Retrospective Theses and Dissertations

1936

The electron-sharing ability of organic radicals: the terpenes and related compounds

Perry Alldredge Moore
Iowa State College

Recommended Citation

NOTE TO USERS

THE ELECTRON-SHARING ABILITY OF ORGANIC RADICALS; THE TERPENES AND RELATED COMPOUNDS.

By

Perry Alldredge Moore

A Thesis Submitted to the Graduate Faculty
for the Degree of

DOCTOR OF PHILOSOPHY

Major Subject - Plant Chemistry

Approved

Signature was redacted for privacy.

In charge of Major work

Signature was redacted for privacy.

Head of Major Department

Signature was redacted for privacy.

Dean of Graduate College

Iowa State College

1936

UMI Number: DP12864

INFORMATION TO USERS

The quality of this reproduction is dependent upon the quality of the copy submitted. Broken or indistinct print, colored or poor quality illustrations and photographs, print bleed-through, substandard margins, and improper alignment can adversely affect reproduction.

In the unlikely event that the author did not send a complete manuscript and there are missing pages, these will be noted. Also, if unauthorized copyright material had to be removed, a note will indicate the deletion.

UMI®

UMI Microform DP12864

ACKNOWLEDGMENT

The writer wishes to express his appreciation to Dr. R. M. Hixon for suggesting the thesis problem and to both Dr. Hixon and Dr. I. B. Johns for their generous help and encouragement throughout its development.

He also wishes to express his appreciation for the assistance given by H. W. Perkins in the preparation of pinyl and bornyl amines.

TABLE OF CONTENTS

INTRODUCTION

The modern electronic theory of valence seems to offer the most adequate explanation of the properties of organic compounds available at the present time. According to this theory the properties of a molecule are dependent upon its electronic configuration and these properties may be varied by shifting this electronic configuration. The introduction of a substituent into an organic molecule, therefore, causes a change in the properties of the molecule because of a difference in the ability of the substituent to share electrons with, or transfer them to or from, the atoms to which they are linked. One of the most readily determined properties of the organic acids and amines is their apparent degree of ionization.

Ostwald (1) was the first to observe that the ionization constant of organic acids changed by a definite amount when a substituent was placed in the same position relative to the carboxyl group. He called those substituents which caused an increase in the dissociation constant of acetic acid negative and those which caused a decrease positive. Wegscheider (2) extended the investigations of Ostwald and summarized the available data into tables of factors which represented the effect of the position of various substituents upon the dissociation constants of organic acids. This "Ostwald Law" has been the basis for a great deal of experimental work. Walker (3) used

it in studying the effect of introducing radicals into dibasic acids and esters. Chandler (4), Adams (5) and Bjerrum (6) used it in the study of the ionization of dibasic acids.

Derick (7) attempted to establish a standard for determining the effect of introducing a radical into a molecule. He attempted to use the acidic and basic dissociation constants of certain hydroxides. If the radical substituted caused the hydroxyl to give hydrogen ions then the degree of ionization would be a measure of the negativity of the radical. If the radical caused a tendency to give hydroxyl ions the degree of ionization would be a measure of its positivity. Derick used two mathematical expressions to determine this "negativity" and "positivity".

$$\text{Negativity} = \frac{-1000}{\log K_A} \; ; \quad \text{Positivity} = \frac{-1000}{\log K_B}$$

Because of the apparent lack of ionization in so many compounds this standard was difficult to apply experimentally.

Hixon and Johns (8) have demonstrated a mathematical relationship which places organic radicals attached to a polar group in a definite order in a series. This relationship for the acids and amines was of the type:

$$\text{Log } K = k e^{ax+b} + C$$

where log K is the logarithm of the dissociation constant and

x is the abscissa value, or "electron-sharing ability", of the radical. The radicals considered must contain no polar group themselves. It was further pointed out that the electron-sharing ability appeared to be a function of the mass of the radical and the spatial configuration of the molecule as well as the potential of the atoms.

In another paper Johns and Hixon (9) applied their conception of the electron-sharing ability of organic radicals to a series of organo-mercury compounds. They used the equilibrium reaction

$$2RHgX \rightleftharpoons R_2Hg + HgX_2 .$$

From this investigation they were able to place the radicals, R, in a series whose order coincided with that obtained in the series RNH_2 and $RCOOH$.

Allison and Hixon (10) pointed out that organic radicals ranged in electron-sharing ability from those more positive than hydrogen to those more negative than chlorine. They pointed out that the literature gave no dissociation constants for unsubstituted amines free from polar groups between the values $5x10^{-5}$ and $1x10^{-9}$. They pointed out that the carbohydrate and terpene amines should give dissociation constants in this range. They prepared 2-glucosyl amine and found its dissociation constant to be $6x10^{-7}$.

Osburn (11) and Ware (12) studied the series R-AsO(OH)$_2$
by conductivity and e.m.f. methods. The series of values for
the electron-sharing ability of the radicals investigated
came in the same order as that reported by Johns and Hixon and
by Allison and Hixon for the R-NH$_2$ and R-COOH series.

Craig and Hixon (13) measured the dissociation constants
of the N-substituted and α-substituted pyrrolidines. They ob-
tained the same order of electron-sharing ability as had been
secured for the series R-NH$_2$, R-COOH, RHgX and R-AsO(OH)$_2$.
Craig (14) in a later paper attempted to correlate toxicity with
structure in a series of α-substituted N-methylpyrrolidines.
He found a relationship similar to the above in respect to
basic strength and polar properties.
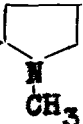
Johns and Hixon (15) have studied the effect upon the
equilibrium constant of changing the radical, R, in the equi-
librium

$$Cl_3CCH(OH)SR \rightleftharpoons Cl_3CCHO + RSH$$
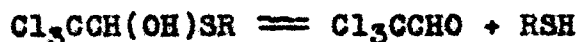
From these data they obtained values for the electron-sharing
ability of the radicals investigated which checked their pre-
vious work.

The bulk of the investigations done on ionization have been
carried out on equilibria in water solutions. Conant (16) and
other recent investigators have pointed out the possibility of

solvent effect upon constants derived from these equilibria.
Goodhue and Hixon (17) studied a series of amines and organic
acids in water, ethyl and methyl alcohol. A comparison of the
values for the dissociation constants gave curves with approx-
imately the same slope, which indicated that the change in
solvent had a constant effect upon the ionization constants of
the organic acids and bases investigated.

Mehltretter (18) extended this investigation by measuring
the ionization constants of a series of secondary amines and
α-substituted N-methylpyrrolidines in absolute methanol. He
obtained the same order of electronegativity of organic radicals
as was found in the data of Goldschmidt and Bader (19). He
also found that substitution of organic radicals in the series
$RNCH_3$, $RNHC_6H_5$ and R- ⌐⌐ affected the dissociation constants
$\overset{\text{N}}{\underset{\text{CH}_3}{}}$

of the compounds in such a way as to give an order of electro-
negativity for the radicals similar to that obtained by Hixon,
Johns and co-workers.

Brent (20) found that the solvent seems to have a constant
effect upon the free energy value for the radicals in a series
investigated by him.

Carr (21) investigated the equilibrium

$$RHgCN + HCl \rightleftharpoons RHgCl + HCN$$

and found values for the electron-sharing ability in agreement
with previous work.

STATEMENT OF THE PROBLEM

As was pointed out in the introduction, there are no amines reported in the literature with dissociation constants falling between approximately 10^{-5} and 10^{-9} except the value for 2-glucozyl amine reported by Allison and Hixon (10). These same authors suggested that other carbohydrate radicals, and also the terpene radicals, should form amines with dissociation constants ranging between the two extremes.

It is the purpose of the present study:

(1) To determine the ionization constants of some terpene amines.

(2) To determine, if possible, some types of structure whose amines might have dissociation constants in the range 10^{-5}—10^{-9}.

(3) To make qualitative observations on the degree of stability of those amines having dissociation constants between 10^{-5}—10^{-9}.

EXPERIMENTAL

Preparation of Compounds

l-Menthyl Amine.

The l-menthyl amine used in this study was obtained from the Eastman Kodak Company. The amine was dissolved in anhydrous ether and the amine hydrochloride precipitated by means of dry hydrogen chloride. The amine hydrochloride was recrystallized twice from water. The benzamide derivative gave a melting point of 156°C.

Analysis of the amine hydrochloride:

Wt. of Sample	cc. N_2	Temp.	Bar. Pres.	Per Cent N_2 Found	Calc.
0.005764	0.386	27°C.	743.4	7.30	7.31
0.005068	0.340	26°C.	732.5	7.22	

Bornyl Amine.

Bornyl amine was prepared by the reduction of camphor oxime.

