CONFORMATIONAL STUDIES OF AMIDES BY NMR

by

ALLAN J. KRAMER

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Approved by:

Joseph V. Rachstein

Major Professor

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THIS BOOK CONTAINS NUMEROUS PAGES WITH DIAGRAMS THAT ARE CROOKED COMPARED TO THE REST OF THE INFORMATION ON THE PAGE.

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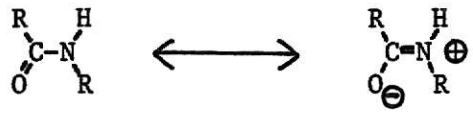
HISTORICAL

In the study of amides, it is known that the NH and CO groups interact with each other in such a manner as to produce a partial double bond character to the C-N bond.[1] The two resonance structures which lead to the partial double bond character are shown in (1). As a result of this partial double



(1)

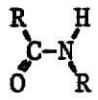
bond character, the set of atoms R-CO-NH-R form a planar group which has considerable rigidity. The best values for the bond lengths and bond angles of this group were determined by Corey and Pauling,[2] by using X-ray spectroscopy on various amides. These values have been confirmed by infrared studies.[3-6]

The calculated resonance energy for amides is 21 Kcal/mole.[7] From this value we see the C-N bond has considerable double bond character and among the possible internal rotational states only the planar cis and trans positions are favored. If the lifetimes of the isomers are greater than .01 sec., it becomes possible to identify the isomers of N-substituted amides by nmr if the chemical shift of the cis and trans protons or groups are different enough. The cis and trans isomers of N-monosubstituted amides[8] have been observed by nmr where the cis and trans alkyl groups are magnetically non-equivalent.

LaPlanche and Rogers have shown that the N-methyl group on N-methyl formamides[9] at higher magnetic fields may be associated with the group cis to the carbonyl oxygen. Their studies of unsymmetrical disubstituted amides[10] revealed that the group cis to the carbonyl oxygen will occur at higher

magnetic field. Buy using nuclear Overhauser effects Anet reported the low field methyl group is cis to the formyl hydrogen in DMF.[11] Infrared studies of cyclic amides[12] have shown that 4-9 membered cyclic amides occur in the cis form due to the steric requirements of the ring. In the larger membered rings, cis-trans isomerism can take place. The 11-members N-methyl cyclic amide has a cis-trans ratio of 55:45[13] and the 13-membered ring has a cis-trans ratio of 40:60.[13] For rings larger than 13 members the trans form predominates.

The trans configuration (2) in N-monosubstituted amides has been shown to predominate over the cis (3) configuration by dipole moment,[14-16] dielec-



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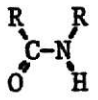


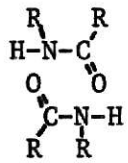
(3)

tric constants[17] and vapor pressure measurements,[18] and by ultraviolet,[14,15] infrared[19,20] and Raman spectroscopy studies.[21-27]

Unsymmetrically N,N-disubstituted amides[9] have been studied by nmr to determine the conformational isomers. It was found that the bulkier groups preferred to be trans to the methyl group of acetamides. If the stability of the isomers depend only on steric factors and the size of the groups is R(alkyl)>CH_3>O>H, then the observed data gave qualitative agreement of steric size and isomer ratio.

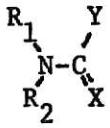
The assignment for cis and trans isomers of N-phenyl-formamide N^{15} and N-methylformamide N^{15} were confirmed by $J_{(N^{15}-H)}$ coupling constants and chemical shifts.[28] The relative amounts of cis and trans forms of N-methyl-formamide N^{15} as determined by integration of the down field N-H absorptions changed with concentration varying from 45% cis at 1.5 mole% to 73% cis at

52.5 mole%. The reason that the trans form predominates at high dillution can be explained in two ways. First, the hydrogen-bonded monosubstituted formamide polymer in the trans form is thermodynamically more stable than the hydrogen-bonded cis form. Second, the trans form even at the high dillutions is stabilized by existence as ring dimers.



By using chemical shifts and coupling constants of formamide N^{15} and N-methylformamide N^{15}, Green[28] reported that N-monosubstituted amides tend to have the amide hydrogen trans to oxygen, thus encouraging the formation of long hydrogen bonded chains of molecules. The hydrogen bond at the trans position to the carboxyl oxygen is favored by about 0.7 kcal/mole over that at the cis position.

N,N-dimethylformamide[29-36] has been the subject of many studies. Some areas of interests that have been undertaken include the effects of protonation and complexation on rotational barriers and on the structure of DMF and other amides.[30,33,34,37,38] The influence of substitution and functional groups (x) on the barriers for restricted rotation about the C-N bond in compounds of type (4) has been observed.[31,36,39-43] Comparisons have been made between the rates of rotation about different bonds in the same molecule.[44,45] The



(4)

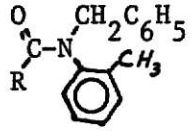
effects of solvents[32,39,44-49] on the internal rotations have been studied

and comparisons have been made between conjugated systems having similar structures for example DMF and 6-dimethylaminofulvene.[50]

A study has been carried out in which formamides and thioformamides with similar N-substituents have been compared to obtain a relationship of the cis-trans isomer ratio. It was found for the thioformamides[51] that the percent cis increased by a factor of two compared with the formamides as an example N-isobutyformamide had 71% trans and 29% cis and N-isobutylthioformamide had 87% trans and 13% cis isomer.

The different chemical shifts of benzyl methylene protons in N-benzyl-N-(o-tolyl) amides has been[52] investigated with respect to the different conformations. NMR spectra of a variety of N,N-disubstituted amides indicate that the nonequivalence does not arise from slow inversion of the pyramidal amide nitrogen, which was proposed by Siddall and Prohaska,[53] but comes from restricted rotation about the aryl-nitrogen bond and the carbonyl-nitrogen bond which gives rise to the cis-trans isomers.

Siddall and Stewart[54] have studied a variety of N-benzyl-N-(o-tolyl) amides varying from the formamide to the pivalamide. The predominant form for the formamide is the cis isomer (5) as compared to the trans isomer (6).



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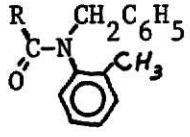


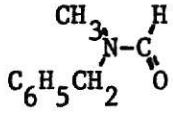
(6)

This is expected because the carbonyl oxygen is larger in size than the formyl proton. For N-substituted analides with larger carbonyl substituents the trans isomer is generally not observed. The calculated value for the rotational barrier of the isobutyl amide (R=isopropyl) is 16 Kcal/mole[55] and the

observed barrier is 5 Kcal/mole larger. This larger value is attributed to the rotation around the benzene-nitrogen bond.

NMR spectra of poly(N-acetylaziridine)exhibit hindered rotation around the amide bond as shown by the splitting of N-CH_2 groups at low temperature and coalescence of the peaks on heating. Rotation around the amide bond on the poly(N,N-dimethylacrylamide)[56] side chain was observed and chemical shift differences of the N-CH_3 groups cis and trans to the carbonyl were measured.

Since the isolation of rotational isomers[57-64] it has ceased to be a property observed only by spectral means. Gutowsky[58] has reported the separation of the N-methyl-N-benzylformamide rotational isomers by complexing (7) with uranyl ion and removing it at low temperatures. Then upon heating, the



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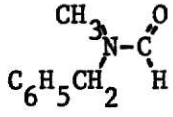


(8)

return to equilibrium of isomer (8) was followed by nmr. With this data he could calculate the rate constants for equilibration. The rates of interconversion have been shown to be dependent on solvent polarity and steric size of substituents. The rotational isomers of N-acylindolines and N-acyltetrahydroquinolines are also stable and could be partially separated.[58,59]

Siddall studied a variety of N-naphthyl-N-ethyl amides[65] and explained the relationship between the ratio of the chemical shifts of the methylene protons as a function of the size of the R-carbonyl substituents as shown below. The

R	$(\upsilon_a - \upsilon_b)$ (ppm)
$C_{10}H_7$	1.02
C_6H_5	.90
CH_2CH_3	.87
Cl	.62

steric size of the substituents determines the more stable conformation of the amide and determines the cis-trans ratio.

Johnson[66] observed that nmr signals of a series of N-benzoyl-2-alkyl-piperidines coalesce at a temperature lower than that for the same protons in similar alkylpiperidine acetamides as a result of the increased steric interactions of the phenyl ring with the piperidine ring. The steric interactions are increased by varying the R-groups on the piperidine ring. The bulkier group tends to be trans to the phenyl ring and increasing the size of the group changes the cis-trans ratio.

A series of N-monosubstituted amides[67] with R_1=Me, Et, Pr, and t-Butyl, and Y=H, Me, Pr, and t-Butyl (see Figure 4) were studied by infrared using the N-H stretching frequencies. The two N-H stretching frequencies at 3410 am^{-1} and 3460 am^{-1} have been shown to result from the cis and trans isomers respectively. The increase in the cis isomer along the series N-methyl, N-ethyl, N-propyl, and N-t-butyl formamide was in qualitative agreement with the nmr data. Although the trans isomer predominates for the mono-substituted formamides, the cis isomer could be detected for N-isopropylacetamide.

Graham and Diel[68] have studied the effects of temperature on the coalescence of N,N-disubstituted amides at 35°. The highly substituted amides are rotating faster about the central C-N bond than the simple amides. They found the barrier to internal rotation (ΔG) varied linearily when the size of the dimethyl amides varied from H to t-Butyl.

Neuman and Jones,[69] in studying N,N-dimethyl amides have shown a relationship between the substituents on the amide molecule and their effect on the barrier to internal rotation. They developed a linear correlation between the standard free energy of the dimethyl amides and the Taft constant σ^* and E_s, the polar and steric substituent constants, respectively. A plot of the

free energy vs ($\sigma^*\rho^* + sE_s$) gives a straight line.

The equilibrium for a variety of N-alkyl-N-picryl amides has been studied by Fisher.[70] The equilibrium constant of the N-alkyl substituents was related to the size and inductive effects of the substituents. A linear correlation was found between the Taft E_s values and the logarithm of the equilibrium constant. A linear correlation was alos found for the Taft σ^* values and the logarithm of the equilibrium constant. However, the correlation with E_s was considerably better.

OBJECTIVES OF THIS INVESTIGATION

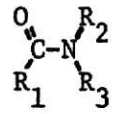
The objectives of this investigation were to determine a correlation between the equilibrium constant of mono- and dialkylamides with Taft's E_s values, Taft's σ^* values, and a combination of Taft's E_s and σ^* values. A correlation will be determined between the equilibrium constant of mono- and dialkylamides and Taft's E_s values by using the equation $\text{Log } K = E_s$. The slope, s, of the line when Log K is plotted vs E_s is a measure of how steric interactions effect the equilibrium constant.

A correlation will also be determined using the equilibrium constant and Taft's σ^* values by using the equation $\text{Log } K = \rho^*\sigma^*$. A measure of how polar effects affect the equilibrium constant is termed ρ^*. This would show if the polarity of the alkyl groups affects the equilibrium constant.

A correlation will be determined between the equilibrium constant and a combination of Taft's E_s and σ^* values by using the equation $\text{Log } K = \rho^*\sigma^* + sE_s$. By checking the statistical[72] F values, one can see if the correlation was improved by using the combination of values.

DISCUSSION OF RESULTS

It has been well established that amides in proteins prefer a planar trans (9) conformation instead of cis (10) conformation by more than 2 Kcal. The reason given, and accepted by almost everyone, is that a steric interaction



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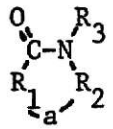


(10)

(a) is largely responsible for the difference in energy between the cis and trans forms. A recent examination of E_s values indicated that E_s values are a good measure of the van der Waal's radius of selected groups.[71]

The objective of this study was to determine the extent of steric effects on the isomer ratios in monoalkyl and dialkylamides. The study was made on several series of amides in which one alkyl substituent was systematically changed. Changes were made in both the amino and the carbonyl substituents of the amide. Several series of amides were examined in different solvents. In each case a linear correlation with the steric size was found but the correlation proved to be solvent dependent. (Compare Figure 7 and Figure 11 in Appendix I.) In general the experimental results confirm that the correlation between E_s values for the substituents was linear with respect to the logarithm of the equilibrium constant. (Compare Figures 3, 5, 7 and 9 in Appendix I.)

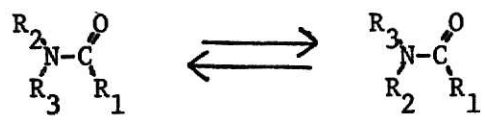
It was possible that the stability of the trans isomer was due to the polarity of the atoms involved. The resonance forms which place a negative charge on the oxygen may polarize the R groups and stabilize the entire molecule. A method to observe this effect was to run a correlation

on the logarithm of the equilibrium constant with respect to the polar substituent constant σ*. In most cases the correlation was poor, however when the values for benzyl and phenethyl were removed the correlation improved. The values for ρ* were also found to be solvent dependent as shown by comparing the slopes in Figures 6 and 10 in Appendix I.

Proposals have been put forth that a combination of steric size and polarity have an effect on the isomer ratios of the amides. This possibility was examined by means of a multiple correlation on the logarithm of the equilibrium constant with respect to a combination of the E_s values and σ* values. In most cases the correlation was not significantly improved as shown by the F values for the correlation.[72]

Since the correlation coefficients are close to unity they do not provide the information necessary to distinguish the significance of the correlation. One must use some other criterion such as the magnitude of the standard error of the estimate or the ratio, F, of the mean squares of the regression and the mean squares of the deviation from the regression. A large value of F corresponds to a small value for the mean squares of the deviation from the regression and is equivalent to the omega test for choice of a functional relationship.

The reaction with which we were concerned was the rotation of substituted amides, in which we can define a forward reaction, k_1, and reverse reaction, k_{-1}, and an equilibrium constant, $K_s = k_1/k_{-1}$. If we assume that on changing



(11) (12)

any one of the R groups the changes in the electronic factors, bond distance

and angles etc., are neglibible and that the equilibrium constant is a reflection of the steric interaction in forms (11) and (12), we can express the equilibrium constant in terms of E_s values for all the alkyl groups on the amide. We assume that the magnitude of the interaction is given as the product of the individual group sizes E_s. Then, if E_1 is the steric size of R_1, and E_{oxy} is the steric size of C=O, etc., we can write the equilibrium as follows, where α is the sensitivity to changes of size.

$$\text{Log } K_s = (E_1 x E_3 + E_2 x E_{oxy} - E_1 x E_2 - E_3 x E_{oxy})\ \alpha$$
$$= (E_1 - E_{oxy})(E_3 - E_2)\ \alpha$$

If only one group is changed on the amide at a time, then the expression can be reduced to one of two forms depending at which end of the amide the groups are varied. If R_1 is varied the equation becomes, $\text{Log } K_s = (E_1 - E_{oxy})A$. If R_3 is varied, the equation becomes $\text{Log } K_s = (E_3 - E_2)B$. Using the expression above one can evaluate A or B since $E_{oxy}A$ and E_2B are constants and the expression reduces to a linear equation in E_1 or E_3. Experimental results suggest, that for the above expression to be valid, an emperical constant term β must be added where β is the intercept ($E_s = 0$). The general expression for the equilibria in amides now becomes

$$\text{Log } K = (E_1 - E_{oxy})(E_3 - E_2)\ \alpha + \beta$$

for a given series of amides. Since α is assumed a constant and only one alkyl group is varied at a time (E_1 or E_3)

α = slope / $E_1 - E_{oxy}$ when R_3 is varied or

α = slope / $E_3 - E_2$ when R_1 is varied.

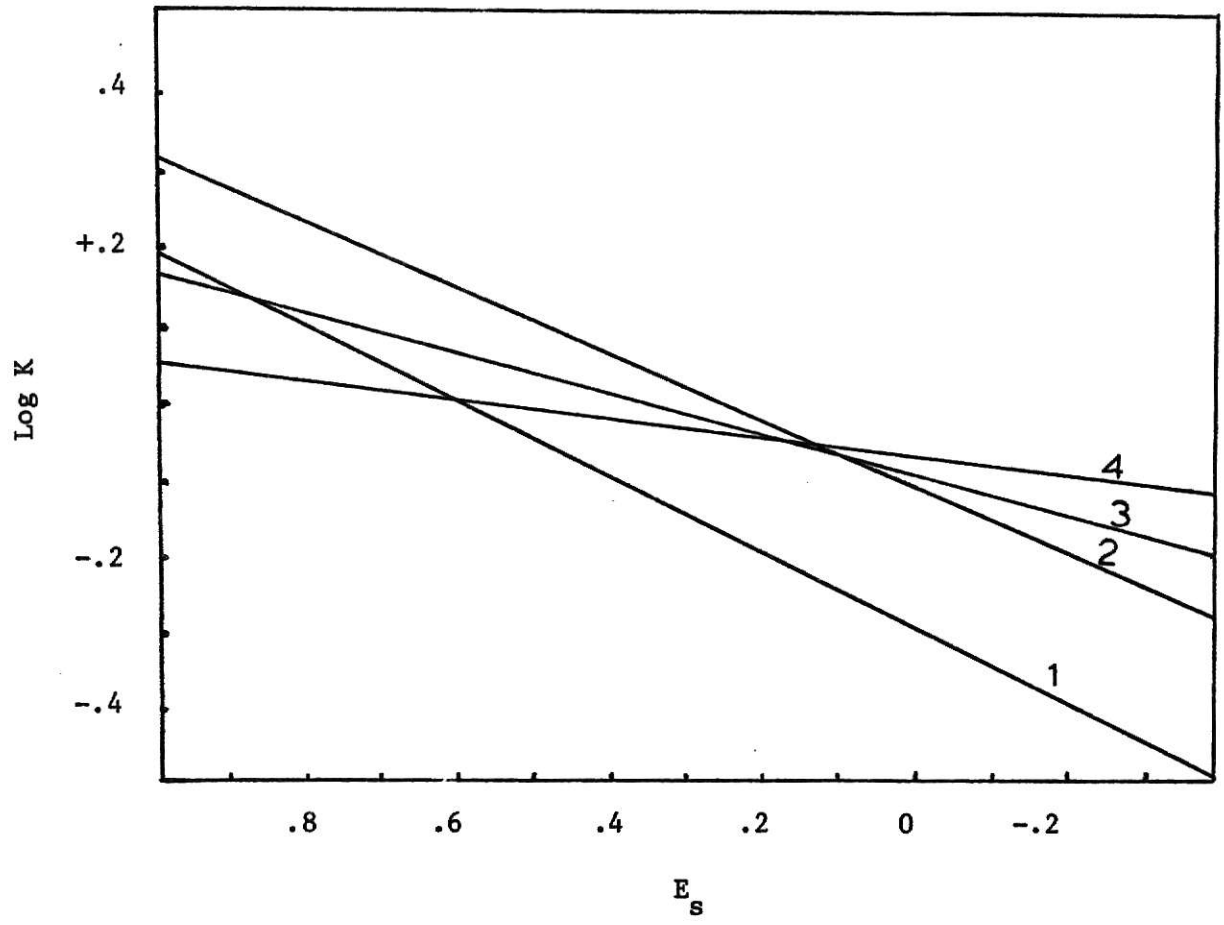
The value for E_{oxy} was determined by using the slope and intercept from a plot of E_s vs Log K_s when R_1 was varied on 4 series of amides. Using the standard equation for a straight line y=mx + b where y = Log K_s = 0 and s = m and b is the intercept, one can calculate a value for E_{oxy}. The values used for s were .257$\pm$ .034, .115 $\pm$ .026, .474 $\pm$ .125 and .430 $\pm$ .075 from series 6b and 7a and the values for the intercept were -.084, -.067, -.296, and -.107 respectively. (See Table 14.) The calculated values for E_{oxy} were also determined from a plot of E_s vs Log K_s when R_1 was varied, when Log K_s = 0 then $E_1 = E_{oxy}$. From the experimental data, the average value for E_{oxy} = .44 $\pm$ .15 (when E_H = 1.24 and E_{CH_3} = .00) as shown in Figure 1. Thus in C = O the oxygen is smaller than methyl but considerably larger than hydrogen.

As can be seen the procedure for obtaining E_{oxy} is not yet adequate because of the relatively large errors in the experiments. For the value to be reliable a number of series should be observed. This is the initial value calculated for E_{oxy} and may be improved when more data is obtained.

Using the calculated value of E_{oxy}, one can determine a ΔE_s for the different series of amides. The ΔE_s values are (E_1-E_{oxy}) when R_3 is varied and (E_3-E_2) when R_1 is varied. The values for the ΔE_s are shown in Table 1. When one plots the ΔE_s values against the s values obtained for the various series of amides (Figure 2) a direct relationship is found between them. The intercept for the line when ΔE_s = 0 was s = 0 which was required for the correlation to be valid. When ΔE_s was calculated for the series of amides when R_1 and R_3 was varied, the four corresponding values for ΔE_s had approximately the same s values, which indicates that R_1 and R_3 are interchangeable.

