SYNTHESES OF NOVEL ANTITUMOR 1,4-ANTHRACENEDIONES AND FUNCTIONIZED CYCLODODECIPTYCENE BASED MOLECULAR GEARS

by

KAIYAN LOU

B.A., Zhejiang University, China, 1996
M.S., East China University of Science and Technology, China, 2001

AN ABSTRACT OF A DISSERTATION

submitted in partial fulfillment of the requirements for the degree

DOCTOR OF PHILOSOPHY

Department of Chemistry
College of Arts and Sciences

KANSAS STATE UNIVERSITY
Manhattan, Kansas

2007

Abstract

The description of this thesis is divided into three chapters following the chronological events of my research development.

In chapter one, a series of new 1,4-anthracenediones were synthesized via functionalizations of the methyl side chain of 6-methyl-1,4-anthracenedione. The new 1,4-anthracenediones were found to exhibit potent cytotoxic activities against human L1210 leukemic and HL-60 cell lines. A key intermediate, 6-bromomethyl-1,4-anthracenedione (**1.44**), was first synthesized through a sequence of reactions including a double Friedel-Crafts reaction, reductive quinone formation, and selective benzylic bromination. The bromide (**1.44**) was further converted to other 1,4-anthracenediones via hydrolysis, subsequent oxidation, and reductive amination or nucleophilic substitution.

Chapter two deals with a continuous research project aiming at macropolycyclic cyclodecitycene or [10]beltene derivative using Diels-Alder reaction as the key strategy for cyclization. A tetraene, *(4aR,5R,7S,7aS,11aR,12R,14S,14aR)*-5,7,12,14-tetrahydroxy-2,3,9,10-tetramethylene-1,4,4a,5,6,7,7a,8,11,11a,12,13,14,14a-tetradecahydro-6,13-*o*-benzenopentacene (**2.51**), was synthesized by following previous work from this laboratory. Unfortunately, the Diels-Alder reaction of tetraene **2.51** with triptycene bisquinone showed predominantly polymerization over intramolecular cyclization. The use of double activated quinone such as 1,4,5,8-naphthodiquinone (**2.64**) and 1,2,4,5-tetraethoxycarbonyl-1,4-benzoquinone (**2.70**) as dienophiles gave monoadducts **2.67** and **2.71** respectively. However, they both failed to cyclize under high dilution conditions at elevated temperature, which may be rationalized by chair conformations adopted in six-membered rings causing unfavorable twist for intramolecular cylization. Further study showed tetraene **2.51** underwent an unexpected furan ring forming reaction.

In chapter three, an unprecedented substituted cyclododeciptycene, 2,4,6,8,10,12,14,16,18,20,22,24-dodecahydro-9,11,21,23-tetramethoxy-(2,14:4,16:6,18:8,20:10,22:12,24)-hexa(*o*-benzeno)-[12]cyclacene-1,3,5,7,13,14,17,19-octaone (**3.138**), was successfully synthesized based on a successful intramolecular Diels-Alder reaction,

which was developed from the above [10]beltene project and previously reported literature work. A series of all *cis*-iptycenequinones were synthesized as bisdienophile building blocks from a sequence of Diels-Alder reactions, separation of individual Diels-Alder adducts, enolization, and oxidative demethoxylation. It was found that each Diels-Alder adduct isomer shows distinguish ^{1}HNMR signals inherent to its structure. The characteristic ^{1}HNMR signals allow the identification of the structures of iptycenequinones derived from the above reactions. A bisdimethoxyanthracene, 6,8,15,17-tetramethoxy-7,16-dihydro-7,16-(*o*-benzeno)heptacene (**3.56**), was synthesized as bisdiene building block, which reacted with *cis,cis*-heptiptycene tetraquinone (**3.23**). The cycloadduct was transformed to cyclododeciptycene **3.138**, whose structure was firmly established by a single-crystal X-ray analysis.

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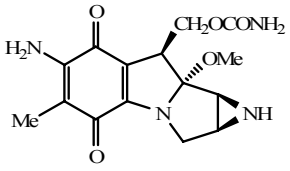

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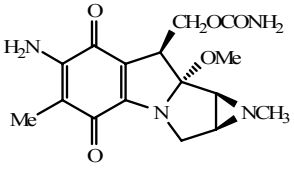

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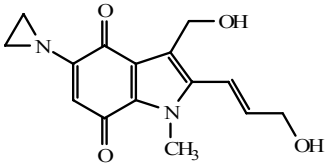

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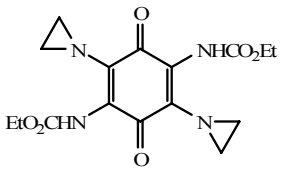

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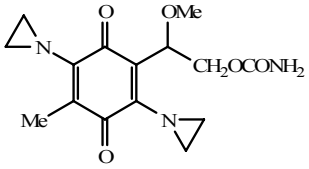

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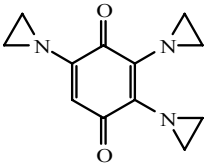

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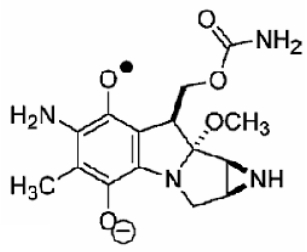

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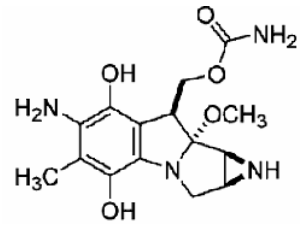

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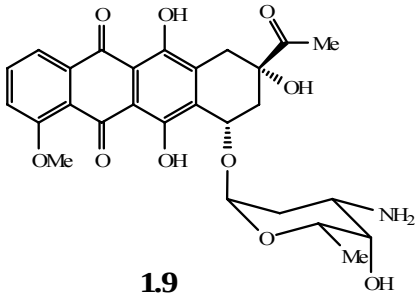

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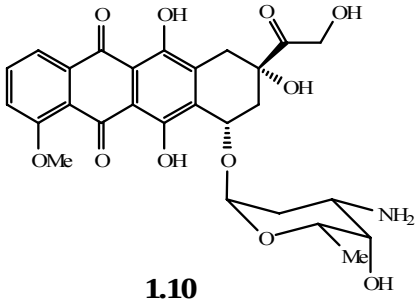

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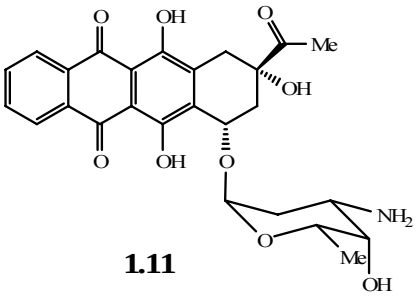

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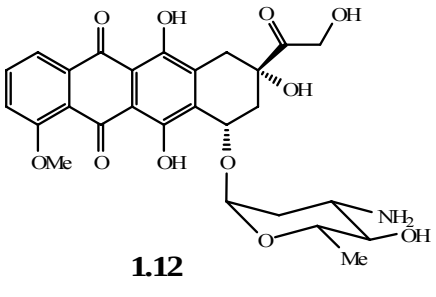

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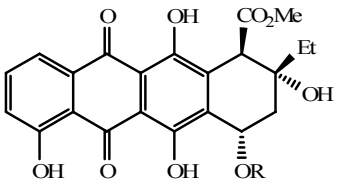

(R=trisaccharide)

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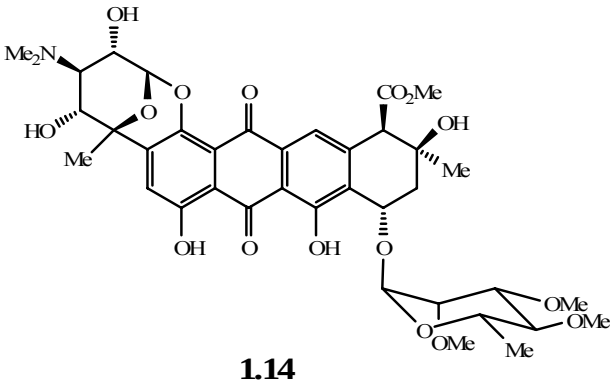

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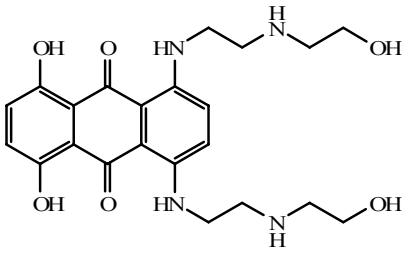

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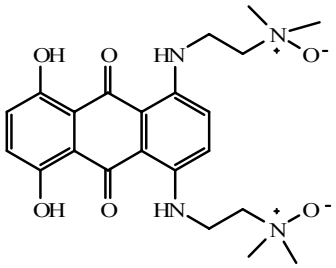

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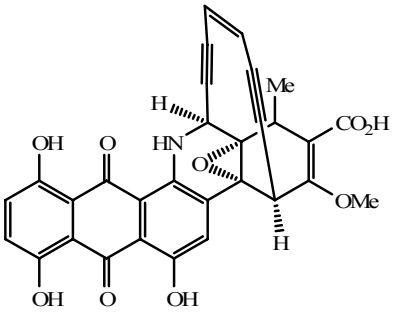

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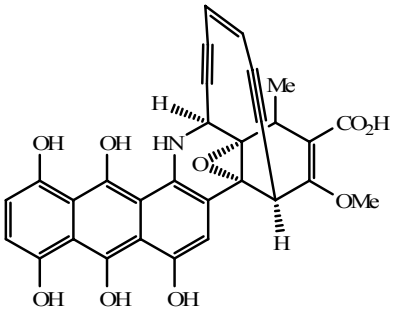

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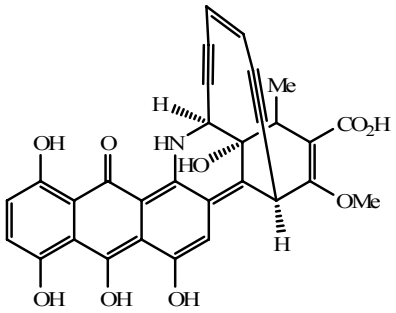

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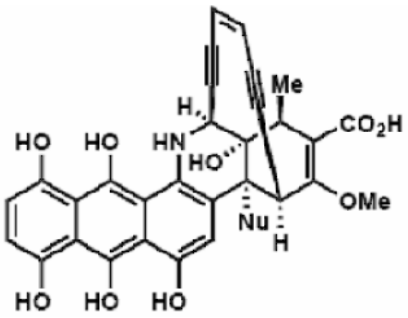

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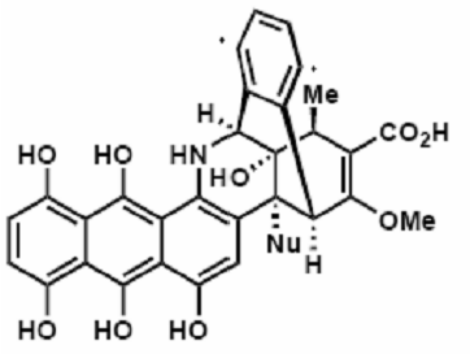

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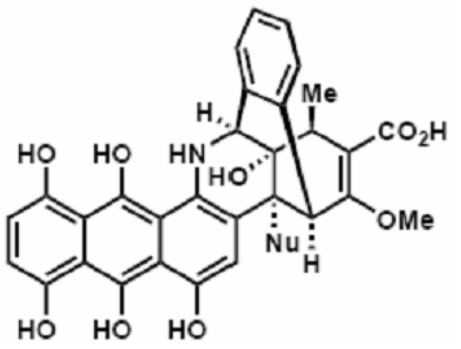

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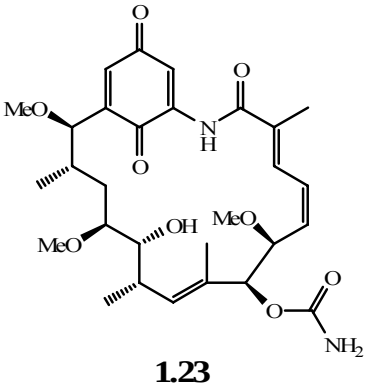

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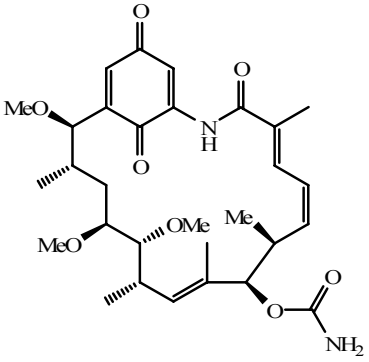

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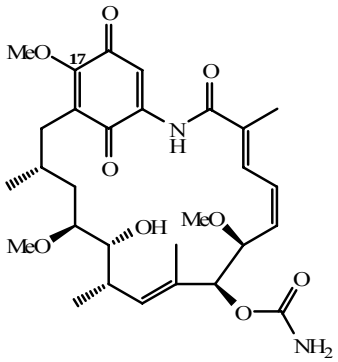

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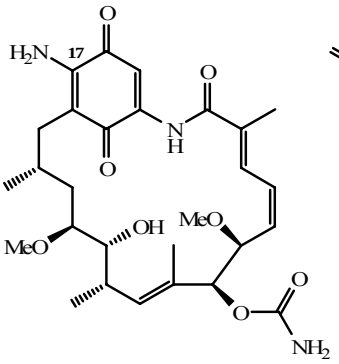

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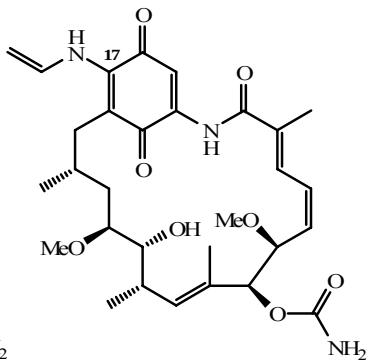

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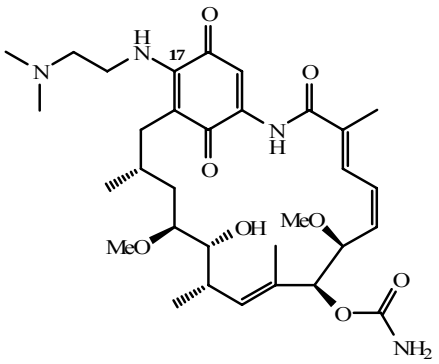

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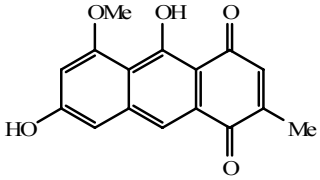

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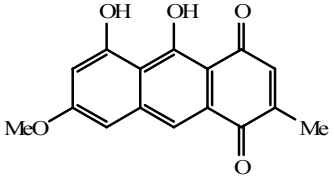

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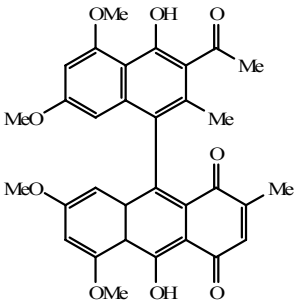

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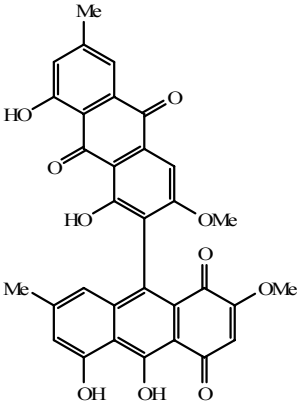

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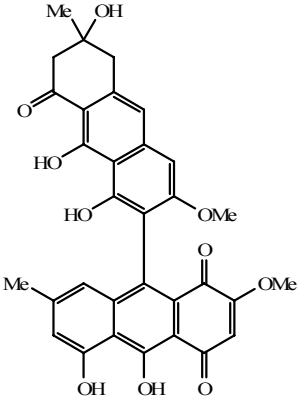

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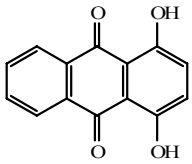

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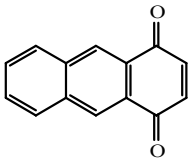

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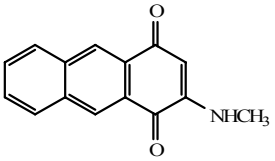

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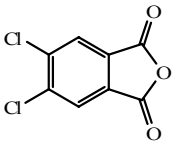

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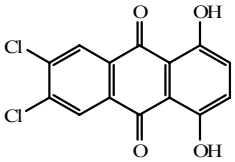

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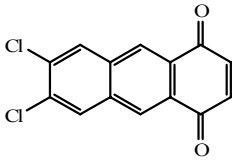

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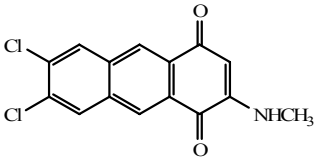

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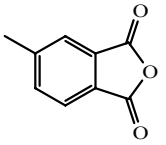

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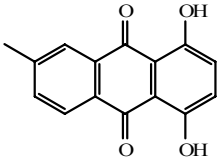

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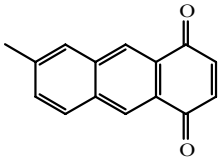

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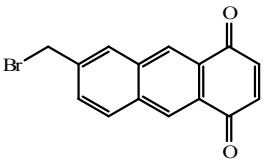

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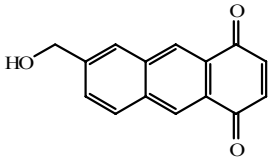

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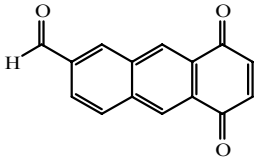

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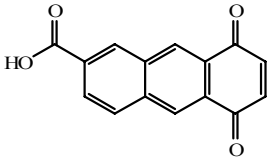

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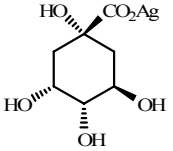

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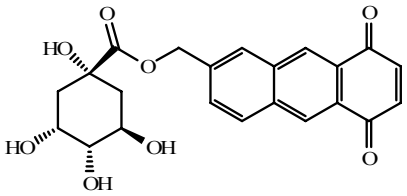

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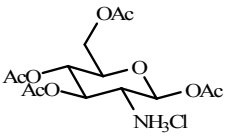

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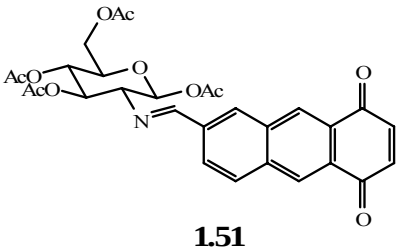

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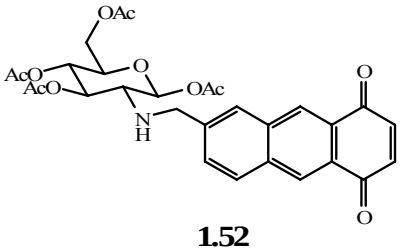

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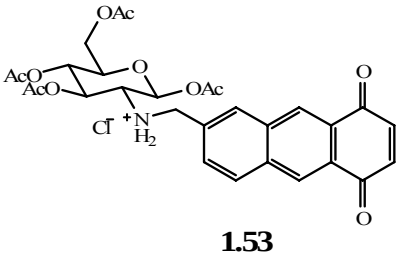

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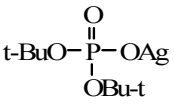

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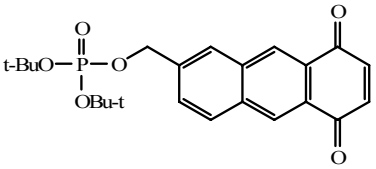

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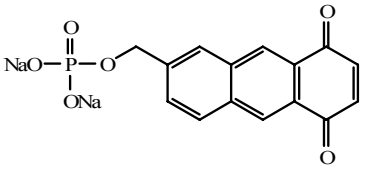

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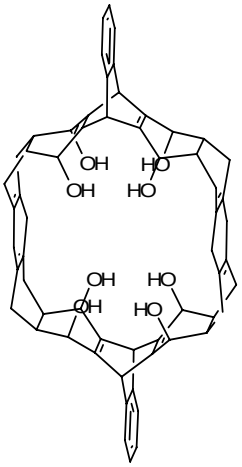

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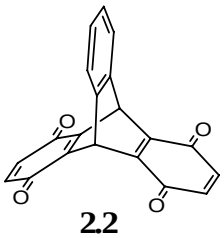

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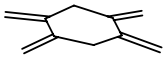

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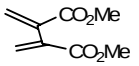

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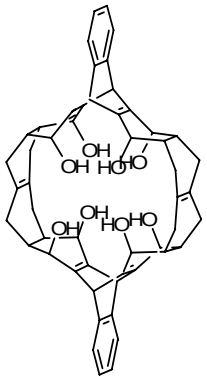

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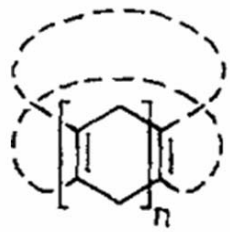

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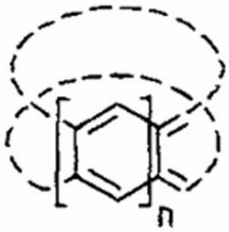

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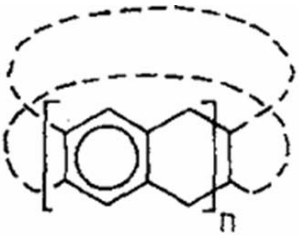

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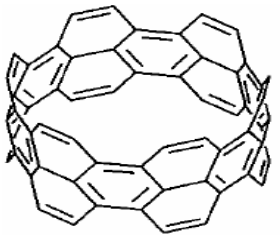

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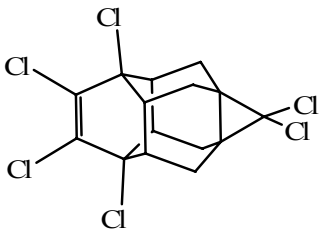

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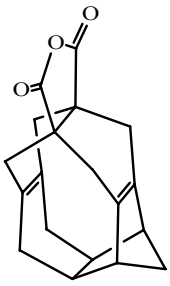

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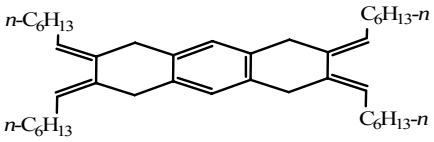

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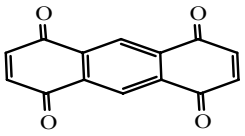

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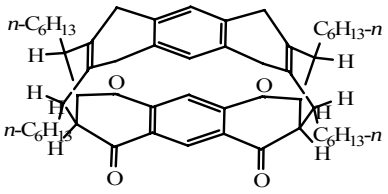

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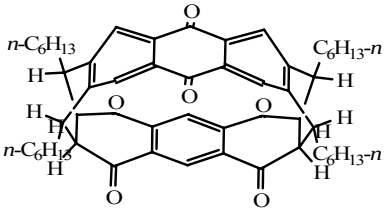

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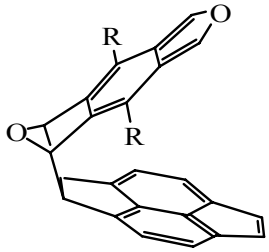

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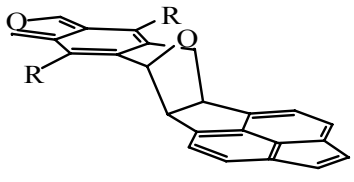

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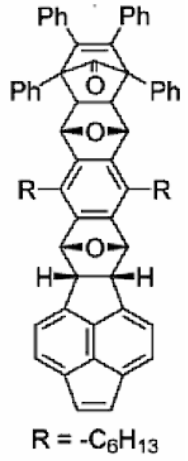

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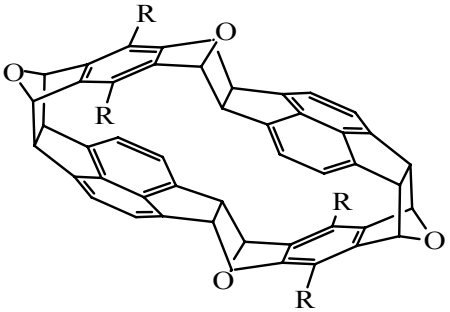

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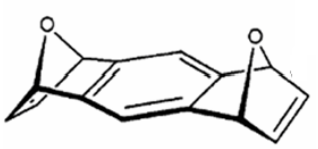

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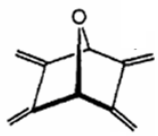

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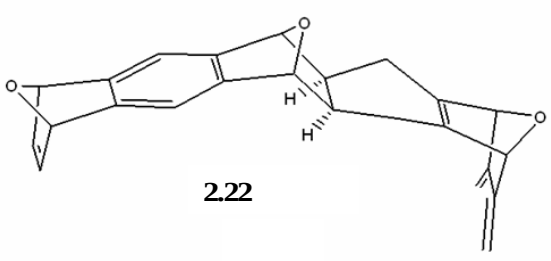

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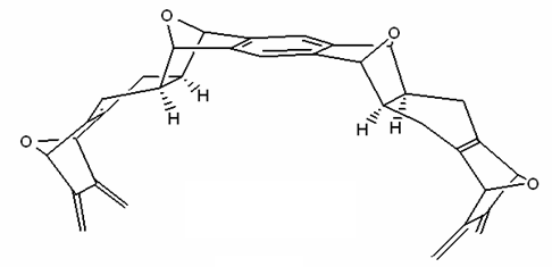

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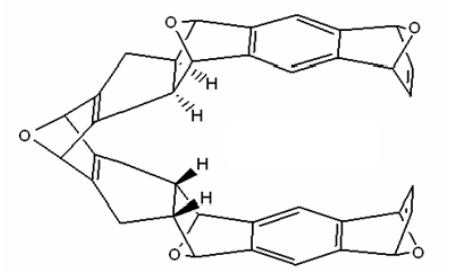

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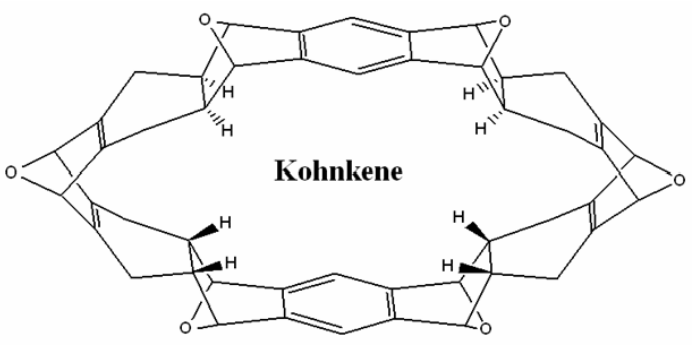

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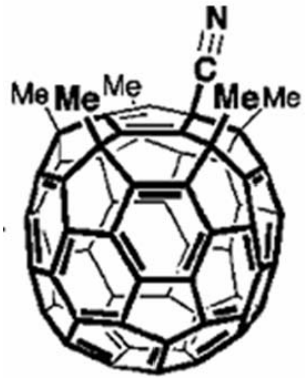

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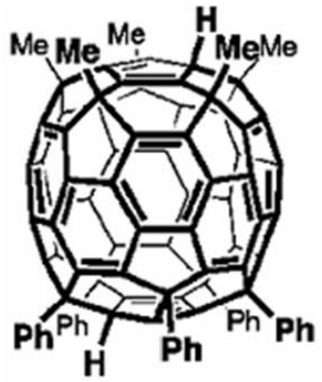

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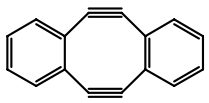

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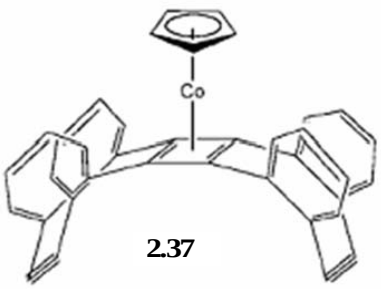

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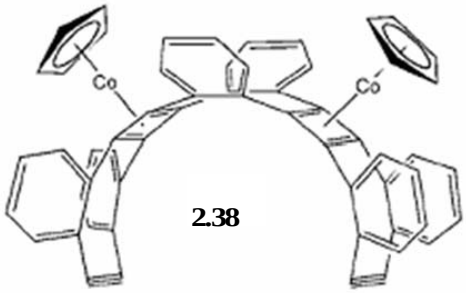

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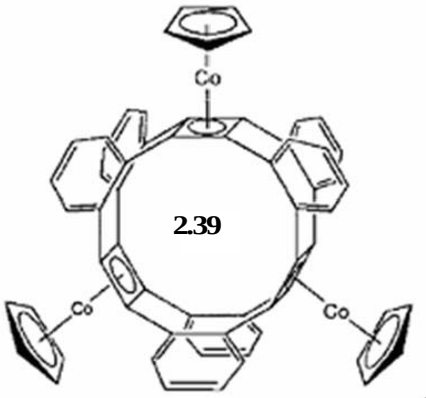

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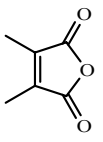

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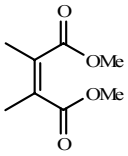

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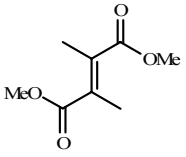

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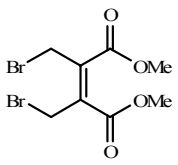

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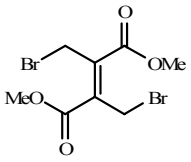

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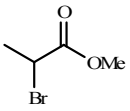

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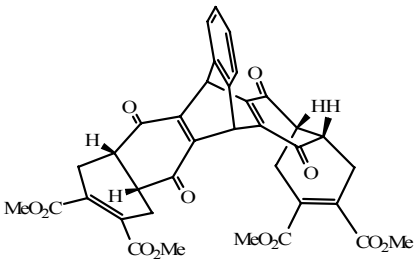

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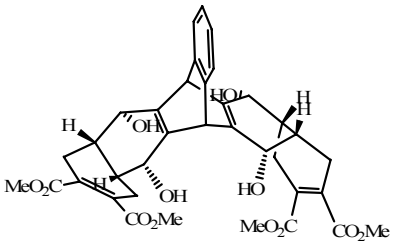

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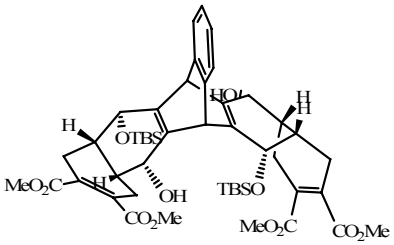

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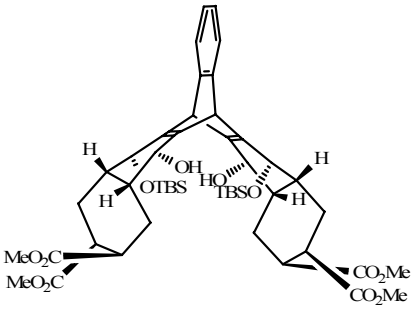

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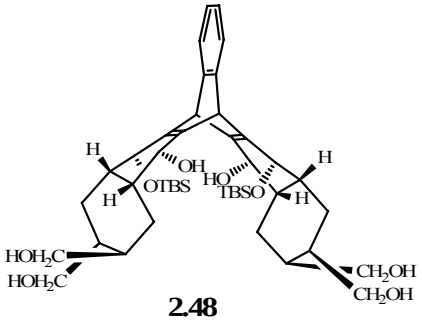

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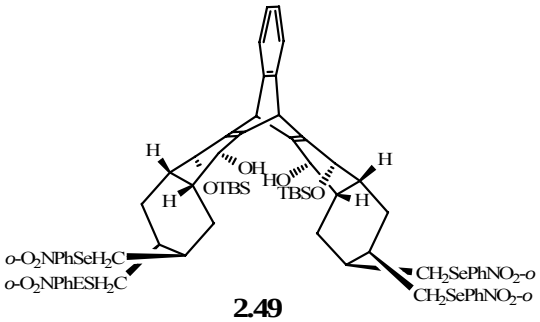

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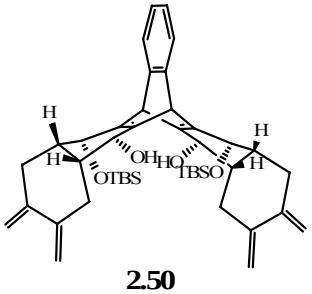

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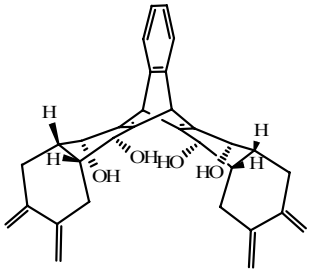

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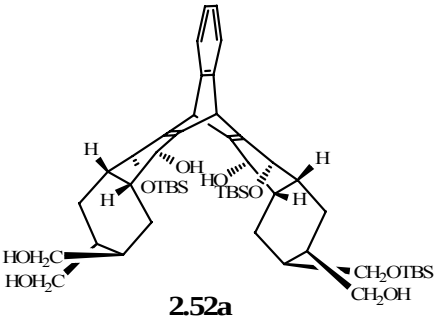

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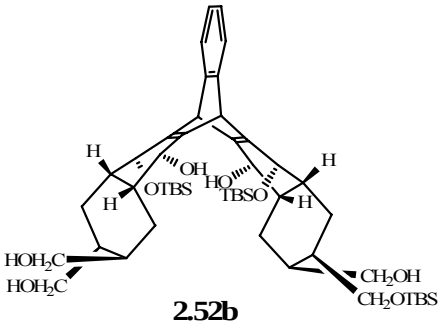

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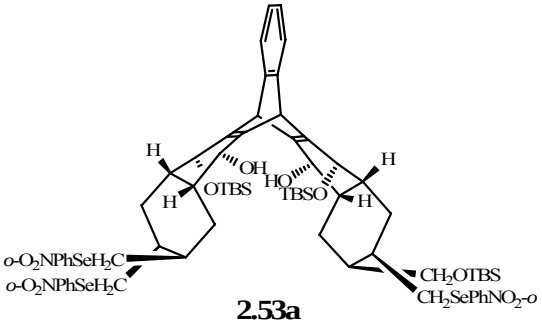

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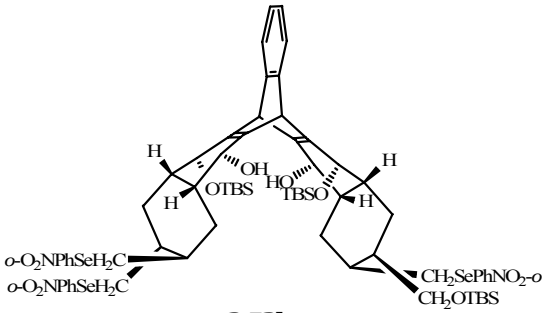

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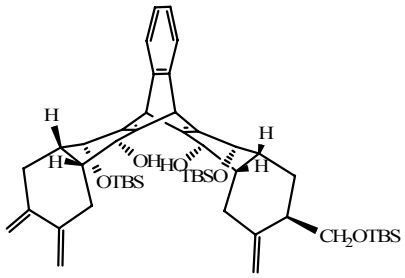

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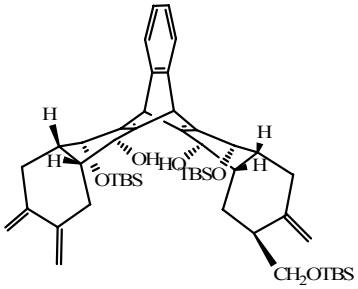

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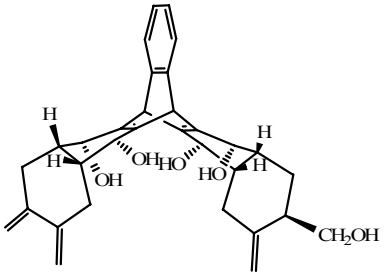

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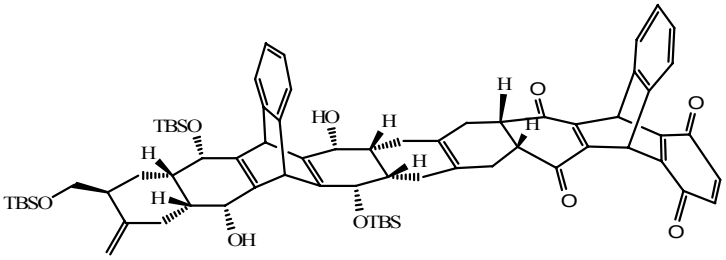

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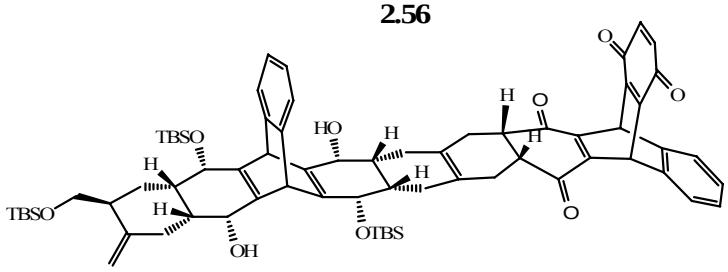

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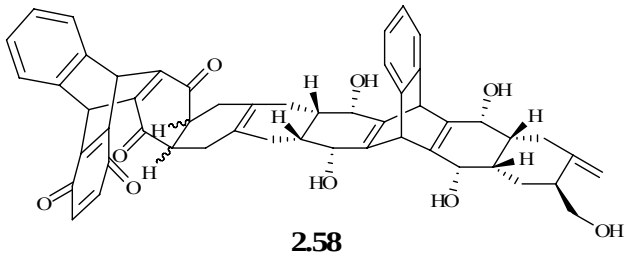

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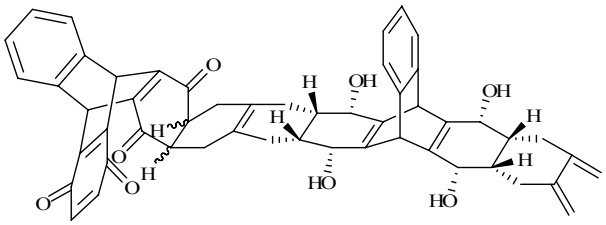

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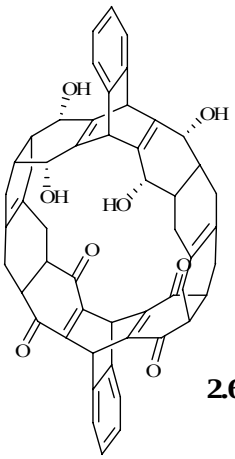

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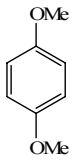

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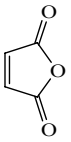

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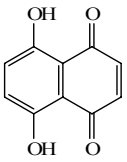

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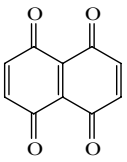

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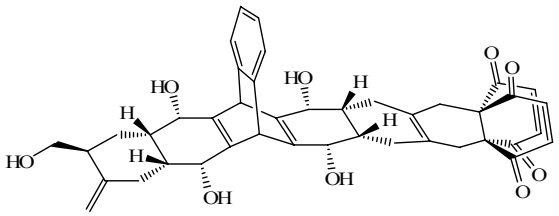

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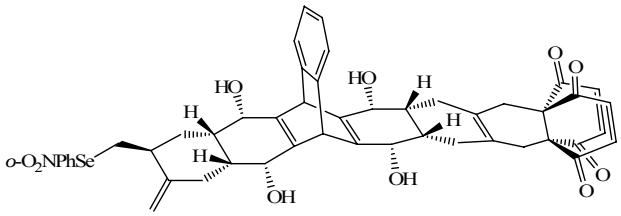

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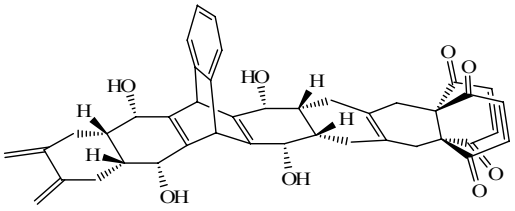

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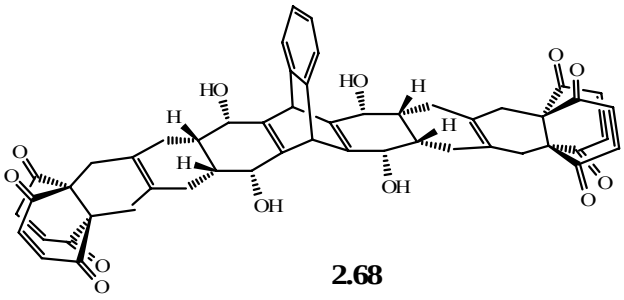

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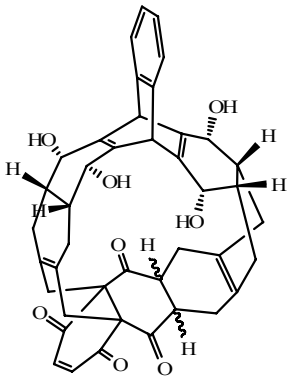

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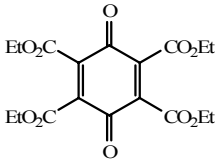

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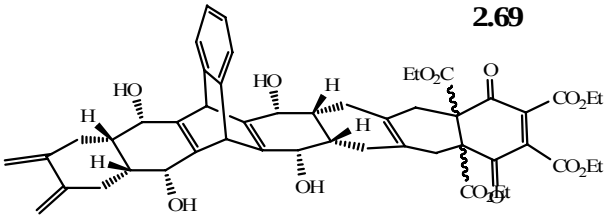

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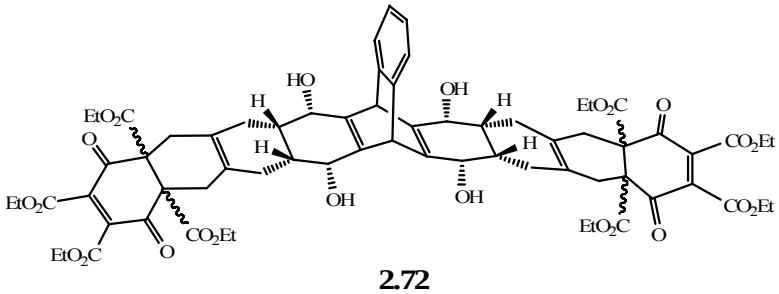

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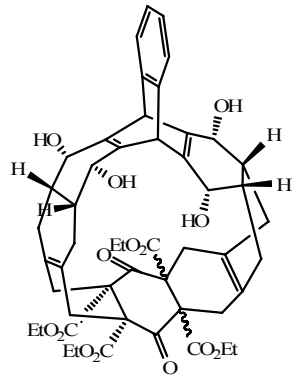

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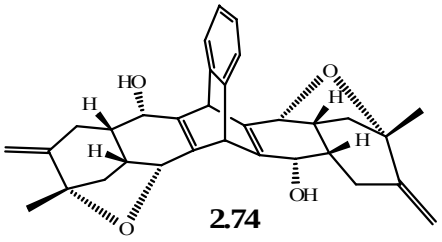

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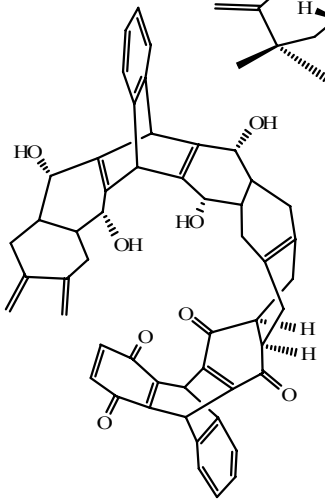

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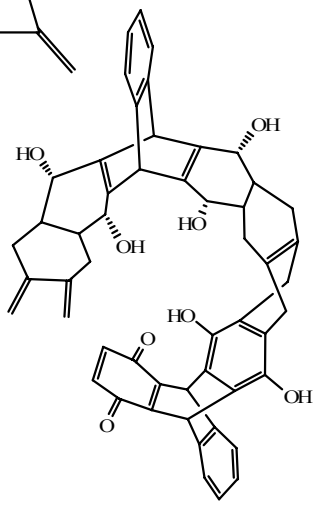

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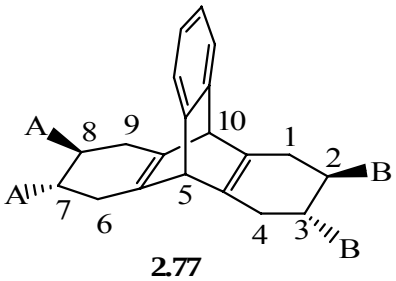

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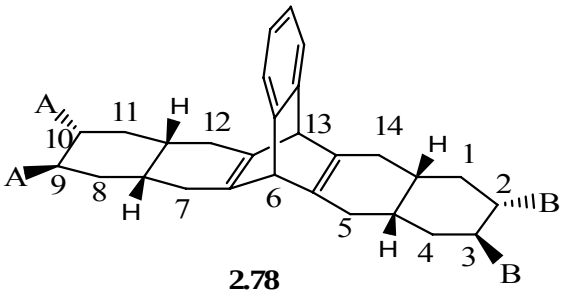

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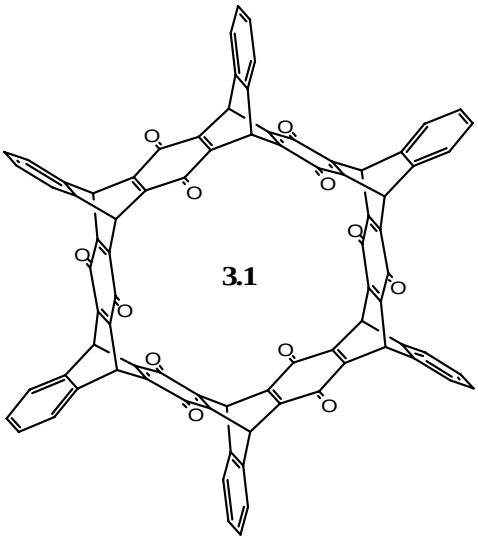

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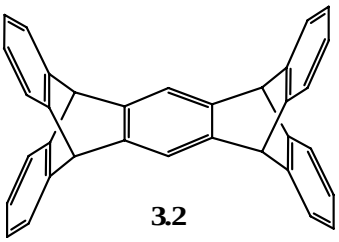

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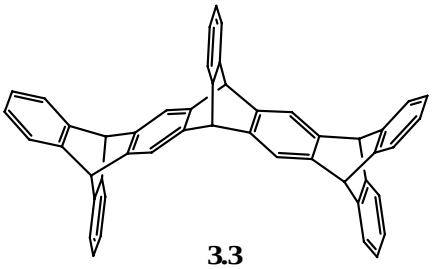

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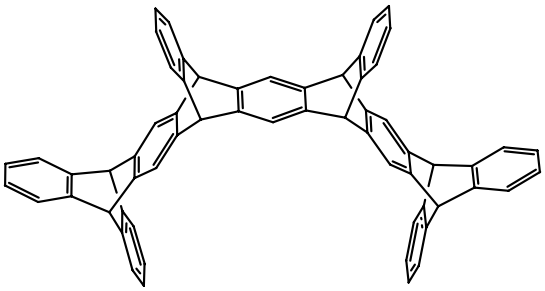

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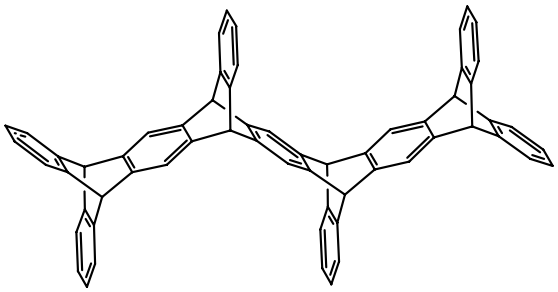

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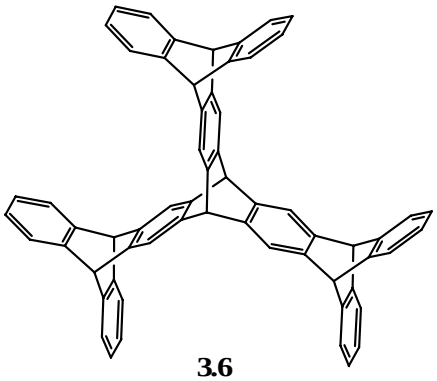

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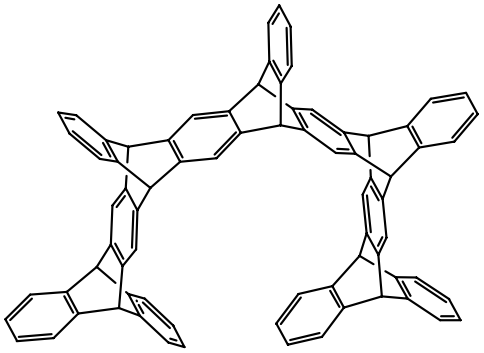

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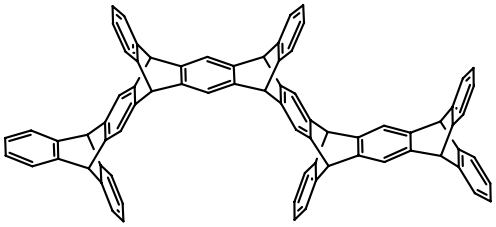

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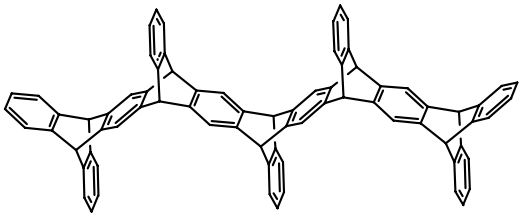

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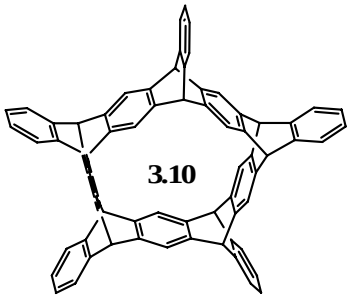

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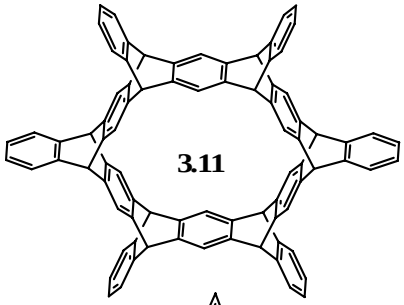

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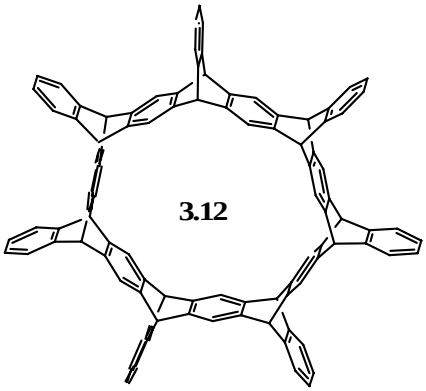

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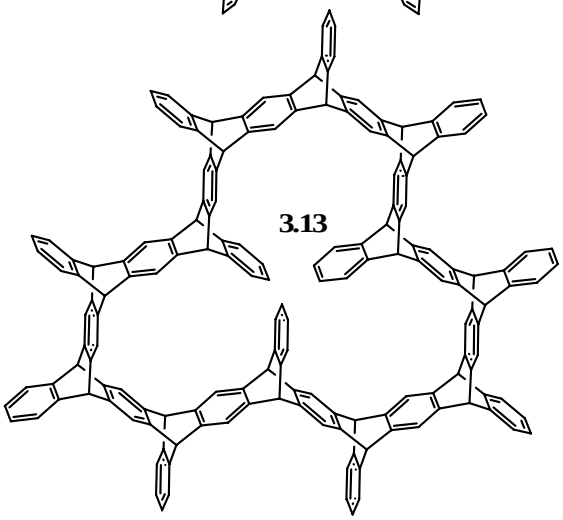

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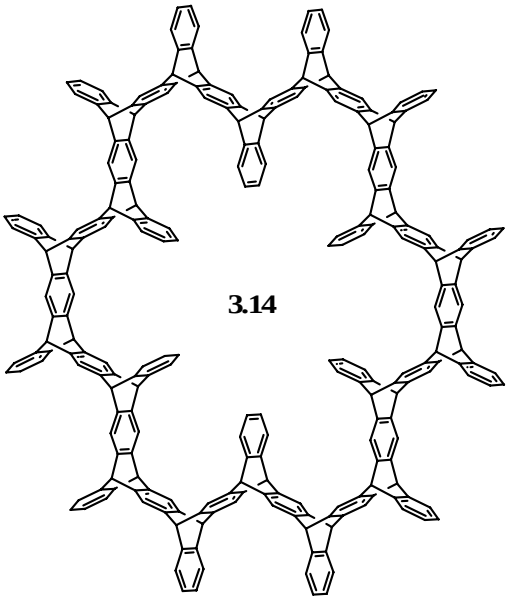

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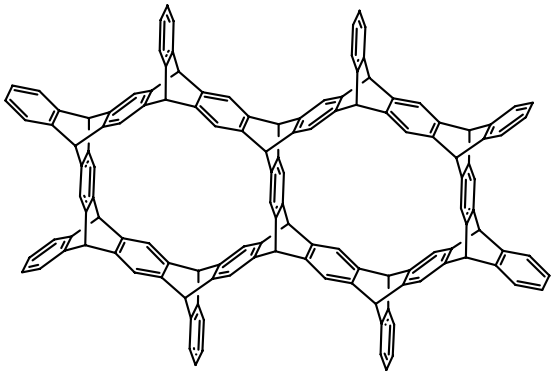

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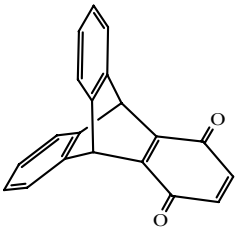

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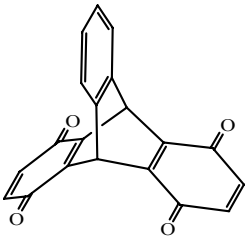

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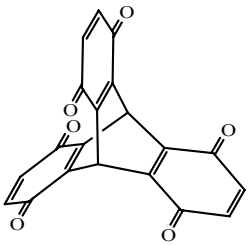

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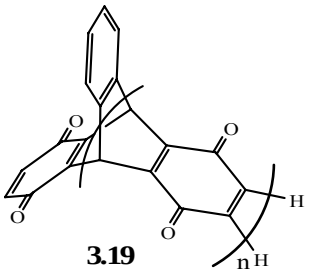

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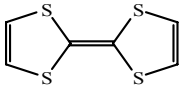

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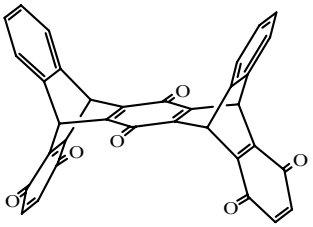

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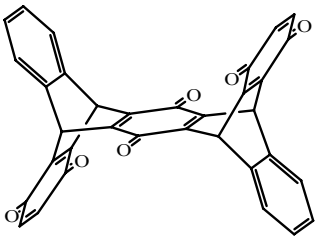

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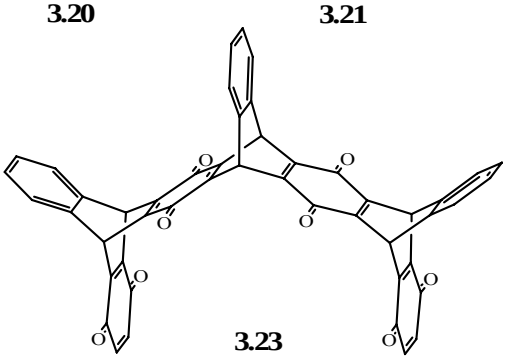

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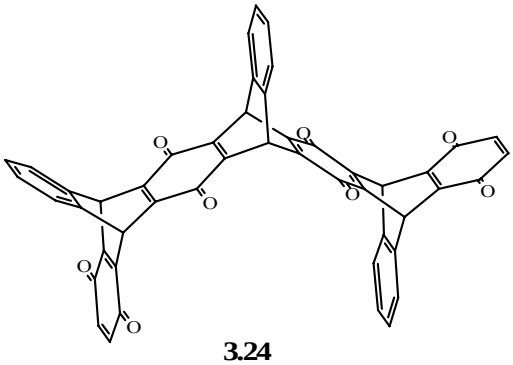

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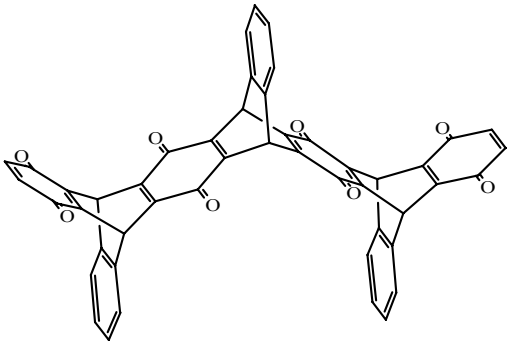

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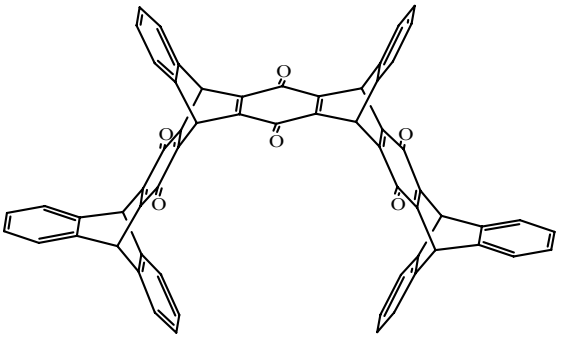

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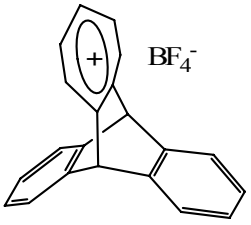

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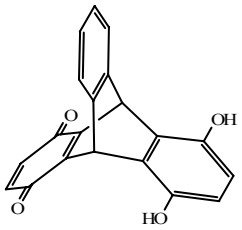

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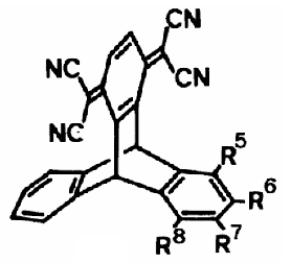
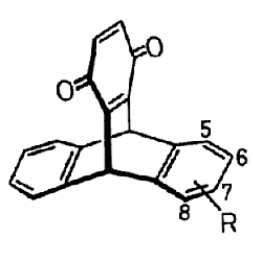


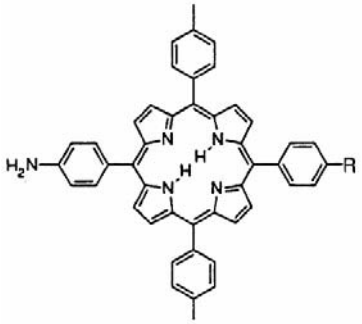
a, $R^5=R^6=R^7=R^8=H$
b, $R^6=OCH_3$, $R^5=R^7=R^8=H$
c, $R^5=OCH_3$, $R^6=R^7=R^8=H$
d, $R^6=R^7=OCH_3$, $R^5=R^8=H$
e, $R^5=R^8=OCH_3$, $R^6=R^7=H$

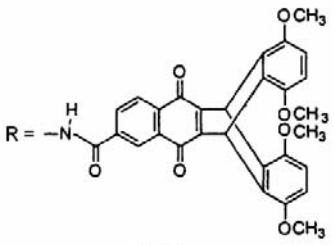
3.29



a, R=H
b, R=5-CH_3
c, R=6-CH_3
d, R=5,8-$(CH_3)_2$
e, R=6,7-$(CH_3)_2$
f, R=5,8-$(OCH_3)_2$
g, R=6,7-$(OCH_3)_2$

3.30





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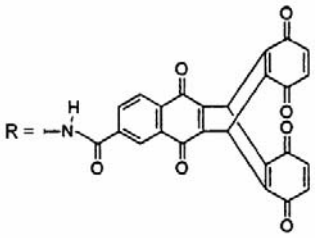

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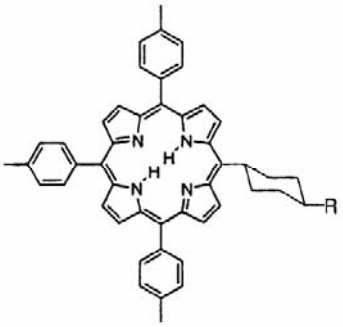

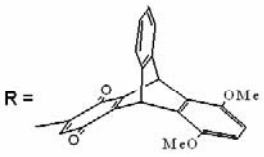

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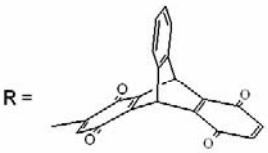

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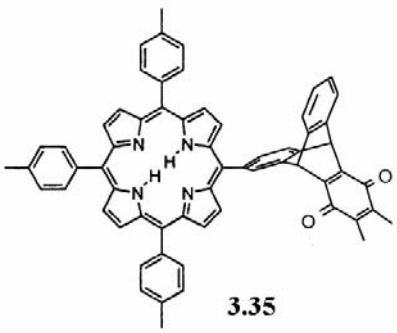

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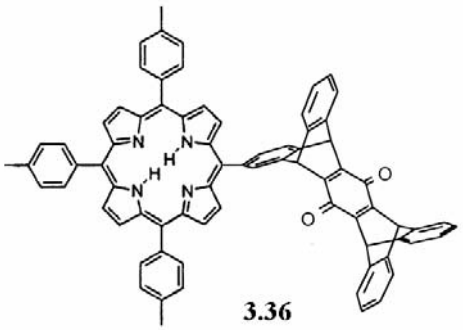

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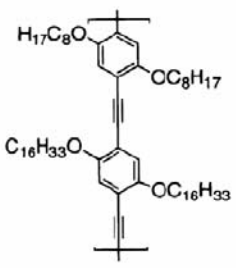

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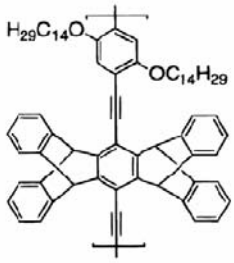

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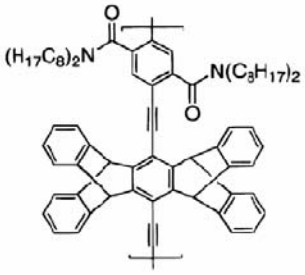

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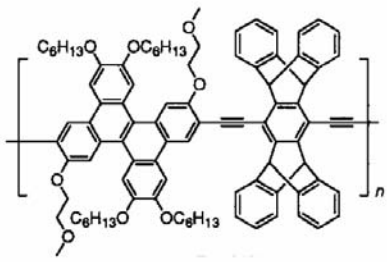

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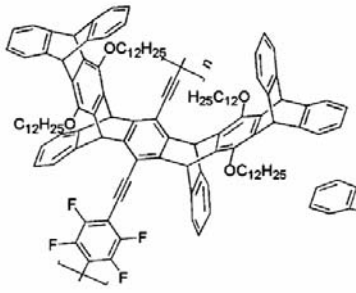

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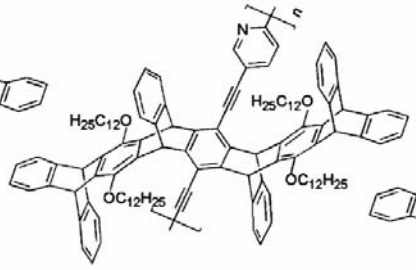

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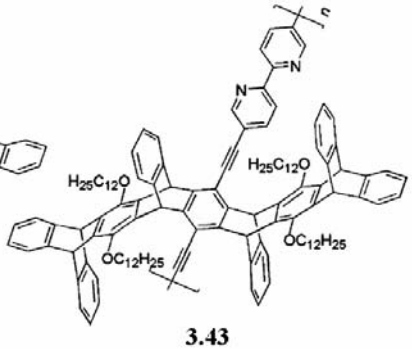

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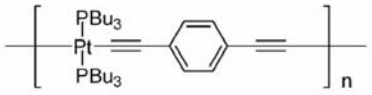

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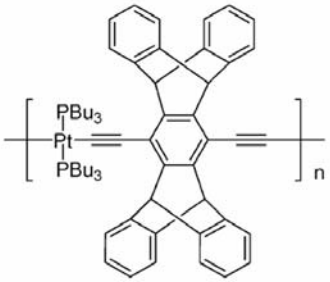

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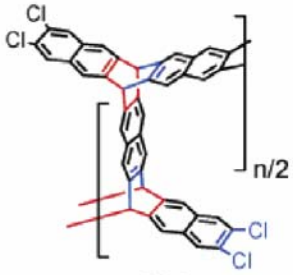

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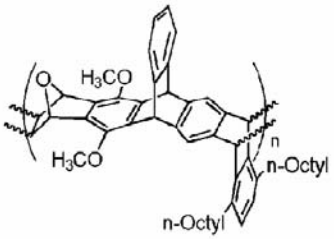

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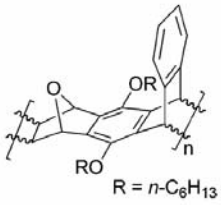

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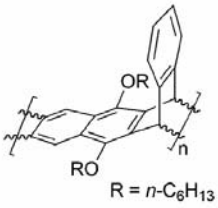

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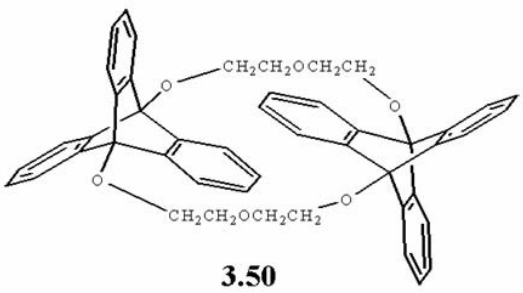

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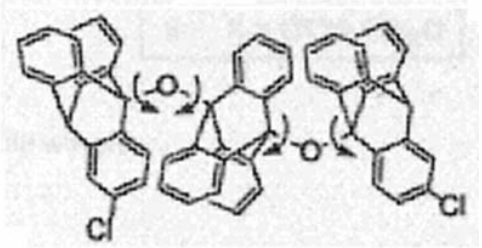

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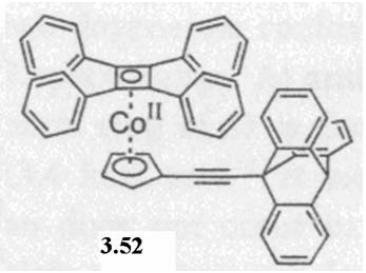

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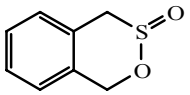

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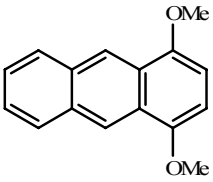

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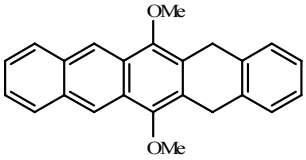

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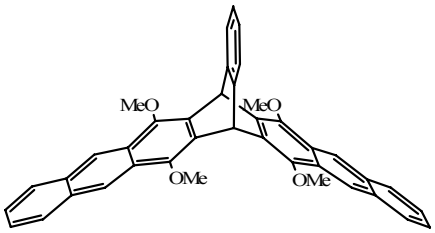

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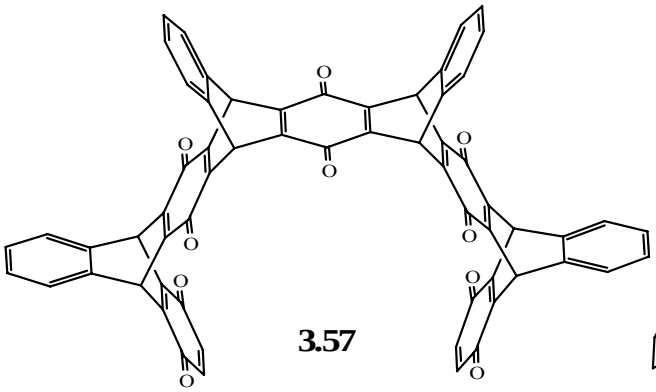

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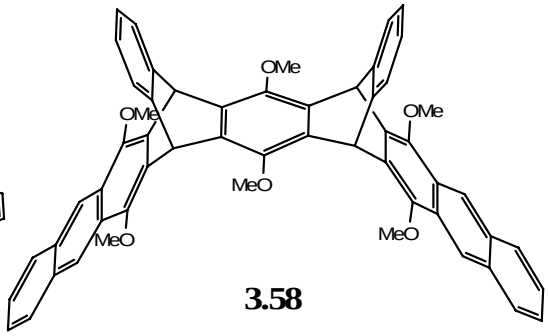

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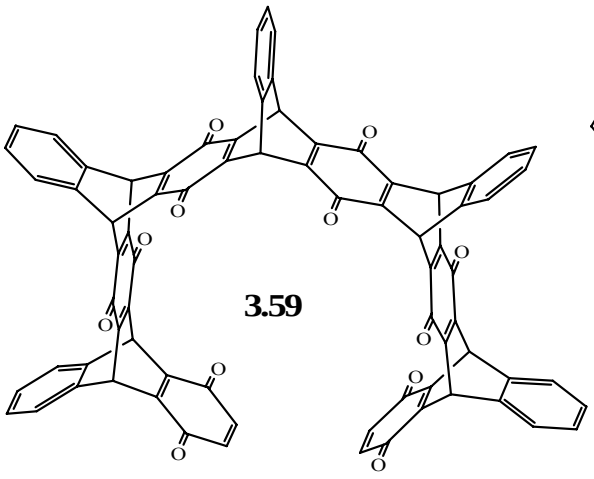

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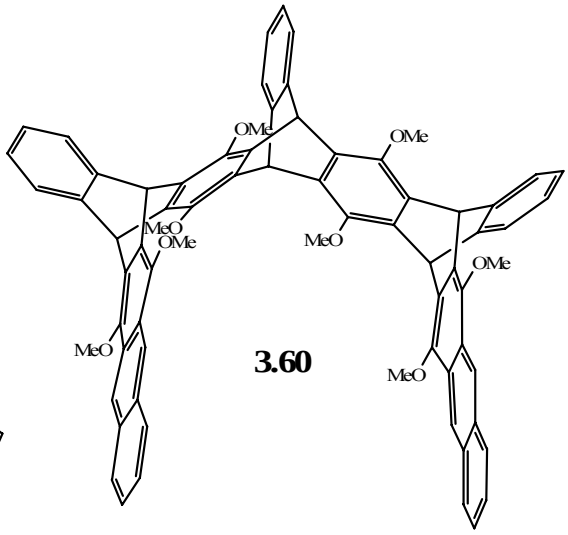

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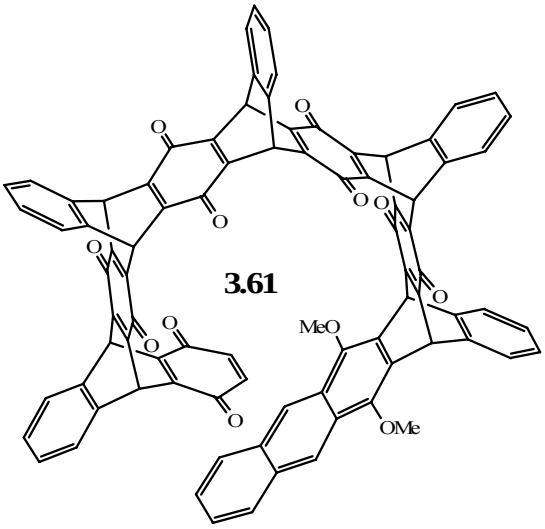

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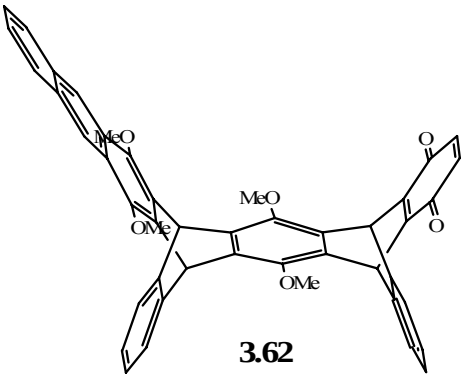

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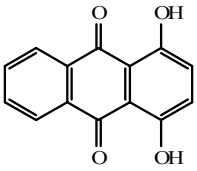

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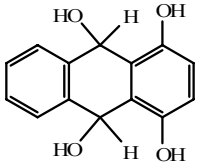

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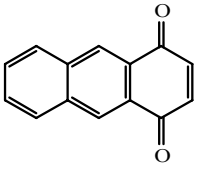

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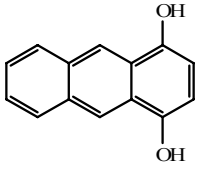

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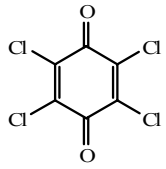

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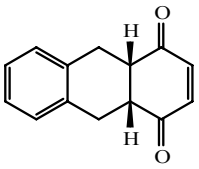

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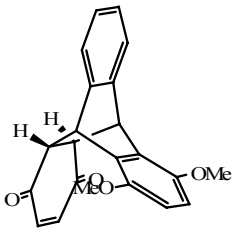

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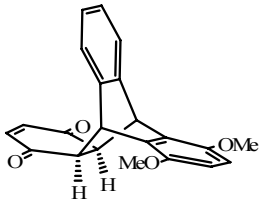

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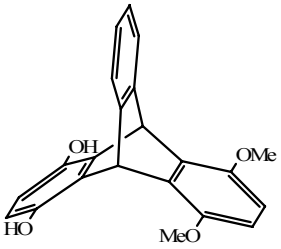

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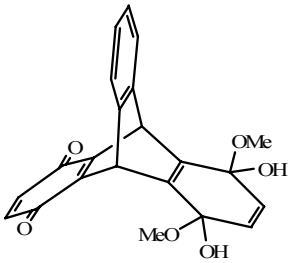

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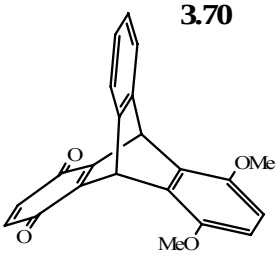

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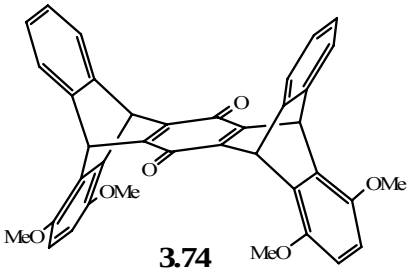

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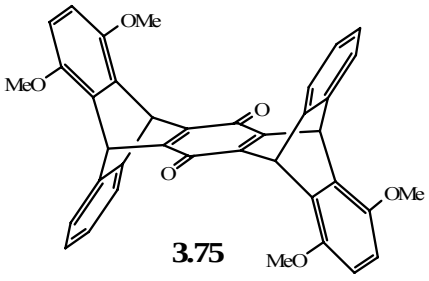

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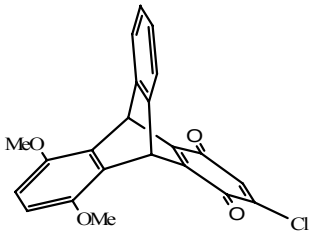

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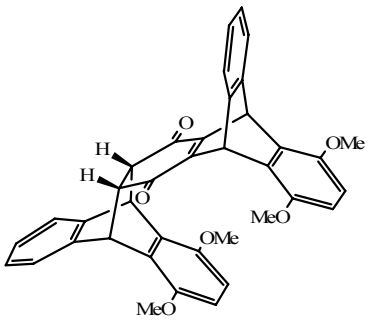

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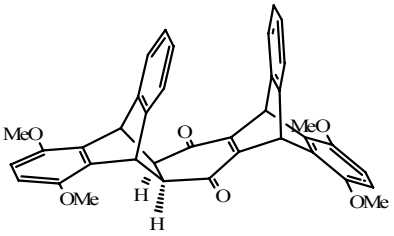

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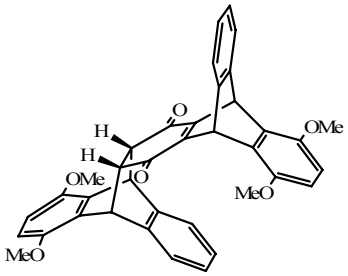

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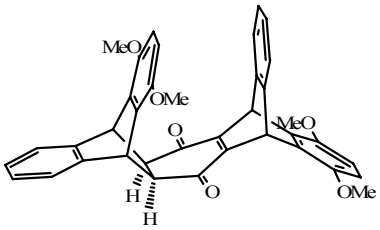

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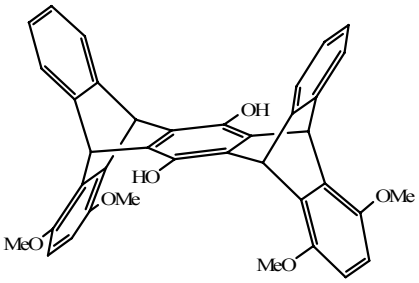

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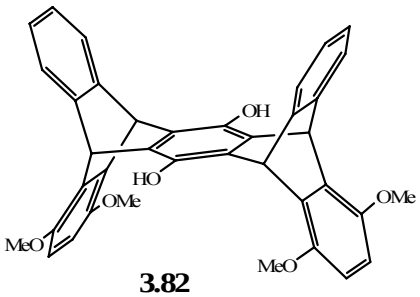

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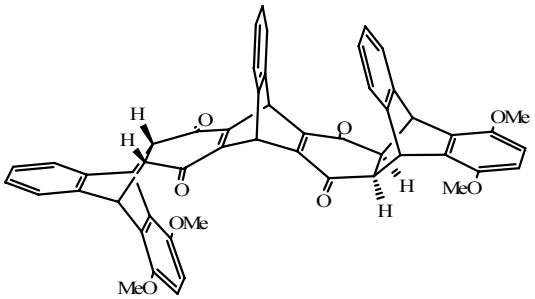

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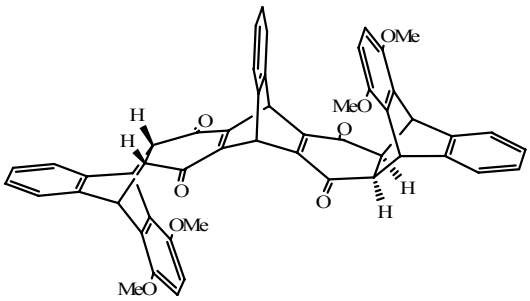

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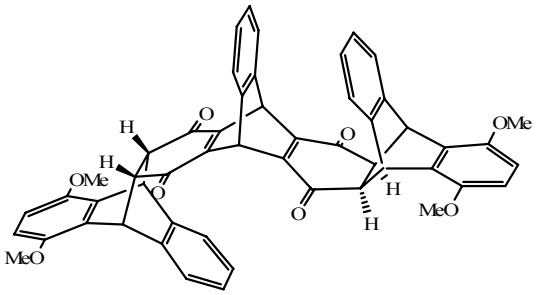

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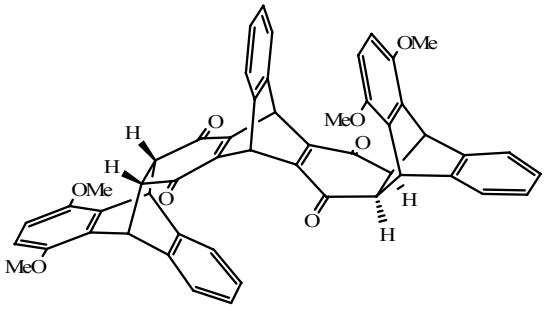

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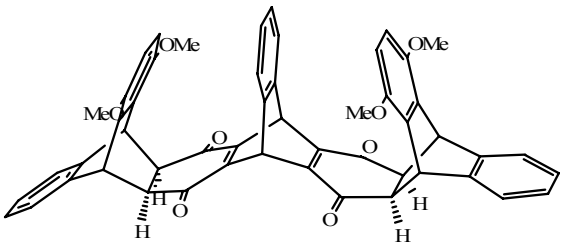

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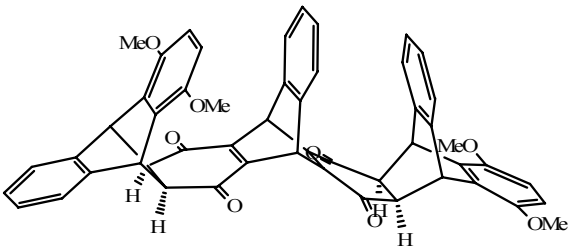

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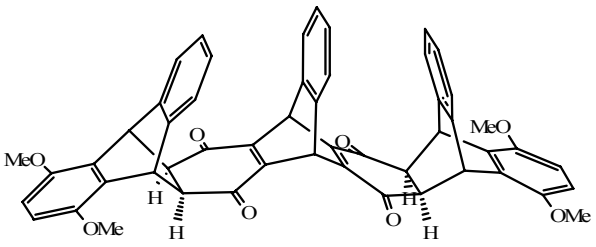

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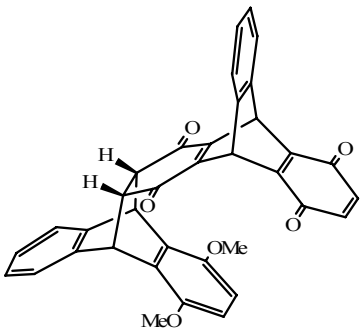

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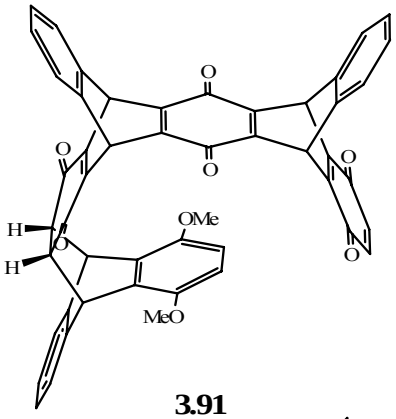

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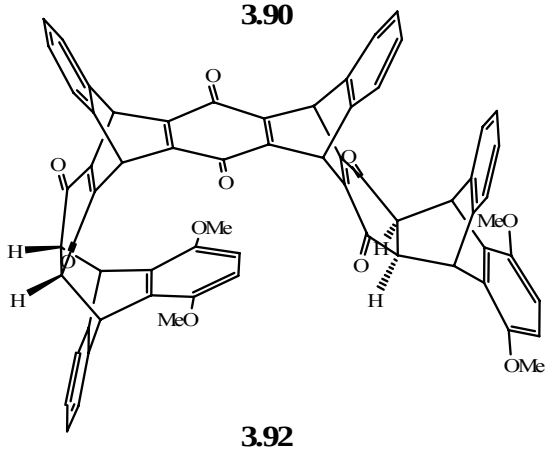

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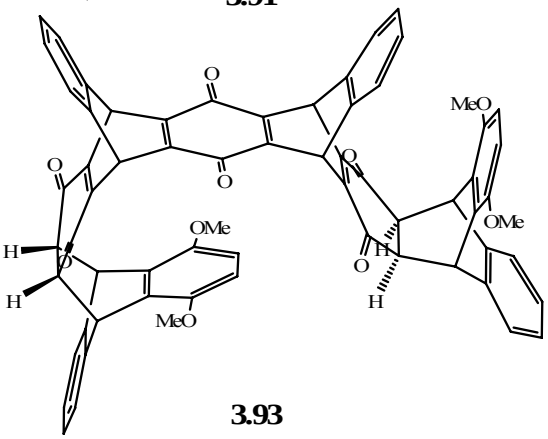

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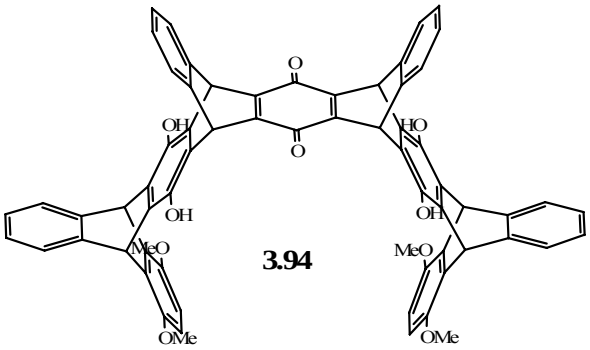

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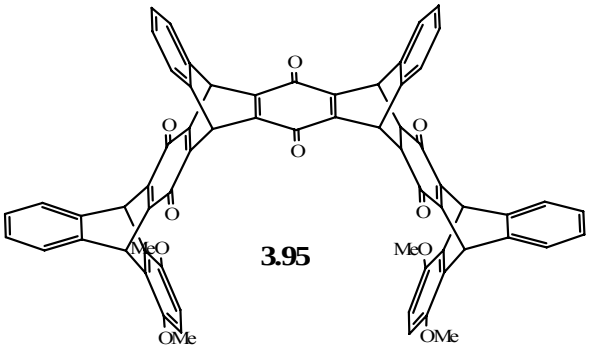

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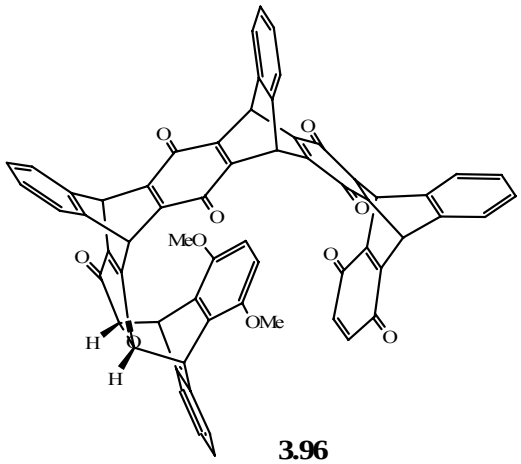

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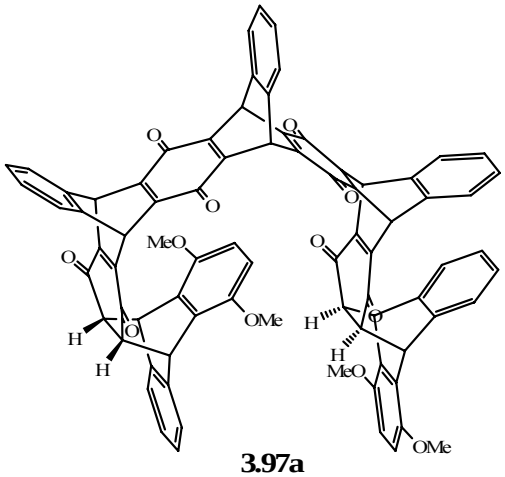

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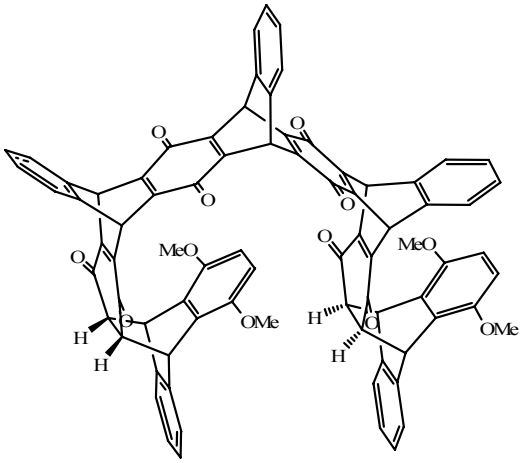

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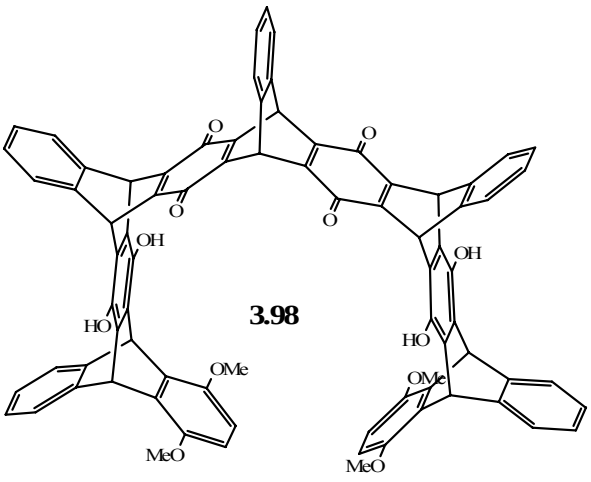

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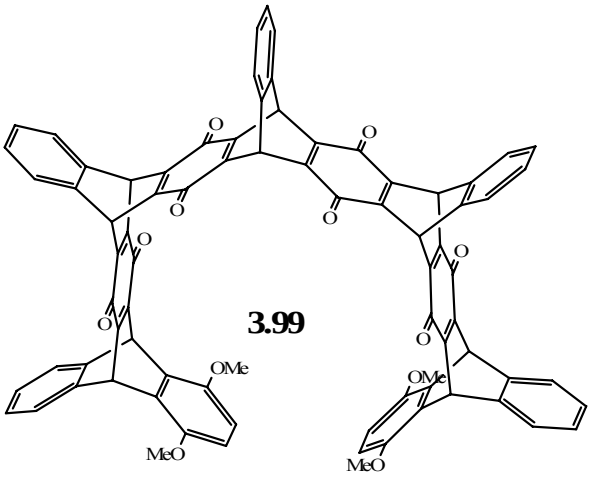

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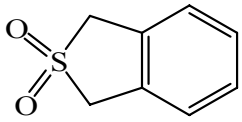

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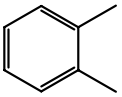

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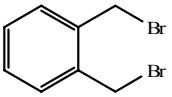

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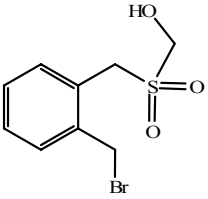

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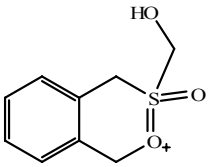

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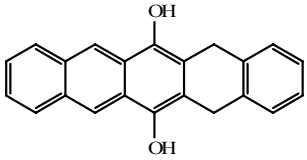

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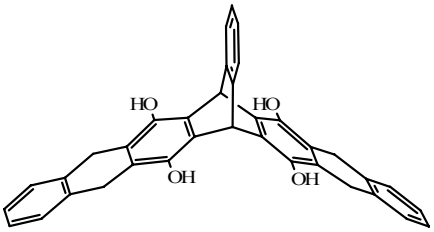

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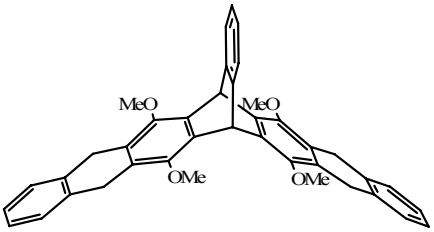

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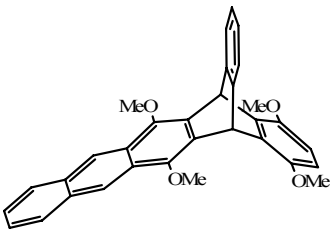

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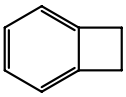

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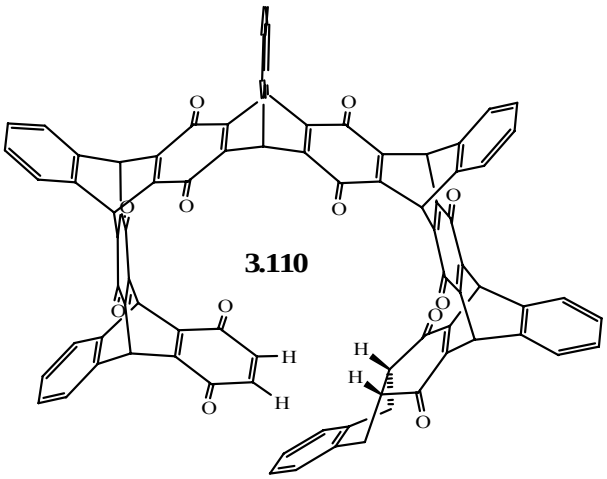

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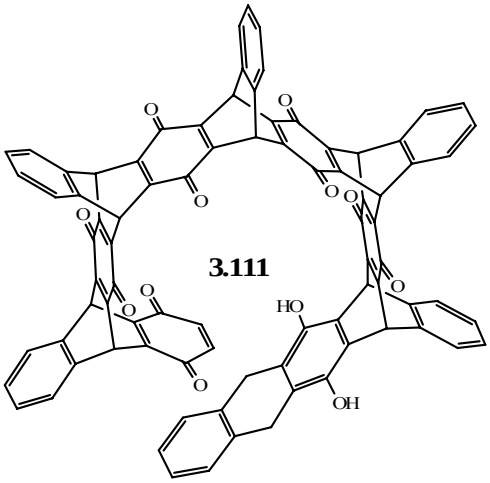

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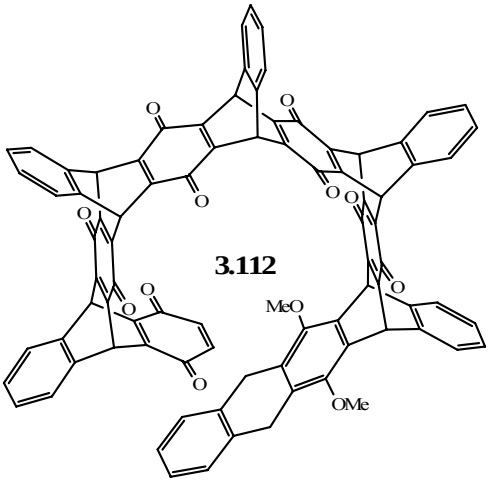

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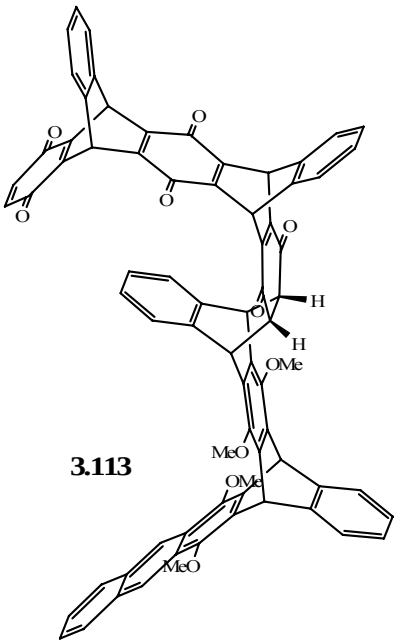

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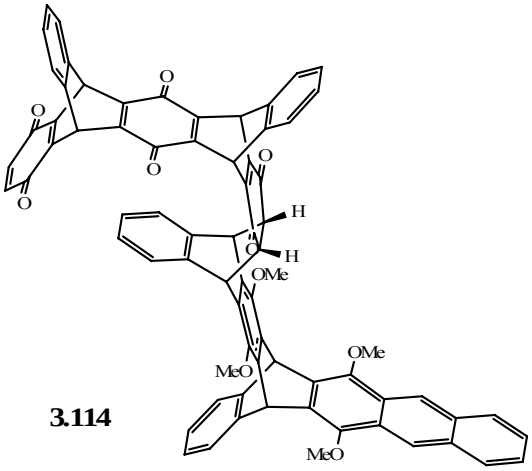

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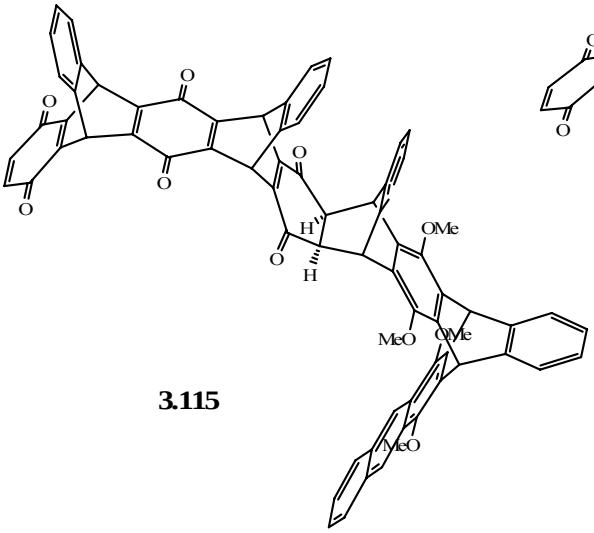

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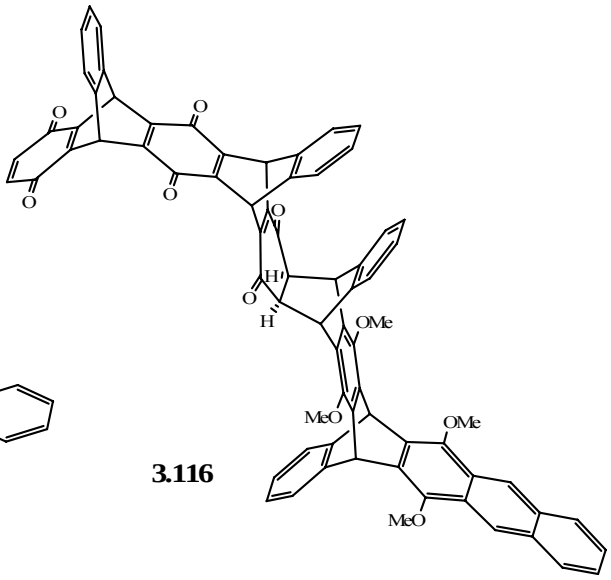

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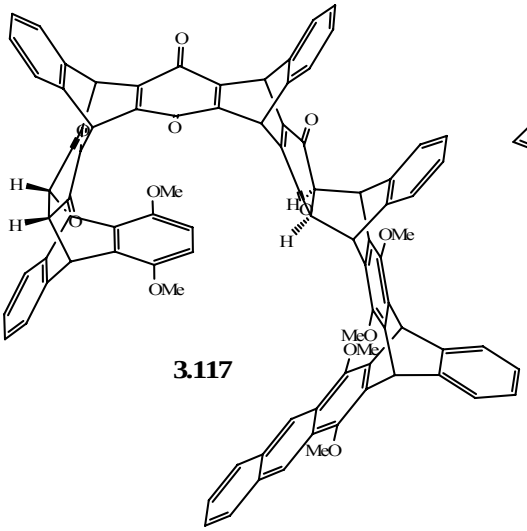

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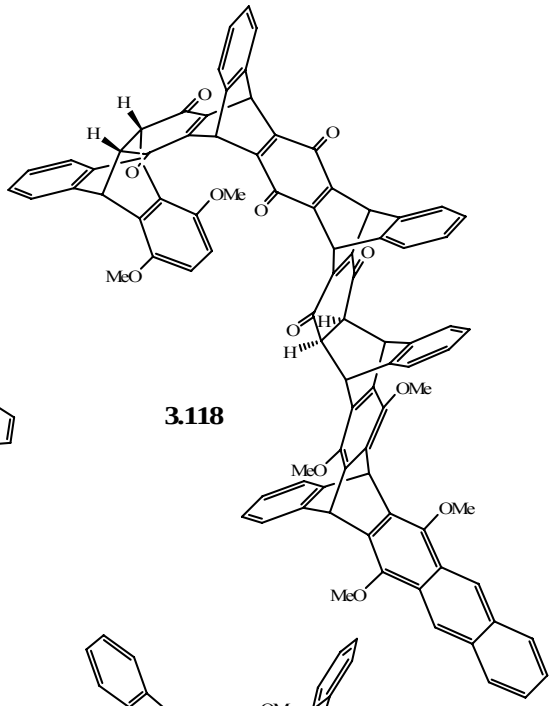

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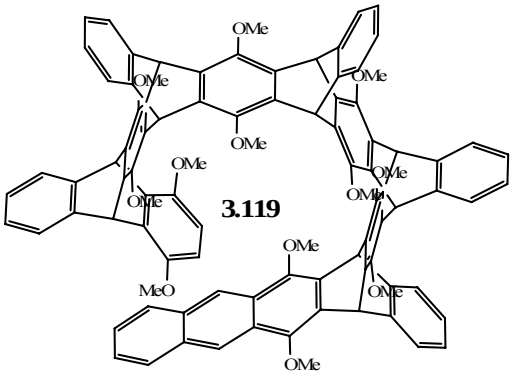

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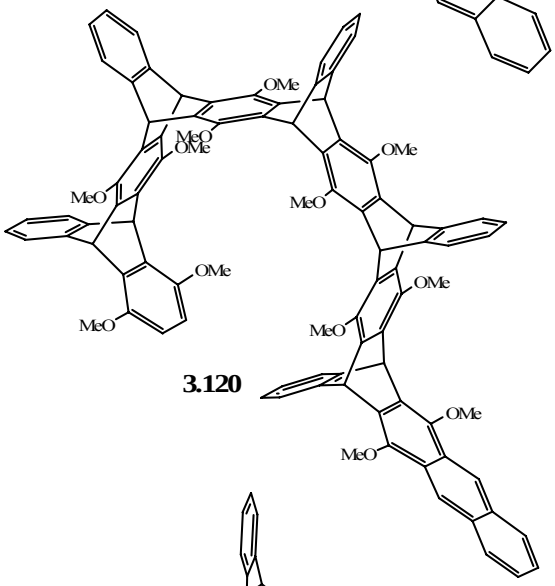

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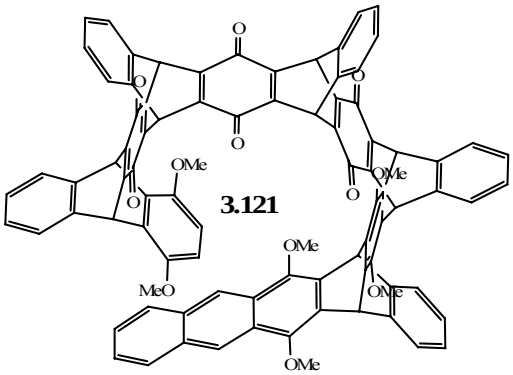

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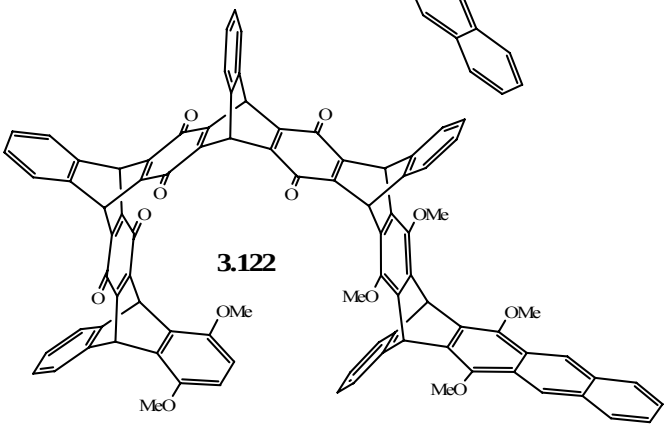

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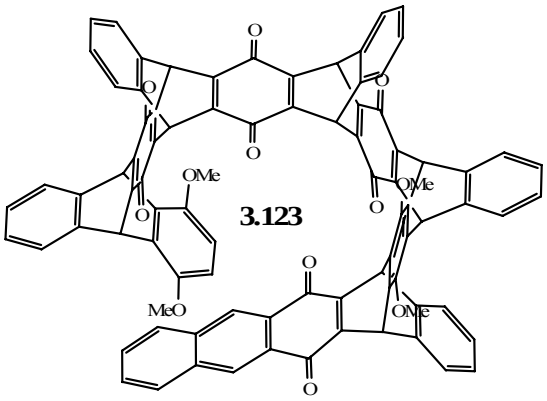

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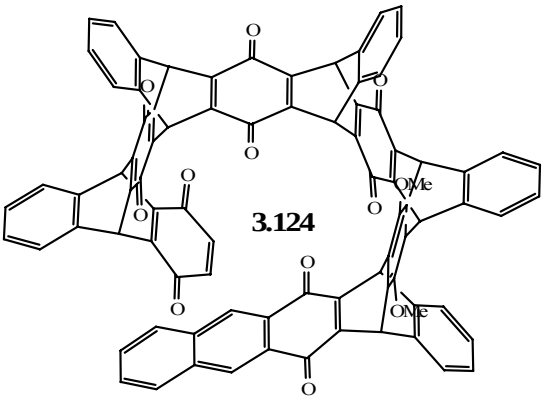

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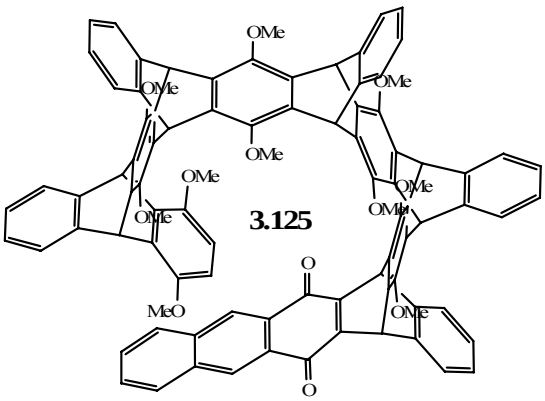

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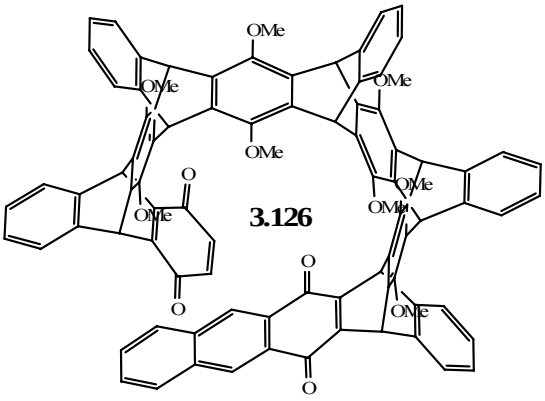

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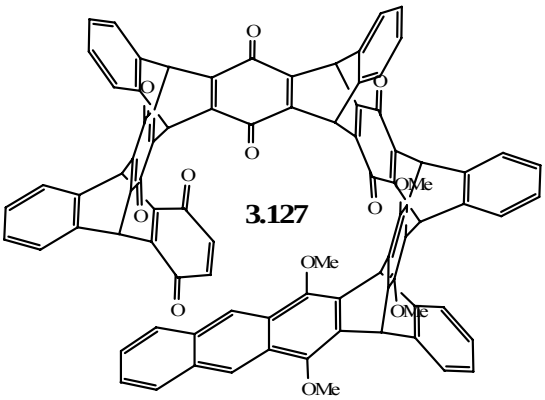

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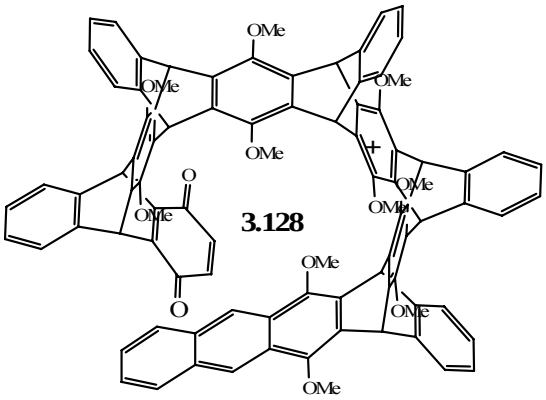

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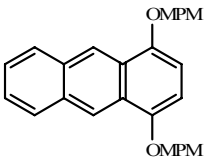

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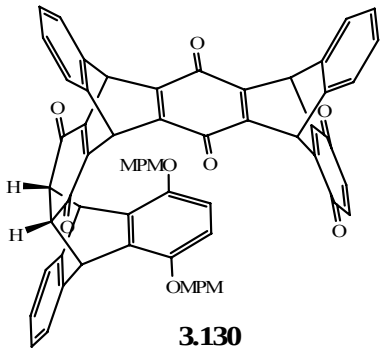

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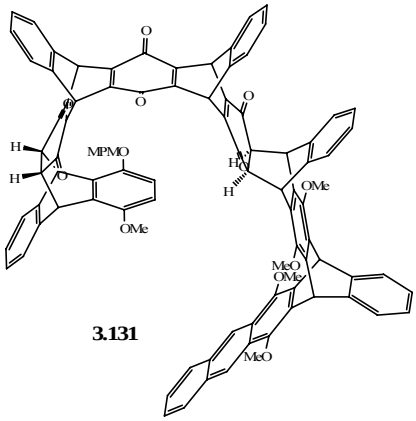

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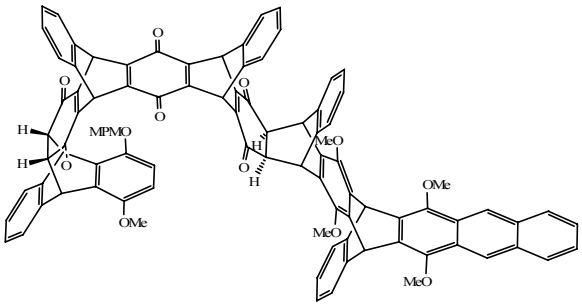

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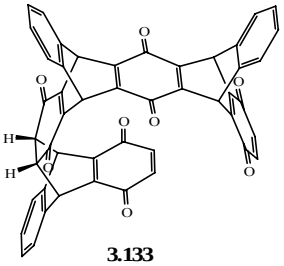

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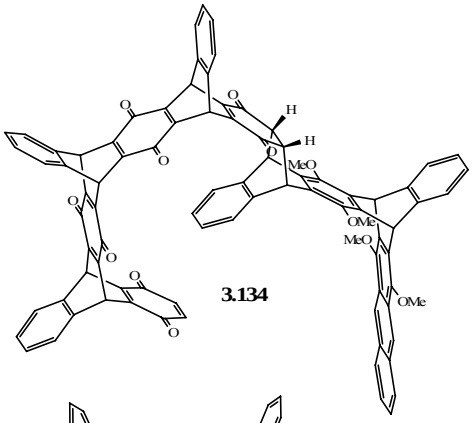

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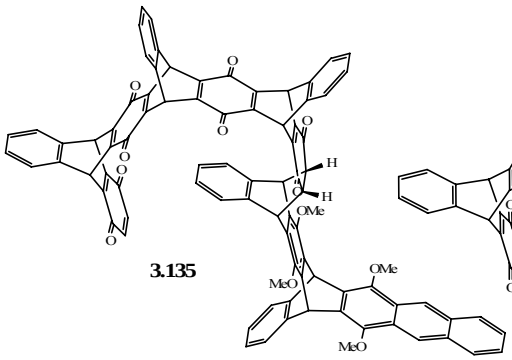

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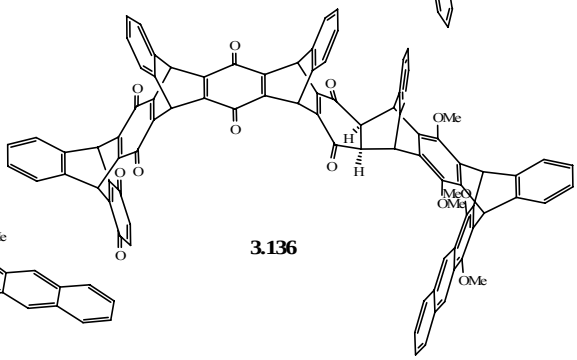

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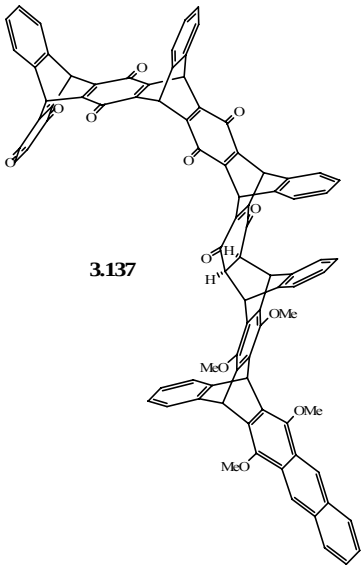

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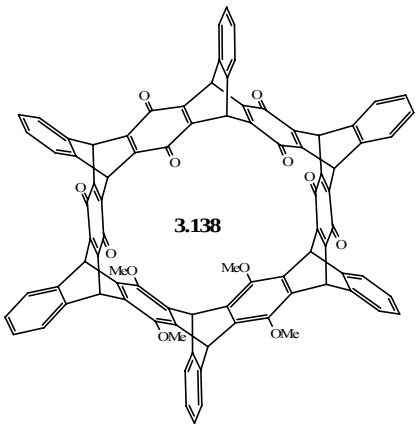

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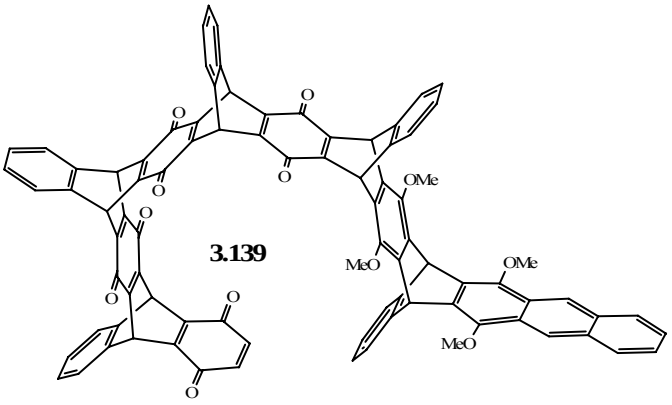

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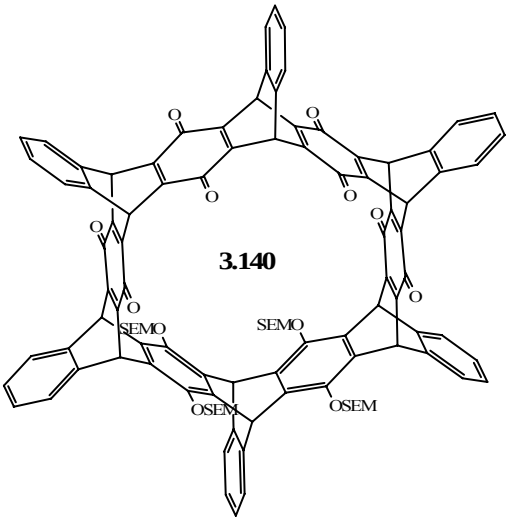

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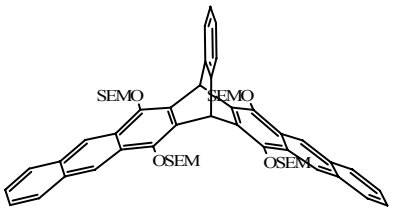

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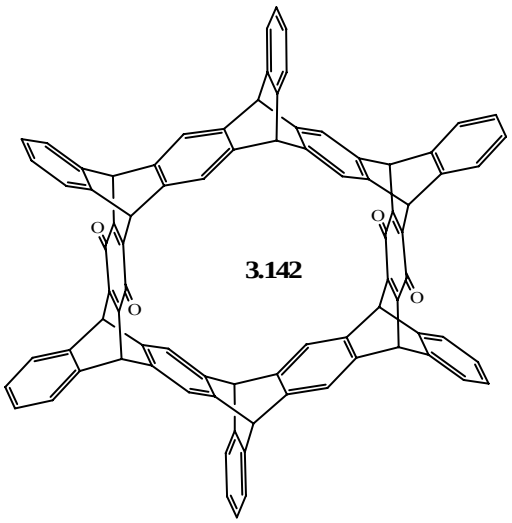

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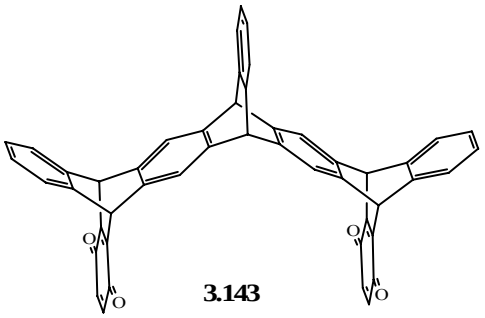

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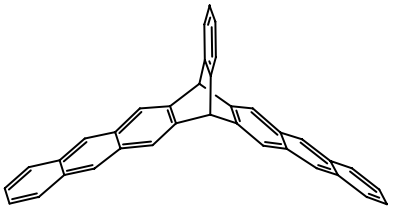

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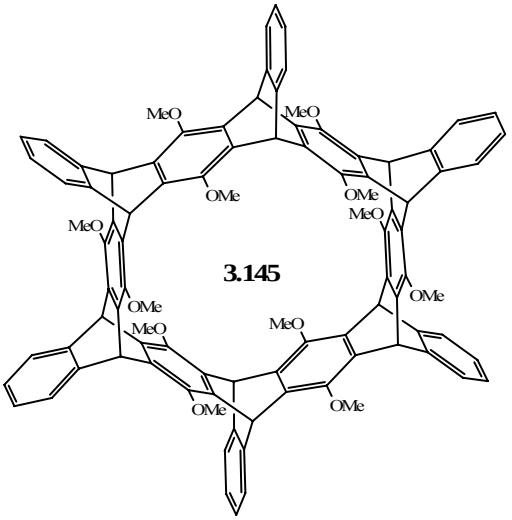

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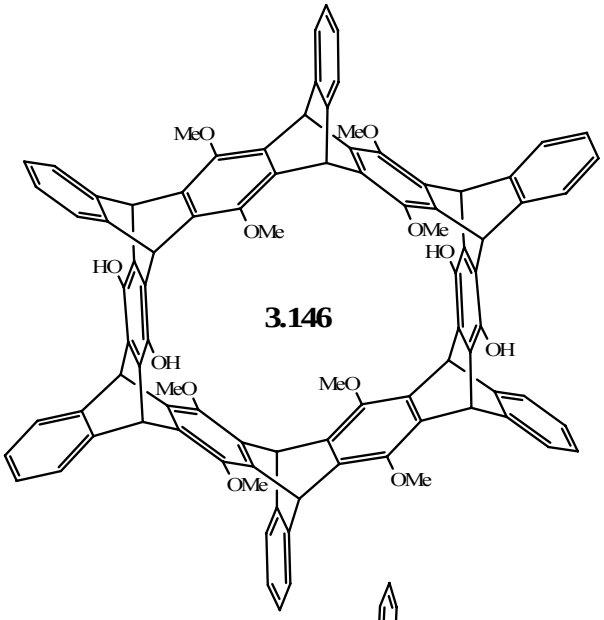

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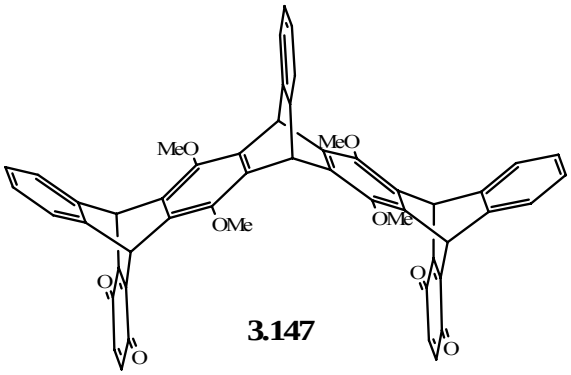

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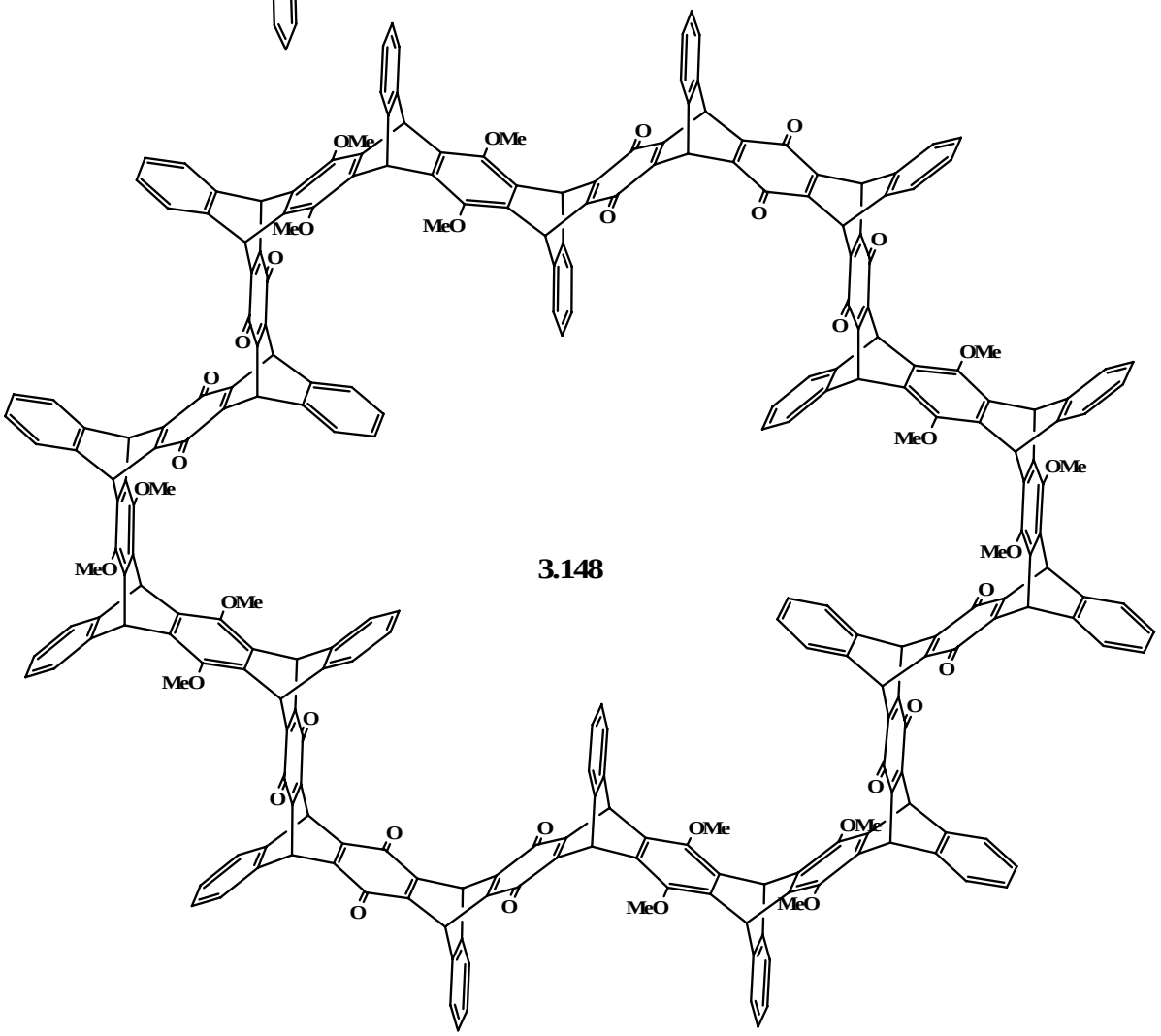

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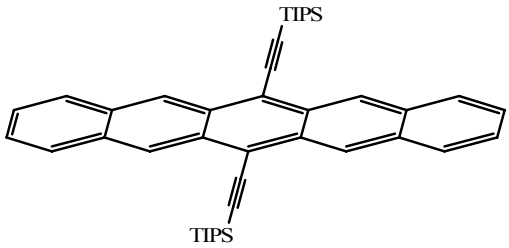

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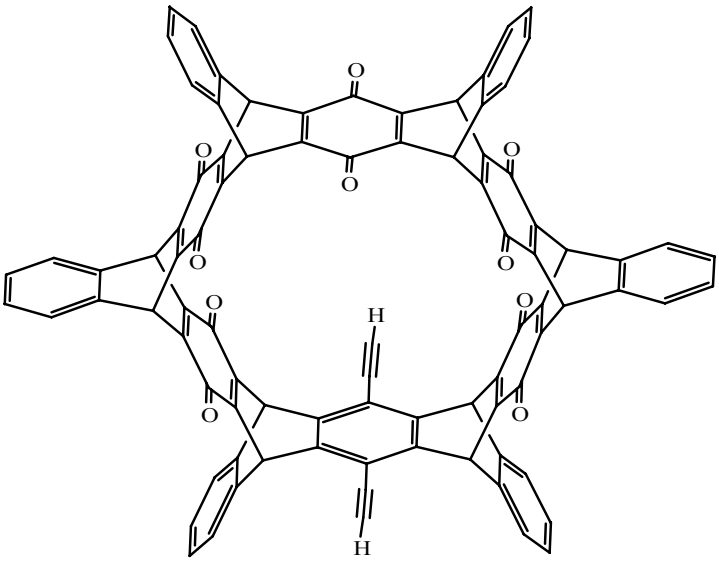

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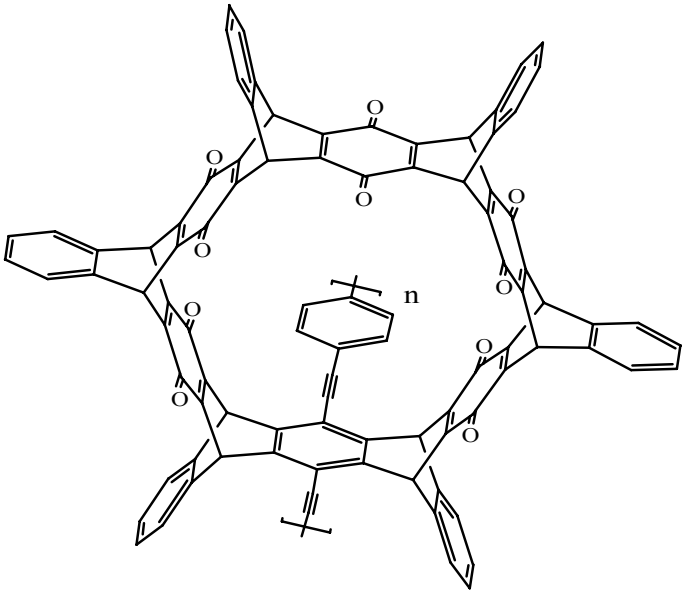

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Acknowledgements

I would like to give my most sincere gratitude to my research advisor, Dr. Duy Hua, for his insightful guidance, constant encouragement, and full support during my Ph. D. period. I have learned a lot from him both in experimental skills and moral character, especially in his dedication and persistent effort towards a scientific goal.

I would also like to thank Dr. Stefan Bossmann, Dr. Stefan Kraft and Dr. Jean-Pierre Perchellet for their time and instructions in serving on my advisory committee. I am also grateful to all other faculty and staff members in the Department of Chemistry for their help and support. Special thanks for Dr. Christer Aakeröy for his help in my application and admission to Kansas State University.

I sincerely thank all former and current members in Dr. Hua's group for their help in research and daily life. Special thanks go to Dr. Xiaodong Huang and Dr. Neil Brown for their previous work in the beltene project. I also thank Huiping Zhao and Bernard Wiredu for providing more materials to continue my projects. I am also grateful to Srinivas Battina, Angelo Aguilar, Ana Jimenez, Sandeep Rana, and Lydia Roberts for their help and friendship.

Finally, I would like to thank my parents in China for their love and support through this period of my life.

CHAPTER 1 - Synthesis of new 1,4-anthracenedione analogs for their study of anticancer activities

1.1 Introduction

Cancer is still one of main killers of human beings in the 21st century. Development of new, more potent anticancer drugs remains a major challenge.[1] New leading compounds have been discovered either by screening new natural products or known synthetic compounds. In our lab, after screening anticancer activity of a number of intermediates towards the synthesis of functionized beltenes (See **Chapter 2**), we found 1,4-anthracenedione and triptycenebisquinone have potent anticancer activities as leading compounds. Synthetic efforts towards their analogs aiming at better anticancer activity were undertaken in our lab. My project mainly involved the synthesis of new 1,4-anthracenedione analogs via functionalization of the methyl side chain of 6-methyl-1,4-anthracenedione.

1.2 Background

1.2.1 Quinone-containing anticancer drugs

Quinones widely exist in biological systems and they are essential to many life processes including biological redox process.[2] Many naturally existing quinones have potent anticancer activity such as doxonubicin and mitomycin C, and have been used in clinical therapy for more than twenty years.[1] Quinone-containing anticancer drugs fall into the following categories based on their structural characteristics and rationalization of their antitumor activity.

1.2.1.1 Mitomycin C and related quinone-containing alkylating agents[3]

This category includes mitomycin C, porfiromycin, diaziquone, carbazilquinone, triaziquone, and EO9 etc. (**Figure 1.1**) They contain a special alkylating group in their structure along with a quinone moiety. The activity of alkylating groups is triggered by enzymatic reduction of the quinone moiety *in vivo* to form covalent linkages with cellular components including proteins, membranes, and DNAs, which accounts for their antitumor activities.[3]

Quinone rings may also contribute to their cytotoxicity through formation of reactive oxygen species during redox cycling.

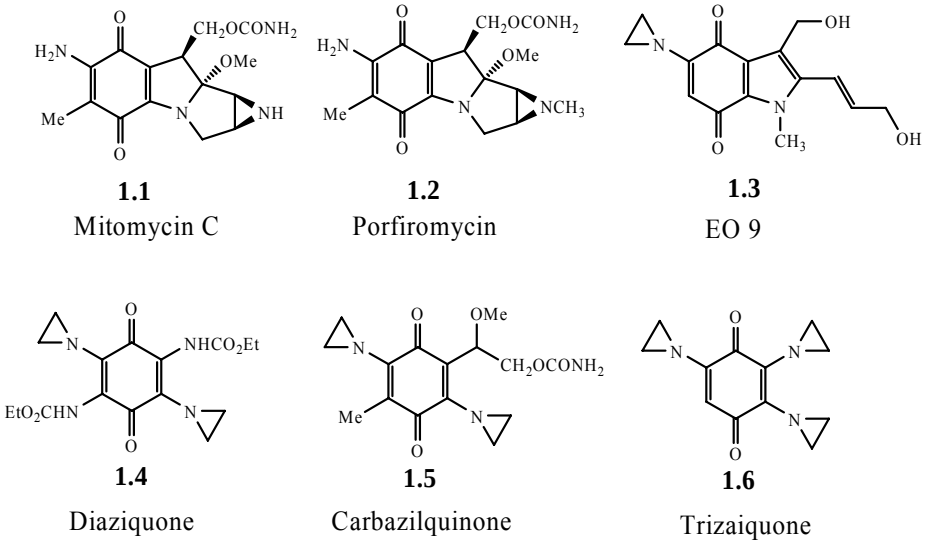
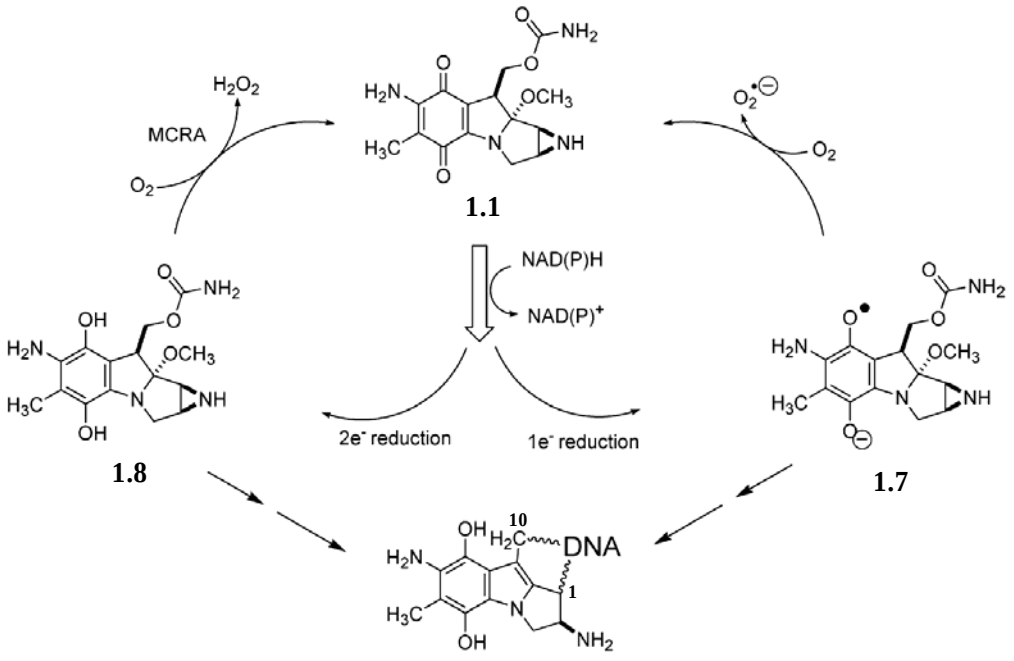


Figure 1.1 Mitomycin C and related quinone-containing alkylating agents.



Scheme 1.1[4] Proposed mechanism for the antitumor activity of mitomycin C. (Taken from reference [4] without permission)

For example, mitomycin C, which has been used clinically for more than 30 years,[5] can be activated by intracellular flavin reductases in either a one- or two-eletron reduction pathway (**Scheme 1.1**). The one-electron pathway forms a semiquinone radical anion (**1.7**), which

transfers an electron to molecular oxygen and produces a superoxide radical anion under aerobic conditions. While in hypoxic conditions, mitomycin is further reduced to its phenol form (**1.8**) in two-electron reduction pathway. The methoxide substituent is then eliminated, which further triggers opening of the aziridine ring which forms a highly reactive species termed mitosene. Mitosene attacks DNA to form crosslinks between C1 and C10 carbon atoms and causes cell damage.[4] This latter pathway is more powerful against cancer cells. Therefore, mitomycin C and related quinone-containing alkylating agents are often used to treat oxygen-deficient solid tumors.

1.2.1.2 Daunorubicin and related anthracycline DNA intercalating agents

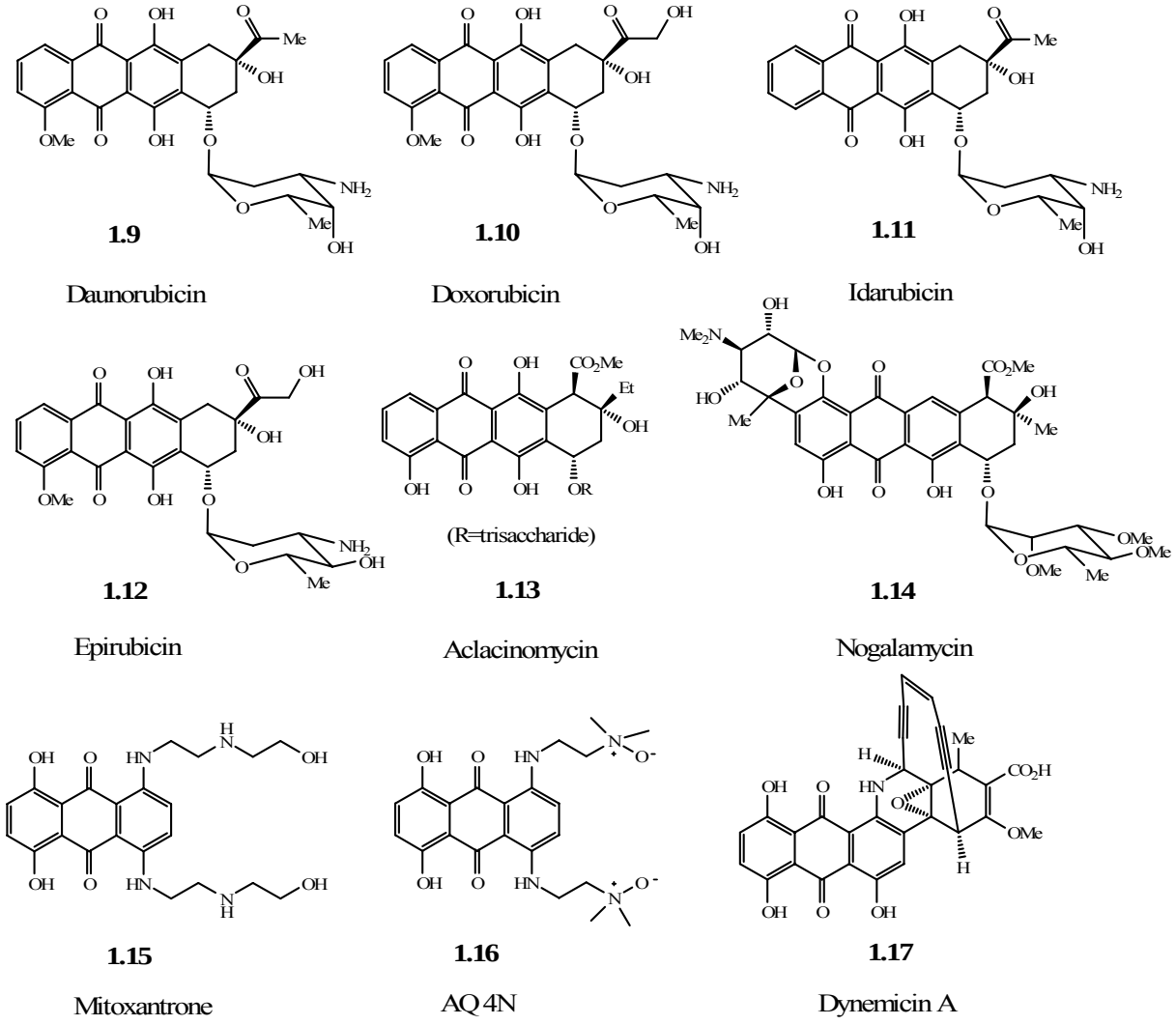


Figure 1.2 Daunorubicin and related anthracycline DNA intercalating agents.

This family of antitumor antibiotics includes daunorubicin, doxorubicin (adriamycin), idarubicin, epirubicin, aclacinomycin, and nogalamycin (**Figure 1.2**). These are dierent from the first category because anthracyclines intercalate to molecular DNA and inhibit DNA replication process.[6] Their structure consists of a flat anthraquinone backbone and a sugar residue with various purposes. In the case of daunorubicin (**1.9**), the duanosamine residue forms hydrogen bonds towards the minor groove of a DNA molecule. Meanwhile, electron-deficient anthracenequinone ring inserts itself into electron-rich purine-pyrimidine bases (**Figure 1.3**), causing a distorted DNA helix, which interferes normal binding activities of DNA polymerases, RNA polymerases, topoisomerases, and other related enzymes required for DNA replication and RNA synthesis.[7,8] Clinically, anthracyclines are used to treat a wide range of cancers, including leukemias, lymphomas, breast, uterine, ovarian, and lung cancers.

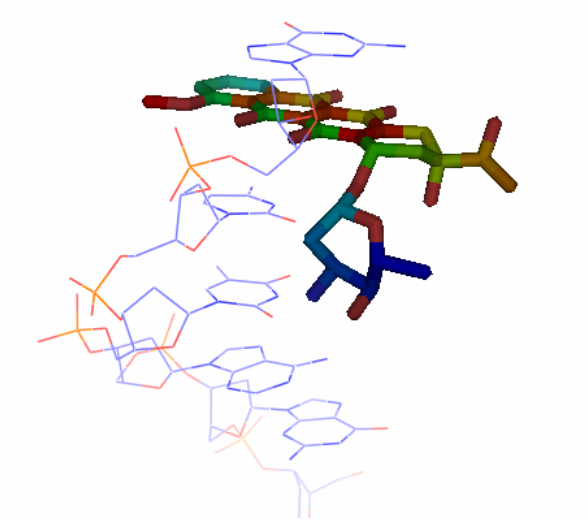
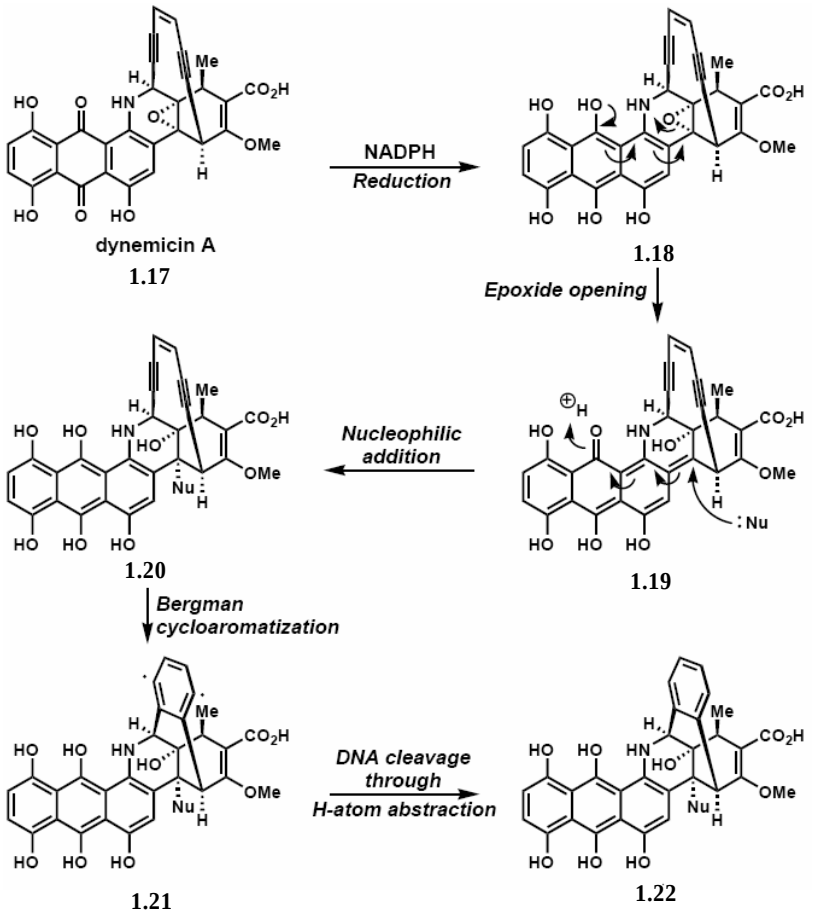


Figure 1.3[8] The crystal structure of d(CGATCG) complexed with daunorobicin (pdb code: 1DA0)

Mitoxantrone (**1.15**), AQ4N (**1.16**), and dynemicin A (**1.17**) have an similar anthraquinone backbone as anthracyclines mentioned above. Their cytotoxicity is also related to their intercalation with DNA. Different from reversible binding of daunorubicin and doxorubicin, mitoxantrone intercalates DNA and cut off DNA, causing DNA aggregation and compaction.[9] AQ4N is structurally related to mitoxantrone but contains a bioreductive N-oxide group, acting as prodrug with increased antitumor activity against hypoxic cancer cells.[10] Dynemicin A is also a reductively activitated antitumor agent. With its unique ten-membered enediyne moiety conjugated with anthraquinone moiety, it causes DNA cleavage via DNA backbone hydrogen

abstraction by a reactive benzenoid diradical formed through a series of reduction, epoxide opening, nucleophilic addition, and Bergman cycloaromatization steps. [11,12] (**Scheme 1.2**)



Scheme 1.2 Proposed mechanism for the antitumor activity of dynemicin A. (Taken from reference[12] without permission)

1.2.1.3 Geldanamycin and related benzoquinone ansamycin Hsp 90 inhibitors

The benzoquinone ansamycin, such as geldanamycin, herbimycin, and macbecin, belong to a family of antitumor antibiotics that were first isolated from actinomycete broth.[13-15] They are characterized by a 20-membered macrocylic lactam ring incorporated with a benzophenone backbone inside it. First described as tyrosine kinase inhibitors, they are now more frequently associated with heat shock protein 90 (Hsp 90), a molecular chaperone involved in maintaining correct conformation and stability of its client proteins required for many key cellular functions such as cell growth, cell survival, apoptosis, angiogenesis, and oncogenesis. Geldanamycin binds with high affinity to the ATP binding pocket of Hsp 90[16] (**Figure 1.5**). As a result, Hsp 90 loses

its ability to act as a chaperone, and the client proteins become misfolded and lose their functions, leading to cell death.[17] To overcome its toxicity and lack of stability as a drug candidate, a number of geldanamycin derivatives such as 17-AG,[18] 17-AAG,[18] and 17-DMAG[19] were developed.

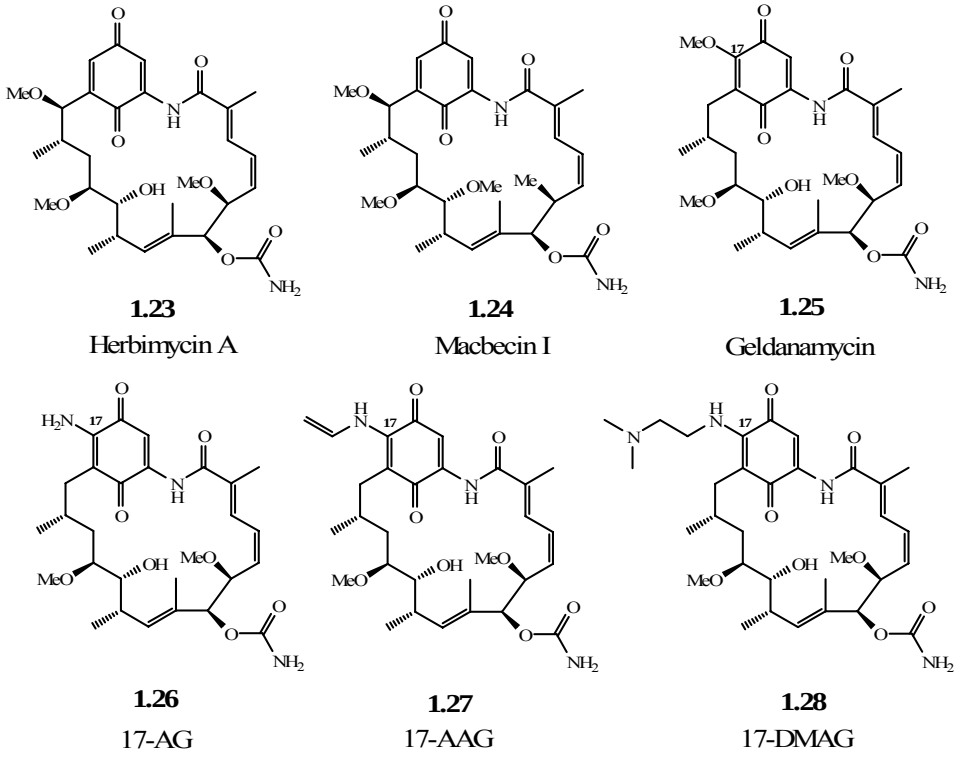


Figure 1.4 Geldanamycin and related benzoquinone ansamycin Hsp 90 inhibitors.

Figure 1.5 The crystal structure of the N-terminal domain of the yeast Hsp90 chaperone complexed with geldanamycin (pdb code:1A4H) [16]

1.2.2 Nature existing 1,4-anthraquinones

Anthracenequiones widely exist in nature mostly as 9, 10-anthraquinones. Very few 1,4-anthraquinones separated from nature have been reported[2] (**Figure 1.6**). The first 1,4-anthraquinones identified in nature were viocristin and isoviocristin isolated from mycelia of *Aspergillus cristatu* in 1980.[20] Biological studies show they have antibiotic activity and inhibitory effect on protein, RNA, and DNA synthesis of *Bacillus brevis* cells.[21, 22] Rrufoolivacin B was isolated from *Cortinarium rufoolivaceus*, which shows antiplasmodial activity against asexual erythrocytic stages of *P. falciparum in vitro* with IC_{50} = 1.67μg/ml.[23] More recently discovered 1,4-anthracenediones in nature are presengulone and segulone.[24] Both were isolated from *Senna sophera*, a medicinal plant used in India. Their biological activities have not yet been investigated. These natural existing compounds show some promise that new anticancer drugs based on 1,4-anthracenequinones may have potential to be as active as those 9, 10-anthracenequinones mentioned above.

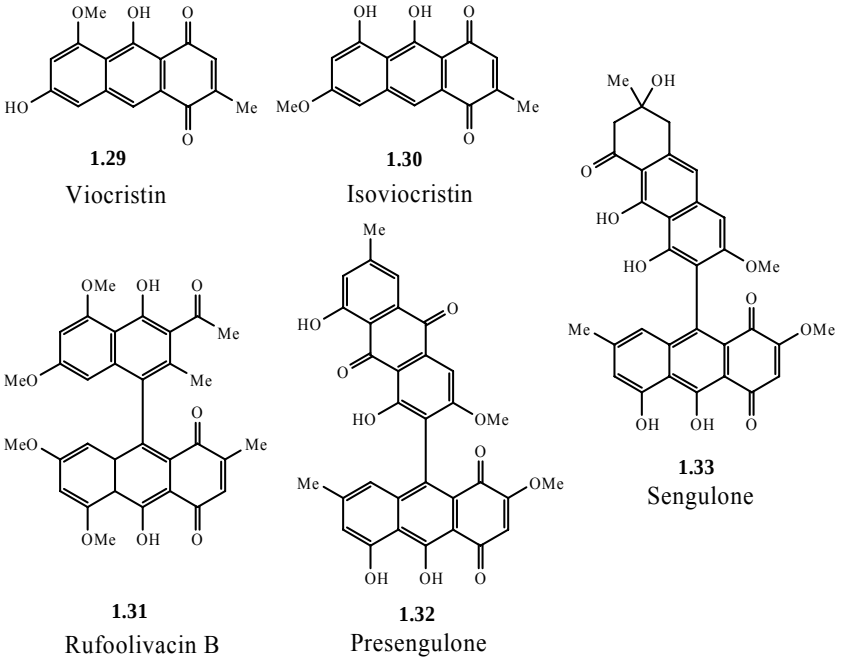
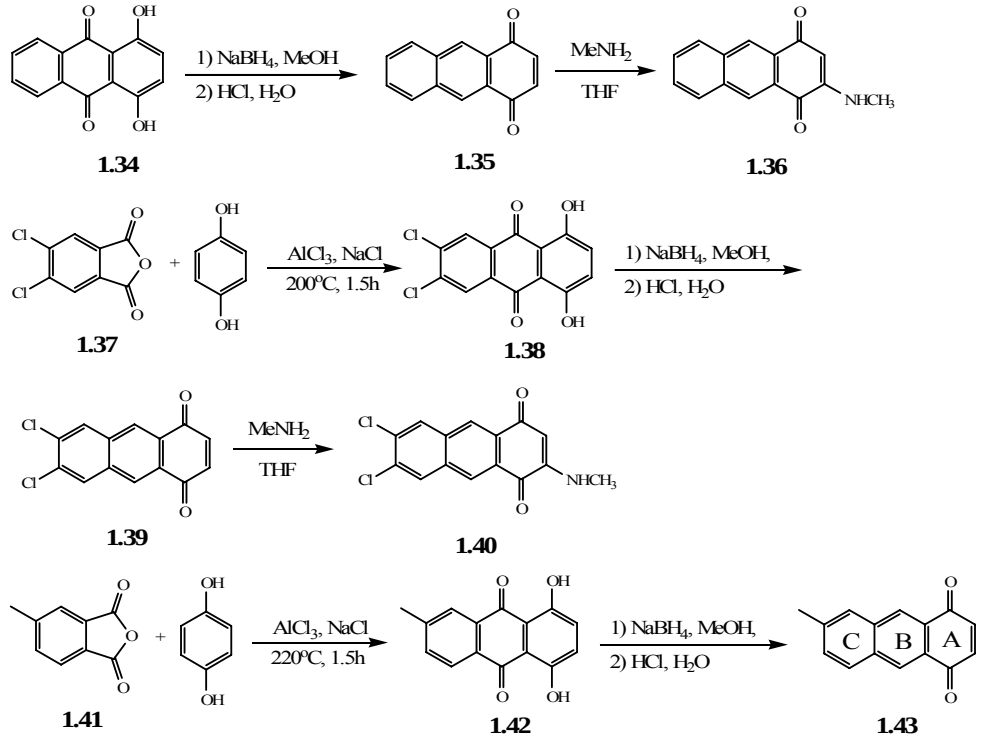


Figure 1.6 Nature existing 1,4-anthraquinones

1.2.3 Previous studies in our lab

Previous studies in our lab have found that 1,4-anthracenedione (**1.35**) showed potent anticancer activity towards L1210 leukemia and human HL-60 tumor cells with IC_{50} = 42.2 nM

and 140.7 nM, respectively, while quinizarine, a 9,10-anthracenedione derivative, was inactive up to 1.6 μM.[25] To study whether other substituted 1,4-anthracenedione showed similar activities against cancer cells, several other 1,4-anthracenedione derivatives were synthesized as shown in **Scheme 1.3**. Their cytotoxicities against L1210 and HL-60 tumor cell lines *in vitro* were given in **Table 1.1**. The data clearly shows that substitution at A-ring decreased antitumor activity, while the substitution at C-ring remained significant antitumor activity for 1,4-anthracenediones.



Scheme 1.3

Compound	L1210, IC_{50} (nM)	HL-60, IC_{50} (nM)
1.34	Not active at 1.6 μM	Not active at 1.6 μM
1.35	42 ± 2	140 ± 7
1.36	Not active at 640 nM	Not active at 640 nM
1.38	Not active at 256 nM	Not active at 256 nM
1.39	84 ± 6	243 ± 16
1.40	Not active at 640 nM	Not active at 640 nM
1.42	Not tested	Not active at 10 μM
1.43	29 ± 1	87 ± 4

Table 1.1 Cytotoxicities of previous synthetic 1,4-anthracenediones *in vitro*.

