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(26) We also observe broadening in the $^1$H NMR spectra of DABCO and DMB during irradiation with TFA.
(27) NIH Postdoctoral Fellow, 1974–1975.

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## Acid Catalyzed CIDNP during Photoinduced Electron Transfer

*Sir:*

We report here an example of chemically induced dynamic nuclear polarization (CIDNP)[1] which occurs only upon acid catalysis.

Triplet α,α,α-trifluoroacetophenone, **1**, is quenched by substituted benzenes via a charge transfer mechanism which presumably involves an exciplex intermediate.[2] Degassed acetonitrile solutions 0.09 M in **1** or in *p*-Cl-**1** (**2**) and 0.0014 M in 1,4-dimethoxybenzene (DMB), upon being irradiated in the cavity of a Varian Model A56/60 NMR spectrometer,[3] can display very weak $^{19}$F emission, E, characteristic of the $CF_3$ group (for **1**, δ 90.2 ($CCl_3F$), t, $J_{FH}$ (ortho) = 1.1 Hz). The signal intensity depends on the solvent's history; in extensively purified solvent there is no emission; when present, the polarization fades during irradiation, leaving the normal weak $^{19}$F absorption of the ketone. This variable weak emission is apparently due to trace impurities which are consumed. In the presence of 0.005–0.1 M acetic acid or *p*-toluenesulfonic acid, strong steady-state $^{19}$F, $^1$H, and $^{13}$C CIDNP[5] signals are evident for **1** itself and also for several ring-substituted derivatives. Figures 1 and 2 display results for **1** and **2**; the acid-catalyzed CIDNP directions, which do not vary from 0.001 to 0.1 M DMB or with length of irradiation, are summarized in Table I. The $^1$H absorption of the DMB is extensively broadened during irradiation.

GC analysis of extensively irradiated samples indicated no disappearance of ketone and no product formation. The 0.0014 M DMB used is sufficient to quench >90% of the ketone triplets formed.[6] The combined redox potentials[7] of the ketones and DMB indicate that dissociation of the exciplex to radical ions is some 6 kcal exothermic;[9] radical ions are expected under such circumstances.[10] Roth has described several examples of CIDNP from radical ions,[11,12] and our observation of broadening of the DMB resonance strongly suggests degenerate electron exchange between $DMB^{+}\cdot$ and DMB.[11] The ketyl radicals can be protonated, as indicated by the acid-catalyzed photoreduction of **1** in benzene.[13]

Kaptein's rules[14] for the direction of polarization resulting from net effects ($\Gamma_\eta = \Delta g \cdot a \cdot \mu \cdot \epsilon$) and multiplet effects ($\Gamma_m = a_i \cdot a_j \cdot J_{ij} \cdot \sigma \cdot \mu \cdot \epsilon$) predict A or emission/absorption (E/A) if Γ is positive. The strong polarization of the carbonyl carbons and of adjacent nuclei of both ketones indicates the involvement of ketyl radicals. The reaction is entirely triplet-derived ($\mu > 0$).[2,6,15] The E/A multiplet for the carbonyl carbons requires an in-cage reaction ($\epsilon > 0$), since $a_C$,[12] $a_F$,[17] $^2J_{CF}$,[18] and σ (both nuclei on same radical) are all positive. Similar arguments for the multiplet polarizations of the $CF_3$ carbon ($^1J_{CF} = -290$ Hz),[19] the fluorines ($^5J_{HF} = 1.1$ Hz),[20] and the ortho-protons also require ϵ to be positive, since $a_H$ (ortho)[21] and $a_{CF_3}$[22] are negative. Moreover, it is not really possible for ϵ to be negative in such a totally revertible photoreaction.[11]

Comparison of the $^{19}$F spectra for **1** and **2** reveals that the acid catalyzed CIDNP results from protonated ketyls rather than from the ketyl radical anions. Since $1^{-}\cdot$ has a *g* value of 2.003 75[23] and $DMB^{+}\cdot$ one of 2.003 68,[24] only a multiplet effect, possibly accompanied by weak A, would be expected from the $1^{-}\cdot$, $DMB^{+}\cdot$ radical pair. In the absence of acid,[25] no steady state CIDNP is seen at all at $[AF_3] > 10^{-3}$ M, but a weak A/E $^{19}$F multiplet can be observed at $[AF_1] < 10^{-3}$ M.[15]

