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Electrostatic Catalysis by Ionic Aggregates. 6. Modulation of Proton-Transfer Equilibria by Lithium Perchlorate–Diethyl Ether Clusters[1]

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Abstract: This study shows that the proton-transfer reaction of tropolone (2-hydroxy-2,4,6-cycloheptatrien-1-one) with amine bases in diethyl ether is subject to substantial changes in the apparent equilibrium constant with changes in the concentration of lithium perchlorate. For example, at 25 °C the apparent equilibrium constant for the reaction of tropolone with pyridine in 4.8×10^{-3} M $LiClO_4$ in ether is 1.9×10^{-3}, but in solution containing 2.95 M lithium perchlorate, the equilibrium constant increases to 23.8, a 12 500-fold increase. Likewise for the other bases used in the study, the apparent equilibrium constant showed a similar dependence on the lithium perchlorate concentration. An analysis of the temperature dependence of the equilibrium constant shows that the enthalpy of the reaction remains essentially constant, but the entropy of the reaction increases markedly with increasing lithium perchlorate concentration. This causes the free energy of reaction to decrease with increasing $LiClO_4$ concentration. The enthalpy of reaction in $LiClO_4$–diethyl ether solutions is −6.0, −4.6, and −3.2 kcal/mol for 4-methylaniline, aniline, and 4-bromoaniline, respectively, and −4.4, −4.0, and −2.9 kcal/mol for 4-methylpyridine, 3-methylpyridine, and pyridine, respectively. Solvation of the ion pairs produced in the proton-transfer equilibrium and their interaction with the solvated lithium perchlorate ion pairs and higher aggregates are discussed.

Lithium perchlorate has been reported to exhibit a very high solubility in diethyl ether, up to 6 M at 30 °C.[2,3] Conductivity measurements of solutions of lithium perchlorate in diethyl ether (LPDE) show a several hundred fold increase in the molar conductivity, despite a large increase in the viscosity of the medium.[3-5] This has been attributed to the transport of single ions within the complex clusters, rather than the movement of the clusters themselves. Vapor pressure data suggest that the solution must be made up of $LiClO_4$·ether complexes, rather than simple $LiClO_4$ clusters.[3]

Using trityl chloride as a sensitive probe of the ionic environment, Pocker and Buchholz[6] showed that the observed equilibrium constant of the dissociation of trityl chloride changes dramatically with varying concentrations of lithium perchlorate in diethyl ether. The equilibrium constant varies from 2.1×10^{-12} in pure ether to 1.4×10^{-2} in 5.05 M LPDE, more than a 10^9-fold increase. The nature of this medium was investigated by producing solubility–temperature curves, measuring the heat of solution, and recording the NMR spectra of lithium perchlorate in diethyl ether.[6] These data suggest that the solution consists of dietherate ions, $Li(OEt_2)_2^+,ClO_4^-$, below 4.25 M LPDE and a mixture of $Li(OEt_2)_2^+,ClO_4^-$ and monoetherate ions $Li(OEt_2)^+,ClO_4^-$ above 4.25 M LPDE. The dielectric constant increased linearly with added salt, but this increase is not nearly large enough to account for the observed catalytic effect seen in this medium.

Pocker and Ellsworth[7] studied the rearrangement of 1-phenylallyl chloride in lithium perchlorate solutions in various solvents. Lithium perchlorate solutions produced large increases in the rate of isomerization. The different solvents used were diethyl ether, tetrahydrofuran, propylene oxide, diethyl carbonate, and dimethylformamide, with the greatest rate increase being observed in solutions of lithium perchlorate in diethyl ether.

Proton-transfer reactions are of fundamental importance in chemistry; however, the effect of LPDE on proton-transfer equilibria, eq 1, has not been studied extensively. Pocker and Rueber[8] have studied the equilibrium reaction of nitrophenols with weak organic bases in LPDE solutions. In the reaction of *p*-nitrophenol with imidazole, the apparent equilibrium constant for the reaction changes from 1.78×10^{-7} in pure ether to ca. 1.0 in 5 M LPDE.

$$HA + B{:} + nLiClO_4 \rightleftharpoons Li^+,A^-{\cdot}(n-m-1)LiClO_4 + BH^+,ClO_4^-{\cdot}mLiClO_4 \quad (1)$$

In the current study, the proton-transfer equilibria between tropolone (2-hydroxy-2,4,6-cycloheptatrien-1-one) and amine bases are used to study the effect of lithium perchlorate in diethyl ether on these types of reactions. Tropolone was chosen because it contains an internal hydrogen-bonded proton. In aqueous solvents, the pK_a of tropolone is 6.71,[9] but in pure ether no proton-transfer reaction could be observed with a variety of bases, indicating that it is a much weaker acid in nonpolar media. Even with a large excess of triethylamine, less than 1% of the tropolone was deprotonated in pure ether, but upon addition of $LiClO_4$ to this solution, the reaction then goes to completion. Pyridine and other weak bases were used so that an equilibrium could be established and the effect of $LiClO_4$ in solution could be measured. The equilibrium constants and thermodynamic parameters were measured for this system.

The lithium perchlorate–ether system has the advantage of possessing relatively mobile ionic clusters[10] that generate appreciable Coulombic fields. The present investigation broadens our understanding of such ionic systems and probes the origin and possible magnitude of their electrostatic effects.

