Chem., Int. Ed. Engl., 11, 850 (1972).
(28) H. Zeldes and R. Livingston, *J. Phys. Chem.*, **76**, 3348 (1972); **77**, 2076 (1973).
(29) R. W. Fessenden and P. Neta, *Chem. Phys. Lett.*, **18**, 14 (1973).
(30) D. Griller and K. U. Ingold, *J. Am. Chem. Soc.*, **96**, 6715 (1974).
(31) J. E. Wertz and J. R. Bolton, "Electron Spin Resonance", McGraw-Hill, New York, N.Y., 1972.
(32) The coupling constants appear to depend to a slight extent on the conditions used to prepare **18**.[33] We have prepared a radical we believe to be **18** (g = 2.00219, a^P = 27.21, $a^H(2H)$ = 3.01) under conditions as close as possible to those used to produce **9**, viz., addition of a trace of Me_3COOH to a solution of the phosphorin in the peroxide and photolysis.
(33) K. Dimroth and H. Weber, unpublished results.
(34) For comparison, cyclohexadienyl itself has two "relatively weak" absorption bands at 512 and 554 nm: J. E. Jordan, D. W. Pratt, and D. E. Wood, *J. Am. Chem. Soc.*, **96**, 5588 (1974).
(35) Phosphorus couplings of ~200 and ~133 G have been reported for analogous radicals.[21f]
(36) B. Maillard and K. U. Ingold, *J. Am. Chem. Soc.*, in press.
(37) For an example of a rearranged adduct to pyridine, see: C. Chachaty, J. C. Ronfard-Haret, A. Lablache-Combier, J. P. Quazebeur, and H. Ofenberg, *J. Chem. Soc., Chem. Commun.*, 579 (1974).
(38) The H atom adduct to pyridine with the B structure has a^N = 5.1 G.[21e] The A structure OH adducts to three pyridinecarboxylic acids have a^N = 2.8–3.4 G.[21i]
(39) In **29**B ($a^{H_2} + a^{H_6})/2 = 8.0 = a^{H_2}$ in **19**.
(40) Note Added in Proof. $a^{^{13}CH_2}$ is not linearly related to a^{HCH_2} in these radicals: J. C. Scaiano and K. U. Ingold, unpublished results.

Kinetics of Degenerate Solvolysis. Reaction of Covalent Amino Adducts of Heteroaromatic Compounds in Liquid Ammonia

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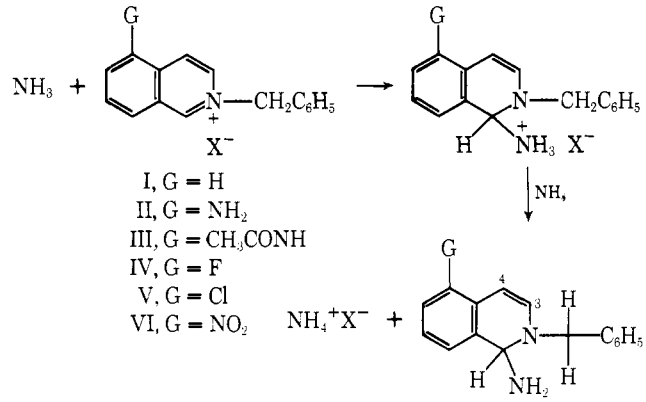
Abstract: Ammonium ion catalyzed solvolysis of covalent complexes formed by the addition of ammonia to quaternized heteroaromatic compounds in liquid ammonia was studied by NMR. Rates of turnover of the amino group were obtained at coalescence of the signals for the diastereotopic *N*-benzyl protons as a function of ammonium salt concentration. By means of Arrhenius plots it was possible to relate reactivities to a common temperature and to obtain relative rates. Relative rates for a series of 5-substituted 1-amino-2-benzyl-1,2-dihydroisoquinoline adducts in ammonia were correlated by linear free energy relationships.

Nucleophilic addition to the annular carbon atoms of carbocyclic and heterocyclic molecules to give ionic or neutral covalent adducts is a common reaction in chemical and biochemical systems.[1-7] Such adducts may be the products of a reaction or they may be intermediates leading to new products. The aim of many current investigations is to obtain data from kinetic, equilibrium, and calorimetric studies for such reactions so that the structural factors which influence rates and equilibria may be determined.