Camphor oxime was prepared by the method used by Wuytz (22). Fifty grams of d-camphor were dissolved in 600 cc. of alcohol and added to a concentrated solution of 50 grams of hydroxylamine hydrochloride in water. To this 75 grams of sodium hydroxide were added followed by 150 cc. of alcohol to clear up the turbid solution. The mixture was refluxed until

a portion of the solution showed no turbidity upon dilution
with a large volume of water. This process required two and
one-half hours. The entire solution was then diluted with a
large volume of water and carefully neutralized with acetic
acid. The camphor oxime separated from the solution upon
neutralization. The melting point of the product obtained was
114-117°C. Yield, 40 grams (73% of the theoretical amount).
This product was used without further purification in the prep-
aration of bornyl amine.

Bornylamine was prepared according to the method described
by Foster (23). Fifty grams of crude camphor oxime were dis-
solved in 500 cc. of amyl alcohol. The solution was placed in
a balloon flask fitted with a reflux condenser and treated
with 50 grams of sodium in 10 gram portions. The temperature
of the reaction mixture was controlled to require about four
hours for complete solution of the sodium. Toward the end of
the reaction time 75 cc. of amyl alcohol were added to prevent
the precipitation of sodium amylate. When solution of the sod-
ium was complete the temperature of the mixture was lowered to
about 60°C. and 325 cc. of water added. Three hundred twenty-
five cubic centimeters of concentrated hydrochloric acid were
next added in small portions with vigorous shaking. Bornyl
amine hydrochloride separated from the solution upon the removal
of the amyl alcohol by steam distillation. Forty grams of the

crude bornylamine hydrochloride (88% of the theoretical amount) were obtained. Initial purification was accomplished by re-crystallization from hot water. For final purification the amine was freed from the hydrochloride by use of sodium hydroxide followed by extraction with ether and reprecipitation of the hydrochloride with hydrogen chloride gas.

The melting point of the amine hydrochloride was 311°C.

Analysis of the amine hydrochloride:

Wt. of Sample	cc. N2	Temp.	Bar. Pres.	Per Cent N2 Found	Calc.
0.004852	0.3234	28°C.	737	7.33	7.38

Pinyl Amine.

Pinyl amine was prepared by the reduction of nitroso-pinene. The nitrosopinene was prepared from pinene nitroso-chloride. α-Pinene nitrosochloride was prepared according to the method used by Wallach (24). The preparation was first at-tempted using d-α-pinene. The yield of nitrosochloride was very poor. When an optically inactive α-pinene was used the yield was satisfactory. This result is in agreement with the obser-vations of Wallach (24)(25). One hundred and forty cubic cen-timeters of l-α-pinene were prepared by adding l-α-pinene to the dextro form until the mixture showed no rotation. To this mixture was added 200 cc. of iso-amyl nitrite and 340 cc. of

glacial acetic acid. It was then cooled in an ice-salt bath.
Eighty cubic centimeters of a mixture of equal volumes of 33%
hydrochloric acid and glacial acetic acid were added very slow-
ly and with constant stirring to the pinene mixture. The blue
color appearing after each addition of the hydrochloric acid
mixture was allowed to disappear before adding the next por-
tion. The reaction mixture was kept cold for about an hour af-
ter the addition of the last portion of the hydrochloric acid
solution. The pinene nitrosochloride, a white crystalline com-
pound, was filtered from the reaction mixture and dissolved in
chloroform. Purification of the nitrosochloride was accomplish-
ed by precipitation from the chloroform solution with methanol.
This product was used in the preparation of nitrosopinene.
Yield, 28 grams (15% of the theoretical amount).

Nitrosopinene was prepared according to the method des-
cribed by Wallach (26). A solution was prepared by dissolving
6 grams of sodium in 150 cc. of 90% alcohol. Fifty grams of
pinene nitrosochloride were added and the whole refluxed for
48 hours. The nitrosopinene was precipitated by the addition
of water to the reaction mixture. Purification was accomplished
by making a paste of the dry nitrosopinene with petroleum
ether, followed by filtration and washing with several portions
of the same solvent. The yield was 39 grams (94% of the theo-
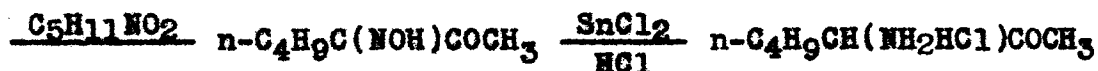retical amount).

The method described by Wallach (26) was used in the
preparation of pinyl amine. Thirty grams of nitrosopinene were
dissolved in 200 cc. of warm glacial acetic acid. The solution
was diluted with water until a slight turbidity appeared. Zinc
dust was added in small portions and the mixture refluxed on a
water bath for about 12 hours. Excess zinc dust was always
present during the reaction. After refluxing, the clear solu-
tion was decanted from the undissolved zinc and diluted with a
large volume of water. The dissolved zinc was precipitated
from the solution by the addition of hydrogen sulfide and the
filtrate concentrated until the solution began to darken.
Pinyl amine nitrate was precipitated from this solution by the
addition of a saturated solution of sodium nitrate. The pinyl
amine nitrate was recrystallized once from hot water. Thirteen
grams were obtained. Further purification was carried out as
follows. The amine was freed from the nitrate by treatment
with sodium hydroxide. The free amine was extracted from the
basic solution with ether and precipitated from the ether solu-
tion as the hydrochloride by means of gaseous hydrogen chloride.
Yield, 12 grams (23% of the theoretical amount). Melting point
of the hydrochloride 229-230°C.

Analysis of the amine hydrochloride:

Wt. of Sample	cc. N_2	Temp.	Bar. Pres.	Per Cent N_2 Found	Per Cent N_2 Calc.
0.003474	0.235	28°C.	737	7.44	7.45

α-Aminoamyl Methyl Ketone.

α-Aminoamyl methyl ketone was prepared by the following series of reactions:

$$n\text{-}C_5H_{11}COOH \xrightarrow{SOCl_2} n\text{-}C_5H_{11}COCl \xrightarrow{CH_3ZnI} n\text{-}C_5H_{11}COCH_3$$

$$\xrightarrow{C_5H_{11}NO_2} n\text{-}C_4H_9C(NOH)COCH_3 \xrightarrow[HCl]{SnCl_2} n\text{-}C_4H_9CH(NH_2HCl)COCH_3$$

n-Caproyl chloride was prepared in 84% yield through the action of thionyl chloride upon n-caproic acid. n-Amyl methyl ketone was prepared in 48% yield by the action of zinc methyl iodide upon n-caproyl chloride. The boiling point of the ketone was 150-151°C. Isonitroso amyl methyl ketone was prepared by the method used by Pezold and Shriner (27) for the preparation of α-nitrosocyclohexanone. One hundred nine grams of amyl methyl ketone and 140 grams of isoamyl nitrite were dissolved in 300 cc. of absolute ether. A second solution was prepared by dissolving 23 grams of sodium in a mixture of 475 cc. of absolute alcohol and 600 cc. of absolute ether. The second solution was cooled by means of an ice salt bath and to it the first solution was added slowly with constant stirring. The stirring and cooling was continued for about three hours after the addition of the first solution was completed. The reaction mixture was extracted with dilute sodium hydroxide solution. The dissolved ether was expelled by heating and the oxime freed

from solution by acidification with acetic acid. Yield, 80 grams of crude compound (58% of the theoretical amount).

α-Aminoamyl methyl ketone was prepared by the method described by Behr and Bregowski (28) for the preparation of α-amino hexylmethyl ketone. Thirty-two grams of isonitroso-amyl methyl ketone were slowly added to a well cooled solution of 99 grams of stannous chloride in 143 grams of concentrated hydrochloric acid. The mixture was stirred constantly during the addition of the oxime and for about twenty-four hours thereafter. Metallic tin was then added and allowed to stand in contact with the reaction mixture over night. After filtering to remove the excess tin the solution was diluted to two liters from which the dissolved tin was precipitated with hydrogen sulfide. The solution was filtered and concentrated to about 200 cc. over a free flame and then evaporated to dryness under vacuum. The amine hydrochloride was extracted from the resultant dry residue with absolute alcohol and recovered by distillation. Yield, 11 grams (29% of the theoretical amount). The amine hydrochloride was recrystallized four times from a mixture of equal volumes of absolute alcohol and petroleum ether. The melting point for the last two crystallizations of the hydrochloride was constant at $130^{\circ}C$.

Analysis of amine hydrochloride:

Wt. of Sample	cc. N_2	Temp.	Bar. Pres.	Per Cent N_2 Found	Calc.
0.004182	0.325	$25.5^{\circ}C$.	735	8.43	8.46

Camphor Amine.

Camphor amine was prepared by reducing isonitrosocamphor.

