SYNTHESIS OF AN OXETENE

by

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B. S., Kansas State College of
Agriculture and Applied Science, 1956

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A THESIS

submitted in partial fulfillment of the

requirements for the degree

MASTER OF SCIENCE

Department of Chemistry

KANSAS STATE COLLEGE
OF AGRICULTURE AND APPLIED SCIENCE

1958

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INTRODUCTION AND HISTORICAL

The oxetene ring system (I) is of theoretical importance
because of its high ring strain and its structural and elec-
tronic similarity to cyclobutadiene (III). The strain would
be greater in an oxetene ring than in an oxetane ring (II)
because of the greater bond angle distortion. The bond angle
is 120° for a double bond (IV) and 109½° for a single bond (V).
If the oxetane and oxetene rings are rectangular, the distor-
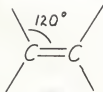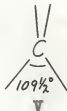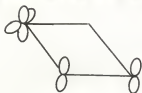tion is 19½° and 30° respectively.

I   II   III

IV   V
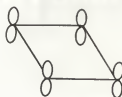
Both oxetene and cyclobutadiene have four membered rings
and both have two pairs of conjugated electrons (Ia, IIa).


IIa   IIIa

The synthesis of cyclobutadiene has been attempted many
times to test the hypothesis that three pairs of conjugated
electrons are necessary in a ring for aromaticity. Since

oxete has the same relationship to cyclobutadiene that α-and
γ-pyran have to benzene, the properties of oxetene may give
some indication of the aromaticity of cyclobutadiene. For
example, oxetene, like the pyrans, may form stable 'onium salts
of "aromatic" character.

α-pyran   γ-pyran   benzene

oxetenonium ion   pyrillium ion
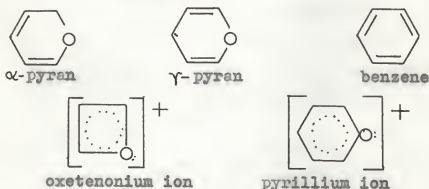
The only example of the oxetene ring system seems to be
3-phenyl-4-ethyloxetene, which Rupe and Huber (14) claimed to
have prepared. Hydroxymethylenephenylacetonitrile (VII) was
reduced to β-phenylhydroxymethylene ethylidenimine (VIII) which
was in turn hydrolyzed, without isolation, to hydroxymethylene-
phenylacetaldehyde (IX). Rupe and Knup (15) reported that
3-hydroxy-2-phenyloxetene (X) may have been one of the products
of the hydrolysis but no attempt was made to isolate or charac-
terize the compound.

Rupe and Huber obtained benzoyloxymethylenephenylacetal-
dehyde (XIa) by benzoylation of hydroxymethylenephenylacetal-
dehyde (IX) (refer to Fig. 1). This was then treated with
ethylmagnesium bromide and the magnesium salt (XIIa) hydrolyzed.
Upon hydrolysis, benzoic acid split out almost quantatively to
form 3-phenyl-4-ethyloxetene (XIV). When methoxymethylene-

phenylacetaldehyde (XIb) was used in place of benzoyloxymethy-lenephenylacetaldehyde (XIa), methanol split out upon hydrolysis of the magnesium salt (VIIb) yielding the same oxetene.

Rupe and Huber's evidence that their compound was 3-phenyl-4-ethyloxetene (XIV) was as follows: (1) The elemental analysis checked fairly well for the empirical formula, $C_{11}H_{12}O$ (Calculated: C, 82.50 per cent; H, 7.50 per cent. Found: C, 81.99 per cent; H, 7.71 per cent.) (2) It was not the isomeric unsaturated aldehyde, as it gave a negative Tollen's test and would not form a semicarbizone.

The boiling point reported for (XIV) of 98-100° centigrade at 11 millimeters seems somewhat low, in view of recent data on related oxetanes, but not unreasonably low. An educated guess that the boiling point of (XIV) would be about 115-120° can be made as follows: 2-Phenyloxetane boils at 87-8° at 8 millimeteers (Pollart, 12), or about 92° at 11 millimeters, and it is likely that 3-phenyloxetane would boil at least as high (2-methyloxetane boils at 60-1°, while 3-methyloxetane boils at 67°). Substitution of an ethyl group for a hydrogen should add 30-40° to the boiling point at atmospheric pressure (2-ethyloxetane boils at 87-9° compared to oxetane at 47°), equivalent to 15-20° at 11 millimeters. It seems reasonable to assume that the presence of a double bond would not lower and might raise the boiling point, (for example: Ethylbenzene boils at 136°, while styrene boils at 146°. Tetrahydrofuran boils at 64-6° compared to 67-9° for 2,5-dihydrofuran).
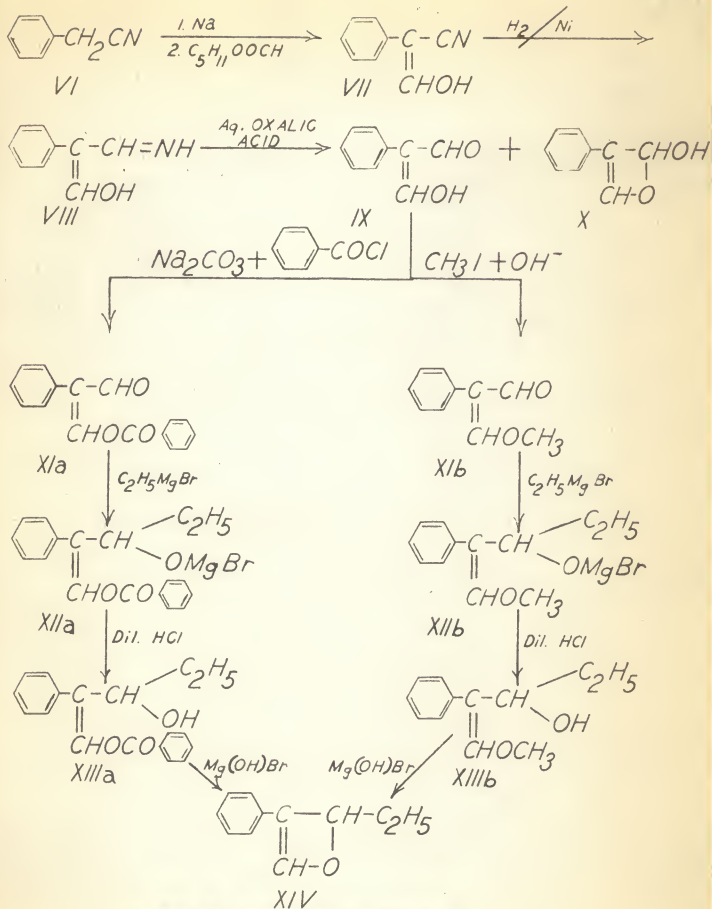
Fig. 1. 3-Phenyl-4-ethyloxetene