We wish to report a study dealing with substituent effects on the rates of solvolysis of some amino adducts of heteroaromatic molecules in liquid ammonia. Our study primarily involves molecules formed by the addition of ammonia to isoquinolinium ions[4] containing a prochiral *N*-benzyl group, Scheme I. A novel application of NMR line shape analysis was employed to determine rates. The kinetic method is expected to be a useful complement to the usual spectrophotometric approaches employed in studying covalent adducts.

Scheme I



Results

Adducts from Isoquinolinium Ions. *N*-Benzylisoquinolinium ions react with liquid ammonia on mixing to give adducts which have the 1-amino-2-benzyl-1,2-dihydroisoquinoline structure (I–VI), Scheme I. Included in this series are the parent ion as well as those ions having at position 5 amino, acetylamino, fluoro, chloro, and nitro substituents. Conversion to adduct is complete; no evidence could be found by NMR for the presence of unreacted starting material in any case. Chemical shifts and coupling constants for these adducts are reported in Table I. The high-field shifts provide direct evidence of the change in structure associated with complex formation.[1,4] The especially interesting feature of the spectra is the nonequivalence of the *N*-methylene hydrogen atoms (diastereotopic protons[8]). Nonequivalence of these protons results because a chiral center is formed when ammonia adds to position 1.

The multiplicity of the *N*-benzyl protons depends on temperature and also on ammonium ion concentration. The AB pair of doublets collapses to a singlet on raising the temperature of a reaction mixture. The temperature required to bring about coalescence is lowered when the ammonium ion concentration is increased. For example, the coalescence temperature of the signal of the complex resulting from 2-benzylisoquinolinium ion decreases from 37 to 26 to 10° as the concentration of ammonium ion increases from 0.34 to 0.86 to 1.86 *M*. Moreover, when powdered KOH is added to a reaction mixture to reduce the ammonium ion concentration, coalescence is not observed even up to 88°. Therefore, the reaction which destroys the nonequivalence of the diastereotopic protons is ammonium ion catalyzed. In some

Table I. Chemical Shifts (τ)[a] and Coupling Constants[b] for Some Amino Adducts in Ammonia

Compd	Carbocyclic H	H-1	H-3	H-4	CH_2	J, Hz
I	2.7–3.1	4.83	3.59	4.55	5.17	$J_{1,3} \cong 1.2$
					5.53	$J_{3,4} = 7.5$
						$J_{CH_2} = 15.5$
II	2.6–3.6	4.82	~3.2	4.37	5.10	$J_{1,3} \cong 1.0$
					5.44	$J_{3,4} = 7.5$
						$J_{CH_2} = 15.25$
III	2.7–3.1	4.86	3.56	4.44	5.20	$J_{1,3} \cong 1.5$
					5.58	$J_{3,4} = 7.5$
						$J_{CH_2} = 15.25$
IV	2.6–3.1	4.77	3.44	4.44	5.16	$J_{1,3} \cong 1.5$
					5.52	$J_{3,4} = 7.5$
						$J_{CH_2} = 15.25$
V	2.6–3.0	4.80	3.39	4.30	5.51	$J_{1,3} \cong 1.5$
					5.17	$J_{3,4} = 7.75$
						$J_{CH_2} = 15.5$
VI	2.1–2.8	4.66	3.06	3.89	5.00	$J_{1,3} \cong 1.5$
					5.32	$J_{3,4} = 7.5$
						$J_{CH_2} = 15.25$
VII	2.4–2.9	4.79	3.17		5.18	$J_{1,3} \cong 1.5$
					5.48	$J_{CH_2} = 15.0$
VIII	2.4–2.7	4.93		2.28	5.05	$J_{CH_2} = 14.0$
					5.29	
IX	2.6–3.6	5.07[c]	4.05	*d*	5.26	$J_{2,3} = 5.0$
						$J_{3,4} = 10.0$
X	2.6–3.5	5.08[c]	4.02	*d*	5.80	$J_{2,3} = 5.0$
					6.05	$J_{3,4} = 9.5$
						$J_{CH_2} = 17.5$

[a] Relative to $(CH_3)_3N$, τ, 7.87. [b] For the sign of geminal couplings see L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd ed, Pergamon Press, New York, N.Y., 1969, Chapter 4-1. [c] H-2. [d] Signal buried in the region for carbocyclic protons.

