Thallation and Coupling of Aromatics[1a]

Patrick M. Henry

Research Center, Hercules Incorporated, Wilmington, Delaware 19899

The replacement of hydrogen in aromatic compounds by thallium(III) (thallation) was found to be an electrophilic reaction by studies of the effect of aromatic structure on rate and product distribution. Furthermore, the rate of thallation was found to increase with increasing acid concentration in aqueous perchloric acid, an effect also observed with mercuration and attributed to "dehydration" of the metal ion. This result suggested that anhydrous weakly complexing acids should be good solvents for thallation and, in fact, methanesulfonic and trifluoroacetic were found to be very good solvents for the reaction. Thus, qualitatively, thallation is very similar to mercuration. Quantitatively thallation is 200–400 times slower than mercuration in aqueous perchloric acid. The main differences between the two are (1) only monothallated aromatics are formed, while polymercuration is very facile, and (2) under many reaction conditions diarylthallium(III) compounds are found. Under more severe conditions Tl^{III} couples aromatics to biphenyl derivatives. With toluene, a mixture of bitolyls consisting of mainly 3,3', 3,4', and 4,4' isomers is obtained. However, the yields are low and the mechanism is uncertain.

The direct replacement of hydrogen in aromatic compounds by mercury(II) to form mercury(II) aryls (mercuration) has been known since about 1900 and

$$\text{C}_6\text{H}_5\text{R} + \text{Hg}^{2+} \longrightarrow \text{R-C}_6\text{H}_4\text{-Hg}^+ + \text{H}^+ \quad (1)$$
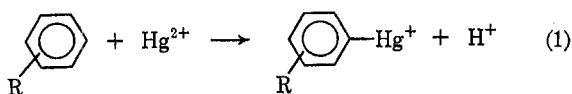
there have been numerous studies of this reaction.[1b] However, the corresponding reaction with thallium(III) (thallation) was first reported in 1943[2] and until recently there have been only two other reports of this reaction.[3,4]

In the isoelectronic series, Hg^{II}, Tl^{III}, and Pb^{IV}, the rates of electrophilic reactions, as evidenced by their reactions with olefins,[5-7] are in the order Hg^{II} > Tl^{III} > Pb^{IV}. The rate of reaction with aromatics, which would also most likely be an electrophilic reaction, would be expected to follow the same order. In keeping with this expectation plumbation occurs only with activated aromatics such as anisole,[8] while mercuration occurs readily even with nonactivated aromatics such as benzene.[9]

The stability of the adducts would be expected to follow the same order as the stability of their adducts with olefins.[6,7,10,11] Mercury(II) aryls are, in fact, very stable,[1] while Pb^{IV} aryls decompose to give coupled products.[8] Thallated aromatics, which would be intermediate in their stability, might thus decompose to give oxidized aromatics.

The reaction of Tl^{III} with aromatics has been studied in these laboratories for the past several years. Recent interest in thallium aryl chemistry[12-15] makes reporting of the general results of these studies timely.

Results

Thallation.—If Tl^{III} in 1 M H$_2$SO$_4$ is heated in the presence of benzene, solids are gradually precipitated. These solids are complex mixtures of phenylthallium-(III), diphenylthallium(III), and Tl^{III} sulfates. Tl^{III} in perchloric acid did not deposit solids when heated with benzene, but treatment of the solution with sodium chloride deposited mixtures of phenylthallium dichloride and diphenylthallium chloride. From the yields of these products it was obvious that thallation was much slower than mercuration. The results of some preliminary rate measurements are listed in Table I. The results indicate that the rates of thallation increase with increasing temperature and electrolyte concentration and are faster for activated aromatics such as toluene and slower for nonactivated aromatics such as benzoic acid.