Isonitrosocamphor was prepared by the method used by
Claisen and Manasse (29). Fifteen and two-tenths grams of sod-
ium shot were added to a solution of 102 grams of camphor in
500 cc. of dry ether. After the reaction had ceased the mix-
ture was cooled with an ice-salt mixture to about -10°C. and a
small portion of isoamyl nitrite added. The reaction mixture
was stirred constantly until a yellow color and a foaming in-
dicated the reaction was under way. When this occurred the re-
mainder of the isoamyl nitrite (78 grams) was added slowly.
Vigorous stirring was continued during the addition of the iso-
amylnitrite and for about twenty minutes after. The tempera-
ture was held near -10°C. This mixture was left standing in
the cold for three hours and then ice water added. The aqueous
layer was removed and extracted three times with ether to re-
move any unreacted camphor. Dissolved ether was removed by
means of a stream of air. The isonitrosocamphor was freed
from the solution by acidifying with acetic acid and used in
the preparation of -aminocamphor without further purification.
Yield, 59 grams (53% of the theoretical amount).

α-Aminocamphor was prepared by a modification of the method
used by Claisen and Manasse (29). Sixty and fifty-six hundredths
grams of isonitrosocamphor were dissolved in a mixture of 340 cc.

of acetic acid and 675 cc. of water. The solution was placed
in a balloon flask fitted with an air cooled condenser and re-
fluxed over a hot-plate for approximately two hours. Small por-
tions of zinc dust were added from time to time during the re-
fluxing. At the end of the refluxing period the undissolved
zinc was filtered from the mixture. Solid NaOH was added until
the precipitated $Zn(OH)_2$ redissolved and a red-yellow waxy oil
separated. The solution was extracted with three portions of
ether and the ether solution dried over KOH. The amine hydro-
chloride was precipitated by passing dry HCl gas into the ether
solution. An attempt to purify a portion of the free amine by
distillation under a vacuum of 15 mm. resulted in decomposition
with the appearance of a waxy camphor-like body and the liber-
ation of a large amount of ammonia. Purification of the amine
hydrochloride was finally accomplished by four recrystalliza-
tions from a mixture of absolute alcohol and acetone. Yield,
57 grams (99% of the theoretical amount) crude amine hydro-
chloride.

The melting point of the hydrochloride was $221^\circ C$.

Analysis of the amine hydrochloride:

Wt. of Sample	cc. N_2	Temp.	Bar. Pres.	Per Cent N_2	
				Found	Calc.
0.006382	0.427	$27^\circ C$.	743	6.80	6.88
0.005594	0.349	$26^\circ C$.	743	6.83	

∝-Amino Cyclohexanone.

An attempt was made to prepare ∝-amino cyclohexanone by the reduction of ∝-nitroso cyclohexanone. The oxime was prepared by the method used by Pezold and Shriner (27). Thirteen and eight-tenths grams of sodium were dissolved in 300 cc. of absolute alcohol. This was diluted with 400 cc. of absolute ether. The sodium ethylate ether mixture was cooled to about -10°C. by means of an ice-salt bath. To this solution was added slowly, with constant stirring, a mixture of 60 grams cyclohexanone, 88.2 grams isoamylnitrite and 900 cc. absolute ether. After three hours continuous stirring a red precipitate, the sodium salt of ∝-nitroso cyclohexanone, separated and was filtered and then washed with absolute ether. The yield was 51 grams, 56% of the theoretical amount.

Attempts were made to reduce ∝-nitroso cyclohexanone both chemically and by catalytic hydrogenation. In neither case could any ∝-amino cyclohexanone be isolated. In one catalytic hydrogenation, using palladium black as a catalyst, 3.8 grams of ∝-nitroso cyclohexanone were suspended in 75 cc. of water to which had been added 0.03M of hydrogen chloride. This mixture absorbed 1330 cc. of hydrogen. The theoretical volume needed to reduce the oxime to the amine is 1340 cc. Upon concentrating the reaction mixture under a vacuum, a white crystalline solid separated and was identified as ammonium chloride. From

the liquid fraction a semi-carbazone was obtained, melting point 165°C. This checked with the melting point of the semi-carbazone of cyclohexanone, 166°C. No amine was detected in the reaction mixture.

Measurement of Dissociation Constants

Method of Measurement.

The method used in the determination of the dissociation constants was essentially the half neutralization method of Carothers, Bickford and Hurwitz (30). Because of the instability of most of the amines used in this investigation, it was found impossible to obtain the free amines in a sufficiently pure condition. The hydrochlorides of the amines, however, proved to be much more stable and could be obtained in a sufficiently pure state. Carothers, Bickford and Hurwitz calculated the dissociation constant from the hydrolysis constant which is equal to the hydrogen ion concentration when the base is half neutralized. They added an half equivalent of hydrogen chloride to a solution of the free amine. It seemed likely that the same result could be obtained by adding an half equivalent of sodium hydroxide to a solution of an amine hydrochloride.

To test this hypothesis the dissociation constant of an-

iline was calculated from the hydrogen ion concentration of a
solution prepared by adding an half equivalent of sodium hy-
droxide to the aniline hydrochloride. The value thus calculat-
ed checked the published value for the dissociation constant of
aniline (31)(32). The following table gives a comparison of
these values.

Wt. Aniline Hydrochloride in 250 cc.	cc's NaOH 0.02885N	Pres-sure mm.Hg	E.M.F. Obs.	E.M.F. 760 mm.	Dissociation Constant	
					Found	Reported
0.2007	26.85	737	0.5133	0.5142	3.5×10^{-10}	3.0×10^{-10} [*]
0.2011	26.95	737	0.5134	0.5143	3.5×10^{-10}	
0.2019	27.01	737	0.5144	0.5153	3.6×10^{-10}	3.7×10^{-10}
0.2004	26.81	737	0.5144	0.5153	3.6×10^{-10}	

[*] Determined at $20^{\circ}C$.

Apparatus Used.

The potentiometer used in this work was the same type as
the electron tube potentiometer described by Goodhue, Schwarte,
and Fulmer (33) and used by Goodhue and Hixon (17).

Two saturated calomel half-cells were used as reference
electrodes. These half-cells gave zero potential when set
against each other and could be used interchangeably in the
measurement of e.m.f.

The hydrogen electrodes used were made of platinum flags

about 7 mm. square and plated with palladium black. A one per
cent solution of palladium chloride in HCl containing a trace
of lead acetate was used in plating. The electrodes were im-
mersed in the palladium chloride solution and a current density
of about 0.4 amperes was applied for three minutes. After be-
ing washed with distilled water the electrodes were electro-
lyzed in dilute sulfuric acid for five minutes, again washed
in distilled water and then in the solution in which they were
to be used.

An attempt was made to use platinum electrodes plated with
platinum black but these proved much less reliable than those
plated with palladium black. This is in agreement with the ob-
servations of Goodhue and Hixon (17).

All e.m.f. measurements made in this investigation were
carried out in a constant temperature air bath at $25° \pm 0.1°$, the
temperature being controlled by a sensitive DeKhotinsky regu-
lator.

Measurement of E.M.F.

The hydrogen half-cell was separated from the saturated
calomel half-cell by a junction through a closed, ungreased
glass stopper. This prevented diffusion of the calomel to the
hydrogen electrode and subsequent poisoning. (See Figure 1.)

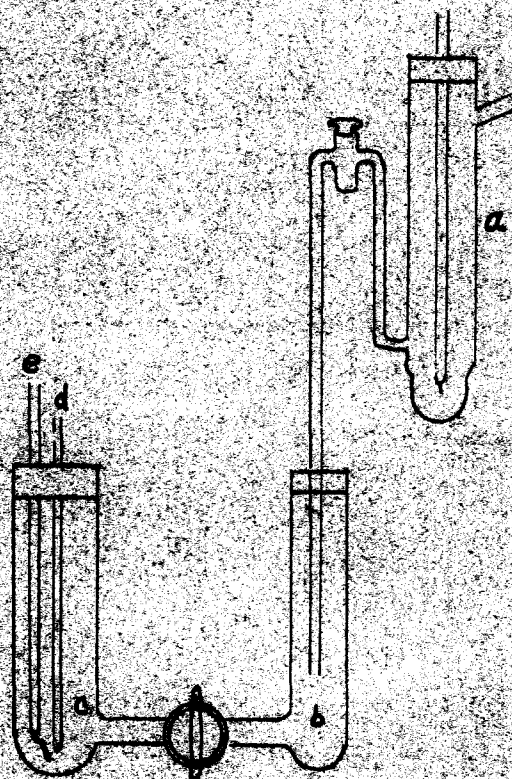The hydrogen electrode was mounted in the cell completely

Figure I. Cell used in e.m.f. measurements.
a, Calomel half-cell; b, saturated KCl
solution; c, half neutralized amine so-
lution; d, hydrogen inlet; e, Pt flag.

immersed in the solution. Hydrogen gas was bubbled from below up over the flags. (See Figure 1.) The hydrogen used was deemed sufficiently pure if the correct e.m.f. was obtained with the hydrogen electrode in 0.05M potassium acid phthalate.