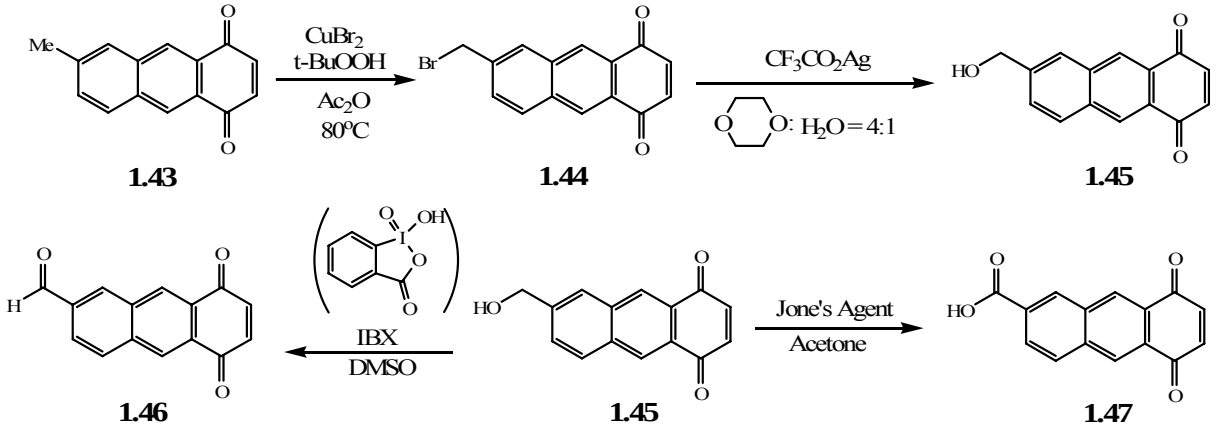
However, low water solubility of these 1,4-anthracenediones may limit drug administration in animal studies and clinical trials. The purpose of this research project was to synthesize new 1,4-anthracenedione derivatives with better water solubility and also investigate their anticancer activities. The most active compound, 6-methyl-1,4-anthracenedione (**1.43**), was chosen for further side-chain modification at 6-methyl position while leaving BC-ring intact for anticancer activity.

1.3 Synthetic efforts towards new 1,4-anthracenedione analogs

1.3.1 Functional group transformation of 6-methyl-1,4-anthracenedione (**1.43**)

The functionization of 6-methyl-1,4-anthracenedione (**1.43**) was started from bromination of the side methyl group. The standard free-radical benzylic bromination using NBS and benzoyl peroxide in refluxing tetrachloromethane failed to give the desired product. Several other conditions also failed.[26] However, radical bromination using copper (II) bromide and *t*-butyl hydroperoxide as radical initiator in acetic anhydride at 80°C successfully gave 6-bromomethyl-1,4-anthracenedione (**1.44**) in 75% yield together with overbrominated byproducts. Compound **1.44** was the key intermediate to synthesize new 1,4-anthracenedione analogs.

Hydrolysis of **1.44** with silver trifluoroacetate in aqueous dioxane at room temperature for two hours to give 92% yield of alcohol **1.45**, which was easily oxidized with IBX (*o*-iodoxybenzoic acid)[27] in DMSO to give 62% yield of aldehyde **1.46** or with Jones reagent to give 82% yield of acid **1.47** (**Scheme 1.4**).

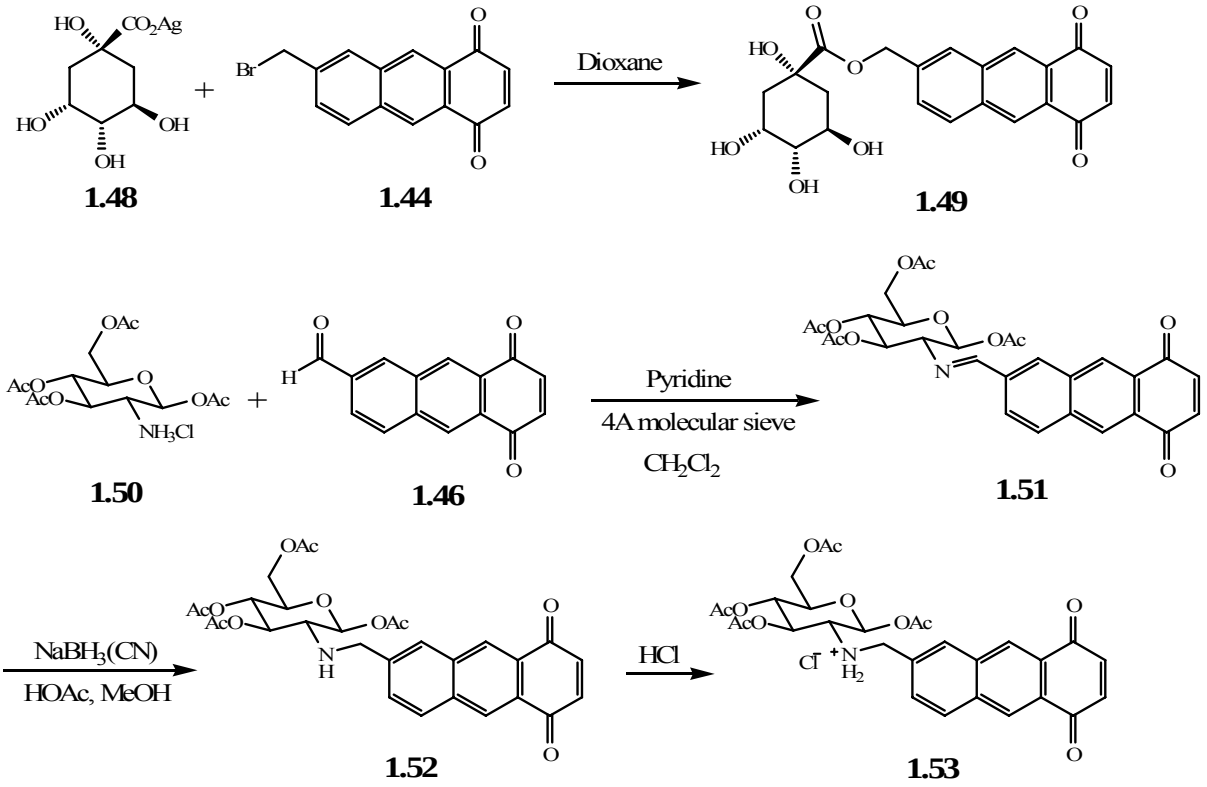


Scheme 1.4

1.3.2 Synthesis of water soluble analogs

We have synthesized several 1,4-anthracenedione analogs with modification at the 6-position. Nonetheless, in order to achieve better water-solubility, a more hydrophilic group such as a sugar or quinic acid group were attached to the molecule.

An ester group can be formed from a bromide reacting with a silver salt of an acid. The quinic acid silver salt **1.48** was easily prepared by stirring silver oxide and quinic acid in ethanol at room temperature overnight. Reaction of bromide **1.44** with the silver salt of (-)-quinic acid (**1.48**) in dioxane afforded ester **1.49** in 46% yield.

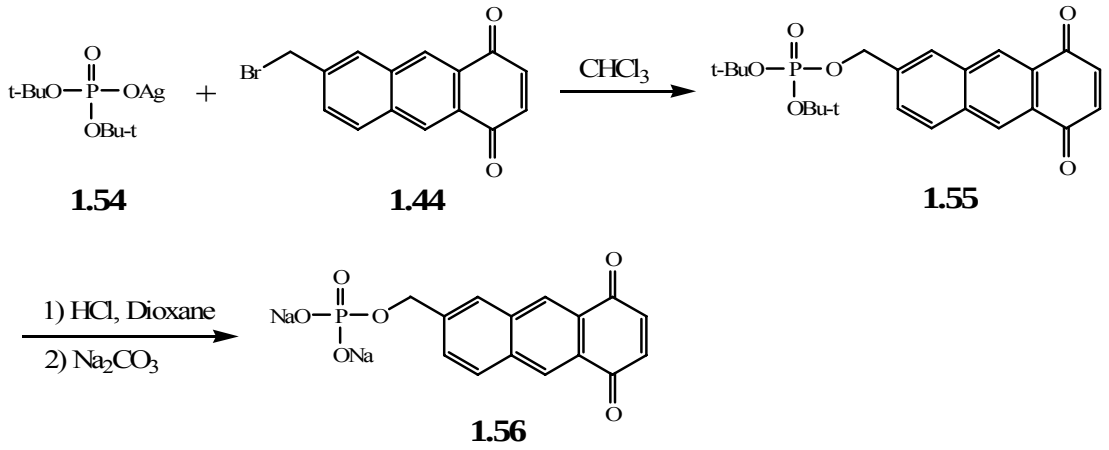


Scheme 1.5

Stepwise reductive amination of aldehyde was used to install an amino sugar group into the molecule. When aldehyde **1.46** reacted with 1,3,4,6-tetra-*O*-acetyl-β-D-glucosamine hydrochloride (**1.50**)[28] in dichloromethane and pyridine, imine **1.51** was formed in 60% yield, which was reduced with sodium cyanoborohydride in acetic acid and methanol to produce the amine **1.52** with protected sugar group. Attempts to remove the acetoxy protecting groups to give a water soluble analog under either basic or acidic conditions were unsuccessful. However, the hydrochloric acid salt of the amine (**1.53**) is soluble in water.

1.3.3 Synthesis of a phosphate ester prodrug

The biological study showed 6-hydroxymethyl-1,4-anthracenedione (**1.45**) has good anticancer activity (Table 1.2). A prodrug approach was used to convert it to a water-soluble phosphate **1.56**, which would release the active quinone **1.45** by phosphatases i*n vivo*. Treatment of bromide **1.44** with silver di-*t*-butyl phosphate **1.54**[29] in refluxing chloroform gave di-*t*-butyl phosphate **1.55** in 48% yield (**Scheme 1.6**), which was deprotected in 4M HCl in dioxane and neutralized with sodium carbonate to afford the water-soluble prodrug disodium phosphate **1.56**.



1.54 **1.44** **1.55**

1.56

Scheme 1.6

1.4 Anticancer activities and conclusions

The biological activity of synthetic 1,4-anthracenedione was carried out in our collaborator Dr. Jean-Pierre Perchellet's Lab. IC_{50} values of new synthetic 1,4-anthracenediones against L1210 and HL-60 leukemic cells at day 4 were summarized in **Table 1.2**. From both **Table 1.1** and **1.2**, the IC_{50} of various 1,4-anthracenediones are in a range of 26 to 462 nM for L1210 cells and 79 to 1260 nM for HL-60 cells with some exceptions. Unexpectedly, increased water-solubility correlated to decreased anti-cancer activities. This may be due to the increased difficulty to cross hydrophobic cell membranes for more water-soluble drugs. 1,4-anthracenedione **1.44** and **1.45** have almost the same anticancer activity against L1210 cells as their mother compound **1.43**. All three compounds show anticancer activities comparable to daunomycin, of which the IC_{50} value is 30 nM in similar conditions.[30] However, their mechanism against cancer cells are somehow different from daunomycin. 1,4-Anthracenediones have broader spectrum of molecular targets in cells. They were found to block nucleoside

transportation, cause DNA fragmentation, and decrease the growth of L1210 leukemic cells.[25, 31] They were also found targeting cytochrome *c*, caspase-9, -3 and -8, poly(ADP-ribose) polymerase-1, and internucleosomal DNA in wild-type and MDR (multidrug-resistant) HL-60 cells by a mechanism partially mediated by caspase-2 activation but not involving Fas signaling.[32] Besides, they can trigger cytochrome *c* release without caspase activation. Most interestingly, they seem to target mitochondria directly to induce a rapid loss of mitochondrial membrane potential together with permeability transition pore opening under experimental conditions, which was not found in daunoymcin.[33, 34] Their wide spectrum of molecular targets and activity against MDR tumor cells make them a potential new synthetic class of quinone-containing-anticancer drugs in chemotherapy.

Compound	L1210, IC_{50} (nM)	HL-60, IC_{50} (nM)
1.44	26 ± 1	79 ± 3
1.45	37 ± 2	125 ± 7
1.46	462 ± 43	1260 ± 104
1.47	Not active at 4.0 μM	Not active at 256 nM
1.49	Not tested	919 ± 78
1.52	Not tested	254 ± 23
1.53	Not tested	1980 ± 176
1.55	Not tested	133 ± 9

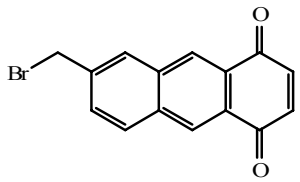
Table 1.2 Cytotoxicities of new synthetic 1,4-anthracenediones *in vitro*.

In conclusion, a series of new 1,4-anthracenediones were synthesized via functionalizations of side chain of 6-methyl-1,4-anthracenedione. They were found to exhibit potent cytotoxic activities against human L1210 leukemic and HL-60 cell lines. A key intermediate, 6-bromomethyl-1,4-anthracenedione (**1.44**), was first synthesized through a sequence of reactions including a double Friedel-Crafts reaction, reductive quinone formation, and selective benzylic bromination. The bromide **1.44** was further converted to other 1,4-anthracenediones via hydrolysis, subsequent oxidation and reductive amination or nucleophilic substitution.

1.5 Experimental Section

General Methods: NMR spectra were obtained at a Varian Unity Plus (400 MHz) or Varian Gemini 2000 (200 MHz). FAB spectra were taken by using Xe beam (8 kV) and *m*-nitrobenzyl alcohol as matrix. Quinizarine, methylamine in THF (2 M solution), 4-methylphthalic anhydride, aluminum trichloride, and *t*-butyl hydroperoxide were commercially available. Davisil silica gel, grade 643 (200–425 mesh), was used for the flash column chromatographic separation.

1.5.1 Synthesis of key intermediate 6-bromomethyl-1,4-anthracenedione



1.44

1.5.1.1) 6-Methyl-1,4-dihydroxy-9,10-anthracenedione (**1.42**)

To a melted (180 ^{o}C) mixture of 37.1 g (27.9 mmol) of aluminum trichloride and 7.25 g (12.4 mmol) of sodium chloride under argon was added a mixture of 5.00 g (30.8 mmol) of 4-methylphthalic anhydride (**1.41**), 3.74 g (34.0 mmol) of hydroquinone, and 15.0 g (113 mmol) of aluminum trichloride in one portion. The mixture was stirred and heated at 220 ^{o}C for 2 h, cooled to room temperature, poured into 300 mL of ice water, and acidified with 12 N HCl. The precipitate was filtered, washed with water, and dried in a vacuum desiccator to give 6.28 g (80% yield) of **1.42**: mp 174~176 ^{o}C (lit[35]: 175~177 ^{o}C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 12.96, 12.92 (2 s, 2 H), 8.25 (d, 1 H, J = 8.0), 8.15 (s, 1 H), 7.64 (d, 1 H, J = 8.0), 7.31 (s, 2 H), 2.56 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 187.5, 187.1, 158.0, 157.9, 146.1, 135.6, 133.6, 131.4, 129.6, 129.3, 127.6, 127.5, 113.1, 113.0, 22.2; MS (MALDI): m/z 255.40 $(M+H)^{+}$.

1.5.1.2) 6-Methyl-1,4-anthracenedione (**1.43**)

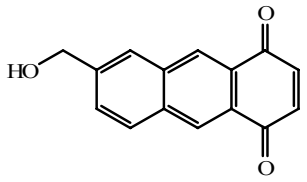
To a suspension of 3.00 g (11.8 mmol) of **1.42** in 50 mL of methanol at 0 ^{o}C under argon, was added 1.80 g (47.6 mmol) of sodium borohydride in portions. The mixture was stirred at 0 ^{o}C for 4 hours and acidified with 6 N HCl. The yellow precipitate was filtered, dried, and applied to flash column chromatograph (silica gel) using a mixture of hexane–ether–CH_2Cl_2 (60:5:1) as an eluent to give 2.57 g (98% yield) of the title compound **1.43:** mp 174~176 ^{o}C (lit[36]:182~183 ^{o}C); ^{1}HNMR ($CDCl_3$, 400 MHz) δ 8.59, 8.54 (2 s, 2 H), 7.97 (d, 1 H, J = 8.4 Hz), 7.84 (bs, 1 H, J = 1.6), 7.53 (dd, 1 H, J_1 = 8.4 Hz, J_2 = 1.6 Hz), 7.06 (s, 2 H), 2.58 (s, 3 H); ^{13}C

NMR ($CDCl_3$, 50 MHz) δ 185.0, 184.9, 140.4, 140.3, 140.1, 135.3, 133.3, 132.2, 130.2, 129.4, 128.9, 128.7, 128.4, 128.0, 22.2; MS (MALDI) m/z 223.11 $(M+H)^+$.

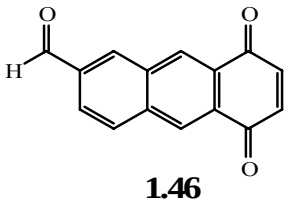
1.5.1.3) 6-Bromomethyl-1,4-anthracenedione (**1.44**)

To a solution of 0.70 g (3.2 mmol) of **1.43** and 1.0 g (4.5 mmol) of copper (II) dibromide in 14 mL of acetic anhydride at 60 ^oC under argon, was added 1.1 mL (5.0 mmol) of *t*-BuOOH (90%) dropwise through a dropping funnel. The solution was stirred at 80 ^oC for 2 h, cooled to room temperature, diluted with 200 mL of water, and extracted with methylene chloride (50 mL ×3). The combined organic layer was washed with brine, dried over $MgSO_4$, concentrated, and applied to column chromatograph on silica gel using a petrol ether-ethyl acetate (17:3) as an eluent to give 0.72 g (75% yield) of the title compound **1.44**: mp 183~184 ^oC; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.59 (s, 1 H), 8.58 (s, 1 H), 8.06 (d, J = 8.4 Hz, 1 H), 8.04 (d, J = 1.8 Hz, 1 H), 7.72 (dd, J = 8.4, 1.8 Hz, 1 H), 7.08 (s, 2 H), 4.67 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 184.7 (2 C, C=O), 140.3, 140.2, 139.4, 135.0, 134.6, 131.2, 130.7, 129.9, 129.1 (2 C), 128.9, 128.7, 32.8. Anal. Calcd for $C_{15}H_9BrO_2 \cdot 0.025H_2O$: C, 58.37; H, 3.21. Found: C, 58.28; H, 2.92.

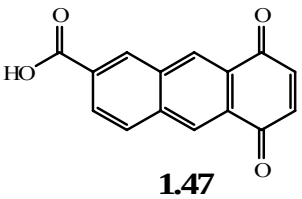
1.5.2 Further function group transformation of 6-bromomethyl- 1,4-anthracenedione



1.45



1.46



1.47

1.5.2.1) 6-Hydroxymethyl-1,4-anthracenedione (**1.45**)

A mixture of 71 mg (0.24 mmol) of the bromide (**1.44**) and 59 mg (0.27 mmol) of silver trifluoroacetate in 2 mL of 1,4-dioxane–water (4:1) was stirred under argon at 25 ^oC for 2 hours, diluted with 10 mL of acetone, and filtered through Celite. The filtrate was concentrated and applied to flash column chromatograph (silica gel) using a mixture of hexane–ethyl acetate (1:1) as an eluent to give 52 mg (92% yield) of the title compound **1.45**: mp 178~179 ^oC (crystallized from toluene); ^1H NMR ($CDCl_3$, 400 MHz) δ 8.58 (s, 1 H), 8.56 (s, 1 H), 8.03 (d, J = 8.4 Hz, 1 H), 8.02 (d, J = 1.4 Hz, 1 H), 7.68 (dd, J_1 = 8.4, J_2 = 1.4 Hz, 1 H), 7.06 (s, 2 H), 4.94 (s, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 184.9 (2 C, C=O), 142.9, 140.3, 140.2, 135.2, 134.5, 130.7, 129.3, 128.9 (2 C), 128.4, 127.3, 125.5, 62.6. Anal. Calcd. For $C_{15}H_{10}O_3 \cdot 0.02H_2O$: C, 74.14; H, 4.37. Found: C, 74.33; H, 4.50.

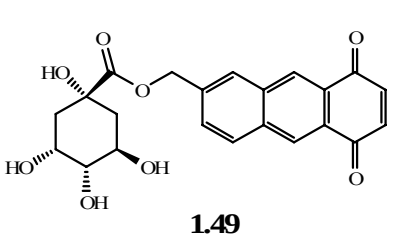
1.5.2.2) 6-Formyl-1,4-anthracenedione (**1.46**)

To a 5 mL of IBX (1M DMSO solution) [27] was added 250 mg (1.05 mmol) of the alcohol **1.45**. The reaction mixture was stirred under argon at room temperature for 12 hours. The mixture was filtered. The filtrate was diluted with wather (100 mL) and extracted with methylene chloride (100 mL ×2). The combined organic layers were washed with water (100 mL), brine (100 mL), dried over anhydrous magnesium sulfate, filtered, concentrated, and applied to flash column chromatograph (silica gel) using a mixture of petrol ether–diethyl ether (2:1) as an eluent to give 154 mg (62% yield) of the title compound **1.46**: mp 185~186 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.25 (s, 1 H, CHO), 8.81 (s, 1 H), 8.69 (s, 1 H), 8.56 (d, J = 1.6 Hz, 1 H), 8.19 (d, J = 8.0 Hz, 1 H), 8.17 (dd, J_1 = 8.0 Hz, J_2 = 1.6 Hz, 1 H), 7.14 (s, 2 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 191.5 (CHO), 184.5 (2 C, C=O), 140.3 (2 C), 138.0, 136.7, 135.7, 134.6, 131.5, 130.7, 130.3, 129.5, 128.8, 126.5; Anal. Calcd For $C_{15}H_8O_3$: C, 76.27; H, 3.41. Found: C, 75.87; H, 3.74.

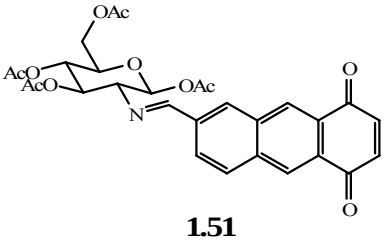
1.5.2.3) 5,8-Dioxo-5,8-dihydroanthracene-2-carboxylic acid (**1.47**)

To a solution of 119 mg (0.500 mmol) of the alcohol in 10 mL of acetone under argon, was added a solution of 0.50 mL (1.4 mmol) of Jones reagent (preparation: 26.72 g of chromium trioxide was dissolved in 23 mL of concentrated H_2SO_4 and then diluted to a volume of 100 mL). The mixture was stirred at 25 ^{o}C for 3 h, and then filtered through Celite, concentrated to dryness. The residue was applied to flash column chromatograph (silica gel) using a mixture of diethyl ether–ethanol (9:1) as an eluent to give 103 mg (82% yield) of the title compound **1.47**: ^{1}H NMR (DMSO-d_6, 200 MHz) δ 8.91 (s, 1 H), 8.81 (s, 1 H), 8.69 (s, 1 H), 8.37 (d, J = 8.4 Hz, 1 H), 8.17 (d, J = 8.4 Hz, 1 H), 7.20 (s, 2 H); ^{13}C NMR (DMSO-d_6, 50 MHz) δ 184.3, 184.1, 166.8, 140.1, 140.0, 136.1, 133.6, 132.3, 131.3, 130.5, 129.7, 129.5, 128.8, 128.5, 127.7; Anal. Calcd For $C_{15}H_8O_4 \cdot 0.03H_2O$: C, 69.35; H, 3.43. Found: C, 69.13; H, 3.75.

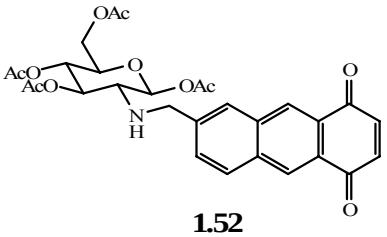
1.5.3 Synthesis of water soluble analogs



1.49



1.51



1.52

1.5.3.1) 5,8-Dioxo-5,8-dihydro-2-anthracenylmethyl-(*1R,3R,4R,5R*)-1,3,4,5-tetrahydroxy-cyclohexanecarboxylate (**1.49**)

A mixture of 0.30 mmol of silver (-)quinate (**1.48**) [prepared from 0.10 g of (-)-quinic acid and 60 mg of Ag_2O in 3mL of ethanol] in 1 mL of 1,4-dioxane was stirred under argon for 24 hours. The reaction mixture was filtered through Celite, concentrated, and applied to column chromatograph (silica gel) using a mixture of ethyl acetate-methanol-water (100:16.5:13.5) as an eluent to give 32 mg (46% yield) of the title compound **1.49**: $[\alpha]^{22}_D$ = -41.7^o (c 0.005, MeOH); ^{1}H NMR (DMSO-d_6, 400 MHz) δ 8.62 (s, 1 H), 8.58 (s, 1 H), 8.28 (d, J = 8.8 Hz, 1 H), 8.26 (d, J = 1.6 Hz, 1 H), 7.77 (dd, J = 8.8, 1.6 Hz, 1 H), 7.16 (s, 2 H), 5.61 (s, 1 H, OH), 5.29 (d, J = 13.2 Hz, 1 H), 5.32 (d, J = 13.2 Hz, 1 H), 4.72 (d, J = 3.6 Hz, 1 H, OH), 4.56 (d, J = 4.4 Hz, 1 H, OH), 4.51 (d, J = 6.4 Hz, 1 H, OH), 3.93 (m, 1 H), 3.81 (m, 1 H), 3.40 (m, 1 H), 2.10~1.70 (m, 4 H); ^{13}C NMR (DMSO-d_6, 50 MHz) δ 184.4 (2 C, C=O), 173.4, 140.1 (2 C), 138.3, 134.1, 133.7, 130.3, 129.0, 128.5, 128.2, 128.0 (2 C), 127.9, 73.8, 72.9, 67.5, 67.3, 65.0, 37.6 (2 C). Anal. Calcd For $C_{22}H_{20}O_8 \bullet 0.02H_2O$: C, 62.81; H, 5.01. Found: C, 62.78; H, 4.84.

1.5.3.2) *N*-[(1,4-Dioxo-1,4-dihydroanthracenyl)methylidene]-2-amino-2-deoxy-1,3,4,6-tetra-*O*-acetyl-β-D-glucopyranose (**1.51**)

A mixture of 21 mg (89 mmol) of the aldehyde **1.46**, 33 mg (95 mmol) of 1,3,4,6-tetra-*O*-acetyl-β-D-glucosamine hydrochloride (**1.50**) [28], 50 μL of pyridine, and 0.20 g of 4 Å molecular sieves in 3 mL of methylene chloride was stirred under argon at room temperature for 24 hours, filtered through Celite, and applied to column chromatograph (silica gel) using a mixture of hexane and diethyl ether (1:1) as an eluent to give 30 mg (60% yield) of the title compound **1.51**: mp 192~193 ^{o}C; $[a]^{22}_D$ = +125^o (c 0.007, MeOH); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.68 (s, 1 H), 8.63 (s, 1 H), 8.45 (s, 1 H), 8.23 (s, 1 H, N=CH), 8.17 (d, J = 8.4 Hz, 1 H), 8.08 (d, J = 8.4 Hz, 1 H), 7.10 (s, 2 H), 6.02 (d, J = 8 Hz, 1 H), 5.51 (t, J = 9.6 Hz, 1 H), 5.19 (t, J = 9.6 Hz, 1 H), 4.40 (dd, J = 12, 4.4 Hz, 1 H), 4.16 (dd, J = 12, 2 Hz, 1 H), 4.02 (m, 1 H), 3.61 (dd, J = 9.6, 8.4 Hz, 1

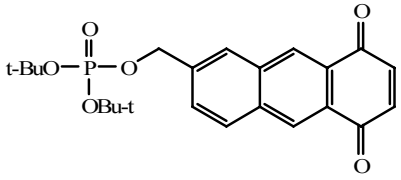
H), 2.12 (s, 3 H), 2.05 (s, 3 H), 2.03 (s, 3 H), 1.89 (s, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 184.3, 184.2, 170.6, 169.8, 169.5, 168.6, 163.9, 140.0, 139.9, 136.3, 136.1, 134.5, 132.3, 130.8, 129.4, 129.2, 128.9, 128.5, 127.3, 92.9, 73.0 (2 C), 72.8, 67.9, 61.7, 20.7, 20.6, 20.5, 20.4. HRMS calcd. for $C_{29}H_{28}NO_{11}$ (M+H) 566.1657, found 566.1430.

1.5.3.3) *N*-[(1,4-Dioxo-1,4-dihydroanthracenyl)methyl]-2-amino-2-deoxy-1,3,4,6-tetra-*O*-acetyl-β-D-glucopyranose (1.52)

To a solution of 25 mg (44 mmol) of the imine **1.51** in 0.1 mL of acetic acid and 1 mL of methanol under argon, was added 11 mg (0.17 mmol) of sodium cyanoborohydride. The solution was stirred at 25 ^{o}C for 3 hours, diluted with 40 mL of water, and extracted twice with 20 mL of dichloromethane. The combined organic layers were washed with brine (40 mL), dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was applied to column chromatograph (silica gel) using a mixture of hexane and ethyl acetate (1:1) as an eluent to give 14 mg (55% yield) of the title compound **1.53**: mp >120 ^{o}C (dec.); $[a]^{22}_{D}$ = +175^{o} (c 0.004, MeOH); ^{1}HNMR ($CDCl_3$, 400 MHz) δ 8.54 (s, 1 H), 8.52 (s, 1 H), 7.99 (d, J = 8 Hz, 1 H), 7.89 (s, 1 H), 7.59 (d, J = 8 Hz, 1 H), 7.05 (s, 2 H), 5.69 (d, J = 8.8 Hz, 1 H), 5.06 (t, J = 9.6 Hz, 1 H), 4.31 (dd, J = 12.4, 4 Hz, 1 H), 4.13 (m, 1 H), 4.10 (d, J = 14.4 Hz, 1 H, CH_2N), 4.04 (d, J = 14.4 Hz, 1 H, CH_2N), 3.83 (m, 1 H), 3.00 (t, J = 8.8 Hz, 1 H), 2.07 (s, 3 H), 2.06 (s, 3 H), 2.05 (s, 3 H), 2.04 (s, 3 H); ^{13}CNMR ($CDCl_3$, 100M Hz) δ 184.6, 184.5, 170.8, 170.5, 169.5, 169.0, 141.9, 139.9, 139.8, 134.7, 134.0, 130.3, 130.0, 129.2, 128.5,128.4, 128.3, 128.2, 94.8, 73.8, 72.4, 68.1, 61.6, 60.3, 51.7, 21.0, 20.8, 20.6, 20.5; HRMS calcd for $C_{29}H_{30}NO_{11}$ (M+H) 568.1819, found 568.1831.

To a solution of 5.0 mg (8.8 mmol) of amine **1.52** in 1 mL of methanol, was added 35 mL (0.14 mmol) of HCl (4 M in dioxane). The solution was stirred for 10 min. and solvent was removed to give 5.3 mg (100% yield) of hydrochloric salt **1.53**.

1.5.4 Synthesis of a phosphate ester pro-drug



1.55

1.5.4.1) (1,4-Dioxo-1,4-dihydroanthracenyl)methyl di-*t*-butylphosphate (1.55)

A mixture of 0.10 g (0.33 mmol) of bromide **1.44** and 0.33 g (0.59 mmol) of silver di-*t*-butyl phosphate (**1.54**)[29] in 15 mL of chloroform was refluxed under argon for 6 hours, filtered through Celite, concentrated, and applied to column chromatograph (silica gel) using a gradient mixture of hexane and ethyl acetate (1:1) as an eluent to give 68 mg (48% yield) of the title compound **1.55**: mp 126~128 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.61 (s, 2 H), 8.07 (d, J = 8.6 Hz, 1 H), 8.05 (s, 1 H), 7.71 (d, J = 8.6 Hz, 1 H), 7.08 (s, 2 H), 5.22 (d, J_{HP} = 7.4 Hz, 2 H, OCH_2), 1.51 (s, 18 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 184.8 (2 C), 140.2 (2 C), 138.9, 138.7, 134.9, 134.6, 130.6, 129.0 (2 C), 128.8 (2 C), 128.2, 83.1 (d, J_{CP} = 7.2 Hz, 2 C), 67.8 (d, J_{CP} = 5.7 Hz, OCH_2), 30.1 (d, J_{CP} = 4.2 Hz, 6 C). Anal. Calcd For $C_{23}H_{27}O_6P \bullet 0.03H_2O$: C, 62.31; H, 6.46. Found: C, 62.49; H, 6.06.

1.5.4.2) Disodium (1,4-dioxo-1,4-dihydroanthracenyl)-methyl phosphate (1.56)

To a solution of 20 mg (47 mmol) of phosphate **1.55** in 1 mL of 1,4-dioxane, was added 0.12 mL (0.47 mmol) of 4 M HCl. The reaction mixture was stirred at room temperature for 1 hour, and 78 mg (0.93 mmol) of $NaHCO_3$ was added, and solvent was removed. To the solids, 2 mL of ethanol was added, and resulting mixture was stirred for 5 min, filtered, and the filtrate was concentrated to give 14 mg (84% yield) of **1.56**. ^{1}H NMR (DMSO-d_6, 400 MHz) δ 8.64 (s, 1 H), 8.60 (s, 1 H), 8.30 (d, J = 8.4 Hz, 1 H), 8.24 (s, 1 H), 7.77 (d, J = 8.4 Hz, 1 H), 7.17 (s, 2 H), 5.11 (d, J_{HP} = 7.6 Hz, 2H, CH_2P).

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CHAPTER 2 - Synthetic efforts toward a macropolycyclic [10]beltene derivative

2.1 Introduction

This project is part of ongoing research in our lab, which has been carried out by three previous students in our lab, Jinmei Fan,[1] Dr. Xiaodong Huang,[2] Dr. Neil Brown[3] since 1996. The initial synthetic target was [12]beltene derivative **2.1**, which could be retrosynthetically constructed from triptycene bisquinone (**2.2**) and 1,2,4,5-tetramethylene cyclohexane (**2.3**). Due to difficulty of synthesis and instability of the tetraene **2.3**,[4,5] we switched to [10]beltene derivative **2.4** for easier synthesis of diene building block **2.5**. The target macropolycyclic [10] beltene **2.4** was expected to undergo self-assembly forming nanotube-like channels.

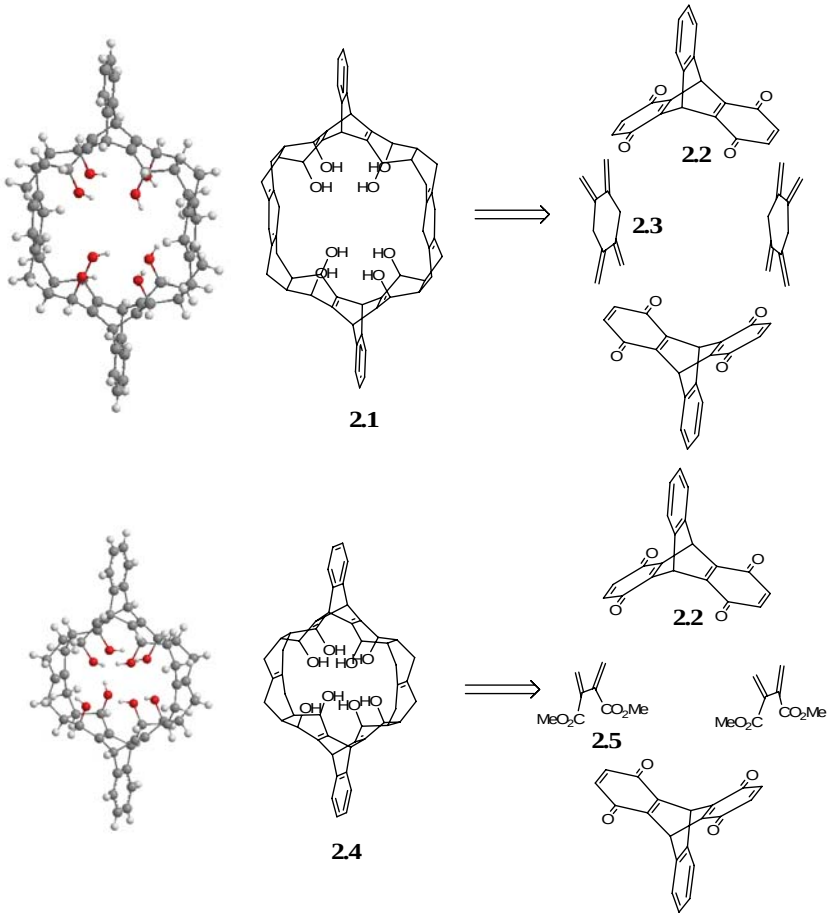
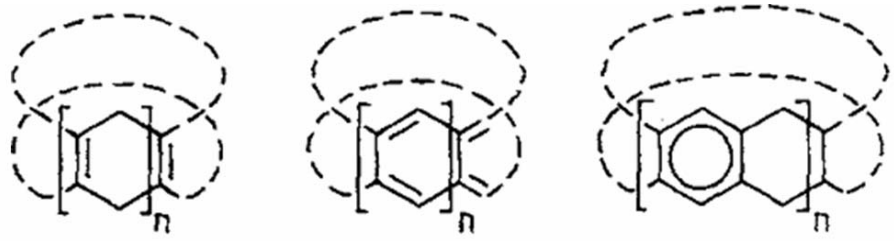


Figure 2.1

2.2 Background

2.2.1 Structure of beltenes and related macropolycycles

Many objects in the macro-world can find their topologically counterparts in micro-molecular level.[6] Belt-shaped macropolycycles are attractive because of their interesting molecular architecture and potential applications in supramolecular chemistry and material science.[7] Vögtle first pointed out that belt-shaped macropolycycles with laterally fused six-membered rings are interesting targets for synthesis.[8] The term "beltenes" was first used by Alder and Sessions to describe the imaginary molecules **2.6** in **Figure 2.2** as "lateral fusion of cyclohexa-1,4-diene rings and linkage into a macrocyclic belt-like assembly".[9] Beltene-related macropolycycles such as cyclacenes and collarenes (**2.7** and **2.8** respectively) share similar carbon backbones with fully or partially aromatized rings around the macropolycycles. Fully conjugated cyclacenes attract more attention both synthetically and theoretically as substructures of fullerenes and single-wall carbon nanotubes (**Figure 2.3**).[10] They may also be possible precursors towards the rational synthesis of these new carbon allotropies.[10] Despite several attempted synthetic endeavors, no beltene and cyclacene has been synthesized yet. Only recently, has a new family of fully conjugated cyclophenacene derivatives been synthesized from C_{60} fullerene.[11-13]



2.6 **2.7** **2.8**

[n]Beltene **[n]Cyclacene** **[2n]Collarene**

[10]Cyclophenacene **"Vögtle Belt"**

2.9 **2.10**

Figure 2.2 Beltenes and their related macropolycycles

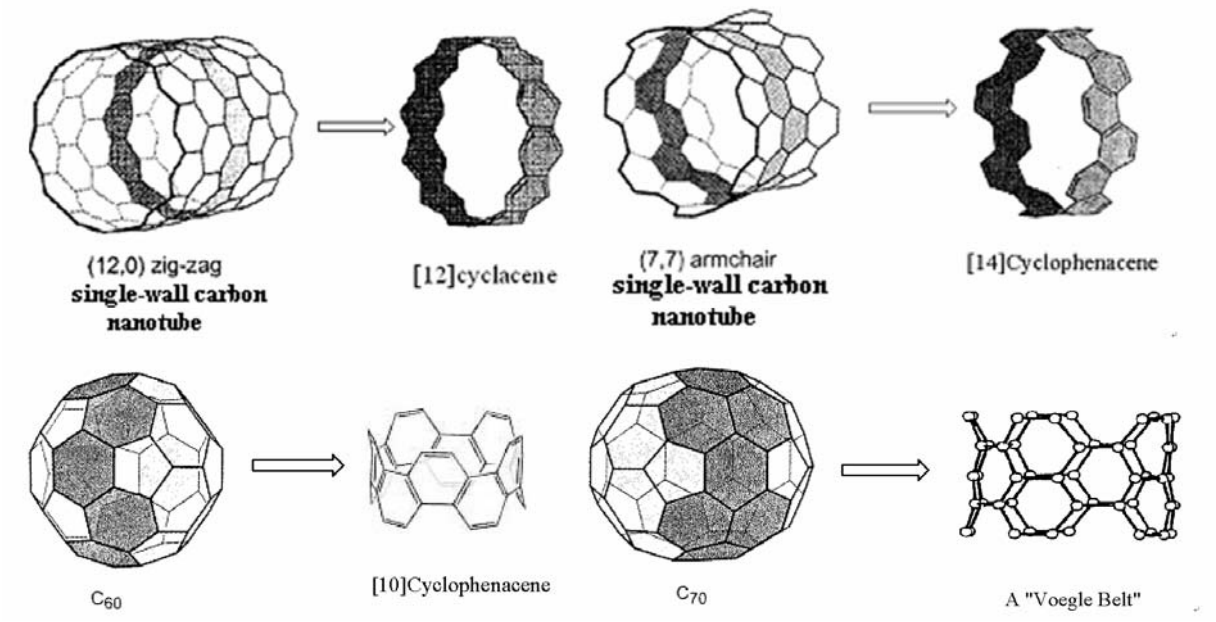


Figure 2.3 Single-wall carbon nanotubes and fullerenes with their belt-like substructures.[10] (Taken from reference [10] without permission)

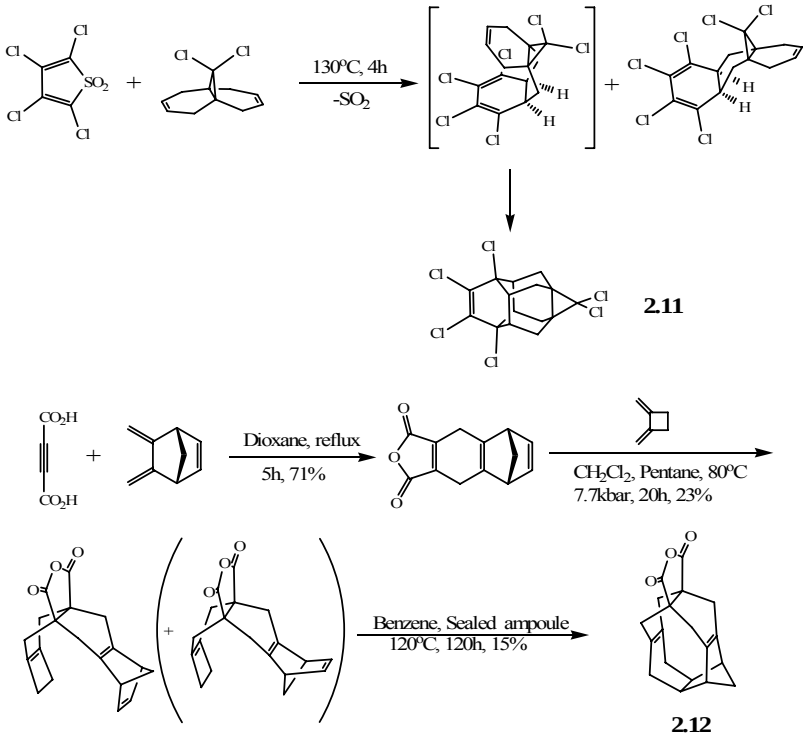
2.2.2 Syntheses of Beltenes and their related macropolycycles

Synthetically, most of the beltene derivatives were constructed by Diels-Alder reactions of rational designed dienes and dienophiles. Diels-Alder adducts were then further converted to their partially aromatized derivatives towards beltenes or cyclacenes. Other approaches such as dearomatization of specific regions of fullerenes[11-13] or metal-templated synthesis[14, 15] were also applied in some cases.

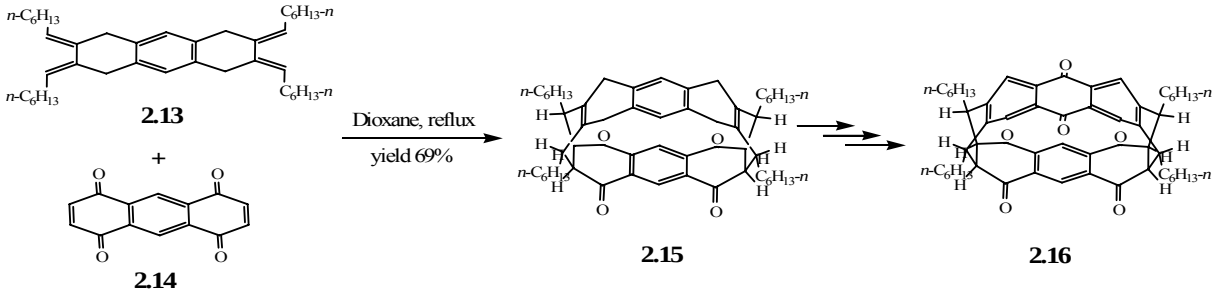
2.2.2.1 Diels-Alder approach

A sequence of Diels-Alder reactions is a powerful method to construct macropolycycles. At least two Diels-Alder reactions are required for cyclization. Adducts in the first Diels-Alder reaction are converted to an intermediate with right-oriented new diene and dienophile moieties to undergo a second intramolecular Diels-Alder reaction. In **Scheme 2.1**, the diene of a thiophene dioxide reacted with a curved bisdienophile in the first Diels-Alder reaction to form *endo*- and *exo*-monoadduct. Both adducts would undergo *in situ* reverse chelotropic reaction to furnish a new diene moiety. However, only *endo*-isomer underwent a second Diels-Alder reaction to give [3]beltene derivative **2.11** since the new formed diene was close to the other

double bond, while in *exo*-adduct two Diels-Alder components were away from each other.[16] In another example, a sequence of three Diels-Alder reactions was applied to give a [4]beltene derivative **2.12**.[17]



Scheme 2.1



Scheme 2.2

Either the intermolecular Diels-Alder reaction of a bisdiene (AA-type, A: acceptor) with a bisdienophile (BB-type, B: donor) or dimerization of an AB-type monomer can be applied to construct larger beltene derivatives. Representative works have been done in three research groups: Cory's group, Stoddart's group, and Schlueter's group.

In Cory's group, an AA-BB type intermolecular double Diels-Alder cyclization of the bisdiene **2.13** and bisquinone **2.14** was applied to construct [8]beltene derivative **2.15**. The yield

was as high as 69% in refluxing dioxane. Derivatization of Diels-Alder adduct **2.15** led to hexaone **2.16**. However, further efforts to make fully conjugated [8]beltene derivatives failed.[18, 19]

A typical example of AB type Diels-Alder cyclization was the construction of a belt-like backbone of fullerene $C_{84}(D_2)$ by Schlueter and coworkers.[20] The dimerization of an AB type curved monomer *exo*-**2.17** or *endo*-**2.17** generated *in situ* from different isomers of **2.18** in the refluxing toluene gave the same cyclized dimer **2.19** in a yield of 45% and 25% respectively. The difference of yields could be rationalized by comparing the different orientation of monomers during cyclization. For the *endo*-**2.17**, cyclization underwent two sequential Diels-Alder reactions of the diene and dienophile moieties in *exo*-orientation. While in case of *exo*-**2.17**, two sequential Diels-Alder reactions are through *endo*-pathway, which is energetically more favorable.

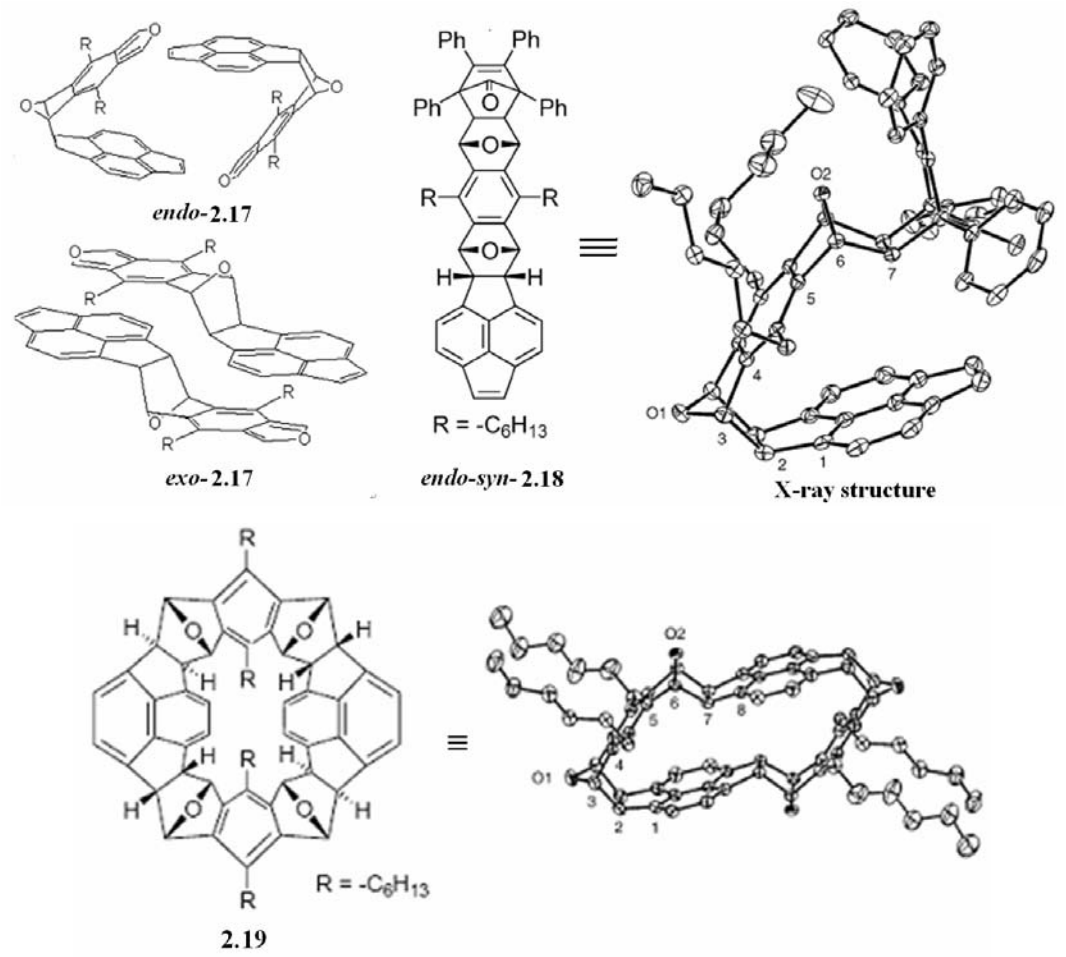
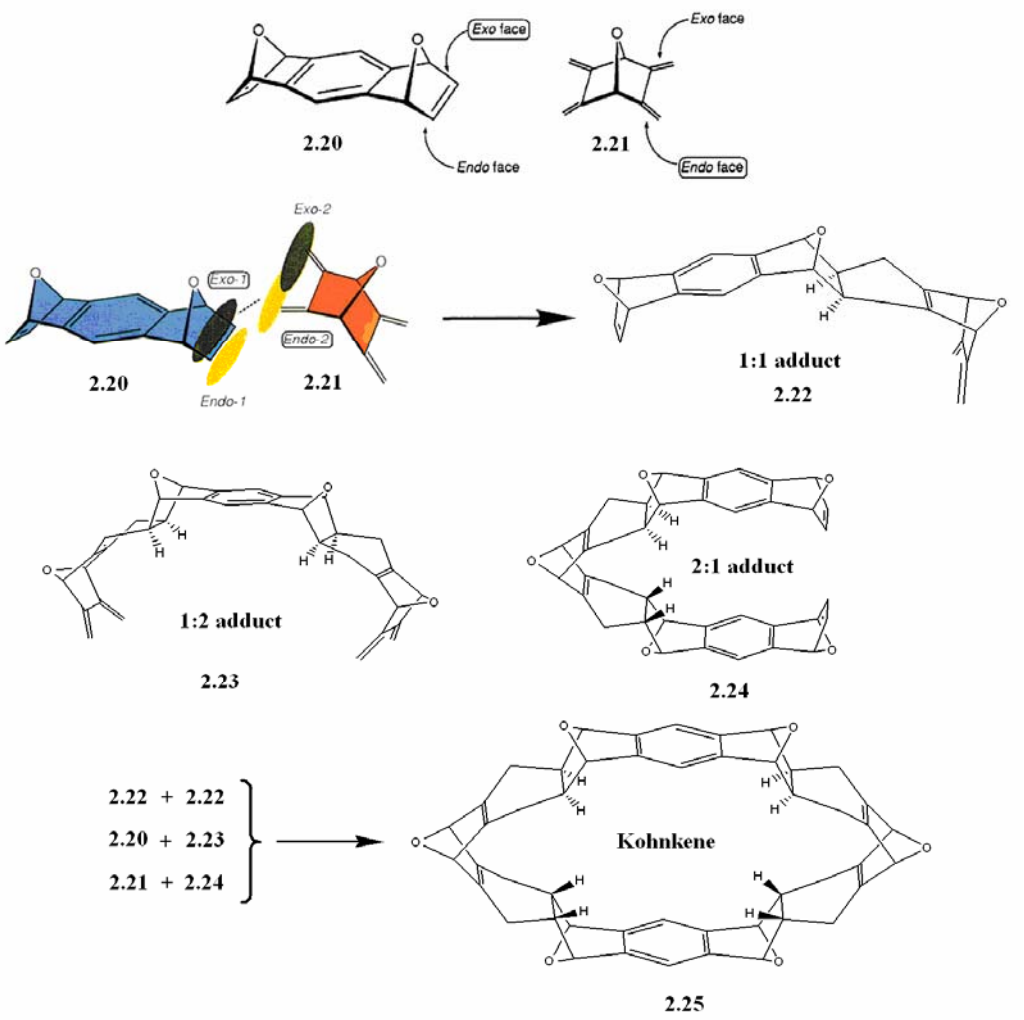


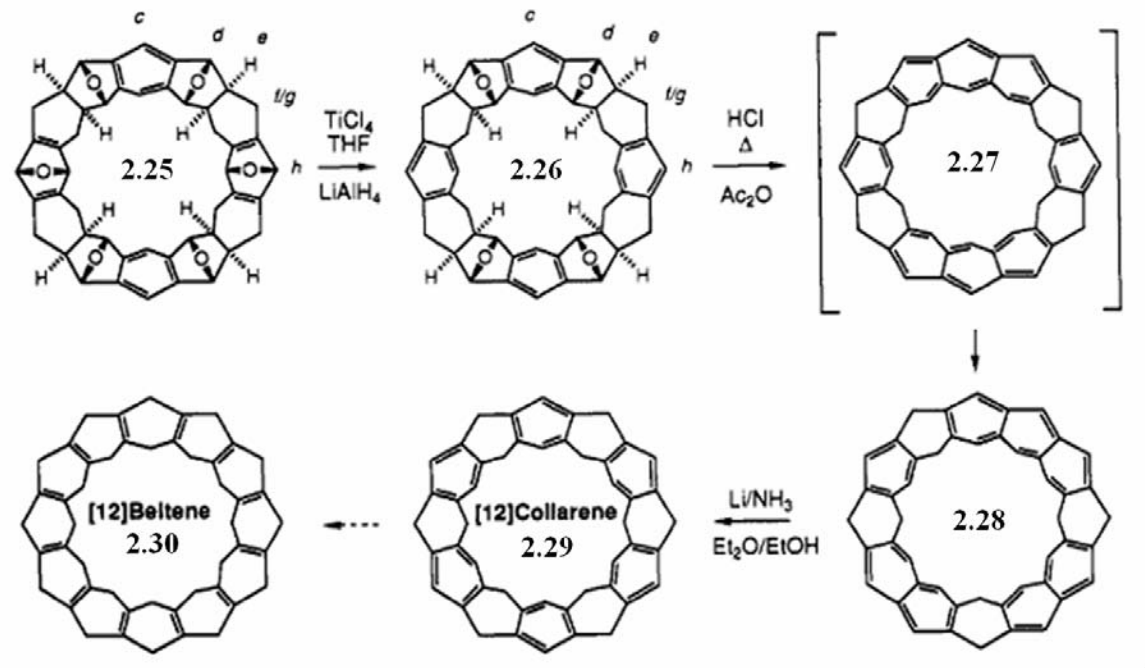
Figure 2.4

Stoddart's synthesis of Kohnkene gave another elegant example of how controlled and predictable Diels-Alder reactions were used to construct a macropolycyclic ring. The bisdienenophile **2.20** and bisdiene **2.21** showed high face selectivity. Their high selectivity is related to the relative electron densities of two faces inherent in their rigid structures.[21] Cycloaddition of **2.20** favors the *exo*-face with higher electron density. While in bisdiene **2.21**, cycloaddition prefers from the *endo*-face with lower electron density. If both faces of diene and dienophile are considered, only one major 1:1 adduct **2.22** is formed out of four possible isomers. Similarly, by changing the ratio of starting materials, 1:2 adduct **2.23** or 2:1 adduct **2.24** would be obtained as the major product. The iterative DA reactions from different combination of intermediates in the same way finally gave the Kohnkene **2.25.**



Scheme 2.3 Construction of Kohnkene utilizing face-selectivity of dienophile **2.20** and diene **2.21**

The transformation of Kohnkene **2.25** towards fully conjugated cyclacene and beltene through a sequence of reductive aromatization, dehydration, and reduction was stopped at [12]collarene **2.29** (**Scheme 2.4**).[21]

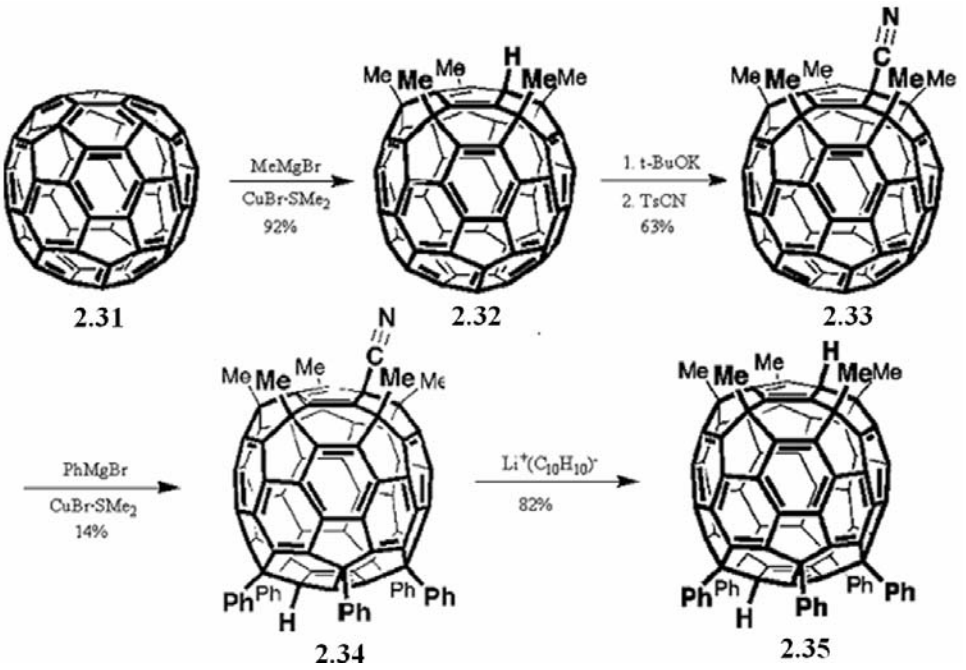


Scheme 2.4 Transformation of Kohnkene **2.25** towards [12]beltene **2.30**.[21] (Taken from reference [21] without permission)

2.2.2.2 Dearomatization of fullerene C_{60}, a substructure-directed synthesis of [10]cyclophenacene derivatives

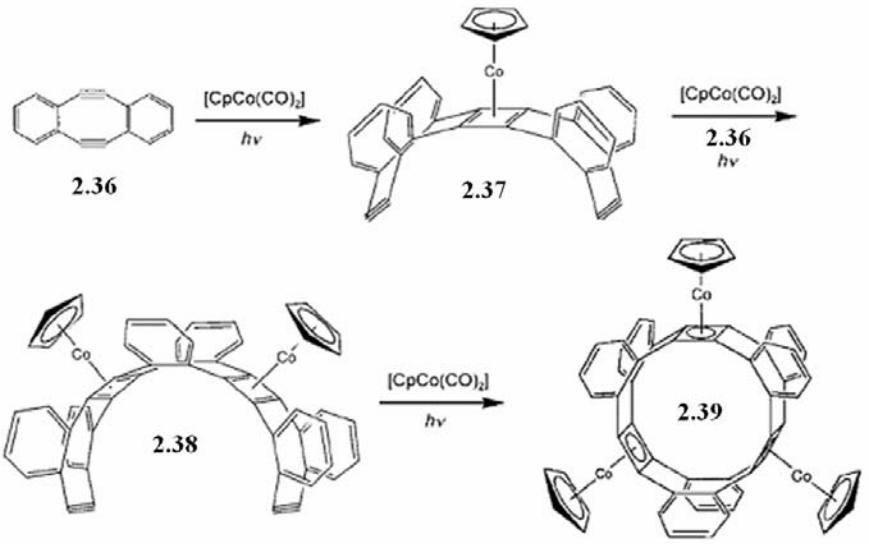
In Nakamura group, several fully conjugated [10]cyclophenacene derivatives have been recently synthesized by dearomatizing specific regions of C_{60}, e.g. the north pole and south pole.[11-13] When an organocopper reagent was used, fullerene C_{60}, a 60 π conjugated system, was successfully converted to 50π system **2.32**. After protection of an acidic proton, a second organocopper addition reaction was applied to transfer **2.32** to a 40 π system **2.33**. Then after deprotection, a hydrocarbon derivative of [10]cyclo-phenacene **2.35** was synthesized (**Scheme 2.5**).[11] Further structure modification led to a double-decker buckyferrocenes, in which 5-membered ring in north pole and south pole were complexed with iron(II), while the cyclophenacene equator remained intact.[13] Since [10]cyclophenacene is a substructure of C_{60},

this approach is a "substructrue-directed synthesis" corresponding to a 'substrate-directed synthesis"of Kohnkene named by Stoddart.[21]



Scheme 2.5 Synthesis of a [10]cyclophenacene from C_{60}. (Taken from reference [11] without permission)

2.2.2.3 Metal templated approach



Scheme 2.6 Synthesis of a CpCo-complexed conjugated beltene.[14] (Taken from reference [14] without permission)

Very recently, a new structure of fully conjugated beltenes has been synthesized by Gleiter and coworkers.[14] The rigid cyclic diyne **2.36,** when irradiated with 254 nm UV light, underwent trimerization in the presence of $CpCo(CO)_2$ with a yield of 14%. The mechanism may be a first step dimerization of **2.36** giving a curved intermediate **2.37.** When the third molecule of **2.36** was added to **2.37**, the newly formed CpCo group was installed on the *exo*-face because of steric hindrance of the *endo*-face. So the open-chain trimer **2.38** has more curved structure to allow two ends close enough for cyclization. Increasing the size of CpCo group by substitution on the Cp ring gave improved yields of cyclization up to 41%.[14]

2.2.3 Potential applications of Beltenes and their related macropolycycles

Beltenes and related macropolycyclic compounds contain unique belt-shaped topology. Their bent surface provides interesting system to study bending π orbitals.[22] Moreover, the inner cavity with regularly oriented π orbitals in a circular pattern makes them new attracting hosts or receptors.[23, 24] They also may be potential precursors for rational syntheses of carbon nanotubes or fullerenes.[10]

2.2.3.1 Interesting systems for study behavior of bent p-orbitals.

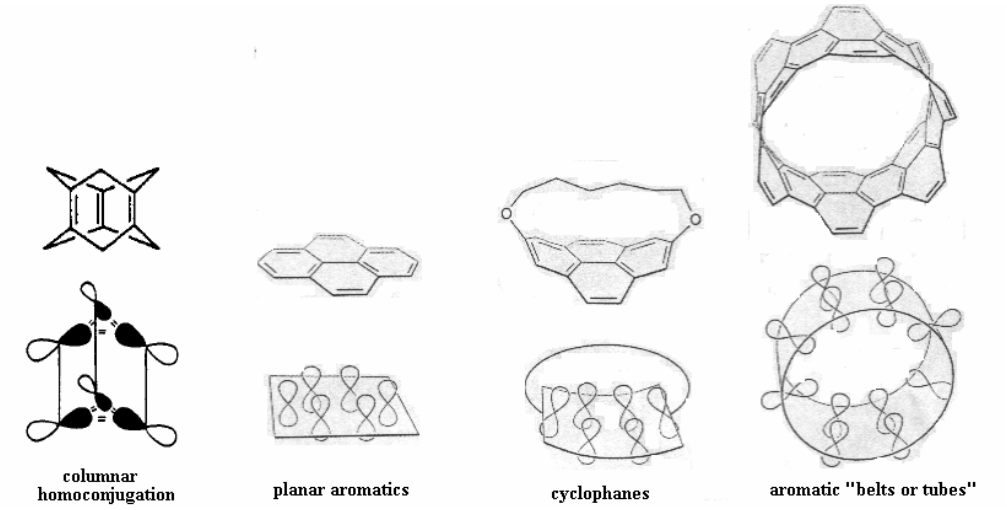


Figure 2.5 Conjugation in curved versus planar surfaces (Taken from reference [10] without permission)

One distinguished structural feature of beltenes and related macropolycycles is that they contain *p* orbitals perpendicular to a curved surface, where conjugation and strain effect counteract with each other. Conjugation effect causes the molecule to adapt plane configuration

for maximum overlaps of orbitals, while the strain inherent in the molecule lowers the degree of conjugation by reducing overlaps. The interaction between the two effects varies from system to system. A study on a series of [n](2,7)pyrenophanes (**Figure 2.6**, the left structure) with a distorted pyrene ring showed that only a small amount of conjugation energy was lost over a wide range of bend.[25] However, in a "picotube" molecule, strain greatly changes conjugation pattern. Although it may be looked upon as four anthracenes connected by single bonds, it is best described as double-bond-joined 1,4-cyclohexadiene.[26] Thus, it would be interesting to study interaction between the two effects in [n]cyclacene for their tunable strain with different numbers of n. For beltene systems, double bonds are separated from each other and no normal conjugation is present, but columnar homoconjugation by through-space interactions of π–orbitals may apply to beltenes.

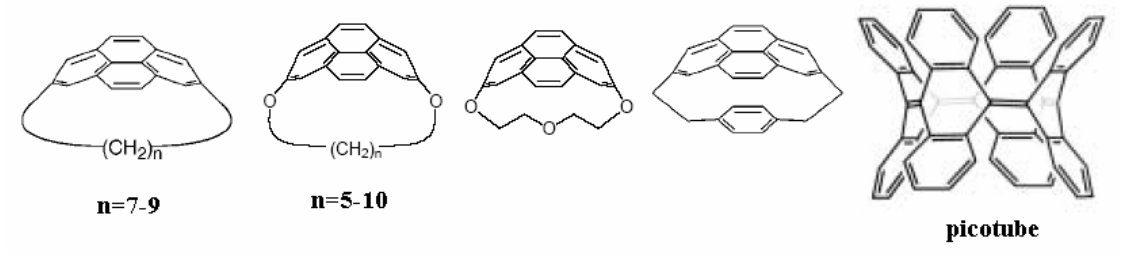


Figure 2.6 A series of [n](2,7)pyrenophanes with distorted pyrene ring synthesized by Bodwell and coworkers[25, 27-29] and a picotube synthesized by Herges and coworkers.[26]

2.2.3.2 Host-guest chemistry of beltenes.

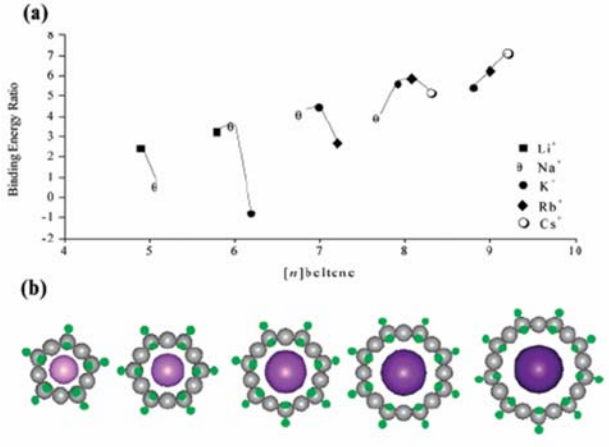


Figure 2.7 a) Binding energy ratios of various [n]beltene-cation complexes. b) Various cations captured by [n]beltenes (Li^+, Na^+, K^+, Rb^+, and Cs^+ are captured by [5], [6], [7], [8], and [9]beltene, respectively)[24] (Taken from reference [24] without permission)

When beltene structures were first proposed by Alder and Session,[9] they were referred to as a potential cavity-based host. Based on MM2 calculation, [9]beltene is a good host for acetylene. Other molecules may be also combined specifically in the cavity by suitable derivatization of beltenes.[9] Since the exact structure of beltene has not been synthesized, the only way to study their potential property is by theoretical calculation.

Recently, theoretical works done by Choi showed collarenes[24] and beltenes[38] may be good ionphores based on cation-π interaction. Beltenes have finer ion selectivity than collarenes.[38] (**Figure 2.7**) From the calculated ion binding energy, it was shown that [5]beltene is specificly combined to Li^+, [6]beltene to Na^+, [7]beltene to K^+, [8]beltene to Rb^+, and [9]beltene to Cs^+.

2.2.3.3 As potential precursors for carbon nanotubes or fullerenes.

Carbon nanotubes and fullerenes, since their discovery in the early 1990's,[30-32] have been an active research area, mainly due to their remarkable physical properties as new materials and molecular electronic devices. However, current arc-discharge methods or similar methods can not control the synthesis of these new carbon allotropies and greatly limit their application.[33] The rational synthesis of carbon nanotubes and fullerenes from smaller organic ring- or belt-like motifs may provide the alternative route to them.[10] Pioneering work on the rational synthesis of C_{60} from polyarene has been achieved despite low yields.[34, 35] Although synthesis of carbon nanotubes from beltenes and related macropolycylces has not been realized yet, it is likely to be achieved in future since many other tube-like structures have been assembled from belt-shaped macrocycles.[7]

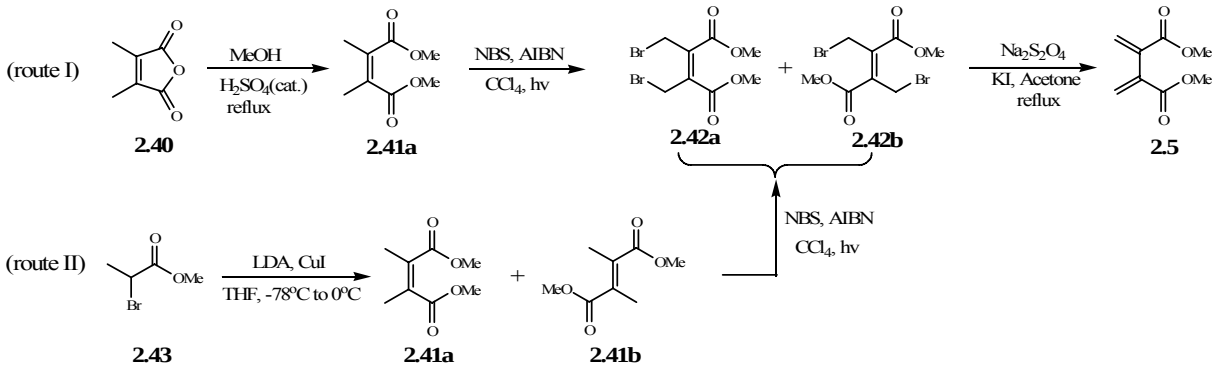
2.3 Synthetic studies towards a macropolycyclic [10]beltene derivative

2.3.1 Previous work in our lab

2.3.1.1 Synthesis of diene component dimethyl 1,3-butadiene-2,3-dicarboxylate (2.5).

Dimethyl 1,3-butadiene-2,3-dicarboxylate (**2.5**) was used as a potential bisdiene components for synthesis of [10]beltene derivative **2.4**. Two ester groups would later be transformed to a diene component for another Diels-Alder reaction. It was synthesized in three steps either from commercially available 2,3-dimethylmaleic acid anhydride (**2.40**) or methyl 2-

bromopropionate (**2.43**)[3] as shown in **Scheme 2.7**. In route I,[2] the acid anhydride **2.40** was first methylated in refluxing methanol with a catalytic amount of sulfuric acid to afford quantitative yield of 2,3-dimethylbutenedioic acid dimethyl ester **2.41a**. A subsequent photo induced radical bromination using azo-bis isobutyronitrile (AIBN) as radical initiator and N-bromosuccinimide (NBS) in tetrachloro methane would afford a mixture of *cis-/trans-* dibromide **2.42a** and **2.42b** in a yield of 90%. Then the mixture of dibromide underwent reductive elimination with potassium iodide and sodium thiosulfate in refluxing acetone to give diene **2.5** in 83% yield. Route II was only different in the first step of making dimethyl ester.[3] The two isomers of diester **2.41a** and **2.41b** instead of one isomer in route I, was synthesized in 96% yield by copper mediated ester couplings with lithium diisopropylamide(LDA) in THF. The mixture of two diesters was then used for the bromidation and elimination to form diene **2.5**. Route II was better for large scale synthesis since the starting material **2.40** used in route I is expensive.

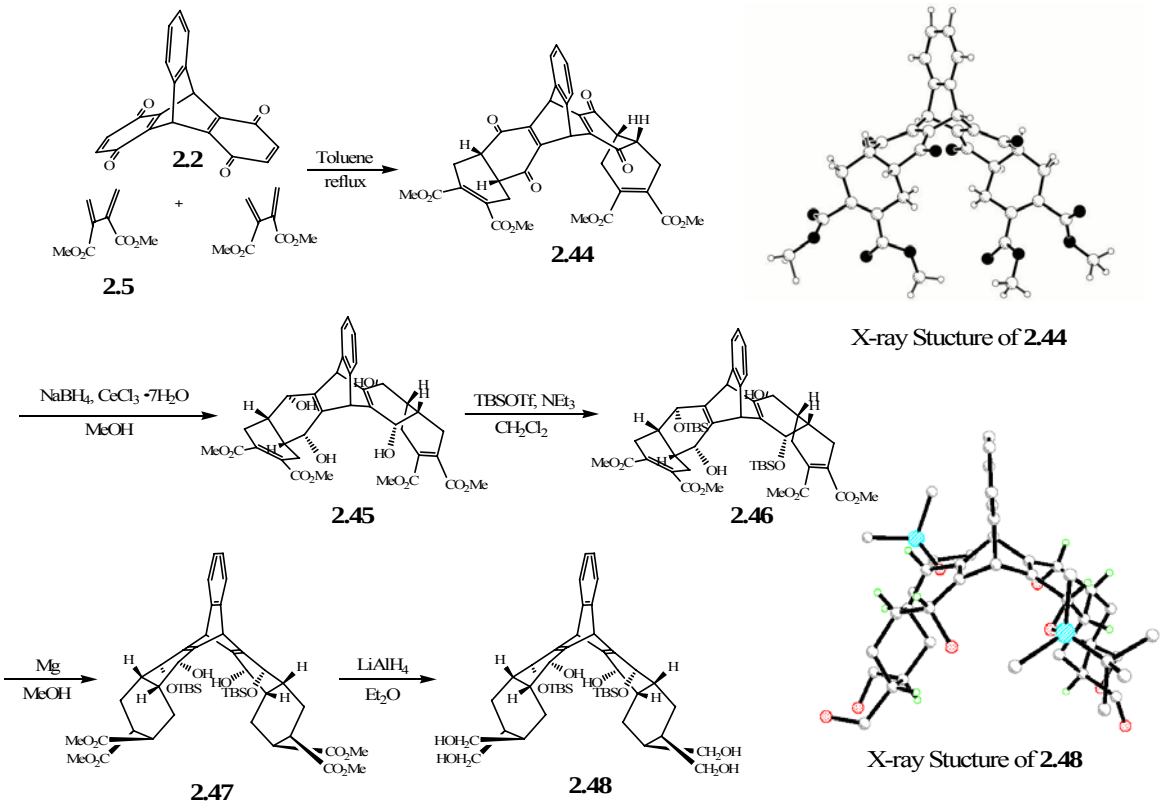


Scheme 2.7 Synthesis of 1,3-butadiene-2,3-dicarboxylate (**2.5)**

2.3.1.2 Synthesis of tetraol (2.48).

Synthesis of tetraol (**2.48**) was first accomplished by Xiaodong Huang in our lab starting from Diels-Alder reaction of triptycene bisquinone **(2.2)** and diene **2.5**.[2] The synthesis of triptycene bisquinone would be discussed later in **Chapter 3**. The Diels-Alder reaction with excess amount of diene **2.5** surprisingly gave only one diadduct in a yield of 87%, which was ascribed to a combination of steric effects and secondary orbital interactions (Reference[3], Page 92). The explanation was not satisfactory, since the quinone ring is sterically not much difference compared with benzene ring. Besides, after the first equivalent of diene was added to triptycene bisquinone **2.2**, there would certainly be an increase in the steric hindrance of *endo*-face and reduce face-selectivity of a second diene molecule. How could the face-selectivity of

the second Diels-Alder reaction remain the same? The so-called through-bond homoconjugation between two quinone rings may be the predominant reason (**Figure 3.7**). The *p*-orbitals of quinone rings on the *endo*-side of triptycene bisquinone **2.2** have more overlap than those on the *exo*-side. In other words, the two quinone rings are somehow "conjugated" in a curved surface with concave *endo*-face having more conjugation than convex *exo*-face. Since a quinone moiety is an electron withdrawing group, the *endo*-face is more electron-deficient than *exo*-face, thus a better dienophile. The structure of **2.44** was proved by X-ray crystallography.



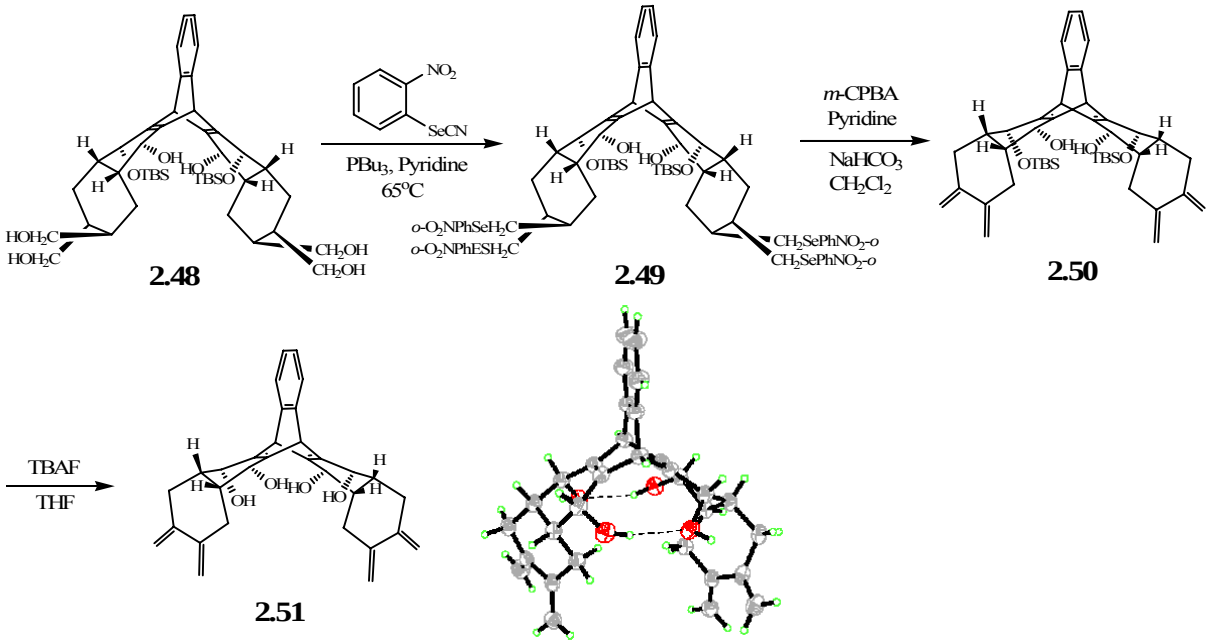
Scheme 2.8 Synthesis of tetraol **2.48**

The next step was reducing ketones in Diels-Alder adducts **2.44** to tetraol **2.45** in 81% yield by treating with sodium borohydride and cerium chloride in methanol at 0°C. The hydride was added from less hindered *exo*-face. The hydroxyl groups in **2.45** had to be protected for further reduction of ester function group. Only two diagonal hydroxyl groups can be protected by bulky *t*-butyldimethylsilyl (TBDMS) group due to the crowd conclave face. The protected product **2.45** was isolated in 70% yield using TBDMSOTf as silylation reagent and triethyl amine as base in methylene chloride at 0°C. After protection, two consecutive reductions by magnesium in methanol and lithium aluminum hydride in THF finally gave the tetrol **2.48** in

78% yield of two steps. The structure of **2.48** was verified by X-ray crystallography. Interestingly, all the hydroxymethyl groups are pointing to the *exo*-face.

2.3.1.3 Formation of tetraene (2.51)

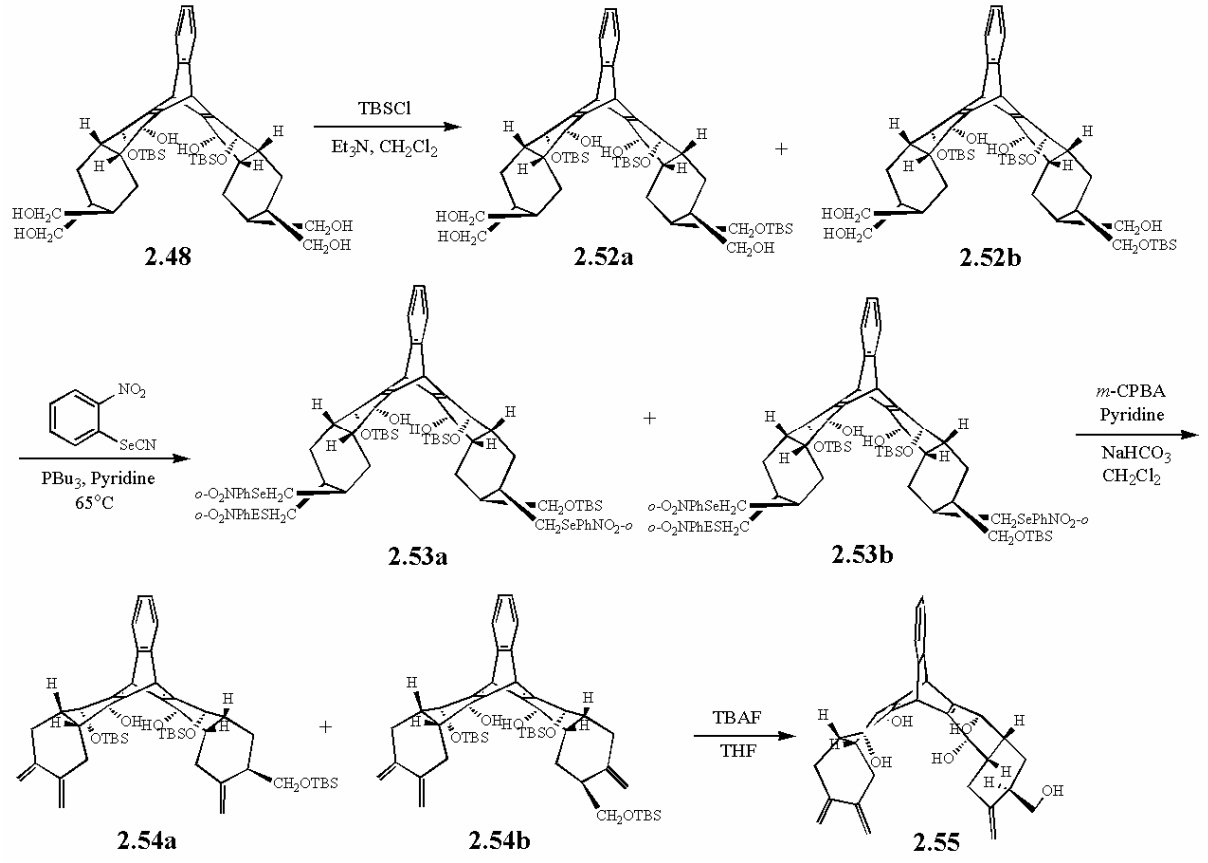
Synthesis of tetraene (**2.51**) was accomplished by Neil Brown, who continued on the beltene project starting from the tetraol **2.48**.[3] The previous study by Xiaodong found that the conversion of tetraol **2.48** either to tetrabromide and tetratosylate failed to give tetraene **2.50** due to terminal furan ring formation.[2] Neil found that treatment of tetraol **2.51** with *o*-nitrophenylselenocyanate and tri-*n*-butyl phosphine in anhydrous pyridine at 65°C for 3 hours would afford the tetraselenide **2.49** in almost quantitative yield.(reference[3], page 99) However, the yield of selenization varied from batch to batch depending largely on condition of solvent and reagents. Then tetraselenide **2.49** was oxidized by *m*-chloroperoxybenzoic acid (mCPBA) to tetraselenoxide, which underwent elimination *in situ* to form tetraene **2.50** in a yield of 65%. Since the bulky *t*-butyldimethylsilyl (TBS) group may prevent final cyclization, it was removed by tetra-*n*-butyl ammonium fluoride (TBAF) to afford the tetraene **2.51** in 63% yield. The crystal structure was later proved by X-ray when I took over the project.



Scheme 2.9 Synthesis of tetraene **2.51**

2.3.1.4 Preliminary Diels-Alder reaction studies

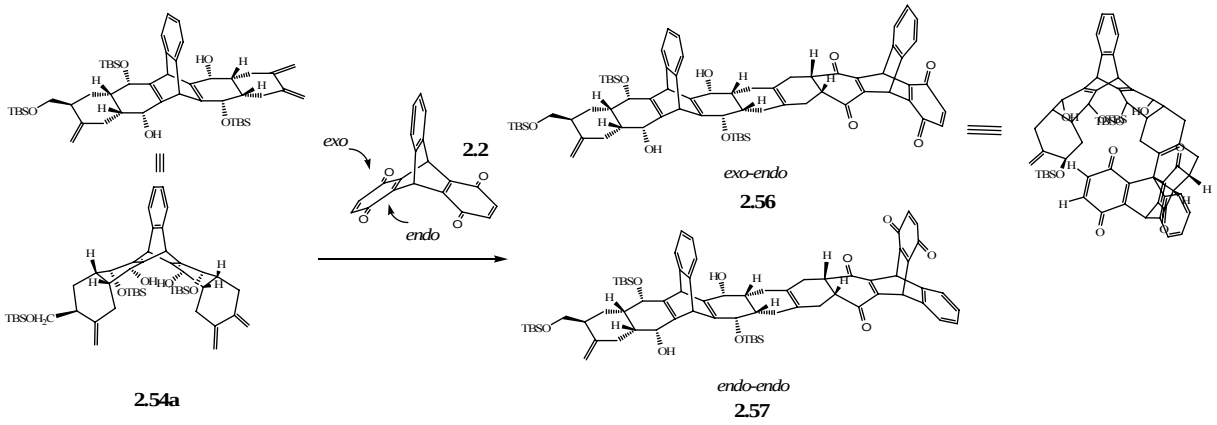
After the synthesis of tetraene **2.50** and **2.51**, Neil Brown explored the Diels-Alder reaction of them. The preliminary results showed there were mainly two problems associated with the Diels-Alder reaction in order to get cyclized Diels-Alder adduct. One was the competition of polymerization and intramolecular cyclization when tetraene (**2.50** or **2.51**) and triptycenebisquinone (**2.2**) were used in DA reaction, since NMR data of crude Diels-Alder reaction mixture showed unidentified broad peaks which indicated possible formation of oligomers or polymers. This problem could be solved by a stepwise strategy through a triene **2.55**, in which only one end can react with dienophile. Then the 1:1 adducts from Diels-Alder reaction were separated and further functional transformation was applied to convert the other end to diene. This detour would afford 1:1 adducts of tetraene with dienophile for further cyclization under high dilution condition (**Scheme 2.12**).



Scheme 2.10 Synthesis of triene **2.55**

The synthesis towards triene **2.55** was carried out by Neil Brown up to one isomer of **2.54**. First protection of one hydroxyl group on **2.48** gave a mixture of two possible triols **2.52a** and

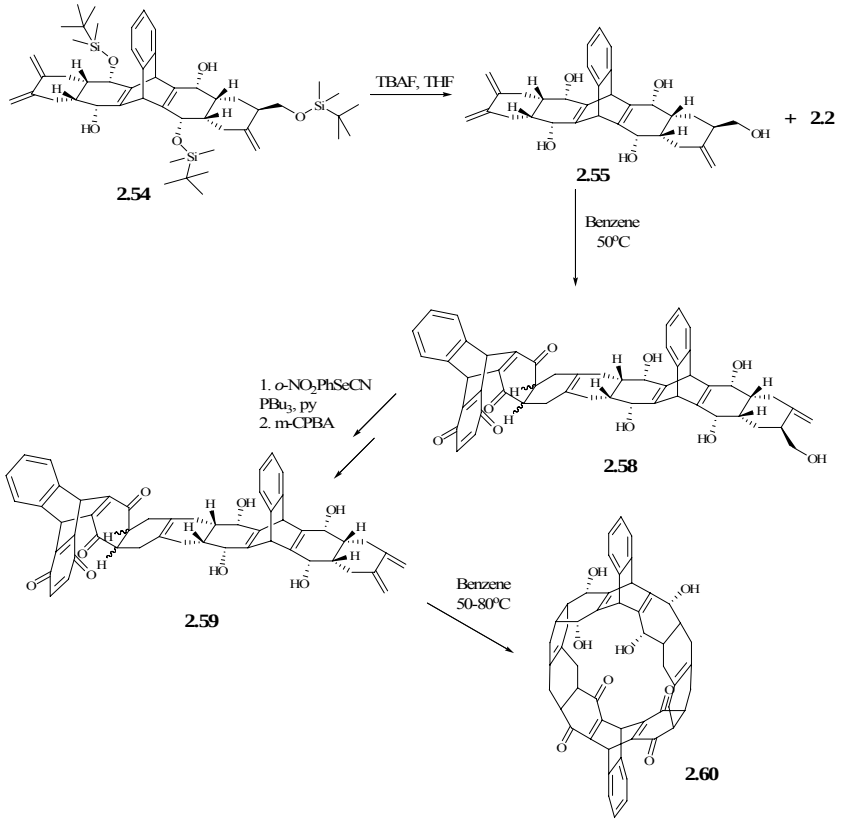
2.53b in 26% yield together with over-protected diols and unreacted starting material **2.48**. Then, selenization of triol **2.52** in similar conditions as that of tetraol **2.48** gave a mixture of two isomer **2.53a** and **2.53b** in 62% yield, which was partially separable in column chromatography. The less polar spot is likely **2.53b** due to the relative upshift of side-TBS group in ^{1}HNMR. (In Neil's thesis, the assignment of structure **2.53a** and **2.53b** to their NMR spectra may not be correct.) Further oxidation of a mixture of **2.53a** and **2.53b** afforded a mixture of **2.54a** and **2.54b** in a yield of 61% according to Neil's thesis (reference,[3] page 109). However, as was later found out, only the less polar isomer of **2.54** was actually separated by Neil Brown. The impurities inside the sample gave over-estimated yield. That might be the reason he thought there were two isomers inside it. Based on ^{1}H NMR, the less polar isomer is most likely **2.54a** and the more polar isomer is **2.54b** since the side TBS group is more congested in **2.54a** so that more Si-Me peaks are found in ^{1}HNMR spectrum due to rotation restriction. The Diels-Alder reaction of the more polar isomer of **2.54** with triptycene bisquinone **2.2** did give 1:1 monoadducts, which was verified by both NMR and MS spectroscopy (reference,[3] page 109). Since Diels-Alder reaction of dienophile triptycene bisquinone is *endo*-face selective while triene **2.55** is likely not, the observed two adducts were most likely *exo-endo*-adduct (**2.56**) and *endo-endo*-adduct (**2.57**).



Scheme 2.11 Possible adducts of triene **2.54a** and triptycene bisquinone **2.2**

Based on above preliminary data, Neil proposed a synthetic route to cyclized adduct **2.60** (**Scheme 2.12**). The 1:1 adducts **2.58** would follow a sequence of selenization, oxidation, and elimination to generate the other diene moiety for cyclization. Apparently, the quinone moiety could not stand selenization condition due to 1.4-addition of phosphine to quinone rings, which makes this route difficult to realize unless there are extra steps of protection and deprotection of quinone rings.

The other problem was the determination of steorochemsitry of Diels-Alder adducts. The successful cyclization depended on the closeness of diene and dienophile moiety. The *exo-endo* adduct **2.56** might undergo cyclization later after generation of a new diene, while *endo-endo* adduct could not because the two ends are opposite to each other. Thus the stereochemistry of Diels-Alder adducts is very important for cyclization. However, it could not be differentiated from ^{1}H NMR spectra, which made the identification of those adducts becoming a difficult issue. For example, in a model reaction, when tetraene **2.51** was reacted with an excess amount of 1,4-benzoquione, only "one" major diadduct was formed as indicated from one set of protons in ^{1}H NMR spectrum. However, we can not tell from ^{1}H NMR whether it is an *endo*-adduct and *exo*-adduct. (reference,[3] page 105) The only way to know whether the desired adduct was formed is through crystallography. A crystal needs to be prepared, which is not available in many cases.



Scheme 2.12 Proposed synthesis of cyclized adduct **2.60** (reference,[3] page 111).

2.3.1.5 Summary

After many years of continuous work, tetraene **2.51** was finally synthesized. The next job was to cyclize it with triptycene bisquinone or another dienophile to make cyclized beltene

derivatives. The major challenges included undetermined structures of Diels-Alder adducts, unfavorable oligomerization, and uncertain cyclization prospects.

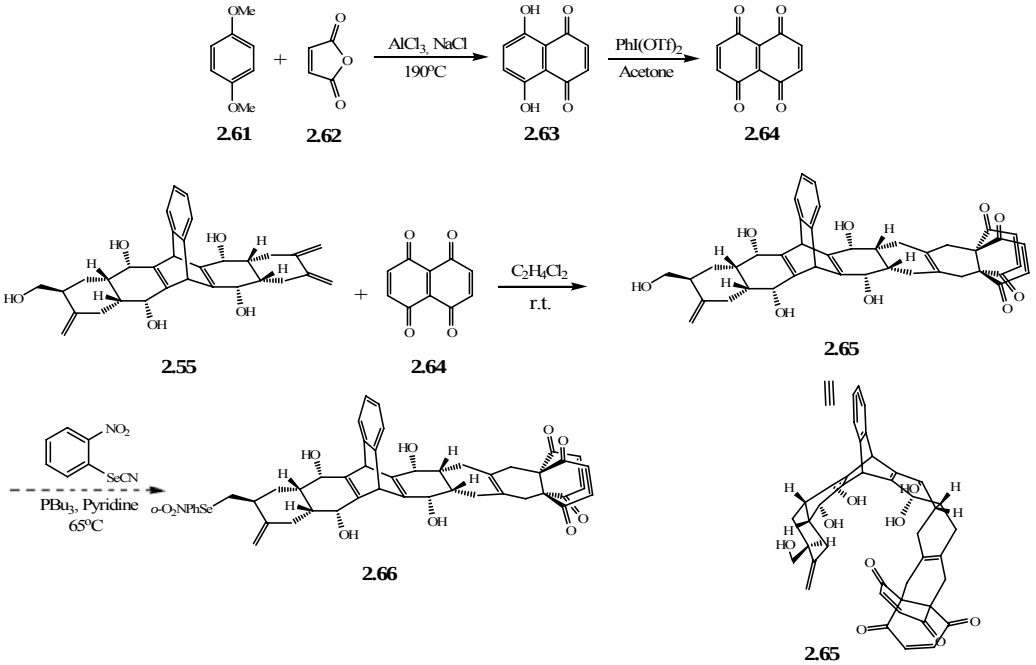
2.3.2 Continuous work towards a macropolycyclic [10]beltene derivative

2.3.2.1 Unsuccessful installation of diene and dienophile in one molecule through triene **2.55**

In previous work, a triene **2.55** was designed to achieve the installation of both diene and dienophile moiety in the same molecule. I started working on this project by following the route proposed in **Scheme 2.12**.

The deprotection of TBDMS group was easily achieved by stirring a mixture of two isomers, **2.54a** and **2.54b**, with 3.6 equivalent of TBAF in THF at room temperature for 3 hours. The deprotected pentiol-triene **2.55** was obtained in 86% yield

The attempted Diels-Alder reaction of deprotected triene **2.55** with triptycene bisquinone **2.2** in refluxing 1,2-dichloroethane gave mainly unidentified polymer-like products together with 1,4-anthracenedione and recovered starting material **2.2**, which indicated decomposition or polymerization might happen under reaction conditions. A more reactive dienophile is needed to be found to react with triene **2.55** which took painfully nine steps to make from triptycene bisquinone **2.2**.



Scheme 2.13

Since both triptycene bisquinone **2.2** and triene **2.55** have unsymmetrical *exo/endo*-faces, problems arouse in identification and separation of different adducts. We resorted to symmetric planar bisquinone **2.64**. In this case, the double-activited inner double bond reacts first with diene moiety and particular symmetry gave only one adduct even the diene moiety has two different faces. Also, the Diels-Alder reaction of **2.64** can happen at a much lower temperature because of its double-activitied nature.

The 1,4,5,8-naphthodiquinone(NDQ) **2.64** was synthesized according to literature procedure.[36] 1.4-dimethoxybenzene was heated with **2.62** in melting salts $AlCl_3$ and NaCl at 190 ^oC to afford 5,8-dihydroxynaphthalene-1,4-dione **2.63** in 20% yield, which was further oxidized by ditrifluoroacetyl-iodobenzene to give NDQ **2.64** in 66% yield.

Diels-Alder reaction of triene **2.55** and bisquinone **2.64** happened at room temperature in 1,2-dichloroethane to give Diels-Alder adduct **2.65** in 82% yield. So far, we have bypassed the face-selectivity problem to afford only one adduct. However, the attempted selenization of **2.65** failed to give expected monoselenide **2.66** for later elimination and generation a new diene moiety. The possible reason might be the incompatibility of cyclohex-2-ene-1,4-dione moiety in the reaction conditions. The synthetic route towards a possible cyclization precursor through triene **2.55** was finally abandoned.

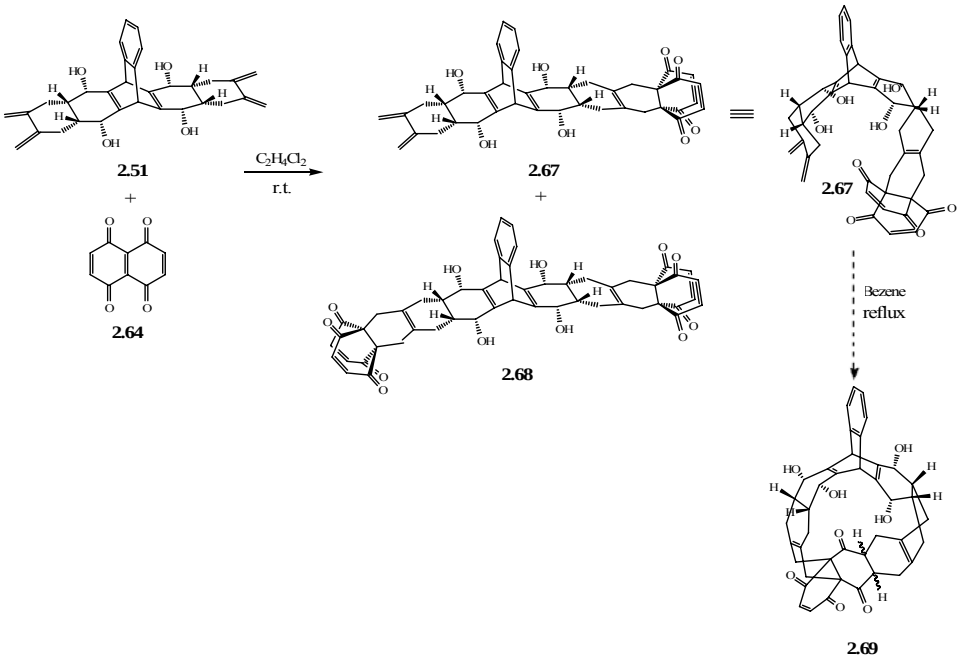
2.3.2.2 Successful installation of diene and dienophile in one molecule with failed cyclization

The successful synthesis of Diels-Alder adduct **2.65** made us believe that in similar conditions, tetraene **2.51** should form similar monoadduct **2.67** with double activated bisquinone **2.64** by carefully controlling the ratio of starting materials.

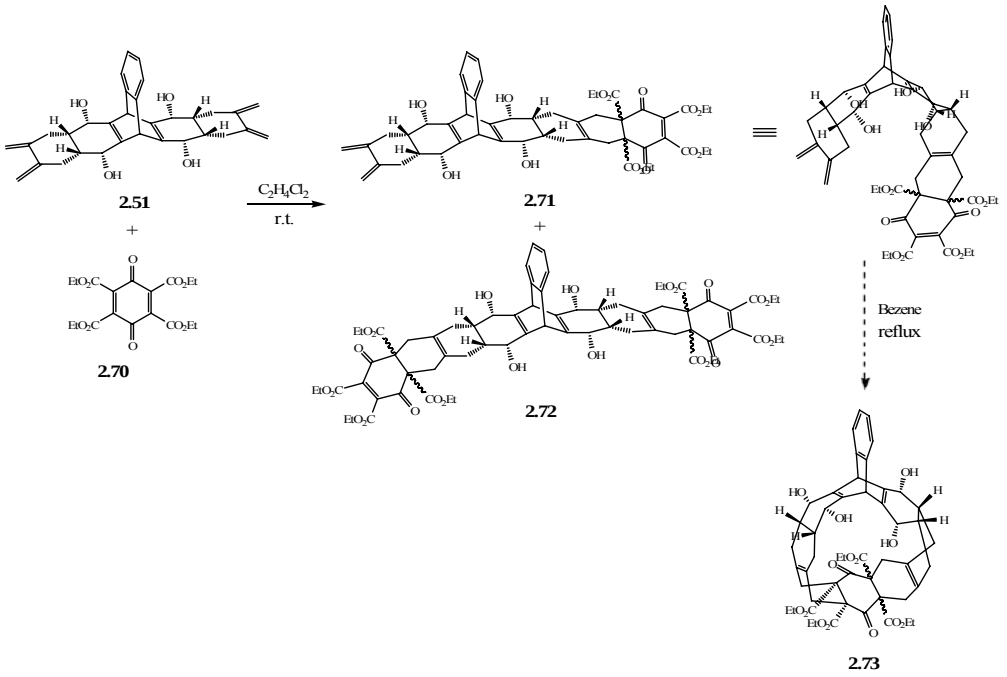
When the tetraene **2.51** was stirred with 0.6 equivalent of the bisquinone **2.64** in 1,2-dichloroethane, monoadduct **2.67** was obtained in 33% yield together with diadduct **2.68** and recovered tetraene. The monoadduct has diene moiety at one end and cyclohex-2-ene-1,4-dione moiety at the other end as the dienophile. The intramolecular cyclization would be expected to happen when heated in a high dilution condition at raised temperature.

However, when a solution of 0.001M of **2.67** was heated in refluxing benzene, no identifiable cyclized product **2.69** was separated. Even if the cyclization happened, the yield was too small to identify. One possible reason might be the dienophile in the **2.67** was not reactive enough for cyclization in low temperature, while raised temperature caused polymerization.

We then resorted to a double-activated quinone **2.70**. The quinone **2.70** contains two double-activated Diels-Alder reaction sites. The monoadduct **2.7**1 would expect to have a much more active dienophile moiety for intramolecular Diels-Alder cyclization even at room temperature (**Scheme 2.15**).



Scheme 2.14

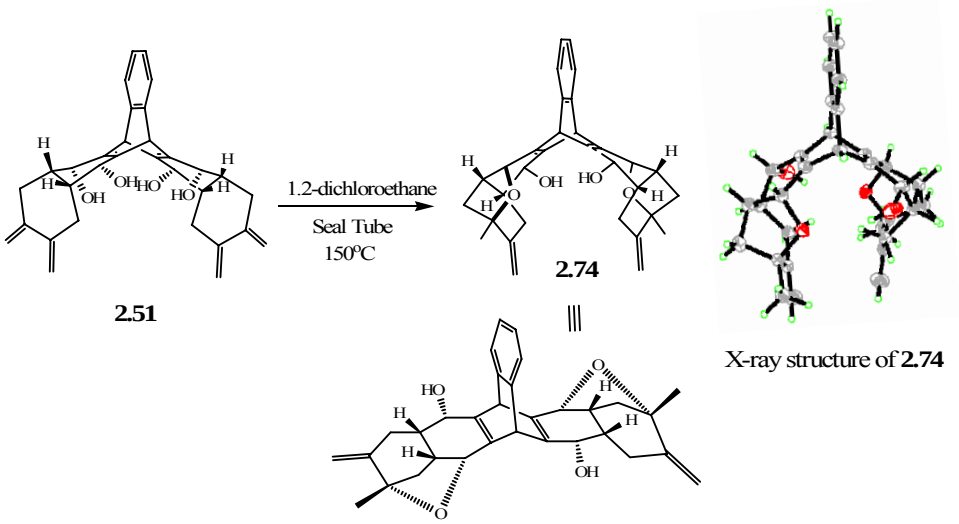


Scheme 2.15

However, only monoadduct **2.71** and diadduct **2.72** were separated when tetraene **2.51** and dienophile **2.70** was stirred in 1,2-dichloroethane at room temperature. No cyclized product **2.73** was separated. From ^{1}H NMR, both **2.71** and **2.72** contain one set of peaks, which mean they most likely consisted of one compound. However, the actual *endo*- or *exo*- conformation was hard to determine. If only steric effects were considered, the less hindered *exo*-face of tetraene **2.51** was preferred in Diels-Alder reaction, so **2.71** was more likely *exo*-adduct, which could not be cyclized. When compound **2.71** was slowly heated to a higher temperature from 50 ^{o}C to 80 ^{o}C in benzene, an undetermined product was formed. The possibility of being **2.73** was excluded by MS spectrum.

2.3.2.3 Isomerization of tetraene 2.51

Frustrated by failure of cyclization by Diels-Alder reaction strategy, we started to look for other cyclization strategies. When tetraene **2.51** was heated with 1st generation Grubb catalyst in refluxing 1,2-dichloroethane overnight, a small amount of **2.74** was separated. We later found that **2.74** was one major product (61%) when tetraene **2.51** was heated in 150^{o}C alone. The structure was proved by X-ray crystallography. To our surprise, diagonal hydroxyl groups added to the nearest double bond to form furan rings.



Scheme 2.16

2.3.2.4 Summary

Although instability of tetraene **2.51** and unsuccessful cyclization by Diels-Alder reaction gave this project a dim prospect, a new chiral clip-shaped molecule **2.74** was synthesized.

2.4 Discussions and conclusion

2.4.1 Requirement for successful cyclization

Failed cyclization of tetraene **2.51** raised a question about what are important factors for successful cyclization by Diels-Alder reactions. A thorough literature research was done and a list of successful examples of AA-BB type cylization and AB type cylization are listed in **Table 2.1** and **Table 2.2**. It seems that all successful cyclization of Diels-Alder reactions were based on rigid or slightly flexible Diels-Alder components with both reacting ends parallel or nearly parallel to each other. Apparently, this would help to bring the remaining diene and dienophile close to each other after first Diels-Alder reaction. On the contrary, the two diene components in the tetraene **2.51** are twisted in an angle because of preferred chair conformation of cyclohexane rings (**Scheme 2.16**). After the first Diels-Alder reaction, the attached quinone moiety extended from one diene end are actually even more far away from the other diene moiety.

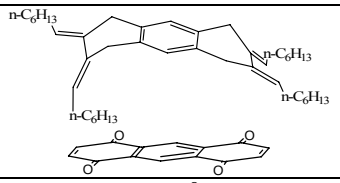
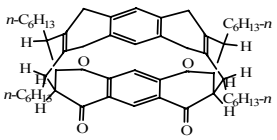
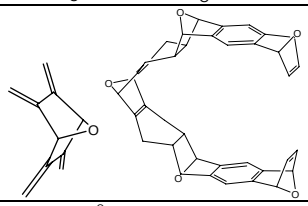
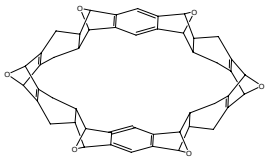
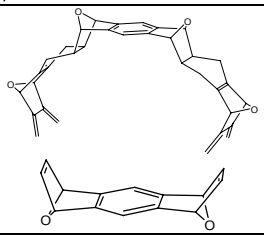
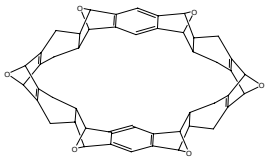
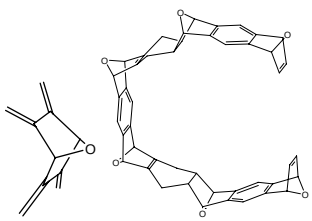
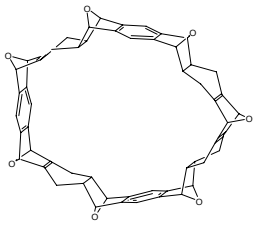
	DA precursors	Product	Reaction condition and yields
I			Dioxane, reflux, (high dilution condition) Yield: 69% [19]
II			Toluene, reflux, 7h, yield: 69%[21]
III			CH_2Cl_2, PTFE high-pressure reaction vessel, 10kbars, 200h, 55-60°C yield: 20%[21]
IV			Toluene, reflux, 12h Yield:78%[21]

Table 2.1 Successful cyclization from AA-BB type Diels-Alder reactions in literature.

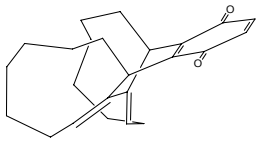
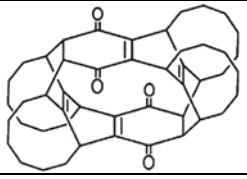
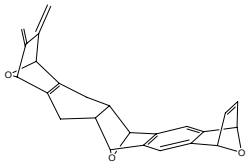
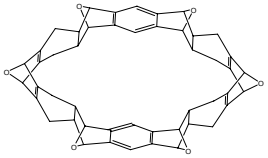
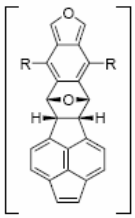
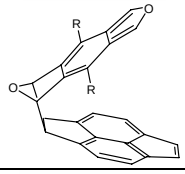
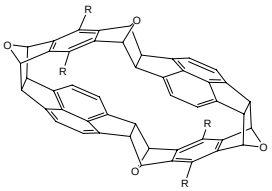
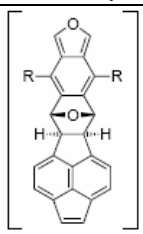
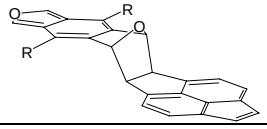
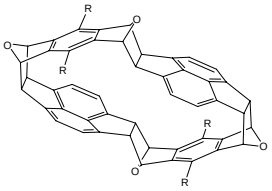
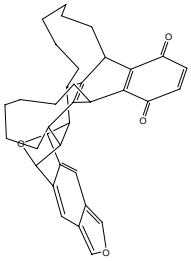
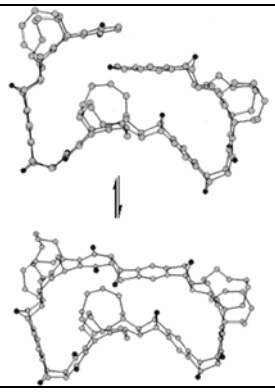
	DA precursors	Product	Reaction condition and yields
I			110°C, yield: 23% to 70% depending on the concentration[37, 38]
II			1)Xylene, reflux, 48h, yield: 3.6% 2) CH_2Cl_2, PTFE high-pressure reaction vessel, 18kbars, 72h, 50°C, yield: 48%[21]
III	 *endo* 		1) Toluene, reflux, yield:25% 2) Neat, 200°C, high-vacuum(0.02mbar), 1h *endo-syn*: no cyclization product observed. *endo-anti*: yield 10%[20]
IV	 *exo* 		1) Toluene, reflux, 2d, *exo-syn*: yield:43% 2) Neat, 200°C, high-vacuum (0.02mbar), 1h *exo-syn*: yield: 40%[20]
V			Toluene, reflux, 60h, open-chain and cyclized trimer together, yield: 6%[39]

Table 2.2 Successful cyclization from AB type Diels-Alder reactions in literature.

An MM2 molecular modeling was done for *exo-endo* adduct of triptycene bisquinone **2.2** with the tetraene **2.51** and the minimized energy conformations were shown in **Figure 2.8**. Since the calculated conformation for tetraene agreed pretty well with X-ray structure, (shown in **Scheme 2.9**) we believed structures calculated by this method are quite close to real ones. For *exo-endo* adduct **2.75** and its enolised derivative **2.76** which was once believed to have better orientation of diene moiety and quinone moiety for cyclization, the belt region is curled in a spiral fashion so that the diene moiety and quinone moiety are pointing away from each other. In order to bring two ends parallel to each other for Diels-Alder cylization, cyclohexane rings within **2.75** and **2.76** have to be all boat conformation, but this is both statistically unlikely and energetically unfavorable to occur. The conclusion drawn from molecular modeling was supported by experimental results that Diels-Alder reaction of **2.51** and **2.2** gave unidentified mixture oligmers and polymers, since monoadducts continued to react with starting materials in reaction conditions. It is also unlikely for twisted two ends of monoadduct **2.75** to undergo dimerization-cyclization for the same reason.

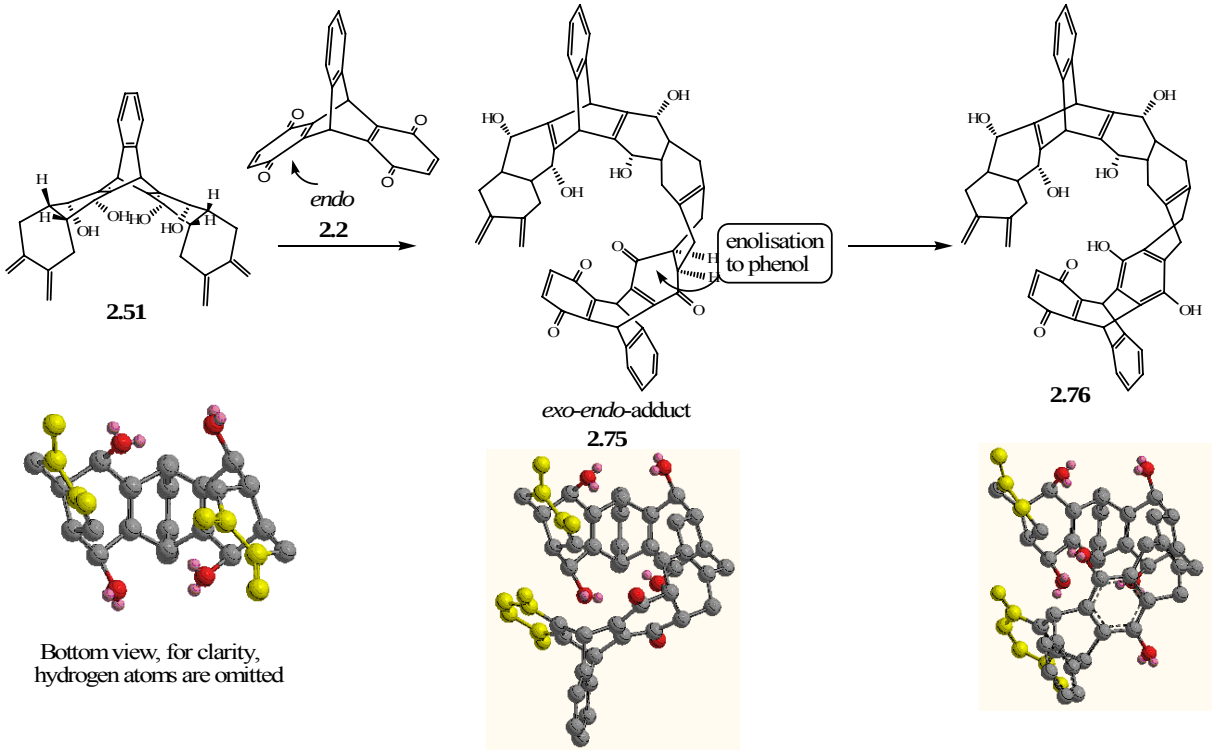


Figure 2.8 Molecular modeling (MM2) of minimized energy conformation for *exo-endo*-adduct of triptycene bisquinone (**2.2**) and tetraene **2.51**. (The two ends were colored yellow for clarity.)

Similar MM2 molecular modeling study was done for monoadduct **2.67**. Again, the molecule encounters a problem of twisted diene and quinone moiety. Besides, the concave skeleton of **2.67** is two cyclohexane rings smaller than **2.75**, which makes it less likely to bring the two ends close to each other to undergo intramolecular Diels-Alder reaction. The calculation matches with experimental findings in that the cyclized product was not detected.

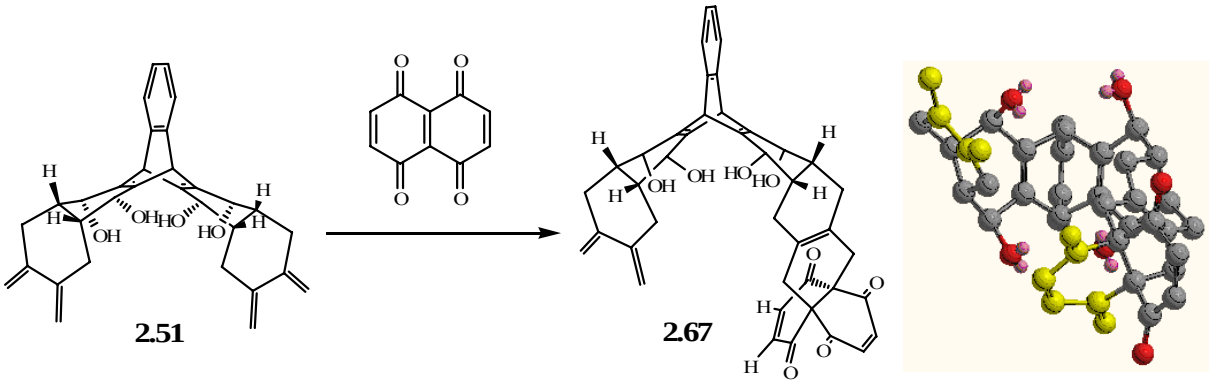


Figure 2.9 Molecular modeling (MM2) of minimized energy conformation for monoadduct **2.67**. (The two ends were colored yellow for clarity.)

In conclusion, three important requirements are learned from both unsuccessful ring closing reactions and molecular modeling analysis for the design of building blocks to construct a macropolycycle by Diels-Alder reactions. First, diene unit and/or dienophile need to parallel to each other in the building blocks. Second, it would be better for dienes and dienophiles to have right face-selectivity to minimize the number of possible Diels-Alder adducts (as in the case of Kohnkene). Otherwise, Diels-Alder adducts would be able to easily differentiate from each other (such as "inherent ^{1}HNMR structural indicators" discussed in **Chapter 3**). Third, for the final cyclization, the intramolecular diene and dienophile moieties should be close to each other and in correct alignment in space. Fulfilling the above three requirements, a functionized cyclododeciptycene was successfully synthesized in **Chapter 3**.

2.4.2 Conformation communication inside tetraene 2.51

Conformation transduction or communication has been reported and studied for tetrasubstituted *cis*-decalins and perhydroanthracenes (**Figure 2.10**).[40-44] When the conformation of one side of a molecule is changed upon a signal stimulus, conformation of the opposite side is changed accordingly. Unexpected intramoleucular furan formation of tetraene **2.51** in diagonal fashion leading to compound **2.74** led us wonder whether conformations in the two sides of

tetraene **2.51** communication with each other. In other word, one conformation in the right side would affect the conformation in the left side to adopt predominantly a specific conformation and vice versa.

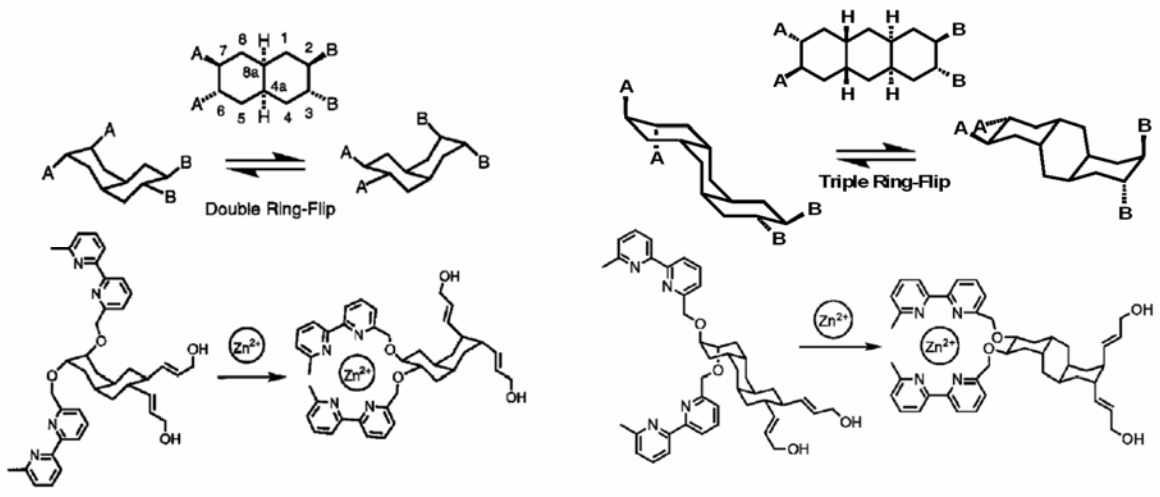


Figure 2.10 Conformation transduction of *cis*-decalin[41] and perhydroanthracene[42].

2.4.2.1 Conformation of tetraene 2.51 in crystal and solution

We first examine the X-ray structure of tetraene **2.51** shown in **Figure 2.11**. It is a low energy conformation of the molecule in crystalline form. Conformations of B, C, and D rings are shown in different views. B ring and D ring clearly adopt *pseudo*-chair conformations with a C_2 symmetry instead of C_S symmetry, which can be explained based on an assumption that a rigid *o*-benzono-bridged 1,4-cyclohexadiene (C ring) responds to ring strain from one side by slightly adjusting conformation of the other side to minimize its total strain energy. In other words, conformations of B and D ring communicate with each other via the C ring. If B ring adopts the *pseudo*-chair conformation shown in **Figure 2.11**, it causes a clockwise twist in the right side of C ring with 13a-carbon atom, a tendency of moving downwards, and 5a-carbon atom, a tendency of moving upwards, and because of rigidity of C ring, the other side of C ring adjusts its twist in opposite direction to release ring strain with 6a-carbon atom moving downwards and 12a-carbon moving upwards. D ring "feels" this movement and adjust its conformation to adopt corresponding *pseudo*-chair conformation.

Based on X-ray structure, groups in axial positions and equatorial positions should show different NMR signals. However, ^{1}H NMR spectrum of tetraene **2.51** taken at room temperature showed no splitting of diastereomeric hydrogens. A rapid conformation interconversion in

solution may have taken place, in which axial groups in one *pseudo*-chair conformation become equatorial groups and vice versa (**Figure 2.12**). During conformation interconversion of tetraene **2.51** from conformation (I) to conformation (II) or vice versa, transformations of BD rings keep communicating with each other. So when the conformation of B ring changes from one *pseudo*-chair conformation to the other, the conformation of D ring changes accordingly.

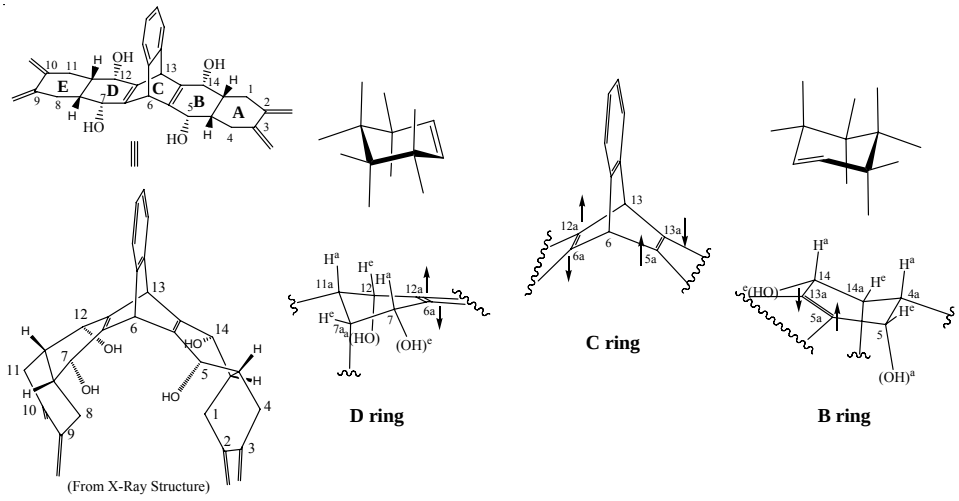


Figure 2.11 BCD ring conformations in X-ray structure of tetraene **2.51**.

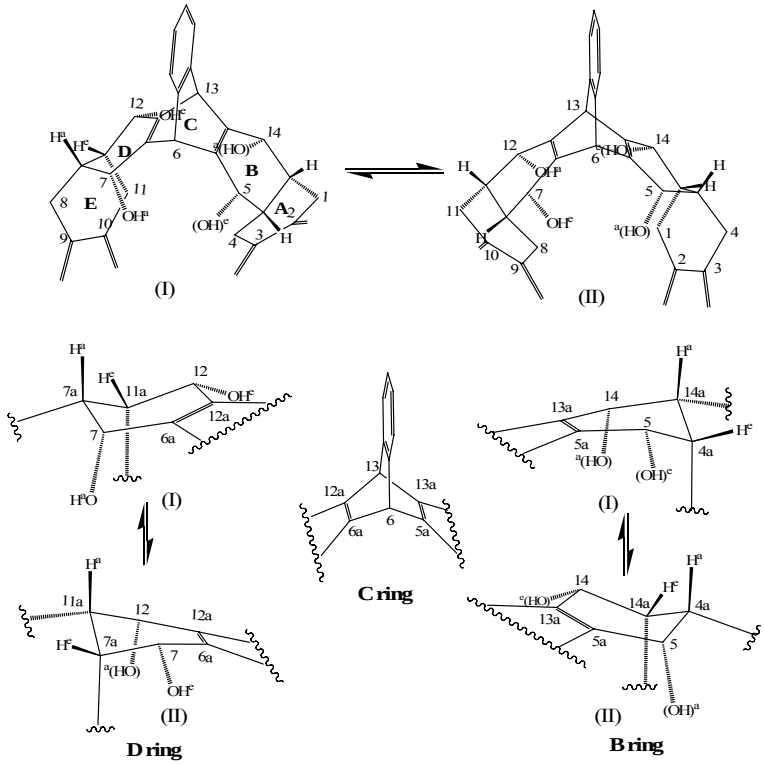


Figure 2.12 Conformation communications of B&D rings during conformation change of **2.51**.

2.4.2.2 Conformation lock by bulky TBS group: ^{1}HNMR analysis of protected tetraene 2.50

At room temperature, conformation (I) and conformation (II) of tetraene **2.51** undergo rapid interconversion in the NMR time scale. However, if a bulky group is introduced and prefers an equatorial position, it would "lock" the molecule to one conformation. In this case, hydrogens in axial position and equatorial position shall show different chemical shifts.

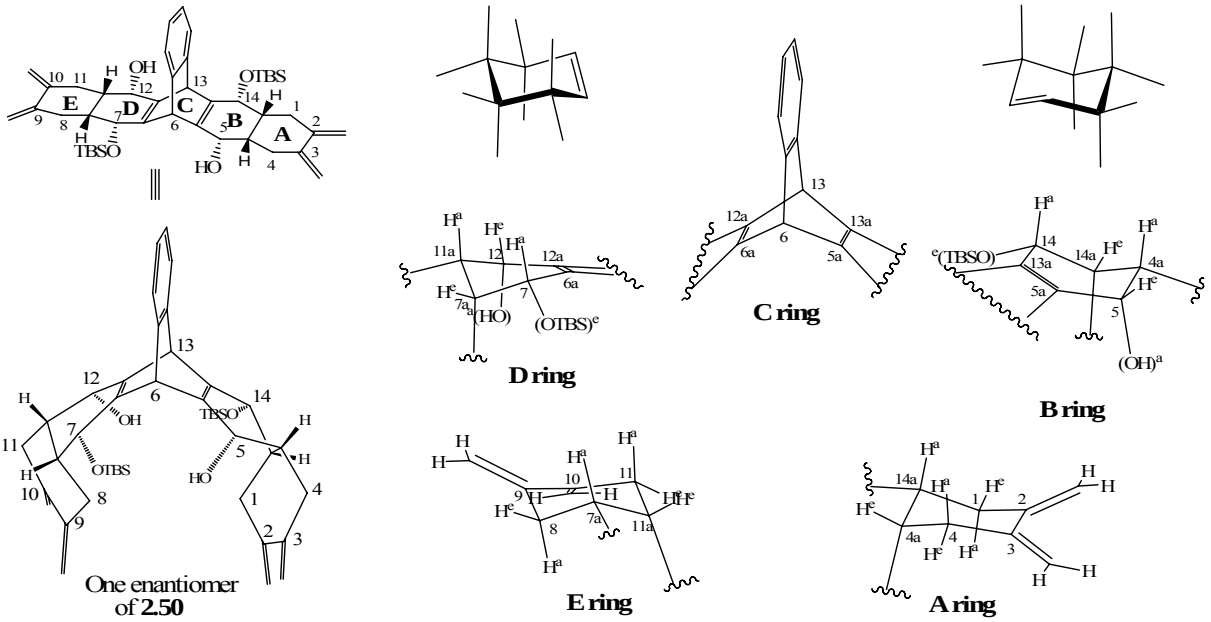


Figure 2.13 Predicted ABCDE ring conformations of protected tetraene **2.50** in solution.

According to the above model, two bulky OTBS groups in compound **2.50** can only occupy equatorial position (7 and 14). The predicted conformation of **2.50** is shown in **Figure 2.13**. Protons in AE rings should have different chemical shifts and a total of six different sets of peaks would be observed. The splitting pattern of each proton can be predicted from coupling constants with its neighboring protons. For example, axial proton in carbon-1 has two neighboring protons; one is an axial proton on carbon-14a with a large coupling constant about 8~14 Hz; the other is an equatorial proton on the same carbon with a geminal coupling constant about 12~18 Hz. It shows a triplet with an average J = 13.6 Hz in the spectrum. For equatorial proton on carbon-1, the coupling constant with axial proton on carbon-14a is small (2~3 Hz) and the geminal coupling constant with axial proton on the carbon-1 is larger (12~18 Hz). It shows a doublet with J = 14.8 Hz in spectrum. Similarly, all the other protons in AE ring can be assigned based on the predicted conformation shown in **Figure 2.13**. Although 2D-NMR studies of **2.50**

are needed to further verify the assignments, the successful prediction of ^{1}H NMR by conformation analysis supports the conformation communication model mentioned above.

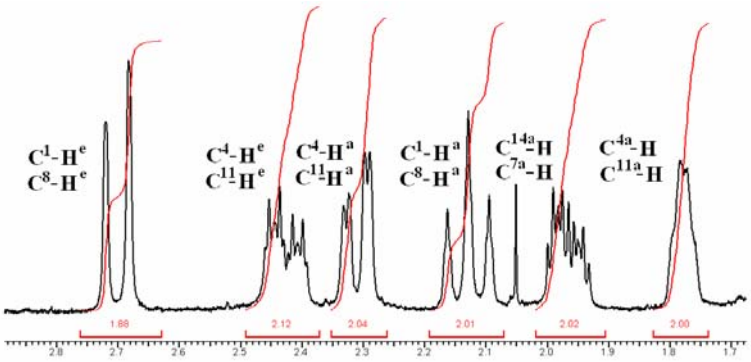


Figure 2.14 Proton assignments of protons in AE rings in ^{1}HNMR (δ 1.7~2.8) of **2.50**

2.4.2.3 Conformation lock by furan ring formation: formation of compound 2.71.

Based on the above model, the diagonal feature of intramolecular furan ring formation in tetraene **2.51** at 150^{o}C can be explained. When the axial hydroxyl group in B ring adds to the C=C at γ position because of space closeness, the conformation of B ring is locked, which causes D ring to adopt a preferred *pseudo*-chair conformation to reduce the strain of C ring. The preferred *pseudo*-chair conformation of D ring, with an axial hydroxyl group being diagonal to the reacted hydroxyl group in B ring, facilitates the second furan formation to form compound **2.71** (**Scheme 2.16** and **Figure 2.15**).

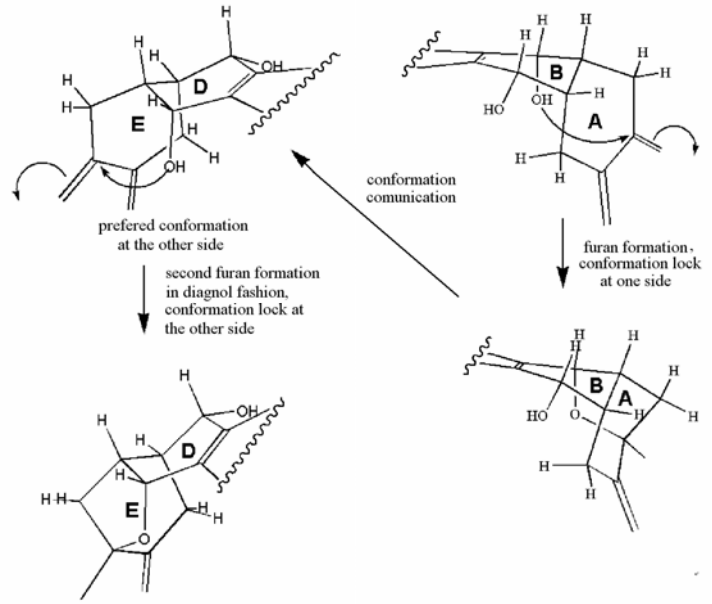


Figure 2.15 Conformation lock and communication leading to formation of diagonal furan rings.

2.4.2.4 Conformation transduction models incorporated with an o-benzono-bridged 1,4-cyclohexadiene ring.

In **Figure 2.10**, transformation transduction models are shown in such a way that if two same groups (such as A) in one side are brought close to each other, the other same groups in the other side (such as B) are brought far away from each other. Two groups are close together because they both occupy equatorial positions. If they both occupy axial positions, they are far away from each other. Similar models can be built for ring systems incorporated with a *o*-benzono-bridged 1,4-cyclohexadiene ring as shown in **Figure 2.16**. The first model **2.77** is equivalent to perhydroanthracene model shown in **Figure 2.10** except for the relative steorochemsitry of two sides. In the second model **2.78**, conformation transduction is conducted unprecedentedly through five rings.

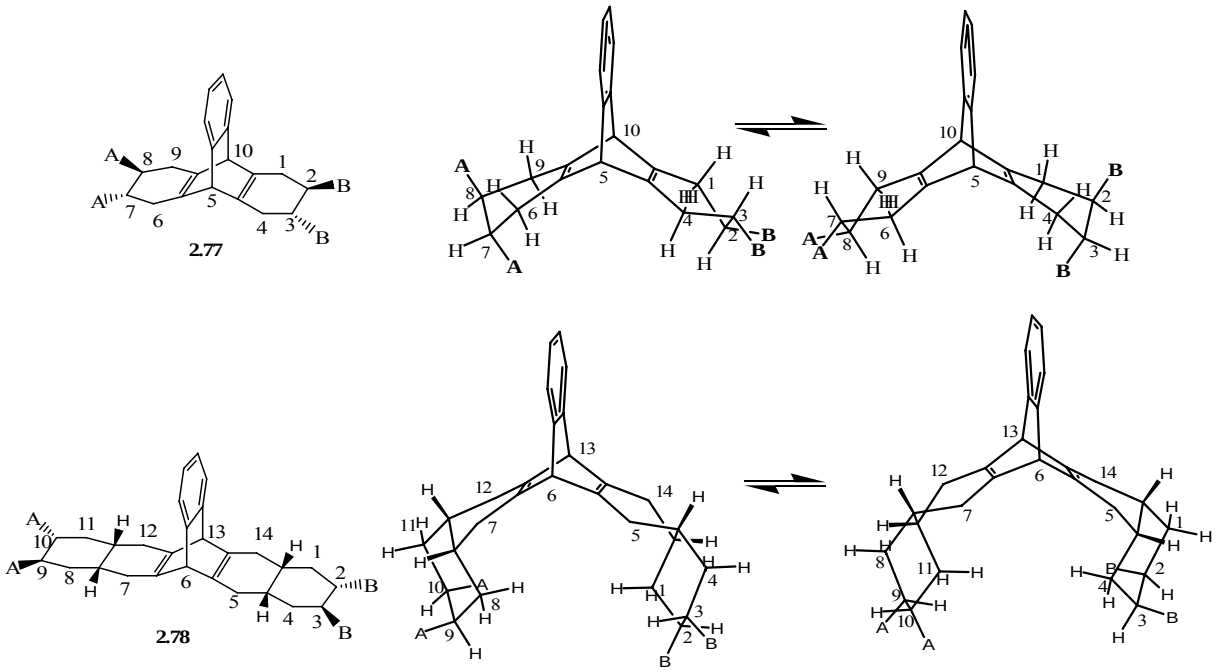


Figure 2.16 Conformation transduction incorporated with an *o*-benzono-bridged 1,4-cyclohexadiene ring

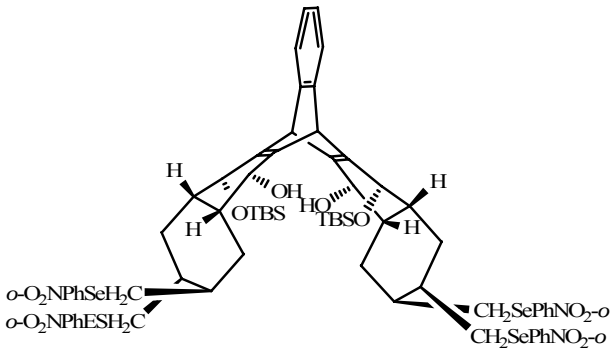
Although the above models of conformation conduction or communication may seem reasonable, they are mostly empirical and descriptive. They raised more questions to be answered. Currently, no detailed calculations regarding to energy differences of all possible conformations of tetraene **2.51** have been studied. The detailed function of *o*-benzono-bridged 1,4-cyclohexadiene ring is also unclear.

2.5 Experimental Section

General Methods: Nuclear magnetic resonance spectra were obtained at Varian Unity Plus (400 MHz) and Varian Gemini 2000 (200 MHz). Mass spectra were taken from a Hewlett Packard 5890A Series II, GC-MS and a Bruker Esquire 3000 Plus electrospray ionization mass spectrometer. FAB spectra were taken by using Xe beam (8 KV) and m-nitrobenzyl alcohol as matrix. Silica gel (200~400 mesh) from Natland International Coporation was used for the flash chromatographic separation. THF and diethyl ether were distilled over sodium and benzophenone. Methylene chloride was distilled over CaH_2. Toluene and benzene were distilled over $LiAlH_4$.

2.5.1 Synthesis of tetraene 2.51

2.5.1.1) (*2R,3S,4aS,5S,7R,7aR,9R,10S,11aS,12S,14R,14aR*)-5,12-Di(*t*-butyldimethylsilan-oxy)-7,14-dihydroxy-2,3,9,10-*tetra*(2-nitrophenylselenyl)methyl-1,2,3,4,4a,5,6,7,7a,8,9,10, 11,11a,12,13,14,14a-octadecahydro-6,13-*o*-benzenopentacene and its enantiomer (**2.49**)

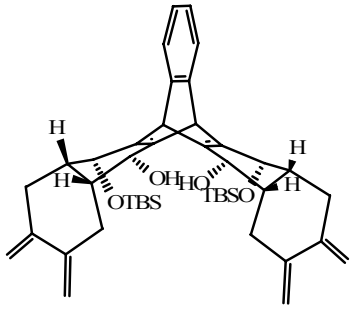


2.49

To a solution of 290 mg (1.28 mmol) of *o*-nitrophenyl selenocyanate in 4 mL of dry pyridine was added 319 μL (1.28 mmol) of tri-*n*-butylphosphine. The resulting deep red solution was stirred at room temperature for 5 minutes. Then a solution of 100 mg (0.128 mmol) of tetraol **2.48** [2] in 4 mL of dry pyridine was added via cannular. The resulting solution was heated to 65 ^{o}C for 3 hours. The reaction mixture was then cooled to room temperature and diluted with 100 ml ethyl acetate. The organic layer was washed with water (2 ×100 mL), brine (100 mL), dried over anhydrous magnesium sulfate, filtered, and concentrated by a rotavapor. The residue was applied to column chromatography (silica gel) using dichloromethane and hexane (3:2) as eluent to give 190 mg (98% yield) of the title compound, **2.49**, as yellow solids: ^{1}H NMR

($CDCl_3$, 200 MHz) δ 8.2~8.3 (m, 4 H), 7.3~7.7 (m, 12 H), 7.18 (dd, J_1 = 5.1 Hz, J_2 = 3.3 Hz, 2 H), 6.98 (dd, J_1 = 5.1 Hz, J_2 = 3.3 Hz, 2 H), 4.93 (s, 2 H), 4.50 (d, J = 7.0 Hz, 2 H), 4.27 (m, 2 H), 3.0~3.3 (m, 4 H), 2.91 (m, 4 H), 2.43 (m, 2 H), 2.1~1.4 (series of multiplets, 12 H) 1.00 (s, 18 H), 0.21 (s, 6 H), 0.10 (s, 6 H).

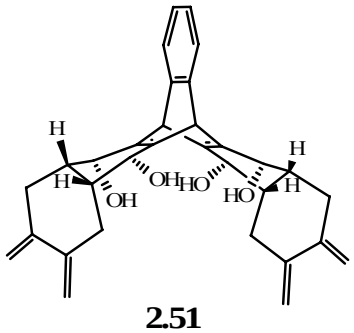
2.5.1.2) ***(4aS,5S,6S,7R,7aR,11aS,12S,13S,14R,14aR)*****-5,12-Di(*t*-butyldimethylsilanoxy)-7,14-dihydroxy-2,3,9,10-tetramethylene-1,4,4a,5,6,7,7a,8,11,11a,12,13,14,14a-tetradecahydro-6,13-o-benzenopentacene and its enantiomer** (**2.50**)



2.50

To a mixture of 20 mg (0.013 mmol) of tetraselenide **2.49**, 11 mg (0.13 mmol) of sodium bicarbonate, and 43 μL (0.53 mmol) of pyridine in 4 mL methylene chloride at room temperature, was added 15.6 mg (0.063 mmol) of 70% *m*-chloroperbenzoic acid. The reaction mixture was stirred overnight at room temperature and then diluted with 50 mL methylene chloride. The organic layer was washed with water (50 mL × 2), brine (50 mL), dried over anhydride magnesium sulfate, filtered, and concentrated by a rotavapor. The residue was then applied to column chromatography (silica gel) using a gradient of petroleum ether and methylene chloride (3:2, V:V) to give 6.9 mg (74% yield) of the title compound **2.50**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.18 (m, 2 H), 6.94 (m, 2 H), 5.04 (m, 4 H), 4.95 (s, 2 H), 4.73 (bs, 2 H), 4.66 (bs, 2 H), 4.46 (dd, 2 H, J_1 = 6.4 Hz, J_2 = 2.0 Hz), 4.25 (d, 2 H, J = 2.7 Hz), 2.70 (d, 2 H, J = 18.8 Hz), 2.42 (m, 2 H), 2.30 (m, 2 H), 2.12 (t, 2 H, J = 14.0 Hz), 1.96 (m, 2 H), 1.78 (m, 2 H), 1.00 (s, 18 H), 0.25 (s, 6 H), 0.15 (s, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.6, 148.4, 147.6, 146.8, 144.8, 124.0, 122.1, 109.2, 108.1, 71.5, 69.1, 41.3, 37.1, 36.6, 30.2, 29.9, 26.3, 18.8, -4.2, -4.4; MS: m/z: 733.589 $(M+Na)^+$.

2.5.1.3) ***(4aR,5R,7S,7aS,11aR,12R,14S,14aR)*****-5,7,12,14-Tetrahydroxy-2,3,9,10-tetramethyl-ene-1,4,4a,5,6,7,7a,8,11,11a,12,13,14,14a-tetradecahydro-6,13-*o*-benzenopentacene** (**2.51**)



2.51

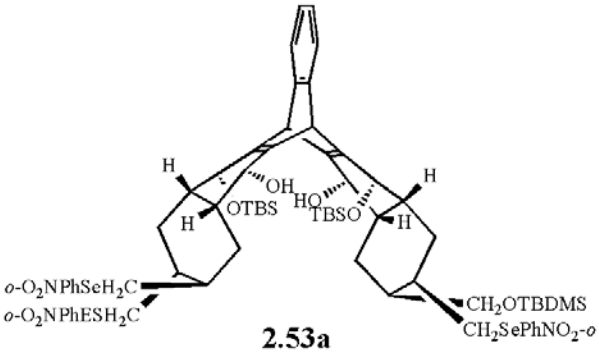
To a solution of 16.7 mg (0.0235 mmol) of tetraene **2.51** in 2.5 mL of THF at 0 ^{o}C (ice-water bath) was added 56.4 μL (0.0564 mmol) of 1M tetrabutylammonium fluoride (TBAF) in THF. The reaction mixture was stirred at room temperature for 2 hours, diluted with 20 mL water and extracted with ethyl acetate (25 mL×2). The organic layer was then washed with water (50 mL) and brine (50 mL), dried over anhydrous magnesium sulfate, filtered, and concentrated by a rotavapor. The residue was then applied to column chromatography using hexane and ethyl acetate (1:2, V:V) as eluent to give 10.1 mg (89 % yield) of the title compound, **2.51**, as white solids: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.28 (dd, J_1 = 5.1 Hz, J_2 = 3.3 Hz, 2 H), 7.01 (dd, J_1 = 5.1 Hz, J_2 = 3.3 Hz, 2 H), 5.17 (s, 2 H), 5.09 (s, 4 H), 4.79 (s, 4 H), 4.55 (bs, 4 H), 2.96 (bs, 4 H), 2.43 (m, 8 H), 2.00 (m, 4 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.5, 147.0, 146.0, 124.3, 122.6, 110.0, 70.7, 50.0, 38.6, 34.0; MS: m/z: 505.35 $(M+Na)^+$.

2.5.2 Synthesis of triene 2.55

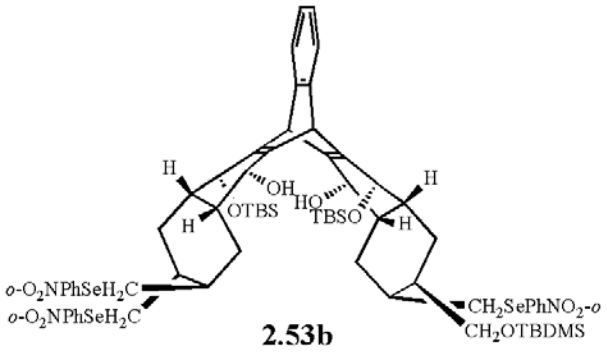
2.5.2.1) ***(2R,3S,4aS,5S,6S,7R,7aR,9R,10S,11aS,12S,13S,14R,14aR)*-2-(*t*-Butyldimethylsilanoxy)methyl-5,12-di(*t*-butyldimethylsilanoxy)-7,14-dihydroxy-3,9,10-*tri*(2-nitrophenylselenyl) methyl-1,2,3,4,4a,5,6,7,7a,8,9,10,11,11a,12,13,14,14a-octadecahydro-6,13-*o*-benzenopentacene and its enantiomer** (**2.53a**)

***(2S,3R,4aR,5R,6S,7S,7aS,9S,10R,11aR,12R,13S,14S,14aS)*-2-(*t*-Butyldimethylsilanoxy)-methyl-7,14-di(*t*-butyldimethylsilanoxy)-5,12-dihydroxy-3,9,10-*tri*(2-nitrophenylselenyl)-methyl-1,2,3,4,4a,5,6,7,7a,8,9,10,11,11a,12,13,14,14a-octadecahydro-6,13-*o*-benzenopentacene and its enantiomer** (**2.53b**)

To a solution of 93 mg (0.41 mmol) of *o*-nitrophenyl selenocyanate in 2 mL of dry pyridine was added 102 μL (0.41 mmol) of tri-*n*-butylphosphine. The resulting deep red solution was stirred at room temperature for 5 minutes. Then a solution of 49 mg (0.055 mmol) of triol



2.53a



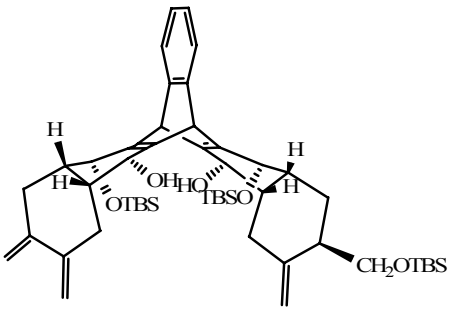
2.53b

2.52a and **2.52b** in 2 mL of dry pyridine was added via cannular. The resulting solution was heated to 65 ^{o}C for 3 hours. The reaction mixture was then cooled to room temperature and diluted with 50 ml ethyl acetate. The organic layer was washed with water (2 $\times$50 mL), brine (50 mL), dried over anhydrous magnesium sulfate, filtered and concentrated by a rotavapor. The residue was applied to column chromatography (silica gel) using a gradient of petrol ether and methylene chloride (from 3:2 to 3:7) as eluent to give 50 mg (62 % yield) of a mixture of title compounds as a yellow solid. Two isomers were partially separated in the column.

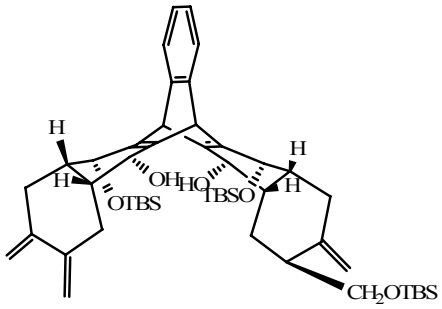
Less polar isomer **2.53b**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.24~8.32 (m, 3 H), 7.40~7.72 (m, 6 H), 7.30 (m, 3 H), 7.18 (m, 2 H), 6.98 (dd, J_1 = 5.1 Hz, J_2 = 3.3 Hz, 2 H), 4.94 (s, 1 H), 4.92 (s, 1 H), 4.48 (m, 2 H), 4.27 (m, 2 H), 4.22 (t, J = 6.0 Hz, 1 H), 3.90 (m, 1 H), 3.62 (m, 1 H), 2.70~3.30 (series of multiplets, 8 H), 1.60~2.50 (series of multiplets, 15 H), 1.01 (s, 9 H), 0.99 (s, 9 H), 0.90 (s, 9 H), 0.25 (s, 3 H), 0.22 (s, 3 H), 0.12 (s, 3 H), 0.09 (s, 3 H), δ 0.06 (s, 3 H), δ 0.04 (s, 3 H).

More polar isomer **2.53a**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.22~8.28 (m, 3 H), 7.42 ~7.71 (m, 6 H), 7.28~7.38 (m, 3 H), 7.19 (dd, J_1 = 5.1 Hz, J_2 = 3.3 Hz, 2 H), 6.98 (dd, J_1 = 5.1 Hz, J_2 = 3.3 Hz, 2 H), 4.98 (s, 1 H), 4.96 (s, 1 H), 4.51 (m, 2 H), 4.28 (m, 2 H), 2.80~3.30 (m, 8 H), 1.60~2.50 (series of multiplets, 16 H), 1.06 (s, 9 H), 1.01 (s, 9 H), 0.85 (s, 9 H), 0.24 (s, 3 H), 0.20 (s, 3 H), 0.16 (s, 3 H), 0.10 (s, 3 H), 0.05 (s, 3 H), 0.02 (s, 3 H).