Table I
Rates of Thallation of Various Aromatics in Aqueous Perchloric Acid[a]

Aromatic	[Aromatic]	[HClO$_4$], M	Temp, °C	k,[b] sec^{-1} × 10^6
Benzene	Saturated	1	70	4.2
Benzene	Saturated	4	70	7
Benzene	Saturated	1	40	<0.2[c]
Benzene	Saturated	4	40	0.35
Benzene	Saturated	6	40	1.8
Benzene	Saturated	6.6	25	1.1
Toluene	Saturated	6.6	25	2.8
Benzoic acid	1 M	8	130	<1[d]

[a] In most runs [Tl^{III}] was about 0.01 M. [b] First-order rate constant based on decrease of [Tl^{III}]. [c] No decrease in [Tl^{III}] in 10 days. [d] No thallated benzoic acid in 7.5 hr.

The products themselves are of interest. Thus, at [HClO$_4$] = 1 M, the main species of thallated benzene present throughout the run is diphenylthallium. At higher [HClO$_4$] the relative rate of thallation compared to diphenylthallium formation must become faster since appreciable amounts of phenylthallium are found under these conditions. Under no conditions was any evidence for dithallated aromatics found in this work.

Anhydrous or nearly anhydrous methanesulfonic acid and anhydrous trifluoroacetic acid were also tried as sol-

(1) (a) Hercules Research Center, Contribution No. 1505; (b) W. Kitching, *Organometal. Chem. Rev.*, **3**, 35 (1968), and references therein.

(2) H. Gilman and R. K. Abbott, *J. Amer. Chem. Soc.*, **65**, 122 (1943).

(3) V. P. Glushkova and K. A. Kocheshkov, *Dokl. Akad. Nauk SSSR*, **103**, 615 (1955).

(4) V. P. Glushkova and K. A. Kocheshkov, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 1186 (1957).

(5) J. Halpern and H. B. Tinker, *J. Amer. Chem. Soc.*, **89**, 6427 (1967).

(6) P. M. Henry, *ibid.* **87**, 990, 4423 (1965); **88**, 1597 (1966).

(7) R. Criegee, "Oxidation in Organic Chemistry," Vol. 5A, K. B. Wiberg, Ed., Academic Press, New York, N. Y., 1965, Chapter 5.

(8) D. R. Harvey and R. O. C. Norman, *J. Chem. Soc.*, 4860 (1964).

(9) C. Perrin and F. H. Westheimer, *J. Amer. Chem. Soc.*, **85**, 2773 (1963).

(10) J. Chatt, *Chem. Rev.*, **48**, 7 (1951).

(11) R. R. Grinstead, *J. Org. Chem.*, **26**, 238 (1961).

(12) J. M. Davidson and C. Triggs, *Chem. Ind. (London)*, 457 (1966).

(13) J. M. Davidson and G. Dyer, *J. Chem. Soc. A*, 1616 (1968).

(14) A. McKillop, L. F. Elsom, and E. C. Taylor, *J. Amer. Chem. Soc.*, **90**, 2423 (1968).

(15) A. McKillop, J. S. Fowler, M. J. Zelesko, J. D. Hunt, E. C. Taylor, and G. McGillivray, *Tetrahedron Lett.*, 2423 (1969).

