monohydrate (25 mg). A drop of several degrees in the distillate temperature indicates removal of ethanol or methanol. Best results were obtained with a rapid distillation and a rate of addition of 1 drop/sec. Distillation was continued (additional benzene may be required) until the distillate temperature returned to 81°. Anhydrous sodium carbonate was then added, and the solution was filtered, concentrated, and distilled under vacuum through a 30-cm column packed with glass helices and heated with an electrical heating tape.

Method B.—The diethyl acetal was prepared as indicated above but was not neutralized with sodium ethoxide. Instead, the benzene was distilled off to remove ethyl formate and ethanol from the reaction mixture (more benzene may be required to bring the distillate temperature to 81°) and the crude residue was then subjected to method A.

Preparation of Bistrichloroethyl Acetals.—Either method A or B may be employed with the following modifications: (1) use 0.1 mol of the acetal and 0.4 mol (59.6 g) of trichloroethanol, (2) add the acetal in xylene to trichloroethanol in xylene, (3) distil until the boiling point of xylene is reached, then distil for one additional hour.

Zinc Elimination.—The trichloroethyl acetal (1.0 g) was refluxed in ethyl acetate or THF with zinc (2.0 g), previously activated by washing with 5% HCl, H_2O, ethanol, ether, and drying *in vacuo* over P_2O_5. The solution was then filtered, enriched with ether, washed with 1% HCl, 5% sodium bicarbonate, brine, dried (sodium sulfate), and evaporated to give the free aldehyde or ketone.

Acid Hydrolysis.—A solution consisting of the acetal (0.05 mol) THF or dioxane (9 ml) water (0.5 ml) and *p*-toluenesulfonic acid monohydrate (50 mg) was refluxed until the nmr of the reaction mixture indicated greater than 95% hydrolysis to the aldehyde or ketone.

Acknowledgment.—We gratefully acknowledge support of this work by the National Institutes of Health, Grant No. A1-10,597-01.

Glyoxal Derivatives. V. Reaction of Alcohols with Glyoxal[1]

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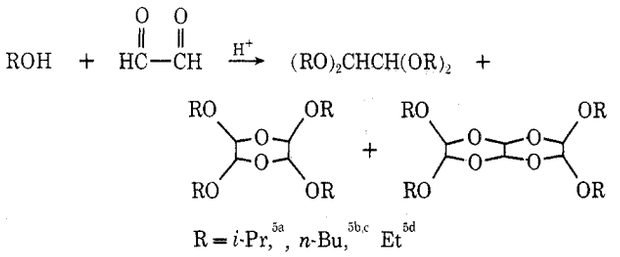
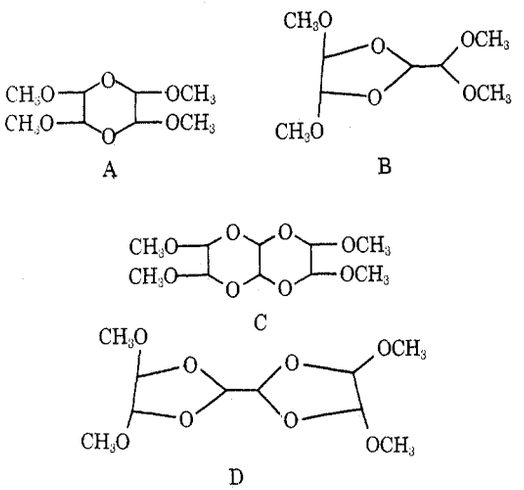
Aqueous glyoxal reacts with alcohols to give glycolates and acetal products consisting of 1,1′,2,2′-tetraalkoxyethanes, 1,3-dioxolanes, and 1,3-bisdioxolanes. It is shown that the dioxolanes are, in fact, the structures which have heretofore been misassigned as dioxane and naphthodioxanes. The relative abundance of any of the acetal products depends on the initial glyoxal concentration as well as the initial ratio of alcohol to glyoxal in the reaction mixture. It is also shown that dioxolane formation can be rationalized not only by the reaction of alcohol with dimeric and trimeric glyoxal, but also *via* the direct reaction of glyoxal with any of the already formed acetals.