STATEMENT OF THE PROBLEM

Two approaches to the synthesis of an oxetene were contemplated. The first to be attempted was to repeat the method of Rupe and Huber (14). This was to be followed by further study on the structure of the product.

Isoamyl formate was to be replaced with ethyl formate in the Claisen ester condensation with benzyl cyanide (VI) because it was more readily available. The hydroxymethylenephenylacetonitrile (VII) obtained was to be partially reduced to β-phenyl-hydroxymethylene ethylidenimine (VIII) with hydrogen over Raney nickel (Mozingo, 11) instead of nickel on Keiselguhr because of the greater convenience of preparation. The hydroxymethylene-phenylacetaldehyde (IX), obtained from the hydrolysis of the imine (VIII), was to be benzoylated with benzoyl chloride. The benzoyloxymethylenephenylacetaldehyde (XIa) would then be treated with ethylmagnesium bromide and the product, (XIIa), hydrolyzed to 3-phenyl-4-ethyl oxetene (XIV).

The second approach, to be employed if the first proved unfruitful, would involve reduction of 1-oxyspiro[3,5]nonan-3-one (XXII) to 1-oxyspiro[3,5]nonan-3-ol (XXIII) followed by dehydration to 1-oxyspiro[3,5]non-2-ene (XXVII) (refer to Fig. 2.). Another name for this compound is 3,3-pentamethyleneoxetene.

The use of the oxetanone (XXII), prepared by Marshall and Walker (9), also allowed verification of their interesting synthesis. 1-Oxyspiro[3,5]nonan-3-one (XXII) was to be prepared by the reaction of diazomethane and 1-acetoxyhexahydrobenzoyl

chloride (XIX) followed by hydrolysis and cyclization of the
intermediate diazoketone (XXI). 1-Oxyspiro$[3,5]$nonan-3-one
was then to be reduced to 1-oxyspiro$[3,5]$nonan-3-ol (XXIII),
with sodium borohydride. It was anticipated that the Tschugaeff
method (19) would be most suitable for dehydration of the
oxetanol to 1-oxyspiro$[3,5]$non-2-ene (XXVII) as it avoids acidic
conditions which could cause cleavage of the oxetane ring.

DISCUSSION

Studies on the syntheses and properties of oxetanes in this
laboratory have created interest in their unsaturated analogs,
oxetenes. The synthesis of an oxetene was attempted using the
method of Rupe and Huber (14). The Claisen condensation of
ethyl formate with benzyl cyanide gave hydroxymethylenebenzyl
cyanide in 84 per cent yield. Ethyl formate was used in place
of isoamyl formate because it was more readily available.

Rupe and Huber used hydrogen over a catalyst to convert
the cyanide (VII) to β-phenylhydroxymethylene ethylidenimine
(VIII), which was not isolated but hydrolyzed with aqueous
oxalic acid. The exact type of catalyst was not mentioned
and no direct reference was given; however, from related work
of that time it is believed that nickel on keiselguhr was used.
Since Raney nickel is a widely applicable catalyst and more
easily prepared than nickel on keiselguhr, it was used.

Hydroxymethylenebenzyl cyanide (VII) was shaken with W-2
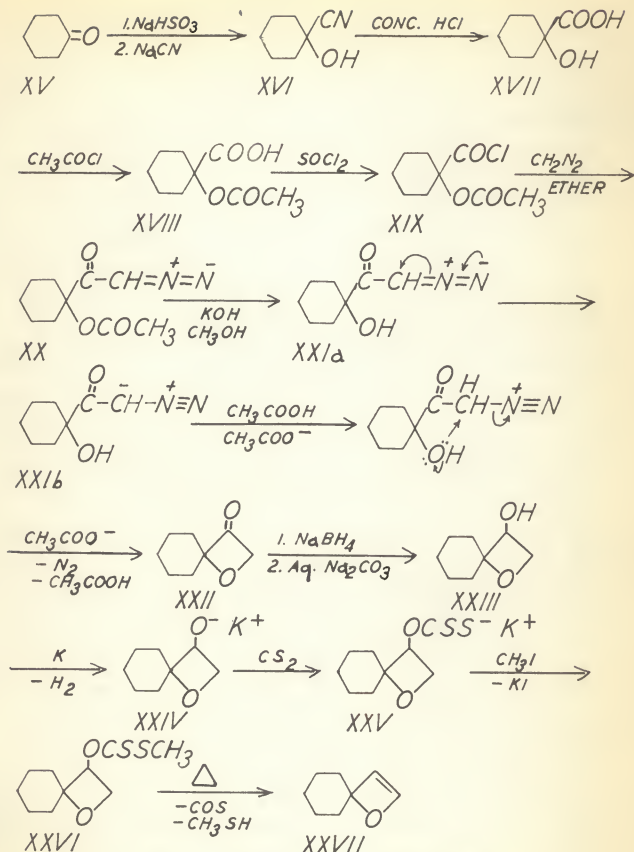Raney nickel (4) under hydrogen at a pressure of 50 pounds per

