energy barrier is believed to be the principal obstacle to the actual proton jump. In ice where the neighboring molecules of water are already aligned, the mobility of protons is several orders of magnitude greater than in water at the same temperature.[14] In 10 *m* n-Bu_4NBr, "ice-like" water is well organized so that the rotational barrier to the proton jump is very small, although it is probably larger than in crystalline ice. It is, then, the diminution in rotational freedom of the water molecules in the quaternary ammonium salt solutions which is responsible for the virtual disappearance of the steric hindrance commonly found with ionol.

Acknowledgments. The support of part of this work by U. S. Atomic Energy Commission Contract AT-(30-1)-2544 is gratefully acknowledged. J. S. thanks the National Research Council of Italy and the Institute of Organic Chemistry of the University of Padua for a research fellowship for some of this work. The late Professor S. Bezzi, former director of the Institute, and Professor E. Scoffone, its present director, were particularly kind. He thanks Professor L. Gotte and Dr. A. Fracassini-Serafini of the Department of Histology of the University for their generous help. Technical assistance by Dr. E. Peggion is deeply appreciated.

The Effect of Conformer Stability on Cation–Ligand Association[1a]

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Abstract: Cation–ligand association constants have been determined by a conductance method for piperidinium, 1-methylpiperidinium, and 1-ethylpiperidinium cations with free amine, triphenylphosphine oxide, and 2,6-dimethylpyridine as ligands in chlorobenzene as solvent and with the first two as ligands in nitrobenzene as solvent, all at 25°. The results are interpreted in terms of equatorial–axial conformational equilibria for the substituted piperidinium cations and amines. Values of the equilibrium constants are calculated and compared with other pertinent values in the literature.

We have determined cation–ligand association constants, K_L (eq 1), for a variety of ligands, L,

$$AH^+ + L \rightleftarrows AH^+,L \qquad K_L = [AH^+,L]/[AH^+][L] \tag{1}$$

principally with tri-n-butylammonium cation in several low dielectric solvents at 25° using a conductance method.[2] We now report the measurement of the conductances of piperidinium ($PipH^+$), 1-methylpiperidinium ($MePipH^+$), and 1-ethylpiperidinium ($EtPipH^+$) picrates with and without added free amine as ligand and added triphenylphosphine oxide (Ph_3PO) as ligand in nitrobenzene ($PhNO_2$) solvent and in chlorobenzene (PhCl) solvent, all at 25°. 2,6-Dimethylpyridine (Lut) was also used as a ligand in the latter solvent. This work was undertaken to extend our information on the effect of cation structure on cation–ligand association.

Experimental Section

Chlorobenzene was purified as before.[2a] Nitrobenzene was purified using a modification[2f] of a procedure due to Witschonke and Kraus.[3] Picric acid (HPi) was recrystallized from ethanol. The piperidines (Columbia Organic Chemicals Co., Inc.) were distilled under reduced pressure, a middle fraction being taken. The picrate salts of each of these amines was prepared in the same way[2a] as the tributylammonium picrate previously used: PipHPi, mp 151–152° (lit.[4] mp 150.5–151.5°); MePipHPi, mp 230–231° (lit.[5] mp 226°); EtPipHPi, mp 172–173° (lit.[5] mp 170°). 2,6-Dimethylpyridine was distilled at atmospheric pressure, a middle fraction being taken. Ph_3PO was purified as before.[2c] Conductance measurements were carried out using the bridge, bath, and cells previously described.[2a] The physical constants of the solvents, $PhNO_2$ and PhCl, have been listed before.[2e,f]

Results

The equivalent conductances, Λ (cm^2 ohm^{-1} $equiv^{-1}$), as a function of molar salt concentration, C, for a number of salts in $PhNO_2$ solvent with and without added ligands, at 25°, appear in Table I. The solvent specific conductance has been subtracted from that of the solution in each case to obtain the specific conductance presumed due to the salt alone. The solvent conductance was no more than 0.2% of that of the most dilute salt solution. No attempt was made to check or correct for polarization. We have already found[2f] that the correction for this effect with a similar salt, Bu_3NHPi, amounted to no more than 0.1%. The conductance data in Table I were treated by the method of Shedlovsky,[6] where S is the Shedlovsky function and $y_{\pm}^2$ is calculated from the Debye–Hückel theory. $\Lambda_0{}^0$ is the limiting

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(1) (a) This research was supported in part by a National Science Foundation Grant, GP-3955; (b) author to whom inquiries should be addressed.

