

on a spinning-band column, b.p. 100–104° (1 mm.); yield, 128 g. (60%).

Anal. Calcd. for $C_7H_{11}BrO_4$: C, 35.1; H, 4.54; Br, 33.4. Found: C, 35.4; H, 4.66; Br, 33.0.

The infrared spectrum contains bands at 3.30, 3.40, 6.75, 7.27, 7.98, 8.12, 8.25, 8.65 (vs), 8.90, 9.30, 9.5 (broad), 10.0, 10.50 (broad), 11.25, and 12.95 μ .

The n.m.r. spectrum consists of a doublet and a narrow A_2B_2 multiplet with an area ratio (by integration) of 2:9, indicating coincidence of the central hydrogen with the methylene groups.

Dibromomalonaldehyde Bisethylene Acetal (VI).—Dibromomalonaldehyde (32 g., 0.139 mole) was refluxed in 200 ml. of benzene with ethylene glycol (18.1 g., 0.291 mole) and sulfuric acid (5 drops). Water was removed continuously. After refluxing overnight, 4.2 ml. of water had been collected. The solution was washed with dilute alkali, the organic layer dried, and the solvent removed.

The residual sirup was distilled *in vacuo*. A viscous oil distilled that contained —OH and carbonyl bands. The pot residue solidified and was recrystallized from carbon tetrachloride, yielding 2.6 g. (6%) of VI, m.p. 70–75°. Two recrystallizations from hexane raised the m.p. to 81–82°.

Anal. Calcd. for $C_7H_{10}Br_2O_4$: C, 26.4; H, 3.14; Br, 50.3. Found: C, 26.9; H, 3.24; Br, 49.7.

The n.m.r. spectrum consisted of a singlet at 4.72 τ and a narrow A_2B_2 multiplet centered at 5.81 τ with an area ratio of 1:4.

Hydrolysis Rates of Acetals IV, V and VI.—Samples of IV, V, and VI were dissolved in minimum amounts of ethanol and treated with 2,4-dinitrophenylhydrazine reagent. Derivative formation, as evidenced by precipitation of a colored solid (which later redissolved in the case of VI) took place in about 30 sec. with compounds IV and V. The acetal VI required about 12 hr. for derivative formation.

Effect of Solvent Composition on the Kinetics of the Cyanoethylation of Methanol

BEN-AMI FEIT, JOEL SINNREICH, AND ALBERT ZILKHA

Department of Organic Chemistry, The Hebrew University, Jerusalem, Israel

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In previous work,¹ the kinetics and mechanism of the alkali metal alkoxide-catalyzed nucleophilic addition of alcohols to acrylonitrile in alcoholic solvents were studied; the rate equation obtained was $R = k[\text{acrylonitrile}][\text{CH}_3\text{O}^-]$. We have investigated further the cyanoethylation of methanol in solvent mixtures of methanol and aprotic solvents such as dimethylformamide (DMF) and dioxane. Dipolar solvents were found to change the nucleophilicity order of nucleophiles in bimolecular substitutions.² Rates of nucleophilic substitution reactions in which anions participate were found to be accelerated by a factor of 10^5 – 10^7 or more^{3,4} on passing from protic to dipolar aprotic solvents⁵; this phenomenon was used with great advantage in the syntheses of many compounds.⁵ It was presumed that this solvent effect must be due largely to the greater reactivity of anions poorly solvated, relative to the transition states of their reactions in dipolar

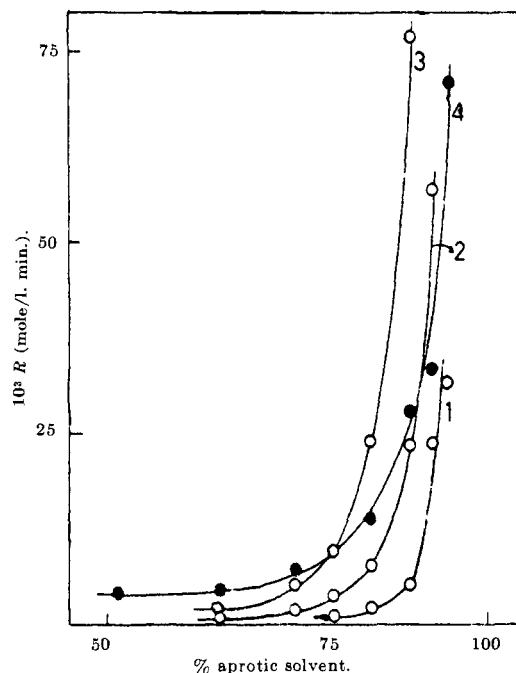


Fig. 1.—Plots of per cent aprotic solvent in the mixed methanol-protic solvent against initial rate (mole/l. min.) in methanol-dimethylformamide mixed solvent: (1) at 0°; (2) at 15°; (3) at 25°; (4) methanol-dioxane mixed solvent at 20°.

