

lated tritium distribution is in very good agreement with the observed results (Table I). Of particular interest is the observation that the process with all carbon positions equivalent, which involves the 3,2 hydride shift, is responsible for 35.2% of the formolysis product, while in the acetolysis under analogous conditions, the contribution of this process is only 10%. This result confirms all previous assumptions³⁻⁶ that more 3,2 shifts occur during formolysis than acetolysis. The finding is in agreement with expectation as the norbornyl cation should have a longer life in formic acid than in acetic acid, thus providing a greater opportunity for the slower 3,2 hydride shifts to take place.

Table II. Calculated Tritium Distribution for the Formolysis of *exo*-I-2-*t* at 25°

Process	% contribution ^a	Calcd % <i>t</i>			
		C-2	C-3	C-1,4,7	C-5,6
Complete equivalence	35.2	3.2	6.4	12.8	12.8
C-1, C-2 equivalent	43.2	21.6		21.6	
C-1, C-2, C-6 equivalent	21.6	5.4		5.4	10.8
Calcd <i>t</i> content		30.2	6.4	39.8	23.6

^a The analogous contributions for the acetolysis of *exo*-I-2-*t* at 25° are 10, 45, and 45%, respectively, for the three processes of complete equivalence, C-1, C-2 equivalent, and C-1, C-2, C-6 equivalent.²

C. C. Lee, L. K. M. Lam

Department of Chemistry and Chemical Engineering
University of Saskatchewan
Saskatoon, Saskatchewan, Canada

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Low-Temperature Kinetics in Protic Solvents. Reactions of *p*-Nitrophenyl Acetate in Methanol and Methanol-*d* at -78°

Sir:

The possibility that water structures resembling crystalline gas hydrates exist in protein cavities and are important in enzyme action¹ has prompted recent measurements of reaction rates in ice.² Interesting rate enhancements are found in this medium, but their nature is unclear because of uncertainties associated with the heterogeneity of the systems. We have extended these studies of the chemistry in cold protic solvents by examining kinetically some nucleophilic reactions of an ester in liquid methanol at low temperature, and we report the results here.

The rate constants for the reaction of methoxide ion with *p*-nitrophenyl acetate (*p*-NPA) in methanol and methanol-*d*³ at -78.2° are given in Table I. The data indicate that the reaction is first order in ester and in methoxide, and that the reaction proceeds 2.6 times faster in methanol-*d* than in methanol.⁴ The rate

(1) F. M. Richards, *Ann. Rev. Biochem.*, **32**, 269 (1963).

(2) H. E. Alburn and N. H. Grant, *J. Am. Chem. Soc.*, **87**, 4174 (1965), and references cited therein.

(3) The purity of these dried solvents was assayed by vapor phase chromatography and found to be satisfactory. Addition of 3% water to the methanol does not perturb the rate constants.

(4) The dielectric constants of methanol and methanol-*d* at -83° are 65.8 and 65.2, respectively: D. W. Davidson, *Can. J. Chem.*, **35**, 458 (1957).

constants for the reaction of excess *n*-butylamine with *p*-NPA in methanol and methanol-*d* at -78.2° are given in Table II. A plot of k_{obsd} vs. [*n*-butylamine] is linear and has a zero intercept, indicating a simple one-term rate expression which is first order in amine. The small amount of methoxide ion present in *n*-butylamine-methanol solutions was shown not to contribute significantly to the reaction because buffering with *n*-butylamine hydrochloride does not change the rate constants. Furthermore, analysis of the reaction products by vapor phase chromatography shows that methyl acetate is produced in less than 10% yield. The observed reaction is mainly nucleophilic attack on the ester by an amine, with little methoxide reaction or general base catalyzed methanolysis. The aminolysis of *p*-nitrophenyl acetate proceeds only 1.12 times faster in methanol-*d* than in methanol, a rate difference which approaches the size of the experimental error.

Table I. The Observed Rate Constants for the Reaction of Methoxide Ion with *p*-Nitrophenyl Acetate in Methanol and Methanol-*d* at -78.2°

[Methoxide], ^{a,d} <i>M</i>	[<i>p</i> -NPA] ^a × 10 ⁴ , <i>M</i>	k_{obsd} × 10 ⁴ , sec ⁻¹	k_2^b × 10 ³ , <i>M</i> ⁻¹ sec ⁻¹
Methanol			
0.236	2.18	11.8	5.00
0.236	2.18	12.2	5.17
0.236	2.18	11.9	5.04
0.117	2.18	6.41	5.48
0.108	2.18	5.82	5.39
0.0694	2.18	3.45	4.97
0.234	4.33	12.1	5.17
$\bar{k}_2 = 5.17$			
Methanol- <i>d</i> ^c			
0.0970	2.18	12.9	13.3
0.0798	2.18	11.1	13.9
0.0554	2.18	7.34	13.2
$\bar{k}_2 = 13.5$			

^a At -78.2 ± 0.3°. ^b $k_2 = k_{\text{obsd}}/[\text{methoxide}]$. ^c >99% deuterium content. ^d Sodium methoxide.

