1954

Part I. Comparison of 1,2- and 1,3- elimination reactions; Part II. Factors which influence the ionization of carboxylic acids

Donald H. Hogle
Iowa State College

Recommended Citation
Hogle, Donald H., "Part I. Comparison of 1,2- and 1,3- elimination reactions; Part II. Factors which influence the ionization of carboxylic acids " (1954). *Retrospective Theses and Dissertations*. 13969.
https://lib.dr.iastate.edu/rtd/13969

PART I. COMPARISON OF 1,2- AND 1,3-ELIMINATION REACTIONS

PART II. FACTORS WHICH INFLUENCE THE IONIZATION OF CARBOXYLIC ACIDS

by

Donald H. Hogle

A Dissertation Submitted to the
Graduate Faculty in Partial Fulfillment of
The Requirements for the Degree of
DOCTOR OF PHILOSOPHY

Major Subject: Physical-Organic Chemistry

Approved:

In Charge of Major Work

Head of Major Department

Dean of Graduate College

Iowa State College
1954

ProQuest Information and Learning Company
300 North Zeeb Road
P.O. Box 1346
Ann Arbor, MI 48106-1346

TABLE OF CONTENTS

PART I. COMPARISON OF 1,2- AND 1,3-ELIMINATION REACTIONS

INTRODUCTION

A vast amount of knowledge has evolved from the extensive studies conducted in the large field of displacement and 1,2-elimination reactions. The mechanism of these reactions has been studied in detail. The factors which influence the rate of the reaction and the distribution of products have been the subject of many investigations. In fact, the study of these processes has contributed greatly to our present day understanding of the nature of organic reactions.

The less widely known and much less frequently occurring 1,3-elimination reactions have received very little attention, however, even though the resulting cyclopropyl system is of considerable theoretical and some practical importance.

Previous discussions of 1,3-elimination reactions, of necessity, have been based almost entirely upon an unproven analogy to the corresponding 1,2-case. It was the purpose of this thesis to elucidate the general features of this reaction, and to compare it directly with the much studied 1,2-elimination by means of a simple system in which both reactions can occur in direct competition with each other.

HISTORICAL REVIEW

Whenever one wishes to study an elimination reaction, it is always necessary to consider the possibility of a concurrent displacement reaction. It is for this reason that these reactions will be considered to some extent whenever they appear to be important in this review, even though the primary purpose of this thesis does not involve a study of displacement reactions.

The subject of elimination and displacement processes has been extensively studied over a considerable period of time. Undoubtedly the largest contribution to the great mass of information has been made by Hughes and Ingold.[1] Since all this information has been very recently compiled and discussed by Ingold,[2] it is appropriate to discuss these contributions mainly on the basis of this excellent discussion.

Previous to the work of these authors, two opposing schools of thought had developed to explain nucleophilic substitution at a carbon atom. One, originally proposed by

---

[1] cf. E. D. Hughes, C. K. Ingold, et. al., J. Chem. Soc., 2093 (1948), for leading references.

[2] C. K. Ingold, "Structure and Mechanism in Organic Chemistry", Cornell University Press, Ithaca, New York, 1953, Chapters VII and VIII.

LeBel,[3] and restated by Lewis,[4] favored the introduction of the entering group and the expulsion of the leaving group as a simultaneous process. The other, proposed by Lowry,[5] maintained that the process occurred in two steps. The process was assumed to be initiated by an ionization process to form a positively charged ion which then combined with the nucleophic reagent. In 1927, Hanhart and Ingold[6] published the first of the long series of papers in which they showed a duality of mechanism which embodied both of the previous concepts. They also proposed mechanisms for the concurrent elimination reactions and proceeded to study the processes on this basis.

The picture of the bimolecular elimination process which evolved from these studies may be summarized as follows:

$$B^- + H\text{-}CR_2\text{-}CR_2\text{-}X \longrightarrow \left[\overset{\delta-}{B}\text{--}H\text{--}CR_2\text{==}CR_2\text{--}\overset{\delta-}{X}\right] \longrightarrow BH + CR_2\text{=}CR_2 + X^-$$

The base, B, attacks a hydrogen situated <u>beta</u> to a leaving group, X. In the transition state both the C-H bond and the C-X bond are stretched giving rise to some bond character to the new C-C bond. In other words, the process is a concerted

---

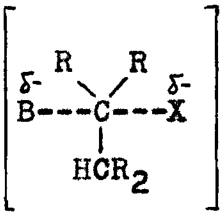
[3] J. A. LeBel, J. Chim. Phys., 9, 323 (1911).

[4] G. N. Lewis, "Valence and the Structure of Atoms and Molecules", Chemical Catalog Co., New York, 1923, p. 113.

[5] T. M. Lowry, Inst. Inter. Chim. Solvay, Conseil Chim. (Brussels), 130 (1925).

[6] W. Hanhart and C. K. Ingold, J. Chem. Soc., 997 (1927).

one, in which both the hydrogen and the leaving group help in forming the new bond. The mechanism for nucleophilic substitution differs only in the respect that the negative charge is dispersed over fewer atoms.



The mechanisms outlined above were supported by several facts. The dependence upon the presence of a strong base was demonstrated by the second order kinetics of the reaction. The mere demonstration of second order kinetics does not make the mechanism of Hughes and Ingold unique, since a prior equilibrium between the substrate and its conjugate base, followed by elimination of the leaving group would give the same dependence upon base concentration.

$$B^{-} + H\text{-}CR_2\text{-}CR_2\text{-}X \xrightleftharpoons{\text{fast}} \overset{-}{C}R_2\text{-}CR_2\text{-}X + BH \xrightarrow{\text{slow}} CR_2{=}CR_2 + X^{-}$$

Since any kinetic procedure would not differentiate between the two mechanisms, Skell and Hauser[7] have demonstrated by an isotopic method that the latter mechanism does not operate. By reacting 2-phenylethyl bromide with sodium ethoxide in

---

[7] P. S. Skell and C. R. Hauser, J. Am. Chem. Soc., 67, 1661 (1945).

deuteroethanol they showed that there was no deuterium exchange between the ethanol and substrate, which would be the case if the above mechanism were operating. Therefore, by a combination of kinetic and isotopic evidence, the only conclusion that may be drawn is that the mechanism is concerted as was proposed by Hughes and Ingold, if only these two mechanism are to be considered.

This is not the case, however, as a third mechanism must be considered also. A two step process with the first step rate-determining must also be considered, since this type of mechanism would also fit the previous data.

$$B^- + H\text{-}CR_2\text{-}CR_2\text{-}X \overset{\text{slow}}{\rightleftharpoons} {}^-CR_2\text{-}CR_2\text{-}X + BH \xrightarrow{\text{fast}} CR_2{=}CR_2 + X^-$$

It has been repeatedly reported that hydrogen halides are eliminated at different rates when the halogen is varied in the substrate molecule. These data very clearly eliminate this possibility, and leave only the concerted mechanism. The following evidence is an example of some recent work on this subject.

The first and second order elimination reactions with several alkoxides in the corresponding alcohol on *t*-amyl halides have been investigated by Brown.[8] The second order

---

[8] H. C. Brown and I. Moritani, *J. Am. Chem. Soc.*, *76*, 455 (1954).

elimination reaction could be made predominant at sufficiently high base concentrations, enabling them to compare the bimolecular elimination rates of t-amyl chloride, bromide, and iodide. It was found that the rate varied markedly with the particular halogen present in the molecule. This fact led Brown to the conclusion that tertiary halides also reacted bimolecularly by means of a concerted mechanism. It was also observed that the rate of elimination decreased as the corresponding base and solvent passed through the series: methanol, ethanol, isopropanol, and t-butanol.

Several factors which influence the course of the reaction have been studied extensively. It was recognized very early by Hanhart and Ingold[6] that the structure of the substrate was important in determining the products, and led to an explanation of the Hofmann and Saytzeff rules on the basis of electromeric and inductive effects, respectively. For example, these authors showed in a study of the bimolecular elimination of 'onium salts where the Hofmann rule holds, that the following series could be constructed with respect to the ease of olefin formation.

primary > secondary > tertiary

On the other hand, the elimination of halides, where the Saytzeff rule applies, gives the reverse order since the transition state in this case is closer to products than reactants, and the stability of the olefin formed is more important than the position of attack.[9]

The competition of substitution and elimination reactions has been noted by many investigators. Hughes and Ingold[10] found that the acid hydrolysis of sec-octyl and isopropyl halides in 60 percent aqueous ethanol at 80° gave 10 percent elimination in the portion of the reaction that was first order. These authors found that in a series of E_1 processes, that the rate varied considerably, but the ratio of elimination to total reaction remained constant under conditions of constant temperature, solvent, and structure while varying the halogen. They also noted a larger difference in rate between the acid hydrolysis of amyl chloride and bromide than between the bromide and iodide.

In a criticism of Taylor's[11] work, Hughes and Ingold[12] found that the rate of bimolecular elimination reactions decreased as the base concentration was increased in the same reaction. Citing the work of Brussoff[13] and that of Segaller[14] who reported opposite relative reactivities of

---

[9] E. R. Alexander, "Principles of Ionic Organic Reactions", John Wiley and Sons, New York, 1950, p. 115.

[10] E. D. Hughes, C. K. Ingold and U. G. Shapiro, J. Chem. Soc., 1277 (1937).

[11] W. Taylor, ibid, 1962 (1937).

[12] E. D. Hughes and C. K. Ingold, ibid, 899 (1940).

[13] S. Brussoff, Z. Physik. Chem., 34, 129 (1900).

[14] D. Segaller, J. Chem. Soc., 103, 1430 (1913).

secondary and tertiary halides, these authors rationalized both results by assuming that a change in kinetics had occurred as the concentration of the base was increased, and as the dielectric constant of the solvent was decreased. In other words, the reaction changed from a unimolecular to a bimolecular mechanism as the concentration of base was increased and as the solvating power of the solvent was decreased.

Shreve and Burtsfield,[15] in a study of the amination of alkyl bromides in liquid ammonia solution found that amination did not occur when the halogen was not in a primary position. Secondary and tertiary halides produced only olefins, while in the primary case a mixture of olefin, primary, secondary, and tertiary amines was obtained. They also noted that the rates of amination of the chlorides were slower than with the bromides and gave a larger ratio of olefin to amine.

Adamson and Kenner[16] found that in the decomposition of primary nitrites in liquid ammonia solution to form primary amine, olefin, and secondary and tertiary alcohols, that increasing the chain length from amyl to decyl resulted in a slight general decrease in the amount of olefin from 30.1 percent for amyl nitrite to 24.4 percent for the nonyl nitrite. The

---

[15] M. K. Shreve and D. R. Burtsfield, Ind. Eng. Chem., 33, 218 (1941).

[16] D. W. Adamson and J. Kenner, J. Chem. Soc., 838 (1934).

yields of total substitution products were in doubt because of the low recovery of primary amine. The yields of secondary alcohol decreased rapidly, however, as the series was ascended.

French and co-workers[17] have studied the effect of concentration and strength of inorganic bases on the elimination reactions of secondary and tertiary halides. The bases employed varied from silver hydroxide to potassium hydroxide in aqueous solution. It was found that an increase in the ratio of base to halide increased the yield of olefin, and that an increase in base strength also caused an increase in the yield of olefin. The reaction rate was observed to be greater in the more dilute solutions.

Vaughn, Vogt, and Niewland[18] in a study of the preparation of ethers in liquid ammonia from primary alkyl halides and sodium alkoxides, estimated that an average yield of 6-8 percent of olefin was formed along with considerable amine.

Hauser[19] has discussed the general mechanism of substitution and elimination reactions and has considered the

---

[17] H. E. French and A. E. Shaeffer, J. Am. Chem. Soc., 57, 1574, 1576 (1935); H. E. French, et. al., ibid, 56, 1346 (1934).

[18] T. H. Vaughn, R. R. Vogt and J. A. Nieuwland, ibid, 57, 510 (1935).

[19] C. Hauser, ibid, 62, 933 (1940).

possibilities of eliminations other than that of the normal 1,2 type. As an example, he cited the elimination of γ-bromobutyric acid to give the γ-lactone.

In 1898 Henry[20] synthesized cyclopropyl cyanide by distillation of γ-chlorobutyronitrile with dry potassium hydroxide and claimed 40-50 percent yields. Bruylants and Stassens[21] attempted the synthesis from γ-chlorobutyronitrile and potassium hydroxide in alcoholic solution and obtained only the substitution product, γ-ethoxybutyronitrile. By another method employing sodium ethoxide and γ-chlorobutyronitrile, Bruylants[22] obtained a mixture of cyclopropyl cyanide and the substitution product. Pyridine and quinoline at water bath temperature gave only allyl cyanide and no cyclopropyl cyanide. Cloke and Anderson,[23] by using sodamide in ether solution, obtained a yield of 75 percent cyclopropyl cyanide after 25 hours of reflux. No other product was isolated.

Sommer, *et. al.*[24] have observed 1,3-elimination when

---

[20] P. Henry, *Bull. Sci. Acad. Roy. Belg.*, (*3*) *36*, 34 (1898); *ibid*, (*3*) *37*, 17 (1899).

[21] P. Bruylants and R. Stassens, *ibid*, (*5*) *7*, 702 (1921).

[22] P. Bruylants, *ibid*, (*5*) *6*, 479 (1920).

[23] J. B. Cloke, E. Anderson, and R. Anderson, *J. Am. Chem. Soc.*, *53*, 2791 (1931).

[24] L. Sommer, R. Van Strien, and F. C. Whitmore, *ibid*, *71*, 3056 (1949).

γ-bromopropyltrimethylsilane was warmed with a catalytic amount of aluminum chloride. A 92 percent yield of cyclopropane was obtained. The chlorosilane gave only a 31 percent yield of cyclopropane when heated with a solution of sodium hydroxide in aqueous ethanol. When the reagents were interchanged in the above procedures, no cyclopropane was obtained. In another experiment, 5-bromopentyltrimethylsilane failed to give any cyclopentane, but gave 1-pentene instead, as would be expected.

Ingold has investigated the competition among displacement, 1,2- and 1,3-elimination reactions by the action of sodium carbonate and potassium hydroxide in methanol on the α-bromoglutaric esters. His results are presented in Table I.

It is seen from Table I that the weak base in every case gave mainly substitution with no detectable 1,2-elimination being observed. On the other hand, the strong base gave predominantly 1,3-elimination, with the strongest tendency to cyclize being observed as the degree of branching increased.

Weston,[25] in order to prepare derivatives of 1-phenylcyclopropylcarboxylic acid, has prepared 1-phenylcyclopropyl cyanide in 51 percent yield by the reaction of phenylacetonitrile and ethylene bromide with sodamide in liquid ammonia. Since the reaction proceeds stepwise, the second stage must

---

[25] A. W. Weston, J. Am. Chem. Soc., 68, 2345 (1946).

Table I

Product distribution in reaction of diethyl glutarates with base

Substrate	Basic conditions[a]	Percent olefin	Percent substitution	Percent cyclization
diethyl α-bromoglutarate	A	0	95	3
diethyl α-bromoglutarate	B	3	16	47
diethyl α,α'-dibromoglutarate	A	0	90	10
diethyl α,α'-dibromoglutarate	B	0	10	90
diethyl α-bromo-β-methylglutarate	A	0	90	10
diethyl α-bromo-β-methylglutarate	B	9	8	64
diethyl α-bromo-β,β-dimethylglutarate	B	0	4	84

[a] Conditions A were 2N sodium carbonate with boiling for twenty hours and conditions B were 6N potassium hydroxide in methanol, with boiling for thirty minutes.

involve a 1,3-elimination reaction of γ-bromo-α-phenylbutyronitrile with a second equivalent of sodamide.

Ingold[2] has generalized the effect of the solvent on elimination reactions on the assumption that any observed effect is due to a difference in solvation of the reactants and the transition state. These effects for SN_2 and E_2 reactions are listed in Table II.

Ingold[2] has also investigated the effect of temperature upon the competitive reactions and has stated that the elimination reaction has an Arrhenius energy of activation which is 1.3 ± 0.4 kcal/mole higher than that of substitution when alkylsulfonium ions are used as substrate. He noted that this appeared to be a general rule. Therefore, one would expect an increase in temperature to increase the proportion of olefin slightly since the elimination reaction would be expected to have the larger temperature coefficient.

Brown[26] has recently obtained evidence which indicated that the direction of elimination in sulfonium and ammonium ions may not be due to an inductive effect, but to the steric requirements of the ion. They have shown that the elimination of alkyl halides may be somewhat controlled by careful selection of the base. Hindered alkoxides such as potassium

---

[26] H. C. Brown and I. Moritani, ibid, 75, 4112 (1953).

Table II

Predicted solvent effects on rates and proportions of olefin formed in bimolecular reactions

	Disposition of charges			Effect of more solvation	
Reaction	Initial state	Transition state	Effect of activation on charge	On rate	On olefin proportion
SN_2	$Y^- + RX$	$\overset{\delta-}{Y}--R--\overset{\delta-}{X}$	Dispersed	Small decrease	Small decrease
E_2		$\overset{\delta-}{Y}--H--C==C--\overset{\delta-}{X}$			
SN_2	$Y + RX$	$\overset{\delta+}{Y}--R--\overset{\delta-}{X}$	Increased	Large increase	?
E_2		$\overset{\delta+}{Y}--H--C==C--\overset{\delta-}{X}$			
SN_2	$Y^- + RX^+$	$\overset{\delta-}{Y}--R--\overset{\delta+}{X}$	Reduced	Large decrease	?
E_2		$\overset{\delta-}{Y}--H--C==C--\overset{\delta+}{X}$			
SN_2	$Y + RX^+$	$\overset{\delta+}{Y}--R--\overset{\delta+}{X}$	Dispersed	Small decrease	Small decrease
E_2		$\overset{\delta+}{Y}--H--C==C--\overset{\delta+}{X}$			

triethylcarboxide gave good yields of olefin with a terminal double bond, while sodium ethoxide produced fairly good yields of the more symetrical olefin. Brown has stated that it is possible to control the elimination by two other methods also. Increasing the steric requirements of the alkyl groups on the incipient double bond and increasing the steric requirements of the group undergoing elimination tend to shift the elimination away from the product predicted by the Hofmann rule.

Isotopic studies on substitution and elimination reactions have been conducted by Shiner.[27] He has measured the rates of the bimolecular substitution and elimination reactions of α-deutero- and β-deutero-isopropyl bromides in alcoholic sodium ethoxide and compared these with the rates observed for ordinary isopropyl bromide. The substitution rate was almost the same for all three compounds, the elimination rate was the same for the ordinary and the α-deutero compounds, while the β-deutero one underwent elimination more slowly than its protium analog by a factor of 6.7. He concluded that both hydrogen and the halide ions are lost simultaneously in the rate-determining step and that substitution and elimination are essentially independent reactions proceeding simultaneously. These conclusions are thus in full agreement with the

---

[27] V. J. Shiner, Jr., *ibid*, *74*, 5285 (1952); *ibid*, *75*, 2925 (1953); *ibid*, *76*, 1603 (1954).

mechanism proposed by Hughes and Ingold.