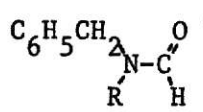
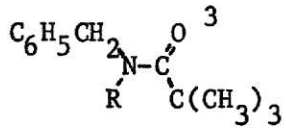
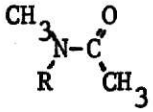
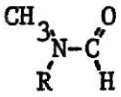
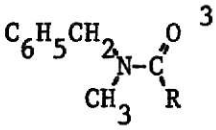
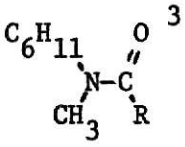
From the correlation of ΔE_s with s, one can conclude that α the sensitivity of the amide to changes in size is a constant for the amides. In a given solvent varying R_1 and R_3 does not effect the value of α. From Table 1 it can be seen that s was solvent dependent for a given series of amides,

Figure 1



1. Series 6 R = primary subst. (Fig. 11 in Appendix 2)
2. Series 6 R = secondary subst. (Fig. 11 in Appendix 2)
3. Series 7 R = primary subst. (Fig. 9 in Appendix 2)
4. Series 7 R = secondary subst. (Fig. 9 in Appendix 2)

Table 1

Series	s value	$\Delta E_s = \lvert E_1 - E_{oxy}^{1} \rvert$
 [3]	.25 ± .04	.80 ± .15
 [3]	.78 ± .11	1.98 ± .15
	.33 ± .07	.80 ± .15
	.13 ± .06	.44 ± .15
	.31 ± .12	.80 ± .15
 [3]	.17 ± .02 .30 ± .12 [2]	$\Delta E_s = \lvert E_3 - E_2 \rvert$ .38 ± .02
 [3]	.26 ± .03	.79 ± .02

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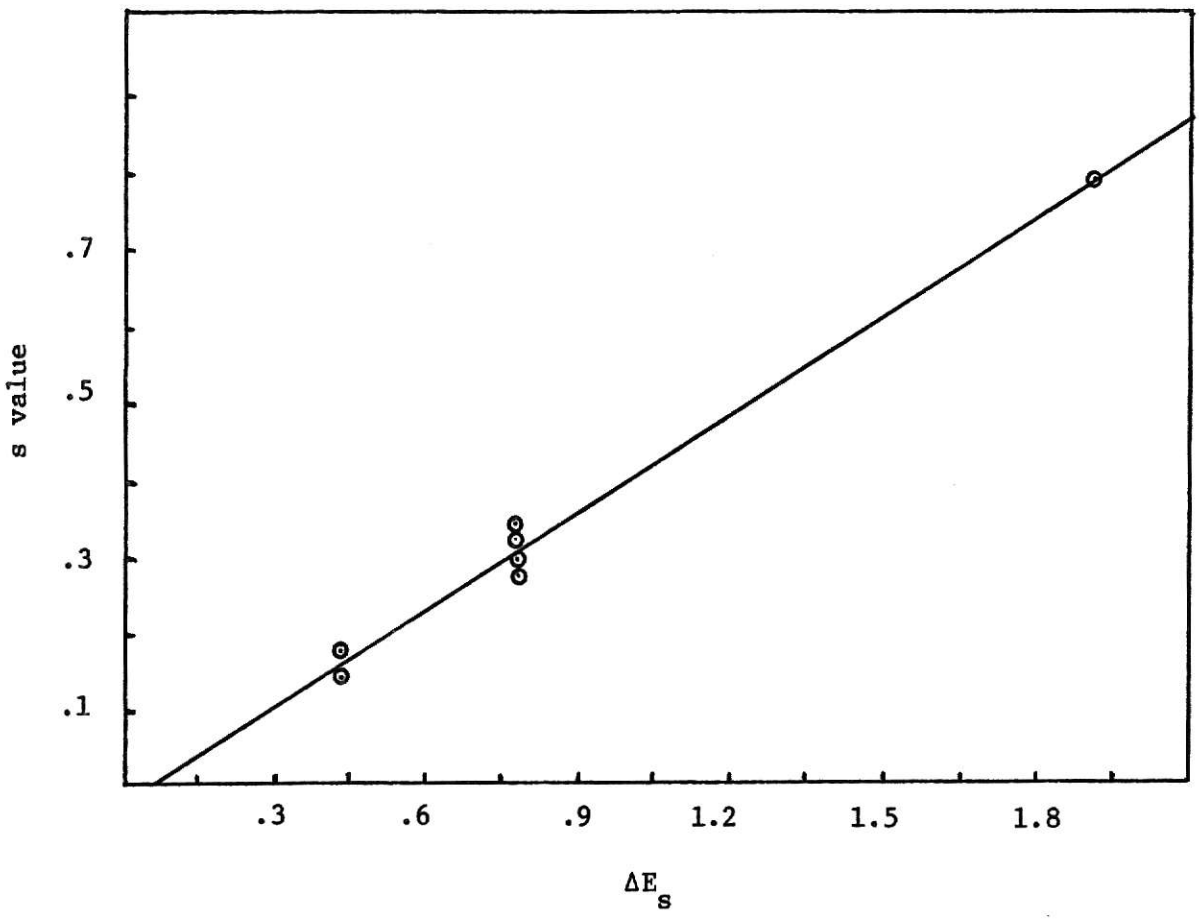
[1] E_{oxy} = .44 ± .15

[2] Value for s in a nonaromatic solvent

[3] R = primary subst.

Figure 2



Values for E_s and s are found in Table 1.

therefore α for the given series will be solvent dependent also. The value for α was calculated to be .38 for the different series of amides using the equation $\alpha = s/E_1-E_{oxy}$ when R_3 is varied or $\alpha = s/E_3-E_2$ when R_1 is varied for a given series of amides.

In conclusion it can be seen that the steric effects have a direct effect on the equilibrium constant of the amide. This was shown when R_1 the carbonyl substituent was varied on the amides. The nature (primary or secondary) alkyl had a direct effect on the equilibrium constant was shown by the different s values for the primary and secondary substituents. (See Figure 3 in Appendix 2.) The correlation of the logarithm of the equilibrium constant with respect to the steric size of the substituent was linear for the series of mono- and dialkylamides studies. (See Figure 3 and Figure 17 in Appendix 2.) The correlation for the different series was solvent dependent. (See Figure 7 and Figure 11 in Appendix 2.)

The correlation of the logarithm of the equilibrium constant with respect to the polarity of the substituents was poorer than with E_s in most cases. Upon removal of the aromatic substituents the correlation improved but the reasons why benzyl groups did not correlate with E_s, σ^* or their combination are not known. This correlation was also dependent on the solvent used. A multiple correlation using steric size and the polarity of the substituent as variable parameters did not significantly improve the correlation with the logarithm of the equilibrium constant. By using the steric size of the substituents, the steric size for the carbonyl oxygen was calculated to be $.44 \pm .15$ for the series studied. The value for α the sensitivity of the amide to change in the size of the substituent was calculated to be .38. A direct relationship was found between the s value, the affect of the steric interaction, and the ΔE_s values for the amides. This implies that the steric size alone can explain the changes in the equilibrium constants of the mono-

and dialkylamides.

NMR SPECTRA

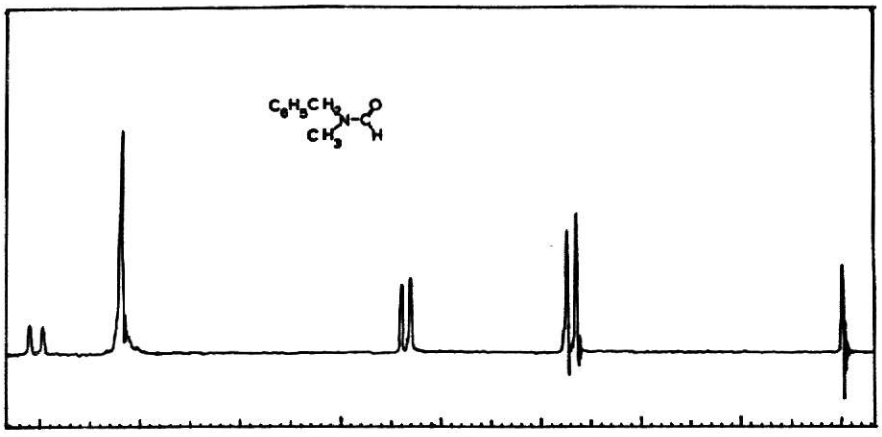
All samples were run as 10% solutions in carbon tetrachloride using TMS as an internal standard.

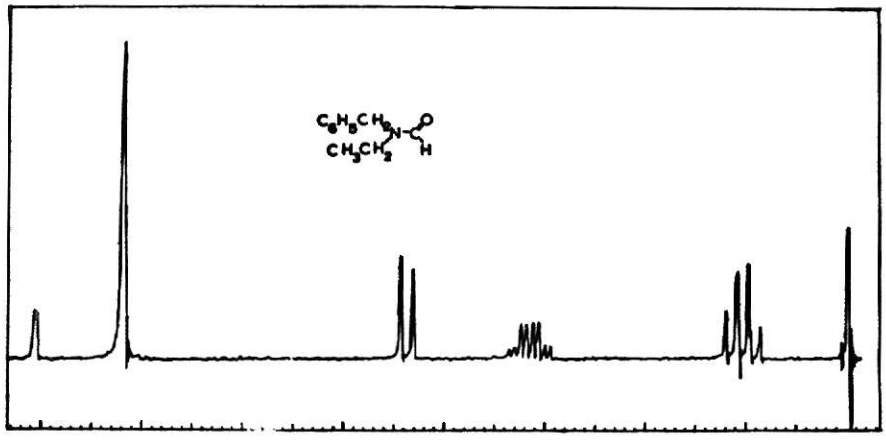
NMR SPECTRA

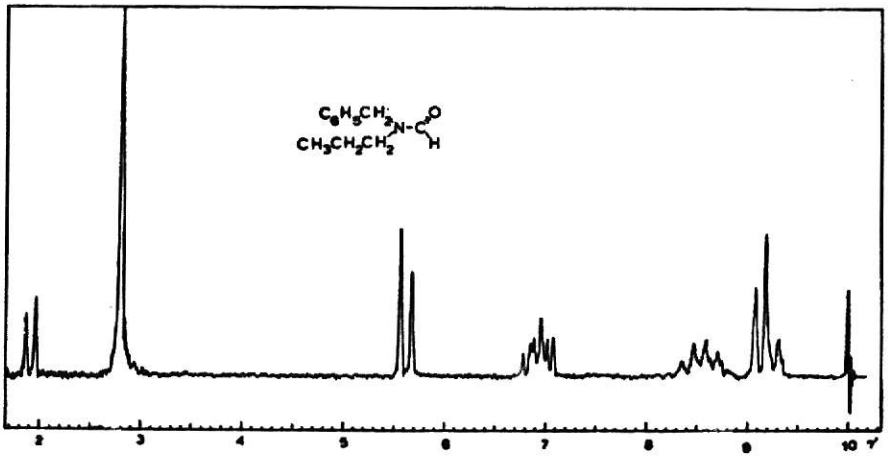
N-benzyl-N-methylformamide

N-benzyl-N-ethylformamide

N-benzyl-N-propylformamide



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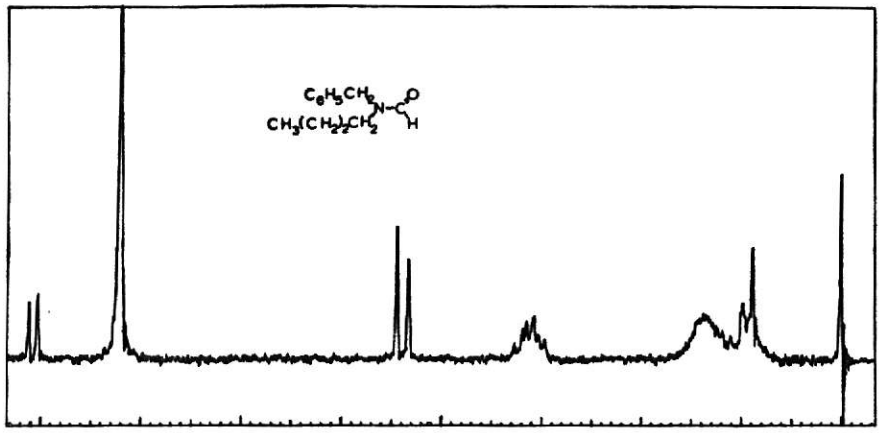
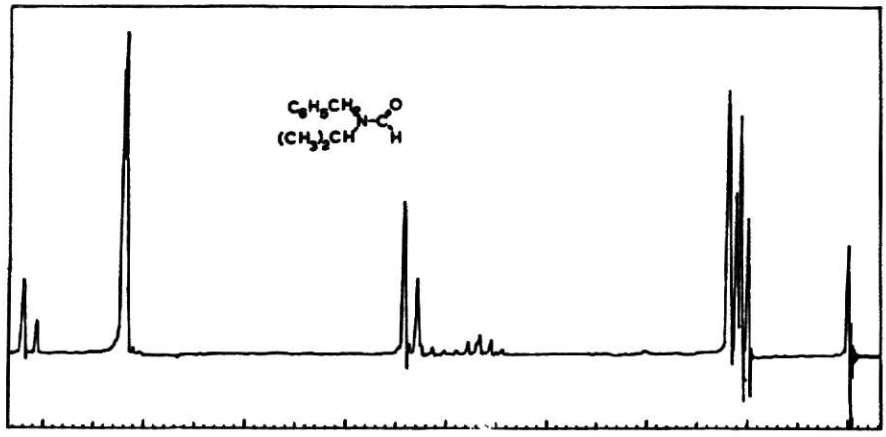
NMR SPECTRA

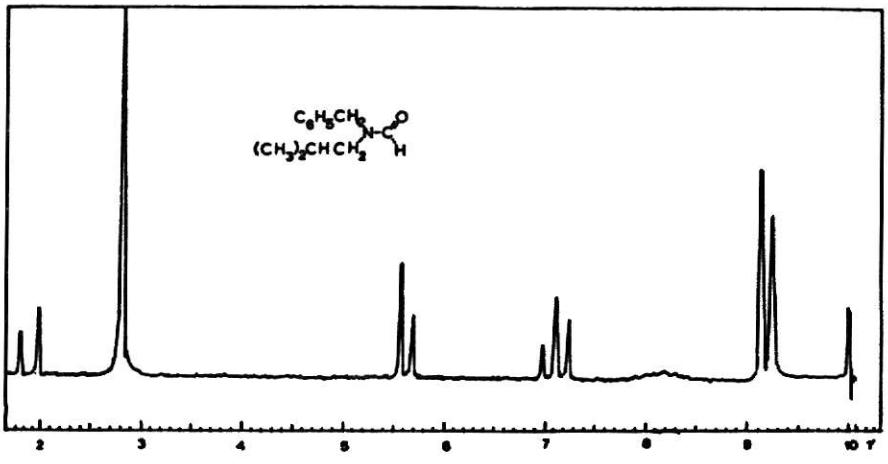
N-benzyl-N-n-butylformamide

N-benzyl-N-isopropylformamide

N-benzyl-N-(2-methylpropyl)formamide


$C_6H_5CH_2$
$CH_3(CH_2)_2CH_2$
N
C
O
H


$C_6H_5CH_2$
$(CH_3)_2CH$
N
C
O
H


$C_6H_5CH_2$
$(CH_3)_2CHCH_2$
N
C
O
H
2
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8
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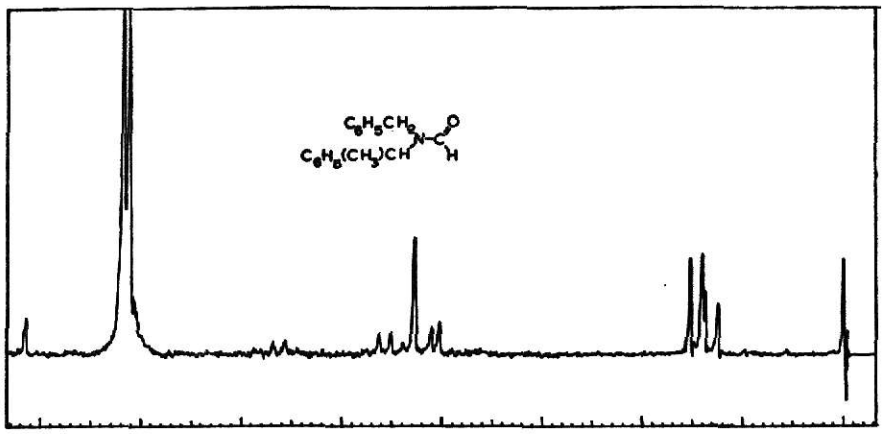
τ

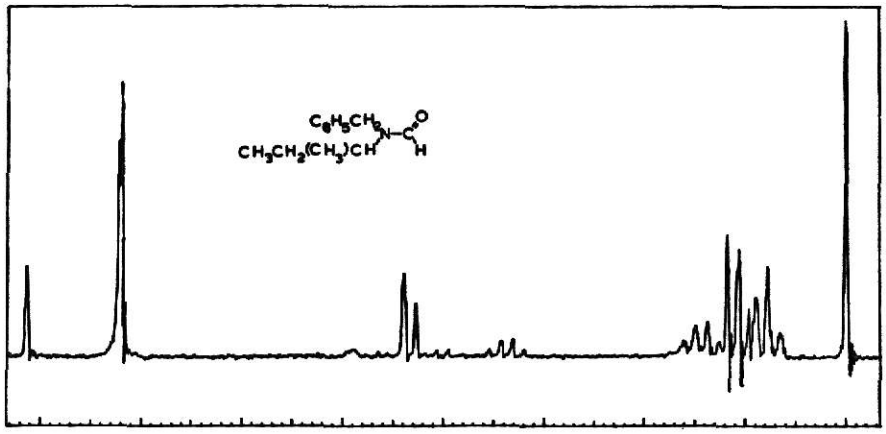
NMR SPECTRA

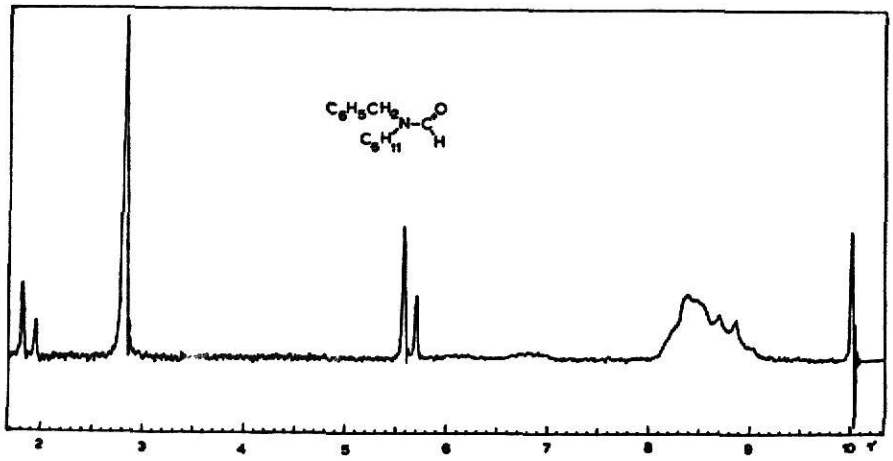
N-benzyl-N-(1-phenylethyl)formamide

N-benzyl-N-2-butylformamide

N-benzyl-N-cyclohexylformamide


$C_6H_5CH_2$
$C_6H_5(CH_3)CH$
N
C
O
H


$C_6H_5CH_2$
$CH_3CH_2(CH_3)CH$
N
C
O
H


$C_6H_5CH_2$
C_6H_{11}
N
C
O
H
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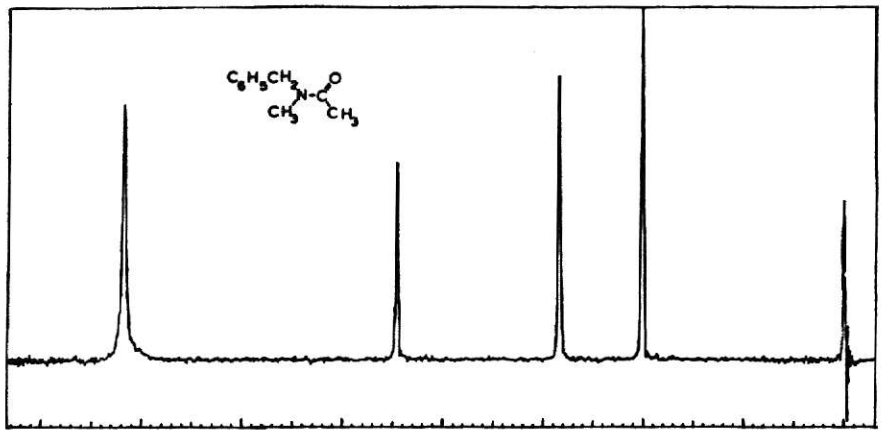
τ

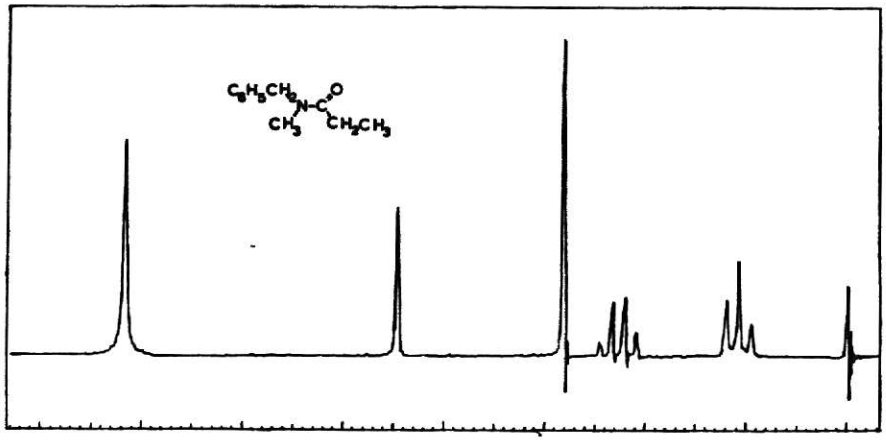
NMR SPECTRA

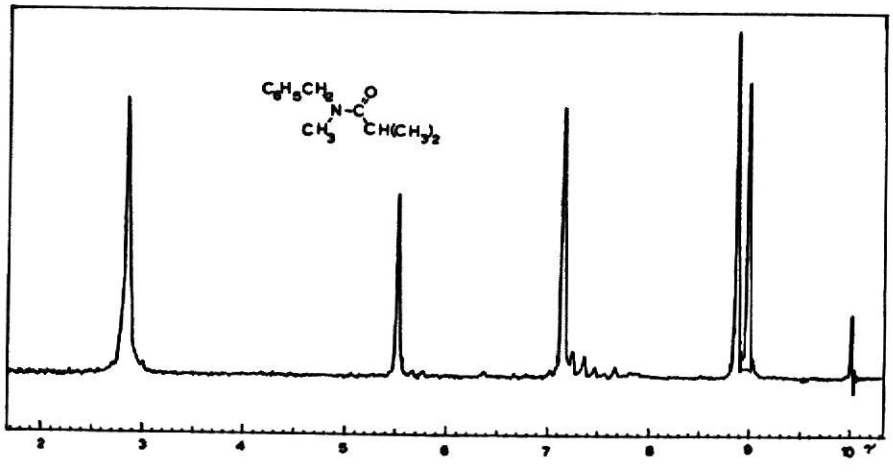
N-benzyl-N-methylacetamide

N-benzyl-N-methylpropionamide

N-benzyl-N-methylisobutylamide


$C_6H_5CH_2$
N
C
O
CH_3
CH_3


$C_6H_5CH_2$
N
C
O
CH_3
CH_2CH_3


$C_6H_5CH_2$
N
C
O
CH_3
$CH(CH_3)_2$
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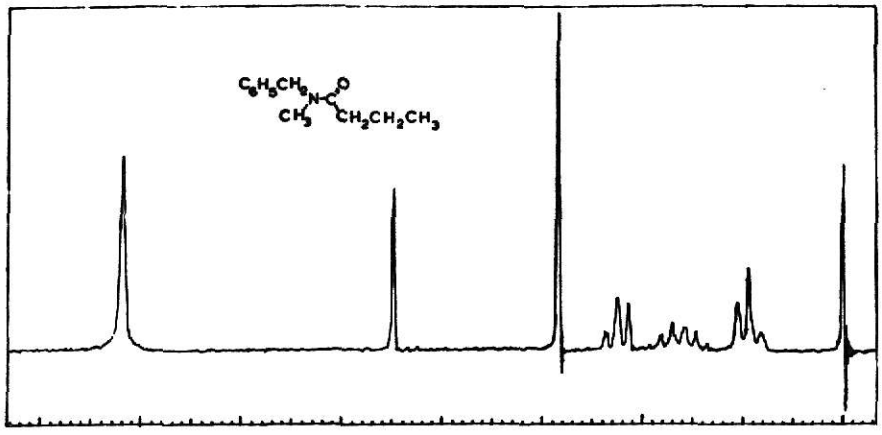
τ