Table II. The Observed Rate Constants for the Reaction of *n*-Butylamine with *p*-Nitrophenyl Acetate in Methanol and Methanol-*d* at -78.2°

[<i>n</i> -Butyl- amine], ^a <i>M</i>	[<i>p</i> -NPA] ^a × 10 ⁴ , <i>M</i>	k_{obsd} × 10 ⁴ , sec ⁻¹	k_2^b × 10 ³ , <i>M</i> ⁻¹ sec ⁻¹
Methanol			
1.52	4.33	15.4	1.01
1.13	4.33	10.8	0.956
1.13 ^d	4.33	10.4	0.920
0.904	4.33	8.69	0.961
0.565	4.33	5.46	0.966
0.225	4.33	2.09	0.929
$\bar{k}_2 = 0.957$			
Methanol- <i>d</i> ^c			
0.226	4.33	2.44	1.08
0.228	4.33	2.41	1.06
$\bar{k}_2 = 1.07$			

^a At -78.2 ± 0.3°. ^b $k_2 = k_{\text{obsd}}/[\textit{n}\text{-butylamine}]$. ^c >97% deuterium content. ^d +0.122 *M* *n*-butylamine hydrochloride.

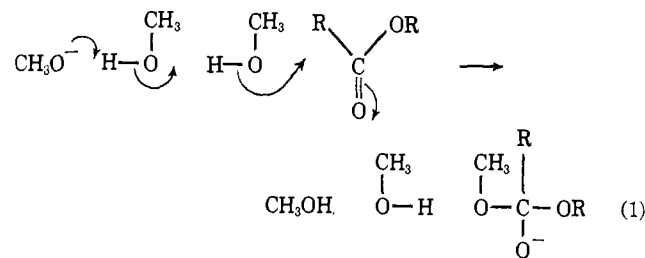
Nucleophilic reactions of nitrogen bases with carboxylic acid derivatives in aqueous solutions are not subject to solvent isotope effects.⁵ In this respect the

(5) M. L. Bender, E. J. Pollock, and M. C. Neveu, *J. Am. Chem. Soc.*, **84**, 595 (1962).

behavior of the aminolysis reaction in methanol at -78.2° is very similar to that of analogous reactions in water at temperatures over 100° higher. On the other hand, the simple kinetics of the low-temperature aminolysis contrasts markedly with those of the aminolysis of esters in ethanol at room temperature which involves terms second and three-halves order in amine.⁶

Reactions of carboxylic acid derivatives in water for which the solvent isotope effect is much greater than unity, as found for the methoxide ion-*p*-NPA system at -78.2° , are well known. Bender and Homer⁷ found that in the alkaline hydrolysis of *p*-nitrophenyl *N*-methylcarbamate $k_{D_2O}/k_{H_2O} = 1.8$, and concluded that the substrate is involved in a solvent-dependent preequilibrium. Bruice and co-workers⁸ attributed the large ratio for the alkaline hydrolysis of 2,2-dichloroethyl acetate to the difference in nucleophilicity of OH^- and OD^- . Clearly neither type of rationale is applicable to the methoxide-*p*-NPA reaction at low temperature because the substrate is nonionizable and the nucleophile is identical in the normal and heavy methanol. The isotope effect for the reaction of methoxide with phenyl benzoate in methanol at 25.0° is smaller than 2.6 but still sizeable ($k_{MeOD}/k_{MeOH} = 1.9$),⁹ showing that low temperature is not necessary for a ratio greater than unity. Differences in solvating properties⁹ of methanol and methanol-*d* must be sufficient to cause the large effects.

The reaction of methoxide ion with *p*-NPA in methanol may involve (A) no intervening reacting solvent molecules or (B) one or more of them (eq 1). Proton transfer in



water is associated with a large isotope effect ($k_{D_2O}/k_{H_2O} \ll 1$),¹⁰ pointing to a nonclassical behavior of the proton. The k_{MeOD}/k_{MeOH} ratio for the methoxide-*p*-NPA reaction would also be expected to be much less than unity if mechanism B applied, particularly if proton tunnelling were important at the reduced temperature. The observation that the ratio is in fact greater than unity (2.6) indicates that mechanism B is incorrect. Desolvation, or partial desolvation, of the nucleophile must be an integral part of the mechanism. Even at the low temperature, where it is more difficult to break solvation bonds, "long-range" reactivity of the methoxide is not present. Clearly in the case of *n*-butyl-aminolysis of *p*-NPA at -78.2° a Grotthuss-like mechanism is not operating through the solvation shell of the amine because little methyl acetate is formed.¹¹

(6) J. F. Bunnett and G. T. Davis, *J. Am. Chem. Soc.*, **82**, 665 (1960).