Experimental Section

Materials. Reagent grade anhydrous $LiClO_4$ (G. Frederick Smith Chemical Co.) was recrystallized twice from distilled water in the form $LiClO_4{\cdot}3H_2O$ and then dried under vacuum at 150 °C (0.5 mm) for 15 h. The salt was stored in a sealed vial in a desiccator until used. It is

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(1) Previous paper in this series: Pocker, Y.; Ellsworth, D. L. *J. Am. Chem. Soc.* **1977**, *99*, 2284–93.

(2) Willard, H. H.; Smith, G. F. *J. Am. Chem. Soc.* **1923**, *45*, 286–97.

(3) Ekelin, K.; Sillén, L. G. *Acta Chem. Scand.* **1953**, *7*, 987–1000.

(4) Chu, J. C. H. Ph.D. Thesis, University of Michigan, Ann Arbor, MI, 1949; *Chem. Abstr.* **1949**, *43*, 8790.

(5) Johnson, O. Ph.D. Thesis, University of Michigan, Ann Arbor, MI, 1948; *Chem. Abstr.* **1949**, *43*, 4543.

(6) Pocker, Y.; Buchholz, R. F. *J. Am. Chem. Soc.* **1970**, *92*, 2075–84.

(7) Pocker, Y.; Ellsworth, D. L. *J. Am. Chem. Soc.* **1977**, *99*, 2276–84.

(8) Pocker, Y.; Rueber, M. S. *Proc. 6th Int. Symp. Solute-Solvent Interactions*, 1982, 5P-13, p 205. Reuber, M. S. Ph.D. Thesis, University of Washington, Seattle, WA, 1987.

(9) Doering, W. v. E.; Knox, L. H. *J. Am. Chem. Soc.* **1951**, *73*, 828–38.

(10) It has not escaped out attention that such ionic clusters in media of low dielectric constant are not only interesting to the physical organic chemist but could also be useful in synthetic chemistry, especially in the use of lithium enolates in asymmetric synthesis (Evans, D. A. in *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York, 1984; Vol. 3, p 21). Other spectacular effects have been noted in cationic and anionic polymerization processes (Takeuchi, K.; Kato, Y.; Okamoto, K. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 3881–82; Pocker, Y.; Miao, E. C., unpublished observations), in the doping of polymers to produce conducting films (Vincent, C. A. *Prog. Solid State Chem.* **1987**, *17*, 145–261), and as electrolytes in lithium batteries (Tobishima, S. I.; Yamaki, J. I.; Okada, T. *Electrochim. Acta* **1984**, *29*, 1471–6).

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necessary to keep $LiClO_4$ completely anhydrous, since the hydrate is not appreciably soluble in ether (0.139 g/100 mL of solution at 25 °C).[2]

Reagent grade anhydrous diethyl ether (Allied Chemical Co.) was refluxed over and distilled from $LiAlH_4$ (Metal Hydrides Inc.) just prior to use.

Aniline (reagent grade, Aldrich Chemical Co.), pyridine (reagent grade, Allied Chemical Co.), 3-picoline (reagent grade, Aldrich Chemical Co.), 4-picoline (reagent grade, Aldrich Chemical Co.), and triethylamine (Baker grade, Baker Chemical Co.) were refluxed over and then distilled from potassium hydroxide pellets at atmospheric pressure under an argon atmosphere.[11] If the amine was not used immediately, it was stored under argon in a desiccator.

p-Toluidine (practical grade, Eastman Organic) and 4-bromoaniline (reagent grade, Aldrich Chemical Co.) were recrystallized from anhydrous ethanol, dried in vacuo, and stored in a desiccator.

Tropolone (Aldrich Chemical Co.) was purified by vacuum sublimation at 0.5 mm, collected on a dry ice/acetone condenser, and stored in a desiccator.

Equilibrium Measurements. All spectrophotometric measurements were done on a Varian Cary Model 210 spectrophotometer interfaced to an Apple IIe computer through a bidirectional parallel interface. The cell compartment of the spectrophotometer was thermostated (±0.1 °C) with a Formatemp Jr. Model 2095-2 constant-temperature bath. All spectra were recorded between 300 and 420 nm and stored on floppy diskettes for later calculation of the equilibrium constant. The maximum absorbance peaks for the compounds monitored are 354 ($\epsilon = 5150$) and 322 nm ($\epsilon = 6650$) for tropolone and 387 ($\epsilon = 11\,300$) and 325 nm ($\epsilon = 12\,300$) for the tropolonate anion. The concentration of tropolone used was ca. 6×10^{-5} M in each case. The concentration of base was adjusted so that the ratio of tropolone to tropolonate anion was greater than 0.1 and less than 10. An equilibrium constant was found for each solution at each temperature by using Beer's law relationships to calculate the concentration of tropolone and tropolonate anion. The apparent equilibrium constant is given by eq 2. In the calculations of the apparent

$$K'_{eq} = \frac{[\text{tropolonate anion}]^2}{[\text{tropolone}] \times ([\text{base}] - [\text{tropolonate anion}])} \qquad (2)$$

equilibrium constants it was assumed that [tropolonate anion] = [protonated base]. The effect of temperature on the equilibrium constant of the proton-transfer reaction between tropolone and various nitrogen bases was measured in varying concentrations of lithium perchlorate in ether. The temperature range used was from 0 to 31 °C, and solutions were corrected for concentration differences due to temperature changes. Plotting $\ln K'_{eq}$ versus $1/T$ and using the relationship $\ln K'_{eq} = -\Delta H/RT + \Delta S/R$, one can find the enthalpy and entropy of reaction for each salt concentration and base.

