CCl:CN, the activation parameters are nearly identical with those obtained in B, S, and ChA:ChN. Comparison of these results with $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ in the cholesteric phase of CCl:CN reveals that solvent order exerts a substantial influence on the reaction mechanism. The large increases in both parameters (Table I) in the cholesteric phase support the out-of-plane mechanism for isomerization, but not the in-plane mechanism.

In a cholesteric mesophase, solvent molecules are arranged in stacked layers in which the constituent molecules display unidirectional alignment of their long axes within an individual layer. Displacement of one layer with respect to its neighbors results in a "twisted" nematic macrostructure.[11] Solute molecules, when dissolved in a cholesteric (or nematic) mesophase, align in the best packing arrangement based upon steric considerations. For example, planar molecules orient their long axis parallel to the long axis of the liquid crystal.[12] Theoretical calculations[13] indicate that anti-azobenzene is planar,[14] whereas the syn isomer is slightly distorted from planarity (the two phenyl rings being twisted ~30° out of the plane of the nitrogen–nitrogen double bond). Therefore, steric factors should orient both azobenzene isomers parallel to the long axis of our liquid crystal. Optical studies performed on solutions of *syn*- and *anti*-azobenzene in compensated nematic liquid crystals are consistent with this hypothesis.[15]

The isomers of azobenzene should perturb the order of a cholesteric liquid crystal similarly since both solutes are of comparable size and shape. It follows that interconversion of the azobenzene isomers via motions within the plane defined by a solvent layer (i.e., the inversion mechanism) will cause a minimal perturbation on the cholesteric structure. Should the interconversion process include severe distortion from planarity (such as those expected if the rotation mechanism is operative), the solvent layers immediately above and below the reacting solute will be disturbed. These hypotheses suggest that $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ for the inversion mechanism should be similar in isotropic and cholesteric phases.[16] However, $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ for the rotation mechanism should both be more positive in a cholesteric phase than in an isotropic phase: rotation will be hindered by the solvent layers directly above and below the solute; the layers will be more disorganized in the transition state than in the ground state. Our results, employing CCl:CN as solvent, are clearly more consistent with the rotation mechanism than the previously preferred inversion mechanism for isomerization.

The experimental approach outlined here demonstrates the utility of cholesteric liquid crystal solvents in the elucidation of reaction mechanisms. We are investigating currently the effects of substituents on the thermal and photochemical pathways for isomerization of other azobenzenes and will report on these in future publications.

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An Isotope Effect Maximum for Proton Transfer between Normal Acids and Bases

Sir:

We wish to report that we have observed a maximum in the dependence of the kinetic isotope effect, on proton transfer between "normal" [1] acids and bases, upon the acid strength of the proton donor. Although a number of such isotope effect maxima are now known for proton transfer to or from carbon,[2] the present case and that described in the accompanying paper[3] are the only known examples for proton transfer limited to oxygen and nitrogen acids and bases.[4] The nature of these maxima has an important bearing on the detailed mechanism of proton transfer between normal acids and bases, and it also offers a ready explanation for the general absence of large isotope effects on these reactions.

Proton transfer between normal acids and bases is usually a very fast reaction.[1] There are systems, however, in which it occurs after an unfavorable equilibrium as part of a complex reaction scheme, and when, in such cases, it is the rate-determining step, it can be studied by classical (slow) kinetic techniques. The reaction between *p*-methoxybenzaldehyde and methoxylamine in the presence of acidic catalysts (eq 1) has been shown to be such a process: under certain conditions of *pH* and catalyst concentration, proton transfer from the catalyst to the alkoxide oxygen of the first-formed zwitterionic intermediate, **1**, is rate determining, eq 2.[7]

$$p\text{-}CH_3OC_6H_4CHO + CH_3ONH_2 \xrightarrow{HA} p\text{-}CH_3OC_6H_4CH{=}NOCH_3 \quad (1)$$

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$$ArCHO + CH_3ONH_2 \rightleftharpoons \underset{\mathbf{1}}{ArCH(O^-)NH_2OCH_3} \xrightarrow[\text{slow}]{HA} \underset{\mathbf{2}}{ArCHNH_2OCH_3} \quad (2)$$