(2) (a) E. R. Ralph, III, and W. R. Gilkerson, *J. Am. Chem. Soc.*, **86**, 4783 (1964); (b) W. R. Gilkerson and E. R. Ralph, III, *ibid.*, **87**, 175 (1965); (c) W. R. Gilkerson and J. B. Ezell, *ibid.*, **87**, 3812 (1965); (d) J. B. Ezell and W. R. Gilkerson, *ibid.*, **88**, 3486 (1966); (e) W. R. Gilkerson and J. B. Ezell, *ibid.*, **89**, 808 (1967); (f) J. B. Ezell and W. R. Gilkerson, *J. Phys. Chem.*, in press.

(3) C. R. Witschonke and C. A. Kraus, *J. Am. Chem. Soc.*, **69**, 2472 (1947).

(4) T. B. Grave, *ibid.*, **46**, 1460 (1924).

(5) W. Magnusson and E. R. Schierz, *Wyoming Univ. Publ.*, 7, 1 (1940); *Chem. Abstr.*, **34**, 6867 (1940).

(6) T. Shedlovsky, *J. Franklin Inst.*, **225**, 739 (1938).

$$AH^+,X^- \rightleftarrows AH^+ + X^- \quad K = [AH^+][X^-]/[AHX] \tag{2}$$

$$1/\Lambda S = 1/\Lambda^0 + \Lambda S C y_\pm{}^2/K\Lambda^{0^2} \tag{3}$$

equivalent conductance in pure solvent, while $\Lambda_a{}^0$ will be used to designate these values obtained in solvent–ligand mixtures. K_0 is the ion-pair dissociation constant (eq 2) for salt in pure solvent, while K is that in the presence of added ligand. The data were analyzed on an IBM 1620 computer using a program written for us by Dr. S. M. Katz. We obtain $\Lambda_0{}^0 = 33.31$ and $K_0 = 1.54 \times 10^{-4}$ for PipHPi. Witschonke and Kraus[3] obtained values of 33.26 and 1.53×10^{-4}, respectively, for these parameters. The values of K and Λ^0 for the three salts studied in the $PhNO_2$–ligand solvent systems are listed in Table II. Only one ligand solution was studied in each case. We shall treat the data as if only a 1:1 complex between cation and ligand is formed (eq 1). Using relations already derived and reported elsewhere,[2c] we have calculated values of K_L and $\Lambda_1{}^0$, the limiting equivalent conductance of the salt, AH^+, L + X^-, for each case where applicable. These values likewise appear in Table II. The uncertainties in the ion-pair dissociation constants, K, are of the order of 7 and 0.3% in Λ^0. The uncertainties in the values of K_L are ~10 and 3% in $\Lambda_1{}^0$.

Table I. Conductances of Piperidinium Salts in $PhNO_2$ Solutions at 25°

10^4C, M	Λ	10^4C, M	Λ
PipHPi		PipHPi + 0.00488 M Ph_3PO	
0.357	27.76	0.6764	24.30
0.685	24.88	1.238	22.17
1.018	22.87	1.831	20.52
1.341	21.39	2.398	19.30
1.640	20.27	2.912	18.39
1.906	19.44	3.386	17.67
2.217	18.59		
PipHPi + 0.0163 M Pip		MePipHPi	
0.5928	27.67	0.5208	25.38
1.272	25.16	1.008	22.06
1.849	23.59	1.456	20.07
2.501	22.19	1.879	18.67
3.071	21.18	2.276	17.61
3.574	20.41	2.637	16.81
MePipHPI + 0.00520 M Ph_3PO		EtPipHPi	
0.5984	25.14	0.3063	28.11
1.219	22.54	0.5791	25.66
1.816	20.77	0.9061	23.58
2.403	19.75	1.164	22.30
2.996	18.38	1.445	21.16
3.474	17.64	1.720	20.22
		2.004	19.40
		2.223	18.84
EtPipHPi + 0.00467 M Ph_3PO		EtPipHPi + 0.0178 M EtPip	
0.6177	25.40	0.6075	25.55
1.148	23.34	1.081	22.78
1.654	21.87	1.592	20.72
2.146	20.72	2.091	19.22
2.571	19.88	2.549	18.15
2.999	19.15	3.010	17.24
		3.349	16.67

