Donor Properties of a Free-Radical Base

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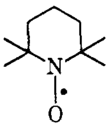
Abstract: Enthalpies of adduct formation of 2,2,6,6-tetramethylpiperidine-*N*-oxyl have been investigated with various hydrogen-bonding acids. The enthalpies and frequency shifts are compared with results from previously reported correlations. The nitrogen hyperfine coupling constant is found to increase regularly with the enthalpy of adduct formation. The donor orbital in the molecule is identified and a model is proposed to account for the increase in A_N with $-\Delta H$. The nmr isotropic shift of the alcohol proton is measured. The difficulties associated with interpreting this shift are presented.

As part of our continued interest in the general area of acid–base chemistry, we have investigated the Lewis basicity of a stable cyclic nitroxide free radical, 2,2,6,6-tetramethylpiperidine-*N*-oxyl, hereafter designated as I.



I

This base differs from any for which quantitative data have been reported[2] in that it contains an unpaired electron. This electron is delocalized approximately 80% on the nitrogen atom and 20% on the oxygen atom.[3,4] Epr spectra of the free radical I in solution have been reported to be solvent sensitive.[5] The correlation of changes in the hyperfine coupling constant (or *g* value) on adduct formation with enthalpies of interaction and with changes in the infrared spectra of the hydrogen-bonding acid upon interaction, $\Delta\nu_{OH}$, can potentially add to the understanding of the nature of hydrogen bonding. In this donor, the unpaired electron is in the highest energy molecular orbital with other potential donor orbitals with large oxygen coefficients nearby in energy. It was of interest to try to ascertain whether the highest energy partially vacant MO or a filled MO was the donor orbital. If a filled MO is the donor orbital, it was of interest to see if these adducts obey the enthalpy–frequency shift correlations reported earlier.[6–8] In this article, the initial results or our investigation are reported.

Experimental Section

Reagent grade carbon tetrachloride, cyclohexane, and hexane were stored over Linde 4A molecular sieves for several days prior to use. Phenol (Mallinckrodt analytical reagent), 1,1,1,3,3,3-hexafluoroisopropyl alcohol (Pierce Chemical sequanol grade), 2,2,2-trifluoroethyl alcohol (Pierce Chemical), and *m*-fluorophenol (J. T. Baker Co.) were purified as previously described.[6,7,9,10] The free radical I was prepared by the method of Briere, Lemaire and Rassat.[5] It was purified by vacuum sublimation prior to use. Owing to the necessity of using a relatively large amount of base in the calorimetric study, the free radical I was recovered from the solution in the case of HFIP and TFE by evaporating off the solvent and, after having dried the resulting precipitate in air on a piece of filter paper, it was sublimed under vacuum. The product was stored over anhydrous calcium chloride for at least 24 hr prior to use. The analysis of the recovered product was in excellent agreement with that expected of the pure material.

The epr spectra were measured with a Varian V-4502 epr spectrometer which was calibrated with Fremy's salt in saturated sodium carbonate solution ($A_N = 13.0 \pm 0.1$ G). The concentration of the free radical in all alcohols was approximately 10^{-3}–10^{-4} *M*. The hyperfine splitting constant, A_N, of the free radical was found to be slightly anisotropic (high-field and low-field values differ by approximately 0.1 G in some cases), and the average value was taken as the observed A_N. Owing to the relatively small change in A_N when the free radical was dissolved in different alcohols, it is important to keep the condition of measurement as constant as possible. The time for running each epr spectrum was 10 min in all cases. Slight variation in the A_N value (~0.1 G) was observed, using different speeds.

The infrared measurements were made on the Perkin-Elmer Model 521. The shifts were corrected for any dependence on the concentrations of the acid and base by extrapolating to infinite dilution. The alcohol concentration was less than 0.02 *M* in all our measurements. The nmr spectra of the alcohol in the presence of a minute amount of the free radical was measured on a Jeolco C-60H. The probe temperature was measured to ±2° with a YS1 Model 42S1 telethermometer. The chemical shift was calibrated by the side-band oscillator technique.

The apparatus, as well as the calorimetric procedure employed, is similar to that previously described.[11]

Results and Discussion

The measured heats for various concentrations of donor and acceptor are presented in Table I and the resulting enthalpies of interaction and equilibrium constants in Table II were calculated simultaneously from the calorimetric data by a reported procedure.[12] The enthalpies measured in CCl_4 are smaller by about 1.1 kcal mol^{-1} than those of the comparable system in cyclohexane. Similar discrepancies have been reported in the past[10,12,13] and can be attributed to either

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(1) Abstracted in part from the Ph.D. Thesis of Y. Y. Lim, University of Illinois, Urbana, Ill., 1971.