Fresh hydrogen electrodes were used for each e.m.f. measurement. They were checked against 0.05M potassium acid phthalate before and after each determination. Values were used only when a reading of 0.4805 volts $\pm$0.5 millivolts was obtained against the acid phthalate. All e.m.f. measurements against the phthalate buffer ranged from 0.4800 to 0.4806 volts.

Solutions whose e.m.f. were to be measured were used immediately after preparation. The amine hydrochloride was weighed, dissolved in water, an half equivalent of sodium hydroxide added and the solution diluted to volume. In each measurement of e.m.f. the voltage rose rapidly to a maximum. The time used in reaching this maximum ranged between four and eight minutes in each case, with the exception of α-aminoamyl methyl ketone. This amine required nearly fifteen minutes to reach a constant e.m.f.

The e.m.f. readings for menthyl amine, bornyl amine and pinyl amine showed a very gradual drift downward from the maximum reading. Check measurements upon the same solutions made from two to five days later gave the same maximum readings and

showed the same slow drift downward. With α-amino amyl methyl ketone the e.m.f. rose very slowly after reaching a constant value. With one sample this upward drift continued for 140 minutes, the e.m.f. changing about 2.5 millivolts. Check readings upon the same solutions made three hours later gave a much lower e.m.f. reading. A solution made up and immediately measured gave a value of 0.7300 volts. This same solution measured three hours later gave a reading of 0.6997 volts. The solutions were turbid and yellow in color, showing evidence of decomposition. Camphor amine gave constant values for the e.m.f. after equilibrium was reached.

In Table I are tabulated the dissociation constants, as -log K_B, for the above amines.

Table I.

Tabulated Results from E.M.F. of
Cells of Half Neutralized Amines

Pd/H_2(1 atm.) amine sol.//KCl(sat.), Hg_2Cl_2/Hg

Substance	Wt. of Amine•HCl	cc's NaOH 0.01586N	Pressure mm. Hg	E.M.F. Obs.	E.M.F. 760 mm.	-log K_B
1-Menthyl amine	0.0859*	14.12	738	0.8478	0.8486	3.81
	0.1023*	16.85	738	0.8489	0.8497	3.79
Bornyl amine	0.1025**	17.04	734	0.8290	0.8299	4.17
	0.0410*	6.82	742	0.8294	0.8302	4.12
Pinyl amine	0.0857*	14.06	734	0.7522	0.7531	5.42
	0.1002*	16.84	734	0.7521	0.7530	5.42
α-Amino amyl methyl ketone	0.0487***	9.27	737	0.7287	0.7296	5.82
	0.0609***	11.55	731	0.7300	0.7310	5.80
	0.0543***	10.34	726	0.7302	0.7313	5.79
Camphor amine	0.2065**	18.13ᵠ	742	0.6644	0.6652	6.91
	0.2052**	18.02ᵠ	742	0.6697	0.6705	6.82
	0.2036**	17.88ᵠ	742	0.6644	0.6652	6.91
	0.2046**	17.96ᵠ	742	0.6611	0.6619	6.96

*Made up to 100 cc. solution.
**Made up to 250 cc. solution.
***Made up to 50 cc. solution.
ᵠNormality 0.02797.

DISCUSSION OF RESULTS

The common classification of organic compounds into the three main classes, aliphatic, heterocyclic and aromatic, makes the study of those compounds of interest to the biologist a difficult matter. A careful study of the free energy of reaction of the so-called aliphatic and aromatic compounds has shown definitely that these two groups, while seemingly quite distinct, tend to merge into each other. This is illustrated by Table II.

An examination of this table shows that the typical aliphatic amines are much stronger bases than the typical aromatic amines. There are, however, certain aliphatic amines which approach aromatic amines in basic strength and some alkyl amines that are even more slightly dissociated than the typically aryl compounds.

Looking critically at the ionization constants listed in Table II, it is noticeable that a distinct gap exists from 10^{-5} to 10^{-9}. There are but few primary amines known which possesses ionization constants within this range. As has been previously stated, there has been some evidence to indicate that the unstable carbohydrate and terpene amines should possess constants of about this magnitude. Thus these compounds should serve as the connecting link between the strictly aliphatic and strictly aromatic types.

Table III shows the constants obtained in several studies on the primary and secondary amines. The radicals in this table are arranged in the same order used in Table II.

The investigations on the ionization constants of the nitrogen heterocyclics, carried out in this laboratory, are summarized in Table IV. Here also, the radicals are arranged in the same order as in Table II.

The work on the ionization constants of the carboxylic and arsonic acids is tabulated in Table V.

Several studies have been made of equilibria not involving ionization. These are summarized in Table VI.

A critical examination of the data presented in Tables II to VI gives rise to a number of interesting points. Each series may be plotted on a curve of the exponential type referred to in the introduction. In each case the order of the radicals plotted as abscissa values is the same. The position of the cyclohexyl radical was determined by the ionization constant given for the amine by Hall and Sprinkle (32) as well as the constants listed in these tables. The tendency of the so-called aliphatic and aromatic amines to merge, when arranged in order of their ionization constants, is found in other series as well. In Tables III, IV, V and VI it will be observed that gaps occur in each series coincidental with that referred to in the discussion of the amines listed in Table II. These gaps

Table II.

Dissociation Constants of Corresponding Polar Compounds of Various Radicals in Water at 25°C. (8).

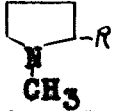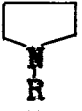| Radical	Amines $RNH_2 \cdot H_2O$	Acid $R \cdot COOH$	Acid RCH_2COOH	Acid RCH_2CH_2COOH	Hydroxide ROH
$(CH_3)_3C-$	3×10^{-4}	1×10^{-5}			
$CH_3CH_2CH_2-$	5×10^{-4}	1×10^{-5}	1×10^{-5}	1×10^{-5}	
CH_3CH_2-	5×10^{-4}	1×10^{-5}	1×10^{-5}	1×10^{-5}	10^{-15}
CH_3-	5×10^{-4}	1×10^{-5}	1×10^{-5}	1×10^{-5}	
$CH_3CH=CHCH_2-$	4×10^{-4}	5×10^{-5}	3×10^{-5}		
$C_6H_5CH_2-$	2×10^{-5}	5×10^{-5}	2×10^{-5}		
$CH_2=CH-$	6×10^{-5}	6×10^{-5}	4×10^{-5}	2×10^{-5}	
$H-$	2×10^{-5}	2×10^{-4}	2×10^{-5}	1×10^{-5}	10^{-14}
$C_6H_4CH_3-p$	2×10^{-9}	5×10^{-5}			
$C_6H_4OCH_3-p$	6×10^{-9}	3×10^{-5}			
$C_6H_4CH_3-m$	6×10^{-10}	5×10^{-5}			
$C_6H_4OCH_3-o$	2×10^{-10}	8×10^{-5}			
C_6H_5-	3×10^{-10}	7×10^{-5}	5×10^{-5}	2×10^{-5}	10^{-10}
$C_6H_4CH_3-o$	3×10^{-10}	1×10^{-4}			
C_6H_4Br-p	2×10^{-10}				
C_6H_4Cl-p	1×10^{-11}	9×10^{-5}			10^{-10}
C_6H_4Br-m	9×10^{-11}	1×10^{-4}			
$C_{10}H_7-$	9×10^{-11}	2×10^{-4}			
C_6H_4Cl-m	6×10^{-12}	2×10^{-4}			
$C_6H_4NO_2-p$	1×10^{-12}	4×10^{-4}			10^{-8}
$C_6H_4NO_2-m$	4×10^{-12}	3×10^{-4}			
H_2IC-		7×10^{-4}	9×10^{-5}	2×10^{-5}	
C_6H_4Cl-o	9×10^{-13}	1×10^{-3}			10^{-9}
CH_3CHCl-		2×10^{-3}	9×10^{-5}		
H_2CBr-		1×10^{-3}	1×10^{-4}	3×10^{-5}	
H_2CCl-		1×10^{-3}	9×10^{-5}	3×10^{-5}	
$C_6H_4NO_2-o$	1×10^{-14}	6×10^{-3}			
$H_2C(NO_2)-$			2×10^{-4}		
$CH_3-C\equiv C-$		3×10^{-3}			
$H_2C(CN)-$		4×10^{-3}			
C_2H_5OOC-			5×10^{-4}	3×10^{-5}	
$HCCl_2-$		5×10^{-2}			
$I-$			8×10^{-4}	9×10^{-5}	
$Br-$			1×10^{-3}	1×10^{-4}	
$Cl-$			1×10^{-3}	9×10^{-5}	10^{-8}
$CN-$			4×10^{-3}		
NO_2-				2×10^{-4}	

Table III.