2.5.2.2) *(2R,4aS,5S,6S,7R,7aR,11aS,12S,13S,14R,14aR)*-2-(*t*-Butyldimethylsilanoxy)methyl-5,12-di(*t*-butyldimethylsilanoxy)-7,14-dihydroxy-3,9,10-trimethylene-1,2,4,4a,5,6,7,7a,8,11,11a,12,13,14,14a-pentidecahydro-6,13-*o*-benzenopentacene and its enantiomer (**2.54a**)
***(2S,4aR,5R,6S,7S,7aS,11aR,12R,13S,14S,14aS)*- 2-(*t*-butyldimethylsilanoxy)methyl-7,14-di-(*t*-butyldimethylsilanoxy)-5,12-dihydroxy-3,9,10-trimethylene-1,2,4a,5,6,7,7a,8,11,11a,12,13,14,14a-pentidecahydro-6,13-*o*-benzenopentacene and its enantiomer** (**2.53b**)



2.54a



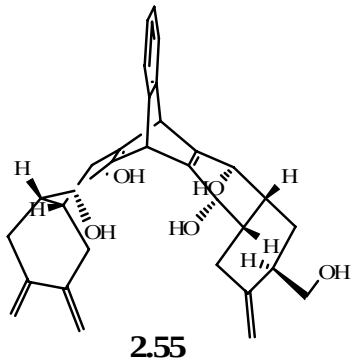
2.54b

To a mixture of 26.5 mg (0.0183 mmol) of triselenides, 59.2 mL (0.73 mmol) of pyridine and 15.4 mg (0.183 mmol) of sodium bicarbonate in 2 mL methylene chloride at 0 ^{o}C (ice-water bath) was added 23 mg (0.092 mmol) of 70% *m*-chloroperbenzoic acid. The reaction mixture was stirred at room temperature under argon for 6 hours and diluted with 20 mL of ethyl acetate. The organic layer was washed with water (20 mL $\times$2) and brine (20 mL), dried over anhydrous magnesium sulfate, and concentrated by a rotavapor. The residue was then applied to column chromatography with methylene chloride and petroleum ether (2:1,V:V) as eluent to give 5.3 mg of less polar isomer **2.54a** and 4.9 mg of the more polar isomer **2.54b** with a combination yield of 66%.

The less polar isomer (**2.54a**): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.19 (m, 2 H), δ 6.96 (m, 2 H), 5.03 (m, 4 H), 4.93 (s, 1 H), 4.20~4.80 (series of multiplets, 7 H), 3.88 (m, 1 H), 3.53 (m, 2 H), 3.09 (m, 2 H), 1.70~2.80 (series of multiplets, 12 H), 1.04 (s, 9 H), 1.00 (s, 9 H), 0.90 (s, 9 H), 0.27 (s, 3 H), 0.23 (s, 3 H), 0.18 (s, 3 H), 0.14 (s, 3 H), 0.07 (s, 3 H), 0.06 (s, 3 H).

The more polar isomer (**2.54b**): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.17 (m, 2 H), δ 6.93 (m, 2 H), 5.02 (m, 2 H), 5.00 (s, 1 H), 4.96 (s, 1 H), 4.84 (bs, 1 H), 4.72 (m, 1 H), 4.66 (bs, 1 H), 4.45 (m 2 H), 4.22 (m, 2 H), 3.60 (m, 2 H), 1.70~2.74 (series of multiplets, 13 H), 1.00 (2 s, 18 H), 0.86 (s, 9 H), 0.25 (s, 3 H), 0.24 (s, 3 H), 0.14 (s, 6 H), 0.13 (s, 3 H), 0.10 (s, 3 H), 0.007 (s, 3 H).

2.5.2.3) ***(2R,4aS,5S,6R,7R,7aR,11aS,12S,13S,14R,14aR)*-2-Hydroxymethyl-3,9,10-trimethyl-ene-5,7,12,14-tetrahydroxy-1,2,4,4a,5,6,7,7a,8,11,11a,12,13,14,14a-pentidecahydro-6,13-*o*-benzenopentacene and its enantiomer** (**2.55**)



2.55

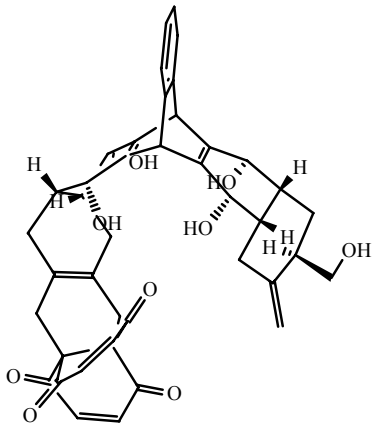
To a solution of 37.8 mg (0.0448 mmol) of triene **2.54a** and **2.54b** in 4 mL of THF at 0°C (ice-water bath) was added 161 μL (0.161 mmol) of 1M tetrabutylammonium fluoride (TBAF) in THF. The reaction mixture was stirred at room temperature for 2 hours, diluted with 20 mL water and extracted with ethyl acetate (25 mL×2). The organic layer was then washed with water (50 mL) and brine (50 mL), dried over anhydrous magnesium sulfate, filtered and concentrated by a rotavapor. The residue was then applied to column chromatography using methylene chloride and methanol (25:1, V:V) as eluent to afford 19.3 mg (86% yield) of the title compound **2.55**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.28 (m, 2 H), 7.00 (m, 2 H), 5.17 (s, 1 H), 5.16 (s, 1 H), 5.09 (bs, 2 H), 4.98 (bs, 1 H), 4.82 (bs, 2 H), 4.79 (bs, 1 H), 4.50~4.60 (m, 4 H), 3.58~3.70 (m, 3 H), 3.30 (m, 1 H), 2.88 (m, 2 H), 2.74 (m. 1 H), 1.77~2.52 (series of multiplets, 12 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 150.0, 149.2, 148.1, 147.9, 147.8, 146.1 (3 C), 145.9, 124.4 (2 C), 122.6 (2 C), 111.0, 110.5, 109.6, 77.2, 71.0, 70.3, 69.9, 64.3, 50.1, 50.0, 44.6, 39.8, 38.5, 37.7, 36.1, 35.5, 34.3, 32.1, 25.3.

2.5.3 Synthesis of Diels-Alder adducts of tetraenr 2.51 and triene 2.55

2.5.3.1) *(4aR,6aS,7S,8S,9R,9aR,11R,13aS,14S,15R,16R,16aR,18S*-11-Hydroxymethyl-12-methylene-7,9,15,17-tetrahydroxy-4a,5,6,6a,7,8,9,9a,10,11,13,13a,14,16,16a,17,18,18a-nonadecahydro-4a,18a-*cis*-ethylenedicarbonyl-8,15-*o*-benzenoheptacene-1,3-dione and its enantiomer (**2.65**)

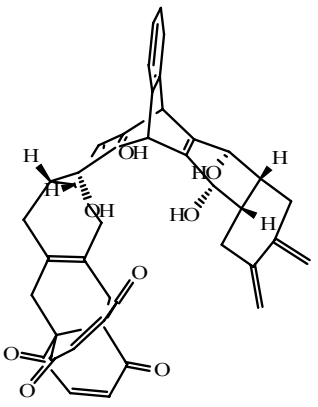
A mixture of 18 mg (0.035 mmol) of triene **2.55** and 8.6 mg (0.046 mmol) of NDQ **2.64** was stirred in 0.5 mL of 1,2-dichloroethane at 0°C, then slowly warmed up to room temperature and stirred at room temperature for 4 hours. Solvent was removed by a rotavapor. The residue was applied to column chromatography (silica gel) using methylene chloride and methanol (25:1, V:V) as eluent to afford 20 mg (82% yield) of the title compound: ^{1}H NMR ($CDCl_3$, 400 MHz) δ

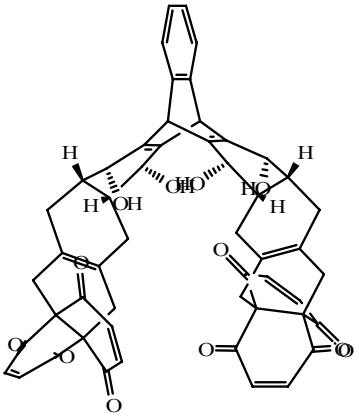
7.30 (m, 2 H), 7.00 (m, 2 H), 6.78~6.80 (m, 4 H), 5.24 (s, 1 H), 5.18 (s, 1 H), 4.93 (bs, 1 H), 4.76 (bs, 1 H), 4.56 (bt, 2 H, J = 8.2 Hz), 4.39 (d, J = 5.0 Hz, 2 H), 3.65 (m, 2 H), 1.60~2.90 (series of multipets, 17 H).



2.65

2.5.3.2) ***(6aS,7S,8S,9R,9aR,13aS,14S,15R,16R,16aR)*-11,12-Dimethylene-7,9,14,16-tetrahydroxy-4a,5,6,6a,7,8,9,9a,10,13,13a,14,16,16a,17,18,18a-octadecahydro-4a,18a-*cis*-ethylenedicarbonyl-8,15-*o*-benzenoheptacene-1,3-dione** (**2.67**)
***(6aS,7S,9R,9aR,17aS,18S,20R,20aR)*-7,9,18,20-Tetrahydroxy-4a,5,6,6a,7,8,9,9a,10,11,11a,15a,16,17,17a,18,19,20,20a,21,22,22a-docosahydro-(4a,22a:11a,15a)-di(*cis*-ethylenedicarbonyl)-8,19-*o*-benzenononacene-1,3,12,15-tetraone** (**2.68**)





2.67 **2.68**

A mixture of 25 mg (0.052 mmol) of tetraene **2.51** and 5.9 mg (0.031 mmol) of NDQ **2.64** was stirred in 10 mL of 1,2-dichloroethane at -78 ^{o}C, then slowly warmed up to 0 ^{o}C and stirred at 0 ^{o}C for 40 min. Solvent was removed by a rotavapor. The residue was applied to

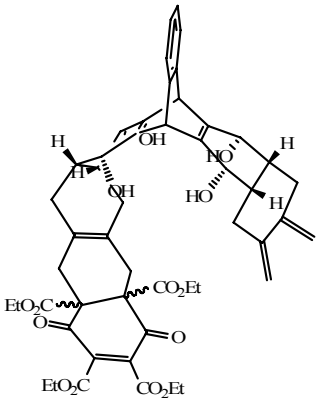
column chromatography (silica gel) using methylene chloride and acetone (20:1, V:V) as eluent to afford 11.6 mg (33 % yield) of monoadduct **2.67** and 2.3 mg (5.0 % yield) of diadduct **2.68**.

Monoadduct **2.67**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.29 (m, 2 H), 7.01 (m, 2 H), 6.81 (s, 2 H), 6.80 (s, 2 H), 5.22 (s, 2 H), 5.07(s, 2 H), 4.76 (s, 2 H), 4.60 (bs, 2 H), 4.37 (bs, 2 H), 3.05 (bs, 2 H), 2,74 (bs, 2 H), 1.74~2.64 (series of multiplets, 16 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 193.7 (2 C), 148.3, 147.0, 146.3, 146.1, 140.0 (2 C), 125.7, 124.4, 122.7, 110.2, 70.9, 70.0, 65.8, 49.9, 38.7, 35.2, 34.2, 31.7, 29.9; MS: m/z 693.29 (M+Na).

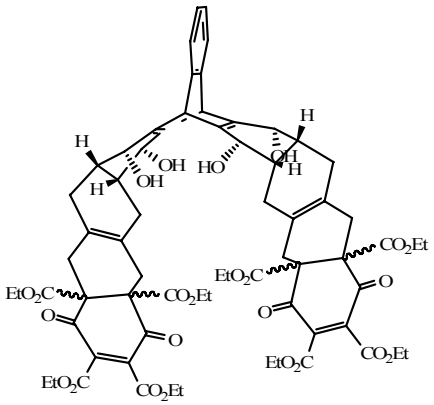
Diadduct **2.68**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.28 (m, 2 H), 7.00 (m, 2 H), 6.80 (s, 4 H), 6.73 (s, 4 H), 5.18 (s, 2 H), 4.37 (bs, 4 H), 2.50 (b, 4 H), 2.36 (bs, 4 H), 2.31 (bs, 4 H), 2.15 (bs, 4 H), 1.89 (bs, 4 H), 1.84 (bs, 4 H); MS: m/z 881.36 (M+Na).

2.5.3.3) (*cis-4a,18a)-(6aR,7R,8R,9S,9aS,13aR,14R,15S,16S,16aS)*-11,12-Dimethylene-7,9,14, 16-tetrahydroxy-2,3,4a,18a-tetraethoxycarbonyl-4a,5,6,6a,7,8,9,9a,10,13,13a,14,16,16a,17, 18,18a-octadecahydro-8,15-*o*-benzenoheptacene-1,3-dione (**2.71**)

(***cis-4a,18a;cis-11a,15a)-(6aR,7R,9S,9aS,17aR,18R,20S,20aS)*-7,9,18,20-Tetrahydroxy-2,3,4a,11a,13,14,15a,22a-octaethoxycarbonyl-4a,5,6,6a,7,8,9,9a,10,11,11a,15a,16,17,17a,18, 19,20,20a,21,22,22a-docosahydro-(4a,22a:11a,15a)-8,19-*o*-benzenononacene-1,3,12,15-tetraone** (**2.72**)



2.71



2.72

A mixture of 26.7 mg (0.0553 mmol) of tetraene **2.51** and 13 mg (0.033 mmol) of the double activated quinone **2.70** was stirred in 33 mL of benzene at 0 ^{o}C, then slowly warmed up to room temperature and stirred at room temperature for overnight. Solvent was removed by a rotavapor. The residue was applied to column chromatography (silica gel) using a gradient of

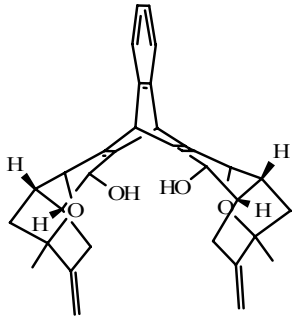
methylene chloride and acetone (25:1 to 9:1, V:V) as eluent to afford 10.4 mg (21% yield) of monoadduct **2.71** and 13.4 mg (19% yield) of diadduct **2.72**.

Monoadduct **2.71**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.29 (m, 2 H), 7.01 (m, 2 H), 5.19 (s, 2 H), 5.13 (bs, 2 H), 4.81 (bs, 2 H), 4.56 (bs, 2 H), 4.38 (bs, 2 H), 4.34 (m, 4 H), 4.25 (m, 4 H), 2.99 (bs, 2 H), 2.75 (bd, 2 H), 2.00~2.70 (series of multiplets, 12 H), 1.79 (bd, 2 H), 1.33 (t, 6 H, J = 7.2 Hz), 1.28 (t, 6 H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 189.3, 167.2, 162.1, 148.0, 147.0, 146.2, 146.1, 138.5, 125.7, 124.4, 122.7, 110.4, 70.8, 70.0, 64.3, 63.5, 62.9, 49.8, 38.6, 35.2, 34.1, 33.1, 29.9, 14.1, 14.0; MS: m/z 901.80 (M+Na).

Diadduct **2.72**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.27 (m, 2 H), 7.00 (m, 2 H), 5.14 (s, 2 H), 4.30~4.40 (m, 12 H), 4.22 (m, 8 H), 2.76 (bd, 4 H), 2.56 (bd, 4 H), 2.17 (bd, 4 H), 2.06 (bs, 4 H), 1.80 (bd, 4 H), 1.32 (t, 12 H, J = 7.6 Hz), 1.25 (t, 12 H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 188.9, 167.2, 162.1, 146.2 (2 C), 138.6, 125.5, 124.4, 122.6, 70.1, 64.3, 63.4, 62.8, 50.0, 35.3, 33.3, 14.1, 14.0; MS: m/z 1297.74 (M+Na).

2.5.4 Isomerization of tetraene 2.51

2.5.4.1) ***(3S,4aR,5R,6R,7S,7aS,11aR,12R,13R,14S,14aS)*****-2,9-Dimethylene-7,14-tetrahydroxy-(3,5:10,12)-bis-oxo-1,3,4,4a,5,6,7,7a,8,10,11,11a,12,13,14,14a-hexadecahydro-6,13-*o*-benzenopentacene** (**2.74**)



2.74

A solution of tetraene **2.51** 20 mg (0.041 mmol) in 3 mL 1,2-dichloroethane under argon was heated in seal tube at 155 ^{o}C for five hours. The solvent was removed by a rotavapor. The residue was applied to column chromatography using a gradient of methylene chloride and acetone (100:1 to 20:1) as eluent to afford 11 mg (55% yield) of the title compound **2.74**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.27 (m, 2 H), 6.99 (m, 2 H), 5.19 (s, 2 H), 4.67 (bs, 2 H), 4.48 (m, 6

H), 2.49 (bs, 2 H), 1.64~2.32 (series of multiplets, 12 H), 1.48 (s, 6 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 151.7, 148.7, 146.2, 143.4, 124.3, 122.6, 104.8, 83.1, 76.0, 71.9, 50.5, 44.7, 40.5, 38.8, 29.1, 22.5; MS: m/z 987.4 (2M+Na).

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CHAPTER 3 - Towards the synthesis of new cyclododeciptycene based molecular gears

3.1 Introduction

This new project was detoured from the previous beltene project. From knowledge gained in pursuing the [10]beltene derivative and literature study, successful cyclization of a molecular ring structure by Diels-Alder reaction depends on both closeness and right alignment of the diene and dienophile ends. In order to bring the two ends close together, a reasonable route coming out was to extend curved backbone of triptycenebisquinone, which led to a series of iptycene quinones with increased curvity. For *cis,cis,cis,cis*-undeciptycenehexaquinone **3.59** (for nomenclature, see below) two quinone ends are both close enough and parallel to each other. If one end was transformed to diene component 1,4-dimethoxyanthracene, the two ends should be close and right on top of the other for intramolecular Diels-Alder cyclization as in **3.112**. The basic idea of extension of simple triptycenebisquinone together with a goal of cyclization would naturally lead to a new beltene derivative cyclododeciptycenehexaquinone, a beautiful gear-shaped molecule with D_{6h} symmetry which was first proposed in my oral proposal in Dec. 2004.

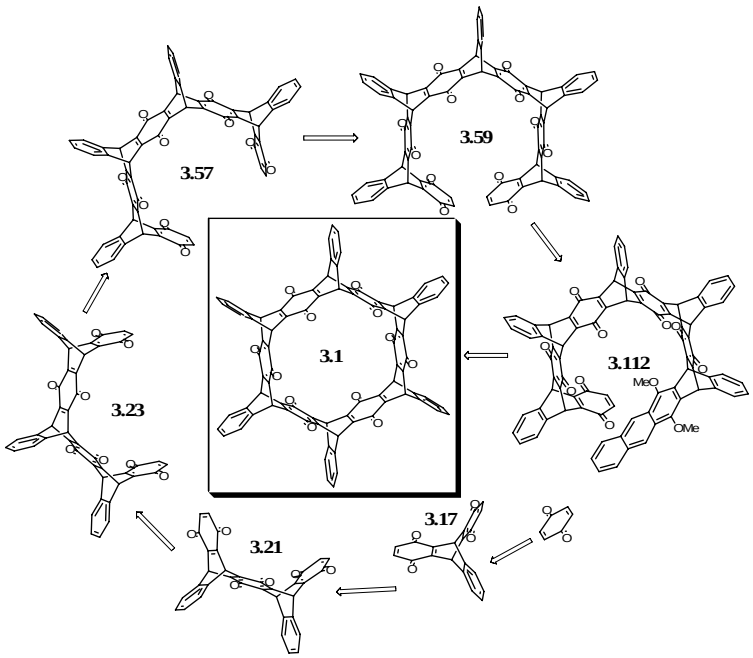


Figure 3.1 From benzoquinone to cyclododeciptycenehexaquinone.

3.2 Background

3.2.1 Iptycenes and iptycene quinones

3.2.1.1 Iptycenes

"Iptycenes", coined by Harold Hart, "are extended triptycenes."[1] They refer to a series of compounds derived from the idea of extension of triptycene in that two nearby triptycene units merged together by sharing a benzene ring (See **Figure 3.2**). The prefix (tri-, pent-, etc.) accounts for the number of benzene planes separated by ring bridges.[1, 2]

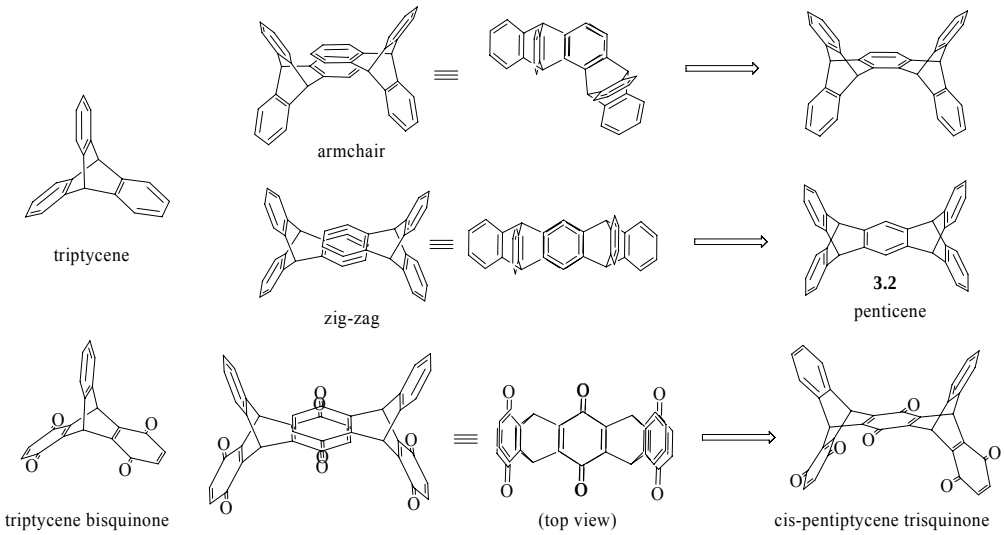


Figure 3.2 Structural correlations between triptycene and pentiptycene; triptycene bisquinonone and pentiptycene trisquinone

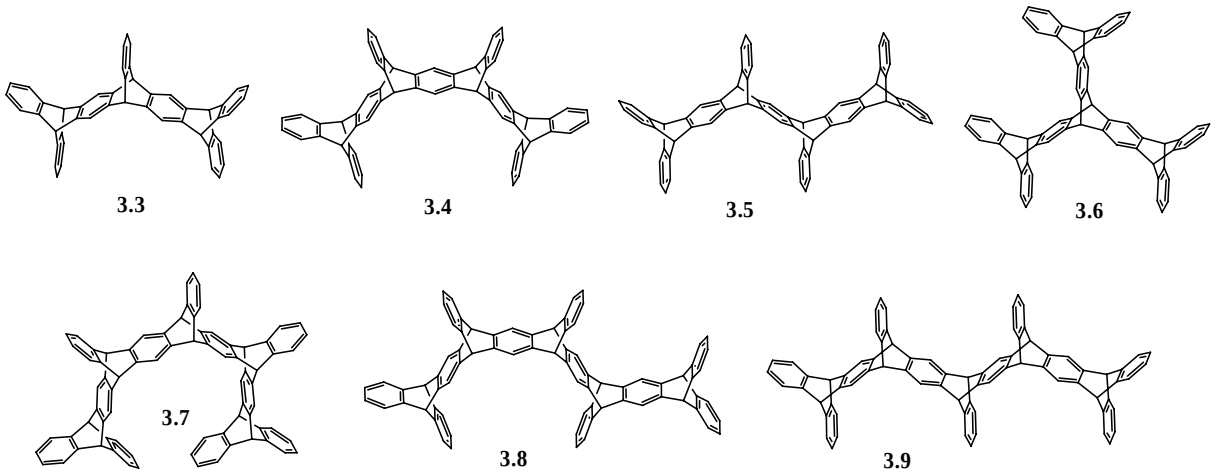
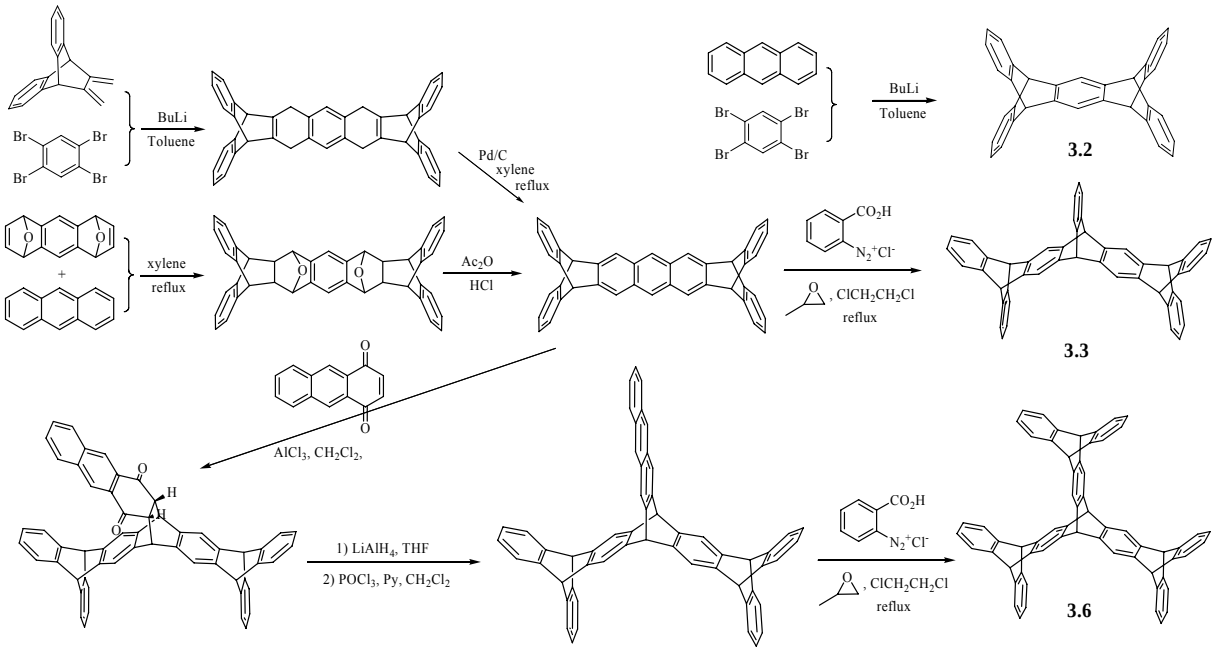


Figure 3.3 Some higher iptycenes.

Triptycene, the simplest member in the iptycene family, was first synthesized by P.D.Bartlett in 1942 for mechanistic study of radicals.[3] Triptycene is a rigid D_{3h} symmetric gear-like molecule, with three benzene rings connected by a [2.2.2] ring bridge, forming the fundamental structural unit for iptycenes.

Pentiptycene, first synthesized in 1974,[4] is the first member of larger iptycenes. Two possible pentiptycenes exist theoretically due to two possible alignments (termed here zig-zag and armchair respectively, for their similarity to zig-zag and armchair carbon nanotubes) when two triptycene "merged" together by overlapping one benzene ring (**Figure 3.2**). [1] Since quinone rings can only be overlaped in a zigzag way, iptycene quinones can only be derivatives of zigzag type of iptycenes. Thus only zigzag type of iptycenes will be discussed in this chapter.



Scheme 3.1 Synthesis of iptycenes

It was Harold Hart who first systematically explored syntheses of higher iptycenes based on aryne and Diels-Alder chemistry.[1, 2, 5-8] A series of building blocks were developed and several higher iptycenes were successfully synthesized. In some cases, several synthetic routes are available. Both the selection of building blocks and the reaction sequence are crucial for achieving good yield. But in most cases, higher iptycenes remain difficult and/or tedious to synthesize and purify. Cycloiptycenes, iptycenes with ring structures, are even more challenging targets for synthesis (**Figure 3.4**).[1, 2] Up to now, no successful synthesis of them or their derivatives have been reported in literature. Among them, cyclododeciptycene (**3.11**) derivatives

have a honeycomb structure with a dihedral angle of 120°, which minimize the strain energy and make them more amenable for synthesis.

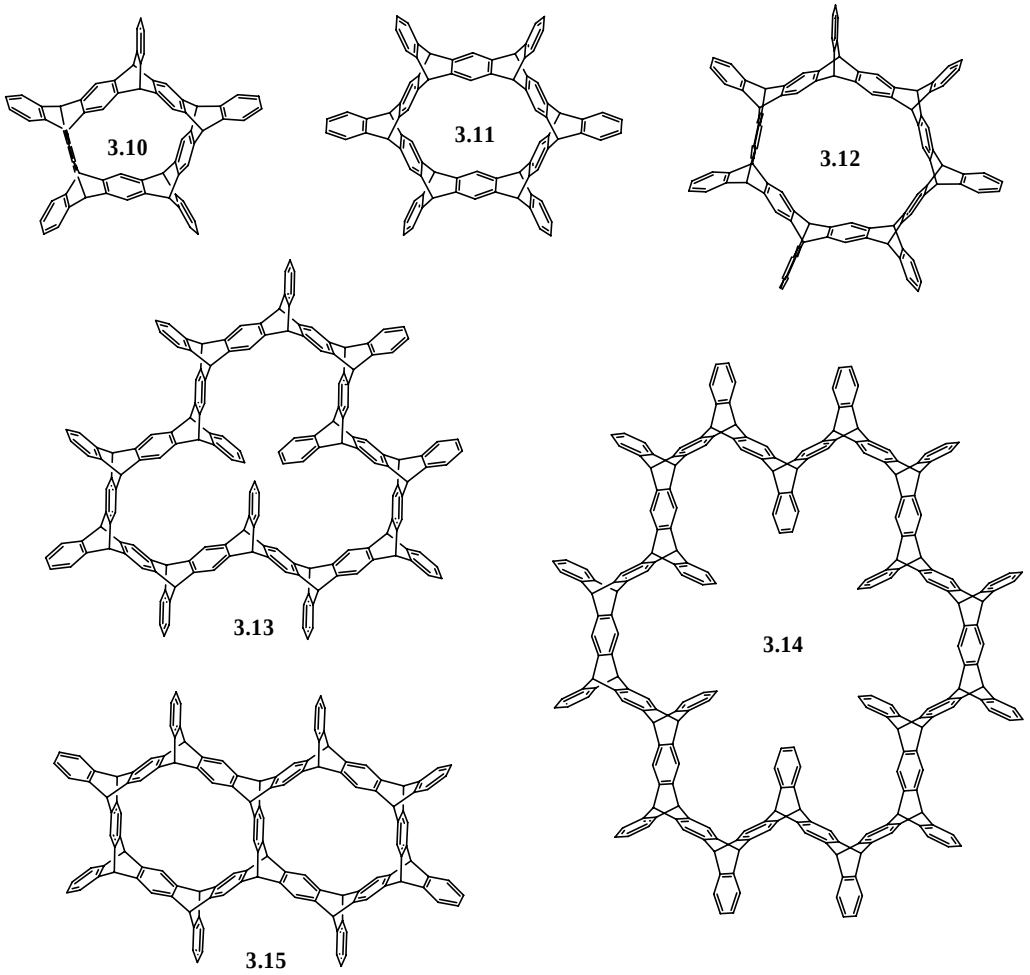


Figure 3.4 Cycloiptycenes.

3.2.1.2 Iptycene quinones

Similarly, iptycenes quinones are extended triptycene quinones (**Figure 3.2**). They can also been seen as iptycene derivatives with one or more benzene rings being replaced by quinone rings. Compared with iptycenes, iptycene quinones have interesting electrochemical and photochemical properties with embedded quinone rings in their structure. Furthermore, they have better derivatization ability,[9] since the quinone ring can be converted to a benzene ring with one position being bromo, iodo, amino, nitro, cyano, or formyl group and its *para*-position being a hydroxy or alkoxy group.[10] They would be important synthetic intermediates leading to a wide

range of iptycene derivatives which have potential applications in supramolecular and material chemistry.

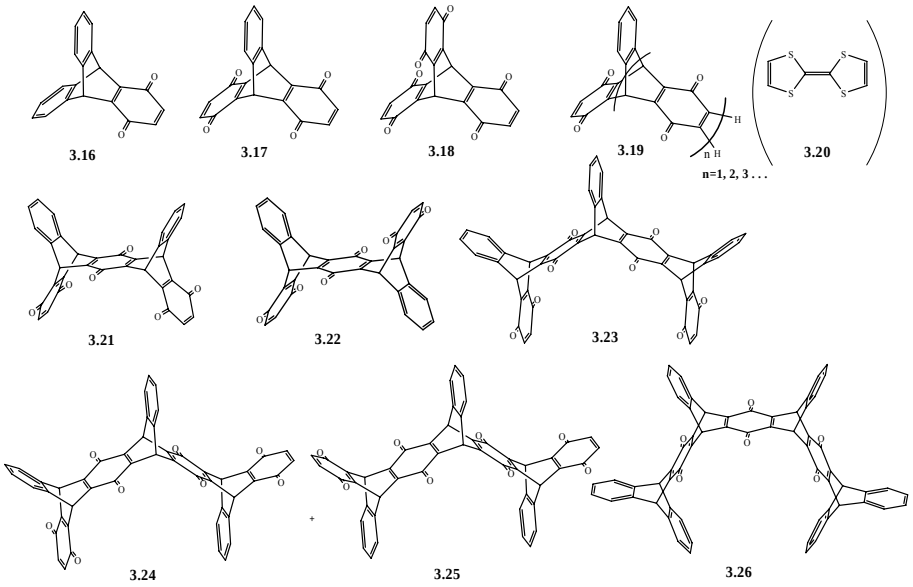
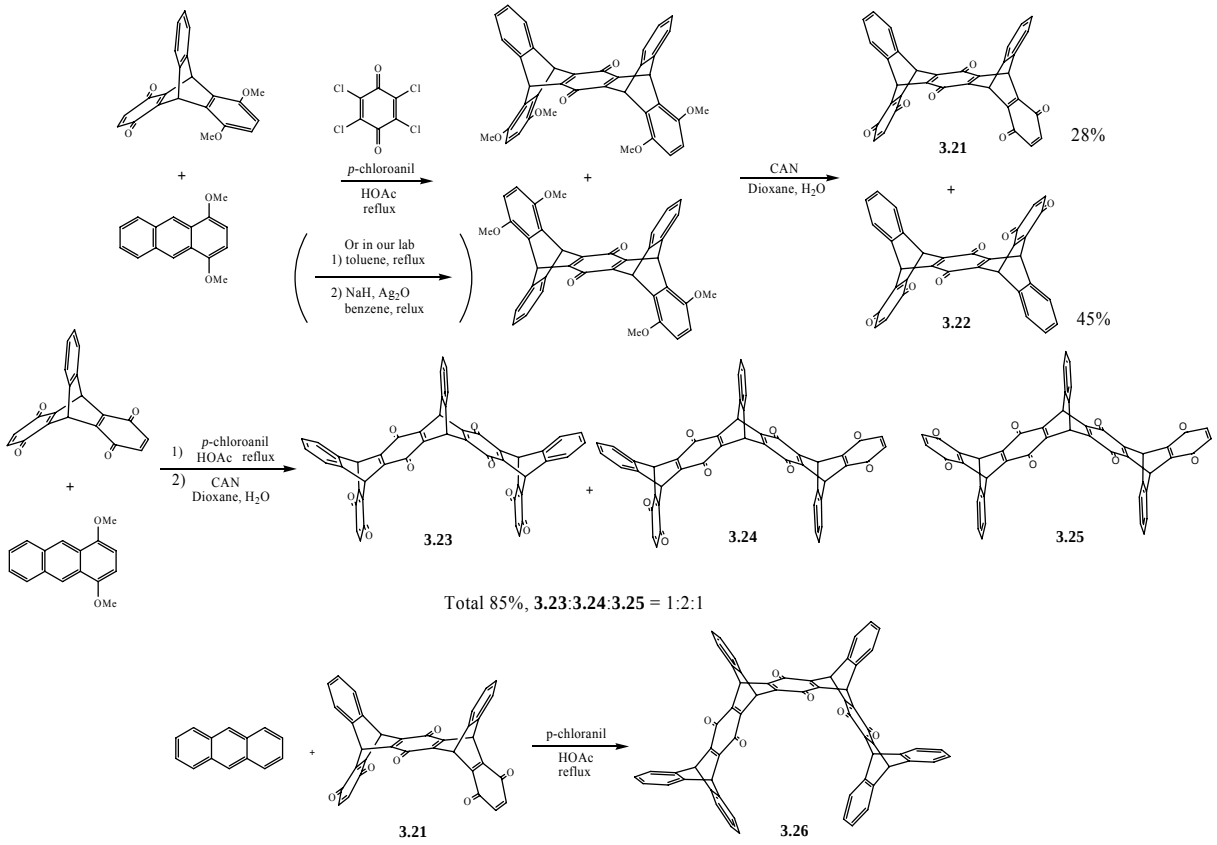


Figure 3.5 iptycenequinones (except **3.20**)



Scheme 3.2 Synthesis of iptycene quinones

The idea of extension of triptycene bisquinone framework was first reported by Iwamura, H. in 1982.[11] He found that triptycene bisquinone has lower electron potential than benzoquinone due to a transannular interaction in triptycene framework. An extended system would expected to show "higher electron affinity and therefore serve as a novel electron acceptor." [11] He then synthesized a series of iptycene quinones (**3.19**, n = 1, 2, 3). It was found that extension of framework does stabilized the 1:2 complex with electron rich 2-(1,3-dithiol-2-ylidene)-1,3-dithiole (**3.20**) especially for compound **3.23**. However, no detailed synthetic routes or structural identification data were provided. Higher iptycene quinones (**3.19**, n = 4, 5) in all *cis*-configuration have not been reported. They contain more units of triptycene bisquinone in a circular form and are predicted to be even better electron acceptors.

It was not until recently a detailed synthesis of higher iptycene quinones was reported by Zhu et.al.[9] Interestingly, their syntheses were more like replica of the simple triptycene bisquione since basically they follow exactly the same reaction sequences. The higher iptycene quinones were synthesized from simpler iptycene quinones and anthracenes just as triptycene bisquinone were synthesized form 1,4-benzoquinone and 1,4-dimethoxyanthracene: a two step synthesis started from an one-pot Diels-Alder–enolization–oxidation reaction followed by another oxidative demethoxylation reaction using CAN as reagent as shown in **Scheme 3.2**. In the first step, the Diels-Alder adducts formed *in situ* were enolized in acetic acid media to form phenols, which was quickly oxidized to quinone rings by *p*-chloroanil. However, a mixture of possible products was formed and it is usually difficult to separate them in this stage. This will increase the task of separation of different products in the final CAN oxidation.

In our lab, we independently synthesized pentiptycene trisquinone **3.21** and **3.22** (LK-4-064, LK-4-070) before the publication of Zhu's paper. We did Diels-Alder reaction in refluxing toluene. Adducts were first separated and then enolized and oxidized in a refluxing benzene with sodium hydride and silver oxide as shown in **Scheme 3.2**. The stepwise method in our lab may seem tedious because of the extra step. It gave the opportunity to separate individual Diels-Alder adduct and identify their structures. Later, we found Diels-Alder adducts containing inherent structural indicators in ^{1}H NMR spectum, which were proved to be very useful to determine the structure of iptycenequinones derived from them. Besides, using a pure single Diels-Alder adduct for later steps would give only one iptycenequinone as product and thus reduced the purification demand in later steps.

3.2.1.3 Properties and applications of iptycene and iptycene quinones

1) Intramolecular charge transfer study.

Charge transfer is a behavior of a partial electronic charge transfer from an electron donor to an electron acceptor in an excited state when these two groups are close to each other. A new and strong band can be observed in UV-Vis spectrum due to charge transfer interaction. Iptycene structure provides unique alignments of electron donors and acceptors for the study of transannular charge transfer behavior.[12-14]

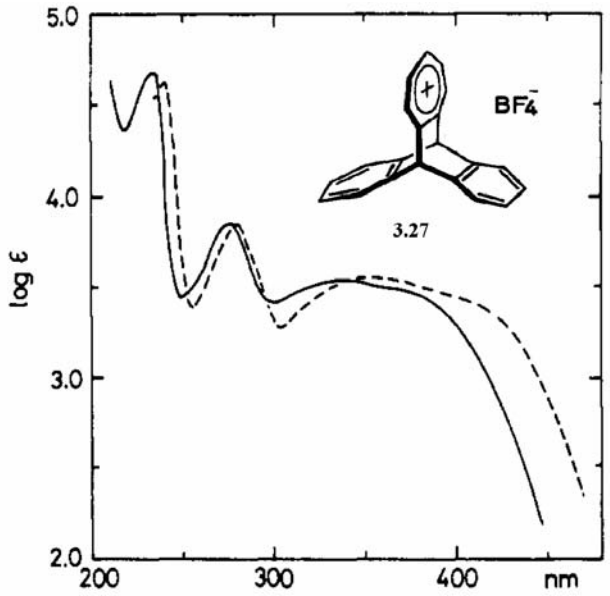


Figure 3.6 Electron spectrum of 9, 10-dihydro-9, 10-(1,2-tropylio)anthracene tetrafluoroborate (**3.27**) in CH_3CN(—) and CH_2Cl_2(---).
(Taken from reference[12] without permission)

The first spectrum evidence of the existence of transannular charge-transfer interaction in the tripycene framework was reported by Murata et.al in 1977.[12] The new broad absorption band at 300~450 nm was formed due to a charge-transfer interaction between tropylium ion and benzene rings. The red-shift of the band from solvent acetonitrile to solvent methylene chloride agreed with that of a charge-transfer band.

A year later, Iwamura et al. reported a new triptycene system incorporated a *p*-benzoquinone ring as the acceptor and a hydroquinone ring as the donor.[13] The observed λ_{max} of charge-transfer band in DMSO is 430 nm, which is almost comparable to that of quinhydrone.[13] The strong charge-transfer band could not be explained simply by the through space interaction between the hydroquinone and *p*-benzoquinone rings in a dihedral angle of 120^o alone. A

through-bond homoconjugation model was proposed by the author as shown in **Figure 3.7**. The carbon-carbon σ orbitals in [2.2.2] bicyclic ring bridge have both high *p*-character and off-center bent bond nature, which facilitate their interaction with π orbital of nearby donor and acceptor rings.[13]

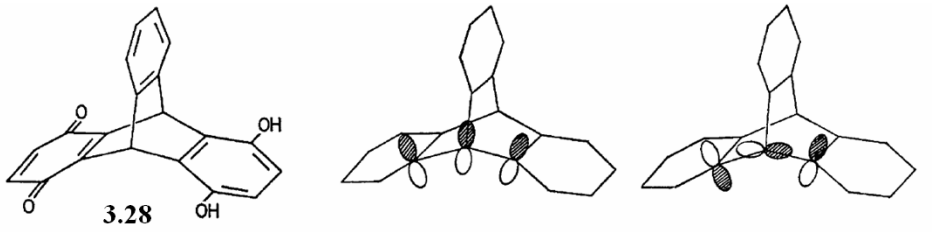


Figure 3.7 Through-bond homoconjugative interaction between hydroquinone and *p*-benzoquinone rings in a triptycene framework.
(Taken from reference[13] without permission)

Murata studied the other two triptycene systems in **Figure 3.8** by focusing the effect of different substitution in the electron donating moiety to the wavelength of charge transfer band.[14] It was found that 5- or 8- substituents showed little effect to λ_{max} of charge-transfer band, while electron donating 6- or 7- substituents caused a significent red-shift, which was rationalized by orbital symmetry analysis.

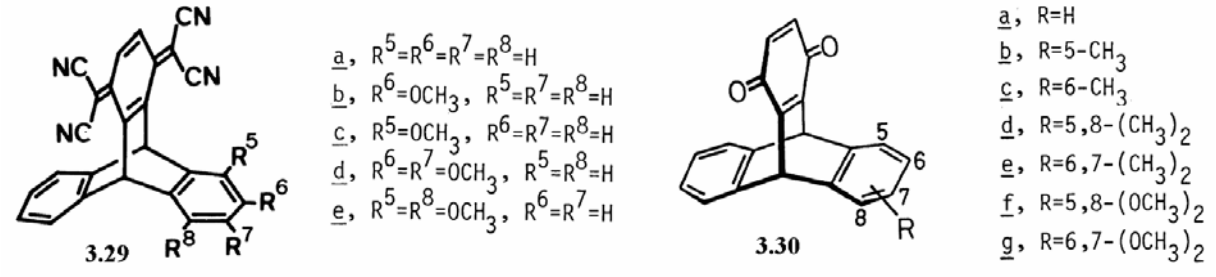


Figure 3.8 Two other triptycene systems with transannular charger-transfer interaction studied by Murata.[14]

2) Photoinduced electron transfer study.

Photoinduced electron transfer (PET) is the key process in photosynthesis, during which light energy is converted to an electronic potential energy due to the separation of charges. Many synthetic PET models containing an electron donor chromophore such as porphyrin linked to acceptor moietie such as quinones in a molecule have been reported.[15]

The rigid structure of iptycene quinones together with the adjustable number of quinone rings and their distances to the donor chromophore make them an ideal acceptor to study the

influence of such factors to PET activities.[16-18] Some reported PET systems with triptycene quinones and pentiptycene quinones are shown in **Figure 3.9**.

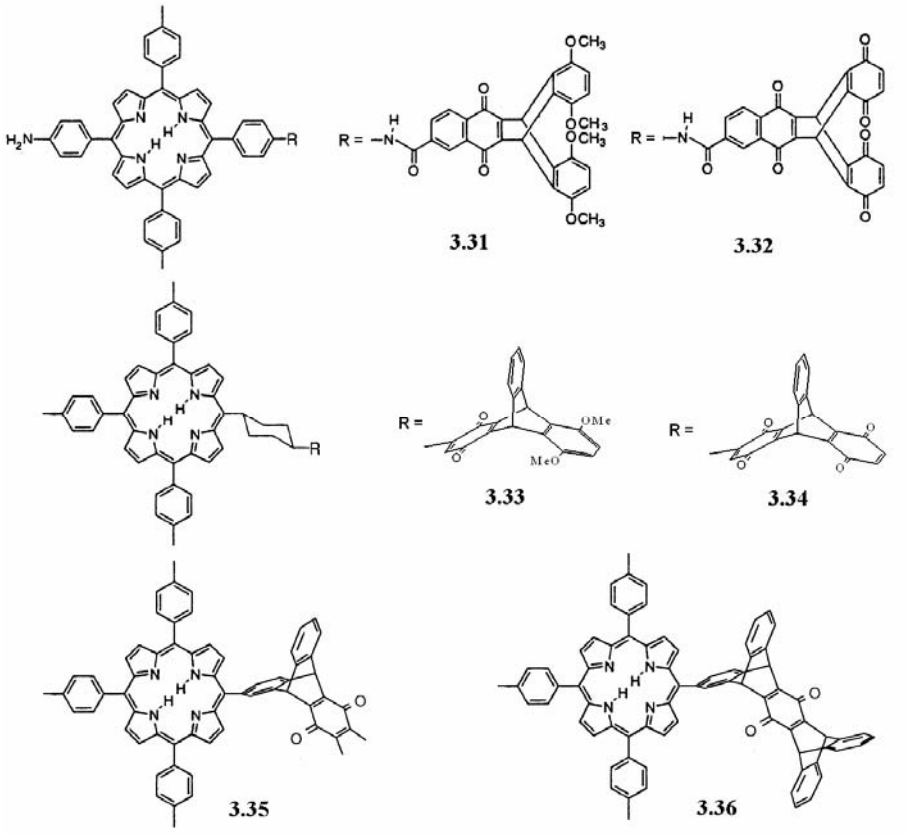


Figure 3.9 Iptycenequinones as electron acceptor in photoinduced electron transfer studies.[17, 18]

3) Intermolecular charge transfer interactions of iptycene quinones with electron donors.

Besides the above intramolecular charge transfer interactions, iptycene quinones form charge-transfer complex with small organic electron donors in solution. Iwamura et al. reported triptycene bisquinone (**3.17**) and *cis,cis,cis*-heptiptycene tetraquinone (**3.23**) formed a 1:2 complex with 2-(1,3-dithiol-2-ylidene)-1,3-dithiole (TTF, **3.20**) in methylene chloride. From theromo-dynamic data listed in **Table 3.1**, compound **3.23** is a better electron acceptor. In a higher TTF concentration, a 1:3 or even 1:4 complexes were formed for **3.23**.[11]

	λ_{CT}(nm)	-ΔH(KJ mol^{-1})	-ΔS (J deg^{-1}mol^{-1})	-ΔG (KJ mol^{-1})
3.17•2TTF	760	37.7 ± 0.4	90.0 ± 1.5	10.4 ± 0.1
3.23•2TTF	774	45.1 ± 2.0	104.6 ± 6.5	13.5 ± 0.6

Table 3.1 Thermodynamic constants for **3.17**•2TTF and **3.23**•2TTF complexes in CH_2Cl_2.[11]

4) Iptycene-containing poly(*p*-phenyleneethynylene)s (**PPE**s) and poly(iptycene)s

Ipytcene-containing polymers have been mainly investigated in Swager's group at MIT since 1998.[19-27] Most of their work is focused on iptycene-containing **PPE**s, which are conjugated polymers with a backbone of alternating benzene rings and acetylenes. Examples of **PPE**s (**3.37**) and iptycene-containing **PPE**s are shown in **Figure 3.10**. In **PPE**s, more efficient electron delocalization and excition migration along polymer backbone allows amplified sensory responses compared with small-molecule-based sensors.[28] However, the usefulness of **PPE**s in thin films is offset by low fluorescence quantum yields due to π-π stacking and interchain excimer/exciplex formation, which also causes a substantial red-shift relative to solution values in the absorption and fluorescence spectrum (**3.37** in **Figure 3.11**). Incoporation of rigid iptycenes in **PPE**s have been found to reduce interchain interactions by spatial isolation of polymer backbones. Thus iptycene-containing **PPE**s show improved photoluminescent stability and quantum yields in the solid state.[20] Correspondently, little or no redshifts in thin film relative to solution values would be found in the absorption and fluorescence spectra. In addition, the "internal free volume" in iptycene moieties provides additional channel-like cavities to facilitate rapid analytes diffusion and achieve faster signal responses (**Figure 3.12**). Also, the insertion of iptycene units into a polymer backbone also lowers its dielectric constant,[24] increases its solubility[25] and improves mechanical properties.[29] Ipytcene containing **PPE**s are potential sensory materials for detecting TNT.[19, 20]

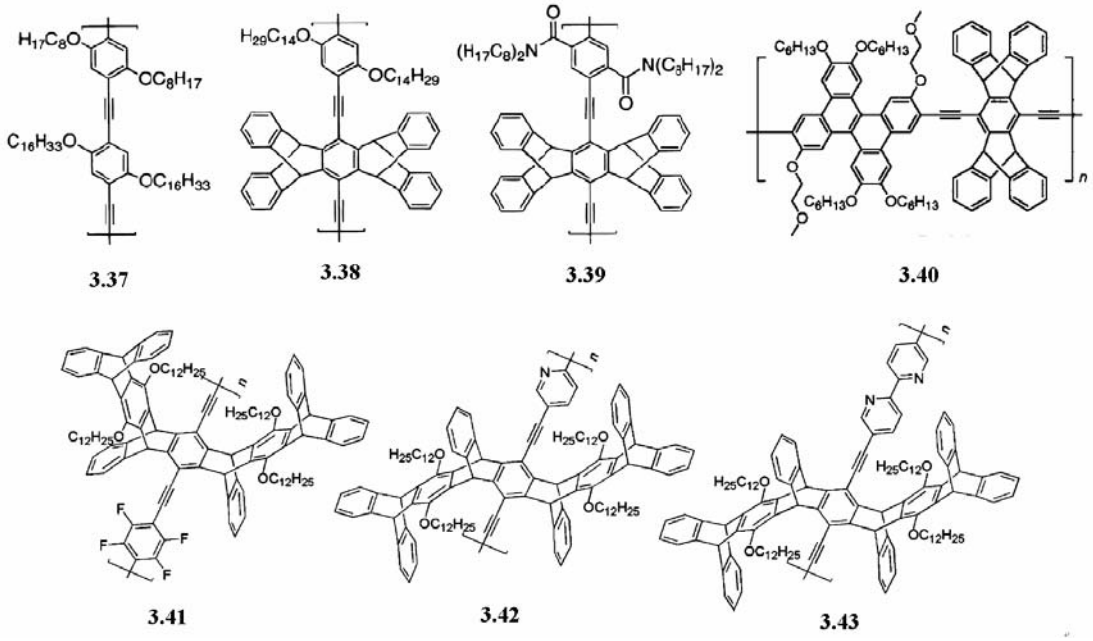


Figure 3.10 Iptycene-containing poly(*p*-phenyleneethynylene)s (**PPE**s)[20, 22, 25, 30]

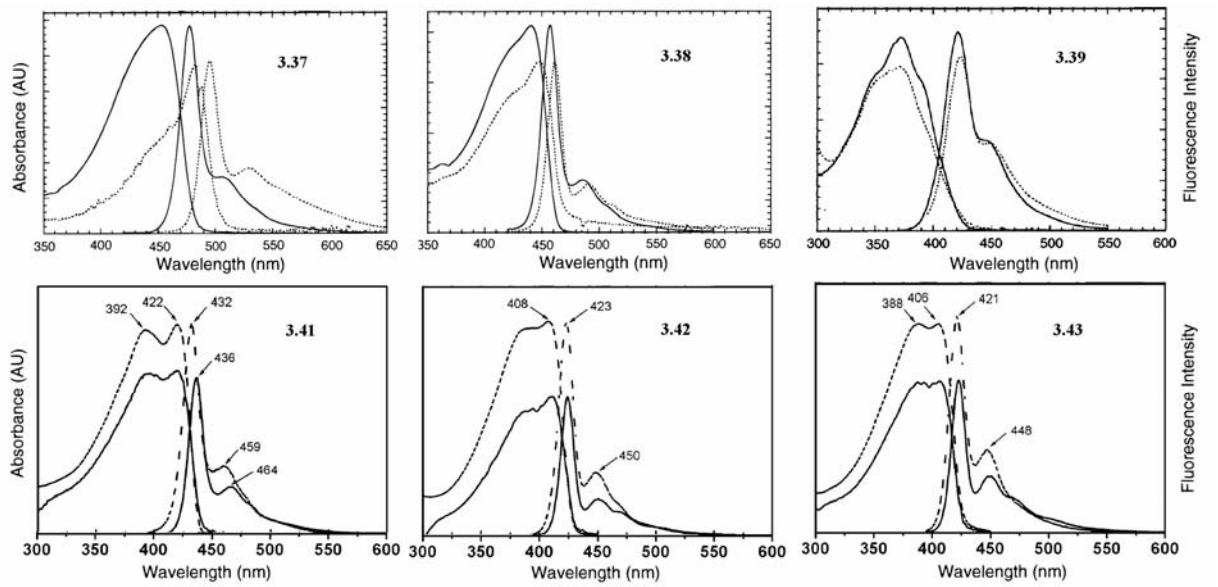


Figure 3.11 Absorption and fluorescence spectra of **3.37**, **3.38**, **3.39** in methylene chloride and **3.41**, **3.42**, **3.43** in chloroform (dash line) and thin films (solid line)[19, 20, 25]
(Taken from reference[19, 20, 25] without permission)

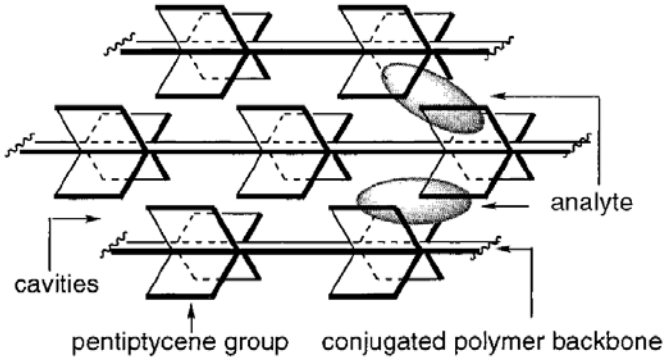


Figure 3.12 Iptycene-containing poly(*p*-phenyleneethynylene)s (**PPE**s) show channel-like cavities [20] (Taken from reference [20] without permission)

Schanze's group reported a platinum acetylide polymer (**3.46**) containing penticene units in the polymer backbone (**Figure 3.13**).[31] Platinum acetylide polymers, such as **3.45**, display phosphorescence at room temperature due to their high efficient intersystem crossing. The optical properties of two polymers **3.45** and **3.46** were studied both in solution and in the solid state. Similar results were drawn. Polymer **3.45** showed phosphorescence emission from an interchain aggregate in solid state, while dominating intrachain phosphorescence emission were observed for polymer **3.46**.

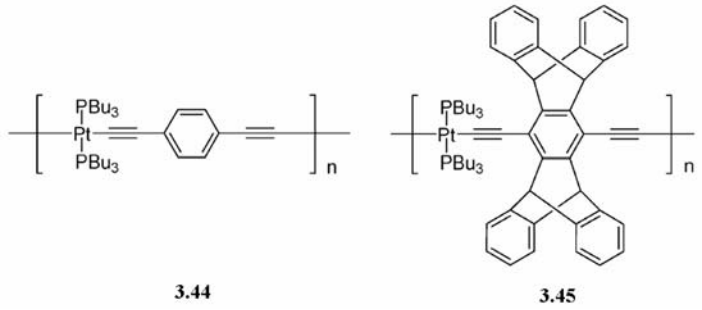


Figure 3.13 Structure of a penticene containing platinum acetylide polymer **3.44** and its parent polymer **3.45**

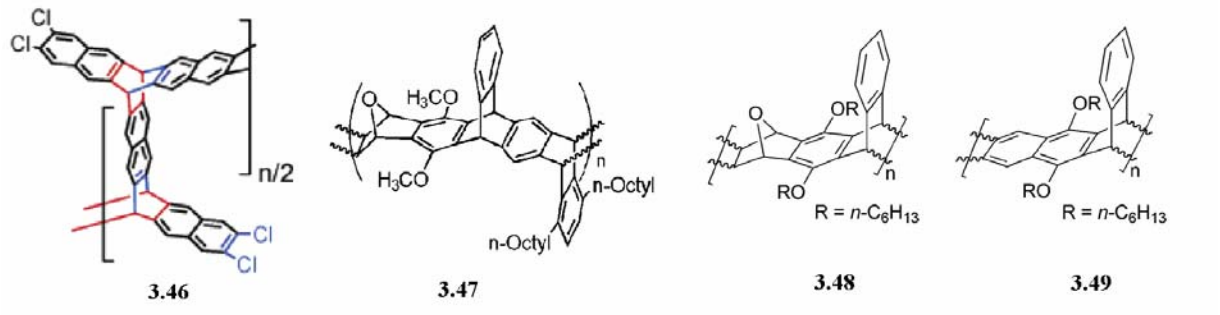


Figure 3.14 Poly(iptycene)s

Another type of iptycene polymers reported are poly(iptycene)s, which contain iptycene units in a extended ladder-like double strand structure (**Figure 3.14**).[27, 32, 33] The unique shape-persistent structure and high free volume inside the polymer has been utilized as a "threading" host for other linear polymer molecules. The polymer **3.47** was found to "align perpendicular to strech-aligned PVC".[33]

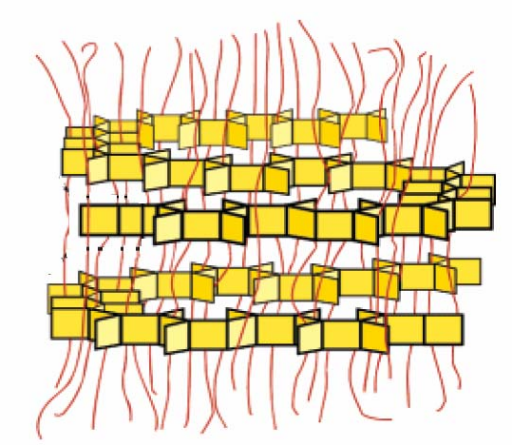


Figure 3.15 Perpendicular alignment of poly(iptycene) **3.45** with stretch-aligned PVC molecules. [33] (Taken from reference [33] without permission)

5) Other properties and applications.

Other properties and applications which have not mentioned above are listed below. First, iptycenes have high melting points and thermal stability, and they could be used in heat-resistant materials.[1] Second, their packing behaviors in crystal structures[34-36] and self-assembly behavior on metal surface[37] have been studied recently, which will further our understanding the interaction of these molecules in microscopic level. Third, their rigid structures have been used to design molecular gate[38] or molecular probe for Cu(II) ion.[39] Moreover, triptyenes have been used as molecular gears, which will be discussed in the coming section. Furthermore, triptycene bisquinone derivatives showed anticancer and antimalaial activities and other bioactivities.[40-42]

Overall, most of reported research on iptycenes were based on triptycenes and pentipycenes systems. There were limited reports on heptipycene and noniptycene derivatives and their applications. No higher iptycene derivatives and cycloiptycenes have ever been synthesized and reported. The synthetic effects to cyclododeciptycenehexaquinone (**3.1**) will bring a series of higher iptycene derivatives, which are expected to show interesting electronic and optical properties and potential applications in supramolecular chemistry and material chemistry due to both their unique structure and properties.

3.2.2 Molecular Gears

3.2.2.1 Molecular gears and their functions

The targeted molecule cyclododeciptycenehexaquinone (**3.1**) forms a perfect molecular gear with a macropolycyclic ring incorporated six *p*-benzoquinonone as the shaft and six benzene rings as teeth. It would be expected to have a potential application as a building part in a molecule machine just as its macroscopic counterparts are important building parts in a machine such as a car or a watch in our daily life. Gears mainly play three functions: 1) transferring the information about the direction of rotation, 2) adjusting the speed of rotation, 3) changing rotational axis.[43] For the first function, as illustrated in **Figure 3.16**, in a molecular gear system **3.50** reported by Bryan et.al.,[44] or a more complicated gear chain system **3.51** reported by Iwamura et.al.[45] the direction of rotation of two neighboring gears are opposite. In this fashion, the information of the directions of rotation is transferred from one end of the gear train to the other end depending on the number of gears (the number of reversion). The last two functions are seen in a molecular bevel gear system reported by Richards et. al.[46] as shown in **Figure 3.17**.

Not only the direction of rotational axis turned 90º from the small gear (triptycene) to the large gear, but also the speed of rotation are different. Since the number of teeth passed the joggle in a certain period of time are same for both gears, it takes the small gear less time to finish a round because it has less teeth attached to it. In other words, small gear rotates faster and big gear rotates slower in a gear system with their relative speed depending on the ratio of the number of teeth in each gear. Currently the number of teeth in a molecular gear can be two (aromatic amide gears), three (triptycenene molecular gears), and four (metallocene molecular gears). The cyclododeciptycene based molecular gears would be first 6-teeth gears in the molecular level.

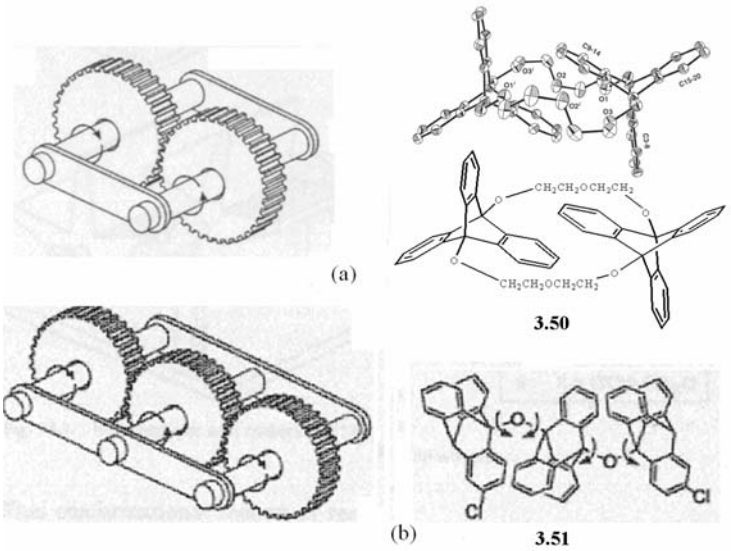


Figure 3.16 Transduction of the direction of rotation in molecular gears: a) two neighboring molecular gears with opposite directions of rotation.(the left picture is taken from reference[47] page 280 without permission, the right crystal structure from reference[44]) b) the transferring of the direction of rotations in a molecular train. (picture from reference[47] page 280 without permission)

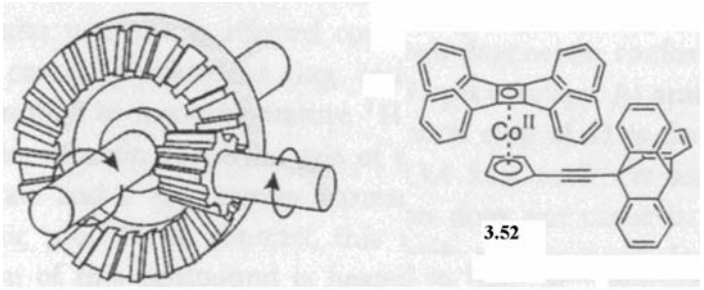


Figure 3.17 A macroscopic and a molecular bevel gear (taken from reference[47] page 280 without permission).

3.2.2.2 Study of rotation behavior of molecular gears.

The most important behavior associated to a molecular gear is its rotation, which is often studied by NMR method. In the gear systems based on triptycene and metallocenes, rotation barriers are usually small. For the simple molecular gear system **3.50**, both triptycene gears rotate very fast on the NMR timescale above 60 ^{o}C, since the aromatic region only show two peaks in NMR. When decreasing temperature, the rotation slows down, reflected by the broadening of aromatic peaks. Finally, under the temperature below -40 ^{o}C, individual sets of signals are seen in NMR.[44]

For the tristriptycene molecular gear train **3.51**, the two benzene rings on the triptycene outside have been labeled with Cl. Two phase isomers *meso*- and racemic *d*-/*l*- can be existed (**Figure 3.18**). It was calculated that the inner rotatory (gear-like rotation) barrier is no higher than 1 kcal/mol, whereas the gear slippage barrier was 43.2 kcal/mol by studying the conversion between two phase isomers in the temperature 238~332 ^{o}C.[48]

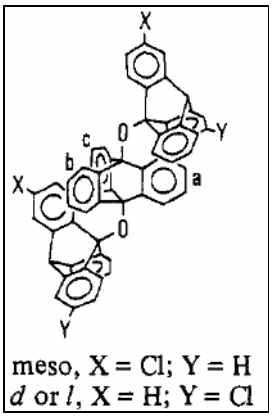


Figure 3.18 [45]

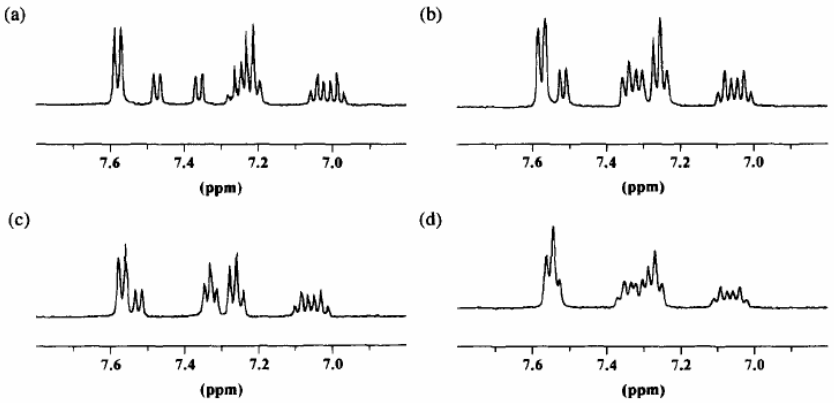
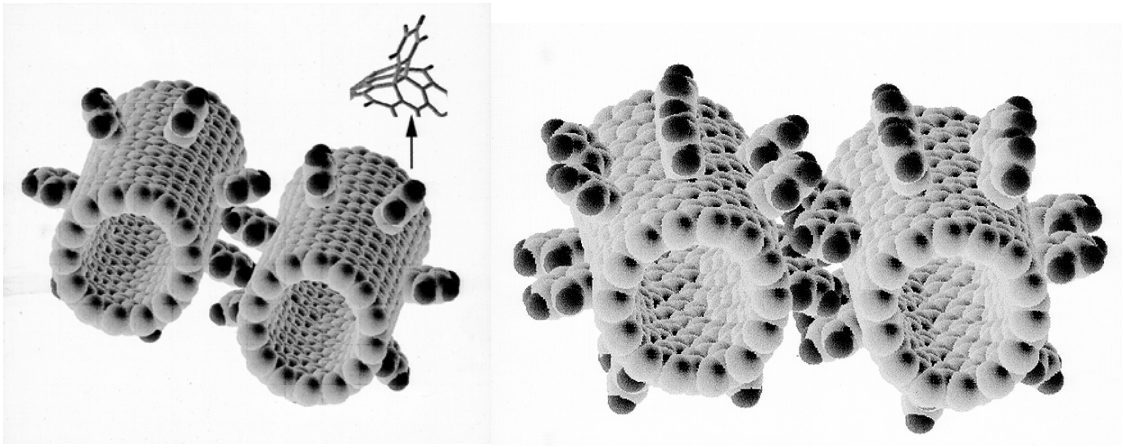


Figure 3.19 NMR of **3.52** at a) 260 K, b) 233 K, c) 220 K, d) 203 K (Taken form reference [45] without permission)

In the case of the molecular bevel gear **3.52**, the simplicity of the NMR peaks in the aromatic region shows the rotations are very fast for both gears on the NMR timescale at 260 K. Then in the spectrum at 203 K, the peaks are broadened a little, which means the ration is slower at lower temperature. (**Figure 3.19**)

Han et.al reported a computer simulation study of the rotation of carbon nanotube-based molecular gears by molecular dynamics.[49] One of the gears was first drove to rotate by charge separation caused by a laser in the simulation condition. The angular momentum was transferred to the other gear. The gears functioned well in the temperature range 600~1000 K with rotation

rates between 50~100 GHz. At higher temperature, these molecular gears did not work well due to the inefficient conversion of input energy to rotational motion.[49]



(a) (b)

Figure 3.20 a) Carbon [14,0]nanotube-based gears with benzyne teeth on every two six-membered ring. b) In-line multiple rows of teeth gears.[49] (Taken form reference [49] without permission)

3.3 Synthetic studies towards cyclododeciptycene based molecular gears

3.3.1 Retrosynthetic analysis of cyclododeciptycenehexaquinone

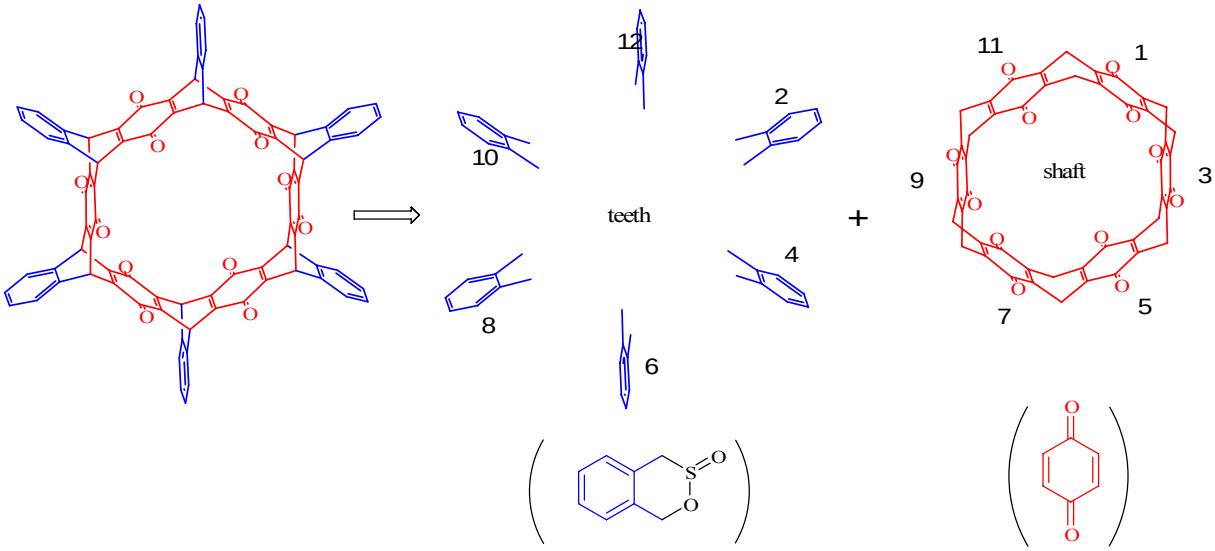


Figure 3.21

The target cyclododeciptycenehexaquinone molecule gear can be conveniently divided as teeth parts and shaft part. Teeth parts are simple benzene rings with two single bonds connected to the shaft, a [12]cyclacene based macropolycycle. For convenience, the six quinone rings in the shaft are named by numbers as 1, 3, 5, 7, 9, 11 according to a clock. The teeth are labelled as 2, 4, 6, 8, 10, 12clockwisely.

There are many different ways to break the molecule to different sizes of fractions in retrosynthetic analysis. For convenience, these small fractions or intermediates are categorized by the number of teeth remained in them. A list of possible intermediates is shown in **Figure 3.22**. Based on these synthetic intermediates, two strategic retrosynthetic routes could be proposed: stepwise and convergent.

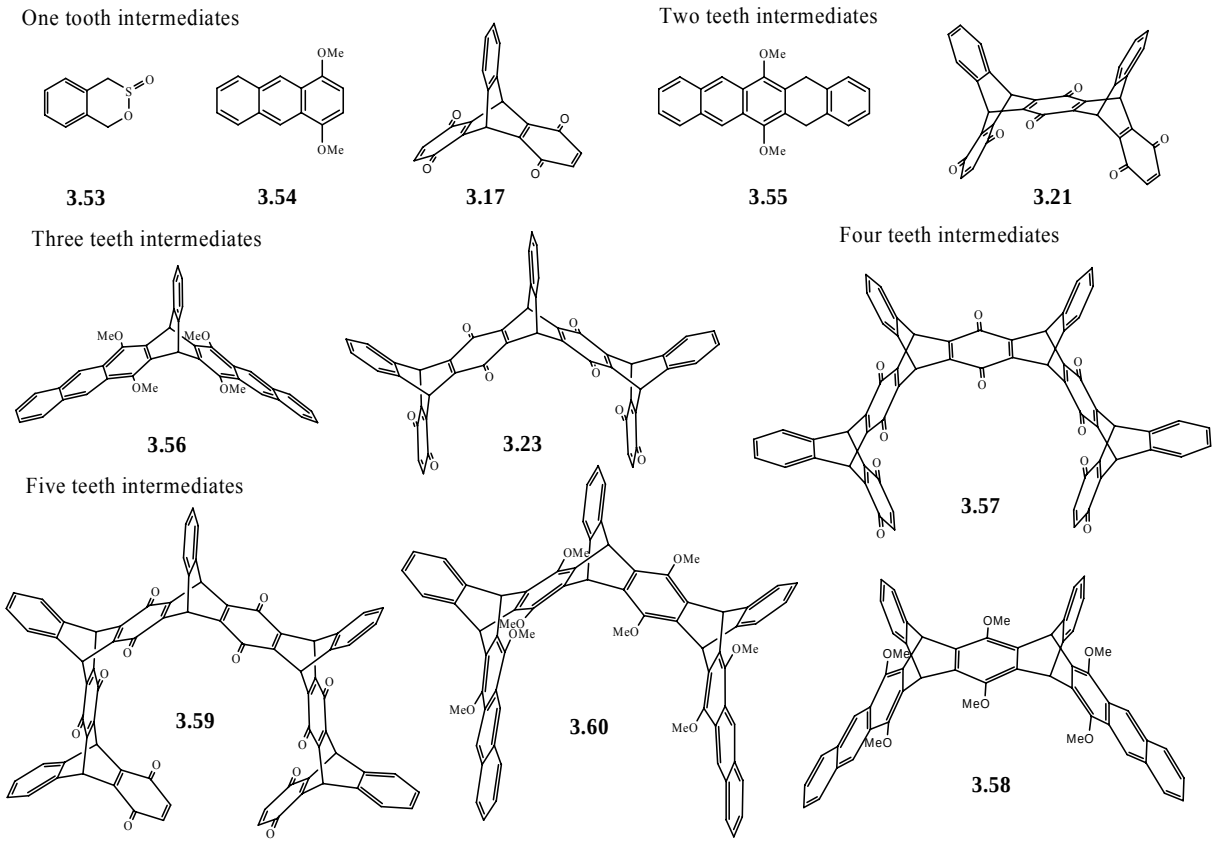
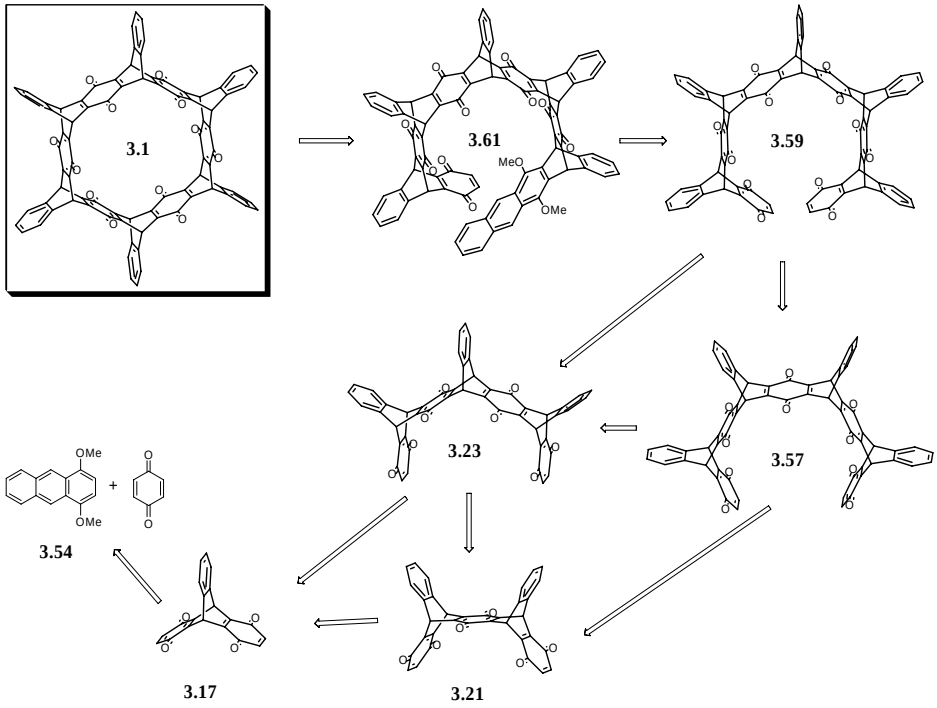


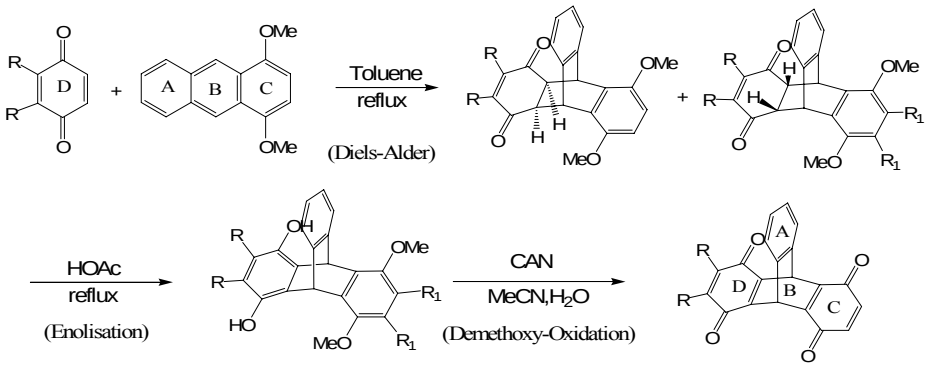
Figure 3.22 Synthetic intermediates for cyclododeciptycenehexaquinone with different number of teeth remained



Scheme 3.3 Proposed stepwise retrosynthetic analysis of cyclododeciptycenehexaquinone to iptycene quinones.

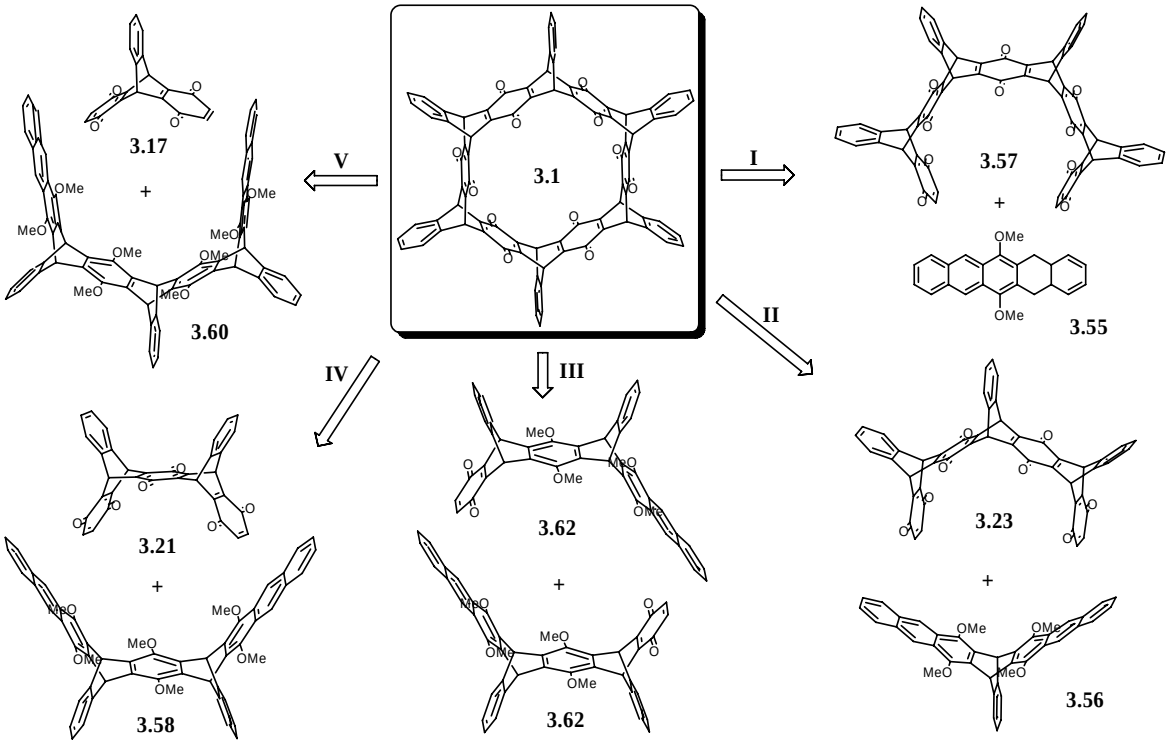
For the stepwise route, a retrosynthetic Diels-Alder transformation converts **3.1** to key synthetic intermediate **3.61** which contains a quinone end and a dimethoxyanthracene end. The disconnection position is between ring No.7 and ring No. 6. From intermediate **3.61**, one tooth is taken off to form 5-teeth intermediate **3.59** by an *o*-quinodimethane Diels-Alder transformation. Then, further teeth reduction transformation to take off either one tooth or two teeth at a time will convert *cis,cis,cis,cis*-undeciptycenehexaquinone **3.59** to lower iptycene quinones **3.57**, **3.23**, **3.21**, and **3.17**. Triptycene bisquinone **3.17** is synthesized from 1,4-dimethoxyanthracene and 1,4-benzoquinone. The transformation of increased teeth number starting from 1,4-benzoquinone to *cis,cis,cis,cis*-undeciptycenehexaquinone **3.59** is generalized in **Scheme 3.4**. One quinone end in an iptycenequinone or benzoquinone is first reacted with 1,4-dimethoxyanthracene, a one tooth intermediate, in toluene. The Diels-Alder adducts are separated and enolized in refluxing acetic acid (sometimes catalyzed by hydrobromic acid). The final oxidative demethoxylation by CAN gives a new iptycenequinone with one more tooth. For iptycene quinone with two quinone ends, two teeth are added if the first Diels-Alder reaction using excess amount of 1,4-dimethoxyanthracene. Theoretically, 5-teeth intermediate **3.59** can be

synthesized in nine steps from 1,4-dimethoxyanthracene and 1,4-benzoquinone through three repititive tooth expansion transformation cycles.



Scheme 3.4 Tooth expansion transformation

For the convergent route, cyclododeciptycenehexaquinone (**3.1)** are retrosynthetically split into two parts, one bisdienophile intermediate such as iptycene quinone. (**3.57**, **3.23**, **3.21**, **3.17**) and one bisdiene tweezer-like intermediate (**3.55**, **3.56**, **3.58**, **3.60**) or two identical three teeth intermediate (**3.62**) which contain both quinone ring and 1,4-dimethoxyanthracene moiety as shown in **Scheme 3.5**. The bisdiene intermediate can be synthesized from corresponding quinone through *o*-quinodimethane Diels-Alder reaction as key transformation. (**Scheme 3.17**)



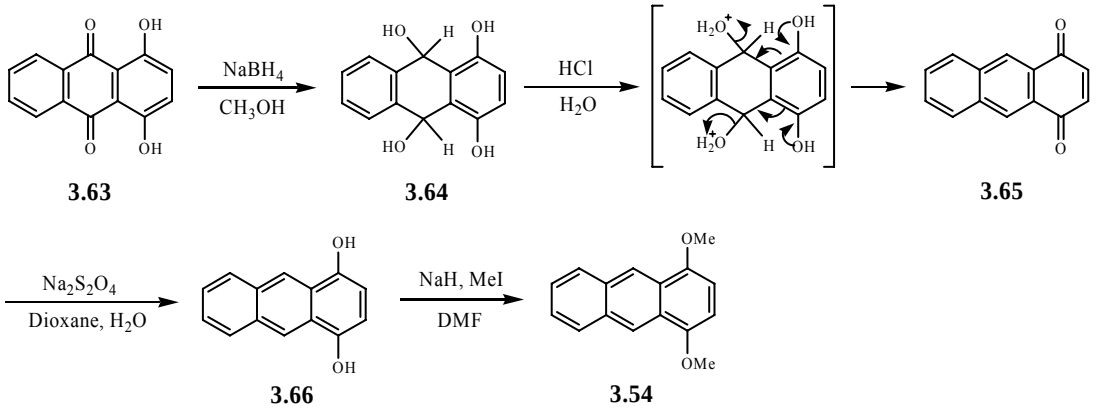
Scheme 3.5 Proposed convergent retrosynthetic analysis of cyclododeciptycenehexaquinone

3.3.2 Synthesis of iptycenequinones

From retrosynthetic analysis, the key intermediates towards the cyclododeciptycene-hexaquinone are iptycenequinones (**3.17**, **3.21**, **3.23**, **3.57**, **3.59**). The prior three of them are known compounds. The latter two have never been synthesized before. The general synthetic strategy follows the tooth expansion transformation outlined in **Scheme 3.4**.

3.3.2.1) Synthesis of 1,4-dimethoxyanthracene (**3.54**)

1,4-Dimethoxyanthracene (**3.54**) is an important one-tooth building block for iptycenequinones. 1,4-dimethoxyanthracene was synthesized from commercially available quinizarin (**3.63**) in three steps.[41] First, quinizarin was reduced with sodium borohydride in methanol at 0^{o}C for 4 hours and then quenched with hydrochloric acid to afford 95% of 1,4-anthracenedione. The reaction mechanism was shown in **Scheme 3.6**. The addition of hydride to the quinone ring to form a tetraol intermediate, which was protonated in acidic condition and underwent elimination of water to form 1,4-anthracenedione (**3.65**). Then 1,4-Anthracenedione (**3.65**) was treated with sodium hydrosulfite in a 1:1 mixture solvent of water and dioxane at room temperature for 10 hours. The 1,4-anthracenediol (**3.66**) was obtained in 82% yield and further methylated in dry DMF solution using sodium hydride as base and methyl iodide as methylation agent to give 1,4-dimethoxyanthracene (**3.54**) in 65% yield.



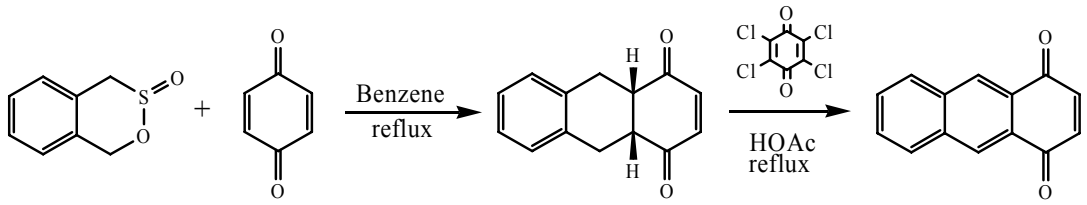
3.63 **3.64** **3.65**

3.66 **3.54**

Scheme 3.6 Synthesis of 1,4-dimethoxyanthracene, an important one-tooth building block

The 1,4-anthracenedione (**3.65**) can also be synthesized starting from 1,4-dihydro-2,3-benzoxathiin-3-oxide (**3.67**) and 1,4-benzoquinone as shown in **Scheme 3.7**. The sultine **3.67** was refluxed in an excess amount of 1,4-benzoquinone in dry benzene for 2 hours. The monoadduct **3.68** was obtained in a yield of 39% after crystallization of the crude mixture from methanol.[50] Then **3.68** was enolized and oxidized in refluxing acetic acid with choranil to get

quantitative yield of 1,4-anthracenedione. This route is not economically better than the route mentioned above, but it shows that the 1,4-dimethoxyanthracene can be synthesized from even smaller building blocks **3.67** and 1,4-benzoquinone. All the iptycenequinones (**3.17**, **3.21**, **3.23**, **3.57**, **3.59**) and the target cyclododeciptycenehexaquinone (**3.1**) are retrieved back to simple one-tooth component (**3.67**) and shaft component (1,4-benzoquinone) in synthesis (**Figure 3.21**).



3.67 **3.68** **3.65**

Scheme 3.7 Another route to 1,4-anthracenedione

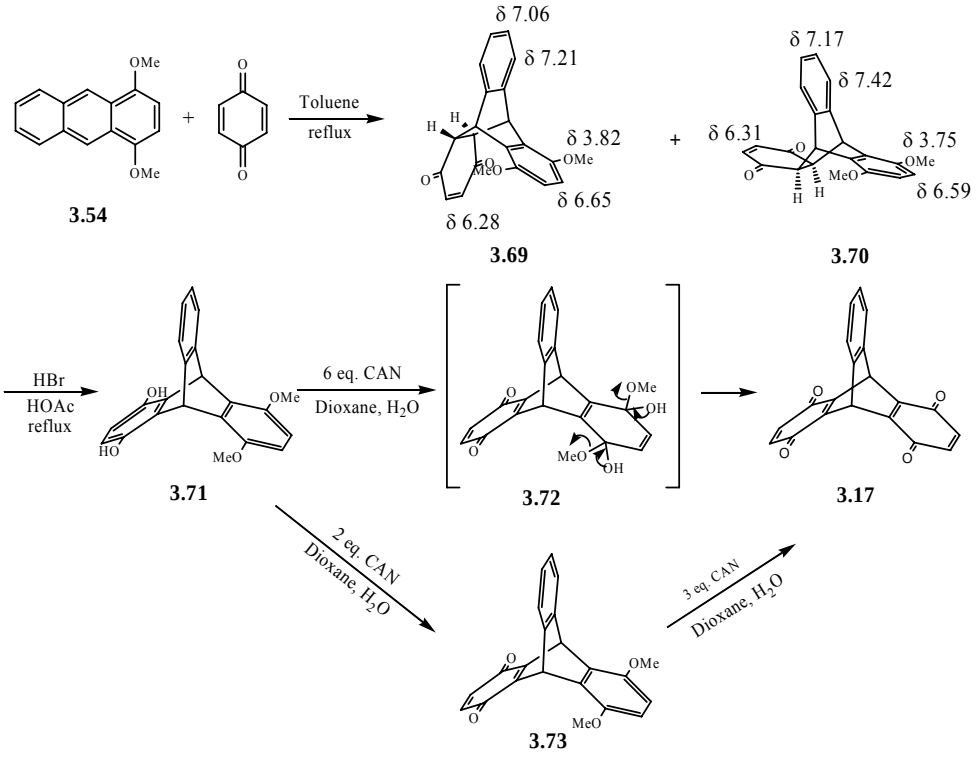
3.3.2.2) Synthesis of triptycene bisquinone (**3.17**)

The synthesis of triptycene bisquinone was first reported by Iwamura in 1978 starting from 1,4-dimethoxyanthracene and 1,4-benzoquinone.[13] We modified the procedure with basically the same reaction sequence described in **Scheme 3.4**. First, the Diels-Alder reaction of 1,4-dimethoxyanthracene and 1,4-benzoquinone in refluxing toluene for 36 hours afforded a mixture of 1:1 *endo*- and *exo*-adducts (**3.69**, **3.70**) in a yield of 96%. The two adducts were partially separable in column chromatography and they can be differentiated by chemical shifts in ^{1}HNMR. It was predicted the chemical shift of methoxy protons of *endo*-adduct should be larger than that of *exo*-adduct, since the methoxy groups in *endo*-adduct are closer to electronegative carbonyl oxygen atoms, as are protons on the 2,3-position of dimethoxybenzene ring. On the contrary, the chemical shift of protons in half-quinone rings of *endo*-adduct should be smaller than that of *exo*-adduct due to the better shielding effect of 1,4-dimethoxybenzene ring in *endo*-adduct compared to benzene ring in *exo*-adduct. The less polar one is believed to be *endo*-adduct **3.69** from its ^{1}H NMR spectrum compared to that of more polar one. Some chemical shifts of two isomers were given in **Scheme 3.8**.

The adducts (**3.69**, **3.70**) were then treated with refluxing acetic acid with a catalytic amount of hydrobromic acid for 10 minutes. An offwhite solid was then precipitated. Simple filtration will give enolized intermediate **3.71** in 87% yield.[42] The enolisation could be done in basic conditions using potassium hydroxide in aqueous dioxane reported by Iwamura.[13] Previous work in our lab showed that the basic condition gave 82% yield of **3.71** after extra acidic workup.

(Reference[51], page 88) Apparently, the acidic conditions gave better yield and an easier procedure. Moreover, based on mechanism, α-protons of carbonyl group were first deprotonated by hydroxyl anion in basic condition to form enolate. This was sometimes difficult because of steric hindrance of the carbonyl α-proton. In acidic condition, there would no such problem because the enolisation is catalyzed by the protonation of more open carbonyl group.

Finally, oxidative demethoxylation of intermediate **3.71** using excess amount of cerium ammoniuim nitrate (CAN) in a mixture of dioxane and water at room temperature for 5 hours gave triptycene bisquinone (**3.17**) in 93% yield. According to the mechanism proposed by Jacob et.al., a bis-methoxyhemiacetal intermediate **3.72** was formed and then methoxy groups was cleaved to form quinone ring.[52]



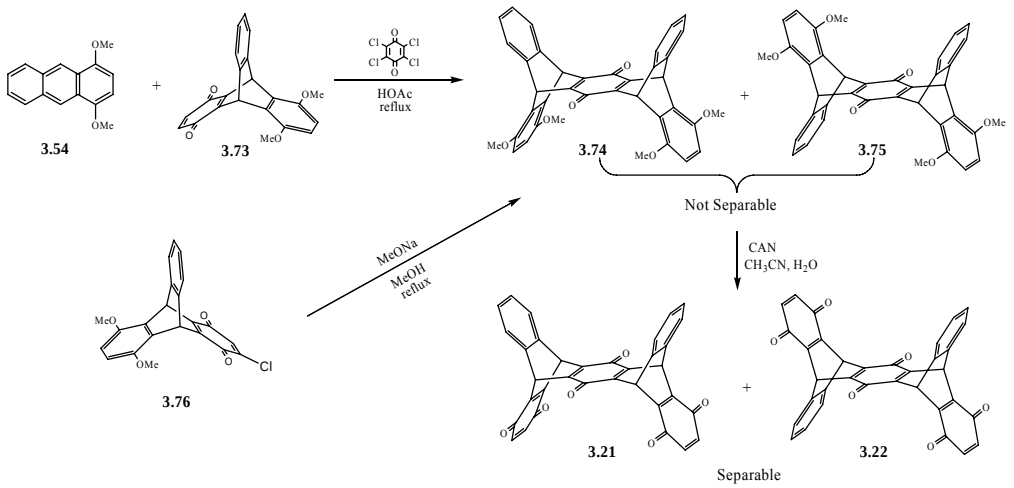
Scheme 3.8 Synthesis of triptycene bisquinone

When 2 eq. of CAN was used instead of 6 eq. in the same reaction condition, dimethoxytriptycene monoquinone **3.73** was formed predominantly because of the much faster rate of phenol oxidation compared to the oxidative demethoxylation of the 1,4-dimethoxybenzene ring. The intermediate **3.73** is synthetically useful as triptycenebisquinone equivalence with one quinone end protected as 1,4-dimethoxybenzene. Compound **3.73** was also

synthesized in one pot by treating the Diels-Alder adducts **3.69** and **3.70** with sodium hydride and silver oxide in refluxing benzene and THF in our lab. (Reference[53], page 57)

3.3.2.3) Synthesis of cis-pentiptycene trisquinone (**3.21**)

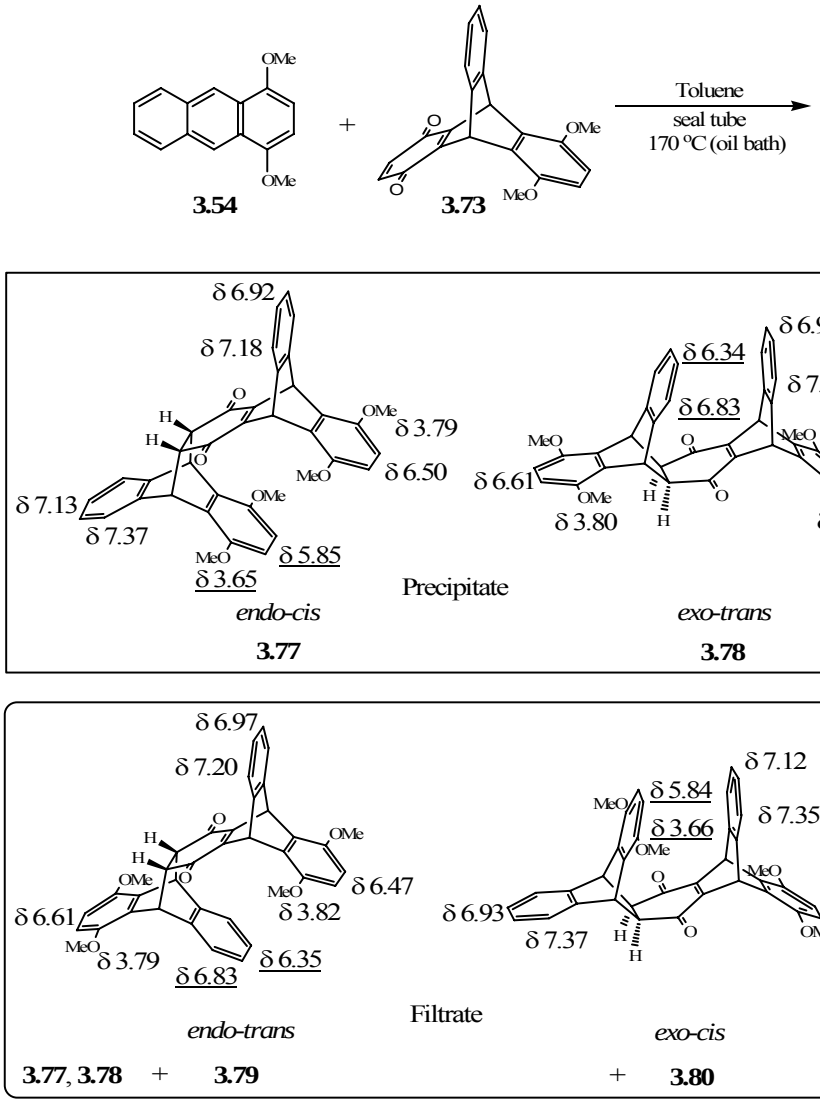
The synthesis of *cis*-pentiptycene trisquinone (**3.21**) has been reported by two other groups.[9, 54] In the recent Zhu and Chen's paper,[9] a modified procedure was taken as shown in **Scheme 3.9**. First, the Diels-Alder reaction of 1,4-dimethoxyanthracene and the dimethoxytriptycene monoquinone **3.73** in refluxing acetic acid with *p*-chloranil as oxidizer afforded a mixture of **3.74** and **3.75** in a yield of 82%. Compounds **3.74** and **3.75** were not separable and used as a mixture for CAN oxidation. Two pentiptycene trisquinones were formed in a yield of 28% and 45% for *cis*-isomer (**3.21**) and *trans*-isomer (**3.22**) respectively, which were separable by column chromatography. The shortcoming of their synthesis was the wanted *cis*-isomer was obtained as minor product. In the other paper by Spyroudis et al., even less yield of the similar synthesis was reported.[54] They also reported an unusual route to compounds **3.74** and **3.75** by reaction of dimethoxytriptycene choloquinone (**3.76**) with sodium methoxide in refluxing methanol with impractical yield of 10%.



Scheme 3.9 Literature syntheses of *cis*-pentiptycene trisquinone

Before the publication of Zhu's work, we synthesized same intermediates **3.74** and **3.75** in two steps (**Scheme 3.2**).The four Diels-Alder adducts of 1,4-dimethoxyanthracene (**3.54**) and dimethoxytriptycene monoquinone (**3.73**) in toluene were first separated and then treated with sodium hydride and silver oxide in refluxing benzene to give a mixture of **3.74** and **3.75**. But the CAN oxidation gave an approximately 2:1 ratio of pentiptycene trisquinones in favor of *cis*-

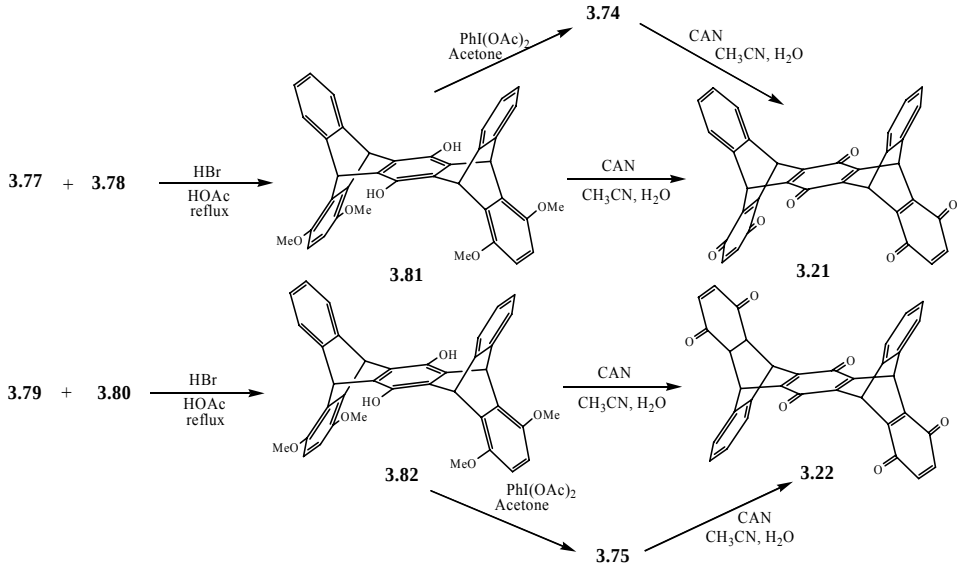
pentiptycene trisquinone (more polar spot in TLC). The only explanation was that the mixture of **3.74** and **3.75** synthesized in our lab have a higher portion of **3.74**.



Scheme 3.10

Later, we modified the synthesis of *cis*-pentiptycene trisquinone. The Diels-Alder reaction of dimethoxytriptycene monoquinone (**3.73**) with 3 eq. of 1,4-dimethoxyanthracene (**3.54**) underwent at 170°C (oil bath temperature) in a sealed tube using dry toluene as solvent for 36 hours. The yellow precipitate was collected by filteration to give 44% yield of a mixture of only two adducts (about 7:3 ratio), which were identified as *endo-cis*-adduct (**3.77**) and *exo-trans*-adduct (**3.78**) based on both NMR methods and derivtization. The filtrate was concentrated and purified by column chromatography (silica gel) to give another 49% yield of a mixture of

four isomers in a ratio of approximately 1:4:7:6 (*endo-cis*-adduct **3.77**, *exo-trans*-adduct **3.78**, *endo-trans*-adduct **3.79**, *exo-cis*-adduct **3.80**) from integrals in ^{1}HNMR. The calculated total yield of four adducts was 93% with 31% for **3.77**, 25% for **3.78**, 19% for **3.79**, 18% for **3.80** respectively. A mixture of two isomers **3.79** and **3.80** could be obtained from column chromatography followed by recrystalization.



Scheme 3.11

The ^{1}HNMR assignments of four adducts were given in **Scheme 3.10**. They were both deduced from the derivatization results and 2D-NOESY/COSY experments. For example, the precipitate containing two isomers only gave more polar *cis*-pentiptycene trisquinone after enolization and oxidative demethoxylation. From the structure of four possible adducts, we knew only *endo-cis* and *exo-trans*-adducts would give *cis*-pentiptycene trisquinone. Thus we knew which two isomers were in the precipitate. Then from the cross peaks in 2D-COSY and 2D-NOESY spectra, the chemical shift of each proton in two isomers could be identified. The upshifted chemical shift values were underlined. They are characteristic to the corresponding structural moiety, which were useful for identifying the structure of Diels-Alder adducts and their derivatized iptycenequinones.

With four Diels-Alder adducts identified, the synthesis of *cis*-pentiptycene trisquinone could be started either from two isomers (**3.77**, **3.78**) or four isomers. Enolisation of adducts in refluxing acetic acid with a catalytic amount of hydrobromic acid gave over 90% yield of tetramethoxypentiptycene monophenol (**3.81** or a mixture of **3.81** and **3.82**). Then CAN

oxidation in aqueous acetonitrile gave over 80% yield of pentiptycene trisquinone (**3.21** or a mixture of **3.21** and **3.22**).

In our synthetic route, the total yield of the three-step-synthesis of *cis*-pentitycene trisquinone was at least 40% compared to 23% yield of two-step synthesis reported by Zhu.[9] Also, pure intermediates **3.74** and **3.75** could be obtained using diacetoxyiodobenzene as oxidant from pure **3.81** or **3.82**, which were derivatized from a mixture of two adducts [(**3.77** and **3.78**) or (**3.79** and **3.80**)]. The tetramethoxypentiptycene monoquinone **3.74** and **3.75** are useful intermediates for derivatization as the middle quinone ring can be converted to many functional groups.[10]

3.3.2.4) Synthesis of cis,cis-heptiptycene tetraquinone (**3.23**)

cis, cis-Heptiptycene tetraquinone (**3.23**) was first reported in 1982,[11] however, its first detailed synthesis was only reported recently in a yield of 11% from triptycene bisquinone (**3.17**) by Zhu et al..[9] Their synthesis was a two step synthesis starting from a one-pot Diels-Alder-enolisation-oxidation reaction of triptycene bisquinone with excess amount of 1,4-dimethoxyanthracene in refluxing acetic acid in the presence of chloranil as oxidizer and then CAN oxidative demethoxylation to give a mixture of three heptiptycene tetraquinones in a ratio about 1:2:1 for *cis,cis*-(**3.23**), *cis,trans*-(**3.24**), *trans,trans*-(**3.25**) isomers respectively. (**Scheme 3.2**)

We tried a Diels-Alder reaction of triptycene bisquinone and 1,4-dimethoxyanthracene at 150 ^{o}C in a sealed tube using toluene as solvent for 2 days. To our surprise, a 1:1 ratio of two adducts (**3.83** and **3.84**) precipitated in 87% yield showed extraordinary face-selectivity in the Diels-Alder reaction. If we considered that two faces of triptycene bisquinone have no facial seletivity, there would be seven possible diadducts formed as shown in **Figure 3.23**. (This conclusion is also applied to iptycenequinone **3.21** and **3.23**)

So what is the face-selectivity and where does it come from? One would guess that since the *endo*-face contains two electron deficient quinone rings compared to only one in the *exo*-face. Thus *endo*-face would attract electron-rich 1,4-dimethoxyanthracene better based on charge-transfer interaction as discussed in the background part. Let's suppose the first equivalent 1,4-dimethoxyanthracene added from *endo*-face of anthracene bisquinone and blocked the second 1,4-dimethoxyanthracene molecule from adding to the same face. Because methoxy groups are electron-donating, the dimethoxybenzene ring (C ring, **Scheme 3.4**) has more electron density

than benzene ring (A ring, **Scheme 3.4**) in the 1,4-dimethoxyanthracene molecule, 1,4-dimethoxyanthracene preferred inward alignment with C ring close to the other quinone ring that was not reacting. The second 1,4-dimethoxyanthracene molecule then had to add from *exo*-face. The 1:1 ratio of two diadducts suggested that the addition of second 1,4-dimethoxyanthracene did not have inward-outward selectivity. That is reasonable since the addition of second molecule of 1,4-dimethoxyanthracene didn't have a quinone ring to induce such selectivity.

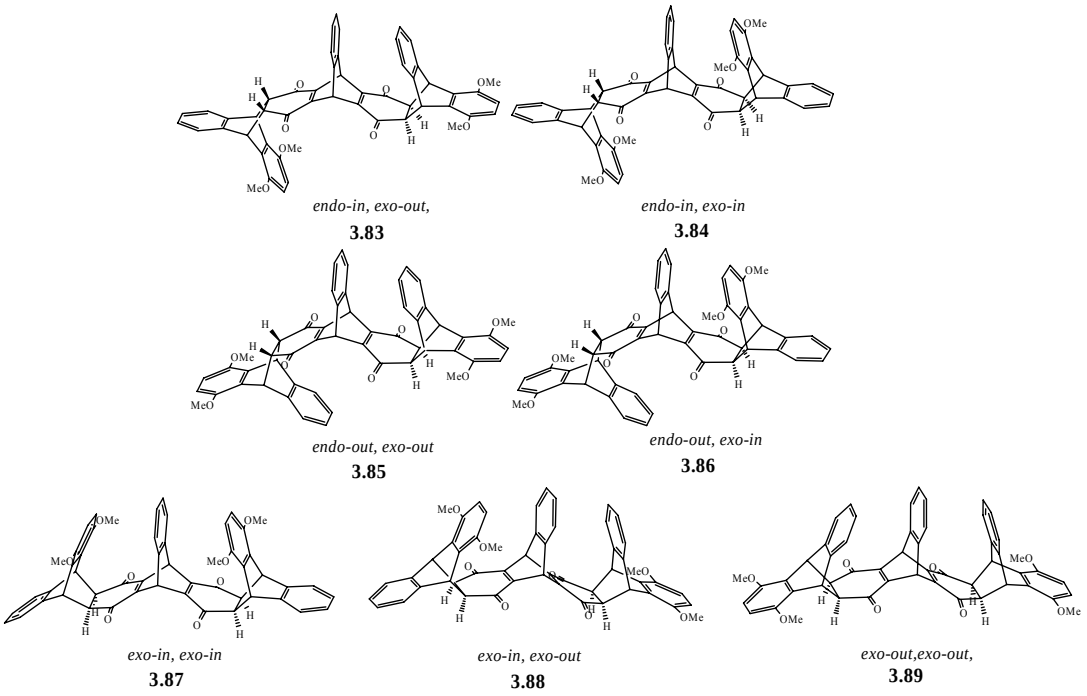
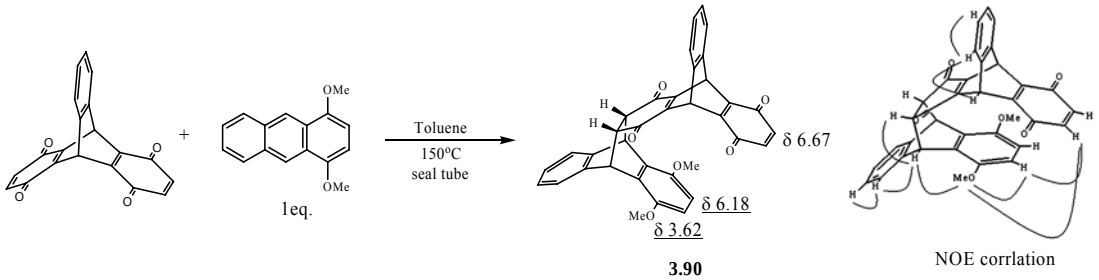
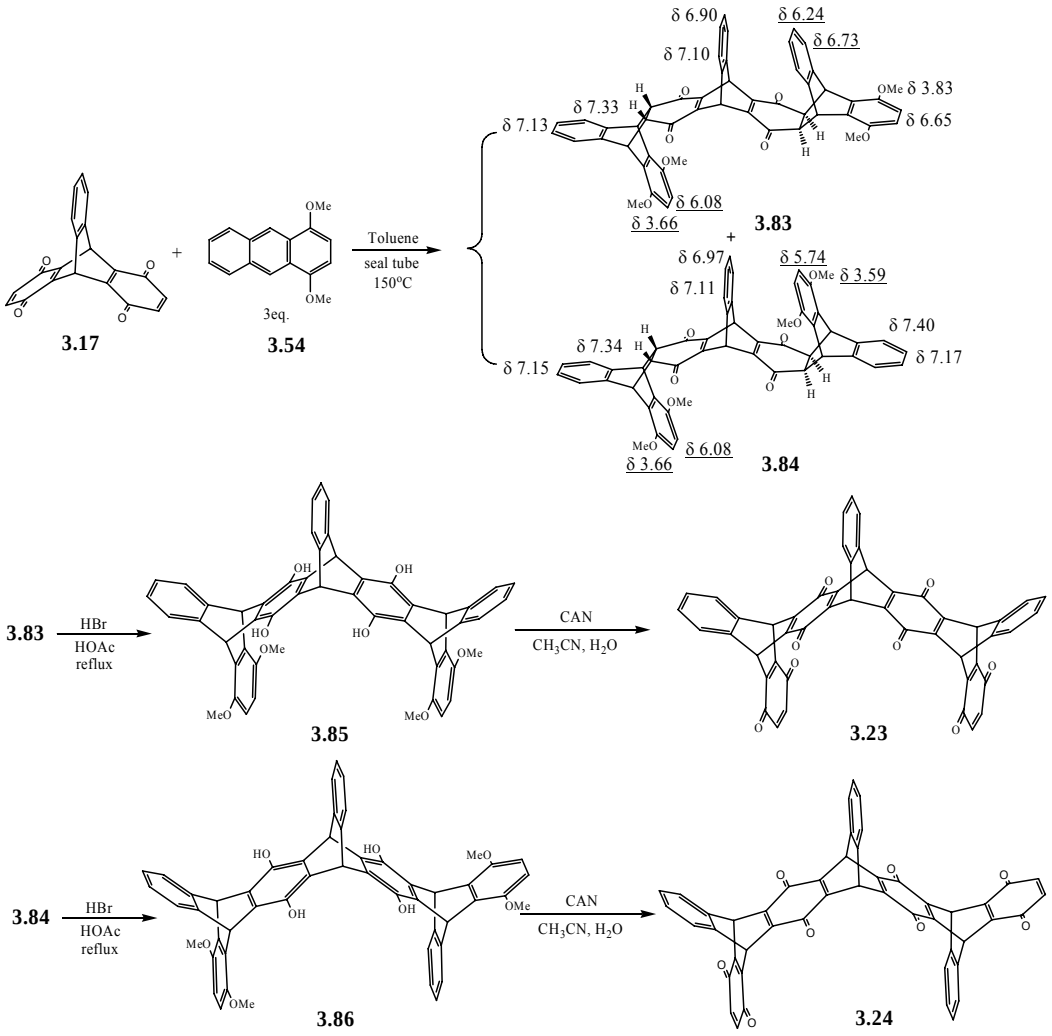


Figure 3.23 Seven possible diadducts formed by triptycene bisquinone and 1,4-demethoxyanthracene. (*in*, means the dimethoxy ring pointing inward to triptycene bisquinone; *out*, means the dimethoxy ring pointing outward to triptycene bisquinone.)

To verify this hypothesis, one equivalent of 1,4-dimethoxyanthracene was reacted with triptycene bisquinone, predominantly one monoadduct was formed. The proposed structure was verified by 2D-NOESY experiment.





Scheme 3.12 Synthesis of *cis,cis*-heptiptycene tetraquinone (**3.23**).

From structure of the monoadduct **3.90**, two diadducts precipitated were deduced as **3.83** and **3.84** respectively. The assignments of chemical shift were based on 2D-COSY and 2D-NOESY. In careful column chromatography conditions, two isomers could be separated with the less polar one being **3.83**. The synthesis of heptiptycene tetraquinone **3.23** and **3.24** were then pretty straight-forward as shown in **Scheme 3.12**. Enolisation of corresponding diadducts **3.83** in refluxing acetic acid with catalytic amount hydrobromic acid would afford corresponding tetramethoxyheptiptycene bisphenol (**3.85**) in 68% yield. Then the CAN oxidative demethoxylation would give the *cis,cis*-heptiptycene tetraquinone (**3.23**) in a yield of 68%. The total yield of **3.23** in three steps was 20% , which was almost twice the yield reported

by Zhu.[9] The structure of **3.23** was further verified by X-ray crystal diffraction as shown in **Figure 3.24**.

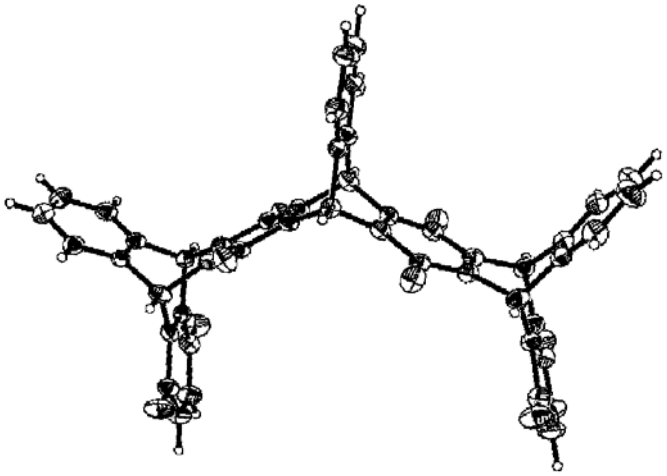
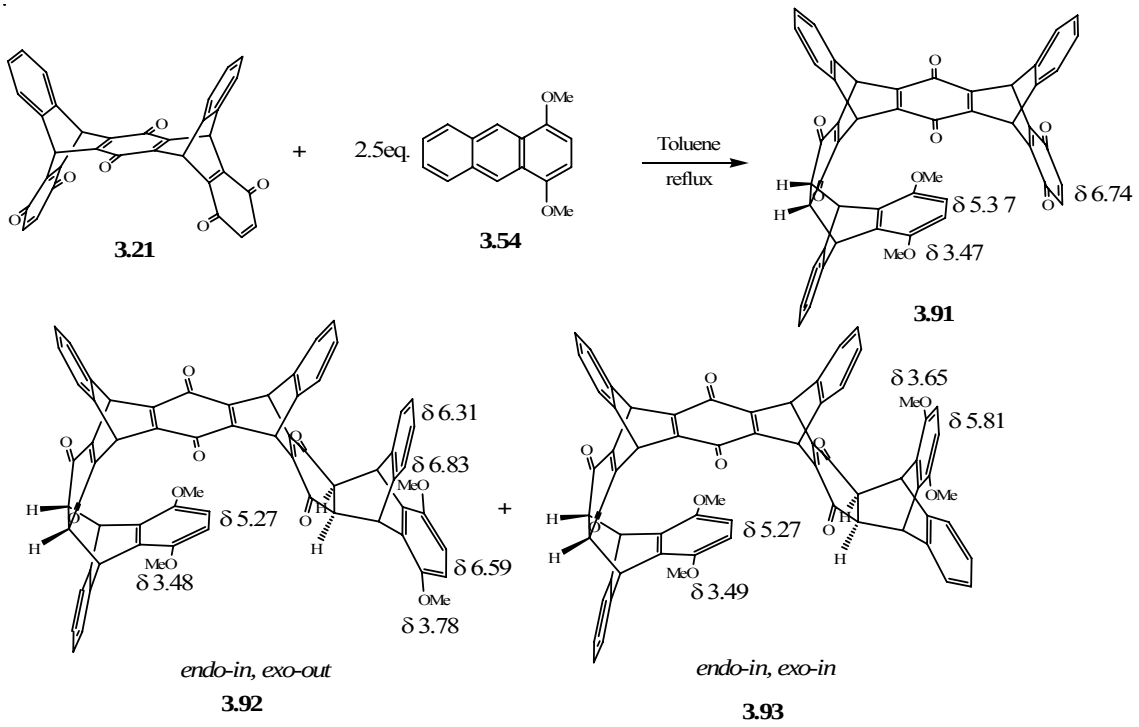


Figure 3.24 X-ray structure of *cis,cis*-heptiptycene tetraquinone (**3.23**)

3.3.2.5) Synthesis of cis,cis,cis-noniptycene pentaquinone (**3.57**)

Similar to the synthesis of *cis,cis*-heptiptycene tetraquinone, the four-teeth iptycene quinone **3.57** was synthesized from *cis*-pentiptycene trisquinone (**3.21**) which is two-teeth less. The Diels-Alder reaction of **3.21** with excess amount of 1,4-dimethoxyanthracene in a sealed tube at 150 ^{o}C using toluene as solvent for 36 hours gave mainly two diadducts which were separated by careful column chromatography. The less polar one corresponded to the (*endo-in, exo-out)*-isomer, while the more polar was the (*endo-in*, *exo-in*)-isomer. The structural assignments were based on so called "structural inherent NMR indicators." In other words, certain structural moieties in Diels-Alder adducts of iptycene quinone have unique patterns of peaks reflected in proton NMR which is inherent to the structure and can be used to identify the existence of this structure. As we seen in adducts **3.78**, **3.83**, the typical two upshift doublet-doublet peaks around δ 6.2~6.3 and 6.7~6.8 suggest an *exo-out* 1,4-methoxyanthracene moiety. The upshift of OMe proton (singlet around 3.6) and the corresponding α aromatic proton (singlet around δ 5.8) in adducts **3.80** and **3.84** indicate an *exo-in* 1,4-dimethoxyanthracene moiety. Here an even stronger upshift of OMe group (singlet around δ 3.5) and the corresponding α aromatic proton (singlet around δ 5.3) for both diadducts **3.92** and **3.93** indicates a common new structural moiety for them. It could only be *endo-in* 1,4-dimethoxyanthracene moiety since *endo-out* should have typical upshifted doublet-doublet peaks and the possiblity of *exo-in* and *exo-out* had already excluded. This is reasonable, since the first equivalent of 1,4-dimethoxyanthracene was

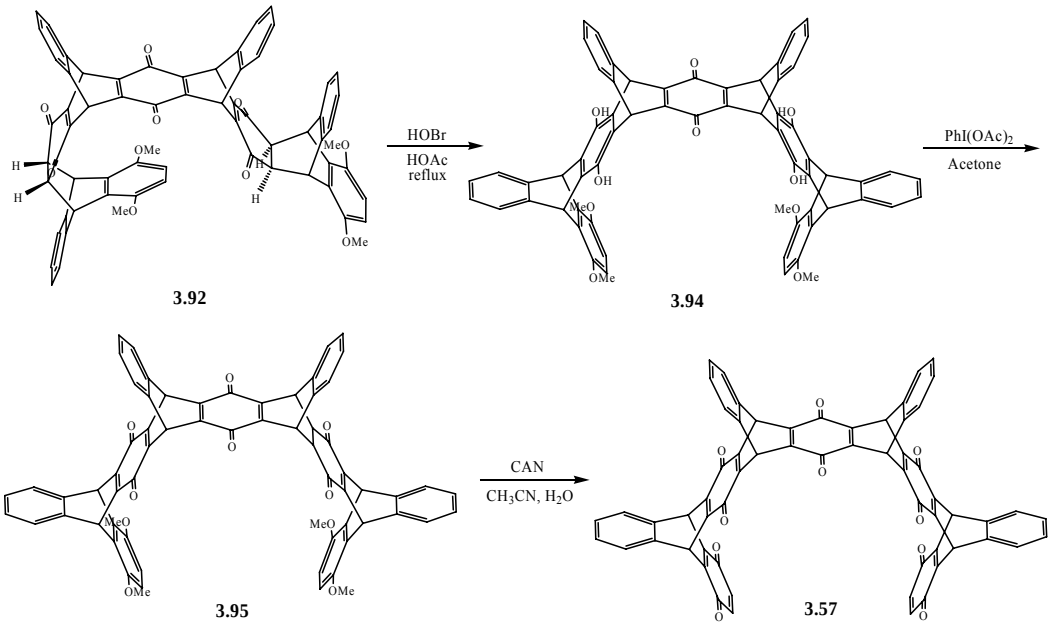
added to the more electrodeficient *endo*-face of *cis*-pentiptycene tetraquinone to form *endo-in* monoadduct **3.91** (Similar to the case of triptycene bisquinone **3.17**), which was also verified from 2D-COSY and 2D-NOESY experiment. Then the second equivalence of 1,4-dimethoxyanthracene added from *exo*-face of the other end quinone moiety with no *in-out* selectivity without the help of the other quinone moieties.



Scheme 3.13

Then pure diadduct **3.92** was treated with refluxing acetic acid and a catalytic amount of hydrobromic acid for 30 minutes. After evaporation of acetic acid, an unexpected messy crude product was formed, and the desired enolised intermediates **3.94** were difficult to purify because of high polarity and are inclined to be oxidized by air. We then treated the crude enolized product with diacetoxyiodobenzene in acetone. The oxidation took about 10 minutes to half an hour. The tetramethoxynoniptycene trisquinone intermediate **3.95** was obtained in a yield of 20%. Final oxidative demethoxylation using CAN would give the *cis, cis, cis*-noniptycene pentiquinone(**3.57**) in 30% of yield. The reduced yield of oxidative demethoxylation was probably because of the electron withdrawing effect of middle quinone rings, which might be caused by through-bond homoconjugative interaction as we discussed in the background part.

The electron density in the terminal 1,4-dimethoxybenzene rings was reduced, as were their susceptiblity to oxidation reagent.



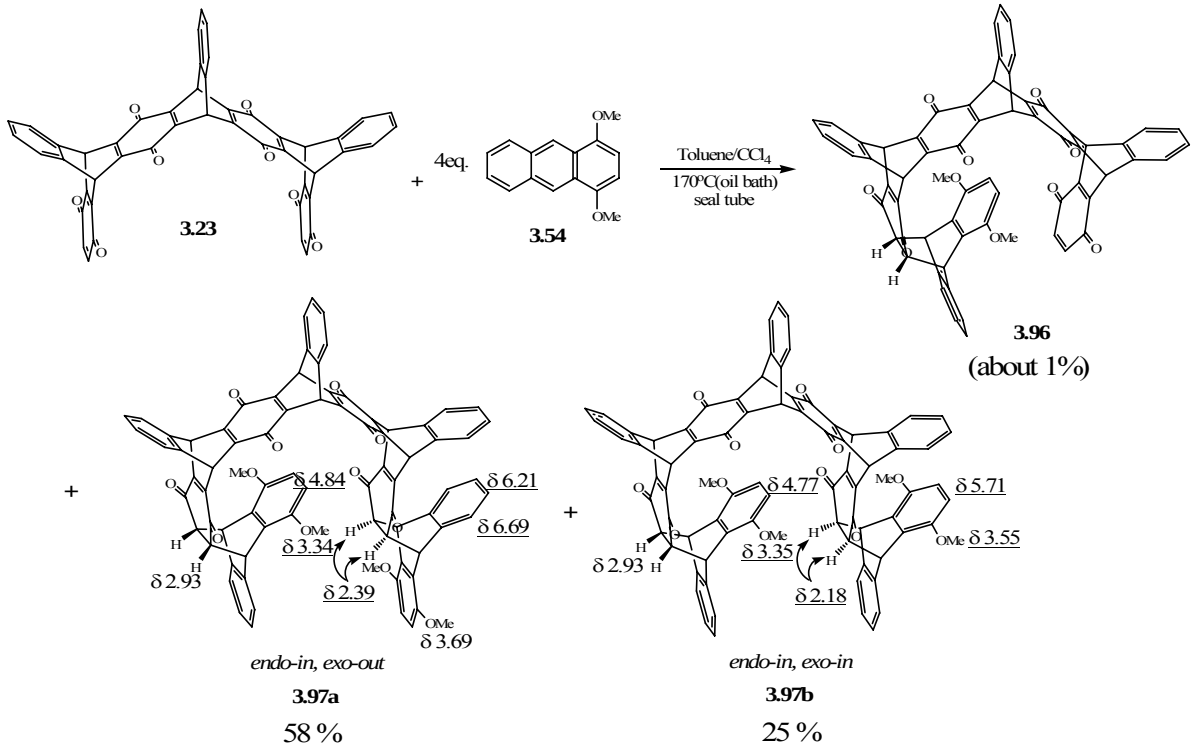
Scheme 3.14 Synthesis of *cis,cis,cis*-noniptycene pentaquinone (**3.57**).

The yield of *cis,cis,cis*-noniptycene pentiquinone (**3.57**) dropped tremendously compared with its one-tooth less *cis,cis*-heptiptycene tetraquinone (**3.23**). Better conditions for enolization and oxidative demethoxylation are needed for practical synthesis of it as a building block for cyclododeciptycenes.

3.3.2.6) Synthesis of cis,cis,cis,cis-undeciptycenehexaquinone (**3.59**)

Similar to the synthesis of four-teeth iptycene quinone, the five-teeth all *cis*-iptycene quinone **3.59** was synthesized from three-teeth *cis,cis*-heptiptycene tetraquinone (**3.23**). The Diels-Alder reaction of **3.23** with excess amount of 1,4-dimethoxyanthracene in a sealed tube at 150^{o}C using toluene and tetrachloromethane as solvent for 36 hours, two diadducts were precipitated in a ratio of 4:1. Tetrachloromethane was used as cosolvent to increase the solubility of the tetraquinone (**3.23**). It is a nonpolar solvent like toluene and would not change the face-selectivity of the Diels-Alder reaction. Similarly, structures of two diadducts were deduced both from "structural inherent NMR indicators" and predicted face-selectivity. As before, we predict the first equivalent of 1,4-dimethoxyanthracene added from *endo*-face and formed *endo-in* monoadduct **3.96** as the major isomer. The second equivalent of 1,4-dimethoxyanthracene reacted from *exo*-face of the other quinone moiety in the other end without *in-out* selectivity.

This prediction was mostly correct. The two isomers in the precipitate showed the predicted "structural inherent NMR patterns". They both have a tremendous upshift OMe protons (singlet, $\delta \approx 3.34$) and corresponding α protons (singlet, $\delta \approx 4.8$), which means they have an *endo-in* dimethoxyanthracene moiety. The major isomer in precipitate (also less polar spot from careful column chromatography) has a characteristic set of two doublet-doublet peaks around δ 6.20 and δ 6.70, which is an indicator for *exo-out* configuration. The major isomer in the precipitate was then identified as the structure **3.97a** in **Scheme 3.15**. The other isomer was determined as **3.97b**.



Scheme 3.15

From the above discussion, one would expect the formation of **3.97a** and **3.97b** be equal. However, after combined recovered diadducts from filtrate, yields for **3.97a** and **3.97b** were 58% and 25% respectively. What was the reason for a less amount of (*endo-in, exo-in*)-diadduct formed in the reaction? We noticed an abnomal upshift of the α protons of carbonyl groups in the *exo*-site for both adducts **3.97a** and **3.97b** with adduct **3.97b** upshifted δ 0.21 more (**Scheme 3.15**, protons labeled with arrow and chemical shift). This big difference in chemical shift means the α protons of carbonyl groups in *exo*-site of **3.97b** are closer to a deshielding 1,4-dimethoxybenzene ring of the *endo-in* dimethoxyanthracene moiety. It may explained by a

"seesaw" model as shown in **Figure 3.25**. The *exo*-dimethoxyanthracene moiety together with the α proton of carbonyl group worked like a "seesaw" with the α carbon of carbonyl as pivot. Because the diemthoxybenzene ring is sterically larger than benzene ring, it is relatively "downward" in isomer **3.97b**. So the α proton of carbonyl group is relatively "upward" and closer to the inner dimethoxy benzene ring, which increases the repulsion between them. The raised repulsion in its closely packed structure caused diadduct **3.97b** being energetically less favorable than the desired (*endo-in, exo-out*)-diadduct **3.97a** used for synthesis of all *cis*-undeciptycenehexaquinone (**3.59**). It was somewhat amazing how a combination of face-seletivity and steric effects would finally afford one out of seven possible isomers in 58% yield in this special case.

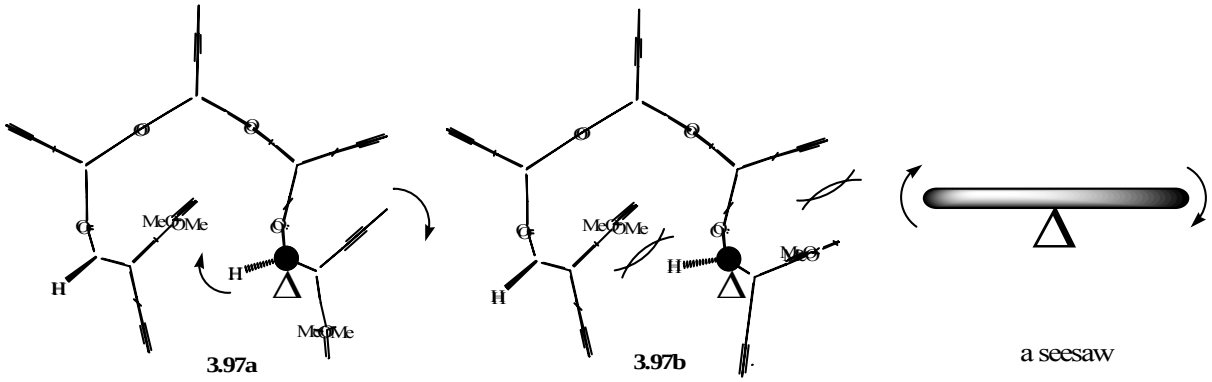
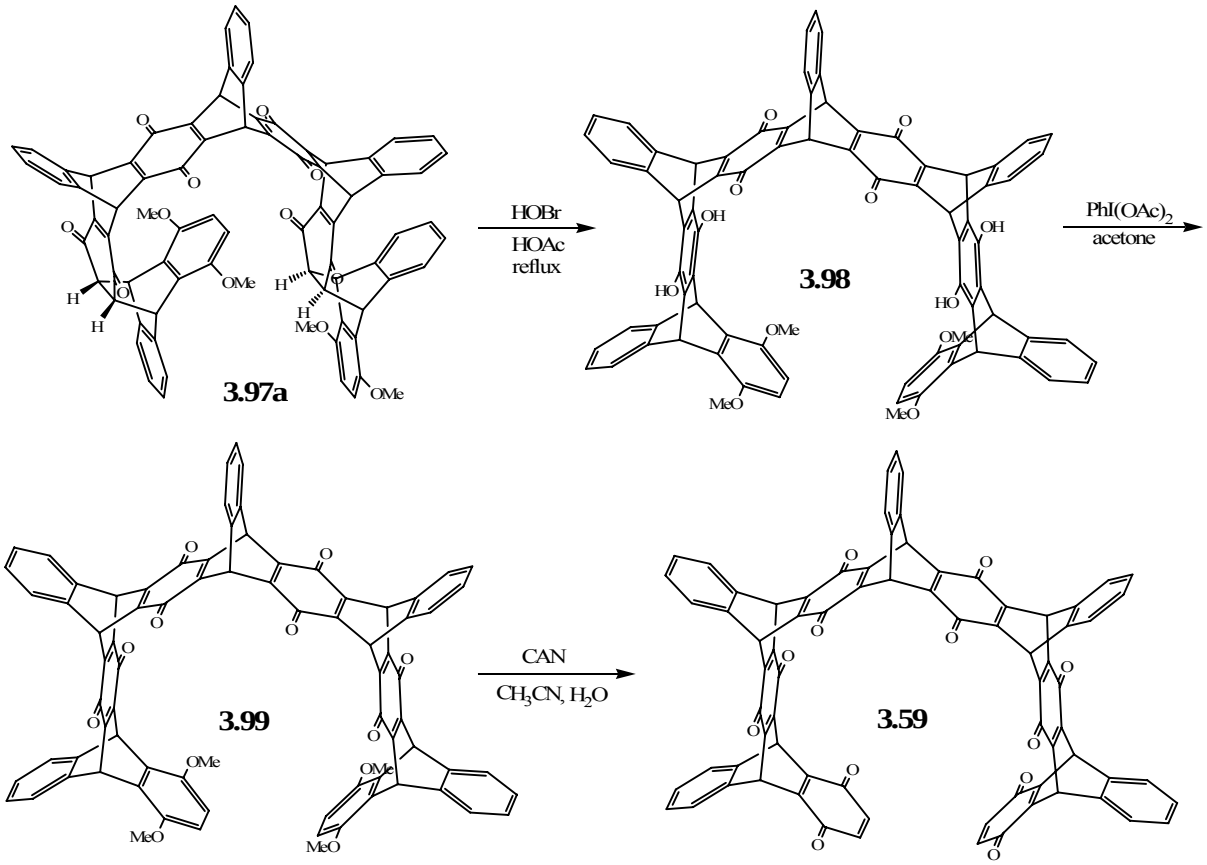


Figure 3.25

Similarly, pure diadduct **3.97** was treated with refluxing acetic acid with catalytic amount of hydrobromic acid for 30 minutes. After evaporizing acetic acid, a messy crude product was formed and the enolised intermediates **3.98** were difficult to purify because of high polarity and inclined to oxidation by air. We then oxidized the crude enolized product with diacetoxyiodobenzene in acetone. The tetramethoxyundeciptycene tetraquinone intermediate **3.99** was obtained in a yield of 29%. Final oxidative demethoxylation using CAN only gave the *cis, cis, cis, cis*-undeciptycene hexaquinone (**3.59**) in a yield of 30%. The low yield was probably related to through-bond homoconjugative interaction of inner quinone moieties. Again, better conditions for enolization and oxidative demethoxylation are need.



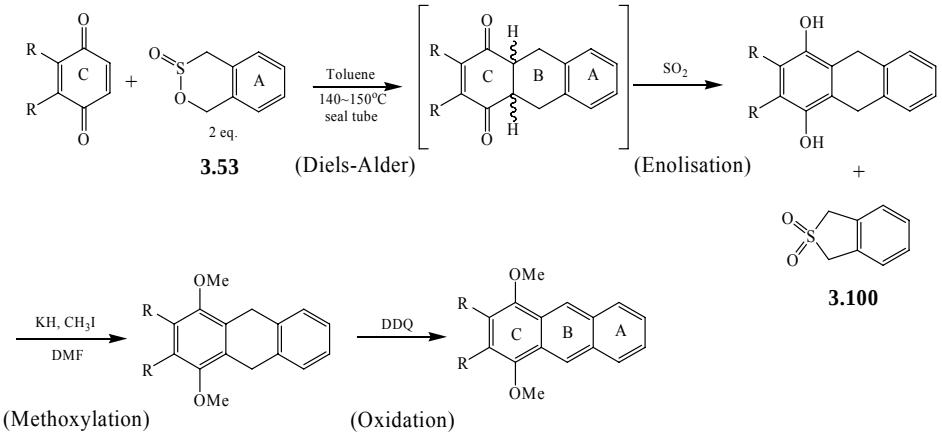
Scheme 3.16 Synthesis of *cis,cis,cis,cis*-undeciptycenehexaquinone (**3.59**).

3.3.3 Synthesis of bisdimethoxyanthracenes

The bisdimethoxyanthracenes (**3.56**, **3.58**, and **3.60**) are bisdiene building blocks for cyclododeciptycenes. Pentacene **3.55** can also be seen as a bisdiene building block. After first Diels-Alder reaction with its anthracene part, the remaing three rings can be aromatized to generate another anthracene unit for a second Diels-Alder reaction. Currently we have only synthesized a 2-teeth bisdiene building block **3.55** and a 3-teeth bisdiene building block **3.56**. The key step to them were the Diels-Alder reaction of corresponding quinone with 1,4-dihydro-2,3-benzoxathiin-3-oxide (**3.53**), an "*o*-quinodimethane" precursor.

"*o*-quinodimethane" is a useful and efficient diene intermediate for Diels-Alder reactions.[55, 56] There are many ways to generate it, including 1,4-elimination of α,α'-dihalo-o-xylenes, thermolysis of benzocyclobutenes, photoenolization of *o*-methylbenzaldehydes, Hoffman elimination of (*o*-methylbenzy1)trimethylammonium hydroxide, decomposition of benzo-fused heterocyclic compounds.[55] We chose 1,4-dihydro-2,3-benzoxathiin-3-oxide (**3.53**)

as precursor because it generates *o*-quinodimethane at mild conditions upon heating around 80 ^{o}C and does not form other organic or inorganic byproducts except for sulfur dioxide in presence of a dienophile. The gereration of sulfur dioxide *in situ* has another advantage. Sulfer dioxide catalyzes the enolisation of initial formed Diels-Alder adducts, so the Diels-Alder reaction and enolisation can be performed in one-pot. If there is no dienophile present, *o*-quinodimethane generated at the reaction temperature will react back with sulfur dioxide to form sideproduct 1,3-dihydro-2-benzothiophene-2,2-dioxide (**3.100**)

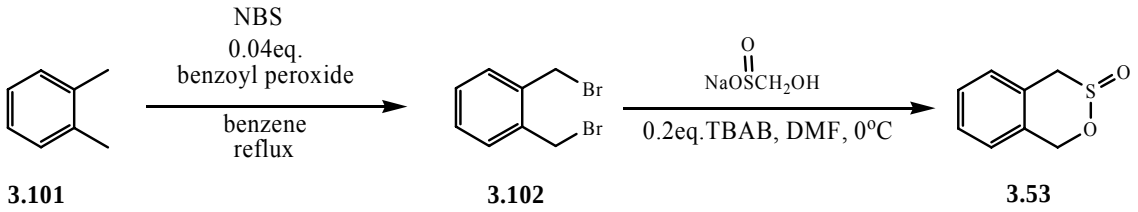


Scheme 3.17 Formation of an 1,4-dimethoxyanthracene from quinone end.

The general reaction sequences and typical reaction conditions for transformation of a quinone to 1,4-dimethoxyanthracene moiety were given in **Scheme 3.17**. The reaction of quinone with excess amount of 1,4-dihydro-2,3-benzoxathiin-3-oxide (**3.53**) in a sealed tube at temperature around 145^{o}C would give phenol as the major product. After methoxylation and oxidation, the 1,4-dimethoxyanthracene unit was installed.

4.3.3.1) Synthesis of 1,4-dihydro-2,3-benzoxathiin-3-oxide (**3.53**)[57]

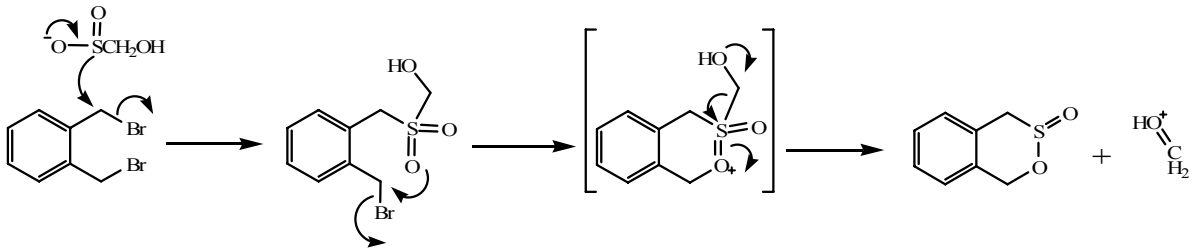
The sultine **3.53** was synthesized in two steps. First, *o*-xylene **3.101** was brominated in refluxing benzene using N-Bromosuccinimide (NBS) as a brominating reagent and benzoyl peroxide as a radical initiator for 2 hours. During concentration of the reaction mixture, dibromide **3.102** was precipited together with succinimide. The latter can be washed away by aqueous workup and the dibromide was obtained in 41% yield. The next step is treatment of dibiromide **3.102** with sodium hydroxymethanesulfinate (Rongalite) and a cataylic amount of tetrabutylammonium bromide (TBAB) in *N,N*-dimethylformamide (DMF) at 0 ^{o}C for 3 hours. The yield for **3.53** was 65% from the dibromide.



3.101 **3.102** **3.53**

Scheme 3.18

The mechanism for the last step was proposed in **Scheme 3.19**. Intermolecular S_N2 reaction of Rongalite with the dibromide first formed sulfone intermediate **3.103**, which underwent intramolecular S_N2 to displace the second bromide anion. The intermediate **3.104** then eliminated a molecule of formaldehyde to give the sultine **3.53**.

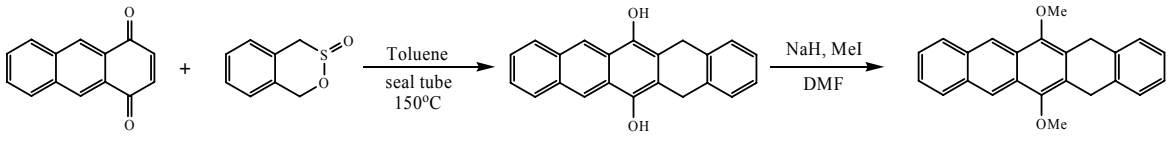


3.102 **3.103** **3.104** **3.53**

Scheme 3.19

3.3.3.2) Synthesis of 6,13-dimethoxy-5,14-dihydropentacene (**3.55**)

As generalized in **Scheme 3.17**, synthesis of the pentacene diene component **3.55** started from the Diels-Alder reaction of 1,4-anthracenedione (**3.65**) and the sultine (**3.53**). When two reactants were refluxed in a sealed tube using toluene as solvent at an oil bath temperature of 150°C for 30 hours, a dark green solid **3.105** precipitated in a yield of 91%. The phenol **3.105** was methylated by methyl iodide in DMF using sodium hydride as base to afford 62% of **3.55**.



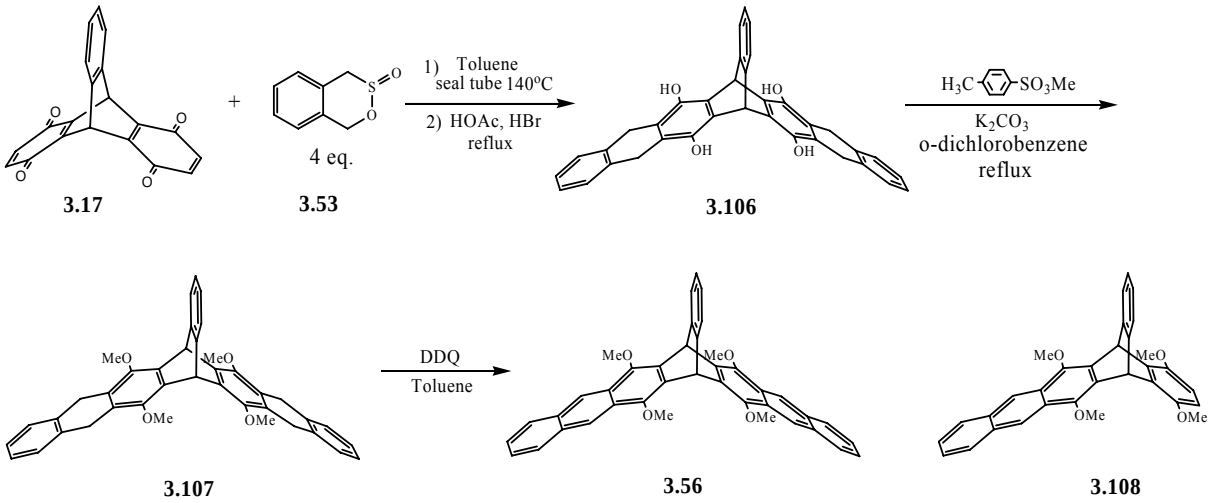
3.65 **3.53** **3.105** **3.55**

Scheme 3.20

3.3.3.3) Synthesis of 6,8,15,17-tetramethoxy-7,16-dihydro-7,16-(o-benzeno)heptacene (**3.56**)

The bisdimethoxyanthracene **3.56** was the diene component used for successful cyclization as we would discuss later. Its synthesis basically followed the general sequence in **Scheme 3.17**, though it had some problems.

First, the Diels-Alder reaction of triptycene bisquinone (**3.17**) and an excess amount of **3.53** in refluxing toluene gave almost exclusively monoadduct. It seemed the Diels-Alder reaction of the second quinone was much slower. Increasing temperature by changing to a sealed tube condition would certainly enhance the reaction rate, but also would increase the rate of decomposition of sultine **3.53** to sulfone **3.100**. The right temperature was important for getting the diadducts. Besides, the monoadducts would cause a purification problem in later steps since it would be converted to monoanthracene **3.108**, which was difficult to separate from bisanthracene **3.56** by column chromatography. It was necessary to find a reliable procedure to get diphenol **3.106** in good purity. A modified procedure was as following. First, Diels-Alder reaction of **3.17** and 4 equivalents of **3.53** was refluxed in a sealed tube at 140^{o} for 24 hours. The precipitate usually contained over 70% of diadducts and partially or fully enolised phenols. An extra step of enolisation in refluxing acetic acid with small amount of hydrobromic acid would give a precipitate which contains mainly diphenol **3.106** since the monophenol derived from monoadduct has better solubility in acetic acid and remained in solution. This enolisation step served as an extra purification step. The diphenol was obtained in a yield of 51% in two steps.



3.17 **3.53** **3.106** **3.107** **3.56** **3.108**

Scheme 3.21 Synthesis of bisdimethoxyanthracene **3.56**.

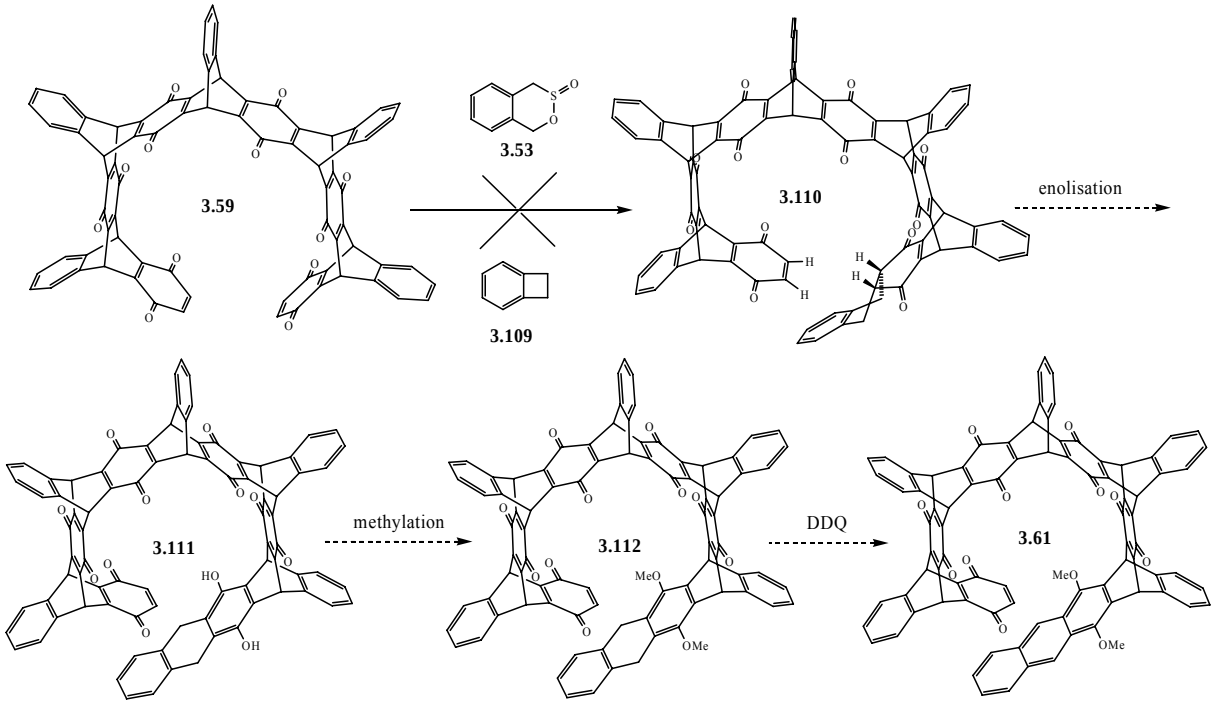
Second, the methylation of diphenol **3.106** also proved difficult at the beginning. The low solubility of **3.106** in DMF caused the previous methylation conditions for **3.105** not feasible here. A harsh methylation condition using methyl *p*-toluenesulfonate, potassium carbonate in refluxing 1,2-dichlorobenzene at around 180 ^{o}C was found and gave a tetramethoxy intermediate **3.107** in a yield of 91%.

