HETEROCYCLIC COMPOUNDS

Volume 5

Five-Membered Heterocycles Containing Two Hetero Atoms and Their Benzo Derivatives

Edited by

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PREFACE

In the present volume of this series, the chemistry of the five-membered heterocycles and their benzo derivatives is considered. Some inconsistencies in the relative amount of space devoted to the various substances will be apparent. Only the 1,3-dioxolanes have been treated. The 1,2-dioxolanes resemble conventional peroxides so closely in their behavior that it was concluded that a detailed discussion of these substances could be omitted. A similar argument might, perhaps, have been used to justify omission of a discussion of the 1,3-dioxolanes, inasmuch as these compounds can properly be regarded merely as cyclic acetals and ketals. However, it was felt that the chemistry of the 1,3-dioxolanes is sufficiently important to warrant a somewhat condensed treatment. Much material pertinent to the chemistry of the 1,3-dioxolanes has been postponed for inclusion in the discussion of the 1,3-dioxanes in Volume 6 of the series, and the reader will probably wish to consult that chapter for further information. Since the sulfur analogs of the dioxolanes present in general no important differences from their oxygen analogs, a discussion of these compounds has been omitted.

What may appear to be an undue amount of space has been devoted to the oxazoles, and, to a lesser extent, to the thiazoles. Justification for a somewhat detailed treatment of the oxazoles is found in the wealth of new material which has appeared since publication of the most recent summarizing articles on these compounds. The thiazole literature is so enormous that this chapter, almost of necessity, attained considerable proportions.

Through circumstances beyond control, publication of this volume has been considerably delayed. Most of the manuscripts have been on hand for several months. This has been the cause of serious editorial problems in so far as inclusion of the most recent work is concerned. Further, this situation has not been helped by the death of one of the senior editors of *Chemical Abstracts* within the past two years, a circumstance which has unavoidably resulted in considerable delay between the appearance of a paper and the appearance of an abstract thereof. Despite these handicaps every effort consistent with mechanical limitations has been made to bring the subject matter up to date as completely as possible. In general, an attempt has been made to cover the major English and German language periodicals through 1955. If important omissions have occurred, I ask the indulgence of the reader.

Continuing the precedent set in earlier volumes of this series, the general practice of omitting hydrogen atoms from cyclic formulas has been followed unless the inclusion of such hydrogen atoms is definitely indicated for reasons of clarity. In all cyclic formulas double bonds are written.

It has been my experience in using previous volumes of this series that the indices have been somewhat overly curtailed. In the present volume an effort has been made to overcome this shortcoming, and a much more comprehensive index has been provided.

As with previous volumes it is a pleasure to acknowledge the encouragement of many friends in the task of providing this volume. I am deeply appreciative of the efforts of the contributors, and especially grateful for their hearty cooperation and forbearance in the face of delays which postponed appearance of the results of their work. To my colleagues and to many graduate students at the University of Michigan I am indebted for many stimulating and fruitful discussions and criticisms. Finally, as in the previous volumes I wish to acknowledge the understanding of my wife during her "book widowhood" and her help in editing, proofreading, and indexing.

ROBERT C. ELDERFIELD
Editor

Ann Arbor, Michigan
August, 1956

CONTENTS

CHAPTER 1

1,3-DIOXOLANE AND DERIVATIVES

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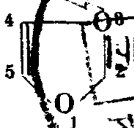
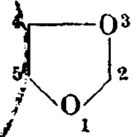
CONTENTS

INTRODUCTION

1,3-Dioxole (I) is the parent substance of 1,3-dioxolane (II). Whereas 1,3-dioxole has apparently not been prepared, and but a few of its derivatives have been reported, the 1,3-dioxolanes, along with the 1,3-dioxanes,



I



II

form a large and relatively important group of substances which can best be considered as cyclic acetals or ketals of polyhydric alcohols. In the older literature, 1,3-dioxolane has been called formaldehyde ethylene acetal, glycol formal, glycol methylene ether, and ethylene methylene dioxide. The numbering system universally used is shown in I and II. The arrangement of carbon and oxygen atoms in 1,3-dioxolane is clearly shown by its formation from one mole of ethylene glycol and one mole of formaldehyde with elimination of one mole of water.[1-3]

In view of the comparative importance of 1,3-dioxolane and its derivatives, these substances will be treated with primary emphasis in the present chapter. 1,3-Dioxole and its derivatives will find a subordinate place at the end of the treatment.

1,3-DIOXOLANE AND ITS DERIVATIVES

Synthesis. Excellent literature summaries on the preparation of 1,3-dioxolanes may be found in papers by Palomaa, Salmi, and Wallin,[4] and by Bersin and Wilfang.[5]

From Aldehydes and 1,2-*Glycols.* Trielat and Cambier[1] first prepared 1,3-dioxolane in 44% yield by heating equimolar quantities of trioxymethylene and ethylene glycol at 100° in the presence of 2% of ferric chloride. However, on the basis of carbon and hydrogen analyses the compound was erroneously assigned the structure $HOCH_2CH_2OCH_2CH_2OH$. The correct structure was subsequently arrived at by means of more accurate analytical data and by the observation that the substance possessed all the properties of an acetal, particularly that of facile cleavage by acid to ethylene glycol and formaldehyde.