The observation that glyoxal reacts readily with alcohols under acid conditions to give 1,1′,2,2′-tetraalkoxyethanes is well documented.[2-4] It has also been reported that higher molecular weight products are also afforded,[4,5] *i.e.*, the corresponding tetraalkoxydioxane and naphthodioxane derivatives.



More recently, we demonstrated[1] that one of the products derived from methyl alcohol and glyoxal was not the expected *p*-dioxane derivative A, but was rather the 1,3-dioxolane derivative B, and that the product derived from glyoxal trimer was not the naphthodioxane product, C, but was, in reality, the bis-1,3-dioxolane, D.



In this paper we shall present our findings on the general reaction of glyoxal with alcohols, as well as a partial insight into the equilibrium reactions of glyoxal with itself.

Results

We have found that, in general, the products of the reaction of glyoxal with alcohols include not only the bisacetals, but also glycolates, dioxolanes and bisdioxolanes (eq 1). The 1,3-dioxolane products were not isolated in addition to the previously presumed *p*-dioxane products, but, in fact, were the same compounds whose structures have been incorrectly assigned.[5]

Furthermore, the relative abundance of any of the acetal products (M, D, or T) depends on the initial

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(1) For previous paper, see J. M. Kliegman, E. B. Whipple, M. Ruta, and R. K. Barnes, *J. Org. Chem.*, **37**, 1276 (1972).

(2) C. B. Purves, U. S. Patent 2,194,405 (March 19, 1940).

(3) L. G. MacDowell and R. W. McNamee, British Patent 559,362 (Feb 16, 1944).

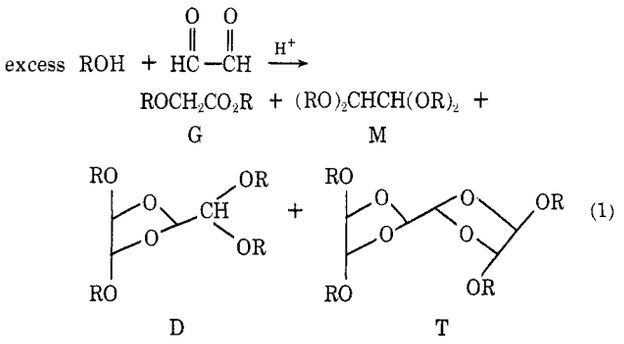
(4) Union Carbide Product Booklet, "General Chemistry of Glyoxal," F-41296, 1965.

(5) (a) O. C. Dermer and J. P. Yuk, *J. Amer. Chem. Soc.*, **77**, 1285 (1955); (b) B. DuVal, R. H. Hall, and B. K. Howe, *J. Appl. Chem.*, **2**, 546 (1952); (c) H. Fiesselmann and F. Horndler, *Chem. Ber.*, **87**, 906 (1954); (d) F. Chartrette, M. Chartrette, J. C. Duplan, and J. Delman, *Tetrahedron*, **27**, 5597 (1971).

TABLE I
PRODUCTS ISOLATED FROM ALCOHOL–GLYOXAL REACTIONS

Alcohol	ROH/glyoxal	% glyoxal	Yields,[a] % G	M	D	T	Residue
Hexanol	5:1	40	8 (1)	90 (2)			
2-Ethylhexanol	5:1	40		88 (3)			10
2-Pentanol	5:1	40	8 (4)	35 (5)	44 (6)		4
Cyclopentanol	5:1	40	8 (7)	73 (8)			10
2-Butanol	5:1	40	10 (9)	31 (10)	42 (11)		
Allyl alcohol	5:1	40	7 (12)	69 (13)	22 (14)		
Allyl alcohol	5:1	80	7	43	16		28 (15), mol wt 750
1-Butanol	5:1	40	10 (16)	80 (17)	8 (18)		
1-Butanol	4:1	80	10	63	16	5 (19)	
1-Butanol	2:1	40	9	10	52	23	
Ethanol	4:1	40	5 (28)	40 (20)	31 (21)		
Methanol	4:1	80	6 (22)	45 (23)	9 (24)		
Methanol	2:1	80	4	7	15	20 (25)	
2-Propanol	4:1	40		[b]	10 (26)	27 (27)	

[a] G is glycolate; M is monomer, based on glyoxal; D is dimer, based on glyoxal; T is trimer, based on glyoxal. [b] We were unable to isolate any monomer acetal. The only open product was a highly reactive material which appeared to be a linear dimer acetal in 15% yield.



glyoxal concentration as well as the ratio of alcohol to glyoxal utilized in the reaction.