Table II. Physical Constants for the Diasterotopic Benzyl Protons in Some Amino Adducts and the Variation in Their Coalescence Temperatures with Ammonium Ion Concentration

Compd	a,[a] Hz	b,[a] Hz	k_c,[b] sec^{-1}	$[NH_4^+]$, M	T_c, °C	k_{rel}[c]
I	42.5	11.5	97.5	0.34	37.5	1.0
				0.86	26	
				1.86	10	
II	41.0	10.5	94.8	0.40	18	3.1
				1.20	0	
				2.50	10	
III	42.5	12.0	96.9	0.27	42	0.78
				0.97	26	
				1.815	17	
IV	41.5	11.0	95.5	0.38	68	0.22
				1.13	46	
				2.34	32	
V	41.0	10.0	95.5	0.28	77	0.17
				1.12	49	
				1.95	38	
VI	40.0	9.5	93.5	0.905	96	0.077
				1.93	75	
				3.05	55.5	
VII	38.5	8.5	90.9	0.44	90	0.10
				1.20	68	
				2.50	46	
VIII	34.0	6.0	82.5	0.50	94	0.071
				1.20	69	
				2.50	54	

[a] Separation between peaks of the AB multiplet: see text. [b] Pseudo-first-order rate constant at coalescence calculated using eq. 1. No correction has been applied for natural line widths which are 1.5–2 Hz in the slow exchange region. This correction is small and approximately constant for the series. [c] At 25°.

instances NH_4I was added to reaction mixtures in order to increase the concentration of acid. In calculating the concentration of ammonium ion in solution it is assumed from the stoichiometry of the reaction leading to an adduct that 1 equiv of ammonium ion is formed along with every mole of adduct, Scheme I. The total concentration is the sum of concentrations from the two sources.

No significant changes in spectra could be detected other than coalescence of the methylene signal. No evidence could be found for the presence of other heterocyclic compounds as the temperature and ammonium ion concentrations were varied. High concentrations of substrate were avoided in order to prevent the formation of an oil.

The coalescence temperatures of the six isoquinoline adducts were determined at three different concentrations of ammonium ion. The nature of the substituent at position 5 of the adducts has a limited influence on the coalescence temperature, Table II. Examining the results in Table II reveals that when the total ammonium ion concentration is about 1 M the coalescence temperature increases in the order $NH_2 < H \sim CH_3CONH < F \sim Cl < NO_2$. These coalescence temperatures range from 0 to 96°.

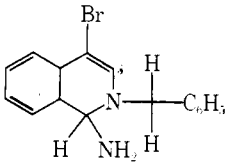
The rate constant, k_c, for the acid catalyzed, pseudo-first-order reaction which leads to coalescence may be estimated at the coalescence temperature using eq 1 where $\Delta^2 = ab$ and $J = (a - b)/2$.[9] The frequency interval between the outermost peaks of the AB multiplet is "a" and the interval between the innermost peaks is "b".[10] Because these parameters are about the same for the six adducts, k_c is about the same for all, having the value ~95 sec^{-1}, Table II. In other words the lifetime, $1/k_c$, of one of the methylene protons in a magnetic environment which is different from that of the other is only about 10 msec at coalescence.

$$k_c = \pi(\Delta^2 + 6J^2)^{1/2}/2^{1/2} \quad (1)$$

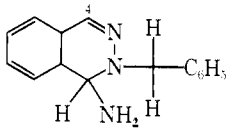
Data for the various compounds can be related to a common temperature by means of Arrhenius plots. Plots of log $(k_c/[NH_4^+])$ vs. $1/T$ are linear for the six isoquinoline substrates. Slopes were calculated by the method of least squares; correlation coefficients range from a low of 0.983 for the parent substrate to a high of 0.999 for the 5-amino complex. Arbitarily selecting 25° as a temperature for comparison gives rise to the following series of relative rates: H, NH_2, CH_3CONH, F, Cl, and NO_2 substrates react in the order 1.0, 3.1, 0.78, 0.22, 0.17, and 0.077. Substituent effects on reactivity are not large, changing only by a factor of 40 on passing from the most (NH_2) to the least (NO_2) reactive adduct.