Tabulation of Ionization Constants of Some Primary and Secondary Amines Measured in Methanol in this Laboratory (17)(18)(34).

Radical	$R-NH_2$ $-\log K_B$	$\dfrac{CH_3CHNH_2}{R}$ $-\log K_B$	$\dfrac{CH_3}{R}NH$ $-\log K_B$	$\dfrac{C_6H_5}{R}NH$ $-\log K_B$	R_2NH $-\log K_B$
$n-C_4H_9-$	4.92		4.95		5.15
C_2H_5-		4.97			
CH_3-				10.98	
CH_2OHCH_2-			5.66	11.41	6.11
$C_6H_5CH_2-$		5.47	6.77	11.73	7.38
$\underline{o}-ClC_6H_4CH_2-$	6.61				
$\underline{o}-ClC_6H_4-$		5.66			
$\underline{p}-CH_3OC_6H_4-$				14.15	13.45
$\underline{p}-CH_3C_6H_4-$	10.00	5.67	10.50	14.31	13.98
C_6H_5-	10.53	5.80		14.50	14.50
$\underline{p}-C_6H_5 \cdot C_6H_4-$		5.90			
$\underline{m}-ClC_6H_4-$	12.14				
$\alpha-C_{10}H_7-$			11.87	14.82	

TABLE IV.

Ionization Constants of Some Substituted Nitrogen Heterocyclics* (13)(17)(18)(35).

Radical	$\text{N}-R$		$\text{N}-R$	$\text{N}-R$ (CH$_3$)	$\text{N}-R$
	Kx10^{-5}		-log K_B	-log K_B	K_B
H—					1.3×10^{-3}
C$_6$H$_{11}$—	64.0	1.3 *	6.05		5.0×10^{-4}
n-C$_4$H$_9$—				6.31*	2.3×10^{-4}
n-C$_3$H$_7$—				6.27*	
C$_2$H$_5$—	27.0		6.09	6.31*	
CH$_3$				6.23*	1.5×10^{-4}
C$_6$H$_5$CH$_2$—	23.0	0.38*	6.92		3.2×10^{-5}
p-CH$_3$O·C$_6$H$_4$—				7.02*	
p-CH$_3$C$_6$H$_4$—	10.0	0.21*	6.41		5.0×10^{-10}
C$_6$H$_5$—	4.0	0.15*	7.25	7.34*	2.0×10^{-10}
p-ClC$_6$H$_4$—				7.66*	
β-Pyrrodyl				8.55*	

*Those values marked with a star were measured in absolute methanol. Unmarked values were obtained from water solutions.

Table V.

Tabulation of Ionization Constants of the
Carboxcylic and Arsonic Acids (11)(12)(17)(36).

Radical	RCOOH* -log K	RAsO(OH)$_2$ K$\times 10^{-4}$
n-C$_4$H$_9$—		0.54
n-C$_3$H$_7$—		0.55
CH$_3$—	9.34	1.06
C$_6$H$_5$C$_3$H$_6$—		0.55
CH$_2$(OH)CH(OH)CH$_2$—		0.99
CH$_3$CH=CH—		1.06
C$_6$H$_5$CH$_2$—		1.20
o-ClC$_6$H$_4$CH$_2$—		1.40
p-CH$_3$C$_6$H$_4$—	9.33	
C$_6$H$_5$—	9.12	2.60
CH$_3$CHBrCHBr—		3.60
p-BrC$_6$H$_4$—	8.74	
p-ClC$_6$H$_4$—		4.20
o-ClC$_6$H$_4$—		4.10
m-ClC$_6$H$_4$—	8.57	5.20

*These values were determined in absolute methanol.

Table VI.

**Tabulation of Equilibrium Constants from
Studies of Non-ionizing Equilibria (9)(15)(21)(37).**

Radical	$2RHgNO_3$ — $R_2Hg+Hg(NO_3)_2$ $Kx10^{-5}$	$2RHgI$ — $R_2Hg+HgI_2$ $Kx10^{-2}$	$RHgCN+HCl$ — $RHgCl+HCN$ $Kx10^{-2}$	$RSH+Cl_3CCHO$ — $Cl_3CCH(OH)SR$ $Kx10^{-2}$
C_6H_{11}—			0.15	
$n-C_4H_9$—	1.2	0.3		0.20
C_2H_5—	7.2	0.6	8.30	0.24
CH_3—	7.5	1.2	4.00	
$C_6H_5CH_2$—	2.0	27.0	5.70	0.28
$o-ClC_6H_4CH_2$—			4.50	
$p-CH_3C_6H_4$—	1.5	70.0	2.50	1.50
C_6H_5—	85.0	100.0	2.60	2.20
$p-ClC_6H_4$—				4.10
$C_{10}H_7$—			1.90	

are particularly noticeable in the series involving ionization equilibria.

As has been stated in the experimental part of this thesis, the e.m.f. readings obtained for cells using half-neutralized solutions of l-menthyl, bornyl and pinyl amines drifted slowly downward after rising rapidly to a maximum. This slow fall in voltage was most noticeable in the case of l-menthyl amine and less evident when bornyl and pinyl amines were used. It seems likely that this slow drop in e.m.f. was caused by the escape of the free amine from solution, aided by the sweeping action of the hydrogen gas. The odor of free amine was very strong from each of the three solutions just mentioned, particularly so in the case of l-menthyl amine.

The gradual increase in voltage previously reported for α-aminoamyl methyl ketone was probably caused by the slow decomposition of the free amine and the subsequent liberation of ammonia. Evidences for this decomposition will be discussed later.

The amines studied in this investigation have ionization constants ranging from 1.6×10^{-4} to 1.2×10^{-7}. It is interesting to note that those terpene amines having the most typical terpene structures have constants of lesser magnitude, while those which have been modified until they more nearly resemble the saturated aliphatic compounds have the greater constants.

This is in agreement with the predictions previously made regarding the terpene amines.

One of the purposes of this investigation was to determine whether the terpene amines, whose ionization constants range between 10^{-5} and 10^{-9}, give evidences of decomposition. These observations of stability are entirely qualitative, since every case in which decomposition occurred was apparently an irreversible process and no method could be devised to study them reversibly.

No evidence of decomposition of l-menthyl amine ($K_B = 1.6 \times 10^{-4}$) could be observed under any ordinary treatment. It could be distilled at atmospheric pressure (B.P. 205°C.). The free amine could be liberated from its hydrochloride by means of strong sodium hydroxide with no evidence of the formation of ammonia.

Bornyl amine ($K_B = 7.2 \times 10^{-5}$) also showed no sign of instability. The free amine (M.P. 163°) is used as a solvent in the microchemical determination of molecular weight. It also may be treated with strong caustic without any sign of liberation of ammonia.

Pinyl amine ($K_B = 3.8 \times 10^{-6}$) shows only slight evidence of instability. Attempts were made to distill it at atmospheric pressure (B.P. 206°C.) the amine turning very dark and perhaps liberating a small amount of ammonia, as evidenced by the odor.

Distillation of the amine is accomplished readily, however, at reduced pressure (90°C. at 12 mm.). This amine gave no evidence of decomposition when treated with strong sodium hydroxide solution.

Camphor amine ($K_B=1.2 \times 10^{-7}$) proved to be rather unstable. An attempt to distill the free amine under a vacuum of 15 mm. resulted in the very rapid evolution of ammonia and the appearance of a white, waxy, camphor-like substance. All attempts to purify the free amine from ammonia proved futile. Purification of the hydrochloride was accomplished.

α-Aminoamyl methyl ketone was prepared for purposes of comparison with camphor amine. Its ionization constant is 1.6×10^{-6}. This indicates that the radical, $(C_4H_9)(CH_3CO)CH-$, is less negative than the camphor radical but more negative than the pinyl and bornyl radicals. This amine is also unstable. The free amine cannot be distilled without some decomposition and the liberation of ammonia. Some difficulty was also experienced in the purification of the amine hydrochloride. Boiling of a solution of the hydrochloride in absolute alcohol— petroleum ether mixture resulted in the slow formation of a precipitate of ammonium chloride. Recrystallization without decomposition was effected at lower temperatures. Liberation of the free amine from the hydrochloride by use of strong caustic results in some decomposition and loss of ammonia.

This is particularly true at higher temperatures.

Attempts were made to prepare a number of other alpha-amino ketones. The attempt to synthesize α-amino cylclohexanone has been described in the experimental part of this thesis. This description gives further evidence of the instability of these α-amino ketones and their tendency to split out ammonia. An effort was made to synthesize α-amino pulegone and α-amino methone from the corresponding oximes. In neither case was reduction carried out successfully.