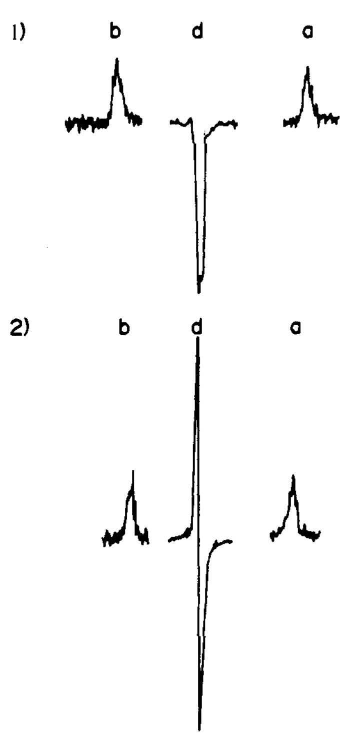
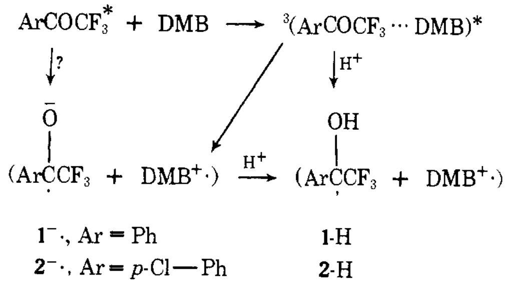


**Figure 1.** $^{19}$F NMR signal at δ 90.2 ($CFCl_3$) of degassed acetonitrile solutions containing $10^{-3}$ M 1,4-dimethoxybenzene, $10^{-2}$ M *p*-toluenesulfonic acid, and (1) 0.1 M **1**; (2) 0.1 M **2**. b, d, and a denote before, during, and after irradiation. Note 2.5-fold decrease in spectrum amplitude during irradiation.

**Table I.** Summary of Polarizations Observed upon Irradiation of 0.09 M **1** and **2** in Acidic Acetonitrile Containing 0.001–0.1 M Dimethoxybenzene[a]

| Nucleus | 1 | 2 |
|---|---|---|
| $^{19}$F | A/E[b] + E | A/E |
| $^1$H(ortho) | A/E | A/E |
| *C* = 0 | E/A | E/A |
| *C*$F_3$ | E/A | E/A |

[a] A ≡ enhanced absorption; E ≡ emission. Low field portion of multiplet signals listed first. [b] Weak.



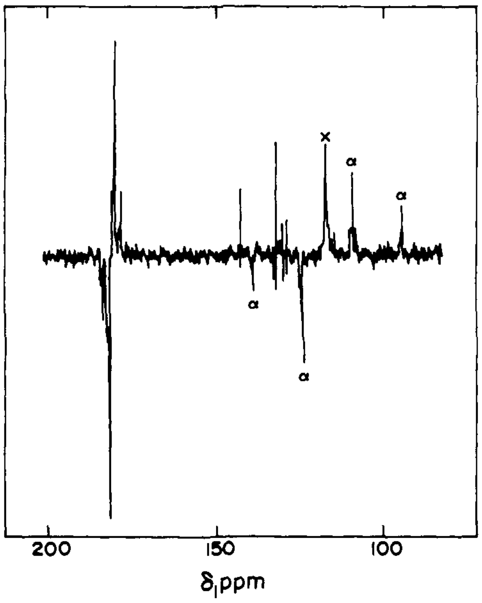
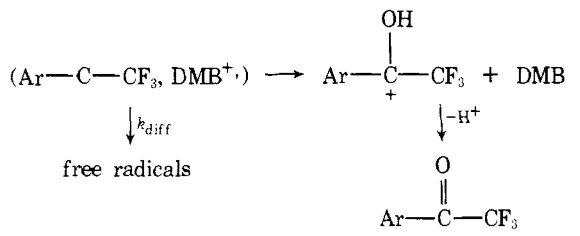


**Figure 2.** Proton-decoupled FT $^{13}C$ NMR spectrum observed after 5400 pulses during continuous irradiation of a degassed acetonitrile solution 0.1 M in *p*-chloro-$\alpha$-trifluoroacetophenone **2**, 0.065 M in DMB, and ~0.3 M in acetic acid. Peaks marked $\alpha$ represent $CF_3$ quartet; peak marked × is a solvent peak; absorbances between $\delta$ 130–150 are aromatic carbons.

Protonation of acetone ketyl lowers its $g$ value by 0.0002.[26] If **1** behaves likewise, $\Delta g$ for (**1**-H, $DMB^{+\cdot}$) would be negative enough to produce the observed $^{19}F$ E. A para-chlorine raises $g$ values of benzyl radicals by 0,0003.[27] A similar effect here would yield a large positive $\Delta g$ for ($\mathbf{2}^{-\cdot}$, $DMB^{+\cdot}$), a near-zero $\Delta g$ for (**2**-H, $DMB^{+\cdot}$). The observed strong $^{19}F$ multiplet for **2** is consistent only with the latter situation. The A/E pattern is expected on the basis of the signs of $a_H$, $a_F$, and $^5J_{HF}$ noted above.