Other Amino Adducts. Rates of solvolysis of several other adducts were examined for comparison purposes. These include adducts formed from 4-bromo-2-benzylisoquinolinium (VII) and 2-benzylphthalazinium (VIII) ions. Here too, addition of ammonia to position 1 takes place[4] and the N-benzyl protons are diastereotopic, Table I. Arrhenius plots were constructed. Relative to the rate of reaction of I, the bromine atom at position 4 of VII and the annular nitrogen atom at position 3 of VIII both retard the rates of racemization of the adducts. Relative rates at 25° are 0.10 and 0.071 for VII and VIII, respectively.

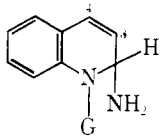
Two N-substituted quinolinium ions were converted to their amino adducts, IX and X. Covalent amination takes place at position 2, Table I.[4] Interestingly, the methylene protons of the N-benzyl group in IX show a singlet pattern. Lowering the temperature of a solution of IX in ammonia to −45° failed to broaden the singlet. Adding excess powdered KOH to reduce the ammonium ion concentration and lowering the temperature to −35° also failed to change the singlet. It seems possible that the singlet signal observed for this adduct is due to accidental degeneracy rather than to a rapid reaction which results in signal averaging.[11,12]



VII



VIII



IX, G = $CH_2C_6H_5$
X, G = CH_2CONH_2

Diastereotopic proton signals were observed for an adduct formed from a quinolinium ion having CH_2CONH_2 bonded to the annular nitrogen atom. Two structures are possible for the complex. One is the amino adduct X shown; the other is an intramolecular, cyclic adduct[13] resulting from the addition of the carbamoyl group to position 2. No attempt was made to decide between these possibilities. Attempting to induce coalescence of the signals by increasing the temperature of the sample only caused the lines to move together before extensive decomposition resulted. Thus, at −58° there was a 5 Hz separation between the main absorption lines of the AB pair; this spacing gradually diminished until it was 2.5 Hz at 6°. At higher temperatures the entire spectrum deteriorated in quality. Such small variations in chemical shift are not unknown[14] and may be due to a variety of factors such as changes in conformation, solvation, and ionization of the carbamoyl group.

Discussion

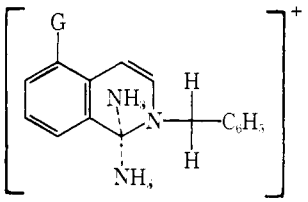
Mechanism. The reaction studied allows the diastereotopic protons of the amino adducts to become enantiotopic; the pair of doublets associated with the *N*-methylene protons coalesces to a singlet. Two characteristic features must be taken into consideration when formulating a mechanism. (1) The reaction is carried out in a nucleophilic moderately polar solvent (dielectric constant is 17 at 25° [15]). (2) Substituents either on the carbocyclic or heterocyclic rings have only a small influence on reactivity, Table II. Note that large substituent effects have been observed on rates and equilibria involving other kinds of uncharged heterocyclic adducts in aqueous solution.[6,7]

Possible reaction pathways involve cleavage of a CN bond; the nitrogen atom in each case is protonated in a preequilibrium step in order to make it a better leaving group. Although the pyramidal annular nitrogen center in an adduct is chiral, inversion is likely to be so fast that the stereochemistry at this center need not be considered.[16-18]

Two mechanisms seem likely and we are unable to select between them. The first is an SN1 reaction in which the rate-limiting step involves loss of ammonia from position 1. In view of the small effect of substituents, this pathway requires that little positive charge be transferred to the ring in the transition state. Hence, only a little of the resonance energy of the heterocyclic ring is generated. This reaction is the reverse of that by which the adducts are first formed, Scheme I. Dissociation-recombination is the generally accepted pathway for ligand turnover involving covalent adducts.[1]

According to the second possibility involving transition state XI, solvent assists the departure of the leaving group. Some positive charge is present on both the nucleophile and leaving group in the transition state. However, only a small amount of charge is transferred to the ring in this SN2 reaction. Of course, it is not unusual for SN2 reactions to show a small rate dependence on substituents because only a small amount of charge may be transferred to the carbon atom undergoing substitution.[19]