In this study, we also show that the formation of acetal products based on dimeric and trimeric glyoxal can be rationalized not only by the reaction of dimeric and trimeric glyoxal with the alcohol, but also from the reaction of glyoxal directly with any of the already formed acetals.

Experimental Section[1,6]

In a typical experiment 5 mol of alcohol and 1 mol of glyoxal were mixed with 1–2 g of *p*-toluenesulfonic acid in a distillation flask. The mixture was brought to reflux and water removed azeotropically by the refluxing alcohol *via* a continuous Dean–Stark tube. In those cases where water solubility prevented separation of the water, another agent was used. Thus, for the reactions of ethanol, methanol, and isopropyl alcohol, the agents were carbon tetrachloride, chloroform, and benzene, respectively. In all cases, the pressure was regulated so that the kettle temperature did not rise above 120°. After water ceased to be generated, the reaction mixture was distilled through a Nester–Faust spinning-band column to give the observed products.

Table I lists the alcohols used in these reactions as well as the yields of glycolate, monomer, dimer, trimer, and residues. The terminology of monomer, dimer, etc., refers to the number of glyoxal residues in the molecule.

Table II lists the physical properties of the products given in Table I.

(6) Melting and boiling points are uncorrected. Infrared, nmr, and mass spectra were recorded on Perkin-Elmer, Varian A60A, and an AIC MS 9 spectrometers. Molecular weights were determined by Crobaugh Laboratories, Cleveland, Ohio. Elemental analysis were performed by the UCC staff.

TABLE II
PHYSICAL PROPERTIES OF PRODUCTS OBSERVED IN TABLE I[a]

Compound	Bp, °C (mm)	$n^{25}D$	Lit. values Bp, °C (mm)	Lit. values n_D
1	119 (3)	1.4321		
2	197 (2)	1.4366		
3	202–212 (3)	1.4455	215–25 (2)[g]	
4	100–110 (3)	1.4202		
5	137 (3)	1.4302		
6	173 (3)	1.4353		
7	101–106 (4)	1.4740		
8	170–180 (4)	Mp 34–37°		
9	90–98 (5)	1.4230	203–204 (743)	$n^{25}D$ 1.4150[b]
10	100–115 (5)	1.4263		
11	115–180 (5)	1.4314		
12	64–70 (3)	1.4475	95–97 (18)	$n^{20}D$ 1.4435[c]
13	92–95 (2)	1.4520	155–160 (25–30)[d]	
14	136–138 (2)	1.4600		
16	95 (10)	1.4234	113–115 (17.5)	$n^{25}D$ 1.4160[e]
17	130–140 (3)	1.4241	159–161 (10)[5c]	
18	160–170 (3)	1.4308	195–202 (10)[5c]	$n^{20}D$ 1.4315[5a]
19	185–205 (1–2)	1.4397		
20	84–85 (10)	1.4035	79 (10)[f]	$n^{20}D$ 1.4051
21	120–121 (4)	1.4238	135 (12)[5d]	
22	58–68 (110)	1.3968	57 (50)	$n^{25}D$ 1.3940[g]
23	83–85 (48)	1.4006	78–79 (50)	$n^{25}D$ 1.4010
24	98–99 (5)	1.4225	[h]	[h]
25	105–108 (5)	Mp 109–110°	[h]	[h]
26	108–110 (3)	1.4216	139 (8–9)	$n^{20}D$ 1.4242[5b]
27	153–155 (2)	Mp 49–58°	165–169 (8)	Mp 48–60[5b]

[a] Satisfactory analytical data (±0.4% for C, H, and ±6.0% for molecular weights (cryoscopic in benzene)) were reported for all new compounds in the table. [b] H. R. Henze and E. N. Kahlenberg, *J. Amer. Chem. Soc.*, **80**, 1664 (1958). [c] General Electric, U. S. Patent 240,659 (1944); *Chem. Abstr.*, **41**, 772 (1947). [d] P. Talet, U. S. Patent 3,197,447 (1965). [e] R. W. McNamee and L. G. McDowell, U. S. Patent 2,366,276 (1945). [f] H. A. Stansbury and D. T. Manning, U. S. Patent 3,130,234 (April 21, 1964). [g] H. Adkins, *et al.*, *J. Amer. Chem. Soc.*, **71**, 3629 (1949); D. J. Loder, U. S. Patent 2,302,618 (1943). [h] *Cf.* ref 1.