TABLE II

THALLATION OF AROMATICS UNDER VARIOUS REACTION CONDITIONS

Aromatic concentration	Solvent	Tl^{III} salt	Temp, °C	Time	Conversion, % aryl Tl^{III} a	Isomer distribution		
						ortho	meta	para
2 M benzene	90% aqueous CH_3SO_3H	0.9 M $Tl(CH_3SO_3)_3$	25	6 days	7			
2 M toluene	90% aqueous CH_3SO_3H	0.9 M $Tl(CH_3SO_3)_3$	25	6 days	22	3.5	18.7	77.8
2 M anisole	90% aqueous CH_3SO_3H	0.9 M $Tl(CH_3SO_3)_3$	25	6 days	1		b	
1 M benzoic acid	CH_3SO_3H	1.5 M $Tl(CH_3SO_3)_3$	130	1 hr	24	40	59	1
1 M benzoic acid	CH_3SO_3H	1.5 M $Tl(CH_3SO_3)_3$	130	6 hr	44	38	60	2
1 M benzoic acid	CH_3SO_3H	1.3 M $Tl(CH_3SO_3)_3$	130	2 hr	21	27	72	1
1 M benzoic acid	CH_3SO_3H	1.3 M $Tl(CH_3SO_3)_3$	130	7 hr	40	57.2	36.5	6.3
2 M benzene	CF_3COOH	0.8 M $Tl(CF_3COO)_3$	25	3 hr	99			
2 M toluene	CF_3COOH	0.8 M $Tl(CF_3COO)_3$	25	3 min	65	4.2	0.5	95.3
2 M anisole	CF_3COOH	0.8 M $Tl(CF_3COO)_3$	25	3 min	24c	100		

a Conversion of monoaryl Tl^{III} based on initial Tl^{III}; no diaryl Tl^{III} detected in any runs. b Distribution not determined. c Some black solids formed.

TABLE III

COUPLING OF AROMATICS BY THALLIC TRIACETATE AND PALLADIUM(II) ACETATE IN REFLUXING ACETIC ACID a

Aromatic	$[Tl(OAc)_3]$, M	$[CH_3SO_3H]$, M	$[Pd(OAc)_2]$, M	Yield, b %	Distribution					
					2,2'	2,3'	2,4'	3,3'	3,4'	4,4'
Benzene	0.25	0.15		8.4						
Benzene	0.25	0.15	0.04	20						
Toluene	0.25	0.15		6.2				36	44	20
Toluene	0.25			3				42	49	9
Toluene	0.25	0.6		2.3				39	42	19
Toluene	0.25	0.15	0.01	76.4	0.4	1.7	2.1	14.8	48	33
Toluene		0.15	0.04	24.5c	1	11	13	16	40	19

a Reaction time was 24 hr. Concentration of aromatic was 2 M. b Based on one coupled aromatic per $Tl(OAc)_3$. Traces of bibenzyl detected in the toluene runs. c Based on one coupled aromatic per $Pd(OAc)_2$.

vents. The results of a series of such experiments are shown in Table II. The thallations were much more facile in these solvents than in aqueous perchloric acid. In fact, even benzoic acid can be thallated in methanesulfonic acid, although a temperature of 130° was required. Note that in two runs quenched at 2 and 7 hr the isomer distribution of thallated benzoic acid changes from a kinetically controlled distribution high in *meta* to an equilibrium distribution high in *ortho* and with much more *para* than in the kinetically controlled distribution. In the runs at 130° some reduction of Tl^{III} occurs, probably because of oxidation of the solvent. However, in all the runs in Table II most of the unreacted Tl^{III} was not reduced at the time of termination of reaction.

Trifluoroacetic acid was by far the best solvent for thallation. In latter work thallic triacetate was used in place of the trifluoroacetate with little loss of reactivity, and this procedure is used in these laboratories as a standard procedure for preparing phenylthallium salts. In both aqueous methanesulfonic acid and trifluoroacetic acid toluene gave predominately the *para* isomer.[16]

In none of the runs in Table II was any evidence found for diarylthallium compounds. This result is in keeping with the observation made in the perchloric acid system that diphenylthallium formation became less important as the water content of the solvent decreased.

Coupling.—In several runs in aqueous perchloric acid at 100° small amounts of organic product were

detected and proved to be diphenyl. It was found that phenylthallium salts in aqueous perchloric acid at 100° were slowly decomposed to diphenyl. In subsequent studies acetic acid was used as a solvent for coupling. In a number of runs palladium(II) acetate was added to determine its effect on the coupling reaction. Typical results are listed in Table III.