The solvolysis reaction is unusual in that both the entering and leaving groups are solvent molecules. In describing the structure of the transition state we are concerned with the difficult question dealing with the organization of the solvent around the heterocycle. Is the solvent unsymmetrically structured (SN1 reaction) around the reaction site or does it have a symmetrical structure (SN2 reaction)? The



XI

problem is related to the much debated question of the extent of solvent assistance in "carbonium ion" reactions. The more nucleophilic is the solvent and the lower its ionizing power, the greater will be its participation in a reaction. As the degree of solvent assistance in a reaction increases, the extent of the electronic effect of substituents decreases.[20]

There is a third mechanism which we disfavor. This pathway involves ring opening by cleavage of the bond between carbon 1 and the annular nitrogen atom. It should be noted that opposing substituent effects are expected on the two steps of the reaction, protonation and ring cleavage. For this pathway, too, the overall effect of substituents could therefore be small. This pathway is disfavored for the following reason. It is possible to generate a 1 adduct from 2-benzylisoquinolinium ion and ethylmercaptide ion in ammonia. Again, as in the solvolysis reaction, ligand turnover is rapid. A singlet signal is found for the *N*-methylene protons and the averaging of free and bonded mercaptide ions gives rise to a common set of signals.[5] The simplest explanation for these observations involves SN1 or SN2 reactions, not ring cleavage. Turnover of the amino and mercaptide ligands probably takes place by similar pathways.

The solvolysis reaction is degenerate in the sense that identical ligands are being exchanged. Such "null reactions" have also been termed "topomerizations".[21]

No attempt was made to determine the kinetic order in ammonium ion catalyst. Because high concentrations of catalyst were employed in our study we expected that ion aggregation and activity coefficient effects would greatly complicate and probably frustrate such a determination.[22-24] It has been firmly established that ammonium salts in ammonia at high concentrations exist largely as aggregates rather than as free ions.[23]

Lack of knowledge of the kinetic order in catalyst has two consequences, neither of which has an important bearing on our conclusions regarding the nature of substituent effects on reactivity. First, energies of activation, E_a, cannot be determined. This may be understood by considering Arrhenius eq 2 in a rearranged form, eq 3, where A has its usual meaning, y expresses the kinetic order of catalyst, and k_c is a rate constant calculated with the aid of eq 1. Both E_a and A are assumed, as usual, to be constants. In our case k_c is a constant as well. Therefore, if y is constant eq 3 has the form of a linear equation; E_a values cannot be determined without a knowledge of y. (Even under favorable circumstances it is not easy to obtain error-free determinations of E_a by NMR methods.[9,18]) Therefore, considering the above, it is not surprising that plots of log $(k_c/[NH_4X])$ vs.

Table III. Elemental Analyses of Substituted 2-Benzyliosquinolinium Salts

Substituent	Anion	Mp, °C	Calcd			Found		
			C	H	N	C	H	N
5-NH_2	ClO_4	195–197	57.41	4.52	8.37	57.33	4.40	8.29
5-CH_3CONH	Cl	186–188	69.10	5.48	8.95	68.98	5.54	8.91
5-Cl	ClO_4	219–221	54.26	3.70	3.95	54.41	3.56	3.94
5-F	Br	85–87	60.40	4.12	4.40	60.10	4.11	4.36
5-NO_2	Br	217–219	55.67	3.80	8.11	55.82	3.87	8.06
4-Br	Br	224–226	50.69	3.46	3.69	50.45	3.41	3.65

$1/T$ used to obtain the relative rate values given in Table II can be linear.

$$\log \frac{k_c}{[NH_4X]^y} = \frac{-E_a}{4.58T} + \log A \quad (2)$$

$$-\log [NH_4X] = \frac{-E_a}{y4.58T} + \frac{1}{y}(\log A - \log k_c) \quad (3)$$