The last step aromatization was an easy step. The tetramethoxy intermediate **3.107** was stirred with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) in toluene to give bisdimethoxyanthracene **3.56** in 89% yield.

3.3.4 Towards the synthesis of cyclododeciptycene based molecular gears

3.3.4.1) Unsuccessful effort starting from cis,cis,cis,cis-undeciptycenehexaquinone (**3.59**)

Since the 5-teeth iptycene quinone **3.59** was the closest building block to the target molecular gear **3.1**, we tried to convert it to 6-tooth intermediate **3.61**, which has a quinone moiety and an anthracene moiety ready for Diesl-Alder reaction. However, the attempted Diels-Alder reaction of either the sultine or benzocylcobutene failed to give the expected adduct **3.110**. The iptycene quinone **3.59** seemed to undergo fragmentation upon heating. The stepwise synthetic route did not work.

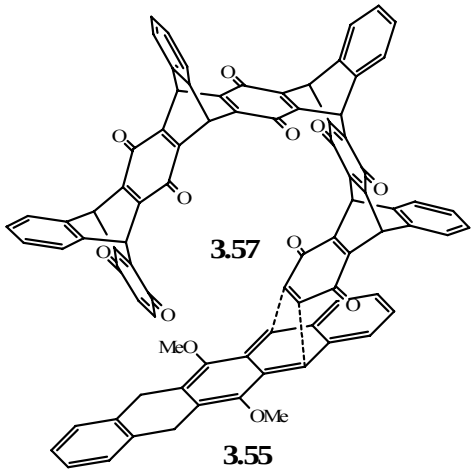


Scheme 3.22

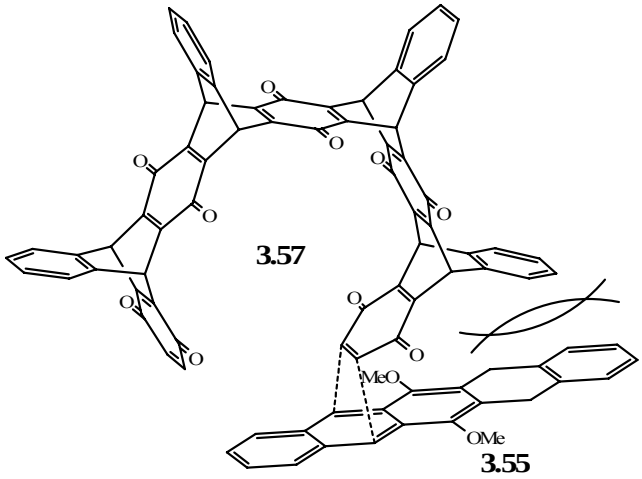
3.3.4.2) Convergent synthesis: finding suitable bisdiene and dienophile components.

The unsuccessful synthesis of stepwise route made us resorted to convergent synthetic routes shown in **Scheme 3.5**. Among five proposed routes, route I and II have starting materials that have already been synthesized.

Route I uses the four-tooth iptycene quinone **3.57** as the dienophile and pentacene **3.55** as the bisdiene component. This route has an advantage over the others because most likely only one adduct will be formed. For a curved structure like **3.57**, the *endo*-face is hindered. If *endo*-adducts are excluded, the remaining two possible adducts would be *exo-in* and *exo-out*-adducts. The transition state energy analysis shows the *exo-in* alignment would be more steric hindered (**Figure 3.26**). Howerver, the pentacene **3.55** turned out to be not a reactive diene component. Usually, the Diels-Alder reaction of 1,4-dimethoxyanthracene with simple quinone happened above 80 ^{o}C. But a model Diels-Alder reaction of the dimethoxy pentacene **3.55** with simple 1,4-benzoquinone was slow even at 150 ^{o}C in a seal tube using toluene as solvent. Since the pentiquinone **3.57** may not be stable in high temperature as hexaquinone **3.59** and also the current synthetic yield to **3.57** was low, this route was abandoned.



exo-out alignment of pentacene

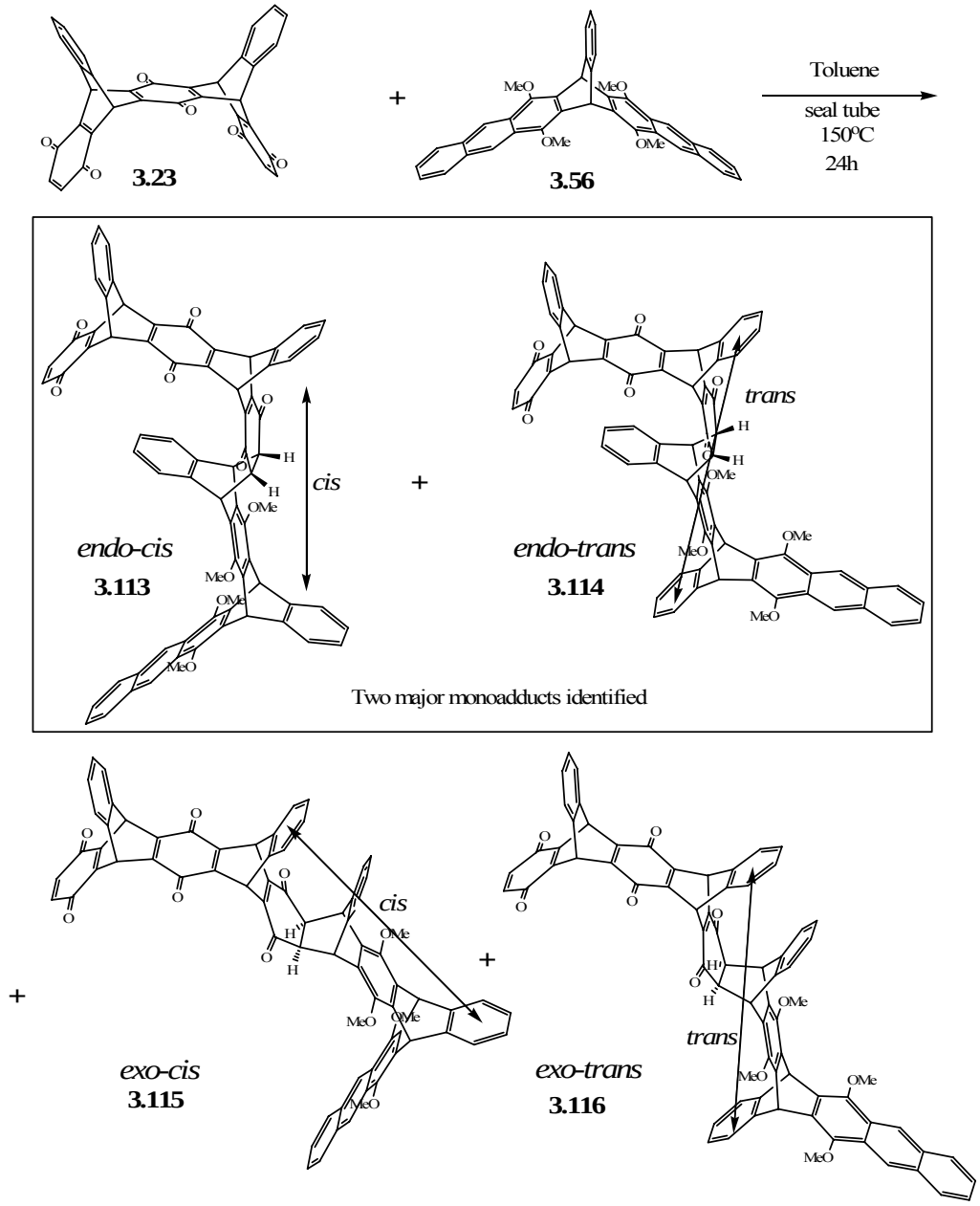


exo-in alignment of pentacene

Figure 3.26

We then resorted to route II. Since slightly change of anthracene structure greatly changed its reactivity in Diels-Alder reaction as in the case of **3.55**, to ensure the reactivity of bisdimethoxyanthracene **3.56**, a model reaction with *cis*-pentiptycene tetraquinone **3.21** was carried out. To our delight, the Diels-Alder reaction happened in refluxing benzene, which means bisdimethoxyanthracene **3.56** is as active as 1,4-dimethoxyanthracene. Two major monoadducts were separated in about 1:1 ratio (**Scheme 3.23**). However, as we looked for typical doublet-doublet peaks around δ 6.2~6.3, which is characteristic for *exo*-adducts as one of "structural inherent NMR indicators", we did not find them. Instead, we found a pair of more

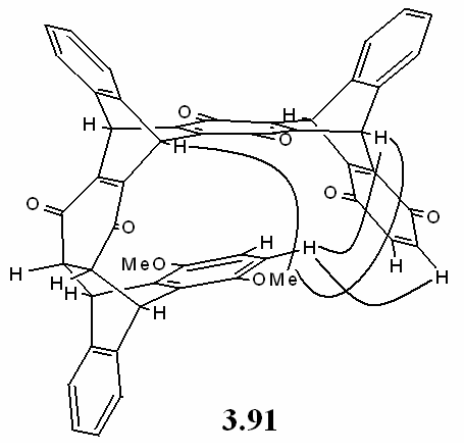
upshifted doublet-doublet peaks around δ 5.9 for two isomers, which could only be explained as *endo*-adducts. The *endo*-face is more electron-deficient and thus, it is easier to form charge-transfer complexes with more readily accessible benzene rings in the dimethoyanthracene moiety.



Scheme 3.23

From this model reaction, we would expect that *cis,cis*-heptiptycene tetraquinone **3.23** react with bisdimethoxyanthracene **3.56** following the same face-seletivity and give the *endo*-adducts as major products. For this reason, the direct use of 3-teeth iptycene quinone **3.23** as

dienophile was initially not considered. Instead, a 3-tooth iptycene quinone equivalent **3.91** was chosen. Compound **3.91** was previously separated in the Diels-Alder reaction of *cis*-pentiptycene trisquinone with excess amount of 1,4-dimethoxyanthracene (**Scheme 3.13**) . Its structure had been verified by NOESY and COSY (**Figure 3.27**). Since the *endo*-face was already blocked by one 1.4-dimethoxyanthracene unit, another diene moiety has to react from *exo*-face unless a retro-Diels-Alder reaction happens and the 1,4-dimethoxyanthracene moiety in *endo*-face was split out.



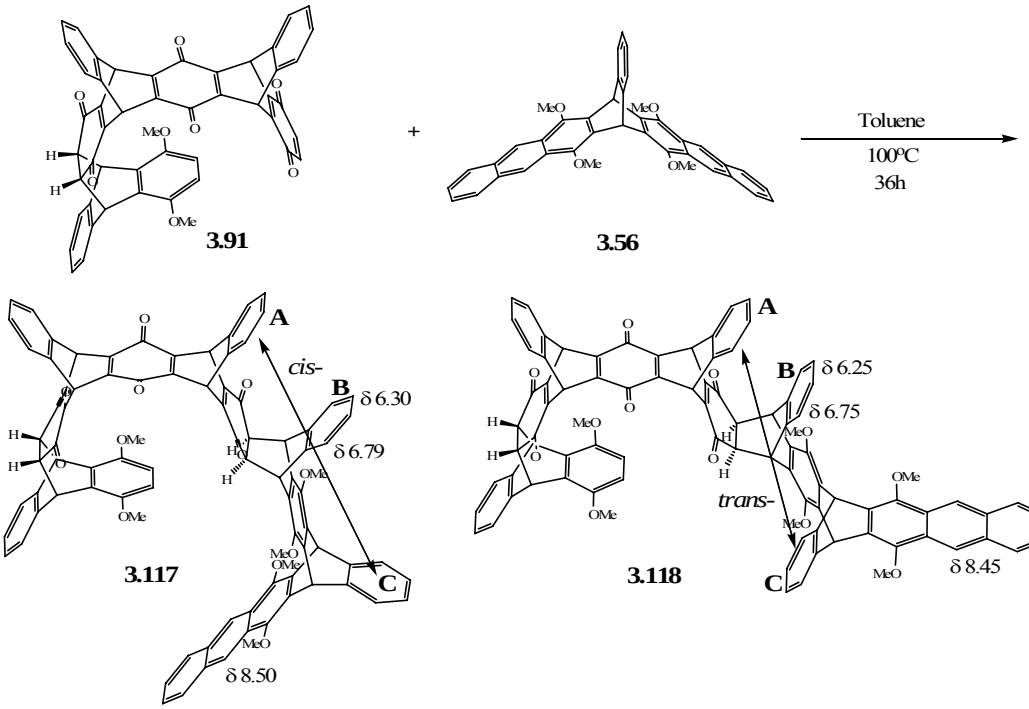
3.91

Figure 3.27 Importane NOE correlations of **3.91**

3.3.4.3) Synthesis of (5R,5aS,7R,9S,10aS,11S,13S,22R,24R,24aR,26S,28S,29aR,30S)-5,5a7,9, 10a,11,13,22,24,24a,26,28,29a,30-Tetradecahydro-1,4,12,14,21,23-hexamethoxy-5,30:7,28:9,26: 11,24:13,22)-penti(o-benzeno)tridecacene-6,8,10,25,27,29-hexaone (**3.117**)

The Diels Alder reaction of *endo*-face blocked dienophile **3.91** with bisdimethoxyanthracene **4.56** in toluene at 100 ^{o}C for 36 hours to give a 3:7 ratio of adducts **3.117** and **3.118** in a yield of 51% (**Scheme 3.24**). They were difficult to separate from each other by column chromatography. But they can be differentiated from ^{1}HNMR. The typical doublet-doublet peaks around chemical shift δ 6.20~6.30 not only verified the addition from *exo*-face, but also reflect slight disturbance of structure due to the "flip" of bisdimethoxyanthracene moiety. Their chemical shifts were δ 6.30 and δ 6.25 for *cis*-isomer **3.117** and *trans*-isomer **3.118**, respectively. From the chemical shifts, we knew the distance between benzene ring A and benzene ring B of *cis*-isomer **3.117** is longer than that of *trans*-isomer **3.118** (**Scheme 3.24**). A seasaw model shown in **Figure 3.28** would give a simplified explaination. The barycenter of bisanthracene moiety for adduct **3.117** is relatively downwards compared with its isomer **3.118**, so the other

benzene end (ring B) moves upward and the distance of two benzene rings were increased. The full assignment of ^{1}H NMR peaks were based on 2D-ROESY experiment.



Scheme 3.24

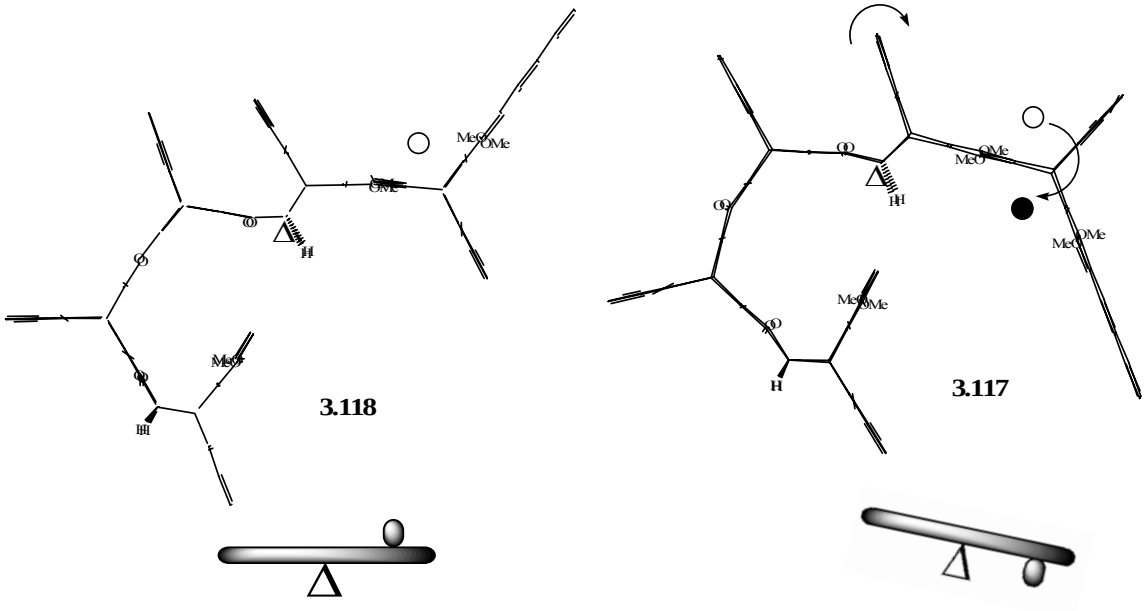
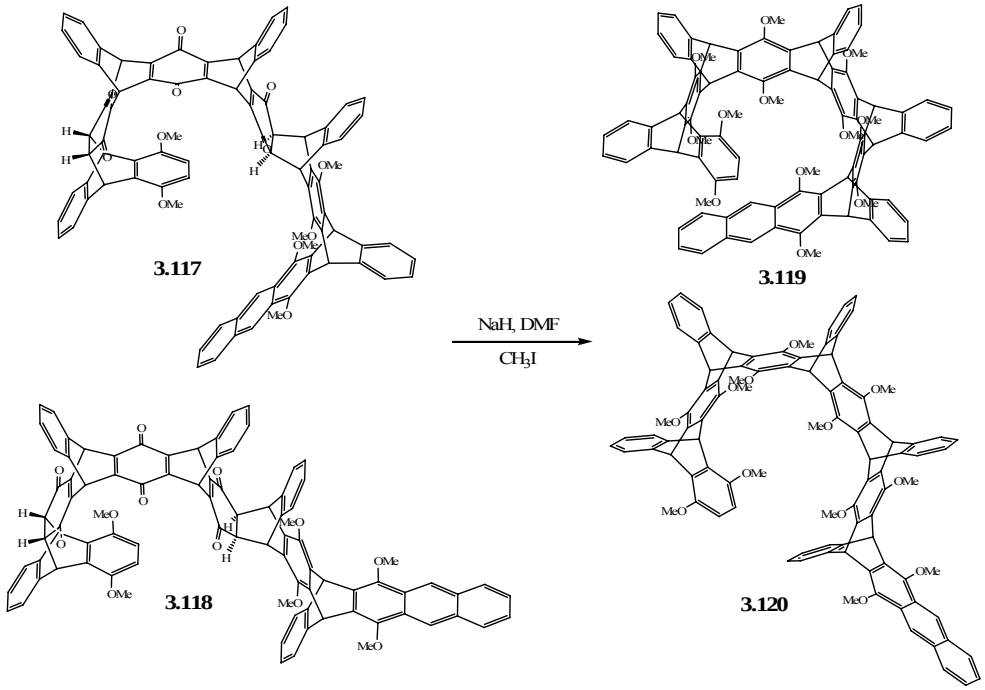


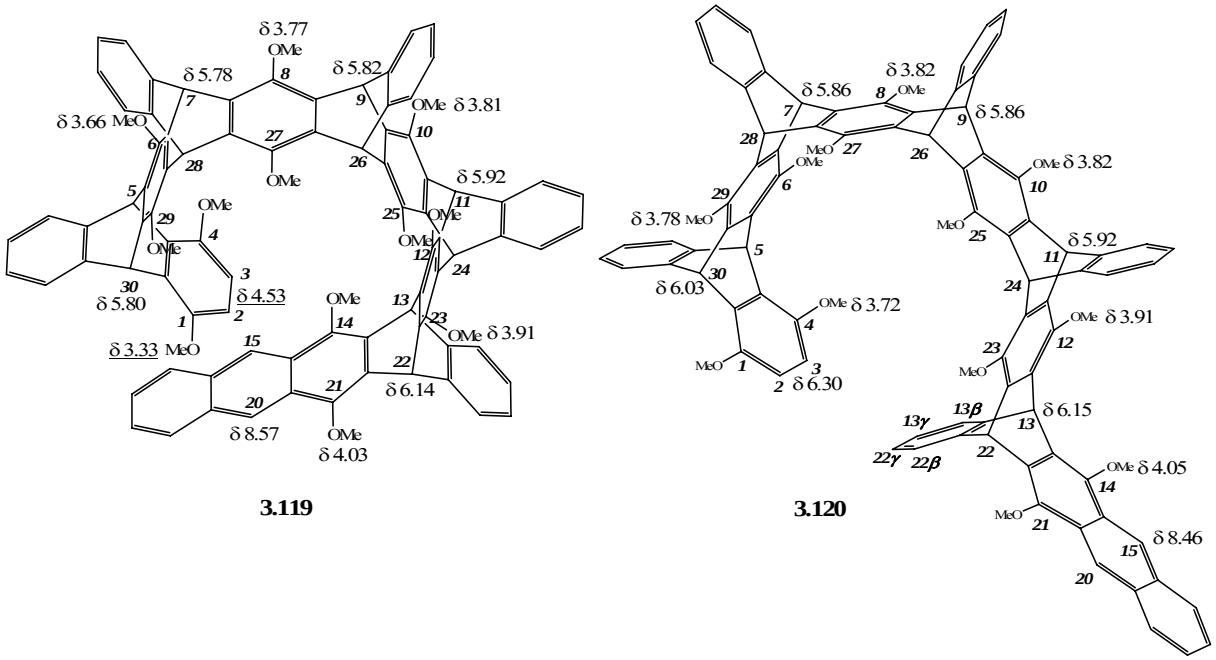
Figure 3.28

3.3.4.4) Enolization of (**3.117**) *under basic conditions to afford (5R,7R,9S,11S,13S,22R, 24R,26S,28S,30S)-5,7,9,11,13,22,24,26,28,30- decahydro-1,4,6,8,10,12,14,21,23,25,27,29-dode-camethoxy-5,30:7,28:9,26:11,24:13,22)-penti(o-benzeno)tridecacene* (**3.119**)

Compound **3.117** has all six teeth installed in all *cis*-fashion. The next step was to enolise two Diels-Alder reaction sites in the molecule to bring two ends closer together. The attempt of enolization in refluxing acetic acid with hydrobromic acid gave messy decomposed products. Then we tried basic conditions using sodium hydride and methyl iodide in DMF, hoping enolate formed *in situ* would be quenched by methyl iodide and give more stable products. Actually, the mixture of two adducts **3.117** and **3.118** was stirred with sodium hydride in dry DMF at 0^{o}C for half an hour before adding methyl iodide and letting the reaction mixture slowly warm up to room temperature over the course of two hours. The typical brown color of charge-transfer band between *endo*-face dimethoxybenzene and quinone rings disappeared. Two new fluorescent spots close to each other in TLC together with several other spots appeared. It was a little of a surprise that these two products might not contain a quinone moiety since if there were fluorescence quenching quinone moiety in the molecule, the whole molecule should show no fluorescent acitivity. The less polar spot was later identified as **3.119**, which was clearly derived from adduct **3.117**. The more polar spot was the corresponding product **3.120** from adduct **3.118**.



Scheme 3.25



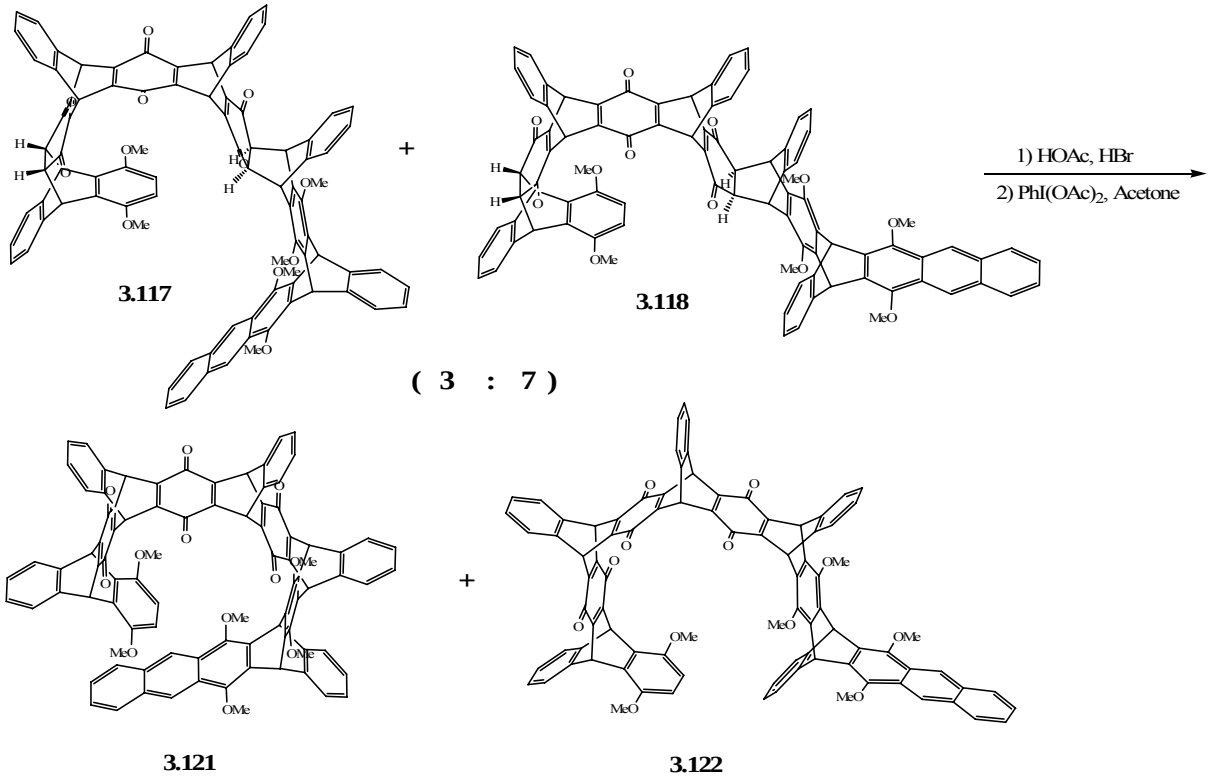
3.119 **3.120**

Figure 3.29

The circular structure of **3.119** was verified by its 2D-ROESY spectrum. From ^{1}H NMR, the peaks of 2,3-H in the terminal dimethoxy benzene was easily distiguished by the big upshift of the chemical shift at δ 4.53. Another group of protons easy to identify are the 15,20-H (δ 8.57) in anthracene ring as the most downshifted protons in the molecule. In 2D-ROESY spectrum, spatially close protons show cross peaks. For molecule **3.119**, we can check for space relationship of nearby protons either starting from 2,3-H or 15,20-H. Since 2,3-H (δ 4.53) is close to 1,4-OMe, this two peaks should show strong crosspeak. Among six OMe peaks, only one (δ 3.33) shows cross peaks with 2,3-H, then we know this peaks corresponds to 1,4-OMe. 1,4-OMe (δ 3.33) shows two crosspeaks with chemical shift δ 4.53 and δ 5.80 respectively. From its structure, we know 1,4-OMe group is close to 2,3-H and 5,30-bridge H. Since we already know δ 4.53 belongs to 2,3-H, δ 5.80 must be of 5,30-H. Then we check the crosspeaks of 5,30-bridge-H (δ 5.80) not counting the already known 1,4-OMe, we find the chemical shift of 6,29-OMe is δ 3.66. In this way, we assigned all the chemical shifts in the "shaft " part of the molecule **3.119**, from 2,3-H to 15,20-H as δ 4.53 (2,3-Ar-H), 3.33 (1,4-OMe), 5.80 (5,30-bridge-H), 3.66 (6,29-OMe), 5.78 (7,28-bridge-H), 3.77 (8,27-OMe), 5.82 (9,26-bridge-H), 3.81 (10,25-OMe), 5.92 (11,24-bridge-H), 3.91 (12,23-OMe), 6.14 (13,22-bridge-H), 4.03 (14,21-OMe), and 8.57 (15,20-Ar-H). Similar crosspeaks can be found in 2D-ROESY of **3.120** for assignment of

chemcal shifts. Besides the nomal crosspeaks indicated by bond connections, a crosspeak of 2,3-H and 15,20-H is found only in 2D-ROESY of **3.119** and not **3.120**, indicating that 2,3-H and 15,20-H are close to each other in space. The strong upshift of 2,3-H is because 2,3-H are strongly shielded by dimethoxyanthracene ring in that close range. From the 2D-ROESY of **3.120**, cheimcal shifts of 2,3-H (δ 6.30) in **3.120** is determined by its abnormal smaller cross peaks with 13,22-βH (larger chemical shift) than 13,22-γH. A bridge-H should have a bigger crosspeak for its β-H than γ-H, because β-H is closer. Based on the 2,3-H in both **3.119** and **3.120**, an estimated 1.77 upfield shift of chemical shift due to the closeness of two ends of **3.119** was deduced.

3.3.4.5) Enolization of (**3.117**) *in acidic conditions to afford (5R,7R,9S,11S,13S,22R, 24R,26S,28S,30S)-5,7,9,11,13,22,24,26,28,30-decahydro-1,4,12,14,21,23-hexamethoxy-(5,30:7,28:9,26:11,24:13,22)-penti(o-benzeno)tridecacene* (**3.121**)

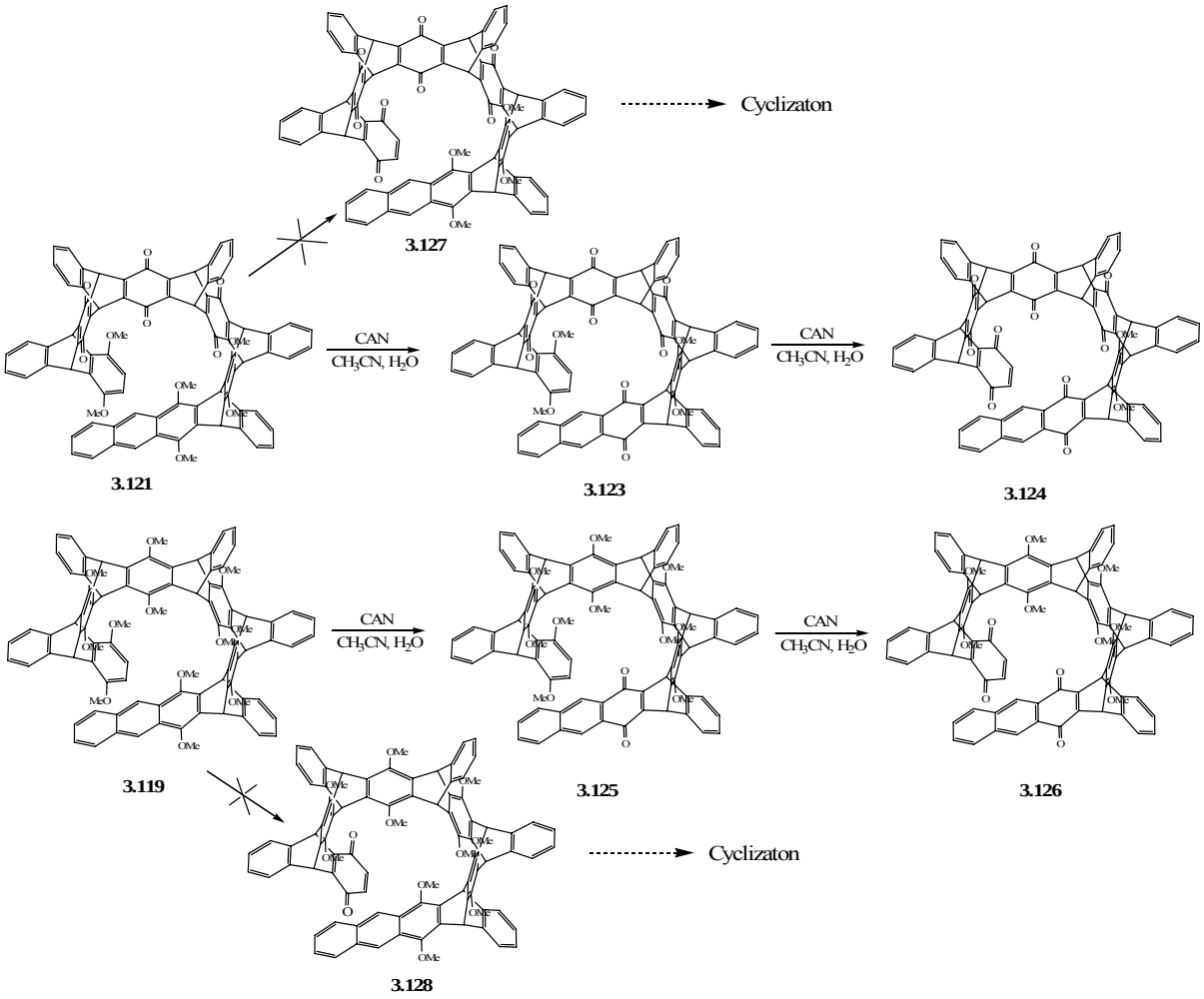


Scheme 3.26

The mixture of six-teeth adduct **3.117** and **3.118** was stirred at room temperature for 36 hours in acetic acid with a catalytic amount of hydrobromic acid. After solvent was removed under vacuum, the residue was dissolved in acetone and oxided with diacetoxyiodobenzene to

afford the enolized product **3.121** and **3.122** in a yield of 25%. Similar to **3.119**, chemical shift of 1,2-H (δ 4.81) in **3.121** is upshifted 1.46 relative to that in **3.122**.

*3.3.4.6) Unsucessful effort to selectively convert 1,4-dimethoxybenzene ring of **3.119** and **3.121** to quinone ring.*



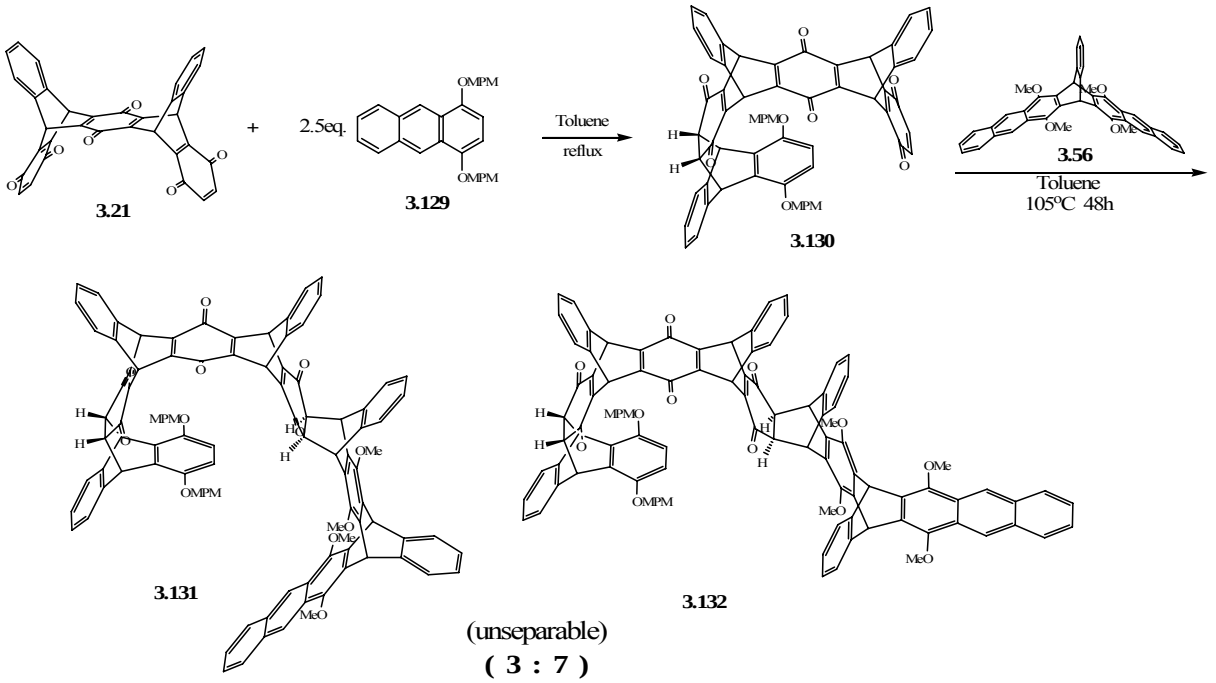
Scheme 3.27

The six-tooth intemediate **3.119** and **3.121** are circular and two ends are close to each other. The next goal is to selectively oxidize the 1,4-dimethoxyanthracene end to quinone and form **3.127** or **3.128**, which are predicted to cyclize under suitable conditions. However, the CAN oxidative demethoxylation of **3.121** and **3.119** gave demethoxylation product at the anthracene ring first. Only **3.123** or **3.125** were separated. If excess amount of CAN was used, compound with two quinone ends, **3.124** or **3.126**, were formed, which cannot be cyclized. Here

we met another dead synthetic route. A rational detour was to change the protecting group in the 1,4-dimethoxybenzene end.

*3.3.4.7) Unsucessful attempt to synthesize **3.127** or **3.128** by introducing p-methoxyphenylmethoxy protecting group.*

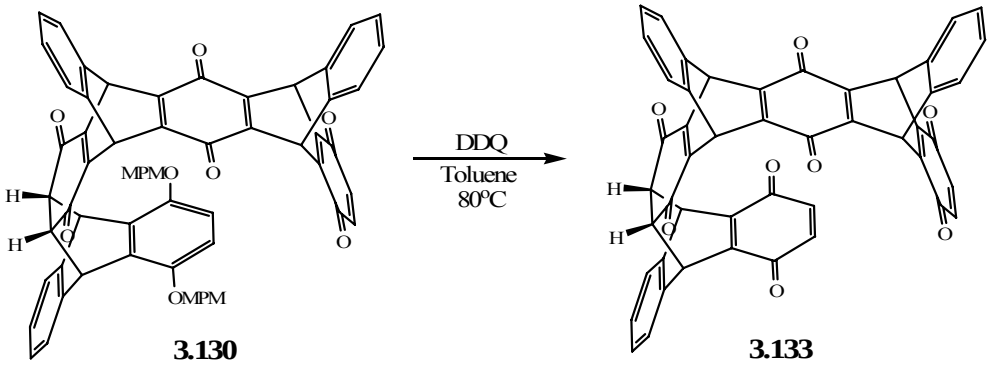
Since the methoxy group on benzene ring was difficult to remove without affecting the methoxy groups in anthracene ring, we started to explore the possible replacement of 1,2-dimethoxy groups in **3.119** or **3.121** by *p*-methoxyphenylmethoxy (MPM) group. The retrosynthetic analysis went back to replacement of methoxy group in 3-teeth quinone intermediated **3.91**, which was easy to realize by reacting the 1,4-di-MPM-anthracene **3.129** with *cis*-penticene trisquinone to afford the MPM protected 3-teeth quinone intermediate **3.130** in 36% yield. Further Diels-Alder reaction with bisdimethoxyanthracene **3.56** at 110°C gave 28% of 3:7 ratio of two adducts **3.131** and **3.132**.



Scheme 3.28

However, when a mixture of **3.131** and **3.132** was treated in either NaH / DMF or HBr / HOAc conditions, no identificable enolised product was isolated. Side reaction became dominant in both conditions. Possible reasons might be in basic conditions, bulky MPM group blocks hydride attacking α-proton of carbonyl group, while in acid conditions, MPM group might come off and destablize the molecule.

How about removing MPM groups in **3.131** and **3.132** first before enolization? The model reaction of deprotection of intermediate **3.130** by DDQ in toluene at 80 ^{o}C for overnight gave deprotected product **3.133** from crude ^{1}H NMR. However compound **3.133** decomposed during workup probably due to loss of stablizing charge-transfer interactions. So, it is not a good idea to remove MPM group before enolization. Besides, it was predicted that deprotection of MPM groups in **3.131** and **3.132** might need even a higher temperature due to steric hinderance. At that temperature, retro-Diels-Alder reaction might also occur.



3.130 **3.133**

Scheme 3.29

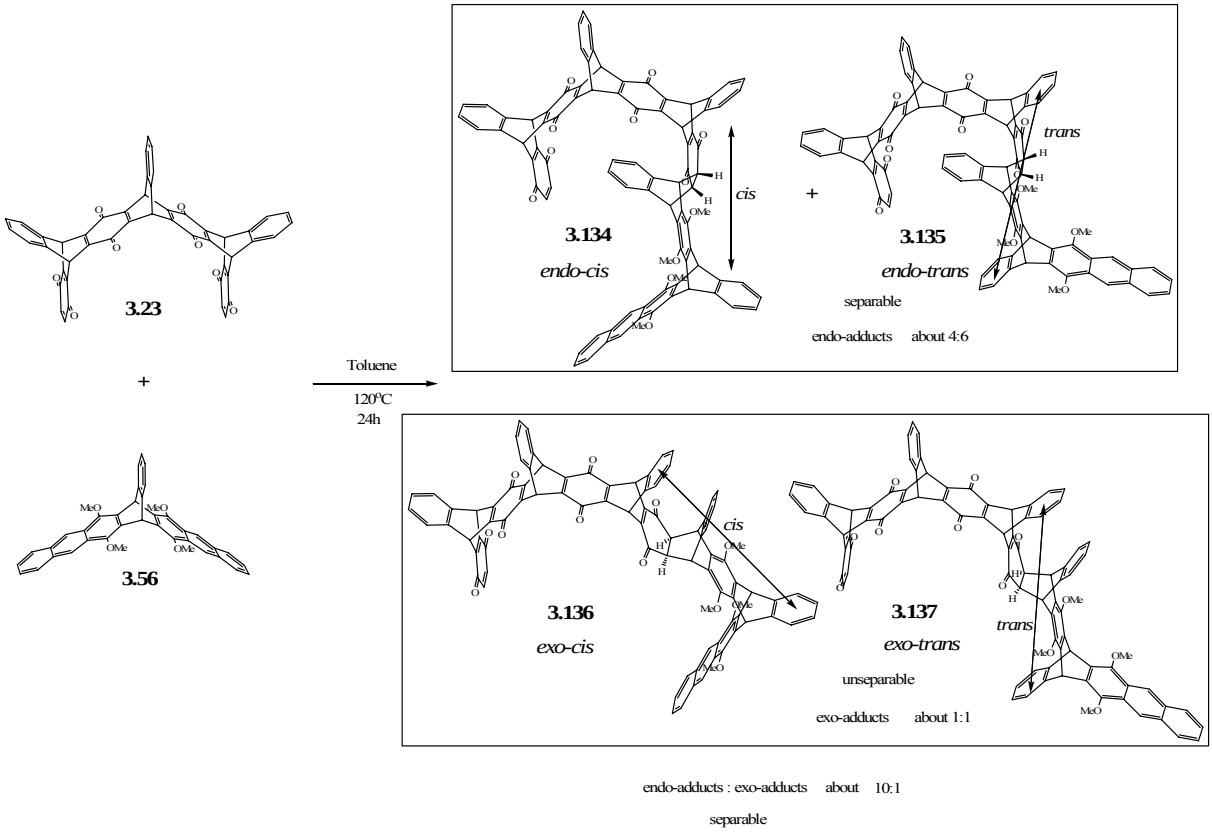
3.3.4.8) Diels-Alder reaction of tetraquinone and bisdimethoxyanthracene and final cyclization

Since both previous efforts of selective demethoxylation to form one quinone end while leaving the other dimethoxyanthracene end intact and protecting group manipulation failed. The direct Diels-Alder reaction between the tetraquinone and bisdimethoxyanthracene seemed to be a possible route left for trying. Although this route was abandoned from previous study because of the formation of predominantly unwanted *endo*-adducts. (That was the reason why previously we tried to go around this face-selectivity problem by so-called *endo*-face blocking strategy.) We hoped a small amount of *exo*-adducts could be separated and identified from proton NMR spectroscopy from their distinguishable structural units. It was predicted the *exo-cis* adduct would undergo cylization after enolization.

When tetraquinone **3.23** and 1 eq. of bisdimethoxyanthracene **3.56** was refluxed in toluene under argon for 24 hours, the crude proton NMR showed predominantly two *endo*-adducts were formed as expected, which was characterized by the upfield shift of newly formed benzene tooth proton up to δ 5.7 because of strong shielding effect of *endo*-face. For *exo*-adducts, the expected new formed benzene tooth proton is around δ 6.3, which was difficult to identify in crude ^{1}HNMR due to overlapping with other signals. We then took a closer look at protons near

the Diels-Alder connection sites. Beside the major δ 4.86 peak, a minor δ 4.93 peak with integral only about 1/10 that of the major pear might be the evidence of forming *exo*-adducts. A similar pattern was found for δ 2.92 and 2.87 in a ratio of 10:1, which are α–protons of carbonyl groups.

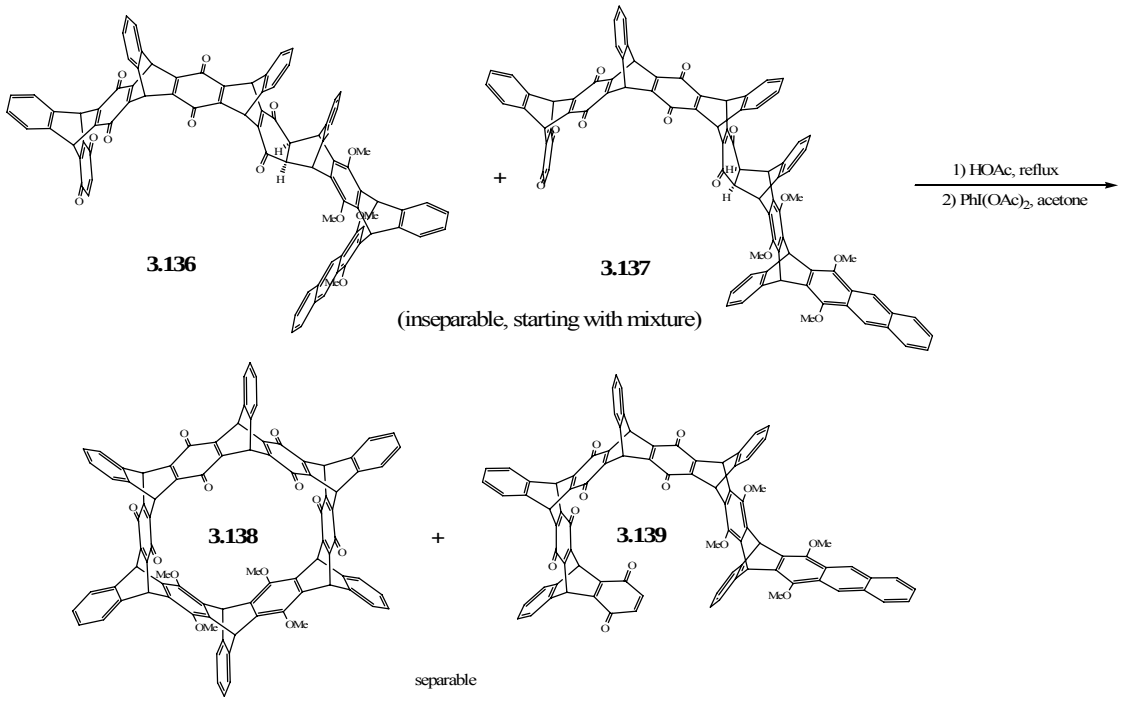
The separation of *endo*-adducts and *exo*-adducts turned out to be difficult. The four 1:1 adducts were only partially separated in column chromatography. Pure samples of each of the two *endo*-adducts together with a mixture of two *endo*-adducts were obtained by PTLC methods using toluene-chloroform-ethyl acetate (25:25:2, V:V:V) as eluent. HPLC conditions for separation of these isomers are absolutely needed later for scaled-up reactions. The yield for *exo*-adducts after purification in the first trial reaction was only about 2.7%. Starting from 57 mg of the tetraquinone and 45 mg of bisdimethoxyanthracene, only 2.8 mg of unseparable two *exo*-adducts **3.136** and **3.137** in a 1:1 ratio was obtained, but, it was enough for a trial of cyclization.



Scheme 3.30 Diels-Alder reaction of tetraene **3.23** and bisanthracene **3.56**.

The small amount of *exo*-adducts was first stirred in acetic acid at room temperature over night for enolizing the keto α-CH. No appreciable change happened after workup. The recovered sample was treated with refluxing acetic acid under argon for half an hour. After aqueous

workup, the residue was dissolved in acetone and treated with diacetoxyiodobenzene to oxidize phenol to quinone. Besides unreacted starting material, TLC showed two newly formed spots with higher Rf. values. After column chromatography, the less polar new spot was isolated in 0.6 mg. ^{1}HNMR showed the disappearance of quinone proton peak (around δ 6.6) and DA adducts characteristic peaks (around δ 4.9, 2.9). The single methoxy peak around δ 3.8 and 1:2:2:1 ratio of bridge proton peaks around δ 6.0 showed symmetry of the molecule, which perfectly matches the predicted cyclized product **3.138** from the *exo-cis* adduct **3.136**. The more polar new spot was isolated in 1.2 mg and it was believed to be derived from the other *exo-trans* adduct **3.137**. It is reasonable that circular molecule **3.138** has higher Rf. value than its open chain analoge **3.139**.



Scheme 3.31 Final cyclization of Diels-Alder adduct **3.136** in refluxing acetic acid.

A single crystal X-ray structure of **3.138** was achieved, which shows unquestionable cyclized structure with a inner ring dimeter about 8.9 Å and the distance between two protons in the opposite teeth about 19.6 Å. However, due to low resolution of current generated structure from X-ray data, positions of methoxy groups are undetermined. An average structure shows a hybridization of one third of 1,4-dimethoxybenzene rings and two thirds of quinone rings in the shaft probablily because of fast rotation of the molecule in the crystal . We also discovered each unit cell in a single crystal contains four **3.138** molecules. Two of them (colored red and green)

are almost parallel to each other and the other two molecules (colored blue and cyan) intercalate between them. (**Figure 3.30**)

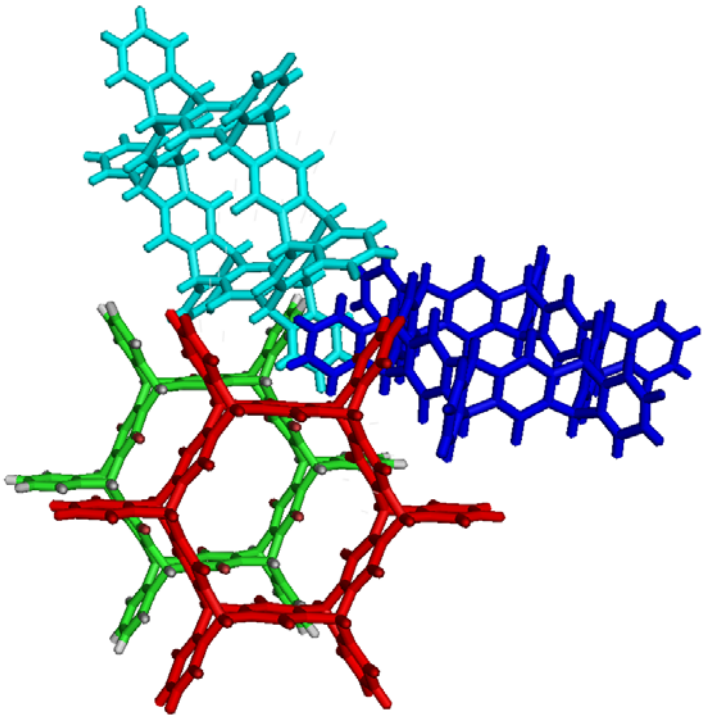


Figure 3.30 Stacking of cyclododeciptycene **3.318** molecules in a unit cell of a single crystal. Methoxy groups are omitted for clarity. (Due to low resolution of current generated structure from X-ray data, the relative positions of methoxy groups are undetermined.)

Although the cyclized cyclododeciptycene derivative was obtained, improving yields and reducing separation work are needed for later property study. First, the low ratio of *exo*- and *endo*-adducts is not acceptable. By simply changing the solvent from toluene to 1,2-dichloroethane, the ratio was improved to about 1:2. But the reaction has to be maintained in a sealed tube for reaction temperature (120 ^{o}C) above boiling point of 1,2-dichloroethane. That was a great improvement, but not enough. How can we improve the ratio of *exo*- and *endo*-adducts even more for favoring *exo*-adducts?

The favored *endo*-selectivity is due to donor-acceptor interaction of electron poor *endo*-face with electron rich diene moiety. If in a reaction solution, a better electron donor was added to "combine" at *endo*-face and "block' the reaction of bisdimethoxyanthracene **3.56** from *endo*-face, this would change the facial selectivity. Based on this assumption, 1,4-dimethoxybenzene, which has a melting point of 54 ^{o}C and a boiling point of 213 ^{o}C, is an ideal electron rich

solvent with high boiling points for Diels-Alder reaction in a wide range of temperatures. Since it was used as a solvent, it also has population advantage over the reactant dimethoxyanthracene. Actually, the ratio of *exo*- and *endo*-adducts was improved to about 3:2 ratio when using 1,4-dimethoxybenzene as solvent. The reaction time was also reduced to four hours at 140 ^{o}C.

After successfully solving the facial selectivity problem of Diels-Alder reaction, we looked into the tedious separation of four Diels-Alder adducts. Since the cyclized product **3.138** has higher Rf. value than its open analog **3.139**. So there would expected similar Rf. value differences between **3.138** and products from *endo*-adducts in refluxing acetic acid condition. A mixture of four adducts was refluxed in acetic acid. To our delight, the introduced two new unwanted products from *endo*-adducts did not increase the task in getting pure **3.138**, since they have almost same Rf. value as **3.139**. However, better conditions for purification of cyclized cyclododeciptycene **3.138** are still need to be developed.

3.3.4.9) Failed *demethoxylation of **3.138** to cyclododeciptycene hexaquione **3.1***

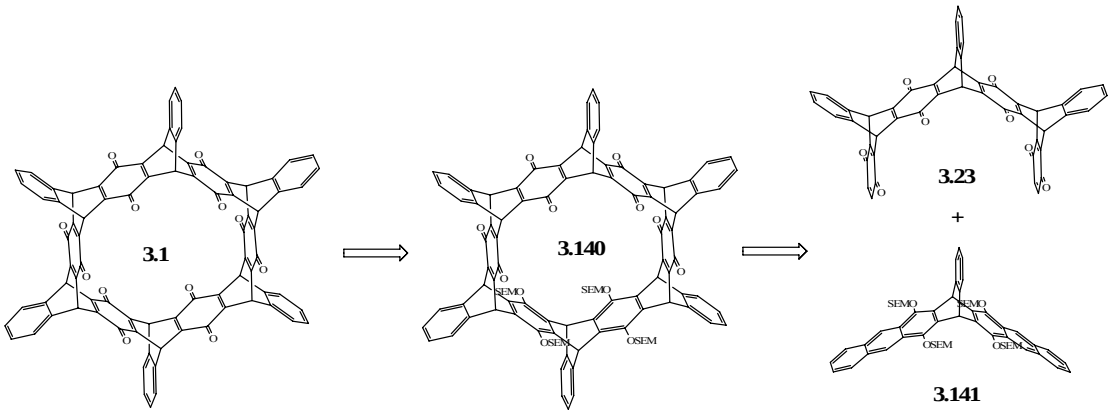
The methoxy group in the molecule **3.318** seemed to be quite inert. An attempted oxy-demethoxylation of **3.138** using CAN failed even at a temperature as high as 80 ^{o}C. The demethoxylation using BBr_3, a strong Louis acid efficient for demethoxylation in many other condtions, also failed to give demethoxylated product. The difficulty of demethoxylation maybe due to highly hindered methoxy groups surrounded by rigid *o*-benzeno "teeth" and carbonyl groups in nearby quinone rings.

3.4 Conclusion and future work

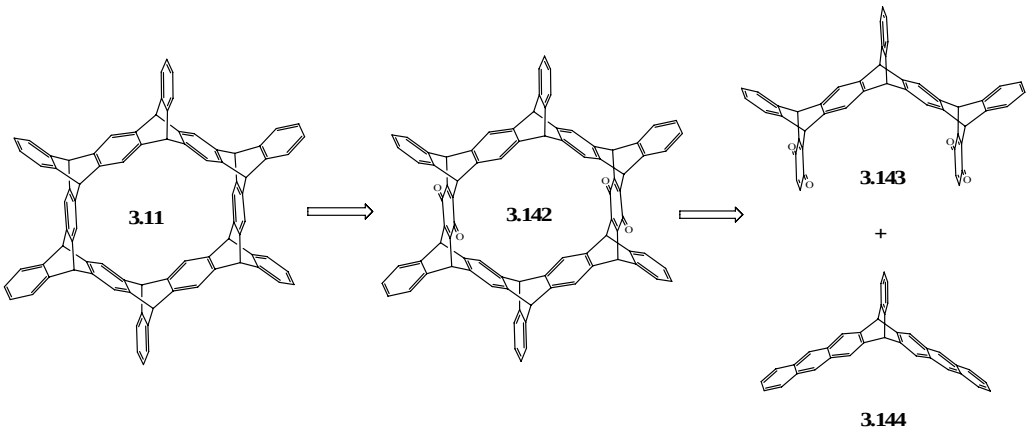
After a year of hardwork and going through many difficulties in synthetic efforts towards cyclododeciptycene hexaquinone, the first cyclododeciptycene derivative **3.318** was synthesized. The work showed how beautifully a complicated molecule such as **3.318** can be assembled from small simple building blocks as *o*-xylene and *p*-benzoquinone. We learned a lot from previous failed synthesis of [10]beltene derivative and literature study. Compared to the previous system of [10] beltene, the key Diels-Alder intemediates tetraquinone **3.23** and bisdimethoxyanthracene **3.56** have rigid and parallel reaction ends. Also inherent NMR structure indicators within the molecule helps to determine structures of Diels-Alder adducts. Besides, the synthetic route was much shorter and convergent.

The synthesis of **3.318** opens possible synthesis of a variety of cyclododeciptycene derivatives with various substitutions by starting from different building blocks. The target cyclododeciptycene hexaquinone **3.1** may be synthesized by bisanthrancene with different protecting groups like 2-(trimethylsilyl)ethoxymethyl (SEM) group which are easier to remove under milder conditions than the methoxy group. The cyclododeciptycene **3.11** would be synthesized from bisanthracene **3.143** and bisquinone **3.144**. Similarly, dodecamethoxy cyclododeciptycene **3.145** would be synthesized from bisdimethoxyanthracene **3.56** and bisquinone **3.147**.

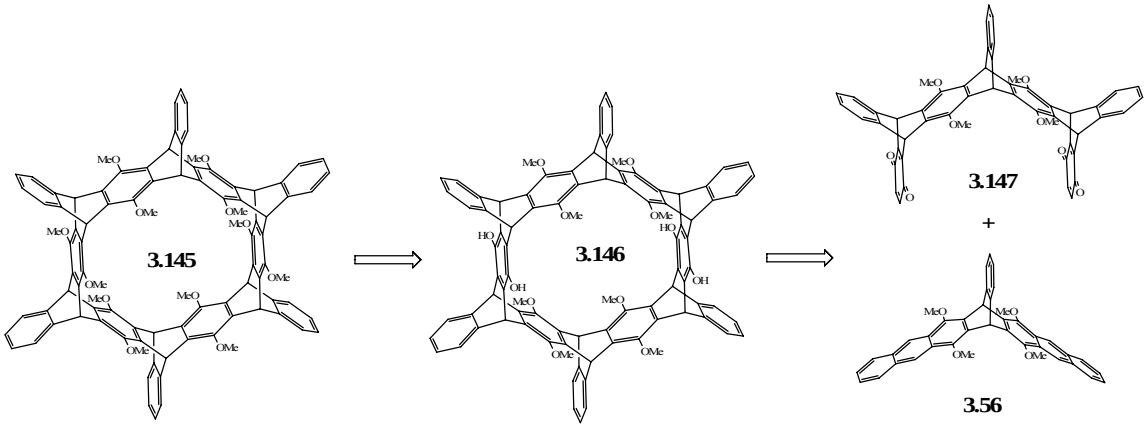
We may also synthesize more complicated cycloiptycene structures shown in **Figure 3.4** such as **3.148**, a [36]cycloiptycene derivative. The compound **3.148** can be assembled by four bisanthracene **3.56**, two triptycene bisquinone **3.17**, and two pentiptycene trisquinone **3.21** through eight Diels-Alder reactions. The purification would be inevitably difficult, but the right intermediate for cyclization still can be figured out by inherent NMR structual indicators.



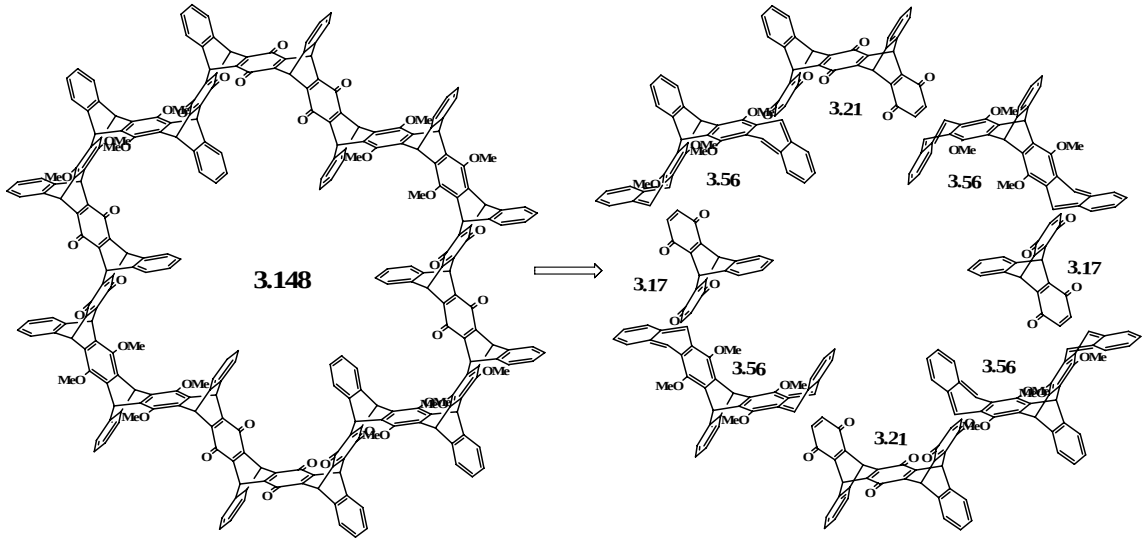
Scheme 3.32



Scheme 3.33

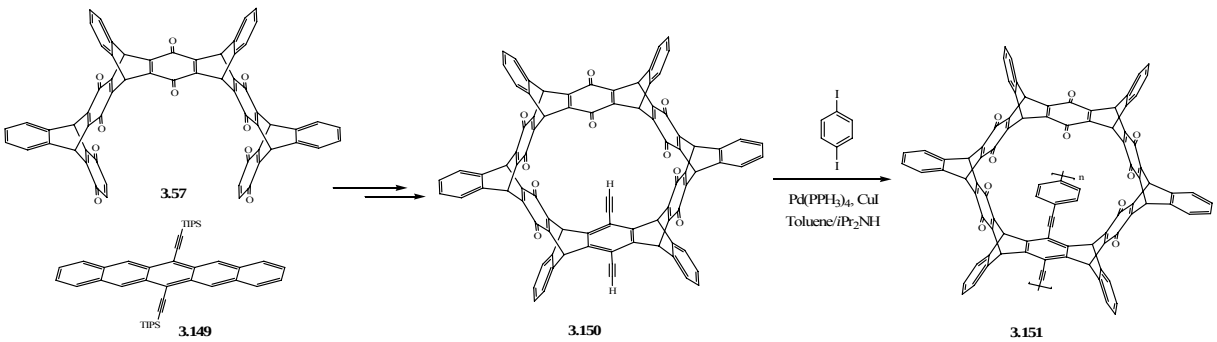


Scheme 3.34



Scheme 3.35

We can also synthesize cycloiptycene-containing poly(*p*-phenyleneethynylene)s similar to what Swager's group has done.[25] This new structure of polymers may have some new interesting properties as new materials.

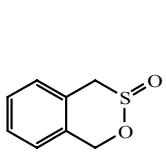


Scheme 3.36

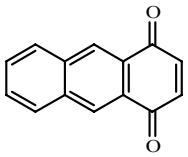
3.5 Experimental section

General Methods: Nuclear magnetic resonance spectra were obtained at Varian Unity Plus (400 MHz) and Varian Gemini 2000 (200 MHz). Mass spectra were taken from a Hewlett Packard 5890A Series II, GC-MS and a Bruker Esquire 3000 Plus electrospray ionization mass spectrometer. FAB spectra were taken by using Xe beam (8 KV) and m-nitrobenzyl alcohol as matrix. Silica gel (200~400 mesh) from Natland International Coporation was used for the flash chromatographic separation. THF and diethyl ether were distilled over sodium and benzophenone. Methylene chloride was distilled over CaH_2. Toluene and benzene were distilled over $LiAlH_4$.

3.5.1 Synthesis of one tooth synthons



3.53



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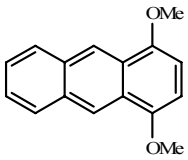

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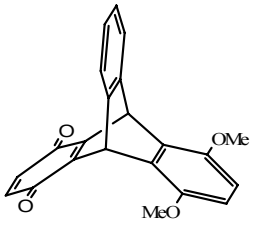
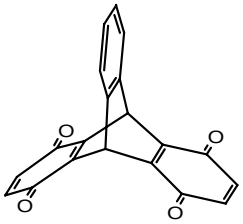


3.73



3.17

3.5.1.1) ***1,4-Dihydro-2,3-benzoxathiin-3-oxide*** **(3.53)**[57]

1) **1,2-Bis(bromomethyl)benzene** (**3.102**)

To a solution of 10 g (94 mmol) of 1,2-dimethylbenzene in 250 mL benzene was added 33.5 g (188 mmol) of *N*-bromosuccinimde and 912 mg (3.77 mmol) of benzoyl peroxide. The mixture was heated to reflux under argon for 2 hours, and then concentrated to about 50 mL by a rotavapor. The white solids precipitated were filtered and redissolved in 200 mL ethyl ether, washed by 150 mL water three times, and 150 mL brine once. The ether layer was dried over anhydrous magnesium sulfate, filtered and then concentrated to give 10.2 g (41% yield) of the title compound, **3.102**, as white solids: m.p. 92~94 ^{o}C (literature:[58] 94~95 ^{o}C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.28~7.40 (m, 4 H), 4.67 (s, 4 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 136.8, 131.3, 129.7, 30.2.

2) **1,4-Dihydro-2,3-benzoxathiin-3-oxide** (**3.53**)[57]

A mixture of 12.4 g (80.6 mmol) of sodium hydroxymethanesulfinate, 2.60 g (8.06 mmol) of tetrabutylammonium bromide, and 10.6 g (40.3 mmol) of 1,2-bis(bromomethyl)benzene

(**3.102**) in 40.3 mL DMF was stirred at 0 ^{o}C for 3 hours. The reaction was worked up by adding 200 mL of ethyl ether, washing with 150 mL water twice and 150 mL brine. The ether layer was dried over anhydrous magnesium sulfate, filtered, and concentrated. The residue was applied to column chromatography using a mixture of petrol ether and ethyl ether (1:1, V:V) as eluent to afford 4.34 g (65% yield) of the title compound, **3.53**, as a light yellow oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.18~7.38 (m, 4 H), 5.28 (d, *J* = 13.2 Hz, 2 H), 4.95 (d, *J* = 13.2 Hz, 2 H), 4.40 (d, *J* = 15.6 Hz, 2 H), 3.54 (d, *J* = 15.6 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 133.8, 129.8, 128.7, 127.9, 126.3, 125.8, 63.1, 57.0.

3.5.1.2) *1,4-Anthracenedione* (3.65)[41]

Route 1: To the solution of 24.0 g (100 mmol) of quinizarin (**3.63**) in 500 mL methanol was added 15.1 g (400 mmol, 4.0 eq.) of sodium borohydride in portions at 0 ^{o}C. The reaction mixture was stirred at 0 ^{o}C for 2 hours and then was added dropwisely to 350 mL of conc. HCl and 1 L of water. The solid precipitated was filtered, washed several times with distilled water, and dried under vacuum to give 19.8g (yield 95%) of the title compound, **3.65**, as yellow solids: m.p. 214~216 ^{o}C (literature:[59] 218~221 ^{o}C); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.64 (s, 2 H), 8.08 (dd, J_1 = 6.3 Hz, J_2 = 3.5 Hz, 2 H), 7.71 (dd, J_1 = 6.1 Hz, J_2 = 3.3 Hz, 2 H), 7.08 (s, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 184.8, 140.2, 135.0, 130.4, 129.7, 129.0, 128.6.

Route 2:

1) ***cis*-4a,9,9a,10-Tetrahydroanthracene-1,4-dione (3.68)**[50]

To a solution of 216 mg (2.00 mmol) of 1,4-benzoquinone in 10 mL of benzene under argon was added 168 mg (1 mmol) of the sultine **3.53**. The reaction mixture was refluxed for 2 hours and benzene was removed by rotavapor. The residue was washed by petrol ether for twice and recrystalized from methanol to afford 83 mg (39% yield) of the title compound, **3.68**, as off-white needles: m.p. 123~125 ^{o}C (literature:[50] 122~123 ^{o}C); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.08~7.14 (m, 4 H), 6.72 (s, 2 H), 3.41 (m, 2 H), 3.16~3.30 (m, 2 H), 2.83~3.00 (m, 2 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 199.8, 139.7, 133.0, 129.1, 126.7, 47.0, 28.6.

2) **1,4-Anthracenedione (3.65)**

A mixture of 52 mg (0.25 mmol) of **3.68** and 181 mg (0.736 mmol) of chloranil was refluxed in acetic acid overnight. The acetic acid was removed by rotavapor. The residue was dissolved in 20 mL of ethyl acetate, washed by water (20 mL), brine (20 mL), dried over anhydrous mageniusm sulfate, and filtered. The filtrate was concentrated and applied to column

chromatography using petrol ether and methylene chloride as eluent to afford 46 mg (90% yield) of the title compound **3.65**.

3.5.1.3) ***1, 4-Dimethoxyanthracene*** **(3.54)** [41]

1) **1, 4-Dihydroxyanthracene** (**3.66**)

To the solution of 20.1 g (100 mmol) 1,4-anthraquinone **3.65** in 625 mL 1,4-dioxane was added a solution of 75.0 g (366 mmol.) 85% sodium hydrosulfite in 625 mL water. The solution was stirred at room temperature for 10 hours and then poured into a solution of 172 mL concentrated HCl in 3 L water. The precipitation was filtered, washed several times with distilled water, and dried under vacuum to give 17.3 g (82%) of the title compound, **3.66**, as green powder: m.p. 165~167 ^{o}C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 9.57 (s, 2 H), 8.66 (s, 2 H), 8.08 (dd, J_1 = 6.3 Hz, J_2 = 3.2 Hz, 2 H), 7.46 (dd, J_1 = 6.2 Hz, J_2 = 3.4 Hz, 2 H), 6.61 (s, 2 H); ^{13}C NMR (DMSO-d_6, 50 MHz) δ 145.4, 136.2, 130.5, 128.4, 125.4, 120.7, 105.6.

2) **1, 4-Dimethoxyanthracene** (**3.54**)

To a cool solution of 5.00 g (23.8 mmol) 1, 4-dihydroxyanthracene **3.66** in 25 mL DMF at 0^{o} C was added 2.29 g sodium hydride (60% in oil, 57.1 mmol) in portions under argon. The reaction mixture was stirred at 0 ^{o}C for half an hour. Then a solution of 3.7 mL methyl iodide in 25 mL DMF was added dropwisely at 0 ^{o}C. The reaction mixture was slowly warmed up to room temperature and stirred in room temperature for 2 hours. The salts precipitated out were filtered and washed with 200 mL ethyl ether. The filtrated was washed with water (150 mL × 2), brine (150 mL), dried over anhydrous magnesium sulfate, concentrated, and applied to column chromatography (silica gel) using a mixture of petroleum ether and methylene chloride (1:1, V:V) as eluent to afford 3.69 g (yield 65%) of the title compound, **3.54**, as yellow crystals: m.p. 131~133 ^{o}C (literature:[60] 134~136 ^{o}C); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.77 (s, 2 H), 8.04 (dd, J_1 = 6.4 Hz, J_2 = 3.4 Hz, 2 H), 7.47 (dd, J_1 = 6.4 Hz, J_2 = 3.0 Hz, 2 H), 6.60 (s, 2 H), 4.03 (s, 6 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 149.7, 131.7, 128.8, 125.7, 121.0, 101.1, 55.9.

3.5.1.4) ***9,10-Dihydro-9,10-(o-benzeno)anthracene-1,4,5,8-tetrone (triptycenebisquinone)*** **(3.17)**

1) **(*4aR,9R,9aS,10S*)-5,8-Dimethoxy-4a,9,9a,10-tetrahydro-9,10-(*o*-benzeno)anthracene-1,4-dione** (**3.69**, *endo*-)

(*4aR,9S,9aS,10R*)-5,8-Dimethoxy-4a,9,9a,10-tetrahydro-9,10-(*o*-benzeno)anthracene-1,4-dione (**3.70**, *exo*-)

A solution of 10.2 g (42.8 mmol) of 1,4-dimethoxyanthracene **3.54** and 6.80 g (60.6 mmol) of 1,4-benzoquinone in 180 mL of toluene was refluxed for 36 h, then cooled to room temperature. The precipitate was filtered and weighted 13.4 g. The filtrate was concentrated to dryness, and applied to column chromatography (silica gel) using an eluent series with increasing polarity starting from petrol ether and methylene chloride (2:3, V:V), to (1:4, V:V), followed by methylene chloride and acetone (50:1, V:V), and finally methylene chloride and acetone (25:1) to afford another batch of the Diels-Alder adducts 0.85 g. Total yield of two adducts **3.69** and **3.70** (in about 1:1 ratio from ^{1}H NMR) was 96%. **3.69** and **3.70** can be partially separated by silica gel column chromatography using petrol ether and methylene chloride (1:2, V:V) with 1% volume of ethyl ether as eluent. The less polar adduct **3.69**: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.21 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2 H), 7.06 (dd, J_1 = 5.4 Hz, J_2 = 4.2 Hz, 2 H), 6.65 (s, 2 H), 6.28 (s, 2 H), 5.31 (t, J = 1.0 Hz, 2 H), 3.82 (s, 6 H), 3.07 (t, J = 1.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 198.6, 148.7, 140.7, 140.2, 131.4, 126.7, 125.1, 109.3, 56.2, 48.7, 42.3. More polar adduct **3.70**: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.42 (dd, J_1 = 5.2 Hz, J_2 = 3.1 Hz, 2 H), 7.17 (dd, J_1 = 5.3 Hz, J_2 = 3.3 Hz, 2 H), 6.59 (s, 2 H), 6.31 (s, 2 H), 5.31 (t, J = 1.0 Hz, 2 H), 3.75 (s, 6 H, Me), 3.07(t, J = 1.0 Hz, 2 H); ^{13}CNMR ($CDCl_3$, 50 MHz) δ 198.3, 149.4, 142.0, 140.5, 129.7, 126.7, 124.2, 110.0, 56.6, 49.0, 42.6.

2) **9,10-Dihydro-1,4-dihydroxy-5,8-dimethoxy-9,10-(*o*-benzeno)anthracene** (**3.71**)

To a suspension of 14.0 g (40.4 mmol) **3.69** & **3.70** (about 1:1 ratio) in 300 mL acetic acid under argon was added 132 drops of hydrobromic acid (40% in water). The mixture was refluxed for 10 min and poured into 100 g ice. The white precipitate was filtered and dried in vacuum to afford 12.7 g (yield 87%) of the title compound **3.71**: ^{1}H NMR (DMSO-d_6, 200 MHz) δ 8.86 (s, 2 H), 7.35 (dd, J_1 = 4.7 Hz, J_2 = 3.2 Hz, 2 H), 6.94 (dd, J_1 = 5.0 Hz, J_2 = 3.3 Hz, 2 H), 6.58 (s, 2 H), 6.30 (s, 2 H), 6.13 (s, 2 H), 3.75 (s, 6 H); ^{13}C NMR (DMSO-d_6, 50 MHz) δ 148.6, 146.2, 144.9, 135.2, 132.3, 124.6, 123.6, 112.9, 109.0, 56.2, 40.4.

3) **9,10-Dihydro-9,10-(*o*-benzeno)anthracene-1,4,5,8-tetrone** (**3.17**)

Route 1: To a stirred solution of 1.0 g (2.9 mmol) of **3.73** in 40 mL acetonitrile and 40 mL THF at 0 ^{o}C was added dropwisely a solution of 4.78 g (8.70 mmol) of ammonium cerium (IV) nitrate (CAN) in 20 mL water. After stirring at 0 ^{o}C for 30 minutes, another portion of 797 mg (1.45 mmol) of CAN was added. The reaction was stirred at 0 ^{o}C for another 30 minutes, then diluted with water (200 mL), extracted with ethyl acetate (150 mL × 2). The combined ethyl

acetate layer was washed by water (150 mL × 2), brine (150 mL), dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was applied to column chromatography (silica gel) using an eluent series with increasing polarity starting from petrol ether and methylene chloride (2:3, V:V), then petrol ether and methylene chloride (1:2, V:V), followed by petrol ether, methylene chloride and ethyl ether (1:2:0.06, V:V:V) to afford 921 mg (100% yield) of the title compound, **3.17**, as yellow solids: m.p. 297~298 ^{o}C, decomp. [literature[13] >220 ^{o}C(decomp.)]; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.49 (dd, J_1 = 5.4 Hz, J_2 = 3.2 Hz, H), 7.08 (dd, J_1 = 5.4 Hz, J_2 = 3.2 Hz, 2 H), 6.65 (s, 4 H), 6.18 (s, 2 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 182.5, 151.8, 142.3, 135.7, 126.2, 125.7, 42.4.

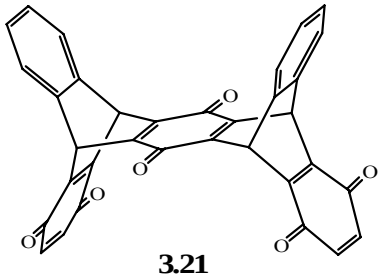
Route 2:

To a suspension of 4.00 g (11.5 mmol) of **3.71** in 200 mL dioxane at 0 ^{o}C was added dropwisely a solution of 25.3 g (46.2 mmol)ammonium cerium (IV) nitrate in 200 mL water. The mixture was stirred at room temperature for 1 hour, diluted with 400 mL water, extracted with 400 mL ethyl acetate for twice. The combined ethyl acetate layer was washed with water (400 mL × 3) and brine (400 mL), dried over anhydrous magnesium sulfate, filtered. The yellow precipitate formed during concentration was filtered to afford 2.66 g of the title compound. The filtrate was concentrated to dryness and applied to column chromatography (silica gel) using an eluent series with increasing polarity starting from petrol ether and methylene chloride (2:3, V:V), then petrol ether and methylene chloride (1:2, V:V), followed by petrol ether, methylene chloride and ethyl ether (1:2:0.06, V:V:V) to afford 698 mg of the title compound. The total yield calculated was 92.6%.

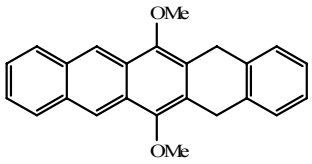
3.5.1.4) ***9,10-Dihydro-5,8-dimethoxy -9,10-(o-benzeno)anthracene-1,4-dione*** **(3.73)**

To a suspension of 3.45 g (10.0 mmol) of **3.71** in 200 mL (actonitrile : H_2O = 6:1, V:V) at 0 ^{o}C was added 10.9 g (20.0 mmol) of CAN. The reaction mixture was stirred at room temperature for half an hour. The red precipitate was filtered to afford 3.30 g (96% yield) of the title compound **3.73**. m.p. 269~270 ^{o}C (literature:[13] 271.5~272.5 ^{o}C); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.44 (dd, J_1 = 5.3 Hz, J_2 = 3.1 Hz, 2 H), 7.01 (dd, J_1 = 5.3 Hz, J_2 = 3.1 Hz, 2 H), 6.57 (s, 2 H), 6.53 (s, 2 H), 6.23 (s, 2 H), 3.80 (s, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 183.8, 153.1, 149.9, 144.4, 135.5, 133.8, 125.5, 124.8, 109.8, 56.6, 41.6.

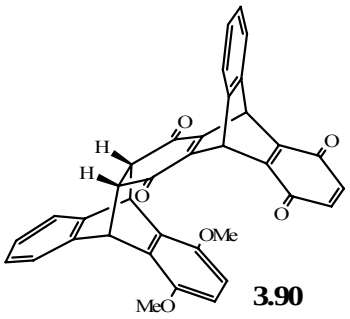
3.5.2 Synthesis of 2-teeth synthons



3.21



3.55



3.90

3.5.2.1) ***(5R,7S,12R,14S)-5,7,12,14-Tetrahydro-5,14:7,12-di(o-benzeno)pentacene-1,4,6,8,11, 13-hexaone*** *(cis-***pentiptycenetrisquinone***)* (**3.21**)

1) **(*5R,5aS,7S,12R,14aR,14S*)-1,4,8,11-Tetramethoxy-5,5a,7,12,14,14a-hexahydro-5,14: 7,12-di(*o*-benzeno)pentacene-6,13-dione** (**3.77**)

(*5R,5aR,7S,12R,14aS,14S*)-1,4,8,11-Tetramethoxy-5,5a,7,12,14,14a-hexahydro-5,14: 7,12-di(*o*-benzeno)pentacene-6,13-dione (**3.78**)

(*5R,5aR,7R,12S,14aS,14S*)-1,4,8,11-Tetramethoxy-5,5a,7,12,14,14a-hexahydro-5,14: 7,12-di(*o*-benzeno)pentacene-6,13-dione (**3.79**)

***(5R,5aS,7R,12S,14aR,14S*)-1,4,8,11-Tetramethoxy-5,5a,7,12,14,14a-hexahydro-5,14: 7,12-di(*o*-benzeno)pentacene-6,13-dione** (**3.80**)

A solution of 1,4-dimethoxyanthracene (715 mg, 3.00 mmol) and 5,8-di-methoxy-9,10-dihydro-9,10-(*o*-benzeno)anthracene-1,4-dione (**3.73**) (689 mg, 2.00 mmol) in 12 mL dry toluene was heated to 170 ^{o}C (oil bath temperature) in a sealed tube for 36 hours. The reaction mixture was cooled to room temperature. The yellow precipitate was filtered, washed with toluene (2 mL) and ethyl ether (5 mL), and dried in vacuum to give 508 mg (44% yield) of a mixture of **3.77** and **3.78** (about 7:3 from ^{1}H NMR) The filtrate was concentrated and purified by column chromatography (silica gel) using a mixture of toluene, chloroform and ethyl acetate (25:25:1, V:V:V) as eluent to give 570 mg (49% yield) of a mixture of four isomers in a ratio of 1:4:7:6. The calculated total yield of four adducts was 93% with 30% for **3.77**, 24% for **3.78**, 49% for **3.79**, and 18% for **3.80**, respectively.

Diels Alder adduct **3.77** (the less polar spot of **3.77** and **3.78**; pure sample was available by careful column chromatography): m.p. 277~278 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.37 (dd, J_1 = 5.6 Hz, J_2 = 3.6 Hz, 2 H), 7.34 (dd, J_1 = 5.4 Hz, J_2 = 3.4 Hz, 2 H), 7.13 (dd, J_1 = 5.6 Hz, J_2 = 3.2 Hz, 2 H), 6.92 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2 H), 6.50 (s, 2 H), 5.94 (s, 2 H), 5.85 (s, 2 H),

5.17 (t, J = 1.2 Hz, 2 H), 3.79 (s, 6 H, OMe), 3.65 (s, 6 H, OMe), 2.98 (t, J = 1.2 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 194.0 (C=O), 157.2, 149.3, 148.7, 144.3, 141.8, 133.8, 128.5, 126.6, 125.3, 124.6, 124.2, 109.6, 109.0, 56.2 (OMe), 56.0 (OMe), 50.4, 43.5, 41.7.

Diels-Alder adduct **3.78** (hard to separate from **3.77**): ^{1}H NMR ($CDCl_3$, 400 MHz) (deduced from ^{1}H NMR, COSY & NOESY of a 7:3 mixture of **3.77** and **3.78**) δ 7.18 (dd, J_1 = 5.2 Hz, J_2 = 3.1 Hz, 2 H), 6.91 (dd, J_1 = 5.6 Hz, J_2 = 2.8 Hz, 2 H), 6.83 (dd, J_1 = 5.2 Hz, J_2 = 3.2 Hz, 2 H), 6.61 (s, 2 H), 6.46 (s, 2 H), 6.34 (dd, J_1 = 5.6 Hz, J_2 = 3.2 Hz, 2 H), 5.94 (s, 2 H), 5.14 (t, J = 1.0 Hz, 2 H), 3.80 (s, 6 H, OMe), 3.76 (s, 6 H, OMe), 3.00 (t, J = 1.2 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) (deduced from ^{13}C NMRs of pure **3.77** and a 7:3 mixture of **3.77** and **3.78**) δ 194.6 (C=O), 157.6, 149.9, 148.8, 143.9, 138.9, 133.6, 131.6, 126.5, 125.1, 124.4, 124.1, 110.1, 109.4, 56.9 (OMe), 56.3 (OMe), 49.9, 43.4, 41.8.

Diels-Alder adduct **3.79** (hard to separate from **3.80**, no pure sample was available)**:** ^{1}HNMR ($CDCl_3$, 400 MHz) (deduced from ^{1}H NMR, COSY, NOESY of a 1:1 mixture of **3.79** and **3.80**) δ 7.35 (dd, J_1 = 5.4 Hz, J_2 = 3.4 Hz, 2 H), 6.93 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2 H), 6.89 (dd, J_1 = 5.2 Hz, J_2 = 3.0 Hz, 2H), 6.61 (s, 2 H), 6.47 (s, 2 H), 6.35 (dd, J_1 = 5.2 Hz, J_2 = 3.2 Hz, 2 H), 5.91 (s, 2 H), 5.13 (t, 2 H, J = 1.2 Hz), 3.82 (s, 6 H, OCH_3), 3.79 (s, 6 H, OCH_3), 3.00 (t, 2 H, J = 1.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) (deduced from ^{13}C NMR of a 1:1 mixture of **3.79** and **3.80** and ^{13}C NMR of a 70% of **3.80** sample) δ 194.7 (C=O), 157.5, 149.8, 148.8, 144.0, 139.1, 133.6, 131.5, 126.3, 125.3, 124.6, 123.9, 110.0, 109.4, 56.9, 56.3, 50.0, 43.5, 41.7.

Diels-Alder adduct **3.80** (hard to separate from **3.79**, only a 70% of **3.80** sample is available by careful column chromatography): ^{1}H NMR ($CDCl_3$, 400 MHz) (deduced from ^{1}HNMR, COSY, NOESY of a 1:1 mixture of **3.79** and **3.80**) δ 7.37 (dd, J_1 = 5.4 Hz, J_2 = 3.4 Hz, 2 H), 7.20 (dd, J_1 = 5.2 Hz, J_2 = 3.6 Hz, 2 H), 7.12 (dd, J_1 = 5.4 Hz, J_2 = 3.4 Hz, 2 H), 6.98 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2 H), 6.46 (s, 2 H), 5.98 (s, 2 H), 5.84 (s, 2 H), 5.17 (t, 2 H, J = 1.2 Hz), 3.76 (s, 6 H, OCH_3), 3.66 (s, 6 H, OCH_3), 3.00 (t, 2 H, J = 1.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) (deduced from ^{13}C NMR of a 1:1 mixture of **3.79** and **3.80** and ^{13}C NMR of a 70% of **3.80** sample) δ 194.0 (C=O), 157.6, 149.7, 148.3, 144.4, 141.9, 133.4, 128.2, 126.5, 125.1, 124.3, 124.2, 109.9, 109.8, 56.8, 56.2, 50.1, 43.3, 41.9.

2) **(*5R,7S,12R,14S*)-6,13-Dihydroxy-5,7,12,14-tetrahydro-1,4,8,11-tetramethoxy-5,14:7,12-di(*o*-benzeno)pentacene** (**3.81**)

A suspension of 7:3 mixture of **3.77** & **3.78** (600 mg, 1.03 mmol) in acetic acid (24 mL) and hydrobromic acid (40% solution, 24 drops) was refluxed for 10 mins. The grey precipitate formed was filtered and washed with toluene (4 mL) and ethyl ether (10 mL) and dried in vacuum to give 564 mg (yield 94.0 %) of the title compound **3.81**: ^{1}H NMR (DMSO-d_6, 400 MHz) δ 8.64 (s, 4 H), 7.30 (dd, J_1 = 4.8 Hz, J_2 = 3.6 Hz, 4 H), 6.87 (dd, J_1 = 4.8 Hz, J_2 = 3.6 Hz, 4 H), 6.52 (s, 4 H), 6.16 (s, 4 H), 3.72 (s, 12 H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 148.2, 146.1, 140.1, 135.1, 131.1, 124.2, 123.4, 108.6, 55.8 (OMe), 40.4.

3) **(*5R,7S,12R,14S*)-5,7,12,14-Tetrahydro-5,14:7,12-di(*o*-benzeno)pentacene-1,4,6,8, 11,13-hexaone** (*cis*-**pentiptycenetrisquinone**) (**3.21**)[9]

To a suspension of **3.81** (442 mg, 0.759 mmol) in 120 mL acetonitrile and 20 mL water at 0^{o}C was added ammonium cerium (IV) nitrate (3.74 g, 6.82 mmol). The reaction mixture was stirred at room temperature for 5 hours, and extracted with chloroform (300 mL), washed with water (200 mL×2) and brine (200 mL), dried over anhydrous magnesium sulfate, filtered and solvent was removed by a rotavapor. The residue was applied to column chromatography using a mixture of toluene, chloroform and ethyl acetate (25:25:1, V:V:V) as eluent to afford 350 mg (89% yield) of the title compound **3.21**: m.p. >300 ^{o}C (literatue:[9] >320 ^{o}C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.42(dd, J_1 = 5.4 Hz, J_2 = 3.4 Hz, 4 H), 7.02 (dd, J_1 = 5.4 Hz, J_2 = 3.4 Hz, 4 H), 6.61 (s, 4 H), 6.15 (s, 4 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 182.3, 177.8, 151.9, 151.3, 142.3, 135.6, 126.2, 125.7, 42.6.

3.5.2.2) *6,13-Dimethoxy-5,14-dihydropentacene* (**3.55**)

1) **5,14-Dihydro-6,13-dihydroxypentacene** (**3.105**)

A suspension of 416 mg (2.0 mmol) of 1,4-anthracenedione (**3.65**) and 672 mg (4.00 mmol) of benzosultine (**3.53**) in 8 mL dry toluene was heated to 150 ^{o}C in a sealed tube for 30 hours. The reaction mixture was cooled to room temperature. The yellow precipitate was filtered, washed with toluene (2 mL) and ethyl ether (5 mL), dried in vacuum to give 568 mg (91% yield) of the title compound **3.105**: ^{1}H NMR (DMSO-d_6, 400 MHz) δ 8.86 (s, 2 H), 8.74 (s, 2 H), 8.06 (dd, J_1 = 6.6 Hz, J_2 = 3.4 Hz, 2 H), 7.45 (dd, J_1 = 6.4 Hz, J_2 = 3.2 Hz, 2 H), 7.37 (dd, J_1 = 5.2 Hz, J_2 = 3.6 Hz, 2 H), 7.21 (dd, J_1 = 6.2 Hz, J_2 = 3.2 Hz, 2 H), 4.12 (s, 4 H); ^{13}C NMR (DMSO-d_6, 50 MHz) δ 140.9, 136.9, 130.2, 128.3, 127.4, 126.1, 125.0 (2 C), 120.4, 118.4, 29.9.

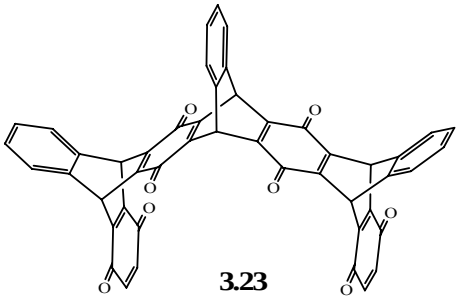
2) **6,13-Dimethoxy-5,14-dihydropentacene** (**3.55**)

To a solution of 100 mg (0.32 mmol) of phenol **3.105** in 2 mL DMF at 0 ^{o}C was added 30.7 mg NaH (60% in oil). The resulting mixture was stirred at 0 ^{o}C for half an hour, then 51.8 μL (0.83 mmol) of methyl iodide was added by syringe. The reaction mixture was stirred at room temperature for 2 hours and diluted with 40 mL ethyl ether. The organic layer was washed with ammonium chloride solution (100 mL), brine (100 mL), dried over anhydrous magnesium sulfate, filtered and concentrated by a rotavapor. The residue was applied to column chromatography using petro ether and ethyl ether (8:1, V:V) as eluent to afford 86 mg (79% yield) of the title compound **3.55**: m.p. 147~148 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.65 (s, 2 H), 8.04 (dd, J_1 = 6.4 Hz, J_2 = 2.8 Hz, 2 H), 7.47 (dd, J_1 = 6.6 Hz, J_2 = 3.0 Hz, 2 H), 7.41 (dd, J_1 = 5.4 Hz, J_2 = 3.4 Hz, 2 H), 7.25 (dd, J_1 = 5.8 Hz, J_2 = 3.4 Hz, 2 H), 4.20 (s, 4 H), 4.06 (s, 6 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.5, 136.8, 131.7, 128.7, 127.8, 126.7, 126.0, 125.7, 121.1, 62.1, 30.5.

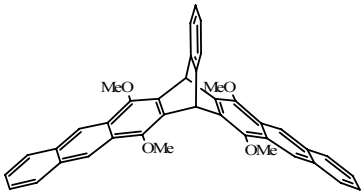
3.5.2.3) ***(5R,6aR,7S,12R,12aS,14S)-8,11-Dimethoxy-5,6a,7,12,12a,14-hexahydro-5,14:7,12-di(o-benzeno)pentacene-6,13-dione*** (**3.90**)

A solution of 1,4-dimethoxyanthracene (119 mg, 0.500 mmol) and triptycene bisquinone (**3.17**) (314 mg, 1.00 mmol) in 10 mL dry toluene was refluxed for 8 h under argon. The reaction mixture was cooled to room temperature. The red precipitate was filtered, washed with toluene (1 mL) and ethyl ether (2 mL), dried in vacuum to give 125 mg crude red precipitate, which was further purified by column chromatography over silica gel using toluene, chloroform and ethyl acetate (25:25:1, V:V:V) as eluent to provide 85 mg (30% yield) of the title compound, **3.90**, as red solids: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.39 (m, 4 H), 7.15 (dd, 2 H), 7.00 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2 H), 6.67 (s, 2 H), 6.18 (s, 2 H), 5.87 (s, 2 H), 5.14 (bs, 2 H), 3.62 (s, 6 H), 3.05 (bs, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 192.9, 188.7, 182.6, 155.6, 150.8, 149.0, 141.9, 141.4, 135.5, 129.3, 126.8, 126.0, 125.5, 124.4, 108.6, 55.9 (OMe), 51.1, 43.5, 42.5.

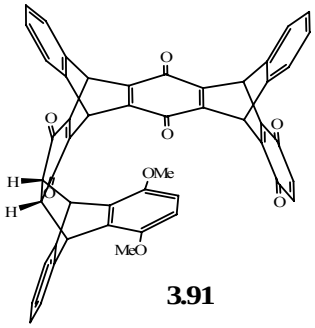
3.5.3 Synthesis of 3-teeth synthons



3.23



3.56



3.91

3.5.3.1) ***(5R,7s,9S,14R,16s,18S)-5,7,9,14,16,18-Hexahydro-5,18:7,16:9,14-tris(o-benzeno)-heptacene-1,4,6,8,10,13,15,17-octaone*** *(cis,cis-**heptiptycenetetraquinone**)* (**3.23**)

1) **(*5R,5aR,7S,8aR,9S,14R,14aS,16S,17aS,18S*)-5,5a,7,8a,9,14,14a,16,17a,18-Decahydro-1,4,10,13-tetramethoxy-5,18:7,16:9,14-tris(*o*-benzeno)heptacene-6,8,15,17-tetraone** (**3.83**)

(*5R,5aS,7R,8aS,9R,14S,14aR,16S,17aR,18S*)-5,5a,7,8a,9,14,14a,16,17a,18-Decahydro-1,4,10,13-tetramethoxy-5,18:7,16:9,14-tris(*o*-benzeno)heptacene-6,8,15,17-tetraone (**3.84**)

A solution of 314 mg (1.00 mmol) of triptycenebisquinone and 715 mg (3.00 mmol) of 1,4-dimethoxyanthracene was heated at 150 ^{o}C in a sealed tube for 2 days. The orange solids precipitate was filtered to afford 690 mg (87%) of 1:1 mixture of two isomers, which can be partially separated by column chromatography (silica gel) using petrol ether–methylene chloride–ether (1:2:0.12, V:V:V) as eluent.

The less polar isomer (**3.83**): m.p. > 220 ^{o}C (decomp.); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.33 (dd, J_1 = 5.4 Hz, J_2 = 3.4 Hz, 2 H), 7.13 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2 H), 7.10 (dd, J_1 = 5.4 Hz, J_2 = 3.4 Hz, 2 H), 6.90 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2 H), 6.73 (dd, J_1 = 5.2 Hz, J_2 = 3.2 Hz, 2 H), 6.65 (s, 2 H), 6.24 (dd, J_1 = 5.6 Hz, J_2 = 2.8 Hz, 2 H), 6.08 (s, 2 H), 5.57 (s, 2 H), 5.10 (bs, 2 H), 5.08 (bs, 2 H), 3.83 (s, 6 H, OMe), 3.66 (s, 6 H, OMe), 3.06 (bs, 2 H), 2.95 (bs, 2 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 193.3, 192.9, 155.2, 155.0, 148.7, 148.6, 141.4, 141.3, 138.4, 131.1, 129.1, 126.7, 126.6, 125.6, 125.1, 124.3, 124.0, 109.3, 108.2, 56.2 (OMe), 55.8 (OMe), 50.9, 50.2, 43.6, 43.4, 42.6.

The more polar isomer (**3.84**): m.p.> 220 ^{o}C (decomp.); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.40 (dd, J_1 = 5.3 Hz, J_2 = 3.3 Hz, 2 H), 7.34 (dd, J_1 = 5.6 Hz, J_2 = 3.4 Hz, 2 H), 7.16 (m, 4 H), 7.11 (dd, J_1 = 5.5 Hz, J_2 = 3.1 Hz, 2 H), 6.97 (dd, J_1 = 5.3 Hz, J_2 = 3.2 Hz, 2 H), 6.08 (s, 2 H),

5.74 (s, 2 H), 5.63 (s, 2 H), 5.14 (t, *J* = 1.2 Hz, 2 H), 5.09 (t, *J* = 1.4 Hz, 2 H), 3.66 (s, 6 H, OMe), 3.59 (s, 6 H, OMe), 3.07 (t, *J* = 1.2 Hz, 2 H), 2.96 (t, *J* = 1.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 192.9, 192.6, 155.4, 155.0, 148.5, 148.0, 141.8, 141.50, 141.46, 128.9, 127.7, 126.8, 126.7, 125.6, 125.0, 124.3, 124.2, 109.6, 109.4, 108.1, 56.0 (OMe), 55.6 (OMe), 50.9, 50.5, 43.4, 43.3, 42.7.

2) **(*5R,7s,9S,14R,16s,18S*)-5,7,9,14,16,18-Hexahydro-6,8,15,17-tetrahydroxy-1,4,10, 13-tetramethoxy-5,18:7,16:9:14-tris(*o*-benzeno)heptacene** (**3.85**)

A suspension of 66 mg (0.083 mmol) of **3.83** in 2 mL acetic acid and 2 drops of 40% hydrobromic acid in water was refluxed under argon for half an hour, and then cooled to room temperature. The gray precipitate was filtered, washed with 2 mL toluene and 5 mL of diethyl ether, and dried in vacuum desiccator to afford 45 mg (68% yield) of the title compound **3.85**: m.p. > 300 ^{o}C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ 8.38 (s, 4 H, -OH), 7.27 (dd, J_1 = 5.4 Hz, J_2 = 3.1 Hz, 4 H), 7.21 (dd, J_1 = 5.2 Hz, J_2 = 3.0 Hz, 2 H), 6.86 (dd, J_1 = 5.2 Hz, J_2 = 3.4 Hz, 4 H), 6.79 (dd, J_1 = 5.2 Hz, J_2 = 3.4 Hz, 2 H), 6.47 (s, 4 H), 6.12 (s, 4 H), 5.99 (s, 2 H), 3.69 (s, 12 H, -OMe); ^{13}C NMR (DMSO-d_6, 50 MHz) δ 148.2, 146.4, 146.2, 139.8, 135.1, 131.4, 131.1, 124.3, 124.1, 123.4, 123.2, 108.5, 55.8, 41.0, 40.5; MS (MALDI-TOF): m/z calcd.for $C_{52}H_{39}O_8$ [$(M+H)^+$] 791.3, found 790.6.

3) **(*5R,7s,9S,14R,16s,18S*)-5,7,9,14,16,18-Hexahydro-5,18:7,16:9,14-tris(*o*-benzeno)-heptacene-1,4,6,8,10,13,15,17-octaone** (*cis,cis*-**heptiptycenetetraquinone**) (**3.23**)

To a suspension of 25 mg (0.032 mmol) of **3.85** in a mixture of 6 mL of acetonitrile and 1 mL of water was added 208 mg (0.380 mmol) of ammonium cerium (IV) nitrate. The mixture was stirred at room temperature for 8 hours and then diluted with ethyl acetate (50 mL), washed with water (50 mL) and brine (50 mL), dried over anhydrous magnesium, filtered, and concentrated. The residue was applied to flash column chromatography using toluene-chloroform-ethyl acetate (25:25:2, V:V:V) as eluent to afford 15.7 mg (68% yield) of the title compound **3.23**: m.p. > 300 ^{o}C (literature:[9] m.p. > 320 ^{o}C); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.40 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 4 H), 7.36 (dd, J_1 = 5.2 Hz, J_2 = 3.2 Hz, 2 H), 7.01 (dd, J_1 = 5.2 Hz, J_2 = 2.8 Hz, 4 H), 6.96 (dd, J_1 = 5.2 Hz, J_2 = 3.2 Hz, 2 H), 6.58 (s, 4 H), 6.12 (s, 2 H), 6.11 (s, 4 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 182.2, 177.7, 151.8, 151.3, 151.2, 142.1, 142.0, 135.5, 126.2 (2 peaks overlap), 125.64, 125.57, 42.5, 42.4.

3.5.3.2) *6,8,15,17-Tetramethoxy-7,16-dihydro-7,16-(o-benzeno)heptacene* (**3.56**)

1) **6,8,15,17-Tetrahydroxy-5,7,9,14,16,18-hexahydro-7,16-(*o*-benzeno)heptacene** (**3.106**)

i) A suspension of 467 mg (1.49 mmol) triptycene bisquinone and 1g (5.94 mmol) benzosultine **3.53** in 15 mL dry toluene was heated to 140 ^{o}C in a sealed tube for 24 hours. The reaction mixture was cooled to room temperature. The yellow precipitate was filtered, washed with toluene (2 mL) and ethyl ether (5 mL), and dried in vacuum to give 523 mg (67% yield) of a mixture of Diels-Alder adducts and their partially enolised derivatives.

ii) A suspension of the above Diels-Alder adducts mixture (400 mg, 0.765 mmol) in acetic acid (10 mL) and hydrobromic acid (40% in water, 10 drops) was refluxed for 10 min. The reaction mixture was cooled to room temperature. The yellow precipitate was filtered, washed with toluene (2 mL) and ethyl ether (5 mL), dried in vacuum to give 306 mg (77% yield) the title compound **3.106**: m.p. > 300 ^{o}C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 8.22 (s, 4 H, OH), 7.35 (dd, J_1 = 5.2 Hz, J_2 = 2.8 Hz, 2 H), 7.24 (dd, J_1 = 5.4 Hz, J_2 = 3.4 Hz, 4 H), 7.12 (dd, J_1 = 5.6 Hz, J_2 = 3.2 Hz, 4 H), 6.92 (dd, J_1 = 5.4 Hz, J_2 = 3.4 Hz, 2 H), 6.28 (s, 2 H), 3.77 (s, 8 H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 146.5, 141.5, 135.7, 130.7, 127.4, 125.7, 124.1, 123.3, 121.5, 40.8, 30.6; MS (MALDI-TOF): m/z calcd.for $C_{36}H_{27}O_4$ [$(M+H)^+$] 523.2, found 522.3.

2) **6,8,15,17-Tetramethoxy-5,7,9,14,16,18-hexahydro-7,16-(*o*-benzeno)heptacene** (**3.107**)

A mixture of **3.106** (300 mg, 0.570 mmol), potassium carbonate (629 mg, 4.55 mmol), and methyl *p*-toluenesulfonate (1.24 g, 6.66 mmol) in 12ml 1,2-dichlorobenzene was refluxed for 24 hours. The reaction mixture was cooled to room temperature and diluted with 150 mL of ethyl acetate. The organic layer was washed with water (100 mL), 1M HCl solution (100 mL), saturated sodium dicarbonate water solution (100 mL), brine (100 mL); dried over anhydrous magnesium sulfate; filtered and ethyl acetate was removed by rotavapor. The remaining dichlorobenzene was removed by vacuum distillation. The residue was applied to flash column chromatography (silica gel) using petrol ether–ethyl ether–methylene chloride (8:2:1, V:V:V) as eluent to afford 299 mg (yield 91%) of the title compound **3.107**: m.p. 286~288 ^{o}C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.44 (dd, J_1 = 5.2 Hz, J_2 = 3.4 Hz, 2 H), 7.25 (dd, J_1 = 5.6 Hz, J_2 = 3.2 Hz, 4 H), 7.13 (dd, J_1 = 5.5 Hz, J_2 = 3.3 Hz, 4 H), 7.00 (dd, J_1 = 5.4 Hz, J_2 = 3.2 Hz, 2 H), 6.15 (s, 2 H), 3.92 (s, 12 H, OMe), 3.86 (s, 8 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 148.8, 145.5, 136.2, 128.2, 127.7, 126.3, 125.6, 123.8, 62.4 (-OMe), 42.8, 29.7.

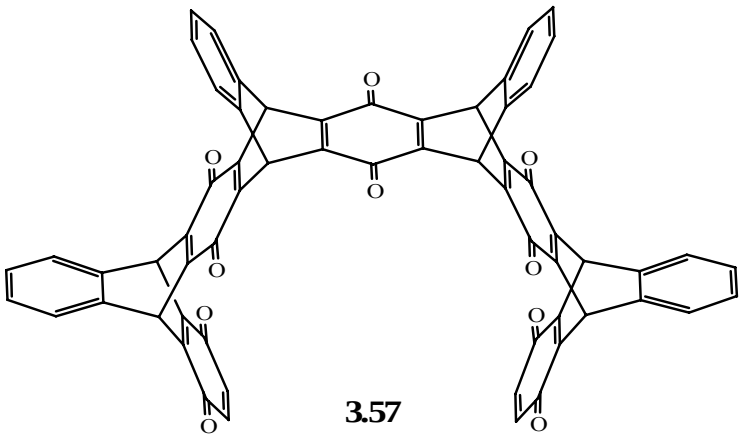
3) **6,8,15,17-Tetramethoxy-7,16-dihydro-7,16-(*o*-benzeno)heptacene** (**3.56**)

To a stirred solution 123 mg (0.210 mmol) of **3.107** in 10 mL toluene at 0 ^{o}C was added 290 mg (1.28 mmol) of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone. The reaction mixture was stirred at room temperature for 24 hours and diluted with 100 mL of ethyl acetate. The organic layer was washed with water (100 mL), saturated sodium thiosulfate water solution (100 mL), saturated sodium bicarbonate water solution (100 mL), brine (100 mL), dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was applied to flash column chromatography (silica gel) using petrol ether–diethyl ether (4:1, V:V) as eluent to afford 109 mg (89% yield) the title compound **3.56**: m.p.>300 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.59 (s, 4 H), 7.98 (dd, J_1 = 6.4 Hz, J_2 = 3.2 Hz, 4 H), 7.62 (dd, J_1 = 5.4 Hz, J_2 = 3.4 Hz, 2 H), 7.43 (dd, J_1 = 6.8 Hz, J_2 = 3.2 Hz, 4 H), 7.17 (dd, J_1 = 5.4 Hz, J_2 = 2.8 Hz, 2 H), 6.52 (s, 2 H), 4.20 (s, 12 H, OMe); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 146.7, 143.5, 131.9, 130.1, 128.6, 126.9, 126.7, 125.7, 124.4, 121.3, 63.3 (-OMe), 41.8.

3.5.3.3) ***(5R,7S,8aR,9S,14R,14aR,16R,18S)-5,7,8a,9,14,14a,16,18-Octahydro-5,18:7,16:9,14-10,13-dimethoxy-tris(o-benzeno)-heptacene-1,4,6,8,15,17-hexaone*** (**3.91**)

A mixture of 556 mg (1.07 mmol) of *cis*-pentiptycene trisquinone (**3.21**) and 225 mg (1.07 mmol) of 1,4-dimethoxyanthracene was refluxed in 50 mL toluene under argon for 36 hours. After cooling to room temperature, the unreacted *cis*-pentiptycene trisquinone was filtered. About 6 g of silica gel was added to the filtrate and concentrated to dryness by rotavapor. The dried silica gel was then applied to column chromatography (silica gel) using toluene-chloroform-ethyl acetate (25:25:1, V:V:V) as eluent to afford 312 mg (38% yield) of the title compound, **3.91**, as red solids: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.45 (dd, J_1 = 5.3 Hz, J_2 = 3.3 Hz, 2 H), 7.32~7.37 (m, 4 H), 7.13 (dd, J_1 = 5.4 Hz, J_2 = 3.2 Hz, 2 H), 7.05 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2 H), 6.95 (dd, J_1 = 5.4 Hz, J_2 = 3.2 Hz, 2 H), 6.75 (s, 2 H), 6.26 (s, 2 H), 5.85 (s, 2 H), 5.37 (s, 2 H), 5.08 (t, J = 1.3 Hz, 2 H), 3.47 (s, 6 H), 3.03 (t, 2 H, J = 1.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 192.8, 182.8, 178.0, 155.0, 152.3, 150.7, 150.1, 148.9, 141.9, 141.6, 141.4, 135.8, 129.6, 126.8, 126.4, 126.1, 125.7, 125.5, 124.3, 106.9, 55.6, 51.1, 43.6, 42.6 (2 peaks overlap).

3.5.4 Synthesis of 4-teeth synthon



3.57

3.5.4.1) ***(5R,7R,9S,11S,16R,18R,20S,22S)-5,7,9,11,16,18,20,22-Octahydro-5,22:7,20:9,18:11,16-tetra(o-benzeno)nonacene-1,4,6,8,10,12,15,17,19,21-decaone (cis,cis,cis-noniptycene-pentiquinone)*** (**3.57**)

1) **(*5R,5aR,7R,8aR,9S,10aR,11S,16R,16aS,18R,20S,21aS,22S*)-5,5a,7,9,10a,11,16,16a,18,20,21a,22-Dodecahydro-1,4,12,15-tetramethoxy-5,22:7,20:9,18:11,16-tetra(*o*-benzeno)-nonacene-6,8,10,17,19,21-hexaone** (**3.92**)

(*5R,5aS,7R,9S,10aS,11R,16S,16aR,18R,20S,21aR,22R*)-5,5a,7,9,10a,11,16,16a,18,20,21a,22-Dodecahydro-1,4,12,15-tetramethoxy-5,22:7,20:9,18:11,16-tetra(*o*-benzeno)nonacene-6,8,10,17,19,21-hexaone (**3.93**)

A mixture of 567 mg (1.09 mmol) of *cis*-pentiptycene trisquinone (**3.21**) and 650 mg (2.73 mmol) of 1,4-dimethoxyanthracene was refluxed in 57 mL toluene under argon for 24 hours. After cooling to room temperature, about 6 g of silica gel was added to the filtrate and concentrated to dryness by rotavapor. The dried silica gel was then applied to column chromatography (silica gel) using toluene-chloroform-ethyl acetate (25:25:2, V:V:V) as eluent to afford 275 mg (25% yield) of the title compound **3.92** (less polar spot) and 315 mg (29% yield) of the title compound **3.93** (more polar spot).

The less polar isomer **3.92**: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.33 (dd, J_1 = 5.6 Hz, J_2 = 3.4 Hz, 2 H), 7.30 (dd, J_1 = 5.2 Hz, J_2 = 3.0 Hz, 2 H), 7.18 (dd, J_1 = 5.5 Hz, J_2 = 3.1 Hz, 2 H), 7.11 (dd, J_1 = 5.5 Hz, J_2 = 3.1 Hz, 2 H), 6.97 (dd, J_1 = 5.5 Hz, J_2 = 3.1 Hz, 2 H), 6.91 (dd, J_1 = 5.4 Hz, J_2 = 3.3 Hz, 2 H), 6.83 (dd, J_1 = 5.3 Hz, J_2 = 3.1 Hz, 2 H), 6.59 (s, 2 H), 6.31 (dd, J_1 = 5.4 Hz, J_2 = 3.2 Hz, 2 H), 5.93 (s, 2 H), 5.77 (s, 2 H), 5.27 (s, 2 H), 5.13 (bs, 2 H), 5.04 (bs, 2 H), 3.78 (s, 6

H), 3.48 (s, 6 H), 3.15 (bs, 2 H), 2.98 (bs, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 194.4, 192.9, 177.9, 156.7, 155.7, 150.3, 149.9, 148.9, 148.8, 141.6 (2 peaks overlap), 141.4, 138.5, 131.0, 129.3, 126.9, 126.8, 126.0, 125.9, 125.4, 125.3, 124.3, 124.1, 109.5, 107.1, 56.2, 55.7, 51.1, 50.3, 43.6 (2 peaks), 42.8, 42.6.

The more polar isomer **3.93**: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.26~7.40 (m, 6 H), 7.21 (dd, J_1 = 5.4 Hz, J_2 = 3.2 Hz, 2 H), 7.10 (dd, J_1 = 5.1 Hz, J_2 = 3.1 Hz, 4 H), 7.02 (dd, J_1 = 5.4 Hz, J_2 = 3.2 Hz, 2 H), 6.91 (dd, J_1 = 5.5 Hz, J_2 = 3.1 Hz, 2 H), 5.98 (s, 2 H), 5.81 (s, 2 H), 5.78 (s, 2 H), 5.23 (s, 2 H), 5.16 (bs, 2 H), 5.04 (bs, 2 H), 3.65 (s, 6 H), 3,59 (s, 6 H), 3.15 (bs, 2 H), 2.98 (bs, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 193.8, 192.9, 177.9, 156.8, 155.7, 150.4, 149.9, 148.9, 148.3, 142.2, 141.7, 141.4 (2 peaks overlap), 129.3, 127.9, 126.9, 126.7, 125.9 (2 peaks), 125.4, 125.2, 124.3, 124.2, 109.9, 107.0, 56.2, 55.7, 51.1, 50.6, 43.5, 43.3, 42.9, 42.5; MS (MALDI-TOF): m/z calcd.for $C_{66}H_{44}O_{10}Na[(M+Na)^+]$ 1019.3, found 1019.4.

2) **(*5R,7R,9S,11S,16R,18R,20S,22S*)-5,7,9,11,16,18,20,22-Octahydro-1,4,12,15-tetramethoxy-5,22:7,20:9,18:11,16-tetra(*o*-benzeno)nonacene-6,8,10,17,19,21-hexaone** (**3.95**)

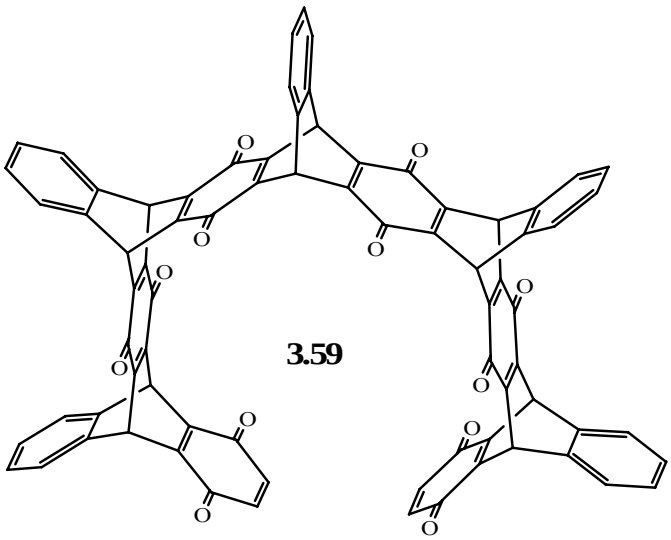
A solution of 37 mg (0.037 mmol) of **3.92** in 5 mL acetic acid and 5 drops of 40% hydrobromic acid was refluxed for 10 minutes under argon. The solvent was removed by a rotavapor. The residue was dissolved in 5 mL of acetone. Diacetoxyiodobenzene (36 mg, 0.11 mmol) was added and the reaction mixture was stirred at room temperature for half an hour. Then acetone was removed by a rotapavor. The residue was appled to column chromatography (silica gel) using petrol ether, methylene chloride and ethyl ether (1:1:0.02, V:V:V) as eluent to afford 7.4 mg (20% yield) of the title compound **3.95**: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.35 (m, 8 H), 7.32 (dd, J_1 = 5.2 Hz, J_2 = 3.0 Hz, 4 H), 6.41 (s, 4 H), 6.12 (s, 4 H), 6.05 (s, 4 H), 3.72 (s, 12 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 178.8, 177.9, 152.3, 151.4, 150.9, 149.8, 144.2, 142.3, 133.9, 126.0, 125.5, 125.4, 124.7, 109.8, 50.7, 42.5, 41.6.

3)***5R,7R,9S,11S,16R,18R,20S,22S*)-5,7,9,11,16,18,20,22-Octahydro-5,22:7,20:9,18:11,16-tetra(*o*-benzeno)nonacene-1,4,6,8,10,12,15,17,19,21-decaone** (***cis,cis,cis*-noniptycene-pentiquinone**) (**3.57**)

To a suspension of 55 mg (0.055 mmol) of **3.95** in 12 mL acetonitrile and 2 mL water was added 182 mg (0.330 mmol) of CAN. The reaction mixture was stirred at room temperature for overnight and diluted with 40 mL of chloroform. The organic layer was washed by water (50 mL ×2), brine (50 mL), dried over anhydrous magnesium sulfate, filtered and concentrated. The

residue was applied to column chromatography using petrol ether, methylene chloride and ethyl ether (1:1:0.04, V:V:V) as eluent to afford 4.8 mg (9.3% yield) of the title compound **3.57**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.38 (dd, J_1 = 5.4 Hz, J_2 = 3.4 Hz, 4 H), 7.34 (dd, J_1 = 5.6 Hz, J_2 = 3.6 Hz, 4 H), 7.00 (dd, J_1 = 5.4 Hz, J_2 = 3.2 Hz, 4 H), 6.95 (dd, J_1 = 5.4 Hz, J_2 = 3.2 Hz, 4 H), 6.55 (s, 4 H), 6.08 (s, 8 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 182.2, 177.6 (2 C), 151.8, 151.3 (2 C), 151.1, 142.1, 141.9, 135.5, 126.1 (2 C), 125.7, 125.6, 42.5, 42.4.

3.5.5 Synthesis of 5-teeth synthon



3.59

3.5.5.1) (*5R,7R,9s,11S,13S,18R,20R,22s,24S,26S*)-5,7,9,11,13,18,20,22,24,26-Decahydro-5,26:7,24:9,22:11,20:13,18-penti(o-benzeno)undecacene-1,4,6,8,10,12,14,17,19,21,23,25-dodecaone (***cis,cis,cis,cis*-undeciptycenehexaquinone**) (**3.59**)

1) **(*5R,5aR,7R,9S,11S,12aR,13S,18R,18aS,20R,22R,24S,25aS,26S*)-5,5a,7,9,11,12a,13,18,18a,20,22,24,25a,26-Tetradecahydro-1,4,14,17-tetramethoxy-5,26:7,24:9,22:11,20:13,18-penti(*o*-benzeno)undecacene-6,8,10,12,19,21,23,25-octaone** (**3.97**)

(*5R,5aS,7R,9R,11S,12aS,13R,18S,18aR,20R,22S,24S,25aR,26S*)-5,5a,7,9,11,12a,13,18,18a,20,22,24,25a,26-Tetradecahydro-1,4,14,17-tetramethoxy-5,26:7,24:9,22:11,20:13,18-penti(*o*-benzeno)undecacene-6,8,10,12,19,21,23,25-octaone (**3.98**)

A mixture of 100 mg (0.138 mmol) of *cis,cis*-heptiptycenetetraquinone (**3.23**) and 131 mg (0.550 mmol) of 1,4-dimethoxyanthracene in 10 ml toluene and 2 ml carbon tetrachloride was heated to 170 ^{o}C (oil bath) in a sealed tube under argon for 24 hours. The precipitation was

filtered to give 80 mg of a mixture of **3.97** and **3.98** in a ratio of 8:1. The filtrate was absorbed in 1 g of silica gel and applied to column chromatography using toluene, chloroform and ethyl acetate (25:25:2, V:V:V) as eluent to give 27 mg of a mixture of **3.97** and **3.98** in a ratio of 3:7. The calculated yield of two isomers is 83% with 58% for **3.97** and 25% for **3.98**.

The less polar isomer **3.97**: m.p. > 240 ^{o}C decomp.; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.20 ~7.38 (m, 6 H), 7.16 (dd, J_1 = 5.6 Hz, J_2 = 3.3 Hz, 2 H), 6.84~7.04 (m, 8 H), 6.69 (dd, J_1 = 5.3 Hz, J_2 = 3.1 Hz, 2 H), 6.47 (s, 2 H), 6.21 (dd, 2 H), 6.15 (s, 2 H), 5.87 (s, 2 H), 5.79 (s, 2 H), 5.00 (bs, 2 H), 4.86 (bs, 2 H), 4.84 (s, 2 H), 3.69 (s, 6 H), 3.34 (s, 6 H), 2.93 (bs, 2 H), 2.39 (bs, 2 H).

The more polar isomer **3.98**: m.p. >240 ^{o}C decomp.; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.35 (dd, J_1 = 5.4 Hz, J_2 = 3.2 Hz, 2 H), 7.30 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2 H), 7.19 (dd, J_1 = 5.2 Hz, J_2 = 3.4 Hz, 4 H), 7.10 (dd, J_1 = 5.2 Hz, J_2 = 3.4 Hz, 2 H), 6.88~7.04 (m, 10 H), 6.17 (s, 2H), 5.92 (s, 2 H), 5.78 (s, 2 H), 5.71 (s, 2 H), 4.98 (bs, 2 H), 4.85 (bs, 2 H), 4.77 (s, 2 H), 3.55 (s, 6 H), 3.35 (s, 6 H), 2.93 (bs, 2 H), 2.18 (bs, 2 H); MALDI-TOF MS: m/z= 1225.4 [$(M+Na)^+$], 1241.4 [$(M+K)^+$]

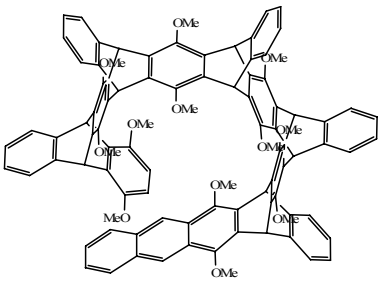
2) **(*5R,7R,9s,11S,13S,18R,20R,22s,24S,26S*)-5,7,9,11,16,18,20,22-Octahydro-1,4,14,17-tetramethoxy-5,26:7,24:9,22:11,20:13,18-penti(*o*-benzeno)undecacene-6,8,10,12,19,21,23,25-Octaone** (**3.99**)

A solution of 50 mg (0.042 mmol) was suspended and heated to reflux in 30 mL acetic acid with 30 drops of HBr (40% water solution) under argon for 45 mins. The acetic acid was removed by a rotavapor. Toluene (25 mL) was added and was removed by the rotavapor for the purpose of further removing remaining acetic acid. The residue was vacuumed for 10 mins before was dissolved in 20 mL acetone. 60 mg (0.186 mmol) of $PhI(OAc)_2$ was added and the reaction mixture was stirred at room temperature for overnight. Silica gel (500 mg)was added and solvent was removed under vacuum. The crude product absorbed in silica gel was applied to column chromatography (Silica gel) using petrol ether, methylene chloride and ethyl ether (1:2:0.03, V:V:V) as eluent to give 14.5 mg (29% yield) of the title compound, **3.99**, as orange solids: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.28~7.38 (m, 10 H), 6.88~6.98 (m, 10 H), 6.28 (s, 4 H), 6.13 (s, 4 H), 6.03 (s, 6 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 178.7, 177.7, 152.1, 152.3, 151.1, 150.8, 149.6, 144.1, 142.3, 142.2, 134.1, 126.0 (2 peaks), 125.5, 125.4 (2 peaks overlap), 124.7, 109.4, 56.5, 42.4 (2 peaks overlap), 41.5; MS (MALDI-TOF): m/z $(M+H)^+$ 1200.2561 (Cal. 1199.3068), $(M+Na)^+$ 1221.2578 (Cal. 1221.2887), $(M+K)^+$ 1237.1980 (Cal. 1237.2626).

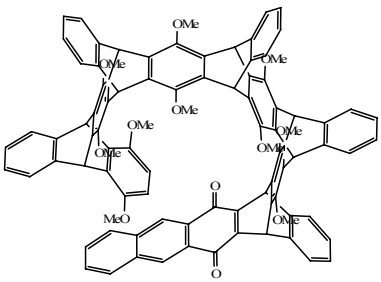
3) **(*5R,7R,9s,11S,13S,18R,20R,22s,24S,26S*)-5,7,9,11,13,18,20,22,24,26-Decahydro-5,26:7,24:9,22:11,20:13,18-penti(o-benzeno)undecacene-1,4,6,8,10,12,14,17,19,21,23,25-dodecaone** (***cis,cis,cis,cis*-undeciptycenehexaquinone**) (**3.59**)

A suspension of 15.0 mg (0.0125 mmol) of **3.99** was suspended in 3 mL acetonitrile. The mixture was sonicated for 30 mins, 0.5 mL water and 41 mg (0.075 mmol) of CAN was added, and the mixture was stirred at room temperature for 2 hours. 40 mL of methylene chloride was added. The organic layer was then washed by water (20 mL × 2) and brine (20 mL), dried over anhydrous magnesium sulfate, filtered, and concentrated by a rotavapor. The residue was purified via column chromatography (silic gel) using a mixture of petrol ether, methylene chloride and ethyl ether (1:2:0.12, V/V/V) to give 4.2 mg (yield 30%) of the title compound, **3.59**, as yellow solids. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.39 (dd, J_1 = 5.4 Hz, J_2 = 3.2 Hz, 4 H), 7.28~7.35 (m, 6 H), 7.00 (dd, J_1 = 5.3 Hz, J_2 = 3.3 Hz, 4 H), 6.88~6.96 (m, 6 H), 6.55 (s, 4 H), 6.07 (s, 4 H), 6.05 (s, 4 H), 6.04 (s, 2 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 182.1, 177.5 (2 peaks), 151.8, 151.1 (3 peaks overlap), 151.0, 142.1 (2 peaks overlap), 141.6, 135.4, 126.2, 126.1 (2 peaks overlap), 125.7, 125.6 (2 peaks overlap), 42.4 (3 peaks overlap); MS (MALDI-TOF): M+Na^+: 1162.3230 (Cal. 1161.1948).

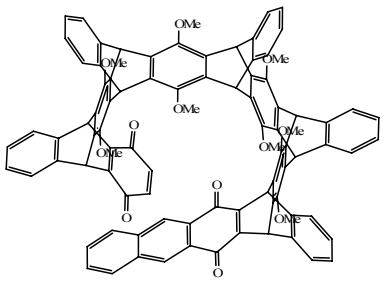
3.5.6 Synthesis of 6-teeth "molecular roll"



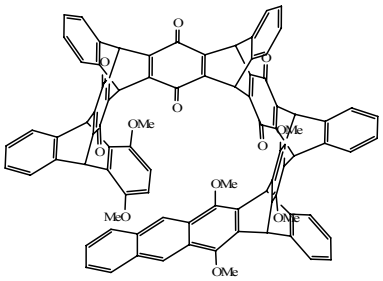
3.119



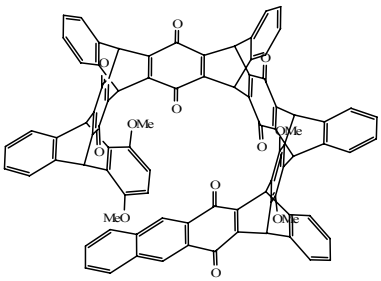
3.125



3.126



3.121



3.123

3.5.6.1) ***(5R,7R,9S,11S,13S,22R,24R,26S,28S,30S)-5,7,9,11,13,22,24,26,28,30-Decahydro-1,4,6,8,10,12,14,21,23,25,27,29-dodecamethoxy-(5,30:7,28:9,26:11,24:13,22)-penti(o-benzeno) tridecacene*** (**3.119**)

1) **(*5R,5aS,7R,9S,10aS,11S,13S,22R,24R,24aR,26S,28S,29aR,30S*)-5,5a7,9,10a,11,13, 22,24,24a,26,28,29a,30-Tetradecahydro-1,4,12,14,21,23-hexamethoxy-(5,30:7,28:9,26:11,24: 13,22)-penti(*o*-benzeno)tridecacene-6,8,10,25,27,29-hexaone** (**3.117**)

(*5R,5aS,7R,9S,10aS,11S,13R,22S,24R,24aR,26S,28S,29aR,30S*)-5,5a7,9,10a,11,13,22, 24,24a,26,28,29a,30-Tetradecahydro-1,4,12,14,21,23-hexamethoxy-(5,30:7,28:9,26:11,24:13, 22)-penti(*o*-benzeno)tridecacene-6,8,10,25,27,29-hexaone (**3.118**)

A mixture of 142 mg (0.187 mmol) of **3.91** and 107 mg (0.197 mmol) of bisdimethoxy-anthracene **3.56** in 10 mL of toluene under argon was heated at 100 ^{o}C for 36 hours. Toluene was removed by a rotavapor. The residue was applied to column chromatography (silica gel) using a mixture of toluene, chloroform and ethyl acetate (25:25:2, V:V:V) as eluent to give 126 mg (51% yield) of a mixture of **3.117** and **3.118** in a ratio of 3:7.

Isomer **3.117** (the minor isomer): ^{1}H NMR ($CDCl_3$, 200 MHz) (deduced from ^{1}H NMR, ROESY of a 3:7 mixture of **3.117** and **3.118**) δ 8.50 (s, 2 H), 7.93 (m, 2 H), 7.49 (m, 2 H), 6.86~7.46 (m, 16 H), 6.79 (m, 2 H), 6.30 (m, 2 H), 6.24 (s, 2 H), 6.89 (s, 2 H), 5.74 (s, 2 H), 5.17 (s, 2 H), 4.98 (bs, 2 H), 4.95 (bs, 2 H), 4.10 (s, 6 H), 3.93 (s, 6 H), 3.41 (s, 6 H), 3.09 (bs, 2 H), 2.94 (bs, 2 H); ^{13}C NMR ($CDCl_3$, 50 MHz) (deduced from ^{13}C NMR of a 3:7 mixture of **3.117** and **3.118**) δ 194.0, 192.9, 177.8, 156.7, 155.6, 150.0, 149.8, 148.7, 146.9, 146.5, 144.0, 141.5, 141.4, 141.2, 138.1, 136.7, 132.7, 131.7, 130.2, 129.5~125.0 (m, 11 C), 124.2, 123.0, 123.9, 121.2, 106.7, 63.5, 63.2, 55.5, 51.0, 50.3, 44.4, 43.4, 42.6, 42.4, 42.0; MS (MALDI-TOF): m/z calcd. for $C_{90}H_{61}O_{12}[(M+H)^{+}]$ 1333.4, found 1333.5; MS (MALDI-TOF) m/z calcd.for $C_{90}H_{61}O_{12}[(M+H)^{+}]$ 1333.4, found 1333.5.

Isomer **3.118** (the major isomer): ^{1}H NMR ($CDCl_3$, 200 MHz) (deduced from ^{1}H NMR, ROESY of a 3:7 mixture of **3.117** and **3.118**) δ 8.45 (s, 2 H), 7.92 (m, 2 H), 7.49 (m, 2 H), 6.86~7.46 (m, 16 H), 6.76 (m, 2 H), 6.25 (m, 2 H), 6.24 (s, 2 H), 6.90 (s, 2 H), 5.76 (s, 2 H), 5.23 (s, 2 H), 5.03 (bs, 2 H), 4.96 (bs, 2 H), 4.06 (s, 6 H), 3.95 (s, 6 H), 3.46 (s, 6 H), 3.09 (bs, 2 H), 2.97 (bs, 2 H); ^{13}C NMR ($CDCl_3$, 50 MHz) (deduced from ^{13}C NMR of a 3:7 mixture of **3.117** and **3.118**) δ 194.0, 192.9, 177.8, 156.7, 155.6, 150.0, 149.8, 148.8, 146.9, 146.4, 144.1, 141.5, 141.4, 141.3, 138.0, 136.6, 132.7, 131.7, 130.2, 129.5~125.0 (m, 11 C), 124.3, 124.1, 123.9,

121.2, 106.8, 63.5, 63.1, 55.6, 51.0, 50.4, 44.4, 43.4, 42.6, 42.4, 42.0; MS (MALDI-TOF): m/z calcd. for $C_{90}H_{61}O_{12}[(M+H)^+]$ 1333.4, found 1333.5.

2) **(*5R,7R,9S,11S,13S,22R,24R,26S,28S,30S*)-5,7,9,11,13,22,24,26,28,30-Decahydro-1,4,6,8,10,12,14,21,23,25,27,29-dodecamethoxy-(5,30:7,28:9,26:11,24:13,22)-penti(*o*-benzeno) tridecacene** (**3.119**)

(*5R,7R,9S,11S,13R,22S,24R,26R,28S,30S*)-5,7,9,11,13,22,24,26,28,30-Decahydro-1,4, 6,8,10,12,14,21,23,25,27,29-dodecamethoxy-(5,30:7,28:9,26:11,24:13,22)-penti(*o*-benzeno)-tridecacene (**3.120**)

To a solution of 87 mg (0.065 mmol) of a mixture of **3.117** and **3.118** in 5 mL DMF at 0^oC was added 26 mg (60% NaH in oil). The reaction mixture was stirred at 0 ^oC for half an hour. Then 162 μL (2.60 mmol) of methyl iodide was added by a syringe. The reaction mixture was then stirred at room temperature for 3 hours, diluted with 30 mL water, and extracted with ethyl acetate (30 mL × 2). The organic layer was washed with 30 mL 1M HCl, conc. sodium bicarbonate solution (30 mL), and brine (30 mL), dried over anhydrous magnesium sulfate, filtered and concentrated by a rotavapor. The residue was appled to column chromatography using toluene, chloroform and ethyl acetate (5:5:1 to 5:5:2, V:V:V) as eluent to afford 23 mg (a mixture of two isomers **3.119** and **3.120** in a ratio of about 1:1. The two isomers are partial separated with the less polar isomer being **3.120** and the more polar isomer being **3.119**.

The more polar isomer **3.119** (not enough materials for ^{13}C NMR): ^1H NMR ($CDCl_3$, 400 MHz) δ 8.57 (s, 2 H), 7.92 (m, 2 H), 7.36 (m, 2 H), 7.30 (m, 2 H), 7.12~7.26 (m, 8 H), 6.95 (m, 2 H), 6.76~6.88 (m, 8 H), 6.14 (s, 2 H), 5.92 (s, 2 H), 5.82 (s, 2 H), 5.80 (s, 2 H), 5.78 (s, 2 H), 4.53 (s, 2 H), 4.03 (s, 6 H), 3.91 (s, 6 H), 3.81 (s, 6 H), 3.77 (s, 6 H), 3.66 (s, 6 H), 3.33 (s, 6 H).

The less polar isomer **3.120** (not enough materials for ^{13}C NMR): ^1H NMR ($CDCl_3$, 200 MHz) δ 8.46 (s, 2 H), 7.92 (m, 2 H), 7.12~7.50 (m, 12 H), 7.08 (m, 2 H), 6.75~6.95 (m, 8 H), 6.30 (s, 2 H), 6.15 (s, 2 H), 6.03 (s, 2 H), 5.92 (s, 2 H), 5,86 (2s overlap, 4 H), 4.05 (s, 6 H), 3.91 (s, 6 H), 3.82 (2s overlap, 12 H), 3.78 (s, 6 H), 3.72 (s, 6 H); MS (MALDI-TOF): m/z calcd.for $C_{96}H_{75}O_{12}$ $[(M+H)^+]$ 1419.5, found 1418.7.

3.5.6.2) (*7R,9R,11R,13R,15R,20S,22S,24S,26S,28S)-7,9,11,13,15,20,22,24,26,28-Decahydro-8,10,12,14,16,19,21,23,25,27-decamethoxy-(7,28:9,26:11,24:13,22)-penti(o-benzeno)-trideca-cene-6,29-dione* (**3.125**)

To a stirred solution of 7.6 mg (5.4 μmol) of **3.119** in 1 mL of CH_3CN and water (6:1) was added 3.0 mg (5.5 μmol) of CAN. The reaction was stirred at room temperature for 5 hours and diluted with 20 mL of ethyl acetate, washed by water (20 mL), brine, dried over anhydrous magnesium sulfate, filtered and concentrated by a rotavapor. The residue was applied to column chromatography using toluene, chloroform and ethyal acetate (5:5:2, V:V:V) as eluent to afford 2.4 mg (32% yield) of the title compound **3.125** (not enough materials for ^{13}C NMR): ^1H NMR ($CDCl_3$, 200 MHz) δ 8.64 (s, 2 H), 7.98 (m, 2 H), 7.55 (m, 2 H), 7.38 (m, 2 H), 7.12~7.30 (m, 8 H), 6.94 (m, 2 H), 6.76~6.90 (m, 8 H), 6.23 (s, 2 H), 5.91 (s, 2 H), 5.85 (2s overlap, 4 H), 5.81 (s, 2 H), 4.70 (s, 2 H), 3.89 (s, 6 H), 3.82 (s, 6 H), 3.80 (s, 6 H), 3.68 (s, 6 H), 3.36 (s, 6 H); MS (MALDI-TOF): m/z calcd.for $C_{94}H_{68}O_{12}Na$ $[(M+Na)^+]$ 1411.5, found 1411.6.

3.5.6.3) ***(5R,7R,9S,11S,13S,22R,24R,26S,28S,30S)-5,7,9,11,13,22,24,26,28,30-Decahydro-6,8,10,12,23,25,27,29-octamethoxy-(5,30:7,28:9,26:11,24:13,22)-penti(o-benzeno)tridecacene-1,4,14,21-tetraone*** (**3.126**)

To a stirred solution of 2.4 mg (1.7 μmol) of **3.119** in 0.5 mL of CH_3CN and water (6:1, V:V) was added 0.8 mg (1.5 μmol) of CAN. The reaction was stirred at room temperature for 5 hours and diluted with 20 mL of ethyl acetate, washed by water (20 mL), brine, dried over anhydrous magnesium sulfate, filtered and concentrated by a rotavapor. The residue was applied to column chromatography using toluene, chloroform and ethyal acetate (5:5:2, V:V:V) as eluent to afford 1.0 mg (43% yield) of the title compound **3.126** (not enough materials for ^{13}C NMR): ^1H NMR ($CDCl_3$, 200 MHz) δ 8.60 (s, 2 H), 8.01 (m, 2 H), 7.57 (m, 2 H), 7.37 (m, 2 H), 7.18~7.34 (m, 8 H), 6.80~6.98 (m, 10 H), 6.25 (s, 2 H), 5.91 (s, 2 H), 5.86 (s, 2 H), 5.81 (s, 2 H), 5.76 (s, 2 H), 4.67 (s, 2 H), 3.89 (s, 6 H), 3.84 (s, 6 H), 3.80 (s, 6 H), 3.67 (s, 6 H); MS (MALDI-TOF): m/z calcd.for $C_{92}H_{62}O_{12}Na[(M+Na)^+]$ 1381.4, found 1381.7.

3.5.6.4) ***(5R,7R,9S,11S,13S,22R,24R,26R,28S,30S)-5,7,9,11,13,22,24,26,28,30-Decahydro-1,4,12,14,21,23-hexamethoxy-(5,30:7,28:9,26:11,24:13,22)-penti(o-benzeno)tridecacene-6,8,10,25,27,29-hexaone*** (**3.121**)

(5R,7R,9S,11S,13R,22S,24R,26R,28S,30S)**-5,7,9,11,13,22,24,26,28,30-Decahydro-1,4,12,14,21,23-hexamethoxy-(5,30:7,28:9,26:11,24:13,22)-penti(*o*-benzeno)tridecacene-6,8,10,25,27,29-hexaone** (**3.122**)

A suspension of 40 mg (0.030 mmol) of **3.117** and **3.118** in 6 mL of acetic acid and 6 drops of 40% hydrobromic acid was stirred at room temperature for 36 hours. The solvent was

removed under reduced pressure. The residue was dissolved in 5 mL of acetone followed by adding 29 mg (0.090 mmol) of diacetoxyiodobenzene. The resulting solution was stirred at room temperature for 5 minutes. 400 mg of silica gel was added and solvent was removed by a rotavapor. The dried silica gel was applied to column chromatography (silica gel) using toluene, chloroform and ethyl acetate (25:25:1, V:V:V) as eluent to afford 10 mg (25% yield) of the mixture of title compounds **3.121** and **3.122**, which could be separated by PTLC using petrol ether, methylene chloride and ethyl ether (1:2:0.06, V:V:V) as eluent.

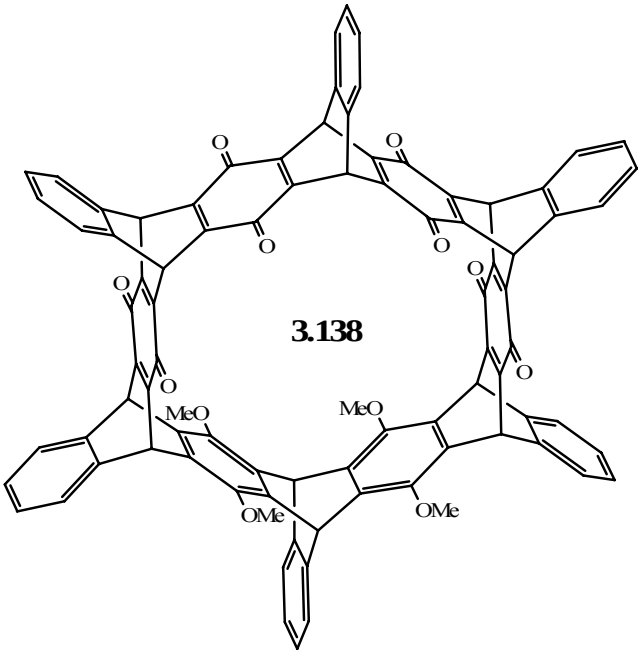
Compound **3.121** (more polar isomer) (not enough materials for ^{13}C NMR): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.57 (s, 2 H), 7.94 (m, 2 H), 7.18~7.42 (m, 12 H), 6.82~7.00 (m, 10 H), 6.16 (s, 2 H), 6.00 (s, 2 H), 5.98 (s, 2 H), 5.96 (s, 2 H), 5.89 (s, 2 H), 4.81 (s, 2 H), 4.07 (s, 6 H), 3.90 (s, 6H), 3.31 (s, 6 H).

Compound **3.122** (less polar isomer) (not enough materials for ^{13}C NMR): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.46 (s, 2 H), 7.93 (m, 2 H), 7.18~7.48 (m, 12 H), 6.82~7.00 (m, 10 H), 6.27 (s, 2 H), 6.16 (s, 2 H), 6.11 (s, 2 H), 6.02 (2 s overlap, 4 H), 5.98 (s,2 H), 4.05 (s, 6 H), 3.87 (s, 6 H), 3.73 (s, 6 H).

3.5.6.5) (*7R,9R,11R,13R,15R,20S,22S,24S,26S,28S)-7,9,11,13,15,20,22,24,26,28-Decahydro-8,10,12,14,16,19,21,23,25,27-decamethoxy-(7,28:9,26:11,24:13,22)-penti(o-benzeno)-trideca-cene-6,29-dione* (3.123)

To a stirred solution of 3 mg (2.3 μmol) of **3.121** in 0.25 mL of CH_3CN and water (6:1, V:V) was added 2.0 mg (3.6 μmol) of CAN. The reaction was stirred at room temperature overnight and diluted with 20 mL of ethyl acetate, washed by water (20 mL), brine, dried over anhydrous magnesium sulfate, filtered and concentrated by a rotavapor. The residue was applied to column chromatography using toluene, chloroform and ethyal acetate (25:25:1, V:V:V) as eluent to afford 1.6 mg (54 % yield) of the title compound **3.123** (not enough materials for ^{13}C NMR): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.63 (s, 2 H), 7.12~7.64 (m, 12 H), 6.80~7.04 (m, 10 H), 6.26 (s, 2 H), 6.01 (s, 2 H), 5.98 (s, 2 H), 5.97 (s, 2 H), 5.93 (s, 2 H), 4.95 (s, 2 H), 3.86 (s, 6 H), 3.34 (s, 6 H).

3.5.7 Synthesis of new cyclododeciptycene based molecular gear 3.318



3.138

3.5.7.1) ***2,4,6,8,10,12,14,16,18,20,22,24-Dodecahydro-9,11,21,23-tetramethoxy-(2,14:4,16:6, 18:8,20:10,22:12,24)-hexa(o-benzeno)-[12]cyclacene-1,3,5,7,13,14,17,19-octaone*** (**3.318**)

1) **(*5R,7R,9S,<u>10aR</u>,11S,<u>13S</u>,<u>22R</u>,24R,<u>24aS</u>,26R,28S,30S*)-5,7,9,10a,11,13,22,24,24a,26, 28,30-Dodecahydro-12,14,21,23-tetramethoxy-(5,30:7,28:9,26:11,24:13,22)-penti(*o*-benzeno) tridecacene-1,4,6,8,10,25,27,29-octaone** (*endo-cis* adduct) (**3.314**)

(*5R,7R,9S,<u>10aR</u>,11S,<u>13R</u>,<u>22S</u>,24R,<u>24aS</u>,26R,28S,30S*)-5,7,9,10a,11,13,22,24,24a,26,28, 30-Dodecahydro-12,14,21,23-tetramethoxy-(5,30:7,28:9,26:11,24:13,22)-penti(*o*-benzeno)-tridecacene-1,4,6,8,10,25,27,29-octaone (*endo-trans* adduct) (**3.315**)

(*5R,7R,9S,<u>10aS</u>,11S,<u>13R</u>,<u>22S</u>,24R,<u>24aR</u>,26R,28S,30S*)-5,7,9,10a,11,13,22,24,24a,26,28, 30-Dodecahydro-12,14,21,23-tetramethoxy-(5,30:7,28:9,26:11,24:13,22)-penti(*o*-benzeno)-tridecacene-1,4,6,8,10,25,27,29-octaone (*exo-cis* adduct) (**3.316**)

(*5R,7R,9S,<u>10aS</u>,11S,<u>13S</u>,<u>22R</u>,24R,<u>24aR</u>,26R,28S,30S*)-5,7,9,10a,11,13,22,24,24a,26,28, 30-Dodecahydro-12,14,21,23-tetramethoxy-(5,30:7,28:9,26:11,24:13,22)-penti(*o*-benzeno)-tridecacene-1,4,6,8,10,25,27,29-octaone (*exo-trans* adduct) (**3.317**)

A mixture of the tetraquinone **3.23** (116 mg, 0.160 mmol) and bisdimethoxyanthracene **3.56** (110 mg, 0.190 mmol) was heated in 1,2-dichloroethane at 120 ^{o}C in a sealed tube for 24 hours. The solvent was removed by a rotavapor. The residue left was applied to column

chromatography (silica gel) using toluene-chloroform-ethyl acetate (25:25:2, V:V:V) as eluent to afford 117 mg (56% yield) of four monoadducts in a ratio about 2:2:1:1 based on ^{1}H NMR.

Endo-cis adduct **3.314** (a small amount of pure sample was obtained by PTLC method using toluene-chloroform-ethyl acetate (25:25:2, V:V:V) as eluent, not enough materials for ^{13}C NMR: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.54 (s, 2 H), 7.97 (m, 2 H), 7.20~7.50 (m, 10 H), 6.87~7.04 (m, 8 H), 6.80 (m, 2 H), 6.33 (s, 2 H), 6.26 (s, 2H), 6.15 (s, 2 H), 6.13 (s, 2 H), 5.74 (s & dd, 4 H), 4.86 (bs, 2 H), 4.14 (s, 6 H, OMe), 3.90 (s, 6 H, OMe), 2.92 (bs, 2 H).

Endo-anti adduct **3.315** (a small amount of pure sample was obtained by PTLC method using toluene-chloroform-ethyl acetate (25:25:2, V:V:V) as eluent, not enough materials for ^{13}C NMR): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.47 (s, 2 H), 7.94 (dd, J_1 = 6.4 Hz, J_2 = 3.4 Hz, 2 H), 7.53 (dd, J_1 = 5.3 Hz, J_2 = 3.1 Hz, 2 H), 7.20~7.44 (m, 8 H), 7.11 (dd, J_1 = 5.2 Hz, J_2 = 3.0 Hz, 2 H), 6.89~7.00 (m, 6 H), 6.77 (dd, J_1 = 5.3 Hz, J_2 = 3.3 Hz, 2 H), 6.26 (s, 2 H), 6.14 (s, 2 H), 6.11 (s, 2 H), 6.08 (s, 2 H), 5.73 (s, 2 H), 5.70 (dd, 2 H), 4.86 (bs, 2 H), 4.07 (s, 6 H, OMe), 3.91 (s, 6 H, OMe), 2.93 (bs, 2 H).

Exo-cis adduct **3.316** (hard to separate from **3.317**, no pure sample was available): ^{1}H NMR ($CDCl_3$, 200 MHz) (deduced from ^{1}H NMR of a 4:6 mixture of **3.316** and **3.317**) δ 8.55 (s, 2 H), 7.98 (m, 2 H), 7.53 (m, 2 H), 6.80~7.48 (m, 10 H), 6.70 (m, 2 H), 6.43 (s, 2 H), 6.29 (m, 2 H), 6.25 (s, 2 H), 6.04 (s, 2 H), 6.03 (s, 2 H), 5.79 (s, 2 H), 4.93 (bs, 2 H), 4.14 (s, 6 H, OMe), 3.91 (s, 6 H, OMe), 2.87 (bs, 2 H).

Exo-trans adduct **3.317** (hard to separate from **3.316**, no pure sample was available): ^{1}H NMR ($CDCl_3$, 200 MHz) (deduced from ^{1}H NMR of a 4:6 mixture of **3.316** and **3.317**) δ 8.45 (s, 2 H), 7.92 (m, 2 H), 6.80~7.48 (m, 12 H), 6.74 (m, 2 H), 6.54 (s, 2 H), 6.26 (s, 2 H), 6.23 (m, 2 H), 6.08 (s, 2 H), 6.04 (s, 2 H), 5.80 (s, 2 H), 4.93 (bs, 2 H), 4.06 (s, 6 H, OMe), 3.93 (s, 6 H, OMe), 2.87 (bs, 2 H).

2) **2,4,6,8,10,12,14,16,18,20,22,24-Dodecahydro-9,11,21,23-tetramethoxy-(2,14:4,16:6,18:8,20:10,22:12,24)-hexa(*o*-benzeno)-[12]cyclacene-1,3,5,7,13,14,17,19-octaone** (**3.138**)

(*5R,7R,9S,11S,13R,22S,24R,26R,28S,30S*)-5,7,9,11,13,22,24,26,28,30-Decahydro-12,14,21,23-tetramethoxy-(5,30:7,28:9,26:11,24:13,22)-penti(*o*-benzeno)tridecacene-1,4,6,8,10,25,27,29-octaone (**3.139**)

A 1:1 mixture of two Diels-Alder adducts (2.8 mg, 2.2 μmol) was refluxed in 2 mL of acetic acid under argon for 30 min. The reaction mixture was poured into 50 mL of water and

extracted with 20 mL of ethyl acetate. The ethyl acetate layer was then washed with water (50 mL×2), concentrated sodium bicarbonate water solution (20 mL×2), brine (20 mL × 2), dried over anhydrous magnesium sulfate, filtered and concentrated. The residue was dissolved in 2 mL acetone. Diacetoxyiodobenzene (2.0 mg, 6.2 μmol) was added and shaked well. Then the solution was applied to PTLC using a mixture of toluene, chloroform, ethyl acetate (25:25:2, V:V:V) as eluent. The Rf. = 0.29 band was cut and eluented with the same eluent [toluene, chloroform, ethyl acetate (25:25:2, V:V:V)], concentrated and was further purified by column chromatography using a mixture of petrol ether, methylene chloride, diethyl ether (1:2:0.12, V:V:V) to give 0.6 mg (43% yield) of the title compound, **3.318**, as orange solids: m.p. > 300 ^{o}C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.25~7.36 (m, 12 H), 6.85~6.98 (m, 12 H), 6.05 (s, 2 H), 6.04 (s, 4 H), 5.95 (s, 4 H), 5.89 (s, 2 H), 3.82 (s, 12 H, OMe); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 178.6, 177.6, 152.0, 151.4, 151.3, 151.0, 147.8, 145.0, 143.5, 141.9, 141.8, 137.4, 135.0, 126.1 (2 peaks overlap), 125.9, 125.7, 125.5(2 peaks overlap), 124.5, 123.8, 63.4 (OMe), 42.4 (3 peaks overlap), 42.2.