The multiplet effects for both ketones are not due to disproportionation of protonated ketyl radicals since no alcohol is observed after extended irradiation and no $^{19}F$ or $^{13}C$ CIDNP was observed for alcohol product during irradiation. We presume that spin polarized ground state ketone is regenerated from the protonated radical pair by a two-step process involving first in-cage electron transfer and then rapid deprotonation.


$$\begin{array}{ccc} (\mathrm{Ar{-}C{-}CF_3,\ DMB^{+\cdot}}) & \longrightarrow & \mathrm{Ar{-}\underset{+}{\overset{OH}{C}}{-}CF_3 + DMB} \\ \downarrow k_{\mathrm{diff}} & & \downarrow -\mathrm{H}^+ \\ \text{free radicals} & & \mathrm{Ar{-}\overset{O}{\overset{\|}{C}}{-}CF_3} \end{array}$$

At the relatively high ketone concentration used, the lack of strong CIDNP in the absence of acid most likely results from almost complete compensation of in-cage polarization by rapid out-of-cage degenerate electron exchange between free polarized ketyls and ground state ketone.[15] It remains to be determined whether it is the exciplex, the caged radical-ion pair, or the free ketyl which gets protonated. The latter is the least likely cause of the observed CIDNP since what should then be observed is a superposition of ketyl radical ion and protonated ketyl polarizations. Since there is evidence that radical pairs responsible for CIDNP have an extended diffusional lifetime,[28] in-cage protonation of the ketyl radical-ion is certainly possible. In a report of CIDNP in the chlorophyll-benzoquinone system, it was pointed out that protonation of semiquinone radical anions could occur but how such protonation would affect the CIDNP observed was not discussed.[12c] There is independent evidence that exciplexes involving triplet ketones are readily protonated.[13,29] Since we also observe strong E by irradiating **1** in the presence of anisole and bromobenzene, neither of which has a low enough oxidation potential to form radical ions directly from triplet **1** and both of whose radical cations have $g$ values higher than that expected for **1**-H, we conclude that a large part of the acid-catalyzed CIDNP which we observe derives from direct protonation of a triplet ketone–aromatic exciplex.

It is important to note that this acid-catalyzed CIDNP is much stronger than the concentration-dependent CIDNP reported separately;[15] the added catalyzed mechanism completely offsets the enhanced absorption seen at high DMB concentrations in nonacidic solutions.

It is now apparent that the charge transfer nature of exciplexes allows them to react more rapidly with many reagents than would either excited partner alone.[30] The proton is certainly one such reagent. In the context of photochemical CIDNP studies, we suggest that most CIDNP phenomena thought to involve radical ion pairs[11,12] should be very sensitive to acids.[31]

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(32) NIH Postdoctoral Fellow, 1974–1975.

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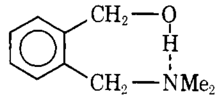
## *o*-(Dimethylaminomethyl)benzyl Alcohol. An Improved Model for Serine Esterases That Is Internally Hydrogen Bonded in Aqueous Solution[1]

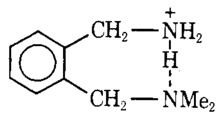
*Sir:*

The action of acetylcholine esterase, $\alpha$-chymotrypsin, and several other enzymes apparently involves attack on a substrate carbonyl group by a serine hydroxyl group that is hydrogen bonded to an imidazole nitrogen atom from a histidine residue.[2-6] Similar mechanisms have been suggested for cleavage of *p*-nitrophenyl acetate[7,8] and other active esters[8] in the presence of various amino alcohols. These amino alcohols are better catalysts than they would be expected to be as amines and give esters as reaction intermediates. Similar evidence for 3-quinuclidinol, where internal hydrogen bonding between hydroxy and amino groups is sterically impossible, shows that attack by the zwitterion form of the amino alcohol can be important.[9] However, catalytic activities of several tertiary-amino alcohols were estimated to be 1.2–6 times as large as expected from a zwitterion mechanism.[8] We have now found that *o*-(dimethylaminomethyl)benzyl alcohol (**1**) is internally hydrogen bonded in aqueous solution and is particularly effective, for its basicity, at cleaving *p*-nitrophenyl acetate via internal amine-assisted attack by its hydroxylic oxygen atom.