The first order solvolysis rates of some deuterated *t*-amyl chlorides have also been reported by Shiner. It was found that deuteration of the methylene group was slightly more effective in reducing the rate than deuteration of the methyl group. Methylene deuteration reduced the olefin production by a factor of nearly 1.5 while methyl deuteration showed no significant effect. Octadeutero-*t*-amyl chloride solvolyzed at a rate about two-fifths as fast as the normal chloride. These facts led the author to propose that solvation of the β-hydrogens is important in the transition state. Further observations of a secondary isotope effect has strengthened Shiner's viewpoint along these lines, and he has proposed that his hypothesis of elimination type driving forces for solvolytic reactions suggests a reinterpretation of the effect of β-branching on solvolysis rates and of the polar effects of alkyl groups in ionic reactions, which are usually explained on the basis of hyperconjugation.

However, this was not the view taken by Lewis and Boozer[28] who have studied the solvolysis of 2-pentyl bromide and have found that the rate was retarded by substitution of deuterium for hydrogen in the 1- and 3- positions. The decrease in rate was attributed to a difference in the loss of

---

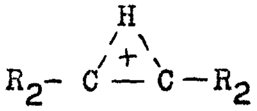
[28] E. S. Lewis and C. E. Boozer, *J. Am. Chem. Soc.*, *76*, 791 (1954).

zero point energy of vibration of the bonds of these hydrogens between the reactant and the transition state. The withdrawal of electrons to satisfy the electron deficiency on carbon by hyperconjugation was believed to be the cause of this loss of zero point energy. They proposed that the extent of rate retardation was a measure of the importance of hyperconjugation and that the solvent and the leaving group modified the resultant electron deficiency on carbon. These authors did not exclude hydrogen bonding of the solvent to the β-hydrogens as an alternate explanation of the observed secondary isotope effect. But since they noted that the isotope effect was reduced with an increase in nucleophilic character of the solvent, they felt it must reduce hyperconjugation and thus the action of solvent on the α-carbon must be more important than that on hydrogen.

Lewis[29] has investigated the solvolysis rates of α-p-tolylethyl chloride which had been deuterated in the para methyl position. A secondary isotope effect was found which compared with that previously reported by Lewis and Boozer. The authors feel that this latest evidence excludes the elimination type driving force favored by Shiner[27] in reactions of this type. Hyperconjugative contributions such as

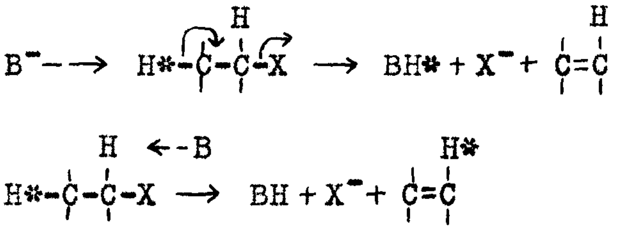
---

[29] E. S. Lewis and G. M. Coppinger, Unpublished communication to J. Am. Chem. Soc., 76 (1954).



are also excluded.

Evidence for α- and β-elimination from deutero alkyl halides has been reported by Hauser[30] and co-workers. It was found that 2-ethylbutyl bromide exhibits only β-elimination, while n-octyl halides exhibit α-elimination as well as β-elimination. Hydrogen halide was eliminated more readily than hydrogen deuteride. The mechanism of the α-elimination was explained by a simultaneous removal of hydrogen and halogen, with a shift of hydrogen from the β- to the α-carbon atom occurring at the same time. The mechanism of β- and α-elimination respectively, was pictured by the author as follows:



The necessity of an α-elimination came from the observation that a loss of deuterium in the α-position was observed. It was established by recovering unreacted substrate that no deuterium-hydrogen exchange took place during the reaction.

---

[30] D. G. Hill, W. Judge, P. Skell, S. Kantor, and C. Hauser, J. Am. Chem. Soc., 74, 5599 (1952).

EXPERIMENTAL

The Synthesis of Materials

γ-Bromobutyronitrile was prepared from trimethylene bromide according to "Organic Syntheses".[31] A solution of 1.2 moles of potassium cyanide in 100 milliliters of water and 350 milliliters of 95 percent ethanol was prepared in a two liter three-necked, round-bottomed flask fitted with a tru-bore stirrer, a reflux condenser, and an addition funnel. One mole of Eastman Kodak White Label trimethylene bromide was added and the mixture was refluxed for about two hours.

The solution was then cooled and diluted with approximately 500 milliliters of water. The bromonitrile was collected by extraction with successive 50 milliliter portions of chloroform. The chloroform solution was then washed with 100 milliliters of saturated calcium chloride solution, and dried over anhydrous calcium chloride.

The majority of the chloroform was then removed by simple distillation. The crude product was placed on a vacuum column and fractionated at 30 millimeters pressure. The pure γ-bromobutyronitrile, b.p. 110°, n_D^{25} 1.4747, was obtained in 35.7 percent yield along with unreacted trimethylene bromide

---

[31] "Organic Syntheses", Coll. Vol. I, edited by A. H. Blatt and H. Gilman, John Wiley and Sons, New York, 1941, p. 156.

and a small amount of trimethylene dicyanide.

γ-Chlorobutyronitrile was prepared in the same manner as the bromo-compound from Eastman White Label trimethylene chlorobromide. A 46.3 percent yield of pure γ-chlorobutyronitrile was obtained by fractionation of the crude product at four millimeters through a vacuum column. The pure material, n_D^{25} 1.4396, boiled at 51.5-53.0° at this pressure.

Cyclopropyl cyanide was synthesized by the method of Cloke and Anderson.[22] Sodamide was prepared by adding sodium metal to a liquid ammonia solution containing a crystal of ferric nitrate. When all of the sodium had reacted, γ-chlorobutyronitrile was added dropwise. The solution was allowed to stand several hours, at which time about 100 milliliters of ether was added, and the ammonia was allowed to evaporate. The sodium chloride was filtered off after the excess sodamide was destroyed by the addition of ammonium chloride.

The ether solution was then placed on the vacuum column, and the solvent was removed under partial vacuum. The crude cyclopropyl cyanide was then fractioned at 33 millimeters pressure giving a 67 percent yield of pure material, n_D^{25} 1.4178, boiling at 49°.

Allyl cyanide was prepared from allyl bromide by reaction with cuprous cyanide by a slight modification of the procedure given in "Organic Synthesis".[32] A slight excess of dry cuprous cyanide was placed in a liter three-necked, round-bottomed flask fitted with a Tru-bore stirrer, an efficient condenser, and an addition funnel. A few milliliters of redistilled Matheson allyl bromide were added, and the flask was warmed with a free flame. After a few minutes of gentle heating the reaction started, and the solid turned dark brown. The remainder of the allyl bromide was then added dropwise at a rate sufficient to produce rapid reflux. The solution was then heated on a steam bath for several hours to complete the reaction.

The crude allyl cyanide was obtained by distillation from the reaction mixture. The product was then fractionated in a glass helix packed column. The fraction, $n_D^{20^\circ}$ 1.4062, boiling at 117.5° was collected in an 87 percent yield.

<u>Cis and trans crotononitrile</u> were prepared from allyl cyanide by the method of Bruylants.[33] Dry hydrogen bromide was prepared by the reaction of bromine with tetralin in a heated flask or was used directly from a cylinder. The gas was passed into allyl cyanide, by means of a bubbler extending to the bottom of a flask, until the liquid was completely

---

[32] Ibid, p. 46.

[33] P. Bruylants, Bull. Soc. Chim. Belg., 31, 175 (1922).

transformed into a mass of crystals. The composition of these crystals was not ascertained, but it was noted that they would decompose into a liquid and hydrogen bromide when either heated or touched with a metal spatula. It seems reasonable that the compound was a hydrogen bromide adduct of β-bromobutyronitrile, probably bound at the nitrile group, and not an olefin-hydrogen bromide adduct which is known to exist at low temperatures. This conclusion is merely a conjecture, however, and is not supported by any strong evidence other than the observation that the crystals did not form until the solution was fairly well saturated with hydrogen bromide.

The solid adduct was then decomposed and the β-bromobutyronitrile was decomposed by the addition of a slight excess of two equivalents of quinoline, followed by distillation of the crude nitriles. The yield of crude crotononitriles was practically quantitative if the solid adduct was formed before elimination.

The crude crotononitriles were then placed on a vacuum column, and rapidly fractionated at 60 millimeters pressure. The lower boiling cis isomer, n_D^{20} 1.4177, was collected @ 41.5°. Since the trans isomer was quite unstable even at this temperature, only a small amount of fairly pure material could be obtained by fractionation.

The melting points of the two isomers allowed a further purification at dry ice temperature. The trans isomer reportedly melts at -51°, while no melting point is given for the cis isomer. By a crude fractional crystallization process, consisting of merely pouring off any liquid remaining upon freezing the impure trans isomer in dry ice, a material, $n_D^{20.1}$ 1.4193, boiling at 51° at the above pressure, was obtained. An infra-red spectrum of each isomer was taken and is reproduced in Figures I and II.

γ-Piperidylbutyronitrile was obtained by the reaction of γ-bromobutyronitrile with piperidine. Excess piperidine was used as solvent. Since the reaction was extremely vigorous, the γ-bromobutyronitrile was added dropwise to the piperidine at room temperature. The piperidine hydrobromide was filtered off and the product fractionated in a vacuum column at 2 mm. pressure giving a product, n_D^{23} 1.4650, which boiled at 59-60°. The literature values are correspondingly n_D^{25} 1.4665, and b.p.$_{25}$ 148-50°.[34]

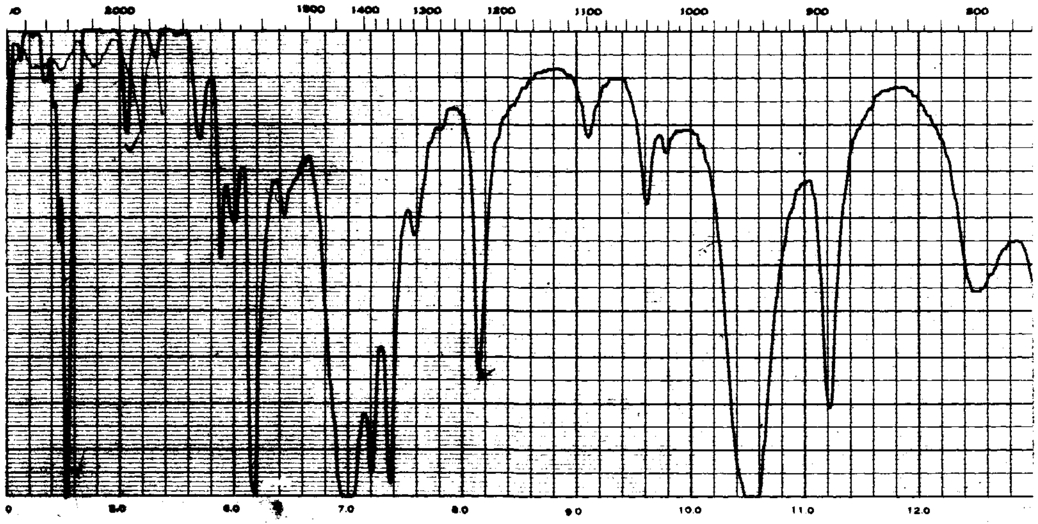
Lithium N-methylanilide was prepared by the action of n-butyl lithium on N-methylaniline. The n-butyl lithium was prepared in one of a pair of 500 milliliter three-necked flasks to which a medium porosity glass sintered disk had been sealed into the bottom thereof. A stopcock was also

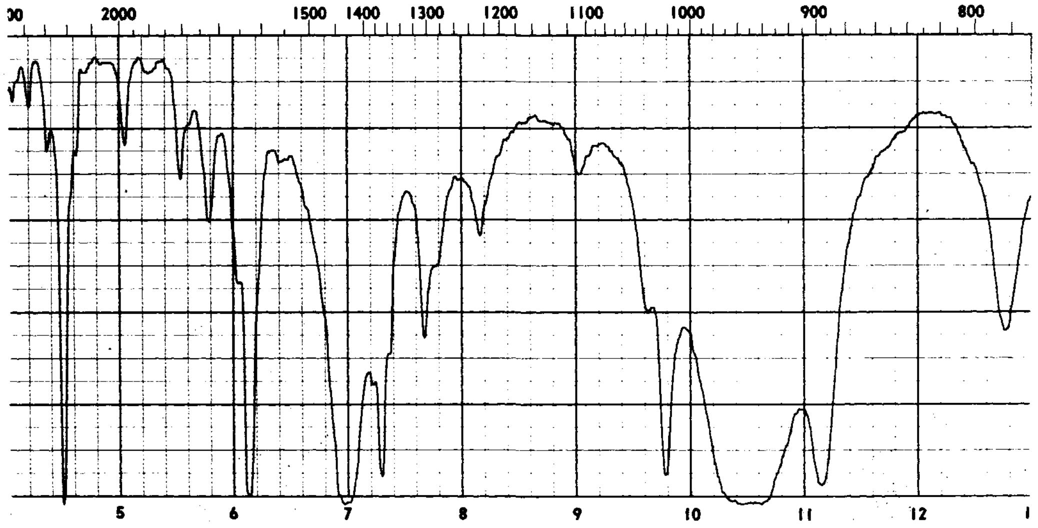
---

[34] F. C. Whitmore, et. al., J. Am. Chem. Soc., 66, 725 (1944).

Figure I. Cis crotononitrile. Cell length: 0.1 mm. Note particularly the bands at 9.6 and 9.8μ.

Figure II. Trans crotononitrile. Cell length: 0.1 mm. Note again the intensities of the 9.6 and 9.8μ bands, and compare them with Figure I.


2000
1500
1400
1300
1200
1100
1000
900
800
5.0
6.0
7.0
8.0
9.0
10.0
11.0
12.0


2000
1500
1400
1300
1200
1100
1000
900
800
5
6
7
8
9
10
11
12

sealed on below the sintered disk to allow a reaction to be conducted in the flask, and then filtered into an identical flask without ever having been exposed to the atmosphere. n-Butyl bromide, purified by drying over Drierite followed by distillation, was placed in the flask with anhydrous ethyl ether, and a slight excess of lithium wire was added while flushing the system with dry nitrogen.

After the reaction was complete, it was filtered into the other flask by application of a slight vacuum on the lower flask and a slight nitrogen pressure on the upper flask. An equivalent of purified N-methyl aniline was then added to the ether solution and the solution was stirred for about three hours. The yellow-orange solution was then evaporated to near dryness leaving an orange precipitate. No suitable solvent could be found to recrystallize the precipitate, which may or may not have been the desired lithium salt. Since the pure salt could not be isolated, so as to distinguish its basic properties from n-butyl lithium, it was not used as a base.

Sodium triphenylmethide was prepared by the reaction of triphenylmethyl chloride with sodium amalgam. The sodium amalgam was prepared as a two percent solution by the procedure given in Organic Reactions.[35] Recrystallized Matheson

---

[35] "Organic Reactions", Vol. I, Roger Adams, Editor-in-Chief, John Wiley and Sons, New York, 1942, p. 284.

triphenylmethyl chloride was dissolved in anhydrous ether and added to the sodium amalgam in a 250 milliliter three-necked flask equipped with a reflux condenser and a Tru-bore stirrer. After about two hours of stirring, the characteristic deep red color of the triphenylmethide ion developed. The stirring was continued for about five hours longer, at which time the solution was allowed to settle overnight.

Tri-p-nitrophenylmethane was prepared by the nitration of triphenylmethane.[36] Eastman White Label triphenylmethane was recrystallized from absolute ethanol, dried and powdered in a mortar. The nitric acid - sulfuric acid mixture was placed in a two-necked liter flask equipped with a Tru-bore stirrer and cooled in an ice-salt bath. The triphenylmethane was added slowly in portions keeping the temperature as low as possible. The reaction mixture was allowed to stir at ice-bath temperature for two hours. The temperature was allowed to rise slowly to room temperature, at which time the mixture was poured onto cracked ice and the yellow precipitate was collected on a Buchner funnel.

The precipitate was boiled with 75 percent acetic acid until the remaining precipitate was reduced to a yellow-green fluorescent crystalline material. The crude tri-p-nitrophenylmethane was recrystallized with a minimum of chloroform to

---

[36] J. Shoesmith, C. Sosson, and A. Hetherington, J. Chem. Soc., 2227 (1927).

which enough anhydrous ether was added to clarify the solution. The solution was cooled in an ice bath for two hours, and the crystals collected on a filter and dried. The pure material, m.p. 213.5°, was obtained in a 42.6 percent yield.

Sodium tri-p-nitrophenylmethide was prepared by reacting an equivalent amount of sodium hydroxide with a pyridine solution of the nitrated hydrocarbon. The solid salt was obtained by evaporation of the pyridine solution.

The solvents, for the most part, were purified by fractionation in a Heli-pak column which was tentatively rated at more than one-hundred theoretical plates. In each case, only the constant boiling fraction was collected. When possible, as in the case of benzene, the purified solvent was stored over sodium chips.

The Kinetics of the Reaction

In order to establish that the reaction under study was truly bimolecular in nature, the kinetics of the reaction of γ-bromobutyronitrile with sodium ethoxide in ethanol were studied. Approximately 4.6 grams of sodium metal were weighed and reacted with ethanol which had been previously dried by reaction with magnesium turnings and distilled from the magnesium ethoxide. The sodium ethoxide solution was then diluted to 500 milliliters and the solution was brought to 24° in a constant temperature bath.

The kinetic run was made by placing a weighed sample of approximately 0.1 mole of γ-bromobutyronitrile in a 250 milliliter volumetric flask, rapidly adding sodium ethoxide solution, and diluting the solution to the mark. A point, arbitrarily designated as zero time, was taken immediately after the solution was shaken thoroughly by pipetting a 10 milliliter aliquot from the reaction mixture and titrating for free base with standard acid. Further points were determined by titration of aliquots every thirty minutes over a period of seven hours, at which time the reaction was approximately 50 percent complete. The data of a typical run are listed in Table III and the second order dependence is shown in Figure III.

Since almost equimolar quantities of substrate and base were used in this study, the integrated rate expression reduces to equation (1), where x is the molar concentration of reactant remaining at any time t, x^o is the initial concentration of reactant, and k_2 the second order rate constant.

$$K_2 t = \frac{1}{x} - \frac{1}{x_o} \qquad (1)$$

A plot of time in hours versus x^{-1} gave the rate constant $k_2 = 0.331$ liter mole^{-1} hour^{-1}.