Fig. 2. 1-Oxyspiro[3,5]non-2-ene

square inch until an equal molar amount had been adsorbed. As in Rupe and Huber's work, hydrolysis with oxalic acid was carried out without attempt to isolate β-phenylhydroxymethylene ethylidenimine. Only a trace of hydroxymethylenephenylacetaldehyde was obtained; the major product was a red-brown, resinous tar. The melting point of the aldehyde was 93-94° (95° was reported by Rupe and Huber). The infrared spectrum showed the aldehyde carbonyl vibration at 5.8 microns and another characteristic vibration at 6.9 microns. The very low yield may have been due to complete reduction to the amine, incomplete reduction to the imine, or polymerization. If incomplete reduction to the imine was the case, then a more active catalyst may be needed; therefore, W-5 Raney nickel (Billicia and Adkins, 3) was prepared.

Reduction of hydroxymethylenebenzyl cyanide (VII) under the same conditions using the more active catalyst again gave only traces of the expected hydroxymethylenephenylacetaldehyde. Reduction of the cyanide was then attempted using both W-2 and W-6 Raney nickel at an initial hydrogen pressure of 150 pounds per square inch. Although the theoretical amount of hydrogen was taken up, only traces of the aldehyde were obtained.

Since Raney nickel was ineffective in the partial reduction of hydroxymethylenebenzyl cyanide, it was thought that possibly the nickel catalyst obtained from hydrogenation of hot nickel oxide, used by Rupe and Huber, was more specific for the reduction of nitriles to imines. Nickel on keiselguhr was prepared

(Adkins and Cramer, 1) and employed as the catalyst in the partial reduction. The hydrogenation mixture was shaken under hydrogen at 50 pounds per square inch until the uptake of hydrogen ceased. This occurred at 2/3 the theoretical amount. The low uptake of hydrogen may have been due to hydrogen occlusion on the catalyst before it was added to the reaction mixture. The β-phenylhydroxymethylene ethylidenimine supposedly formed was hydrolyzed with dilute hydrochloric acid without isolation. After extracting with ether, drying of the extract, and removal of the solvent, only a red-brown noncrystallizable tar remained.

A Stephen's reduction (Stephen and Stephen, 18) of hydroxy-methylenebenzyl cyanide (VII) was then attempted (refer to Fig. 3). A 55 per cent yield of the crude complex (XXVIII) was ob-tained. Upon hydrolysis of the complex only a trace of hydroxy-methylenephenylacetaldehyde (IX) was isolated along with a large amount of resinous material.

Hesse and Schrodel (8) reported the use of sodium triethoxy-aluminum hydride as a specific reducing agent for reducing cyanides to imines. They reported good yields (70-92 per cent) with aromatic nitriles and 25-30 per cent with aliphatic nitriles. A model experiment was performed using the readily available benzyl cyanide (refer to Chart III). Sodium triethoxyaluminum hydride (XXX) was prepared in ether solution. This solution was used in the attempted reduction without isolation of the reducing agent. An aliquot of the solution, however, was evaporated to

give a white residue, which reacted smoothly with water, giving
a gentle evolution of hydrogen. Evidently the reagent was
present. Treatment of benzyl cyanide (VI) with the ethereal
solution of sodium triethoxyaluminum hydride (XXX) followed by
hydrolysis of the reaction mixture, expected to contain the
imine complex (XXXI), gave no phenylacetaldehyde. 85-90 per
cent of the benzyl cyanide was recovered. Since the reduction
of benzyl cyanide was unsuccessful, this method was not employed
on   hydroxymethylenebenzyl cyanide (VII).

Since the partial reduction of   hydroxymethylenebenzyl
cyanide was unsuccessful, the alternate method of oxetene
synthesis was investigated. The method of Marshall and Walker
(9) provided a synthesis of 1-oxyspiro[3,5]nonan-3-one (XXII),
a possible intermediate in the synthesis of 1-oxyspiro[3,5]non-
2-ene (XXVII). Cyclohexanone cyanohydrin (XVI) was prepared
from cyclohexanone (XV) by the addition of sodium cyanide to
the bisulfite addition compound of cyclohexanone. The crude
cyanohydrin was converted to 1-hydroxyhexahydrobenzoic acid
(XVII) by hydrolysis with concentrated hydrochloric acid (Bucherer,
4). The yield of 1-hydroxyhexahydrobenzoic acid, based on cyclo-
hexanone, was 43 per cent. The hydroxy acid (XVII) was acetylat-
ed with acetyl chloride (Bucherer and Dahlem, 5) to give 1-acet-
oxyhexahydrobenzoic acid (XVIII) in 72-73.5 per cent yield. The
addition of acetyl chloride to the hydroxy acid in the absence
of a solvent or a weak base, such as pyridine, resulted in a
smooth reaction and easy purification of the acetoxy acid (XVIII).