In all runs more than 98% of the Tl^{III} was reduced and less than 1% thallated aromatics were detected. The main points are that yields are low in the absence of Pd^{II} and the distributions with toluene are not those expected for electrophilic attack followed by coupling from the position of Tl^{III} attachment. Pd(OAc)$_2$ gave a distribution similar to that found in the $Tl(OAc)_3$ couplings alone.

In one run phenylthallium dichloride was refluxed in acetic acid for 6 hr. Only a 1% yield of diphenyl was detected.

No coupled products were detected in the benzoic acid reaction mixtures. However, if preformed thallated benzoic acid is refluxed in acetic acid, a yield of about 50% of coupled benzoic acid is produced.

Discussion

Thallation.—The effect of aromatic structure on rate (Table I) and the product distributions found with toluene, anisole, and benzoic acid (Table II) indicate that thallation is an electrophilic reaction, in agreement with other reports on ease of thallation and product distributions.[8,12,15] The change in distribution with time for the benzoic acid runs (Table II) suggests thallation is reversible, and the increase in rate of reaction with increasing salt concentration is not surprising, since the reaction of Tl^{III} with olefins displays this same effect.[6]

(16) In a recent preliminary communication,[15] exactly the same procedure was reported to give exclusively *para* isomer. The difference may be that we isolated all the thallated toluene by precipitation with aqueous sodium chloride, while the other workers isolated only the insoluble portion.

Thus, mercuration and thallation are qualitatively very similar. Both show the characteristics of an electrophilic reaction, both are apparently reversible, and the rates of both are accelerated by lowering of water activity. Quantitatively in aqueous perchloric acid at 40°, the rates of mercuration[9] are 200–400 times as fast as thallation, a result in agreement with the relative rates of reaction with olefins.[5,6]

There are, however, differences between the two reactions. First, under many conditions Ar_2Tl^+ is the main product of thallation. With only two aromatics has this been the case with mercuration.[17,18] Secondly, only monothallation occurred with all the aromatics we studied, while polymercuration occurs very readily.[9,19,20] Thus Tl^{III} must deactivate an aromatic ring much more strongly than does Hg^{II}, a result in keeping with the higher charge of Tl^{III}.

The increase in rate of thallation with increasing acid concentration is related to decreasing water activity.[6,9] Thus, noncomplexing solvents containing little or no water should promote thallation. Indeed, thallation was much faster in methanesulfonic and trifluoroacetic acids. Trifluoroacetic acid, by far the more effective of the two, has recently been used by other workers for a variety of thallation reactions.[15] Our own choice of trifluoroacetic acid was prompted by the report that mercuration was very rapid in this solvent.[21]

The thallation of anisole in trifluoroacetic acid appears anomolous since yields are low for such an activated arene and only the *ortho* adduct is formed. However, ether linkages in the presence of strong acids are apparently strongly hydrogen bonded thus decreasing the electron releasing ability of the ether linkage.[22,23] Also, in such a poor complexing solvent as trifluoroacetic acid the ether might well be complexed to the thallic ion thus putting the thallic ion in position for an ortho attack. A similar effect has been observed for benzoic acid in trifluoroacetic acid.[15]
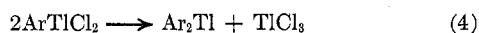
The formation of diarylthallium compounds must occur either by disproportionation

$$2ArTl^{2+} \longrightarrow Ar_2Tl^+ + Tl^{3+} \qquad (2)$$

or by attack of the monoaryl on a second aromatic.

$$ArTl^{2+} + ArH \longrightarrow Ar_2Tl + H^+ \qquad (3)$$
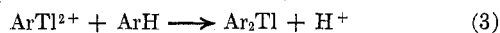
The fact that phenylthallium dichloride disproportionates in the absence of aromatic[24] (eq 4) suggests the

$$2ArTlCl_2 \longrightarrow Ar_2Tl + TlCl_3 \qquad (4)$$

first mechanism (eq 2) is operable.