Structural Assignments

The structures of our products were deduced from their infrared spectra, molecular weight, elemental analysis, and nuclear magnetic resonance spectra. The glycolates were identified by a comparison of their infrared spectra with the infrared spectra of the known glycolates of 2-butanol, allyl alcohol, and 1-butanol. The unknown glycolates were identified from their infrared and mass spectra. Our analysis of the nuclear magnetic resonance spectra of the remaining acetals provides the bulk of the proof of structure of these

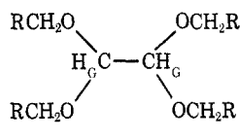
TABLE III
NMR SPECTRA OF ACETAL PRODUCTS[a]

Compd	ROH	Solvent	Acetal proton	R protons -C(H)O-	R protons CH_2	R protons CH	R protons CH_3	Dioxolane protons $C_{4,5}$ H	Dioxolane protons $C_{2,\alpha}$ H	R protons -C(H)O-	R protons CH_2	R protons CH	R protons CH_3
2	Hexanol	Neat	4.27 (s)	3.55 (m)	1.38 (m)		0.95 (tr)						
3	2-Ethyl-hexanol	Neat	4.25 (s)	3.45 (m)	1.33 (m)	1.33 (m)	0.92 (m)						
5	2-Pentanol	Neat	4.17 (d, 2.0 Hz)	3.66 (m)	1.42 (m)		1.03 (d, 5.0 Hz) 0.90 (tr)						
8	Cyclopentanol	Neat	4.20 (s)	4.20	1.62								
		CS_2	4.17 (s)	4.17	1.60								
		Pyridine	4.45 (s)	4.30 (m)	1.68								
		CCl_4	4.20 (s)	4.20	1.62								
10	2-Butanol	Neat	4.28 (d, 1.0 Hz)	3.65 (q, 6.0 Hz)	1.40 (q, 6.0 Hz)		1.10 (d, 6.0 Hz) 0.90 (tr, 6.0 Hz)						
13	Allyl alcohol	Neat	4.42 (s)	4.20 (m)	5.33 (m) 5.08 (m)	5.83 (m)							
17	1-Butanol	Neat	4.18 (s)	3.50 (m)	1.47 (m)		0.73 (m)						
20	Ethanol	Neat	4.28 (s)	3.58 (q, d, 7.0 Hz, 2.0 Hz)			0.73 (m) 1.13 (tr, 7.0 Hz)						
6	2-Pentanol	Neat						4.92 (d)	4.90 (d, 5.0 Hz) 4.28 (d, 5.0 Hz)	3.67 (m)	1.40 (m)		1.15 (m) 0.90 (m)
11	2-Butanol	CCl_4						5.00 (d)	4.98 (d, 6.0 Hz) 4.28 (d, 6.0 Hz)	3.63 (m)	1.43 (q, 6.0 Hz)		1.12 (d, 6.0 Hz) 0.90 (tr, 7.0 Hz)
14	Allyl alcohol	Neat						5.10 (d)	5.00 (obscured) 4.38 (d, 6.0 Hz)	4.12 (m)	5.37 (m) 5.08 (m)	5.83 (m)	
18	1-Butanol	Neat						4.97 (d)	5.12 (d, 6.0 Hz) 4.30 (d, 6.0 Hz)	3.58 (m)	1.50 (m)		0.92 (tr, 6.0 Hz)
21	Ethanol	CCl_4						4.83 (d)	5.05 (d, 6.0 Hz) 4.12 (d, 6.0 Hz)	3.58 (m)			1.16 (tr, 7.0 Hz)
26	2-Propanol	Neat						4.95 (d)	4.95 (d, 6.0 Hz) 4.24 (d, 6.0 Hz)	3.82 (m)			1.09 (d, 4.0 Hz)
19	1-Butanol	CCl_4						5.0–5.1 (3 peaks)	3.65 (m)	1.50 (m)			0.92 (tr)
27	2-Propanol	Neat						4.94–4.98 (3 peaks)	3.90 (m)				1.15 (d, tr, 5.0 Hz 1.0 Hz)

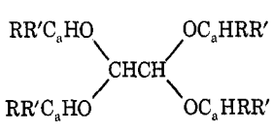
[a] All resonances are given in ppm from TMS with multiplicity and couplings in parentheses.

compounds. The results of these nmr analysis are given in Table III.