It seems evident from the material presented above that, as the ionization constants of the amines decrease from 10^{-5} to 10^{-7}, the tendency of the amines to decompose, with the liberation of ammonia, increases. This conclusion is strengthened by the observations of Allison and Hixon (10) upon the decomposition of 2-glucosyl amine, referred to in the introduction. It would be interesting to prepare amines with ionization constants between 10^{-7} and 10^{-9} and study their stabilities. This is beyond the scope of the present investigation. It seems likely to the author, however, that the stability of the amines may pass through a minimum in those compounds possessing ionization constants between 10^{-5} and 10^{-9}. Whether such a minimum actually exists or whether there is merely an instability range has not been determined in this investigation. Some method of quantitatively measuring the instability of this type of com-

pound must be devised before the question can be answered. Study should also be made of the correlation between stability and equilibrium constant of other types of polar compounds. A beginning has been made in the work of Johns, Peterson and Hixon (37) on the stability of certain $RHgNO_3$ compounds and in the study by Carr (21) of the stability of some $RHgCN$ compounds.

When an attempt is made to correlate a gradient series based upon some fundamental property with some other property, the appearance of irregularities is not unusual. In the inorganic field, there are many cases in which the stability of a series of compounds runs directly contrary to our present theories of the relationship between potential and affinity. We might cite, for example, such discrepancies with the electrochemical series.

The fundamental assumptions of the electrochemical conception of valence have been expressed as follows by Hildebrandt (38): "The basis of the 'replacement series' is the ease with which elements lose or gain electrons. As we now usually say, sodium is a very positive element because it has a loosely held outer electron, which readily passes to a chlorine atom, where it is tightly held, completing a stable octet. In potassium the outer or valence electron is more loosely held, so that potassium chloride is formed with greater evolution of energy than is sodium chloride. The ease with which

electrons are lost or gained has been measured directly as ion-
ization potential".

In Table VII are listed some elements in order of their
increasing ionization potentials. Included in this table are
the heats of formation of the oxides, hydroxides, fluorides
and chlorides. The heats of reaction for the following chem-
ical changes are also tabulated:

1. $R_2O + H_2O = 2\ ROH + \Delta H_1$

2. $ROH + HCl = RCl + H_2O + \Delta H_2$

3. $R_2O + HCl = ROH + RCl + \Delta H_3$

4. $3R_2O + 2Al = 6R + Al_2O_3 + 3\Delta H_4$

If a smooth curve be drawn (ΔH_1 in Figure II) and the
values for ΔH_1 from Table VII be placed upon it, abscissa
values for the elements will be obtained which may be called
the electron-sharing ability of the elements. Curves for the
data in Table VII are plotted in Figures II and III. It will
be observed that the magnitudes of the heats of formation of
the chlorides (ΔH_{RCl}) are in the relative order required by
our present theories of valence. The heats of formation of
the fluorides (ΔH_{RF}), of the hydroxides (ΔH_{ROH}) and of the ox-
ides (ΔH_{R_2O}) are not in this order and are examples which are
discrepant with the electrochemical theory of valence. While
the magnitudes of the heats of formation of the oxides and hy-

droxides are discrepant with our present ideas of affinity, yet
when they are combined as in reactions 1, 2 and 3, the magni-
tudes of the heats of reaction ΔH_1, ΔH_2 and ΔH_3 are in harmony
with the theory. On the other hand, the summation of the heats
of reaction as in equation 4 is quite abnormal so far as theory
is concerned.

The curves in Figures II and III show clearly that the dis-
crepancies which exist when an attempt is made to correlate cer-
tain other properties of the elements with their ionization po-
tentials may be more fancied than real. The apparently dis-
crepant properties plot smooth curves, in some cases possessing
maxima or minima. This same condition could also exist in a
series of amines, in which stability plotted against electron-
sharing ability might show a minimum. This unstable range is
indicated in Figure IV, where the electron-sharing abilities of
the radicals are plotted against the ionization constants for
the amines.

Table VII.

Tabular Comparisons of the Heats of Formation and Heats of Reaction for a Series of Elements in the "Replacement Series"