Table II. Conductance Parameters in $PhNO_2$ at 25°

Salt	Ligand[a]	10^4K	$\Lambda_0{}^0$ (or $\Lambda_a{}^0$)	K_L	$\Lambda_1{}^0$
PipHPi		1.54	33.31		
	Pip	4.38	31.36	113	30.4
	Ph_3PO	3.30	28.85	234	25.1
MePipHPi		1.38	32.96		
	Ph_3PO	3.07	29.67	236	26.9
EtPipHPi		1.75	32.58		
	EtPip	1.73	32.77	0	
	Ph_3PO	3.69	29.42	238	26.4

[a] Concentrations of ligands are given in Table I.

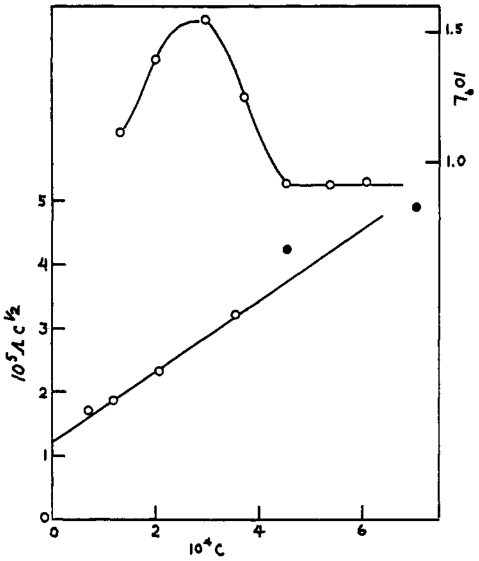


Figure 1. PipHPi in PhCl at 25°. Lower curve, Fuoss and Kraus plot: open circles, PipHPi alone; closed circles, with added HPi. Upper curve; titration of 4.56×10^{-4} M Pip with HPi in PhCl: specific conductance, L, $vs.$ concentration of HPi, C, in resulting solution.

The piperidinium picrates are very weak electrolytes in PhCl solvent. The conductances of salt solutions of the order of 10^{-4} M are only ten times the conductance of the solvent itself, in spite of precautions in preparing the latter. It is necessary to work at such low salt concentrations in order to minimize the effects of triple ion formation.[2f,7] Despite the relatively poor quality of the data from the point of view of a conductance expert, the results are quite useful, as we shall see. We present all of the results obtained in PhCl in graphical form. PipHPi in pure PhCl showed evidence of triple ion formation in the 10^{-4} M region; a Fuoss and Kraus plot[7] of these data is shown in Figure 1. The intercept yields a value of $K_0 = 6 \times 10^{-14}$. We estimated[2a,f] a value of $\Lambda_0 = 50$ for this salt in PhCl. K_0 for Bu_3NHPi is ten times greater in this solvent.[2a]

We next undertook titration experiments. The upper curve in Figure 1 shows the effect on the specific conductance of the addition of increments of a solution of HPi in PhCl to a 4.56×10^{-4} M solution of piperidine in PhCl. The stoichiometric concentration of picric acid in the resulting solution is denoted C in this plot. It can be seen that, after the equivalence point, the conductance of the solution is unaffected by the addition of excess HPi. The piperidines were then added in weighed increments to solutions of HPi in PhCl. Plots of the values of Λ^2C $vs.$ total ligand concentration obtained from these experiments appear in Figure 2 for the systems HPi + Pip, HPi + MePip, and HPi + EtPip. Here C is the concentration of picrate salt taken as being equal to the stoichiometric concentration of amine prior to the equivalence point, and equal to the stoichiometric concentration of HPi beyond the equivalence point. [L]

(7) R. M. Fuoss and C. A. Kraus, *J. Am. Chem. Soc.*, 55, 2387 (1933).