The band just below the cyclized product (Rf. = 0.26) was cut and eluented with toluene-chloroform-ethyl acetate (25:25:2, V:V:V), concentrated to afford 1.2 mg (86% yield) of compound **3.139** (not enough materials for ^{13}C NMR): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.47 (s, 2 H), 7.93 (m, 2 H), 7.20~7.70 (m, 12 H), 6.80~7.00 (m, 12 H), 6.63 (s, 2 H), 6.14 (s, 2 H), 6.07 (s, 2 H), 6.04 (s, 2 H), 6.03 (s, 2 H), 5.99 (s, 2 H), 4.05 (s, 6 H), 3.88 (s. 6 H).

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Appendix

^{1}H-NMR SPECTRA, ^{13}C-NMR SPECTRA AND MASS SPECTRA

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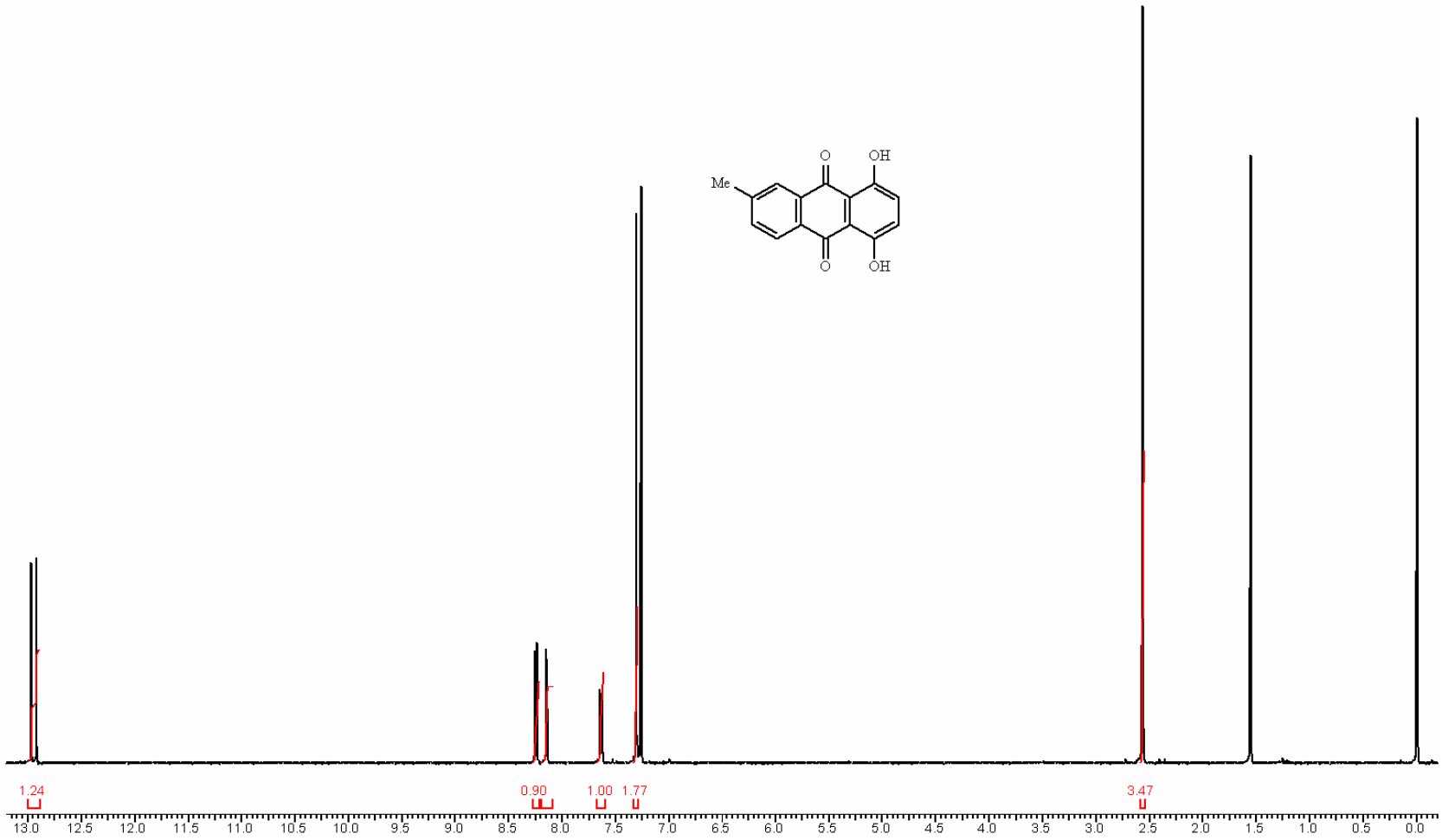
Solvent	CDCl3	***Sweep Width (Hz)***	7000.35	***Temperature (grad C)***	29.000		



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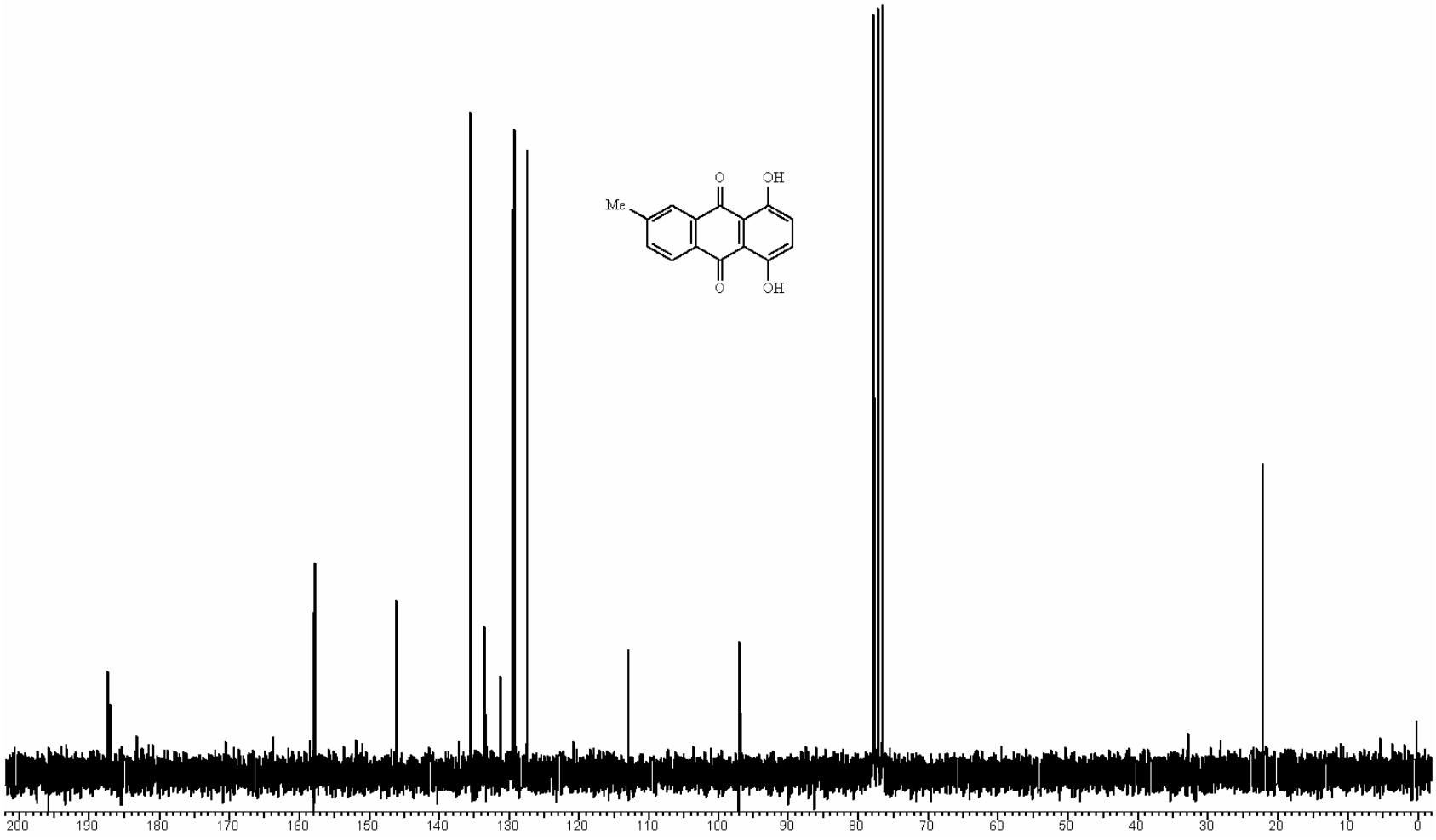

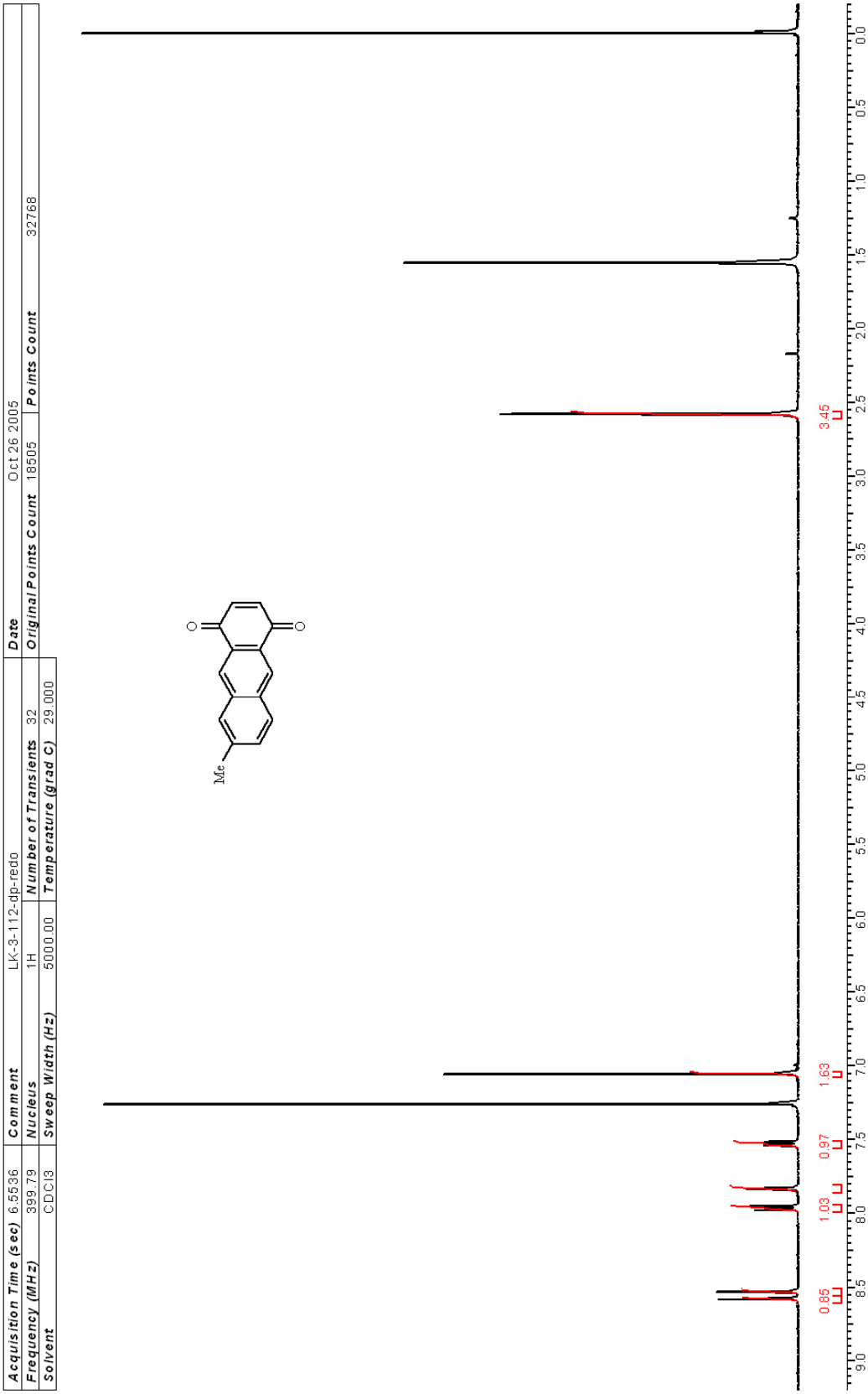
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Original Points Count 18505
Points Count 32768
Solvent CDCl3
Sweep Width (Hz) 5000.00
Temperature (grad C) 29.000
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1.03
0.97
1.63
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8.5
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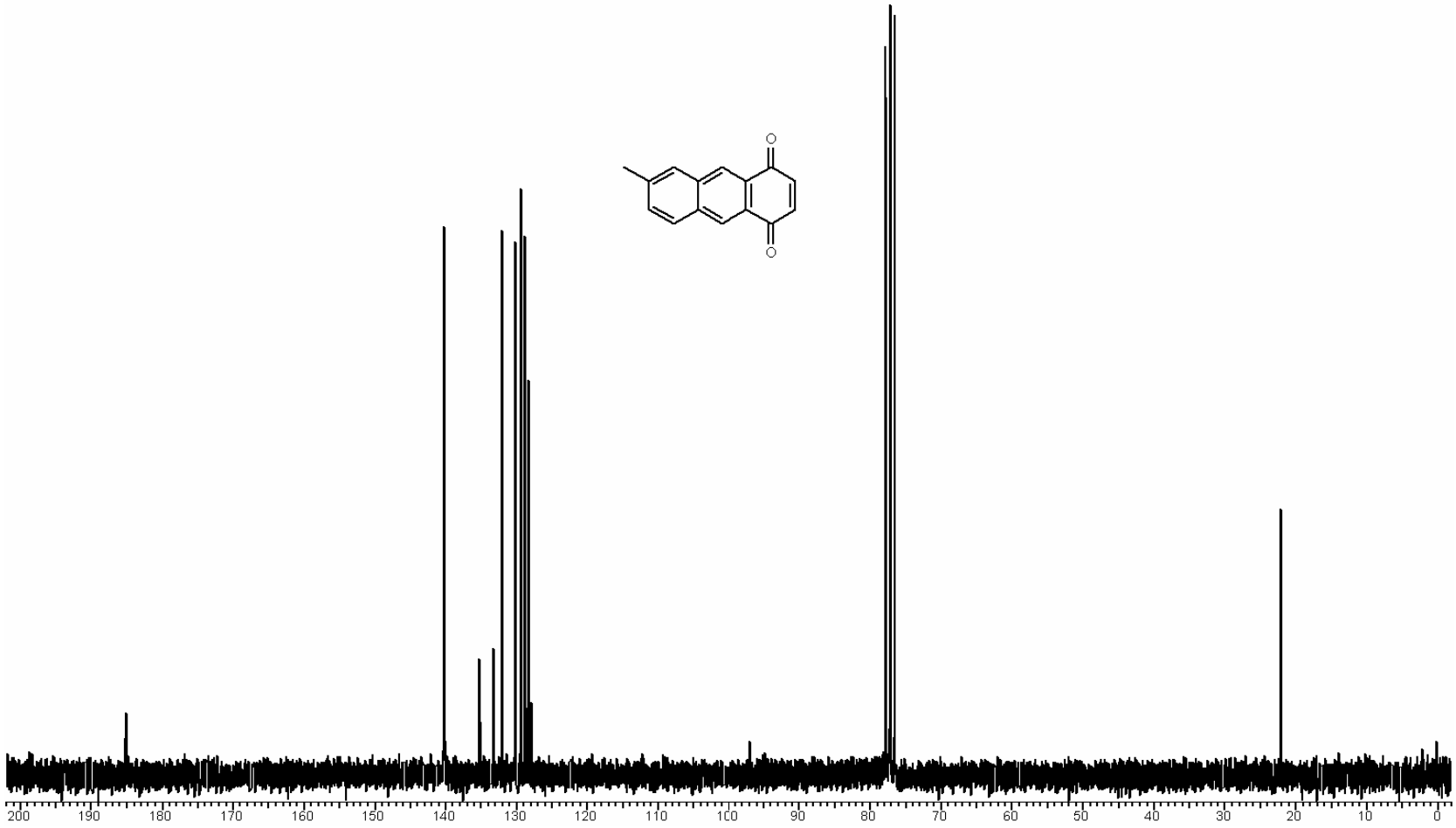
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

Acquisition Time (sec)	2.6214	*Comment*	LK-3-112-dp-c13-redo		*Date*	Oct 26 2005	
Frequency (MHz)	50.29	*Nucleus*	13C	*Number of Transients* 20000	*Original Points Count*	18720	*Points Count* 32768
Solvent	CDCl3	*Sweep Width (Hz)*	12500.00		*Temperature (grad C)*	29.000	



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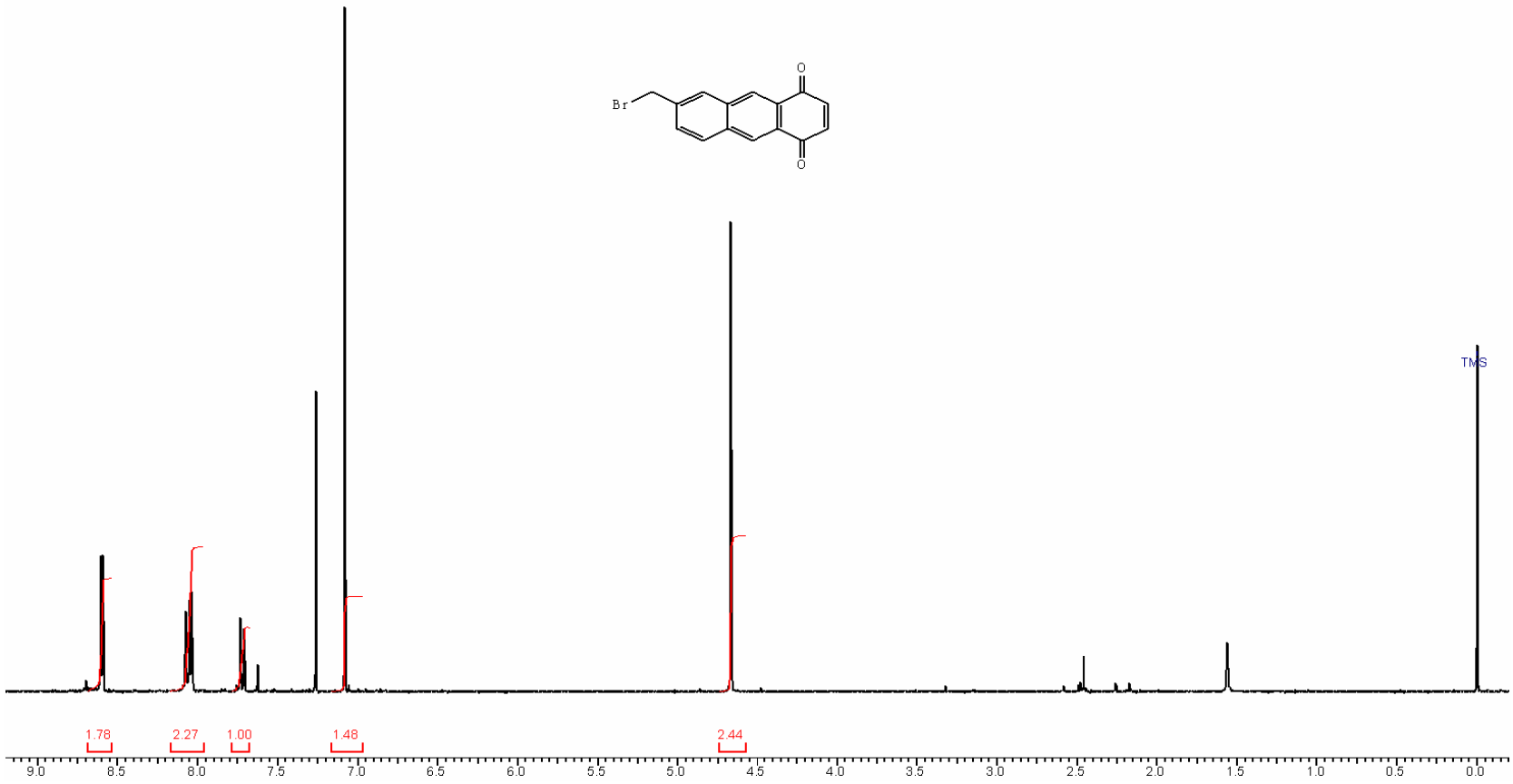
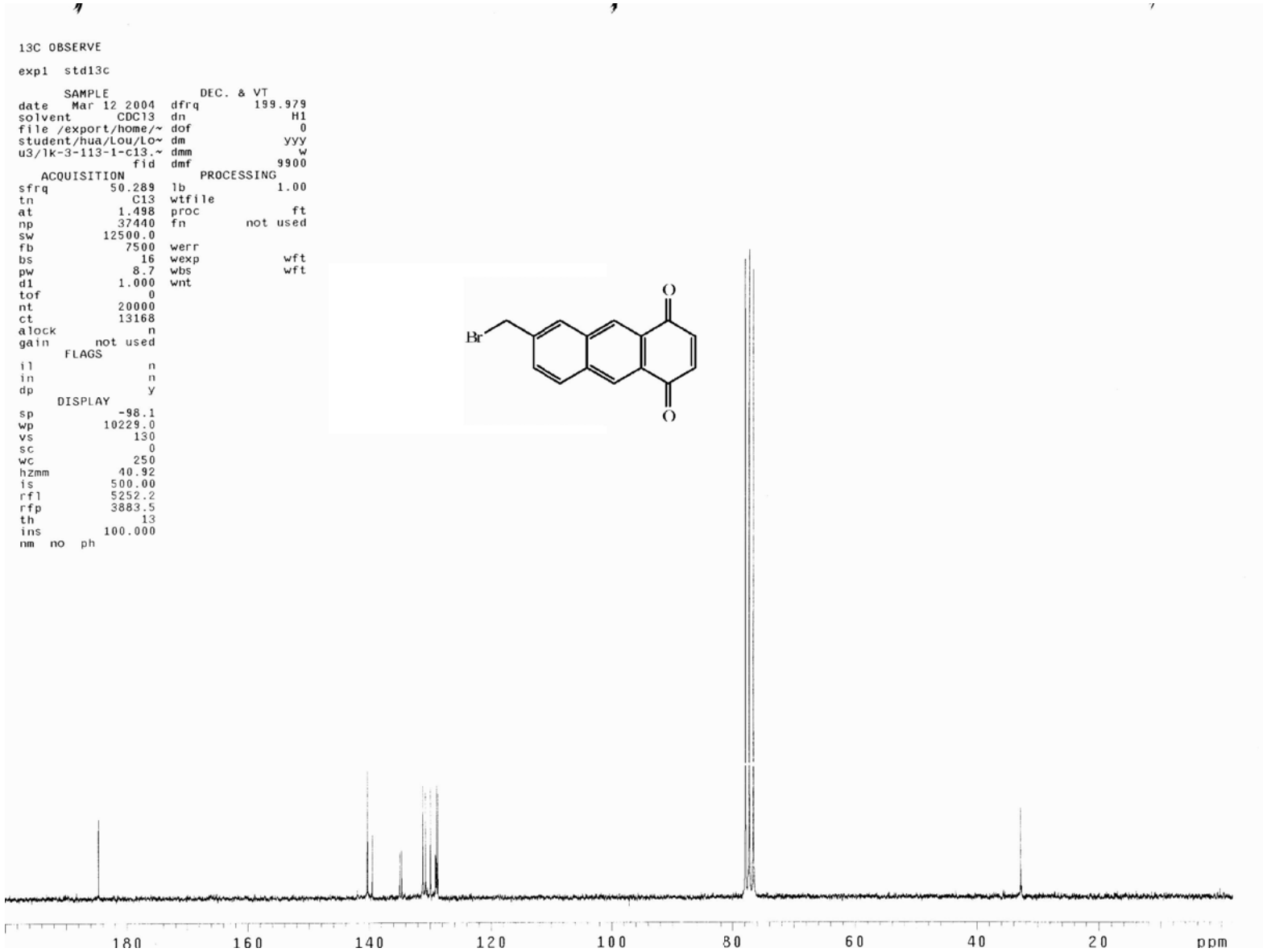
Temperature (grad C)	29.000								

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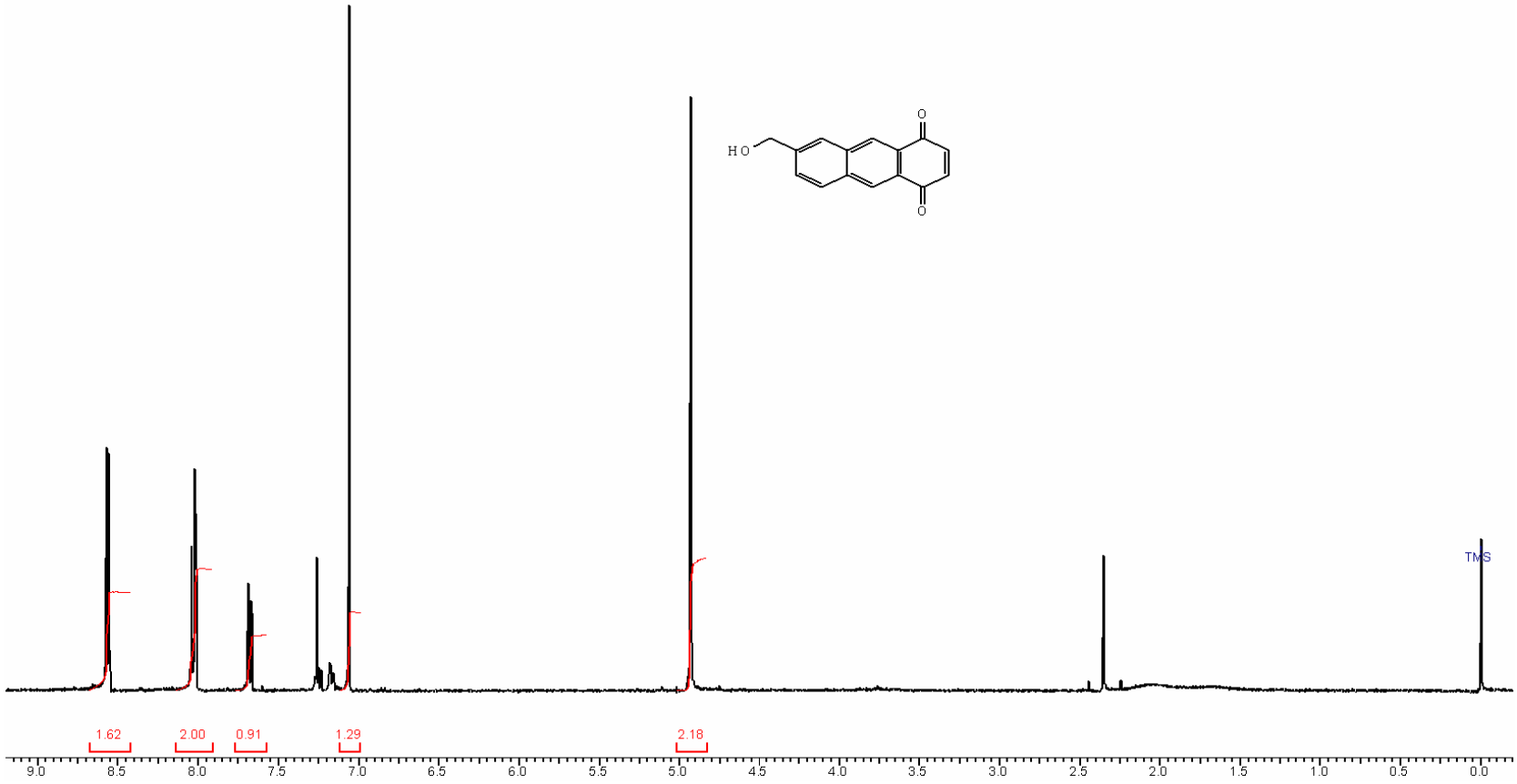

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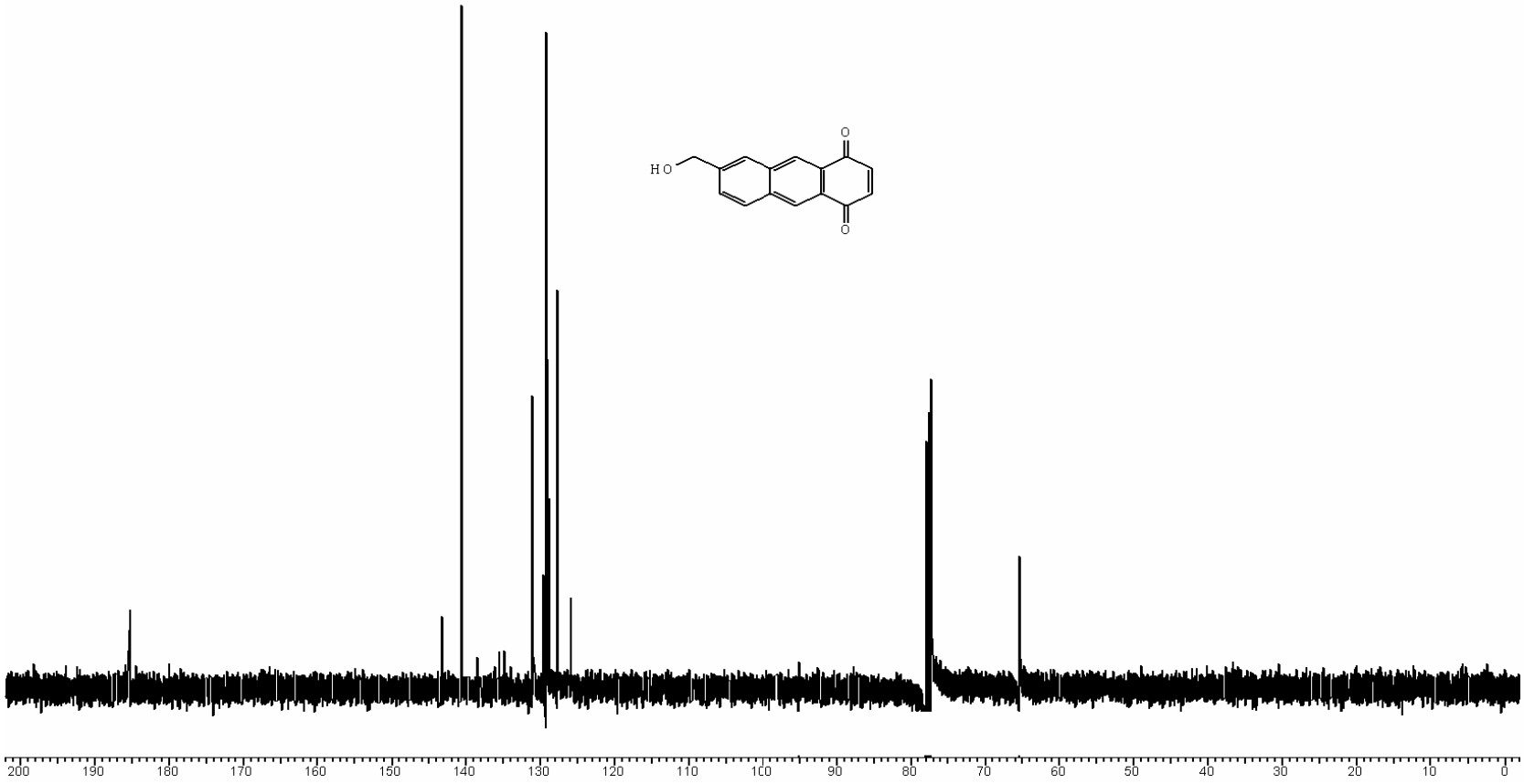

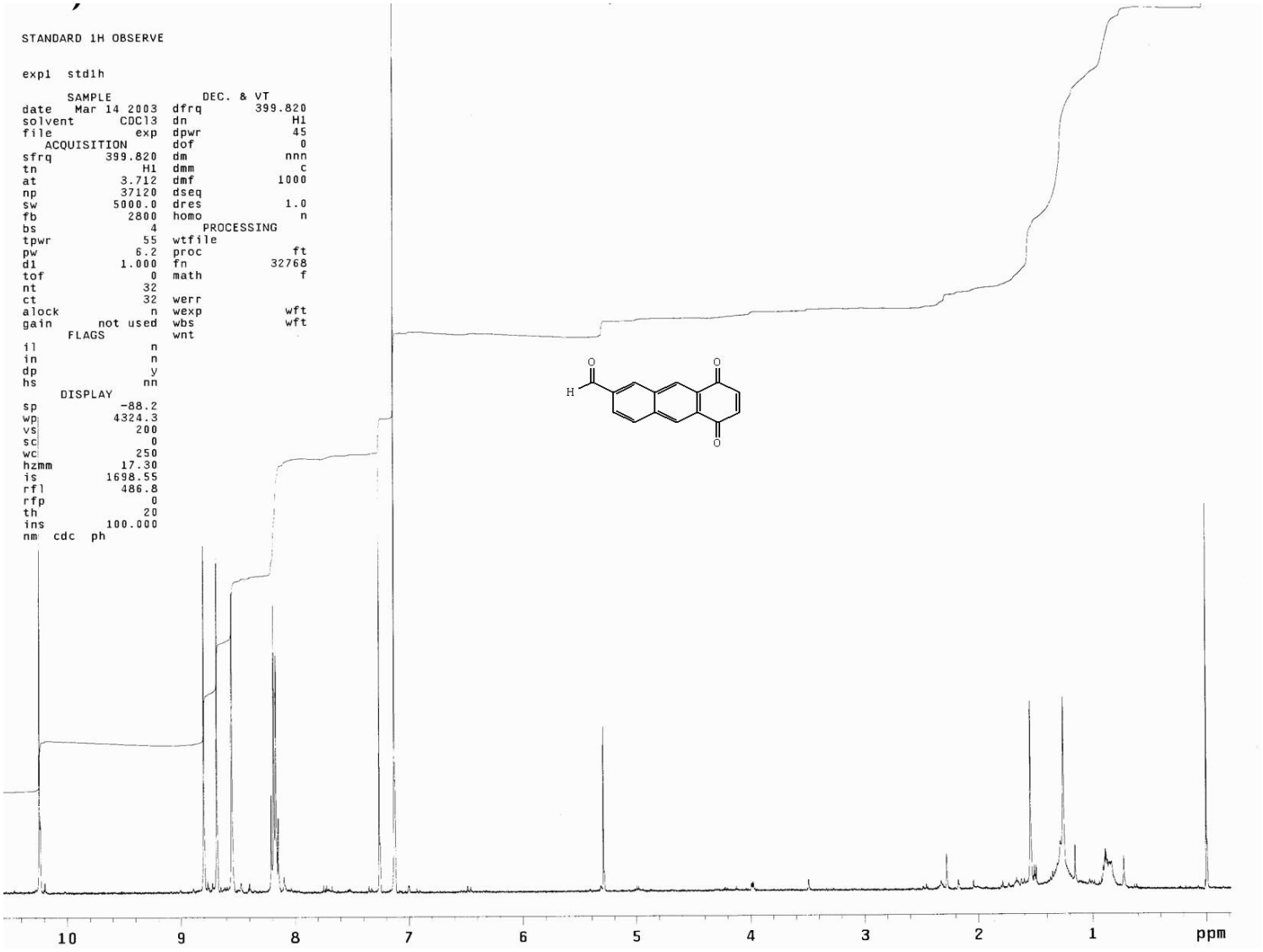
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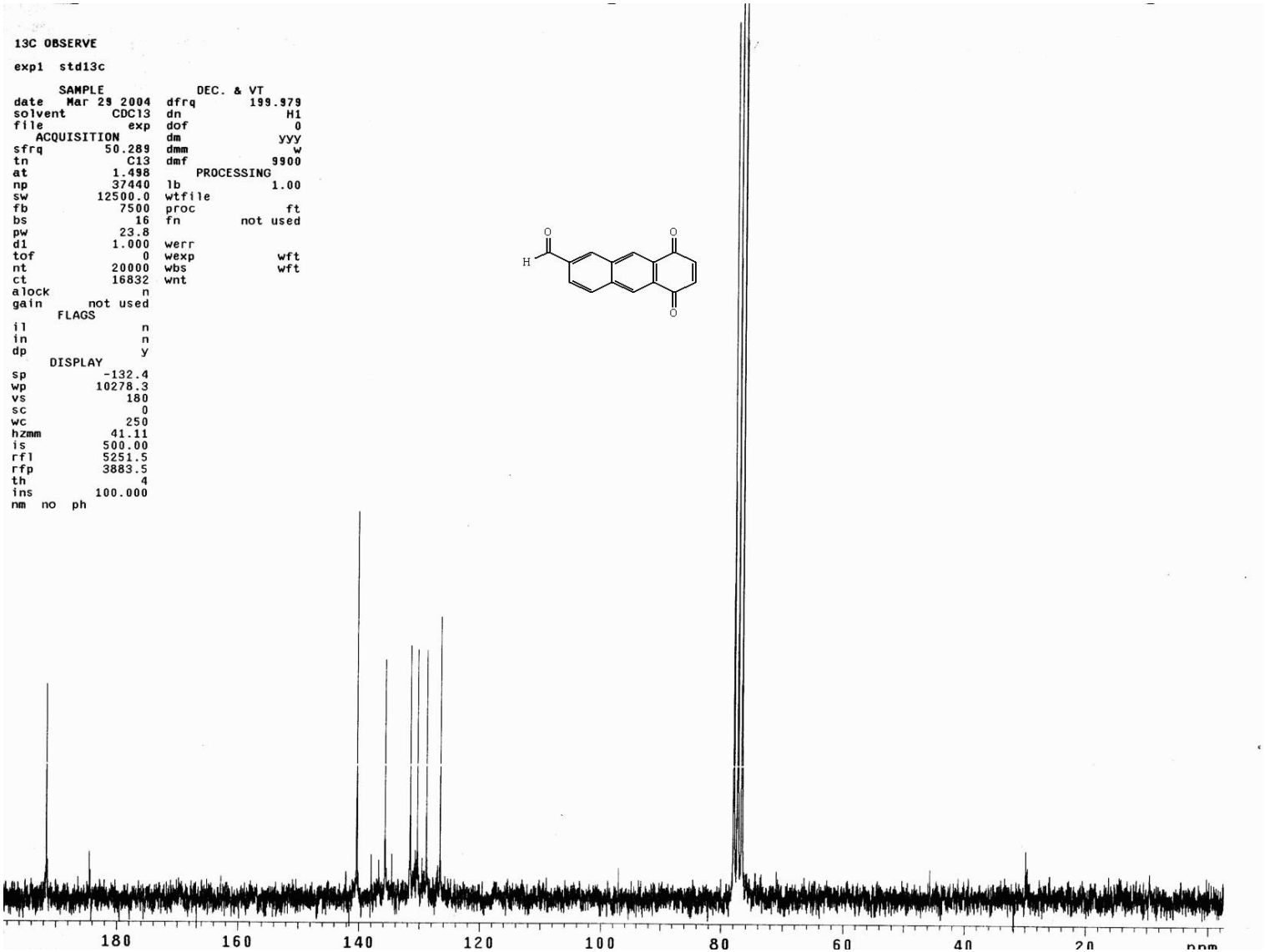
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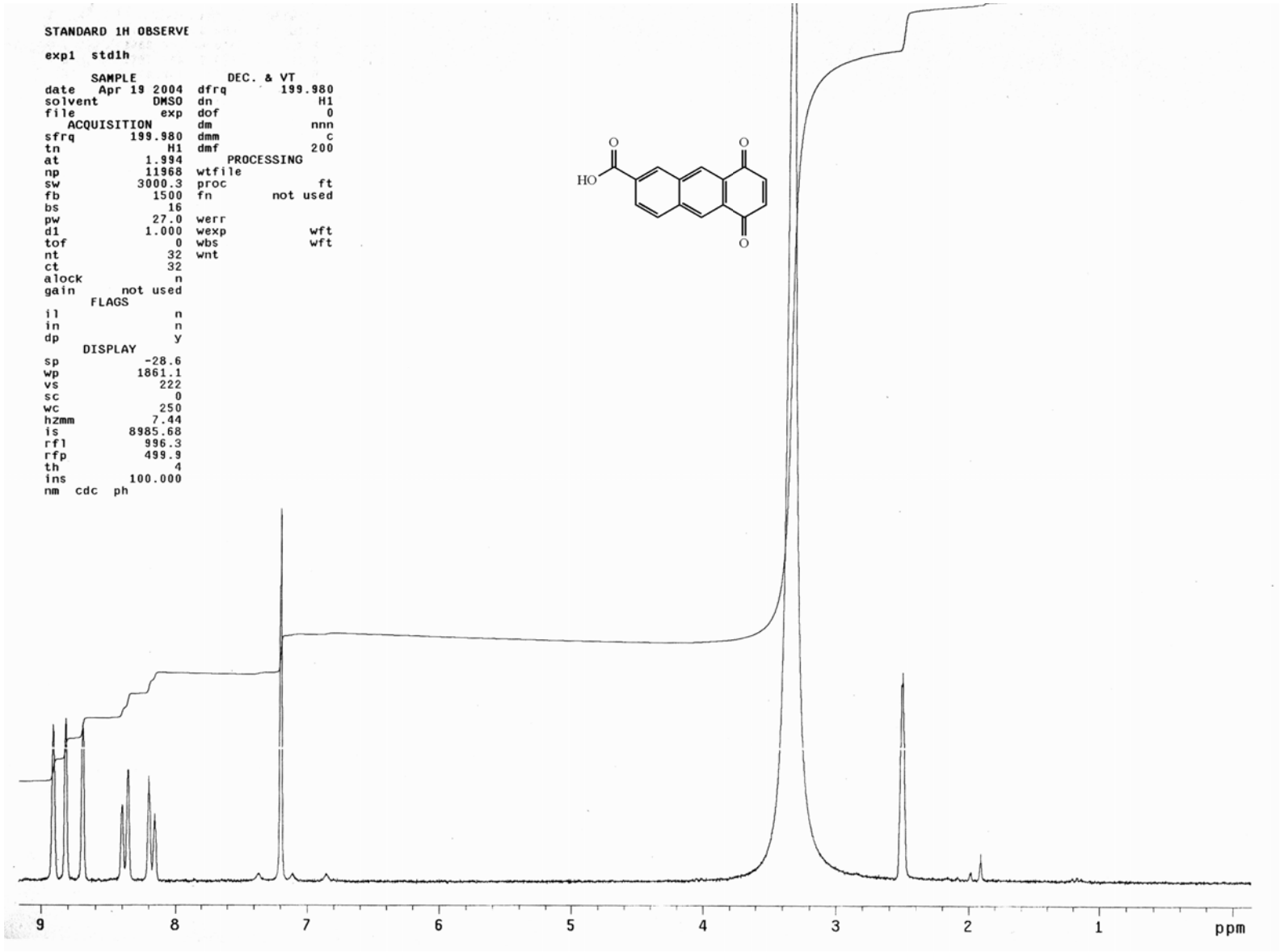
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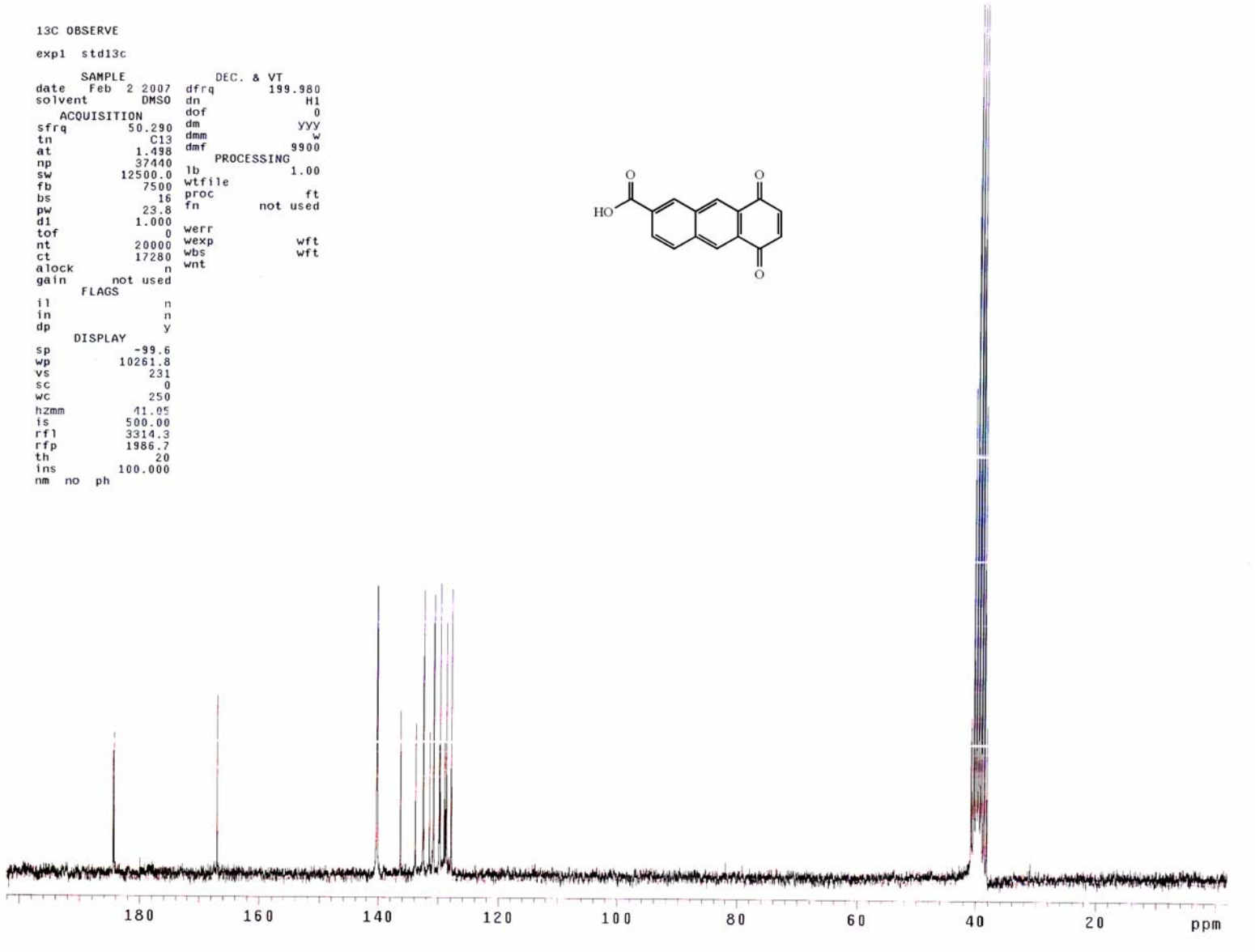
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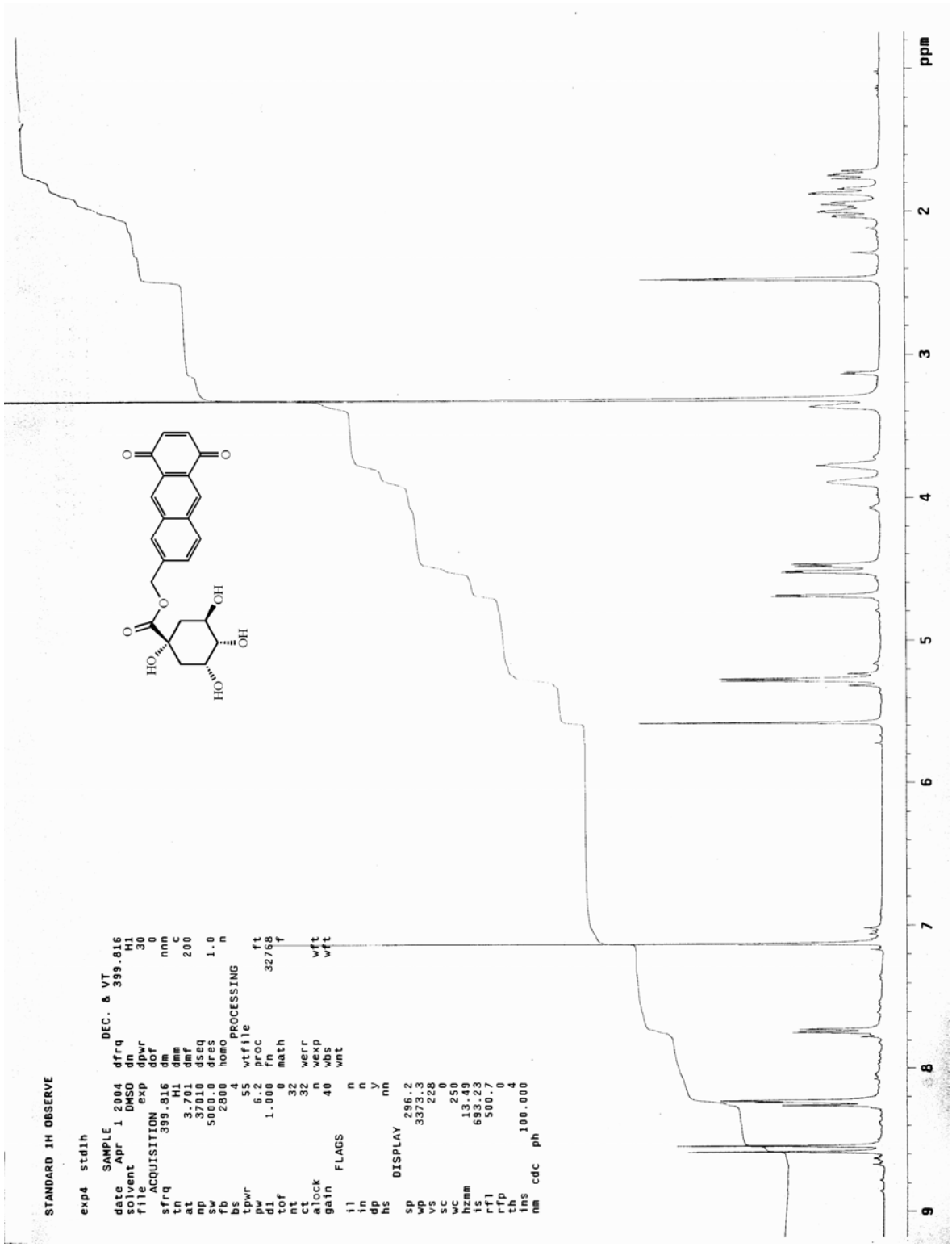
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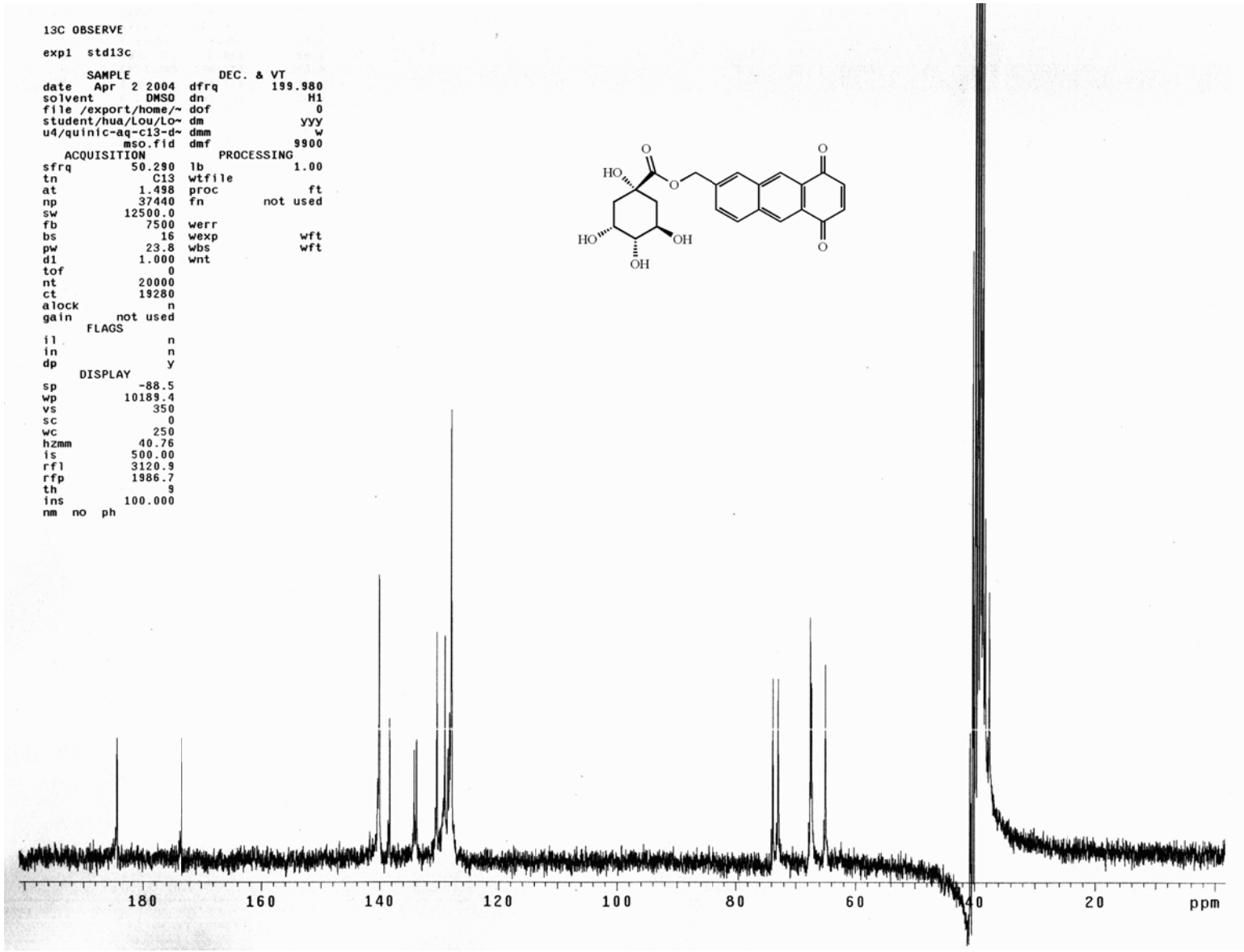
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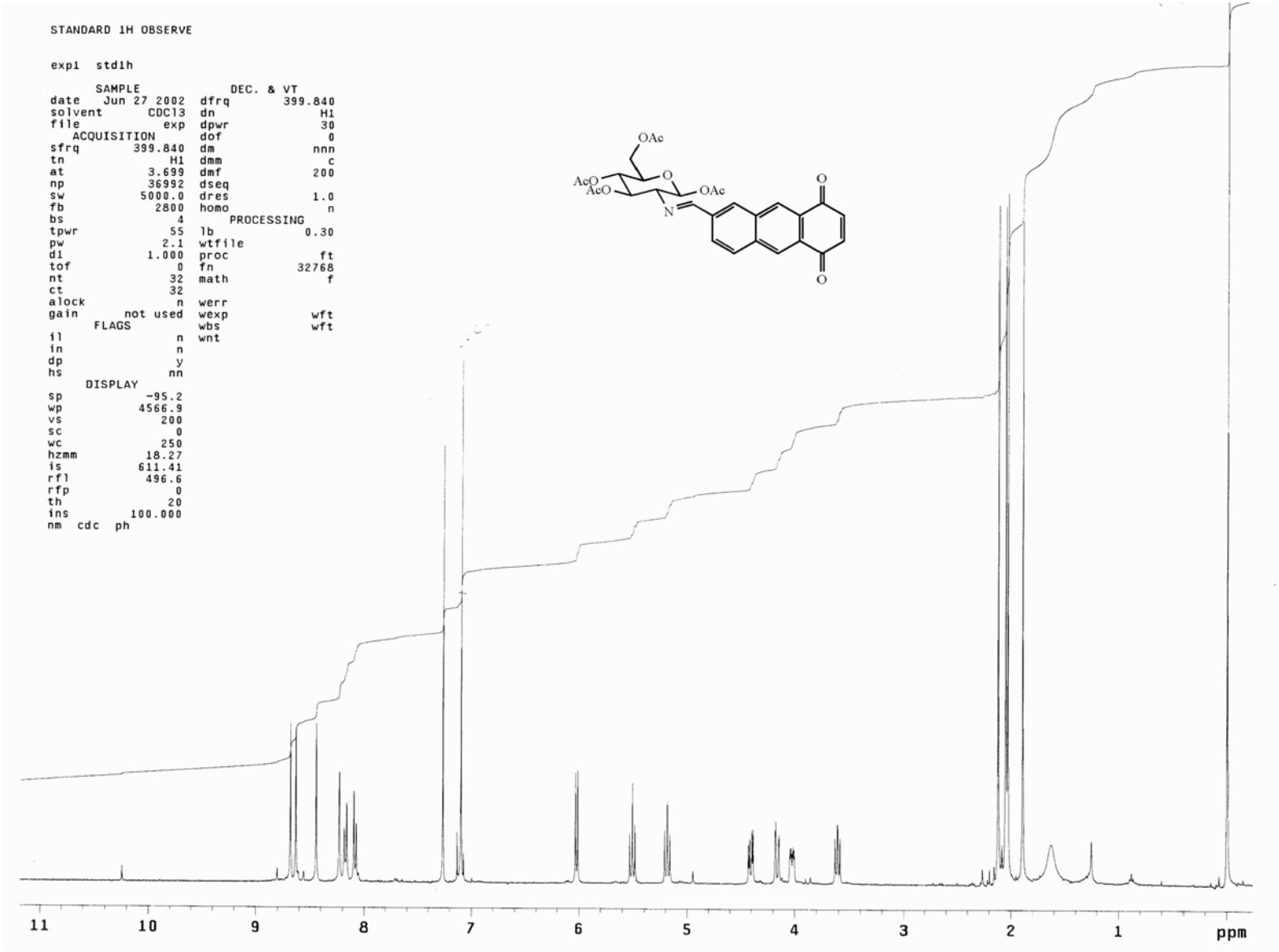
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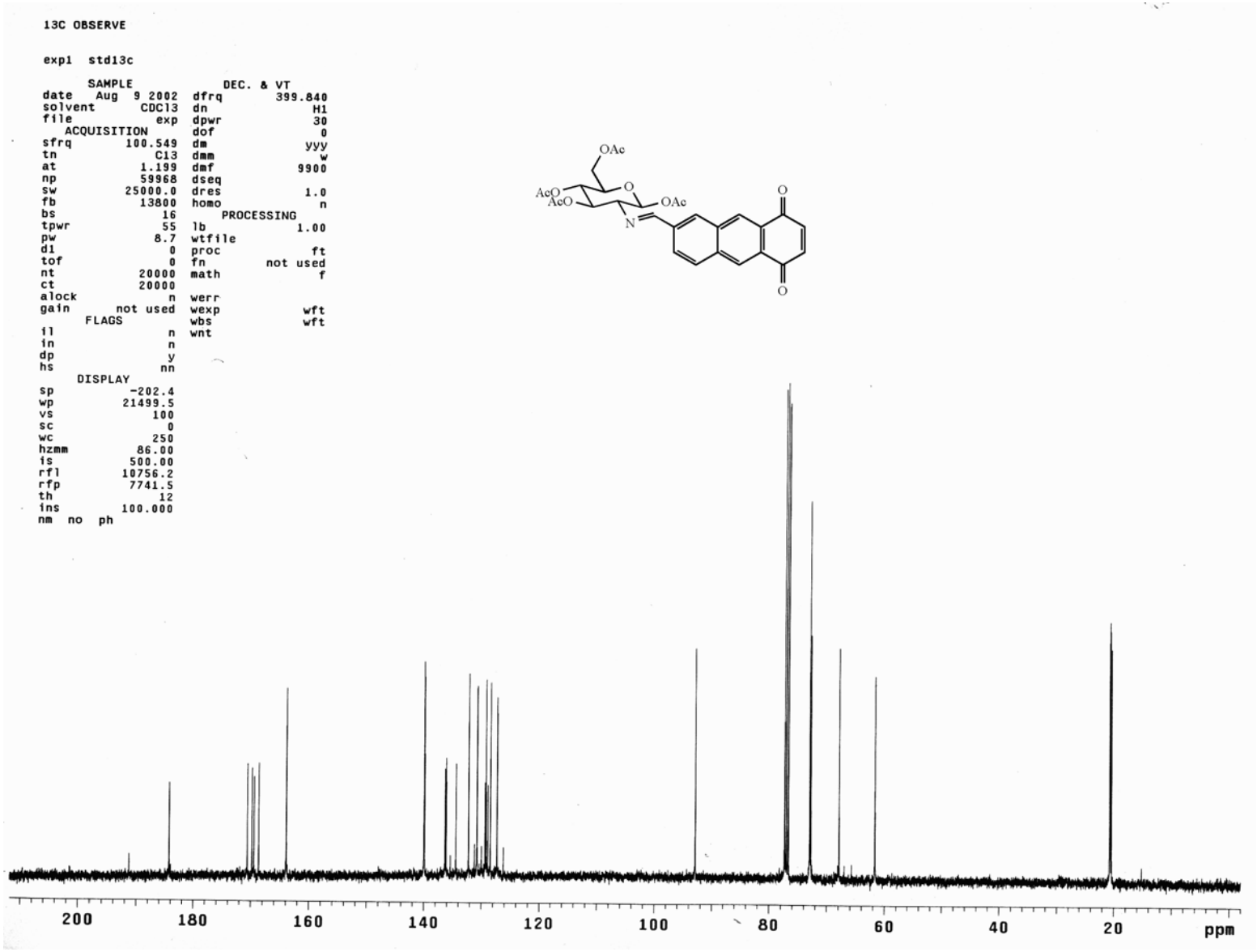
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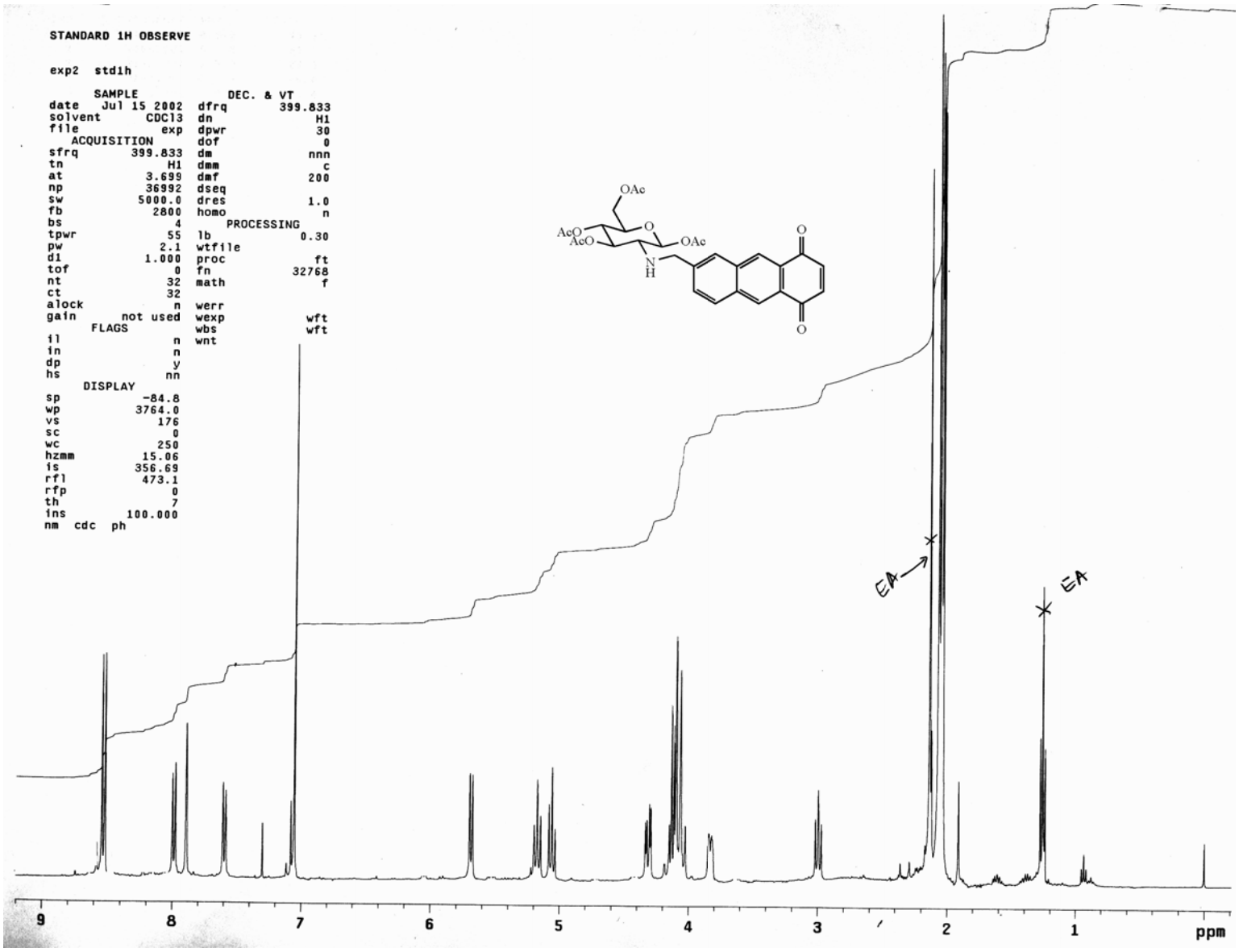
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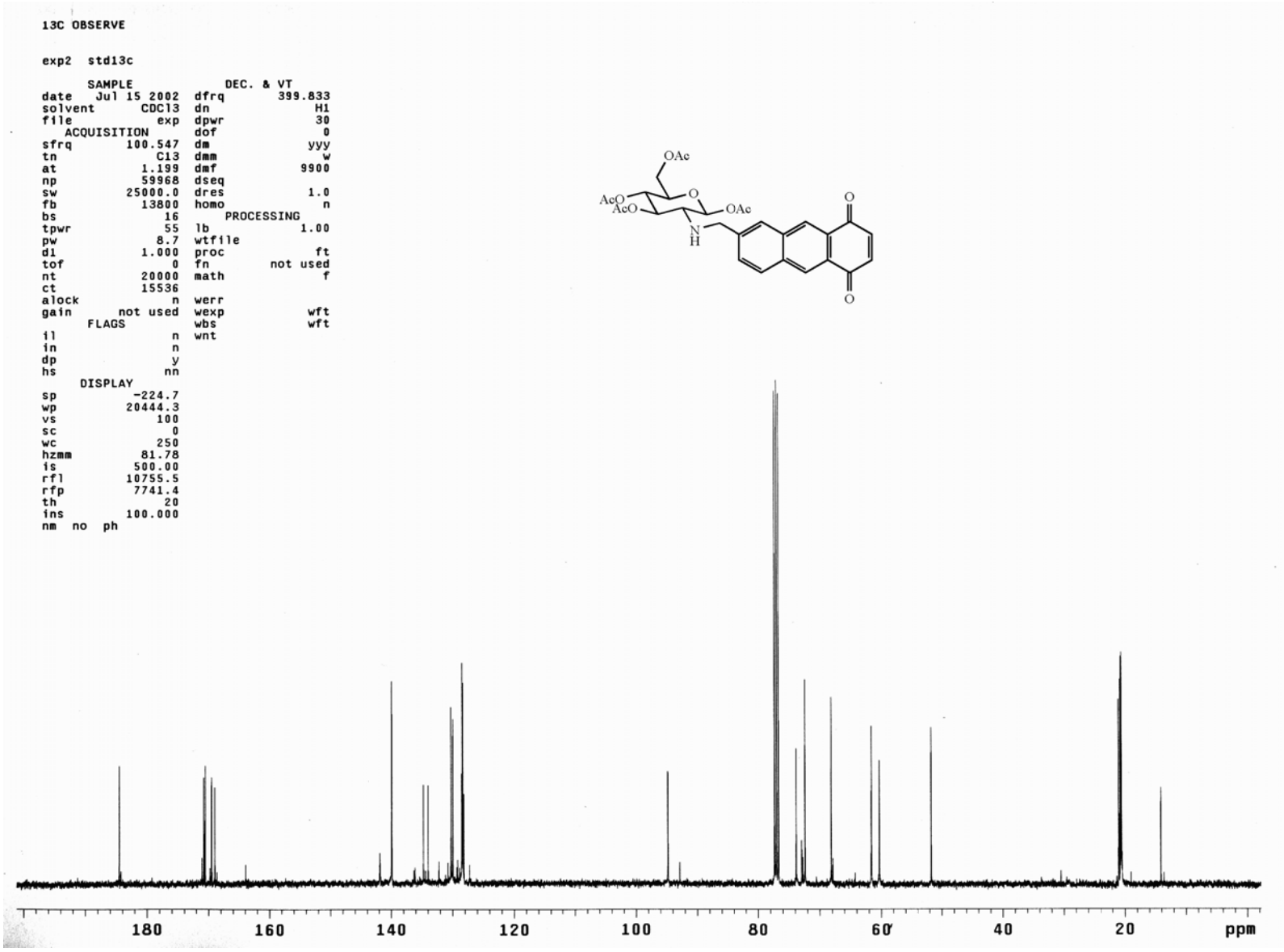
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
lb 0.30
wtfile
proc ft
fn 32768
math f
werr
wexp wft
wbs wft
wnt
OAc
AcO
AcO
O
OAc
N
H
O
O
EA
EA
9
8
7
6
5
4
3
2
1
ppm


13C OBSERVE
exp2 std13c
SAMPLE
date Jul 15 2002
solvent CDCl3
file exp
ACQUISITION
sfrq 100.547
tn C13
at 1.199
np 59968
sw 25000.0
fb 13800
bs 16
tpwr 55
pw 8.7
d1 1.000
tof 0
nt 20000
ct 15536
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -224.7
wp 20444.3
vs 100
sc 0
wc 250
hzmm 81.78
is 500.00
rfl 10755.5
rfp 7741.4
th 20
ins 100.000
nm no ph
DEC. & VT
dfrq 399.833
dn H1
dpwr 30
dof 0
dm yyy
dmm w
dmf 9900
dseq
dres 1.0
homo n
PROCESSING
lb 1.00
wtfile
proc ft
fn not used
math f
werr
wexp wft
wbs wft
wnt
OAc
AcO
AcO
O
OAc
N
H
O
O
180
160
140
120
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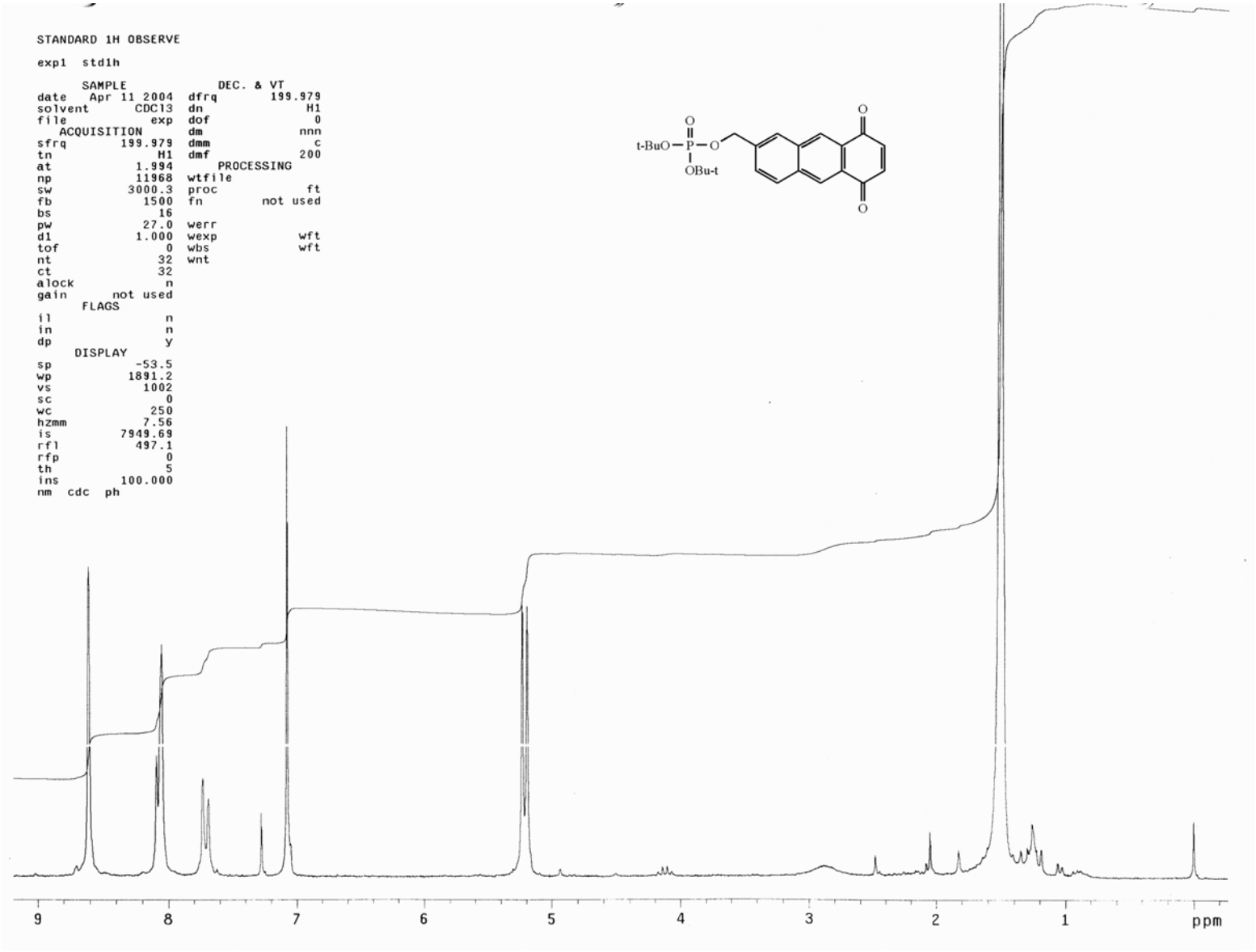
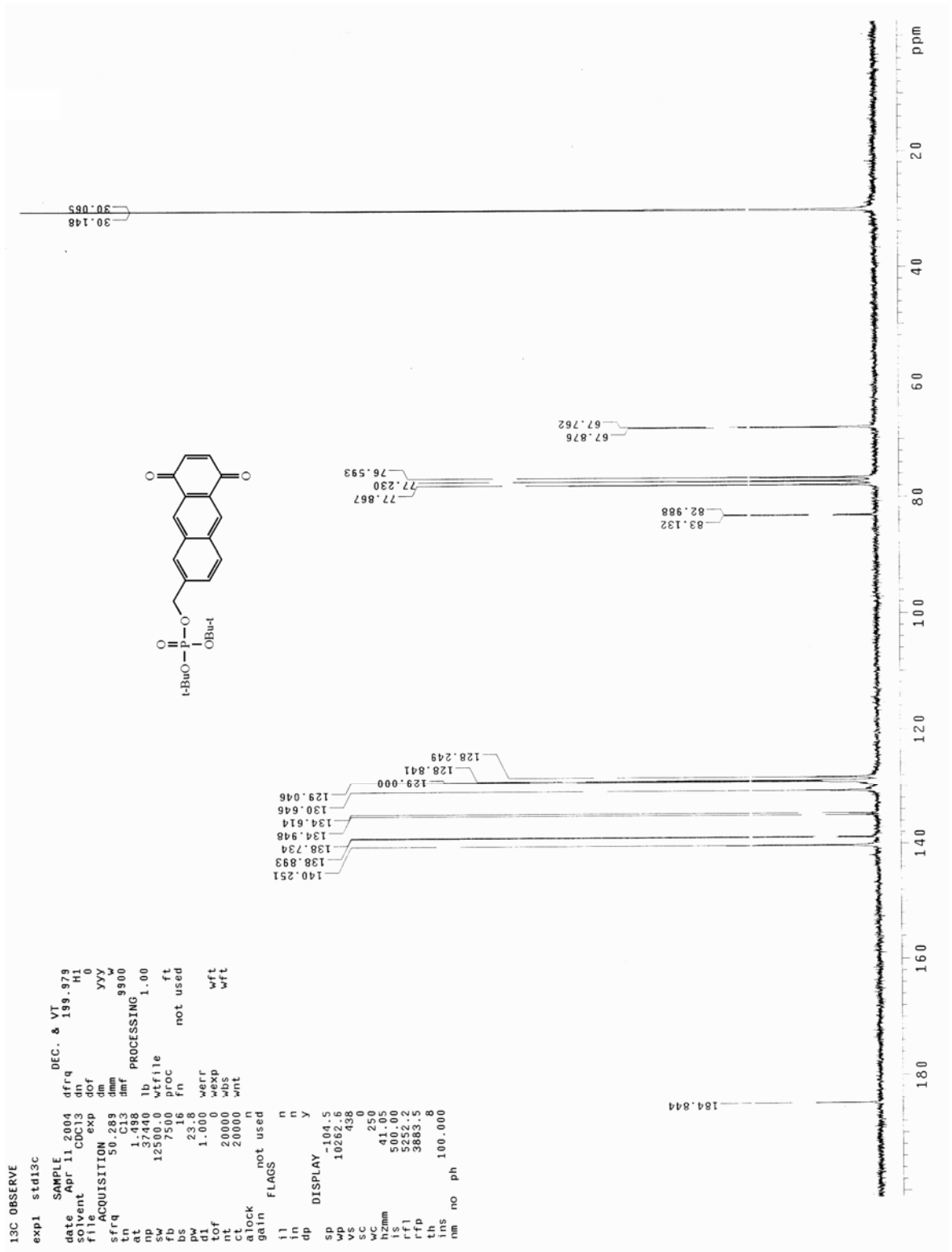
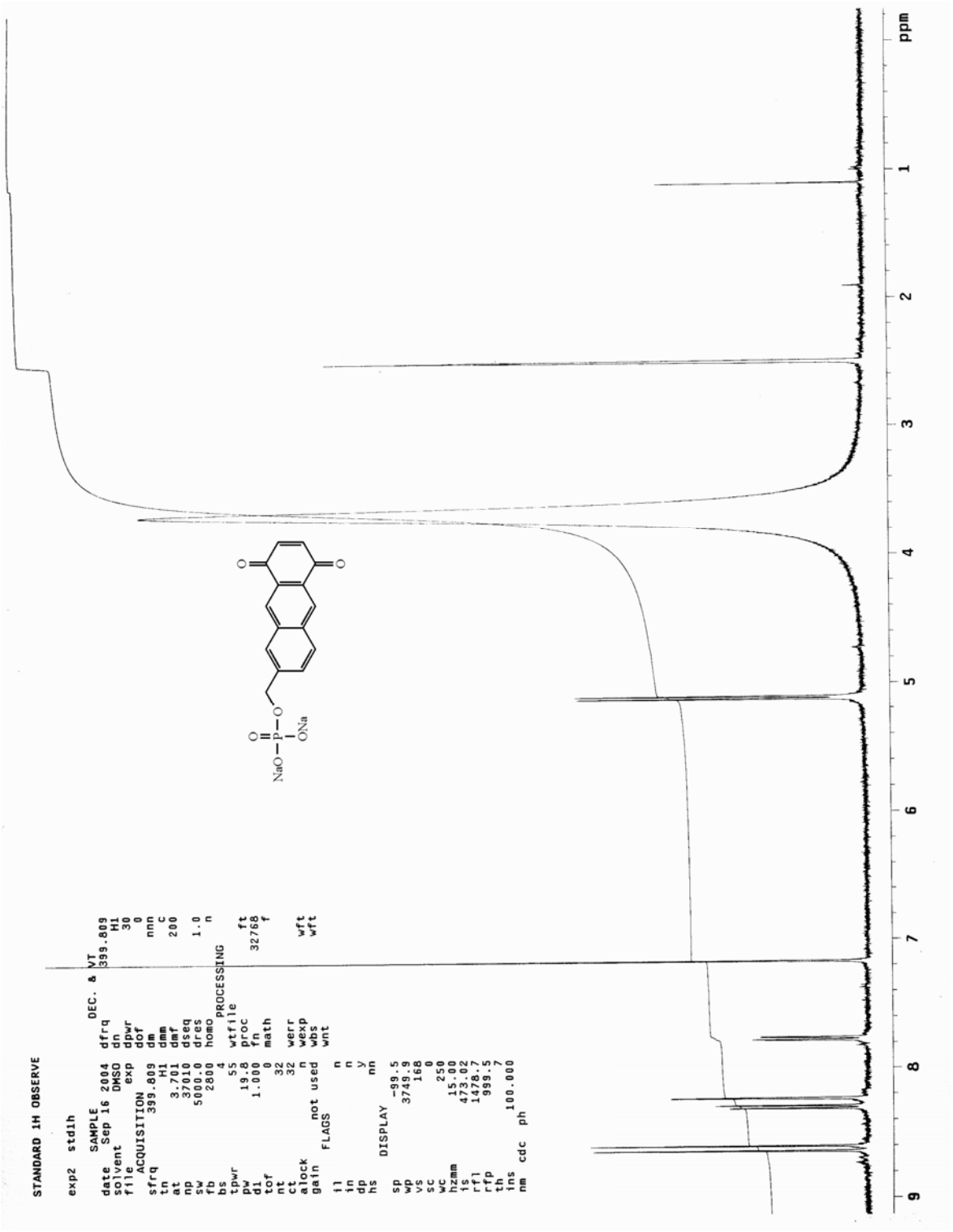
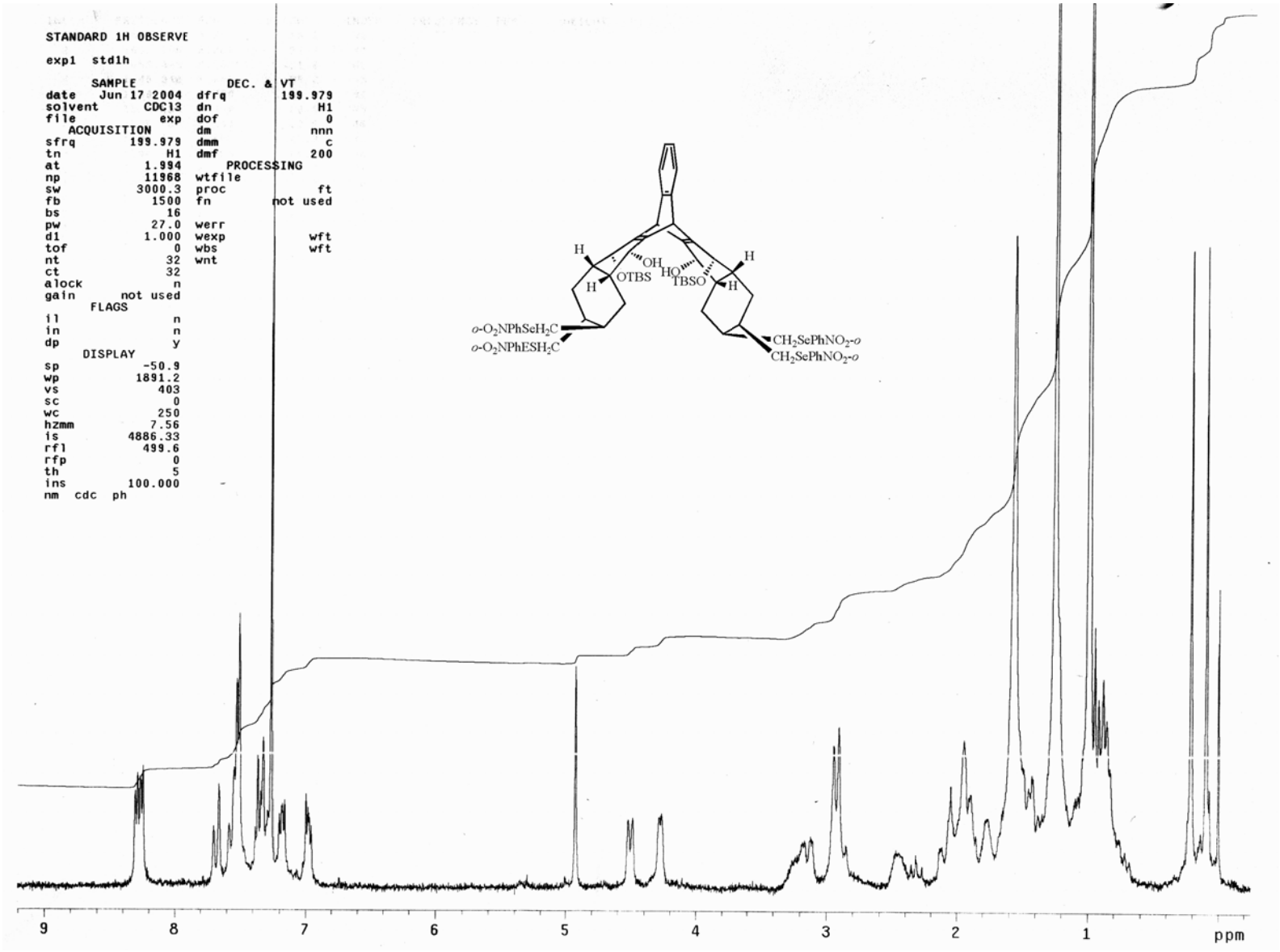
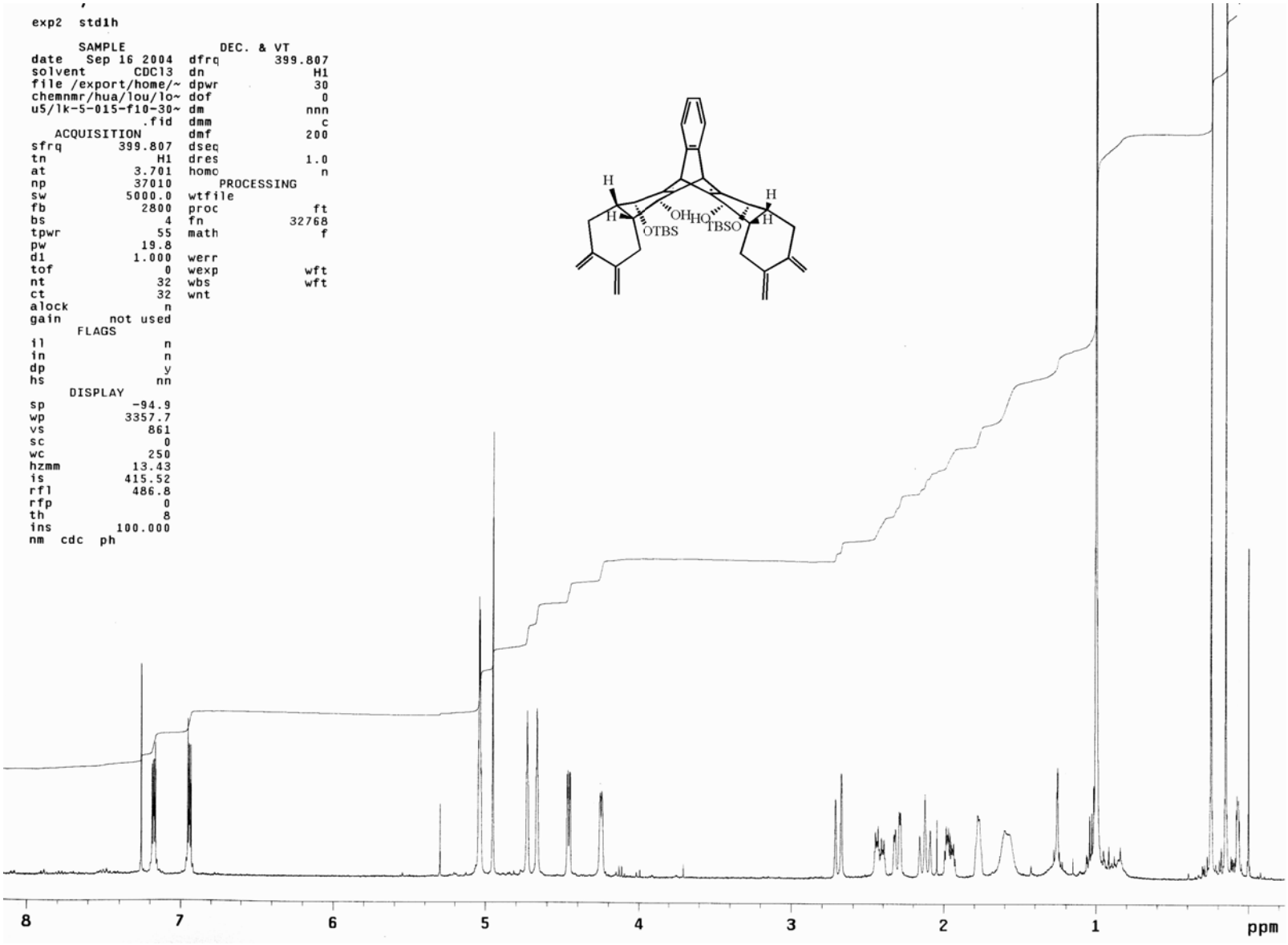
60
40
20
ppm

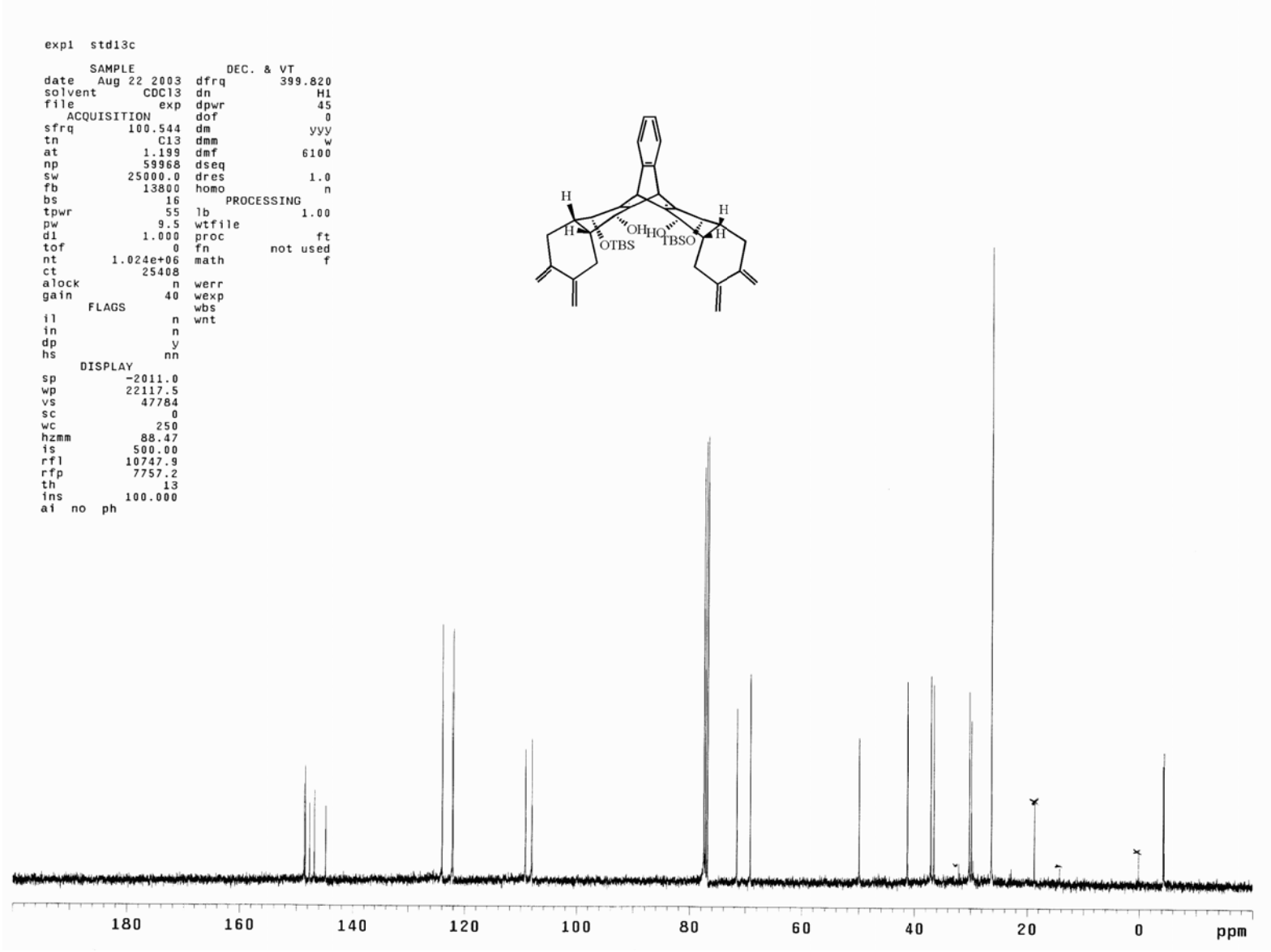

STANDARD 1H OBSERVE
exp1 std1h
SAMPLE
date Apr 11 2004
solvent CDCl3
file exp
ACQUISITION
sfrq 199.979
tn H1
at 1.994
np 11968
sw 3000.3
fb 1500
bs 16
pw 27.0
d1 1.000
tof 0
nt 32
ct 32
alock n
gain not used
FLAGS
il n
in n
dp y
DISPLAY
sp -53.5
wp 1891.2
vs 1002
sc 0
wc 250
hzmm 7.56
is 7949.69
rfl 497.1
rfp 0
th 5
ins 100.000
nm cdc ph
DEC. & VT
dfrq 199.979
dn H1
dof 0
dm nnn
dmm c
dmf 200
PROCESSING
wtfile
proc ft
fn not used
werr
wexp wft
wbs wft
wnt
t-BuO
OBu-t
9
8
7
6
5
4
3
2
1
ppm

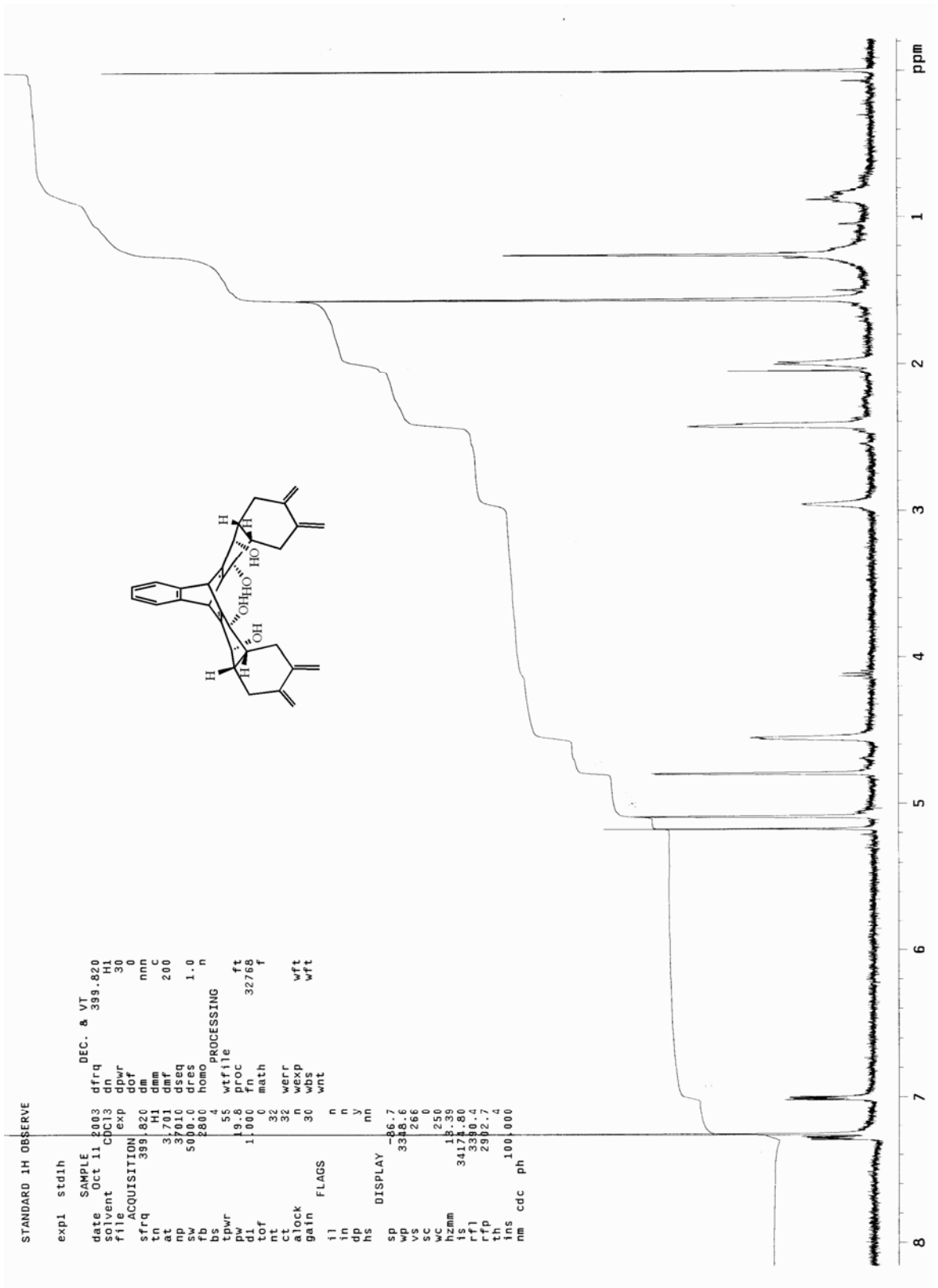

13C OBSERVE
exp1 std13c
SAMPLE
date Apr 11 2004
solvent CDCl3
file exp
ACQUISITION
sfrq 50.289
tn C13
at 1.498
np 37440
sw 12500.0
fb 7500
bs 16
pw 23.8
d1 1.000
tof 0
nt 20000
ct 20000
alock n
gain not used
FLAGS
il n
in n
dp y
DISPLAY
sp -104.5
wp 10262.6
vs 438
sc 0
wc 250
hzmm 41.05
is 500.00
rfl 5252.2
rfp 3883.5
th 8
ins 100.000
nm no ph
DEC. & VT
dfrq 199.979
dn H1
dof 0
dm yyy
dmm w
dmf 9900
PROCESSING
lb 1.00
wtfile
proc ft
fn not used
werr
wexp wft
wbs wft
wnt
30.065
30.148
67.762
67.876
76.593
77.230
77.867
82.988
83.132
128.249
128.841
129.000
129.046
130.646
134.614
134.948
138.734
138.893
140.251
184.844
t-BuO
OBu-t
ppm


STANDARD 1H OBSERVE
exp2 stdih
DEC. & VT
SAMPLE 399.809
date Sep 16 2004 dfrq 399.809
solvent DMSO dn H1
file exp nt 30
ACQUISITION ct 0
sfrq 399.809 dm nnn
tn H1 dmm c
at 3.701 dmf 200
np 37010 dseq
sw 5000.0 dres 1.0
fb 2800 homo n
bs 4 PROCESSING
tpwr 55 wtfile
pw 19.8 proc ft
dl 1.000 fn 32768
tof 0 math f
nt 32 werr
ct 32 wexp wft
alock n wbs wft
gain not used wnt
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -99.5
wp 3749.9
vs 168
sc 0
wc 250
hzmm 15.00
is 473.02
rfl 1478.7
rfp 999.5
th 7
ins 100.000
nm cdc ph
NaO
P
O
ONa
ppm
9
8
7
6
5
4
3
2
1

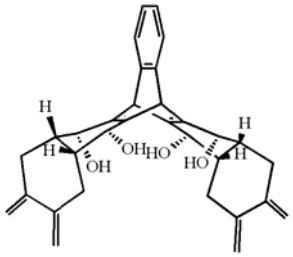

STANDARD 1H OBSERVE
exp1 std1h
SAMPLE
date Jun 17 2004
solvent CDCl3
file exp
ACQUISITION
sfrq 199.979
tn H1
at 1.994
np 11968
sw 3000.3
fb 1500
bs 16
pw 27.0
d1 1.000
tof 0
nt 32
ct 32
alock n
gain not used
FLAGS
il n
in n
dp y
DISPLAY
sp -50.9
wp 1891.2
vs 403
sc 0
wc 250
hzmm 7.56
is 4886.33
rfl 499.6
rfp 0
th 5
ins 100.000
nm cdc ph
DEC. & VT
dfrq 199.979
dn H1
dof 0
dm nnn
dmm c
dmf 200
PROCESSING
wtfile
proc ft
fn not used
werr
wexp wft
wbs wft
wnt
H
OH
HO
H
OTBS
TBSO
H
H
o-O2NPhSeH2C
o-O2NPhESH2C
CH2SePhNO2-o
CH2SePhNO2-o
9
8
7
6
5
4
3
2
1
ppm

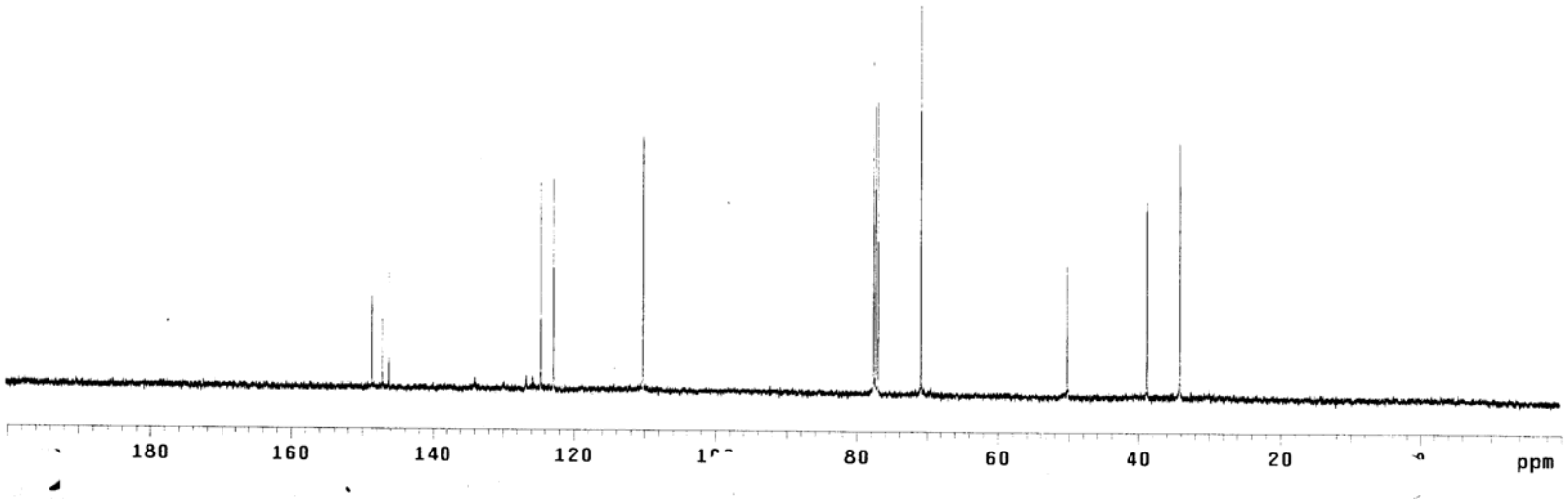

exp2 std1h
SAMPLE
date Sep 16 2004
solvent CDCl3
file /export/home/~
chemnmr/hua/lou/lo~
u5/lk-5-015-f10-30~
.fid
ACQUISITION
sfrq 399.807
tn H1
at 3.701
np 37010
sw 5000.0
fb 2800
bs 4
tpwr 55
pw 19.8
d1 1.000
tof 0
nt 32
ct 32
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -94.9
wp 3357.7
vs 861
sc 0
wc 250
hzmm 13.43
is 415.52
rfl 486.8
rfp 0
th 8
ins 100.000
nm cdc ph
DEC. & VT
dfrq 399.807
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn 32768
math f
werr
wexp wft
wbs wft
wnt
H
H
OTBS
OH
HO
TBSO
H
H
8
7
6
5
4
3
2
1
ppm

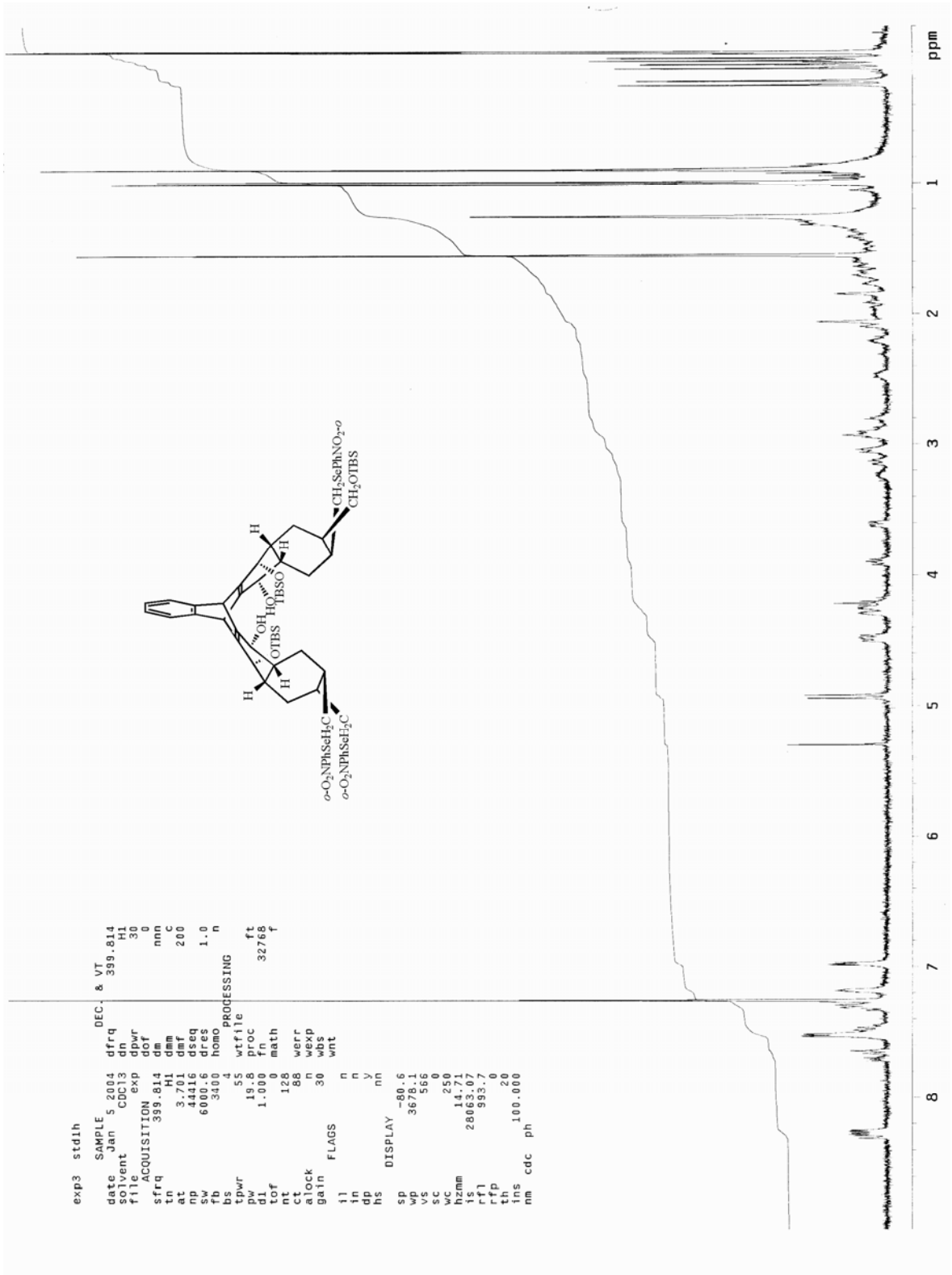

exp1 std13c
SAMPLE
date Aug 22 2003
solvent CDCl3
file exp
ACQUISITION
sfrq 100.544
tn C13
at 1.199
np 59968
sw 25000.0
fb 13800
bs 16
tpwr 55
pw 9.5
d1 1.000
tof 0
nt 1.024e+06
ct 25408
alock n
gain 40
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -2011.0
wp 22117.5
vs 47784
sc 0
wc 250
hzmm 88.47
is 500.00
rfl 10747.9
rfp 7757.2
th 13
ins 100.000
ai no ph
DEC. & VT
dfrq 399.820
dn H1
dpwr 45
dof 0
dm yyy
dmm w
dmf 6100
dseq
dres 1.0
homo n
PROCESSING
lb 1.00
wtfile
proc ft
fn not used
math f
werr
wexp
wbs
wnt
H
H
OTBS
OH
HO
TBSO
H
H
180
160
140
120
100
80
60
40
20
0
ppm

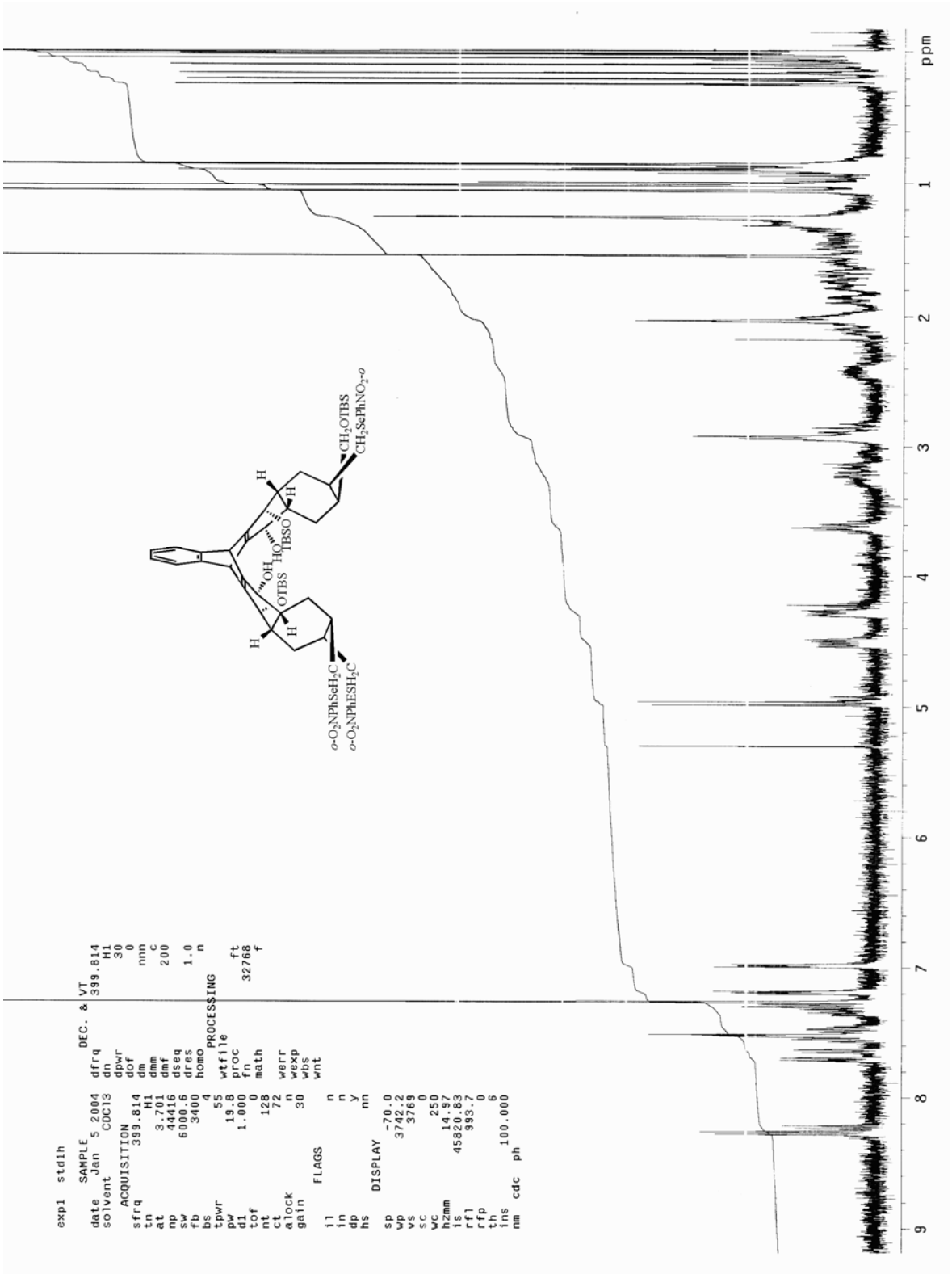

STANDARD 1H OBSERVE
expl stdih
SAMPLE
date Oct 11 2003
solvent CDCl3
file exp
ACQUISITION
sfrq 399.820
tn H1
at 3.701
np 37010
sw 5000.0
fb 2800
bs 4
tpwr 55
pw 19.8
d1 1.000
tof 0
nt 32
ct 32
alock n
gain 30
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -86.7
wp 3348.6
vs 266
sc 0
wc 250
hzmm 13.39
is 3417.80
rfl 3390.4
rfp 2902.7
th 4
ins 100.000
nm cdc ph
DEC. & VT
dfrq 399.820
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn 32768
math f
werr
wexp wft
wbs wft
wnt
H
OH
HO
ppm
8
7
6
5
4
3
2
1

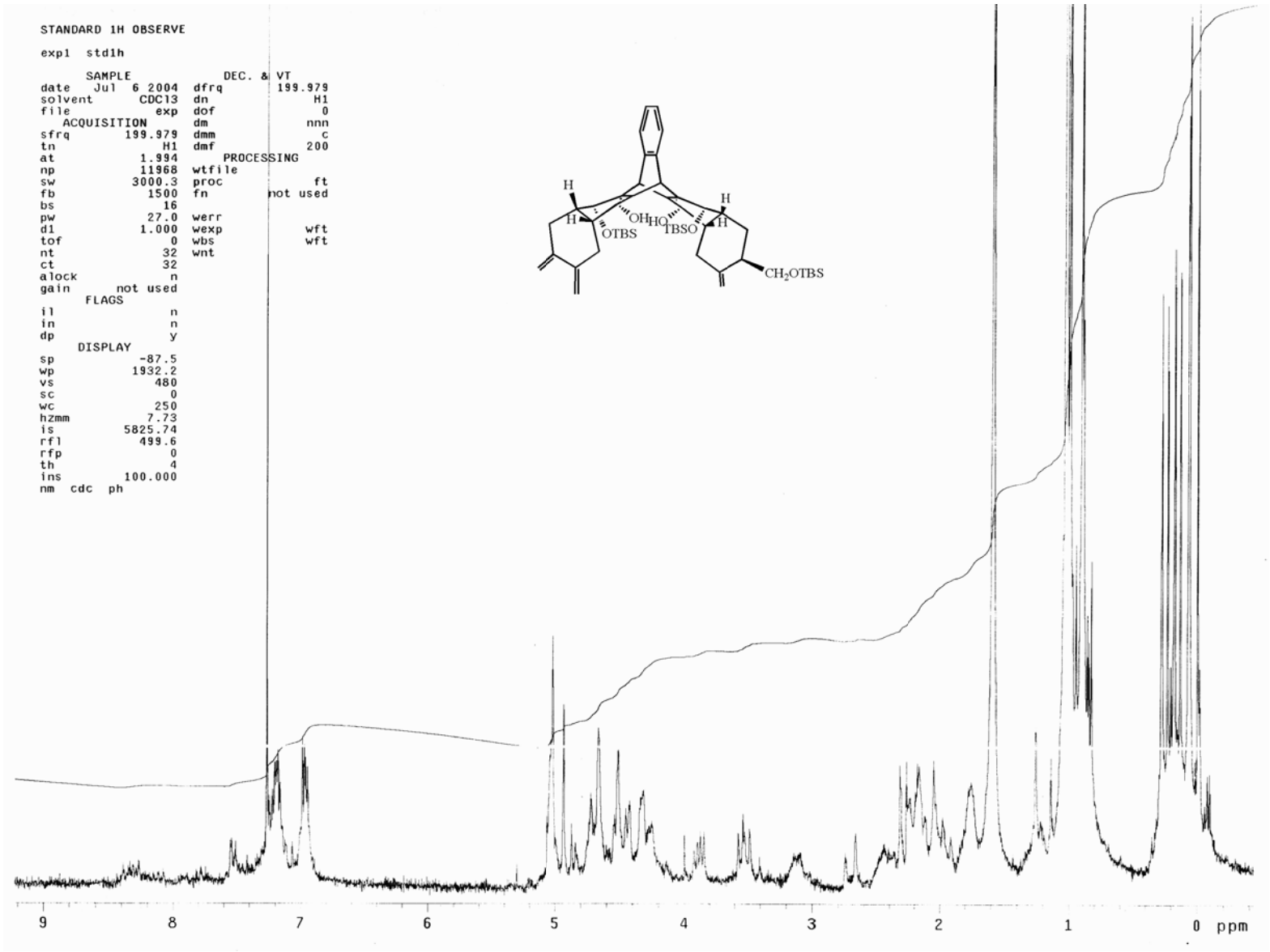
```
exp1  std13c

       SAMPLE
date    Feb 26 2004
solvent       CDCl3
file             exp
    ACQUISITION
sfrq         100.542
tn               C13
at               1.199
np               59968
sw           25000.0
fb               13800
bs                  16
tpwr                55
pw                 9.2
d1                  0
tof                 0
nt          1.024e+06
ct                39520
alock               n
gain        not used
       FLAGS
il                  n
in                  n
dp                  y
hs                 nn
     DISPLAY
sp            -2011.1
wp            22116.8
vs                 32
sc                  0
wc                250
hzmm            88.47
is              500.00
rfl           10748.6
rfp            7757.1
th                  2
ins           100.000
nm  no  ph

       DEC. & VT
dfrq          399.814
dn                 H1
dpwr               45
dof                 0
dm                yyy
dmm                 w
dmf              6100
dseq
dres              1.0
homo                n
     PROCESSING
lb                1.00
wtfile
proc               ft
fn          not used
math                f
werr
wexp
wbs
wnt
```

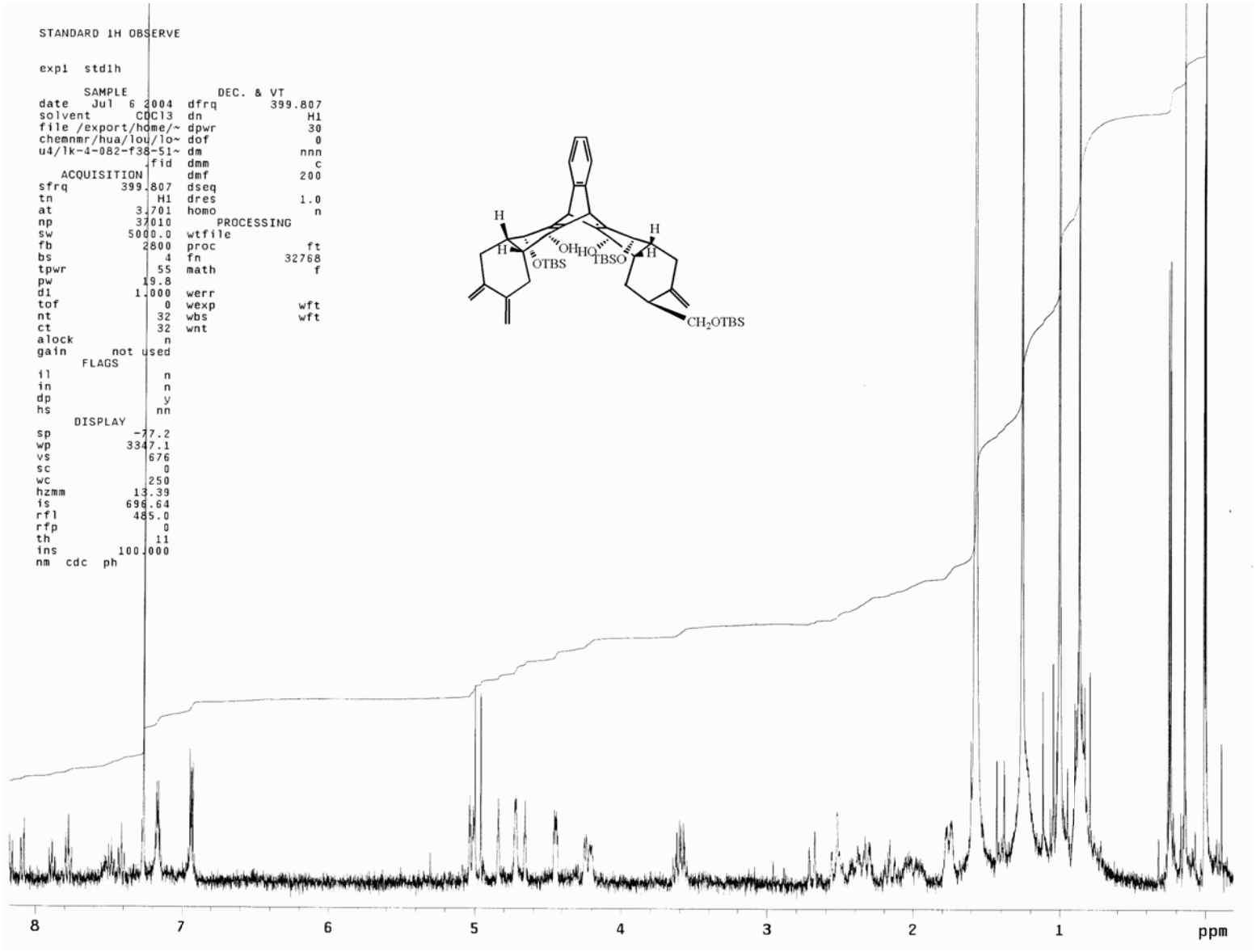


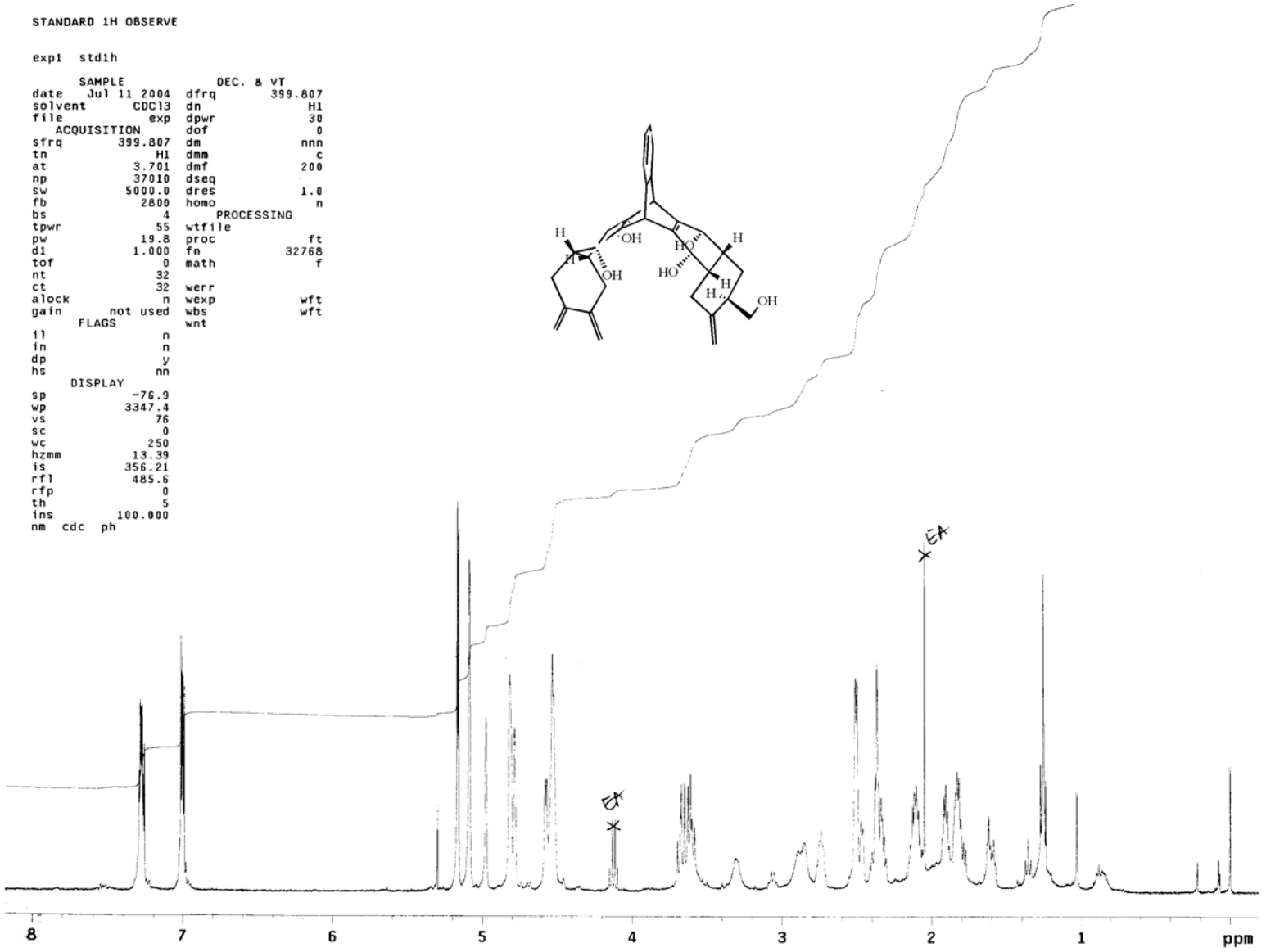


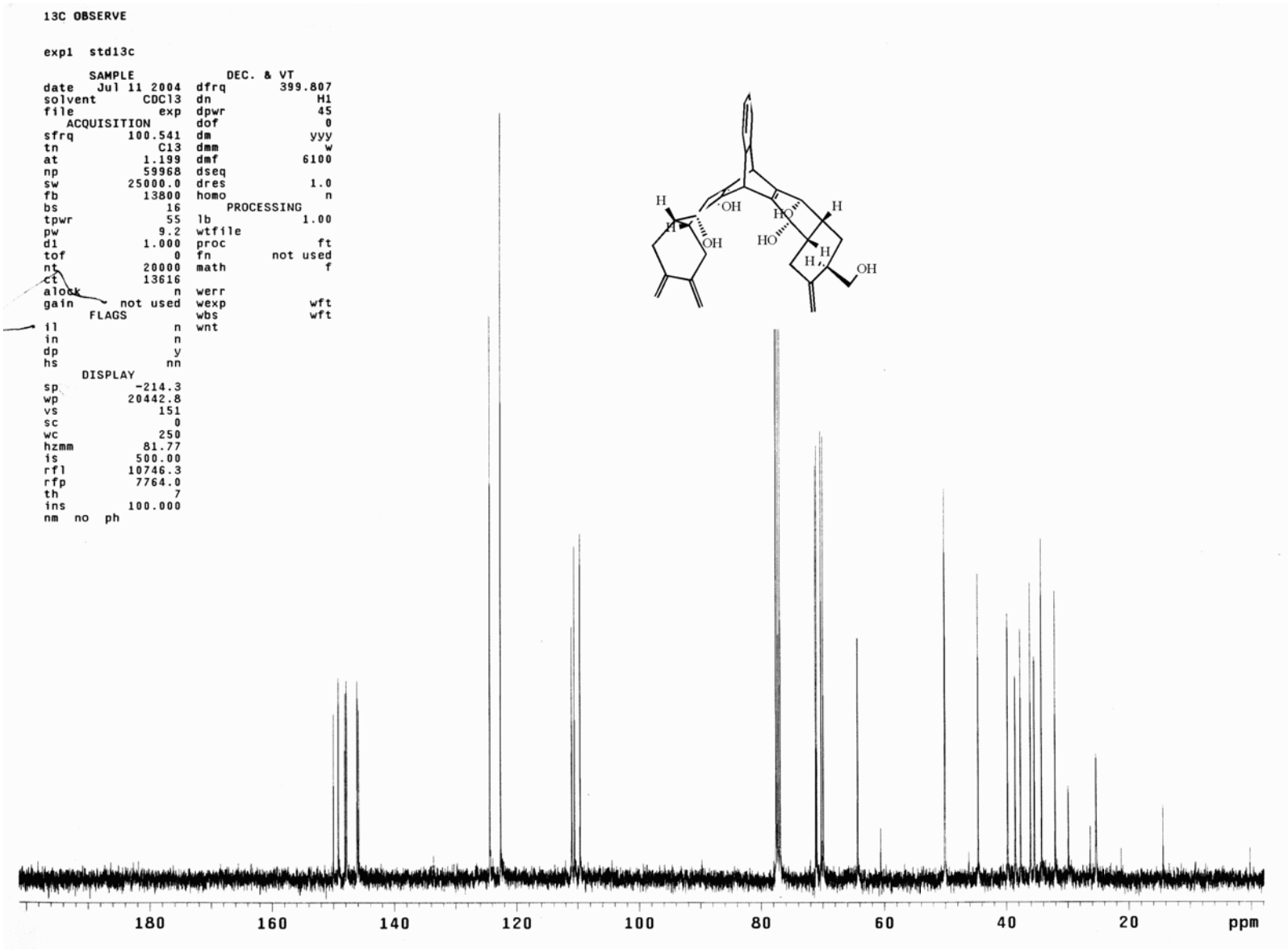

exp3 std1h
SAMPLE
date Jan 5 2004
solvent CDCl3
file exp
ACQUISITION
sfrq 399.814
tn H1
at 3.701
np 44416
sw 6000.6
fb 3400
bs 4
tpwr 55
pw 19.8
d1 1.000
tof 0
nt 128
ct 88
alock n
gain 30
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -80.6
wp 3678.1
vs 566
sc 0
wc 250
hzmm 14.71
is 28063.07
rfl 993.7
rfp 0
th 20
ins 100.000
nm cdc ph
DEC. & VT
dfrq 399.814
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn 32768
math f
werr
wexp
wbs
wnt
ppm
1
2
3
4
5
6
7
8
OTBS
OH
HO
TBSO
H
H
H
H
CH2OTBS
CH2SePhNO2-o
o-O2NPhSeH2C
o-O2NPhSeH2C

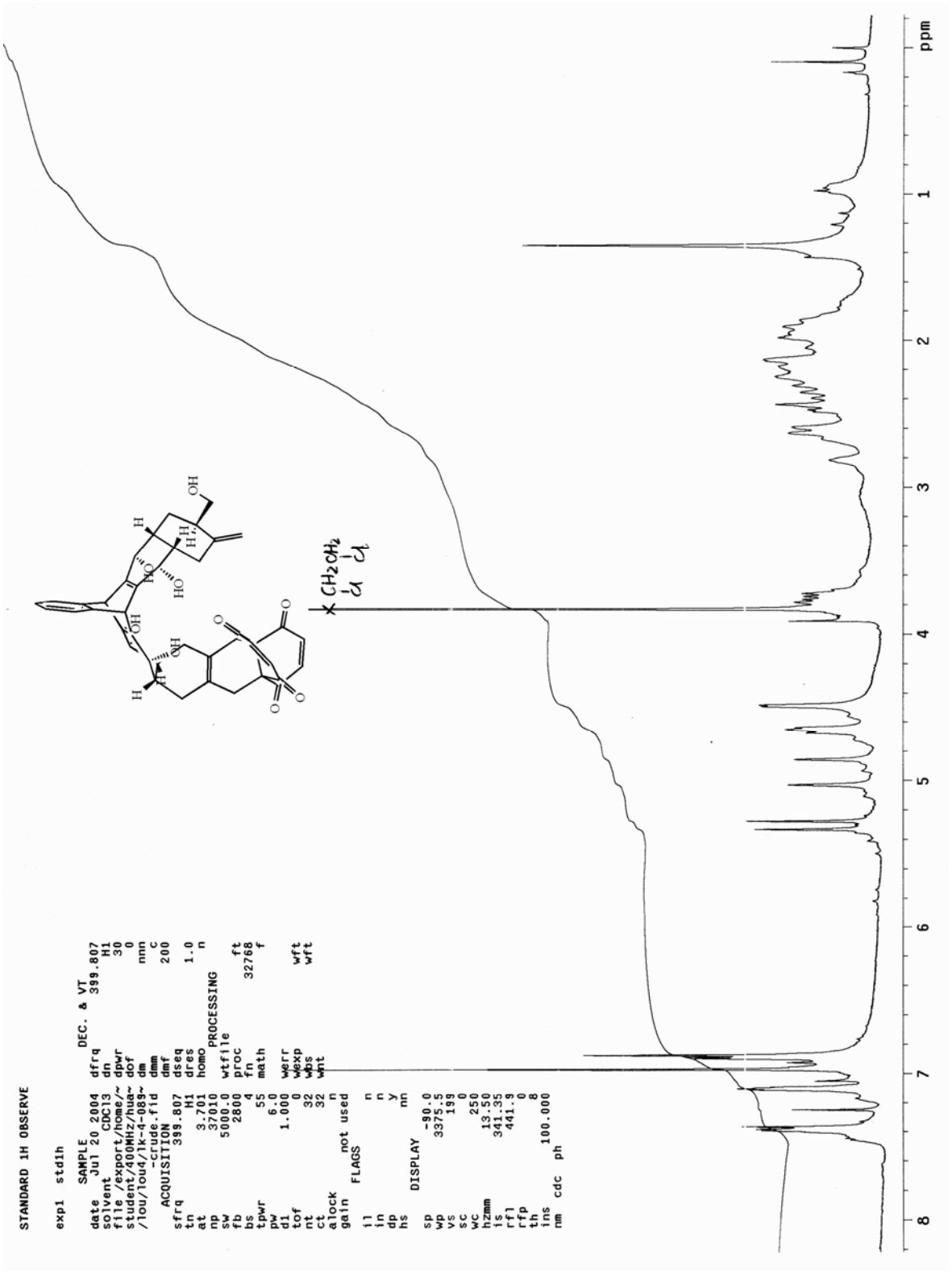

expl stdih
SAMPLE
date Jan 5 2004
solvent CDCl3
ACQUISITION
sfrq 399.814
tn H1
at 3.701
np 44416
sw 6000.6
fb 3400
bs 4
tpwr 55
pw 19.8
d1 1.000
tof 0
nt 128
ct 72
alock n
gain 30
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -70.0
wp 3742.2
vs 3768
sc 0
wc 250
hzmm 14.97
is 45820.83
rfl 993.7
rfp 0
th 6
ins 100.000
nm cdc ph
DEC. & VT
dfrq 399.814
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn 32768
math f
werr
wexp
wbs
wnt
OTBS
OH
TBSO
H
o-O2NPhSeH2C
o-O2NPhESH2C
CH2OTBS
CH2SePhNO2-o
ppm
9
8
7
6
5
4
3
2
1

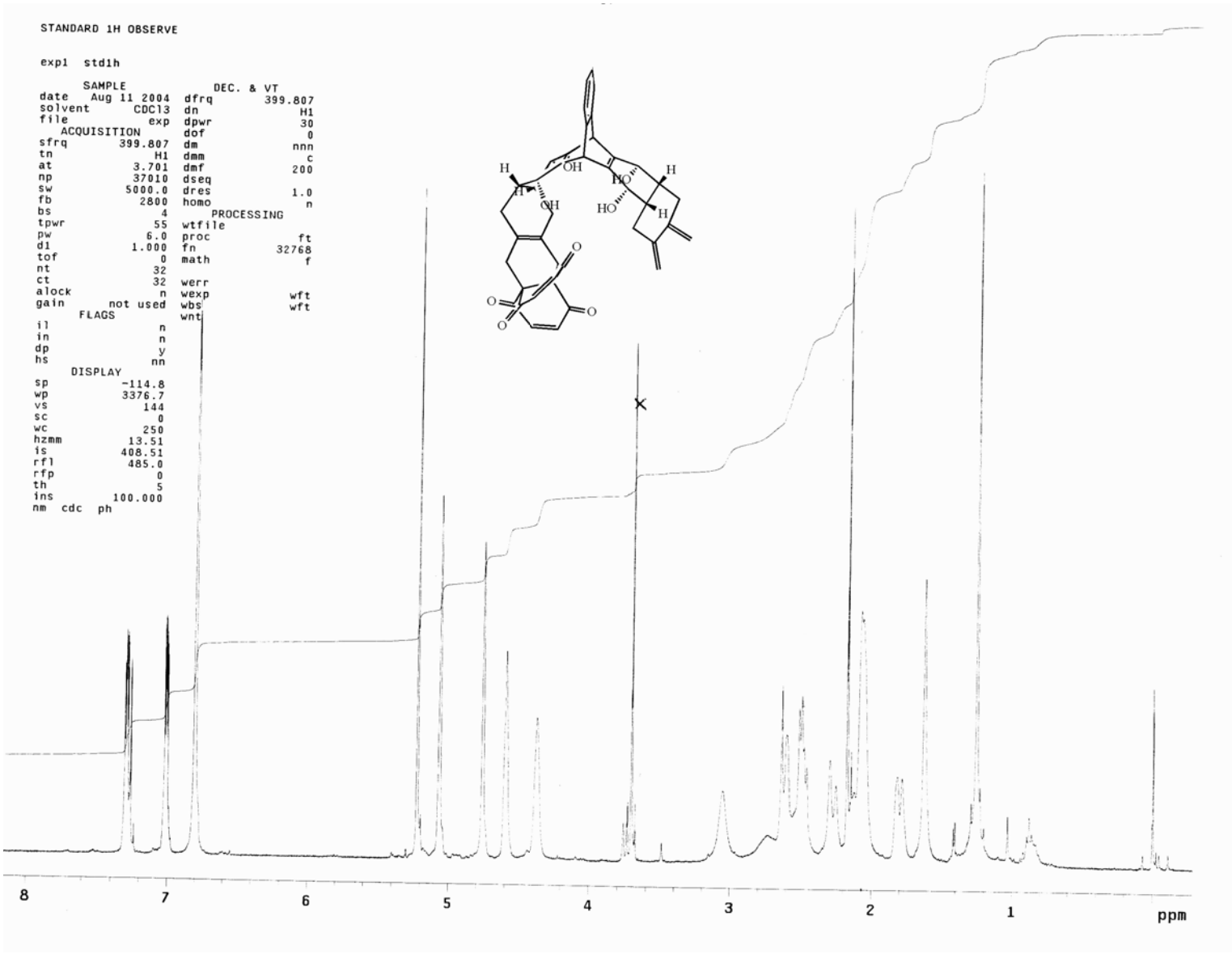

STANDARD 1H OBSERVE
exp1 std1h
SAMPLE
date Jul 6 2004
solvent CDCl3
file exp
ACQUISITION
sfrq 199.979
tn H1
at 1.994
np 11968
sw 3000.3
fb 1500
bs 16
pw 27.0
d1 1.000
tof 0
nt 32
ct 32
alock n
gain not used
FLAGS
il n
in n
dp y
DISPLAY
sp -87.5
wp 1932.2
vs 480
sc 0
wc 250
hzmm 7.73
is 5825.74
rfl 499.6
rfp 0
th 4
ins 100.000
nm cdc ph
DEC. & VT
dfrq 199.979
dn H1
dof 0
dm nnn
dmm c
dmf 200
PROCESSING
wtfile
proc ft
fn not used
werr
wexp wft
wbs wft
wnt
H
H
OTBS
OH
HO
TBSO
H
H
CH2OTBS
9
8
7
6
5
4
3
2
1
0 ppm

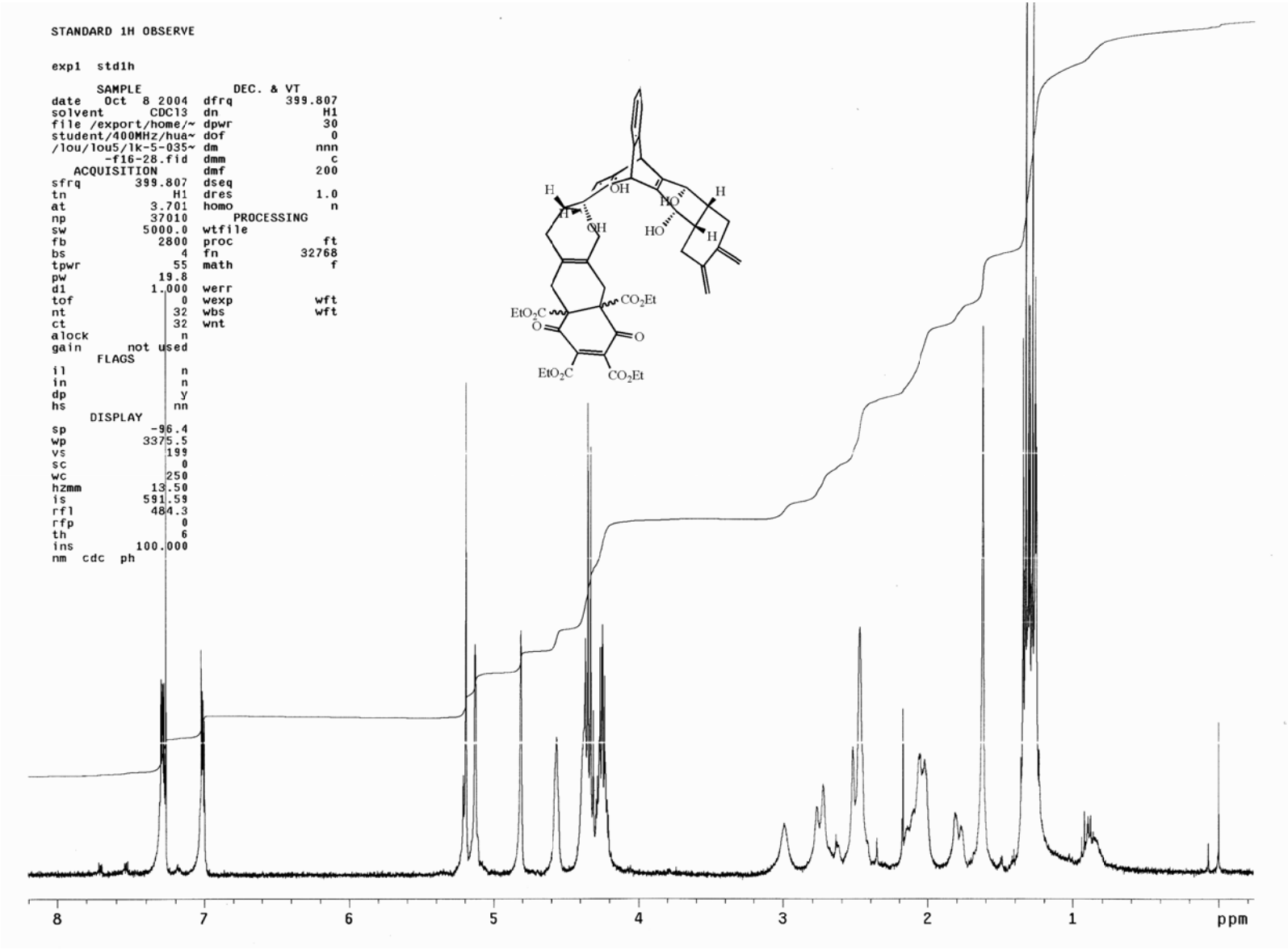

STANDARD 1H OBSERVE
exp1 std1h
SAMPLE
date Jul 6 2004
solvent CDCl3
file /export/home/~
chemnmr/hua/lou/lo~
u4/lk-4-082-f38-51~
.fid
ACQUISITION
sfrq 399.807
tn H1
at 3.701
np 37010
sw 5000.0
fb 2800
bs 4
tpwr 55
pw 19.8
d1 1.000
tof 0
nt 32
ct 32
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -77.2
wp 3347.1
vs 676
sc 0
wc 250
hzmm 13.39
is 696.64
rfl 485.0
rfp 0
th 11
ins 100.000
nm cdc ph
DEC. & VT
dfrq 399.807
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn 32768
math f
werr
wexp wft
wbs wft
wnt
H
H
OTBS
OH
HO
TBSO
H
CH2OTBS
8
7
6
5
4
3
2
1
ppm

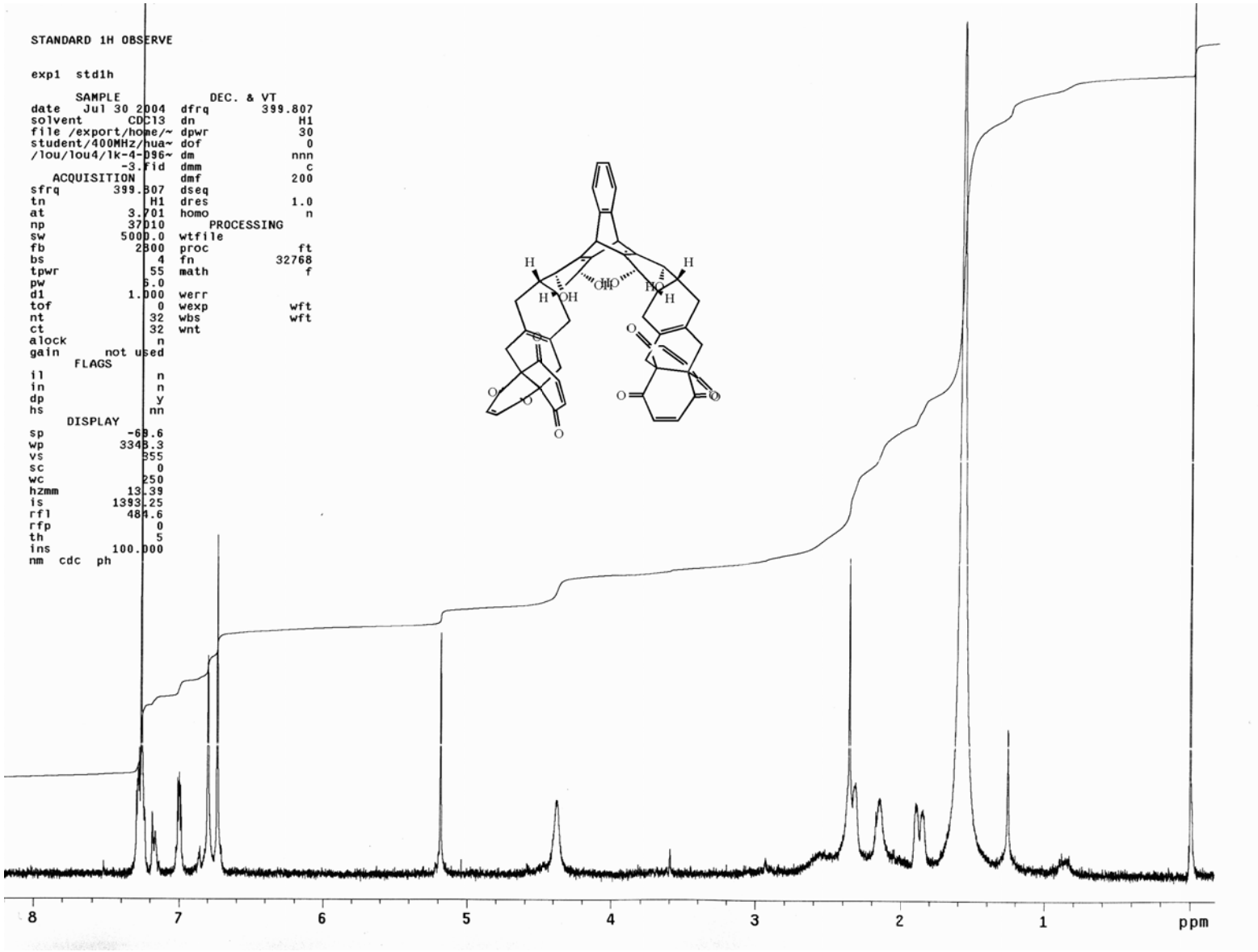

STANDARD 1H OBSERVE
expl stdlh
SAMPLE
date Jul 11 2004
solvent CDCl3
file exp
ACQUISITION
sfrq 399.807
tn H1
at 3.701
np 37010
sw 5000.0
fb 2800
bs 4
tpwr 55
pw 19.8
d1 1.000
tof 0
nt 32
ct 32
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -76.9
wp 3347.4
vs 76
sc 0
wc 250
hzmm 13.39
is 356.21
rfl 485.6
rfp 0
th 5
ins 100.000
nm cdc ph
DEC. & VT
dfrq 399.807
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn 32768
math f
werr
wexp wft
wbs wft
wnt
OH
HO
HO
OH
OH
EA
EA
8
7
6
5
4
3
2
1
ppm

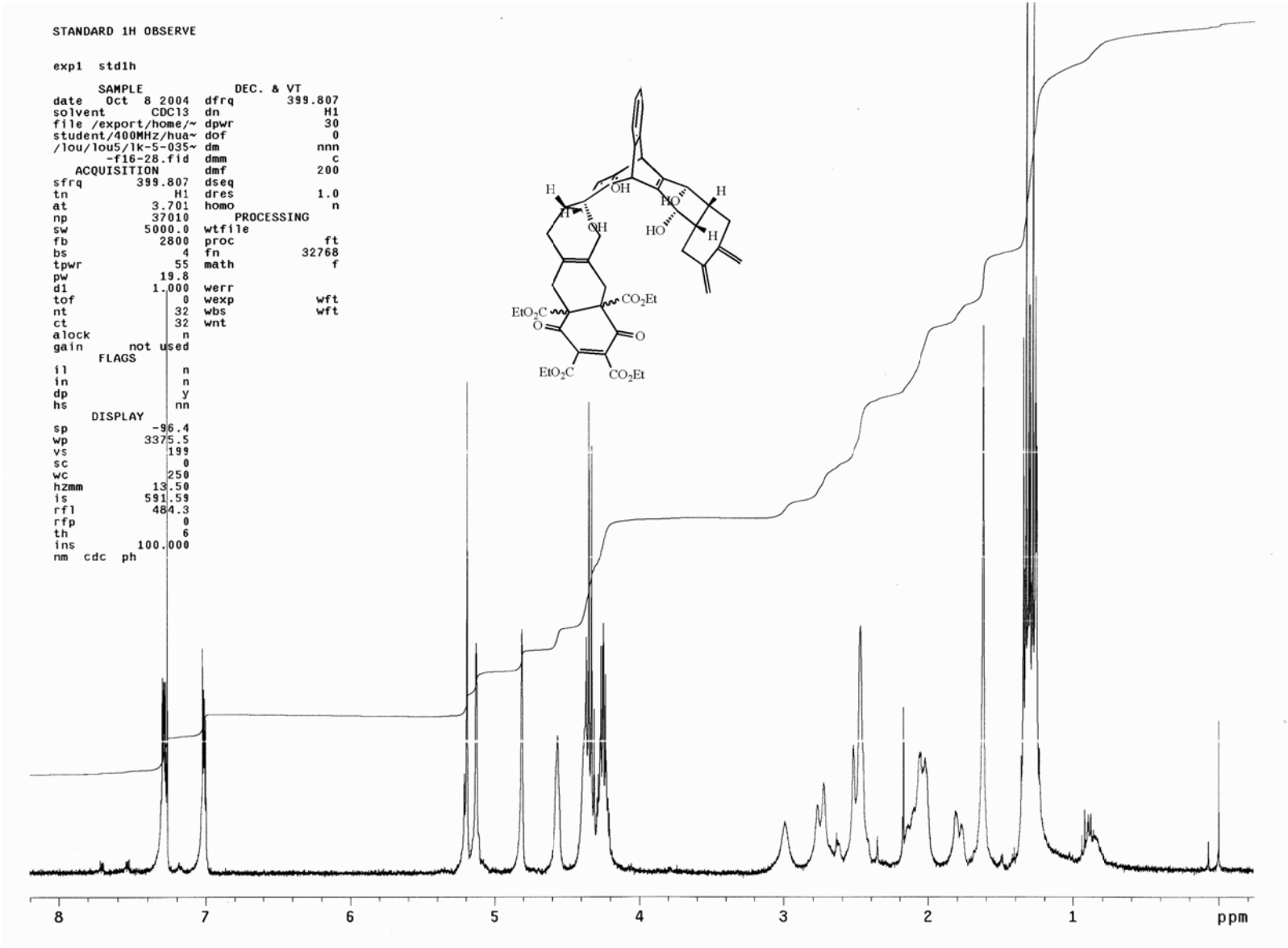

13C OBSERVE
exp1 std13c
SAMPLE
date Jul 11 2004
solvent CDCl3
file exp
ACQUISITION
sfrq 100.541
tn C13
at 1.199
np 59968
sw 25000.0
fb 13800
bs 16
tpwr 55
pw 9.2
d1 1.000
tof 0
nt 20000
ct 13616
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -214.3
wp 20442.8
vs 151
sc 0
wc 250
hzmm 81.77
is 500.00
rfl 10746.3
rfp 7764.0
th 7
ins 100.000
nm no ph
DEC. & VT
dfrq 399.807
dn H1
dpwr 45
dof 0
dm yyy
dmm w
dmf 6100
dseq
dres 1.0
homo n
PROCESSING
lb 1.00
wtfile
proc ft
fn not used
math f
werr
wexp wft
wbs wft
wnt
H
OH
H
OH
HO
HO
H
H
H
OH
180
160
140
120
100
80
60
40
20
ppm