aprotic solvents.⁵ A similar solvent effect is to be expected in the case of cyanoethylation and related addition reactions, involving a nucleophilic attack of anions on acidic double bonds. Very little is known at present in this field; thus, the rate of addition of *p*-toluene thiolate to phenylacetylene in ethanol-dimethylformamide mixtures was found to increase greatly in the presence of high dimethylformamide concentrations.⁶

Results and Discussion

The kinetics of the cyanoethylation of methanol was studied in mixtures of methanol-dimethylformamide, at various temperatures, using lithium methoxide as basic catalyst, and in methanol-dioxane mixtures at 20° using potassium methoxide. Rates of reaction were calculated from the initial slopes of conversion *vs.* time plots. The rate increased progressively with decrease in the proportion of methanol in the mixed solvents (Fig. 1). A very great increase in rate was noticed in the range of low methanol concentrations, which in the case of methanol-dioxane mixtures obviously cannot be attributed solely to the effect of lowering of the dielectric constant on the rate of reaction between an ion and a neutral molecule.⁷ In the case of methanol (ϵ 34)⁸ and dimethylformamide (ϵ 37.6)⁹ mixtures, the increase in rate has but little to do with change in the dielectric constant.

In all cases the rate of reaction was first order in acrylonitrile. First-order rate constants were calculated from the linear plots of $\log [\text{acrylonitrile}]_t$ *vs.* time (Tables I, II). The rate of reaction was also approximately first order in catalyst; its value was 1.2

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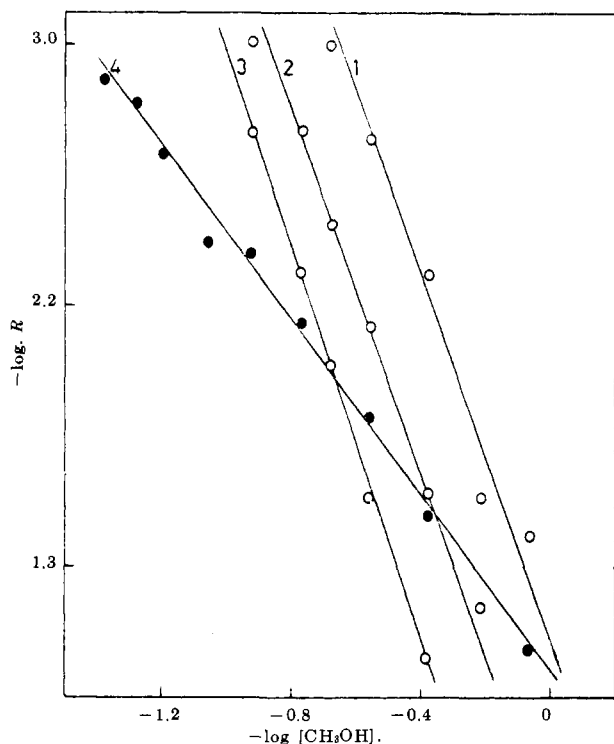


Fig. 2.—Order plots of logarithm of methanol concentration against logarithm of initial rate in methanol-dimethylformamide mixed solvent: (1) at 0°, slope -2.75 ; (2) at 15°, slope -2.75 ; (3) at 25°, slope -2.97 ; (4) methanol-dioxane mixed solvent at 20°, slope -1.33 .