Using published methods,[7] we have determined kinetic isotope effects on this reaction catalyzed by 13 carboxylic acids and ammonium ions. The data (Figure 1) give $k_H/k_D = 1$ for the relatively strong acids $CNCH_2CO_2H$ and HCO_2H, rise to a maximum just short of $k_H/k_D = 3$ for $CNCH_2CH_2NH_3^+$, $O(CH_2CH_2)_2NH_2^+$, and $C_6H_5CH_2NH_3^+$, and drop back to below $k_H/k_D = 2$ for $CH_3OCH_2CH_2CH_2NH_3^+$ and $CH_3CH_2CH_2NH_3^+$.

These isotope effects were necessarily determined using D_2O as the solvent for k_D measurements, and the values of k_H/k_D therefore contain solvent and/or secondary isotope effects. The fact that $k_H/k_D = 0.90$ and 1.0 for catalysis by $CNCH_2CO_2H$ and HCO_2H, respectively, suggests that, for examples of this reaction at the strong-acid end of the series, solvent and/or secondary isotope effects are small; it is likely that they will be small for examples at the other end as well. Solvent and secondary isotope effects, moreover, are likely to vary monotonically along a series such as this, and it is doubtful that they would show an extremum like the maximum observed here. It seems safe to conclude, therefore, that at least the larger of the present isotope effects have a sizable primary isotope effect component. This provides strong confirmatory evidence for the validity of the mechanism of eq 2.

Primary kinetic isotope effects on proton-transfer reactions have maximum values when the proton affinities of the bases between which the proton is moving, as measured, for example, by the pK_a's of the proton donor and the protonated proton acceptor, are approximately evenly matched ($\Delta pK_a = 0$). It is significant, therefore, that the present isotope effect maximum comes at pK_a (catalyst) = 8–9, for the pK_a of the carbinol ammonium ion **2** has been estimated to be 9.0.[7] This estimate is confirmed by the Brønsted plot for this reaction: proton transfers between normal acids and bases are known to give biphasic Brønsted plots with breaks at $\Delta pK_a = 0$, and such a plot with its break at pK(catalyst) = 8–9 has been observed for this reaction.[7] The original data which demonstrated this, supplemented by the present measurements, are shown in Figure 2.

Proton transfer between normal acids and bases may be split up into three kinetically significant steps: (1) encounter of the reactants, (2) proton transfer, and (3) separation of the products.

$$B + HA \overset{1}{\rightleftharpoons} B \cdot HA \overset{2}{\rightleftharpoons} BH \cdot A \overset{3}{\rightleftharpoons} BH + A \quad (3)$$

It is generally agreed that encounter is rate-determining when $\Delta pK_a \ll 0$, and that separation is the slow step when $\Delta pK_a \gg 0$. The situation at $\Delta pK_a = 0$ is less clear. The encounter pair formed in the first step is generally regarded as being a hydrogen-bonded complex, and proton transfer down a hydrogen bond is known to be much faster than the rate of diffusion together of two reactants in ordinary aqueous solution.[1,8] The general absence of large hydrogen kinetic isotope effects on these reactions also supports a completely diffusion-controlled process. On the other hand, experimental determination of rates of proton transfer between normal acids and bases generally gives values at $\Delta pK_a = 0$ which fall one to two orders of magnitude below the diffusion-controlled limit.[9]

The isotope effects observed here and those found in the accompanying study[7] provide direct evidence on this point: they show that proton transfer is kinetically significant in the region near $\Delta pK_a = 0$. In both cases, however, the maximum isotope effect observed falls considerably short of the value expected