Coupling.—Thallic acetate in refluxing acetic acid reacts with benzene and toluene to give low yields of coupled aromatics (Table III). In spite of the low yields the thallic acetate is completely reduced, presumably by oxidation of the solvent, and only traces of thallated aromatics are found in the final reaction mix-

tures. Since thallated aromatics are formed under the reaction conditions,[12] it seems likely that they are intermediates in the reaction. In that case the thallated toluene must have arrived at an equilibrium distribution of isomers before coupling, since so large an amount of 3,3' and 3,4' isomers is present. Coupling of a kinetic-controlled distribution would have predicted large amounts of 4,4' but little 3,3' or 3,4'. The lack of 2,2', 2,3', and 2,4' isomers could result from steric hindrance to coupling.

To obtain evidence for thallated aromatic intermediates, $Pd(OAc)_2$ was added to the reaction mixture. Hopefully, the initially formed intermediate would rapidly transfer aryl to Pd^{II} followed by rapid coupling. Arylmercury(II) compounds[25,26] as well as phenylboronic acids[27] transfer aryl to Pd^{II} followed by coupling of the Pd^{II} aryls. Thus a change in distribution from 3,3' and 3,4' to 4,4' would be evidence for arylthallium intermediates which were coupled by $Pd(OAc)_2$. In a similar study[28] it was found that addition of Hg^{II} changed the distribution of a Pd^{II} coupling of toluene from mainly 3,4' and 3,3' to mainly 4,4'.

In the present case the yields were increased but the 3,4' and 3,3' isomers still predominated. Thus, either equilibration was occurring before transfer of aryl to Pd^{II} or else Tl^{III} was only reoxidizing the Pd^0 back to Pd^{II}.

It is possible that the interesting coupling reactions reported by McKillop, Elsom, and Taylor[14] proceed by decomposition of Tl^{III} aryls to give coupled products. However, more work is necessary to determine the mechanisms of both couplings.

Experimental Section

Reagents.—Thallic oxide was purchased from the Fairmount Chemical Company. Preparation and analysis of thallic stock solutions has been described previously.[6] Standards of phenylthallium dichloride or diphenylthallium chloride were prepared by literature procedures.[24,29] (All other chemicals were of reagent grade.)

Identification of Products.—Phenylthallium salts were precipitated as their chlorides and separated into the monophenyl and diphenyl compounds by solubility characteristics. They were identified by their X-ray powder patterns. To determine if any dithallation occurred, the phenyl thallation adducts were treated by bromine using the procedure described by Wright.[19] The presence or absence of dibromobenzenes was then determined by vapor phase chromatography (vpc) using a 20-ft 10% 4,4'-dimethoxyazoxybenzene on 45–60 mesh Chromosorb W. The temperature was 120° and the flow rate 75 ml/min.

The product distributions for the thallated toluenes, anisoles, and benzoic acids were also determined by treatment with bromine followed by vpc analysis. For the bromotoluenes the same vpc procedure was employed as was used for the bromobenzenes. The bromoanisoles were separated using a 20-ft. Ucon 75h column with a gas flow of 100 ml/min. The temperature was programmed from 130 to 205° at 4.6°/min. The bromobenzoic acids were esterified with diazomethane and the distributions of methyl esters determined using 6 ft of 5% bentone 34 + 5% didecyl phthalate on Chromosorb W. The temperature was 150° and the flow rate 80 ml/min. Identification of brominated products was determined by comparison of retention times with standards. In several cases peaks were collected from vpc and identification confirmed by infrared spectra.

(17) P. I. Petrovich, *Zh. Obshch. Khim.*, **30**, 2808 (1960).

(18) G. B. Deacon and F. B. Taylor, *Inorg. Nucl. Chem. Lett.*, **5**, 477 (1969).

(19) M. Malaiyandi, H. Sawatzky, and G. F. Wright, *Can. J. Chem.*, **39**, 1827 (1961).

(20) K. Sewall McMahon and K. A. Kobe, *Ind. Eng. Chem.*, **49**, 42 (1957).