| Element	Ionizing Potential	Heat of Formation				Heat of Reactions			
		ΔH_{R_2O}	ΔH_{ROH}	ΔH_{RF}	ΔH_{RCl}	ΔH_1	ΔH_2	ΔH_3	ΔH_4
Cs	3.88	83	102	107	106	53	48	101	44
Rb	4.16	84	102	108	105	52	47	99	43
K	4.32	87	104	109	105	53	45	98	40
Na	5.12	101	103	111	99	37	43	77	26
1/2 Ba	5.19	126	109	112	98	24	33	57	1
Li	5.37	142	115	120	97	20	26	46	-15
1/2 Sr	5.67	140	112	117	98	17	30	46	-13
1/2 Ca	6.09	152	116	119	95	12	23	35	-23
1/2 Mg	7.61	144	108	105	75	5	11	15	-17
1/3 Al		127	99	83	54	3	1	2	0
H	13.54	68	68	38	24	0	0	0	59
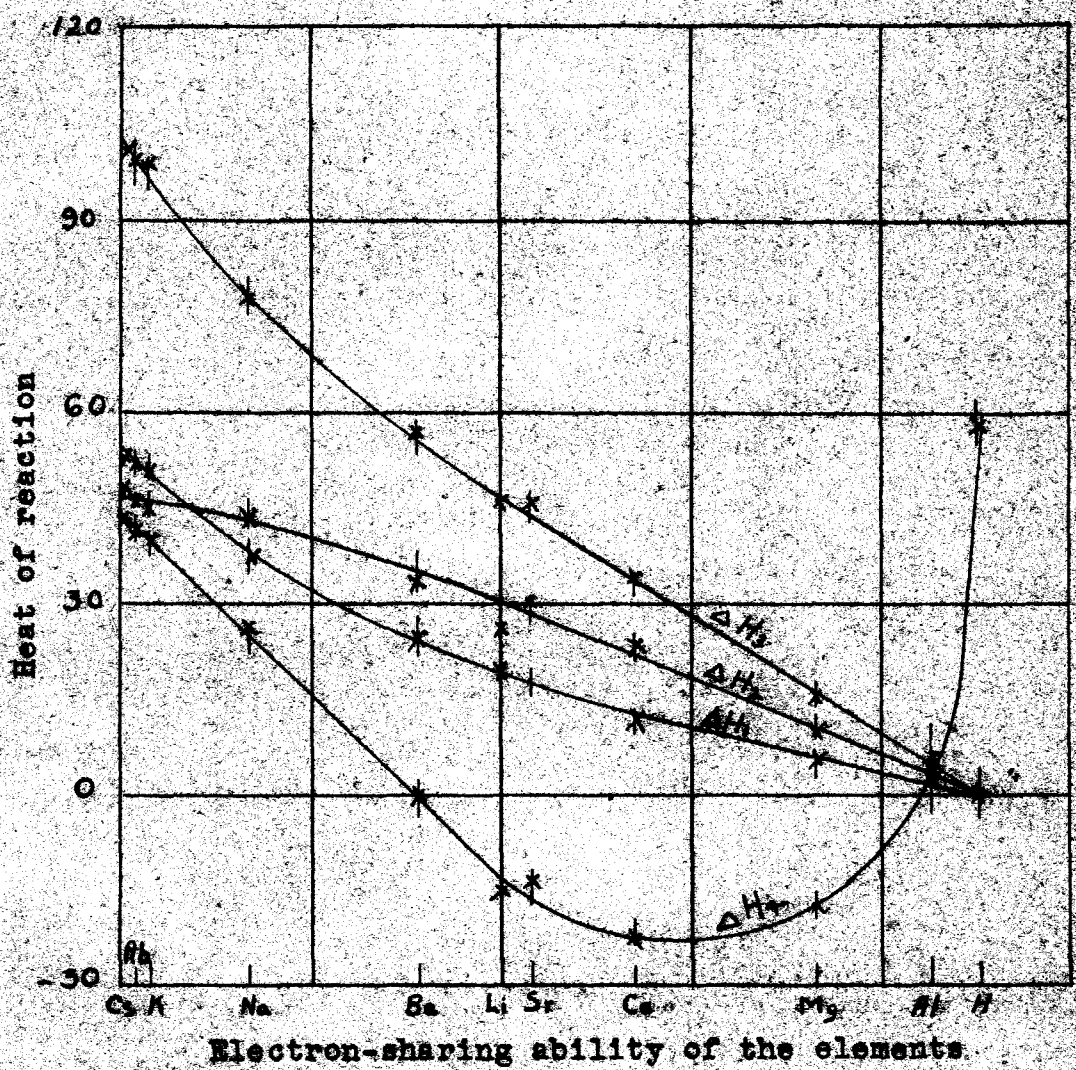
Figure II. Relation of heats of reaction to the electron-sharing ability of the elements. The equation of the curve H_1 is $H_1 = 13.1(e^{-0.18x} - 1)$.
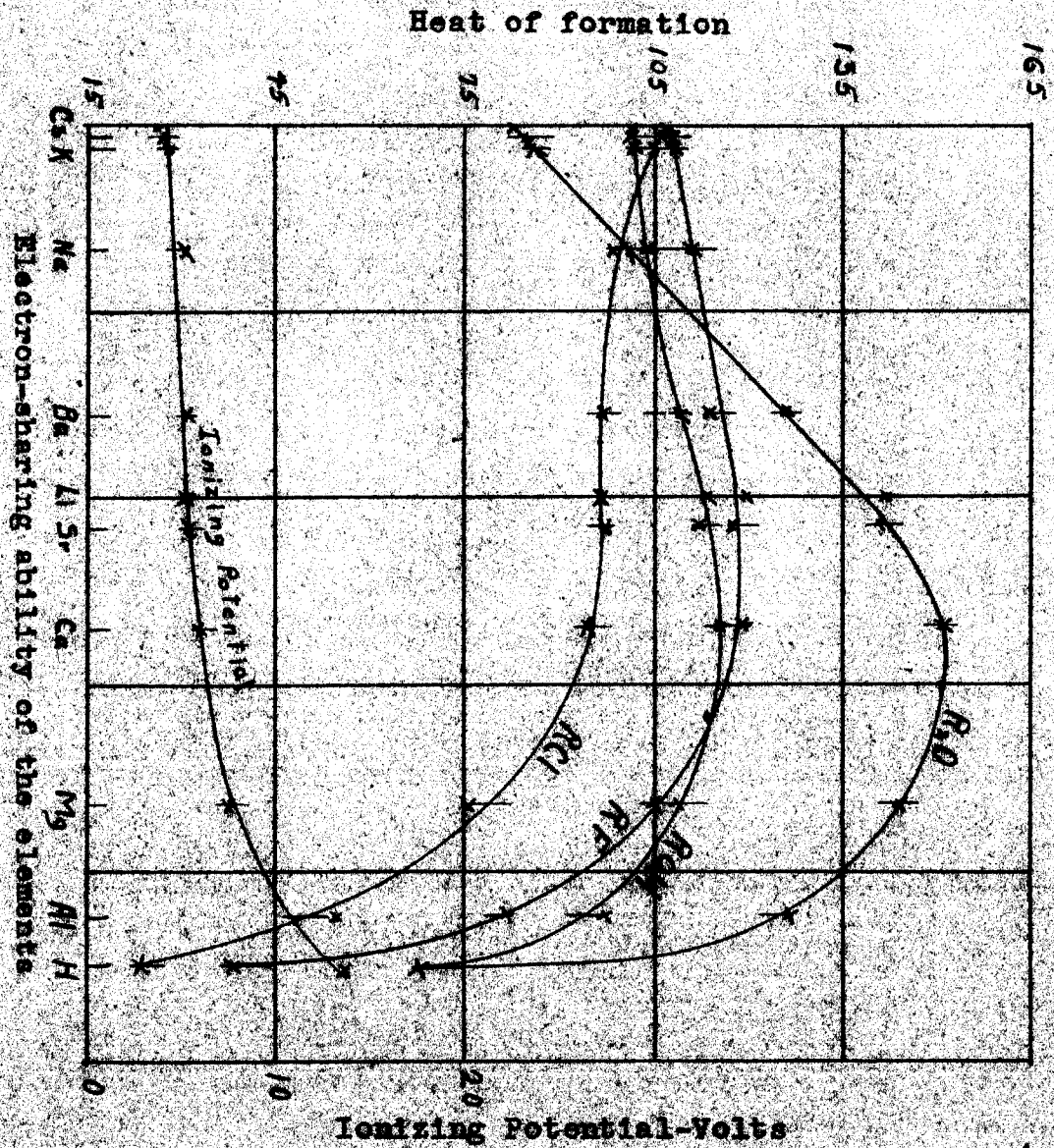
Figure III. Relation between the heat of formation of the oxide, hydroxide, fluoride and chloride of various elements arranged in the order of their electron-sharing ability.
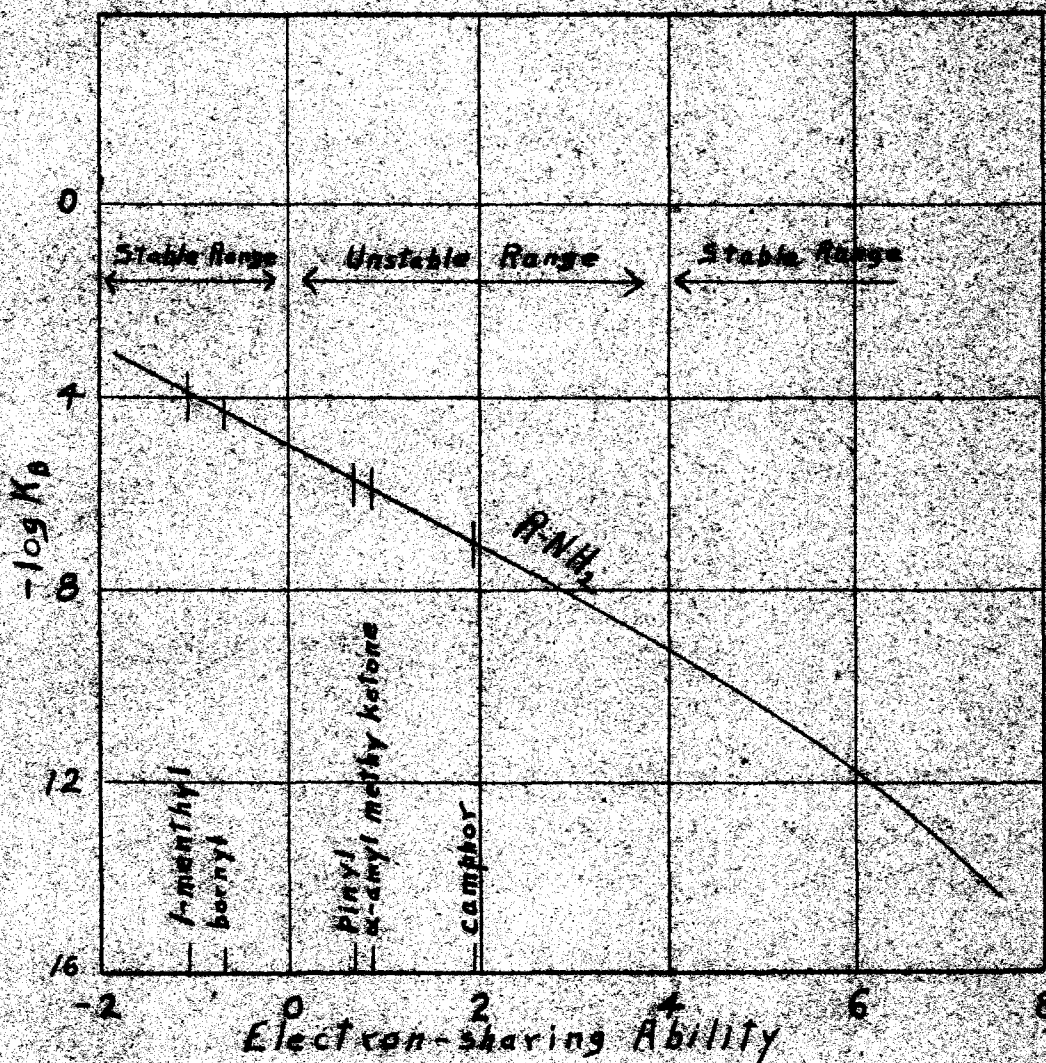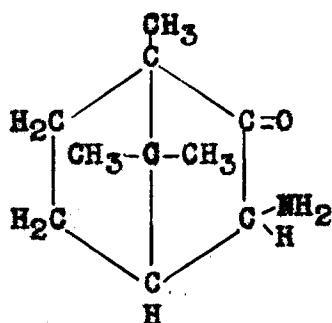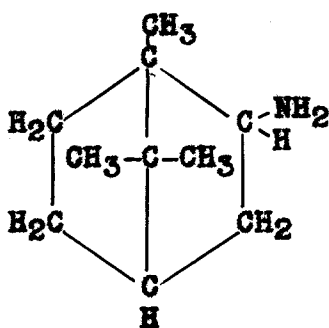
Figure IV. Electron-sharing ability of organic
radicals plotted against -log K_B.