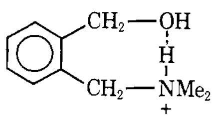
*o*-(Dimethylaminomethyl)benzylamine, a bifunctional catalyst for dedeuteration of acetone-$d_6$,[10] is about 15 times as basic as would be expected from data on benzylamine, *N,N*-dimethylbenzylamine, and other reference compounds.[11] This increased basicity is evidence for stabilization of the monoprotonated form of the amine (**2**) by internal hydrogen bonding. Such internal hydrogen bonding in **1** should decrease its basicity, but this decrease could be offset by stabilization of the conjugate acid of **1** (**3**) by internal hydrogen bonding. The internal hydrogen bonding suggested for **1** would be impossible for the corresponding methyl ether, but hydrogen bonding of the type shown for **3** would be possible for the protonated methyl ether. The decreased basicity of alcohol **1** relative to its methyl ether (see Table I) is therefore evidence for internal hydrogen bonding in **1**.[12]



**1**



**2**



**3**

*N,N*-Dimethylbenzylamine and especially *o*-(dimethylaminomethyl)benzyl methyl ether were taken as models for the catalytic activity to be expected from the tertiary amino group of **1**. Table I shows that at ionic strength 0.20, where the greater solubility of the amines permits more reliable rate constants to be obtained, **1** is more than 100 times as good a catalyst for the decomposition of *p*-nitrophenyl acetate as either of the two models (in spite of the greater basicity of the models).

**Table I.** Catalysis of the Decomposition of *p*-Nitrophenyl Acetate in Water at 25 °C

| Catalyst | Ionic strength | $100k$,[a] $M^{-1}\,s^{-1}$ | p$K$ |
|---|---|---|---|
| $o$-Me$_2$NCH$_2$C$_6$H$_4$CH$_2$OH | 1.00 | 4.90 (0.06) | 8.77 |
| | 0.20 | 5.05 (0.08) | |
| $o$-Me$_2$NCH$_2$C$_6$H$_4$CH$_2$OMe | 1.00 | <0.1[b] | 9.09 |
| | 0.20 | <0.03[b] | |
| C$_6$H$_5$CH$_2$NMe$_2$ | 1.00 | <0.03[b] | 9.03 |
| | 0.20 | 0.034 (0.019) | |
| $o$-Me$_3$NCH$_2$C$_6$H$_4$CH$_2$OH$^+$ + OH$^-$ | 1.00 | 10200 (900)[c] | |

[a] The parenthesized numbers are estimated standard deviations. In each case the reaction was shown to be first order in catalyst by varying the catalyst concentration by at least tenfold. [b] These are estimated upper limits; the least-squares values were slightly negative. [c] $M^{-2}\,s^{-1}$.

Studies using $o$-HOCH$_2$C$_6$H$_4$CH$_2$NMe$_3{}^+$Br$^-$ (**4**) showed that the catalytic activity of **1** is also much greater than would be expected for attack by its zwitterion form. We assume that the acidity of the hydroxylic proton in **4** is the same as that in the conjugate acid of **1** and that the rate constants for attack of zwitterion forms of **1** and **4** on *p*-nitrophenyl acetate are the same, We define $K_w$ as the autoprotolysis constant of water, $K_{1H}$ as the acidity constant of protonated **1**, $k_n$ as the total catalysis constant for electrically neutral forms of **1**, $k_z$ as that part of $k_n$ that arises from attack by the zwitterion, and $k_{qb}$ as the rate constant for the term of the form $k_{qb}[\mathbf{4}][\mathrm{OH}^-][\mathrm{pNPA}]$ observed when *p*-nitrophenyl acetate is hydrolyzed in the presence of **4**. It follows that

$$k_z = k_{qb}K_w/K_{1H}$$

From the values of $K_w$, $K_{1H}$, and $k_{qb}$ (Table I) a value of 0.0012 $M^{-1}\,s^{-1}$ is obtained for $k_z$. The $k_n$ value for **1** listed in Table I is 40 times this large. This is much larger than the factors estimated for other amino alcohols[8] and hence much more likely to be larger than the errors in the estimate of $k_z$.

The necessity for having the alcohol and amine groups in the same molecule is shown by the observation that 0.035 M benzyl alcohol has no detectable effect on the rates of reaction in the presence of 0.01–0.05 M *N,N*-dimethylbenzylamine.

The hydrolysis of *p*-nitrophenyl acetate in the presence of **1** gave the acetate of **1** as a reaction intermediate. This was shown by a ferric acetohydroxamate analysis[15] and by the infrared spectra of cyclohexane extracts of the reaction solutions.

Other amino alcohols that are significantly less basic than their methyl ethers will be attractive possible models for serine enzymes if their hydroxy groups are not too hindered sterically.

**Supplementary Material Available:** A table of p$K$ values for corresponding methoxy and hydroxy amines (2 pages). Ordering information is given on any current masthead page.

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(1) This research was supported in part by Grant GM 18593 from the National Institute of General Medical Sciences.

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