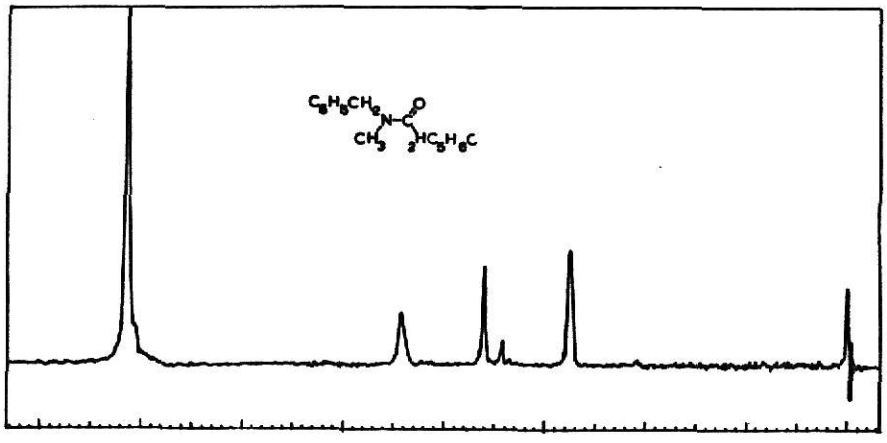
NMR SPECTRA

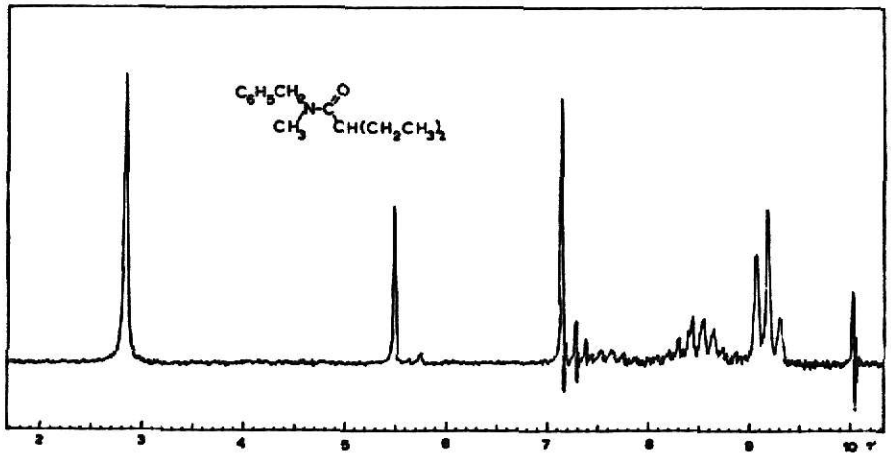
N-benzyl-N-methylbutylamide

N-benzyl-N-methyl-2-phenylacetamide

N-benzyl-N-methyl-2-ethylbutylamide


$C_6H_5CH_2$
N
O
CH_3
$CH_2CH_2CH_3$


$C_6H_5CH_2$
N
O
CH_3
$CH(C_2H_5)_2$


$C_6H_5CH_2$
N
O
CH_3
$CH(CH_2CH_3)_2$
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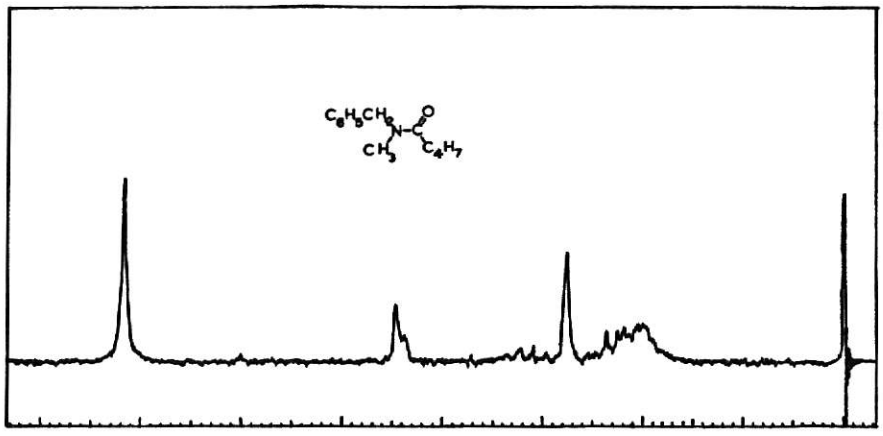
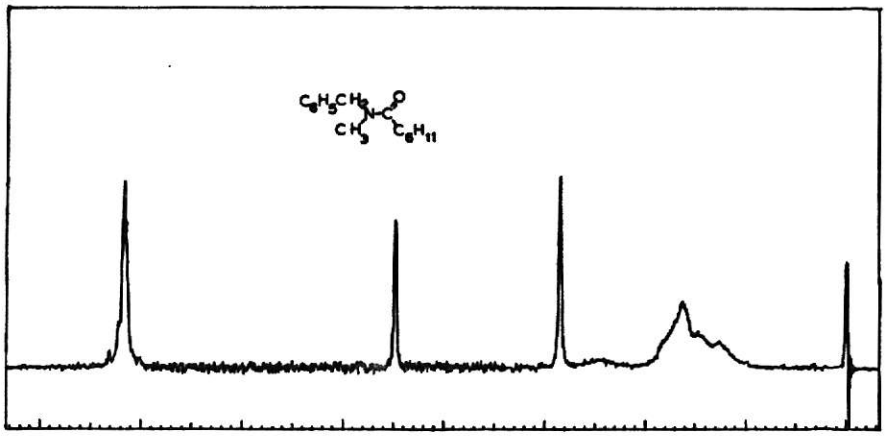
NMR SPECTRA

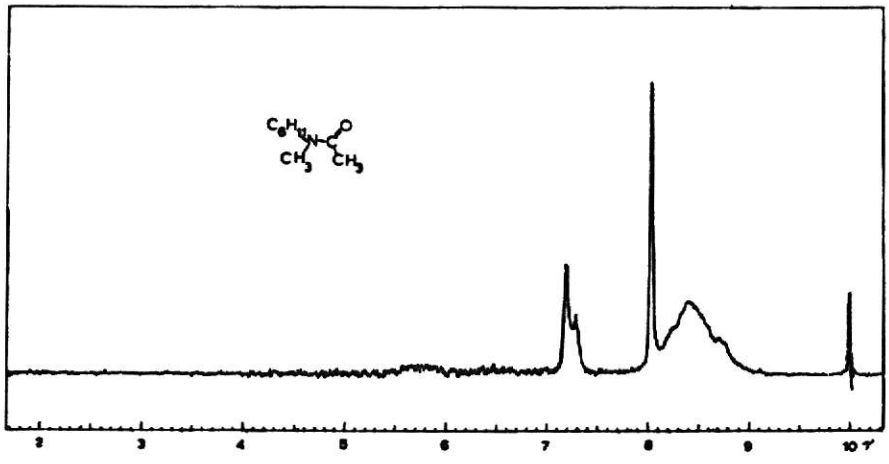
N-benzyl-N-methylcyclobutanecarboxamide

N-benzyl-N-methylcyclohexanecarboxamide

N-cyclohexyl-N-methylacetamide



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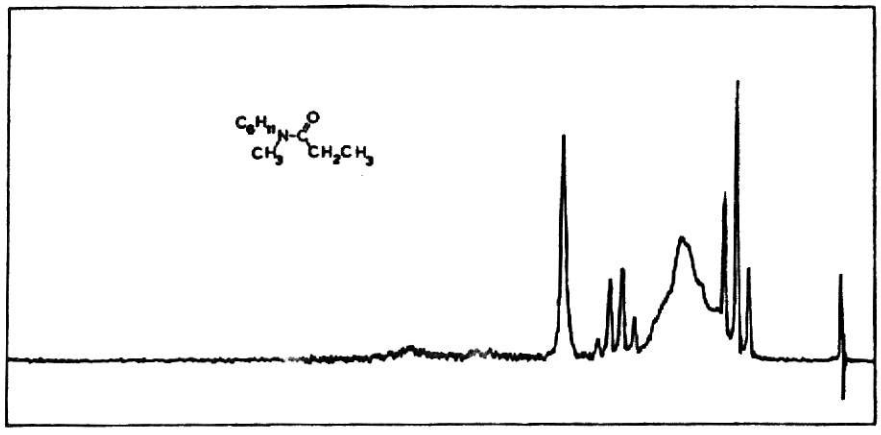
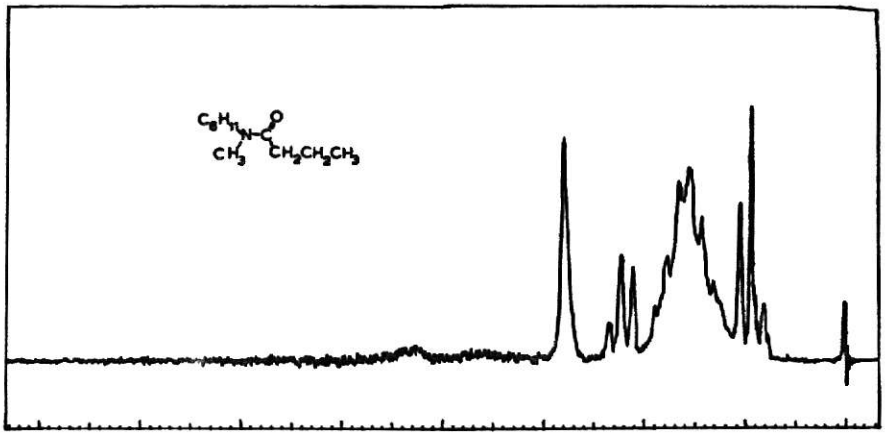
NMR SPECTRA

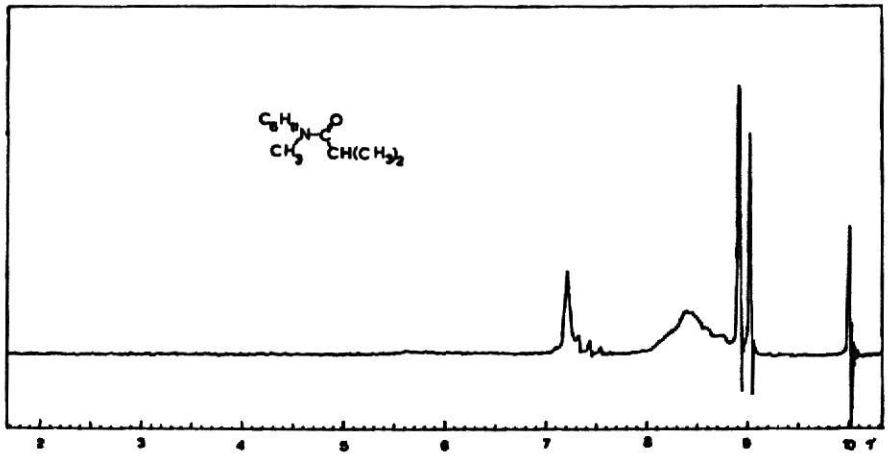
N-cyclohexyl-N-methylpropionamide

N-cyclohexyl-N-methylbutylamide

N-cyclohexyl-N-methyl-2-methylpropionamide



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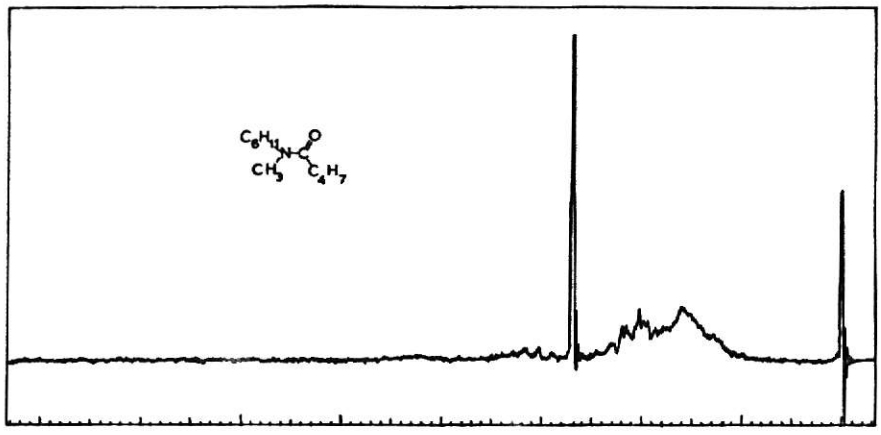
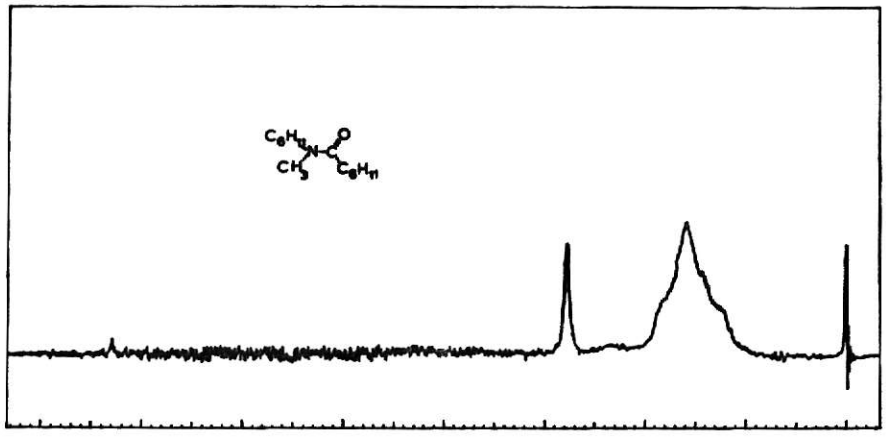
NMR SPECTRA

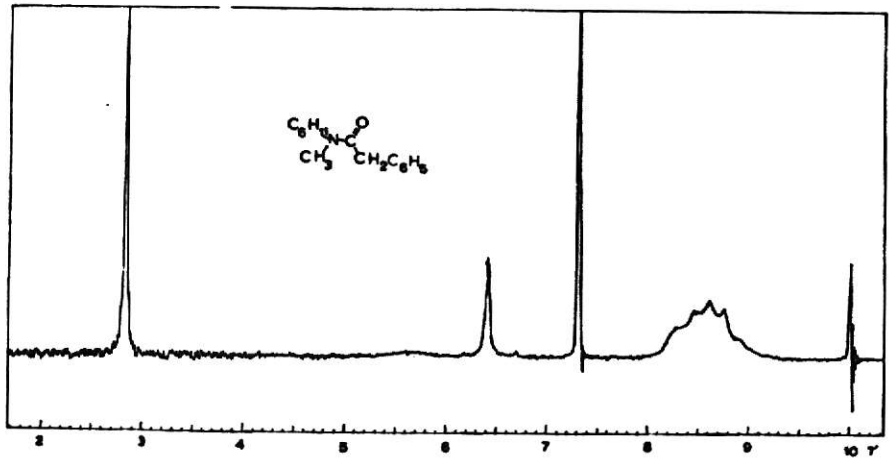
N-cyclohexyl-N-methylcyclobutanecarboxamide

N-cyclohexyl-N-methylcyclohexanecarboxamide

N-cyclohexyl-N-methylphenylacetamide



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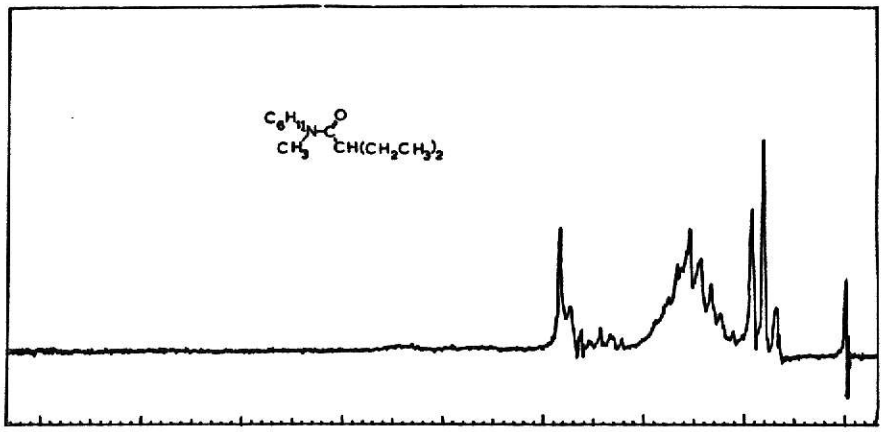
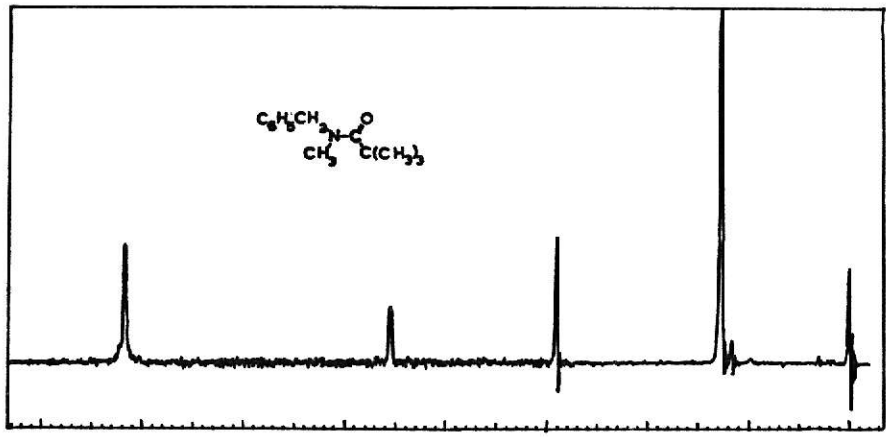
NMR SPECTRA

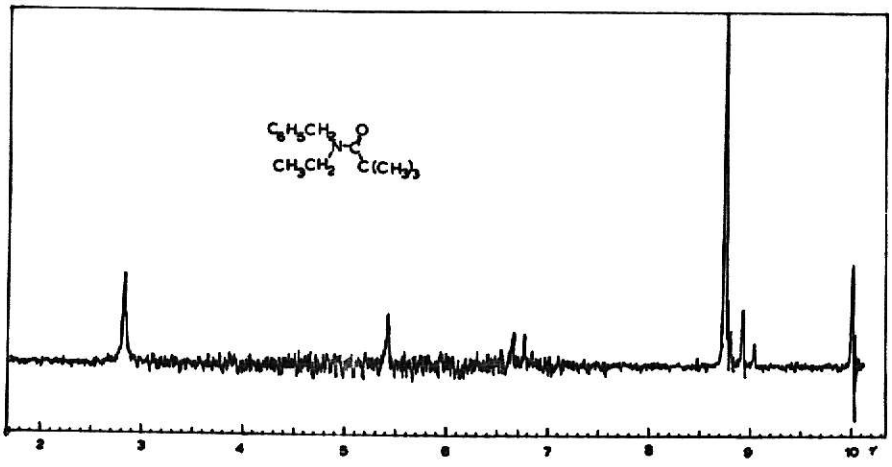
N-cyclohexyl-N-methyl-2-ethylbutylamide

N-benzyl-N-methylpivalamide

N-benzyl-N-ethylpivalamide



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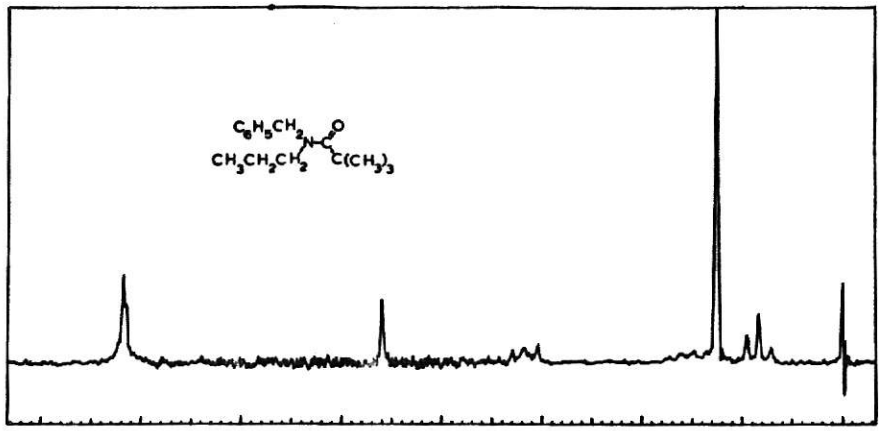
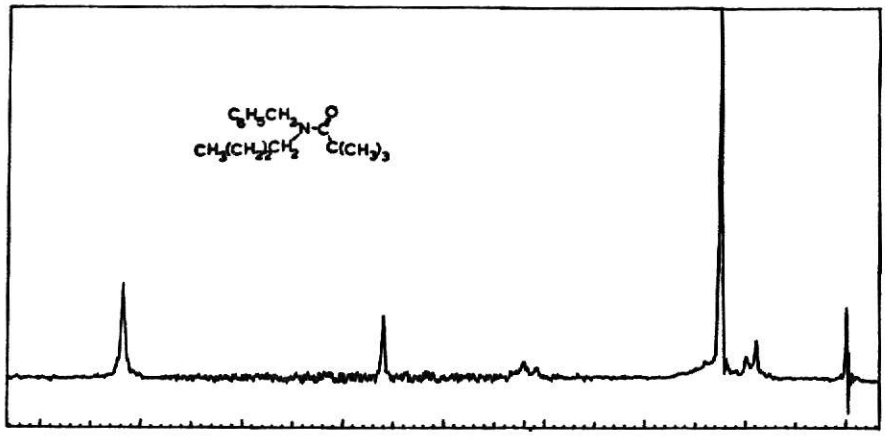
NMR SPECTRA

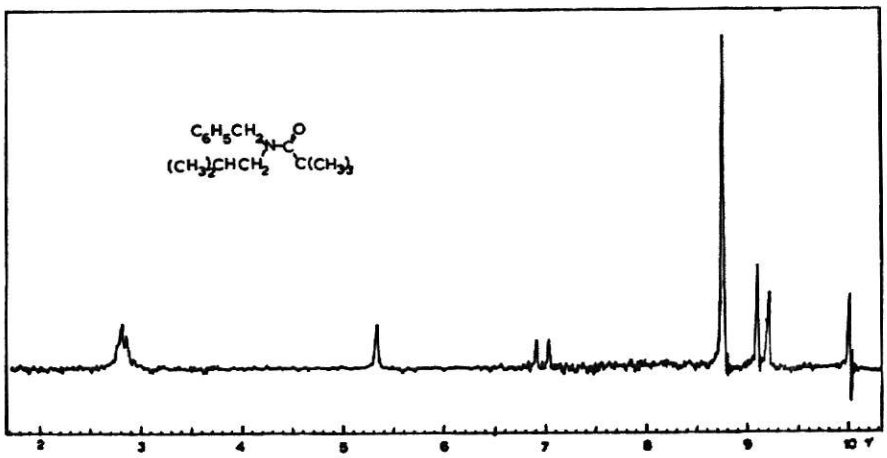
N-benzyl-N-propylpivalamide

N-benzyl-N-butylpivalamide

N-benzyl-N(2-methylpropyl)pivalamide


$C_6H_5CH_2$
$CH_3CH_2CH_2$
$C(CH_3)_3$


$C_6H_5CH_2$
$CH_3(CH_2)_2CH_2$
$C(CH_3)_3$


$C_6H_5CH_2$
$(CH_3)_2CHCH_2$
$C(CH_3)_3$
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EXPERIMENTAL

N-benzyl-N-methylacetamide. To a stirred solution of 3.03 g (.025 mole) of benzylmethylamine in 10 ml of 20% NaOH solution was added 1.95 g (.025 mole) of acetyl chloride. After 30 minutes the solution was extracted three times with ether. The combined ether extracts were dried with magnesium sulfate and excess solvent removed. The oil obtained was distilled to yield 1.96 g (48% yield) of N-benzyl-N-methylacetamide: m.p. 40°; (lit. m.p. 40-41°);[73] ir (CCl_4) 1656,1401,1019,725,698 cm^{-1}; nmr (CCl_4) 2.75 (s, 5H), 5.57 (s, 2H), 7.17 (s, 3H), 8.01 (s, 3H).