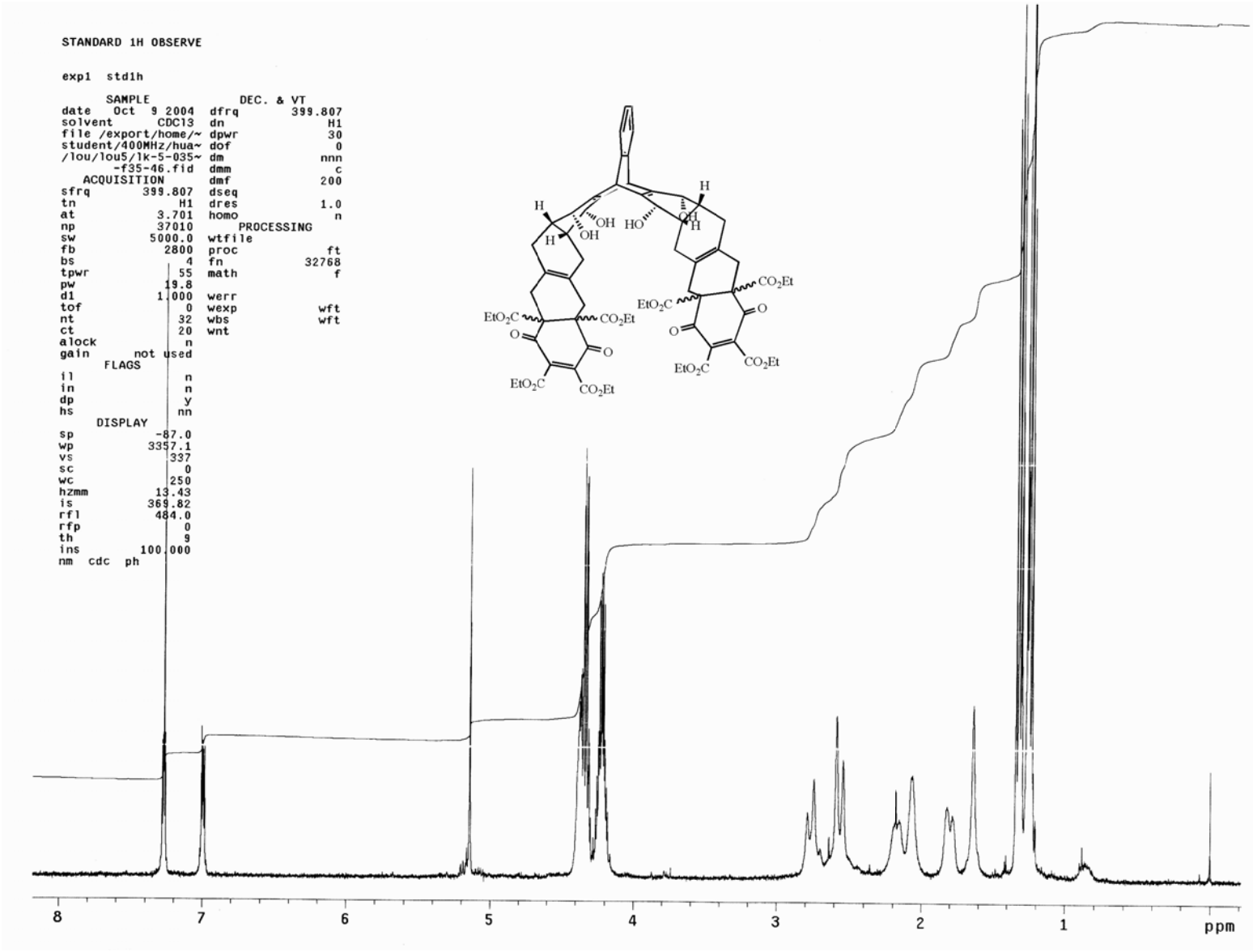

STANDARD 1H OBSERVE
exp1 std1h
SAMPLE
date Jul 20 2004
solvent CDCl3
file /export/home/~
stuident/400MHz/hua~
/lou/lou4/lk-4-089~
-crude.fid
ACQUISITION
sfrq 399.807
tn H1
at 3.701
np 37010
sw 5000.0
fb 2800
bs 4
tpwr 55
pw 6.0
d1 1.000
tof 0
nt 32
ct 32
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -90.0
wp 3375.5
vs 199
sc 0
wc 250
hzmm 13.50
is 341.35
rfl 441.9
rfp 0
th 8
ins 100.000
nm cdc ph
DEC. & VT
dfrq 399.807
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
homo 1.0
n
PROCESSING
wtfile
proc ft
fn 32768
math f
werr
wexp wft
wbs wft
wnt
ppm

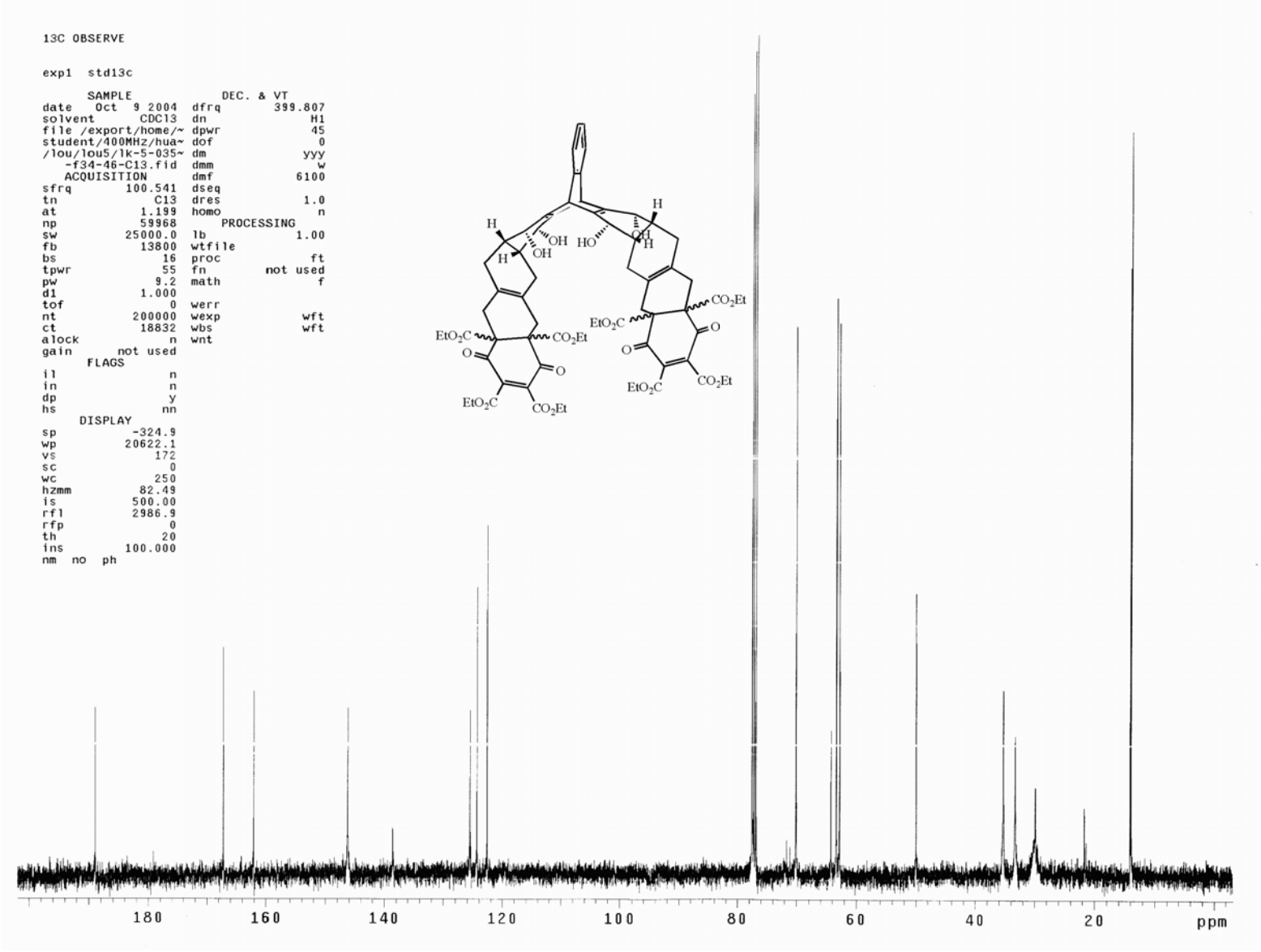

STANDARD 1H OBSERVE
expl std1h
SAMPLE
date Aug 11 2004
solvent CDCl3
file exp
ACQUISITION
sfrq 399.807
tn H1
at 3.701
np 37010
sw 5000.0
fb 2800
bs 4
tpwr 55
pw 6.0
d1 1.000
tof 0
nt 32
ct 32
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -114.8
wp 3376.7
vs 144
sc 0
wc 250
hzmm 13.51
is 408.51
rfl 485.0
rfp 0
th 5
ins 100.000
nm cdc ph
DEC. & VT
dfrq 399.807
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn 32768
math f
werr
wexp wft
wbs wft
wnt
8
7
6
5
4
3
2
1
ppm

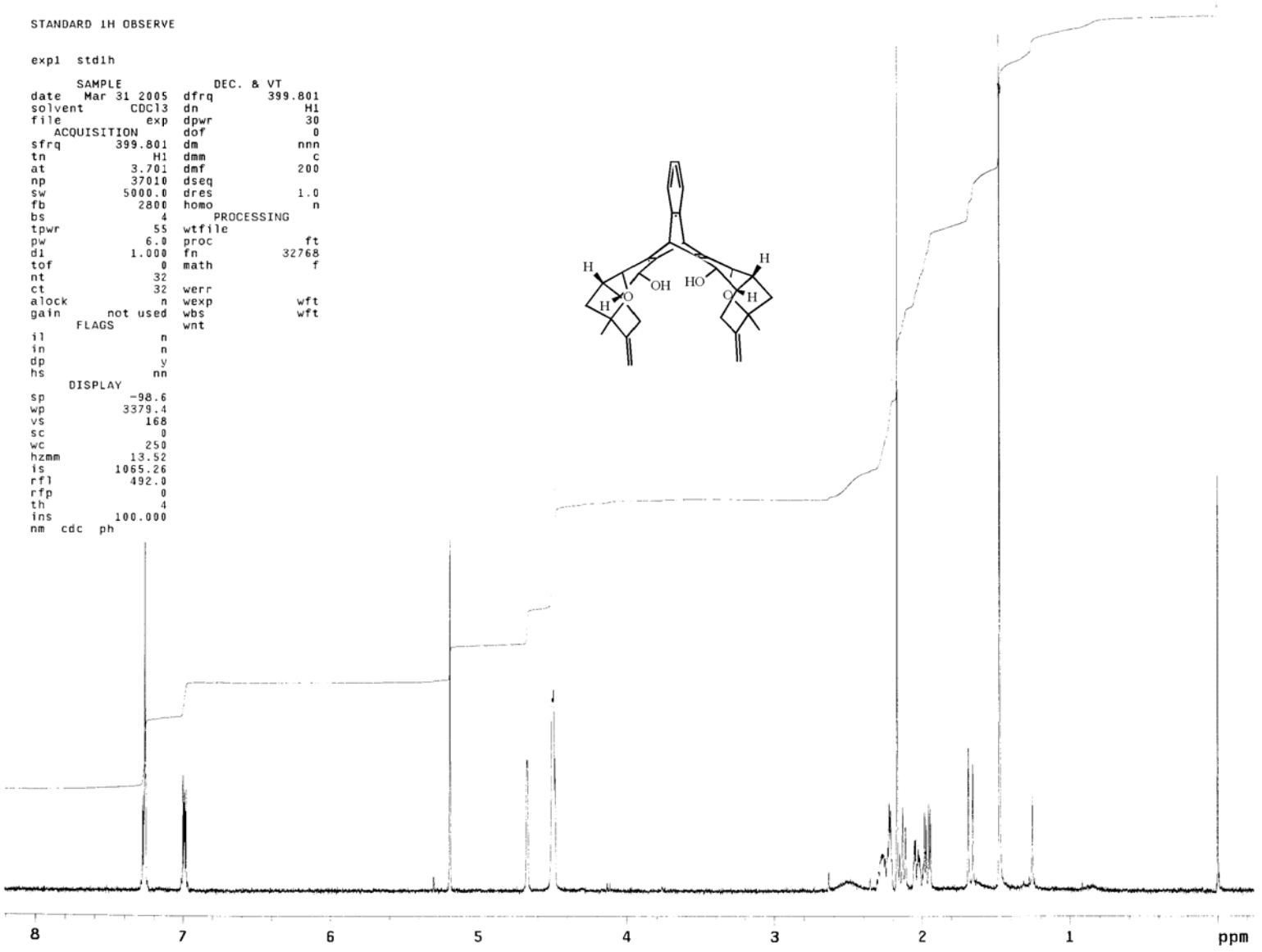

STANDARD 1H OBSERVE
exp1 std1h
SAMPLE
date Oct 8 2004
solvent CDCl3
file /export/home/~
student/400MHz/hua~
/lou/lou5/lk-5-035~
-f16-28.fid
ACQUISITION
sfrq 399.807
tn H1
at 3.701
np 37010
sw 5000.0
fb 2800
bs 4
tpwr 55
pw 19.8
d1 1.000
tof 0
nt 32
ct 32
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -96.4
wp 3375.5
vs 199
sc 0
wc 250
hzmm 13.50
is 591.59
rfl 484.3
rfp 0
th 6
ins 100.000
nm cdc ph
DEC. & VT
dfrq 399.807
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn 32768
math f
werr
wexp wft
wbs wft
wnt
8
7
6
5
4
3
2
1
ppm

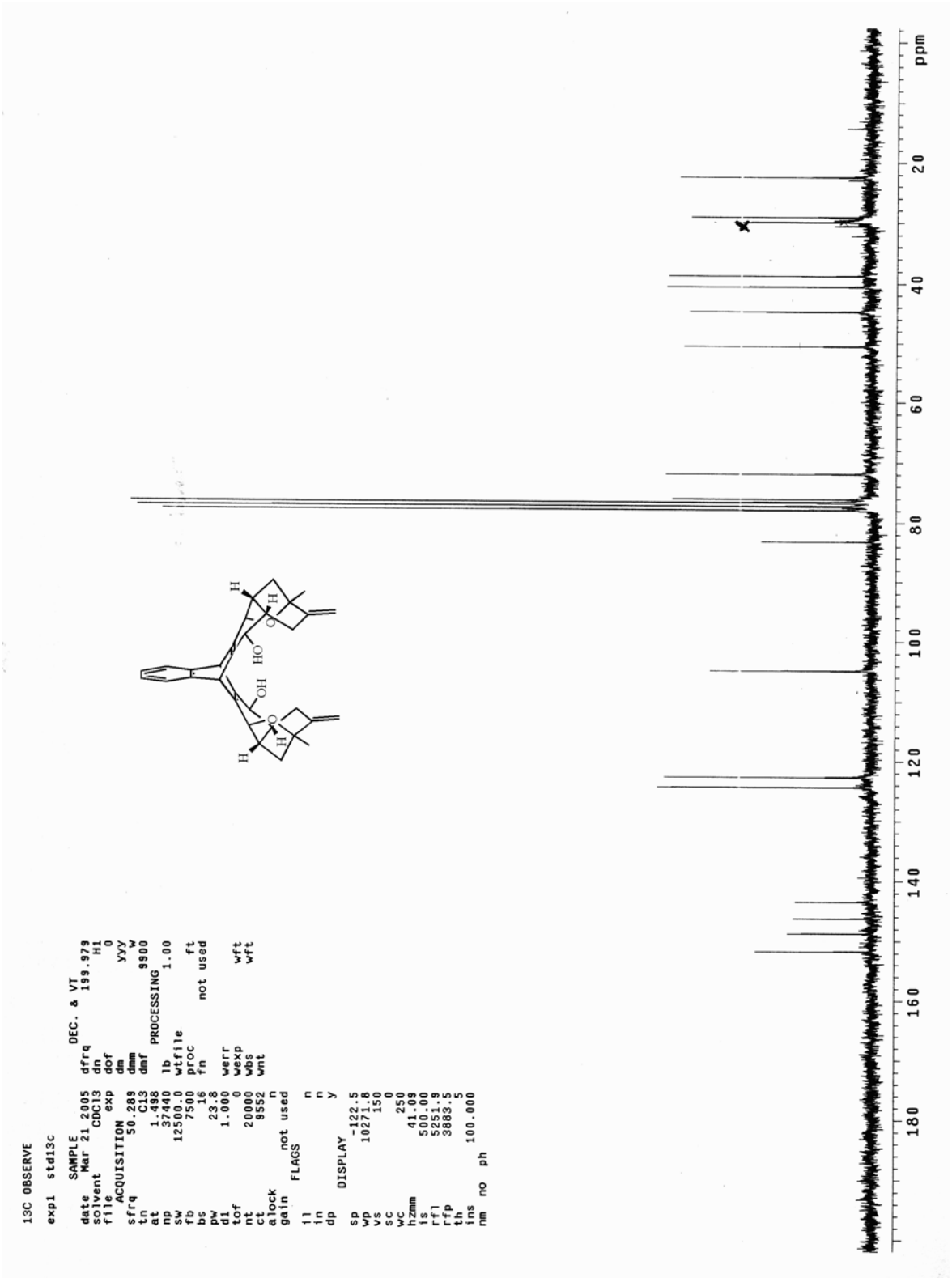

STANDARD 1H OBSERVE
exp1 std1h
SAMPLE
date Jul 30 2004
solvent CDCl3
file /export/home/~
student/400MHz/hua~
/lou/lou4/lk-4-096~
-3.fid
ACQUISITION
sfrq 399.807
tn H1
at 3.701
np 37010
sw 5000.0
fb 2800
bs 4
tpwr 55
pw 6.0
d1 1.000
tof 0
nt 32
ct 32
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -68.6
wp 3348.3
vs 355
sc 0
wc 250
hzmm 13.39
is 1393.25
rfl 484.6
rfp 0
th 5
ins 100.000
nm cdc ph
DEC. & VT
dfrq 399.807
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn 32768
math f
werr
wexp wft
wbs wft
wnt
8
7
6
5
4
3
2
1
ppm

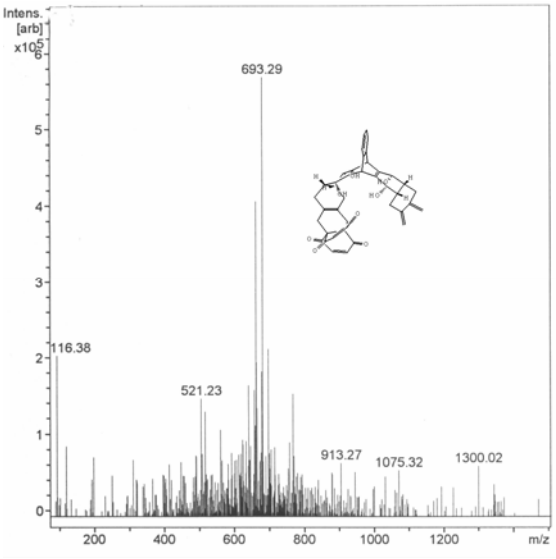

STANDARD 1H OBSERVE
exp1 std1h
SAMPLE
date Oct 8 2004
solvent CDCl3
file /export/home/~
student/400MHz/hua~
/lou/lou5/lk-5-035~
-f16-28.fid
ACQUISITION
sfrq 399.807
tn H1
at 3.701
np 37010
sw 5000.0
fb 2800
bs 4
tpwr 55
pw 19.8
d1 1.000
tof 0
nt 32
ct 32
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -96.4
wp 3375.5
vs 199
sc 0
wc 250
hzmm 13.50
is 591.59
rfl 484.3
rfp 0
th 6
ins 100.000
nm cdc ph
DEC. & VT
dfrq 399.807
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn 32768
math f
werr
wexp wft
wbs wft
wnt
8
7
6
5
4
3
2
1
ppm

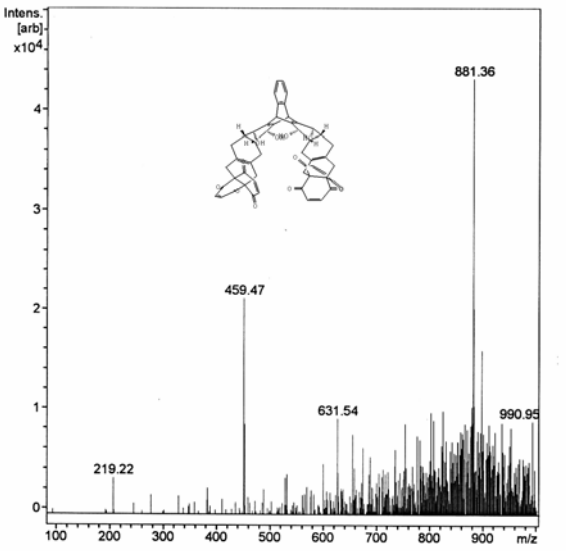

STANDARD 1H OBSERVE
exp1 std1h
SAMPLE
date Oct 9 2004
solvent CDCl3
file /export/home/~
student/400MHz/hua~
/lou/lou5/lk-5-035~
-f35-46.fid
ACQUISITION
sfrq 399.807
tn H1
at 3.701
np 37010
sw 5000.0
fb 2800
bs 4
tpwr 55
pw 19.8
d1 1.000
tof 0
nt 32
ct 20
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -87.0
wp 3357.1
vs 337
sc 0
wc 250
hzmm 13.43
is 369.82
rfl 484.0
rfp 0
th 9
ins 100.000
nm cdc ph
DEC. & VT
dfrq 399.807
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn 32768
math f
werr
wexp wft
wbs wft
wnt
8
7
6
5
4
3
2
1
ppm

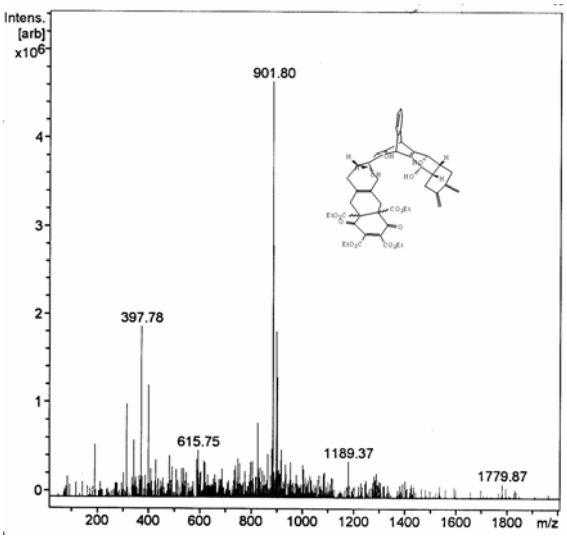

13C OBSERVE
exp1 std13c
SAMPLE
date Oct 9 2004
solvent CDCl3
file /export/home/~
student/400MHz/hua~
/lou/lou5/lk-5-035~
-f34-46-C13.fid
ACQUISITION
sfrq 100.541
tn C13
at 1.199
np 59968
sw 25000.0
fb 13800
bs 16
tpwr 55
pw 9.2
d1 1.000
tof 0
nt 200000
ct 18832
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -324.9
wp 20622.1
vs 172
sc 0
wc 250
hzmm 82.49
is 500.00
rfl 2986.9
rfp 0
th 20
ins 100.000
nm no ph
DEC. & VT
dfrq 399.807
dn H1
dpwr 45
dof 0
dm yyy
dmm w
dmf 6100
dseq
dres 1.0
homo n
PROCESSING
lb 1.00
wtfile
proc ft
fn not used
math f
werr
wexp wft
wbs wft
wnt
180
160
140
120
100
80
60
40
20
ppm

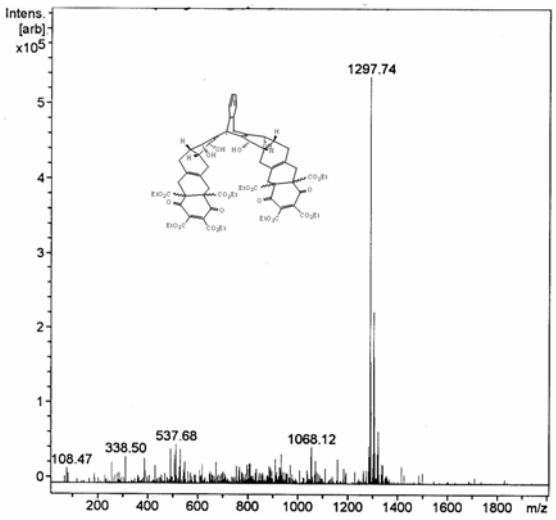

STANDARD 1H OBSERVE
expl std1h
SAMPLE
date Mar 31 2005
solvent CDCl3
file exp
ACQUISITION
sfrq 399.801
tn H1
at 3.701
np 37010
sw 5000.0
fb 2800
bs 4
tpwr 55
pw 6.0
d1 1.000
tof 0
nt 32
ct 32
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -98.6
wp 3379.4
vs 168
sc 0
wc 250
hzmm 13.52
is 1065.26
rfl 492.0
rfp 0
th 4
ins 100.000
nm cdc ph
DEC. & VT
dfrq 399.801
dn H1
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn 32768
math f
werr
wexp wft
wbs wft
wnt
H
OH
HO
H
O
O
H
H
8
7
6
5
4
3
2
1
ppm

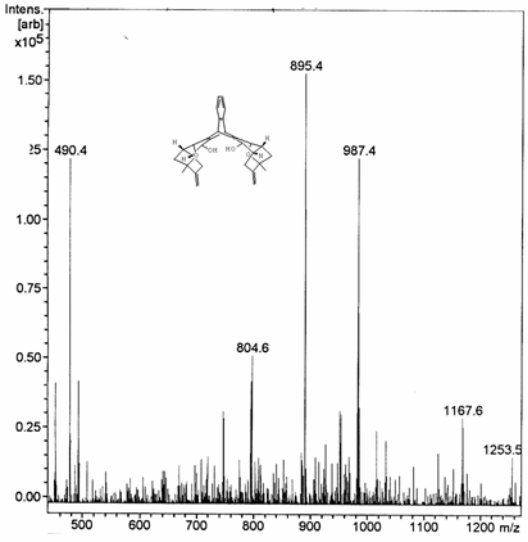

13C OBSERVE
exp1 std13c
SAMPLE
date Mar 21 2005
solvent CDCl3
file exp
ACQUISITION
sfrq 50.289
tn C13
at 1.498
np 37440
sw 12500.0
fb 7500
bs 16
pw 23.8
d1 1.000
tof 0
nt 20000
ct 9552
alock n
gain not used
FLAGS
il n
in n
dp y
DISPLAY
sp -122.5
wp 10271.8
vs 150
sc 0
wc 250
hzmm 41.09
is 500.00
rfl 5251.9
rfp 3883.5
th 5
ins 100.000
nm no ph
DEC. & VT
dfrq 199.979
dn H1
dof 0
dm yyy
dmm w
dmf 9900
PROCESSING
lb 1.00
wtfile
proc ft
fn not used
werr
wexp wft
wbs wft
wnt
OH
HO
H
O
ppm
180
160
140
120
100
80
60
40
20


Intens.
[arb]
x10^5
693.29
116.38
521.23
913.27
1075.32
1300.02
m/z

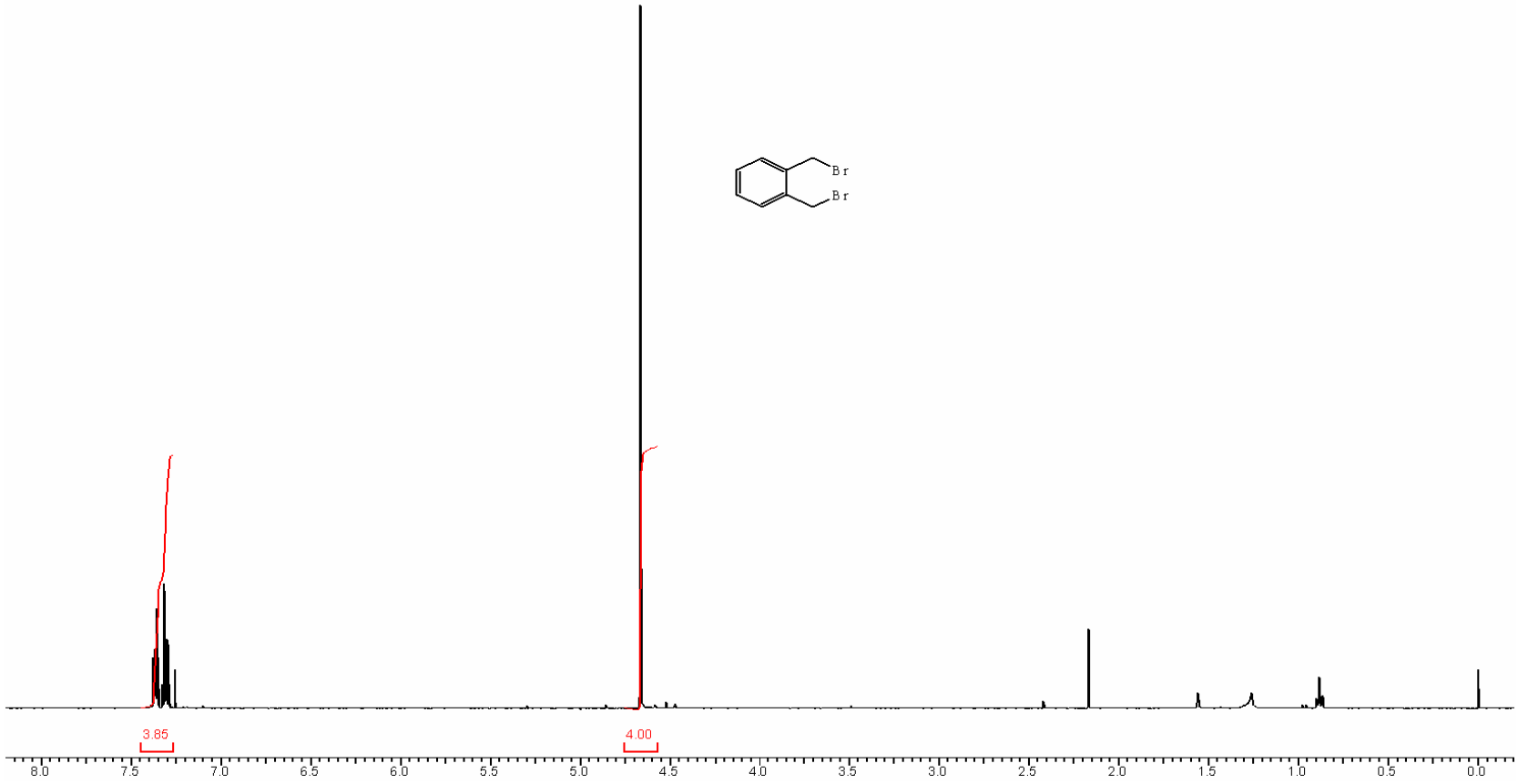

Intens.
[arb]
x10^4
881.36
459.47
631.54
990.95
219.22
m/z

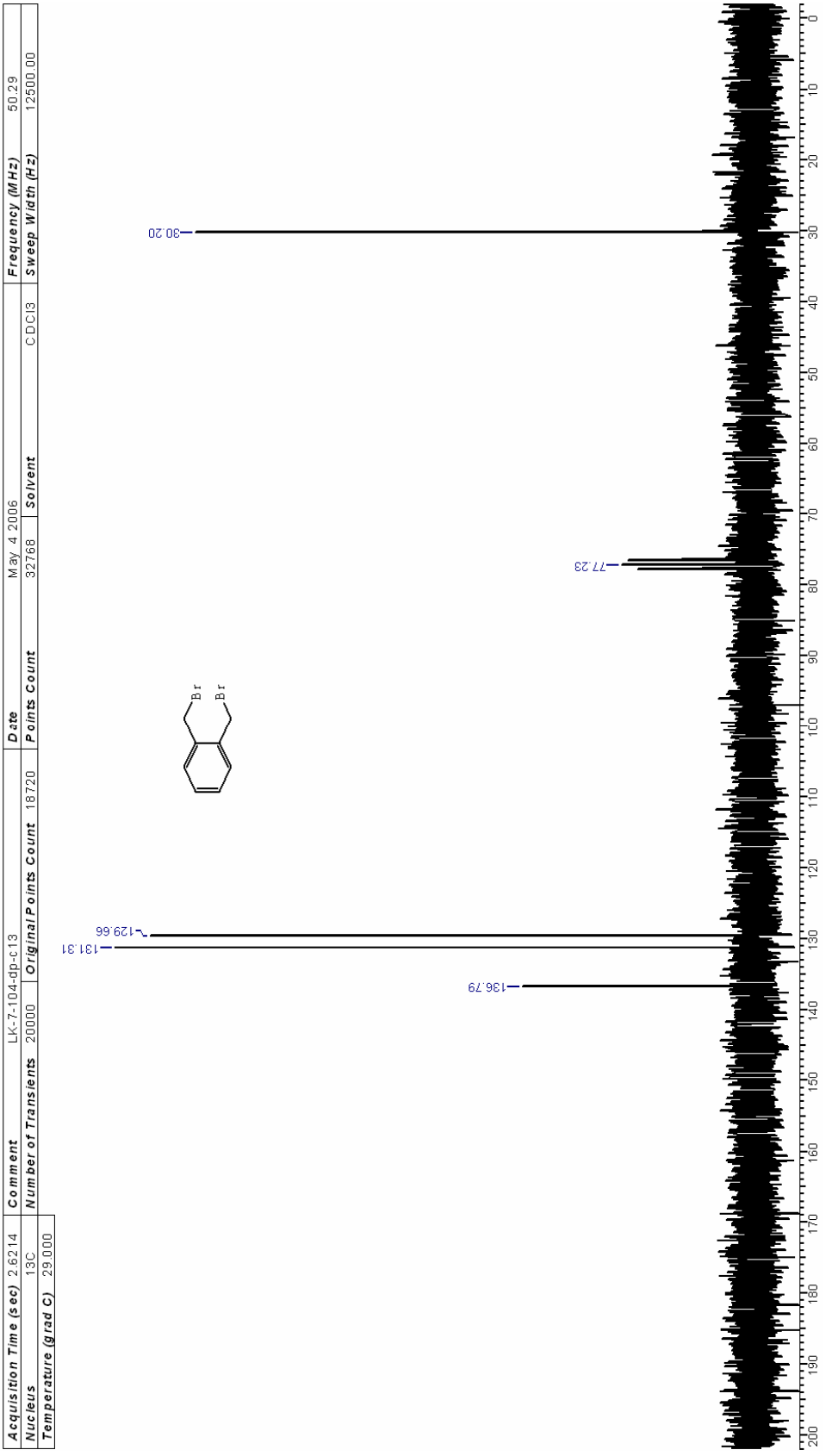

Intens.
[arb]
x10^6
901.80
397.78
615.75
1189.37
1779.87
m/z


Intens.
[arb]
x10^5
1297.74
108.47
338.50
537.68
1068.12
m/z

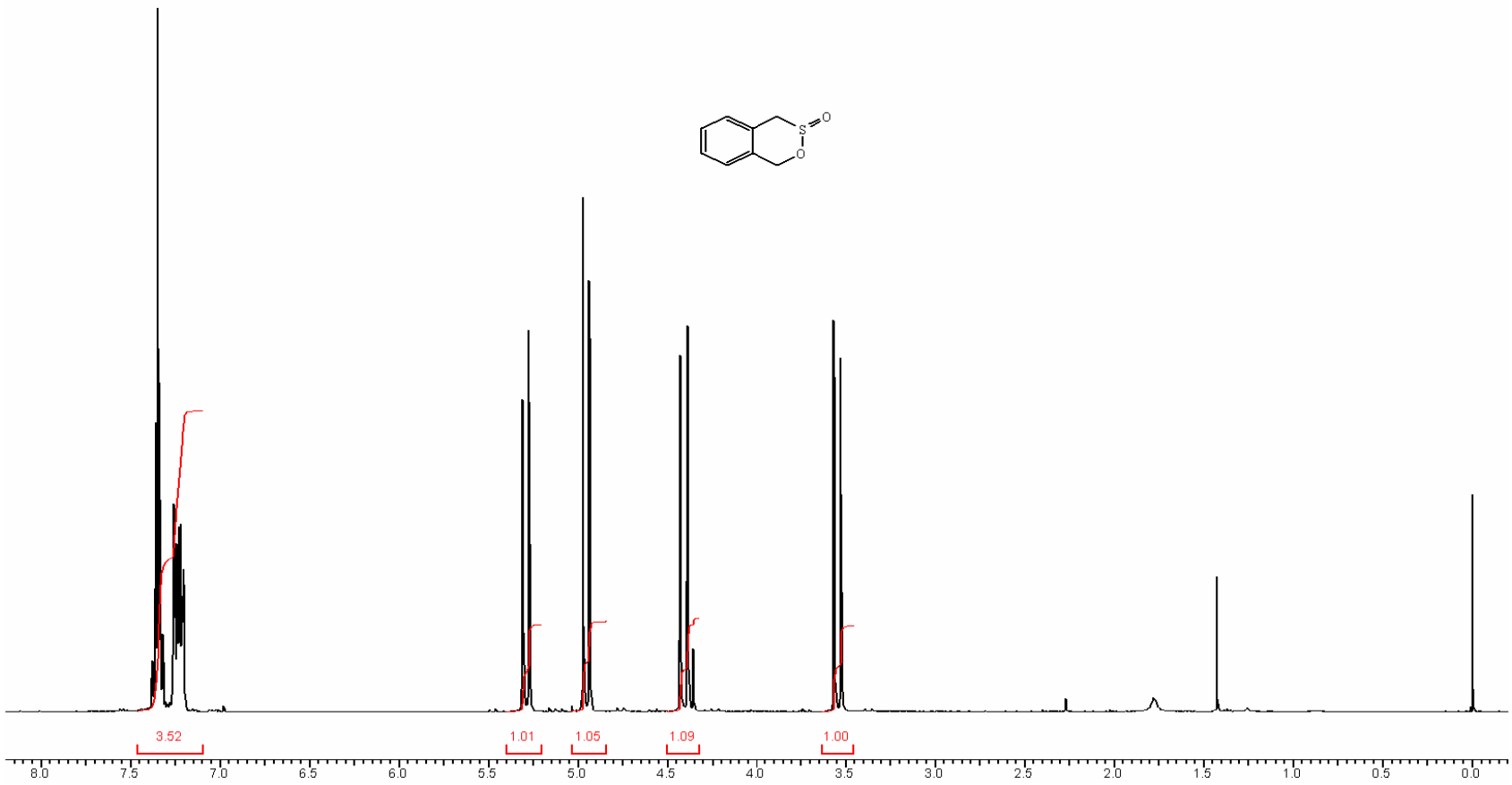

Intens.
[arb]
x10^5
895.4
490.4
987.4
804.6
1167.6
1253.5
m/z

Acquisition Time (sec)	6.5536	***Comment***	LK-7-104-dp		***Date***	Nov 27 2005		***Frequency (MHz)***	399.79
Nucleus	1H	***Number of Transients***	128	***Original Points Count*** 18505	***Points Count***	32768	***Solvent*** CDCl3	***Sweep Width (Hz)***	5000.00
Temperature (grad C)	29.000								

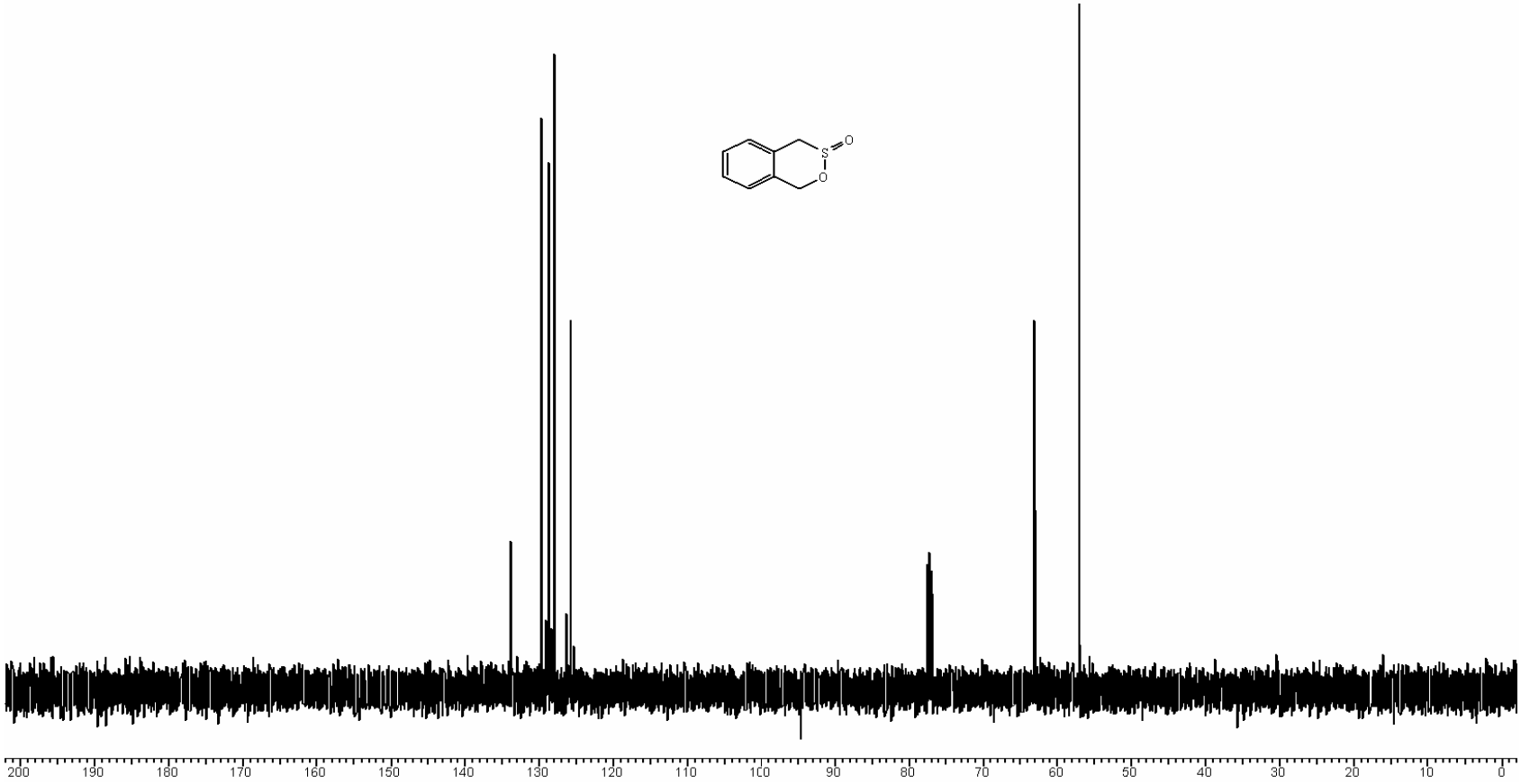


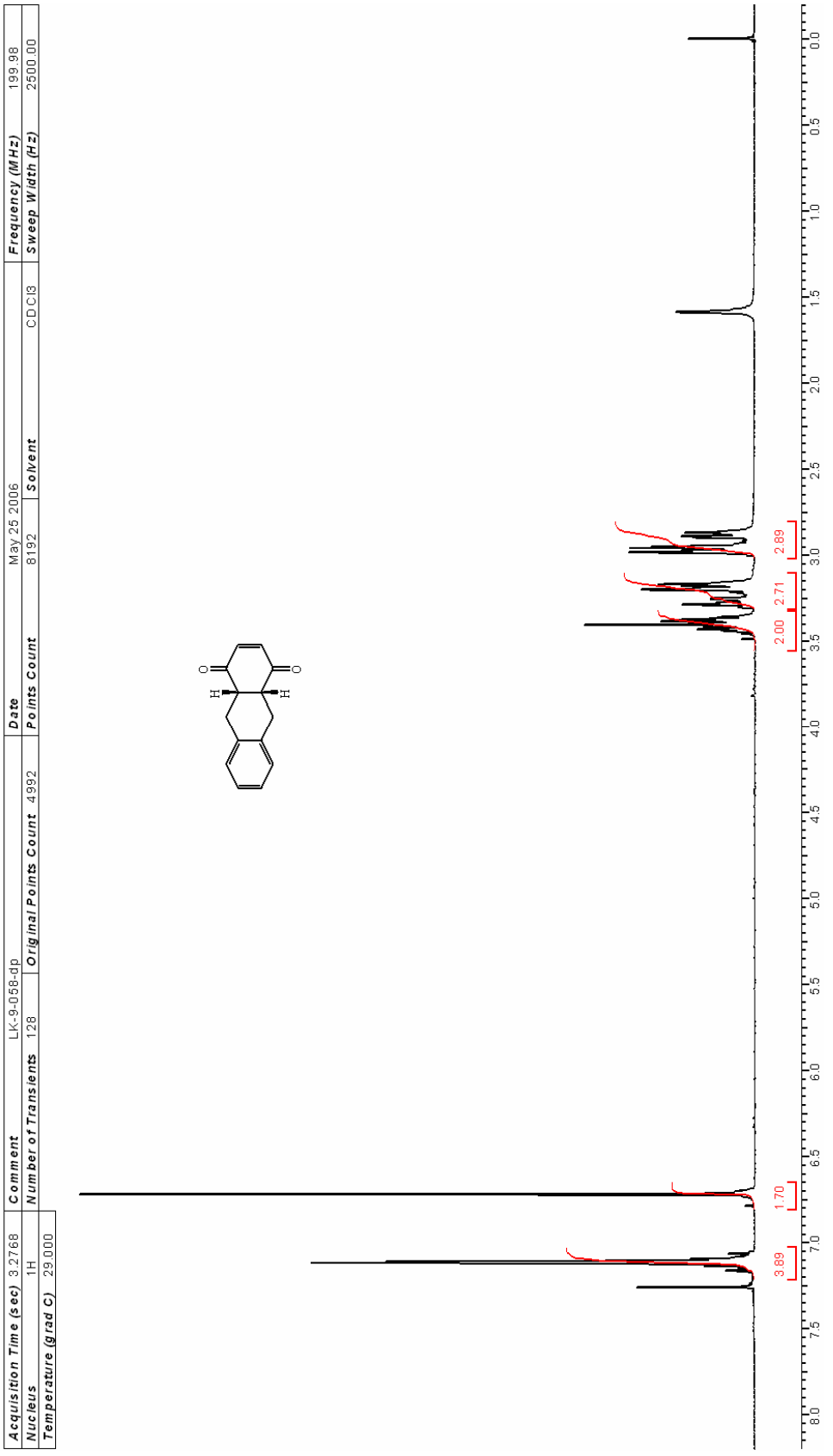

Acquisition Time (sec) 2.6214
Comment LK-7-104-dp-c13
Date May 4 2006
Frequency (MHz) 50.29
Nucleus 13C
Number of Transients 20000
Original Points Count 18720
Points Count 32768
Solvent CDCl3
Sweep Width (Hz) 12500.00
Temperature (grad C) 29.000
30.20
77.23
129.66
131.31
136.79
Br
Br

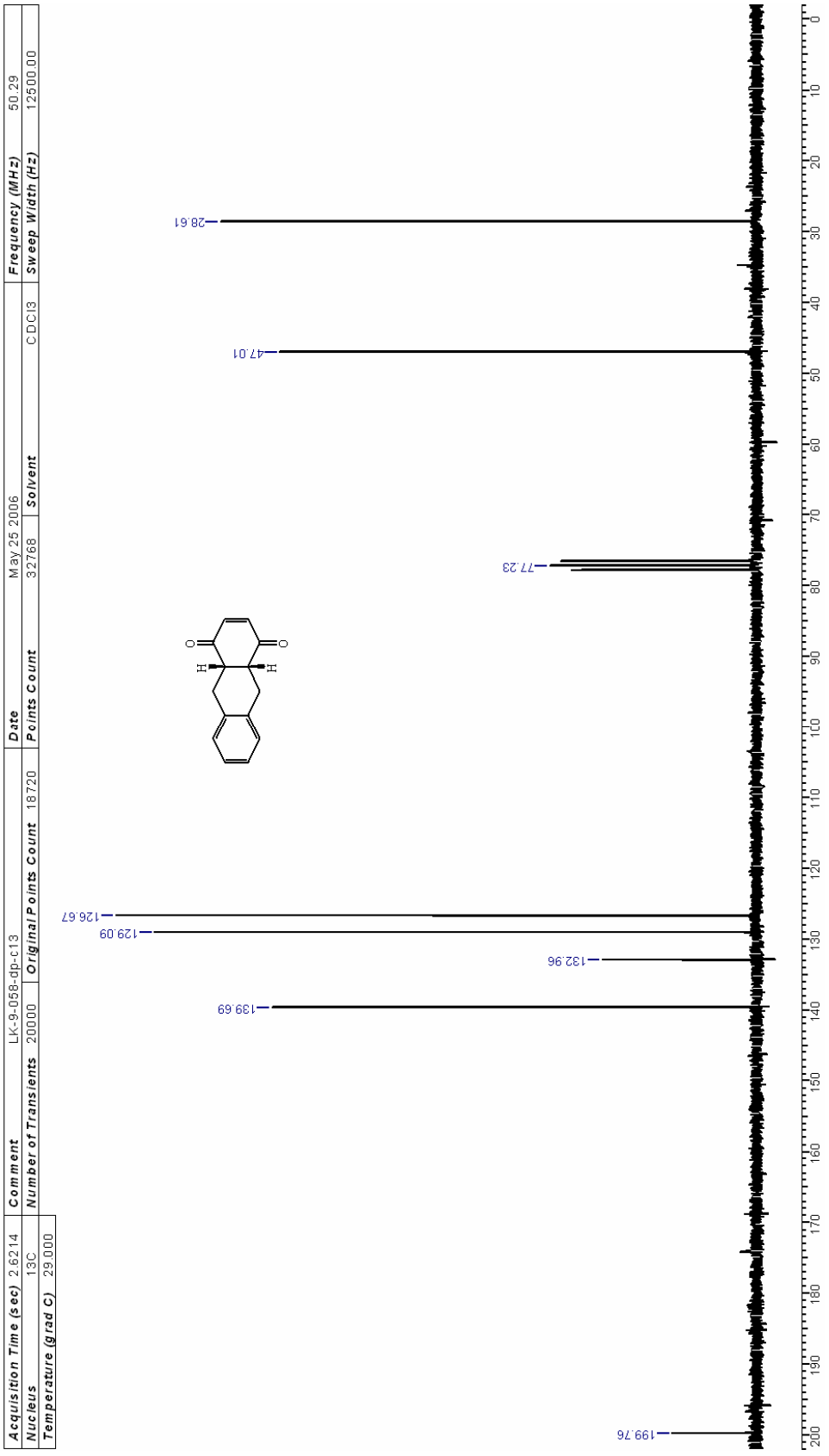
Acquisition Time (sec)	6.5536	***Comment***	LK-9-091-dp		***Date***	Nov 14 2005		***Frequency (MHz)***	399.79
Nucleus	1H	***Number of Transients***	128	***Original Points Count*** 18505	***Points Count***	32768	***Solvent*** CDCl3	***Sweep Width (Hz)***	5000.00
Temperature (grad C)	29.000								

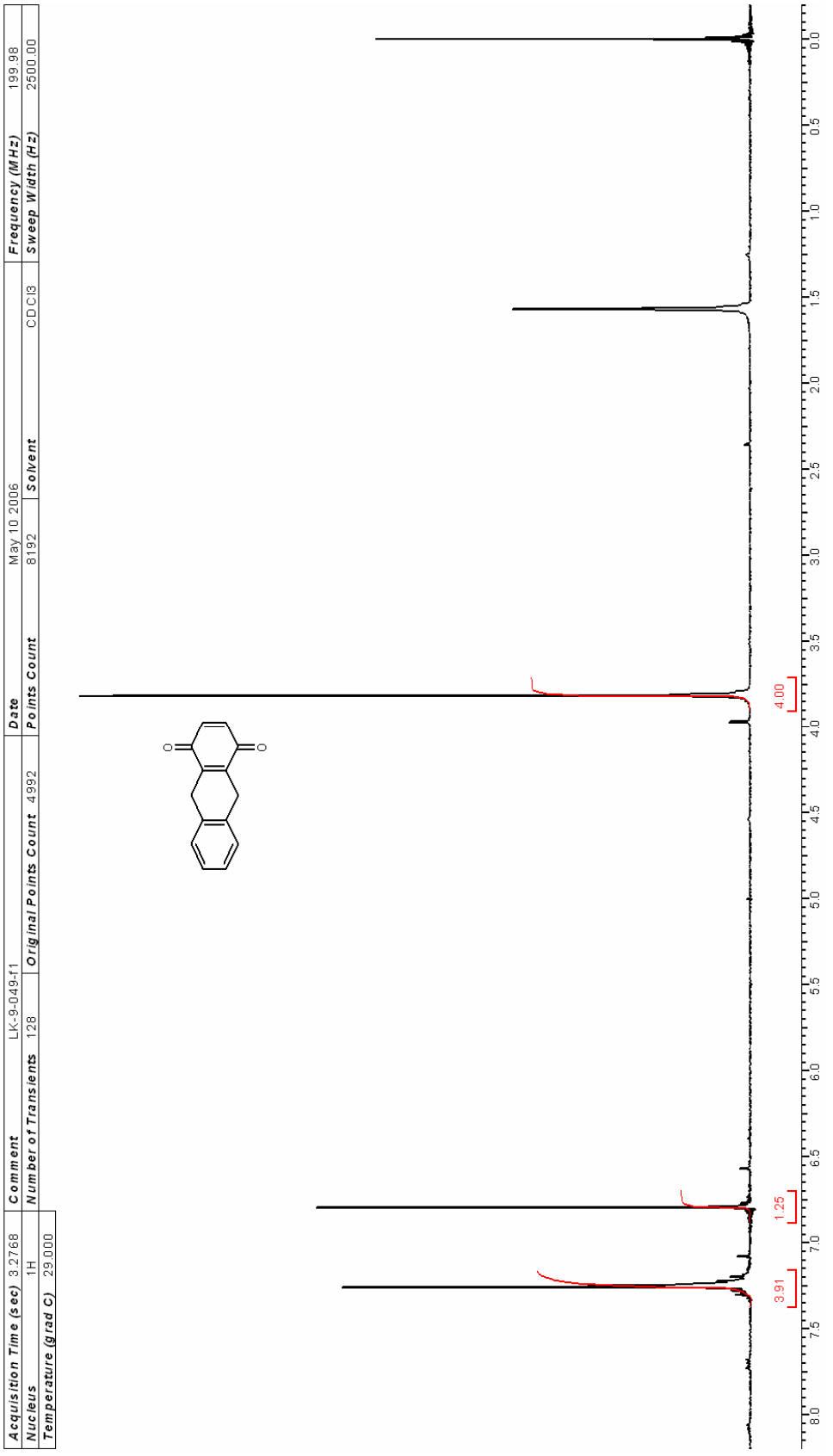


Acquisition Time (sec)	1.3107	***Comment***	LK-7-091-dp-c13		***Date***	Nov 15 2005		***Frequency (MHz)***	100.54
Nucleus	13C	***Number of Transients***	20000	***Original Points Count*** 29984	***Points Count***	32768	***Solvent*** CDCl3	***Sweep Width (Hz)***	25000.00
Temperature (grad C)	29.000								

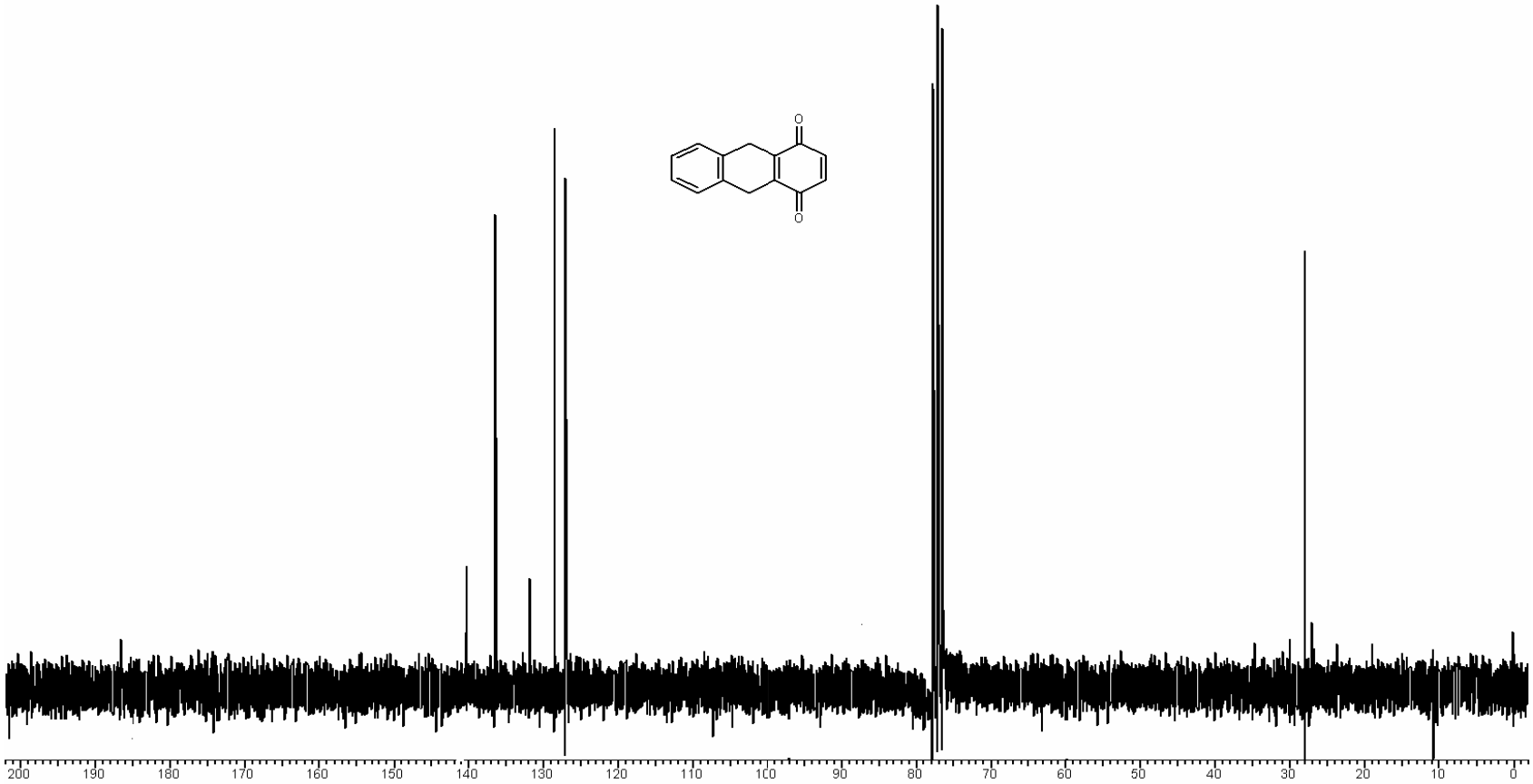



Acquisition Time (sec) 3.2768
Comment LK-9-058-dp
Date May 25 2006
Frequency (MHz) 199.98
Nucleus 1H
Number of Transients 128
Original Points Count 4992
Points Count 8192
Solvent CDCl3
Sweep Width (Hz) 2500.00
Temperature (grad C) 29.000
O
H
H
O
3.89
1.70
2.00
2.71
2.89
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

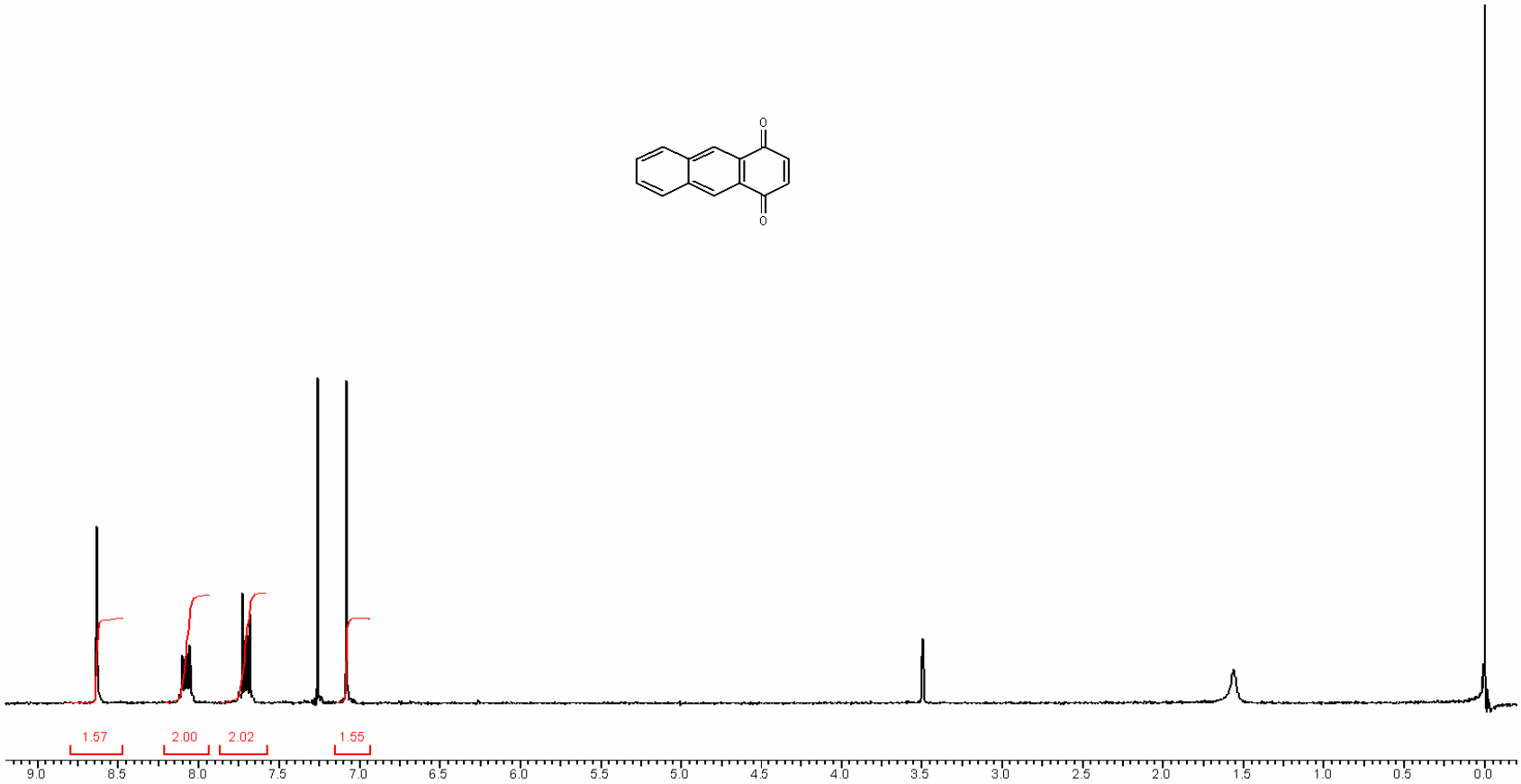

Acquisition Time (sec) 2.6214
Comment LK-9-058-dp-c13
Date May 25 2006
Frequency (MHz) 50.29
Nucleus 13C
Number of Transients 20000
Original Points Count 18720
Points Count 32768
Solvent CDCl3
Sweep Width (Hz) 12500.00
Temperature (grad C) 29.000
199.76
139.69
132.96
129.09
126.67
77.23
47.01
28.61

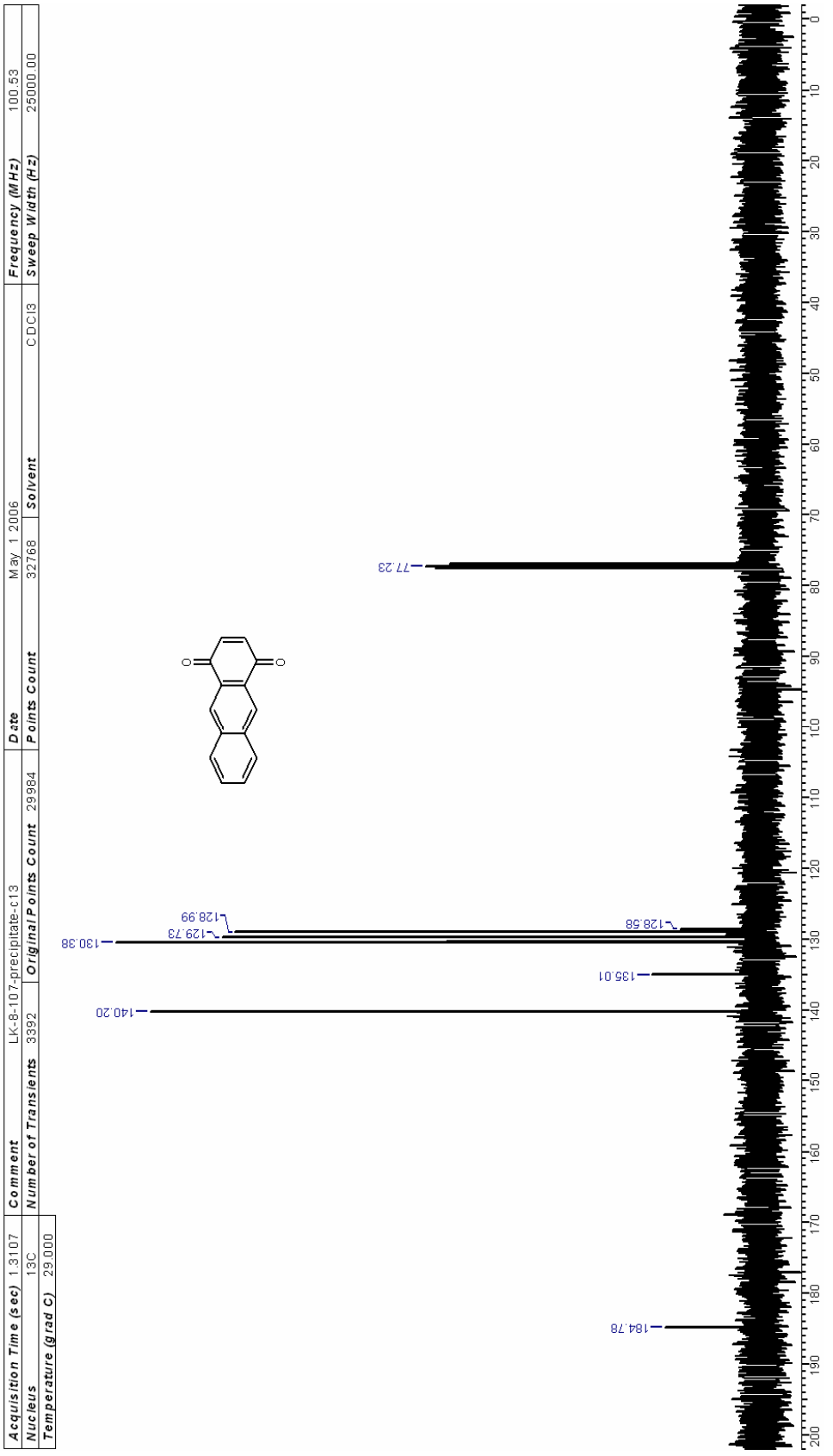

Acquisition Time (sec) 3.2768
Comment LK-9-049-f1
Date May 10 2006
Frequency (MHz) 199.98
Nucleus 1H
Number of Transients 128
Original Points Count 4992
Points Count 8192
Solvent CDCl3
Sweep Width (Hz) 2500.00
Temperature (grad C) 29.000
O
O
3.91
1.25
4.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

Acquisition Time (sec)	2.6214	***Comment***	LK-9-049-f1-c13		***Date***	May 10 2006		***Frequency (MHz)***	50.29
Nucleus	13C	***Number of Transients***	20000	***Original Points Count*** 18720	***Points Count***	32768	***Solvent*** CDCl3	***Sweep Width (Hz)***	12500.00
Temperature (grad C)	29.000								

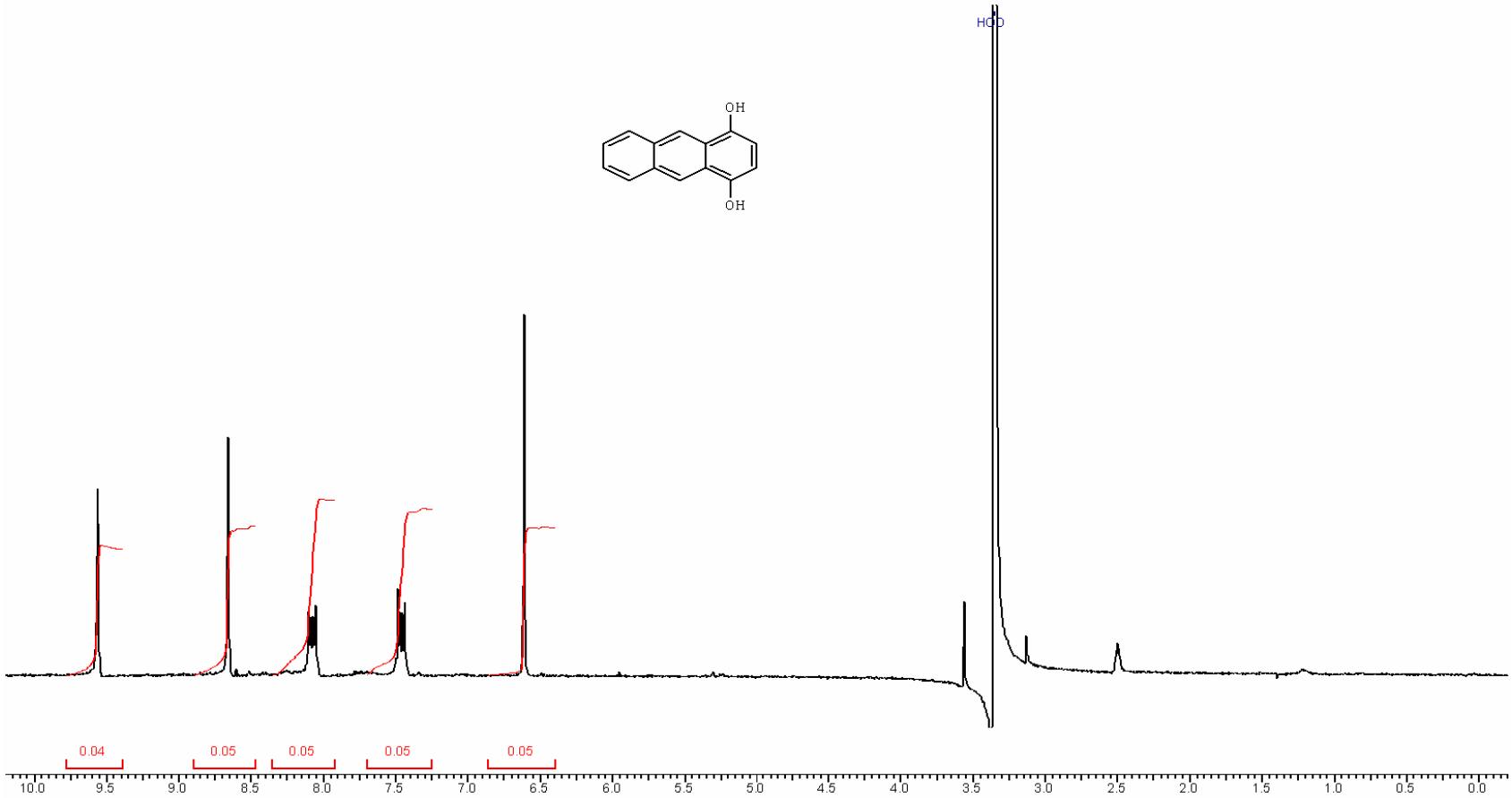


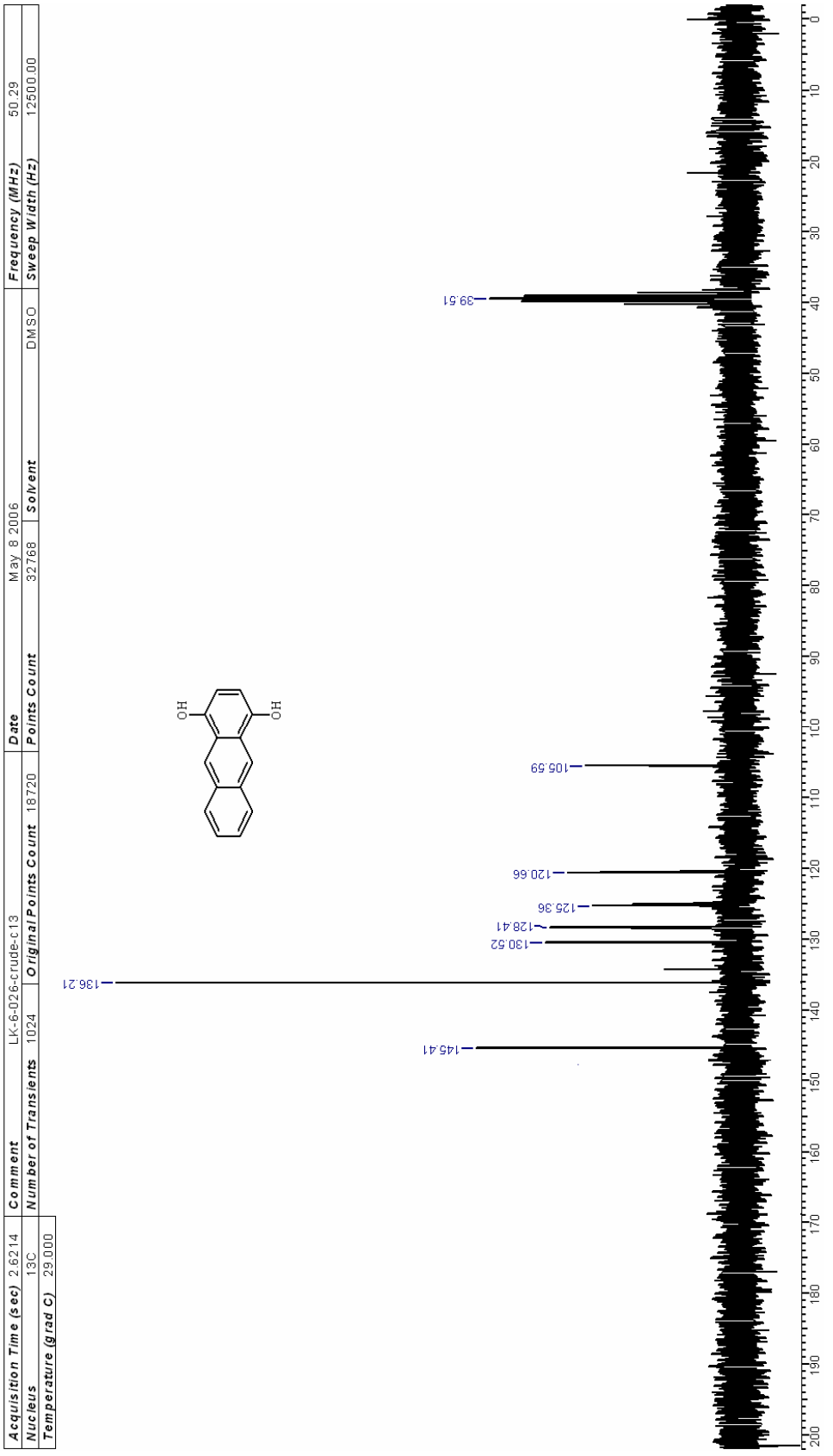
Acquisition Time (sec)	3.2768	***Comment***	LK-8-107-precipitate		***Date***	Mar 20 2006		***Frequency (MHz)***	199.98
Nucleus	1H	***Number of Transients***	128	***Original Points Count*** 4992	***Points Count***	8192	***Solvent*** CDCl3	***Sweep Width (Hz)***	2500.00
Temperature (grad C)	29.000								



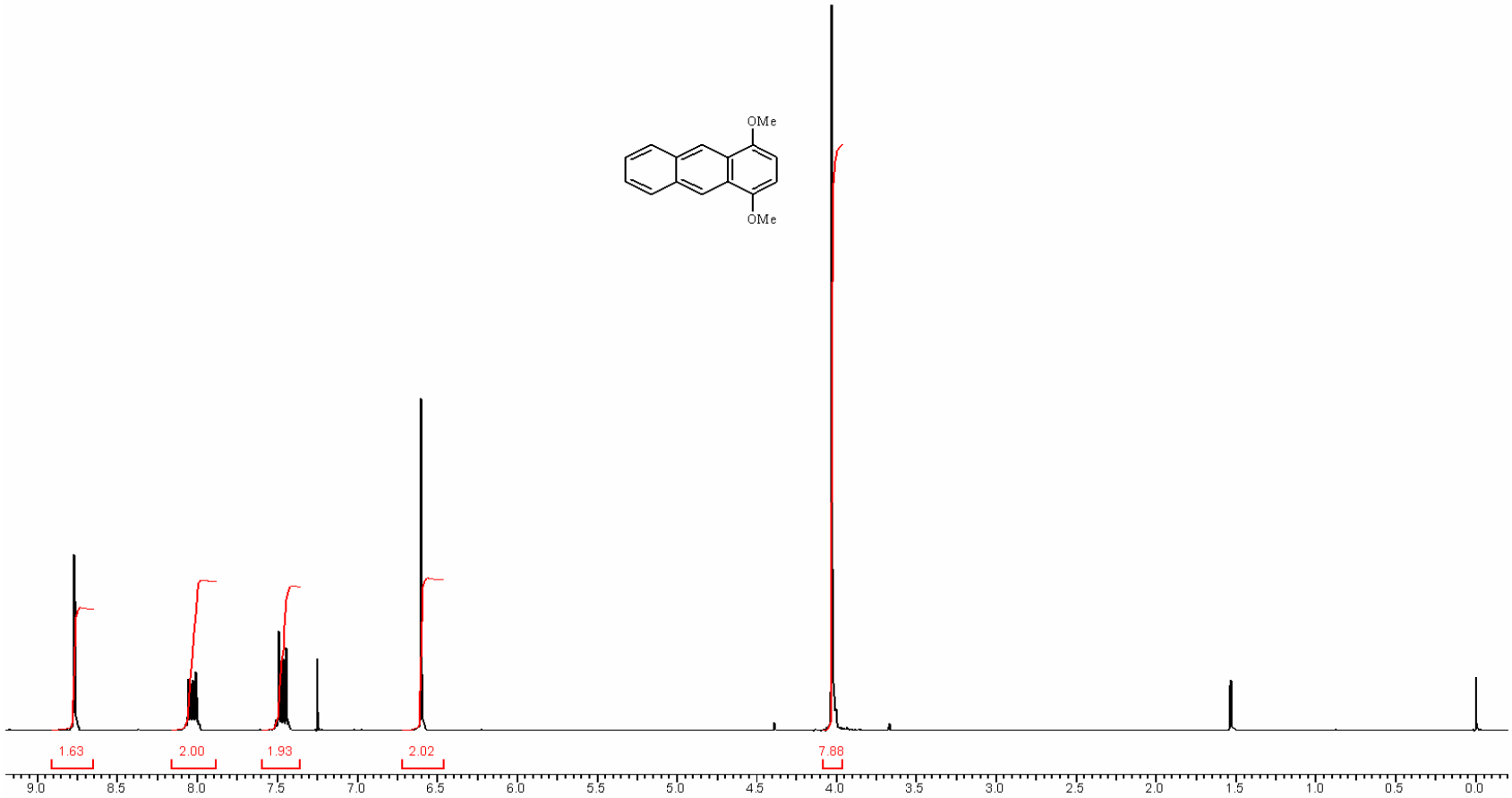

Acquisition Time (sec) 1.3107
Comment LK-8-107-precipitate-c13
Date May 1 2006
Frequency (MHz) 100.53
Nucleus 13C
Number of Transients 3392
Original Points Count 29984
Points Count 32768
Solvent CDCl3
Sweep Width (Hz) 25000.00
Temperature (grad C) 29.000
O
O
184.78
140.20
135.01
130.38
129.73
128.99
128.58
77.23

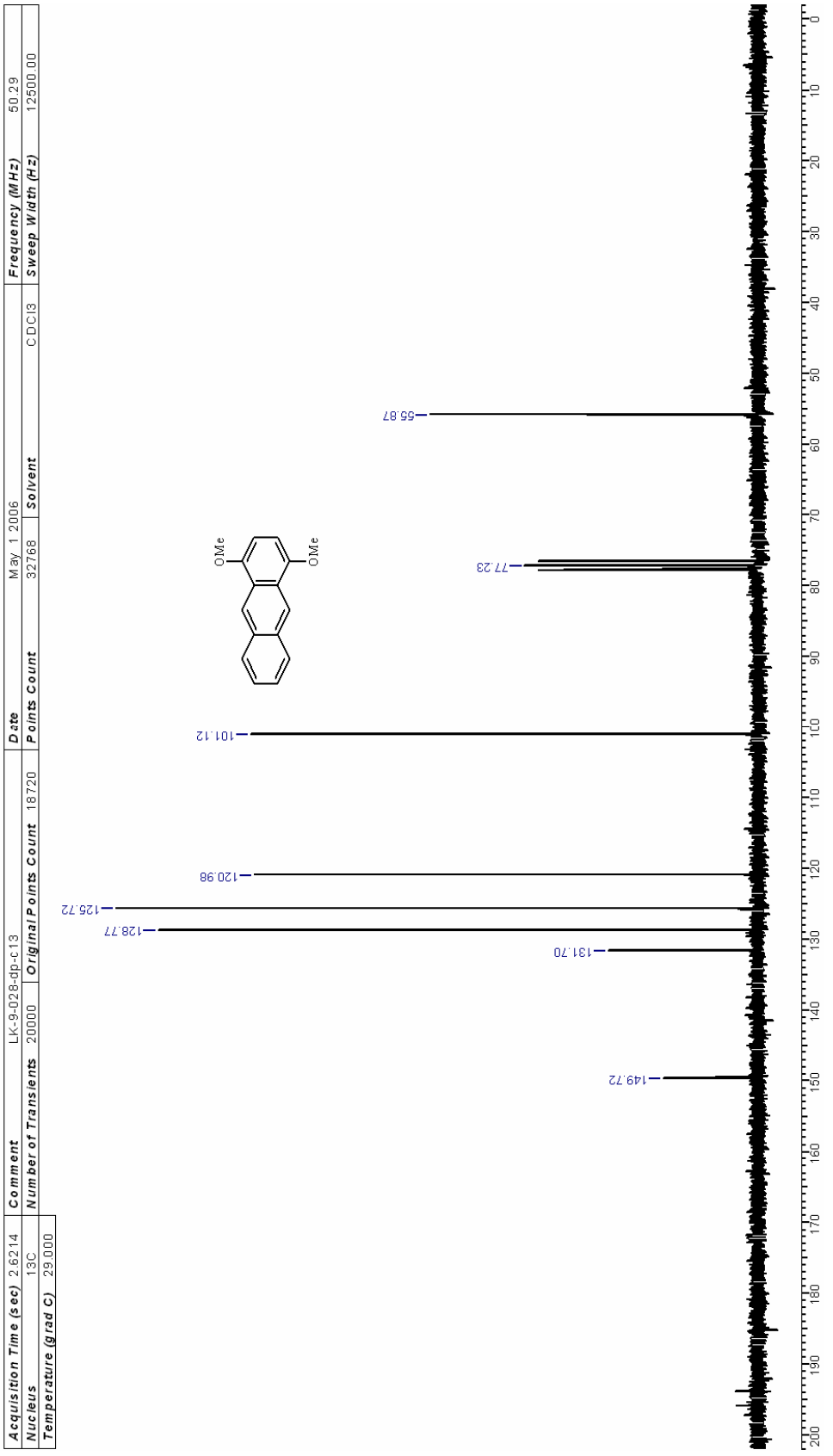
Acquisition Time (sec) 2.7304	***Comment*** LK-6-026-crude		***Date*** Mar 24 2005			***Frequency (MHz)*** 199.98			
Nucleus 1H	***Number of Transients*** 32	***Original Points Count*** 5984	***Points Count*** 8192	***Solvent*** DMSO		***Sweep Width (Hz)*** 3000.30			
Temperature (grad C) 29.000									



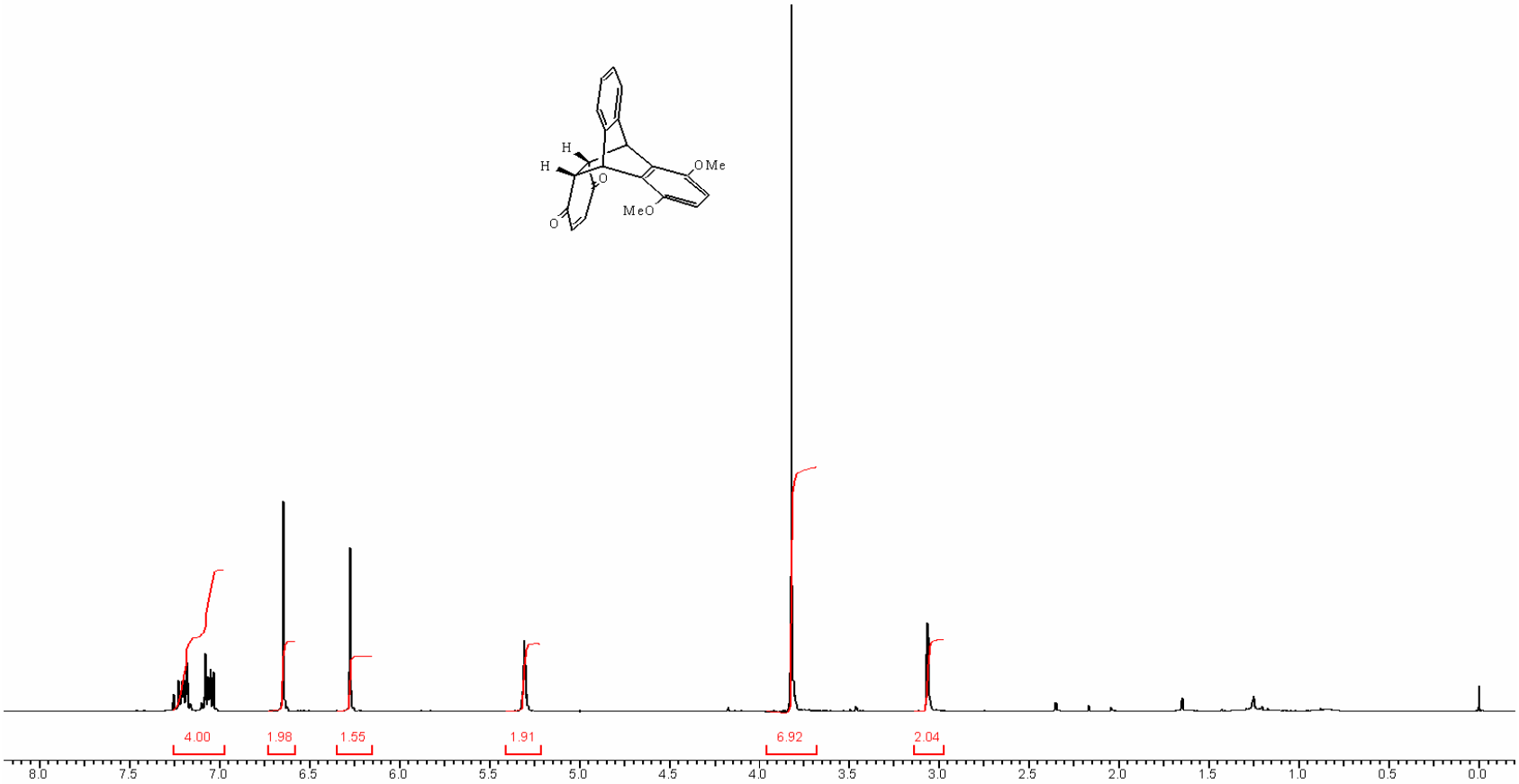

Acquisition Time (sec) 2.6214
Comment LK-6-026-crude-c13
Date May 8 2006
Frequency (MHz) 50.29
Nucleus 13C
Number of Transients 1024
Original Points Count 18720
Points Count 32768
Solvent DMSO
Sweep Width (Hz) 12500.00
Temperature (grad C) 29.000
OH
OH
136.21
145.41
130.52
128.41
125.36
120.66
105.59
39.51
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200

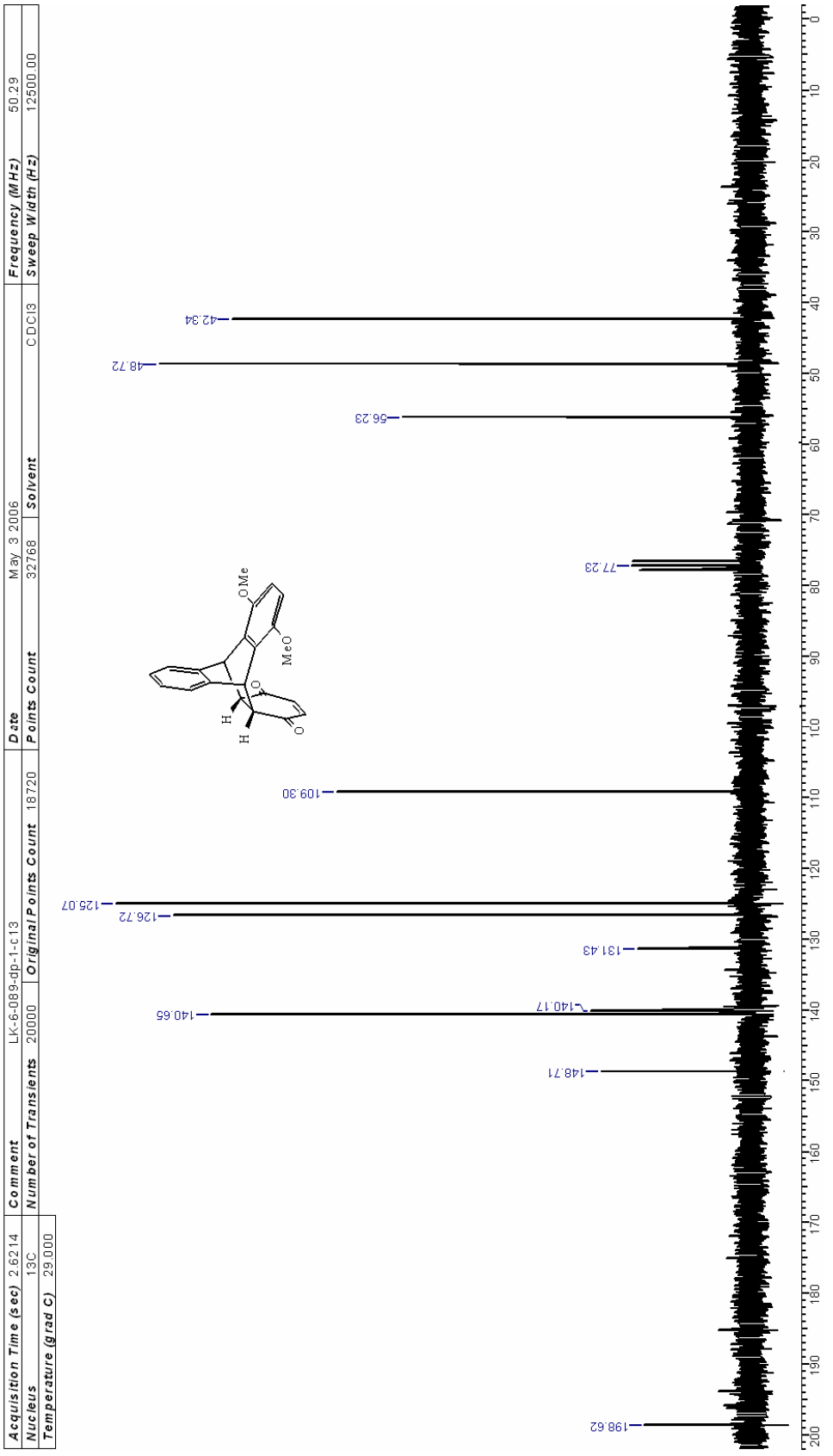
Acquisition Time (sec)	3.2768	*Comment*	LK-9-028-dp		*Date*	May 1 2006		*Frequency (MHz)*	199.98
Nucleus	1H	*Number of Transients*	128	*Original Points Count* 4992	*Points Count*	8192	*Solvent* CDCl3	*Sweep Width (Hz)*	2500.00
Temperature (grad C)	29.000								



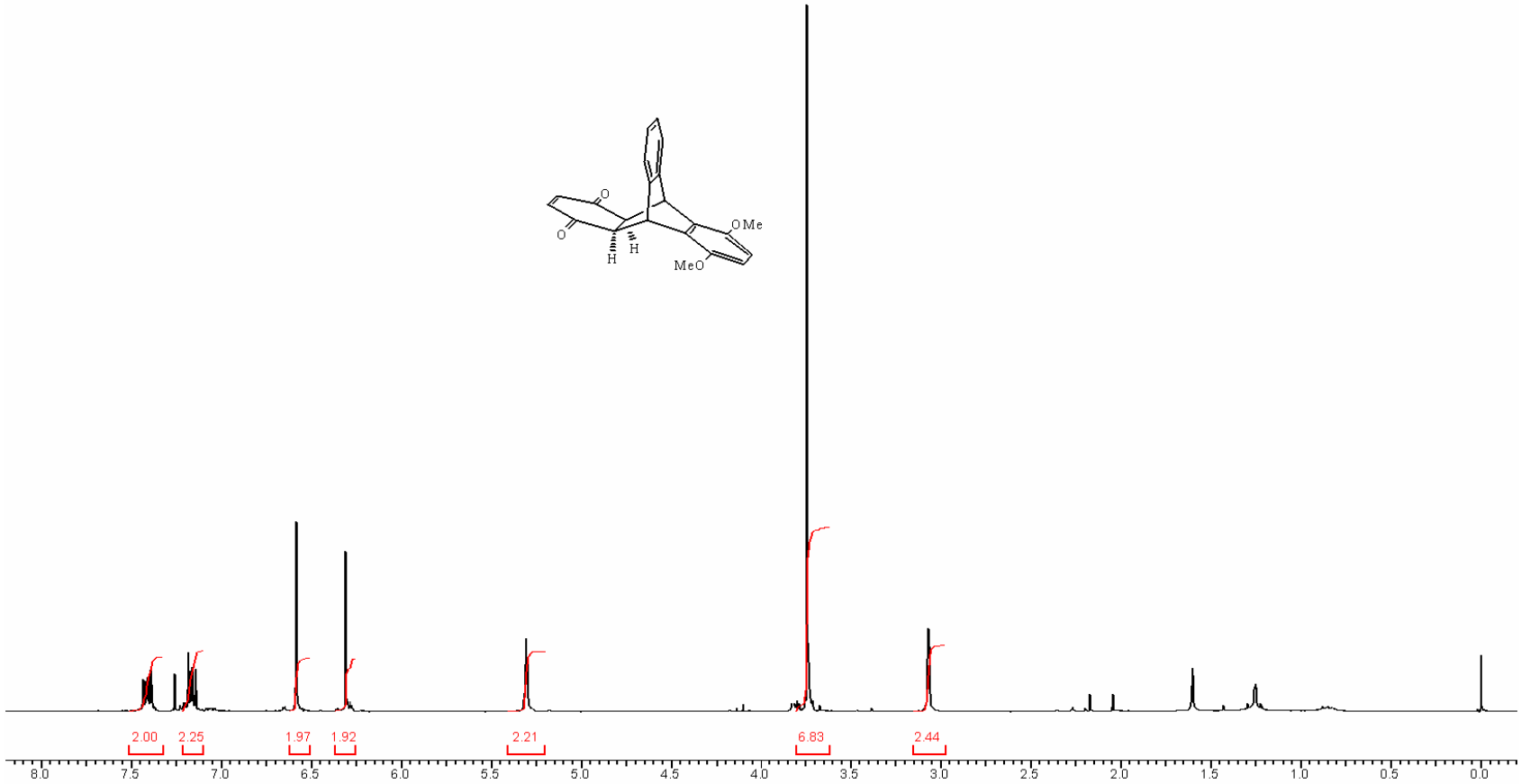

Acquisition Time (sec) 2.6214
Comment LK-9-028-dp-c13
Date May 1 2006
Frequency (MHz) 50.29
Nucleus 13C
Number of Transients 20000
Original Points Count 18720
Points Count 32768
Solvent CDCl3
Sweep Width (Hz) 12500.00
Temperature (grad C) 29.000
OMe
OMe
149.72
131.70
128.77
125.72
120.98
101.12
77.23
55.87

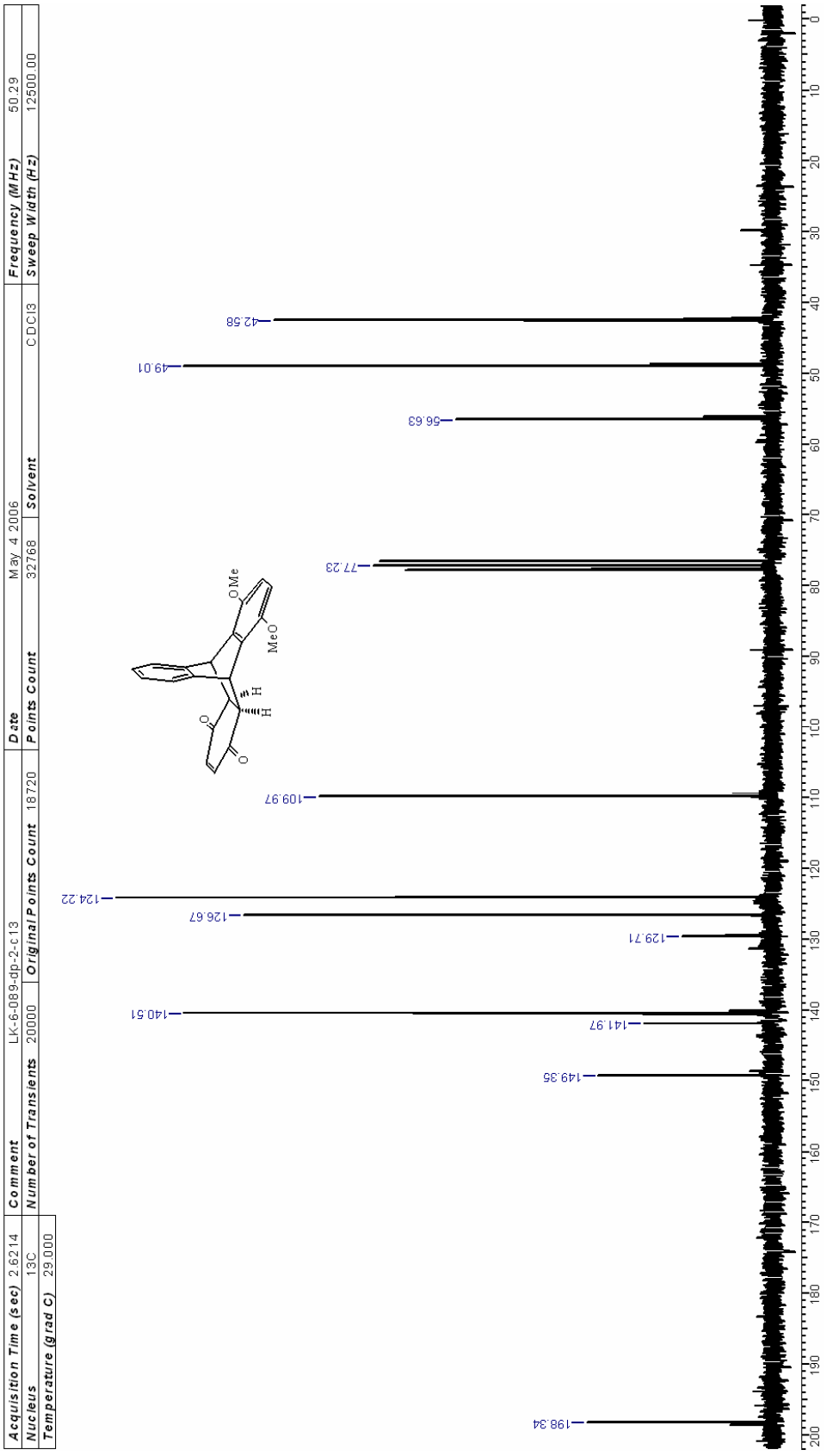
Acquisition Time (sec)	3.2768	***Comment***	LK-6-089-dp-1		***Date***	May 3 2006		***Frequency (MHz)***	199.98
Nucleus	1H	***Number of Transients***	128	***Original Points Count*** 4992	***Points Count***	8192	***Solvent*** CDCl3	***Sweep Width (Hz)***	2500.00
Temperature (grad C)	29.000								



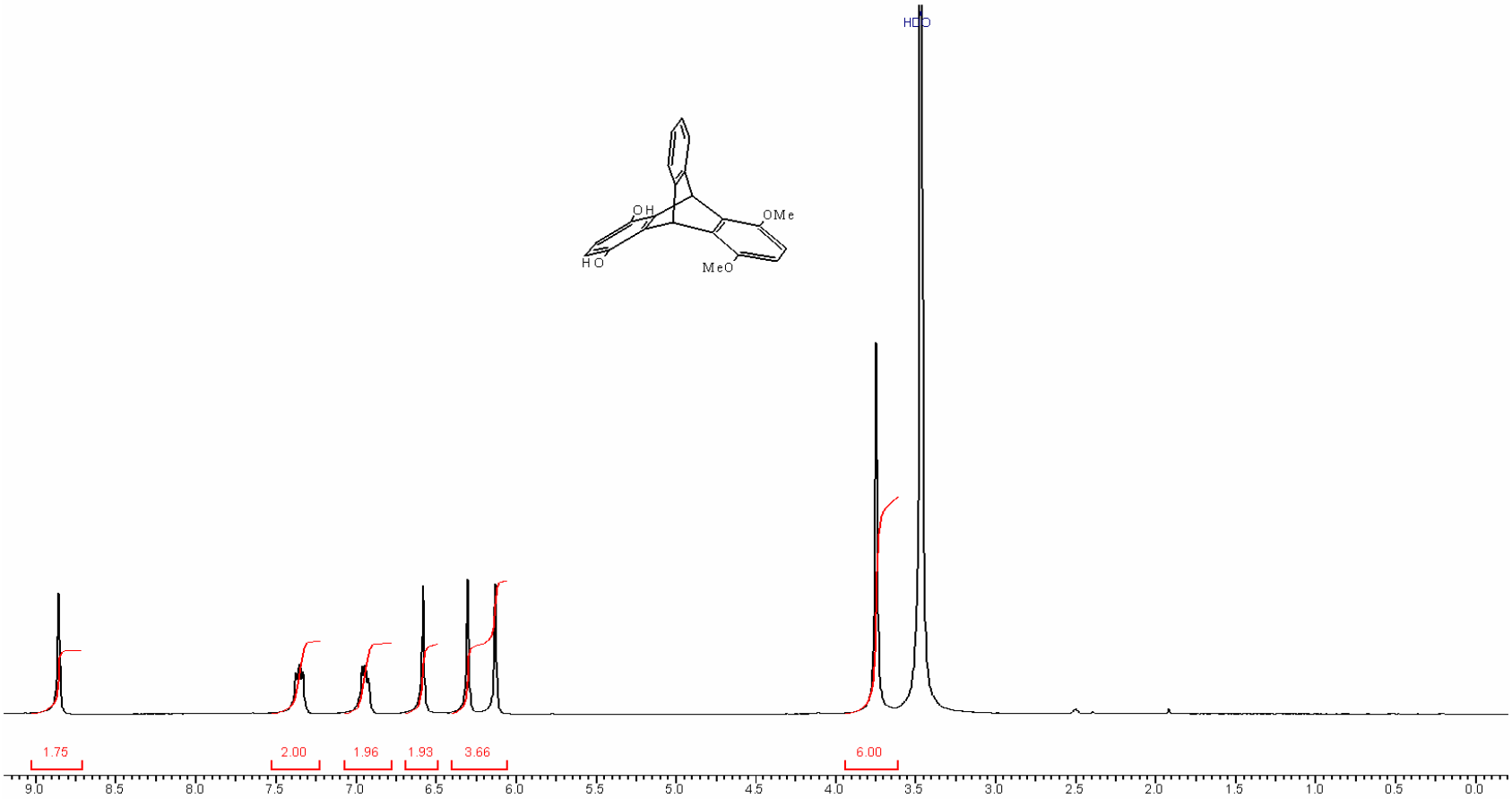

Acquisition Time (sec) 2.6214
Comment LK-6-089-dp-1-c13
Date May 3 2006
Frequency (MHz) 50.29
Nucleus 13C
Number of Transients 20000
Original Points Count 18720
Points Count 32768
Solvent CDCl3
Sweep Width (Hz) 12500.00
Temperature (grad C) 29.000
42.34
48.72
56.23
77.23
109.30
125.07
126.72
131.43
140.17
140.65
148.71
198.62
OMe
MeO
O
H
H
O

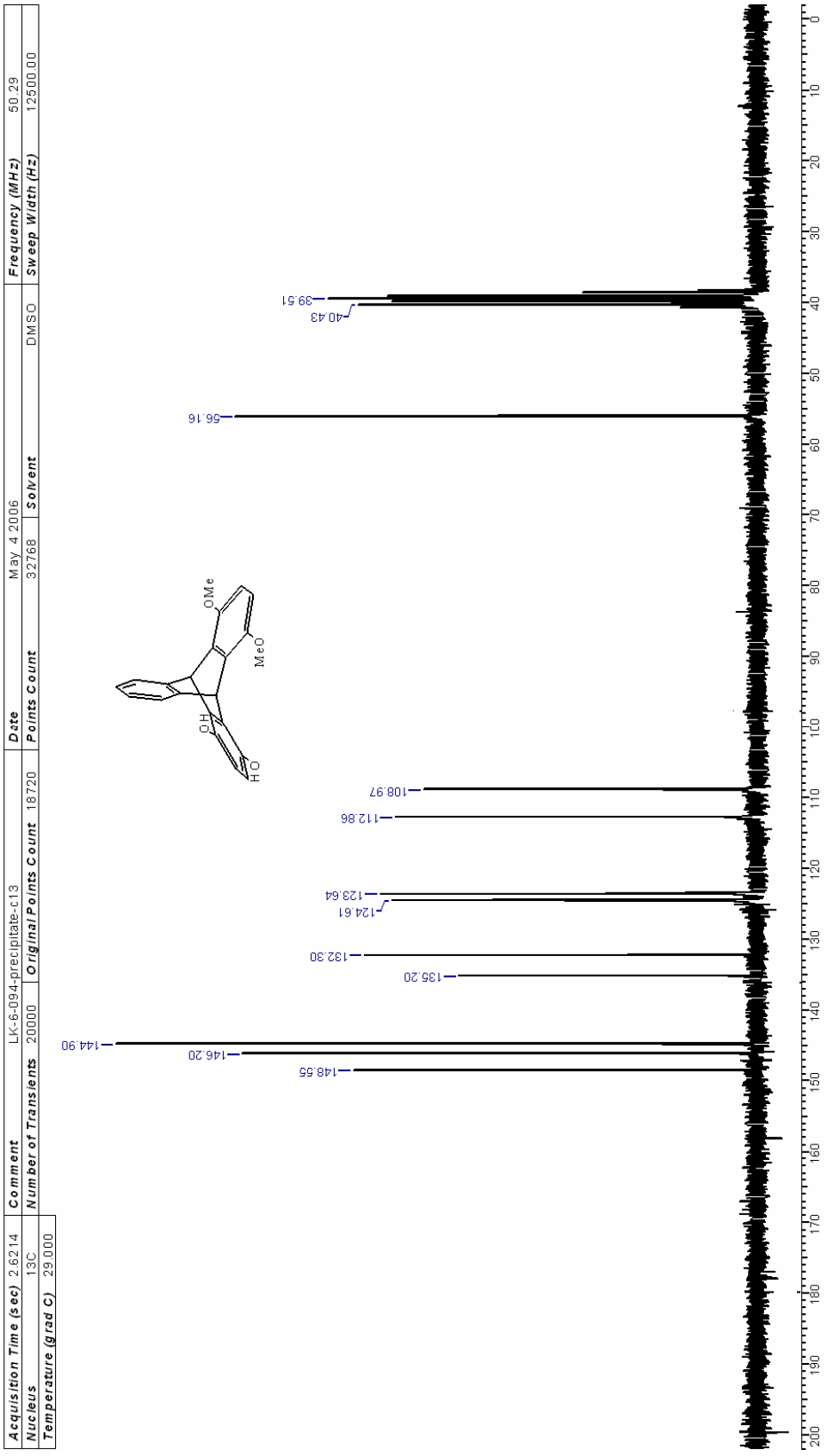
Acquisition Time (sec)	3.2768	***Comment***	LK-6-089-dp-2		***Date***	May 4 2006		***Frequency (MHz)***	199.98
Nucleus	1H	***Number of Transients***	128	***Original Points Count*** 4992	***Points Count***	8192	***Solvent*** CDCl3	***Sweep Width (Hz)***	2500.00
Temperature (grad C)	29.000								



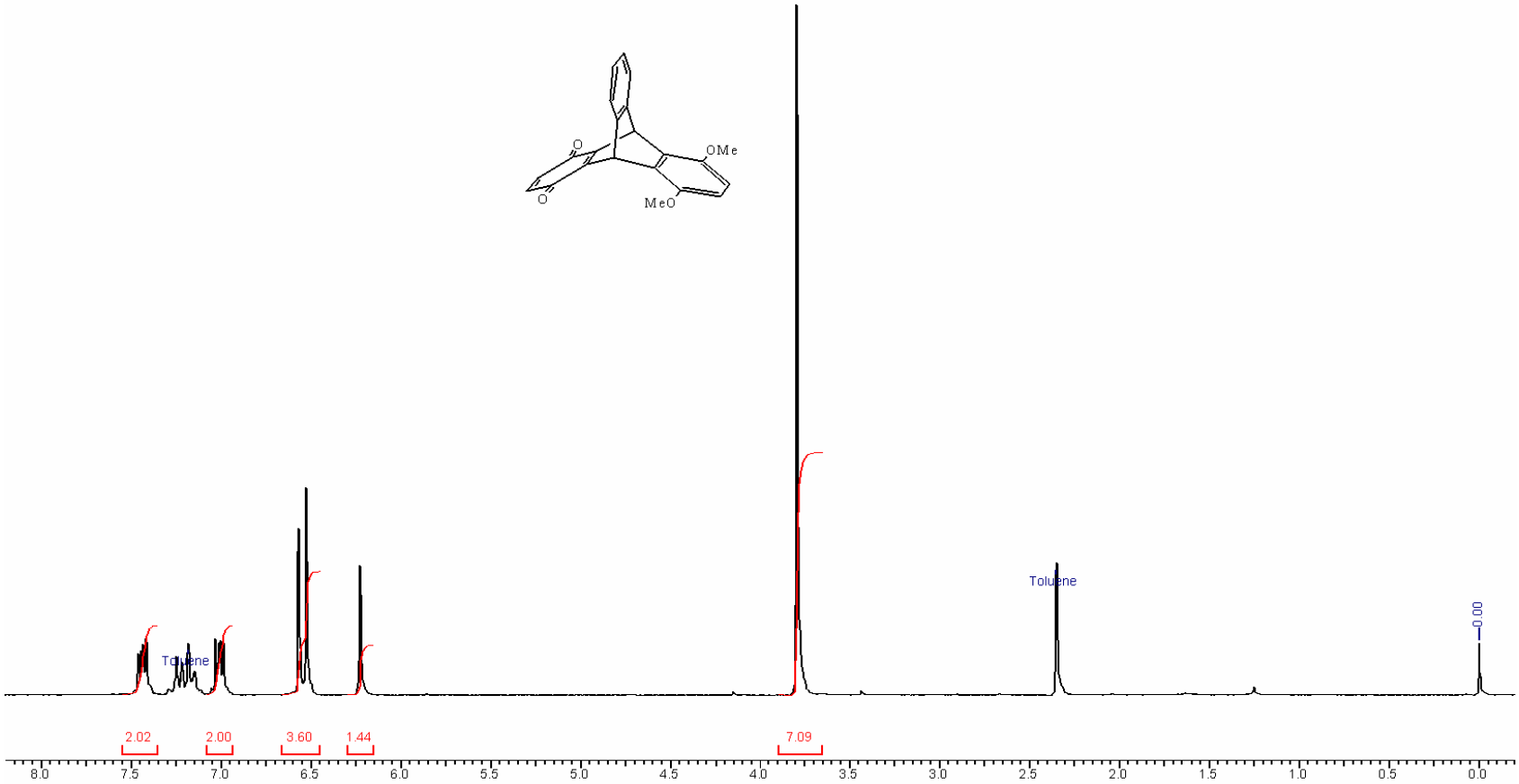

Acquisition Time (sec) 2.6214
Comment LK-6-089-dp-2-c13
Date May 4 2006
Frequency (MHz) 50.29
Nucleus 13C
Number of Transients 20000
Original Points Count 18720
Points Count 32768
Solvent CDCl3
Sweep Width (Hz) 12500.00
Temperature (grad C) 29.000
42.58
49.01
56.63
77.23
109.97
124.22
126.67
129.71
140.51
141.97
149.35
198.34
OMe
MeO
H
H
O
O

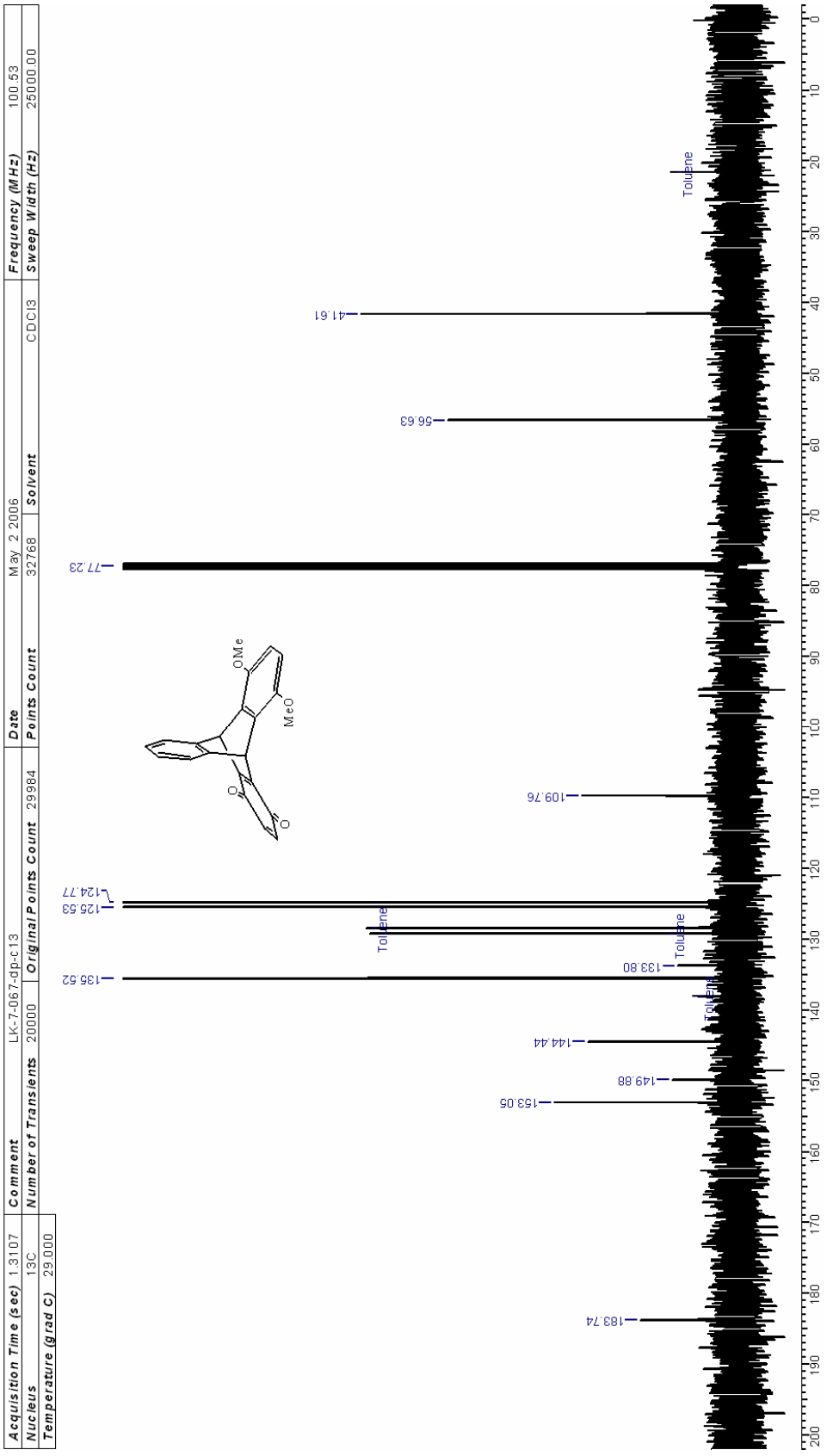
Acquisition Time (sec)	2.7304	***Comment***	LK-6-094-precipitate		***Date***	May 4 2006		***Frequency (MHz)***	199.98
Nucleus	1H	***Number of Transients***	128	***Original Points Count*** 5984	***Points Count***	8192	***Solvent*** DMSO	***Sweep Width (Hz)***	3000.30
Temperature (grad C)	29.000								



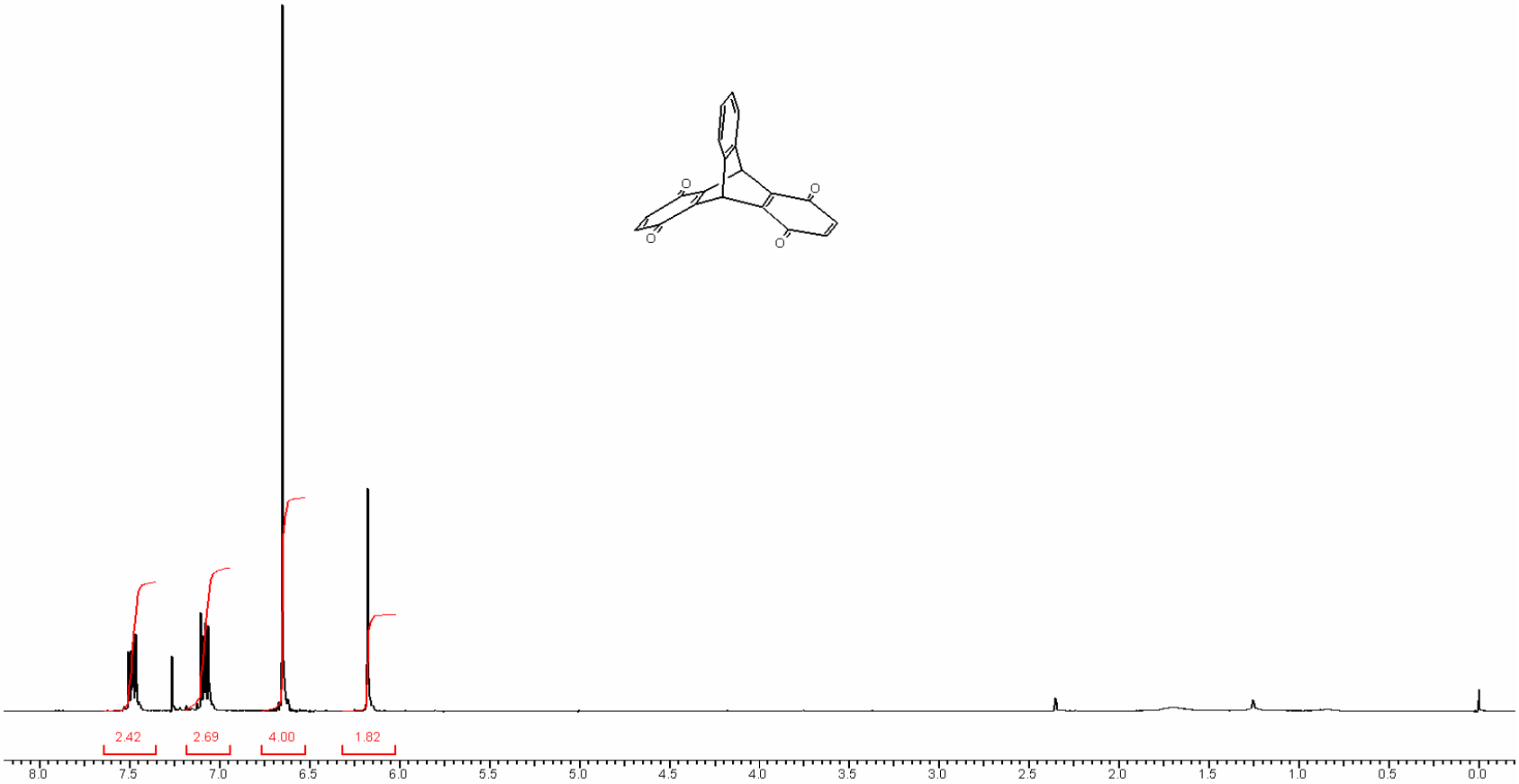

Acquisition Time (sec) 2.6214
Comment LK-6-094-precipitate-c13
Date May 4 2006
Frequency (MHz) 50.29
Nucleus 13C
Number of Transients 20000
Original Points Count 18720
Points Count 32768
Solvent DMSO
Sweep Width (Hz) 12500.00
Temperature (grad C) 29.000
39.51
40.43
56.16
108.97
112.86
123.64
124.61
132.30
135.20
144.90
146.20
148.55
OMe
MeO
OH
HO

Acquisition Time (sec)	3.2768	***Comment***	LK-7-067-dp		***Date***	May 2 2006		***Frequency (MHz)***	199.98
Nucleus	1H	***Number of Transients***	128	***Original Points Count*** 4992	***Points Count***	8192	***Solvent*** CDCl3	***Sweep Width (Hz)***	2500.00
Temperature (grad C)	29.000								

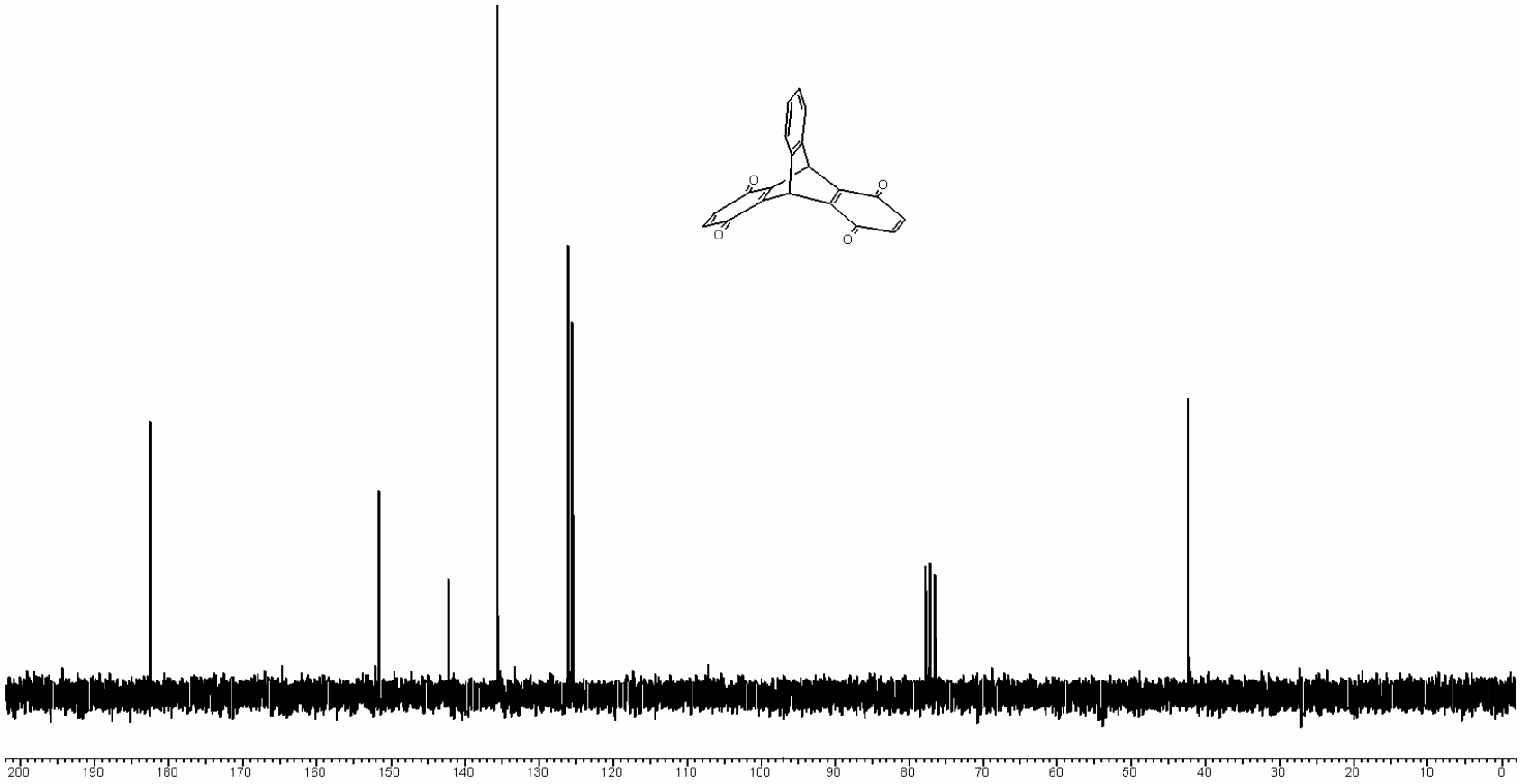



Acquisition Time (sec) 1.3107
Comment LK-7-067-dp-c13
Date May 2 2006
Frequency (MHz) 100.53
Nucleus 13C
Number of Transients 20000
Original Points Count 29984
Points Count 32768
Solvent CDCl3
Sweep Width (Hz) 25000.00
Temperature (grad C) 29.000
OMe
MeO
O
O
77.23
41.61
56.63
109.76
124.77
125.53
135.52
133.80
144.44
149.88
153.05
183.74
Toluene
Toluene
Toluene
Toluene

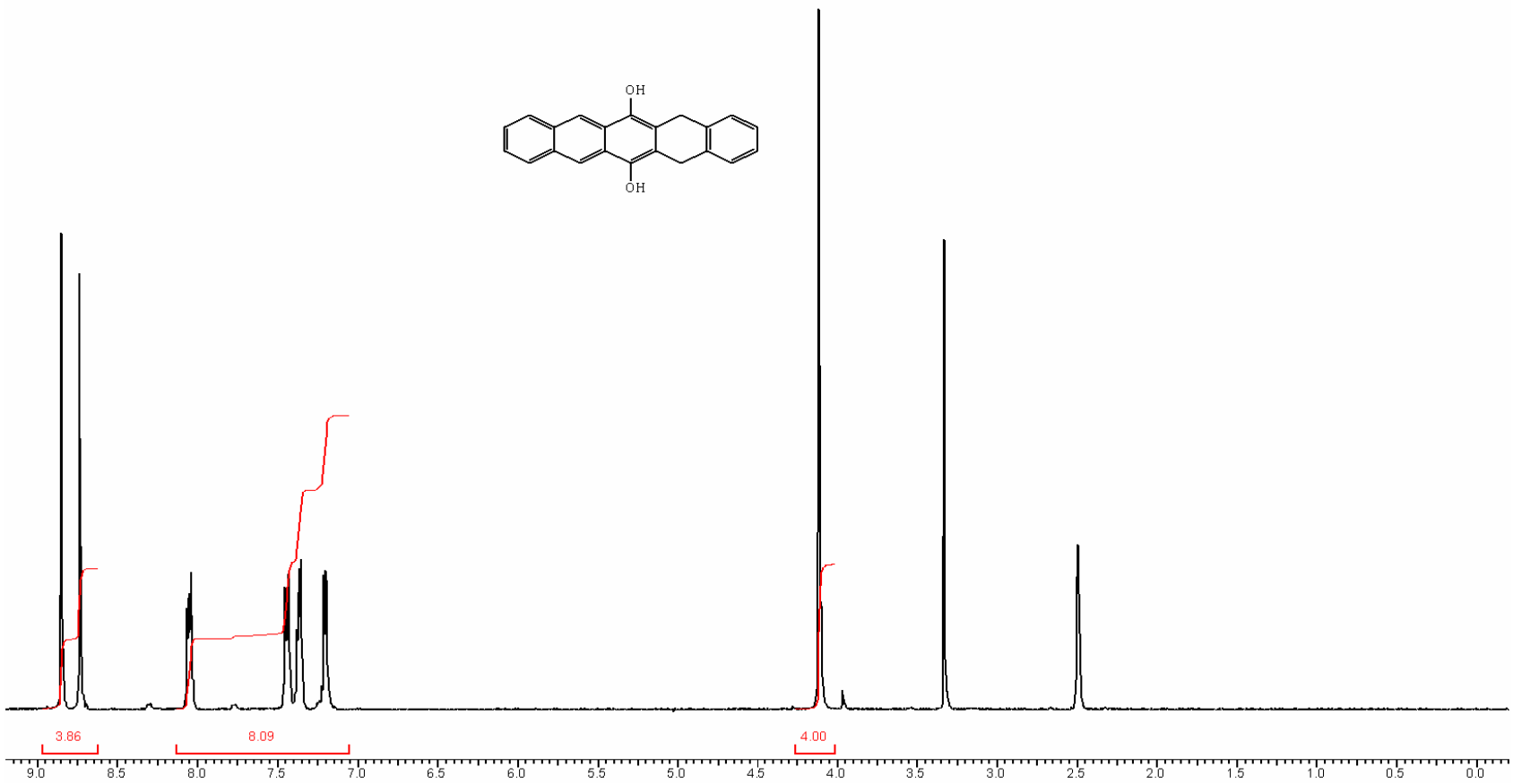
Acquisition Time (sec)	3.2768	***Comment***	LK-9-046-f2		***Date***	Apr 30 2006		***Frequency (MHz)***	199.98
Nucleus	1H	***Number of Transients***	128	***Original Points Count*** 4992	***Points Count***	8192	***Solvent*** CDCl3	***Sweep Width (Hz)***	2500.00
Temperature (grad C)	29.000								

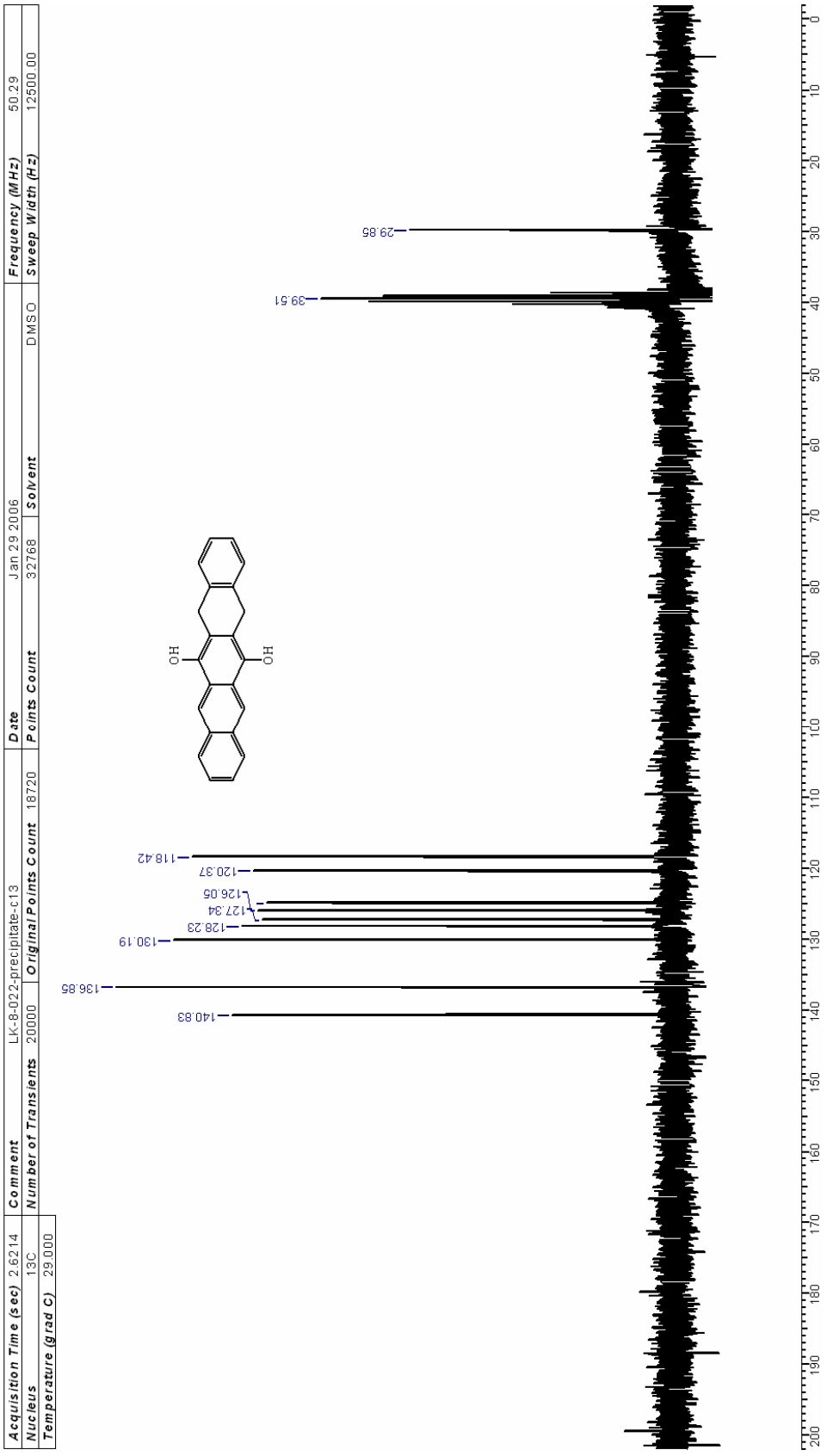


Acquisition Time (sec)	2.6214	***Comment***	LK-9-046-f2-c13		***Date***	Apr 30 2006		***Frequency (MHz)***	50.29
Nucleus	13C	***Number of Transients***	20000	***Original Points Count*** 18720	***Points Count***	32768	***Solvent*** CDCl3	***Sweep Width (Hz)***	12500.00
Temperature (grad C)	29.000								

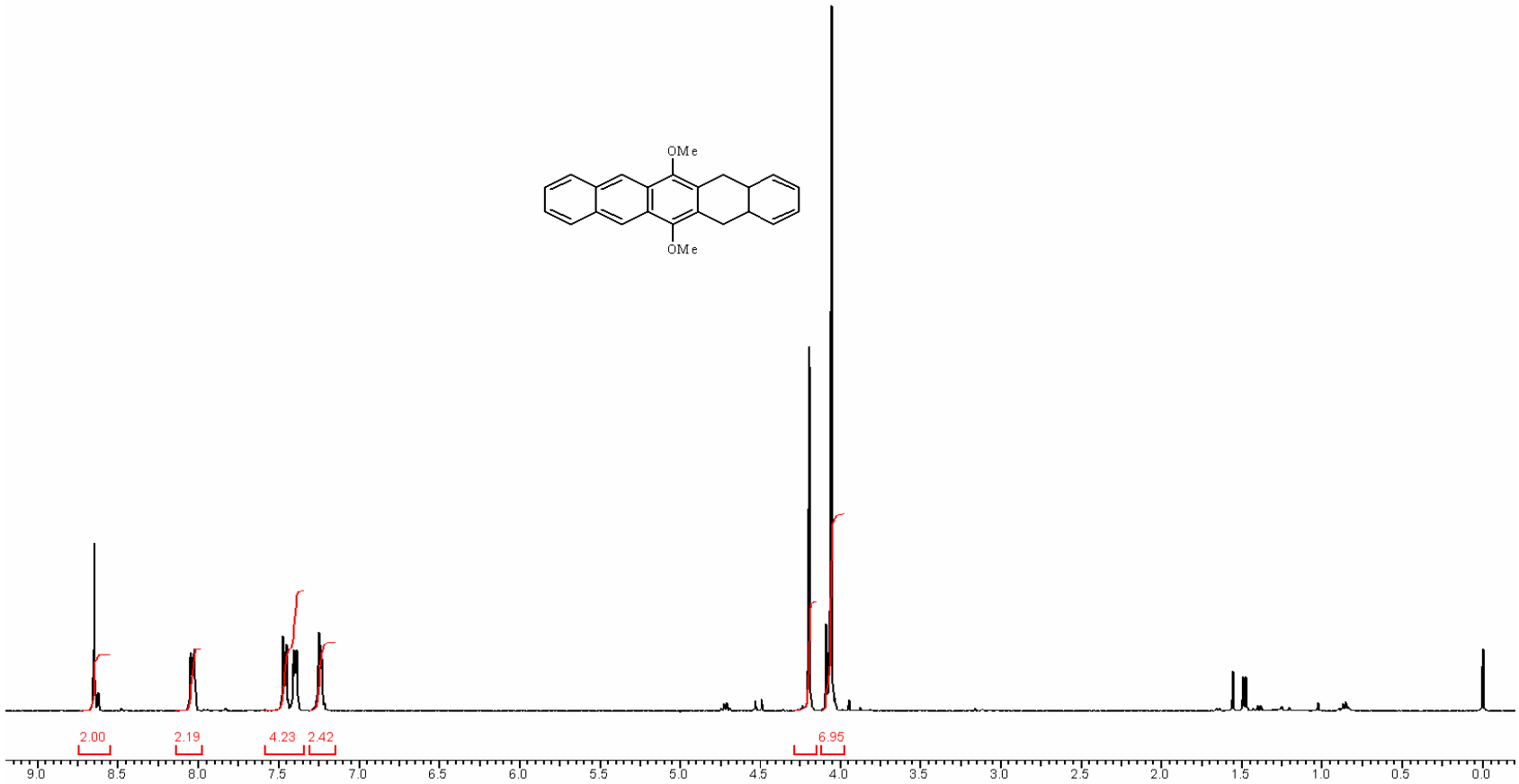


Acquisition Time (sec)	6.5536	***Comment***	LK-8-022-precipitate		***Date***	Jan 29 2006		***Frequency (MHz)***	399.78
Nucleus	1H	***Number of Transients***	128	***Original Points Count*** 18505	***Points Count***	32768	***Solvent*** DMSO	***Sweep Width (Hz)***	5000.00
Temperature (grad C)	29.000								

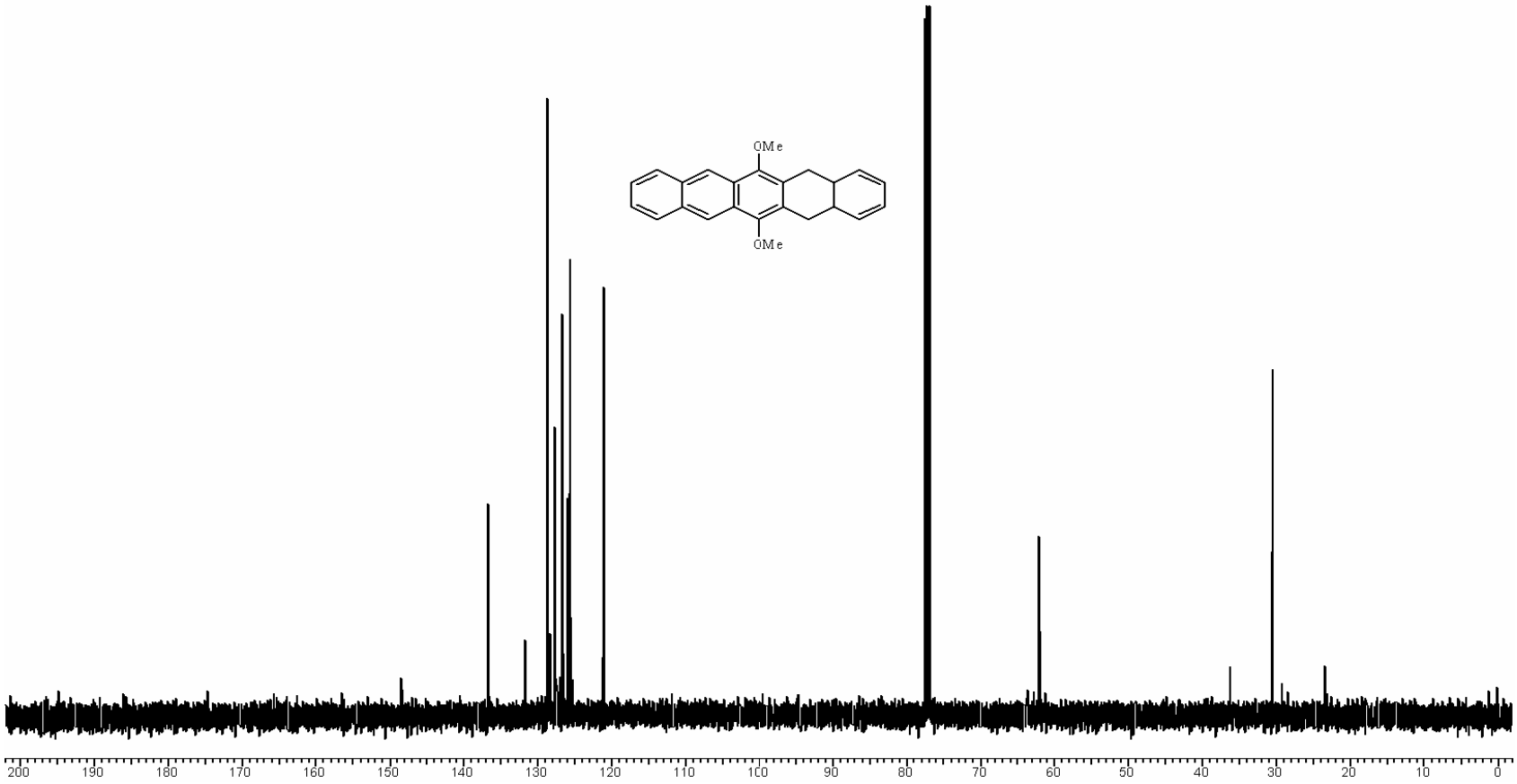



Acquisition Time (sec) 2.6214
Comment LK-8-022-precipitate-c13
Date Jan 29 2006
Frequency (MHz) 50.29
Nucleus 13C
Number of Transients 20000
Original Points Count 18720
Points Count 32768
Solvent DMSO
Sweep Width (Hz) 12500.00
Temperature (grad C) 29.000
OH
OH
29.86
39.51
118.42
120.37
126.05
127.34
128.23
130.19
136.85
140.83

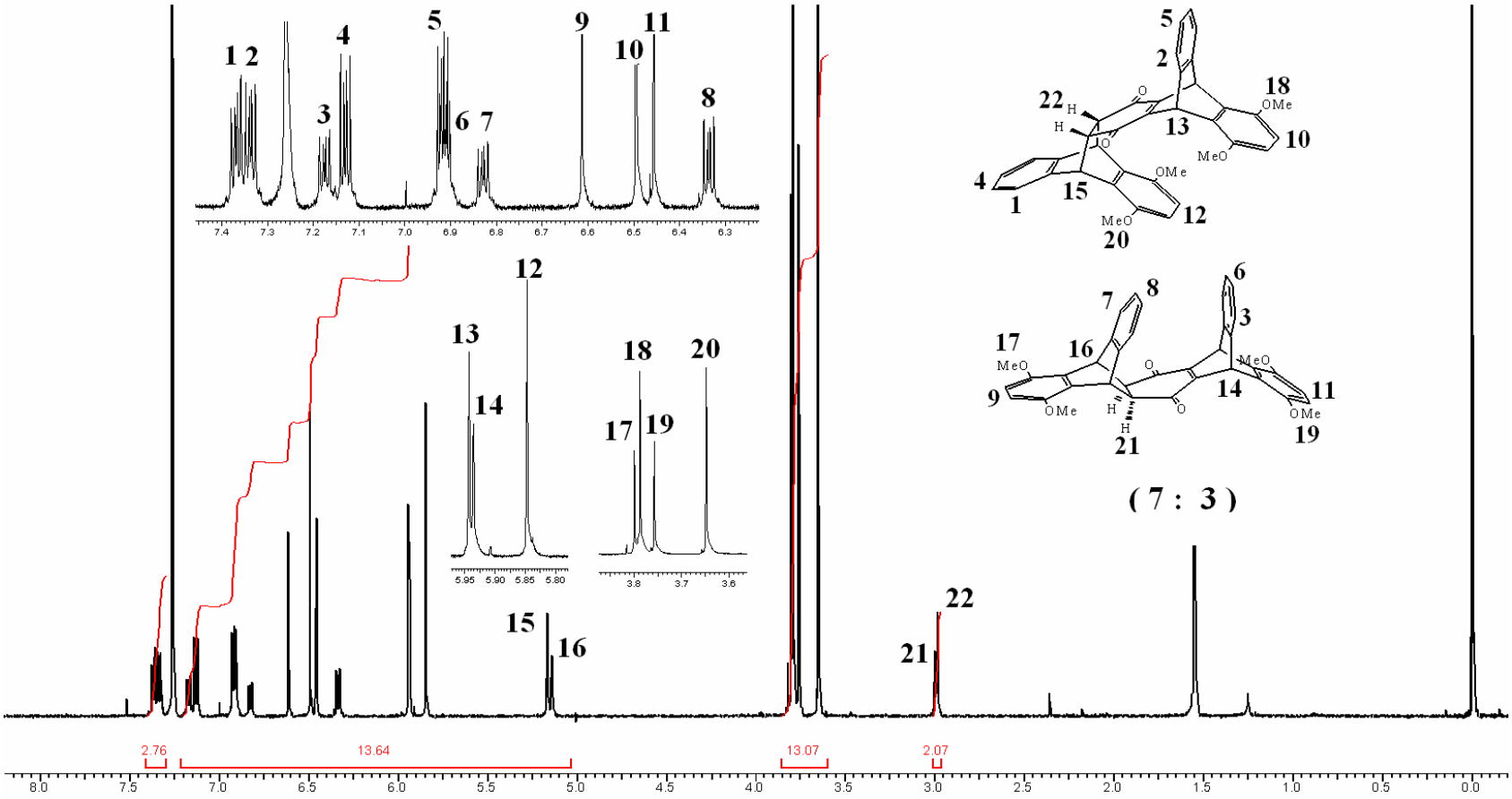
Acquisition Time (sec)	6.5536	***Comment***	LK-8-066-f4		***Date***	Jan 30 2006		***Frequency (MHz)***	399.78
Nucleus	1H	***Number of Transients***	128	***Original Points Count*** 18505	***Points Count***	32768	***Solvent*** CDCl3	***Sweep Width (Hz)***	5000.00
Temperature (grad C)	29.000								



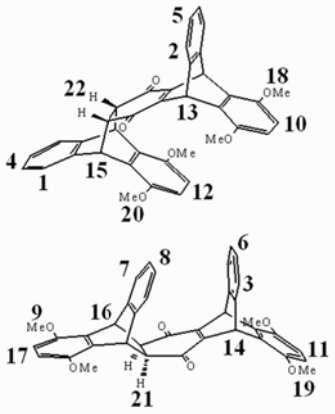
Acquisition Time (sec)	1.3107	***Comment***	LK-8-066-f4-c13		***Date***	Jan 30 2006		***Frequency (MHz)***	100.53
Nucleus	13C	***Number of Transients***	20000	***Original Points Count*** 29984	***Points Count***	32768	***Solvent*** CDCl3	***Sweep Width (Hz)***	25000.00
Temperature (grad C)	29.000								

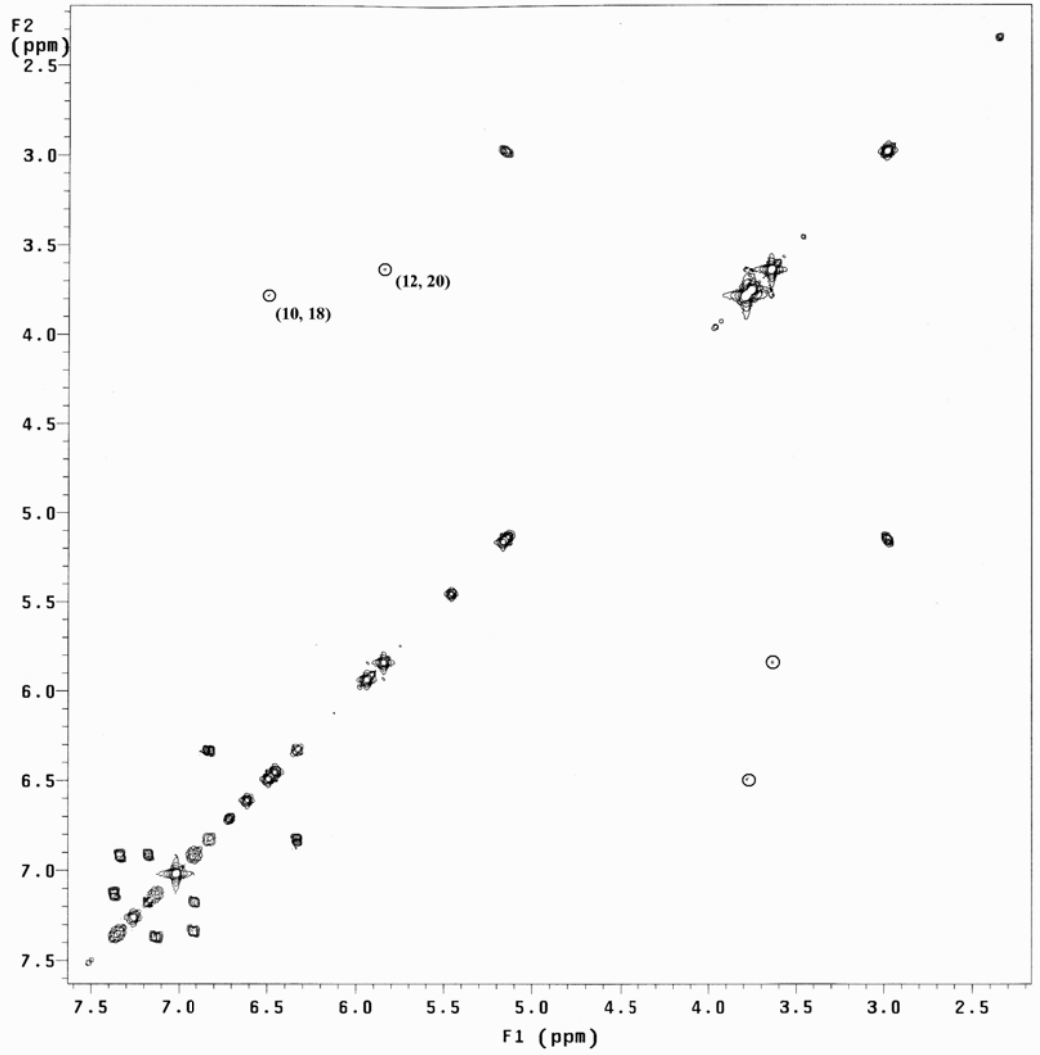


Acquisition Time (sec)	6.5536	*Comment*	LK-7-076-precipitate		*Date*	Nov 4 2005		*Frequency (MHz)*	399.79
Nucleus	1H	*Number of Transients*	128	*Original Points Count*	18505	*Points Count*	32768	*Solvent*	CDCl3	*Sweep Width (Hz)*	5000.00
Temperature (grad C)	29.000								