(2) For a review, see G. C. Vogel, R. S. Drago, and T. E. Needham, submitted for publication.

(3) A. M. Vasserman and A. L. Buchachenko, *J. Struct. Chem.*, **7**, 633 (1966).

(4) The exact amount of unpaired electron on N or O is still controversial. Some claim $\zeta_\pi^N \simeq 0.3$, while others claim $\zeta_\pi^N \simeq 0.9$. However, we are not concerned with the exact amount of unpaired spin density here.

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Table I

[Acid], *M*	[Base], *M*	Total vol, ml (solvent)	Measd heat (*h*′), cal
[CF_3CH_2OH]		(CCl_4)	
0.01668	0.01910	110.1	2.137[a]
0.01709	0.04550	110.1	3.947
0.01688	0.1152	110.1	6.168
0.01714	0.2064	110.2	7.562
[C_6H_5OH]		(CCl_4)	
0.01549	0.01813	110.7	2.716[b]
0.01556	0.02709	110.8	3.642
0.01566	0.06033	110.8	5.728
0.01569	0.09277	110.8	6.890
0.01551	0.2195	110.8	8.467
[C_6H_5OH]		(C_6H_{12})	
0.01479	0.01757	110.5	4.653[c]
0.01451	0.02581	110.5	5.791
0.01430	0.04684	110.6	7.466
0.01444	0.07197	110.5	8.506
0.01424	0.09017	110.5	8.942
0.01487	0.1986	110.5	10.516
[$(CF_3)_2CHOH$]		(CCl_4)	
0.01775	0.02752	110.0	8.821[d]
0.01789	0.05569	110.0	11.012
0.01787	0.1110	110.2	12.001
0.01646	0.1769	110.1	11.718
0.01784	0.2917	110.4	13.075
[$(CF_3)_2CHOH$]		(C_6H_{14})	
0.01229	0.02268	110.0	8.588[e]
0.01288	0.08471	110.0	10.612
0.01269	0.1096	110.0	10.565
0.01288	0.1909	110.0	11.178
0.01251	0.04827	110.0	9.726
[*m*-F_6H_4OH]		(C_6H_{12})	
0.01323	0.02231	110.0	7.443[f]
0.01339	0.03283	110.0	8.577
0.01270	0.05169	110.0	8.958
0.01307	0.07410	110.0	9.669
0.01251	0.1006	110.1	9.690
0.01280	0.2304	110.2	10.298

[a] Corrected for $\Delta H_{soln} = 5.16 \pm 0.01$ kcal mol^{-1}.[8] [b] Corrected for ΔH_{soln} of 3.548 *M* stock phenol solution = 3.33 ± 0.03 kcal/mol. [c] Corrected for ΔH_{soln} of approximately 3.17 *M* stock phenol solution = 4.59 ± 0.05 kcal/mol. [d] Corrected for ΔH_{soln} in CCl_4 = 4.77 ± 0.01 kcal/mol.[7] [e] Corrected for ΔH_{soln} in C_6H_{14} = 5.05 ± 0.04 kcal/mol. [f] Corrected for ΔH_{soln} in C_6H_{12} = 4.94 ± 0.06 kcal/mol.[10]

Table II. Summary of the Thermodynamic Data

Acid	Solvent	*K*, l. mol^{-1} (temp, °K)	$-\Delta H$, kcal/mol	$-\Delta H$, kcal/mol[b]
C_6H_5OH	CCl_4	27 ± 1 (298)	5.8 ± 0.2	6.1
C_6H_5OH	C_6H_{12}	60 ± 5 (299)	6.9 ± 0.2	
m-FC_6H_4OH	C_6H_{12}	160 ± 19 (299)	7.5 ± 0.2	6.4
HFIP	CCl_4	127 ± 38 (298)	6.7 ± 0.2	7.6
HFIP	C_6H_{14}	312 ± 198 (298)	7.9 ± 0.2	
TFE	CCl_4	19 ± 1 (297)	5.0 ± 0.2	5.9
	C_6H_{14}		6.1 ± 0.2[a]	

[a] Corrected for solvent effects by adding 1.1 to the CCl_4 heat. [b] Calculated from ΔH *vs.* $\Delta\nu$ correlation: for phenol, $-\Delta H = 0.0105\Delta\nu_{OH} + 2.99$;[6] for HFIP, $-\Delta H = 0.115\Delta\nu_{OH} + 3.6$;[7] for TFE, $-\Delta H = 0.0121\Delta\nu_{OH} + 2.70$;[8] for *m*-fluorophenol, $-\Delta H = 0.0103\Delta\nu_{OH} + 3.08$.[6]

specific interactions of the donors with CCl_4 or to extensive association of polar donors in the nonpolar solvent providing a solvation shell of polar donor molecules around the adduct.