N-benzyl-N-methylpropionamide. The procedure is the same as described above: yield 40%; b.p. 92° (0.15mm); ir (film) 1639,1064,735,698 cm^{-1}; nmr (CCl_4) 2.87 (s, 5H), 5.56 (s, 2H), 7.19 (s, 3H), 7.75 (q, 2H), 8.93 (t, 3H).

N-benzyl-N-methylbutylamide. The procedure is the same as described above: yield 57%; b.p. 102° (0.10mm)(lit. b.p. 115° (2.5mm)[74]); ir (film) 2899,1647,733,699 cm^{-1}; nmr (CCl_4) 2.86 (s, 5H), 5.56 (s, 2H), 7.21 (s, 2H), 7.77 (t, 2H), 8.38 (m, 2H), 9.10 (t, 3H).

N-benzyl-N-methylisobutylamide. The procedure is the same as described above: yield 49%; b.p. 104° (0.10mm); ir (film) 1642,1089,733,699 cm^{-1}; nmr (CCl_4) 2.86 (s, 5H), 5.54 (s, 2H), 7.16 (s, 3H), 7.25 (m, 1H), 8.75 (d, 6H).

N-benzyl-N-methylcyclohexanecarboxamide. The procedure is the same as described above: yield 69%; b.p. 122° (0.15mm); (lit. b.p. 146° (1.0mm)[75]); ir (film) 2890,1645,733,700 cm^{-1}; nmr (CCl_4) 2.84 (s, 5H), 5.53 (s, 2H), 7.16 (s, 3H), 8.08-8.95 (m, 11H).

N-benzyl-N-methylphenylacetamide. The procedure is the same as described above; yield 62%; b.p. 140° (0.41mm); ir (film) 1642,1449,733,698 cm^{-1}; nmr (CCl_4) 2.88 (s, 10H), 5.61 (s, 2H), 6.45 (s, 2H), 7.28 (s, 3H).

N-benzyl-N-methylcyclobutanecarboxamide. The procedure is the same as described above: yield 24%; b.p. 117° (0.18mm); ir (film) 2890,1642,734,699 cm^{-1}; nmr (CCl_4) 2.84 (s, 5H), 5.59 (br s, 2H), 6.78 (m, 1H), 7.25 (s, 3H), 7.58-8.21 (m, 6H).

N-benzyl-N-methyl-2-ethylbutyramide. The procedure is the same as described above: yield 49%; b.p. 112° (0.37mm); ir (film) 2899,1642,733,699 cm^{-1}; nmr (CCl_4) 2.84 (s, 5H), 5.48 (s, 2H), 7.15 (s, 3H), 7.32-7.78 (m, 1H), 8.18-8.78 (m, 4H), 9.18 (t, 6H).

N-cyclohexyl-N-methylacetamide. To a stirred solution of 3.39 g (.03 mole) of N-methylcyclohexylamine in 10 ml of 20% NaOH solution was added 2.76 g (.03 mole) of acetyl chloride. After 1 hr the solution was extracted three times with ether. The combined ether extracts were dried with magnesium sulfate and excess solvent removed. The oil obtained was distilled to yield 3.30 g (65% yield) of N-cyclohexyl-N-methylacetamide: b.p. 70° (0.30mm); (lit. b.p. 249° (740mm)[76]); ir (film) 2907,1642,1403,1024 cm^{-1}; nmr (CCl_4) 7.27 (d, 3H), 8.46 (s, 3H), 7.97-9.06 (m, 11H).

N-cyclohexyl-N-methylpropionamide. The procedure is the same as described above: yield 64%; b.p. 90° (0.20mm); ir (film) 2890,1642,1408,1066 cm^{-1}; nmr (CCl_4) 7.23 (s, 3H), 7.76 (q, 2H), 8.00-8.93 (m, 11H), 8.96 (t, 3H).

N-cyclohexyl-N-methylbutylamide. The procedure is the same as described above: yield 68%; b.p. 88° (0.30mm); ir (film) 2874,1645,1449,1075 cm^{-1}; nmr (CCl_4) 7.21 (br s, 3H), 7.78 (t, 2H), 7.97-8.92 (m, 13H), 9.08 (t, 3H).

N-cyclohexyl-N-methylphenylacetamide. The procedure is the same as described above: yield 65%; b.p. 140° (0.40mm); ir (film) 2890,1626,1445,1403, 1100,710,696 cm^{-1}; nmr (CCl_4) 2.84 (s, 5H), 6.42 (s, 2H), 7.32 (s, 3H), 8.07-9.07 (m, 11H).

N-cyclohexyl-N-methyl-2-methylpropionamide. The procedure is the same as described above: yield 82%; b.p. 86° (0.50mm); ir (film) 2874,1639,1404, 1085 cm^{-1}; nmr (CCl_4) 7.16 (s, 3H), 6.98-9.02 (m,11H), 8.98 (d, 6H).

N-cyclohexyl-N-methylcyclohexanecarboxamide. The procedure is the same as described above: yield 79%; m.p. 49°; ir (CCl_4) 2890,1645,1447,1406 cm^{-1}; nmr (CCl_4) 7.23 (s, 3H), 7.97-9.05 (m, 22H).

N-cyclohexyl-N-methyl-2-ethylbutylamide. The procedure is the same as described above: yield 46%; b.p. 94° (0.40mm); ir (film) 2890,1639,1463, 1092 cm^{-1}; nmr (CCl_4) 7.24 (d, 3H), 7.34-8.82 (m, 1H), 7.96-9.02 (m, 15H), 9.20 (t, 6H).

N-cyclohexyl-N-methylcyclobutanecarboxamide. The procedure is the same as described above: yield 29%; b.p. 124° (0.21mm); ir (film) 2890,1639,1449, 1408 cm^{-1}; nmr (CCl_4) 6.68-7.17 (m, 1H), 7.32 (s, 3H), 7.51-9.06 (m, 17H).

N-benzyl-N-methylpivalamide. To a stirred solution of 3.03 g (.025 mole) of benzylmethylamine in 10 ml of a 20% NaOH solution was added 3.00 g (.025 mole) of pivalyl chloride. After 2 hr the solution was extracted three times with ether. The combined ether extracts were dried with magnessium sulfate and excess solvent removed. The solid formed was recrystalized from a water-ethanol solution to yield 4. 5 g (78% yield) of N-benzyl-N-methyl-2, 2-dimethylpropionamide: m.p. 44-45°; ir (CCl_4) 2950,1634,1190,1096,697 cm^{-1}; nmr (CCl_4) 2.84 (s, 5H), 5.47 (s, 2H), 7.10 (s, 3H), 8.74 (s, 9H).

N-benzyl-N-ethylpivalamide. The procedure is the same as described above: yield 56%; m.p. 51-52°; ir (CCl_4) 2924,1637,1414,1185,698 cm^{-1}; nmr (CCl_4) 2.84 (s, 5H), 5.43 (s, 2H), 6.71 (q, 2H), 8.75 (s, 9H), 8.91 (t, 3H).

N-benzyl-N-propylpivalamide. The procedure is the same as described above: yield 58%; m.p. 51°; ir (CCl_4) 2941,1639,1410,1183,699 cm^{-1}; nmr (CCl_4) 2.84 (s, 5H), 5.40 (s, 2H), 6.83 (t, 2H), 8.21-8.91 (m, 2H), 8.76 (s, 9H), 9.17 (t, 3H).

N-benzyl-N-butylpivalamide. The procedure is the same as described above: yield 53%; m.p. 51-52°; ir (CCl_4) 2915,1637,1410,1186,697 cm^{-1}; nmr (CCl_4) 2.83 (s, 5H), 5.40 (s, 2H), 6.79 (t, 2H), 8.34-8.94 (m, 4H), 8.75 (s, 9H), 9.11 (t, 3H).

N-benzyl-N-2-methylpropylpivalamide. The procedure is the same as described above: yield 49%; m.p. 66-67°; ir (CCl_4) 2915,1634,1408,1185,697 cm^{-1}; nmr (CCl_4) 2.84 (d, 5H), 5.33 (s, 2H), 6.98 (d, 2H), 8.77 (s, 9H), 9.17 (d, 6H).

N-benzyl-N-2-methylpropylformamide. To a stirred solution of 4.07 g (.025 mole) of 2-methylpropylbenzylamine in 10 ml of benzene was added 1.15 g (.025 mole) of formic acid. The solution was refluxed for 12 hr and the water was removed by using a Dean-Stark apparatus. The excess solvent was removed and the oil obtained was distilled to yield 2.68 g (57% yield) of N-benzyl-N-2-methylpropylformamide: b.p. 112° (0.90mm); ir (film) 2899, 1675,1422,738,699 cm^{-1}; nmr (CCl_4) 1.93 (d, 1H), 2.83 (s, 5H), 5.63 (d, 2H), 7.10 (t, 2HO, 7.84-8.53 (m, 1H), 9.20 (d, 6H).

N-benzyl-N-methylformamide. The procedure is the same as described above: yield 53%; b.p. 91° (0.20mm); ir (film) 3195,1650,1372,765,701 cm^{-1}; nmr (CCl_4) 1.97 (d, 1H), 2.84 (s, 5H), 5.67 (d, 2H), 7.32 (d, 3H).

N-benzyl-N-ethylformamide. The procedure is the same as described above: yield 59%; b.p. 86° (0.20mm) ir (film) 1667,1425,1080,740,704 cm^{-1}; nmr (CCl_4) 1.93 (d, 1H), 2.81 (s, 5H), 5.64 (d, 2H), 6.86 (q, 2H), 8.98 (t, 3H).

N-benzyl-N-isopropylformamide. The procedure is the same as described above: yield 61% b.p. 95° (0.35mm); (lit. b.p. 158° (13mm)[57]); ir (film) 1667,1416,734,698 cm^{-1}; nmr (CCl_4) 1.88 (d, 1H), 2.86 (s, 5H), 5.70 (d, 2H), 6.36 (m, 1H), 8.89 (d, 6H).

N-benzyl-N-propylformamide. The procedures is the same as described above: yield 52%; b.p. 98° (0.35mm); ir (film) 1667,1425,740,702 cm^{-1}; nmr (CCl_4) 1.89 (d, 1H), 2.80 (s, 5H), 5.63 (d, 2H), 6.93 (t, 2H), 8.26-8.87 (m, 2H), 9.19 (t, 3H).

N-benzyl-N-n-butylformamide. The procedure is the same as described above: yield 56%; b.p. 106° (0.30mm); ir (film) 1667,1425,735,703 cm^{-1}; nmr (CCl_4) 1.94 (d, 1H), 2.83 (s, 5H), 5.63 (d, 2H), 6.69-6.95 (m, 2H), 8.24-8.95 (m, 4H), 9.14 (t, 3H).

N-benzyl-N-cyclohexylformamide. The procedure is the same as described above: yield 71%; b.p. 105° (0.25mm); (lit. b.p. 135-140° (3mm)[77]); ir (film) 2865,1667,741,713 cm^{-1}; nmr (CCl_4) 1.88 (d, 1H), 2.84 (s, 5H), 5.64 (d, 2H), 8.08-9.09 (m, 11H).

N-benzyl-N-(1-phenylethyl)formamide. The procedure is the same as described above: yield 54%; b.p. 144° (0.20mm); ir (film) 1667,1408,734,699 cm^{-1}; nmr (CCl_4) 1.74 (d, 1H), 2.82 (s, 5H), 2.92 (s, 5H), 5.42 (q, 1H), 5.83 (d, 2H), 8.56 (d. 3H).

N-benzyl-N-2-butylformamide. The procedure is the same as described above: yield 81%; b.p. 92° (0.15mm); ir (film) 1699,1422,737,702 cm^{-1}; nmr (CCl_4) 1.86 (s, 1H), 2.80(s, 5H), 5.68 (d, 2H), 6.64 (m, 1H), 8.58 (q, 2H), 8.92 (d, 3H), 9.27 (t, 3H).

General: Infrared spectra were taken on a Perkin Elmer Model 137. Solids were run as solutions in carbon tetrachloride. Liquid samples were placed between sodium chloride plates, and the spectra were taken of thin films without solvent. Nuclear Magnetic Resonance spectra were obtained from a Varian A-60. Samples were run as 10% solutions in carbon tetrachloride using TMS as an internal standard. Melting points were obtained using Fisher Johns melting point apparatus. All melting points and boiling points are uncorrected.

APPENDICES

APPENDIX 1

Calculation of equilibrium constants for different series of amides.

Table 2

Identification of compounds with series numbers.

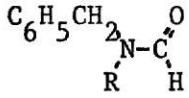
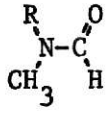
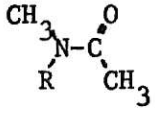
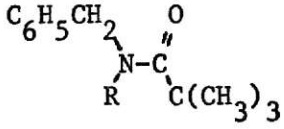
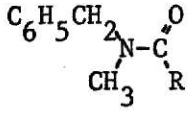
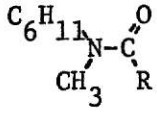
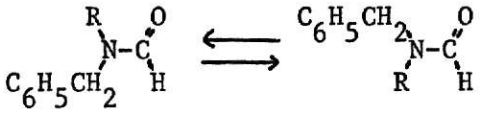
Compound	Series Number
	Series 1
	Series 2
	Series 3
	Series 4
	Series 5
	Series 6
	Series 7

Table 3[1]

Equilibrium constants for series 1.



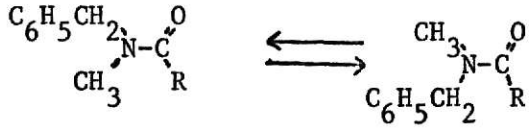
R.	Low Field (mm)[2]	High Field (mm)	K	Log K
$-CH_3$	87.5 ± 2	95.5 ± 1.5	1.090	+.038
$-CH_2CH_3$	93.5 ± 2.5	89.6 ± 2	.960	-.018
$-CH_2-CH_2-CH_3$	103.0 ± 1	77.5 ± 1	.755	-.123
$-CH(CH_3)_2$	104.0 ± 1	59.3 ± 1	.565	-.248
$-CH_2CH(CH_3)_2$	96.8 ± 2	59.3 ± 1.5	.614	-.212
$-CH(C_6H_5)(CH_3)$	71.5 ± 1.5	32.4 ± 1.5	.454	-.342
$-C_6H_{11}$	101.0 ± 2	50.0 ± 1	.500	-.300
$-CH(CH_3)CH_2CH_3$	95.0 ± 1.5	43.3 ± 1	.455	-.341
$-CH_2CH_2CH_2CH_3$	95.0 ± 1.5	78.1 ± 2	.820	-.087

[1] In CCl_4 at 37° C. 6% mole ratio

[2] Integrated heights of peaks

Table 4[1]

Equilibrium constants for series 6 in CS_2



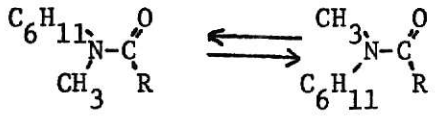
R.	Low Field (mm)[2]	High Field (mm)	K	Log K
$-CH_3$	105.0 ± 2	58.1 ± 2	.552	- .258
$-CH_2CH_3$	101.1 ± 2	42.5 ± 1.5	.420	- .377
$-CH_2CH_2CH_3$	117.0 ± 2	41.3 ± 1.5	.348	- .458
$-CH(CH_3)_2$	83.1 ± 2.5	50.1 ± 1	.603	- .220
$-C_6H_{11}$	110.0 ± 2	68.1 ± 1	.618	- .208
$-C_4H_7$	107.1 ± 1.5	48.4 ± 1	.445	- .352
$-CH(CH_2CH_3)_2$	115.4 ± 1	9.5 ± 1	.084	-1.074

[1] At 0° in CS_2 6% mole ratio

[2] Integrated heights of peaks

Table 5[1]

Equilibrium constants for series 7 in CS_2.



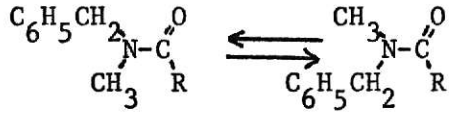
R.	Low Field (mm)[2]	High Field (mm)	K	Log K
$-CH_3$	136.0 ± 2	95.2 ± 2	.700	-.154
$-CH_2CH_3$	116.4 ± 1.5	67.4 ± 1.5	.575	-.241
$-CH_2CH_2CH_3$	97.8 ± 2	62.4 ± 2	.638	-.195
$-CH(CH_3)_2$	95.2 ± 1.5	74.1 ± 1.5	.780	-.108
$-C_6H_{11}$	88.5 ± 2	47.6 ± 1.5	.540	-.267
$-CH_2C_6H_5$	98.0 ± 2	46.8 ± 1.5	.473	-.325
$-C_4H_7$	78.6 ± 2	42.5 ± 1	.543	-.265
$CH(CH_2CH_3)_2$	116.4 ± 1.5	74.1 ± 1	.640	-.194

[1] At o° in CS_2 6% mole ratio

[2] Integrated heights of peaks

Table 6[1]

Equilibrium constants for series 6 in Toluene.



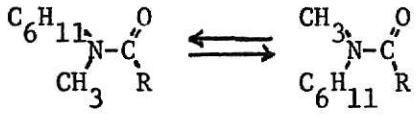
R.	Low Field (mm)[2]	High Field (mm)	K	Log K
$-CH_3$	115.7 ± 2	73.4 ± 1.5	.633	-.198
$-CH_2CH_3$	101.2 ± 2	60.5 ± 1.5	.600	-.222
$-CH_2CH_2CH_3$	118.1 ± 1.5	68.1 ± 1.5	.578	-.238
$-CH(CH_3)_2$	114.4 ± 2	59.7 ± 1.5	.521	-.282
$-C_6H_{11}$	109.5 ± 2	41.4 ± 1.5	.378	-.410
$-CH_2C_6H_5$	125.0 ± 1	73.4 ± 1.5	.587	-.232
$-C_4H_7$	106.0 ± 1.5	55.0 ± .525	.525	-.280
$-CH(CH_2CH_3)_2$	74.2 ± 1.5	28.0 ± 1	.375	-.420

[1] At -1°C. in Ø-CH_3 6% mole ratio

[2] Integrated heights of peaks

Table 7[1]

Equilibrium constants for series 7 in Chlorobenzene.



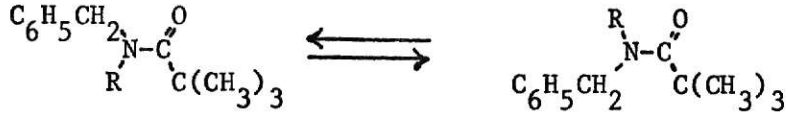
R	Low Field (mm)[2]	High Field (mm)	K	Log K
-H	56.0 ± 1	101.0 ± 1	.560	-.253
$-CH_3$	77.0 ± 1	103.0 ± 1	.745	-.127
$-CH_2CH_3$	63.0 ± 1.5	87.5 ± 1.5	.720	-.143
$-CH_2CH_2CH_3$	55.1 ± 1	80.4 ± 1	.690	-.162
$-CH(CH_3)_2$	66.4 ± 1.5	89.0 ± 1	.745	-.127
$-C_6H_{11}$	48.7 ± 1.5	76.9 ± 1	.633	-.200
$-CH_2C_6H_5$	72.1 ± 1.5	94.0 ± 1.5	.740	-.132
$-C_4H_7$	51.2 ± 1.5	57.1 ± 1.5	.920	-.045
$-CH(CH_2CH_3)_2$	50.6 ± 1.5	95.1 ± 1.5	.526	-.280

[1] At 0°C. in ø-Cl 6% mole ratio

[2] Integrated heights of peaks

Table 8[1]

Equilibrium constants for series 5.



R	Low Field $(mm)^2$	High Field (mm)	K	Log K
$-CH_3$	50.2 ± 1	78.6 ± 1	1.57	+.196
$-CH_2CH_3$	66.7 ± 1.5	85.3 ± 1.5	1.29	.111
$-CH_2CH_2CH_3$	62.0 ± 1.5	65.6 ± 1	1.06	.026
$-CH_2CH_2CH_2CH_3$	70.0 ± 1.5	70.7 ± 1	1.01	.004
$-CH_2CH(CH_3)_2$	99.0 ± 1.5	26.6 ± 1	.272	-.556

[1] -60°C in SO_2 6% mole ratio

[2] Integrated heights of peaks

Table 9[2]

Equilibrium constants for series 2 (Lambing).