$$\text{Ph}-\underset{\underset{\text{VII}}{\overset{|}{\text{CHOH}}}}{\overset{\text{O}}{\underset{\|}{\text{C}}}}-\text{CN} \xrightarrow{\text{2 HCl}} \text{Ph}-\overset{\text{O}}{\underset{\underset{\text{CHOH}}{\overset{|}{}}}{\underset{\|}{\text{C}}}}-\text{CCl}=\text{NH}\cdot\text{HCl}$$

$$\xrightarrow[\text{HCl}]{\text{SnCl}_2} \text{Ph}-\overset{\text{O}}{\underset{\underset{\text{XXVIII}}{\overset{|}{\text{CHOH}}}}{\underset{\|}{\text{C}}}}-\text{CH}=\text{NH}\cdot\text{HCl} \xrightarrow{\text{HYDROLYSIS}}$$

$$\text{Ph}-\overset{\text{O}}{\underset{\underset{\text{IX}}{\overset{|}{\text{CHOH}}}}{\underset{\|}{\text{C}}}}-\text{CHO}$$

$$\underset{\text{XXIX}}{\text{Al}\left(\text{OCH}_2\text{CH}_3\right)_3} + \text{NaH} \xrightarrow{\text{LiAlH}_4} \underset{\text{XXX}}{\text{NaAlH}\left(\text{OCH}_2\text{CH}_3\right)_3}$$

$$\xrightarrow{\text{Ph}-\text{CH}_2\text{CN}} \underset{\text{XXXI}}{\text{Ph}-\text{CH}_2\text{CH}=\text{NH}\cdot\text{Al}\left(\text{OCH}_2\text{CH}_3\right)_3}$$

$$\xrightarrow{\text{HYDROLYSIS}} \underset{\text{XXXII}}{\text{Ph}-\text{CH}_2\text{CHO}}$$
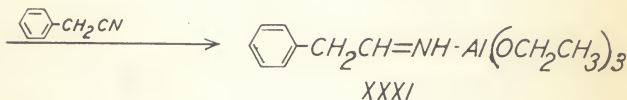
Fig. 3. Stephen and Sodium
Triethoxyaluminum Hydride Reductions

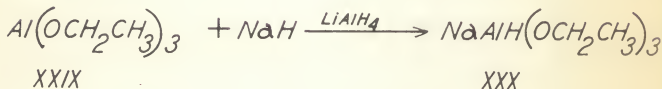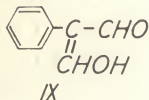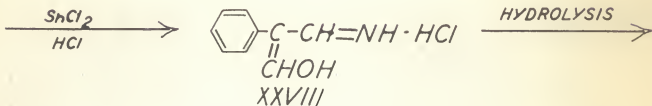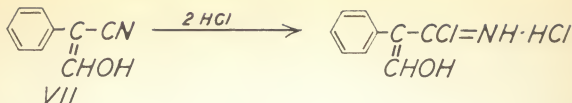1-Acetoxyhexahydrobenzoic acid (XVIII) was treated with thionyl chloride in the absence of a solvent (Marshall and Walker, 9) to give 1-acetoxyhexahydrobenzoyl chloride (XIX) in 42-93 per cent yield. The yield of the acid chloride is largely dependent on the reflux time of the reaction mixture, the optimum reflux time being approximately 10 minutes. Refluxing 20 minutes resulted in a 42 per cent yield of the 1-acetoxyhexahydrobenzoyl chloride with a large amount of resinous material being formed.

The next step in the reaction sequence was the addition of diazomethane to 1-acetoxyhydrobenzoyl chloride (XIX). Diazomethane was first prepared by the method of DeBoer and Backer (6). This method involved the decomposition of N-methyl-N-nitroso-_p_ -toluenesulfonamide with aqueous alcoholic potassium hydroxide at 60-65°. An ethereal solution of N-methyl-N-nitroso-_p_-toluene-sulfonamide was added dropwise to the hot aqueous alcoholic potassium hydroxide solution. Diazomethane and ether distilled off and were collected in cold traps. The addition of 1-acetoxy-hexahydrobenzoyl chloride (XIX) to the ethereal diazomethane was followed by hydrolysis of the acetoxy-group with methanolic potassium hydroxide, then cyclization by the action of glacial acetic acid. No 1-oxyspiro[3,5]nonan-3-one (XXII) could be isolated. It was found that ethanol, from the aqueous alcoholic potassium hydroxide, was carried over into the ethereal diazomethane. This ethanol would react with the acid chloride to give an ester and not the expected diazoketone (XX). Drying the ethereal diazomethane with potassium hydroxide followed by sodium gave

little increase in the yield. The decomposition of N-methyl-N-nitroso-*p*-toluenesulfonamide was then attempted using concentrated aqueous potassium hydroxide. The decomposition did not occur, probably because of the insolubility of the sulfonamide. Since alcohol must be excluded from the decomposition mixture, an intermediate which could be decomposed with aqueous potassium hydroxide was needed; therefore, N-methyl-N-nitrosourea was used to prepare diazomethane (Arndt, 2).

The addition of 1-acetoxyhexahydrobenzoyl chloride (XIX) to a dry ethereal solution of diazomethane followed by hydrolysis of the acetoxy group and cyclization of the 1-hydroxyhexahydrophenyldiazomethyl ketone (XXI) resulted in the isolation of 1-oxyspiro $[3,5]$ nonan-3-one (XXII) in 40-49 per cent yield. 1-Acetoxyhexahydrophenyldiazomethyl ketone (XX) was hydrolyzed to 1-hydroxyhexahydrophenyldiazomethyl ketone (XXI) with methanolic potassium hydroxide at room temperature to prevent hydrolysis of the diazo group. The cyclization of 1-hydroxyhexahydrophenyldiazomethyl ketone (XXI) was effected by the addition of glacial acetic acid. Since oxetanes are unstable in acid solutions, the low yield of 1-oxyspiro $[3,5]$ nonan-3-one (XXII) may be due, in part, to hydrolytic cleavage of the oxetane ring.