The molecular weight determination of the free radical in the latter solvents ($\simeq$0.04 *M*) by vapor pressure osmometry indicates that the free radicals are present predominantly in the monomeric form, and hence the extrasolvation effect that was observed in the case of *N*,*N*-dimethylacetamide[6] does not account for the discrepancy here. We conclude that there must be some kind of specific interaction of the free radical I with CCl_4, so that CCl_4 is not an "inert" solvent toward this donor. Interactions of this sort are proposed with sulfur donors[13] and pyridine,[14] and the present study supports a similar interaction with this radical. It is interesting to note that the nitrogen hyperfine splitting constant of the radical in CCl_4 as compared with the values in acetone and cyclohexane has increased slightly. The value lies within the limits of experimental uncertainty, but is consistent with the radical interacting with CCl_4. As will be discussed shortly, adduct formation increases A_N. The possibility that the cause of this discrepancy arises from phenol or aliphatic alcohols interacting with CCl_4 has recently been suggested.[15] However, data in the literature at the time of this suggestion and results obtained subsequently[13] enable us to set an upper limit of 0.2 kcal on this effect. Since this is within experimental error, this effect can be ignored for our purposes. The ΔH values for adducts of the free radical with HFIP or TFE in hexane agree reasonably well with those predicted from the constant-acid enthalpy–frequency shift correlations which have been reported.[7,8] The appropriate equations describing these correlations are summarized in Table II. However, in the case of phenols, the heats measured in cyclohexane are considerably greater than those predicted from the frequency shifts, and it is not clear at present why phenols should behave so differently from the aliphatic alcohols. Further investigation is in progress, and this example again supports our repeated warning that, before enthalpies are estimated from the frequency shift correlations for a new class of donors, several enthalpies must be determined with this class of donors to check the validity of such an extrapolation. Even though this free-radical donor does not fall on our constant-acid plots, a constant-base plot does exist[16] (*i.e.*, $\Delta\nu_{OH}$ for the various alcohols with a given base can be plotted *vs.* $-\Delta H$ to give a line with a near-zero intercept). The sulfur donors also gave constant-base plots even though these donors did not fall on our constant-acid plots.[13] From the constant-base plot, the enthalpy of 1:1 adduct formation of our free-radical donor with several hydrogen-bonding alcohols can be predicted; *i.e.*, one is led to expect that $\Delta\nu_{OH}$ for a series of acids toward this given donor should be related to the magnitude of interactions.

The data in Table III illustrate the increase observed in the magnitude of the electron–nitrogen hyperfine coupling constant as the magnitude of the hydrogen-bonding interaction increases. It has previously been

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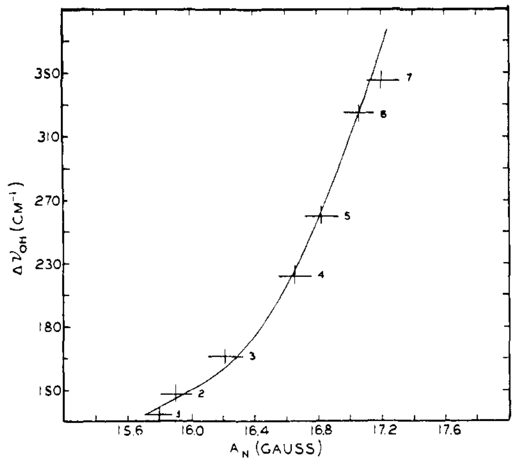


Figure 1. Infrared frequency shift *vs.* nitrogen hyperfine coupling constant (see Table III for acid numbering system).