The monomeric acetal structures



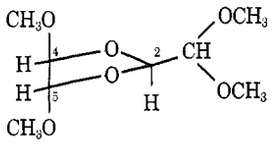
are distinguished by the appearance of the glyoxal aldehydic proton, H_G, as a single peak at 4.17–4.42 ppm. The two exceptions to this observation are with the 2-pentanol and 2-butanol compounds. In these cases, an asymmetric center is present at the carbon,



C_a connected to the acetal oxygen. This provides for at least two magnetically nonequivalent structures corresponding to the stereoisomeric enantiomers. Thus, the doublet shown is not really a doublet, but two singlets each from different stereoisomeric structures. The remainder of the spectrum corresponds normally to that expected for the alcohol portions of the molecule.

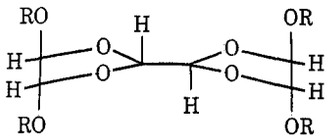
The acetal structures based on glyoxal dimer were deduced by a comparison of their nmr spectra with that

observed for the dimer acetal of glyoxal and methanol (compound **24**[1])



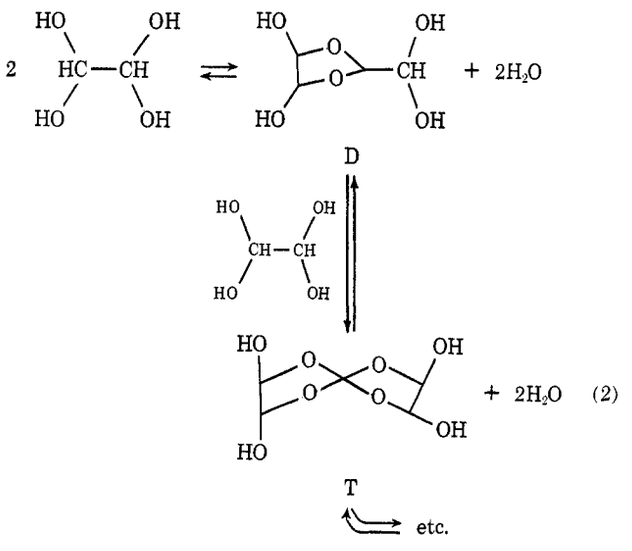
In that study, the dioxolane ring protons in the 4 and 5 positions appeared as two uncoupled peaks at 4.60 ppm, while the proton in the 2 position and the side-chain proton appeared as an AB pair with doublets at 4.78 and 3.82 ppm (J = 6–7 Hz), typical for vicinal, nonequivalent protons. The similarity between that spectrum and those observed in this case is striking. In the present dimer acetals, the adjacent dioxolane ring protons appear as two single peaks at 4.9–5.1 ppm. The AB pair derived from the 2 proton and side-chain proton are at 4.78 and 4.3 ppm (J = 6 Hz). The remaining portions of the spectra corresponding to the alcohol portion of the molecules were normal, and as expected.

The acetal structures based on glyoxal trimer, compounds **19** and **27**, were deduced by comparing their nmr spectra with that of the trimer isolated from the reaction of glyoxal with methanol **25**.[1] An extremely complicated group of peakes at 4.99–5.10 ppm corresponds to the dioxolane ring protons. The remaining



peaks correspond to the butyl and isopropyl group protons.

Mechanism.—Whipple has shown that the major portion of aqueous glyoxal dimers and trimers also are of the dioxolane type and they exist as an equilibrium between monomeric, dimeric, trimeric, etc., species[7] (eq 2). Equation 2 represents the major components of



40% aqueous glyoxal, with very small contributions from dioxane-type structures. This equilibrium is easily shifted by the removal of water. Thus, whereas in 40% solution the major form is the monomer, the dimer and trimer structures predominate in 80% glyoxal.