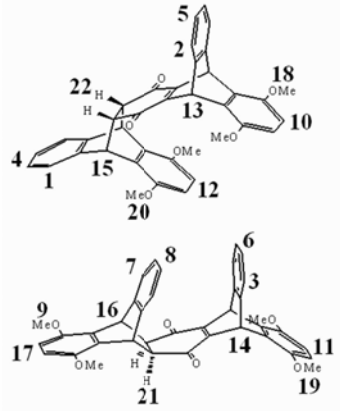


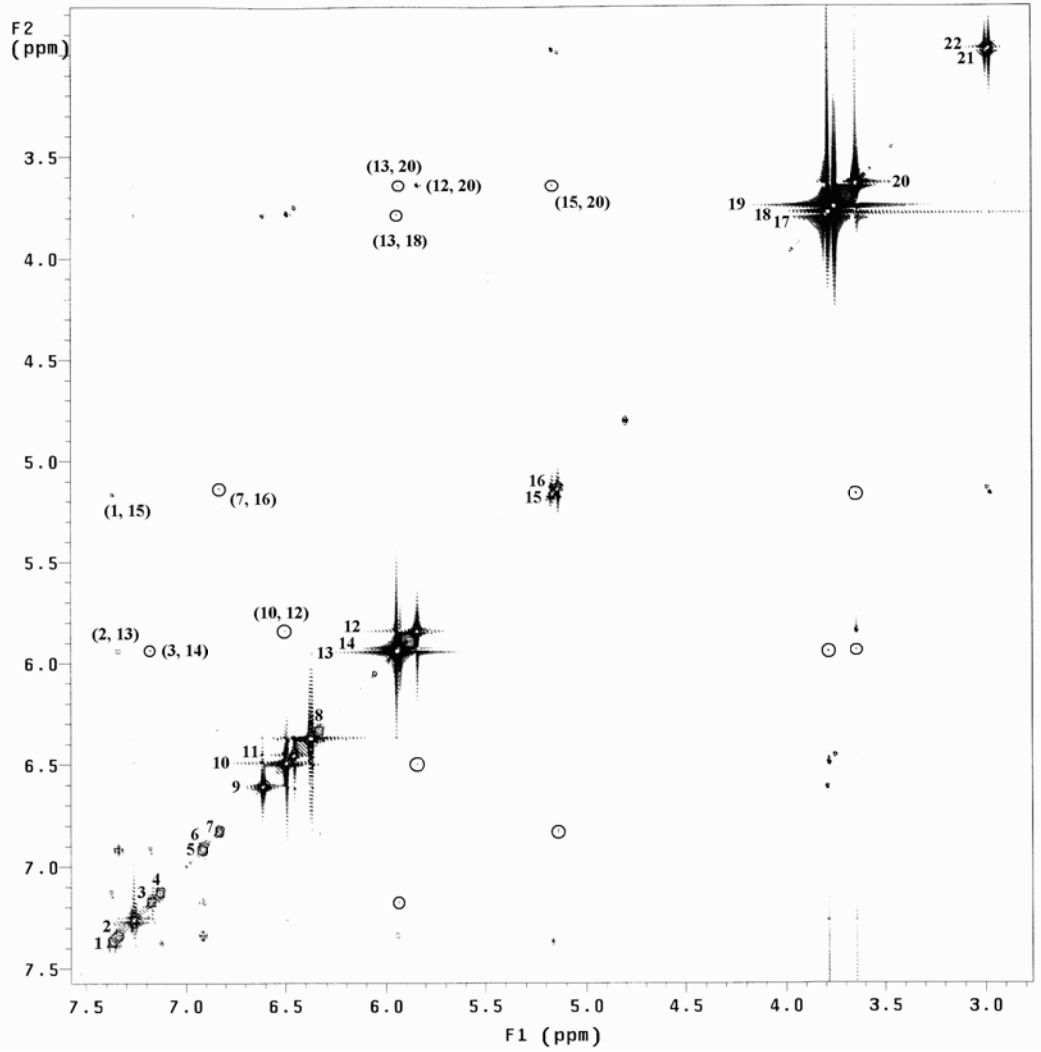
LK-7-076-pecipitate-cosy



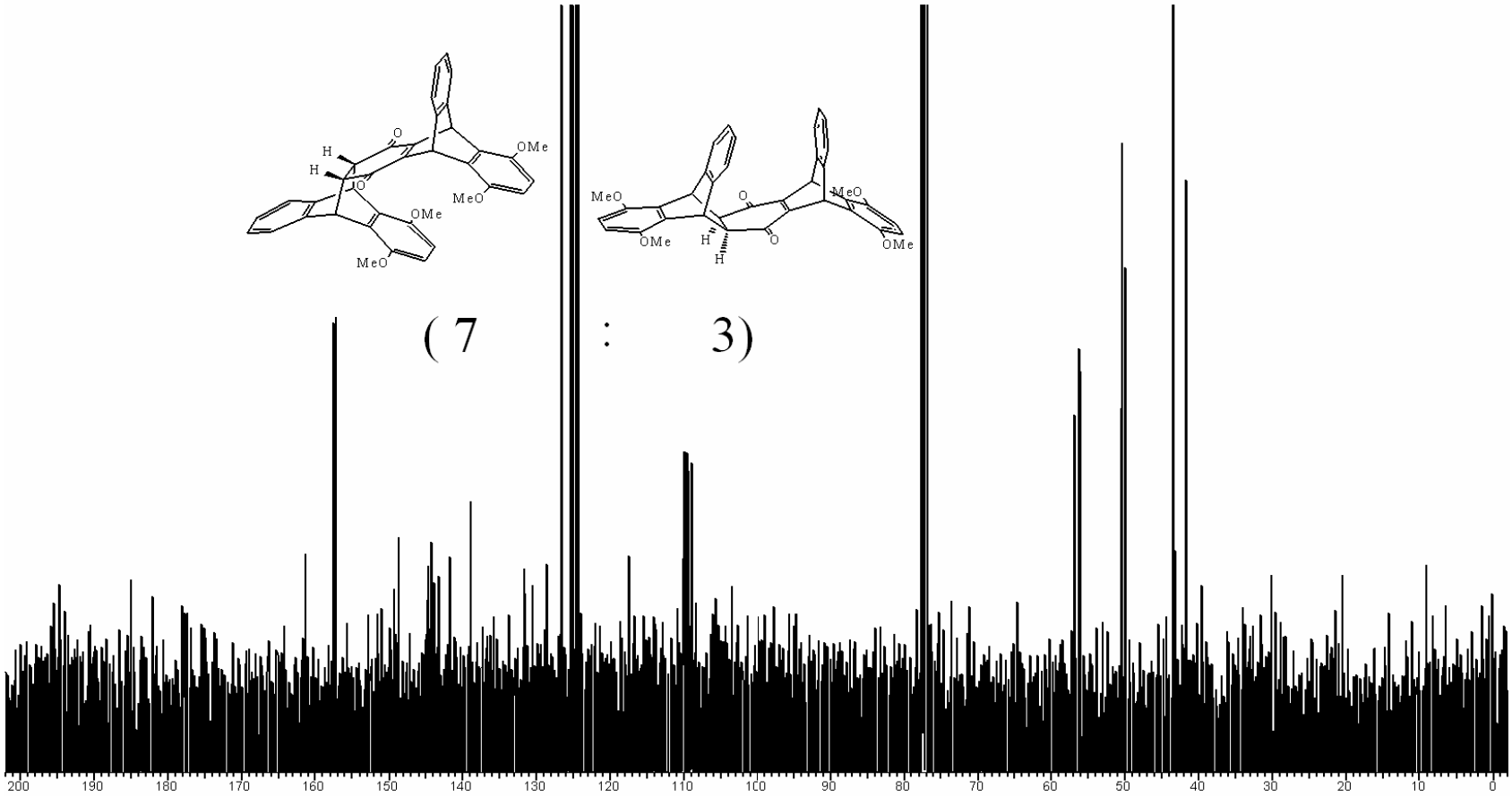


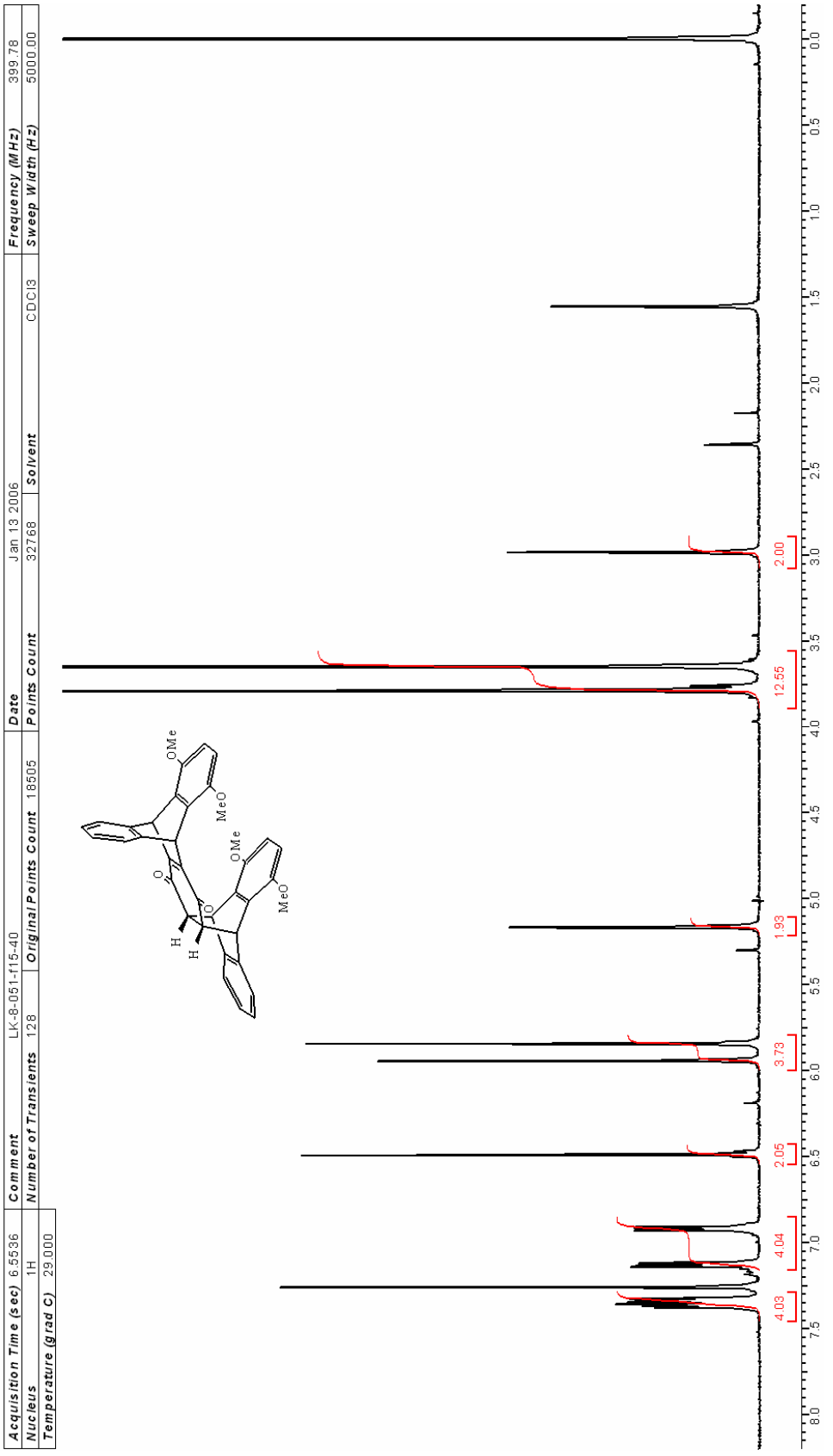
LK-7-076-precipitate-noesy



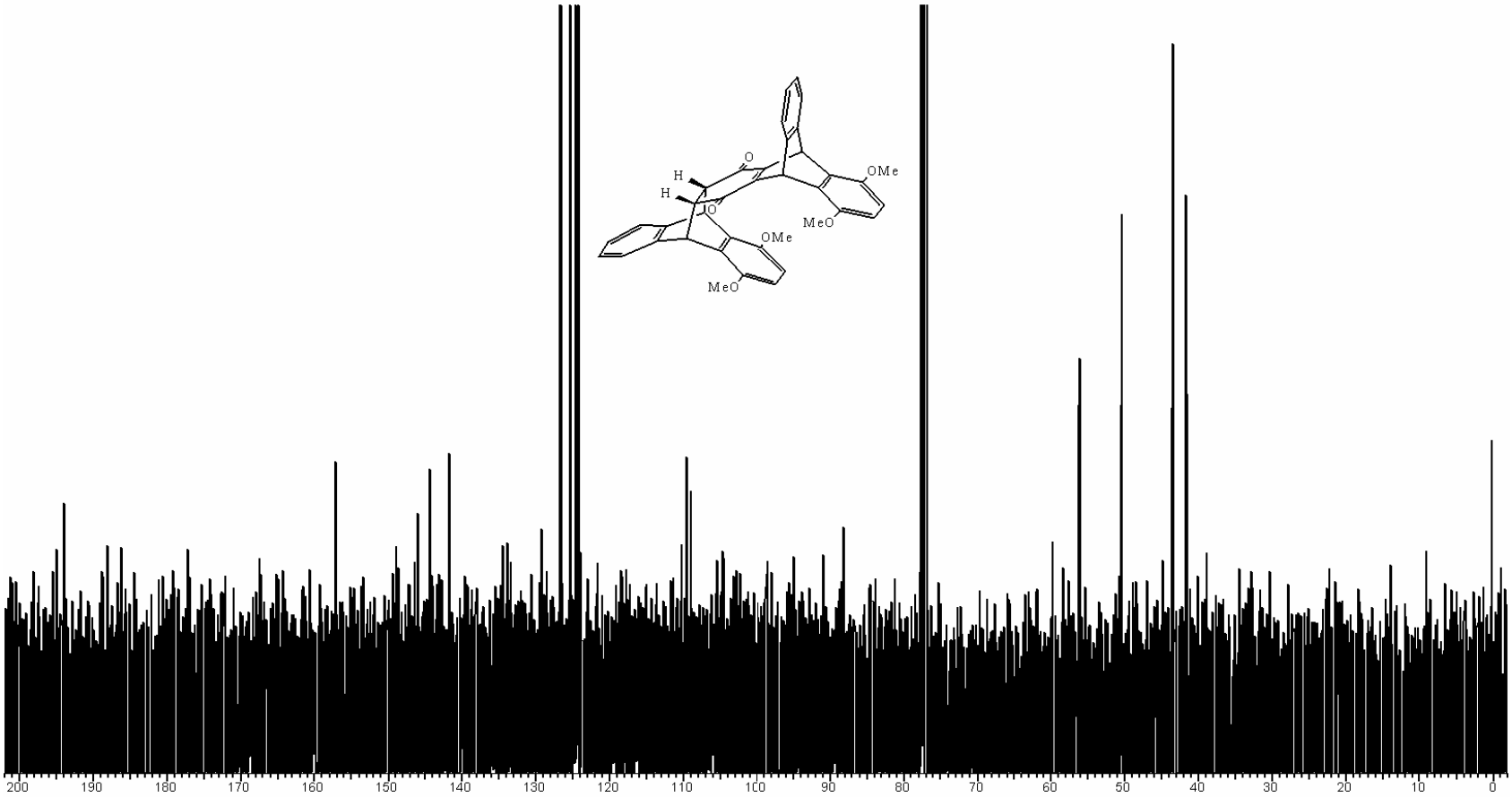


Acquisition Time (sec)	1.3107	*Comment*	LK-7-076-precipitate-c13		*Date*	Jan 6 2006		*Frequency (MHz)*	100.53
Nucleus	13C	*Number of Transients*	6784	*Original Points Count* 29984	*Points Count*	32768	*Solvent* CDCl3	*Sweep Width (Hz)*	25000.00
Temperature (grad C)	29.000								

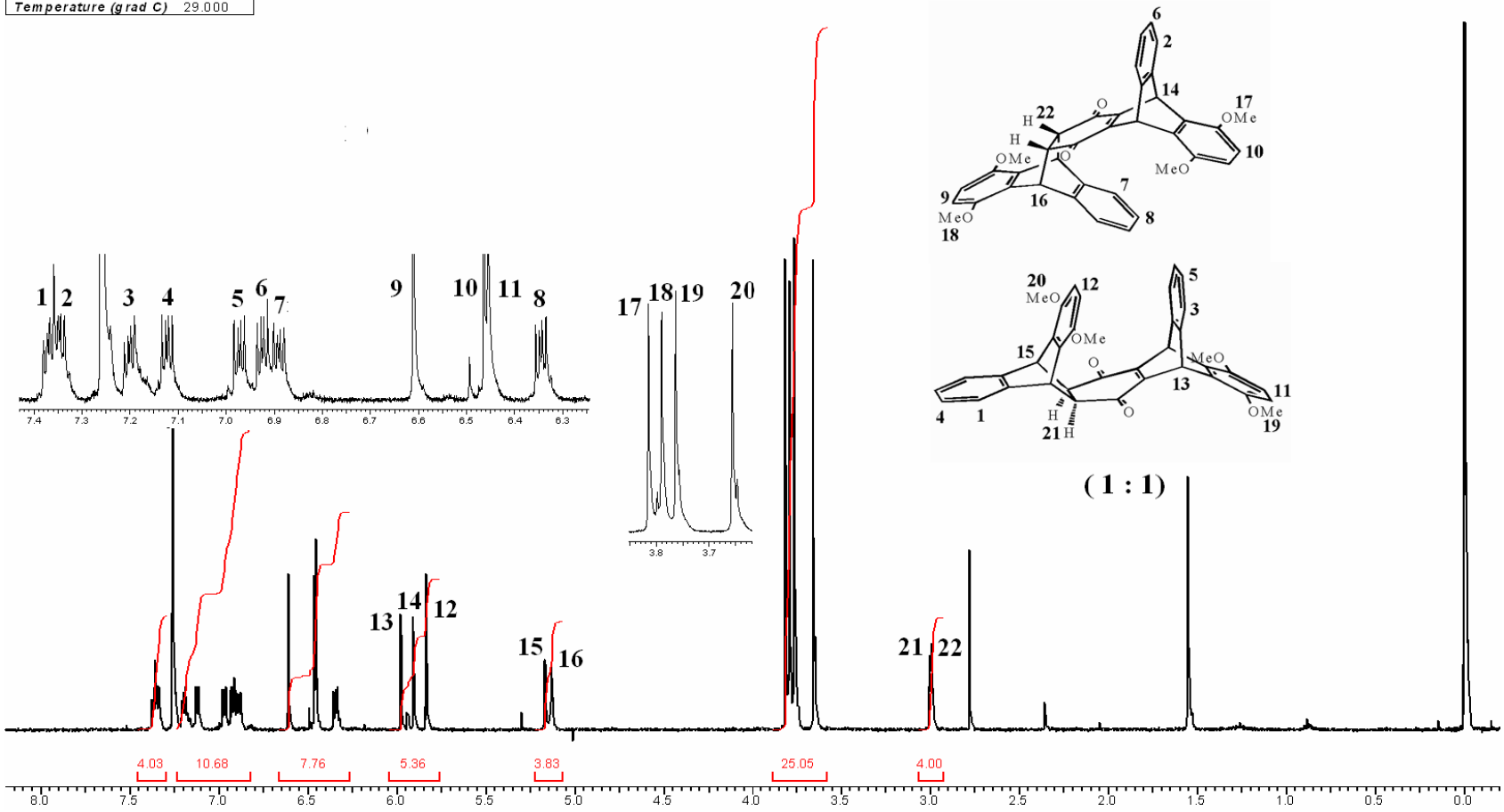



Acquisition Time (sec) 6.5536
Comment LK-8-051-f15-40
Date Jan 13 2006
Frequency (MHz) 399.78
Nucleus 1H
Number of Transients 128
Original Points Count 18505
Points Count 32768
Solvent CDCl3
Sweep Width (Hz) 5000.00
Temperature (grad C) 29.000
OMe
MeO
OMe
MeO
O
O
H
H
4.03
4.04
2.05
3.73
1.93
12.55
2.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

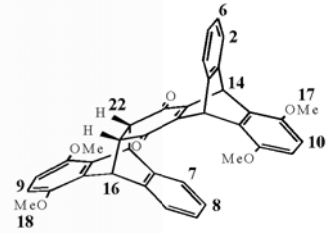
Acquisition Time (sec)	1.3107	***Comment***	LK-8-051-f15-40-c13			***Date***	Jan 13 2006	***Frequency (MHz)***	100.53
Nucleus	13C	***Original Points Count***	29984	***Points Count***	32768	***Solvent***	CDCl3	***Sweep Width (Hz)***	25000.00
Temperature (grad C)	29.000								

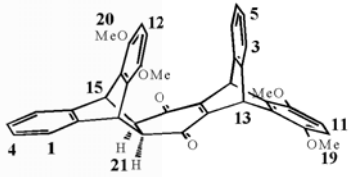


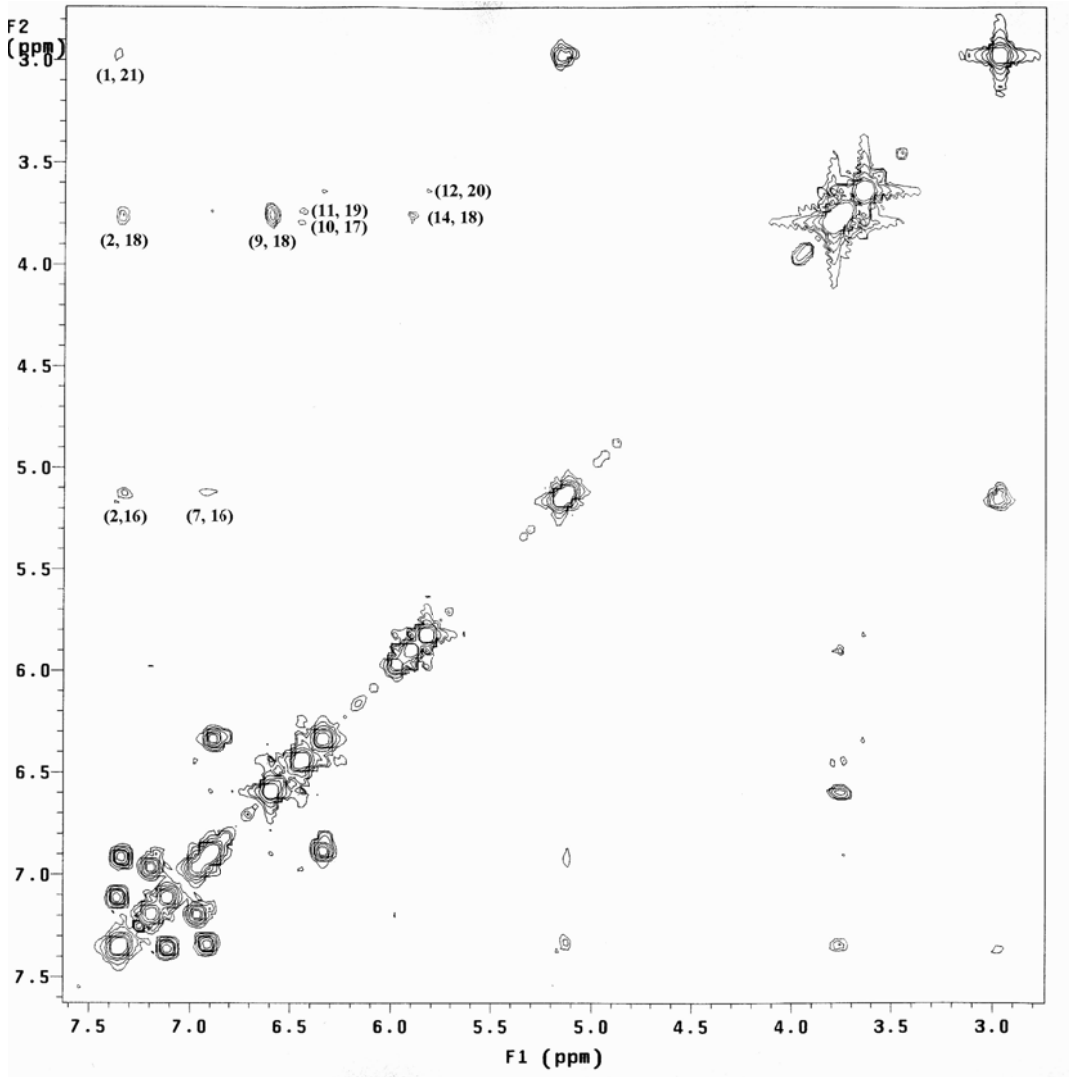
Acquisition Time (sec)	6.5536	*Comment*	LK-8-030-filtrate-recrystal		*Date*	Jan 13 2006		*Frequency (MHz)*	399.78
Nucleus	1H	*Number of Transients*	128	*Original Points Count* 18505	*Points Count*	32768	*Solvent* CDCl3	*Sweep Width (Hz)*	5000.00
Temperature (grad C)	29.000								



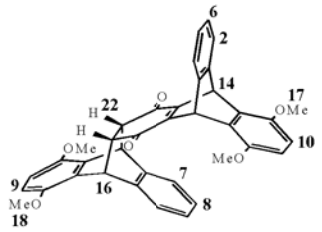
LK-8-030-3-cosy

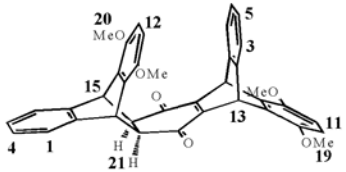




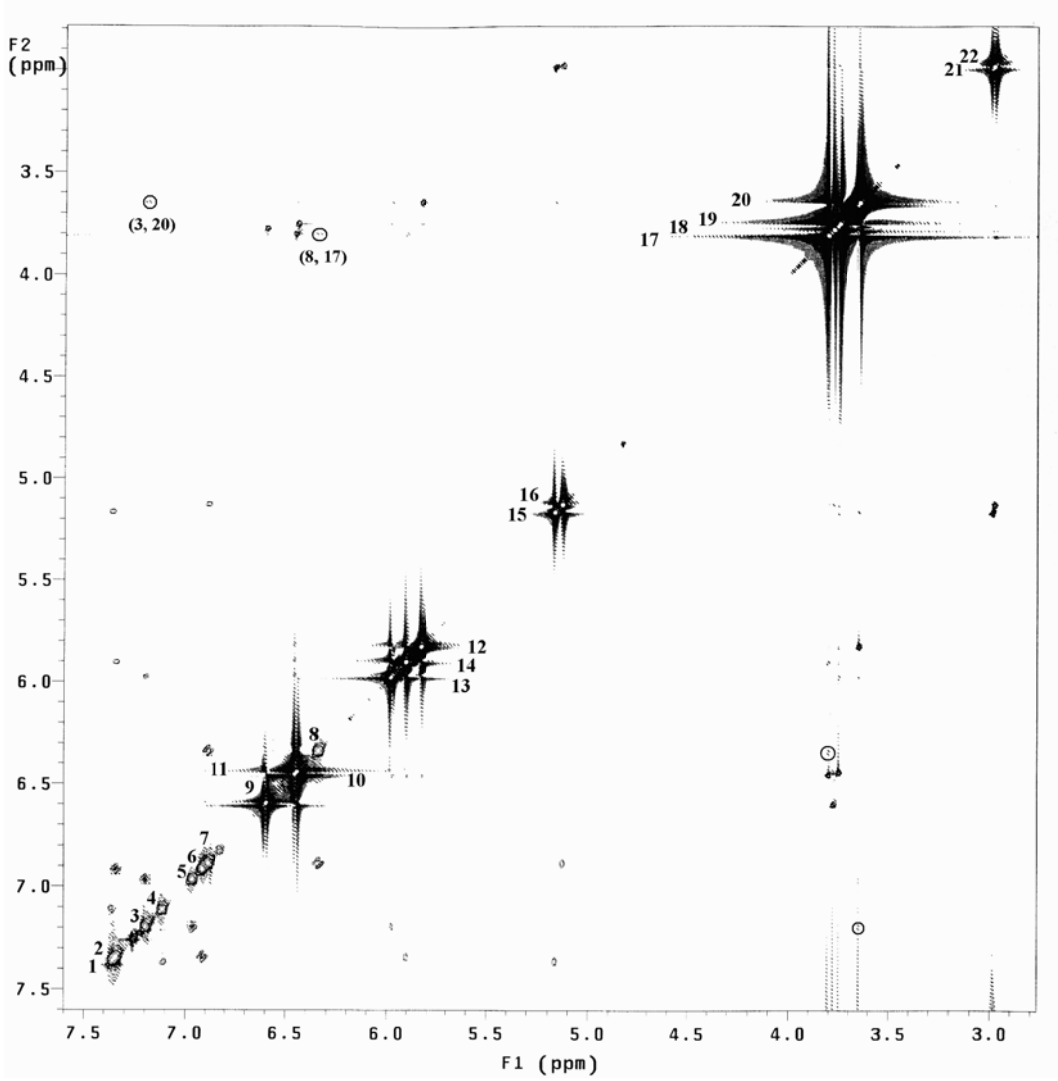


LK-8-30-3-noesy

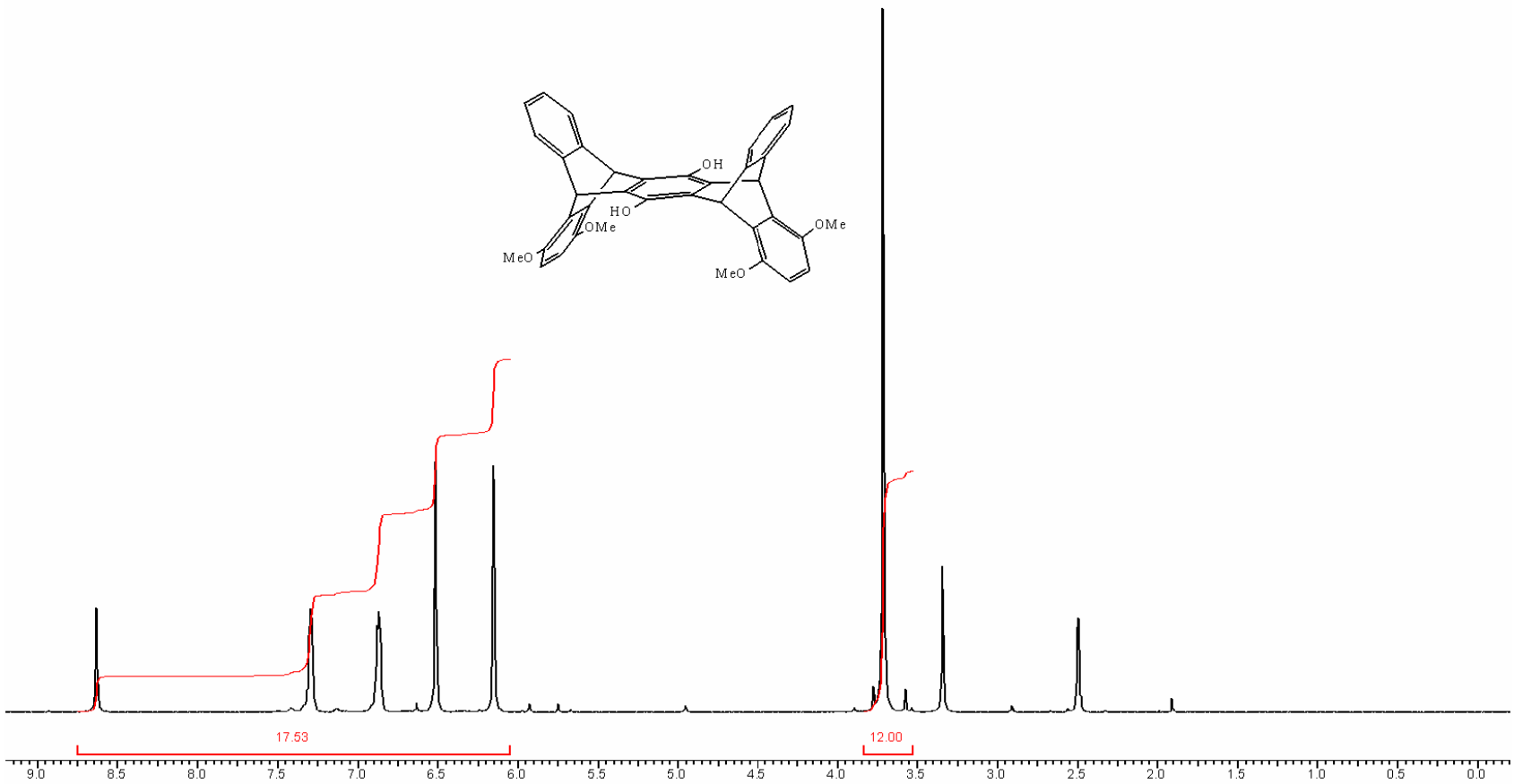


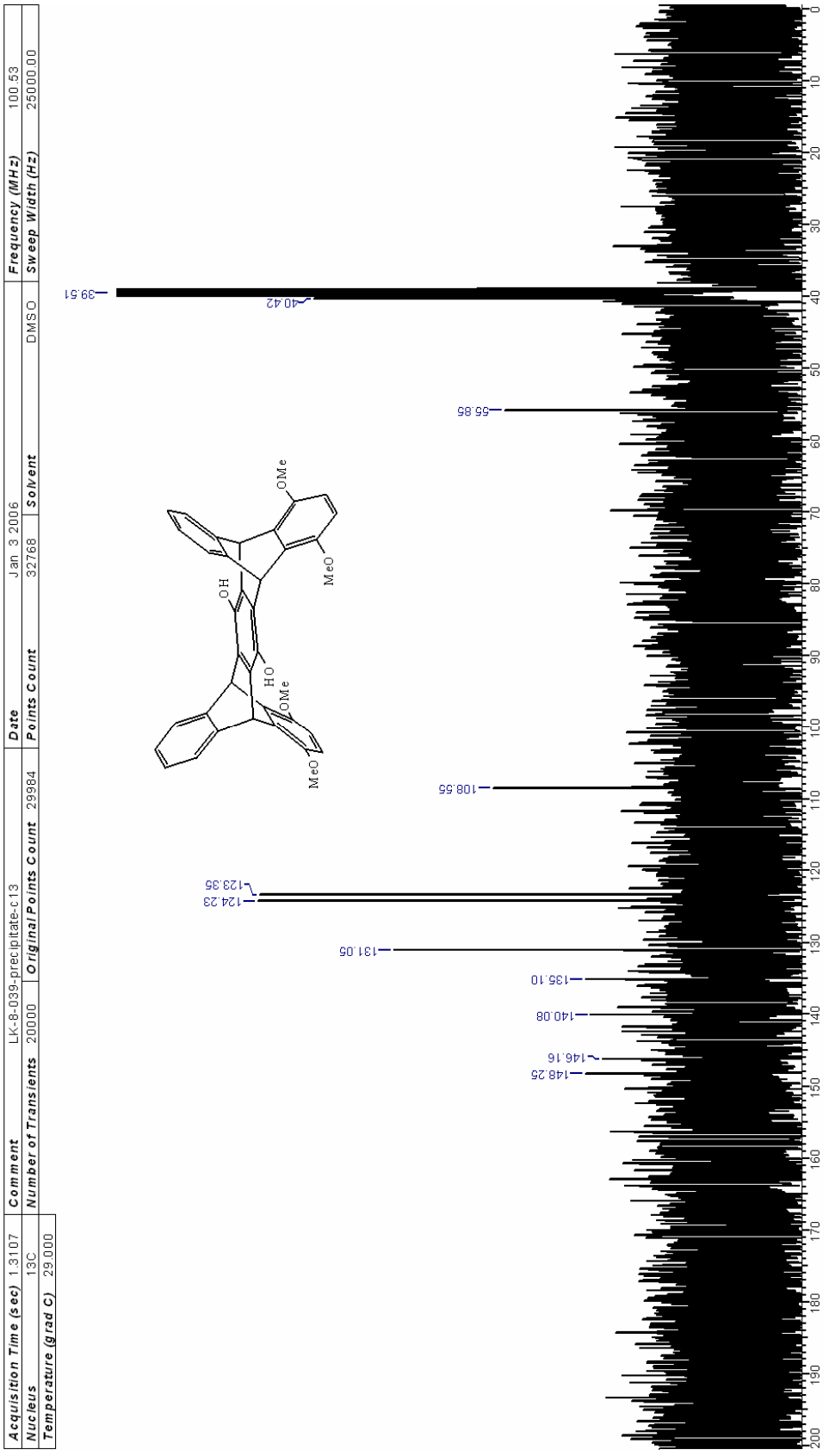


(important through-space NOE cross-peaks are noted with circles)

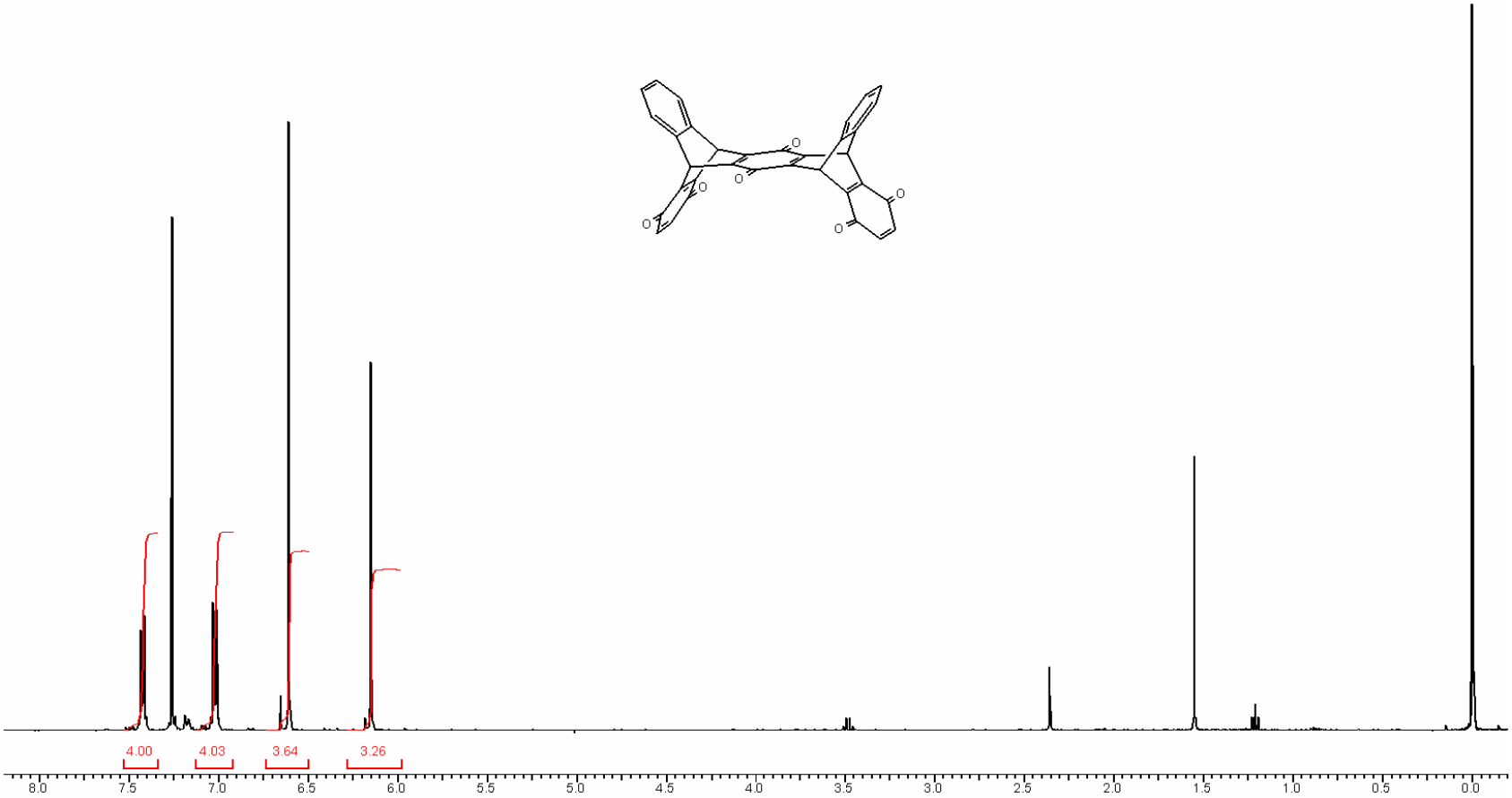


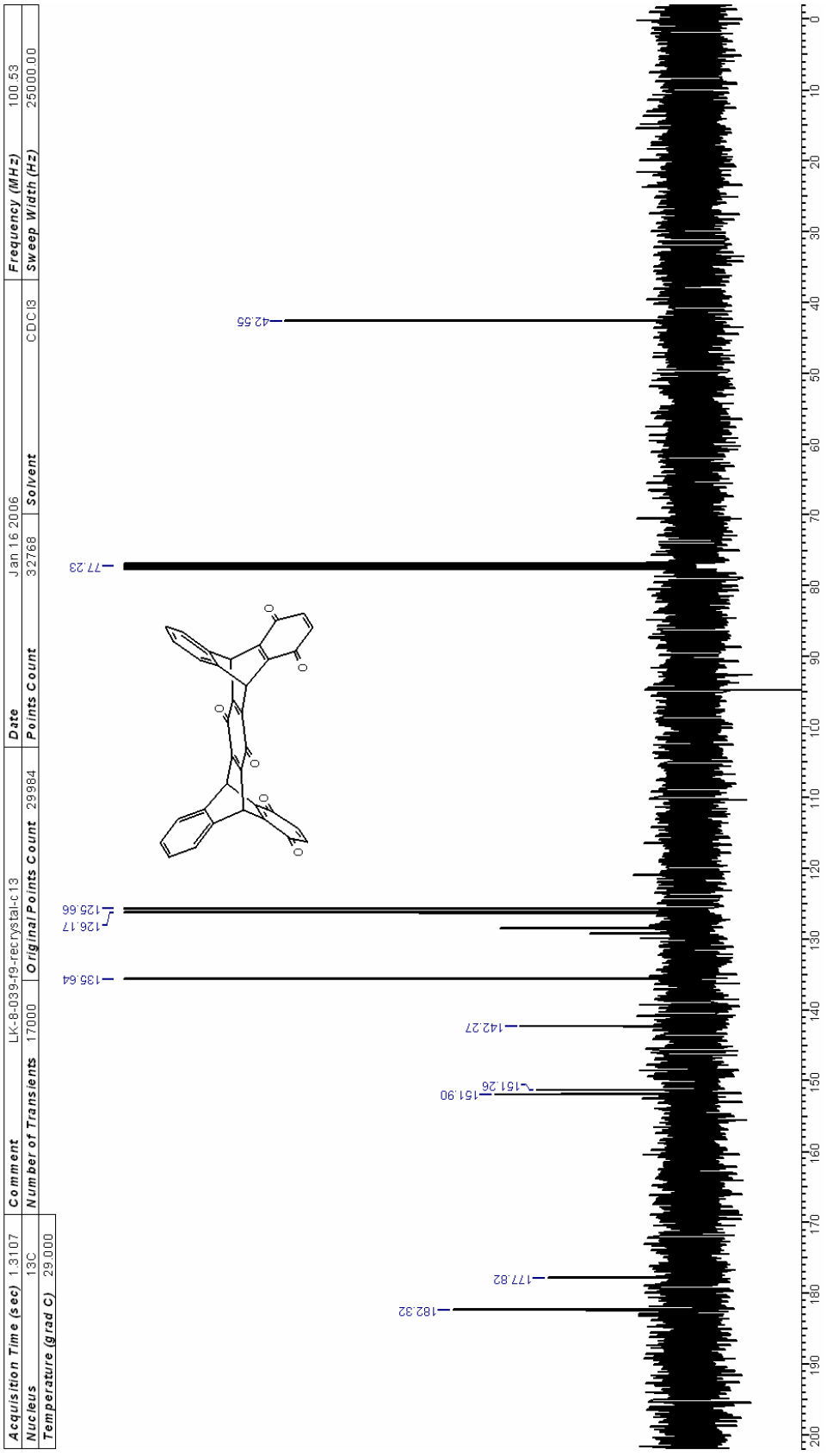
Acquisition Time (sec)	6.5536	***Comment***	LK-8-039-precipitate		***Date***	Jan 3 2006		***Frequency (MHz)***	399.78
Nucleus	1H	***Number of Transients***	128	***Original Points Count*** 18505	***Points Count***	32768	***Solvent*** DMSO	***Sweep Width (Hz)***	5000.00
Temperature (grad C)	29.000								



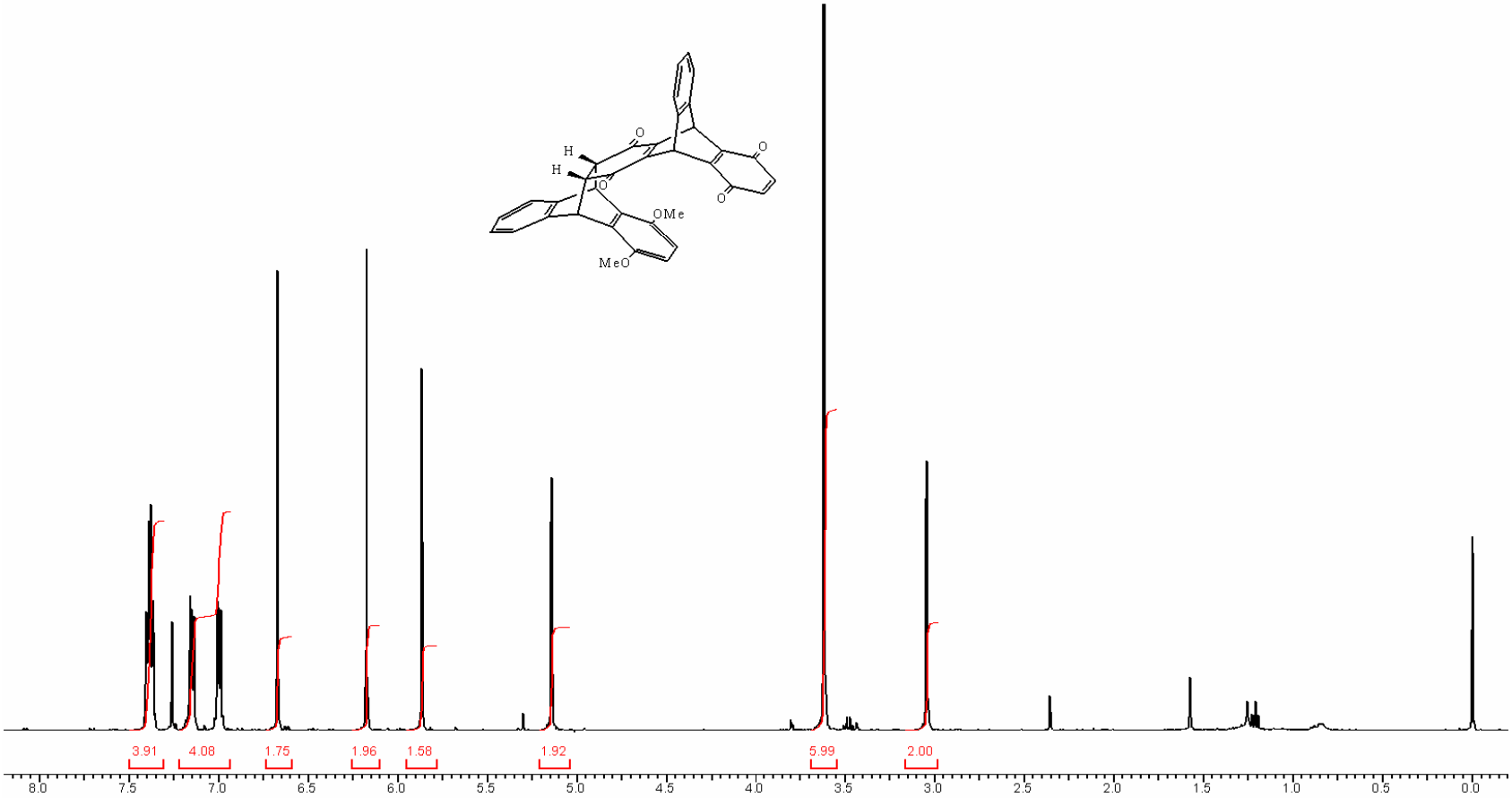

Acquisition Time (sec) 1.3107
Comment LK-8-039-precipitate-c13
Date Jan 3 2006
Frequency (MHz) 100.53
Nucleus 13C
Number of Transients 20000
Original Points Count 29984
Points Count 32768
Solvent DMSO
Sweep Width (Hz) 25000.00
Temperature (grad C) 29.000
39.51
40.42
55.85
108.55
123.35
124.23
131.05
135.10
140.08
146.16
148.25
OMe
MeO
OH
HO
OMe
MeO

Acquisition Time (sec)	6.5536	***Comment***	LK-8-052-f9-recrystal		***Date***	Jan 12 2006		***Frequency (MHz)***	399.78
Nucleus	1H	***Number of Transients***	128	***Original Points Count*** 18505	***Points Count***	32768	***Solvent*** CDCl3	***Sweep Width (Hz)***	5000.00
Temperature (grad C)	29.000								

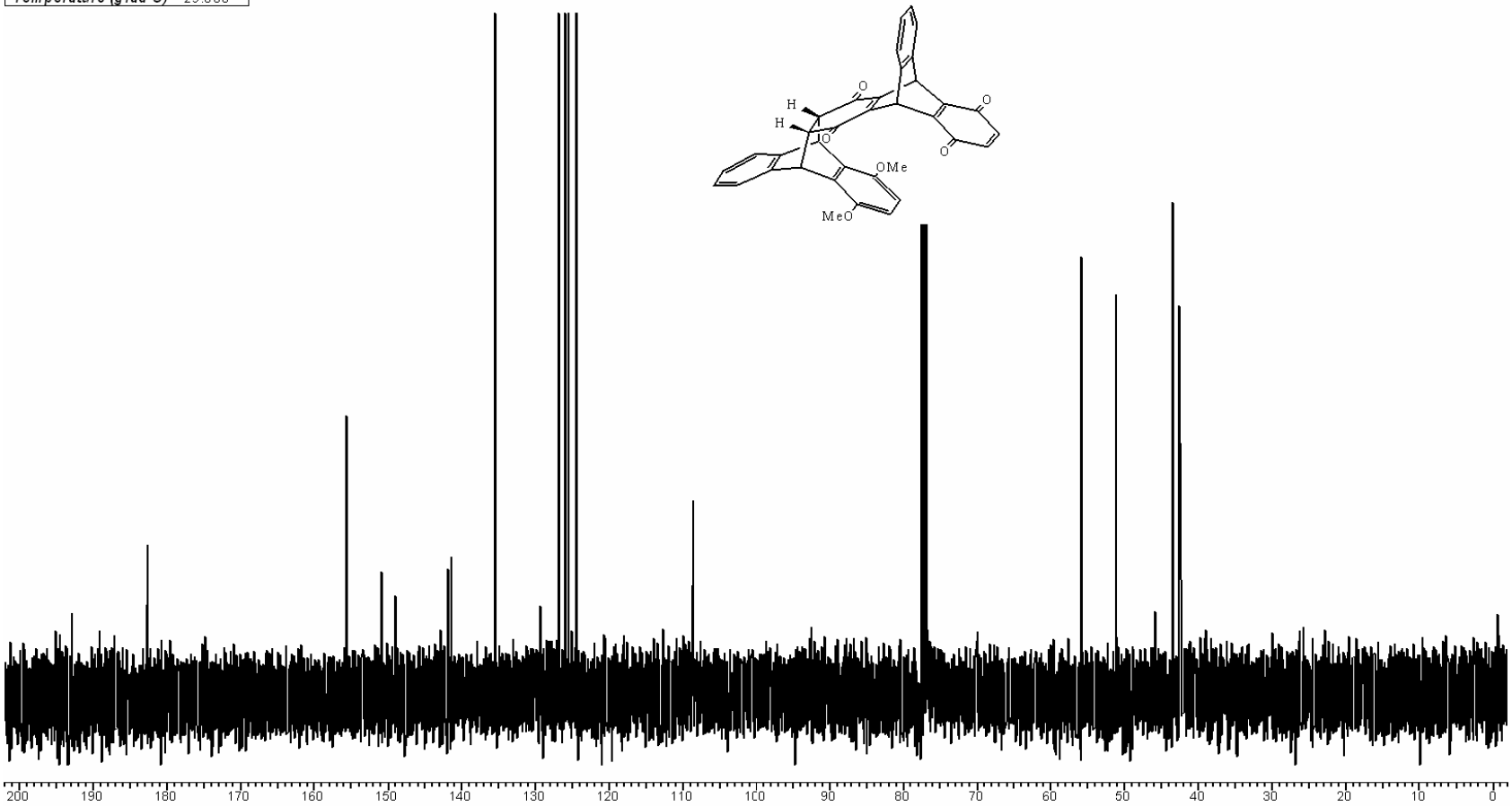


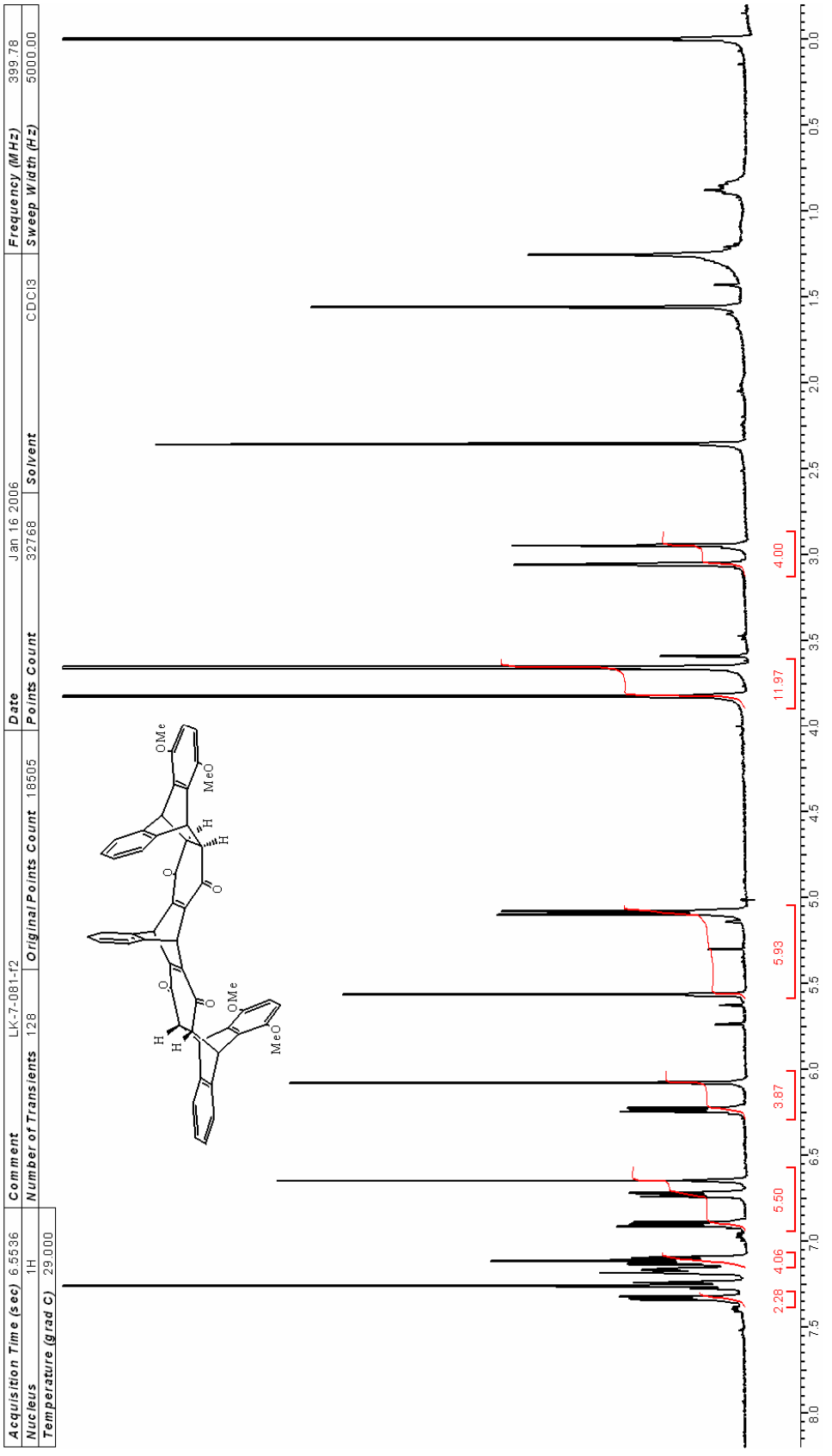

Acquisition Time (sec) 1.3107
Comment LK-8-039-f9-recrystal-c13
Date Jan 16 2006
Frequency (MHz) 100.53
Nucleus 13C
Number of Transients 17000
Original Points Count 29984
Points Count 32768
Solvent CDCl3
Sweep Width (Hz) 25000.00
Temperature (grad C) 29.000
42.55
77.23
125.66
126.17
135.64
142.27
151.26
151.90
177.82
182.32

Acquisition Time (sec)	6.5536	*Comment*	LK-8-034-f1		*Date*	Dec 26 2005		*Frequency (MHz)*	399.78
Nucleus	1H	*Number of Transients*	128	*Original Points Count* 18505	*Points Count*	32768	*Solvent* CDCl3	*Sweep Width (Hz)*	5000.00
Temperature (grad C)	29.000								

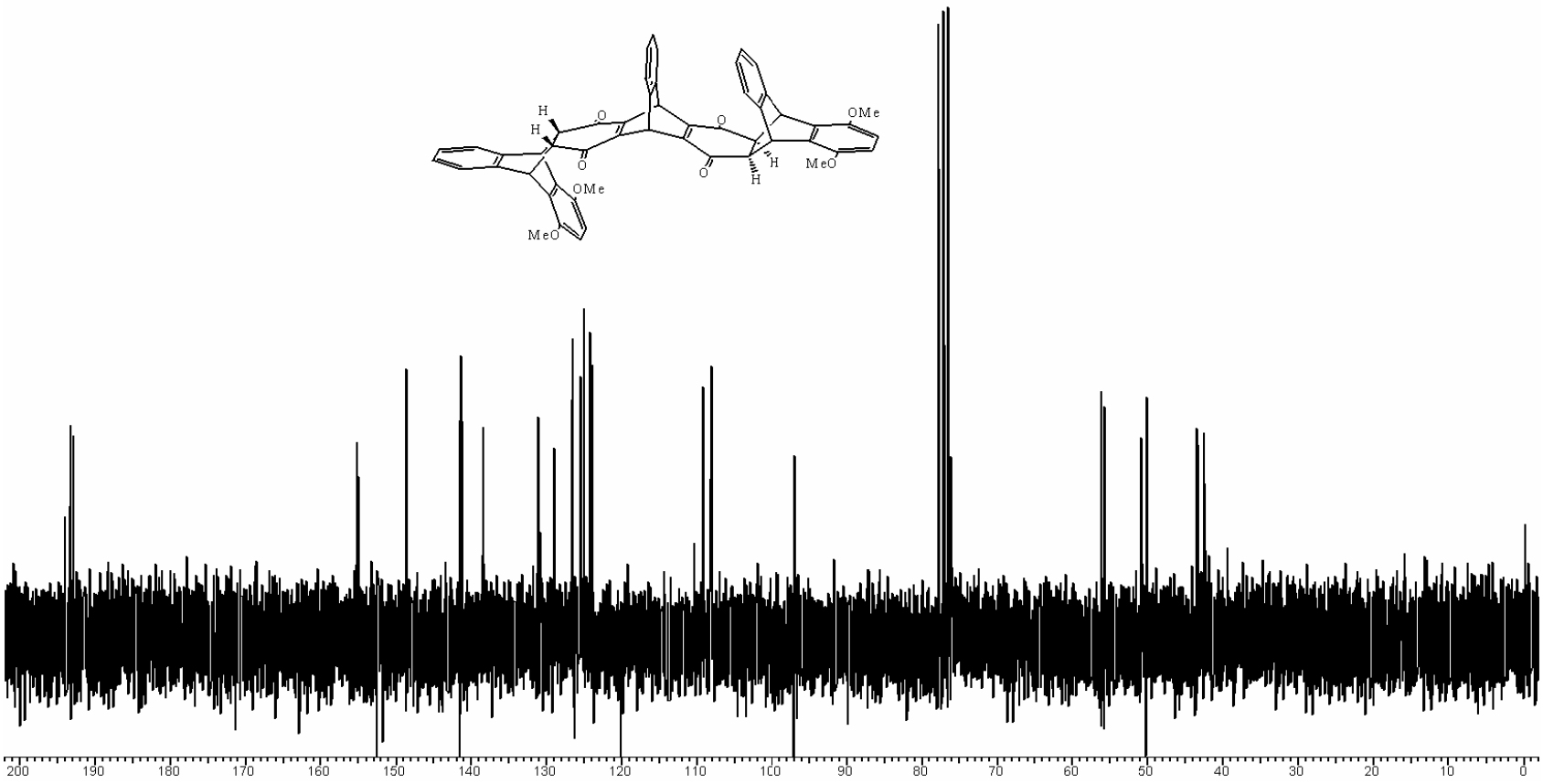


Acquisition Time (sec)	1.3107	*Comment*	LK-8-034-f1-c13		*Date*	Dec 26 2005		*Frequency (MHz)*	100.53
Nucleus	13C	*Number of Transients*	20000	*Original Points Count* 29984	*Points Count*	32768	*Solvent* CDCl3	*Sweep Width (Hz)*	25000.00
Temperature (grad C)	29.000								

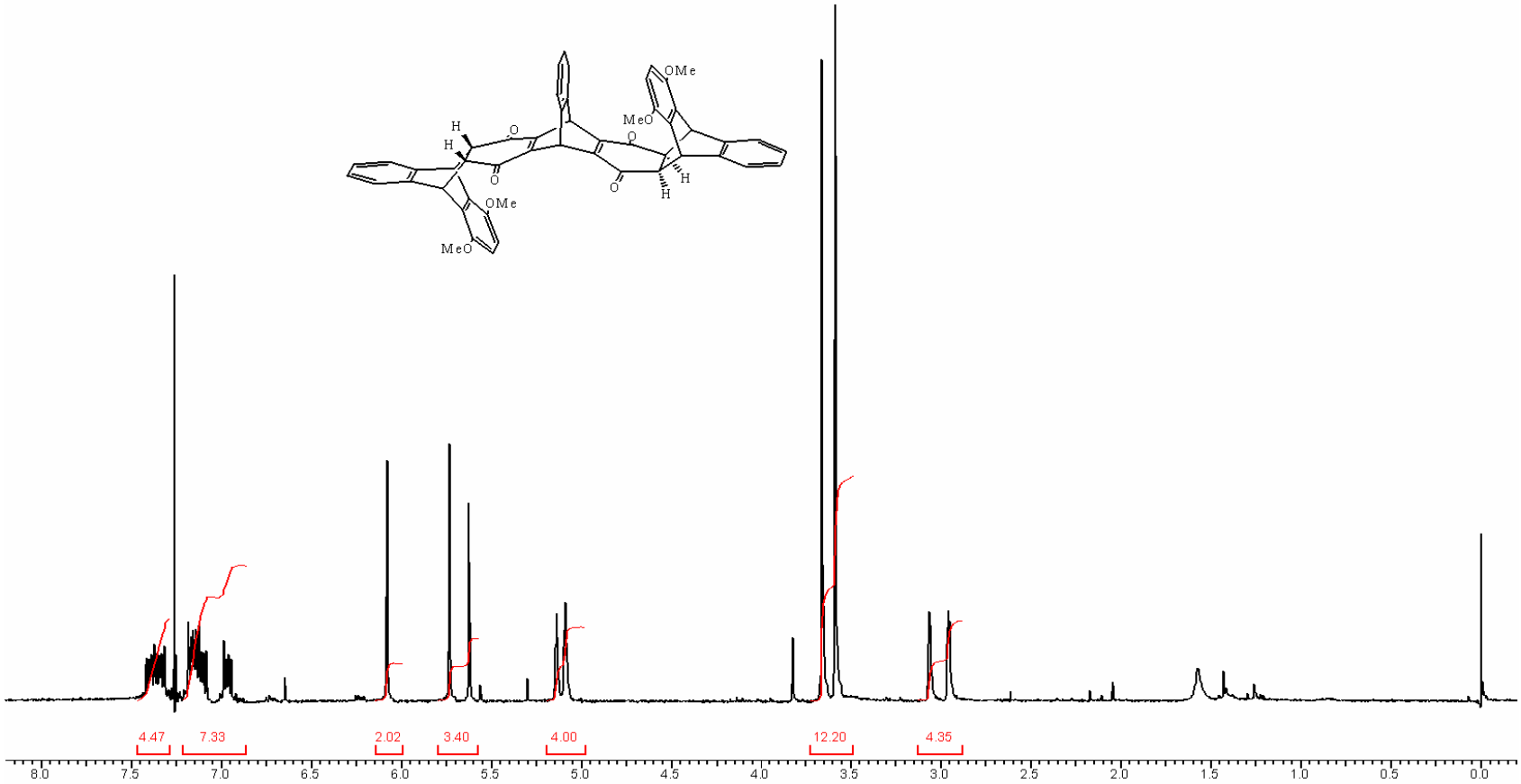



Acquisition Time (sec) 6.5536
Comment LK-7-081-f2
Date Jan 16 2006
Frequency (MHz) 399.78
Nucleus 1H
Number of Transients 128
Original Points Count 18505
Points Count 32768
Solvent CDCl3
Sweep Width (Hz) 5000.00
Temperature (grad C) 29.000
OMe
MeO
H
H
O
O
OMe
MeO
2.28
4.06
5.50
3.87
5.93
11.97
4.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

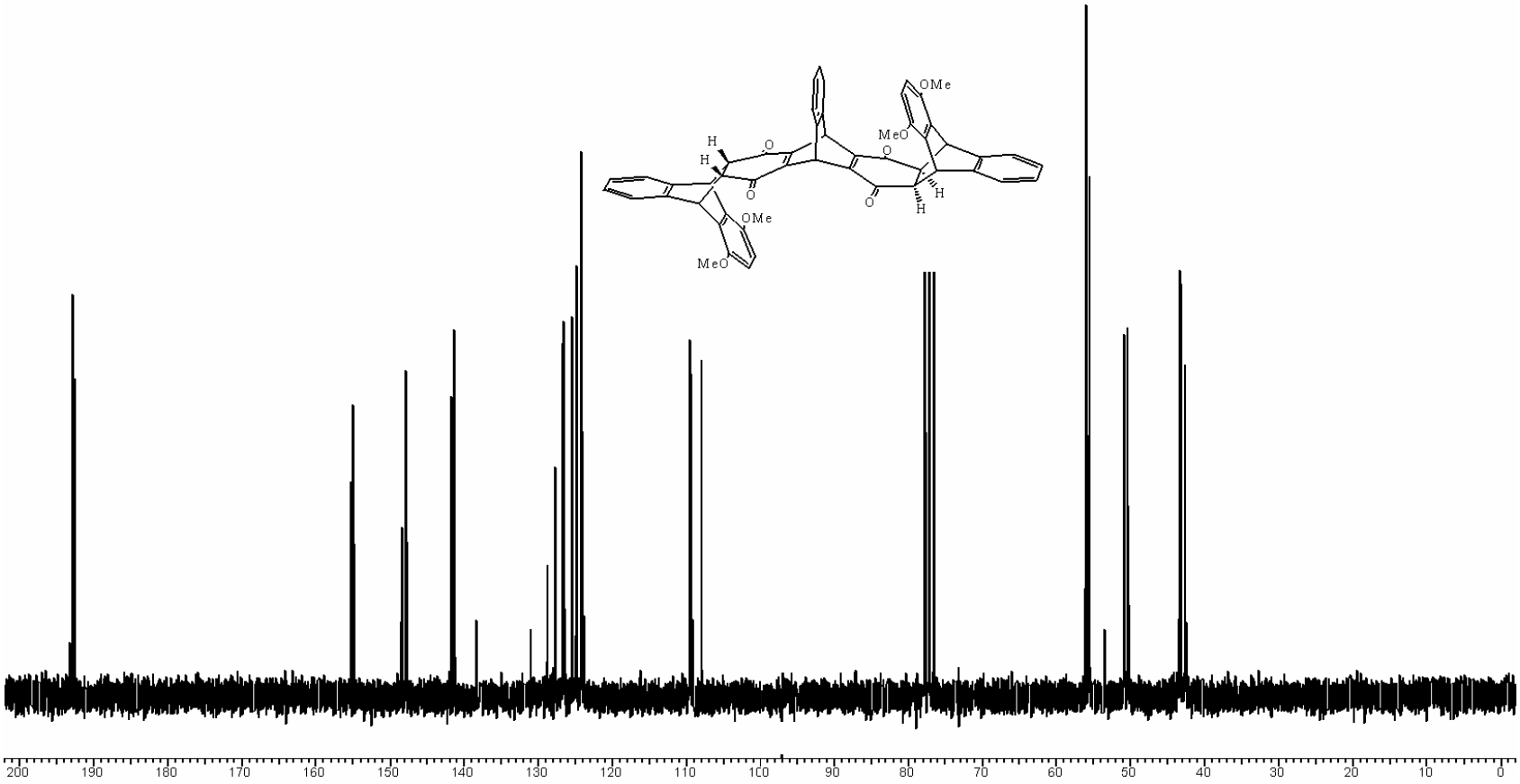
Acquisition Time (sec) 2.6214	***Comment***	LK-7-081-dp-C13		***Date***	Sep 28 2006			***Frequency (MHz)***	50.29
Nucleus 13C	***Number of Transients***	20000	***Original Points Count*** 18720	***Points Count***	32768	***Solvent***	CDCl3	***Sweep Width (Hz)***	12500.00
Temperature (grad C) 29.000									



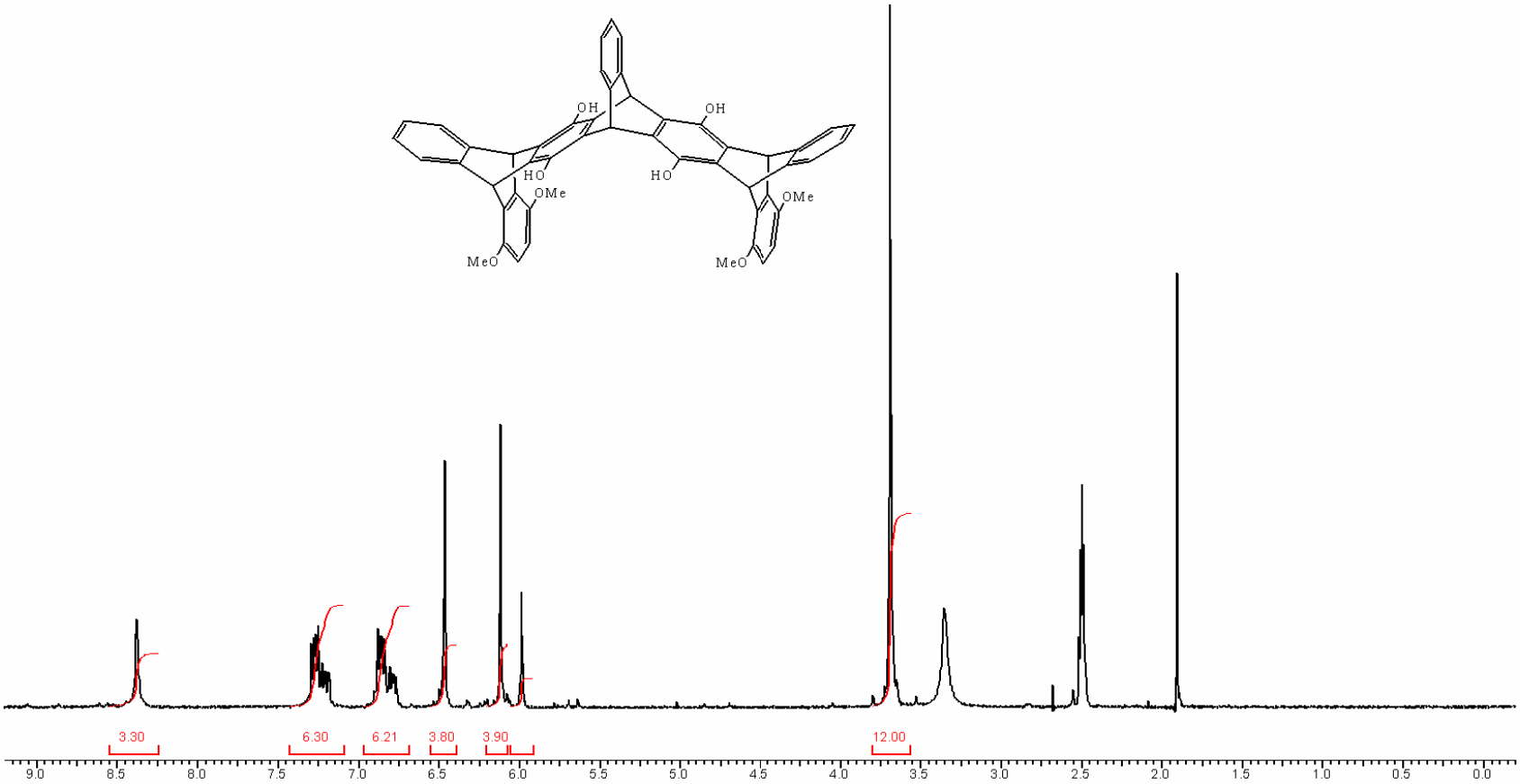
Acquisition Time (sec)	3.2768	***Comment***	LK-8-070-2		***Date***	Feb 7 2006		***Frequency (MHz)***	199.98
Nucleus	1H	***Number of Transients***	128	***Original Points Count*** 4992	***Points Count***	8192	***Solvent*** CDCl3	***Sweep Width (Hz)***	2500.00
Temperature (grad C)	29.000								

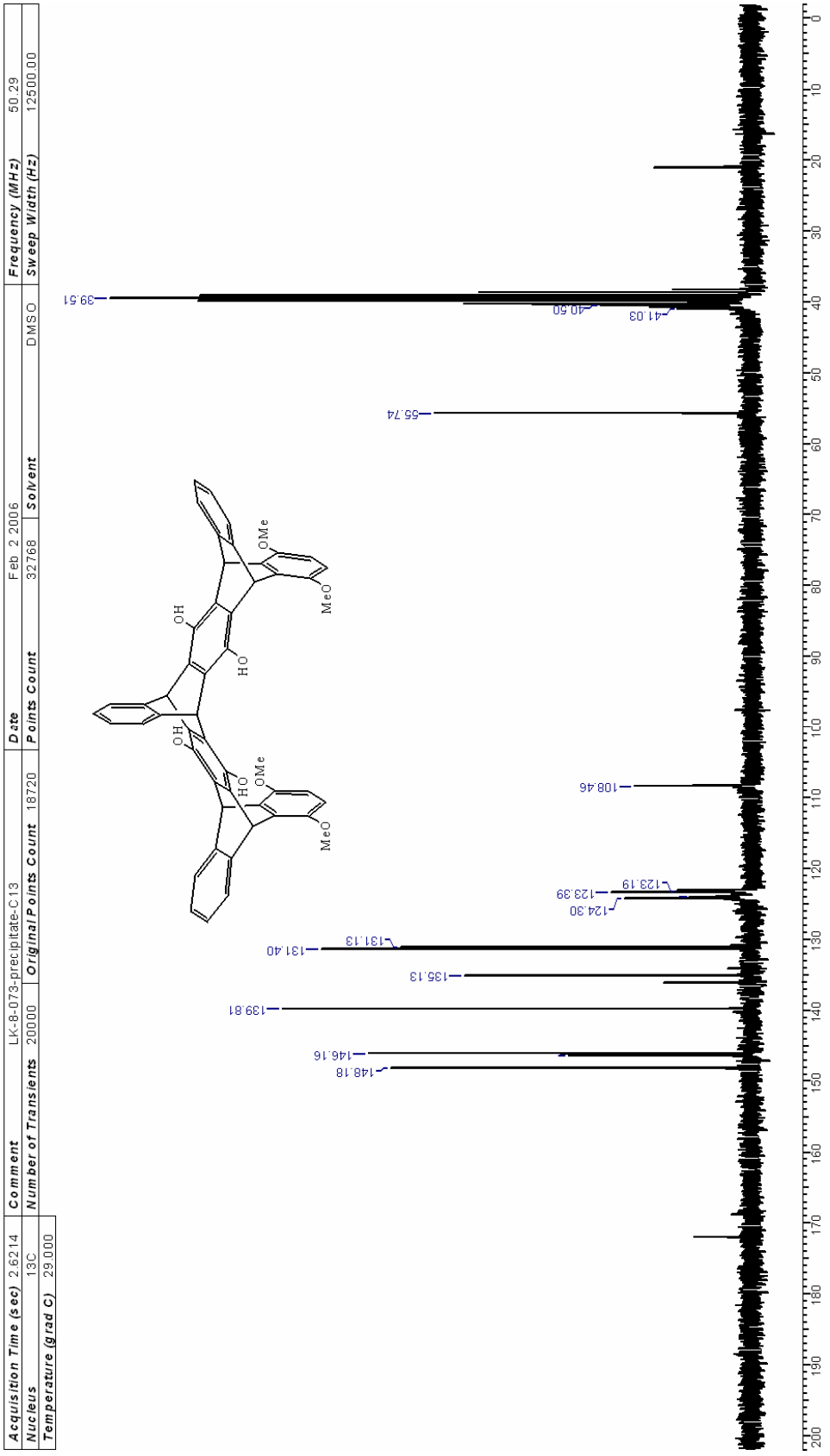


Acquisition Time (sec) 2.6214	***Comment***	LK-7-081-dp-isomer-c13		***Date***	Sep 29 2006			***Frequency (MHz)***	50.29
Nucleus 13C	***Number of Transients***	20000	***Original Points Count*** 18720	***Points Count***	32768	***Solvent***	CDCl3	***Sweep Width (Hz)***	12500.00
Temperature (grad C) 29.000									

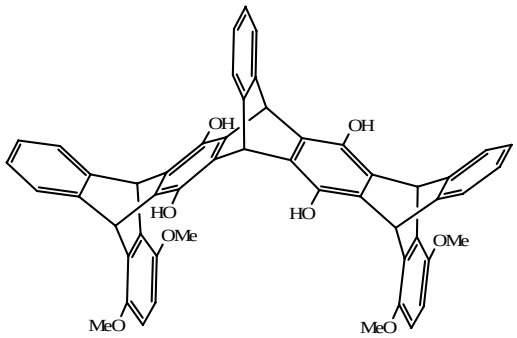


Acquisition Time (sec)	3.2768	***Comment***	LK-8-073-precipitate		***Date***	Feb 1 2006		***Frequency (MHz)***	199.98
Nucleus	1H	***Number of Transients***	128	***Original Points Count*** 4992	***Points Count***	8192	***Solvent*** DMSO	***Sweep Width (Hz)***	2500.00
Temperature (grad C)	29.000								




Acquisition Time (sec) 2.6214
Comment LK-8-073-precipitate-C13
Date Feb 2 2006
Frequency (MHz) 50.29
Nucleus 13C
Number of Transients 20000
Original Points Count 18720
Points Count 32768
Solvent DMSO
Sweep Width (Hz) 12500.00
Temperature (grad C) 29.000
39.51
40.50
41.03
55.74
108.46
123.19
123.39
124.30
131.13
131.40
135.13
139.81
146.16
148.18
OMe
MeO
OH
HO
OH
HO
OMe
MeO

LK-8-073-precipitate



$(M+H)^+$: $C_{52}H_{39}O_8$

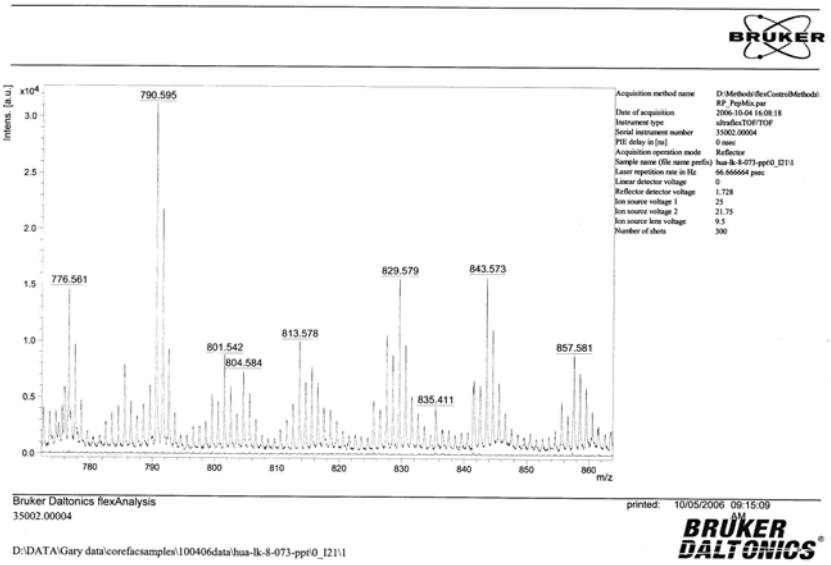
Exact Mass: 791.2645
m/z: 791.26 (100.0%), 792.27 (57.0%), 793.27 (17.6%), 794.27 (3.7%)

$(M+Na)^+$: $C_{52}H_{38}O_8Na$

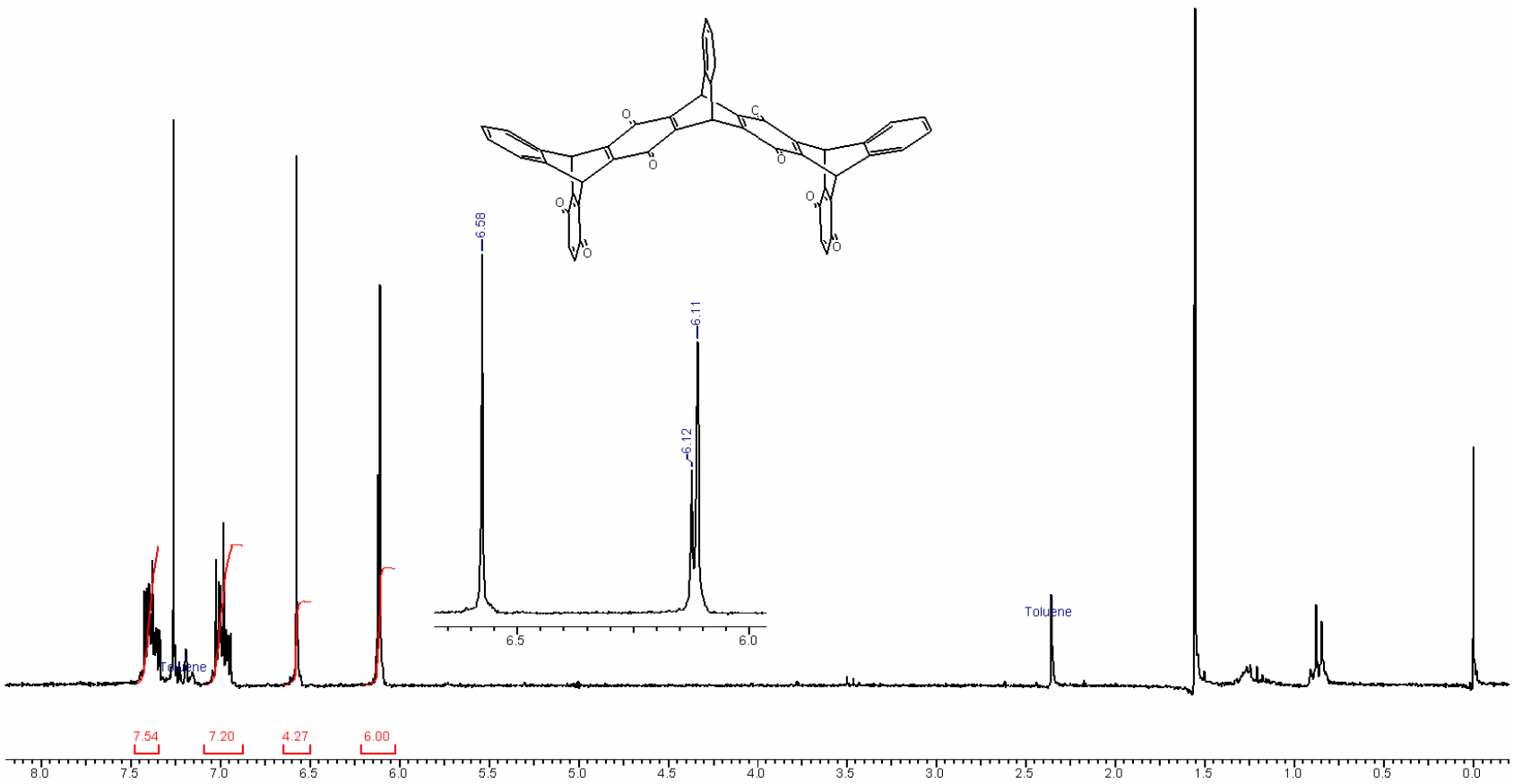
Exact Mass: 813.2464
m/z: 813.25 (100.0%), 814.25 (57.0%), 815.25 (17.3%), 816.26 (2.9%)

$(M+K)^+$: $C_{52}H_{38}O_8K$

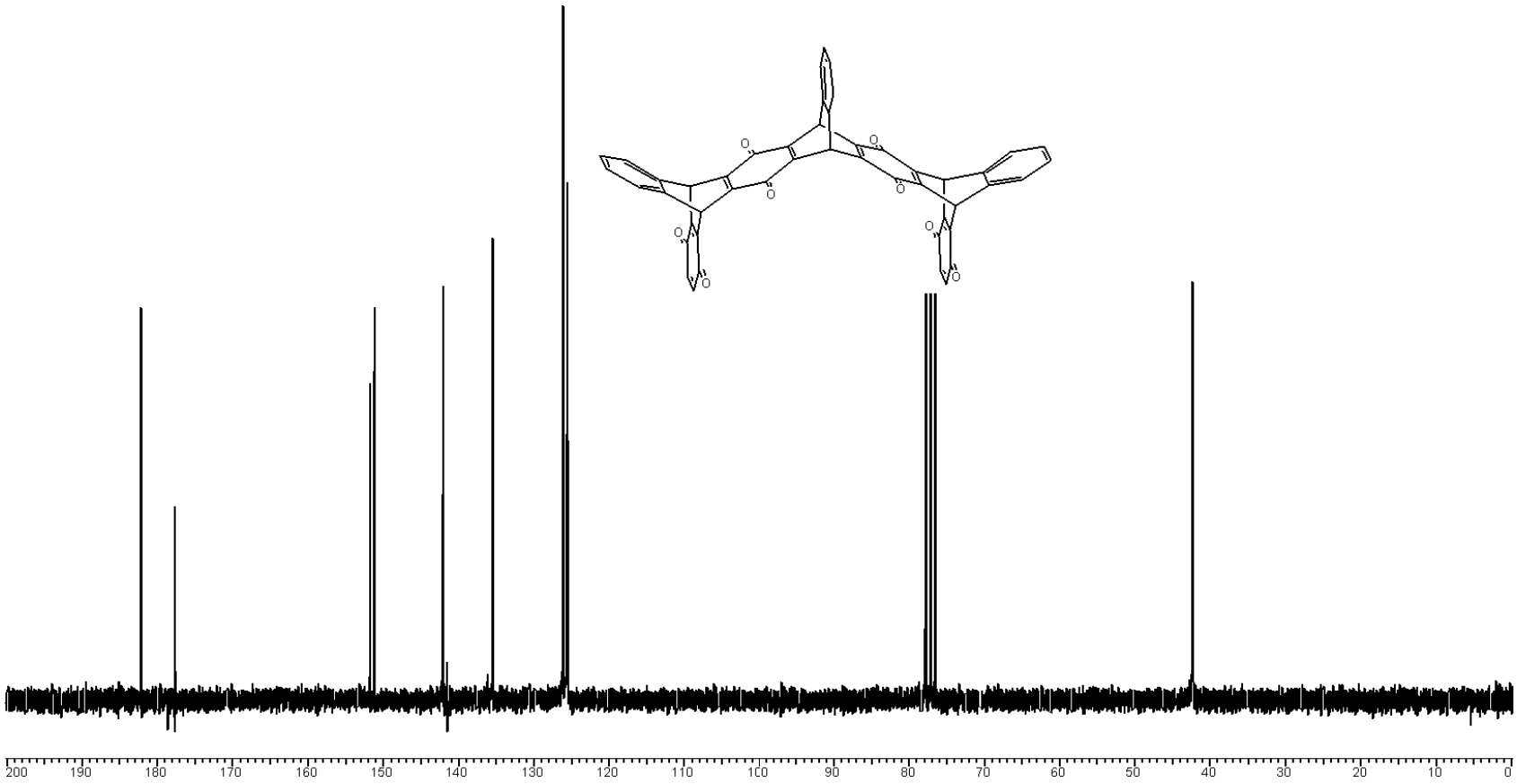
Exact Mass: 829.2204
m/z: 829.22 (100.0%), 830.22 (56.6%), 831.23 (15.9%), 831.22 (8.9%), 832.22 (4.1%), 832.23 (3.9%), 833.23 (1.8%)



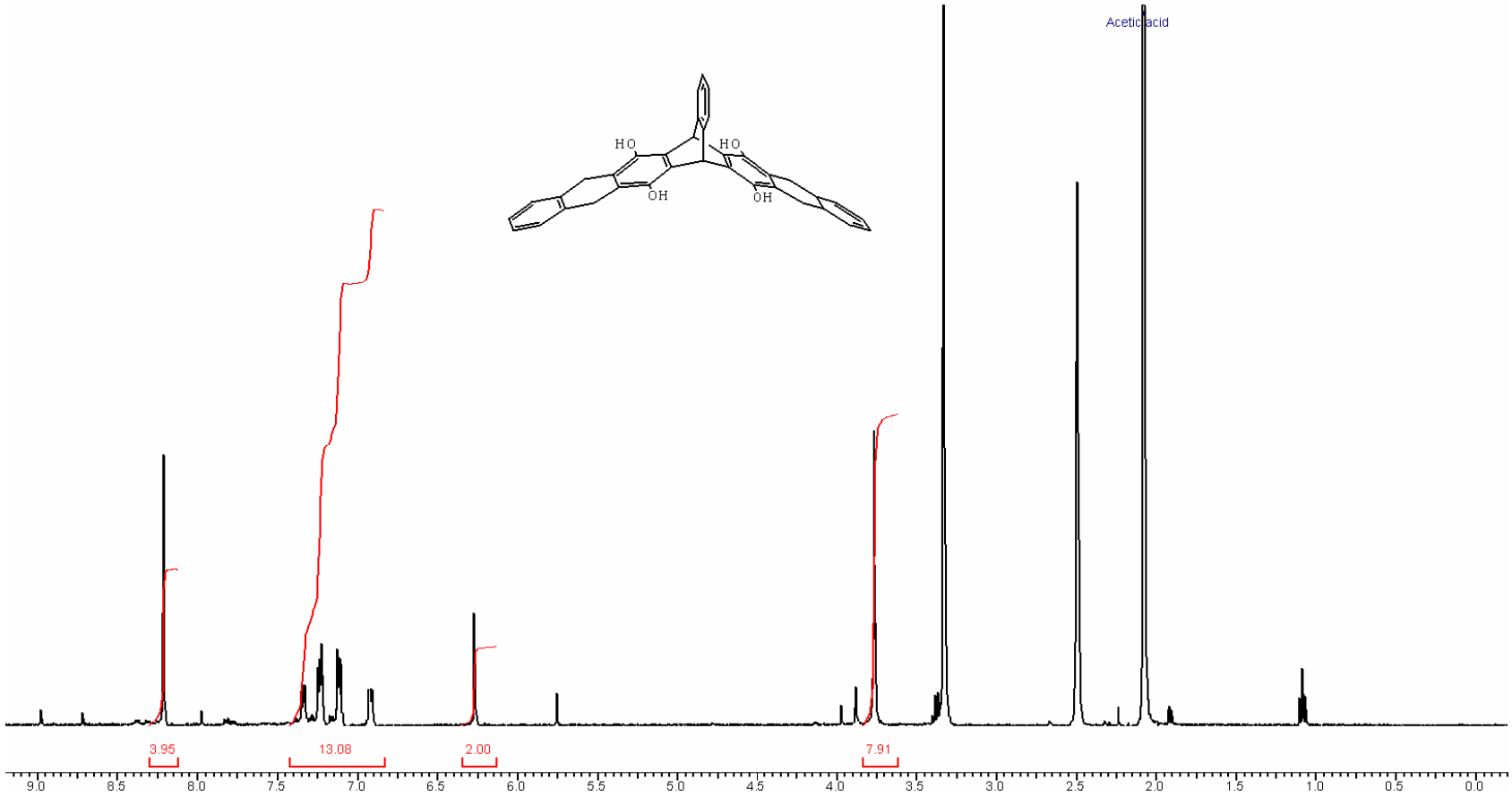
Acquisition Time (sec)	3.2768	***Comment***	LK-8-104-f9-11-recrystal		***Date***	Mar 16 2006		***Frequency (MHz)***	199.98
Nucleus	1H	***Number of Transients***	128	***Original Points Count*** 4992	***Points Count***	8192	***Solvent*** CDCl3	***Sweep Width (Hz)***	2500.00
Temperature (grad C)	29.000								

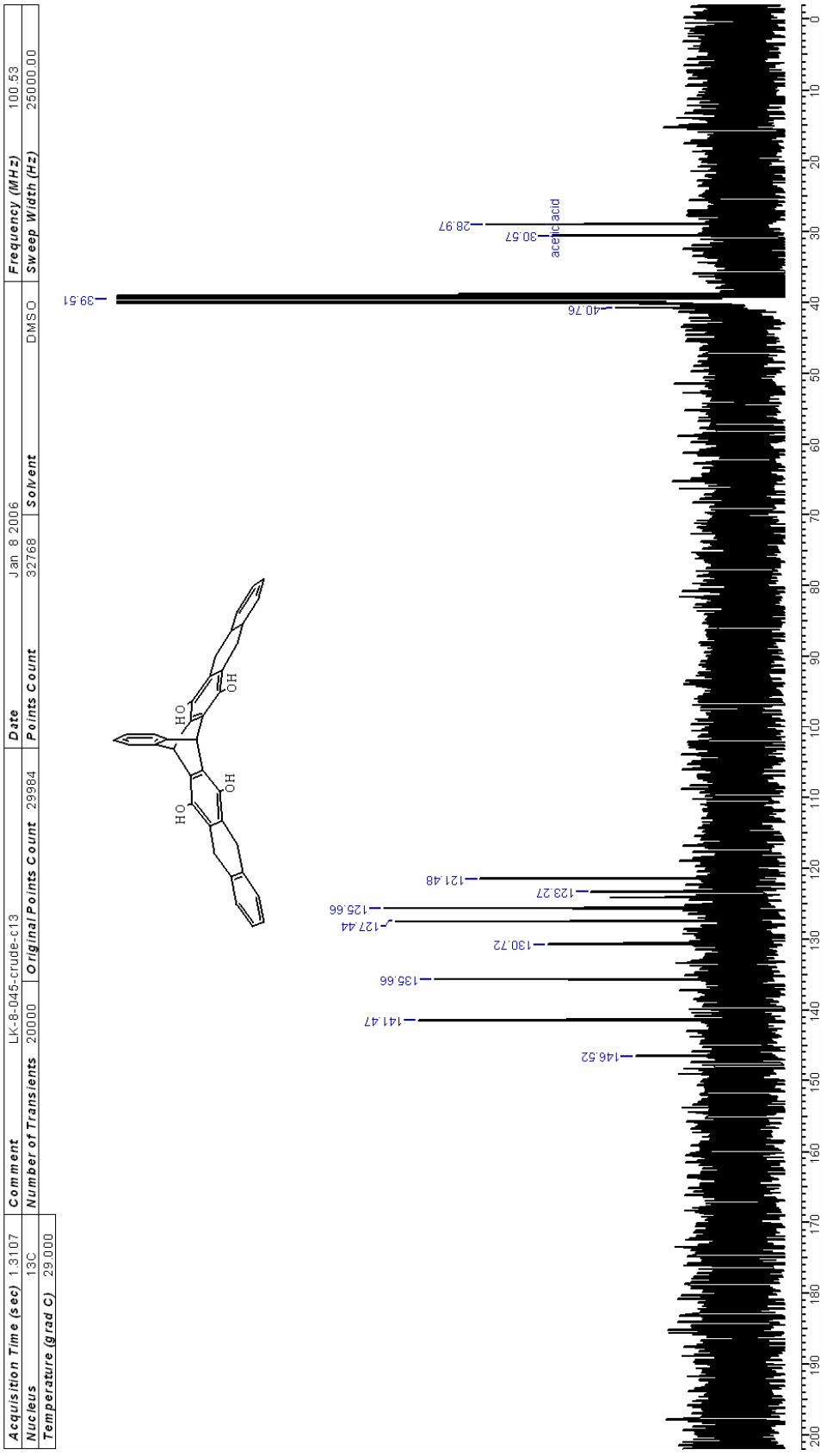


Acquisition Time (sec) 2.6214	***Comment*** LK-8-104-dp-c13			***Date*** Apr 21 2006				***Frequency (MHz)***	50.29
Nucleus 13C	***Number of Transients*** 20000	***Original Points Count*** 18720		***Points Count*** 32768		***Solvent*** CDCl3		***Sweep Width (Hz)***	12500.00
Temperature (grad C) 29.000									

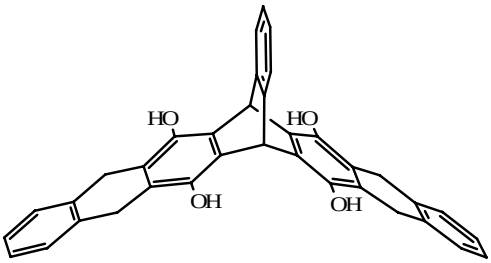


Acquisition Time (sec)	6.5536	***Comment***	LK-8-045-crude	***Date***	Jan 5 2006			***Frequency (MHz)***	399.78
Nucleus	1H	***Number of Transients***	128	***Original Points Count***	18505	***Points Count***	32768	***Solvent***	DMSO	***Sweep Width (Hz)***	5000.00
Temperature (grad C)	29.000										




Acquisition Time (sec) 1.3107
Comment LK-8-045-crude-c13
Date Jan 8 2006
Frequency (MHz) 100.53
Nucleus 13C
Number of Transients 20000
Original Points Count 29984
Points Count 32768
Solvent DMSO
Sweep Width (Hz) 25000.00
Temperature (grad C) 29.000
HO
OH
HO
OH
146.52
141.47
135.66
130.72
127.44
125.66
123.27
121.48
39.51
40.76
30.57
28.97
acetic acid
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200

LK-10-043-dp



$(M+H)^+$: $C_{36}H_{27}O_4$

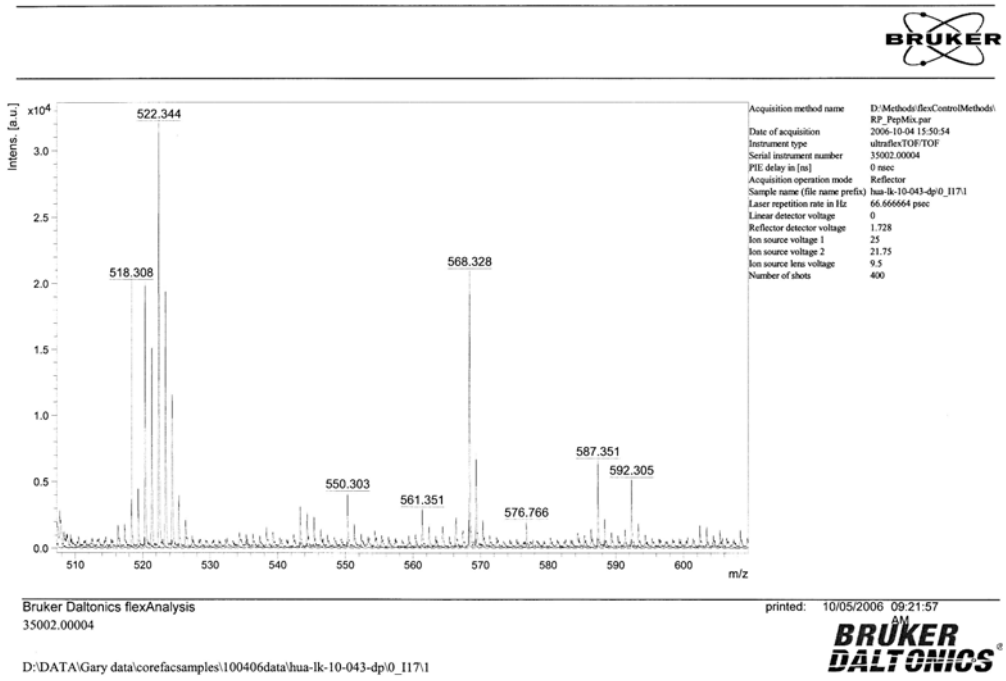
Exact Mass: 523.1909
m/z: 523.19 (100.0%), 524.19 (38.9%), 525.20 (8.4%), 526.20 (1.3%)

$(M+Na)^+$: $C_{36}H_{26}O_4Na$

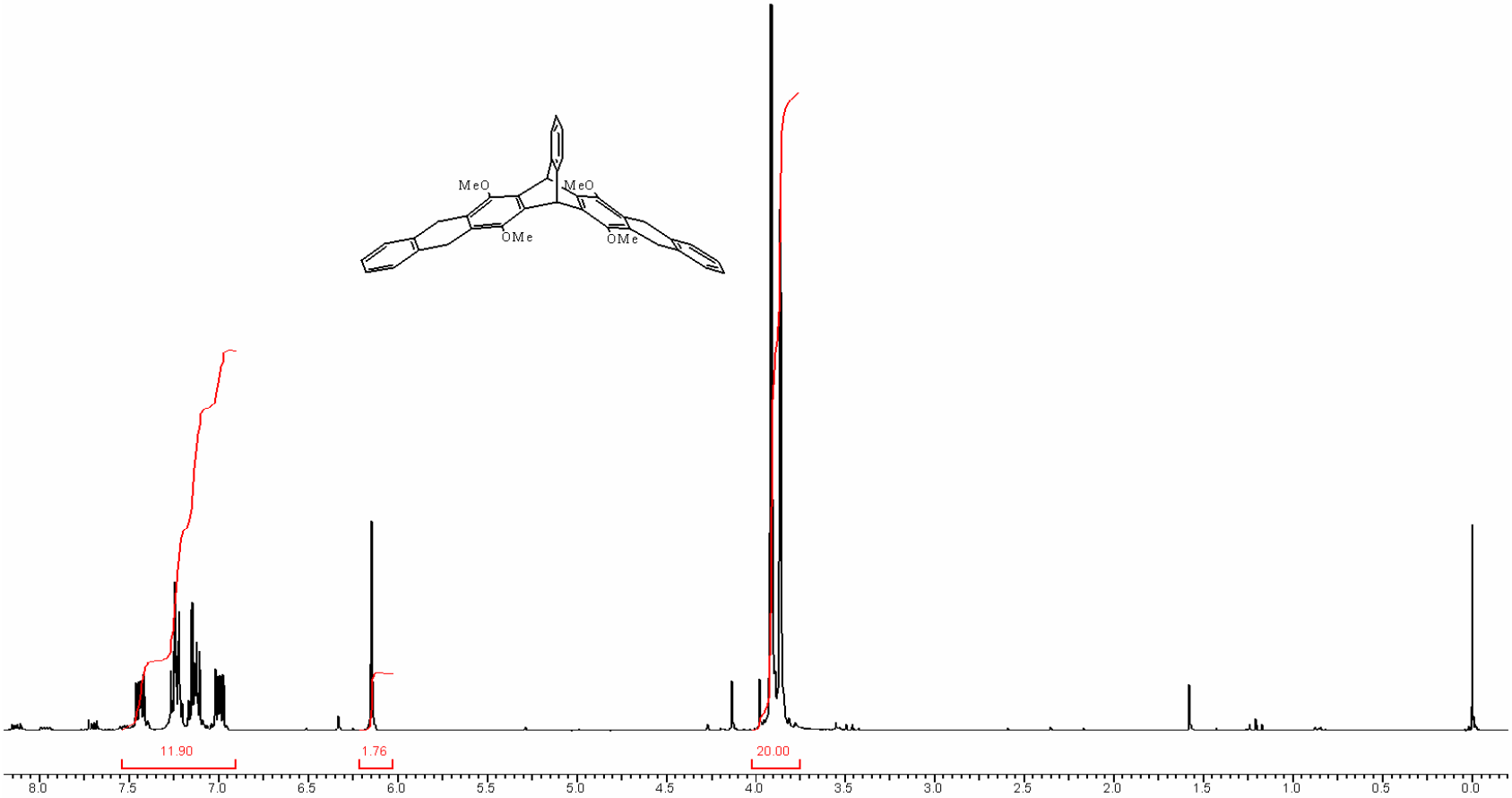
Exact Mass: 545.1729
m/z: 545.17 (100.0%), 546.18 (39.4%), 547.18 (8.4%), 548.18 (1.2%)

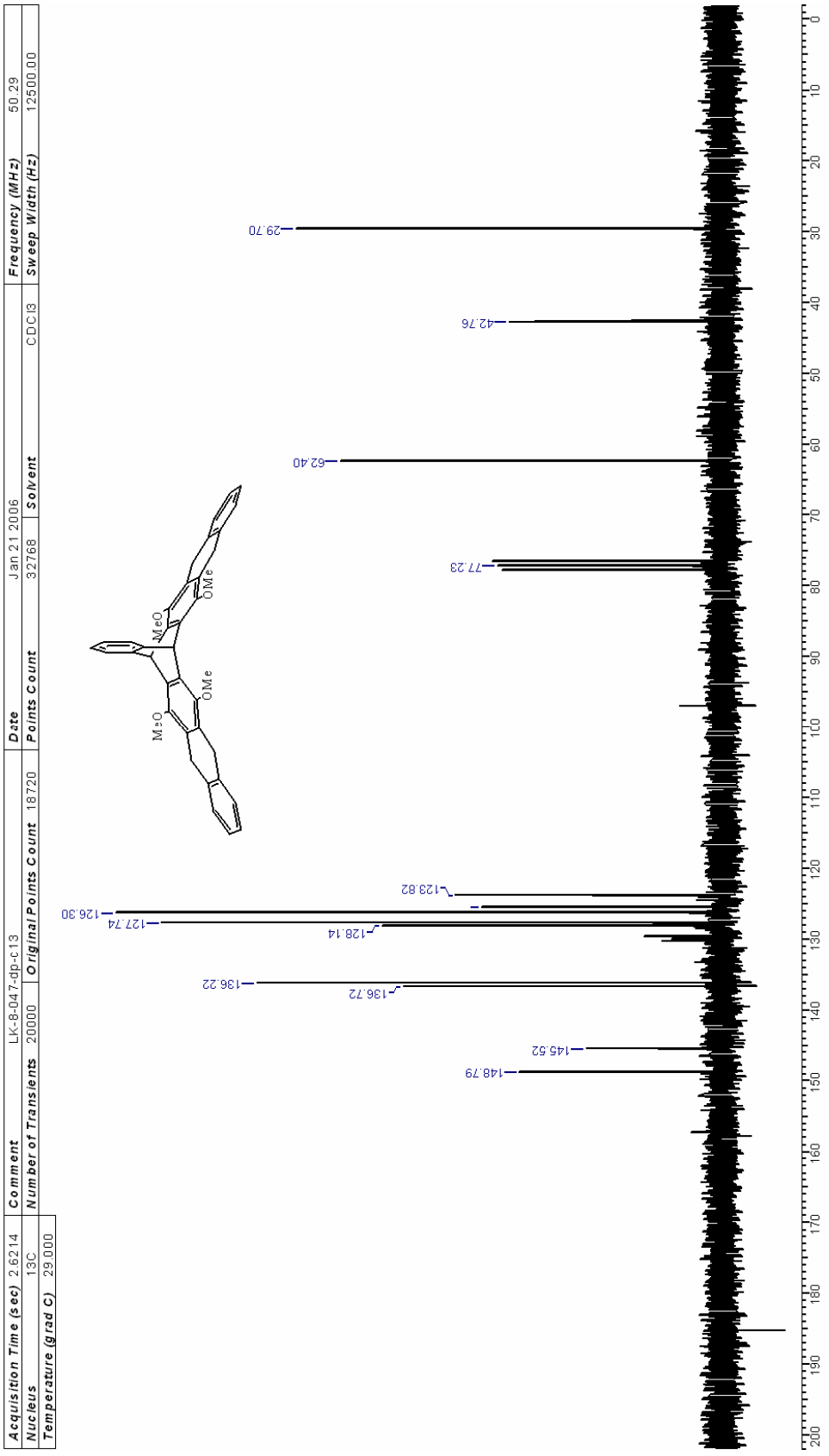
$(M+K)^+$: $C_{36}H_{26}O_4K$

Exact Mass: 561.1468
m/z: 561.15 (100.0%), 562.15 (39.4%), 563.15 (8.3%), 563.14 (7.2%), 564.15 (3.2%)

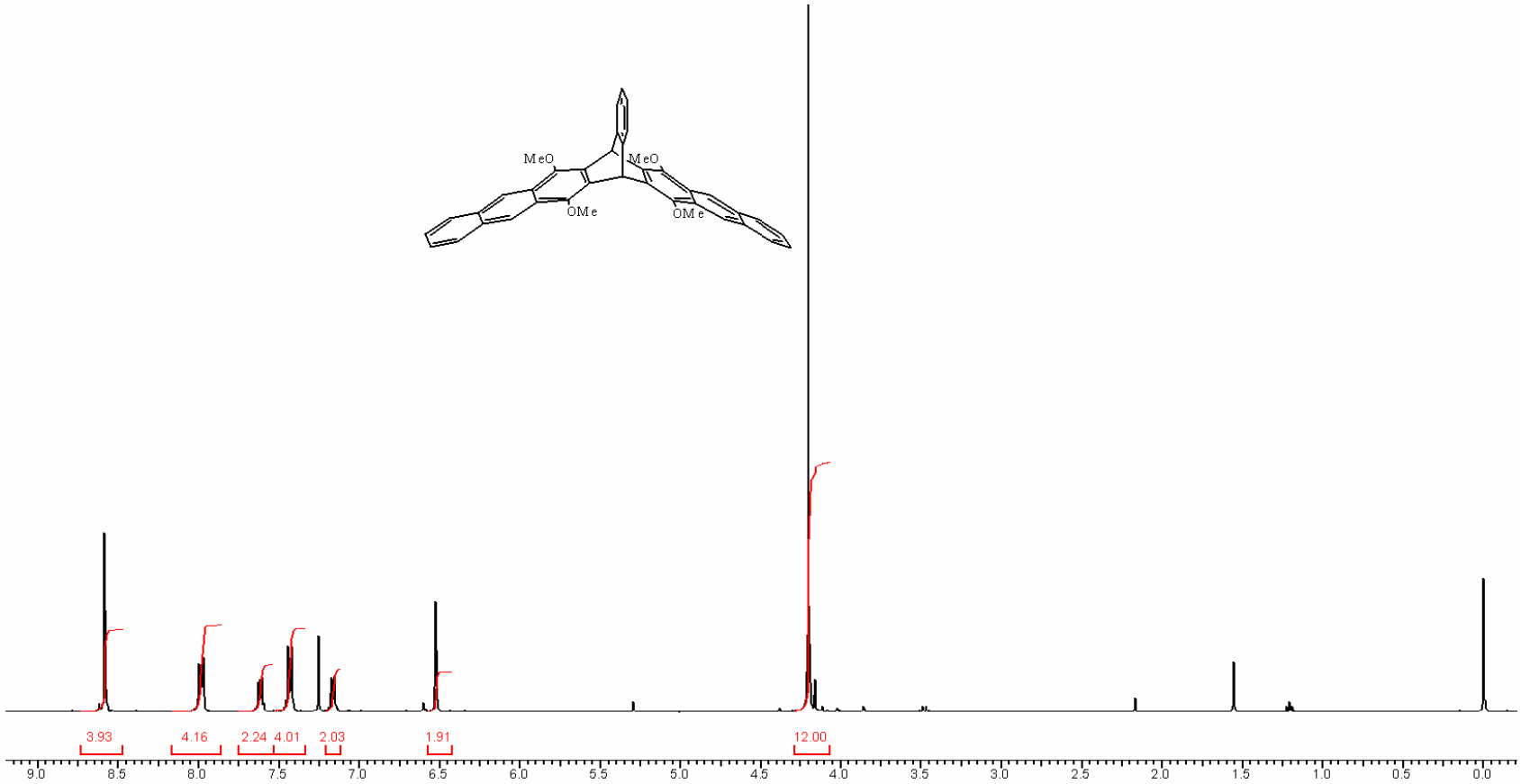


Acquisition Time (sec)	3.2768	***Comment***	LK-8-047-f8-20-crystal		***Date***	Jan 21 2006		***Frequency (MHz)***	199.98
Nucleus	1H	***Number of Transients***	128	***Original Points Count*** 4992	***Points Count***	8192	***Solvent*** CDCl3	***Sweep Width (Hz)***	2500.00
Temperature (grad C)	29.000								

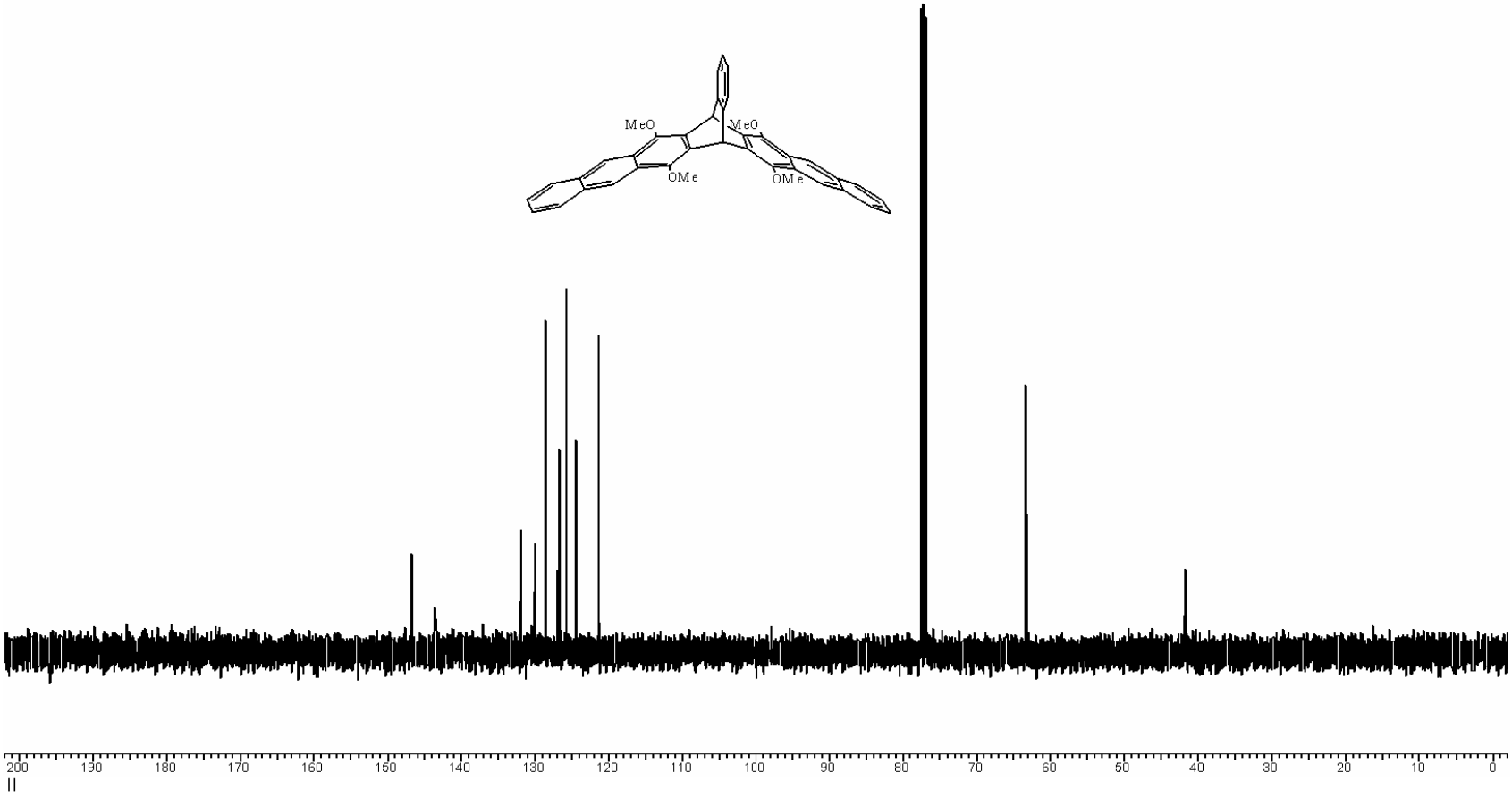



Acquisition Time (sec) 2.6214
Comment LK-8-047-dp-c13
Date Jan 21 2006
Frequency (MHz) 50.29
Nucleus 13C
Number of Transients 20000
Original Points Count 18720
Points Count 32768
Solvent CDCl3
Sweep Width (Hz) 12500.00
Temperature (grad C) 29.000
29.70
42.76
62.40
77.23
123.82
126.30
127.74
128.14
136.22
136.72
145.52
148.79
MeO
OMe
OMe
MeO

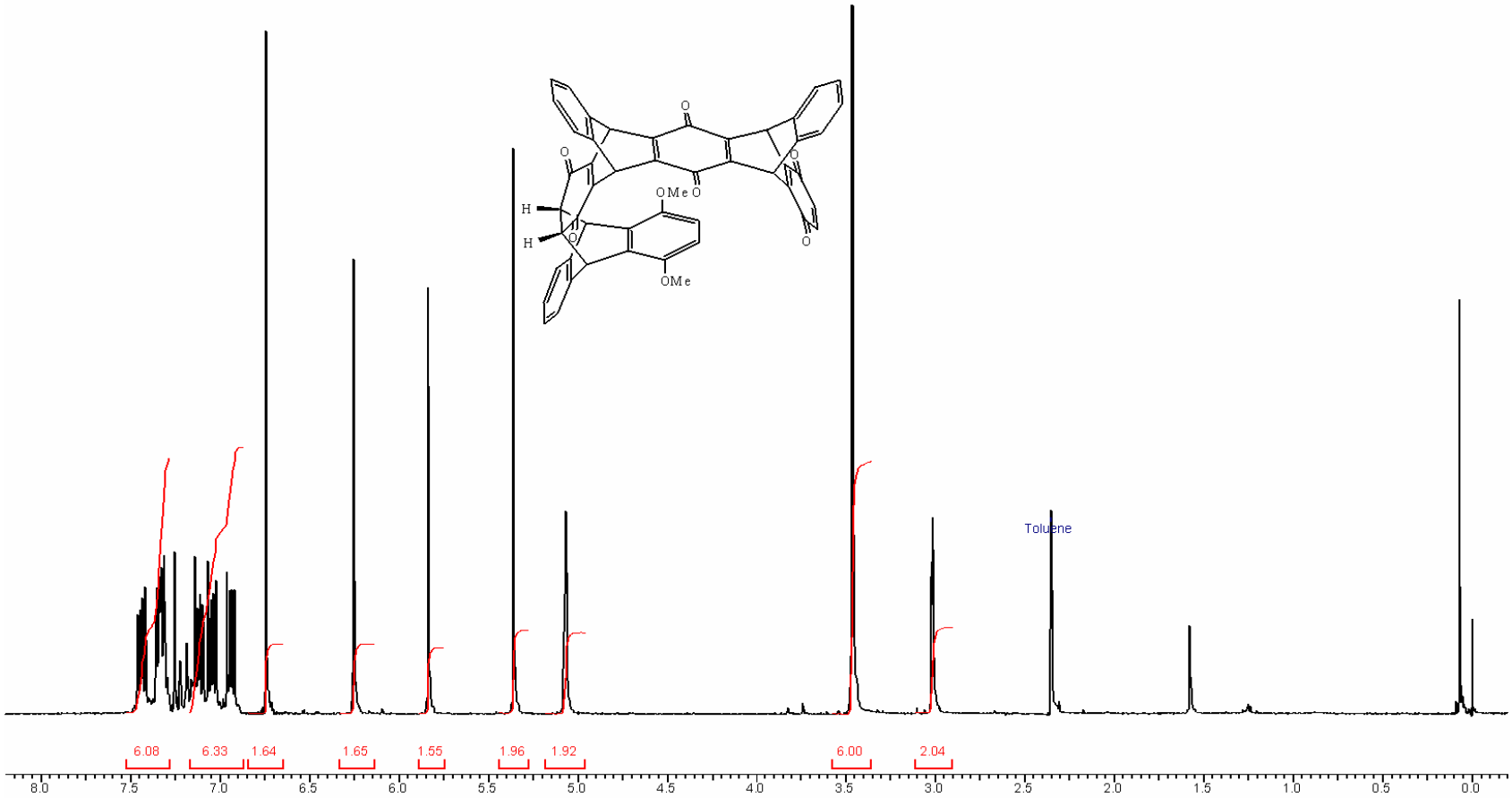
Acquisition Time (sec)	6.5536	***Comment***	LK-8-024-dp		***Date***	Dec 19 2005		***Frequency (MHz)***	399.78
Nucleus	1H	***Number of Transients***	128	***Original Points Count*** 18505	***Points Count***	32768	***Solvent*** CDCl3	***Sweep Width (Hz)***	5000.00
Temperature (grad C)	29.000								



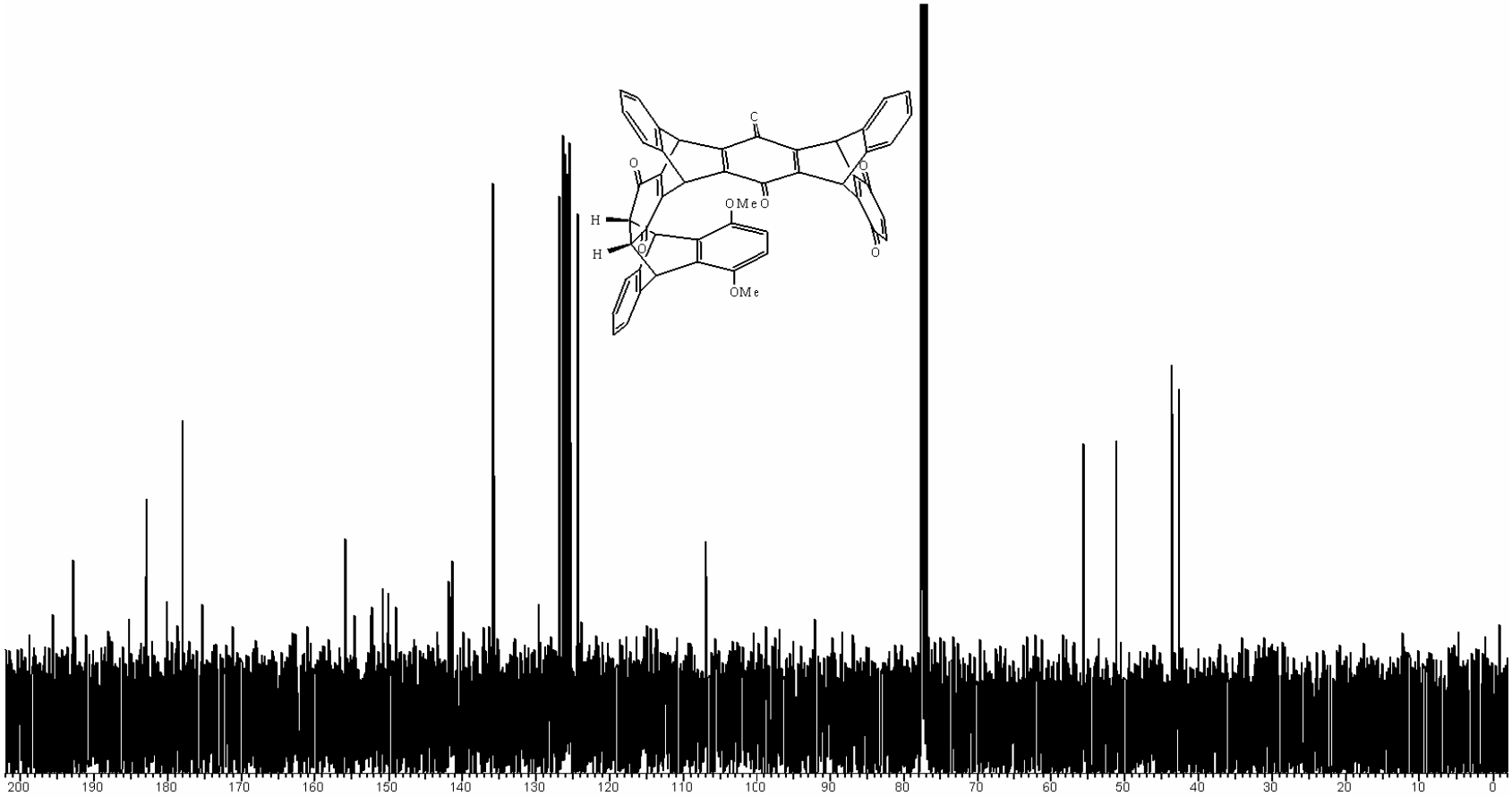
Acquisition Time (sec)	1.3107	***Comment***	LK-8-024-dp		***Date***	Dec 19 2005		***Frequency (MHz)***	100.53
Nucleus	13C	***Number of Transients***	20000	***Original Points Count*** 29984	***Points Count***	32768	***Solvent*** CDCl3	***Sweep Width (Hz)***	25000.00
Temperature (grad C)	29.000								

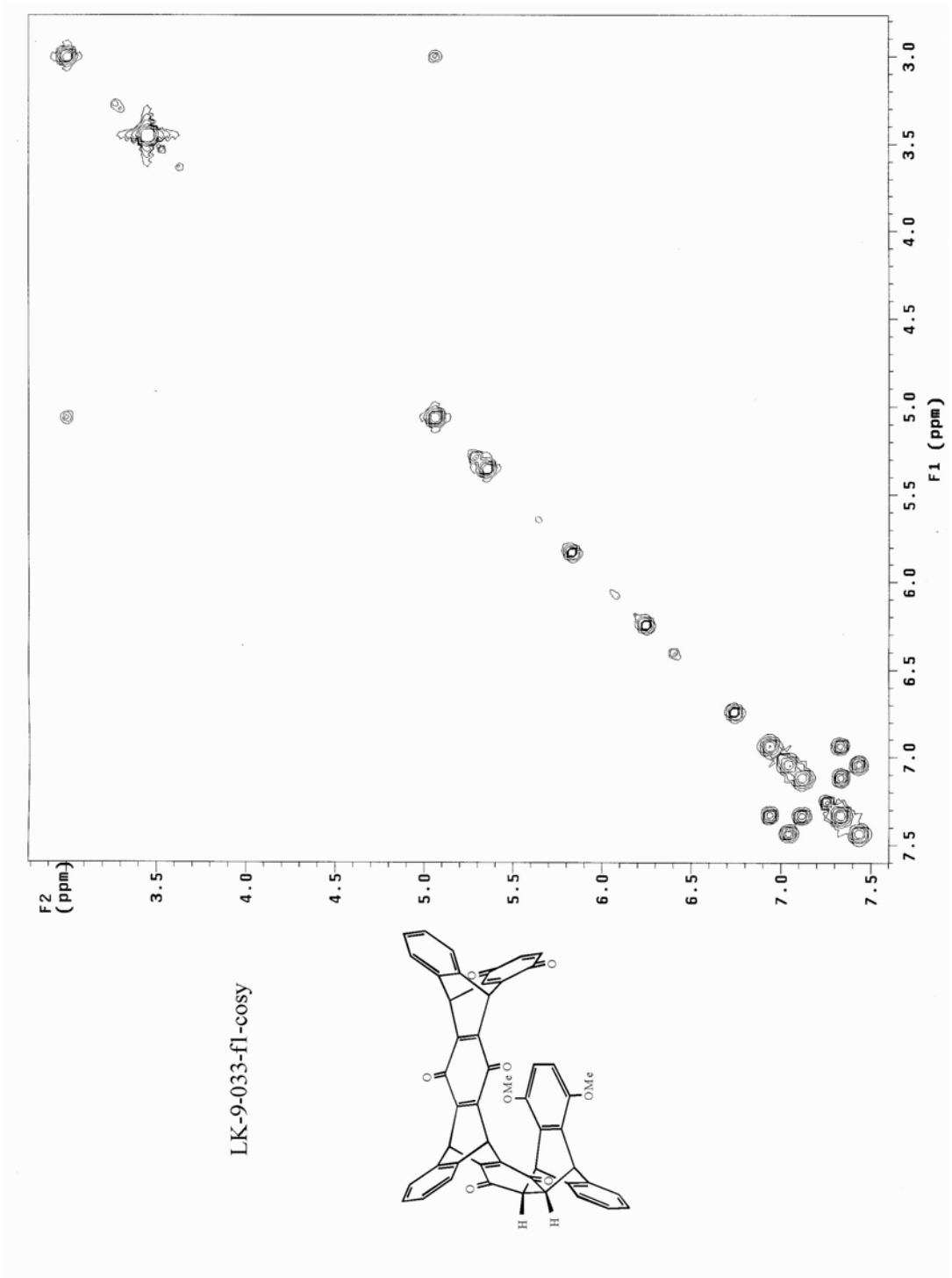


Acquisition Time (sec)	3.2768	***Comment***	LK-9-033-f1		***Date***	Apr 13 2006		***Frequency (MHz)***	199.98
Nucleus	1H	***Number of Transients***	128	***Original Points Count*** 4992	***Points Count***	8192	***Solvent*** CDCl3	***Sweep Width (Hz)***	2500.00
Temperature (grad C)	29.000								



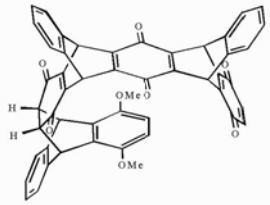
Acquisition Time (sec) 1.3107	***Comment*** LK-9-0330f1-c13			***Date*** Apr 23 2006				***Frequency (MHz)***	100.53
Nucleus 13C	***Number of Transients*** 20000	***Original Points Count*** 29984		***Points Count*** 32768		***Solvent*** CDCl3		***Sweep Width (Hz)***	25000.00
Temperature (grad C) 29.000									



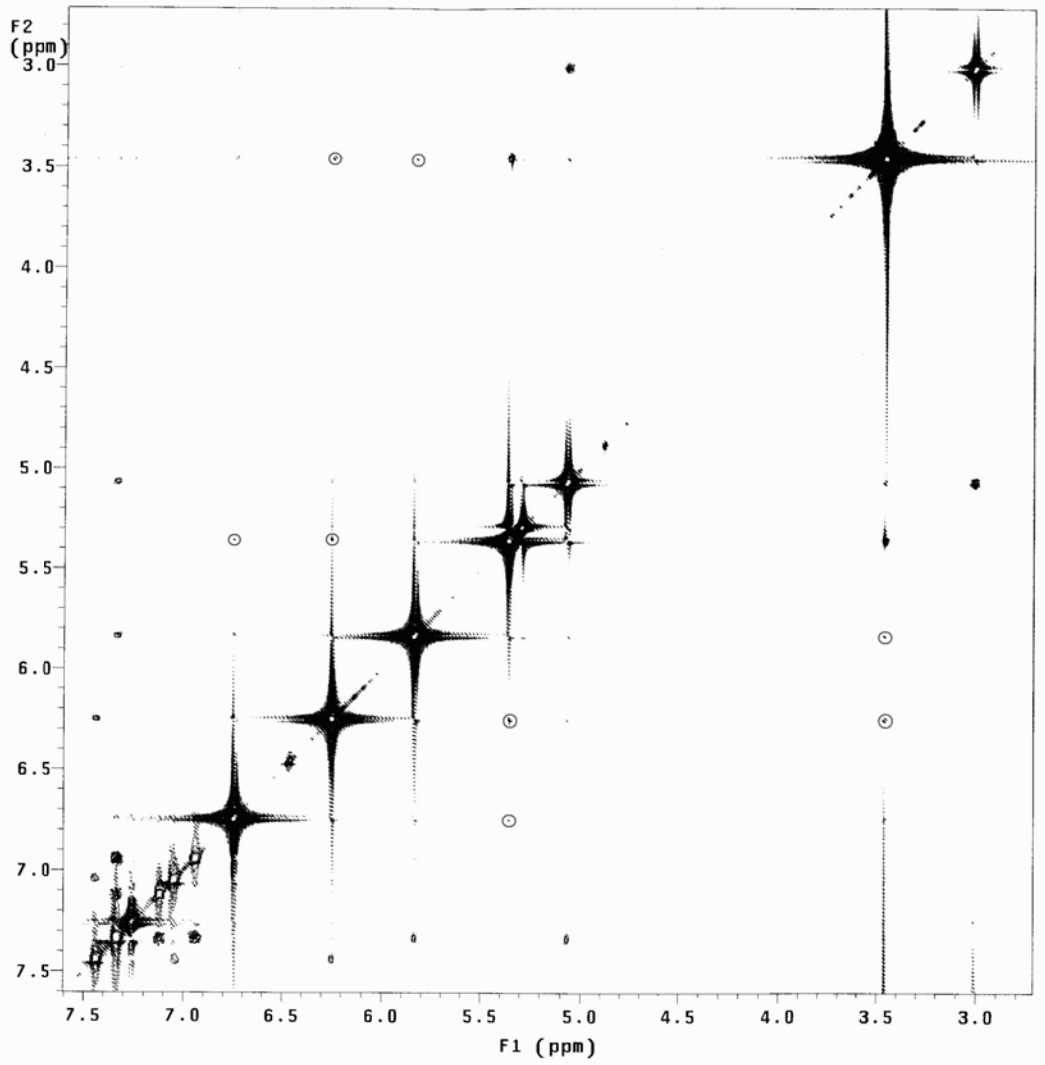


LK-9-033-f1-cosy

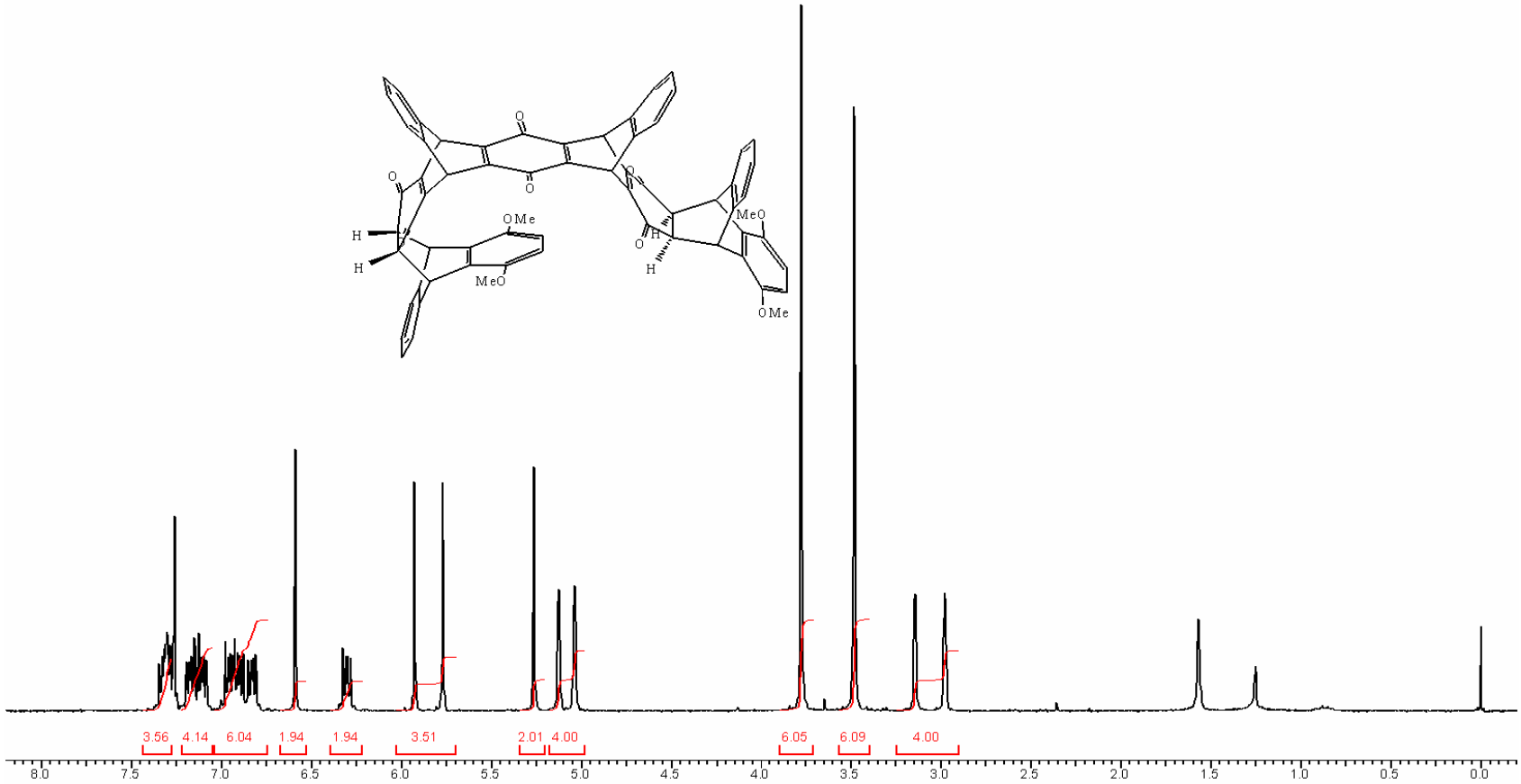
LK-9-033-f1-noesy



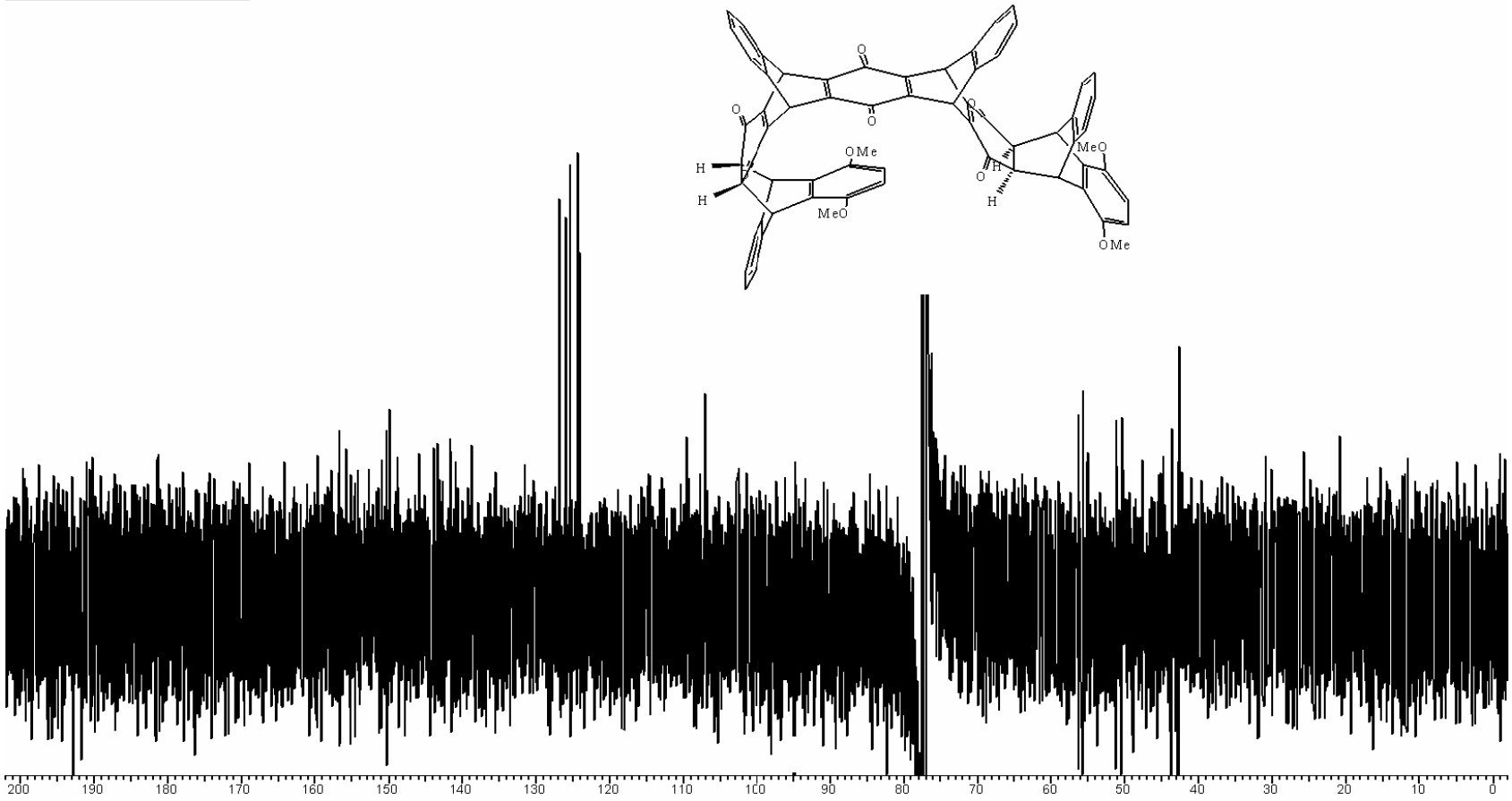
(important through-space NOE cross-peaks are noted with circles)



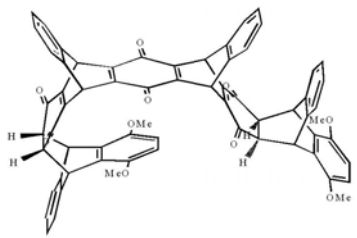
Acquisition Time (sec)	3.2768	***Comment***	LK-9-033-dp		***Date***	Apr 21 2006		***Frequency (MHz)***	199.98
Nucleus	1H	***Number of Transients***	128	***Original Points Count*** 4992	***Points Count***	8192	***Solvent*** CDCl3	***Sweep Width (Hz)***	2500.00
Temperature (grad C)	29.000								

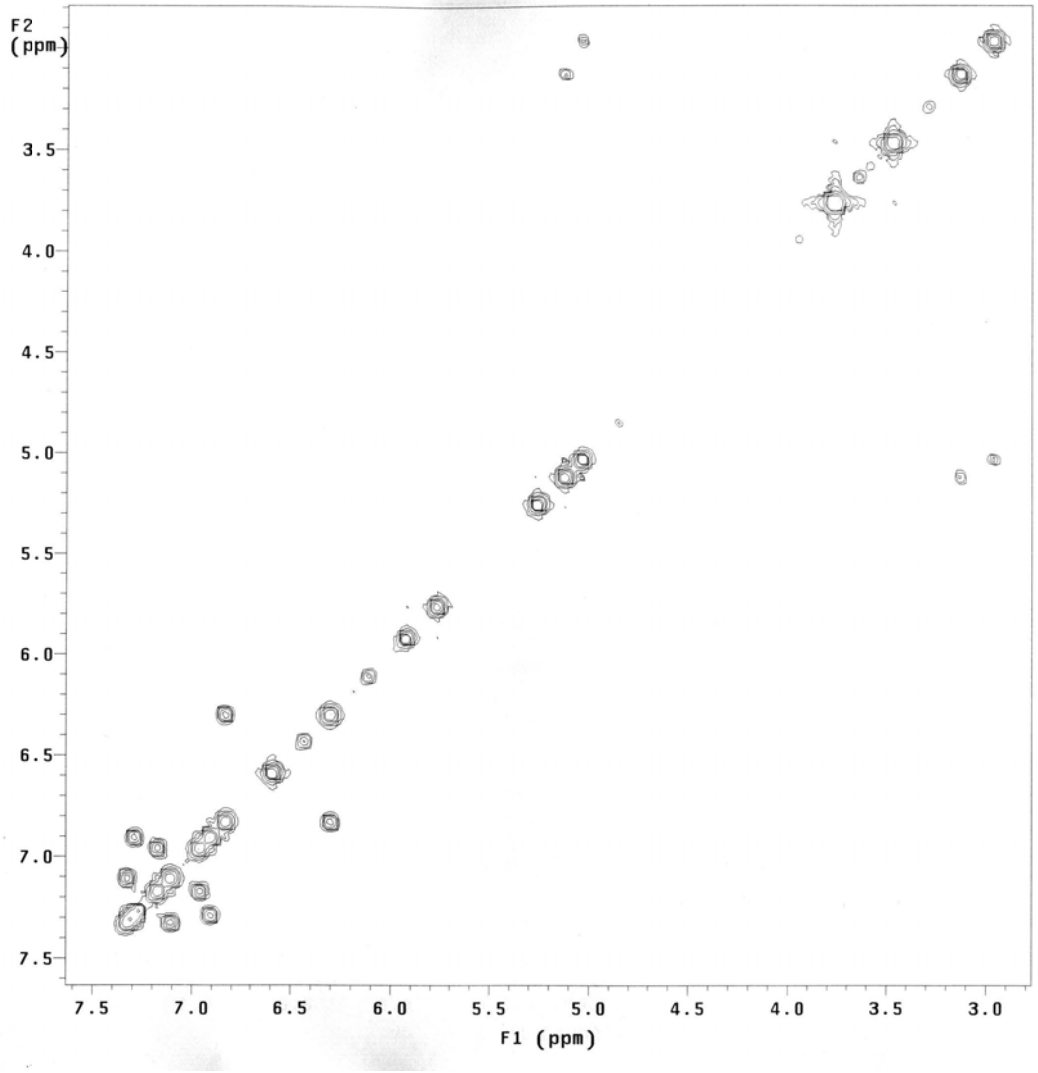


Acquisition Time (sec) 1.3107	***Comment*** LK-9-033-dp-c13			***Date*** Apr 22 2006				***Frequency (MHz)***	100.53
Nucleus 13C	***Number of Transients*** 20000	***Original Points Count*** 29984		***Points Count*** 32768		***Solvent*** CDCl3		***Sweep Width (Hz)***	25000.00
Temperature (grad C) 29.000									

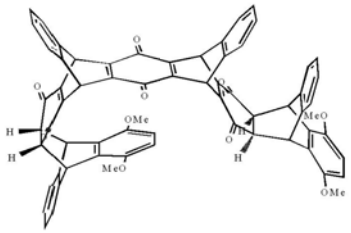


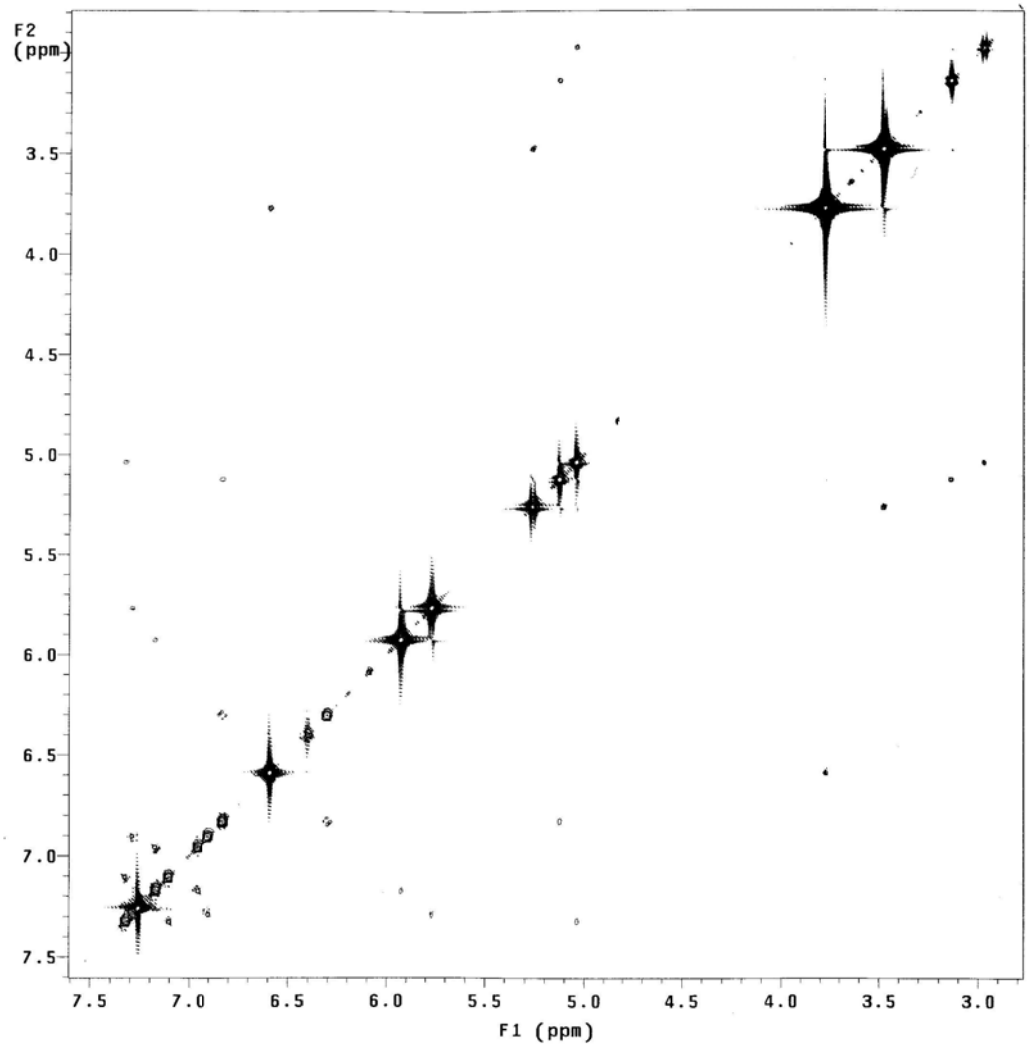
LK-9-033-dp-cosy



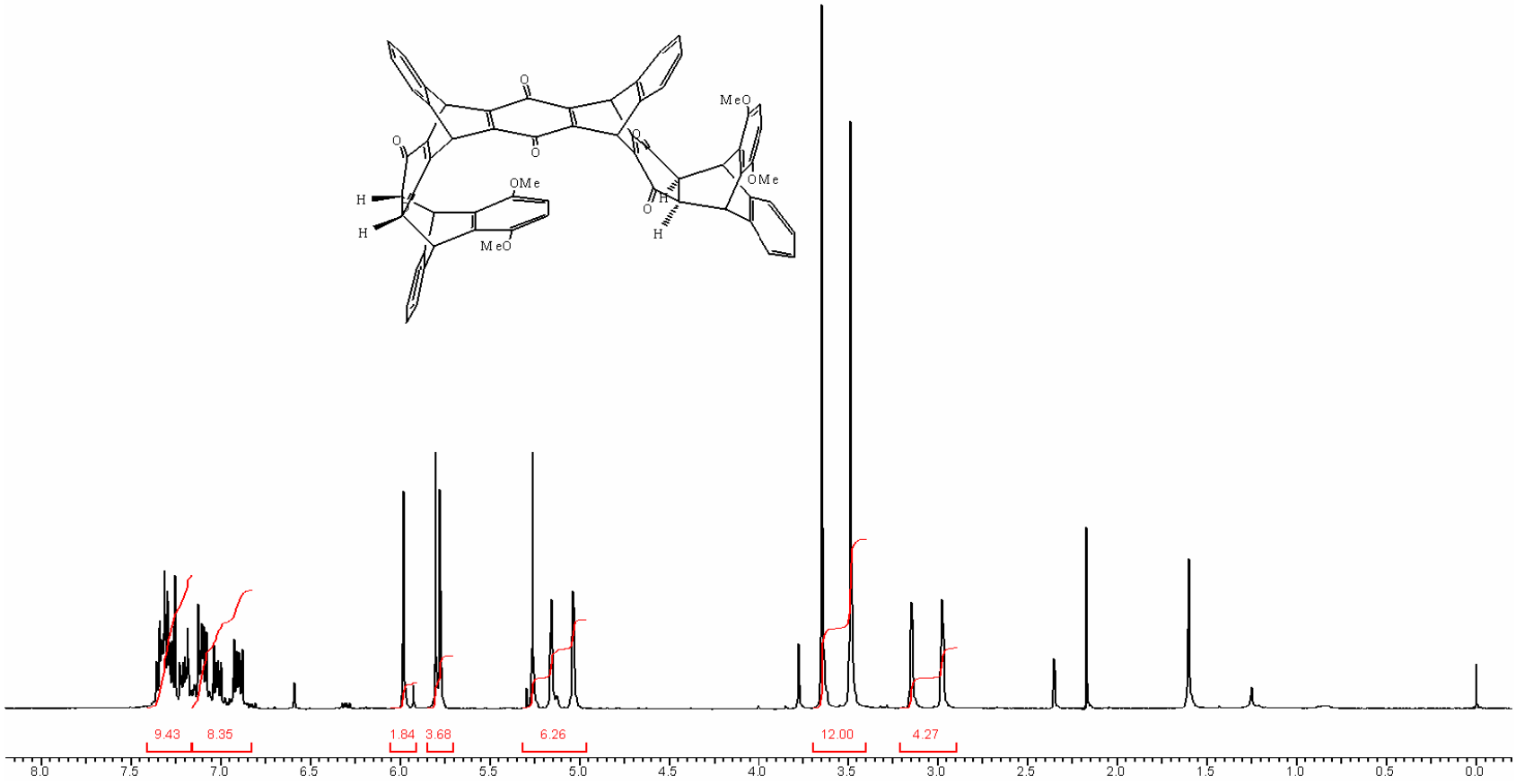


LK-9-033-dp-noesy

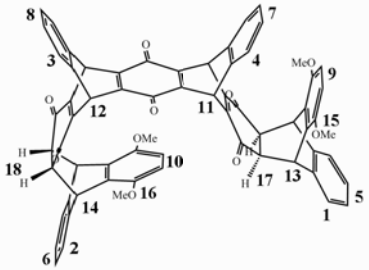


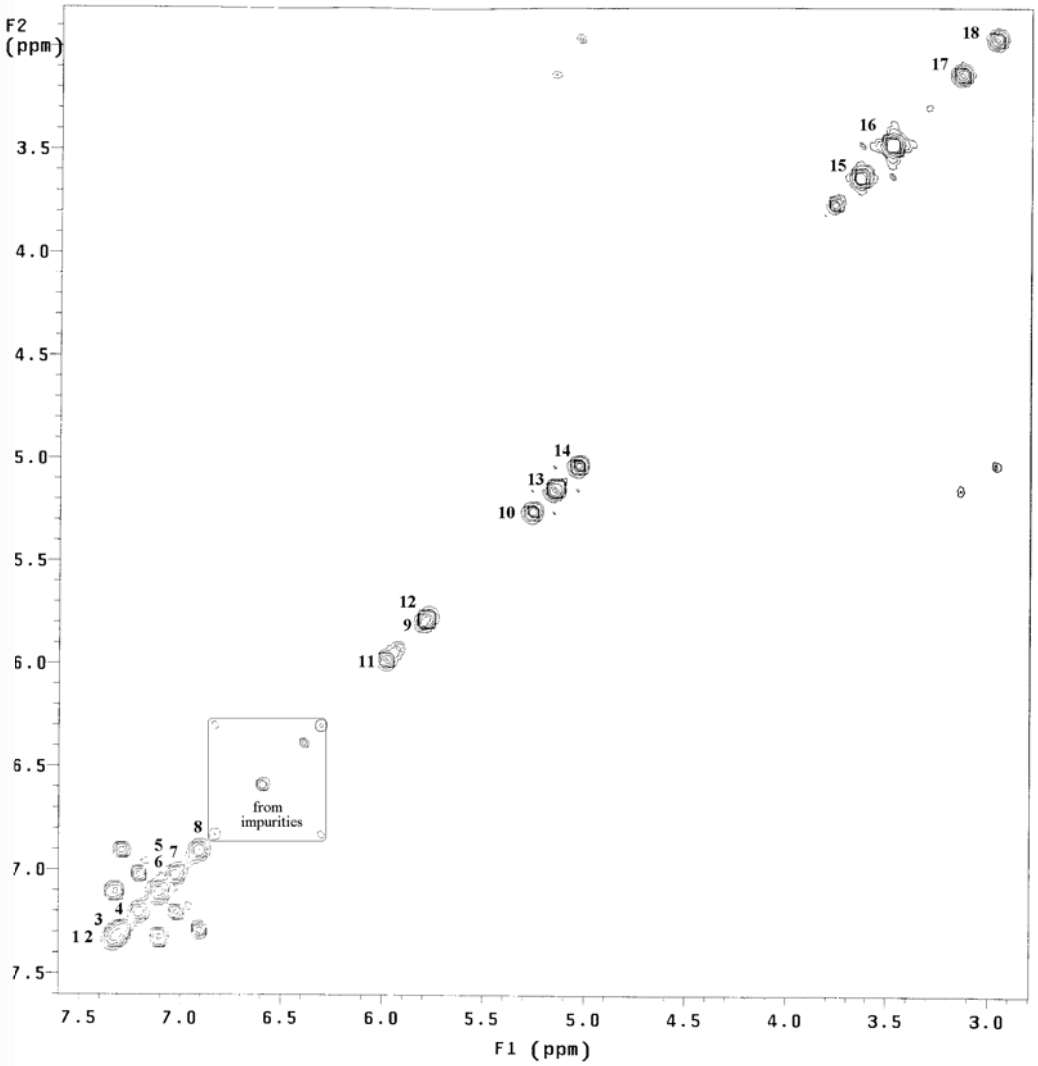


Acquisition Time (sec)	3.2768	***Comment***	LK-9-033-dp-isomer		***Date***	Apr 29 2006		***Frequency (MHz)***	199.98
Nucleus	1H	***Number of Transients***	128	***Original Points Count*** 4992	***Points Count***	8192	***Solvent*** CDCl3	***Sweep Width (Hz)***	2500.00
Temperature (grad C)	29.000								