Table III

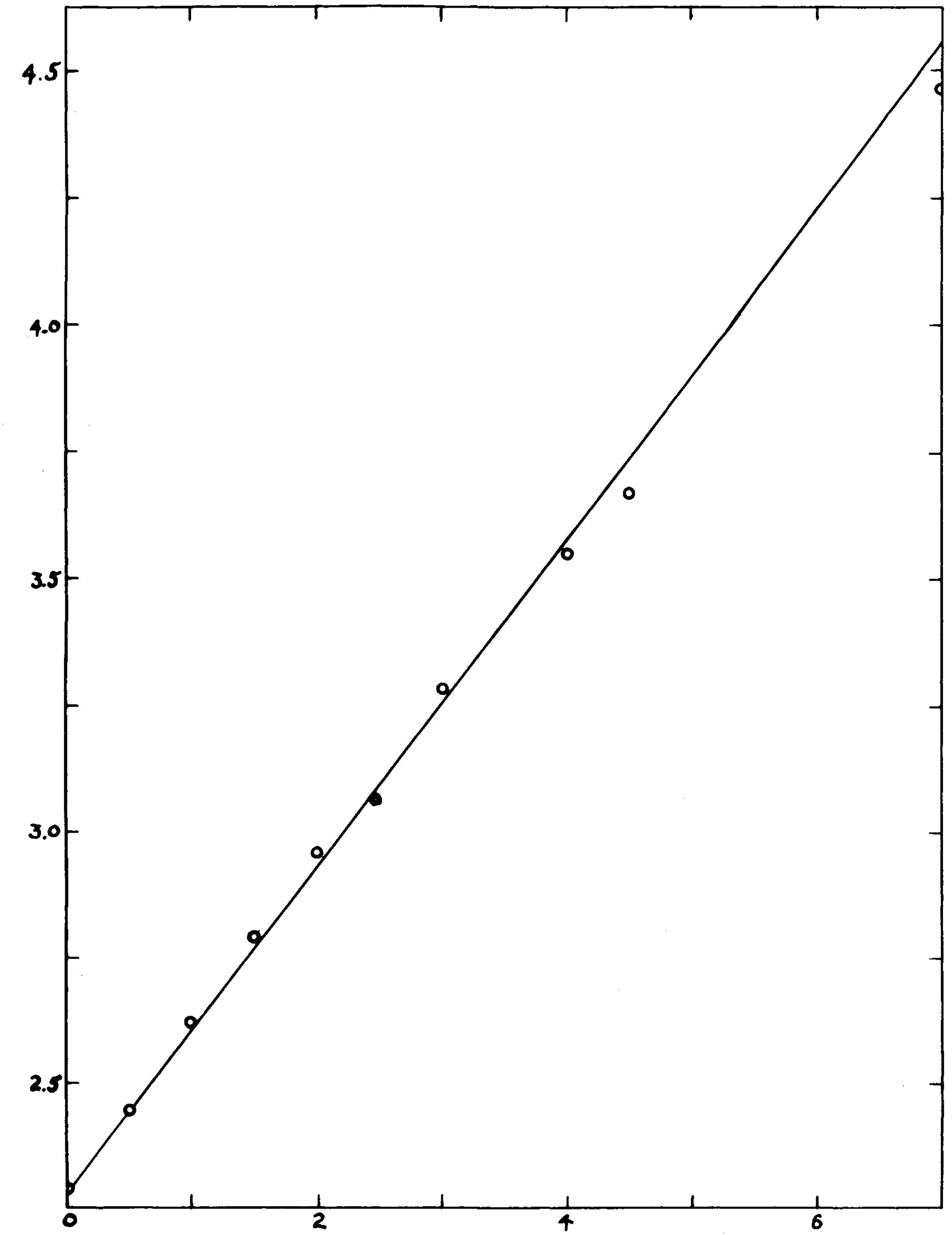
Kinetic data for reaction of equimolar γ-bromobutyronitrile and sodium ethoxide in ethanol at 24°

Time in hours	Acid titer in ml.	Molar concentration sodium ethoxide
0	19.15	0.438
0.5	17.90	0.409
1.0	16.70	0.382
1.5	15.55	0.358
2.0	14.70	0.338
2.5	14.00	0.320
3.0	13.30	0.304
4.0	12.30	0.282
4.5	11.95	0.273
7.12	9.80	0.224

Figure III. γ-Bromobutyronitrile with sodium methoxide in methanol @ 24°.

Ordinate - x^{-1} in liter $mole^{-1}$.

Abscissa - time in hours.


4.5
4.0
3.5
3.0
2.5
0
2
4
6

Product Analysis

The chemical method

An extensive preliminary investigation was conducted in order to find a reliable analytical procedure for the determination of product distribution in the reaction mixture. A refinement of the procedure outlined by Siggia[37] was used, since crotononitrile is a conjugated olefin and is brominated with difficulty.

Siggia's bromination procedure utilizes a mercuric sulfate catalyst and uses potassium bromate as an analytical source of bromine. It was found that in order to obtain consistent results, a very rigid technique must be developed. The order of addition of reagents and the concentration of reagents were extremely critical in this system. For example, if the olefin was added before the catalyst had been complexed with free bromine, little or no bromination occurred.

A procedure which gave consistent and accurate results to within one percent error, if followed rigorously, consisted in placing an estimated one hundred percent excess of potassium bromate solution in an iodine flask and evacuating the

---

[37] S. Siggia, "Quantitative Organic Analysis via Functional Groups", John Wiley and Sons, New York, 1949, p. 34.

flask with an aspirator. A slight excess of 4N sulfuric acid was then sucked into the flask and time was allowed for complete liberation of the bromine. Four milliliters of a 0.2N mercuric sulfate solution in 4N sulfuric acid was then added, followed by enough water to wash in all of the catalyst solution.

The flask was shaken, the sample to be analyzed was then added and washed in with distilled water. The flask was again shaken for at least fifteen minutes. A freshly prepared solution of potassium iodide was then added and the flask again vigorously shaken. No careful control of the amount of potassium iodide was made, but care was taken to add an excess. The salt was also tested to insure that no potassium iodate impurity was present before being used to destroy excess bromine.

The vacuum was then released from the iodine flask, and a small piece of dry ice, about one-half gram, was added and the apparatus was rinsed with distilled water. The liberated iodine was finally titrated with standard sodium thiosulfate solution to a starch-iodine endpoint. It was observed that a starch solution not stabilized with a mercuric salt would, upon standing, give a poor endpoint.

It was possible by this procedure to differentiate between allyl cyanide and crotononitrile. Allyl cyanide brominated readily at ice bath temperature, while crotononitrile was unaffected. It was hoped, at one time, that a complete analysis could be effected by bromination of a mixture of allyl cyanide, crotononitrile, and cyclopropyl cyanide at different temperatures. Cyclopropyl cyanide would not react with bromine at room temperature, but a solution would take up bromine at elevated temperatures when acetic acid was used to give a homogeneous solution. It evolved, however, that even in a dark flask, mercuric sulfate catalyzed a reaction with acetic acid, since very little reaction occurred with no acetic acid present.

The extreme catalytic ability of mercuric sulfate proved to limit the usefulness of this procedure drastically. It was found that alcohols and ethers reacted sufficiently to forbid its use when alkoxides were used as bases in the competitive elimination and displacement reactions.

Efforts were then directed towards finding a method of changing solvents after the reaction was run. A series of azeotropic distillations was devised, but it was quickly ascertained that a mixture of cyclopropyl cyanide and crotononitrile decomposed materially even when the solvent was removed at low temperatures. It was for this reason that the method was abandoned in favor of an infra-red analysis.

The infra-red analysis

Originally an attempt was made to use a Model B, Baird infra-red recording spectrophotometer in order to analyze reaction mixtures. However, when it was discovered that a change of solvent was impractical, little hope was held for any success along this line, since the solvents to be used in the elimination study were not ideally suited for infra-red work.

The availability of a Model 112 Perkin-Elmer recording spectrophotometer changed this picture since it was discovered that the nitrile bands of crotononitrile and cyclopropyl cyanide, which occur between 4.2-4.8 microns, were sufficiently resolved to enable an analysis of a mixture when calcium fluoride optics were used. The background of several potential solvents were such that the method seemed feasible even though it would require matching the unknown solution with carefully prepared known mixtures because of an overlap of the two partially unresolved bands.

The method was never utilized, however, because of the discovery of several bands which obeyed the Beer-Lambert Law, and which could be resolved from interferring solvent bands on the Model 13, Perkin-Elmer direct ratio infra-red spectrophotometer using sodium chloride optics and 0.1 millimeter matched cells.

The bands utilized in each of the solvents are summarized in Table IV. Calibration lines were constructed from curves obtained from five standard solutions for each solvent. In the case of benzene, standard solutions were run with 1M alcohol present in the standard solution and in the reference cells since the alcohols had interferring bands close to the analytical bands.

Selected examples of the calibration lines obtained are presented in Figures IV and V and the infra-red spectra of cyclopropyl cyanide and allyl cyanide are presented in Figures VI and VII.

The Beer-Lambert lines were constructed by a procedure which differed somewhat from the conventional manner. First, a point on the spectrum was chosen so that all of the particular series, including the unknown mixture, could be shifted on the graph to the same relative position. This point, designated as a reference point, was chosen at a wave length at which the sample and the reference beam were of equal intensity, so that the initial light intensity, I_o, was at a maximum. In other words, the curve at this point should have indicated one-hundred percent transmission, but for some reason usually did not. The highest transmission at this point in the series of spectra was arbitrarily chosen as a standard, and the difference in transmission of the remaining spectra was then applied as an additive correction for the I_o and I values read from these spectra.

Table IV

Infra-red absorption bands[a] used for analysis of crotononitrile and cyclopropyl cyanide

Solvent	Crotononitrile	Cyclopropyl cyanide
benzene	10.54	9.4,[b] 9.6, 10.76
nitrobenzene	10.54	9.6, 10.76
benzonitrile	6.1, 10.54	10.76
n-butanol	6.1	10.76
sec-butanol	6.1	9.6,[b] 10.76
t-butanol	6.1	10.76
dimethylformamide	10.54	10.76

[a] All wave lengths are given in microns.

[b] Apparent extinction coefficient was very low.

Figure IV. Calibration lines.

A. Crotononitrile in benzonitrile, 10.54 μ band.

B. Crotononitrile in benzonitrile, 6.1 μ band.

C. γ-Piperidylbutyronitrile in benzene.

Ordinate - $\frac{I_0}{I}$ (log scale).

Abscissa - molar concentration.

Figure V. Cyclopropyl cyanide calibration lines.

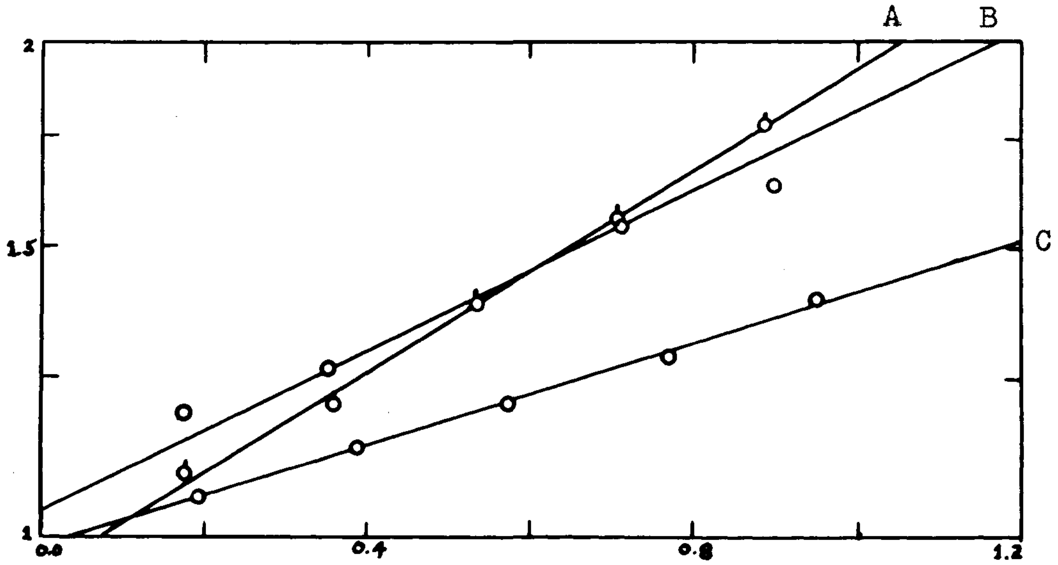
A. 10.76 μ band in benzonitrile.

B. 9.6 μ band in nitrobenzene.

C. 9.4 μ band in benzene.

Ordinate - $\frac{I_0}{I}$ (log scale).

Abscissa - molar concentration


A
B
C
2
1.5
1
0.0
0.4
0.8
1.2

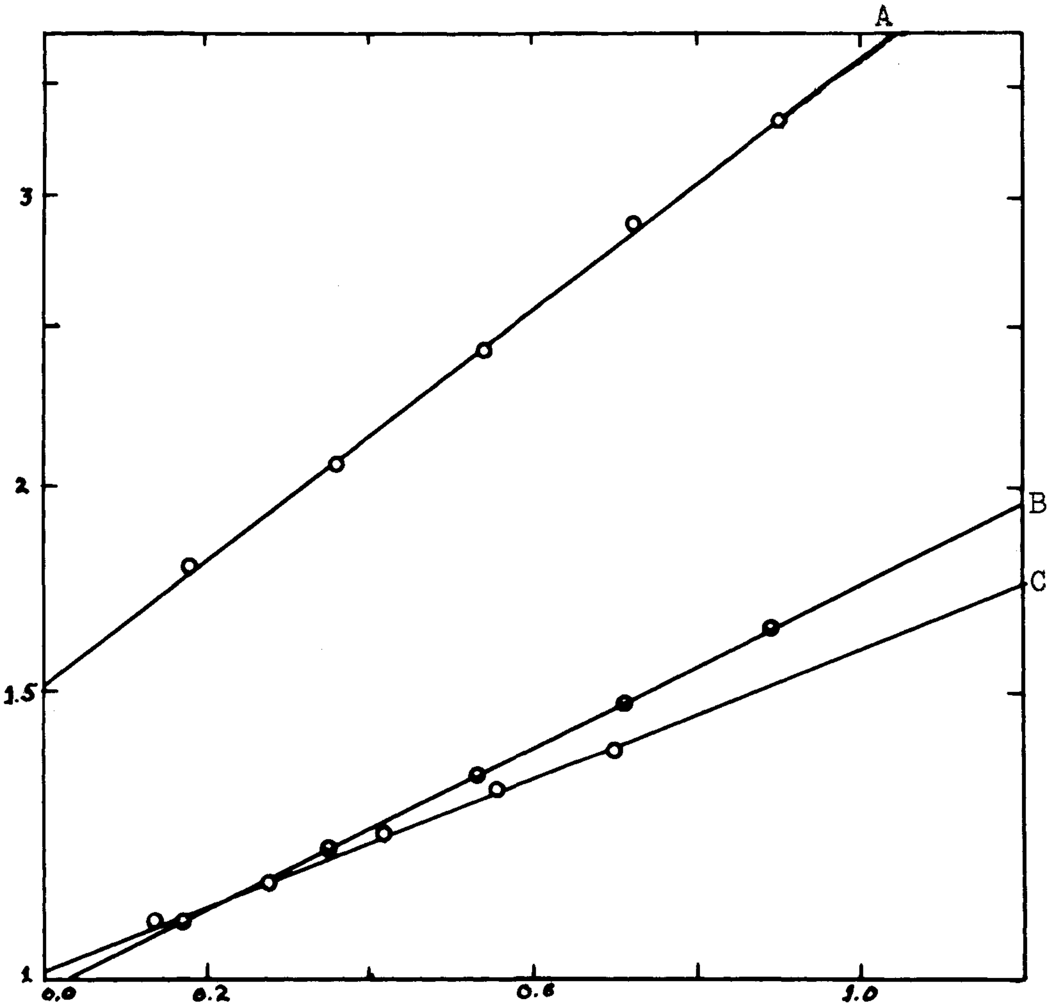
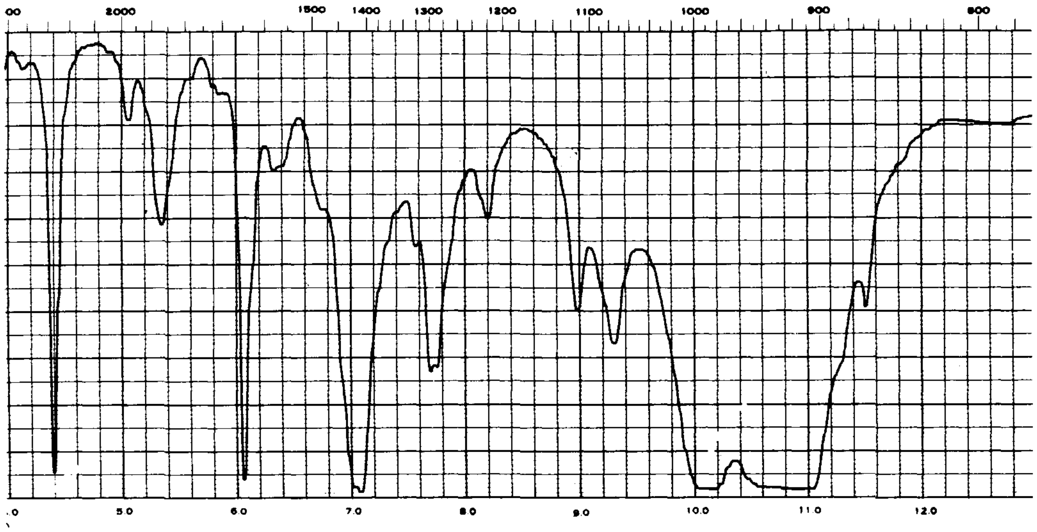
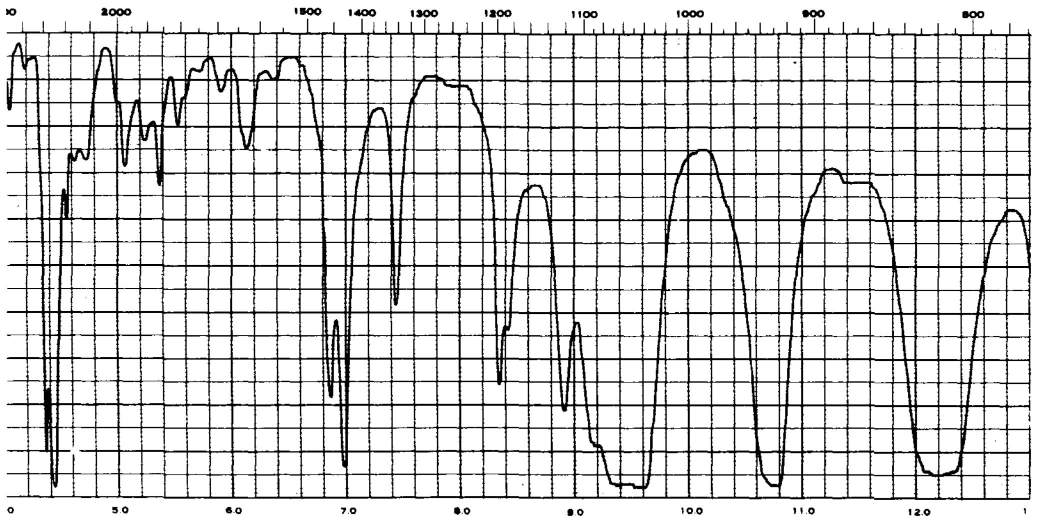

A
B
C
3
2
1.5
1
0.0
0.2
0.6
1.0

Figure VI. Allyl cyanide. Cell length: 0.1 mm. Note the strong band between 10 and 11 microns where both crotononitrile and cyclopropyl cyanide absorb.