TABLE IV
PRODUCT DEPENDENCE ON GLYOXAL CONCENTRATION

Glyoxal concn, %	Alc/gly	Product yield, % G	M	D	T	Higher
40	BuOH 5:1	10	80	8		
80	BuOH 5:1	10	63	16	5	
40	BuOH 2:1	9	10	52	23	
40	Allyl 5:1	7	69	22		
80	Allyl 5:1	7	43	16		28 (mol wt 750)

The reaction of alcohols with aqueous glyoxal gives products whose structures are directly analogous with the above equilibrium of glyoxal in water. The differences in yields of monomeric and dimeric acetals, and the nonobservance of dimeric acetals with cyclopentanol, hexanol, and 2-ethylhexanol might be explained by the solubility of glyoxal monomer (tetrahydroxyethane) in the reacting alcohol. In those reactions which are two phase, one would expect the majority of the reactions to take place at the interface of the layers. If the complex equilibrium of glyoxal

SCHEME I

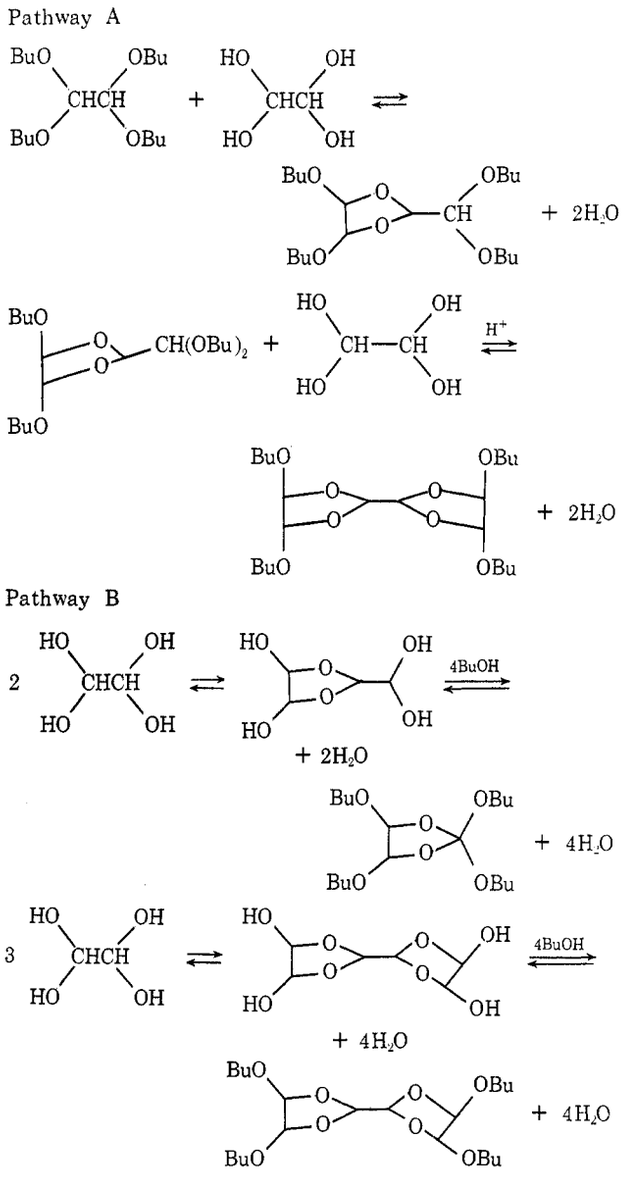


Table V
Reactions of 1,1′,2,2′-Tetrabutoxyethane[a]

Reactants	Products yield,[b] % Unreacted acetal	1,3-Dioxolane (dimer)	Bis-dioxolane (trimer)	Butanol
Water	38.8	37.0	5.4	26.4
Aqueous glyoxal	6.6	51.7	34.4	22.0

[a] The stoichiometry of the reaction with glyoxal was 1:1. The water reaction was run with the same water stoichiometry as was present in the reaction with glyoxal. [b] No free glyoxal was observed in these reaction mixtures.

in water, described by Whipple, is further complicated by an equilibrium between the water layer and water-insoluble alcohol, one might expect to see a wide range of yields of products. For example, if only tetrahydroxyethane goes into the hexanol layer the result would be (1) the formation of more acetal based on glyoxal monomer and (2) a decrease in the amount of dimer present in the aqueous phase. Another explanation might lie in the relative rates of acetal formation and exchange of the various species in the glyoxal solution.