Results and Discussion

Proton-Transfer Equilibria of Tropolone with Amine Bases. The proton-transfer equilibria of tropolone with various amine bases was studied in lithium perchlorate–diethyl ether solutions. The bases used in the equilibrium constant determinations are 4-methylaniline, aniline, 4-bromoaniline, 4-methylpyridine, 3-methylpyridine, and pyridine. No reaction was observed with bases having acidity constants of their conjugate acids less than 10^{-3}, while stronger bases gave a quantitative yield of products. The concentration of $LiClO_4$ ranged from 0.004 to 4.00 M. Higher concentrations were not used because the reactions go essentially to completion, and the ratio of products to reactants could not be measured accurately.

Table I. Equilibrium Constants for the Proton-Transfer Reaction of Tropolone with Pyridine Bases at 25.0 °C

base	$[LiClO_4]$, M	[HA],[a] $\times 10^5$ M	$[A^-]$,[b] $\times 10^5$ M	[base],[c] $\times 10^5$ M	K'_{eq}[d]
4-methylpyridine	1.04	0.63	7.10	10.9	20.8
	0.310	3.72	4.98	7.56	2.59
	0.101	2.62	4.56	21.9	0.46
	0.034	4.39	2.75	21.9	0.091
	0.013	3.49	2.94	84.0	0.031
	0.010	6.33	1.63	21.9	0.021
	0.0065	4.39	2.16	84.0	0.013
3-methylpyridine	2.12	1.14	6.84	8.51	24.5
	1.16	1.30	8.70	14.3	10.3
	0.31	3.68	6.96	14.3	1.78
	0.11	3.53	4.19	25.5	0.23
	0.10	4.10	4.34	28.7	0.19
	0.035	5.23	2.64	25.5	0.058
	0.035	5.94	2.62	28.7	0.044
	0.010	7.24	1.49	28.7	0.011
pyridine	2.95	0.75	4.10	5.04	23.8
	2.01	1.06	3.78	5.04	10.8
	1.44	2.35	4.61	5.95	6.74
	0.99	2.18	4.59	6.51	5.04
	0.55	3.01	3.87	6.51	1.85
	0.33	3.88	3.19	6.51	0.792
	0.17	1.28	3.48	42.8	0.240
	0.10	1.81	2.85	42.8	0.113
	0.052	2.19	4.86	311	0.0353
	0.031	2.93	3.91	311	0.0170
	0.010	4.45	2.74	311	0.0055
	0.0065	2.10	4.32	294	0.0030
	0.0048	3.80	1.47	301	0.0019

[a] Concentration of tropolone in solution as determined by eq 4. [b] Concentration of tropolonate anion in solution as determined by eq 4. [c] Initial concentration of base. [d] Apparent equilibrium constant calculated from eq 2.

Table II. Equilibrium Constants for the Proton-Transfer Reaction of Tropolone with Aniline Bases at 25.0 °C

base	$[LiClO_4]$, M	[HA],[a] $\times 10^5$ M	$[A^-]$,[b] $\times 10^5$ M	[base],[c] $\times 10^5$ M	K'_{eq}[d]
4-methylaniline	2.00	1.16	6.17	7.29	29.3
	1.04	1.65	4.89	6.21	10.3
	0.98	2.05	5.54	7.29	8.63
	0.49	2.89	4.81	7.29	3.22
	0.25	1.84	6.38	23.7	1.28
	0.10	1.93	5.80	105	0.177
	0.05	3.34	4.35	105	0.0566
	0.02	3.75	2.24	77.6	0.0177
	0.01	6.15	1.48	105	0.0034
aniline	4.00	0.89	5.94	7.38	27.4
	2.96	1.36	5.69	7.38	14.0
	2.05	1.78	5.18	7.47	6.57
	1.00	1.17	5.14	11.1	3.78
	0.50	1.02	5.58	40.3	0.88
	0.31	3.46	4.22	18.7	0.355
	0.10	4.16	2.64	40.3	0.0445
	0.10	5.75	2.05	18.7	0.0440
	0.01	5.40	3.78	2100	0.0013
4-bromoaniline	3.95	2.55	3.41	4.74	3.42
	3.08	3.13	2.76	4.74	1.23
	3.00	2.48	2.90	5.43	1.34
	1.99	5.17	3.60	10.5	0.489
	1.98	3.86	2.18	4.74	0.482
	1.08	1.81	3.43	36.8	0.194
	1.03	1.70	3.67	45.5	0.190
	0.59	2.55	2.73	36.8	0.0862
	0.49	2.70	2.83	45.5	0.0696
	0.25	3.83	1.83	45.5	0.0148
	0.11	3.90	1.57	61.3	0.0053
	0.02	7.44	0.38	1120	0.0002

[a] Concentration of tropolone in solution as determined by eq 4. [b] Concentration of tropolonate anion in solution as determined by eq 4. [c] Initial concentration of base. [d] Apparent equilibrium constant calculated from eq 2.

The apparent equilibrium constants (K'_{eq}) obtained at each concentration are listed in Table I for the pyridine bases and Table II for the aniline bases. These values were calculated from eq 2, by measuring the concentrations of tropolone and tropolonate anion in solution, and from the known initial base concentration. It was assumed that the protonated base concentration is equal to the tropolonate anion concentration. Molar absorptivities were measured for tropolone and tropolonate anion at wavelengths in the range 300–420 nm (the range of greatest spectral change between tropolone and its anion). Assuming Beer's law behavior is obeyed by the individual species, one can write the absorbance of the solution as

$$A(\lambda) = \sum_i \epsilon_i(\lambda) c_i \qquad (3)$$

where λ is a particular wavelength, $A(\lambda)$ is the absorbance at wavelength λ, $\epsilon_i(\lambda)$ is the molar absorptivity of the *i*th species at

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[11] Vogel, A. I. *A Textbook of Practical Organic Chemistry*; Longmans, Green and Co.: New York, 1948; pp 173–4.