Figure VII. Cyclopropyl cyanide. Cell length: 0.1 mm. The broad band between 9.2 and 9.6 microns resolves into two bands, 9.4 µ and 9.6 µ.


00
2000
1500
1400
1300
1200
1100
1000
900
800
.0
5.0
6.0
7.0
8.0
9.0
10.0
11.0
12.0


0
2000
1500
1400
1300
1200
1100
1000
900
800
0
5.0
6.0
7.0
8.0
9.0
10.0
11.0
12.0
1

Then, two stable points on either side of the band to be analyzed were chosen in order to define a base line. These points were chosen with particular reference to the spectrum of the unknown mixture. The wave length of maximum absorption in the band under question was then determined. The intensity I, was determined by adding the correction to the transmission observed at this point. I_o was determined similarly by adding the correction to the transmission at this wave length on the base line. The ratio $\frac{I_o}{I}$ was calculated, and log $\frac{I_o}{I}$ plotted against the molar concentration of the standard solutions. Excellent linear plots were obtained in every case. The method is illustrated in Figures VIII, IX, and X.

It should be pointed out that a molar extinction coefficient obtained by this method would not have the same value as one obtained in the conventional manner. For this reason, the extinction coefficient was not used as a measure of the sensitivity of the band to changes in concentration.

The competition reactions

The competitive reactions were run under as nearly equivalent conditions as the nature of the reactants would allow. A standard procedure was set up since the method was

Figure VIII. Crotononitrile and cyclopropyl cyanide mixture in *n*-butanol. The numbers are counter markings and should not be confused with wave lengths. The sharp band on the right is at 6.1μ, the band marked at right center is at 9.6μ, and the one at left center is at 10.76μ. The zero point is marked at 9.5 counter reading. Both components are ca. 0.9M in this solution.

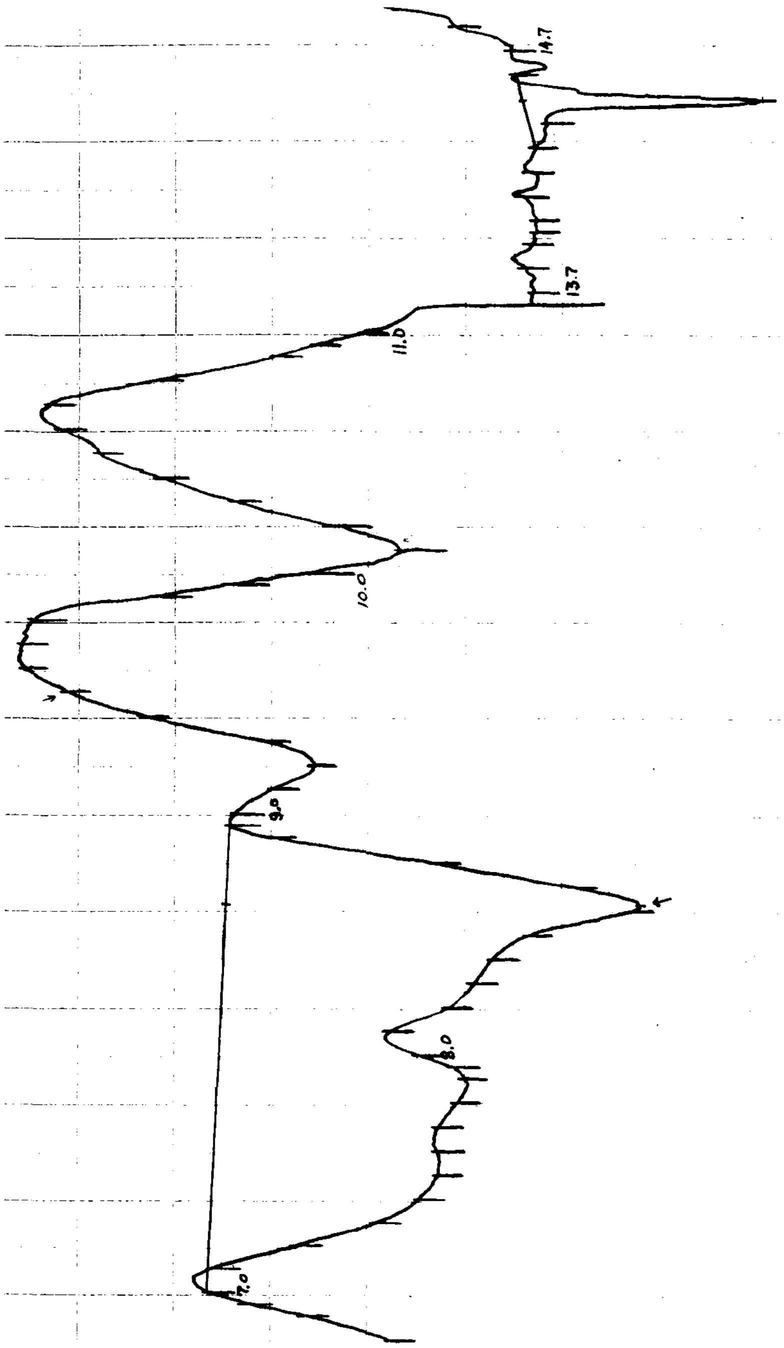
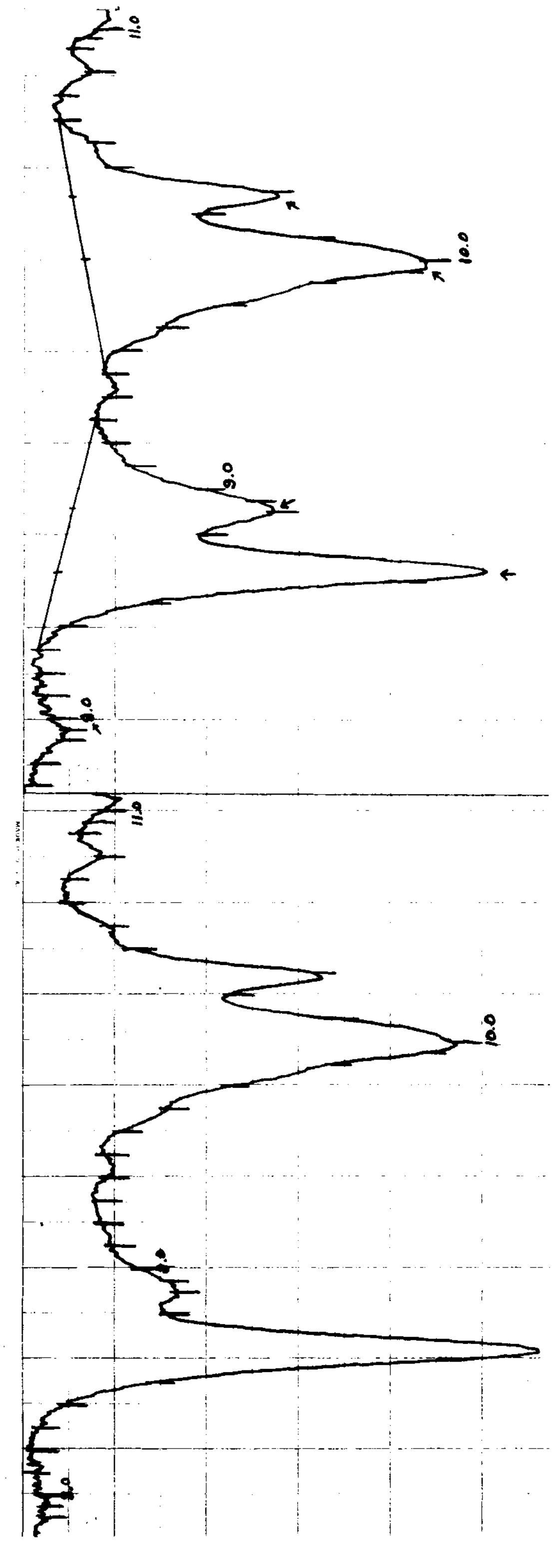

7.0
8.0
9.0
10.0
11.0
13.7
14.7

Figure IX. Cyclopropyl cyanide and crotononitrile in benzene. Compare the intensities of these bands with those in Figure X. Cyclopropyl cyanide is 0.562 M and crotononitrile is 0.1803 M.

Figure X. Cyclopropyl cyanide and crotononitrile. The analytical bands are marked. Reading from left to right, they are 10.76, 10.54, 9.6, and 9.4 microns. Cyclopropyl cyanide is 0.422 M and crotononitrile is 0.180 M.


11.0
10.0
9.0
8.0
11.0
10.0

such that variations in procedure could have led to discrepancies in the results.

When an alcohol was used as solvent, 1.10 grams of potassium metal was weighed as accurately as possible under mineral oil on a triple beam balance and added to a 50 milliliter three-necked, pear-shaped flask containing 17 milliliters of the alcohol. The flask was previously dried thoroughly in an oven at 110° and the system flushed with a stream of dry nitrogen connected through a drying tube to the flask. A reflux condenser containing another drying tube which was used as an outlet, and a small Tru-bore stirrer completed the apparatus. A variac controlled oil bath was placed under the flask, so that the formation of the alkoxide could be assisted by higher temperatures. When solution of the potassium metal was complete, enough of the halonitrile was added to the alkoxide solution to give an approximately one molar solution when the total volume after reaction was 25 milliliters. The reaction mixture was then stirred at room temperature until the reaction was complete. In the case of γ-bromobutyronitrile the reaction mixture was allowed to stand approximately twelve hours, while in the case of γ-chlorobutyronitrile the reaction mixture was allowed to stand an average of three days.

The potassium halide was then filtered off by very gentle suction, and the flask was rinsed and the precipitate was washed carefully with small portions of enough fresh solvent to dilute the reaction mixture to 25 milliliters. The infrared analysis was then carried out as previously described. The extent of total reaction was determined by dilution of the potassium halide to 250 milliliters to give an approximately 0.1N solution, followed by titration of an aliquot by the Volhard method for halide ion.

When benzene was used as solvent, 3.00 grams of alcohol were weighed out on a triple beam balance and reacted with the potassium metal. Benzene was added from time to time in order to keep a homogeneous solution. When all of the potassium had reacted, the solution was diluted to approximately 18 milliliters with benzene, and treated as described previously. In the remainder of the cases, just enough benzene was added in order to obtain a complete reaction with the potassium. The benzene was then completely removed under vacuum. The system was thoroughly flushed with nitrogen, and the solvent was added.

Since benzonitrile and dimethylformamide reacted slowly with the alkoxides, the halobutyronitrile was added immediately in order to minimize this reaction. The reactivity of nitrobenzene was too great to allow its use when an alkoxide was to be used as the base. For this reason, it could be used only in the case of the weak base, piperidine. Even though dimethylformamide could be used as a solvent with γ-bromobutyronitrile, its use was discontinued when it was discovered that even a potassium bromide saturated solution would etch the infra-red cells. The use of methanol and ethanol as solvents was prohibited for the same reason.

The dielectric constants of the pure solvents employed are listed in Table V. It should be pointed out that these values were not the exact dielectric strengths of the medium, particularly near the end of the reaction. The various alcohols were regenerated during the reaction, either raising or lowering the dielectric strength of the medium depending upon its initial value. Similarly, the ambient ionic strengths varied as the reactions progressed.

The data for the competitive elimination reactions are listed in Tables VI and VII. γ-Chlorobutyronitrile was used in the runs followed by the letter C while γ-bromobutyronitrile was used in the remainder of the runs. The product distributions listed in Table VII have been corrected for incomplete reaction of the substrate. In the cases where no indication of a product was found upon examination of the infra-red spectrum the yield of this compound has been listed as zero, even though the stoichiometry of the reaction may have been poor.

Allyl cyanide was never observed to be present in any of the product mixtures, which simplified the infra-red analysis considerably as Figure VI clearly shows. In order to determine how rapidly and how thoroughly allyl cyanide was

Table V

Dielectric constants of the pure solvents

Solvent	Dielectric constant	Temperature °C	Reference
benzene	2.28	20	a
_t_-butyl alcohol	11.4	19	b
sec-butyl alcohol	15.8	25	a
_n_-butyl alcohol	17.1	25	a
benzonitrile	25.2	25	a
dimethylformamide	37.65	20	c
nitrobenzene	34.8	25	a

[a] National Bureau of Standards Circular 514.

[b] International Critical Tables.

[c] G. R. Leader, and J. F. Gormley, _J. Am. Chem. Soc._, _73_, 5731 (1951).

Table VI

Variation in conditions of the reaction between γ-halobutyronitrile and base

Run	Molar concentration substrate	Base	Solvent	Approximate temperature °C
7	1.003	piperidine	benzene	25
11	1.993	piperidine	nitrobenzene	25
30	1.000	potassium *n*-butoxide	benzene	60
31-C	1.000	potassium *n*-butoxide	benzene	60
19	1.000	potassium *n*-butoxide	*n*-butanol	25
27-C	0.998	potassium *n*-butoxide	*n*-butanol	25
24	0.999	potassium *n*-butoxide	benzonitrile	60
28-C	0.999	potassium *n*-butoxide	benzonitrile	60
22	1.001	potassium *sec*-butoxide	benzene	60
18	0.999	potassium *sec*-butoxide	*sec*-butanol	25
26-C	0.999	potassium *sec*-butoxide	*sec*-butanol	25
20	0.992	potassium *sec*-butoxide	benzonitrile	60
29-C	0.993	potassium *sec*-butoxide	benzonitrile	60

Table VI (Continued)

Run	Molar concentration substrate	Base	Solvent	Approximate temperature °C
23	0.999	potassium *sec*-butoxide	dimethylformamide	60
12	1.003	potassium *sec*-octoxide	benzene	60
10	1.001	potassium *t*-butoxide	benzene	60
32-C	0.960	potassium *t*-butoxide	benzene	60
16	0.990	potassium *t*-butoxide	*t*-butanol	25
25-C	0.992	potassium *t*-butoxide	*t*-butanol	25

Table VII

Product distribution in the reaction between γ-halobutyronitrile and base

Run[a]	Percent total reaction	Percent substitution[b]	Percent elimination[b]	
			1,2-	1,3-
7	96.0	98.0	0	0
11	94.0	90.0	0	0
30	97.7	0	c,d	c,d
31-C	83.2	0	c,d	c,d
19	96.0	0	74	15
27-C	82.2	0	29	53
24	97.5	0	74	27
28-C	74.0	0	0	46

---

[a] The runs followed by the letter C contained γ-chlorobutyronitrile while the remainder contained γ-bromobutyronitrile.

[b] The percentages reported here have been corrected for incomplete reaction.

[c] These runs could not be analyzed quantitatively.

[d] Refer to the discussion section for the qualitative analysis of these runs.

Table VII (Continued)

Run[a]	Percent total reaction	Percent substitution[b]	Percent elimination[b]	
			1,2-	1,3-
22	98.0	0	63	67
18	97.2	0	43	48
26-C	89.2	0	40	81
20	93.7	0	54	49
29-C	56.4	0	07	64
23	83.8	d,e	d,e	d,e
12	99.0	0	0	100
10	98.0	0	0	91
32-C	84.6	0	0	100
16	98.0	0	0	94
25-C	95.8	0	0	87

---

[d] Refer to the discussion section for the qualitative analysis of these runs.

[e] The use of dimethylformamide was discontinued before a quantitative analysis was obtained.

tautomerized by base, a standard solution of allyl cyanide in <u>sec</u>-butanol was prepared and allowed to stand for twelve hours in the presence of a small amount of potassium <u>sec</u>-butoxide. An infra-red analysis showed that the solute had completely isomerized to crotononitrile. For this reason, a slight excess of base was employed in each case, and no analysis for allyl cyanide was made.

DISCUSSION

The data presented in Tables VI and VII summarize the effect of base strength and solvent upon the product distribution for both the bromo- and the chloronitrile. The data are arranged in the order of increasing base strength. For each base, the solvents have been listed in the order of increasing dielectric strength.

The first general observation that should be made in reference to Table VII, is the absence of any substitution product when a strong base was used in the reaction. On the other hand, γ-piperidylbutyronitrile was the only product observed when the relatively weak base, piperidine, was employed. This is surprising in view of the fact that Bruylants[22] reported that only allyl cyanide was produced when pyridine or quinoline was reacted with γ-chlorobutyronitrile at steam bath temperature. It should be remembered, however, that the band utilized in the analysis of these runs was very near that of crotononitrile, which could have been present in too small a concentration to be detected. The difference in temperature could easily account for a smaller difference in products, but the absence of olefin must be attributed to other causes. The difference between bromine and chlorine as a leaving group does not provide a ready explanation, since again the observed product difference is too great. A possible explanation may arise from the fact that allyl cyanide could easily have been produced from an intermediately formed quartenary ammonium salt.

The results observed in this work are much easier to explain than that of Bruylants. Since piperidine or pyridine and quinoline are nitrogen bases, the nucleophilicity of the molecule outweighs its basicity,* and a much greater tendency for the displacement reaction should be observed.

Considering now the remainder of the runs listed in Tables VI and VII, in which an alkoxide was used as base, it is seen that in no case was any displacement product observed. These observations are completely in accord with the above reasoning, since in these cases the basicity of the attacking species is by far the controlling factor.

In fact, these bases all fall in the category of very strong bases by conventional standards, since even the weakest base employed is considerably stronger than hydroxide ion. A differentiation in base strength can be made, however, since it is well known that the base strength of an alkoxide increases as the number of alkyl substituents on the <u>alpha</u> carbon atom is increased. Furthermore, increasing the chain

---

*A distinction between nucleophilicity and basicity has been made here on the basis that even though the two terms are not entirely separable, the basicity measures the ability to abstract a hydrogen from carbon, while the nucleophilicity is also a function of the polarizability of the atom or molecule.

length of the substituent group also increases the base strength of the alkoxide.