Substantially all direct syntheses of 1,3-dioxolane and its derivatives, with the exception of those from acetylene and ethylene oxide, proceed by condensation of a 1,2-glycol with a carbonyl compound, and for optimum results an acid catalyst is desirable. The carbonyl component may be either an aldehyde or a ketone, and the 1,2-glycol may be a 1,2-glycol as such or a related derivative such as an α-hydroxy acid. From the latter compounds 1,3-dioxalan-4-ones result (p. 27). By far the greatest application of dioxolanes has been in the field of sugar chemistry, in which the familiar isopropylidene ethers and benzylidene ethers which arise from the condensation of a variety of carbohydrates with acetone and benzaldehyde, respectively, are familiar to the majority of organic chemists.

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[1] Trielat and Cambier, *Bull. soc. chim. France*, [3] **11**, 759 (1894).

[2] Verley, *Bull. soc. chim. France*, [3] **21**, 275 (1899).

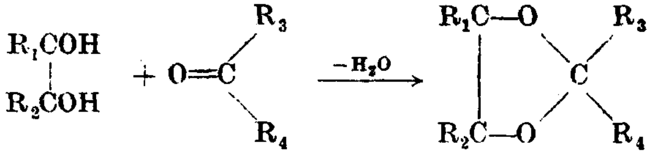
[3] Clarke, *J. Chem. Soc.*, **101**, 1788 (1912).

[4] Palomaa, Salmi, and Wallin, *Ber.*, **68**, 609 (1935).

[5] Bersin and Willfang, *Ber.*, **70**, 2167 (1937).

This phase of the chemistry of 1,3-dioxolane will be afforded a minor part in the present treatment.

The over-all reaction which results in the formation of a 1,3-dioxolane may be represented by the following generalized equation.



R_1 and R_2 = H, alkyl, or aryl; R_3 = H, alkyl, or aryl; = R_4H or alkyl

When an acid is the catalyst, a hemiacetal is the probable intermediate.

Wurtz[6] apparently was the first to prepare ethylideneglycol (2-methyl-1,3-dioxolane) by heating ethylene glycol with acetaldehyde for several hours at 100°. Shortly thereafter 2-*n*-butyl- and 2-phenyl-1,3-dioxolane were prepared by the same method from valeraldehyde and benzaldehyde, respectively.[7]

Meunier,[8] Schulz and Tollens,[9] and Fischer[10] prepared a number of 1,3-dioxolanes from ethylene glycol, glycerol, and various sugar alcohols and benzaldehyde, acetaldehyde, or formaldehyde with the aid of sulfuric or hydrochloric acid as catalyst. Use of sirupy phosphoric acid[2, 3] or of phosphorus pentoxide[11] as catalyst has resulted in improved yields of cleaner products in many instances.

As with any acetal formation, the reactions involve equilibria. As first noted by Gerhardt,[12] this equilibrium between the acetal and its hydrolysis products may be displaced in favor of the 1,3-dioxolane by removal of the water formed by distillation. This method has been developed to give good yields of 1,3-dioxolanes by addition of a catalytic amount of benzene- or *p*-toluene-sulfonic acid with concurrent use of a suitable solvent for removal of the water formed by azeotropic distillation.[13, 14]

A list of representative 1,3-dioxolanes which have been prepared from 1,2-glycols and aldehydes is given in Table 1. This is by no means complete but serves to indicate the types of compounds which can be prepared.

Certain special 1,3-dioxolanes of the type listed in the table merit further discussion. Whereas benzaldehyde readily undergoes condensation

[6] Wurtz, *Ann.*, **120**, 328 (1861).

[7] Harnitzky and Menschutkin, *Ann.*, **136**, 126 (1865).

[8] Meunier *Ann. chim. et. phys.* [6] **22**, 412 (1891).

[9] Schulz and Tollens, *Ann.*, **289**, 20 (1896).

[10] Fischer, *Ber.*, **27**, 1524 (1897).

[11] Tsuzuki, *Bull. Chem. Soc. Japan*, **11**, 362 (1936).

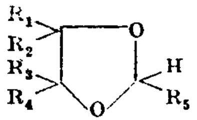
[12] Ger. pat. 253,083 [*C. A.*, **7**, 868 (1913)].

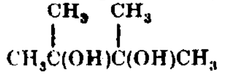
[13] Salmi and Pohjolainen, *Ber.*, **72**, 798 (1939).

[14] Sulzbacher, Bergmann, and Pariser, *J. Am. Chem. Soc.*, **70**, 2827 (1948), inter alia.