The reduction of 1-oxyspiro $[3,5]$ nonan-3-one (XXII) to 1-oxyspiro $[3,5]$ nonan-3-ol (XXIII) was effected by sodium borohydride in methanol. Sodium borohydride was used for two reasons: 1) It will not reduce the oxetane ring, resulting in cleavage. 2) It is not very sensitive to water or alcohols and,

therefore, can be used in aqueous, alcoholic, or aqueous-alcoholic solutions. The oxetanone reacted smoothly at 0-5° in methanol. After hydrolysis of the unreacted sodium borohydride, 1-oxyspiro [3,5]nonan-3-ol (XXIII) was isolated in 87-89 per cent yield. Since the oxetane ring is unstable in acid solution, basic hydrolysis of the sodium borohydride using aqueous sodium carbonate was employed.

The dehydration of 1-oxyspiro [3,5]nonan-3-ol (XXIII) was effected using the method of Tschugaeff (19). Tetrahydrofuran was substituted for ether as a solvent for two reasons: 1) Tetrahydrofuran has a higher boiling point, thus allowing a higher reaction temperature. 2) The potassium salt of the oxetanol (XXIII), precipitating in the course of the reaction, seems to form an emulsion with ether but not tetrahydrofuran. The crude xanthate (boiling point 120-135° at 1 millimeter) decomposed, upon heating above 220°, to yield 2.5 grams (25 per cent yield) of crude 1-oxyspiro [3,5]non-2-ene (XXVII). The infrared spectrum showed C=C stretching at 6.1 microns, C-H stretching at 3.4 microns, =C-H stretching at 3.2 microns, and four membered ring bending at 10.1 microns.

The bromine addition compound of the oxetene (XXVII), presumable 2,3-dibromo-1-oxyspiro [3,5]nonane, was made by adding the quantitative amount of bromine (0.64 grams) in carbon tetrachloride to 0.5 grams of the oxetene. It boiled at 80° at 1 millimeter and its infrared spectrum showed C-H stretching at 3.3 microns, the four membered ring bending at 10.3 microns,

and a band at 14.9 microns which is probably C-Br vibration.
In the spectra of both the oxetene (XXVII) and the bromine
addition compound, a carbonyl band appeared at 5.8 microns.
This band may be due to contamination with cyclohexylideneacet-
aldehyde, arising from hydrolysis of the oxetene ring.

In going from the oxetanol (XXIII) to the oxetene (XXVII),
the four membered ring bending band shifted from 10.3-10.5
microns to 10.1 microns showing that oxetene has the more rigid
ring.

EXPERIMENTAL

Hydroxymethylenebenzyl Cyanide (VII)

Hydroxymethylenebenzyl cyanide was prepared from benzyl
cyanide and ethyl formate by the method of Ghosh (7) in 88 per
cent yield.

Hydrogenation Catalysts

(A) Raney nickel catalyst of low activity (W-2) was pre-
pared by the procedure reported by Mozingo (11).

(B) Raney nickel catalyst, which was pyrophoric (W-5), was
prepared by the procedure of Billicia and Adkins (3).

(C) Nickel on keiselguhr was prepared by the method of
Adkins and Cramer (1).

Hydrogenation of Hydroxymethylenebenzyl Cyanide (VII)

(A) Over Raney nickel at low pressure.   Hydroxymethylene-

benzyl cyanide (14.5 grams, 0.1 mole) was dissolved in 100
millileters of 95 per cent ethanol. Approximately 5 grams of
W-2 Raney nickel were added and the solution shaken under
hydrogen at room temperature until 0.1 mole of hydrogen had
been taken up. The pressure drop for 0.1 mole was from 50 to
47.4 pounds per square inch. The catalyst was then filtered
and washed with ethanol. The ethanol was removed by steam
distillation. Oxalic acid (7.5 grams), dissolved in a minimum
of water, was added to the cooled residue. The residue consist-
ed of a yellowish aqueous solution containing a red-brown resin-
ous material in the bottom. The residue, containing the oxalic
acid, was allowed to sit at room temperature for two hours. It
was then subjected to steam distillation to remove the   hydroxy-
phenylacetaldehyde from the hydrolysis mixture. In order to
test for the complete removal of   hydroxymethylenephenylacet-
aldehyde from the hydrolysis mixture an aliquot of the distillate,
was treated with ferric chloride. The appearance of a blue
color, due to a ferrate complex of the enol form of the aldehyde,
showed incomplete distillation. The distillate was exhaustively
extracted with ether and the resulting ethereal solution shaken
with dilute hydrochloric acid to insure complete hydrolysis.
The ethereal solution was then washed with 10 per cent sodium
bicarbonate solution and dried over anhydrous magnesium sulfate.
Removal of the ether under reduced pressure left only a few
platelets of   hydroxymethylenephenylacetaldehyde (IX) and a
considerable amount of red-brown tar. The melting point of the

platelets was 93-94°. The melting point of hydroxymethylene-
phenylacetaldehyde reported by Rupe and Huber (14) was 95°. The
infrared spectrum of the compound showed the enol hydroxyl stretch
at 2.9 microns, the carbonyl vibration at 5.8 microns and another
band, characteristic for aldehydes, at 6.9 microns.

The use of the more active W-5 Raney nickel under the above
conditions resulted in only a trace of hydroxymethylenephenyl-
acetaldehyde (IX).

(B) Over Raney nickel at high pressure. Hydroxymethylene-
benzyl cyanide (15.6 grams) was dissolved in 130 millileters of
95 per cent ethanol. Water (90 milliliters) was added and the
solution placed in a hydrogenation bomb with 15-20 grams of
catalyst (Raney nickel, W-2). The mixture was shaken in a
hydrogen atmosphere at an initial pressure of 150 pounds per
square inch until an equal molar amount of hydrogen had been
taken up. The procedure from this point was the same as for
the low pressure hydrogenation.

Only traces of hydroxymethylenephenylacetaldehyde were
isolated from the above procedure using W-2 or W-5 Raney nickel.