Table III. Equilibrium Constants for the Proton-Transfer Reaction of Tropolone with Aniline and Pyridine Bases at 25.0 °C

base	pK_{aq}[a]	pK'_{eq}[b]
4-bromoaniline	2.85	2.28
aniline	2.11	1.35
4-methylaniline	1.63	0.75
pyridine	1.46	0.95
3-methylpyridine	1.08	0.72
4-methylpyridine	0.68	0.33

[a] Equilibrium constant calculated for the reaction of tropolone with the amine bases in aqueous solution from $pK_{aq} = pK_{TrH} + pK_B - pK_w$; $pK_{TrH} = 6.71$ and pK_B taken from ref 12. [b] Equilibrium constant for the reaction with tropolone in 0.10 M LPDE.

Table IV. Effect of $LiClO_4$ on the Apparent Equilibrium Constant[a]

base	$[LiClO_4]$, M	increase in K'_{eq}
4-methylaniline	0.01–1.0	2800
aniline	0.01–1.0	3000
4-bromoaniline	0.02–2.0[b]	2500
4-methylpyridine	0.01–1.0	1300
3-methylpyridine	0.01–1.0	1000
pyridine	0.01–1.0	1000

[a] Determined at 25.0 °C in diethyl ether. [b] Too weak a base to accurately determine the equilibrium constant below 0.02 M LPDE.

wavelength λ, and c_i is the concentration of the ith species. For two absorbing species, this equation can be arranged to give eq 4. Using absorbance and molar absorptivity data from various

$$A(\lambda)/\epsilon_1(\lambda) = c_1 + [\epsilon_2(\lambda)/\epsilon_1(\lambda)]c_2 \qquad (4)$$

wavelengths, one can plot $[\epsilon_2(\lambda)/\epsilon_1(\lambda)]$ versus $A(\lambda)/\epsilon_1(\lambda)$, yielding a slope of c_2, the tropolonate anion concentration, and an intercept equal to c_1, the tropolone concentration.

In observing the equilibrium constant at a particular concentration of lithium perchlorate, we see that K'_{eq} of the bases in LPDE parallel their values in aqueous solutions for each class of bases[12,13] (Table III). This is not too surprising because the proton affinities of the bases in the gas phase are proportional to their basicities in aqueous solutions as well.[14,15] The aniline and pyridine bases are too weak for the equilibrium constant in pure ether to be measured. The maximum value of the equilibrium constant for the reaction of tropolone with pyridine or aniline bases in pure diethyl ether is assumed to be less than that for the reaction of triethylamine with tropolone in the same solvent, which has a value of 1×10^{-5}, since the compounds used in the study are all weaker bases than triethylamine.

As can be seen from the data presented in Tables I and II, the acid–base equilibrium is very sensitive to the concentration of salt in the solution. From the data in Table IV, a 100-fold increase in the concentration of $LiClO_4$ causes approximately a 3000-fold increase in the apparent equilibrium constant for the aniline bases and approximately a 1000-fold increase for the pyridine bases.[16]

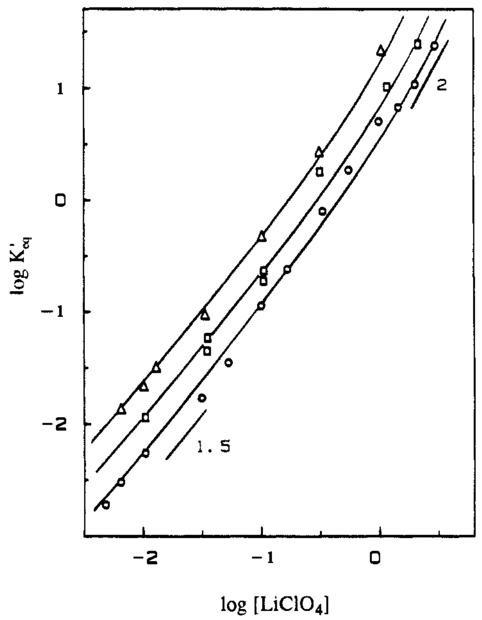

Figure 1. Plot of log K'_{eq} of the proton-transfer equilibrium of tropolone with pyridine bases versus log $[LiClO_4]$ at 25 °C: 4-methylpyridine (△), 3-methylpyridine (□), and pyridine (○). A slope of 1.5 is observed below 1 M LPDE, and a slope of 2 at 2 M LPDE.

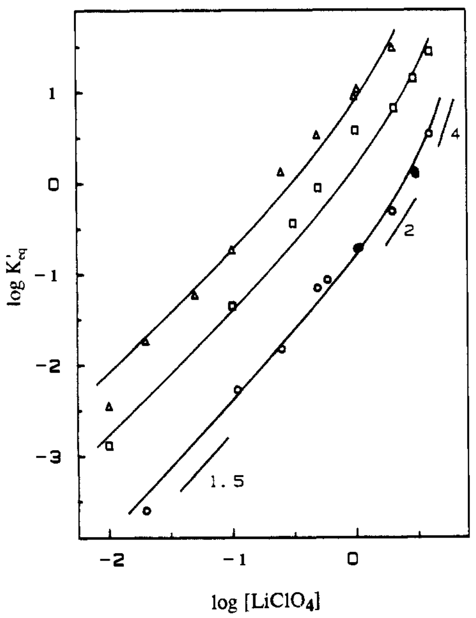

Figure 2. Plot of log K'_{eq} of the proton-transfer equilibrium of tropolone with aniline bases versus log $[LiClO_4]$ at 25 °C: 4-methylaniline (△), aniline (□), and 4-bromoaniline (○). A slope of 1.5 is observed below 0.3 M LPDE, a slope of 2 at 2 M LPDE, and a slope of 4 at 4 M LPDE.