(21) H. C. Brown and R. A. Wirkkala, *J. Amer. Chem. Soc.*, **88**, 1447, 1453 (1966).

(22) R. F. Taft, E. Price, I. R. Fox, I. C. Lewis, K. K. Andersen, and G. T. Davis, *ibid.*, **85**, 709 (1963).

(23) P. E. Peterson, C. Casey, E. V. P. Tao, A. Agtarap, and G. Thompson, *ibid.*, **87**, 5163 (1965).

(24) F. Challenger and B. Parker, *J. Chem. Soc.*, 1462 (1931).

(25) R. R. Josephson, Hercules Inc., unpublished results.

(26) P. M. Henry, *Tetrahedron Lett.*, 2285 (1968).

(27) J. M. Davidson and C. Triggs, *J. Chem. Soc. A*, 1324 (1968).

(28) M. O. Unger and R. A. Fouty, *J. Org. Chem.*, **34**, 18 (1969).

(29) V. P. Glushkova and K. A. Kocheshkov, *Dokl. Akad. Nauk SSSR* **116**, 233 (1957).

The product distributions of all the coupled products except the coupled benzoic acids were carried out using a 12-ft 15% Apiezon N column at 250°. Flow rate was 60 ml/min. The identity of the 2,2′, 3,3′, and 4,4′ bitolyls was determined from vpc by fortification with an authentic sample of each isomer. The identity of the 2,3′, 2,4′, and 3,4′ mixed bitolyls was inferred from their reported order of elution under very similar vpc conditions.[30] Further support for the assignment by vpc retention times was obtained by the ultraviolet spectra of samples collected from the vpc eluent. Because of the small samples and similarities in spectra it was difficult to make positive identification. However, the comparison of these spectra with published spectra[31] of the isomers lent support to the assignments by vpc retention time. The coupled benzoic acids were esterified by diazomethane and the esters analyzed using a 6-ft Apiezon N column at 260°. Flow rate was 60 ml/min.

Kinetic Runs.—Quantitative analyses were by polarographic analysis. The wave for monoarylthallium(III) compounds falls between the waves for Tl^{III} and diarylthallium(III) compounds. The kinetic runs were made using a soft-drink bottle

(30) E. A. Johnson, *J. Chem. Soc.*, 4155 (1957).

(31) G. H. Beaven and E. A. Johnson, *Spectrochim. Acta*, **14**, 67 (1959).

stirred with a magnetic stirring bar. The bottle was capped with a metal cap having holes sealed by a rubber liner through which samples for analysis could be withdrawn using a syringe with needle attached. Two-milliliter aliquots were withdrawn and quenched by addition of 1 ml of 4 *M* NaCl. The sample was diluted to 10 ml with water for analysis. These samples were analyzed at 25° using a Sargent Model XXI polarograph. The $E_{1/2}$ for Tl^{3+} occurred at -0.1 V vs. a standard calomel electrode, the $E_{1/2}$ for phenyl thallium at -0.2 V, and the $E_{1/2}$ for diphenylthallium at -0.5 V. The i_d for the Tl^{3+} was directly proportional to Tl^{3+} concentration in the bulk of the solution. Control runs showed no disproportion took place in the time required for analysis.

Substituent Effect Transmission from Heavy Atoms.
Microscopic Dissociation Constants of Selenoglycolic Acid

JOSEPH L. KURZ AND JUDITH COBURN HARRIS[1]