Comparing only the runs in which γ-bromobutyronitrile was used as the substrate, it is seen that in any given solvent, the product distribution changed from predominantly olefin to the complete formation of cyclopropyl cyanide as the base is varied through the series, n-butoxide, sec-butoxide, t-butoxide. Even in the cases where the stoichiometry is poor, the trend is well pronounced.

When the distribution of products is compared in the runs with a constant base and varied solvent, the differences are much smaller. In some cases where the stoichiometry is poor, it is difficult to interpret the results. On the whole, however, a definite trend is noted which favored olefin formation as the dielectric constant of the solvent was increased. The trend is more pronounced with n-butoxide than with sec-butoxide, and of course is nonexistent in the case of t-butoxide. This latter fact alone shows that the transition states are more sensitive to the base than to the solvent. Thus one is led to believe that the transition state which leads to cyclization is quite similar to that which leads to 1,2-elimination.

If dimethylformamide could have been used as a solvent, the trends could have been more significant, since it appeared qualitatively that the ratio of products was definitely in favor of 1,2-elimination. A band also appeared in the region where the substitution product should have absorbed, but it was not ascertained whether any substitution had taken place. The fact that potassium t-butoxide was insoluble in benzonitrile, and also reacted with it quite rapidly also restricts a complete comparison of the solvent effect with the strongest base.

A comparison of the product distribution when γ-bromobutyronitrile was used with the results from the γ-chlorobutyronitrile runs clearly shows that 1,3-elimination is favored in the latter case. The effect is quite striking in every case, even with the runs in benzene which could not be analyzed quantitatively. Run 31-C, containing γ-chlorobutyronitrile, was only 83.2 percent complete while run 30, the corresponding reaction with γ-bromobutyronitrile, was 97.7 percent complete. Even so, the amount of cyclopropyl cyanide formation was about the same, while considerably more crotononitrile was present in run 30. Thus when these results are corrected for incomplete reaction, it is seen that 1,3-elimination is definitely favored.

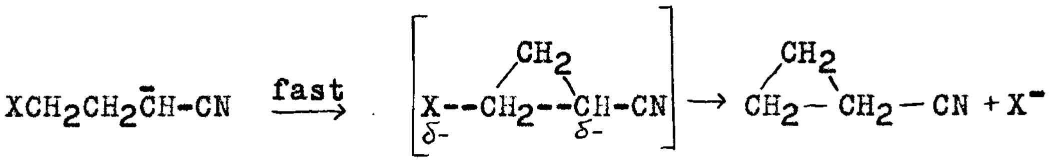
It should be noted that the extent of reaction in the chloronitrile runs was invariably smaller than the corresponding bromonitrile runs except when potassium t-butoxide was used. This could arise from one or more of several possible causes. The differences in rate, which will be discussed below, could have been the cause. In the case of the benzonitrile runs, reaction of the base with the solvent was undoubtedly a factor, since what appeared to be an organic precipitate was isolated along with the potassium chloride. The slower rate of reaction of the chloronitrile could also have allowed more air oxidation of the primary or secondary alkoxide, since these substances were quite sensitive to oxygen.

The rates of the reaction differed considerably depending on whether γ-bromobutyronitrile or γ-chlorobutyronitrile was used as the substrate. The bromonitrile reacted quite vigorously at 60°, and had to be added cautiously when an elevated temperature was employed in order to obtain a homogeneous reaction. The chloronitrile, on the other hand, could be added under these conditions with no turbidity arising for several minutes. As has been stated above, the incomplete reaction of the substrate with the base no doubt can be largely attributed to the unreactivity of the chloronitrile.

Rate differences were also noted with the various bases and also with the various solvents employed. Potassium *n*-butoxide in benzene reacted quite rapidly with γ-bromobutyronitrile while the same base in benzonitrile reacted quite slowly in comparison. It is therefore not surprising that only a 74 yield was obtained when potassium *n*-butoxide in benzonitrile was reacted with the chloronitrile for four days.

Since the check on the kinetic order of the reaction gave satisfactory evidence that the reaction is bimolecular, there are three mechanisms for 1,3-elimination that should be seriously considered. The first one involves a rate-determining abstraction of hydrogen

$$XCH_2CH_2CH_2CN + B^- \xrightleftharpoons{slow} XCH_2CH_2\overset{-}{C}HCN + BH$$



$$XCH_2CH_2\overset{-}{C}H{-}CN \xrightarrow{fast} \left[\underset{\delta-}{X}{-}{-}CH_2{-}{-}\overset{CH_2}{\underset{\delta-}{C}}H{-}CN\right] \rightarrow \overset{CH_2}{CH_2{-}CH_2}{-}CN + X^-$$

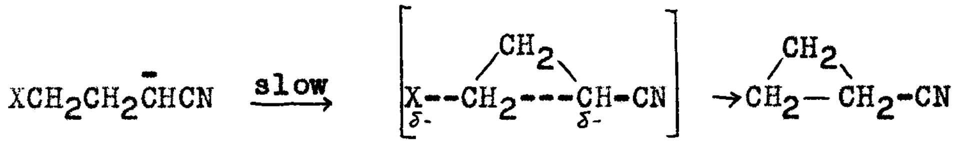
from the substrate, followed by a rapid elimination of halogen by the anion. This process seems logical since anion formation would be favored by the electrophilic cyano group, and the anion, if formed, would be stabilized by resonance.

$$[XCH_2CH_2\overset{-}{C}HCN] \longleftrightarrow [XCH_2CH_2CH{=}C{=}\overset{-}{N}]$$

Furthermore, the mechanism would fit second order kinetics, since both the base and the substrate are involved in the rate-determining step. It is not in agreement with the qualitative observations of the relative rates, however. The fact that γ-bromobutyronitrile reacted considerably faster than the chloronitrile is sufficient evidence to discard this process as the mechanism.

A second mechanism to be considered involves the same steps as in the above case with the second step rate-determining.

$$XCH_2CH_2CH_2CN + B^- \rightleftharpoons XCH_2CH_2\overset{-}{C}HCN + BH$$



$$XCH_2CH_2\overset{-}{C}HCN \xrightarrow{slow} \left[\overset{\delta-}{X}\text{--}CH_2\text{---}\overset{\delta-}{C}H\text{-}CN\right] \rightarrow CH_2\text{—}CH_2\text{-}CN$$

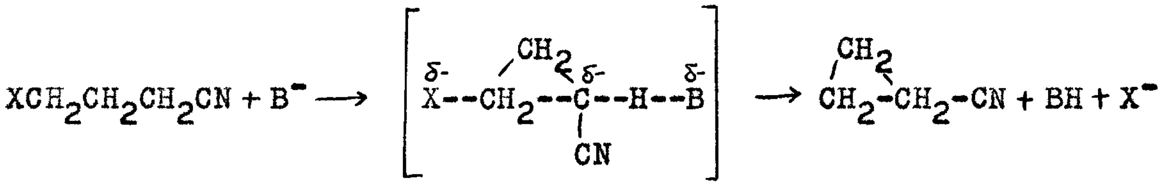
This mechanism also would follow second order kinetics since the rate law would be of the form

$$\frac{d[A]}{dt} = k_2K\,[AH]\,[B^-]$$

where A is the anion, B^- is the base, k_2 the rate constant, and K is the equilibrium constant for formation of the anion. The distribution of products would also be affected by the strength of the base, since the magnitude of the equilibrium constant would be expected to change with base strength. Since 1,2-elimination reactions have been shown to be concerted, a shift in the equilibrium to the right would result in a larger cyclopropyl cyanide yield because of a concentration factor.

The optimum conditions for 1,3-elimination reactions were found to be high base strength and low dielectric constant of the solvent. Since the transition state in this mechanism would involve a distribution of a full negative charge over three atoms, the reaction rate should increase slightly with a decrease in the dielectric strength of the solvent. At the same time a lower dielectric medium could lower the ionization constant somewhat, thereby reducing the observed rate constant, k_2K. Whether or not the solvent effect on the ionization would be of sufficient magnitude to counteract the effect of the charge distribution in the transition state appears to be a moot question on the basis of the data at hand. Therefore this two step process cannot be discarded at this time and should be considered as a conceivable mechanism.

A third possibility which arises is a concerted mechanism analogous to the established mechanism for 1,2-elimination, in which both the hydrogen and the halogen atoms are removed simultaneously.



$$XCH_2CH_2CH_2CN + B^- \longrightarrow \left[\overset{\delta-}{X}--CH_2--\underset{CN}{\overset{CH_2\ \delta-}{C}}--H--\overset{\delta-}{B} \right] \longrightarrow \overset{CH_2}{CH_2-CH_2}-CN + BH + X^-$$

The kinetics for this mechanism are obviously second order, and the rates of the bromo- and chloronitrile should differ as in the 1,2-elimination case.

The transition state in this mechanism might well have more charge distribution than the last case, which should increase the rate and favor cyclization with lower dielectric media. Since this picture is not complicated by any possible side effects as the previous mechanism may or may not be, this process also offers a possible mechanism.

It is apparent that further data must be obtained in order to eliminate one of the two previous mechanisms. Since further kinetic data would not differentiate between the two processes, a device such as deuterium exchange must be resorted to. This would in effect be repeating the experiment of Skell and Hauser[7] on this system. A stereochemical approach was undertaken in this work, but since it was not carried to a successful conclusion, no details are presented here. Therefore, as far as this thesis is concerned, both mechanisms must be considered.

A question arises as to the desirability of differentiating between an ionic process and a concerted one in an inert solvent like benzene. Surely in such a solvent, there are very few, if any, free ions in solution. One might expect that the ion-pairs which are present in such a solution would give rise to a somewhat concerted process, thus degenerating the ionic mechanism to the concerted one.

Even if this is the case, it is possible to differentiate between the two possible proposed mechanisms. Two transition states would exist in the first case, with the second one being rate-determining, while the latter mechanism has only a single free energy maximum. The only essential difference between a truly ionic process and one involving ion-pairs would be the inclusion of the metal ions in all of the transition states.

Before any possible mechanism for 1,3-elimination can be accepted, it must be consistent with the accumulated evidence for the competitive 1,2-elimination and a possible competitive displacement reaction. Such a picture can now be constructed on the basis of the accumulated evidence. Since a displacement reaction in competition with the elimination reactions was found to be unimportant in this system when a strong base was employed, it will be sufficient to discuss only the competitive elimination reactions.

Three factors were observed to affect the competition between 1,2- and 1,3-elimination reactions. Since it has been demonstrated that 1,2-elimination reactions derive a large part of their driving force from the departure of the leaving group, the new carbon-carbon bond is no doubt fairly well made, and the old bonds fairly well broken in the transition state. In other words, the transition state in this process resembles neither products nor reactants. The distribution of charge thus favors the reaction in low dielectric media as in the 1,3-elimination case. The results of this investigation show that the charge is more dispersed in the 1,3- case than in the 1,2-elimination, since the ratio of cyclopropyl cyanide to crotononitrile increased as the dielectric constant of the solvent was decreased.

It therefore seems clear in the 1,3-elimination that the negative charge must be distributed over the cyano group as well as the remainder of the molecule, as it is for 1,2-elimination. Whether or not an ionic, two-step mechanism or a concerted one is involved is still a mute question at this time.

The strength of the attacking base was found to be an important factor in the competing elimination reactions. The fact that a stronger base is required for the cyclization process may be evidence in favor of the concerted process. A greater basic strength would be required to overcome the greater distance over which the halogen must exert its influence in a 1,3- process. Since the cyano group would make the alpha hydrogens quite acidic, it does not seem necessary to require the stronger base to form an anion. But again, it is difficult to assess the relative magnitudes of the driving force in 1,2-elimination with that of anion formation.

The observed differences in the rates of the reaction and a distinct change in the product distribution when chlorine is substituted for bromine in the halonitrile leads to a significant conclusion. The fact that the rate of the reaction was greater when γ-bromobutyronitrile was the substrate than when the chloronitrile was employed signified that the substitution of bromine for chlorine decreased the free energy of activation of both processes. The added fact that the ratio of crotononitrile to cyclopropyl cyanide increased at the same time signifies that the free energy change was greater for the 1,2-elimination process than the corresponding free energy change for the 1,3-elimination. This in turn indicates that the driving force of the 1,2-elimination reaction is enhanced significantly by the increased polarizability of bromine over that of chlorine, since the relative ground state energies of both reactants and products are probably similar enough to cancel in the comparison. This is entirely reasonable since the stretching of the carbon-halogen bond is the source of some of the driving force of 1,2-eliminations.

In the case of the 1,3-elimination it is also reasonable that the transition state should be less sensitive to the leaving group. In the first place the cyano group must absorb some of the negative charge regardless of whether an anion is formed or the reaction is concerted. Also the strain involved in forming a three membered ring must place the departing halogen at a significantly greater distance from the site of the attacking negative center. Thus the increased polarizability is not acting to full advantage in this case, whereas it is ideally situated to do so in the 1,2-elimination.

SUMMARY

The competitive 1,2- and 1,3-eliminations have been studied. γ-Bromo- and γ-chlorobutyronitrile were reacted with a series of alkoxides in solvents of varied dielectric constant.

It was found that 1,3-elimination is favored by high basic strength of the attacking species and a low dielectric constant of the solvent. γ-Bromobutyronitrile reacted at a greater rate than the γ-chloronitrile, but γ-chlorobutyronitrile produced a larger proportion of cyclopropyl cyanide. A weakly basic nucleophile was found to give only substitution when reacted with the bromonitrile.

The combined rate and product distribution data have been interpreted as evidence that bromine promotes 1,2-elimination to a greater extent than it does the 1,3-elimination. The fact that the reaction rate with a given base increased when the dielectric constant of the solvent was decreased is an indication that the charge distribution of the 1,3-elimination transition state is greater than in the 1,2- case.

These facts are consistent with two mechanisms, one of which is a completely concerted process. The second mechanism involves prior anion formation, followed by a rate-determining displacement of halogen. The two mechanisms cannot be distinguished on the basis of the present data.

PART II. FACTORS WHICH INFLUENCE THE IONIZATION OF CARBOXYLIC ACIDS

INTRODUCTION

Many investigations have been conducted in order to elucidate the acid strengths of organic acids. These investigations have been the basis of a large part of the present knowledge of relation of structure to reactivity in organic chemistry.

Several attempts have been made to calculate ionization constants of organic acids on the basis of relatively simple models. None of these calculations were successful until it was discovered that the solvent played a more important role in determining the acid strength than had been previously realized.

The emphasis in the majority of previous studies on steric hindrance and free energy relationships has been on the structure of the acid, and not on the medium in which it is dissolved.

It was, therefore, the purpose of this thesis to demonstrate that the ionization constants of sterically hindered aliphatic acids could be adequately explained on the basis of steric hindrance to solvation of the acid anions, and to demonstrate the dependence of linear free energy relationships on the solvation of benzoic acids.

HISTORICAL REVIEW

Qualitative Attempts to Correlate Acid Strengths

It has long been recognized that several factors are involved in the ionization of organic acids and bases. As early as 1894, Meyer[38] noted that the strengths of <u>ortho</u> substituted benzoic acids depended not so much on the chemical characteristics of the substituent as it did on the size of the group. This idea was further developed by Flurscheim[39] who assumed that steric hindrance would operate only in the reverse process of the equilibrium

$$RCOOH + H_2O \rightleftharpoons RCOO^- + H_3O^+$$

His argument recast in modern terms implies that the anion is thermodynamically more stable than the undissociated acid because of a repulsion of the proton by the <u>ortho</u> substituents. Ingold[40] has since pointed out that this argument is not valid because of two reasons. First, when an atom becomes negatively charged it undergoes an increase in size, and secondly,

---

[38] H. Meyer, <u>Ber.</u>, <u>27</u>, 1580 (1894); <u>ibid</u>, <u>28</u>, 1254 (1895).

[39] B. Flurscheim, <u>J. Chem. Soc.</u>, 725 (1909).

[40] C. K. Ingold, "Structure and Mechanism in Organic Chemistry", Cornell University Press, Ithaca, New York, 1953, pp. 743-50.

an ionic group is much stronger solvated than a neutral group.

Dippy[41] measured the strengths of several *ortho* substituted benzoic acids and came to the same general conclusion as Flurscheim. He recognized that the bulk of the *ortho* substituent failed to entirely account for the "*ortho* effect". Dippy felt that group interaction occurred, and in fact was the major factor to be considered in some cases.

This view was also held by Bennett and Mosses[42] who compared the geometry of the terminal methyl group with the *ortho* position of *o*-toluic acid. They postulated that the abnormalities in acid strength had a common origin, and arose from hydrogen bonding of the methyl group with the carboxylate anion. The effect was considered to be less effective in the fatty acid because of the lack of rigidity in that system as compared with the aromatic system.

Dippy[41] previously had noted that the dissociation constants of isobutyric and diethyl acetic acids are also relatively high, which to him indicated that the same phenomenon was operative. Because of the increased extent of branching, he was convinced that this was the explanation for the sequence

---

[41] J. F. J. Dippy, *Chem. Revs.*, *25*, 151 (1939); J. F. J. Dippy, *et. al.*, *J. Chem. Soc.*, 1421 (1937).

[42] Bennett and Mosses, *ibid*, 2364 (1930).

of acidities,

diethylacetic > isovaleric > *n*-butyric

which is the converse of the order to be expected from consideration of inductive effects alone.

A view somewhat reminiscent, but ascribed to steric hindrance, has been expressed by Newman and co-workers[43] who have formulated an empirical rule of six, which stated that the greater the number of atoms in the six position the greater will be the steric effect. The six position was defined by numbering the carbonyl oxygen in carboxylic acids as one and then counting back along the chain. These authors showed that substitution of hydrogen atoms in the β-position by methyl groups decreased the rate of acid-catalyzed esterification to a greater degree than substitution in the α- or γ- positions.

Ingold[40] has further discussed the role of steric hindrance in benzoic acids and in *cis* isomers of α,β-unsaturated acids. In the case of the benzoic acids, he has pointed out that resonance interaction of the carboxyl function with the benzene nucleus weakens the acid. If bulky groups are present in the *ortho* positions, however, the carboxyl group may be

---

[43] M. S. Newman, *J. Am. Chem. Soc.*, *72*, 4783 (1950); K. L. Leoning, A. B. Garrett, and M. S. Newman, *ibid*, *74*, 3929 (1952).

twisted out of the plane of the ring and consequently the charge on the carboxyl oxygens is not dispersed by resonance interaction, and the acid is strengthened. The same interpretation applies to olefinic acids. The size of the group located <u>cis</u> to the carboxyl function may twist the carboxyl group out of the plane of the trigonal carbon atoms, strengthening the acid.