reported that coordination to this free radical by Lewis acids results in an increase in A_N.[17] In Figure 1, A_N is plotted *vs.* our estimate of the magnitude of the interactions from $\Delta\nu_{OH}$, demonstrating that as the strength of the hydrogen-bonding interactions increases, the hyperfine splitting constant A_N also increases. Since A_N is nearly isotropic and the isotropic coupling constant is related to the unpaired spin density at the nucleus, $\psi^2(0)$, by the relation

$$A_N = \frac{8\pi}{3} g g_N \beta \beta_N \psi_{ns}(0)^2$$

where g and g_N are electron and nuclear g factors and β and β_N are the electron Bohr magneton and the nuclear magneton, respectively, the magnitude of A_N is a direct measure of the unpaired electron density at the nitrogen nucleus. Coordination of the acid to nitrogen, involving the MO containing the unpaired electron, would be expected to decrease A_N because of extensive delocalization of the unpaired electron onto the acid. The increased value of A_N with extent of interaction supports coordination to a MO which is largely a lone-pair oxygen orbital. Coordination to oxygen is expected to lower the VSIP of oxygen more than of nitrogen, so the oxygen atom contributions to the lower energy filled MO's increase and the nitrogen contribution to the MO containing the electron increases. In valence-bond formulation, the increase in A_N could be attributed to stabilization of form A below by coordination to oxygen.

Table III

No. in Figure 1	Solvent	A_N ± 0.1 G	$\Delta\nu_{OH}$ ± 5 cm^{-1}
	CCl_4	15.28	
	C_6H_{12}	15.21	
	Acetone	15.21	
	CH_2Cl_2	15.77	
1	Ethyl alcohol	15.80	135
2	*tert*-Butyl alcohol	15.90	148
3	Benzyl alcohol	16.21	171
4	2,2-Dichloroethyl alcohol	16.65	222
5	TFE	16.82	260 (±8 cm^{-1})
	H_2O	16.91	
6	*m*-Fluorophenol	17.06	325
7	HFIP	17.21	345
	Pyrrole	16.38	

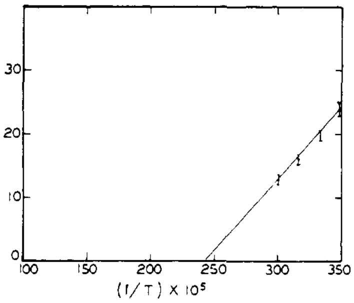
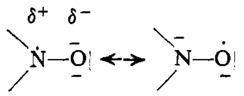


Figure 2. Curie law test of the nmr isotropic shift.



A B

In terms of either description, a stronger acid would be expected to increase the value of A_N if coordination occurred with an essentially oxygen lone pair. It is also possible that the inductive effects from coordination to the oxygen causes a change in geometry around the nitrogen, placing more nitrogen s character in the molecular orbital containing the unpaired electron.

It is of interest to point out here that the results of the nmr contact-shift experiment summarized in Table IV indicate that negative spin density is delocalized onto the acid hydroxyl proton. Coordination of the proton to a filled MO which is mainly oxygen could produce negative spin density at the proton *via* the spin-polarization mechanism found for ammonia coordinated to nickel(II), where α spin on the nitrogen produces β spin on the proton.[18] If the proton were hydrogen bonded to the nitrogen and if the proton coefficient in the nonbonding three-center MO containing the unpaired electron were small, spin polarization could again lead to negative spin density at the proton. In a

Table IV. Variation of the Observed Shifts with Temperatures[a]

ν_0, cps	ν_d ± 0.2 cps	$\nu_0 - \nu_d$	T, °K	$1/T$
−215 (±1.0)	−239.1	24.1	287.5	0.00348
−204.8 (±0.5)	−224.4	19.6	299.5	0.00334
−189.0 (±0.5)	−204.9	15.9	317	0.00316
−174.2 (±0.5)	−187.2	13.0	332	0.00302

[a] Mole fraction of radical **I** = 0.00459; mole fraction of CF_3CH_2OH = 0.9954.

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previous report[19] from this laboratory involving hydrogen bonding of chloroform, negative spin density was observed on the chloroform proton. Thus the contact shift is consistent with oxygen coordination, but not definitive.

The complexity of the contact-shift data is indicated in the plot shown in Figure 2. The data deviate badly from the straight-line plot with zero intercept expected for Curie law behavior. Several potential causes for this behavior have been recently proposed.[20] Clearly, one cannot derive a meaningful value of A_H from a single measurement, as has recently been claimed.[21] The cause of the nonzero intercept is not clear, but it could arise from different extents of hydrogen bonding as the temperature is varied (*i.e.*, changes in the size of the hydrogen-bonding acid cluster). It has been shown[18] that hydrogen-bonding interaction in the second coordination sphere (in this case $B \cdots H(H){-}O \cdots H{-}OH$) can cause appreciable contact shifts at the proton involved. Thus the proton shifts from this experiment are very difficult to interpret.

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