To calculate the dependence of the equilibrium constant on changing lithium perchlorate concentrations for the reaction of tropolone with various bases, we plotted values of log K'_{eq} against log $[LiClO_4]$. From the slope of these plots, n, the minimum order of participation of $LiClO_4$ in the equilibrium could be determined.

$$K_{eq} = \frac{[Li^+,Tr^-\cdot(n-m-1)LiClO_4][BH^+,ClO_4^-\cdot mLiClO_4]}{[TrH][B:][LiClO_4]^n} \qquad (5)$$

$$K'_{eq} = \frac{[Li^+,Tr^-\cdot(n-m-1)LiClO_4][BH^+,ClO_4^-\cdot mLiClO_4]}{[TrH][B:]} \qquad (6)$$

$$\log K'_{eq} = n \log [LiClO_4] + \log K_{eq} \qquad (7)$$

For all the bases used in this study, the order in lithium perchlorate increases with increasing lithium perchlorate concentration. From Figure 1, it can be seen that the order approaches 1.5 at low concentrations and 2 at high concentrations for the

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(12) Rappoport, Z. *CRC Handbook of Tables for Organic Compound Identification*, 3rd ed.; CRC: Boca Raton, FL, 1967; pp 436–9.

(13) A moderate change in the pH of aqueous solutions of acids can also be induced by concentrated salt solutions: Critchfield, F. E.; Johnson, J. B. *Anal. Chem.* **1959**, *31*, 570–1.

(14) Summerhay, K. D.; Pollack, S. K.; Taft, R. W.; Hehre, W. J. *J. Am. Chem. Soc.* **1977**, *99*, 4585–7.

(15) Aue, D. H.; Webb, H. M.; Bowers, M. T.; Liotta, C. L.; Alexander, C. J.; Hopkins, H. P., Jr. *J. Am. Chem. Soc.* **1976**, *98*, 854–6.

(16) Using the estimated equilibrium constant for this reaction in pure ether, one finds an increase of 3×10^7 in the K'_{eq} for the reaction of 4-methylaniline with tropolone upon changing the solvent from diethyl ether to 2.0 M LPDE. The same order of magnitude is observed for the ionization equilibrium of triphenylmethyl chloride in this same solvent system.[6] A similar increase in the equilibrium constant is observed with the other bases used in the study.

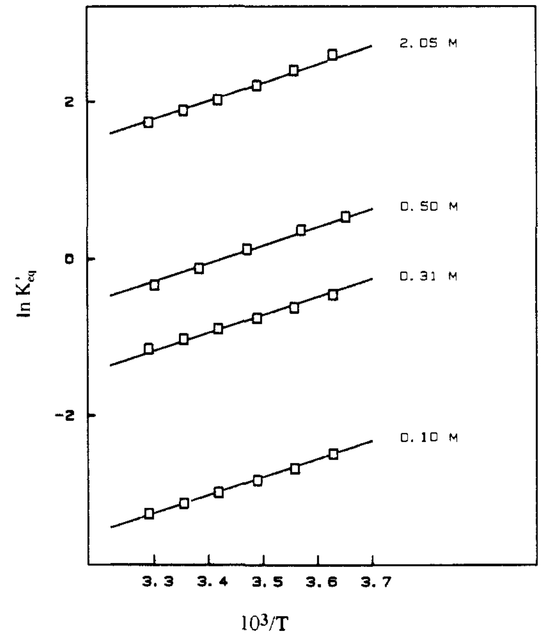
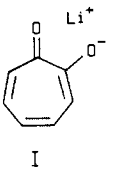


Figure 3. Determination of temperature dependence of the observed equilibrium constant for the reaction of aniline with tropolone in various concentrations of LPDE.

pyridine bases. From Figure 2 for the aniline bases, the slopes of the graphs reach 1.5 at low concentrations, and increase to approximately 4 at high concentrations. Since the acid is the same in both systems, the difference in the order of participation of lithium perchlorate must be due to differences in the structures of the bases. At higher concentrations of lithium perchlorate, more ions are able to interact with the anilinium ions than with the pyridinium ions, thus stabilizing the anilinium ions better than the pyridinium ions. This fact is seen in Table IV, where the same increase in $LiClO_4$ concentration causes the apparent equilibrium constant of the aniline bases to increase ca. 3 times that of the pyridine bases. The anilinium cations have three protons that can interact with ions in the solution, but there is only one proton in the pyridinium cations that can interact.

Previous studies on the effect of lithium perchlorate in various solvents all showed increases in the order of participation of lithium perchlorate of at least 4,[1,6-8,17] and in the ionization of trityl chloride to trityl cation and chloride anion, orders of lithium perchlorate as high as 12 were observed.[6] One exception was the reaction of imidazole with *o*-nitrophenol in lithium perchlorate solutions in diethyl ether, which showed an order increase of 1–2.[8] This is the same result as is observed for the reaction of tropolone with pyridine bases.