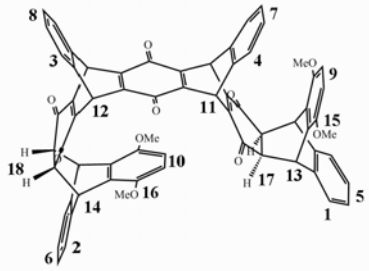


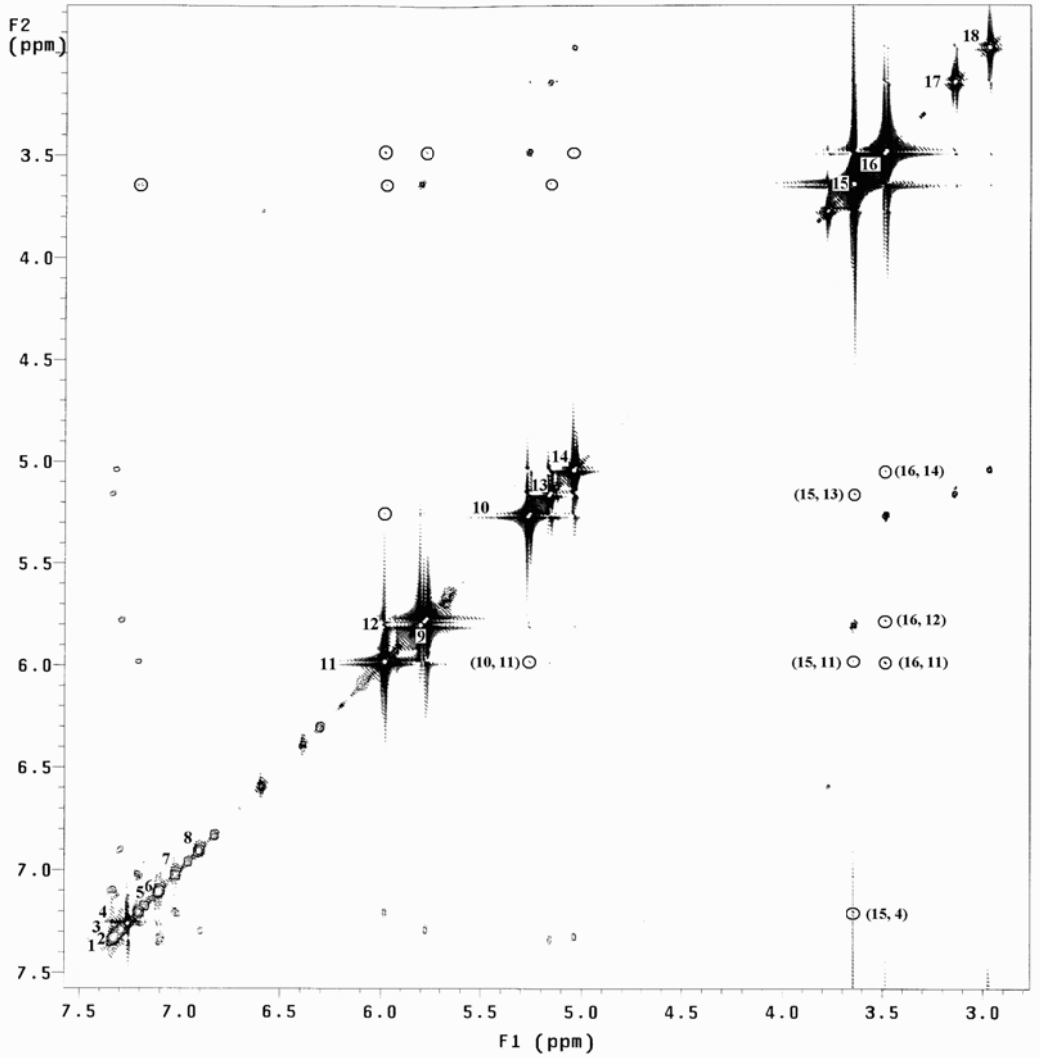
LK-9-033-dp-isomer-cosy



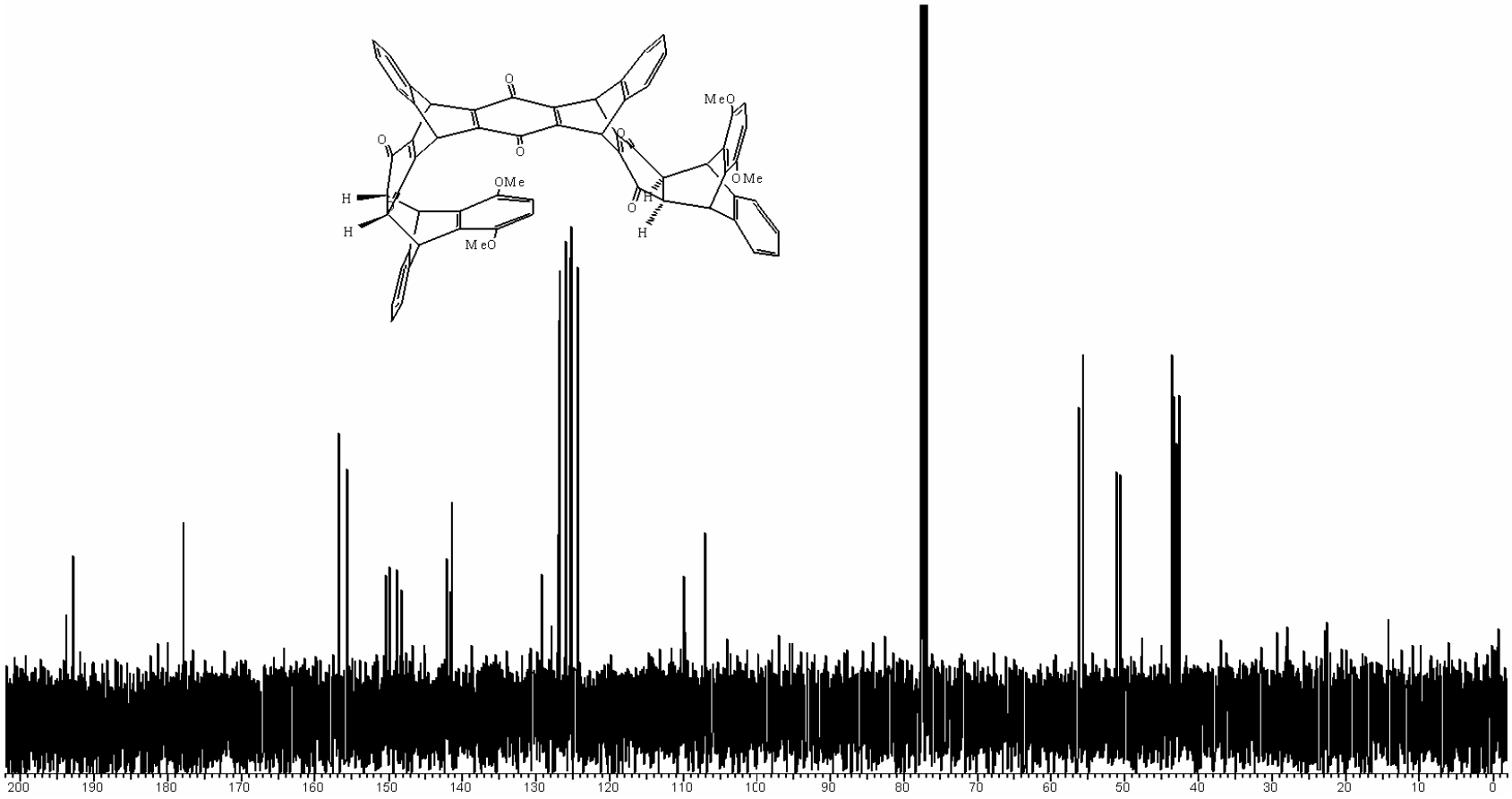


LK-9-033-dp-isomer-noesy

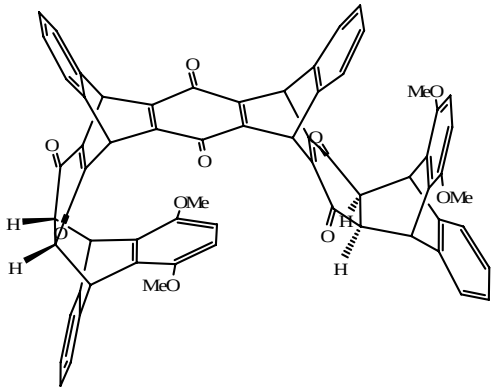




Acquisition Time (sec)	1.3107	***Comment***	LK-9-033-dp-isomer-c13			***Date***	Apr 30 2006	***Frequency (MHz)***	100.53
Nucleus	13C	***Original Points Count***	29984	***Points Count***	32768	***Solvent***	CDCl3	***Sweep Width (Hz)***	25000.00
Temperature (grad C)	29.000								



LK-9-033-dp-isomer



$(M+Na)^+$: $C_{66}H_{44}O_{10}Na$

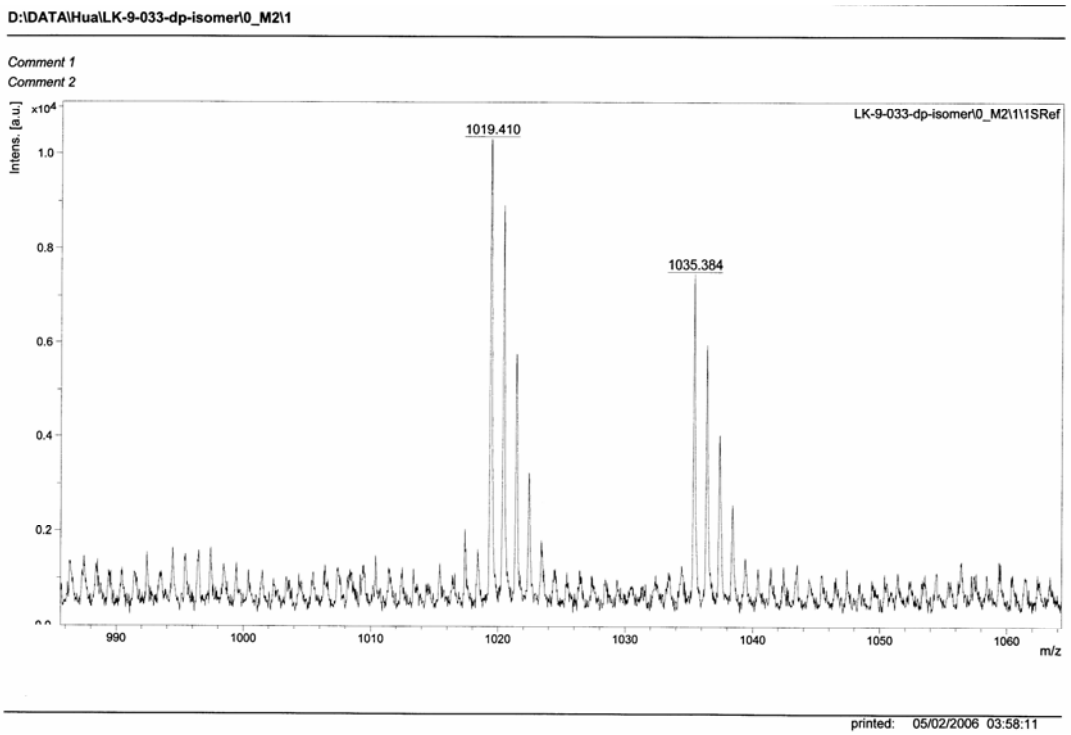
Exact Mass: 1019.2832

m/z: 1019.28 (100.0%), 1020.29 (72.3%), 1021.29 (27.8%), 1022.29 (7.4%), 1023.30 (1.0%)

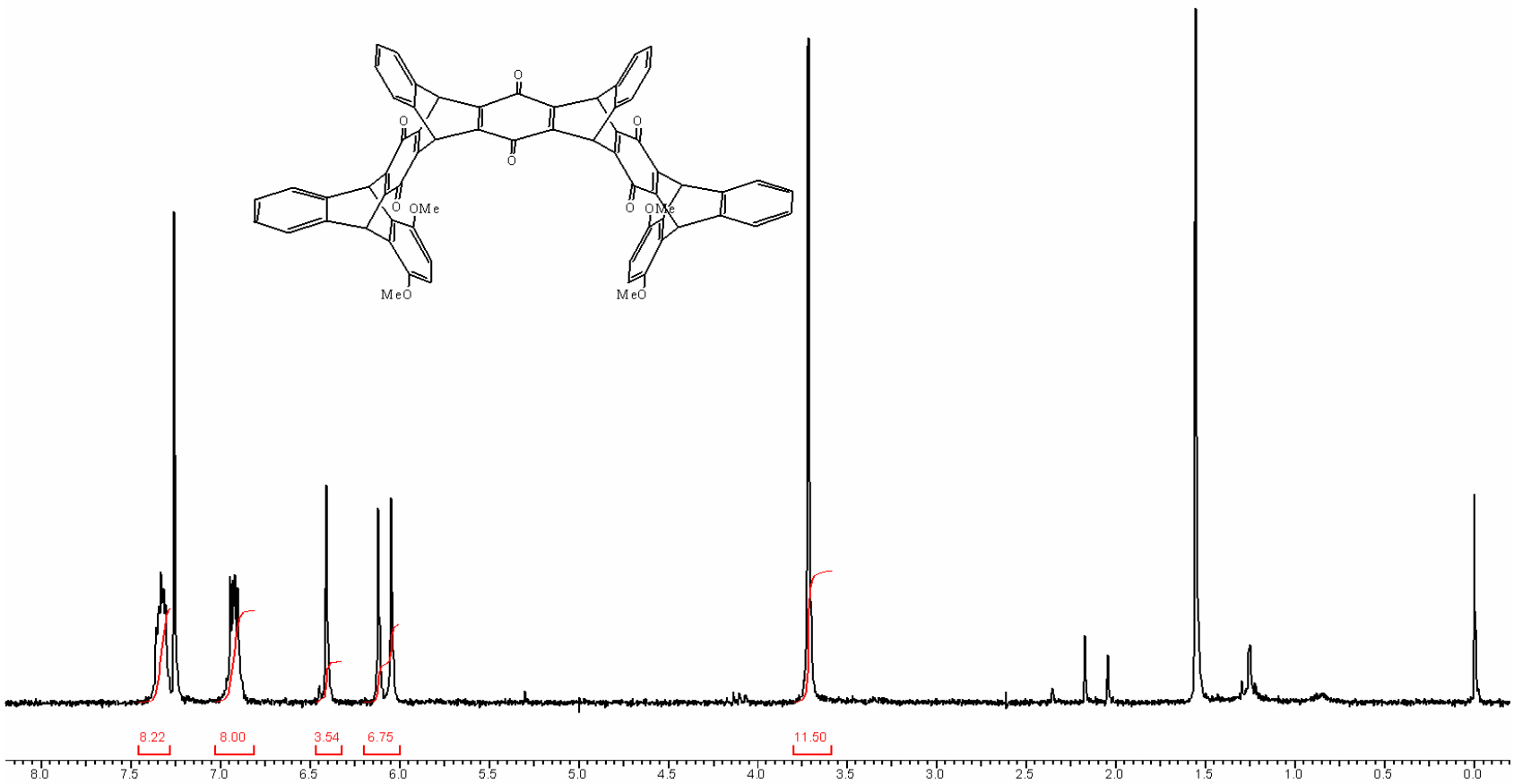
$(M+K)^+$: $C_{66}H_{44}O_{10}K$

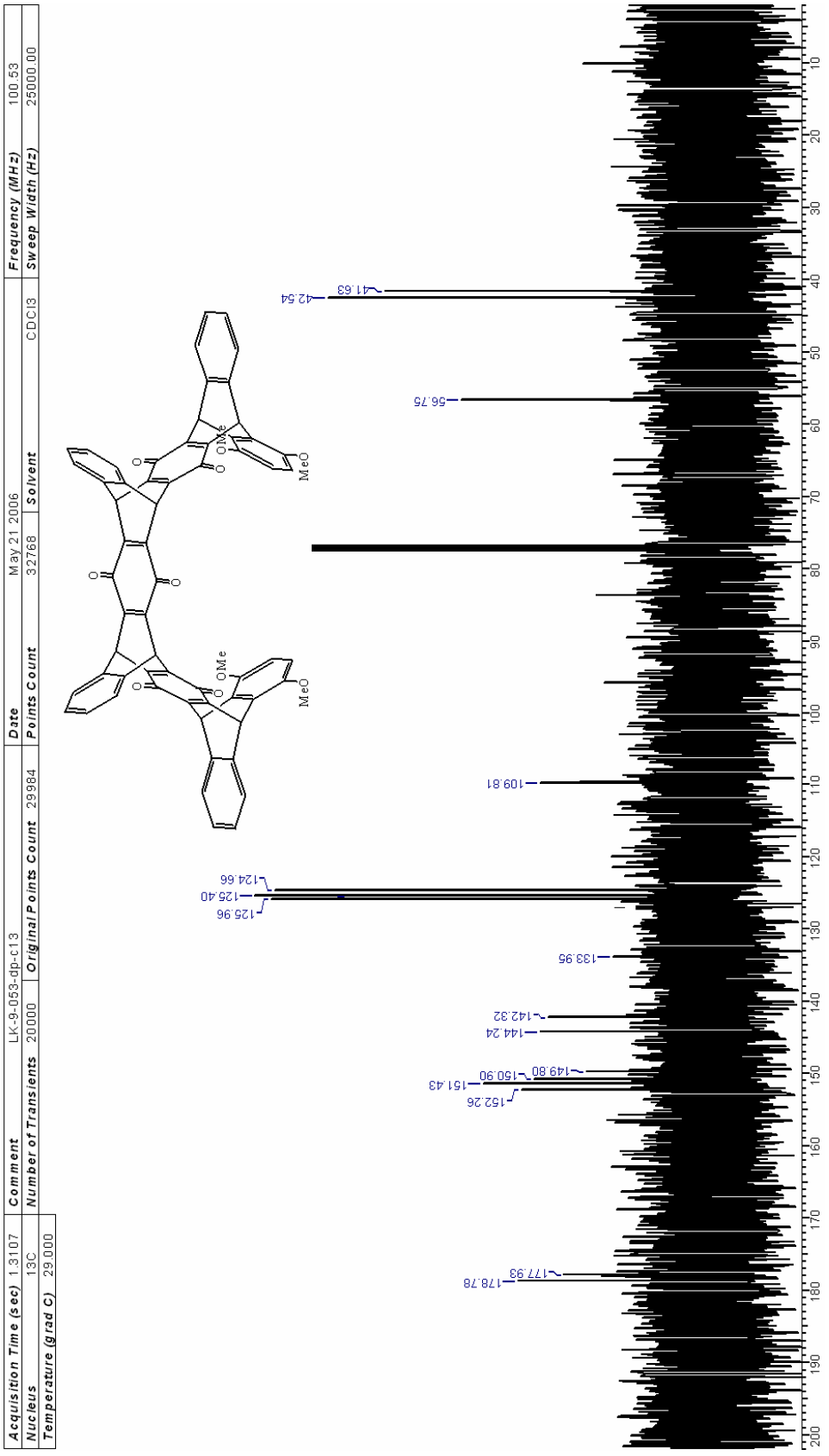
Exact Mass: 1035.2572

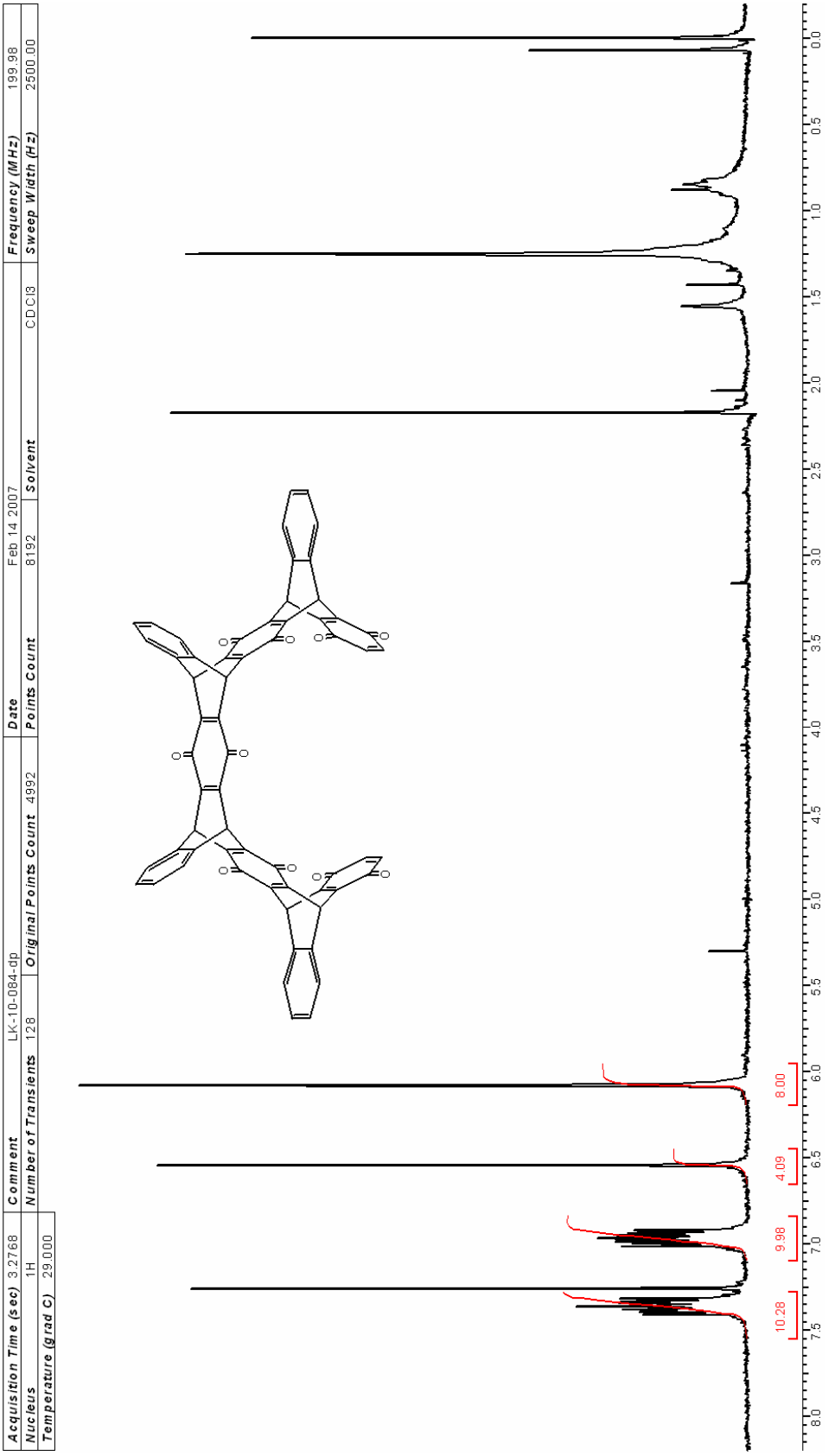
m/z: 1035.26 (100.0%), 1036.26 (72.3%), 1037.26 (34.6%), 1038.26 (6.7%), 1038.27 (6.0%), 1039.26 (2.0%), 1039.27 (1.6%)



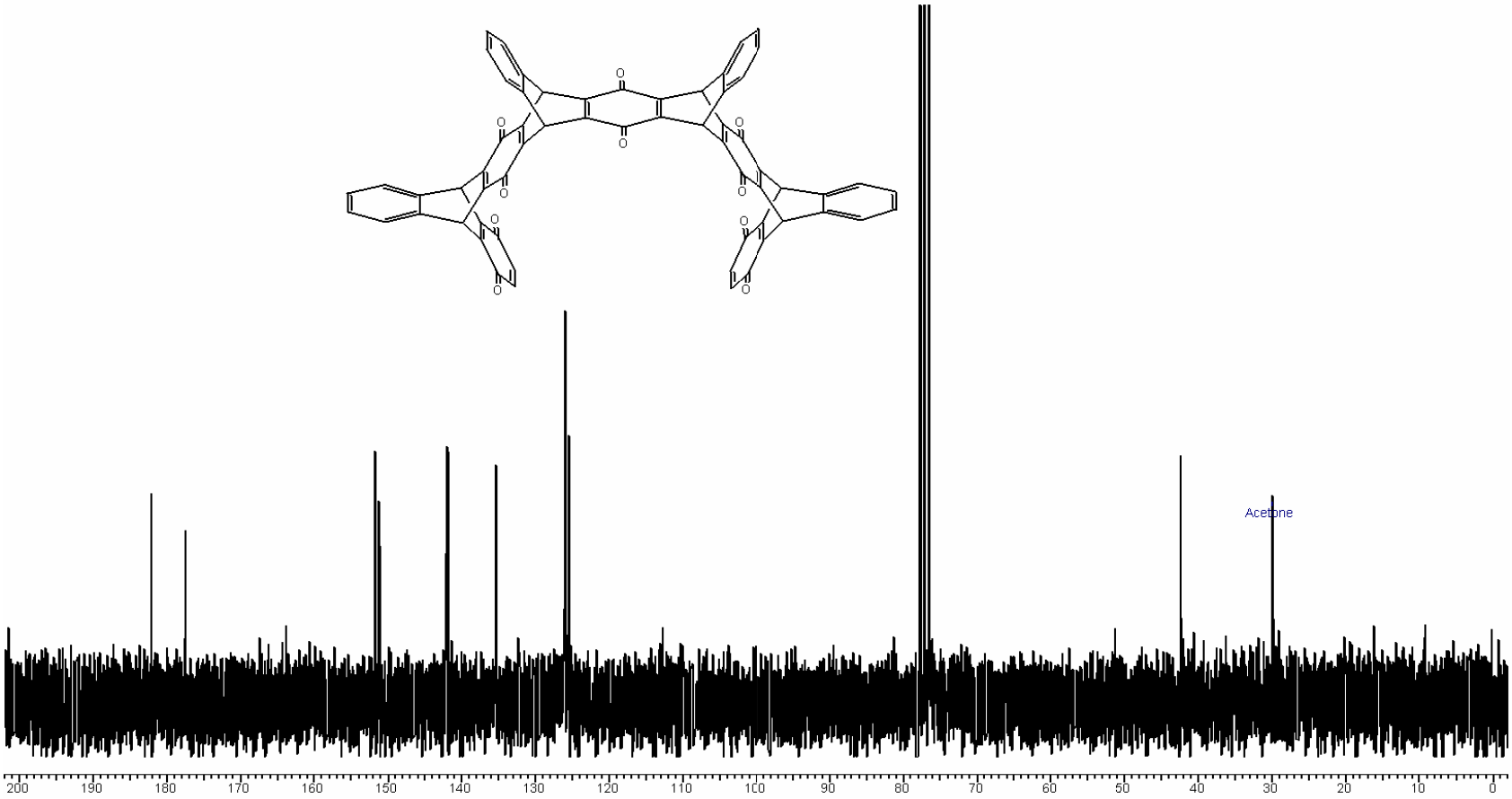
Acquisition Time (sec)	3.2768	***Comment***	LK-9-053-dp		***Date***	May 18 2006		***Frequency (MHz)***	199.98
Nucleus	1H	***Number of Transients***	128	***Original Points Count*** 4992	***Points Count***	8192	***Solvent*** CDCl3	***Sweep Width (Hz)***	2500.00
Temperature (grad C)	29.000								



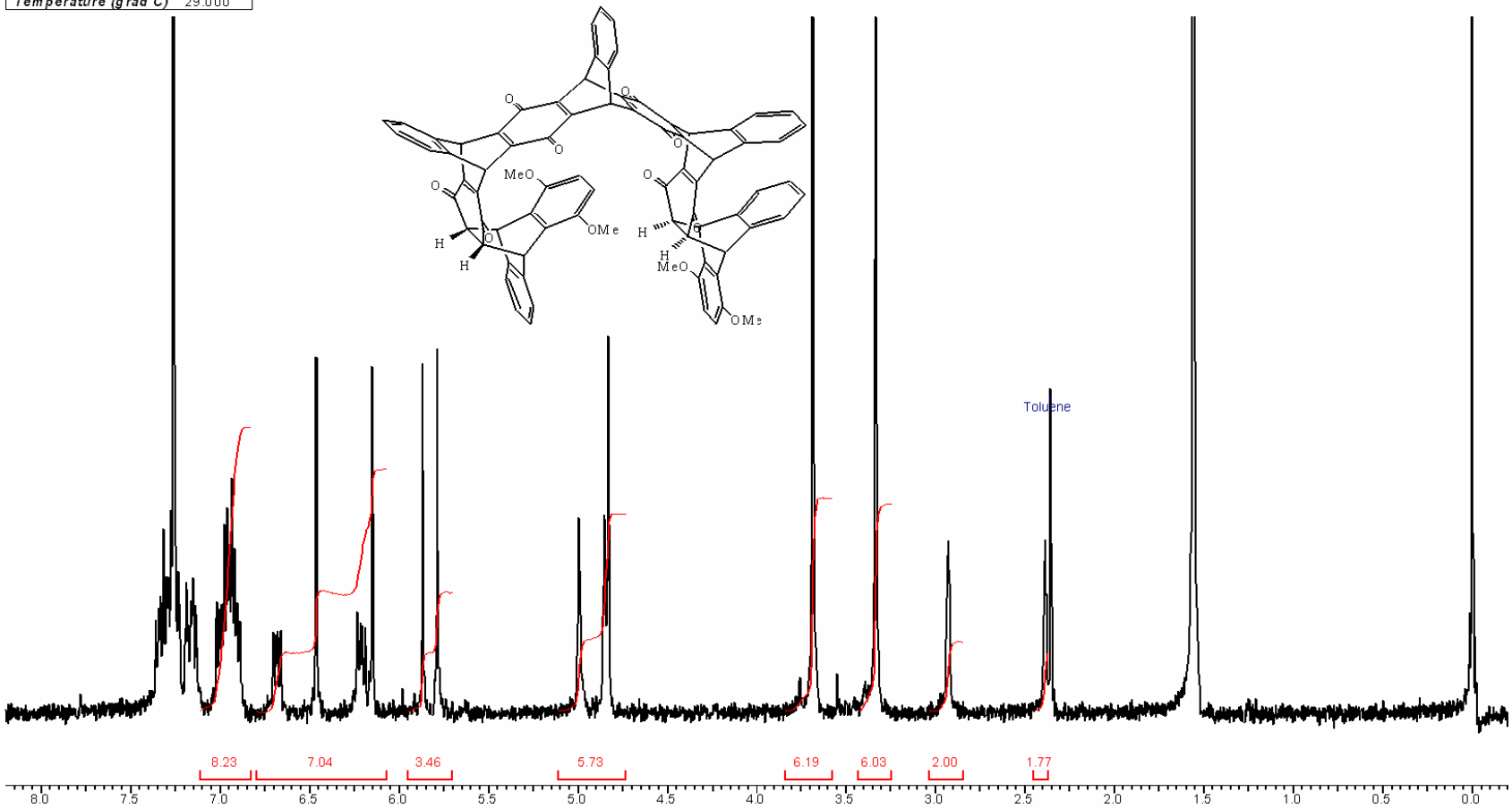

Acquisition Time (sec) 1.3107
Comment LK-9-053-dp-c13
Date May 21 2006
Frequency (MHz) 100.53
Nucleus 13C
Number of Transients 20000
Original Points Count 29984
Points Count 32768
Solvent CDCl3
Sweep Width (Hz) 25000.00
Temperature (grad C) 29.000
OMe
MeO
41.63
42.54
56.75
109.81
124.66
125.40
125.96
133.95
142.32
144.24
149.80
150.90
151.43
152.26
177.93
178.78


Acquisition Time (sec) 3.2768
Comment LK-10-084-dp
Date Feb 14 2007
Frequency (MHz) 199.98
Nucleus 1H
Number of Transients 128
Original Points Count 4992
Points Count 8192
Solvent CDCl3
Sweep Width (Hz) 2500.00
Temperature (grad C) 29.000
10.28
9.98
4.09
8.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

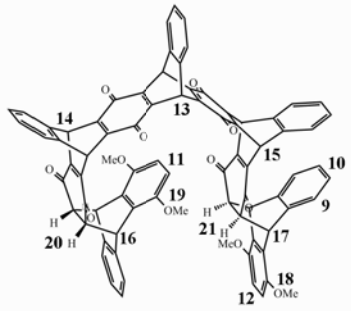
Acquisition Time (sec)	2.6214	*Comment*	LK-10-084-dp-C 13		*Date*	Feb 14 2007		*Frequency (MHz)*	50.29
Nucleus	13C	*Number of Transients*	20000	*Original Points Count* 18720	*Points Count*	32768	*Solvent* CDCl3	*Sweep Width (Hz)*	12500.00
Temperature (grad C)	29.000								

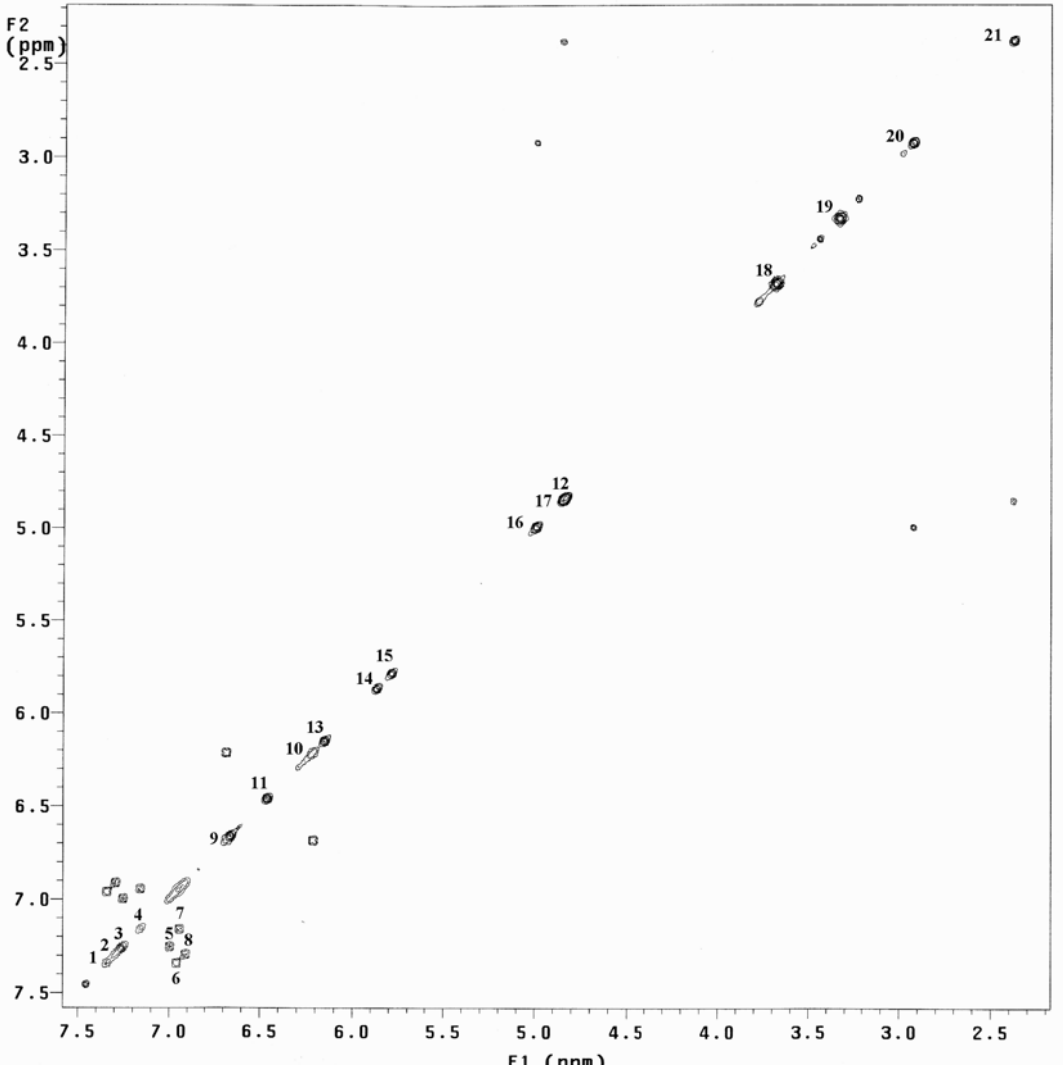


Acquisition Time (sec)	3.2768	***Comment***	LK-9-030-precipitate-2		***Date***	Apr 9 2006		***Frequency (MHz)***	199.98
Nucleus	1H	***Number of Transients***	128	***Original Points Count*** 4976	***Points Count***	8192	***Solvent*** CDCl3	***Sweep Width (Hz)***	2500.00
Temperature (grad C)	29.000								

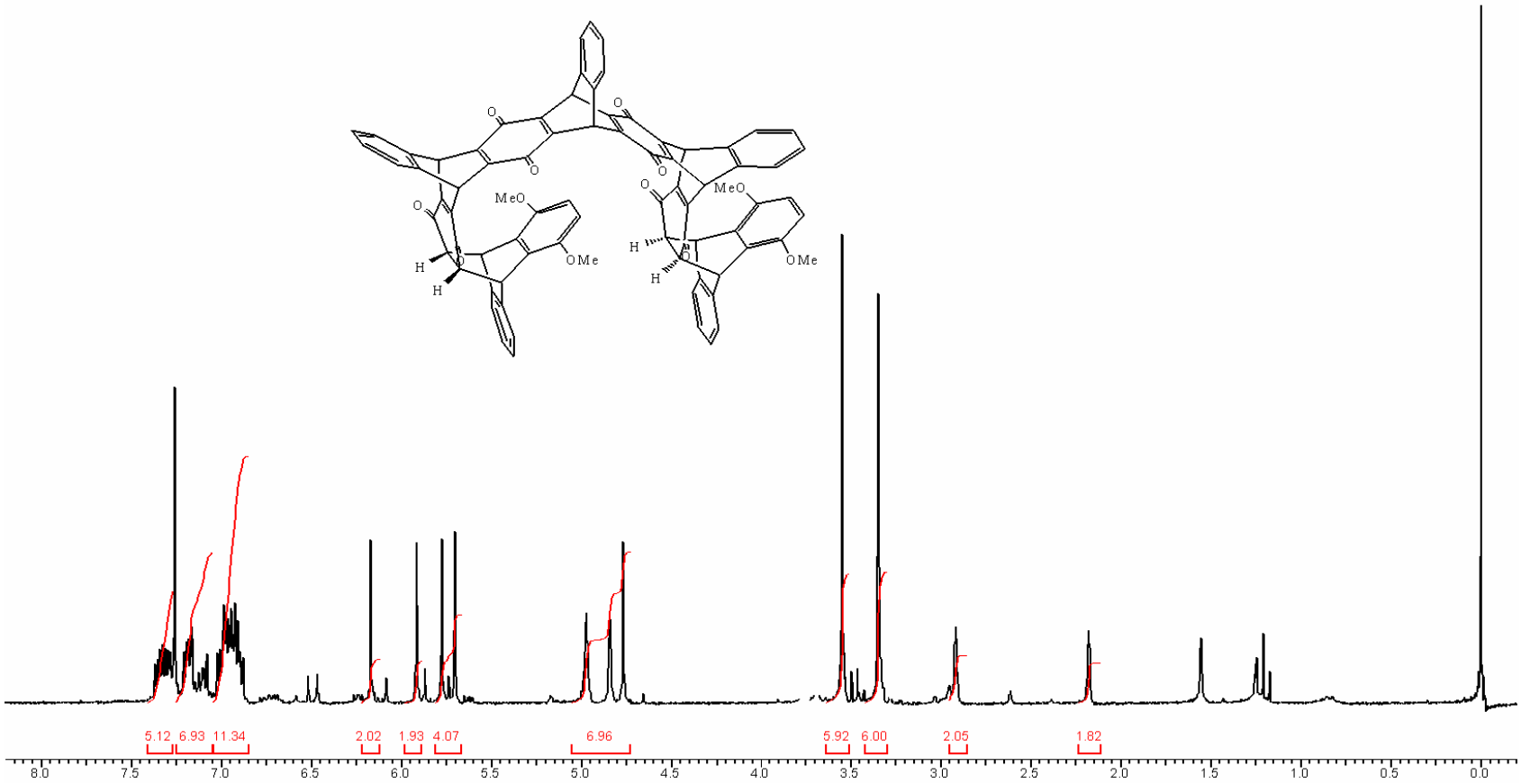


LK-9-047-f3-cosy

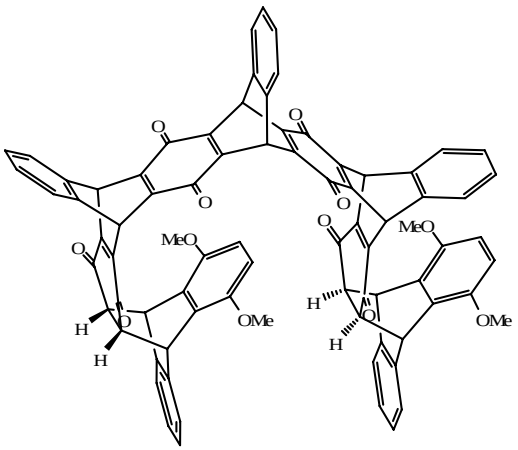




Acquisition Time (sec)	3.2768	***Comment***	LK-9-047-dp-isomer		***Date***	May 1 2006		***Frequency (MHz)***	199.98
Nucleus	1H	***Number of Transients***	128	***Original Points Count*** 4992	***Points Count***	8192	***Solvent*** CDCl3	***Sweep Width (Hz)***	2500.00
Temperature (grad C)	29.000								



LK-9-047-f10

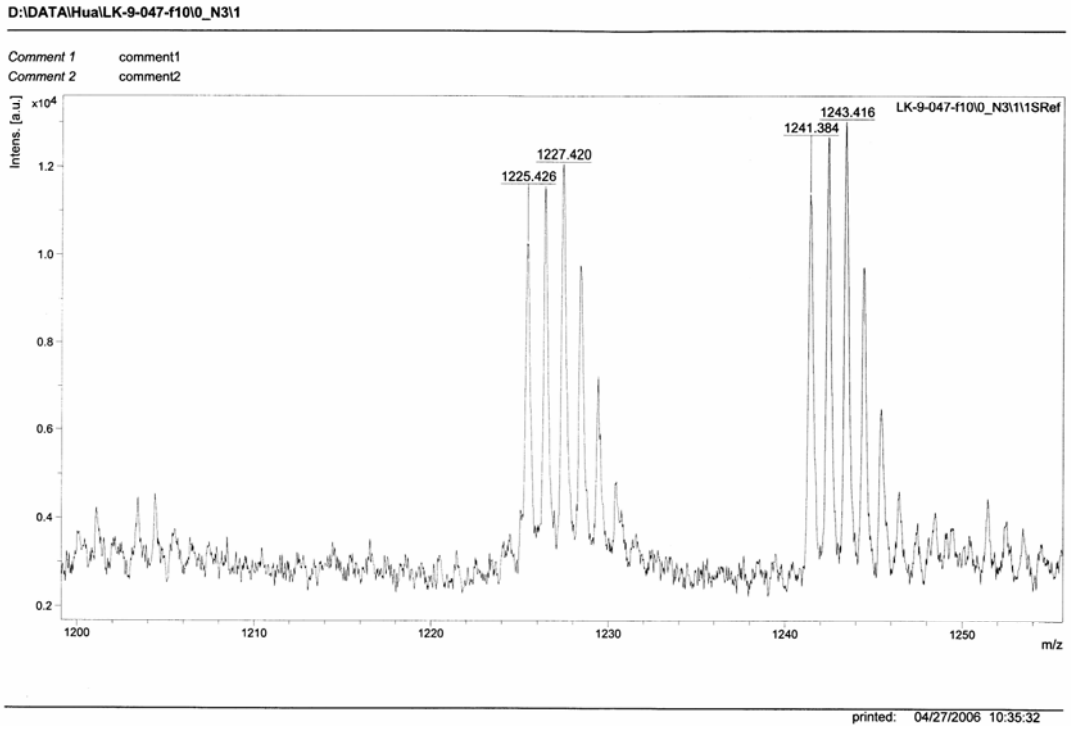


$(M+Na)^+$: $C_{80}H_{50}O_{12}Na$

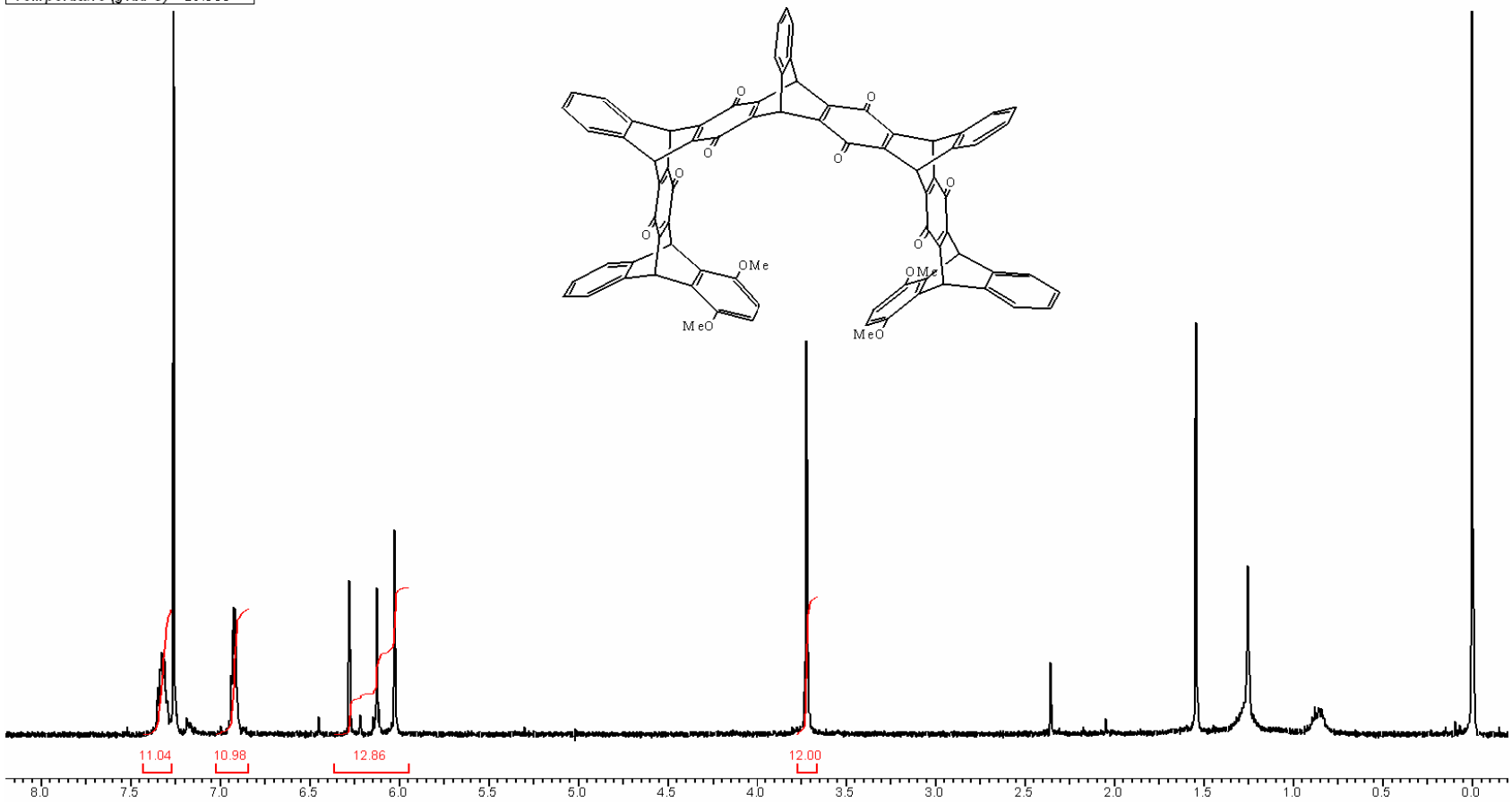
Exact Mass: 1225.3200
m/z: 1225.32 (100.0%), 1226.32 (87.0%), 1227.33 (37.9%), 1228.33 (12.9%), 1229.33 (3.2%), 1227.32 (2.5%)

$(M+K)^+$: $C_{80}H_{50}O_{12}K$

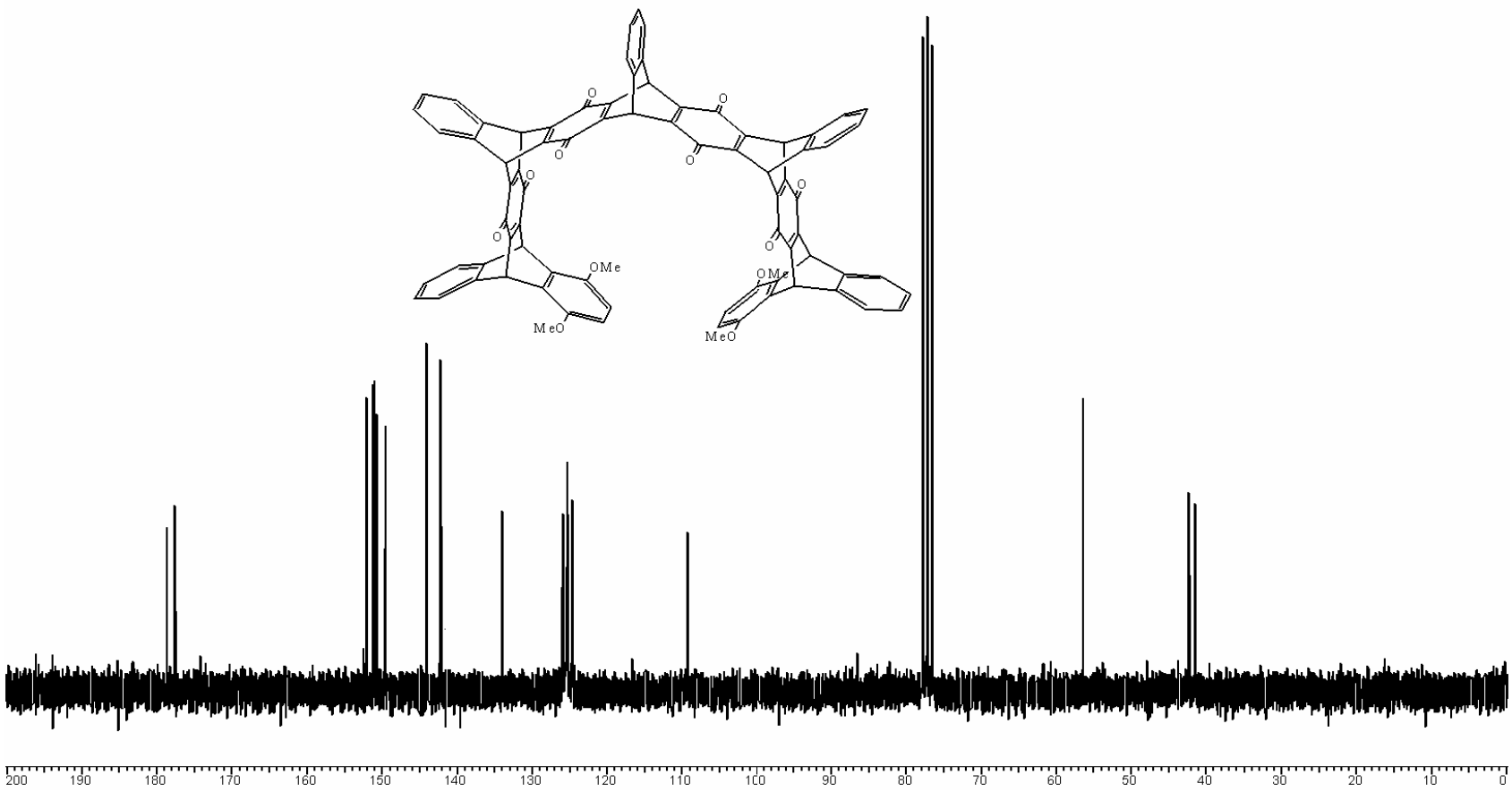
Exact Mass: 1241.2939
m/z: 1241.29 (100.0%), 1242.30 (87.6%), 1243.30 (40.3%), 1244.30 (19.0%), 1243.29 (7.2%), 1245.30 (3.9%), 1245.31 (2.3%)

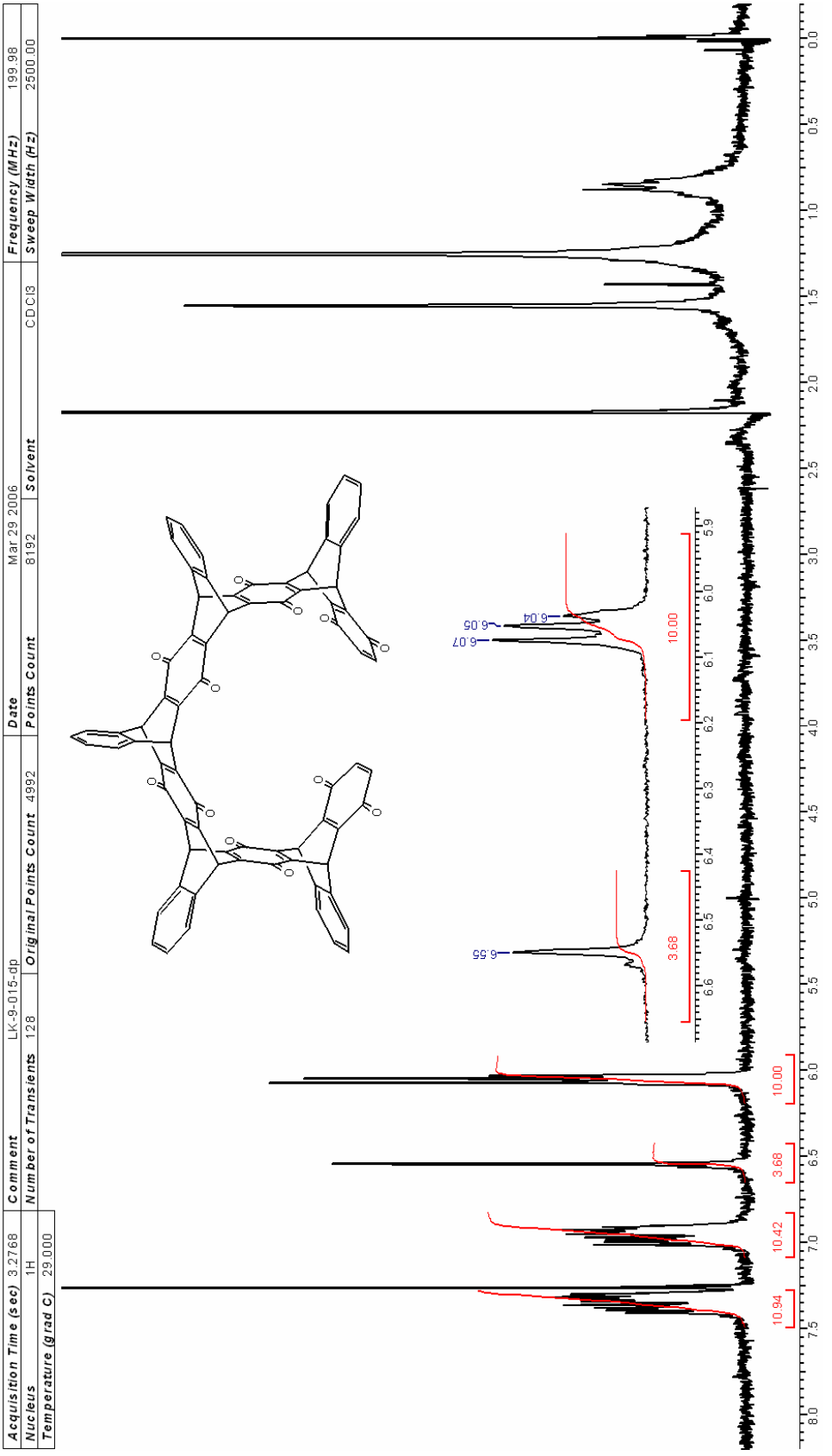


Acquisition Time (sec)	5.4608	*Comment*	LK-8-092-dp		*Date*	Feb 26 2006		*Frequency (MHz)*	399.78
Nucleus	1H	*Number of Transients*	32	*Original Points Count* 22208	*Points Count*	32768	*Solvent* CDCl3	*Sweep Width (Hz)*	6000.60
Temperature (grad C)	29.000								

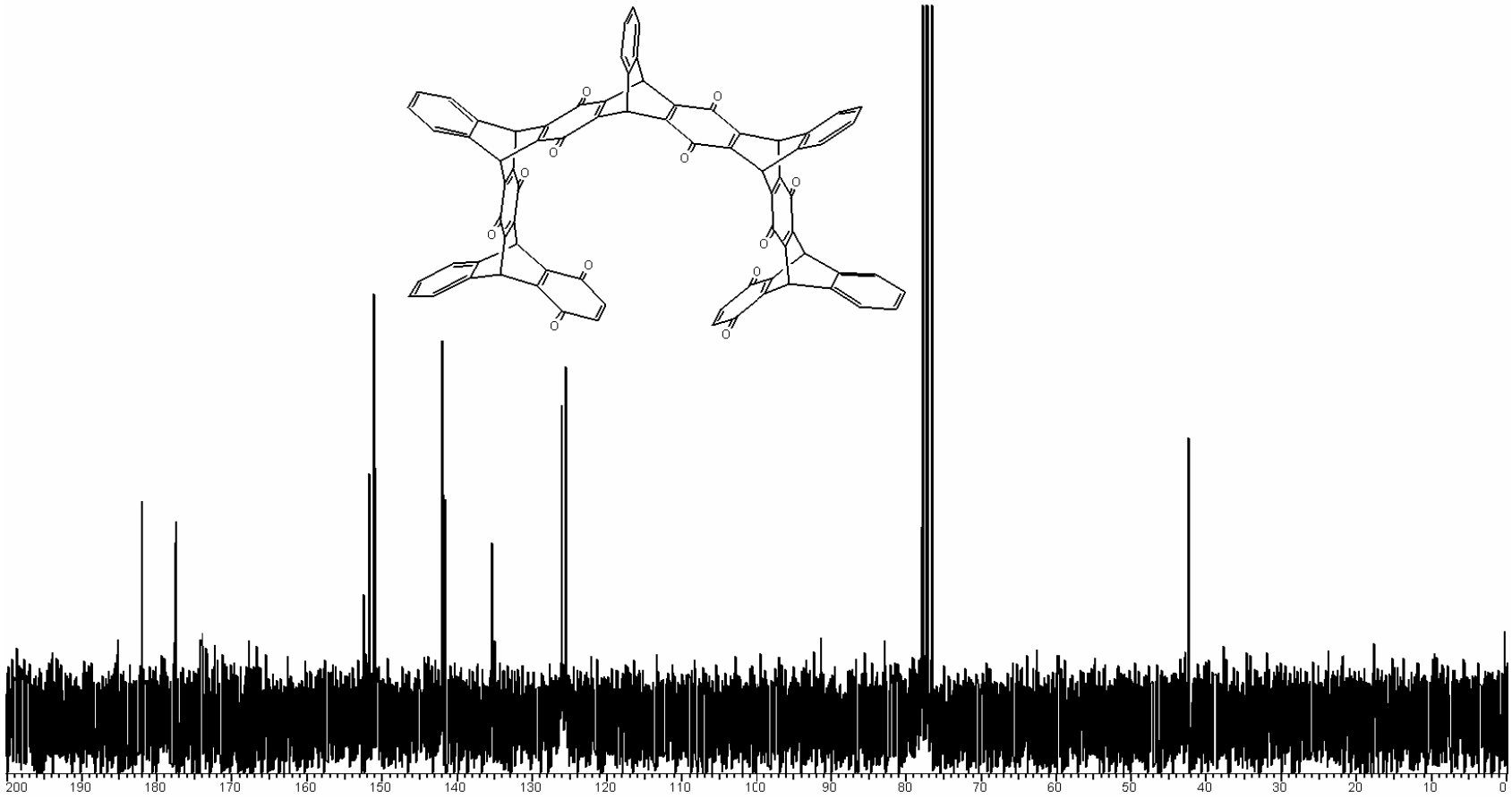


Acquisition Time (sec)	2.6214	*Comment*	LK-9-026-dp-c13		*Date*	Apr 8 2006		*Frequency (MHz)*	50.29
Nucleus	13C	*Number of Transients*	20000	*Original Points Count* 18720	*Points Count*	32768	*Solvent* CDCl3	*Sweep Width (Hz)*	12500.00
Temperature (grad C)	29.000								

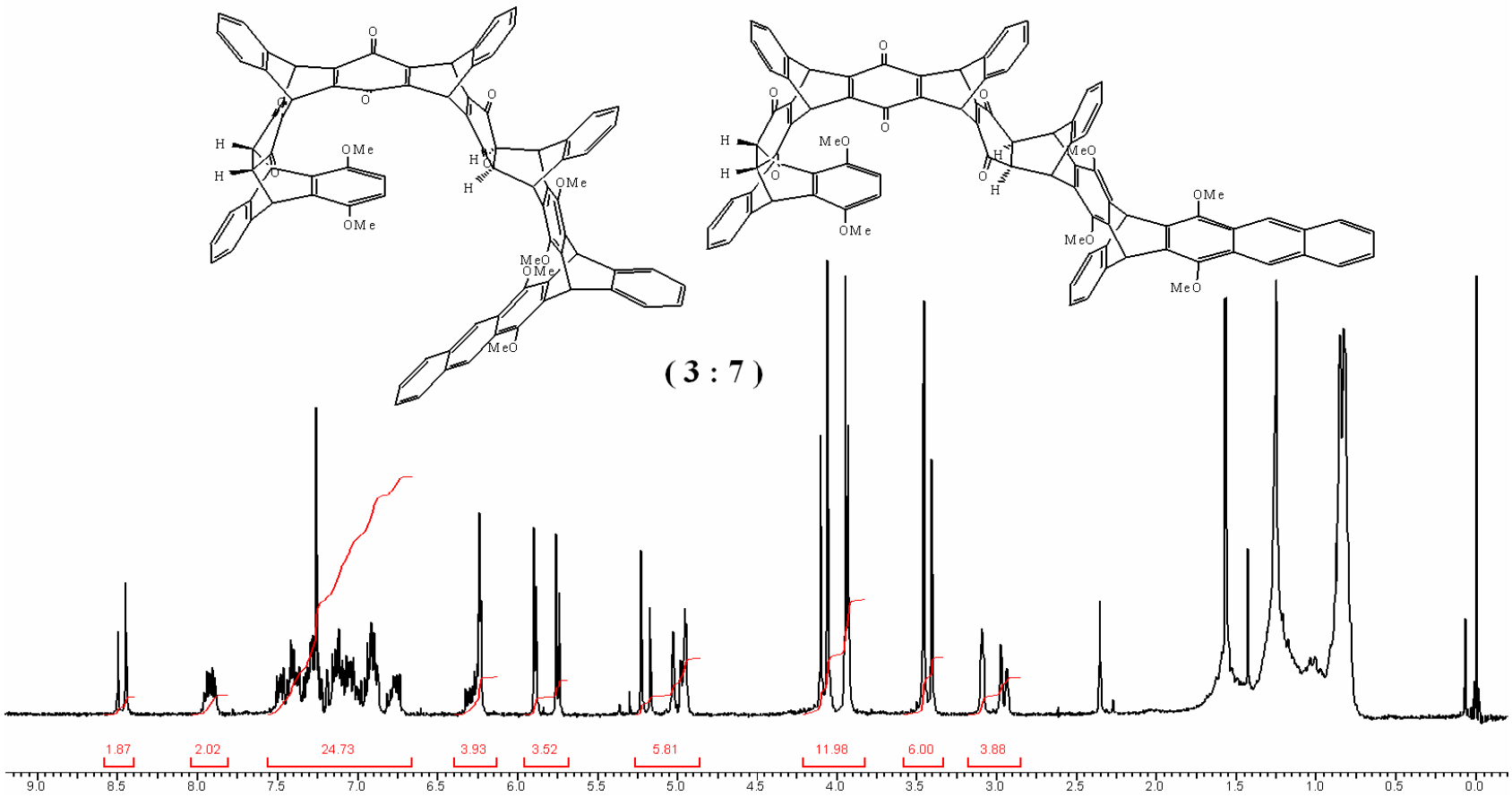



Acquisition Time (sec) 3.2768
Comment LK-9-015-dp
Date Mar 29 2006
Frequency (MHz) 199.98
Nucleus 1H
Number of Transients 128
Original Points Count 4992
Points Count 8192
Solvent CDCl3
Sweep Width (Hz) 2500.00
Temperature (grad C) 29.000
6.55
6.04
6.05
6.07
10.94
10.42
3.68
10.00
3.68
10.00

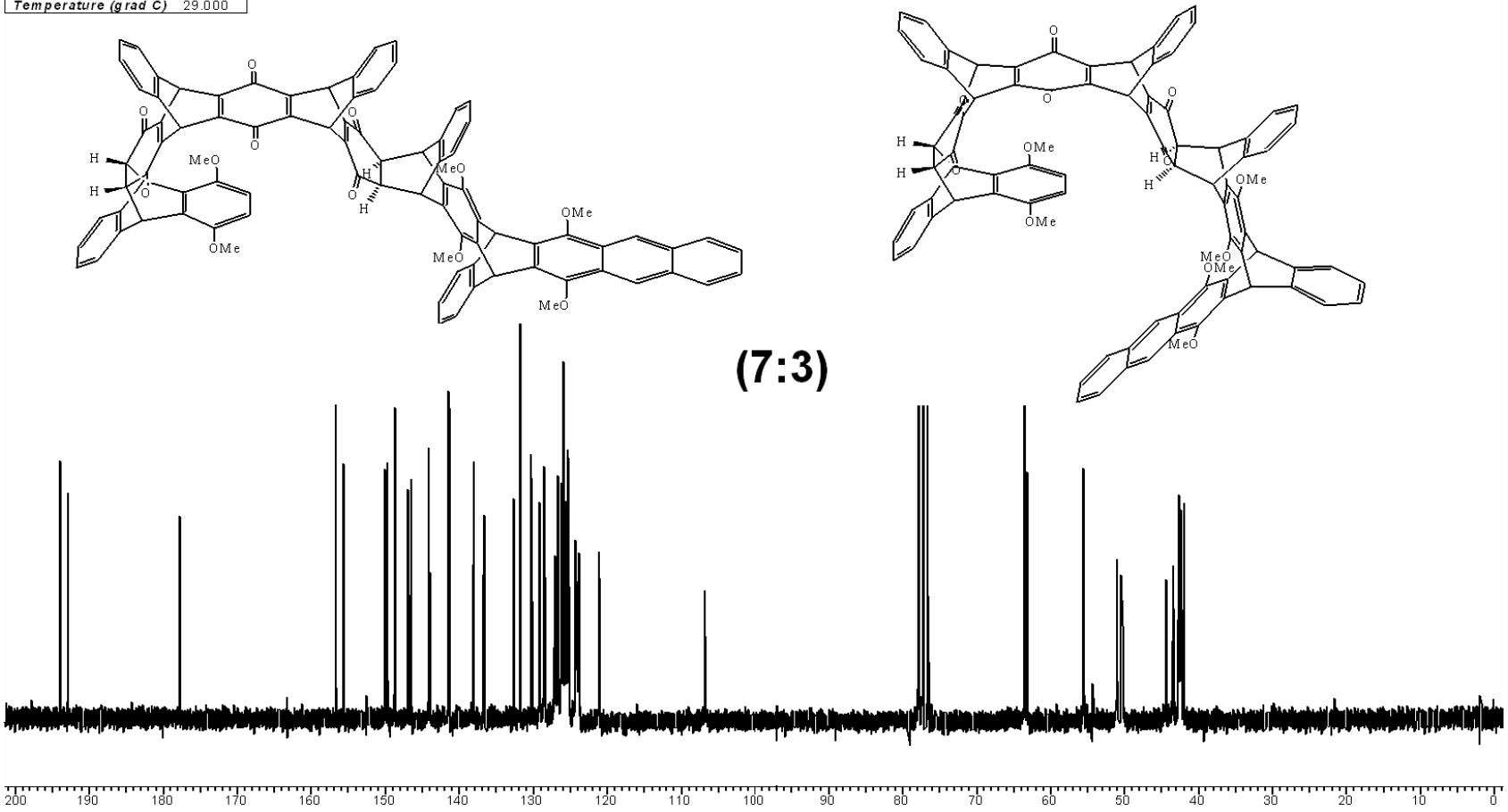
Acquisition Time (sec) 2.6214	***Comment*** LK-9-039-dp-c13			***Date*** Apr 17 2006				***Frequency (MHz)***	50.29
Nucleus 13C	***Number of Transients*** 20000	***Original Points Count*** 18720		***Points Count*** 32768		***Solvent*** CDCl3		***Sweep Width (Hz)***	12500.00
Temperature (grad C) 29.000									



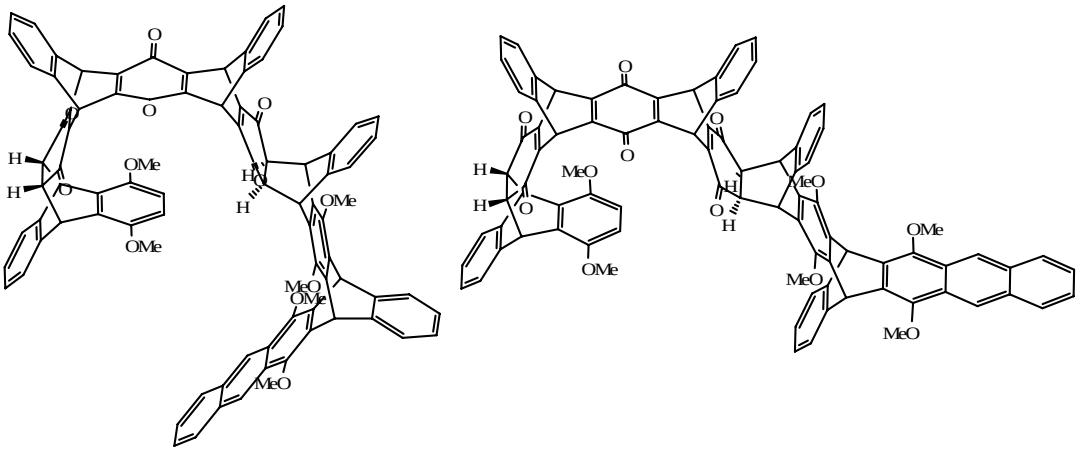
Acquisition Time (sec)	3.2768	*Comment*	LK-9-042-f6		*Date*	Apr 16 2006		*Frequency (MHz)*	199.98
Nucleus	1H	*Number of Transients*	128	*Original Points Count* 4992	*Points Count*	8192	*Solvent* CDCl3	*Sweep Width (Hz)*	2500.00
Temperature (grad C)	29.000								



Acquisition Time (sec)	2.6214	***Comment***	LK-9-107-dp-C13		***Date***	Aug 17 2006		***Frequency (MHz)***	50.29
Nucleus	13C	***Number of Transients***	20000	***Original Points Count*** 18720	***Points Count***	32768	***Solvent*** CDCl3	***Sweep Width (Hz)***	12500.00
Temperature (grad C)	29.000								

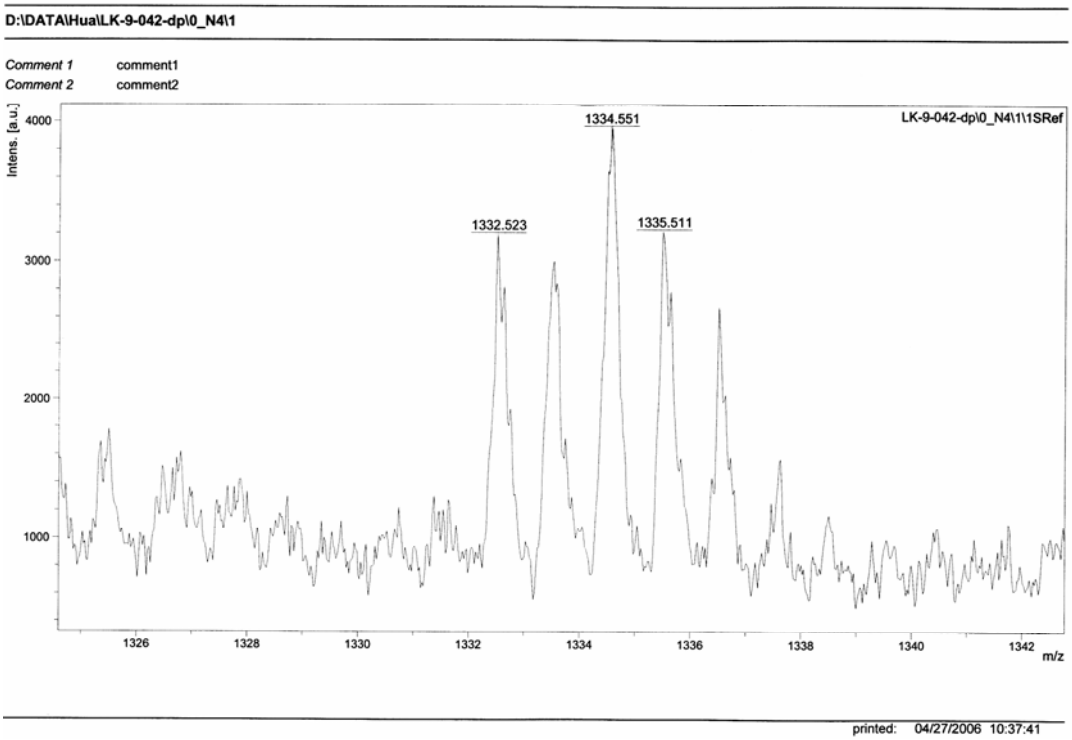


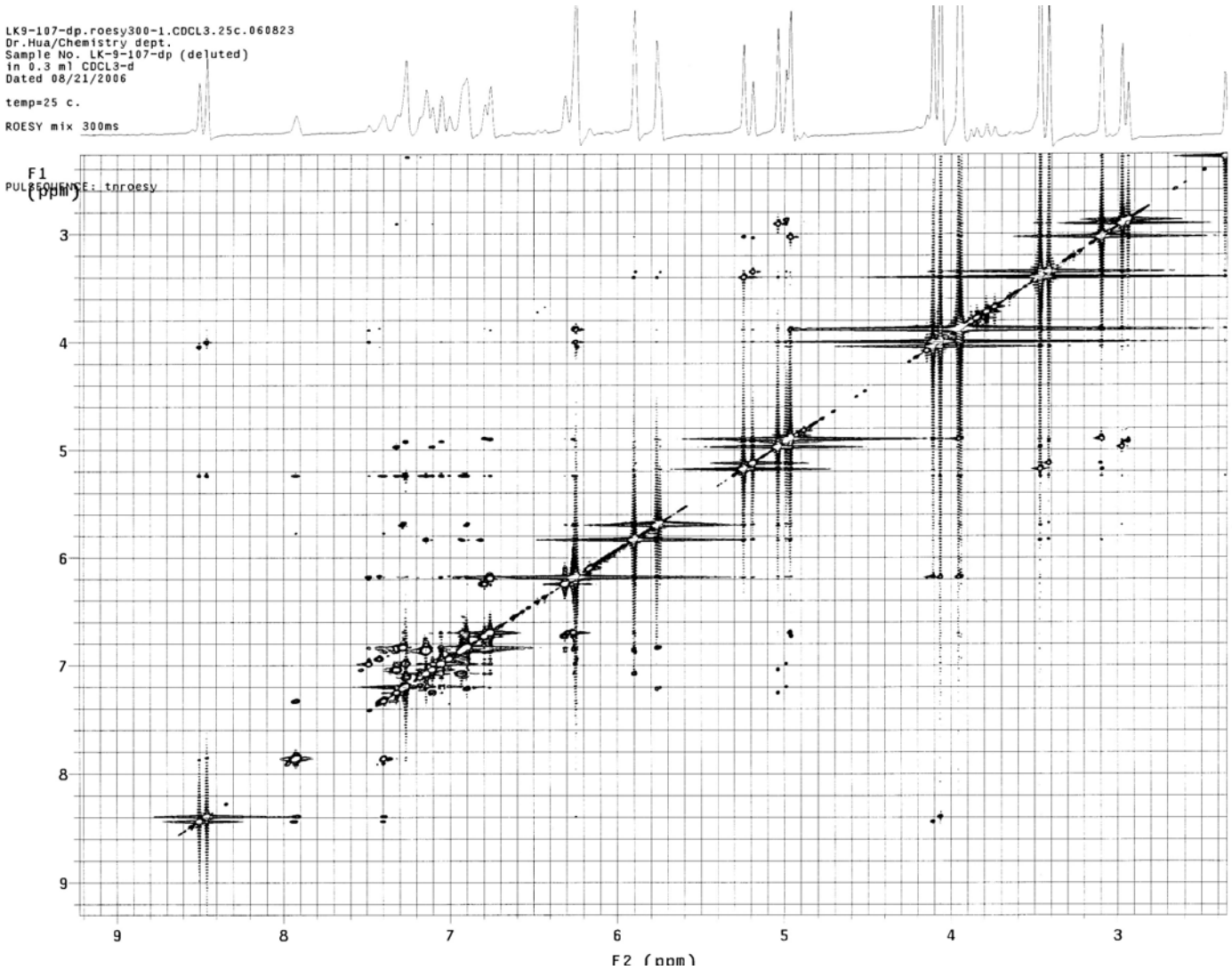
LK-9-042-dp



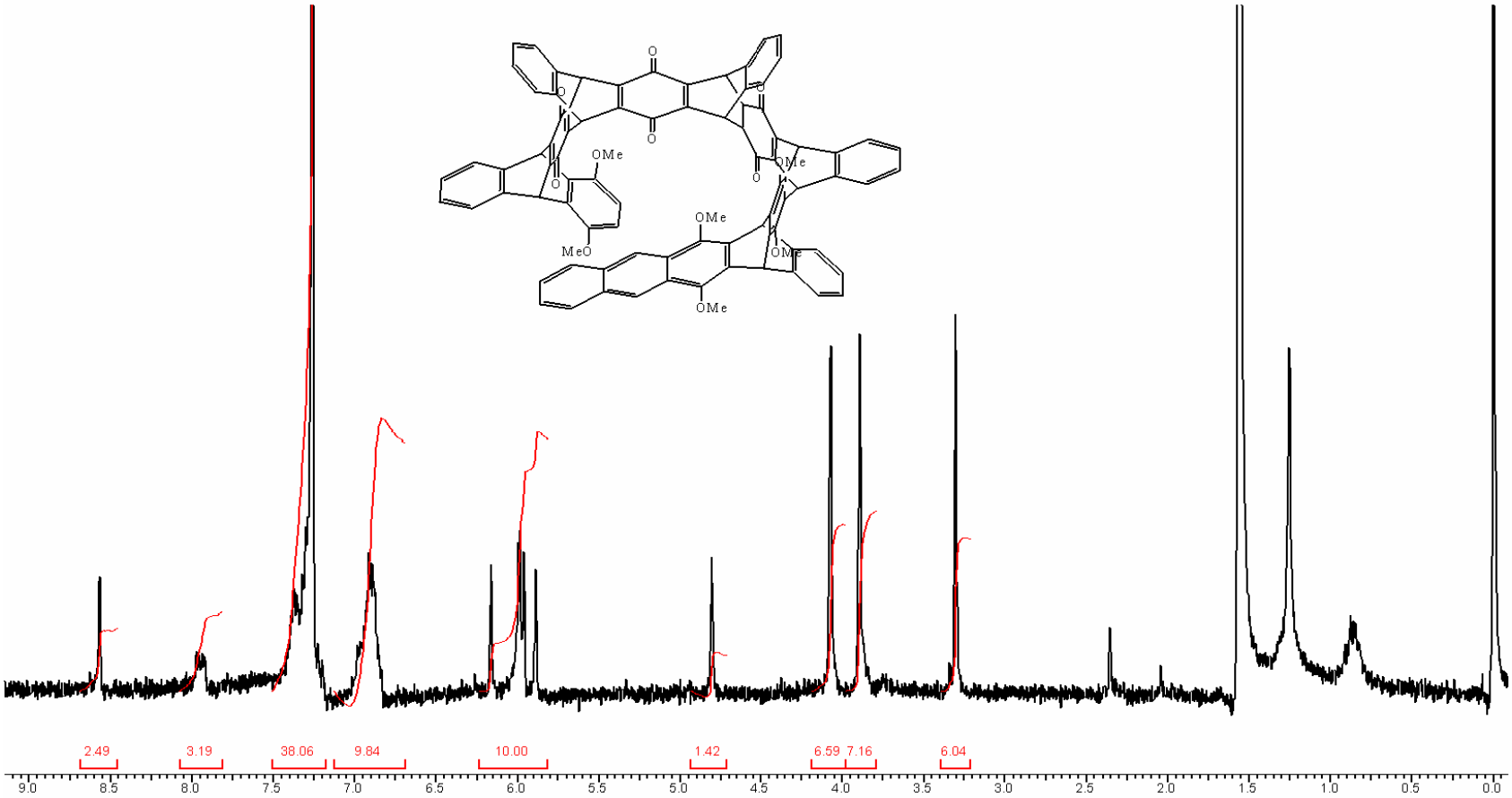
$(M+H)^+$: $C_{90}H_{61}O_{12}$

Exact Mass: 1333.4163
m/z: 1333.42 (100.0%), 1334.42 (98.5%), 1335.
42 (49.8%), 1336.43 (15.4%), 1337.43 (4.8%), 1336.42 (2.4%), 1338.43 (1.1%)

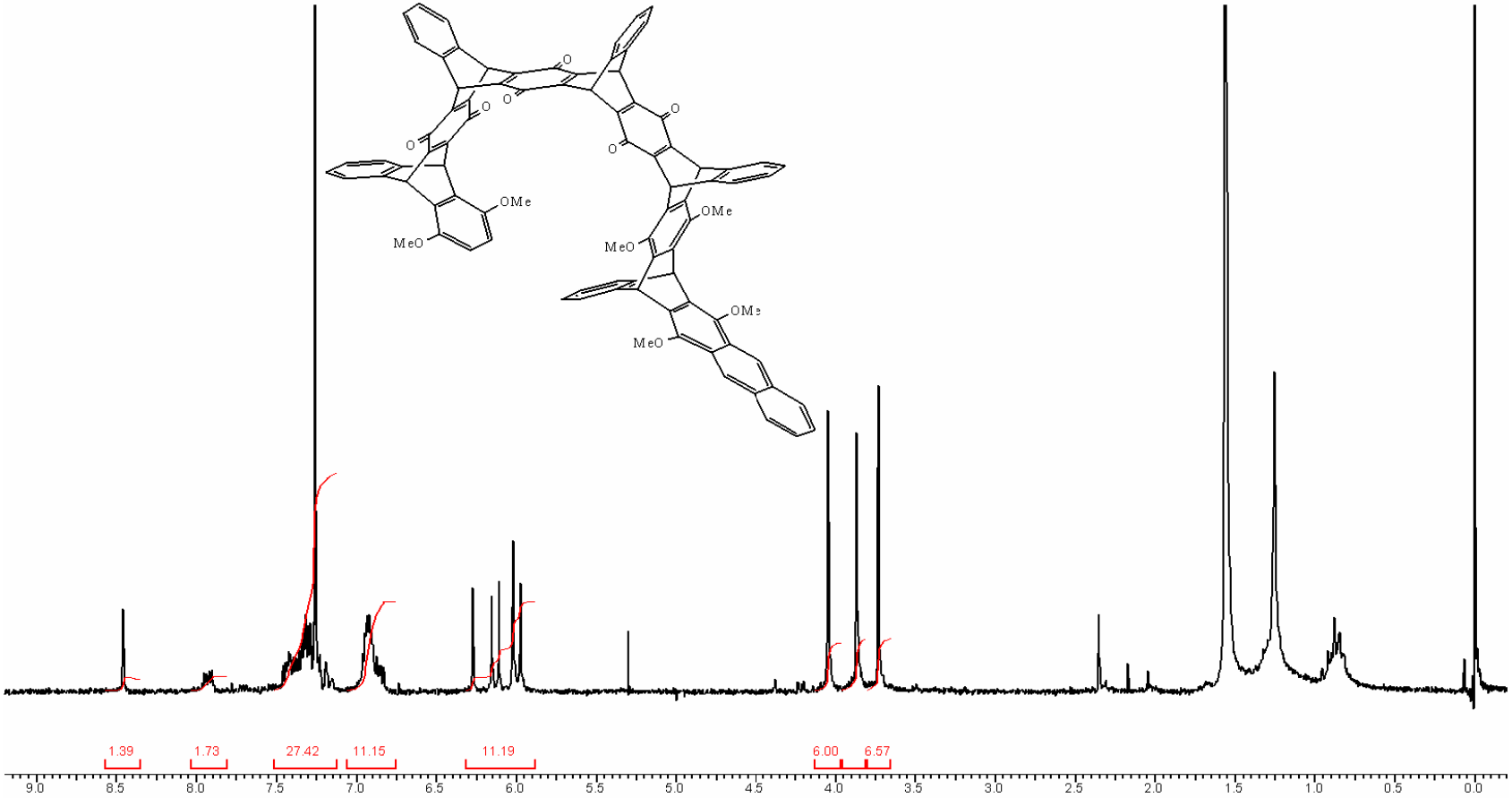


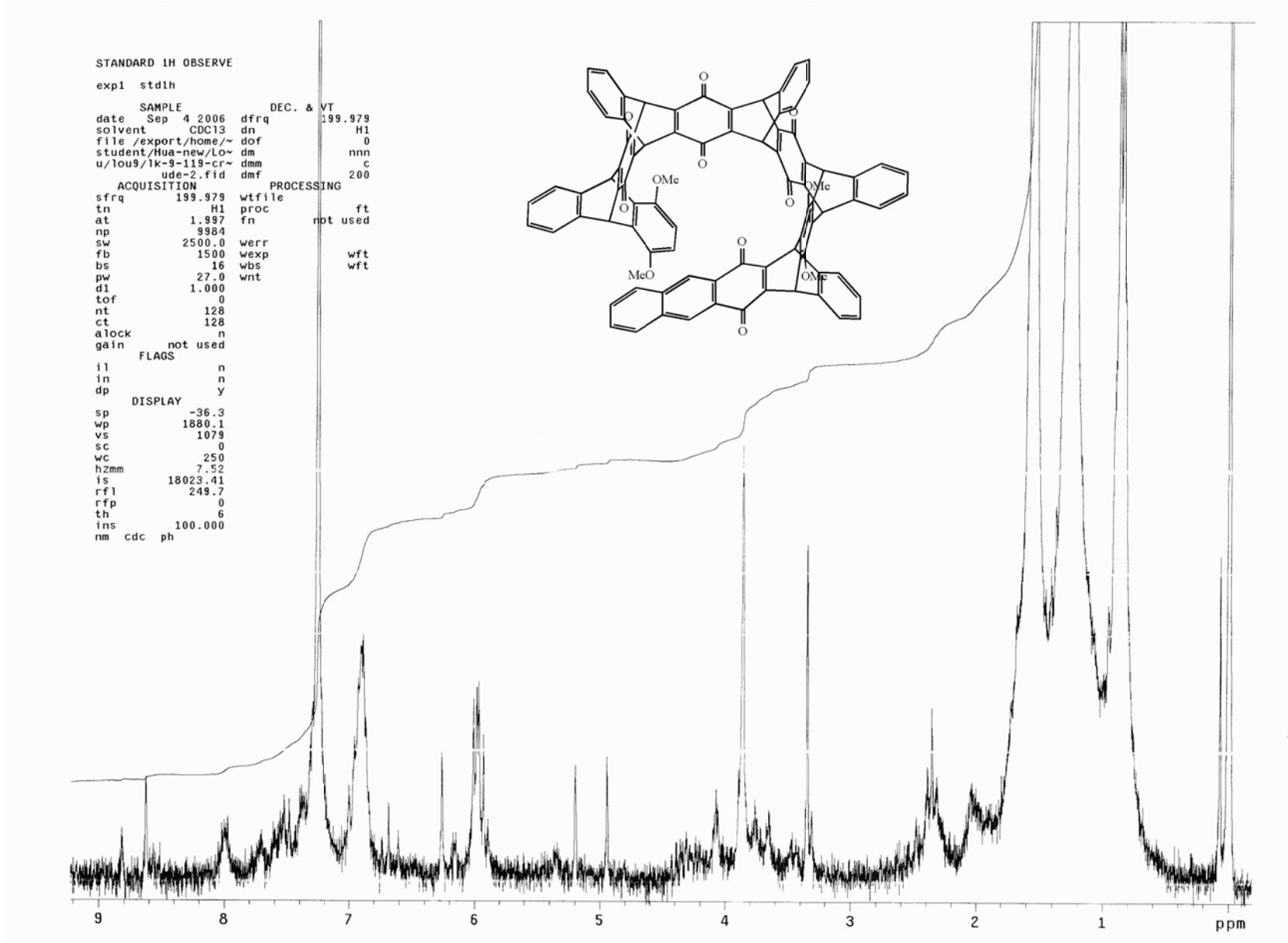

LK9-107-dp.roesy300-1.CDCL3.25c.060823
Dr.Hua/Chemistry dept.
Sample No. LK-9-107-dp (deluted)
in 0.3 ml CDCL3-d
Dated 08/21/2006
temp=25 c.
ROESY mix 300ms
PULSESEQUENCE: tnroesy
F1 (ppm)
3
4
5
6
7
8
9
9
8
7
6
5
4
3
F2 (ppm)

Acquisition Time (sec)	3.2768	***Comment***	LK-9-116-dp		***Date***	Aug 24 2006		***Frequency (MHz)***	199.98
Nucleus	1H	***Number of Transients***	128	***Original Points Count*** 4992	***Points Count***	8192	***Solvent*** CDCl3	***Sweep Width (Hz)***	2500.00
Temperature (grad C)	29.000								

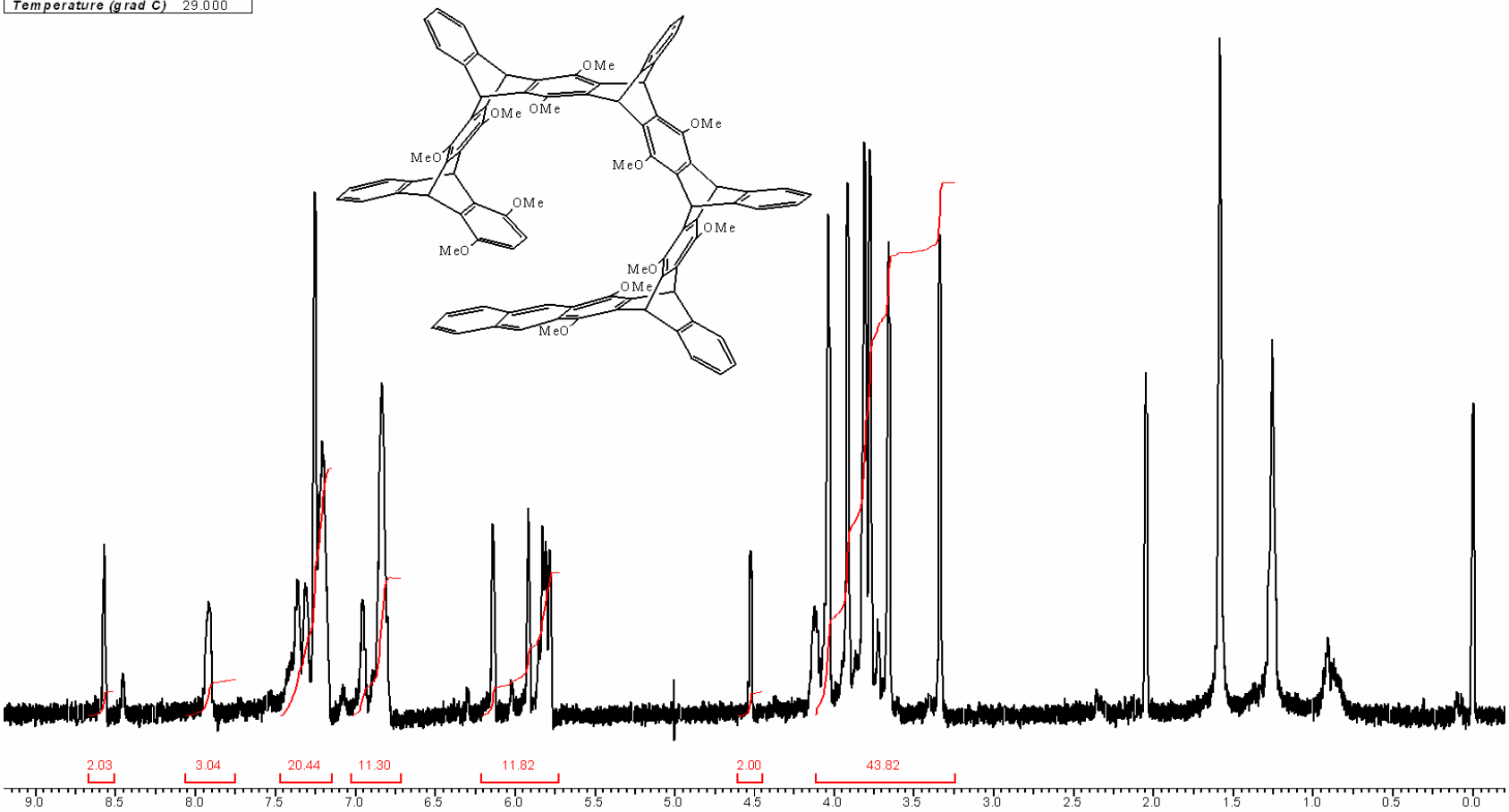


Acquisition Time (sec)	3.2768	***Comment***	LK-9-116-isomer		***Date***	Aug 25 2006		***Frequency (MHz)***	199.98
Nucleus	1H	***Number of Transients***	128	***Original Points Count*** 4992	***Points Count***	8192	***Solvent*** CDCl3	***Sweep Width (Hz)***	2500.00
Temperature (grad C)	29.000								

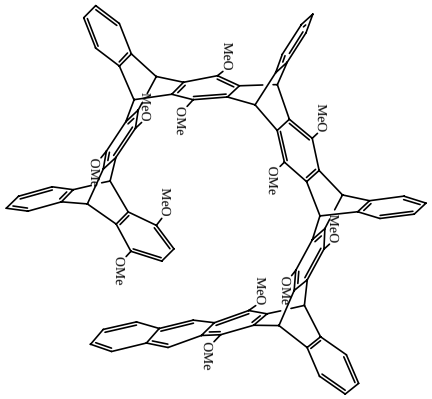


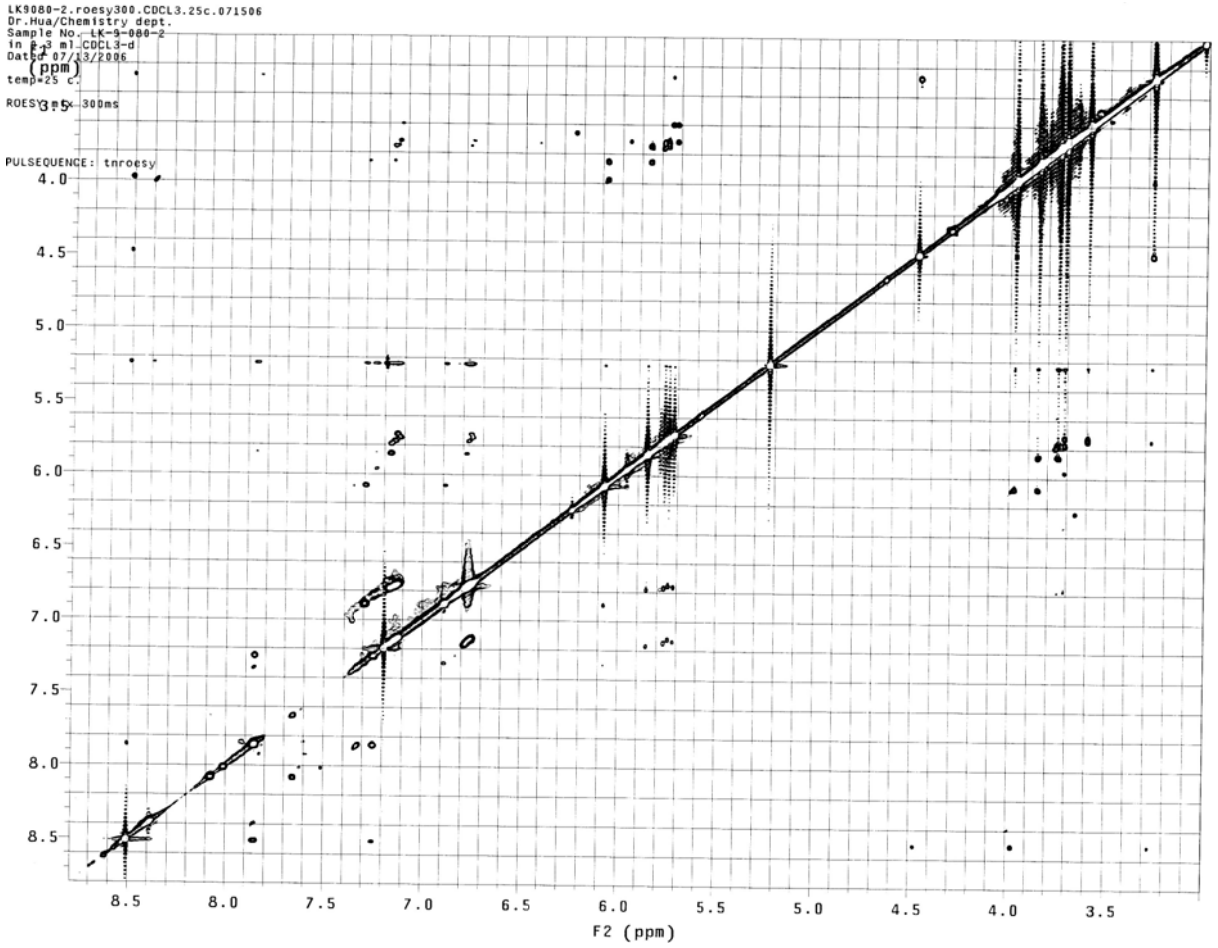

STANDARD 1H OBSERVE
exp1 std1h
SAMPLE
date Sep 4 2006
solvent CDCl3
file /export/home/~
student/Hua-new/Lo~
u/lou9/lk-9-119-cr~
ude-2.fid
ACQUISITION
sfrq 199.979
tn H1
at 1.997
np 9984
sw 2500.0
fb 1500
bs 16
pw 27.0
d1 1.000
tof 0
nt 128
ct 128
alock n
gain not used
FLAGS
il n
in n
dp y
DISPLAY
sp -36.3
wp 1880.1
vs 1079
sc 0
wc 250
hzmm 7.52
is 18023.41
rfl 249.7
rfp 0
th 6
ins 100.000
nm cdc ph
DEC. & VT
dfrq 199.979
dn H1
dof 0
dm nnn
dmm c
dmf 200
PROCESSING
wtfile
proc ft
fn not used
werr
wexp wft
wbs wft
wnt
OMe
MeO
9
8
7
6
5
4
3
2
1
ppm

Acquisition Time (sec)	6.5536	***Comment***	LK-9-082-dp		***Date***	Jul 17 2006		***Frequency (MHz)***	399.78
Nucleus	1H	***Number of Transients***	128	***Original Points Count*** 18505	***Points Count***	32768	***Solvent*** CDCl3	***Sweep Width (Hz)***	5000.00
Temperature (grad C)	29.000								

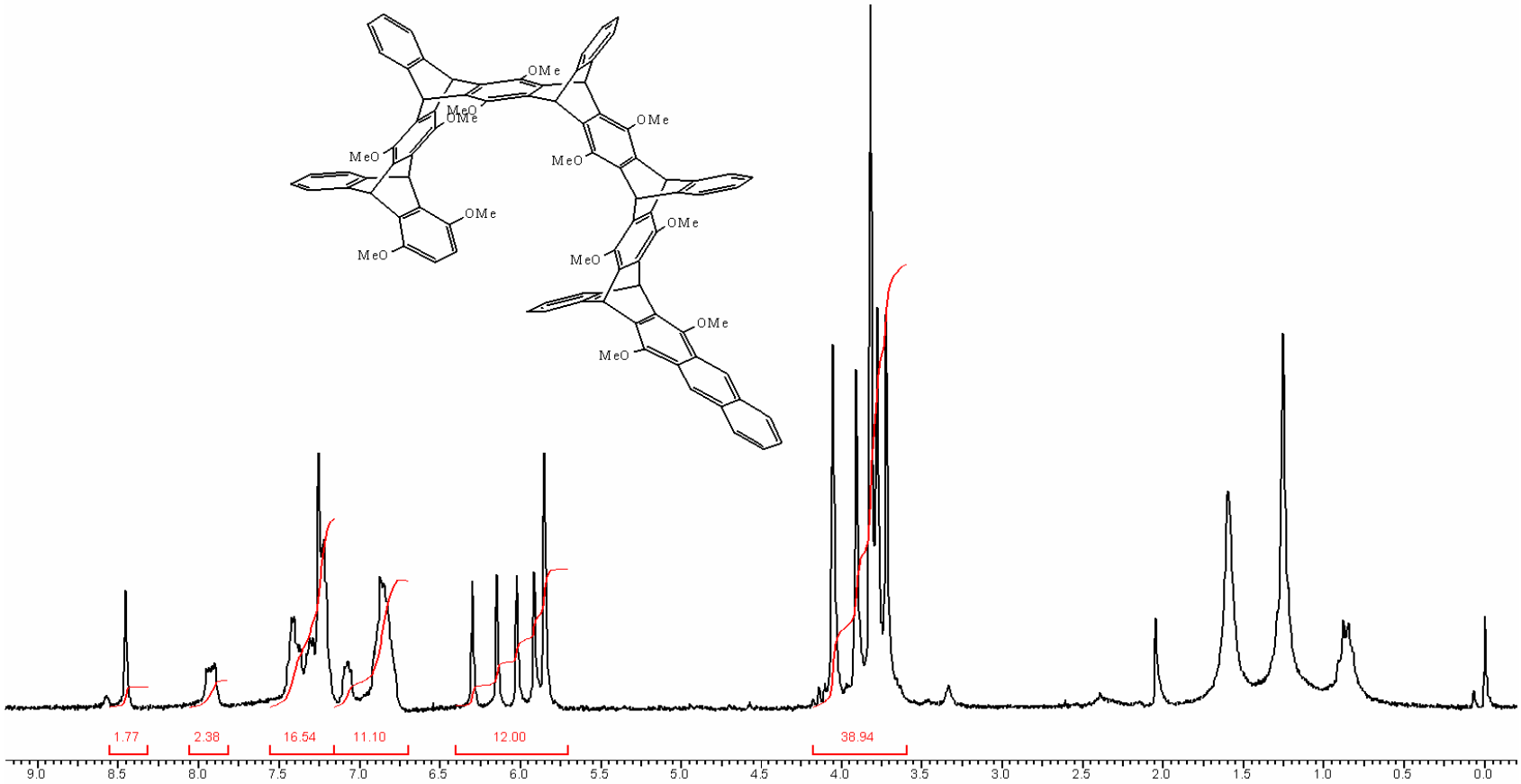


LK-9-080-2-ROESY

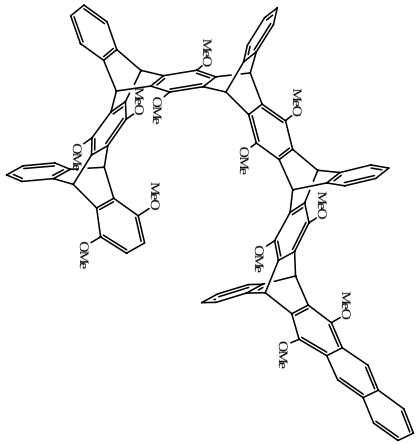


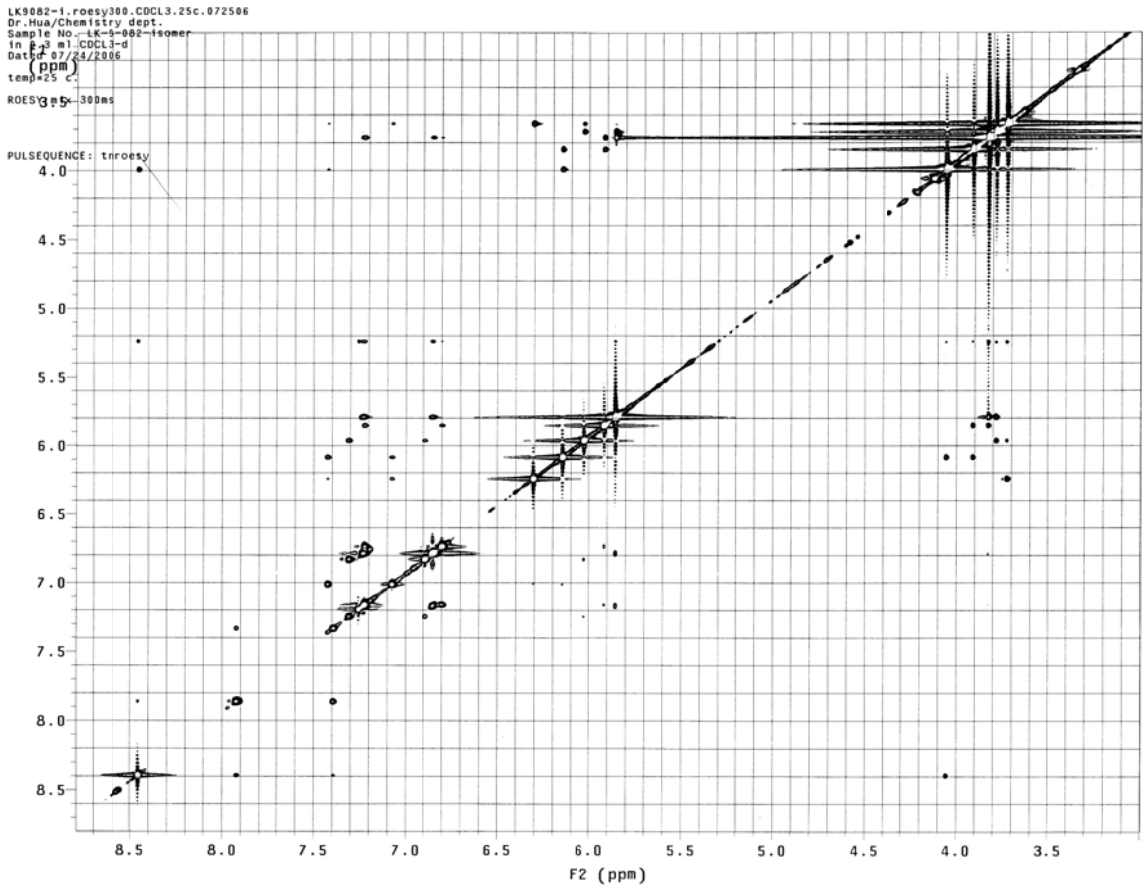


Acquisition Time (sec)	3.2768	***Comment***	LK-9-082-isomer		***Date***	Jul 24 2006		***Frequency (MHz)***	199.98
Nucleus	1H	***Number of Transients***	128	***Original Points Count*** 4992	***Points Count***	8192	***Solvent*** CDCl3	***Sweep Width (Hz)***	2500.00
Temperature (grad C)	29.000								

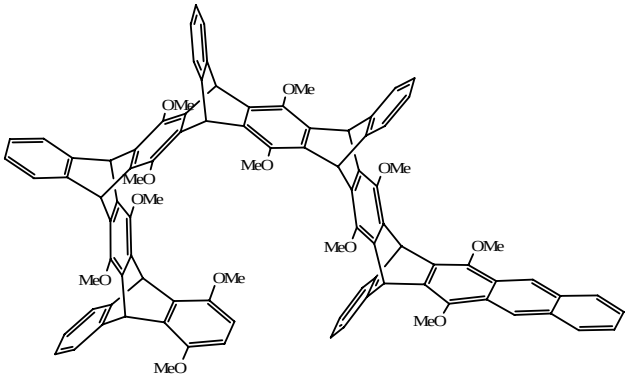


LK-9-082-isomer-ROESY





LK-9-080-1



$(M+H)^+$: $C_{96}H_{75}O_{12}$

Exact Mass: 1419.5259

m/z: 1420.53 (100.0%), 1419.53 (95.1%), 1421.53 (53.5%), 1422.54 (17.9%), 1423.54 (5.8%), 1422.53 (2.4%), 1424.54 (1.3%)

$(M+Na)^+$: $C_{96}H_{74}O_{12}Na$

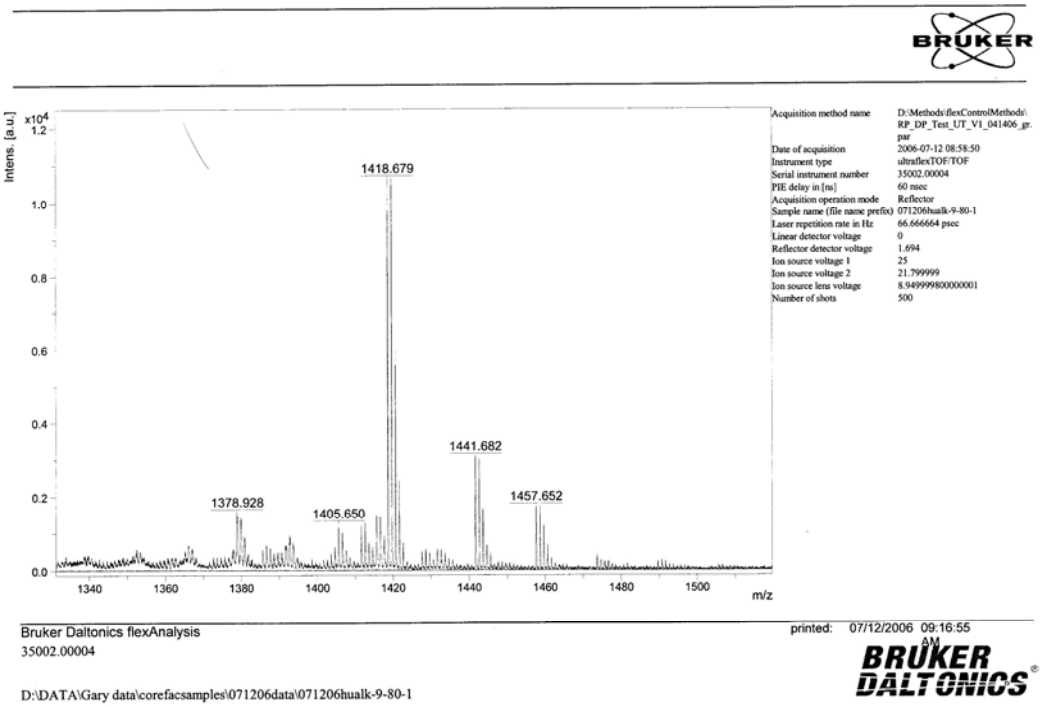
Exact Mass: 1441.5078

m/z: 1442.51 (100.0%), 1441.51 (95.1%), 1443.51 (53.1%), 1444.52 (20.3%), 1445.52 (5.8%), 1446.52 (1.3%), 1443.52 (1.3%)

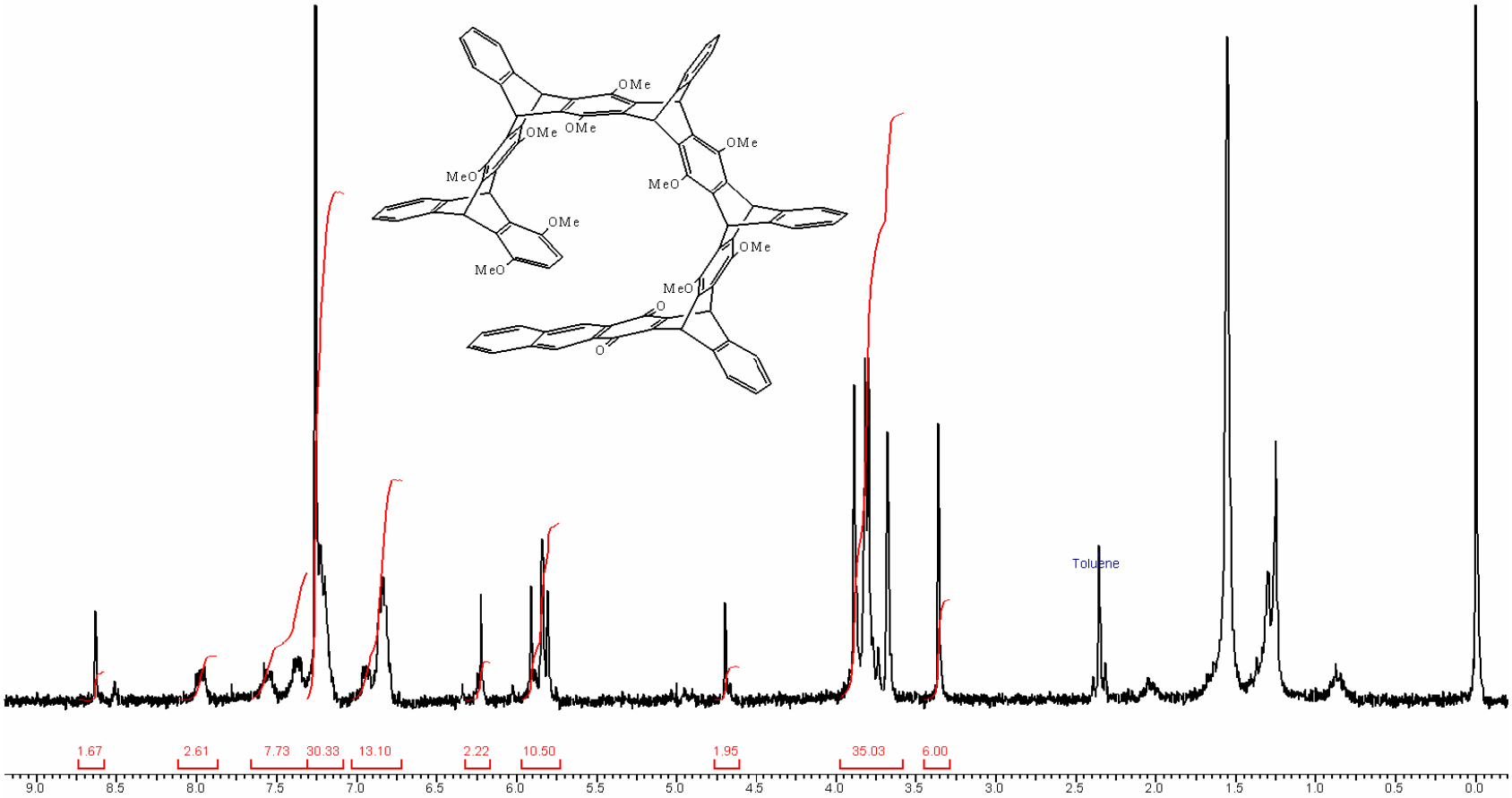
$(M+K)^+$: $C_{96}H_{74}O_{12}K$

Exact Mass: 1457.4817

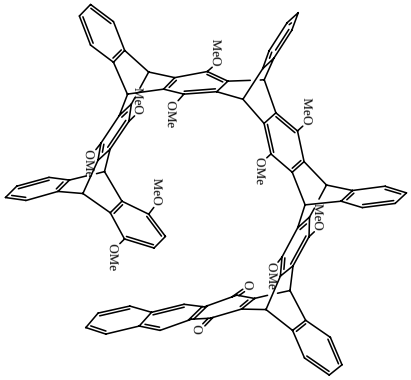
m/z: 1458.49 (100.0%), 1457.48 (95.1%), 1459.49 (54.4%), 1460.49 (20.4%), 1460.48 (7.2%), 1459.48 (6.9%), 1461.49 (5.0%), 1461.50 (4.6%), 1462.49 (1.5%), 1462.50 (1.3%)

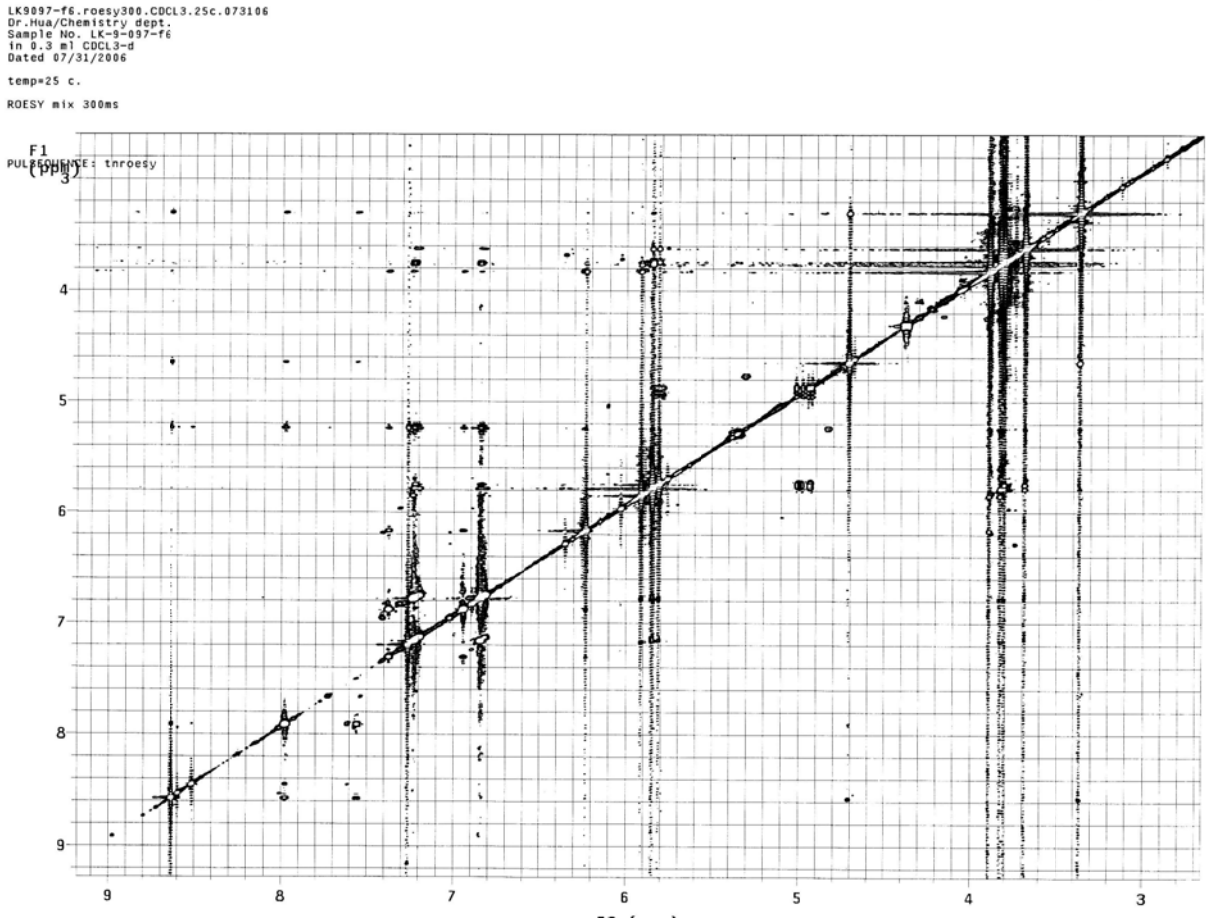


Acquisition Time (sec)	3.2768	*Comment*	LK-9-097-f6		*Date*	Jul 30 2006		*Frequency (MHz)*	199.98
Nucleus	1H	*Number of Transients*	128	*Original Points Count* 4992	*Points Count*	8192	*Solvent* CDCl3	*Sweep Width (Hz)*	2500.00
Temperature (grad C)	29.000								

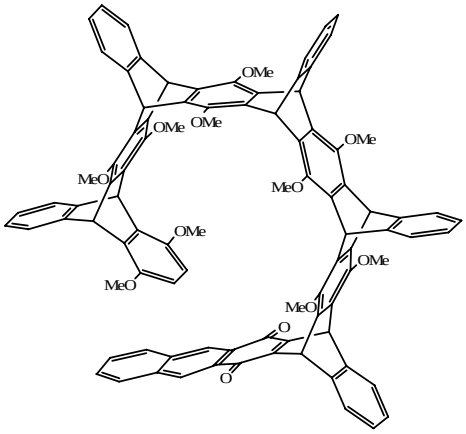


LK-9-097-f6-ROESY





LK-9-097-f6



$(M+H)^+$: $C_{94}H_{69}O_{12}$

Exact Mass: 1389.4789

m/z: 1390.48 (100.0%), 1389.48 (97.9%), 1391.49 (51.3%), 1392.49 (19.7%), 1393.49 (5.5%), 1391.48 (2.4%)

$(M+Na)^+$: $C_{94}H_{68}O_{12}Na$

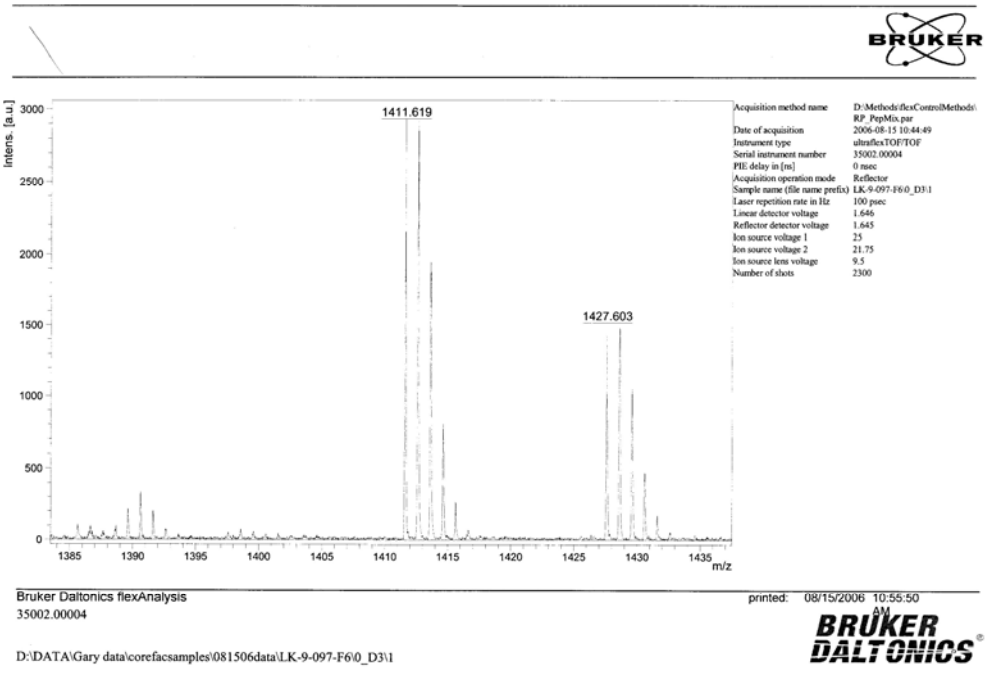
Exact Mass: 1411.4608

m/z: 1412.46 (100.0%), 1411.46 (98.4%), 1413.47 (54.0%), 1414.47 (19.8%), 1415.47 (5.4%), 1416.48 (1.3%), 1412.47 (1.2%)

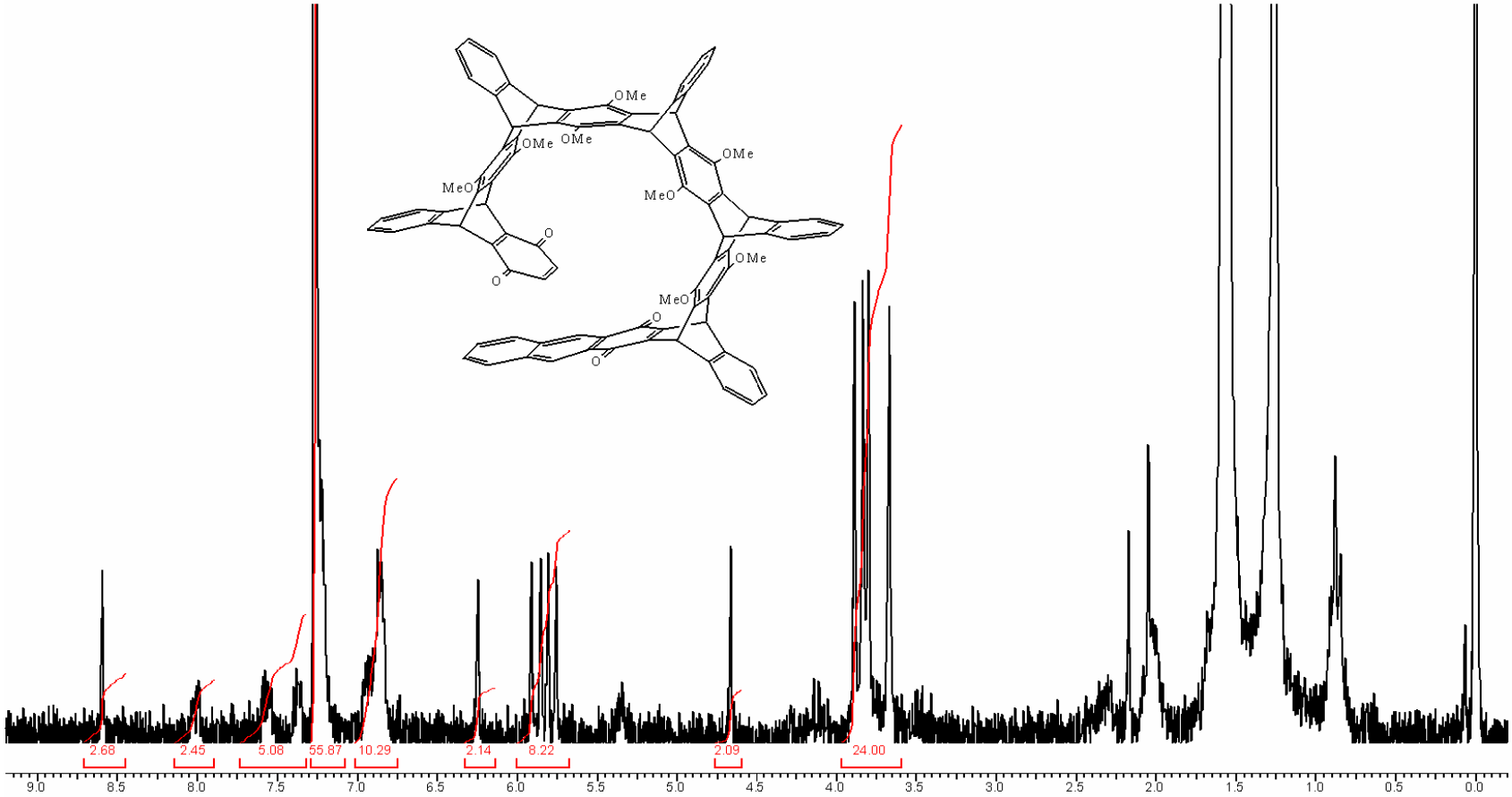
$(M+K)^+$: $C_{94}H_{68}O_{12}K$

Exact Mass: 1427.4348

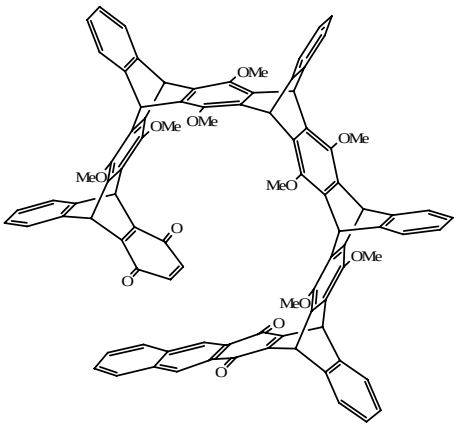
m/z: 1428.44 (100.0%), 1427.43 (97.2%), 1429.44 (53.3%), 1430.44 (26.1%), 1429.43 (7.0%), 1431.45 (5.5%), 1431.44 (3.9%), 1432.44 (1.4%), 1432.45 (1.3%)



Acquisition Time (sec)	3.2768	***Comment***	LK-9-098-dp		***Date***	Aug 4 2006		***Frequency (MHz)***	199.98
Nucleus	1H	***Number of Transients***	256	***Original Points Count*** 4992	***Points Count***	8192	***Solvent*** CDCl3	***Sweep Width (Hz)***	2500.00
Temperature (grad C)	29.000								



LK-9-098-dp



$(M+H)^+$: $C_{92}H_{63}O_{12}$

Exact Mass: 1359.432

m/z: 1360.44 (100.0%), 1359.43 (99.3%), 1361.44 (52.3%), 1362.44 (18.8%), 1363.45 (4.0%), 1363.44 (1.2%), 1364.45 (1.2%)

$(M+Na)^+$: $C_{92}H_{62}O_{12}Na$

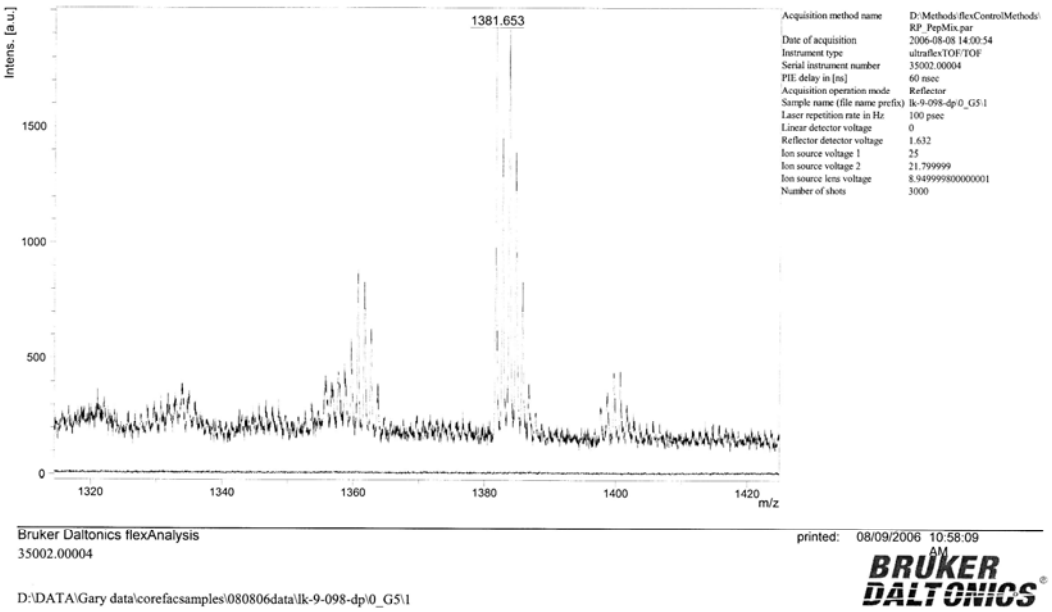
Exact Mass: 1381.4139

m/z: 1382.42 (100.0%), 1381.41 (99.3%), 1383.42 (52.2%), 1384.42 (18.5%), 1385.43 (4.0%), 1385.42 (1.2%), 1386.43 (1.2%)

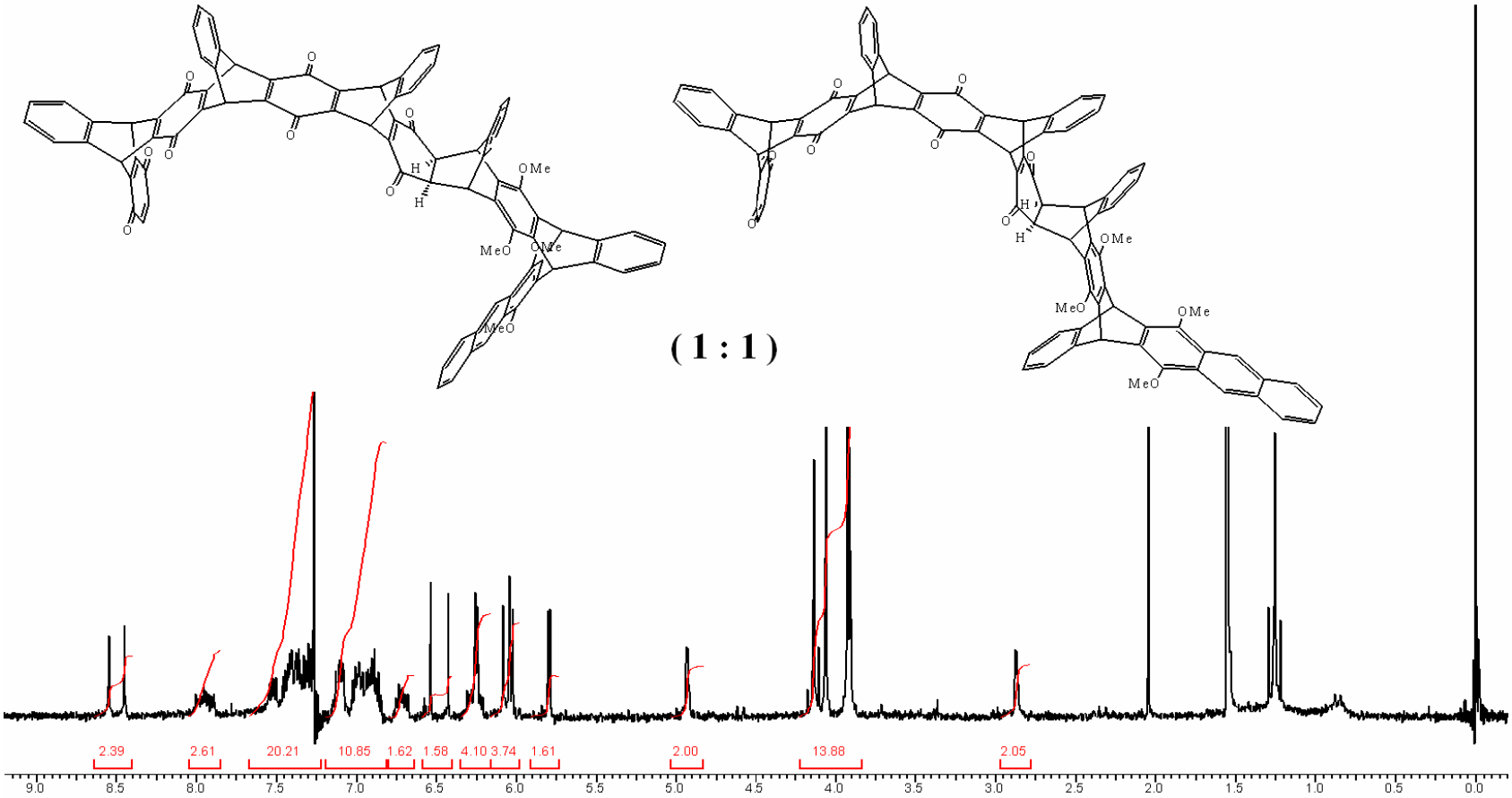
$(M+K)^+$: $C_{92}H_{62}O_{12}K$

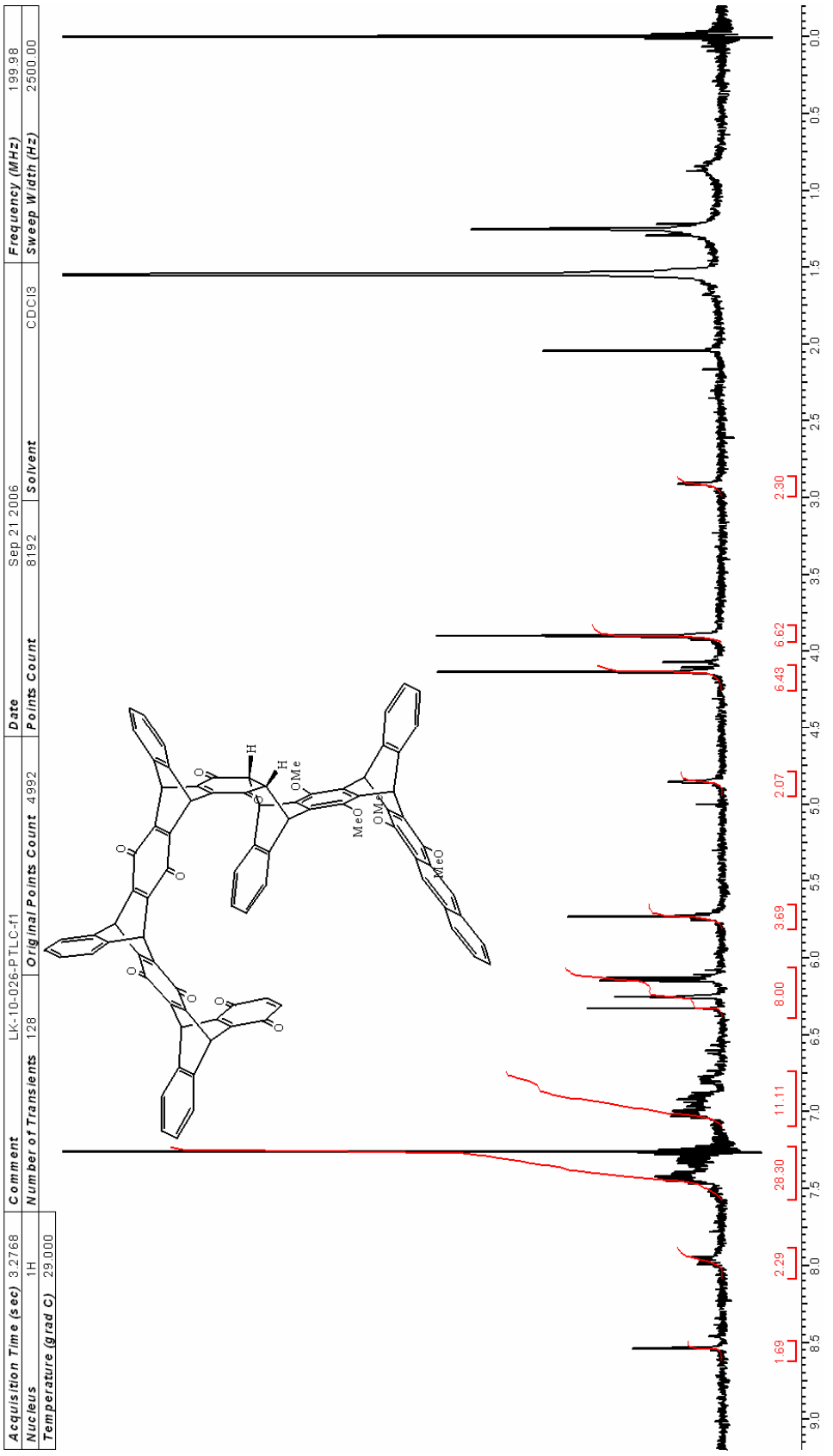
Exact Mass: 1397.3878

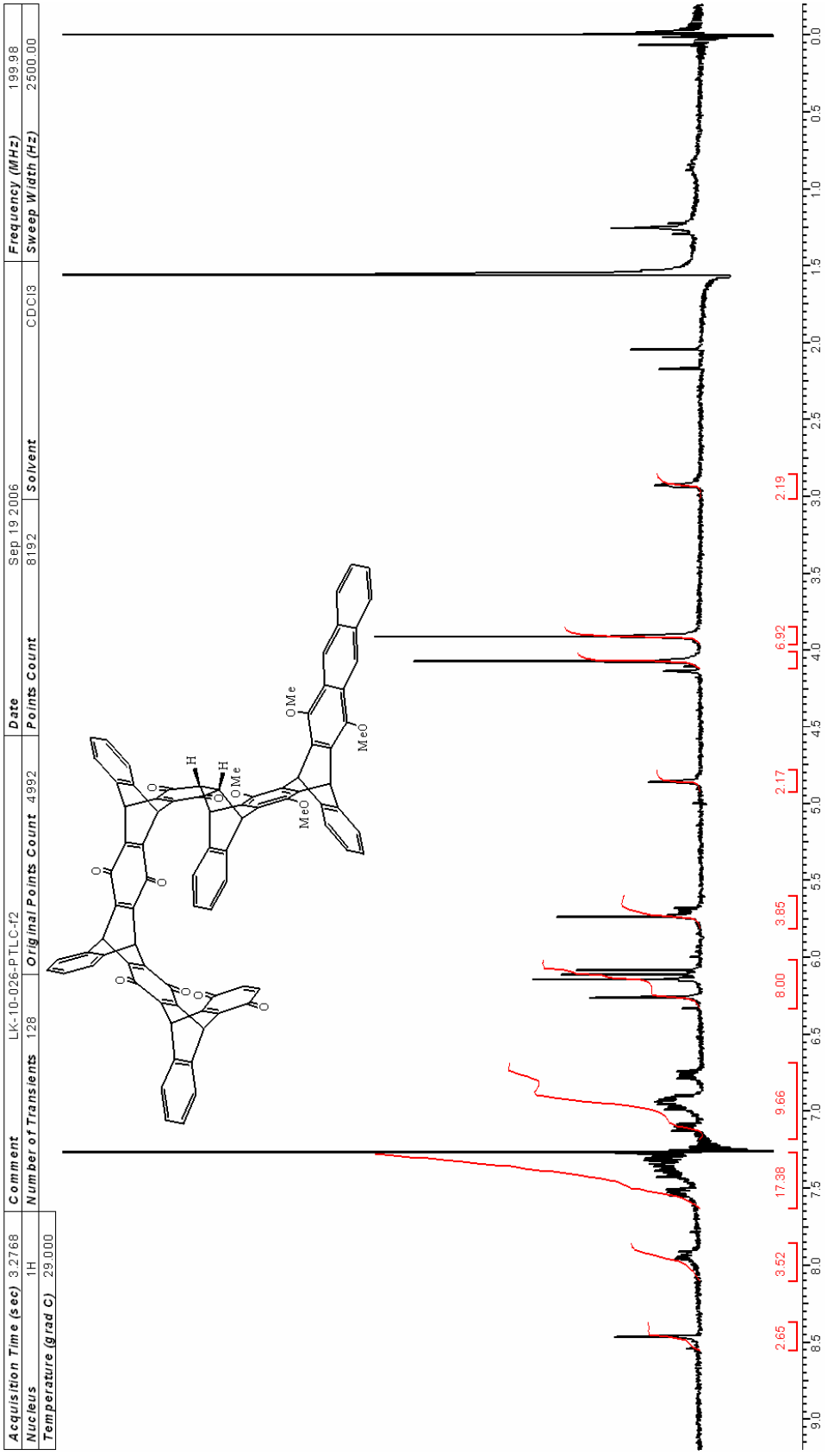
m/z: 1398.39 (100.0%), 1397.39 (99.3%), 1399.39 (58.3%), 1400.40 (18.8%), 1400.39 (7.2%), 1401.40 (5.3%), 1401.39 (3.7%), 1402.40 (2.3%), 1399.40 (1.2%)

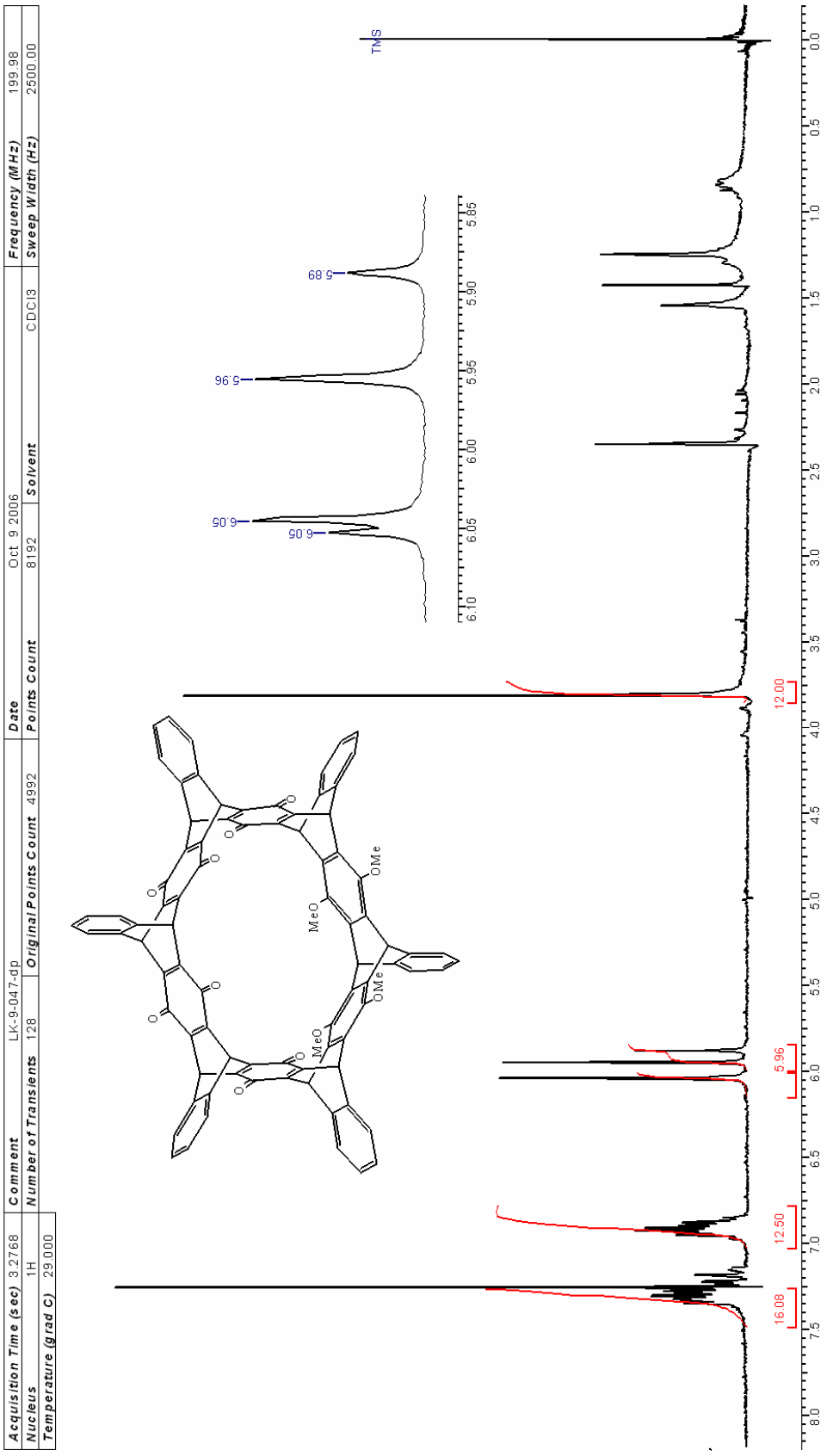


Acquisition Time (sec)	3.2768	*Comment*	LK-10-026-PTLC-f3		*Date*	Sep 18 2006		*Frequency (MHz)*	199.98
Nucleus	1H	*Number of Transients*	128	*Original Points Count* 4992	*Points Count*	8192	*Solvent* CDCl3	*Sweep Width (Hz)*	2500.00
Temperature (grad C)	29.000								




Acquisition Time (sec) 3.2768
Comment LK-10-026-PTLC-f1
Date Sep 21 2006
Frequency (MHz) 199.98
Nucleus 1H
Number of Transients 128
Original Points Count 4992
Points Count 8192
Solvent CDCl3
Sweep Width (Hz) 2500.00
Temperature (grad C) 29.000
MeO
OMe
1.69
2.29
28.30
11.11
8.00
3.69
2.07
6.43
6.62
2.30


Acquisition Time (sec) 3.2768
Comment LK-10-026-PTLC-f2
Date Sep 19 2006
Frequency (MHz) 199.98
Nucleus 1H
Number of Transients 128
Original Points Count 4992
Points Count 8192
Solvent CDCl3
Sweep Width (Hz) 2500.00
Temperature (grad C) 29.000
OMe
MeO
H
O
2.65
3.52
17.38
9.66
8.00
3.85
2.17
6.92
2.19


Acquisition Time (sec) 3.2768
Comment LK-9-047-dp
Date Oct 9 2006
Frequency (MHz) 199.98
Nucleus 1H
Number of Transients 128
Original Points Count 4992
Points Count 8192
Solvent CDCl3
Sweep Width (Hz) 2500.00
Temperature (grad C) 29.000
TMS
5.89
5.96
6.05
6.05
MeO
OMe
MeO
OMe
12.00
5.96
12.50
16.08

Acquisition Time (sec) 2.6214	***Comment*** LK-10-050-dp-C13			***Date*** Oct 14 2006		***Frequency (MHz)*** 50.29	
Nucleus 13C	***Original Points Count*** 18720	***Points Count*** 32768		***Solvent*** CDCl3	***Sweep Width (Hz)*** 12500.00		
Temperature (grad C) 29.000