(7) M. L. Bender and R. B. Homer, *J. Org. Chem.*, **30**, 3975 (1965).

(8) T. C. Bruice, T. H. Fife, J. J. Bruno, and P. Benkovic, *J. Am. Chem. Soc.*, **84**, 3012 (1962).

(9) R. E. Robertson and P. M. Laughton, *Can. J. Chem.*, **35**, 1319 (1957); C. A. Bunton and V. J. Shiner, *J. Am. Chem. Soc.*, **83**, 3207, 3214 (1961).

(10) M. Eigen, *Angew. Chem. Intern. Ed. Engl.*, **3**, 1 (1964).

(11) A more detailed analysis and a description of further experiments in this area are forthcoming.

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F. M. Menger

Department of Chemistry, Emory University
Atlanta, Georgia

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The Intermediacy of Protonated Cyclopropanes in the Addition of Bromine to Cyclopropane

Sir:

Baird and Aboderin reported that addition of D_2SO_4 to cyclopropane in 57% D_2SO_4 produced monodeuterated 1-propanol and monodeuterated 1-propyl hydrogen sulfate with deuterium on C-1, C-2, and C-3.¹ It was reasoned that other addition reactions of cyclopropane should show similar complexity.

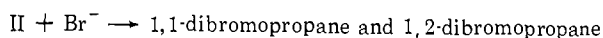
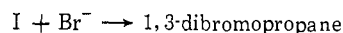
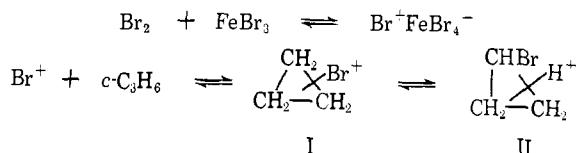
The addition of Br_2 to cyclopropane has now been examined, and 1,1-dibromopropane, 1,2-dibromopropane, and 1,3-dibromopropane are all produced. The results are presented in Table I.

Table I. Products from the Reaction of Br_2 and Cyclopropane

Temp, °C	Time, hr	Catalyst (g/100 g of Br_2)	% yields based on Br—			
			Dibromopropanes 1,1	1,2	1,3	$CH_3-CHBr-CHBr^a$
-15	12	Fe (1)	<i>b</i>	46	39	2.5
60	1	Fe (1)	<i>b</i>	60	10	12
65	0.25	$AlCl_3$ (6.7)	~5	~5	30	12
25	240 ^c	$AlBr_3$ (0.5)	3.8	2.8	15	3

^a The pmr spectrum consisted of a doublet ($J = 6.5$ cps) at δ 1.90, a complex multiplet at 4.3-4.7, and a doublet at 5.96 ($J = 3$ cps). This is definitive along with the boiling point of 200-201° (G. B. Bachman, *J. Am. Chem. Soc.*, **57**, 1090 (1935); B. K. Mereshkowsky, *Ann.*, **431**, 239 (1923)). The yield was computed on the basis that the gc band area had the same proportionality to weight as the dibromopropanes using a thermal conductivity detector. ^b The 1,1-dibromopropane is unstable under the reaction conditions. However, it does not produce the isomeric dibromopropanes on decomposition. The 1,2 and 1,3 isomers are stable. ^c The reaction was largely incomplete.

The production of all three dibromopropanes is interpreted to be the result of equilibration between intermediate protonated monobromocyclopropanes, $c-C_3H_6Br^+$. The interpretation parallels the equilibration of intermediate isomeric $c-C_3H_6D^+$ species, which were proposed by Baird and Aboderin to rationalize the deuterium scrambling in the addition of D_2SO_4 to cyclopropane.¹



(1) R. L. Baird and A. A. Aboderin, *J. Am. Chem. Soc.*, **86**, 252 (1964). This result has been confirmed with minor revision in 57% D_2SO_4 and throughout the 57-96% D_2SO_4 range. Also confirmed was the report that monodeuteriocyclopropane was formed (A. A. Aboderin and R. L. Baird, *Tetrahedron Letters*, 235 (1963)), and this result has now been extended to 57-96% D_2SO_4 .