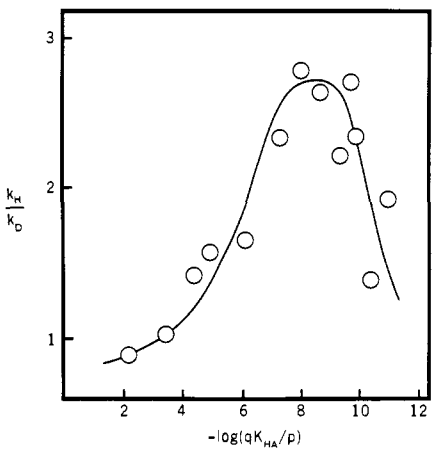

Figure 1. Isotope effects on proton transfer to the alkoxide oxygen of the zwitterion formed by addition of methoxylamine to *p*-methoxybenzaldehyde. Proton donors, from left to right: $CNCH_2CO_2H$, HCO_2H, CH_3CO_2H, $CH_3ONH_3^+$, $CF_3CH_2NH_3^+$, $O(CH_2CH_2)_2NHCH_3^+$, $CNCH_2CH_2NH_3^+$, $O(CH_2CH_2)_2NH_2^+$, $^+NH_3CH_2CH_2CH_2NH_3^+$, $C_6H_5CH_2NH_3^+$, $HOCH_2CH_2NH_3^+$, $CH_3OCH_2CH_2CH_2NH_3^+$, $CH_3CH_2CH_2NH_3^+$.

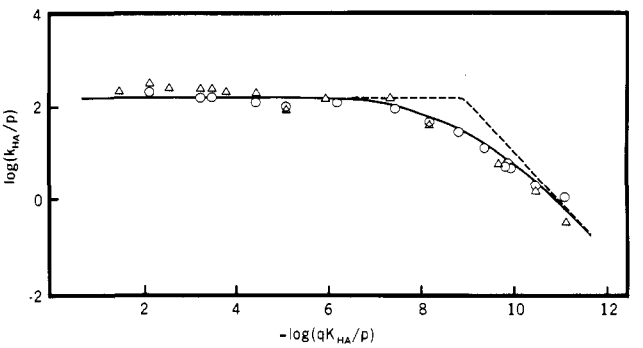

Figure 2. Brønsted plot for proton transfer to the alkoxide oxygen of the zwitterion formed by addition of methoxylamine to *p*-methoxybenzaldehyde: circles, this work; triangles, ref 3.

for proton transfer from oxygen or nitrogen through a symmetrical transition state, and that suggests that proton transfer never becomes fully rate determining. In fact, a model in which encounter, proton transfer, and separation occur at approximately equal rates when $\Delta pK = 0$ is consistent with the experimental data.

The isotope effect maximum observed here is quite narrow: its width at half-height is only a few pK_a units, whereas those reported for other proton-transfer reactions are generally an order of magnitude broader.[2] This is consistent with the fact that these other maxima all occur in systems where proton transfer is to or from carbon, and the reactions are intrinsically much slower than the proton transfers between normal acids and bases studied here. It is tempting to elaborate on this difference by saying that fast reactions have transition states whose structures change more rapidly with ΔpK_a, and isotope effects in such systems consequently should be more sensitive functions of this variable.[10] This may well be so, but the present data offer no proof, for the isotope effect maximum observed here could be caused entirely by an influence of the diffusion steps. In a system where encounter, proton transfer, and separation all occur at comparable rates at $\Delta pK_a = 0$, a shift of only one or two pK_a units to either side of this point will make either encounter or separation fully rate determining. Since the latter steps can be expected to show only small isotope effects, the result of such changes in rate-determining step will be to reduce the observed isotope effect quite sharply on either side of $\Delta pK_a = 0$.

In any event, the fact remains that the isotope effect maxi-

mum observed here is sharp and that this sharpness may be traced back to the great speed of the proton-transfer step. This suggests that isotope effect maxima for proton transfer between normal acids and bases may always be fairly narrow, and that a close match of donor and acceptor pK_a's will be required to produce an isotope effect with a significant primary component. Isotope effects large enough to be identified unmistakably as primary may therefore be scarce in such reactions simply because the necessary close match of pK_a's has seldom been achieved.[2d] A similar reason may apply to the general absence of large isotope effects from systems in which proton transfer between normal acid–base centers is accompanied by heavy-atom reorganization.[11]

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General Acid Catalysis of the Aminolysis of Phenyl Acetate by a Preassociation Mechanism[1]

Sir:

We wish to report evidence that the methoxyaminolysis of phenyl acetate is subject to general acid catalysis through a preassociation mechanism in which strong acids provide enforced general acid catalysis of amine attack by hydrogen bonding, weaker acids give partiallly rate-determining proton transfer to the addition intermediate, $T^{\pm}$, and weak acids lead to rate-determining separation of the encounter pair $T^{+}\cdot A^{-}$. The proton-transfer step gives rise to a solvent deuterium isotope effect with a sharp maximum at $pK_{HA} \sim 7$.