(C) Over nickel on keiselguhr. Hydroxymethylenebenzyl
cyanide (5 grams) was dissolved in 40 milliliters of ethanol,
30 milliliters of water were added. Nickel on keiselguhr (10
grams) was added and the resulting mixture was shaken under
hydrogen at room temperature at an initial pressure of 50 pounds
per square inch. After two days 2/3 of the theoretical amount
of hydrogen had been taken up. The procedure from this point

was the same as for low pressure hydrogenation over Raney nickel. Only a trace of the expected hydroxymethylenephenylacetaldehyde (IX) was observed with a large amount of red-brown tar.

Attempted Stephen Reduction of Hydroxymethylenebenzyl Cyanide

Anhydrous stannous chloride (26.6 grams, 0.14 mole) was placed in 250 milliliters of ethyl acetate and the mixture cooled to 0°. Dry hydrogen chloride was bubbled into the mixture until the stannous chloride was dissolved. Dry hydrogen chloride was bubbled into a solution of 21 grams (0.14 mole) of hydroxymethylenebenzyl cyanide (VII) at 0° until the solution became saturated. The two solutions were mixed and the product isolated according to the method of Stephen and Stephen (18). The crystalline product was not purified because only a very small amount was isolated. The melting point was 150-154°, showing that the substance was not the expected hydroxymethylenephenylacetaldehyde (IX) but was probably recovered hydroxymethylenebenzyl cyanide (VII).

Attempted Reduction of Benzyl Cyanide (VI) with Sodium Triethoxyaluminum Hydride (XXX)

Aluminum ethoxide (XXIX) was prepared by the method of Meister, Lucius, and Bruning (10). Sodium triethoxyaluminum hydride was prepared from 30 grams (0.18 mole) of aluminum ethoxide and 4.2 grams (0.18 mole) of sodium hydride using lithium aluminum hydride as a catalyst according to the method of O. Schmitz-Dumont (16). Since ether was used as a solvent

for the reduction, the reagent was not isolated but used directly in its ether solution.

The reduction of benzyl cyanide by sodium triethoxyaluminum hydride was attempted using the method Hesse and Schrödel (8). A solution of 5.85 grams (0.05 mole) of benzyl cyanide in 50 milliliters of ether was placed in a round bottom flask fitted with a reflux condenser attached to a drying tube, a stirrer, and a dropping funnel. One third of the ethereal sodium tri-ethoxyaluminum hydride, theoretically containing 0.06 mole of the reagent, was added slowly to the benzyl cyanide. The reduc-tion mixture was refluxed on a steam bath two hours. The cooled ethereal solution was shaken with 20 milliliters of 20 per cent sodium bicarbonate solution to hydrolyze the expected β-phenyl-hydroxymethylene ethylidenimine-aluminum ethoxide complex. The aqueous layer was separated and washed with a small amount of ether. The ether wash was combined with the main ethereal solu-tion. The combined solutions were dried over anhydrous magnesium sulfate. Fractional distillation of the dry ethereal solution gave no phenylacetaldehyde, however, 85-90 per cent of the benzyl cyanide was recovered, distilling at 113-115° at 20 millimeters.

1-Hydroxyhexahydrobenzoic Acid (XVII)

Cyclohexanone (500 grams) was slowly added, with stirring, to a solution of 530 grams of sodium bisulfite and 550 milli-liters of water in a 2 liter beaker. A white, flocculent pre-cipitate formed and the temperature increased to approximately

70°. A concentrated solution of aqueous sodium cyanide was added to the warm mixture with stirring. The precipitate disappeared and the reaction mixture separated into two liquid layers. The mixture was stirred occasionally and allowed to cool overnight.

The two layers were separated and the bottom, aqueous, layer was extracted twice with ether. The ether and cyclohexanone cyanohydrin layers were combined and 490 milliliters of hydrochloric acid added. The mixture was allowed to sit overnight and was then heated on a steam bath with stirring for 10 hours. After cooling the precipitate formed was triturated with hot benzene and the ammonium chloride filtered. As the benzene solution cooled 1-hydroxyhexahydrobenzoic acid (XVII) crystallized. It was then recrystallized from a benzene-petroleum ether solution as white platelets.

The purified acid amounted to 314 grams, which was a 43 per cent yield based on cyclohexanone. After drying over concentrated sulfuric acid, the acid melted at 107°, the same as reported by Bucherer (4).

1-Acetoxyhexahydrobenzoic Acid (XVIII)

Acetyl chloride (60.8 grams, 0.775 mole) was added to 70.5 grams (0.49 mole) of 1-hydroxyhexahydrobenzoic acid (XVII) in a round bottom flask fitted with a reflux condenser. Reaction began immediately, evidenced by the evolution of hydrogen chloride. After standing at room temperature for one hour, the

reaction mixture was heated on a steam bath until the cessation of hydrogen chloride evolution, approximately 1/2 hour. The excess acetyl chloride was removed under reduced pressure leaving a light yellow crystalline solid. The solid was recrystallized from benzene to give 66.8 grams (73.5 per cent yield) of 1-acetoxyhexahydrobenzoic acid. The melting point was found to be 101-2°. The assigned structure was confirmed by its infrared spectrum, which showed absorption bands for OH stretching vibration at 28 microns, ester carbonyl stretching vibration at 5.7 microns, and acid carbonyl stretching vibration at 5.8 microns. The melting point of 111° reported in Chemical Abstracts (5) appears to be a misprint.

1-Acetoxyhexahydrobenzoyl Chloride (XIX)

The method of Marshall and Walker (9) was employed in the synthesis of 1-acetoxyhexahydrobenzoyl chloride. Purified 1-acetoxyhexahydrobenzoic acid (62 grams, 0.34 mole) was refluxed with 70 milliliters of thionyl chloride for ten minutes and the excess thionyl chloride removed immediately under reduced pressure. Distillation of the residue gave 63.2 grams (93 per cent yield) of the acid chloride collected at 84° at 1 millimeter.