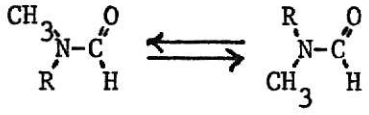
R	K[1]	Log K
$-CH_3$	.078	-1.10
$-CH_2CH_3$	.138	-.864
$-CH(CH_3)_2$	.178	-.750
$-t-C_4H_9$	.332	-.480
$-C_6H_5$	.525	-.280
$-CH_2CH_2OH$	.200	-.700
$-CH_2C_6H_5$	.136	-.868

[1]At 37° in a neat solution

[2]The following series of compounds was synthesized by Larry Lambing

Table 10

Equilibrium constants for series 3.

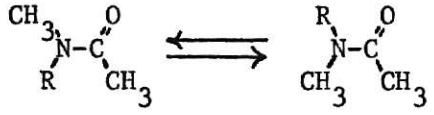


R	K[1]	Log K
$-CH_3$	1.00	.00
$-CH_2CH_3$	.660	-.180
$-CH_2CH_2CH_2CH_3$	.640	-.194
-cyclo-C_6H_{11}	.515	-.289
$-CH(CH_3)_2$	.490	-.310
-t-C_4H_9	.124	-.910
$-CH_2C_6H_5$	.850	-.071
$-CH(CH_3)C_6H_5$	.560	-.252
-H	11.00	1.05

[1]Values for K were obtained from L. A. LaPlanche and M. T. Rogers, J. Am. Chem. Soc., 85 3729 (1964) and W. Walter and G. Marten, Liebigs Ann. Chem. 712 60 (1968).

Table 11

Equilibrium constants for series 4.

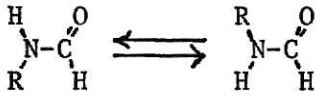


R	K[1]	Log K
$-CH_3$	1.00	.00
$-CH_2CH_3$	.960	-.018
$-CH_2CH_2CH_2CH_3$	.885	-.053
-cyclo-C_6H_{11}	.820	-.087
$-CH_2C_6H_5$	.803	-.094
$-CH(CH_3)_2$	.715	-.146

[1] Values for K were obtained from L. A. LaPlanche and M. T. Rogers, J. Am. Chem. Soc., 85 3729 (1964) and W. Walter and G. Maerten, Liebigs, An. Cham., 712, 60 (1968).

Table 12

Equilibriun constants for series 2(LaPlanche and Rogers).



R	K[1]	Log K
$-CH_3$	.087	-1.06
$-CH_2CH_3$	.137	-.864
$-CH(CH_3)_2$	.137	-.864
$-CH_2CH(CH_3)_2$	.150	-.824
$-CH_2C_6H_5$	.110	-.960
$-CH(CH_3)C_6H_5$	.150	-.824
$-t-C_4H_9$	.222	-.654

[1]Values for K were obtained from L. A. LaPlanche and M. T. Rogers, J. Am. Chem. Soc., 85 3729 (1964) and W. Walter and G. Maerten, Liebigs Ann. Chem., 712 60 (1968).

Table 13

Values for E_s and σ^*.

R	E_s[1]	σ^*[2]
$-CH_3$	-.00	-.00
$-CH_2CH_3$	-.07	-.10
$-CH_2CH_2CH_3$	-.36	-.115
$-CH_2CH_2CH_2CH_3$	-.39	-.130
$-CH(CH_3)_2$	-.47	-.190
$-CH_2CH(CH_3)_2$	-.93	-.125
$-CH(C_6H_5)CH_3$	-1.19	-.210
-cyclo-C_6H_{11}	-.79	-.150
$-CH(CH_3)CH_2CH_3$	-1.18	-.110
$-CH_2C_6H_5$	-.39	+.215
-cyclo-C_4H_7	-.06	-.182[3]
$-CH(CH_2CH_3)_2$	-1.98	-.225
H	+1.24	+.50

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[1] J. E. Leffler and E. Grunwald, Rates and Equilibria of Organic Reactions, John Wiley and Sons, Inc., New York, 1963, p. 228.

[2] Ibid., p. 222.

[3] R. Hahan, T. Corbin and H. Scheckter, J. Am. Chm. Soc., 90, 3404 (1968).
(See page 58.)

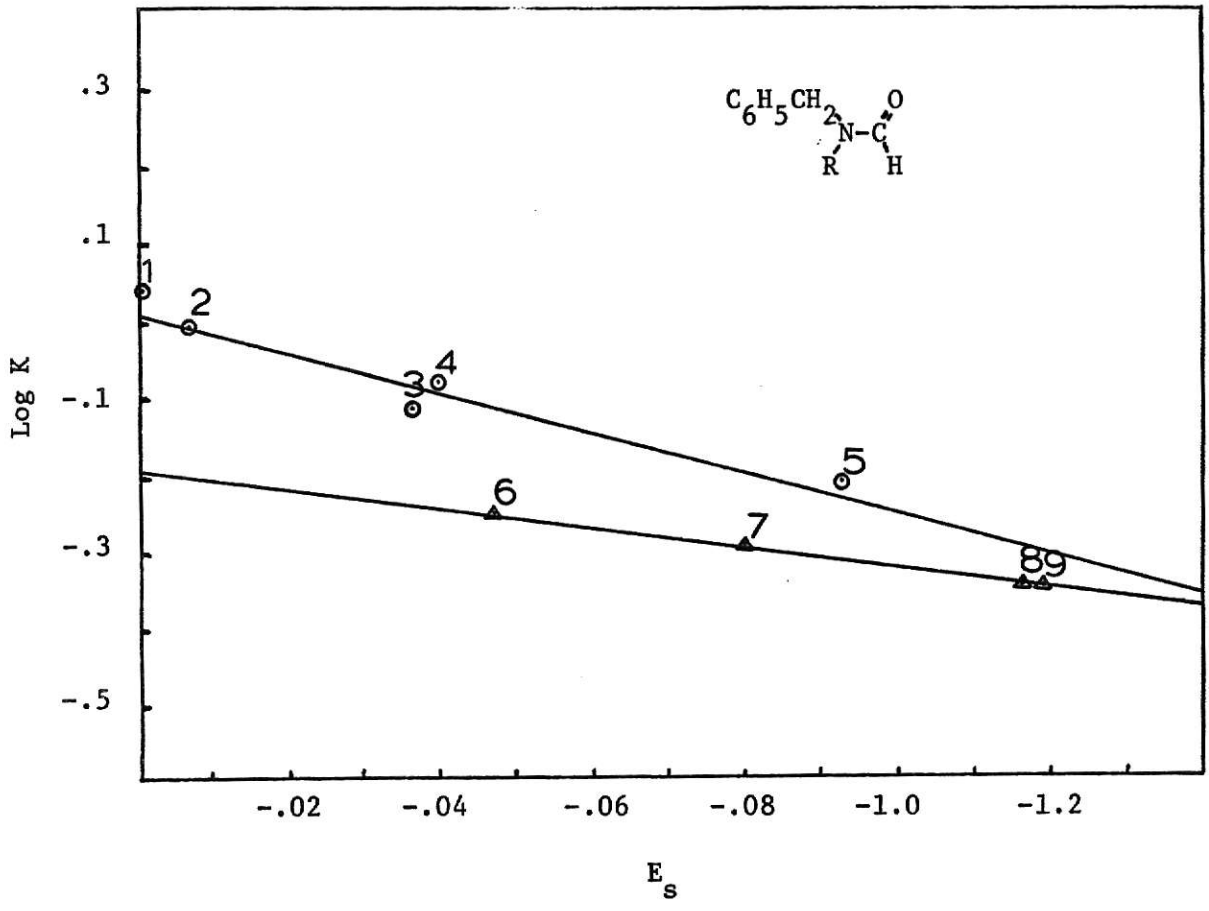
[3]Scheckter has reported the ionization constants of cycloalkyl substituted benzoic acids. The values for cyclohexyl, cyclopentyl, cyclobutyl and isopropyl substituents were 1.28, 1.28, 1.30, and 1.30 x 10^6 respectively. The ionization constant for benzoic acid was 2.01 x 10^6. The σ^* values for cyclohexyl, cyclopentyl, and isopropyl have been determined[2] and for these values a ρ^* for the reaction was determined to be $\rho^* = -1.04$. Using $\rho^* = -1.04$ the σ^* value for the cyclobutyl subst. was calculated to be -.182.

APPENDIX 2

Plots of Log K vs E_s and Log K vs σ^* for the series of amides.

Figure 3

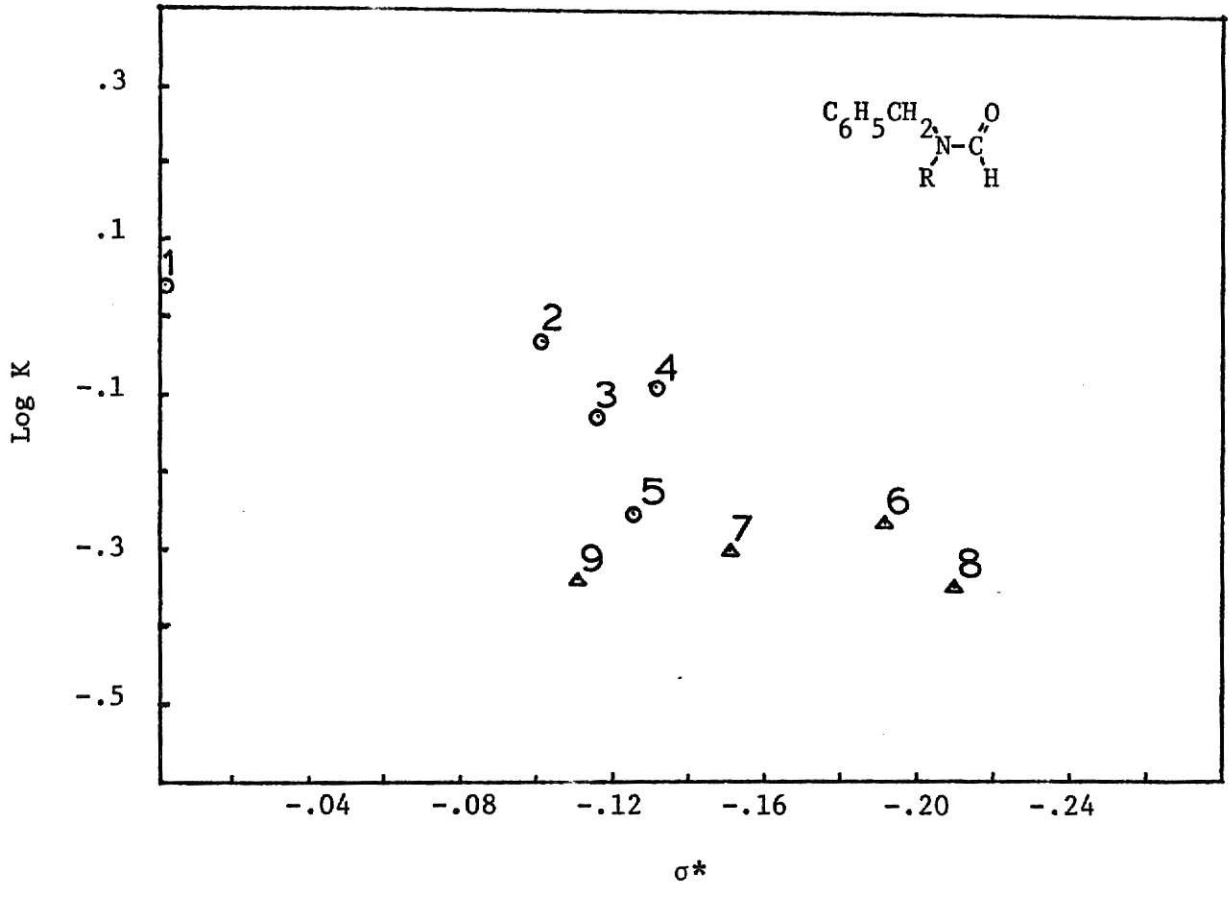
Plot of Log K vs E_s for series 1.



1. R = CH_3
2. R = CH_2CH_3
3. R = $CH_2CH_2CH_3$
4. R = $CH_2CH_2CH_2CH_3$
5. R = $CH_2CH(CH_3)_2$
6. R = $CH(CH_3)_2$
7. R = C_6H_{11}
8. R = $CH(CH_3)CH_2CH_3$
9. R = $CH(C_6H_5)CH_2CH_3$

Figure 4

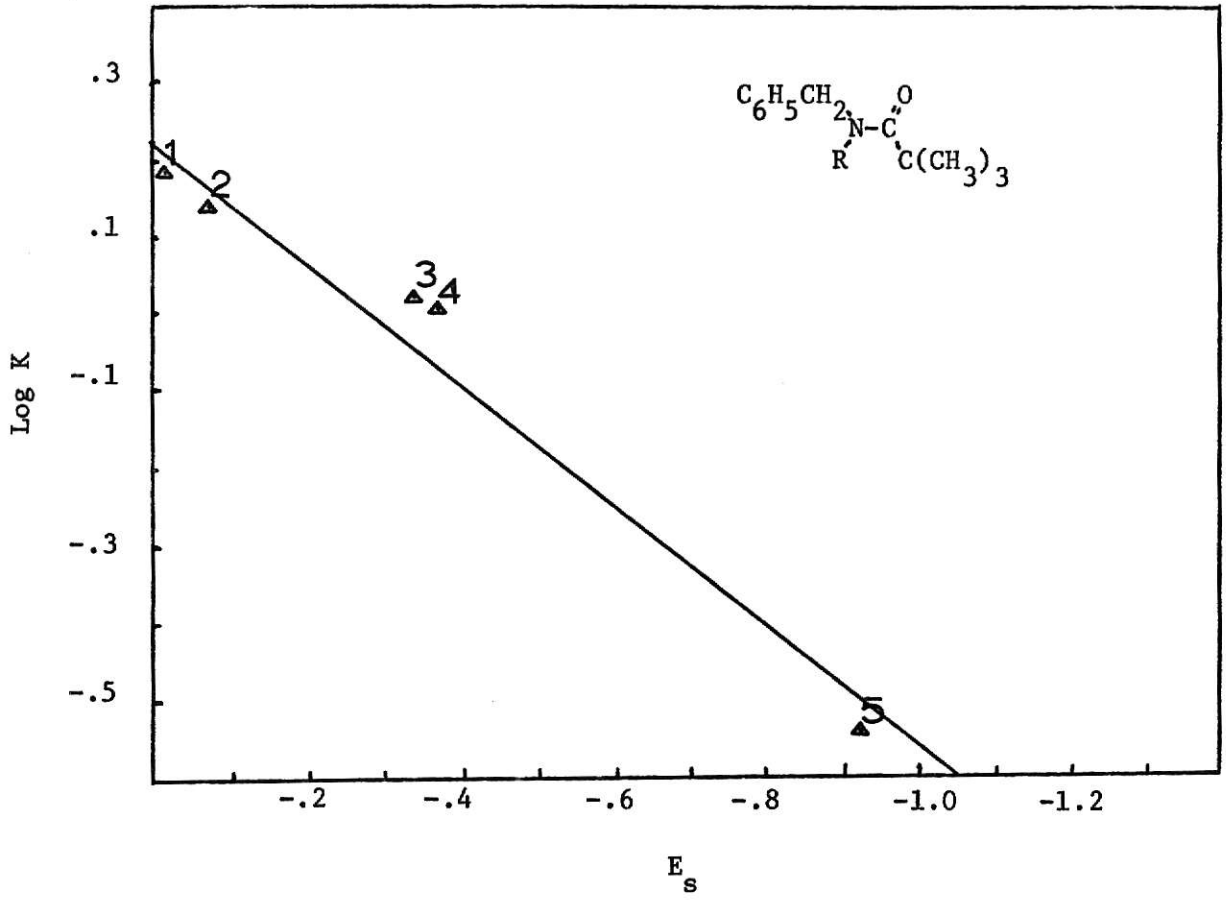
Plot of Log K vs σ* for series 1.



1. R = CH_3
2. R = CH_2CH_3
3. R = $CH_2CH_2CH_3$
4. R = $CH_2CH_2CH_2CH_3$
5. R = $CH_2CH(CH_3)_2$
6. R = $CH(CH_3)_2$
7. R = C_6H_{11}
8. R = $CH(CH_3)CH_2CH_3$
9. R = $CH(C_6H_5)CH_2CH_3$

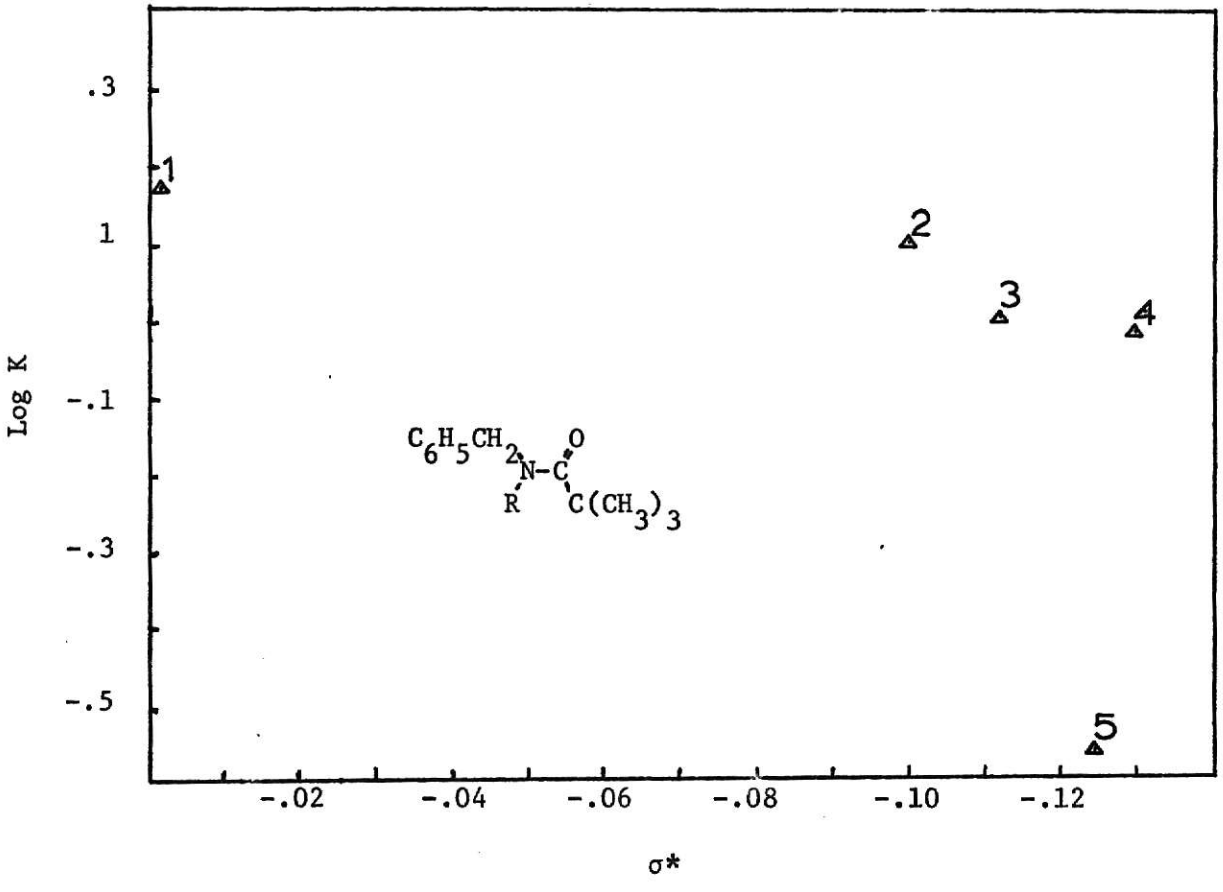
Figure 5

Plot of Log K vs E_s for series 5.



1. R = CH_3
2. R = CH_2CH_3
3. R = $CH_2CH_2CH_3$
4. R = $CH_2CH_2CH_2CH_3$
5. R = $CH_2CH(CH_3)_2$

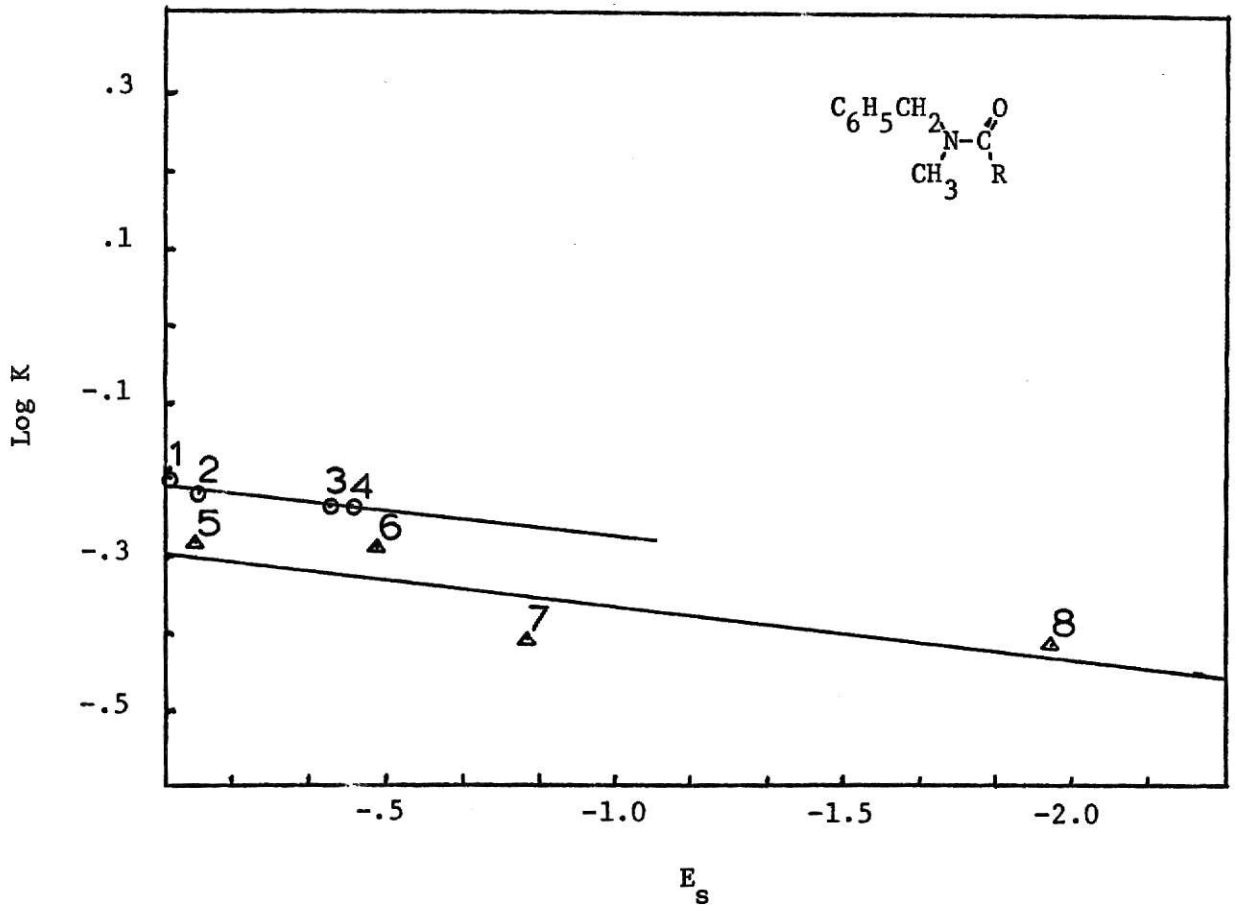
Figure 6
Plot of Log K vs σ* for series t.