A second consequence of the unknown kinetic order in catalyst is that the true magnitude of the relative rate scale is unknown. An equivalent way to view the relative rate scale expressed in Table II makes use of eq 3. In effect, the concentration of catalyst required to bring about coalescence at 25°, $[NH_4X]_{25}$, the reference temperature, is calculated. This value depends for a given substrate on the value assumed for y. Comparison of the quantities $k_c/[NH_4X]_{25}$ gives relative rate constants. Now, since the catalyst concentrations are similar in all experiments, it is likely that the kinetic order is the same for all substrates. Because large aggregates of ions often are less reactive than small ones,[23,25] it is unlikely that the kinetic order is >1. However, it is possible that y is <1[23] and the true scale is smaller than the one given in Table II where it was assumed arbitarily that $y = 1$. Consider, for example, the consequence of a kinetic order of one-half on the magnitude of the scale of relative rates for the 5-substituted isoquinoline adducts. This smaller kinetic order would decrease the scale by the square root of that given in Table II; the spread from the most (amino) to the least (nitro) reactive adduct would decrease from a factor of 40 to 6.3. Clearly, regardless of an accurate knowledge of kinetic order, it can be stated that substituent effects on reactivity are small.

Hammett Correlations. Relative rates of turnover of the amino group of the isoquinoline adducts are correlated by a simple Hammett equation. A satisfactory fit (correlation coefficient 0.96) is obtained using meta substituent constants,[26] eq 4. Standard derivations are indicated in parentheses; t tests indicate the ρ value has a confidence limit >99.5% and the intercept statistically does not appear to be different from zero.[27] Other substituent constants, σ_p and σ_p^0, give inferior correlations. Note that the use of a kinetic order for ammonium ion other than the one employed will change the value of ρ. For example, assuming the reaction to be one-half order in ammonium ion reduces the ρ value by one-half, indicating a lower sensitivity to substituent effects.

$$\log k_{rel} = -1.85(\pm 0.3)\sigma_m + 0.1(\pm 0.1) \quad (4)$$

The kinetic results can also be correlated by the extended Hammett equation which considers the inductive and resonance effects of substituents separately. Four correlations were attempted using the four current sets of resonance parameters.[28] The best correlation, eq 5, results with σ_R^+ resonance values (correlation coefficient 0.994). These resonance effect parameters indicate that effects involving electron-donating groups are enhanced. The confidence limits of the F test are >99.5%, indicating a statistically meaningful correlation. Both ρ values have confidence limits >99% as indicated by t tests; the intercept is not significantly different from zero.[27] This correlation indicates that the inductive effect is the major factor controlling reactivity for all substituents except the amino group. For the latter, the major effect is resonance. We emphasize that these statements about the nature of the electronic effects of the substituents are valid and in no way are tied to a particular mechanism.

$$\log k_{rel} = -1.74(\pm 0.17)\sigma_I - 0.41(\pm 0.06)\sigma_R^+ - 0.01(\pm 0.08) \quad (5)$$

Generalizations. The NMR method is expected to be applicable to studies of other kinds of adducts in various solvents. The method is especially attractive for reactions involving preequilibrium proton transfer because the desired level of reactivity can be obtained by changing the concentration of catalyst. Moreover, when line shape analysis is employed to extend rate measurements outside the coalescence condition, even greater flexibility results. The NMR method is expected to supplement the spectrophotometric methods now used in conjunction with flow and/or relaxation techniques to obtain rate constants for fast reactions. Owing to the requirement of diastereotopic protons, the NMR method is more limited in scope than spectrophotometric methods but the general availability of the NMR equipment and the simplicity of the method make it extremely attractive.

Experimental Section

General Method of *N*-Alkylation. Isoquinoline, a substituted isoquinoline,[29] quinoline, or phthalazine was allowed to stir at room temperature with an alkylating agent which was benzyl chloride or bromide or chloroacetamide. Addition of ethyl acetate generally resulted in the formation of a solid. Recovered solid often was recrystallized from ethanol–ethyl acetate. The reaction mixtures containing 5-amino-2-benzylisoquinolium ion and 1-carbamoylmethylquinolinium ion were added to a mixture of 1:2:10 (v/v) 70% $HClO_4$:ethanol:ethyl acetate; on standing the perchlorate salt precipitated. A methanolic solution of the 5-chloro-2-benzylisoquinolinium ion was converted to a perchlorate salt using the same perchloric acid–ethanol–ethyl acetate solution. Yields of recovered salts were not less than 60%. Elemental analyses and melting points are reported in Table III for isoquinolinium ions. 1-Carbamoylmethylquinolinium perchlorate, mp 248–250°.

Anal. Calcd for $C_{11}H_{11}N_2O_5Cl$: C, 46.09; H, 3.87; N, 9.77. Found: C, 46.24; H, 3.99; N, 9.78.