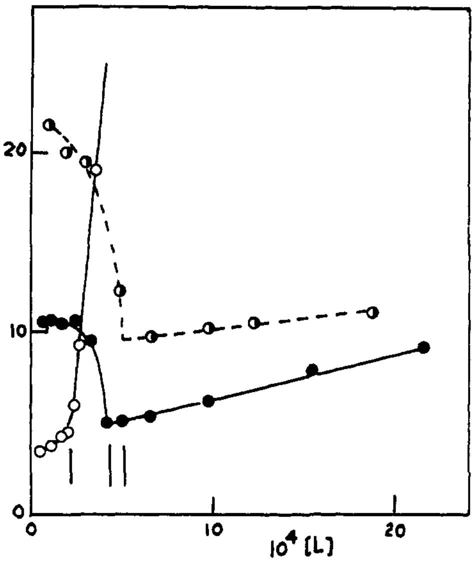


Figure 2. Plots of Λ^2C *vs.* concentration of piperidine, *C*, from titrations of HPi with piperidines in PhCl at 25°: ○, piperidine; ●, 1-methylpiperidine; ◑, 1-ethylpiperidine. Perpendicular lines below the breaks in the curves indicate the equivalence points.

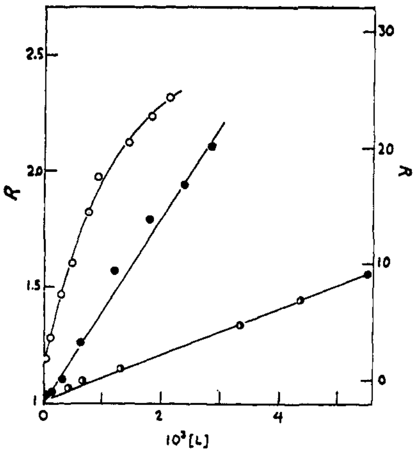


Figure 3. The ratios, *R*, for 2.56 × 10^{-4} *M* PipHPi + Pip, ○, right-hand ordinate; for 3.48 × 10^{-4} *M* MePipHPi + MePip, ●, left-hand ordinate; and for 5.52 × 10^{-4} *M* EtPipHPi + EtPip, ◑, left-hand ordinate.

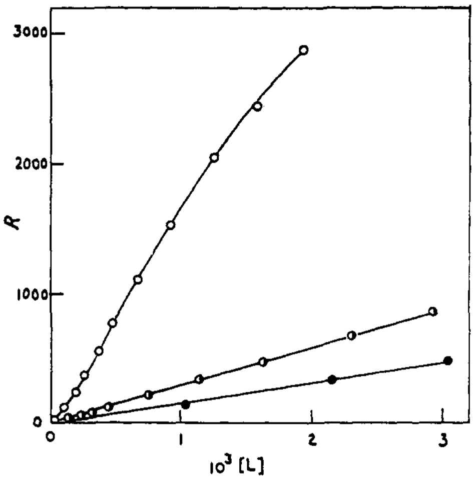


Figure 4. Ph_3PO as ligand in PhCl: ○, 3.70 × 10^{-4} *M* PipHPi; ●, 2.92 × 10^{-4} *M* MePipHPi; ◑, 2.79 × 10^{-4} *M* EtPipHPi.

here denotes the total concentration of amine. All concentrations have been corrected for volume changes in the course of the titrations. Note the differences in the behavior of the product, Λ^2C in the case of Pip compared to MePip and EtPip. The former values increase as [Pip] increases and at the equivalence point become steeply linear. The same quantities in the case of MePip and EtPip show curvature downward until the equivalence point and subsequently are linear (as [L] increases) with a relatively small slope. The shape of the curves prior to the equivalence point for the substituted piperidines might lead one to suspect that they are due to suppression of acid–base dissociation of the ion pairs by the excess HPi present. If this were the case, however, the increases in Λ^2C after the equivalence point should at least be equal to or greater than those before the end point is reached. These complexities in the case of excess HPi should be investigated further. We need values of $(\Lambda^2C)_{L=0}$ at the equivalence point in order to determine values of K_L[2d,f] (eq 1) from plots of $R = (\Lambda^2C)_L/(\Lambda^2C)_{L=0}$ *vs.* [L] for these systems. The required values can be easily obtained from graphs such as Figure 2. We show in Figure 3 values of the ratios *R* plotted *vs.* concentration of the respective piperidine in excess for the three systems studied. Three titrations were carried out for Pip, two for MePip and one for EtPip. The plots for the substituted piperidines were reasonably linear. The slopes of these, K_L, are given in Table III. The plot for Pip itself shows a decreasing slope at higher [Pip]. We believe this to be due to a molecule of the amine complexing with the ion pair, $PipH^+$, Pi^-, itself[2a] (eq 4). It has been shown[2a] that the ratio *R* becomes