There is evidence that general acid catalysis of the aminolysis of phenyl acetate by basic amines involves rate-determining trapping of the dipolar addition intermediate, $T^{\pm}$, upon encounter with buffer acids.[2] This catalysis is enforced by the short lifetime of the intermediate, which was estimated to revert to reactants with a rate constant on the order of 10^9 s^{-1}. The experiments reported here were carried out to test the prediction that a less basic amine would give a still less stable intermediate, so that the lowest energy path for catalysis would become an enforced preassociation mechanism in which the attack of the amine on the ester must take place in the presence of the acid catalyst.[3,4]

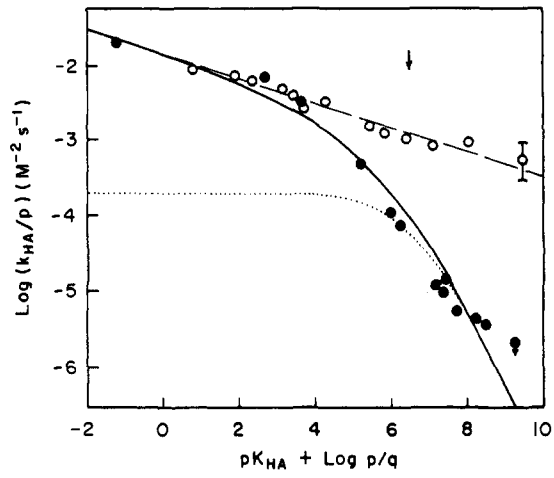

Figure 1. Brønsted plot for general acid catalysis of the methoxyaminolysis of phenyl acetate at 25 °C, ionic strength 1.0 (KCl). The rate constants were determined as described previously.[2,7,17] The closed circles represent monofunctional catalysts and open circles represent bifunctional catalysts. The dotted and solid curves are calculated[7,9] lines for trapping and preassociation mechanisms, respectively. The arrow at $pK = 6.5$ shows the calculated pK of T^{+}. The smallest rate constant represents an upper limit.

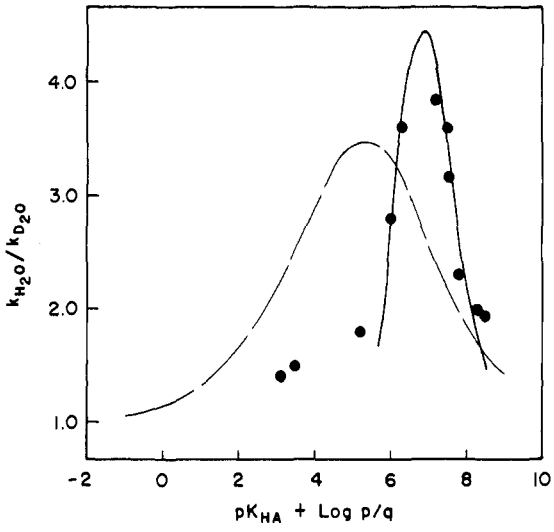

Figure 2. Solvent deuterium isotope effects for monofunctional general acid catalysis of the methoxyaminolysis of phenyl acetate. The dashed and solid lines were calculated assuming constant and changing isotope effects on the k_p step, respectively.[9,13]

The Brønsted plot for general acid catalysis of the methoxyaminolysis of phenyl acetate is shown in Figure 1. The rate constants for monofunctional catalysts (protonated amines and the proton) are shown as solid symbols and follow a curved line that approaches a slope of $\alpha = 1.0$ for weak acids and a slope of $\alpha = 0.16$ for the stronger acids. The rate constants for bifunctional catalysts (carboxylic acids and inorganic oxyacids) are shown as open symbols and are similar to those for monofunctional acids of $pK < 4$. However, for weak acids the

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