Branch and Calvin[44] treat solvation effects of certain carboxylic acids in the following manner. An acid which has hydrogens that may be strongly hydrogen bonded with the solvent may lose some of its hydrogen bonding upon ionization, since the anion will tend to make these hydrogens less available to strong solvation with the solvent. The neutral acid is stabilized with respect to the anion, and as a result the acid is weakened. When the acidic hydrogens are replaced by alkyl groups, less stabilization energy is lost upon ionization. Thus the following order of acidities are explained by a solvation effect.

$$R_3\overset{+}{N}CH_2COOH > R_2\overset{+}{N}CH_2COOH > R\overset{+}{N}H_2CH_2COOH > H_3\overset{+}{N}CH_2COOH$$

In a further discussion of the factors contributing to the "<u>ortho</u> effect" they present arguments for reversed direction

---

[44] G. Branch and M. Calvin, "The Theory of Organic Chemistry", Prentice-Hall, Inc., New York, 1941, p. 229 ff.

of dipoles of ortho substituents, chelation of the ortho group with carboxyl function, twisting of groups such as o-nitro out of the plane of the ring, and repulsion of the groups occupying the 1,2- and 1,6-positions increasing the potential energy of the molecule.

Brown[45] has proposed a steric strain theory designated as "B-Strain", which he has used to explain the acidity of ortho substituted anilinium ions. He argues that when a fourth group is added to nitrogen in an ortho substituted aniline or a trialkylamine, the groups already present are forced back from essentially a trigonal to a tetrahedral configuration causing steric strain. Thus, even the attack of a proton is sufficient to cause "B-Strain" and consequently makes the molecule a weaker acid.

Pearson,[46] on the other hand, has measured the catalytic effect of alkylamines on the ionization of nitroethane and has reported that successive replacement of the hydrogen atoms in ammonia by alkyl groups led to an increase in the relative rates of ionization. A comparison of piperidine and quinuclidine with diethylamine and triethyl amine showed that the presence of the ring structure in the former amines caused

---

[45] H. C. Brown and A. Cahn, J. Am. Chem. Soc., 72, 2939 (1950).

[46] R. G. Pearson and F. V. Williams, ibid, 76, 258 (1954).

a further increase in rate. Pearson concluded that "F-Strain", that is, "Frontal Strain", is operative in decreasing the rate of proton removal by the amine. He felt that this effect is compensated by an inductive effect which increases the nucleophilicity of the nitrogen atom. He also suggested that the ionization constants of tertiary amines in solvents of low dielectric are reduced by a decrease in the solvation energy in the 'onium ion as is shown by Table VIII presented in his paper.

Table VIII

pK_b of anilines in various solvents

	Water	Ethanol	_m_-Cresol	Chlorobenzene
aniline	9.36	13.8	8.10	- 1.0
N-methylaniline	9.15	14.6	7.26	- 1.8
N,N-dimethylaniline	8.99	15.1	6.18	- 2.8

Pearson pointed out that the basicities of the _n_-butylamines increased regularly in chlorobenzene with alkyl substitution, whereas the basicity in water solution decreased considerably in passing from _n_-butylamine to di-_n_-butylamine and only increased slightly with tri-n-butylamine. The basicities observed in chlorobenzene agreed with the observations in his investigation, while the basicities in water solution did not agree. It was for this reason that Pearson concluded that "B-Strain" was unimportant.

Stillson and co-workers[47] have reported the abnormal behavior of di-ortho-substituted phenols. They found that 2,6-dimethyl-4-t-butylphenol was soluble in 10 percent sodium hydroxide solution and 2,4-dimethyl-6-t-butylphenol was not, while 2,4,6-tri-t-butylphenol is even insoluble in a methanolic potassium hydroxide solution. These results are highly indicative of the stability of the acid form over the phenoxide ion. Undoubtedly the steric requirements of the phenoxide ion together with its molecule(s) of solvation entirely prohibit the ionization.

Goering, Rubin and Newman[48] have studied the alkaline saponification rates of methyl 4-x-2,6-dimethylbenzoates in dioxane-water solution and have concluded that cleavage occurred by an SN_2 reaction at the methyl group in the ester from consideration of the magnitudes of the entropy term and the Hammett rho constant.[49] The authors did not exclude the

---

[47] G. H. Stillson, D. W. Sawyer, and C. K. Hunt, ibid, 67, 303 (1945).

[48] H. L. Goering, T. Rubin, and M. S. Newman, ibid, 76, 787 (1954).

[49] L. P. Hammett, "Physical Organic Chemistry", McGraw-Hill Company, New York, 1940, pp. 186 ffl.

possibility that the small rho constant might have been due to nonplanarity of the ester function with the benzene nucleus, a factor of no small significance.

The authors concluded, therefore, that both polar transmission and solvation effects are operating in conjunction with the steric factor. They felt that the coplanarity of the carboxylate function is not greatly affected by the presence of one *ortho*-substituent but that the presence of the second group is sufficient to limit interaction of the ring and the carboxyl group.

It is also interesting to note that these authors measured the ionization constants of a number of *para*-substituted benzoic acids in 26.5 and 43.5 percent dioxane-water solution. By plotting the relative pK_A values for these acids against the Hammett sigma constant, *rho* values of 1.23 and 1.35 were obtained for the two solutions. A plot of *rho* against the weight percent dioxane in an aqueous mixture yielded a straight line for dioxane concentrations as high as 43.5 percent.

Bright and Briscoe[50] have measured the apparent ionization constants of a number of substituted benzoic acids as well as aliphatic acids in various ethanol-water and methanol-

---

[50] W. L. Bright and H. T. Briscoe, *J. Phys. Chem.*, *37*, 787 (1933).

water mixtures. The measurements were made by potentiometric titration using a potentiometer to obtain the titration curve. Since it will be of interest to compare the results of this work with the data of these authors, a partial compilation of their data is listed in Table IX.

Table IX

Acid strengths in methanol-water

Acid	pK_A in % by volume methanol		Acid	pK_A in % by volume methanol	
	50	70		50	70
benzoic	5.15	5.72	*n*-valeric	6.04	6.54
propionic	5.84	6.41	isovaleric	5.89	6.41
n-butyric	5.88	6.41	*n*-caproic	5.91	6.44
isobutyric	6.23	6.70	isocaproic	5.90	6.40

Quantitative Attempts to Correlate Acid Strengths

Several attempts to correlate acid strengths utilizing a relatively simple electrostatic model are recorded in the literature. The earliest of these was developed by Bjerrum[51]

---

[51] N. Bjerrum, *Z. Physik. Chem.*, *106*, 219 (1923).

who assumed that the molecule consisted of point charges embedded in a uniform medium with a dielectric constant equal to that of the solvent. He regarded the free energy of ionization for a dibasic acid to equal the work necessary to remove a proton from a distance, r, to infinity. The distance, r, is the normal distance between the undissociated proton and the other carboxyl group in the acid. Using classical electrostatic theory, this leads to the equation

$$\ln \frac{K_1}{K_2} = \frac{Ne^2}{RTDr} \qquad (1)$$

where K_1/K_2 is the ratio of the first to the second ionization constant, D is the dielectric constant, N is Avogadro's number, and e is the charge on the proton. Since accurate values are not known for r, and since theoretically it may vary over a rather wide range depending on whether the molecule is fully extended, partially extended, or fully coiled, Bjerrum's equation was quite often used to calculate this distance. It was found that the equation gave quite reasonable values in the cases where the molecule under consideration was long and thin, but failed miserably when it was short and rather thick.

A treatment rather similar to that of Bjerrum's was developed by Eucken[52] for acids with dipolar substituents, and has been discussed by Wheland.[53] The treatment, which is based on the equilibrium between chloroacetic acid, acetate ion and their conjugate base and acid, respectively yields the following equation:

$$\ln \frac{K_c}{K_a} = \frac{Ne\mu \cos \theta}{RTDr^2} \qquad (2)$$

The value e, is again the protonic charge, μ is the magnitude of the carbon-chlorine bond moment, K_c and K_a are the ionization constants of chloroacetic and acetic acids, respectively, r is the distance between the center of the carbon-chlorine bond and the ionizable proton, and θ is the carbon-carbon-chlorine angle in chloroacetic acid. This equation gives unreasonably low values of r unless a small value, in the neighborhood of 1 to 5, is used for the dielectric constant. Smallwood[54] has pointed out that an effective dielectric constant of 1 is quite reasonable since the inductive effect of the carbon-chlorine dipole is transmitted not through the solvent, but through the molecule.

---

[52] A. Eucken, Angew. Chem., 45, 203 (1932).

[53] G. W. Wheland, "Advanced Organic Chemistry", Second Edition, John Wiley and Sons, New York, 1949, pp. 440 ffl.

[54] H. M. Smallwood, J. Am. Chem. Soc., 54, 3048 (1932).

Thus the Smallwood model is the extreme of that of Bjerrum, in that he visualizes point charges embedded in a molecule of infinite volume.

Kirkwood and Westheimer[55] subsequently developed a model which was more reasonable than either of the two previously discussed. They treated the molecule as either a sphere or an ellipsoid with radius b with an arbitrary charge distribution and immersed in a uniform solvent of dielectric D. The rather complex derived equation in the case of the ellipsoidal model may be simplified, and for the case in which the acid HA, has a charge in excess of the acid HA_2, it may be written in the following form:

$$\triangle pK = e^2/2.303\ D_E RkT \qquad (3)$$

D_E is an effective dielectric constant defined in terms of the Bjerrum equation. In the case in which HA_1 contains a dipole in excess of HA_2, the equation may be written in the following manner:

$$\triangle pK = eM\ \cos L/2.303\ D_E R^2 kT \qquad (4)$$

R is defined as the distance from the proton to the point dipole, and L is its angle of inclination to the line joining

---

[55] J. G. Kirkwood and F. H. Westheimer, J. Chem. Phys., 6, 506 (1938); F. H. Westheimer and J. G. Kirkwood, ibid, 6, 513 (1938); F. H. Westheimer and M. W. Shookhoff, J. Am. Chem. Soc., 61, 55 (1939).

it to the proton.

Since the effective dielectric constant involves terms relating both the dielectric of the solvent and the molecule, it can be shown that the equation can be reduced to include either the Bjerrum or the Smallwood models. Consequently, calculations of the distance r based on this model gave much more reasonable values for r with both types of dibasic acids than the simpler models as is shown by Table X taken from Wheland.[53]

Table X

Computed length of acid molecule in A°

Acid	Bjerrum model (D = 80)	Modified Smallwood model (D = 1)	Kirkwood-Westheimer model	Fully extended	Free rotation
adipic	8.1	635	7.8	9.0	5.6
chloro-acetic	0.6	5.1	3.0	3.4	3.0

Sarmousakis[56] has extended the Westheimer-Kirkwood treatment by considering the molecule to be an oblate spheroid with

---

[56] J. N. Sarmousakis, J. Chem. Phys., 12, 277 (1944).

charges on the focal disks with all dissociating protons and substitutent dipoles on the focal circles.* He used the oblate spheroidal coordinates ξ, η, and ϕ which are defined as:

$$x = c(1+\xi^2)^{\frac{1}{2}}(1-\eta^2)^{\frac{1}{2}}\cos\phi \qquad (5)$$

$$y = c(1+\xi^2)^{\frac{1}{2}}(1-\eta^2)^{\frac{1}{2}}\sin\phi \qquad (6)$$

$$z = c\eta\xi \qquad (7)$$

where ξ, η, and ϕ define orthogonal families of oblate spheroids, hyperoloids of one sheet, and half planes, respectively. The focal ring of the spheroids and hyperboloids has a radius, c. By making use of the expressions for the electrostatic potential obtained by solution of Laplace's equation in three coordinates, the following relation similar to Bjerrum was obtained, which was then applied to substituted benzoic acids.

$$\log \frac{K_1}{K_2\sigma} = \frac{e^2}{(2.303kTrD_E)} \qquad (8)$$

where

$$\frac{1}{D_E} = \frac{1}{D_1} + \left(\frac{1}{D} - \frac{1}{D_1}\right) \sum_{n=0}^{\infty} \sum_{m=0}^{n} \frac{r}{c} \frac{\alpha_n^m}{1-(D_1/D)\gamma_n^m} \cos m\phi \qquad (9)$$

---

*An oblate spheroid is generated when an ellipse is rotated about its minor axis. For a further discussion cf. H. Morgenau and G. Murphy, "The Mathematics of Physics and Chemistry", D. Van Nostrand Co., New York, 1943, p. 177.

$$\alpha_n^m = i(2-\delta_m^0)(2n+1) \quad \frac{\left[(n-m)!\,(n+m)!\right]^2 Q_n^m(i\zeta_o)}{\left[2^n \left(\frac{n-m}{2}\right)! \left(\frac{n+m}{2}\right)!\right]^4 P_n^m(i\zeta_o)} \tag{10}$$

and

$$Y_n^m = \frac{m\zeta_o + (1+\zeta_o^2)^{\frac{1}{2}} P_n^{m+1}(i\zeta_o)/P_n^m(i\zeta_o)}{m\zeta_o + (1+\zeta_o^2)^{\frac{1}{2}} Q_n^{m+1}(i\zeta_o)/Q_n^m(i\zeta_o)} \tag{11}$$

In the above relationships, K_1 and K_2 are the first and second dissociation constants, σ is the statistical factor, c is the charge on the proton, k is Boltzmann's constant, T is the absolute temperature, r is the distance between the dissociating protons, and D_E is the effective dielectric constant. D_i and D are the dielectric constants of the cavity and the solvent, respectively, $\frac{r}{c}$ takes on the values 1, $\sqrt{3}$, and 2 and ϕ, the angle between the radii of the focal circle to the dissociating protons, assumes the values 60°, 120°, and 150° depending on whether the acid is ortho-, meta-, or para- substituted. $P_n^m(i\zeta_o)$ and $Q_n^m(i\zeta_o)$ are associated Legendre functions of the first and second kind defined for imaginary variables. The parameter ζ_o defines the boundary of the molecular cavity.

It is then possible by various manipulations and graphical interpolations to simplify the complex function above to the following:

$$\log K_{A_x B_o} = \frac{1}{2.303kT}\left[\frac{-e|\mu_\xi|\cos(\mu_\xi, i_1, r)}{r^2 D_\xi} - \frac{e|\mu_\phi| \cos(\mu_\phi, i_2, r)}{r^2 D_\phi}\right] \tag{12}$$

where

$$\frac{1}{D_\xi} = \frac{g_1}{D_i} + \frac{g_2}{D} \tag{13}$$

$$\frac{1}{D_\phi} = \frac{h_1}{D_1} + \frac{h_2}{D} \tag{14}$$

The terms μ_ξ and μ_ϕ are components of the dipole along i_1 and i_2, the unit vector directed from the center of the focal circle along the radius to the dipole, making an angle ϕ with the radius of the dissociating proton and the corresponding vector tangent to the focal circle in the direction of increasing ϕ, respectively. D_ξ and D_ϕ are the dielectric constants corresponding to the dipoles μ_ξ and μ_ϕ. The values g_1, g_2, h_1 and h_2 are determined graphically from values of ξ_o, depending on whether the substituent is in the _ortho_, _meta_ or _para_ position.

The value of ξ_o for each acid was determined from the equation

$$\frac{\Upsilon}{c^3} = \frac{4\pi}{3}\,\xi_o\,(1+\xi_o^2) \tag{15}$$

in which Υ is the cavity volume. For the calculation of the ionization constants in water, $\frac{\Upsilon w}{c^3}$ was calculated by making use of the dimensions of the benzene ring and van der Waals radii. For the remainder of the solvents, the experimental value of the ionization constants was substituted in the equations, and Υ was calculated. In water solution, the agreement between the calculated and the experimental values was excellent. Sarmousakis has pointed out that as the dielectric constant of the solvent decreases from water to propanol the calculated values of Υ increased. He also noted that in general for pure solvents, that $\Delta \log K$ was fairly constant but this was not true for dioxane-water mixtures. His interpretation of this phenomenon was that in the dioxane-water solution, a certain amount of unmixing occurred which contributed an unknown amount of free energy to the experimentally measured log K term.

Wynne-Jones[57] has proposed that the ionization constant of a given acid measured relative to some standard acid in a series of solvents should be inversely proportional to the dielectric constant of the medium. He considered the intercept of this linear relationship to be a measure of the intrinsic acid strength of the substance in question.

---

[57] W. F. K. Wynne-Jones, Proc. Roy. Soc. (London), A140, 440 (1933).

Kilpatrick and co-workers[58] have experimentally measured the dissociation constants of a series of *ortho*, *meta*, and *para* substituted benzoic acids relative to benzoic acid in methanol, ethanol, propanol, ethylene glycol, *n*-butanol, and in several dioxane-water mixtures. They found that the Wynne-Jones relationship held for solvents with dielectric constant greater than 25. The failure of a linear relationship with low dielectric solvents was attributed by them to dipole-dipole interactions between the molecule and the solvent. They also stated that no correlation was found for the ionization constants in dioxane-water solutions, and attributed this behavior to partial unmixing of the solvent. Using the data for the ionization constants in varied media, Kilpatrick found a correlation between Hammett's *rho* and the dielectric constant of the solvent, in the cases where a pure solvent had a dielectric constant greater than 25.

---

[58] J. H. Elliott and M. Kilpatrick, *J. Phys. Chem.*, *45*, 454, 466, 472, 485 (1941); *ibid*, *46*, 221 (1942); Mason and M. Kilpatrick, *J. Am. Chem. Soc.*, *59*, 576 (1937).

EXPERIMENTAL

The Purification of Materials

Acetic acid was purified by refluxing ninety-nine percent commercial grade acid over potassium permanganate for several hours in order to remove all oxidizable material. It was then fractionated by distillation through a glass helix packed column from acetic anhydride. Only the middle constant boiling fraction was collected.

The remainder of the acids listed below were obtained from M. S. Newman of Ohio State University. The acids, for the most part, were originally prepared by the late F. C. Whitmore's students at Pennsylvania State College, and the methods of preparation can only be inferred from the published methods of synthesis indicated for each.

Methylneopentylacetic acid was fractionated in a glass center rod column at ca. 1 mm. pressure, b.p. 86° (uncorrected); $n_D^{20.1^\circ}$ 1.4231; literature[59] b.p. 217° (730 mm.); $n_D^{20^\circ}$ 1.4233. The neutral equivalent was found to be 145, and the calculated value was 144.

Dimethylneopentylacetic acid was used without further

---

[59] F. C. Whitmore, et. al., J. Am. Chem. Soc., 63, 643, 2028 (1941).

purification, m.p. 45°; literature[60] m.p. 45°. The neutral equivalent was found to be 156, and the calculated value was 156.