$$PiPH^+,Pi^- + Pip \rightleftarrows (Pip)_2H^+,Pi^-$$

$$K_2 = [(Pip)_2HPi]/[PipHPi][Pip] \qquad (4)$$

$R = (1 + K_L[L])/(1 + K_2[L])$. Rearranging, we obtain eq 5. A plot of $(R - 1)/[L]$ *vs.* *R* yielded a value of K_L

$$(R - 1)/[L] = K_L - K_2R \qquad (5)$$

(Table III) from the intercept as $R \rightarrow 1$, and a value of $K_2 = 500 \pm 10$ was calculated from the slope. The estimated uncertainties in the values of K_L are: 5% (Pip), 16% (MePip), and 6% (EtPip).

Table III. Cation–Ligand Association in PhCl at 25°

Ligand	$10^{-3}K_L$ PipH$^+$	MePipH$^+$	EtPipH$^+$
R-Pip[a]	21	0.38	0.10
2,6-Dimethylpyridine	3.9	0.75	0.44
Ph_3PO	650	150	280

[a] R-Pip represents the free amine corresponding to the cation.

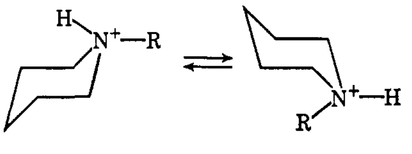
Results of titrations of PhCl solutions of the three piperidinium picrates with Ph_3PO are shown in Figure 4, where values of *R* are plotted *vs.* [Ph_3PO]. The increases in conductances are quite large for this ligand. Distinct curvature is apparent in the case of PipHPi. The increasing slope at low [Ph_3PO] we believe is due to a second molecule of ligand being added to the cation–ligand complex, $PipH^+$, $OPPh_3$. The decreasing slope at higher phosphine oxide concentration may be due to the ligand forming a complex with the ion pair itself. For the moment, we are not interested in the complexity of this system, so we obtained the value of K_L (as $[Ph_3PO] \rightarrow 0$) listed in Table III from a plot of $(R - 1)/[L]$ *vs.* [L]. Values of K_L for the other two salts were obtained from the slopes of the R *vs.* $[Ph_3PO]$ graphs. The estimated uncertainties in these values of K_L are 8% ($PipH^+$), 13% ($MePipH^+$), and 7% ($EtPipH^+$).

Results of titrations of PhCl solutions of the three piperidinium salts with 2,6-dimethylpyridine are shown in Figure 5, where the ratios R are plotted *vs.* [Lut]. The plots for both MePipHPi and EtPipHPi show curvature upward at higher [Lut]. We used the limiting slopes at low ligand concentration to obtain the values of K_L listed in Table III. We estimate the uncertainty in these two values of K_L to be ~20%. The plot for PipHPi does not show significant curvature; the uncertainty in this value of K_L is estimated to be 3%.

We have neglected possible changes in Λ^0 for the salts upon complexation in PhCl. This factor could introduce an error of the order of 10–15% in all of the foregoing values of K_L, in this solvent.

Discussion

Our principal aim in undertaking this work was to investigate the effect on cation–ligand association of substituting methyl and ethyl groups for hydrogen on the nitrogen atom in piperidinium cation. Our results can best be understood in terms of the conformational



$K_{ea} = [AH^+]_a/[AH^+]_e$ (6)

equilibrium (eq 6) between the equatorial conformer (e) and the axial conformer (a). Values for the equilibrium constant, K_{ea}, for the protonated piperidines have not been reported to our knowledge. Allinger[8] has reported a value of $\Delta F_{ea}{}^\circ$ for the unprotonated methylpiperidine in benzene at 25° from which we obtain $K_{ea} \simeq 0.05$. Lewin and Winstein[9] reported values of $\Delta F_{ea}{}^\circ$ for methyl- and ethylcyclohexane in CCl_4 at 30° from which one estimates $K_{ea} = 0.054$ for both compounds at 25°.