1. R = CH_3
2. R = CH_2CH_3
3. R = $CH_2CH_2CH_3$
4. R = $CH_2CH_2CH_2CH_3$
5. R = $CH_2CH(CH_3)_2$

Figure 7

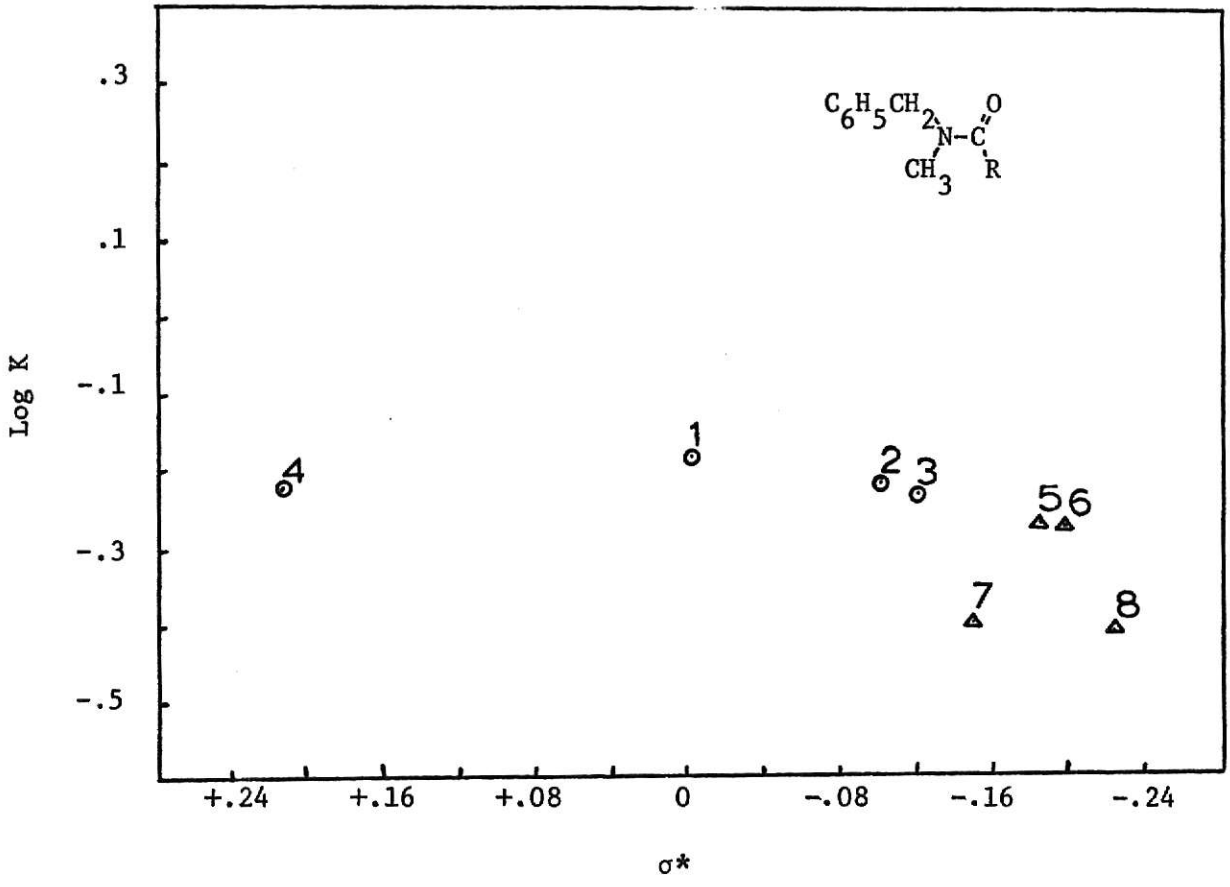
Plot for Log K vs E_s for series 6 (in CS_2).



1. R = CH_3
2. R = CH_2CH_3
3. R = $CH_2CH_2CH_3$
4. R = $CH_2C_6H_5$
5. R = cyclo-C_4H_7
6. R = $CH(CH_3)_2$
7. R = cyclo-C_6H_{11}
8. R = $CH(CH_2CH_3)_2$

Figure 8

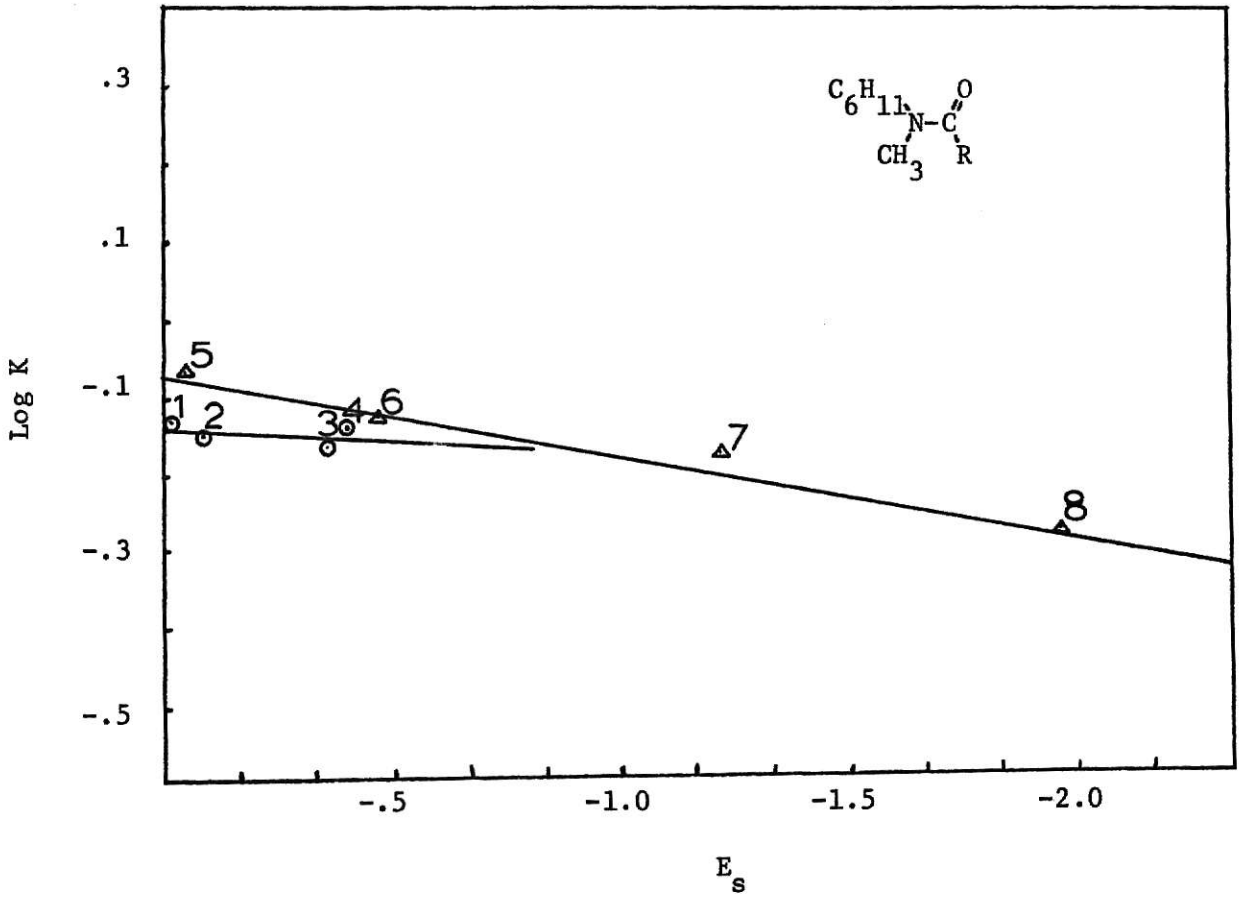
Plot of Log K vs σ* for series 6 (in CS_2)



1. R = CH_3
2. R = CH_2CH_3
3. R = $CH_2CH_2CH_3$
4. R = $CH_2C_6H_5$
5. R = cyclo-C_4H_7
6. R = $CH(CH_3)_2$
7. R = cyclo-C_6H_{11}
8. R = $CH(CH_2CH_3)_2$

Figure 9

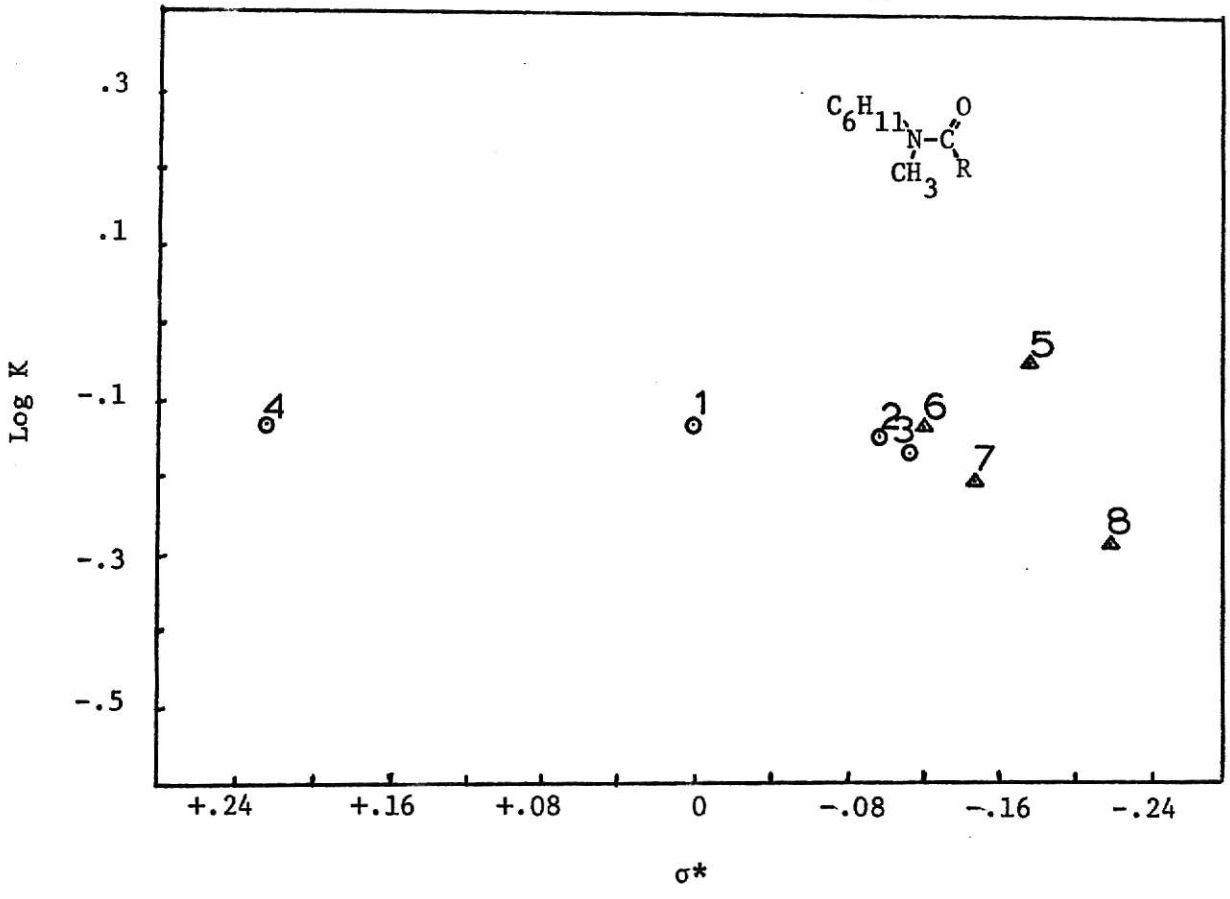
Plot of Log K vs E_s for series 7 (in CS_2).



1. R = CH_3
2. R = CH_2CH_3
3. R = $CH_2CH_2CH_3$
4. R = $CH_2C_6H_5$
5. R = cyclo-C_4H_7
6. R = $CH(CH_3)_2$
7. R = cyclo-C_6H_{11}
8. R = $CH(CH_2CH_3)_2$

Figure 10

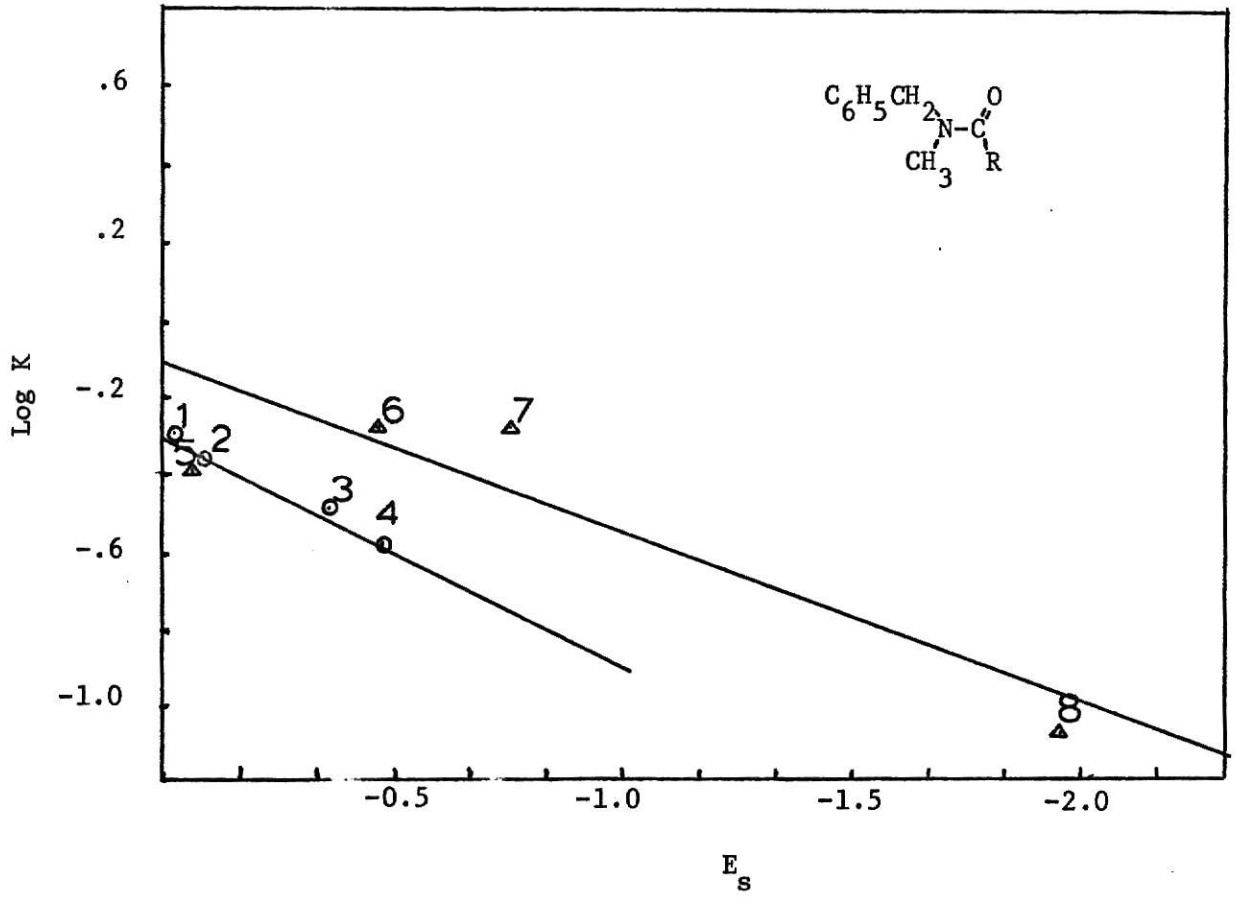
Plot of Log K vs σ* for series 7 (in CS_2).



1. R = CH_3
2. R = CH_2CH_3
3. R = $CH_2CH_2CH_3$
4. R = $CH_2C_6H_5$
5. R = cyclo-C_4H_7
6. R = $CH(CH_3)_2$
7. R = cyclo-C_6H_{11}
8. R = $CH(CH_2CH_3)_2$

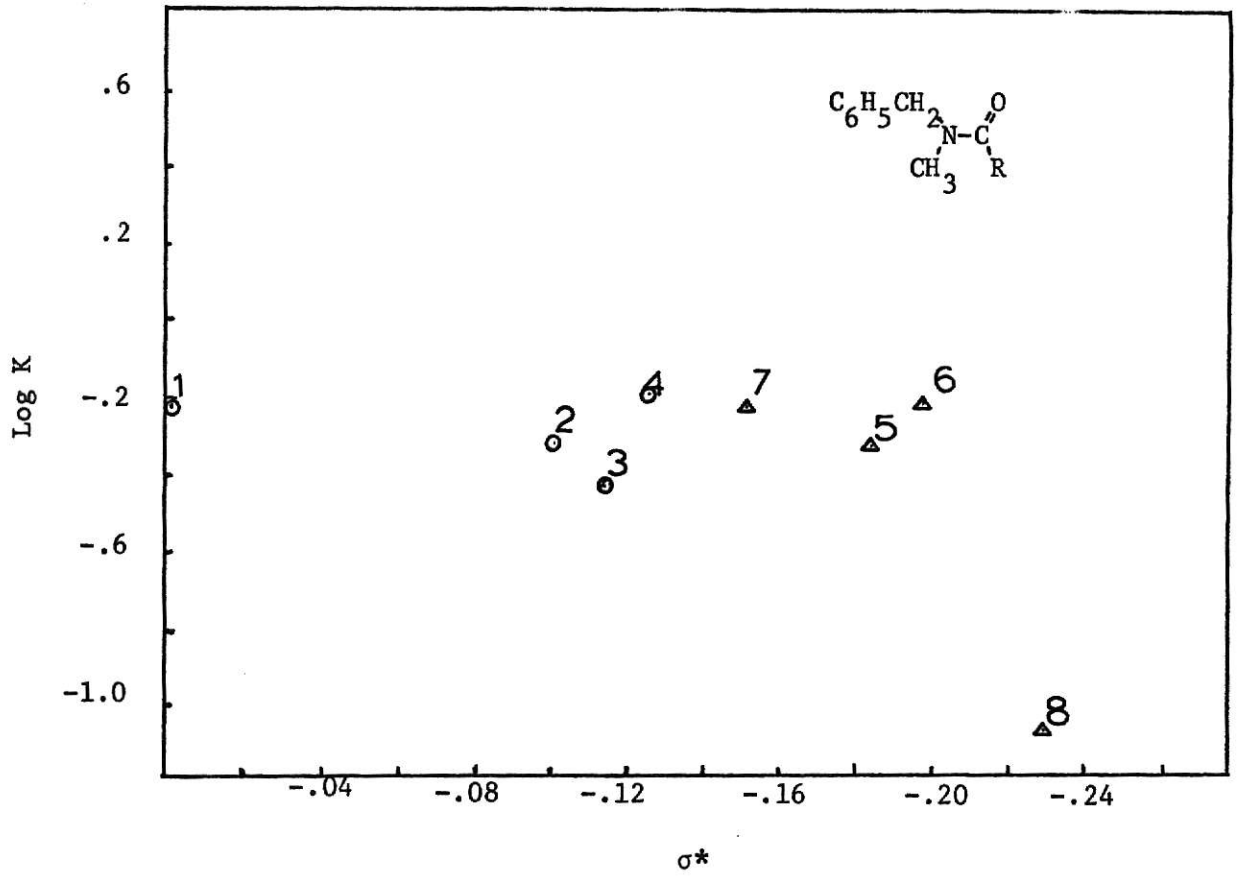
Figure 11

Plot of Log K vs E_s for series 6 (in Toluene).



1. R = CH_3
2. R = CH_2CH_3
3. R = $CH_2CH_2CH_3$
4. R = $CH_2C_6H_5$
5. R = cyclo-C_4H_7
6. R = $CH(CH_3)_2$
7. R = cyclo-C_6H_{11}
8. R = $CH(CH_2CH_3)_2$

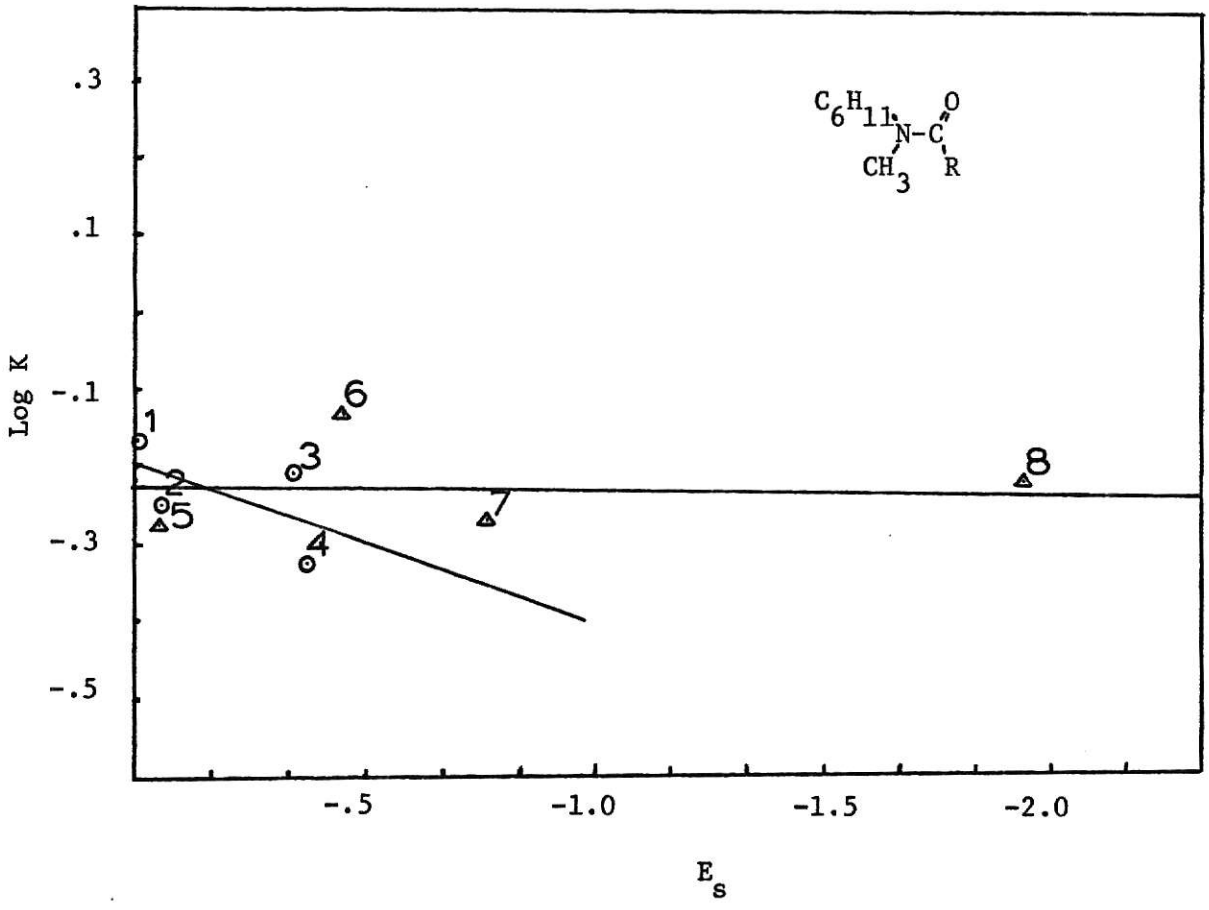
Figure 12
Plot of Log K vs σ* for series 6 (in Toluene).