Support for the above consideration of the complex equilibria of glyoxal in water comes from those experiments in which the concentration of glyoxal was varied as well as the molar ratio of alcohol to glyoxal (Table IV).

This table (IV) clearly shows that the change in equilibrium in going from 40 to 80% glyoxal provides higher yields of dimeric, trimeric, and even higher products. Even more striking is the reaction in which only half as much alcohol is present per mole of tetrahydroxyethane (hydrated glyoxal). It is in that case that we see the largest yield of dimer and trimer product.

The equilibrium reactions in Scheme I represent the two most probable mechanistic pathways to our observed products in which pathway B represents the glyoxal equilibria to products, and pathway A proposes the direct insertion reaction of glyoxal with acetals.

Support for the above pathways and equilibria was obtained by a study of the reactions of 1,1′,2,2′-tetrabutoxyethane with water and with aqueous glyoxal. The results of those reactions are given in Table V.

The reaction of 1,1′,2,2′-tetrabutoxyethane with water gives a 61% conversion of acetal whereas with glyoxal the conversion was 94%. In both cases the butanol yield indicates the same degree of hydrolysis reaction took place; so the only difference must be in the availability and concentration of glyoxal for direct insertion. This conclusion is augmented by the relatively unchanged yield of dimeric product and the six- to sevenfold increase in trimeric product.

We conclude from this study that this direct insertion reaction is a viable pathway and, indeed, plays a part in controlling the product mixture in the multiphase reactions described earlier.

The formation of glycolates in these reactions will not be discussed in this report, but will be taken up in a future publication.

Registry No.—**1,** 37160-54-6; **2,** 37160-55-7; **3,** 37160-56-8; **4,** 37160-57-9; **5,** 37160-58-0; **6,** 37160-59-1; **7,** 37160-60-4; **8,** 37406-80-7; **9,** 37160-61-5; **10,** 37160-62-6; **11,** 37160-63-7; **12,** 4704-23-8; **13,** 16646-44-9; **14,** 37160-66-0; **16,** 7397-62-8; **17,** 6284-81-7; **18,** 37160-68-2; **19,** 37160-69-3; **20,** 3975-14-2; **21,** 37160-71-7; **22,** 96-35-5; **23,** 2517-44-4; **24,** 33834-49-8; **25,** 33834-90-1; **26,** 37160-75-1; **27,** 37160-76-2; glyoxal, 107-22-2.

Acknowledgment.—We should like to thank Mr. B. E. Wilkes for the mass spectra and Mr. R. A. Thursack for helpful discussions of the nmr spectra.

Inductive Effect in Dithiocarbamate Decomposition Mechanism

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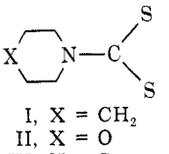
The acid-induced decomposition of $X(C_2H_4)_2NCS_2^-$ ions (X = CH_2, O, S, HN, CH_3N) was spectrophotometrically studied in pseudo-first-order conditions by varying ionic strength, dielectric constant, pH, and temperature. The reaction is first order with respect to the H^+ and dithiocarbamate ions. Activation parameters and activated complex radius values are also reported.

Some authors[1-6] have studied the dithiocarbamate ion decomposition mechanism using polarographic, potentiometric, or spectrophotometric techniques. Although some aspects of the problem have been clarified, we believe that this subject has not been completely dissected. In fact, ionic strength and the type of acid catalysis have never been considered, and the influence of dielectric constant variation has not been well defined. Moreover, increases of even 100-fold in decomposition rate constants have been explained by referring to steric and sometimes to electronic factors. In this paper we intend to carry out a more detailed treatment using a homogeneous series of ions, where it is possible to point out the inductive effects, such as shown below.



I, X = CH_2
II, X = O
III, X = S
IV, X = NH
V, X = CH_3N

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