Department of Chemistry, Washington University, St. Louis, Missouri 63130

An unusual enhancement of the substitutent effect of a negative charge on the pK_a of a carboxyl group has been observed to be present when that charge is located on a selenium atom. A method for preparing solutions of pure selenols from the corresponding diselenides is described, and such solutions have been used in determining the extents of dissociation of the SeH groups in $HSeCH_2CO_2CH_3$ and $HSeCH_2CO_2H$ as functions of pH. Values for the microscopic dissociation constants of the latter acid have been derived from those data, and are: for the SeH groups, $pk_a = 4.7$, $pk_d = 7.3$; for the CO_2H group, $pk_b = 4.1$, $pk_c = 6.7$. Relative to the effect on the acidity of a carboxyl group which is produced by a charge located on nitrogen or oxygen, the substitutent effects of charges located on S and Se in $^-SCH_2CO_2H$ and $^-SeCH_2CO_2H$ are too large by 0.6 and 0.8 pK units, respectively. It is shown that this enhancement of the substituent effect is within the range attributable to a decrease in the effective dielectric constant arising from the increase in atomic radius in the sequence O, S, Se. An uncertain fraction of this increase in ΔpK probably arises from a decrease in the interaction between the charge on CO_2^- and the XH dipole moment as X varies through the same sequence.

The effect of charged substituents on the acidity of carboxylic acids has been studied extensively,[2-4] and for several classes of acids it has been shown[3] that such effects can be predicted from a suitably modified electrostatic model with an uncertainty not exceeding a few tenths of a pK unit. However, tests of such electrostatic predictions, as well as of purely empirical correlations of pK with the distance between the charge and the acidic site,[5-7] have been almost completely restricted to acids in which the charge is borne by a first-row atom, N or O. In connection with other work in these laboratories, it became necessary to make similar estimates for the effect of charges located on heavier atoms.

Very few pK values are available for dibasic acids in which one or both protons are bound to non-first-row atoms, and most which have been reported are apparent

values measured at high or unspecified ionic strength. It is known that ΔpK for acids in which two protons are bound to the same basic atom can vary widely as that atom is changed (*e.g.*, H_3O^+ *vs.* H_2O, $\Delta pK = 17.4$; H_2S *vs.* HS^-, $\Delta pK = 7.6$,[8] in at least qualitative agreement with an electrostatic prediction based on the relative size of O and S). However, the scarcity of data makes it uncertain whether any such variation persists when the protons are not bound to the same atom and the nonelectrostatic effects which contribute[8] to those very large differences are therefore no longer operative. That changes in effective dielectric constant, D_E, arising from an increase in the radius of the atom bearing the charge might be important is suggested by the observation[4] that the acid-strengthening effect of a positive charge on quaternary nitrogen is greater than that of a charge on less highly substituted nitrogen. (*E.g.*, at 25° (a) for $H_3N^+CH_2CO_2H$ *vs.* $(CH_3)_3N^+-CH_2CO_2H$, $\Delta pK = 0.5$,[9] (b) for amine salts derived from the 1,4-diazabicyclo[2.2.2]octane ring system, $HN^+(CH_2CH_2)_3NH^+$ has $pK_a = 2.67$, $CH_3N^+(CH_2-$

(1) National Science Foundation Graduate Fellow, 1968-1969.

(2) (a) J. G. Kirkwood and F. H. Westheimer, *J. Chem. Phys.*, **6**, 506 (1938); (b) F. H. Westheimer and J. G. Kirkwood, *ibid.*, **6**, 513 (1938); (c) F. H. Westheimer and M. W. Shookhoff, *J. Amer. Chem. Soc.*, **61**, 555 (1939).

(3) C. Tanford, *ibid.*, **79**, 5348 (1957).

(4) C. F. Wilcox, Jr. and J. S. McIntyre, *J. Org. Chem.*, **30**, 777 (1965).

(5) G. E. K. Branch and M. Calvin, "The Theory of Organic Chemistry," Prentice-Hall, Englewood Cliffs, N. J., 1941, Chapter 6.

(6) J. L. Kurz and J. I. Coburn, *J. Amer. Chem. Soc.*, **89**, 3528 (1967).

(7) J. C. McGowan, *J. Appl. Chem.*, **10**, 312 (1960).

(8) R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959, p 92.

(9) D. D. Perrin, "Dissociation Constants of Organic Bases in Aqueous Solution," Butterworths, London, 1965.