In both cases, a tertiary amine (e.g., imidazole or pyridine) is reacting with an intramolecularly hydrogen-bonded acid. It is apparent from these results that fewer ions are needed or able to interact with the conjugate base of an intramolecularly hydrogen-bonded acid. It is possible to think of the lithium ion as replacing the proton in the hydrogen bond as is shown in I and II. Further intimate interactions with other ions or ion pairs are not necessary, and any stabilization of the lithium–conjugate base ion pair with increased lithium perchlorate concentration is due to an increase in the ionic environment.



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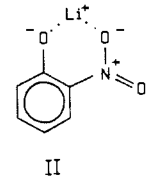

II

Thermodynamic Parameters for the Proton-Transfer Equilibrium of Tropolone with Amine Bases. The temperature dependence of the equilibrium constant of the proton-transfer reaction was measured at various lithium perchlorate concentrations for each base. The temperature was varied from 0 to 31 °C. Graphs of ln K'_{eq} versus reciprocal temperature were generated so that the enthalpy and entropy of the equilibrium reaction could be calculated. The results are given in Table V. Representative plots for the bases used in the study are shown for aniline (Figure 3) and pyridine (Figure 4). The van't Hoff plots for the other bases were of equal quality. From Table V, it can be seen that the free energy of reaction, ΔG, decreases with increasing $LiClO_4$ concentration. This decrease in free energy is due to an increase in the entropy of the equilibrium reaction. The enthalpy of reaction remains essentially constant, as can be seen from the slopes in Figures 3 and 4. As found in earlier work in this media,[1,7,17] the largest effect of the electrostatic fields generated by these solutions is in the entropy term.

Table V. Thermodynamic Parameters for the Proton-Transfer Equilibrium of Tropolone with Amine Bases at 25.0 °C

base	$[LiClO_4]$, M	ΔG,[a] kcal/mol	ΔH,[b] kcal/mol	ΔS,[c] cal/(deg mol)
4-bromoaniline	3.00	−0.3	−3.3	−10.2
	2.03	+0.4	−3.2	−12.0
	1.08	+1.0	−3.2	−14.0
	0.59	+1.4	−3.2	−15.6
	0.11	+3.1	−3.2	−21.3
aniline	2.05	−1.1	−4.6	−11.7
	0.50	−0.3	−5.0	−15.8
	0.31	+0.8	−4.4	−17.6
	0.10	+2.0	−4.5	−21.9
4-methylaniline	2.00	−2.0	−6.1	−13.9
	0.98	−1.5	−6.2	−15.9
	0.49	−0.3	−5.6	−17.9
	0.05	+1.9	−5.8	−25.8
pyridine	1.00	−0.9	−2.8	−6.5
	0.55	−0.4	−2.9	−8.5
	0.17	+0.9	−2.9	−12.6
	0.03	+2.6	−2.9	−18.5
3-methylpyridine	1.16	−1.2	−3.8	−8.8
	0.32	−0.5	−3.9	−11.5
	0.10	+0.6	−4.2	−16.2
	0.01	+2.4	−4.2	−22.3
4-methylpyridine	1.04	−1.7	−4.3	−8.7
	0.30	−0.6	−4.3	−12.5
	0.10	+0.4	−4.4	−16.1
	0.01	+2.3	−4.4	−22.3

[a] Calculated from $\Delta G = -RT \ln K'_{eq}$ for the particular salt concentration and base. [b] Calculated from the slopes of van't Hoff plots for each base studied: slope = $-\Delta H/R$. [c] Calculated from the intercepts of van't Hoff plots for each base studied: intercept = $\Delta S/R$.

The enthalpy term for reaction 1 can be separated into two terms, the internal enthalpy, intrinsic to the reaction products, ΔH_{int}, and the external enthalpy, ΔH_{ext}, which takes into account the solvent and intermolecular ion interactions.[18,19] From the data for the systems studied, the enthalpy is constant with respect to changes in the concentrations of lithium perchlorate.

$$\Delta H_{eq} = \Delta H_{int} + \Delta H_{ext} \tag{8}$$

$$\Delta H'_{eq} - \Delta H_{eq} = (\Delta H'_{int} - \Delta H_{int}) + (\Delta H'_{ext} - \Delta H_{ext}) \approx 0 \tag{9}$$

In eq 9 and those following, $\Delta H'$ and ΔH indicate enthalpies for two different concentrations of lithium perchlorate. The internal enthalpy is the same for the two solutions since only the concentration of the lithium perchlorate changes. ΔH_{ext} can be further separated into specific interactions for each of the different species in solution:

$$\Delta H_{ext} = \left(\Delta H_{ip}^{Li^+A^-} + \Delta H_{ip}^{BH^+ClO_4^-} + \Delta H_{solv}^{Li^+A^-} + \Delta H_{solv}^{BH^+ClO_4^-}\right) - \left(\Delta H_{solv}^{HA} + \Delta H_{solv}^{B:} + \Delta H_{ip}^{Li^+ClO_4^-} + \Delta H_{solv}^{Li^+ClO_4^-}\right) \tag{10}$$