Kinetic Procedure. Substrate and ammonium iodide, if desired, were weighed into an NMR tube. (Ammonium iodide was extracted with boiling ether to remove the yellow coloration prior to use.) Ammonia was condensed in the tube using an acetone–Dry Ice bath and 2 ml of trimethylamine vapor (τ 7.87) was added by syringe. The tube was sealed with a torch and the seal was tested by placing the tube in a water bath heated about 20° above the temperature at which the tube was to be heated in the NMR spectrometer. Standard thin wall tubes (0.4 mm) were used at temperatures up to about 30°; at higher temperatures medium wall (0.75 mm) tubes were employed.

The level of ammonia in the tube was measured with a ruler at room temperature. This measurement then was converted to a volume measurement by the use of a calibration curve which was con-

structed by adding known volumes of water to an NMR tube and by measuring the level of the liquid in the tube at room temperature. Concentrations are not corrected for thermal expansion at higher temperatures. Substrate concentrations were about 0.4 M.

Spectra were recorded on a Varian A-60A spectrometer equipped with a V-6040 variable-temperature controller. The probe temperature was measured by the chemical shift method using a sample of methanol and a calibration chart provided by Varian Associates. The level of liquid was kept below the spinner to ensure uniform sample temperatures. Using a sweep width of 100 Hz, the coalescence temperature was determined. The coalescence temperature was taken to be the lowest temperature at which there was no separation between the halves of the AB multiplet.[9]

Constants for least-squares correlation lines involving log (k_c/[NH_4X]) vs. $1/T$ were obtained. The first value multiplied by the constant -10^3 gives the slope; the second value gives the intercept: I, 2.33, 9.91; II, 2.20, 9.96; III, 2.98, 11.99; IV, 2.26, 9.025; V, 2.40, 9.38; VI, 1.58, 6.28; VII, 1.97, 7.72; VIII, 2.04, 7.79.

Recovery of Starting Materials from Ammonia. 2-Benzylisoquinolinium perchlorate, 5-acetylamino-2-benzylisoquinolinium chloride, or 5-nitro-2-benzylisoquinolinium bromide (0.40–0.50 g) was added to approximately 25 ml of ammonia. After the solutions were allowed to reflux for 10 min the mixture was evaporated to dryness. The resultant solid was washed with ether or chloroform and then recrystallized from methanol or ethanol. Starting material was recovered in 60–85% yield.

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References and Notes

(1) For review articles see: W. L. F. Armarego, *Adv. Heterocycl. Chem.*, **1**, 253 (1963); A. Albert and W. L. F. Armarego, *Ibid.*, **4**, 1 (1965); D. D. Perrin, *Ibid.*, **4**, 43 (1965); D. Beke, *Ibid.*, **1**, 167 (1963); A. Albert, *Angew. Chem., Int. Ed. Engl.*, **6**, 919 (1967); M. J. Strauss, *Chem. Rev.*, **70**, 667 (1970); M. R. Crampton, *Adv. Phys. Org. Chem.*, **7**, 211 (1969); E. Buncel, A. R. Norris, and K. E. Russel, *Q. Rev. Chem. Soc.*, **22**, 123 (1968); P. Buck, *Angew. Chem., Int. Ed. Engl.*, **8**, 120 (1969); T. C. Bruice and S. J. Benkovic, "Bioorganic Mechanisms", Vol. II, W. A. Benjamin, New York, N.Y., 1966, Chapter 9.

(2) I. H. Pitman, M. J. Cho, and G. S. Rork, *J. Am. Chem. Soc.*, **96**, 1840 (1974); M. J. Cho and I. H. Pitman, *Ibid.*, **96**, 1843 (1974); J. W. Bunting and W. G. Meathrel, *Can. J. Chem.*, **52**, 303, 962 (1974); **51**, 1965 (1973); **50**, 917 (1972).

(3) J. A. Zoltewicz and L. S. Helmick, *J. Am. Chem. Soc.*, **94**, 682 (1972); J. A. Zoltewicz, L. S. Helmick, T. M. Oestreich, R. W. King, and P. E. Kandetzki, *J. Org. Chem.*, **38**, 1947 (1973).