We find in $PhNO_2$ that K_L with L = Ph_3PO is independent of the substituent on N. $PhNO_2$ is a good solvating agent for cations[2e,f] as aromatic nonbasic solvents go. We would expect, from examination of space-filling models, that the ligand or specifically solvating solvent molecule would overwhelmingly prefer to attach itself to the cation conformer in which the methyl or ethyl group is in the axial conformation. This is in agreement with observation (Table II), provided as before[2e,f] we assume that $PhNO_2$ specifically solvates piperidinium cations as it appears to solvate tributylammonium cation. In short we suppose that the 1-methylpiperidinium and 1-ethylpiperidinium cations exist in nitrobenzene solvent preferentially in the axial conformation whether they are free (solvated) or in a cation–ligand complex. We observe a complex between $PipH^+$ and Pip in $PhNO_2$, but there is no indication of the formation of the corresponding complex between $EtPipH^+$ and EtPip. This can be explained by recalling that while $PhNO_2$ solvates the cation, forcing it into the axial conformation, the free amine, bearing no net charge, would not be expected to interact with solvent to nearly the extent the cation would. The free amine then would preferentially exist in the equatorial conformation. The amine then would have to undergo an equatorial-to-axial flip in order to form the most stable cation–ligand complex.

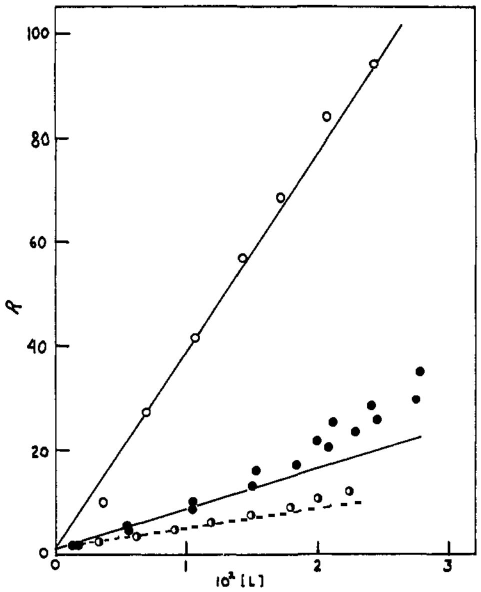
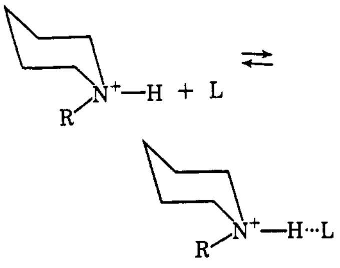


Figure 5. 2,6-Dimethylpyridine (Lut) as ligand in PhCl: ○, 2.62 × 10^{-4} *M* PipHPi; ●, 3.13 × 10^{-4} *M* MePipHPi; ◐, 2.94 × 10^{-4} *M* EtPipHPi.

The effects of alkyl substituents bonded to nitrogen in piperidinium cations on K_L values in PhCl solvent are quite marked (Table III). PhCl is a much poorer specifically solvating solvent for cations than is $PhNO_2$.[2e,f] We first consider 2,6-dimethylpyridine as a ligand. This compound was chosen with the thought in mind that it certainly would prefer (based on steric considerations) to form a cation–ligand complex with the axial conformers of the alkylpiperidinium cations



$K_L^a = [AH^+,L]_a/[AH^+][L]$ (7)

where the subscripts a on the concentrations of the cations denote the axial conformers. In the following analysis, we shall make the assumptions (i) only a negligible fraction of cation–ligand complex has an N-alkyl substituent in an equatorial conformation, (ii) the axial conformers of 1-methylpiperidinium and 1-ethylpiperidinium cations have the same affinity for Lut as does piperidinium cation itself; *i.e.*, $K_L{}^a$ is the same for all three cations with this ligand. Then the observed value of K_L becomes

$$K_L = [AH^+,L]_a/[AH^+]_{total}[L] = K_L{}^a K_{ea}/(1 + K_{ea}) \quad (8)$$

where $[AH^+]_{total} = [AH^+]_a + [AH^+]_e = [AH^+]_a(1 + 1/$

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[8] N. L. Allinger, J. G. D. Carpenter, and F. M. Karkowski, *J. Am. Chem. Soc.*, **87**, 1232 (1965).