Methyl-t-butylneopentylacetic acid was not of sufficient purity to warrant its use without purification. It was dissolved in methanolic sodium hydroxide and extracted with pentane to remove what was believed to be 2,2,3,5,5-pentamethylhexane, which could have easily been formed on long standing by decarboxylation of the original acid. The alkaline solution was acidified and the acid extracted with pentane. After this procedure was repeated several times, the melting point of the material had risen from 102-116° to 116-126°, and the neutral equivalent decreased from 270 to 250, the calculated value being 200. The small size of the sample prevented any further purification. The literature[59,61] lists the melting point of the pure material to be 130°. The neutral material obtained by extraction from the basic methanolic-solution, was obtained only in trace amounts, and could not be identified.

Dineopentylacetic acid was used without further purification, m.p. 52-53°; literature[62] m.p. 53-55°. The neutral

---

[60] F. C. Whitmore, et. al., ibid, 63, 2035, 3237 (1941).

[61] F. C. Whitmore, et. al., ibid, 56, 1128 (1934).

[62] J. G. Aston, J. T. Clarke, K. A. Burgess, and R. B. Grienburg, ibid, 64, 300 (1942).

equivalent was calculated to be 132, and experimentally found to be 130.

Dimethyl-t-butylacetic acid was also used without further purification, m.p. 200°, literature[63] m.p. 196-7°. The neutral equivalent was found to be 146, while the calculated value was 144.

Ethyl-t-butylacetic acid was used without further purification, m.p. 79.5-80.5°; literature[64] 76-77°. The neutral equivalent was found to be 146, while the calculated value was 144.

Triethylacetic acid was also used without further purification, m.p. 39°; literature[65] m.p. 39°. The neutral equivalent was calculated to be 144, and found experimentally to be 142.

Diisopropylacetic acid was obtained also in a pure state, b.p. 82-3° at 2 mm. pressure, $n_D^{24.4}$ 1.4243, $d^{24.4}$ 0.9080 and was used without purification. The neutral equivalent was calculated to be 144.2, and found experimentally to be 144.7.

---

[63] F. C. Whitmore, et. al., ibid, 63, 1626 (1941).

[64] K. L. Loening, A. B. Garrett, and M. S. Newman, ibid, 74, 3929 (1952).

[65] F. C. Whitmore, et. al., ibid, 64, 2964 (1942).

The Measurement of the Ionization Constants

The apparent ionization constants of the acids were measured potentiometrically in 50 "volume percent" methanol-water solution at 40° by the method of one-quarter, one-half, and three-quarter points in the titration curve. A Beckman pH meter, model G, was used with calomel and glass electrodes, and was standardized repeatedly against buffer solutions at pH 4 and pH 7. The cell was one of approximately 200 milliliter capacity and was water jacketed. A rubber stopper placed in the top of the cell, was fitted with holes for the electrodes, an air driven stirrer, an offset tip for a five-milliliter micro burette, and a thermometer. The cell was thermostated by water which was pumped from a regulated water bath. All electrical equipment in the bath, as well as the pH meter, was well grounded in order to obtain reproducible readings.

In a typical titration, approximately 0.75 milliequivalents of the acid were weighed and dissolved in 100 milliliters of 50 "volume percent" methanol-water solution. The methanol-water solution was prepared by mixing equal volumes of freshly distilled water and methanol, which had been previously purified by fractional distillation through a Heli-pak column rated over one hundred plates. After solution was complete, and thermal equilibrium was established, approximately

0.2 milliliters of 0.0957 N carbonate free sodium hydroxide in 50 "volume percent" methanol was added. After a minute or so, the air stirrer and all of the electrical equipment except the pump in the water bath was disconnected, and the reading was taken. This procedure was repeated until the pH meter indicated a slight excess of base was present in the solution. If this procedure was not followed rigorously, it was found that random readings of the pH meter were obtained. However, the sample titration curves in Figure XI show that satisfactory readings were obtained. Also, in order to keep constant check on the validity of the readings, the meter was standardized at pH 4 and pH 7 with standard buffer solutions before and after each titration.

The apparent ionization constants were calculated by reading the endpoint from the curve, since this could be done more accurately than a calculation based on the strength of the base, and the one-quarter, one-half and three-quarter strengths were determined by the following relationships.

$$pK_A = pH_{\frac{1}{4}} + \log 3 \qquad (16)$$

$$pK_A = pH_{\frac{1}{2}} \qquad (17)$$

$$pK_A = pH_{3/4} - \log 3 \qquad (18)$$

These data are listed in Table XI, as well as the apparent ionization constants.

Figure XI. Titration curves for hindered acids.

Top curve - methyl-t-butylneopentylacetic acid.

Center curve - triethylacetic acid.

Lower curve - methylneopentylacetic acid.

Ordinate - pH.

Abscissa - milliliters of base.

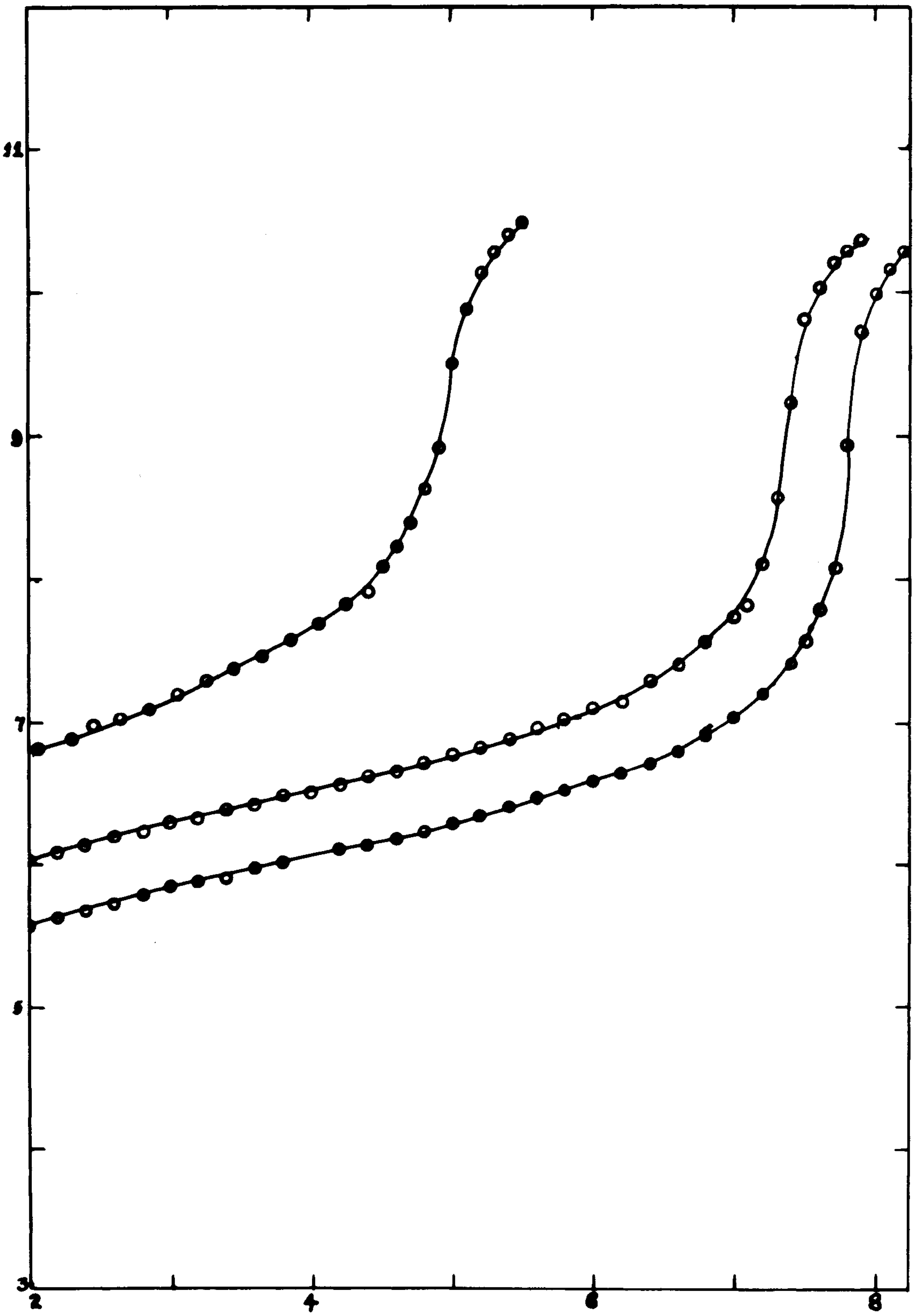

11
9
7
5
3
2
4
6
8

Table XI

Ionization constants of hindered acids in 50 "volume percent" methanol-water at 40°

Acid	Apparent pK_A			
	1/4	1/2	3/4	$Kx10^7$
acetic	5.57	5.55	5.55	27.6
methylneopentylacetic	6.04	6.05	6.07	8.90
methyl-t-butylacetic	6.25	6.25	6.24	5.63
ethyl-t-butylacetic	6.31	6.32	6.31	4.90
diisopropylacetic	6.40	6.40	6.39	3.98
triethylacetic	6.44	6.44	6.44	3.62
dimethylneopentylacetic	6.49	6.51	6.51	3.13
dineopentylacetic	6.51	6.54	6.62	2.75
dimethyl-t-butylacetic	6.74	6.72	6.71	1.91
methyl-t-butylneopentylacetic	6.88	6.97	7.02	1.10

The solvent was chosen with two criteria in mind. First, the non-ideal behavior of electrolytes in non-aqueous solvents dictated that a large percentage of water must be present in the solvent. On the other hand, however, the slight solubility of these acids in water dictated that a considerable portion of the solvent must be organic. A 50 "volume percent" methanol-water solution coupled with a slightly elevated temperature in order to dissolve the most hindered of the acids thus seemed to be the best compromise available. The junction potential in this solvent was assumed to be small and constant throughout the series of acids. It was also assumed that the activities of the ions were very nearly the same as in water, and any deviation was neglected in the calculations.

DISCUSSION

The Ionization of Sterically Hindered Acids

The effects that have been proposed to account for the strength of organic acids may be placed in two categories; those which are acid strengthening, and those that are acid weakening. The bulk of those in the first category were designed to explain the enhancement of acidity in ortho substituted benzoic acids. The views of the earlier workers[38,39,41] who explained the increased acidity by an interaction between the carboxyl function and the ortho substituent, have been supplanted by the more logical explanation of steric inhibition of resonance.[40] That is to say, the carboxyl group is forced out of the plane of the benzene ring preventing resonance interaction of that group with the ring. No conclusive evidence has been introduced, but a far better understanding of chemical structure has made the older views much less tenable than they appeared at the time of their proposal. For example, the argument that the hydrogens on the methyl group in o-toluic acid or in isobutyric acid are hydrogen bonded with the carboxyl function is weak because of the complete lack of any evidence for a hydrogen bond of any consequence existing between carbon and oxygen.

The concept of Brown[45] involves the acid strengthening effect of steric inhibition of resonance as well as the acid weakening effect of increased strain in the essentially tetrahedral configuration of the anilinium ion as compared with the essentially trigonal configuration of the aniline. This argument assumes that the predominant effect is due only to the increased steric requirements of the anilinium ion, since Brown has proposed that the variation in acidity constants may be taken as a criterian for the estimation of internal strains of neutral "homomorphs" of the anilinium ions.

The work of Pearson[46] has shown that Brown was not considering the problem in its entirety, since the former author found that the catalytic effect of amines on the ionization of nitroethane increased when Brown's steric strain theory predicted it should decrease. Pearson, therefore, attributed Brown's observations to a decrease in solvation of the 'onium ion as the number of alkyl groups attached to nitrogen increased. As supporting evidence, Pearson presented the ionization constant data listed in Table VIII of this thesis, and showed that his results paralleled the base strengths in solvents of varied dielectric strength.

It follows then, that the strengths of ortho substituted benzoic acids are the result of two factors, one which is acid strengthening arising from steric inhibition of resonance, and the other acid weakening, arising from decreased solvation of the carboxylate anion. In this case, it is apparent that steric inhibition of resonance is the predominant effect, and masks the relatively small stabilization of the undissociated acid due to the screening of the anion by the _ortho_ substituents.

In the case of the di-_ortho_ substituted phenols reported by Stillson,[47] steric inhibition of resonance no doubt is unimportant until both _ortho_ positions are occupied by larger groups than methyl. This may be illustrated by the fact that 2,6-dimethyl-4-_t_-butylphenol is soluble in sodium hydroxide solution, and also that a model of the compound allows the hydroxyl group to remain in the plane of the ring. This is also true of 2,4-dimethyl-6-_t_-butylphenol even though it is insoluble in sodium hydroxide solution. In 2,4,6-tri-_t_-butylphenol the model shows that the hydroxyl group is somewhat hindered by the adjacent _t_-butyl groups, and may be forced somewhat out of the plane of the ring. It appears quite clear, then, that 2,4-dimethyl-6-_t_-butylphenol is a weak acid because of steric hindrance to solvation of the phenoxide ion. The extreme insolubility of the tri-_t_-butylphenol may be explained as the result of both effects operating, since steric inhibition of resonance in this case tends to weaken the acid.

Even though the qualitative data already available for the hindered phenols indicates these compounds represent a good case for illustrating the importance of solvation effects, a better case may be presented for hindered aliphatic acids, since they are not complicated by any steric inhibition of resonance in the anion. A comparison of the data presented in Table XI of this thesis with that of Bright and Briscoe[50] listed in Table X shows that the sterically hindered acids are weaker than their straight chain analogues. The two sets of data are not directly comparable since a pK_A of 5.62 @ 23° obtained in this work for benzoic acid does not compare favorably with the value of 5.15 @ 25° obtained by Bright and Briscoe. It could not be ascertained from their description of the work whether ratios of alcohol to water or the true volume percent had been used. At any rate, it is seen that if one arbitrarily assumes a value of 60 percent by volume for comparison, the normal and iso-acids are not as weak as any but the strongest listed in Table XI. The magnitude of the effect is also of a different order of magnitude than observed by Dippy[66] for α-substitution of acetic acid, since the weakest acid measured, methyl-t-butylneopentylacetic is 25 times weaker than acetic acid.

If one carefully scrutinizes the results, it is seen that in every case when the corresponding t-butyl and neopentyl acetic acids are compared, the t-butyl acetic acid is weaker than the neopentyl acetic acids by a factor of

---

[66] J. F. J. Dippy, J. Chem. Soc., 1222 (1938).

approximately 1.5. When the Fischer-Hirshfelder models of these compounds are constructed, it is noted that in each case the <u>t</u>-butyl group more efficiently surrounds the carboxyl group, screening it from the solvent than does the corresponding neopentyl group. The neopentyl group presents a larger bulk, and in the case of dimethylneopentylacetic acid the model can be constructed only with difficulty even though the resulting molecule has a more open structure than the less bulky dimethyl-<u>t</u>-butylacetic acid.

The above facts tend to indicate that a somewhat smaller bulk situated closer to the carboxyl function has a greater acid weakening effect than a greater bulk somewhat removed from the site of the carboxyl group. The general trend of the data illustrates this point, since all of the tri-substituted acetic acids are weaker than the most hindered disubstituted acid. A case in point is triethylacetic acid with relatively small bulk, but weaker than its bulky isomer, methylneopentylacetic acid, by a factor of 2.8.

A comparison of the ionization constants of the hindered acids presented herein with the empirical rule of six proposed by Newman[43] proves to be interesting. If one writes down the six numbers for the acids listed in Table XI, it is seen that the number increases as the strength of the acid decreases, as long as one stays in either disubstituted or trisubstituted acids, but an overall correlation with acid strength is not found. It should be pointed out, however, that the significance of the six number is quite obvious, and any correlation within a given sequence of similar acids should be expected.

As was also to be expected, a plot of log $\frac{K}{K_o}$ for the acid catalyzed esterification of several of these acids versus log $\frac{K}{K_o}$ for the ionization constants gave a scattering of points. The reference compound in each case was acetic acid. Since the proposed solvation effect is involved in the free energies as an entropy term, it is gratifying that no linear free energy relationship was observed.

When one considers the supporting evidence as a whole, it is quite clear that the large acid weakening effect reported here is the result of the effect of bulky alkyl groups on the carboxylate anion. The close proximity of these groups lowers the effective dielectric constant in the vicinity of the carboxyl group increasing its electrostatic free energy. At the same time the solvent becomes less available for hydrogen bonding at the carboxylate oxygens which should also increase its free energy. These effects are both acid weakening, and since they are concurrent effects in the hindered aliphatic acids, they cannot be differentiated by the data presented here. In addition, it is quite possible that the steric requirements of the acidic hydrogen atom makes a small contribution to the acidity of these compounds. However, one can be quite certain that steric inhibition of solvation is of such a magnitude that it completely overshadows proton repulsion.

The Correlation of Rho Constants With Effective Dielectric Constants

Hammett[67] has stated that the greatest weakness of the field theory in its present state is its inability to account for differences in the magnitude of the quantity rho in different reactions. The Westheimer-Kirkwood treatment improves the simpler theories somewhat, but still is not at all satisfactory. The Sarmousakis treatment is a refinement of the Westheimer-Kirkwood theory in that he has chosen a more flexible and realistic model for describing the interaction of the dipoles with the solvent and the molecule. The most promising aspect of this refinement is the fact that it made allowances for changes in solvent.

The ionization of benzoic acids is a process that has been studied extensively, and also has the advantage that these acids may be correlated by a linear free energy relationship, such as that of Hammett. Furthermore, attempts

---

[67] L. P. Hammett, "Physical Organic Chemistry", McGraw-Hill Company, New York, 1940, p. 203.

have already been made to correlate acid strength with dielectric constant of the ionizing medium. The results of these attempts have always given approximately the same results, namely that a correlation exists only for pure solvents with dielectric constant greater than 25.

In order to establish the interdependence of ionization constants of benzoic acids, Hammett's rho, and dielectric constant, it is necessary only to write the following relationships:

$$\log \frac{K}{K_o} = \rho\sigma \qquad (19)$$

$$\log \frac{K}{K_o} = e^2/2.303kTrD_e = F\left(\frac{1}{D_e}\right) \qquad (20)$$

where equation (19) is the Hammett equation and equation (20) is a simple form of the field theory derived by Sarmousakis. It follows directly that

$$\log \frac{K}{K_o} = \rho\sigma = F\left(\frac{1}{D_e}\right) \qquad (21)$$

If water is now chosen as the standard solvent, as is the established convention, then the relationship becomes

$$\log \frac{K_w}{K_{ow}} = \rho_w\sigma = F\left(\frac{1}{D_e}\right)_w \qquad (22)$$

where $\rho_w = 1$ by definition.