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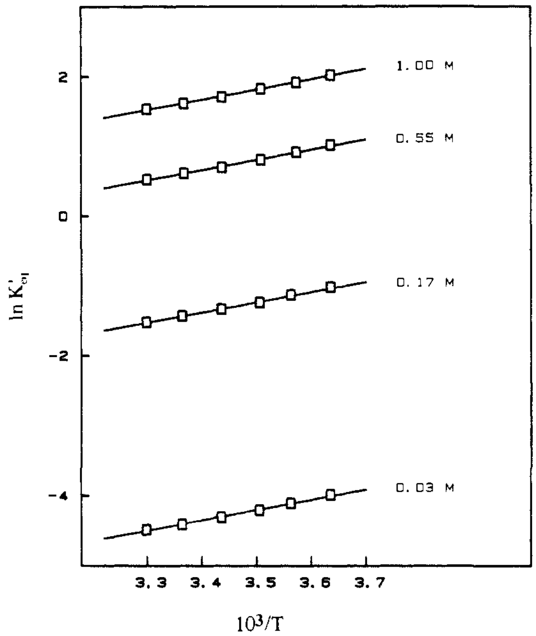

Figure 4. Determination of temperature dependence of the observed equilibrium constant for the reaction of pyridine with tropolone in various concentrations of LPDE.

where the ΔH_{solv} is the enthalpy of solvation of the particular species and ΔH_{ip} is the enthalpy of ion pair formation. Ion–dipole interactions are, in general, small compared to ion–ion interaction, so that in the difference of the external enthalpies, the contributions due to the solvation of the neutral species can be ignored.[20]

$$\Delta H'_{\text{eq}} - \Delta H_{\text{eq}} = \Delta H'_{\text{ext}} - \Delta H_{\text{ext}} \approx 0 \qquad (11)$$

$$\begin{aligned}\Delta H'_{\text{ext}} - \Delta H_{\text{ext}} \approx {} & \left[\left(\Delta H'^{\text{Li}^+\text{A}^-}_{\text{ip}} - \Delta H^{\text{Li}^+\text{A}^-}_{\text{ip}}\right) + \left(\Delta H'^{\text{Li}^+\text{A}^-}_{\text{solv}} - \Delta H^{\text{Li}^+\text{A}^-}_{\text{solv}}\right) + \right. \\ & \left.\left(\Delta H'^{\text{BH}^+\text{ClO}_4^-}_{\text{ip}} - \Delta H^{\text{BH}^+\text{ClO}_4^-}_{\text{ip}}\right) + \left(\Delta H'^{\text{BH}^+\text{ClO}_4^-}_{\text{solv}} - \Delta H^{\text{BH}^+\text{ClO}_4^-}_{\text{solv}}\right)\right] - \\ & \left[\left(\Delta H'^{\text{Li}^+\text{ClO}_4^-}_{\text{ip}} - \Delta H^{\text{Li}^+\text{ClO}_4^-}_{\text{ip}}\right) + \left(\Delta H'^{\text{Li}^+\text{ClO}_4^-}_{\text{solv}} - \Delta H^{\text{Li}^+\text{ClO}_4}_{\text{solv}}\right)\right] \qquad (12)\end{aligned}$$

The difference in enthalpy is made up of terms for ion pair formation and ion pair solvation. At low $LiClO_4$ concentrations, the partners of the various ion pairs or ion pair dimers interact strongly, because this medium cannot stabilize ionic entities efficiently. As more $LiClO_4$ is added to the solution, larger clusters of ions form.[2] Any given ion, in the cluster, interacts with many ions of the aggregate, so that the individual interaction enthalpy, i.e., the ion pair formation, ΔH_{ip}, will be less than that for a single ion pair or dimer in solution.[21,22] The ions involved in a cluster are stabilized by the ionic environment generated by the cluster, so that the solvation enthalpy, ΔH_{solv}, increases. The loss of enthalpy of the specific ion pair interaction, ΔH_{ip}, is compensated for by an equal gain in solvation enthalpy, ΔH_{solv}, as the $LiClO_4$ concentration is increased. A consequence of this relationship is that, as the enthalpy of the ion pair interaction decreases, the enthalpy of ion pair solvation increases, and the net effect is that the enthalpy of reaction remains essentially independent of the $LiClO_4$ concentration, in agreement with our experimental results.

From Figure 5, it can be seen that the entropy of the process increases rapidly with increasing lithium perchlorate concentration for both the pyridine and aniline bases. At any given concentration of lithium perchlorate, the entropy is algebraically smaller for the proton-transfer equilibria involving aniline bases. This can be partially attributed to the fact that anilinium ions cause a higher degree of organization in the LPDE solvent than the pyridinium ions. This organization comes from the capacity of anilinium ion to hydrogen bond to more entities than the pyridinium ion by way of the three nitrogen protons versus the one in the pyridinium ion.[23-25] This same result was seen in the order of participation in lithium perchlorate pairs that react with anilinium ions versus pyridinium ions.

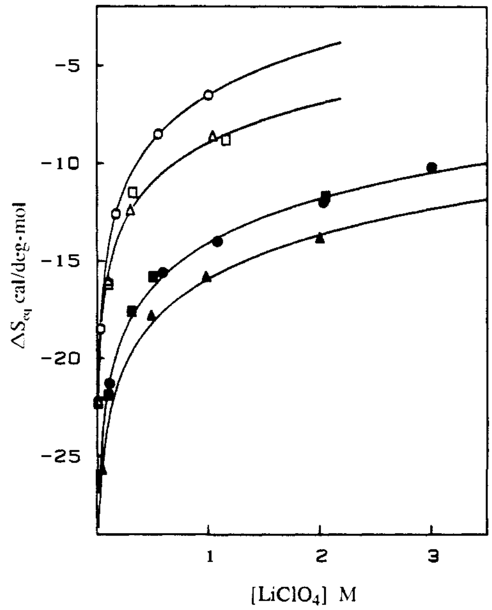

Figure 5. Plot of ΔS of reaction for the proton transfer of tropolone with amine bases versus $[LiClO_4]$ at 25 °C: 4-methylpyridine (△), 3-methylpyridine (□), pyridine (○), 4-methylaniline (▲), aniline (■), and 4-bromoaniline (●).