TABLE I

FIRST-ORDER RATE CONSTANTS FOR THE CYANOETHYLATION OF METHANOL IN DMF-METHANOL MIXTURES^a

DMF, % by volume	10^3k_1 (min. ⁻¹) at 0°	10^3k_1 (min. ⁻¹) at 15°	10^3k_1 (min. ⁻¹) at 25°
50	1.23
65	...	1.80	3.70
75	...	4.16	11.41
80	1.84	9.47	22.26
85	4.61	19.39	56.66
90 ^b	10.80	64.36	187.75
93	50.83	164.29	...
95°	109.01

^a Experimental conditions: initial concentration of acrylonitrile, 0.506 mole/l.; of lithium methoxide, 3.333×10^{-4} mole/l. Rate measurements were carried out as previously described.¹ ^b Under otherwise constant conditions, 10^3k_1 (min.⁻¹) values at various base concentrations, $10^4[\text{CH}_3\text{OLi}]$, shown in parentheses (moles/liter) were: 8.75 (0.83), 33.45 (1.67), 64.36 (3.33), 115.00 (5.00), 163.09 (6.67). ^c At low equivalent concentrations of methanol, polymerization of excess acrylonitrile occurs. See B.-A. Feit and A. Zilkha, *J. Appl. Polymer Sci.*, **7**, 287 (1963).

in the case of methanol-dimethylformamide solvent (containing 90% by volume of dimethylformamide) at 15°, and 1.1 in the case of methanol-dioxane (93% dioxane) at 20°. Negative values were found for the order of reaction in methanol (Fig. 2). In methanol-dimethylformamide mixtures, the order in methanol was approximately -3 at all three reaction temperatures, whereas in methanol-dioxane mixtures it was -1.3 . It might well be assumed, therefore, that methanol itself participates in the reaction, for example, by solvation of the methoxide anions. An equilibrium involving free methoxide anions and solvated ones, the former being much more reactive, may exist: CH_3O^-

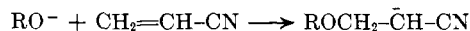
TABLE II

FIRST-ORDER RATE CONSTANTS FOR THE CYANOETHYLATION OF METHANOL IN DIOXANE-METHANOL MIXTURES^a

Dioxane, % by volume	10^3k_1 (min. ⁻¹) at 20°	Dioxane, % by volume	10^3k_1 (min. ⁻¹) at 20°
0	2.31	75	15.81
20.7	3.57	85	29.27
34.5	5.11	90	56.61
51.7	8.42	93 ^b	123.21
65	10.22	95	281.75

^a Experimental conditions: initial concentration of acrylonitrile, 0.506 mole/l.; of potassium methoxide 6.720×10^{-3} mole/l. ^b Under otherwise constant conditions 10^3k_1 (min.⁻¹) values at base concentrations, $10^4[\text{CH}_3\text{OK}]$, shown in parentheses (moles/liter) were: 9.50 (8.33), 33.81 (20.00).

$n\text{-CH}_3\text{OH} \rightleftharpoons \text{CH}_3\text{O}^- + n\text{-CH}_3\text{OH}$. Such an equilibrium followed by a rate determining nucleophilic attack¹ may be responsible for the negative order in methanol.



Support for the above can be found from the work of Cram, *et al.*,⁴ on the sodium methoxide-catalyzed H-D exchange, where the reaction was 10^9 times faster in dimethyl sulfoxide than in methanol, due to a strong solvation of methoxide anions in methanol by hydrogen bonds, and a very poor one in dimethyl sulfoxide. Cavell and Speed¹⁰ found a large increase in the rate of the isotopic exchange reaction of radioactive iodine with butyl iodide in mixed methanol-acetonitrile (ϵ 36) solvent, with increasing acetonitrile proportion. They too suggested that the existence of the equilibrium, $\text{I}^-\text{CH}_3\text{OH} \rightleftharpoons \text{I}^- + \text{CH}_3\text{OH}$, and the much greater reactivity of the free I^- as compared to the solvated one is responsible for this increase in rate.

The results of the present work offer possibilities for the shortening of reaction time and for obtaining higher yields in suitable nucleophilic additions.

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Oxidation of Thiols by Dimethyl Sulfoxide

C. N. YIANNIOS AND J. V. KARABINOS

Chemicals Division, Olin Mathieson Chemical Corporation,
New Haven, Connecticut

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Various oxidizing agents such as nitric acid, hydrogen peroxide, oxygen, and potassium ferricyanide have been employed for the conversion of thiols to disulfides. However, most of these reagents are also capable of reacting with other oxidizable sites such as aldehyde and amino groups.

We wish to report a convenient laboratory synthesis of disulfides from the corresponding thiols by selective oxidation of the latter with dimethyl sulfoxide.

While most oxidizable functional groups are quite stable to dimethyl sulfoxide, there are several reports in the literature of its use as a unique oxidizing agent, for example, in the conversion of α -bromo ketones to gly-