(4) J. A. Zoltewicz, T. M. Oestreich, J. K. O'Halloran, and L. S. Helmick, *Ibid.*, 1949 (1973).

(5) J. A. Zoltewicz and J. K. O'Halloran, unpublished observations.

(6) C. J. Cooksey and M. D. Johnson, *J. Chem. Soc. B*, 1191 (1968).

(7) R. N. Linquist and E. H. Cordes, *J. Am. Chem. Soc.*, **90**, 1269 (1968).

(8) K. Mislow and M. Raban, *Top. Stereochem.*, 1, 1 (1967); T. H. Siddall and W. E. Stewart, *Prog. Nucl. Magn. Reson. Spectrosc.*, **5**, 33 (1969); M. van Gorkom and G. E. Hall, *Q. Rev. Chem. Soc.*, **22**, 14 (1968).

(9) G. Binsch, *Top. Stereochem.*, **3**, 97 (1968); D. Kost, E. H. Carlson, and M. Raban, *Chem. Commun.*, 656 (1971).

(10) P. Diehl, E. Fluck, and R. Kosfeld, "NMR. Basic Principles and Progress", Vol. 5, Springer-Verlag, New York, N.Y., 1971, Chapter IV.

(11) A. Rauk, L. C. Allen, and K. Mislow, *Angew. Chem., Int. Ed. Engl.*, **9**, 400 (1970).

(12) G. M. Whitesides, D. Holtz, and J. D. Roberts, *J. Am. Chem. Soc.*, **86**, 2628 (1964).

(13) U. Habermalz and F. Krohnke, *Chem. Ber.*, **106**, 1549 (1973).

(14) H. W. Gibson, *J. Org. Chem.*, **38**, 2851 (1973); T. H. Siddall, *J. Phys. Chem.*, **70**, 2249 (1966).

(15) J. J. Lagowski and G. A. Moczygemba in "The Chemistry of Non-Aqueous Solvents", Vol. II, J. J. Lagowski, Ed., Academic Press, New York, N.Y., 1967, Chapter 7.

(16) J. M. Lehn, *Top. Curr. Chem.*, **15**, 311 (1970).

(17) J. B. Lambert, *Top. Stereochem.*, **6**, 19 (1971).

(18) H. Kessler, *Angew. Chem., Int. Ed. Engl.*, **9**, 219 (1970).

(19) C. K. Ingold, "Structure and Mechanism in Organic Chemistry", 2nd ed, Cornell University Press, Ithaca, N.Y., 1969, Chapter VII.

(20) See, for example, F. L. Schadt and P. v. R. Schleyer, *J. Am. Chem. Soc.*, **95**, 7860 (1973); D. J. Raber and J. M. Harris, *J. Chem. Educ.*, **49**, 60 (1972).

(21) G. Binsch, E. L. Eliel, and H. Kessler, *Angew. Chem., Int. Ed. Engl.*, **10**, 570 (1971).

(22) M. R. Crampton and H. A. Khan, *J. Chem. Soc., Perkin Trans. 2*, 2286 (1972).

(23) D. R. Clutter and T. J. Swift, *J. Am. Chem. Soc.*, **90**, 601 (1968).

(24) E. C. Fohn, R. E. Cuthrell, and J. J. Lagowski, *Inorg. Chem.*, **5**, 111 (1966).

(25) J. F. Garst in "Solute-Solvent Interactions", J. F. Coetzee and C. D. Ritchie, Ed., Marcel Dekker, New York, N.Y., 1969, Chapter 8.

(26) P. R. Wells, "Linear Free Energy Relationships", Academic Press, New York, N.Y., 1968.

(27) G. W. Snedecor and W. G. Cochran, "Statistical Methods", 6th ed, Iowa State University Press, Ames, Iowa, 1967.

(28) S. Ehrenson, R. T. C. Brownlee, and R. W. Taft, *Prog. Phys. Org. Chem.*, **10**, 1 (1973).

(29) A. Roe and C. E. Teague, Jr., *J. Am. Chem. Soc.*, **73**, 687 (1951); R. H. F. Manske and M. Kulka, *Can. J. Res., Sect. B*, **27**, 161 (1949); J. J. Craig and W. E. Cass, *J. Am. Chem. Soc.*, **64**, 783 (1942).