1. R = CH_3
2. R = CH_2CH_3
3. R = $CH_2CH_2CH_3$
4. R = $CH_2C_6H_5$
5. R = cyclo-C_4H_7
6. R = $CH(CH_3)_2$
7. R = cyclo-C_6H_{11}
8. R = $CH(CH_2CH_3)_2$

Figure 13

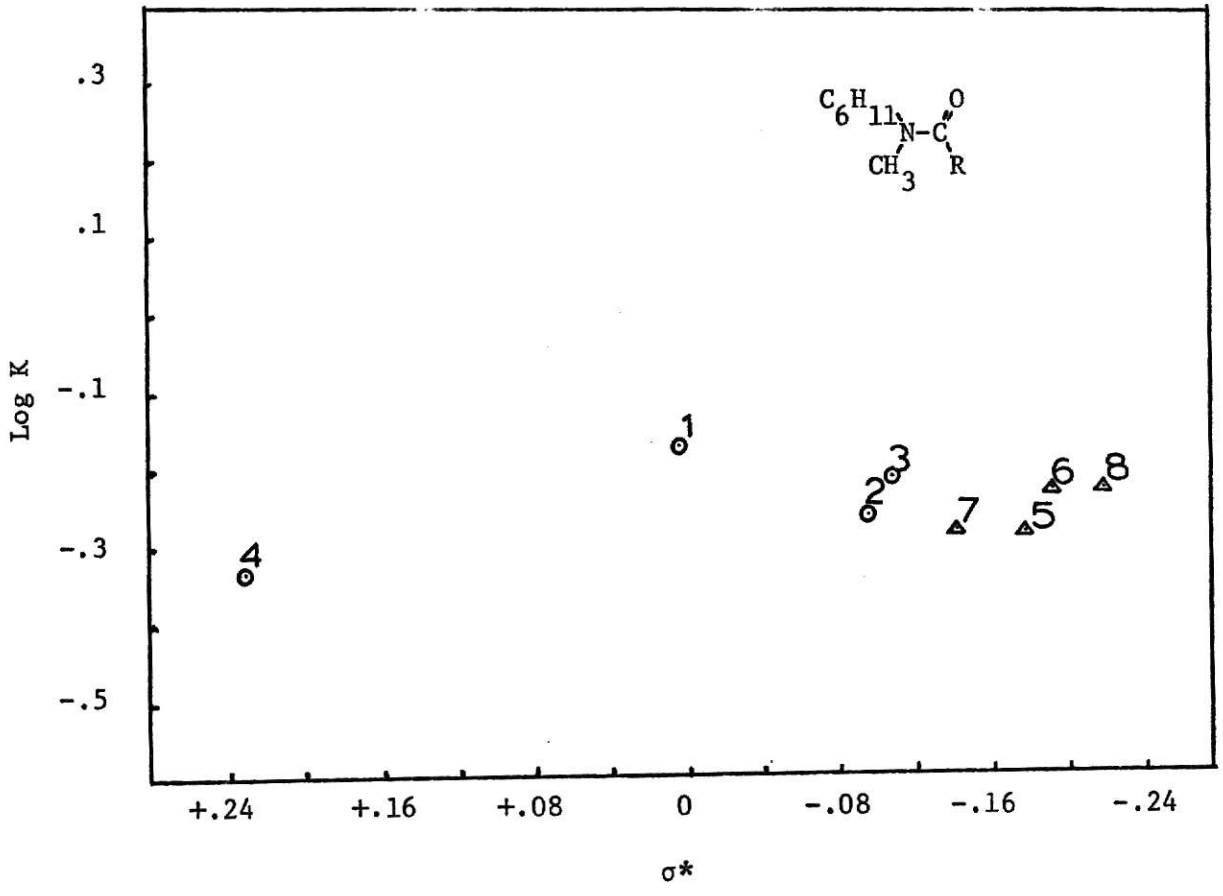
Plot of Log K vs E_s for series 7 (in Chlorobenzene).



1. R = CH_3
2. R = CH_2CH_3
3. R = $CH_2CH_2CH_3$
4. R = $CH_2C_6H_5$
5. R = cyclo-C_4H_7
6. R = $CH(CH_3)_2$
7. R = cyclo-C_6H_{11}
8. R = $CH(CH_2CH_3)_2$

Figure 14

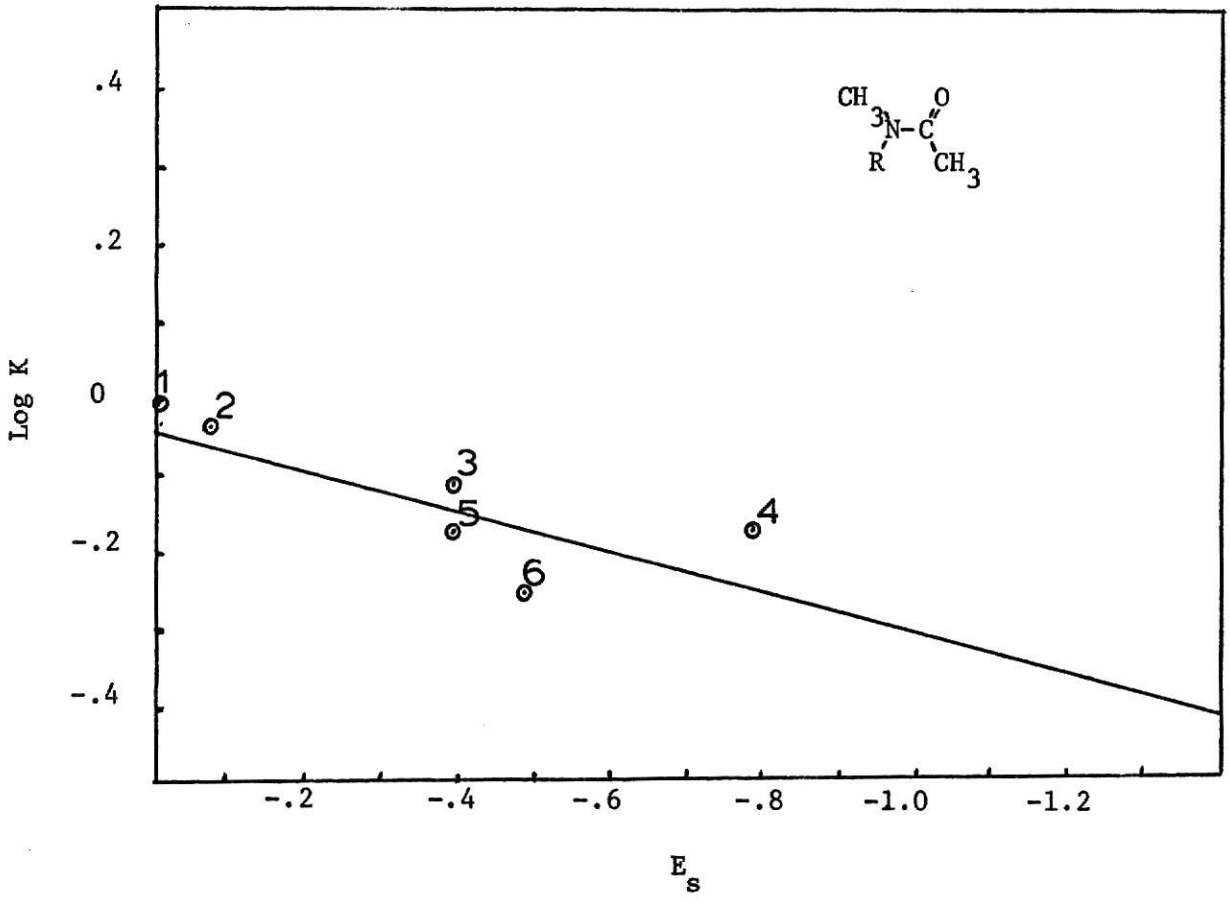
Plot of Log K vs σ* for series 7 (in Chlorobenzene).



1. R = CH_3
2. R = CH_2CH_3
3. R = $CH_2CH_2CH_3$
4. R = $CH_2C_6H_5$
5. R = cyclo-C_4H_7
6. R = $CH(CH_3)_2$
7. R = cyclo-C_6H_{11}
8. R = $CH(CH_2CH_3)_2$

Figure 15

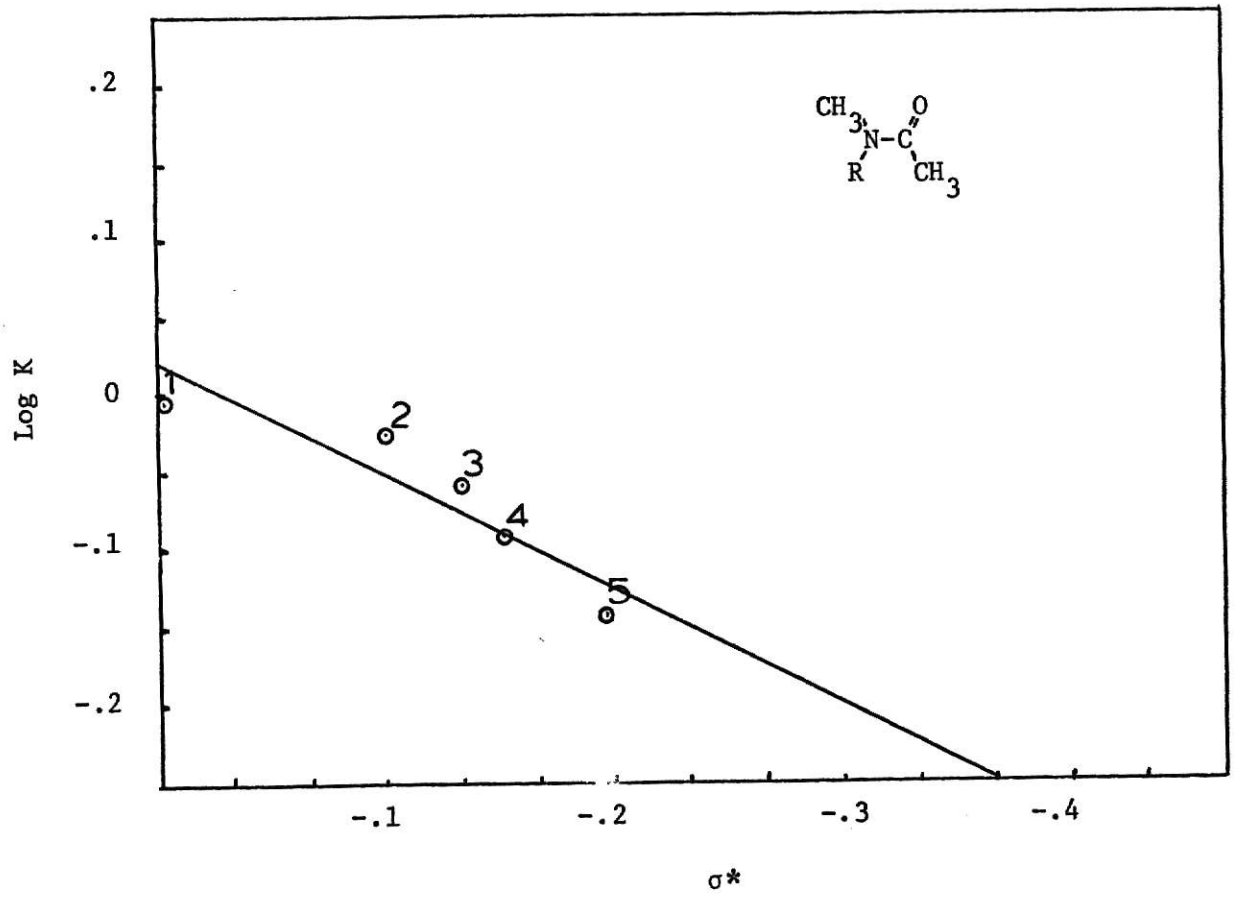
Plot of Log K vs E_s for series 4.



1. R = CH_3
2. R = CH_2CH_3
3. R = $CH_2CH_2CH_2CH_3$
4. R = cyclo-C_6H_{11}
5. R = $CH_2C_6H_5$
6. R = $CH(CH_3)_2$

Figure 16

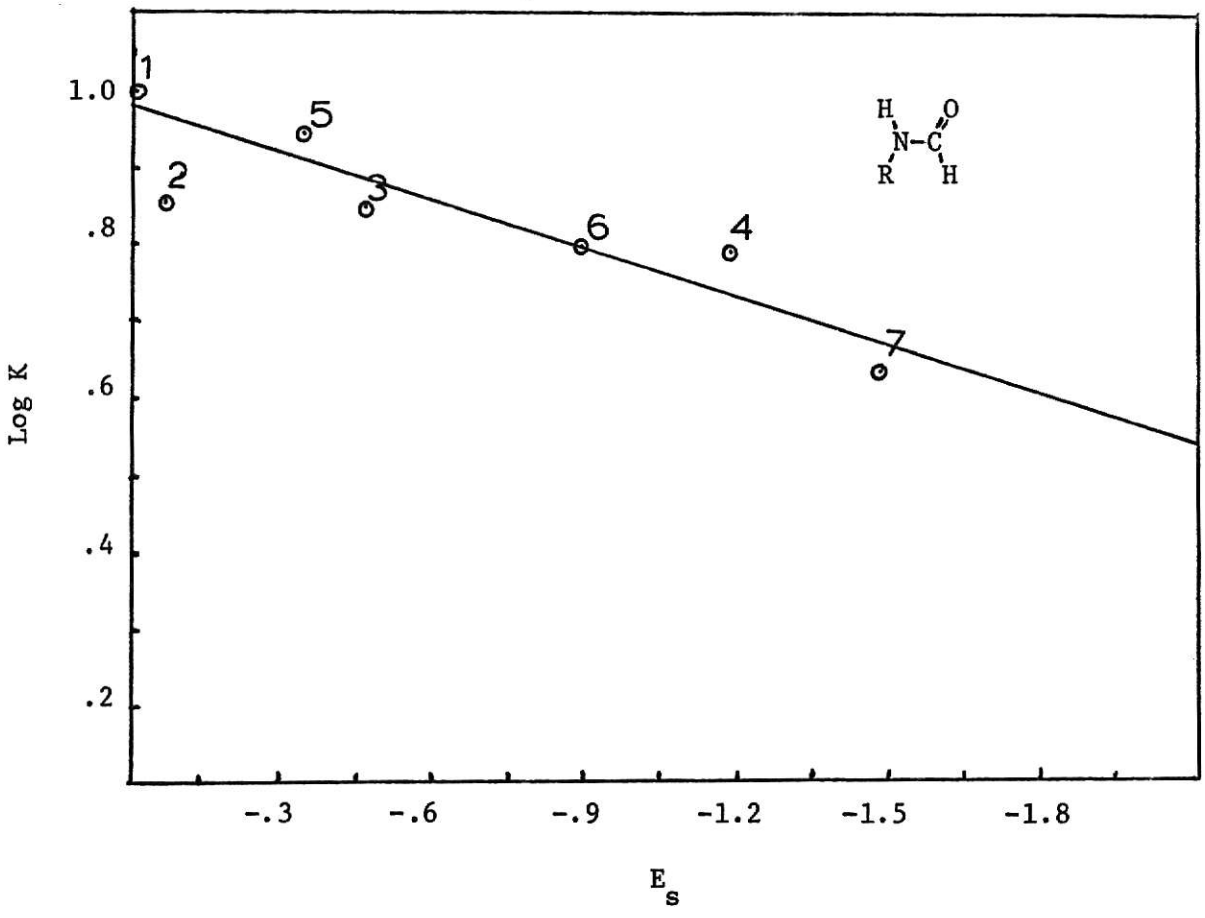
Plot of Log K vs σ* for series 4.



1. R = CH_3
2. R = CH_2CH_3
3. R = $CH_2CH_2CH_2CH_3$
4. R = cyclo-C_6H_{11}
5. R = $CH(CH_3)_2$

Figure 17

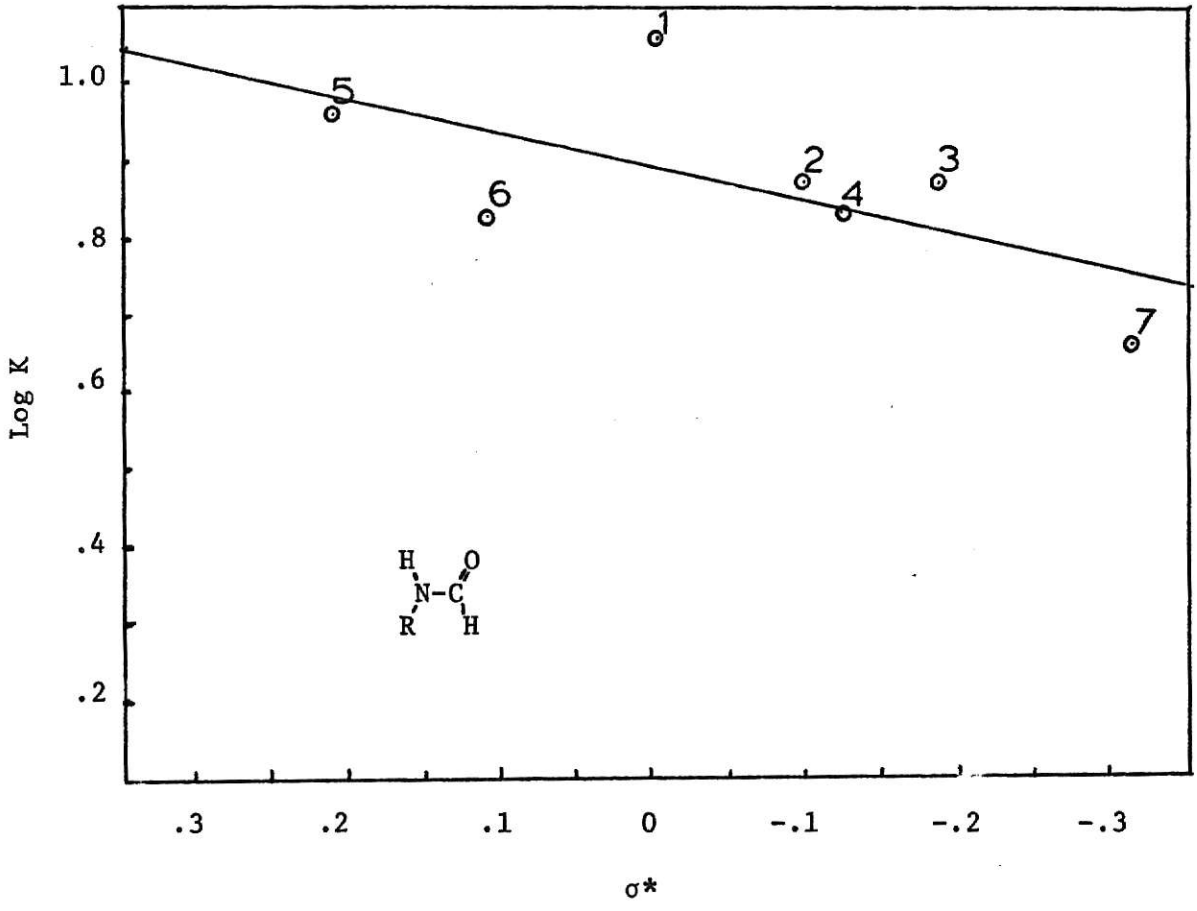
Plot of Log K vs E_s for series 2 (Lambing).