[9] A. H. Lewin and S. Winstein, *ibid.*, **84**, 2464 (1962).

K_{ea}). Taking $K_L{}^a = K_L$ for piperidinium cation with Lut as ligand, we calculated the values of K_{ea} listed in Table IV. These values are greater than that quoted[8] for the unprotonated methylpiperidine in benzene. We have already noted that we expect a large specific solvent effect to be operative in the case of the cations and not in the case of the free amines. The results in $PhNO_2$ solvent (Table II) support the conclusion that K_{ea} may even be greater than unity for the cations in that solvent. We attribute the larger values of K_{ea} for the cations in PhCl compared to the amine in benzene to the polar PhCl specifically solvating the cations in such a manner as to lower the free energy of that conformer with the substituent in the axial position, compared to the value it would have in benzene solvent.

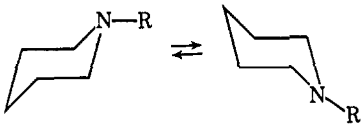
Table IV. Conformational Equilibrium Constants, K_{ea}, in PhCl at 25°

Ligand	Lut	Ph_3PO	R-Pip[a]
Cation			
$MePipH^+$	0.24	0.30	0.10
$EtPipH^+$	0.13	0.76	0.043

[a] R-Pip represents the free amine corresponding to the cation. These are values of $K_{ea}{}^L$, for the ligands themselves, calculated as described in the text.

The values of K_{ea} for the same cations calculated using K_L values for Ph_3PO as ligand are also listed in Table IV. Note that for $MePipH^+$ K_{ea}, using Ph_3PO as a ligand, is the same as that obtained using Lut as ligand, within the limits of the assumptions made and the experimental error. K_{ea} for the $EtPipH^+$ cation with Ph_3PO is six times greater than that obtained using Lut. We think this is a significant difference. The enhancement using Ph_3PO we think is due to specific interaction between a hydrogen on the terminal methyl of the ethyl group attached to nitrogen and the second lone pair of electrons on the phosphoryl oxygen atom. The first lone pair is involved in the interaction with the proton on nitrogen. Experiments to test predictions based on the foregoing explanation have been carried out, and these results form the content of another report to be submitted.

The values of K_L using the free amines as ligands (Table III), decrease drastically as one substitutes methyl for hydrogen, and then ethyl for methyl on the ring nitrogen. The results with the amines as ligands in $PhNO_2$ solvent seemed to require that the ethylpiperidine undergo an unfavorable e → a conversion to form the complex with the already (by solvation) converted cation. Now, in PhCl as solvent, it appears that both cation and amine must be required to undergo the e → a conversion prior to or during the cation–ligand complex formation. Then in addition to eq 6 and 7, we have



$K_{ea}^L = [L]_a/[L]_e$ (9)

Using the same assumptions as before, i and ii, we obtain

$$K_{ea}{}^L = K_L(1 + K_{ea})/[K_{ea}K_L{}^a - K_L(1 + K_{ea})] \quad (10)$$

We now calculate values of $K_{ea}{}^L$, using eq 10, for the ligands themselves, taking $K_L{}^a = K_L$ for $PipH^+$ + Pip. These values of $K_{ea}{}^L$ appear in Table IV in the last column. These values bracket that reported by Allinger[8] for MePip. The nature and number of the assumptions made in calculating these values of $K_{ea}{}^L$ are such that much significance cannot be attached to the observation that the value for MePip is greater than that for EtPip. We do observe the same order for the cations. In conclusion, these values of equatorial-to-axial equilibrium constants are not precision numbers by any means, but we do believe they are quite close to the real values. An examination of trends in K_L for other ligands with the 1-substituted piperidines might help clear up some of the uncertainties in this regard.