Some observations upon the structures of the amines studied
in this investigation might prove of interest. Camphor amine,

$$CH_3$$
$$C$$
$$H_2C \qquad C=O$$
$$CH_3-C-CH_3$$
$$H_2C \qquad C-NH_2 \quad H$$
$$C$$
$$H$$

with an ionization constant of $1x10^{-7}$, was the most negative.
Bornyl amine,

$$CH_3$$
$$C$$
$$H_2C \qquad C-NH_2 \quad H$$
$$CH_3-C-CH_3$$
$$H_2C \qquad CH_2$$
$$C$$
$$H$$

with a similar structure, proved to be much more positive
$(K=7x10^{-5})$. Even though the amino group is on the 4-position
in the first case and on the 3-position in the second, the only
major difference between the two compounds is the presence of a
carbonyl group in camphor amine. The larger part of the differ-
ence in the ionization constants of these two compounds must be

due to the negativity of this grouping. This contention is further strengthened by the constant obtained for α-aminoamyl methyl ketone (1.6×10^{-6})

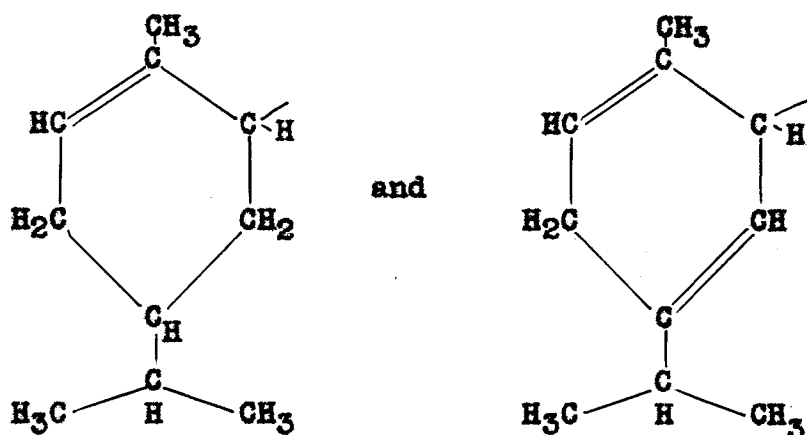$$C_4H_9 - \underset{\underset{NH_2}{|}}{CH} - \underset{\underset{O}{||}}{C} - CH_3$$
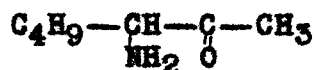
All previous data obtained in this laboratory indicate that, if the oxygen in the above compound be replaced by two hydrogen atoms, the magnitude of the ionization constant should increase to about 10^{-4}. The ring structure of camphor probably accounts for the lower ionization constant of its amine. The effect of the bridge-ring is also observable in the cases of menthyl and bornyl amines. (See Figure IV.) Pinyl amine
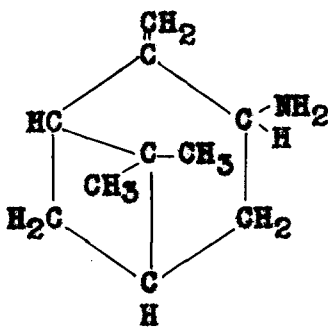
illustrates the effect of the four membered bridge-ring as contrasted with the five membered ring of the bornyl radical. The methylene group one carbon removed from the amino radical without doubt contributed to the negativity of the pinyl structure.

Some bicyclic terpene amines containing a three membered ring may possibly prove still more negative. Terpene radicals of the type

$$
\begin{array}{ccc}
& CH_3 & \\
& C & \\
HC & & C \diagdown H \\
H_2C & & CH_2 \\
& C \\
& H \\
& C \\
H_3C & H & CH_3
\end{array}
\qquad \text{and} \qquad
\begin{array}{ccc}
& CH_3 & \\
& C & \\
HC & & C \diagdown H \\
H_2C & & CH \\
& C \\
& H \\
H_3C & H & CH_3
\end{array}
$$

might form amines with ionization constants of lesser magnitude than any of those measured in this study. The lack of any evidence in the literature for the existence of such amines, combined with the known instability of other compounds containing such radicals, makes the extension of this investigation to include them very difficult.

CONCLUSIONS

From the data presented in this study the following conclusions may be drawn:

1. The terpene amines have ionization constants ranging from about 10^{-4} to 10^{-7}.

2. There is evidence of instability in those amines with constants of the order of 10^{-6} to 10^{-7}.

3. There is qualitative evidence indicating the existence of a minimum stability range in the electron-sharing ability curve for amines.

4. The instability of primary amines of the terpene type explains the lack of values in the literature for ionization constants ranging from 10^{-5} to 10^{-9}.

5. So-called aliphatic amines may be modified by placing a carboxyl group in the alpha position, to give ionization constants and stabilities within this unstable range.

6. Ionization constants may be determined by a modification of the half neutralization method, using the amine hydrochloride and an half-equivalent of NaOH instead of the usual procedure.

SUMMARY

1. Bornyl amine hydrochloride has been prepared and purified.

2. Pinyl amine hydrochloride has been prepared and purified.

3. α-Aminoamyl methyl ketone hydrochloride has been prepared and purified.

4. Camphor amine hydrochloride has been prepared and purified.

5. The ionization constants for l-menthyl amine, bornyl amine, pinyl amine, α-aminoamyl methyl ketone and camphor amine have been measured.

6. Observations have been made on the stability of terpene amines and related amines.

7. A modification of the half neutralization method for the determination of ionization constants has been reported.

8. The terpene and certain other amines possess ionization constants falling within the range 10^{-5} to 10^{-9}.

BIBLIOGRAPHY

1. Ostwald, J. prakt. Chem., 31, 433 (1885); Z. physik. Chem., 3, 170 (1889).

2. Wegscheider, Monatsh., 23, 287 (1902).

3. Walker, J. Chem. Soc., 61, 715 (1892).

4. Chandler, J. Am. Chem. Soc., 30, 694 (1908).

5. Adams, J. Am. Chem. Soc., 38, 1503 (1916).

6. Bjerrum, Z. physik. Chem., 106, 219 (1923).

7. Derick, J. Am. Chem. Soc., 33, 1152, 1162, 1181 (1911); 34, 74 (1912).

8. Hixon and Johns, J. Am. Chem. Soc., 49, 1786 (1927).

9. Johns and Hixon, J. Phys. Chem., 34, 2226 (1930).

10. Allison and Hixon, J. Am. Chem. Soc., 50, 168 (1928).

11. Osburn, O. L., The Effect of the Electron-sharing Ability of Organic Radicals on the Conductance and Toxicity of Certain Organic Arsenical Compounds. Unpublished Thesis, Library, Iowa State College, Ames, Iowa (1930).

12. Ware, F. E., The Electron-sharing Ability of Organic Radicals. Orthochlorobenzyl Radical. Unpublished Thesis, Library, Iowa State College, Ames, Iowa (1930).

13. Craig and Hixon, J. Am. Chem. Soc., 53, 4367 (1931).

14. Craig, J. Am. Chem. Soc., 55, 2543 (1933).

15. Johns and Hixon, J. Am. Chem. Soc., 56, 1333 (1934).

16. Conant, Ind. Eng. Chem., 24, 466 (1932).

17. Goodhue and Hixon, J. Am. Chem. Soc., 56, 1329 (1934).

18. Mehltretter, C. L., The Ionization Constants of Some Secondary Amines in Methanol. Unpublished Thesis, Library, Iowa State College, Ames, Iowa (1934).

19. Goldschmidt and Bader, Ann., **473**, 137 (1929).

20. Brent, J. Am. Chem. Soc., **53**, 1794 (1931).

21. Carr, E., The Reversible Splitting of Organomercuric Cyanides with Hydrogen Chloride. Unpublished Thesis, Library, Iowa State College, Ames, Iowa (1934).

22. Wuytz, Ber., **36**, 868 (1903).

23. Foster, J. Chem. Soc., **73**, 390 (1898).

24. Wallach, Ann., **245**, 251 (1888).

25. Wallach, Ann., **252**, 130 (1889).

26. Wallach, Ann., **268**, 197 (1892).

27. Pezold and Shriner, J. Am. Chem. Soc., **54**, 4710 (1932).

28. Behr and Bregowski, Ber., **30**, 1515 (1897).

29. Claisen and Monasse, Ann., **274**, 71 (1893).

30. Carothers, Bickford and Hurwitz, J. Am. Chem. Soc., **49**, 2908 (1927).

31. Pring, Trans. Farad. Soc., **19**, 705 (1923).

32. Hall and Sprinkle, J. Am. Chem. Soc., **54**, 3469 (1932).

33. Goodhue, Schwarte and Fulmer, Iowa State Coll. J. Sci., **7**, 111 (1933).

34. Burch, J. M., The Dissociation Constants and Rotations of Some Alpha-substituted Ethylamines. Unpublished Thesis, Library, Iowa State College, Ames, Iowa (1935).

35. Starr, Bulbrook and Hixon, J. Am. Chem. Soc., **54**, 3971 (1932).

36. Cole, O. D., The Effect of Substitution on the Electron Sharing Ability of the Two- and Three- Carbon Radicals. Unpublished Thesis, Library, Iowa State College, Ames, Iowa (1931).

37. Johns, Peterson and Hixon, J. Phys. Chem., **34**, 2218 (1930).

38. Hildebrandt, Chem. Reviews, **2**, 394 (1926).