Diazomethane

Diazomethane was prepared from aqueous alcoholic potassium hydroxide decomposition of N-methyl-N-nitroso-p-toluenesulfonamide according to the procedure of DeBoer and Backer (6). The

ethereal diazomethane was found to contain ethanol which could
not be completely removed by treatment with potassium hydroxide
and sodium.

The second preparation of diazomethane, proposed by Arndt
(2), was the decomposition of N-methyl-N-nitrosourea with
aqueous potassium hydroxide. This gave an alcohol-free solution
of diazomethane which was dried with potassium hydroxide and
sodium.

1-Oxyspiro[3,5]nonan-3-one (XVII)

The procedure of Marshall and Walker (9) was employed for
the preparation of 1-oxyspiro[3,5]nonan-3-one. 1-Acetoxyhexa-
hydrobenzoyl chloride (XIX) (25 grams) in 25 milliliters of dry
ether was added to a dry solution of approximately 11 grams of
diazomethane in 500 milliliters of ether. The oxetanone (XXII)
was isolated, in 40-49 per cent yield after hydrolysis and
cyclization of 1-acetoxyhexahydrophenyldiazomethyl ketone (XX),
by distillation. The boiling point was found to be 84-86° at 24
millimeters (86° at 28 millimeters was reported (Marshall and
Walker, 9)); n_D^{20} 1.4640 (reported: n_D^{19} 1.4631 (Marshall and
Walker, 9)). The infrared spectrum shows the carbonyl stretch-
ing vibration at 5.4 microns for the oxetanone compared to
approximately 5.6 microns for the carbonyl stretching in cyclo-
butanone (Randell, 13). Also, there was a C-H stretching band
at 3.4 microns and a strong four-membered ring bending band at
10.5 microns. No O-H stretching band was observed.

1-Oxyspiro[3,5]nonan-3-ol (XXIII)

Sodium borohydride (2.0 grams, 0.053 mole) was dissolved
in 50 milliliters of cold methanol and placed in a 200 milli-
liters three necked round bottom flask fitted with a mechanical
stirrer, a dropping funnel, and a condenser. 1-Oxyspiro[3,5]nonan-
3-one (XXII) (7.5 grams, 0.053 mole), dissolved in 50 milliliters
of cold methanol, was added to the sodium borohydride solution
dropwise over a 20 minute period. The sodium borohydride re-
acted slightly with the methanol and hydrogen was evolved through-
out the oxetanone addition. The reaction mixture was allowed to
sit overnight and then refluxed 1 1/2 hours on a steam bath.
After refluxing, methanol was distilled off at atmospheric
pressure until 30-50 milliliters of the reaction mixture remain-
ed. A solution of 20 grams of sodium carbonate in 80 milliliters
of water was added to the cool residue and the mixture heated on
a steam bath for 1/2 hour. White, feathery crystals of borax
appeared upon cooling. The cool hydrolysis mixture was exhaustive-
ly extracted with ether and the extract dried over anhydrous
potassium carbonate. The drying agent was filtered and the
filtrate fractionally distilled. The main fraction was collect-
ed from 85-90° at 0.3 millimeters and amounted to 6.6 grams (88
per cent yield). This was again distilled and the fraction
boiling from 90-92° at 0.5 millimeters collected, n_D^{20} 1.4855,
density 1.097 grams per cubic centimeter. The infrared spectrum
showed the O-H stretch at 2.8 microns, the C-H stretch at 3.4
microns and the four-membered ring bending band at 10.3-10.5

microns. No carbonyl band was present. _Analysis._ Calculated
for C, H, and O: C, 67.57 per cent; H, 9.92 per cent; O, 22.50
per cent. Found: C, 67.40 per cent; H, 10.02 per cent.

The phenylurethane, prepared in the usual manner (20), had
a melting point of 125-6°. _Analysis._ Calculated for C, H, O,
and N: C, 68.94 per cent; H, 7.33 per cent; O, 18.37 per cent;
N, 5.36 per cent. Found: N, 5.52 per cent.

1-Oxyspiro [3,5] non-2-ene (XXVII)

1-Oxyspiro [3,5] nonan-3-ol (11.5 grams, 0.081 mole) was
added to 3.7 grams (0.094 mole) of potassium in dry tetrahydro-
furan according to the procedure of Tschugaeff (19). The mixture
was stirred at room temperature until the reaction ceased then
refluxed on a steam bath until nearly all the potassium had re-
acted. Two small pieces of potassium would not react and were
removed from the cooled mixture with a wire. Carbon disulfide
(9.1 milliliters, 0.15 mole) was added dropwise to the cool
reaction mixture over a 1/2 hour period. After stirring 2
hours 14.0 milliliters (0.226 moles) of methyl iodide were
added over a 20 minute period. The reaction mixture was stirred
at room temperature for six hours then refluxed for one hour.
To the cooled reaction mixture 100 milliliters of ether and 100
milliliters of water were added. The ether layer was washed
twice with water and dried over anhydrous sodium sulfate. The
drying agent was filtered off and washed with ether. The filtrate
was fractionally distilled and the xanthate ester (XXI) collected

from 120-135° at 1 millimeter.

The xanthate ester (XXVI) was then heated in an oil bath. Decomposition began at 220°. Four fractions were taken: (1) 45-70°, (2) 70-110°, (3) 110-140°, (4) 140-over 200°. Cuts 2 and 3 were distilled through a column packed with glass helices. A cut from 140-1° was taken for analysis, n_D^{20} 1.5023. The compound decolorized bromine in carbontetrachloride and reduced potassium permanganate. A sample was taken for analysis, but was lost enroute. The infrared spectrum showed C-H stretching at 3.4 microns, C=C stretching at 6.1 microns, =C-H stretching at 3.2 microns, and four membered ring bending at 10.1 microns.