1. R = CH_3
2. R = CH_2CH_3
3. R = $CH(CH_3)_2$
4. R = $CH_2CH(CH_3)_2$
5. R = $CH_2C_6H_5$
6. R = $CH(CH_3)C_6H_5$
7. R = t-C_4H_9

Figure 18

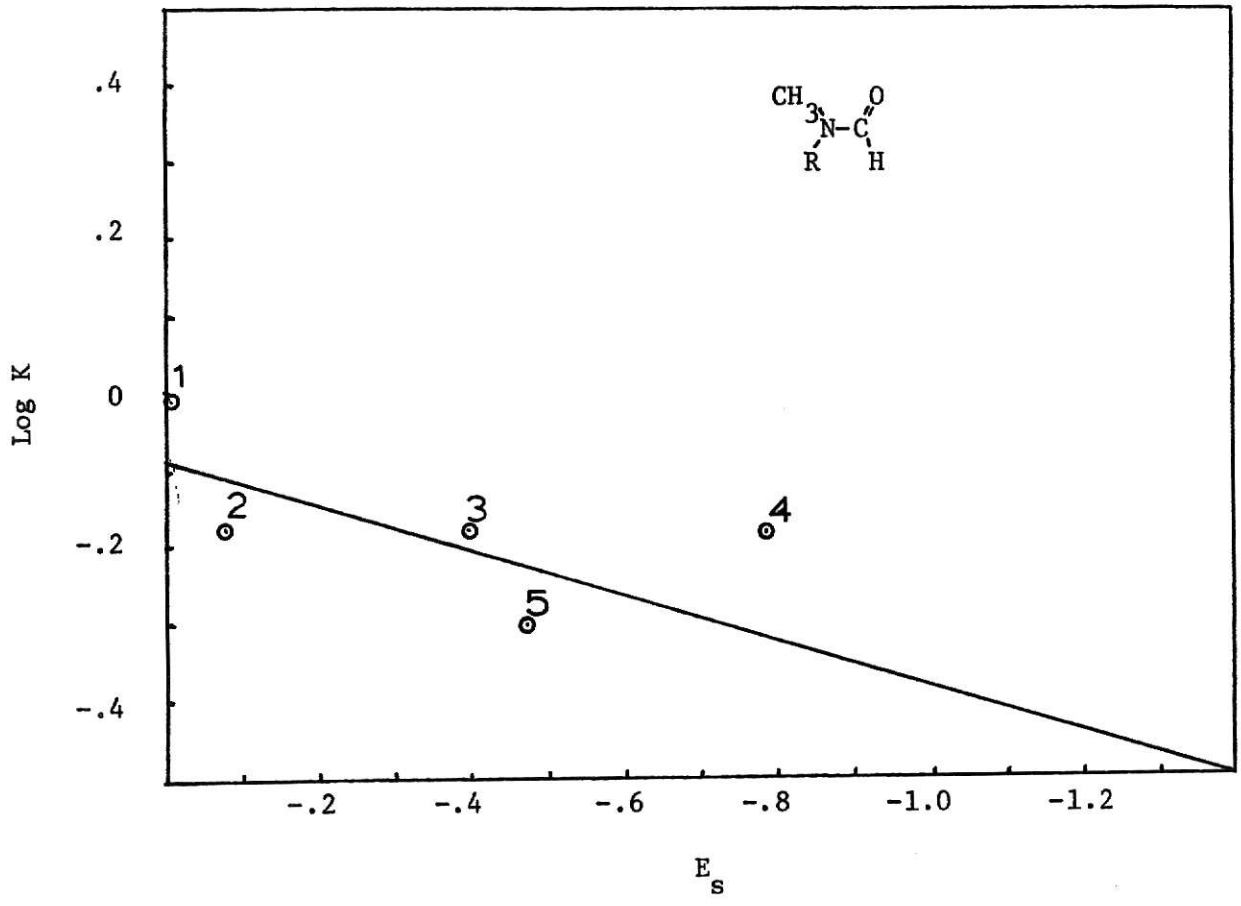
Plot of Log K vs σ* for series 2 (Lambing).



1. R = CH_3
2. R = CH_2CH_3
3. R = $CH(CH_3)_2$
4. R = $CH_2CH(CH_3)_2$
5. R = $CH_2C_6H_5$
6. R = $CH(CH_3)C_6H_5$
7. R = $t\text{-}C_4H_9$

Figure 19

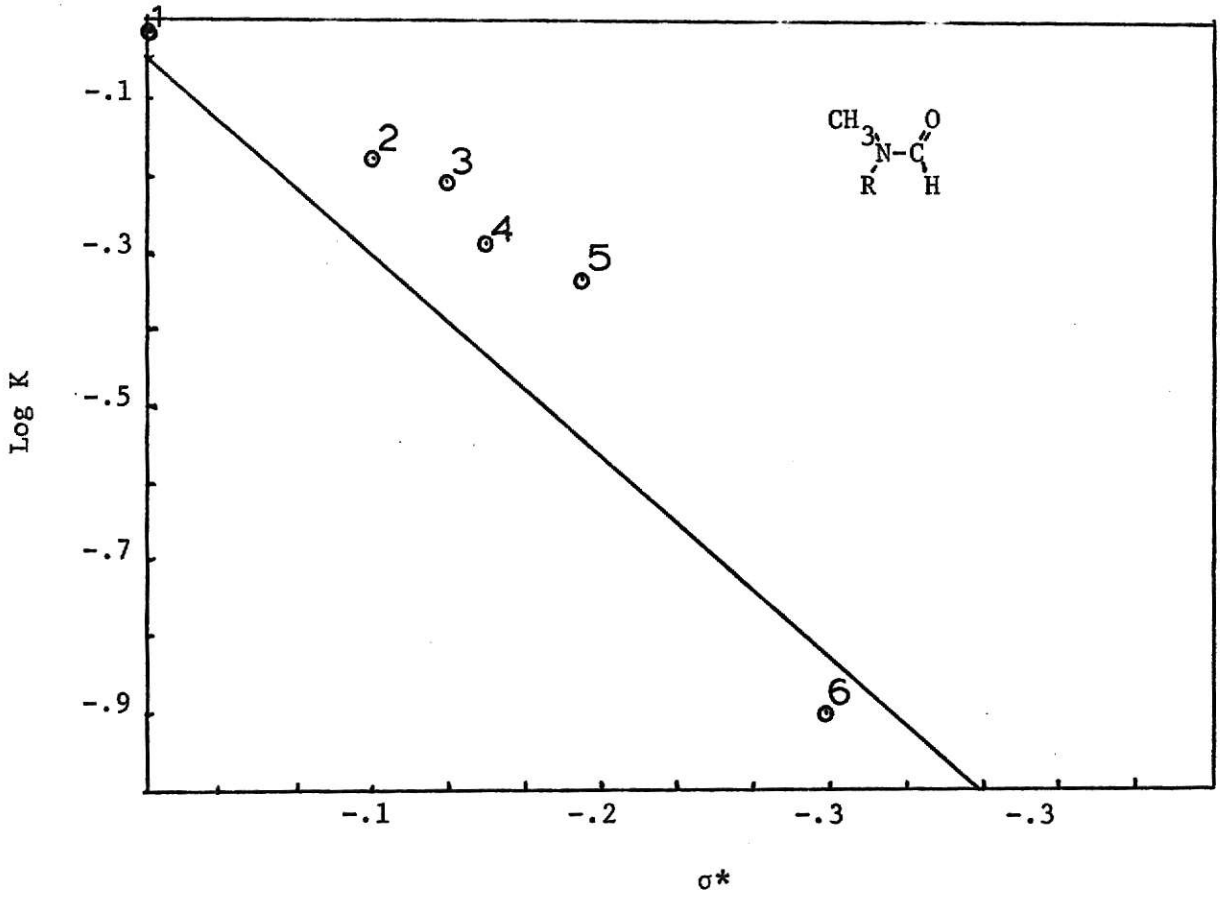
Plot of Log K vs E_s for series 3.



1. R = CH_3
2. R = CH_2CH_3
3. R = $CH_2CH_2CH_2CH_3$
4. R = cyclo-C_6H_{11}
5. R = $CH(CH_3)_2$

Figure 20

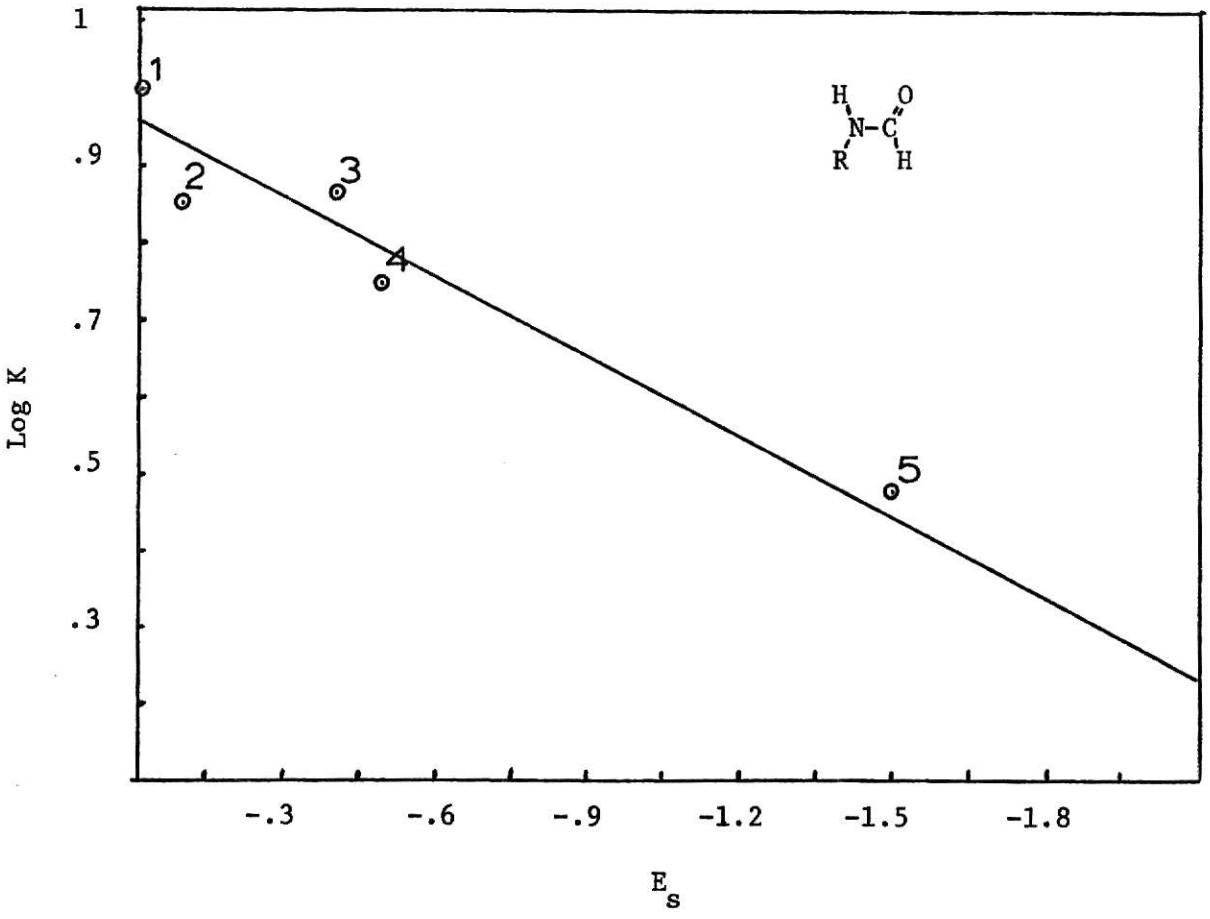
Plot of Log K vs σ* for series 3.



1. R = CH_3
2. R = CH_2CH_3
3. R = $CH_2CH_2CH_2CH_3$
4. R = cyclo-C_6H_{11}
5. R = $CH(CH_3)_2$
6. R = t-C_4H_9

Figure 21

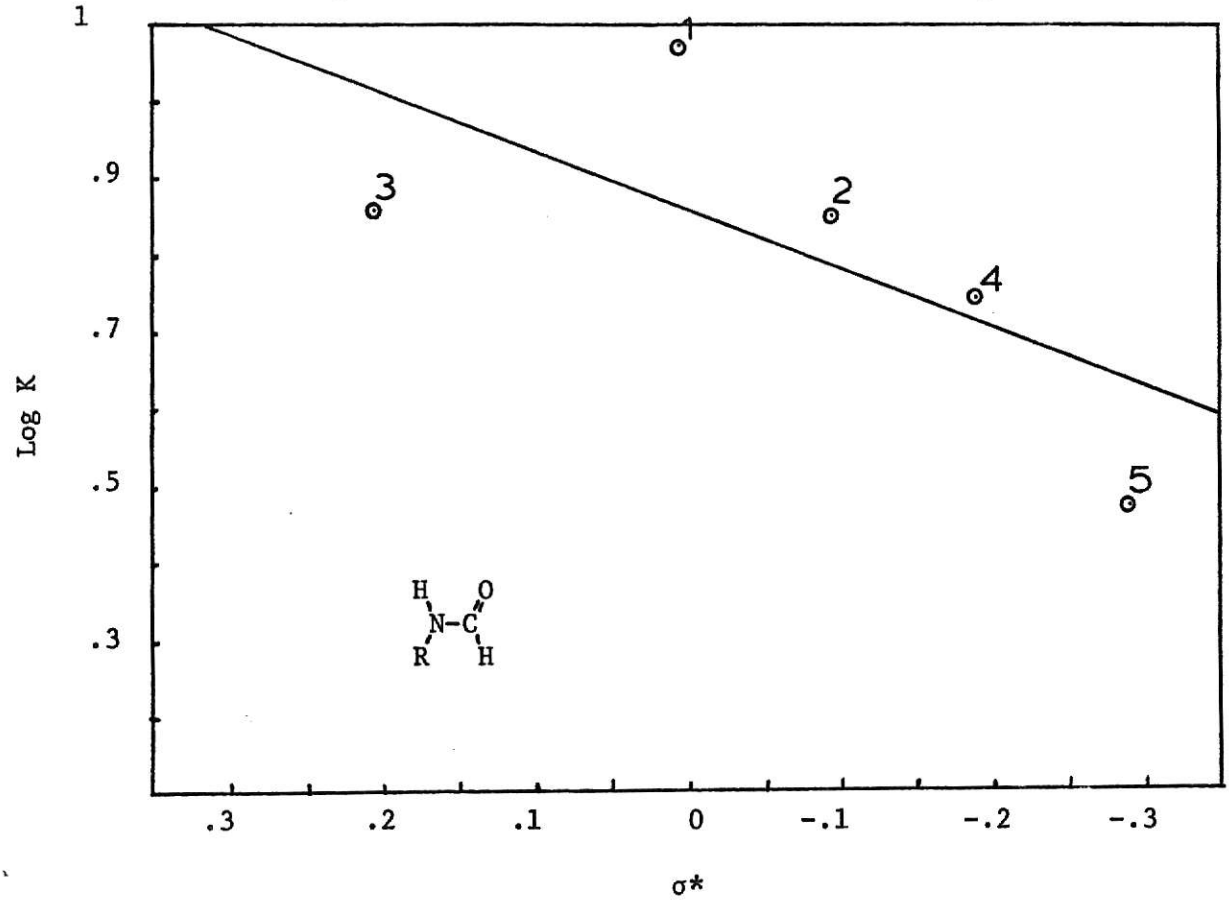
Plot of Log K vs E_s for series 2 (LaPlanche and Rogers).



1. R = CH_3
2. R = CH_2CH_3
3. R = $CH_2C_6H_5$
4. R = $CH(CH_3)_2$
5. R = t-C_4H_9

Figure 22

Plot of Log K vs σ* for series 2 (LaPlanche and Rogers).



1. R = CH_3
2. R = CH_2CH_3
3. R = $CH_2C_6H_5$
4. R = $CH(CH_3)_2$
5. R = t-C_4H_9

APPENDIX 3

Tables of values for correlation of Log K with E_s and σ^*.

Table 14[1]

Series	Type[2]	s values[3]	ρ* values[3]	Corr.[4]	Incpt.[5]	F[6]
1	P(5)	$s = .252 \pm .04$		.961	.007	36.60
1	S(4)	$s = .129 \pm .009$		.994	-.191	178.2
1	P(5)		$\rho^* = .013 \pm .65$	.770	.049	4.39
1	S(4)		$\rho^* = .141 \pm .18$	.470	-.323	0.56
1	P(5)	$s = .208 \pm .04$	$\rho^* = .464 \pm .315$	.981	.036	26.46
1	S(4)	$s = .130 \pm .01$	$\rho^* = .008 \pm .03$	.994	-.189	47.27
2	P+S(5)	$s = .337 \pm .079$		.926	.987	18.19
2	P+S(5)		$\rho^* = .760 \pm .494$	.663	.868	2.35
2	P+S(5)	$s = .297 \pm .111$	$\rho^* = .209 \pm .350$	.937	.975	7.29
3	P+S(6)	$s = .310 \pm .129$		.810	-.087	5.75
3	P+S(6)		$\rho^* = 1.29 \pm .543$	.938	.118	29.45
3	P+S(6)	$s = .312 \pm .187$	$\rho^* = 1.13 \pm 1.06$	.968	.049	22.70
4	P+S(6)	$s = .134 \pm .060$		.740	-.018	4.84
4	P+S(6)		$\rho^* = .722 \pm .214$	.889	.021	11.36
4	P+S(6)	$s = .025 \pm .087$	$\rho^* = .634 \pm .392$	.894	.020	3.99
5	P(5)	$s = .784 \pm .113$		.970	.230	47.18
5	P(5)		$\rho^* = .001 \pm .000$	.131	.006	.05

Table 14 (cont.)

Series	Type	s values	ρ* values	Corr.	Incpt.	F
5	P(5)	$s = .853 \pm .16$	$\rho^* = .803 \pm 1.09$	.976	.180	20.51
6a	P(5)	$s = .174 \pm .015$		.988	-.185	124.8
6a	S(4)	$s = .076 \pm .038$		.814	-.284	3.95
6a	P(4)		$\rho^* = .004 \pm .081$	.038	-.225	.01
6a	S(4)		$\rho^* = .205 \pm 1.77$	.081	-.309	.02
6a	P(4)	$s = .099 \pm .041$	$\rho^* = .091 \pm .033$	.939	-.204	3.75
6a	S(4)	$s = .017 \pm .56$	$\rho^* = .118 \pm .021$	.984	-.584	16.13
6b	P(4)	$s = .474 \pm .125$		.901	-.296	4.31
6b	S(4)	$s = .430 \pm .075$		.867	-.107	6.05
6b	P(4)		$\rho^* = 1.15 \pm .466$	.957	-.253	10.90
6b	S(4)		$\rho^* = 2.11 \pm 4.91$	.852	1.165	5.32
6b	P(4)	$s = .228 \pm .004$	$\rho^* = 1.10 \pm .015$	.990	-.258	15.40
6b	S(4)	$s = .271 \pm .193$	$\rho^* = 1.67 \pm 5.17$	.953	1.102	4.95
7a	P(4)	$s = .257 \pm .034$		.974	-.084	57.16
7a	S(4)	$s = .115 \pm .026$		.951	-.067	19.19
7a	P(4)		$\rho^* = .077 \pm .047$	.775	.140	2.66

Table 14 (cont.)

Series	Type	s values	ρ* values	Corr.	Incpt.	F
7a	S(4)		$\rho^* = .012 \pm 2.12$	.383	-.074	0.34
7a	P(4)	$s = .023 \pm .059$	$\rho^* = .114 \pm .153$	.980	.092	24.61
7a	S(4)	$s = .141 \pm .021$	$\rho^* = 1.11 \pm .568$	.990	.260	26.65
7b	P(4)	$s = .221 \pm .208$		.600	-.183	1.12
7b	S(4)	$s = .012 \pm .063$		.141	-.219	0.04
7b	P(4)		$\rho^* = .336 \pm .24$	.679	-.228	1.89
7b	S(4)		$\rho^* = 1.11 \pm 1.51$	.475	-.424	0.58
7b	P(4)	$s = .142 \pm .249$	$\rho^* = .263 \pm .326$	.782	-.199	0.79
7b	S(4)	$s = .023 \pm .100$	$\rho^* = 1.15 \pm 2.68$	.516	-.479	0.18

[1] s, ρ*, Corr., Incpt. and F were computed using IBM MULTIREG program.

[2] P = primary subst. S = secondary subst. () = number of values used in correlation.

[3] s = slope of graph of Log K vs E_s. ρ* = slope of graph of Log K vs σ*. Values for the combination of Log K vs E_s and σ* are shown together under s values and ρ* values.

[4] Corr. = Correlation coefficient.

[5] Incpt. = Intercept.

[6] F = statistical F value for correlation.

APPENDIX 4

Chemical shift differences for rotational isomers.

Table 15

Difference in chemical shifts of disubstituted amides

Series 6[1]	$N-CH_2-R$ (δcis-δtrans)
R = CH_3	30.1
R = CH_2CH_3	28.2
R = $CH_2CH_2CH_3$	25.6
R = $CH(CH_3)_2$	23.1
R = $CH_2C_6H_5$	24.0
R = cyclo-C_4H_7	31.2
R = cyclo-C_6H_{11}	18.6
R = $CH(CH_2CH_3)_2$	25.4

[1] In ϕ-CH_3 at 0° C

Series 6[2]	$N-CH_2-R$
R = CH_3	3.2
R = CH_2CH_3	1.2
R = $CH_2CH_2CH_3$	2.0
R = $CH(CH_3)_2$	5.4
R = $CH_2C_6H_5$	0.8
R = cyclo-C_4H_7	4.6
R = cyclo-C_6H_{11}	6.8
R = $CH(CH_2CH_3)_2$	16.7

[2] In CS_2 at 0° C

Table 16

Difference in chemical shifts of disubstituted amides

Series 7[1]	N-CH_3
R = CH_3	12.5
R = CH_2CH_3	13.6
R = $CH_2CH_2CH_3$	12.8
R = $CH(CH_3)_2$	9.0
R = $CH_2C_6H_5$	12.6
R = cyclo-C_4H_7	16.6
R = cyclo-C_6H_{11}	7.8
R = $CH(CH_2CH_3)_2$	8.4

[1] In Ø-Cl at 0° C

Series 7[2]	N-CH_3
R = CH_3	8.8
R = CH_2CH_3	6.6
R = $CH_2CH_2CH_3$	4.0
R = $CH(CH_3)_2$	10.1
R = $CH_2C_6H_5$	2.2
R = cyclo-C_4H_7	4.2
R = cyclo-C_6H_{11}	10.1
R = $CH(CH_2CH_3)_2$	8.2

[2] In CS_2 at 0° C

Table 17

Difference in chemical shifts in disubstituted amides

Series 1[1]	$N-CH_2-R$	O=C-H
$R = CH_3$	5.5	8.0
$R = CH_2CH_3$	8.0	7.5
$R = CH(CH_3)_2$	8.0	8.0
$R = CH_2CH_2CH_3$	7.0	5.5
$R = CH_2CH_2CH_2CH_3$	7.0	5.5
$R = CH_2CH(CH_3)_2$	6.5	11.5
R = cyclo-C_6H_{11}	7.5	8.0
$R = CH(CH_3)CH_2CH_3$	7.5	8.0
$R = CH(C_6H_5)CH_2CH_3$	12.5	13.0

[1] In CCl_4 at 37° C

Series 5[2]	$N-CH_2-R$
$R = CH_3$	17.5
$R = CH_2CH_3$	18.2
$R = CH_2CH_2CH_3$	18.6
$R = CH_2CH_2CH_2CH_3$	18.6
$R = CH_2CH(CH_3)_2$	15.6

[2] In SO_2 at -60°C

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CONFORMATIONAL STUDIES

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by

ALLAN J. KRAMER

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ABSTRACT

A correlation was determined between the equilibrium constant of mono- and dialkylamides and Taft's E_s values by using the equation Log K = sE_s. In general the experimental results confirm that the correlation between the E_s values for the alkyl substituents was linear with respect to the logarithm of the equilibrium constant.

A correlation was determined between the equilibrium constant and Taft's σ^* values by using the equation Log K = $\rho^*\sigma^*$. There was a poor correlation between the σ^* values for the alkyl substituents and the logarithm of the equilibrim constant.

A correlation was also determined between the equilibrium constant and a combination of Taft's E_s and σ^* values by using the equation Log K = $\rho^*\sigma^* + sE_s$. The correlation was not improved by using the combination of values as was shown by comparing the F values for the correlation.