The variation of entropy with salt concentrations is understandable if interpreted as the loss of freedom of solvent and of $Li(OEt_2)_2{}^+,ClO_4{}^-$ ion pairs when "frozen" around the ions BH^+ and A^-. Ether molecules are quite free in the liquid state and, on freezing, a large decrease in entropy occurs. If these molecules are bound tightly to BH^+ and A^- ions, a large negative entropy change would be expected. On the other hand, highly polar liquids such as concentrated LPDE solutions contain progressively smaller amounts of free ether and already exist in a state of partially ordered clusters[26] because of the strong interionic forces. The introduction of successive amounts of BH^+ and A^- ions produced by the proton-transfer equilibrium to an already organized assembly of ionic clusters would cause considerably less reorganization of these ionic clusters at high salt concentrations than at low ones.[27,28] Hence, while strongly bound to the ions BH^+ and A^- such ionic aggregates suffer a relatively small entropy decrease.

Conclusion

From the data, it can be seen that these solutions of lithium perchlorate in diethyl ether can greatly enhance and stabilize the formation of ionic products. These LPDE clusters provide a particularly effective system for increasing the apparent equilibrium constant of proton-transfer reactions between neutral acids and bases. Since a great many reactions are modulated by proton-transfer processes, kinetic studies utilizing such salt solutions would probably exhibit features that have little precedent in

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physical-organic chemistry and would complement the equilibrium studies presented here.

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Alkyl Group Effects on the Rate Constants and Equilibrium Constants for Formation of Cyclic Tetrahedral Intermediates

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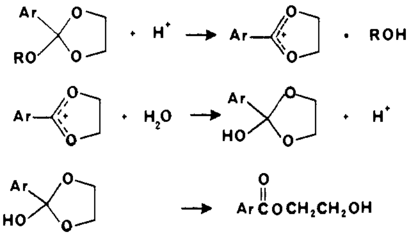
Abstract: 2-Hydroxy-2-alkyl-1,3-dioxolanes T are the cyclic tetrahedral intermediates of the degenerate intramolecular ester interchange reactions of ethylene glycol monoalkanoates A, in which alkanoyl groups transfer from one end of ethylene glycol to the other. This study reports equilibrium constants for the cyclization A $\rightleftarrows$ T to the tetrahedral intermediate stage with 10 alkanoate derivatives. These equilibrium constants, which when written as [A]/[T] are all large (10^7–10^9) in favor of the ring-opened form, were obtained as the ratio of rate constants for equilibration occurring with H^+ catalysis. Rate constants for the ring opening of T were directly measured through a study of the kinetics of the hydrolysis of 2-methoxy-2-alkyl-1,3-dioxolane ortho esters. These hydrolyses proceed via T, and under acid conditions the breakdown of this intermediate is rate-limiting. Rate constants in the ring-closing direction were obtained by preparing $HOCH_2CD_2OOCR$ and, with the use of ^1H NMR spectroscopy, measuring the kinetics of isomerization to an equilibrium mixture with $RCOOCH_2CD_2OH$. The reaction under investigation is an intramolecular analogue of H^+-catalyzed alkanoate ester hydrolysis, whose rate constants define the steric substituent parameter E_s. The ring-closure rate constants for A → T do show an excellent correlation with E_s. However, the rate constants for ring-opening T → A and the overall equilibrium constants are badly correlated, showing quite different behavior for series with α and β branching in the alkyl group. Thus, for this system the E_s parameter does not correlate free energy differences between the acyl derivative and tetrahedral intermediate. It is only the free energy differences between the acyl form and the transition state leading to the intermediate that fit E_s.

A three-stage reaction mechanism is now well established for the H^+-catalyzed hydrolysis of ortho esters.[1,2] Until recently, kinetic studies were generally carried out under conditions with the first stage (eq 1), generation of the dialkoxycarbocation intermediate, rate-limiting. However, there have now been encountered a number of ortho esters that have stage 1 rate-limiting at high pH, with a changeover at low pH to rate-limiting stage 3, the breakdown of the hydrogen ortho ester intermediate to products. This situation arises for those ortho esters that have a rate constant for H^+ catalysis of stage 3 which is smaller than that of stage 1. Thus, providing that the solution is acidic, stage 3 is a slower process than stage 1. Stage 3 is also efficiently catalyzed by OH^-. This causes stage 3 to be faster than stage 1 at high pH, with a resultant change in rate-limiting step.



(1)

(2)

(3)

A hydrogen ortho ester is also the tetrahedral intermediate of an ester alcoholysis reaction and is obviously also closely related to the tetrahedral intermediate of ester hydrolysis. The kinetic procedure usually employed in studies of ortho ester hydrolysis involves the monitoring of the appearance of the ester product, taking advantage of its carbonyl chromophore. This means that under the conditions where stage 3 is rate-limiting, the observed rate constants measure directly the breakdown of a tetrahedral intermediate.[2-5] Such rate constants cannot be obtained in investigations of the corresponding ester alcoholysis, where the tetrahedral intermediate is present only in very small stationary-state amounts. Moreover, by coupling these breakdown rate constants with rate constants for formation from appropriate acyl precursors, it has been possible to directly measure equilibrium constants for tetrahedral intermediate formation.[3a,f,4e] These equilibria substantially favor the acyl derivative, and thus the

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