2,3-Dibromo-1-oxyspiro[3,5]nonane was prepared by the addition of the theoretical amount of bromine (0.64 grams) in carbon tetrachloride to 0.5 grams of 1-oxyspiro[3,5]non-2-ene. The reaction mixture turned pink during the addition and dark brown upon standing. The dibromo compound was distilled and collected at 80° at 0.1 millimeters, n_D^{20} 1.5665. _Analysis_. Calculated: C, 33.80 per cent; H, 4.23 per cent; O, 5.63 per cent; br, 56.34 per cent. Found: Br, 58.23 per cent. The high per cent of bromine is probably due to some bromine substitution on the molecule.

SUMMARY

The synthesis of an oxetene was undertaken to compare its physical and chemical properties to those of oxetane and to prove that the oxetene ring system can exist. An oxetene was

reported once previously by Rupe and Huber but the structure
of their compound was not proven.

An attempt was made to prepare 3-phenyl-4-ethyloxetene
(XIV) by the method of Rupe and Huber (14), but difficulty was
encountered in reduction of hydroxymethylenebenzyl cyanide
(VII) to β-phenylhydroxymethylene ethylidenimine with hydrogen
over Raney nickel or over nickel on keiselguhr. Chemical re-
duction by Stephen's method was unsuccessful, and the use of a
new reagent, sodium triethoxyaluminum hydride, appeared unpromis-
ing.

In a second approach 1-acetoxyhexahydrobenzoyl chloride,
obtained in three steps from cyclohexanone cyanohydrin, was
treated with diazomethane by the process of Marshall and Walker
forming 1-oxyspiro[3,5]nonan-3-one (XXII). This ketone was re-
duced to the corresponding alcohol, 1-oxyspiro[3,5]nonan-3-ol
(XXIII), by the action of sodium borohydride. The structure
of 1-oxyspiro[3,5]nonan-3-ol, which is the first oxetanol to
be reported, was established by analysis, qualitative tests,
and infrared. It was dehydrated by the Tschugaeff reaction
to 1-oxyspiro[3,5]non-2-ene (XXII), which may also be called
3,3-pentamethyleneoxetene.

The yield of 1-oxyspiro[3,5]nonan-3-one (XXII) from the
addition of 1-acetoxyhexahydrobenzoyl chloride (XIX) to diazo-
methane depends largely on the dryness of the ethereal solution
of diazomethane. It seems that the acid chloride is hydrolyzed
more rapidly than it reacts with diazomethane.

Reduction of the oxetanone (XXII) to 1-oxyspiro[3,5]nonan-3-ol (XXIII) proceeded smoothly with sodium borohydride in methanol. Dehydration of the oxetanol was accomplished by pyrolysis of the xanthate ester (XXVI). This method of dehydration was used to avoid acidic reagents since acid media cleave the oxetane ring.

ACKNOWLEDGMENT

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THE SYNTHESIS OF AN OXETENE

by

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Agriculture and Applied Science, 1956

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AN ABSTRACT OF A THESIS

submitted in partial fulfillment of the

requirements for the degree

MASTER OF SCIENCE

Department of Chemistry

KANSAS STATE COLLEGE
OF AGRICULTURE AND APPLIED SCIENCE

1958

The only previous report of an oxetene (H. Rupe and A. Huber, Helv., 10, 846 (1927)) did not absolutely prove the existence of such a ring system. An attempt was made to repeat this work to verify the procedure and to study further the character of the oxetene ring system.

The partial hydrogenation of hydroxymethylenebenzyl cyanide to β-phenylhydroxymethylene ethylidenimine using Raney nickel or nickel on keiselguhr as a catalyst proved unsuccessful. Hydrolysis of the unisolated imine gave only traces of the expected hydroxymethylenephenylacetaldehyde, along with a considerable amount of tar. Chemical reduction, by the Stephen's reaction, also proved fruitless. A new reagent, sodium triethoxyaluminum hydride, did not appear promising (benzyl cyanide was recovered unchanged upon treatment with the reagent).

The synthesis of an oxetene was effected using 1-oxyspiro-[3,5]nonan-3-one (J. R. Marshall and J. Walker, J. Chem. Soc., 467 (1952)) as an intermediate. 1-Acetoxyhexahydrobenzoyl chloride was prepared in good yield from cyclohexanonecyanohydrin in three steps. This acid chloride was then added to dry ethereal diazomethane, resulting in 1-acetoxyhexahydrophenyldiazomethyl ketone. The unisolated ketone was treated with methanolic KOH to hydrolyze the acetoxy-group. Glacial acetic acid was then added to promote cyclization to the oxetanone. The diazomethane solution had to be free of water and alcohol or the yield of the diazomethyl ketone was drastically reduced due to side reactions of the acid chloride.

The oxetanone, 1-oxyspiro[3,5]nonan-3-one, when treated with methanolic sodium borohydride, gave the corresponding alcohol, 1-oxyspiro[3,5]nonan-3-ol (b. p. 90-92° at 0.5 millimeters, n_D^{20} 1.4855) in 87-89 per cent yield. This alcohol is the first oxetanol ever reported. The structure postulated is based on infrared spectrum, qualitative tests, and analysis. The phenylurethane derivative was prepared, melting point 125-126°.

1-Oxyspiro[3,5]nonan-3-ol was converted to its xanthate ester, by the method of Tschugaeff (Ber., 33, 735 (1900)) and subsequently pyrolyzed. Decomposition began at 220° and gave a 25 per cent yield of 1-oxyspiro[3,5]non-2-ene (boiling point 140-141°, n_D^{20} 1.5023). The assigned structure is based on the infrared spectrum, and qualitative tests. The bromine addition compound was prepared, boiling point 80° at 0.1 millimeters, n_D^{20} 1.5665.