In some other solvent, the equation becomes

$$\log \frac{K_s}{K_{os}} = \rho_s \sigma = F\left(\frac{1}{D_e}\right)_s \qquad (23)$$

Dividing (23) by (22) one obtains

$$\log \frac{K_s}{K_{os}} \bigg/ \log \frac{K_w}{K_{ow}} = \rho_s = F\left(\frac{1}{D_e}\right)_s \bigg/ F\left(\frac{1}{D_e}\right)_w \qquad (24)$$

If e and r are assumed constant and T is held constant in equation (20), then

$$\log \frac{K_s}{K_{os}} \bigg/ \log \frac{K_w}{K_{ow}} = \rho_s = \frac{D_{ew}}{D_{es}} \qquad (25)$$

Thus the usual plot of $\log \frac{K_s}{K_{os}}$ against sigma constant, or better in this case, a single set of data for the ionization constants of benzoic acids in water, since sigma constants are average values derived from a large amount of data from different sources, will yield a value of rho for the ionization of benzoic acids in a particular solvent. Then by suitable assumptions, as will be explained, the effective dielectric constants for a series of solvents may be calculated. Then a plot of rho versus the reciprocal of the effective dielectric constant should give a straight line with a slope equal to the effective dielectric constant of water.

In order to calculate the effective dielectric constants for a series of solvents, Sarmousakis made use of existing data for van der Waals radii and the geometry of aromatic compounds to calculate Υ_w, the average cavity volume of a particular benzoic acid in water solution. Ellipsoids with axes of different lengths rather than oblate spheroids were used. The length of the major axis was set equal to the distance between the outermost atoms along the axis of symetry plus the sum of the van der Waals radii of these atoms. The length of the mean axis was set equal to the distance between the two ortho hydrogens plus twice the van der Waals thickness of the benzene ring. The ellipsoidal shell around the molecule was assumed to arbitrarily have a thickness $\delta =$ 0.80 A^o, the average distance between the van der Waals radius and the covalent radius of any atom. These values of Υ_w were then used in order to calculate the pK$_A$ of each acid in water solution. In the case of the other solvents, the reverse procedure was used. That is, the pK$_A$ value of the acid in a given solvent was utilized in order to calculate a cavity volume Υ for that acid in the solvent in question. Consequently a table of Υ_w values for a large number of benzoic acids in several solvents was presented by Sarmousakis.

It should be noted in the previous discussion[68] of this work, that the effective dielectric constant is split into two components, one designated as D_γ and the other D_ϕ. In the case of a meta substituted acid, both of these components enter the calculations, but with para substituted acids, only the term involving D_γ appears. Since the rho values include both meta and para substituted benzoic acids, the effective dielectric constants were calculated on the basis that all of the acids were para substituted.

In order to calculate a value of Υ_w to be used in conjunction with rho values, an average value of Υ_w was taken from Sarmousakis' work excluding those calculated values that deviated markedly from the mean value. This was done essentially because of the sensitivity of the effective dielectric constant to changes in the cavity volume. A constant value, $c = 3.30A^o$, was taken for the radius of the focal ring of the ellipsoid. Then by successive approximations, a value of ξ_0 defining the boundary of the cavity was obtained from the equation

$$\frac{\Upsilon_w}{c^3} = \frac{4\pi}{3}\xi_0\left(1+\xi^2\right) \qquad (26)$$

The values of ξ_0 obtained in this manner are listed in Table XII along with the average cavity volume, Υ_w.

---

[68] p. 87, this thesis.

For the sake of comparison, the same procedure was followed except that a constant value of $\tau_w = 261A^{o3}$ was used. This procedure, of course, gives a constant value of λ_0 which, in this case, is equal to 0.9. Having found the value determining the boundary of the cavity, this sets the corresponding g_1 and g_2 parameters which have been found graphically by Sarmousakis at 0.1792 and 0.9648, respectively, in the last mentioned case and as listed in Table XIII for the first case.

Table XII

Average values of λ_0 and τ_w for meta substituted benzoic acids in various solvents

Solvent	λ_0	τ_w	Solvent	λ_0	τ_w
water	0.97	257	butanol	1.15	359
ethylene glycol	1.10	336	26.5% dioxane-water	1.04	296
methanol	1.18	385	43.5% dioxane-water	1.06	311
ethanol	1.18	387	73.5% dioxane-water	1.04	299
propanol	1.18	385	∞	0.93	238.

The effective dielectric constants were then calculated from the following relation.

$$\frac{1}{D_{\mathcal{J}}} = \frac{g_1}{D_i} + \frac{g_2}{D} \qquad (27)$$

D_i is the internal dielectric constant of the molecule arbitrarily set at a value of 2, and D is the dielectric constant

Table XIII

g_1 and g_2 values for meta substituted benzoic acids in various solvents

$\mathcal{J}_0$	g_1	g_2	$\mathcal{J}_0$	g_1	g_2
0.93	0.2742	0.9206	1.08	0.3912	0.8110
0.97	0.3059	0.8932	1.10	0.4066	0.7943
1.04	0.3605	0.8413	1.15	0.4425	0.7540
1.06	0.3758	0.8256	1.18	0.4640	0.7296

of the solvent. The results of this calculation are summarized in Table XIV for both cases being considered. The values of rho in each case are also included.

When rho is plotted against $1/D_{\mathcal{J}}$ for cases I and II in Figures XII and XIII, quite different results are observed. In case I, a definite trend of values shows that the relation between the ratio of ionization constants and the dielectric

Table XIV

Effective dielectric constants and rho constants for various solvents

Solvent	Dielectric constant D	Effective dielectric constant-D_E	D_E^{-1}		Rho
		Case I[a]	Case I	Case II	
water	78.5	8.08	0.1239	0.1019	1.00
26.5% dioxane-water	55	6.63	0.1510	0.1071	1.28
43.5% dioxane-water	40	6.12	0.1635	0.1135	1.35
ethylene glycol	37.5	5.63	0.1776	0.1153	1.24
methanol	31.5	4.86	0.2058	0.1202	1.40
ethanol	24.2	4.69	0.2134	0.1295	1.46
propanol	20.1	4.53	0.2203	0.1376	1.50
butanol	17.1	4.57	0.2192	0.1460	1.44
73.5% dioxane-water	15	5.33	0.1877	0.1440	1.53

[a] γ_w varies in Case I, and is constant in Case II.

Figure XII. Correlation of *rho* constant and dielectric constant, Case I.

Ordinate - *rho* constant, ρ

Abscissa - $\frac{1}{D_s} \times 10^2$

1. - water
2. - 26.5% dioxane-water
3. - 43.5% dioxane-water
4. - 73.5% dioxane-water
5. - ethylene glycol
6. - methanol
7. - ethanol
8. - *n*-propanol
9. - *n*-butanol

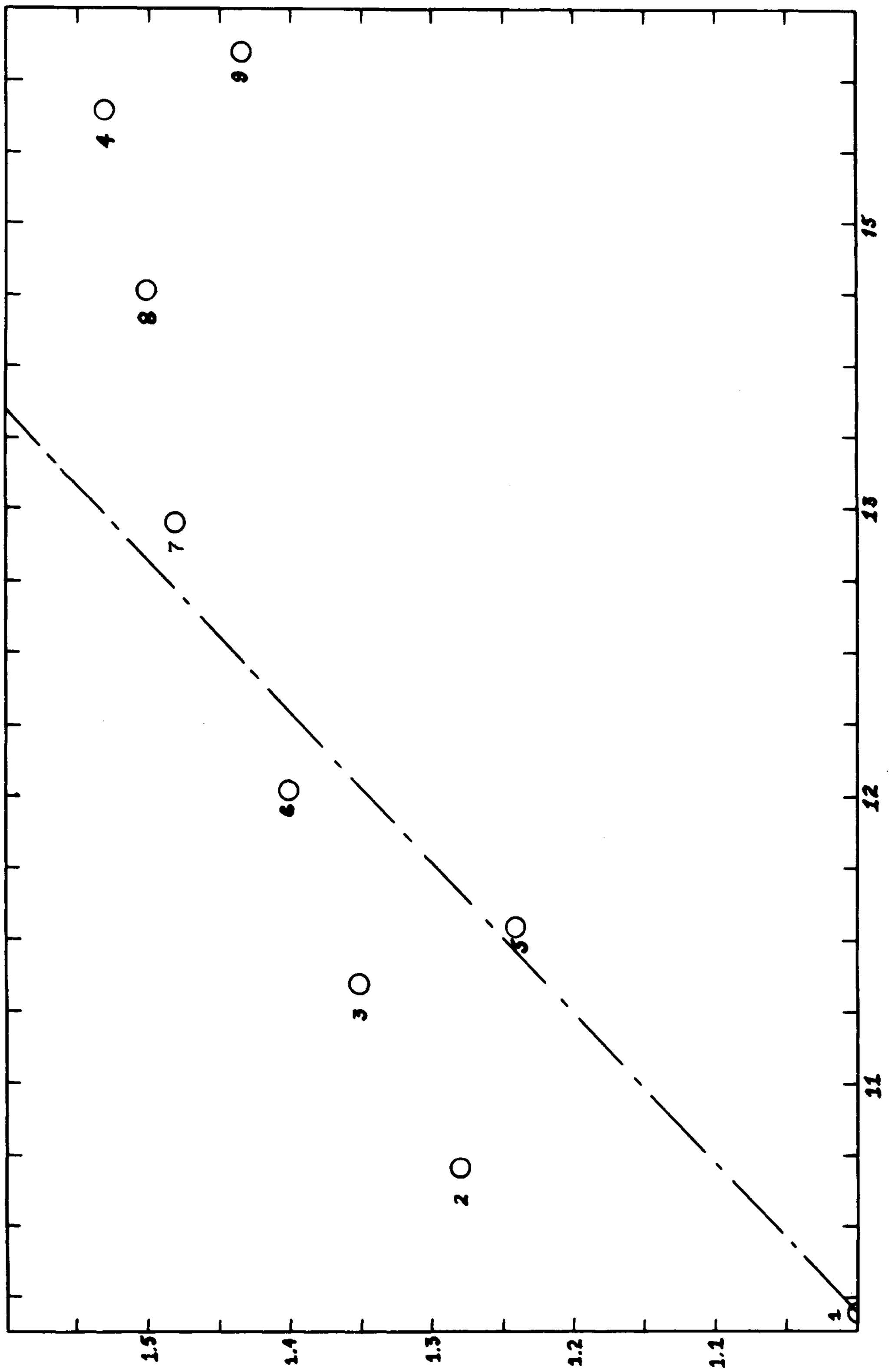
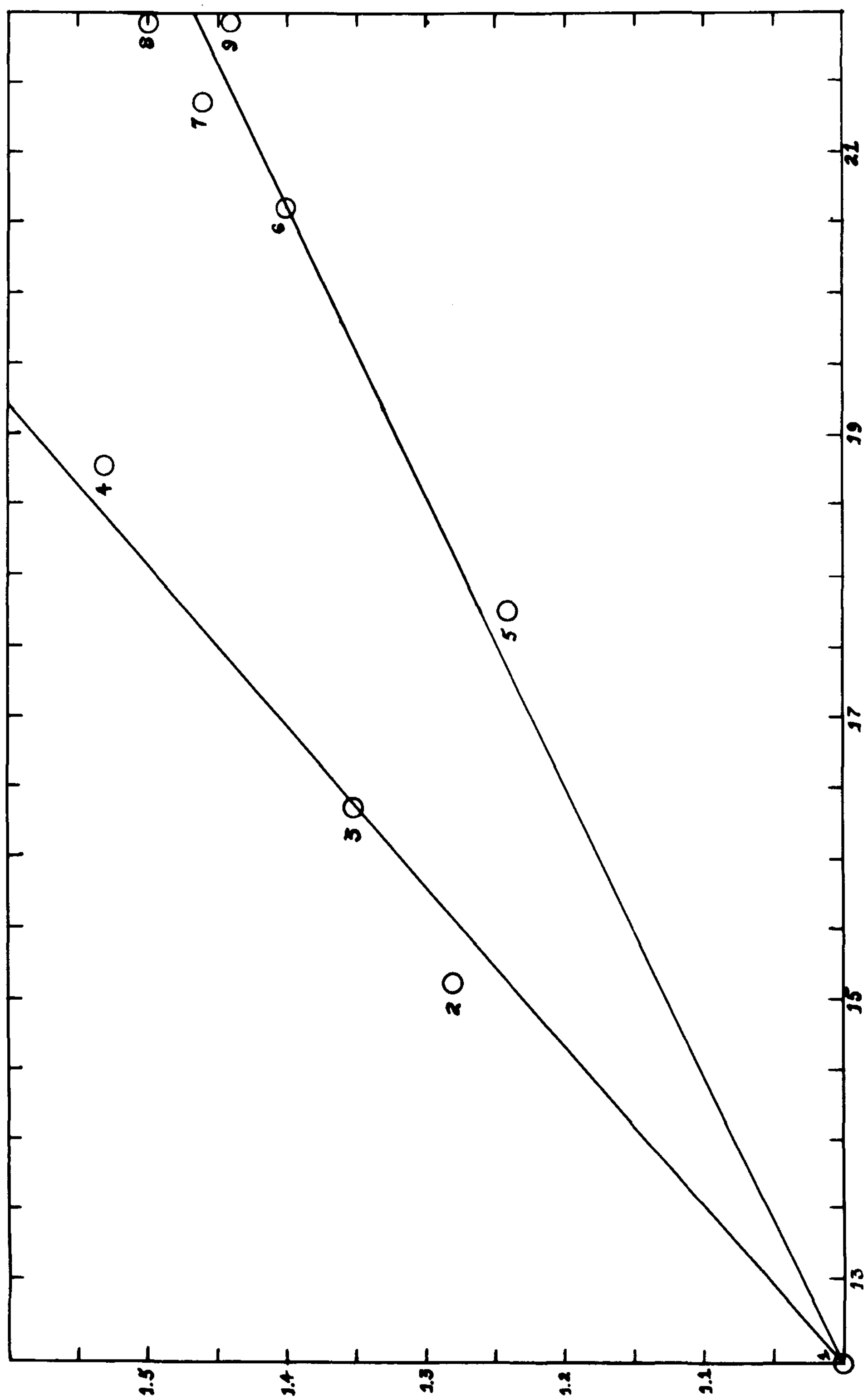

1.5
1.4
1.3
1.2
1.1
11
12
13
15
1
2
3
4
5
6
7
8
9

Figure XIII. Correlation of rho constant with dielectric constant, Case II.

Ordinate - rho constant, ρ

Abscissa - $\frac{1}{D_J} \times 10^2$

The numbers are the same as in Figure XII.


1.5
1.4
1.3
1.2
1.1
13
15
17
19
21
1
2
3
4
5
6
7
8
9

constant is not a simple function. The dashed line corresponds to the correlation that has been made by Kilpatrick[58] and others. It is quite obvious that a simple dielectric constant, which the effective dielectric constant is in this case, is entirely unsatisfactory to account for the observed *rho* constants. It should be noted that all of the dioxane-water mixtures and the pure solvents of low dielectric constant deviate considerably from the rough linear relationship.

However, in Case II there are quite definitely two linear relationships. The pure hydroxylic solvents form one line, while the dioxane-water mixtures form the other. The deviations are quite small considering that the cavity volumes used in the calculation of the effective dielectric constants were weighed averages of a considerable number of substituted acids. This factor was of particular importance in the case of the dioxane-water solutions, since the individual cavity volumes varied considerably. It was in these cases that the large deviations were disregarded in computing the average *rho* value.

The slopes of the two lines are considerably different. It will be remembered that equation (25) predicted that the slope of the line resulting from the plot of *rho* versus $1/D_f$ should be equal to the effective dielectric constant of water. The slope of the dioxane-water line is very nearly this value, being 8.8 as compared with 8.1 for the theoretical line. The pure solvent line, on the other hand, has a slope of only 4.8, which is very nearly one-half the theoretical value.

There seems to be a quite reasonable explanation for this deviation, however. In arriving at the simplified relationship expressed by equation (25), it was assumed that both e and r remained constant, and thus cancelled when the ratio was taken. If e is not assumed constant, but varies with a change in dielectric constant, equation (25) becomes

$$\log \frac{K_s}{K_{os}} \Big/ \log \frac{K_w}{K_{ow}} = \rho_s = e_s^2 D_{ew} \Big/ e_w^2 D_{es} \qquad (28)$$

The field theory upon which equations (25) and (28) depend was derived from a consideration of the work necessary in order to remove a proton from the undissociated acid to a point infinitely distant under the influence of the dipolar substituents. It is easy to visualize that the proton in water solution has its charge fairly well dispersed throughout the cluster of water molecules which solvate the ion. In a solvent of dielectric constant lower than that of water, the dispersion of charge should be less and in fact should be related to the magnitude of the dielectric constant of the solvent. Therefore, it seems quite reasonable to expect the slope of the pure solvent line to be less than in a mixed water solvent in which the water present no doubt solvates the proton almost exclusively. The slope of the line in this case should then very closely approximate the theoretical value.

The correlation obtained with the pure solvents is not restricted only to those which have a high dielectric constant, since propanol and butanol deviate only slightly from the best straight line through the six points plotted. The success of this treatment illustrates the importance of the degree of solvation in organic reactions in general. The values of Υ_w listed in Table XII show that a decrease in dielectric constant first causes an increase in cavity volume, and then a subsequent decrease. This behavior is in agreement with a picture in which the dipolar groups are strongly solvated in a solvent of high dielectric, and the benzene ring solvated in a medium of low dielectric constant. Of course, the physical picture of solvation cannot be too clear from a treatment of this sort, since the charges have been assumed to be concentrated on the surface of a hypothetical ellipsoid.

SUMMARY

The ionization constants of a series of highly hindered aliphatic carboxylic acids have been measured. The data are consistent with the hypothesis that two factors are sufficient to explain the acidity of hindered organic acids.

Since steric inhibition of resonance is not a factor in these aliphatic carboxylic acids, the acid weakening effect observed may be assigned to the second factor, steric hindrance to solvation of the carboxylate anion.

A treatment of substituted benzoic acids based on an oblate spheroidal model has been modified slightly in order to calculate effective dielectric constants for these acids in various solvents. These effective dielectric constants were then correlated with Hammett's rho constant.

A linear relationship was obtained for pure solvents regardless of their dielectric constant. Another linear relationship was obtained for dioxane-water mixtures of widely varied compositions. It was shown that the work necessary to remove a proton from an acid was proportional to the effective dielectric constant in the case of a pure solvent, but was proportional to that of water in dioxane-water mixtures.

ACKNOWLEDGMENTS

The author would like to express his appreciation for the many hours of encouragement and guidance given him by Dr. George S. Hammond.

The use of the infra-red equipment by the Institute for Atomic Research is also gratefully acknowledged. The author is particularly indebted in this respect to Mr. Richard M. Hedges.

Appreciation is also expressed for the Union Carbide and Carbon Fellowship for the year 1953-54.