TABLE 1

2-MONOSUBSTITUTED 1,3-DIOXOLANES



1,2-Glycol	Aldehyde	Substituents in Product (H unless otherwise indicated)					Reference
		R_1	R_2	R_3	R_4	R_5	
$HOCH_2CH_2OH$	$HCHO$						3, 13
$HOCH_2CH_2OH$	CH_3CHO					CH_3	2, 3, 15
$HOCH_2CH_2OH$	iso-C_3H_7CHO					iso-C_3H_7	2, 15
$HOCH_2CH_2OH$	C_6H_5CHO					C_6H_5	14
$HOCH_2CH_2OH$	*p*-$CH_3OC_6H_4CHO$					*p*-$CH_3OC_6H_4$	14
$HOCH_2CH_2OH$	*o*-ClC_6H_4CHO					*o*-ClC_6H_4	14
$HOCH_2CH_2OH$	C_2H_5CHO					C_2H_5	15
$HOCH_2CH_2OH$	$(CH_3)_3CCHO$					$(CH_3)_3C$	15
$HOCH_2CH_2OH$	CH_2ClCHO					CH_2Cl	15
$HOCH_2CH_2OH$	$CHCl_2CHO$					$CHCl_2$	15
$HOCH_2CH_2OH$	CCl_3CHO					CCl_3	15
$HOCH_2CHOHCH_3$	Furfural	CH_3				2-Furyl	16
$HOCH_2CHOHCH_3$	$HCHO$	CH_3					3
$HOCH_2CHOHCH_3$	$C_6H_5CH{=}CHCHO$	CH_3				$C_6H_5CH{=}CH$	17
 $CH_3\overset{\overset{CH_3}{\vert}}{C}(OH)\overset{\overset{CH_3}{\vert}}{C}(OH)CH_3$	$(CH_3)_2CHCHO$	CH_3	CH_3	CH_3	CH_3	$CH(CH_3)_2$	18
$CH_2OHCHOHCOOCH_3$	CH_3CHO	$COOCH_3$				CH_3	19
Diethyl tartrate	Aromatic and aliphatic aldehydes	$COOC_2H_5$		$COOC_2H_5$		Depends on aldehyde	11, 20
$HOCH_2CHOHCH_2O(CH_2)_2OH$	CH_3CHO	$CH_2O(CH_2)_2OH$				CH_3	21

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[15] Hibbert, Morazain, and Paquet, *Can. J. Research*, **2**, 131 (1930).

[16] Salmi and Jansson, *Suomen Kemistilehti*, **12B**, 28 (1939) [*C. A.*, **34**, 423 (1940)].

[17] Salmi and Loukenkuru, *Suomen Kemistilehti*, **20B**, 5 (1947) [*C. A.*, **42**, 537 (1948)].

[18] Dworzak and Lasch, *Monatsh.*, **51**, 59 (1929).

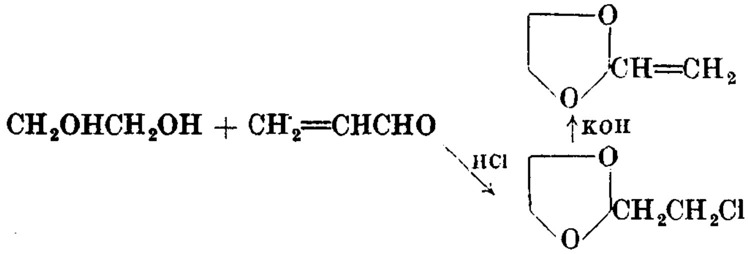
[19] Hermann and Baer, *Helv. Chim. Acta*, **16**, 534 (1933).

[20] Tsuzuki, *Bull. Chem. Soc. Japan*, **14**, 35 (1949).

[21] Kharasch and Nudenberg, *J. Org. Chem.*, **8**, 189 (1943); U.S. pat. 2,428,805 [*C. A.*, **42**, 618 (1948)].

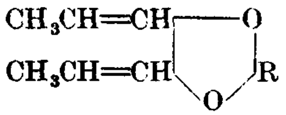
with ethylene glycol, it has been reported[22] that *m*-methyl- and *p*-methoxy-benzaldehyde fail to give 1,3-dioxolanes with sulfuric or hydrochloric acid as catalyst. On the other hand, all three nitrobenzaldehydes, chlorobenzaldehydes, *o*- and *m*-hydroxybenzaldehyde, and *p*-methoxybenzaldehyde condense with ethylene glycol in the presence of phosphorus pentoxide.[20]

Under hydrochloric acid catalysis as usually carried out, acrolein does not condense with ethylene glycol.[23] When acrolein is heated for several weeks with glycerol at 50–60° in the absence of a catalyst, a 10% yield of 2-vinyl-1,3-dioxolane-3-methanol results. However when acrolein is dropped into ethylene glycol containing hydrogen chloride at 0°, 2-(β-chloroethyl)-1,3-dioxolane results. From this 2-vinyl-1,3-dioxolane is formed on treatment with alkali.

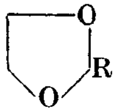


Other unsaturated aldehydes, cinnamic, crotonic, or α-methyl-β-ethylacrolein, show little tendency to condense with ethylene glycol with dilute sulfuric or phosphoric acid catalysts. However, cinnamic aldehyde readily condenses with ethylene or propylene glycol in the presence of *p*-toluenesulfonic acid when the water liberated is removed by azeotropic distillation.[17] α-Chlorocinnamic and α-chlorocrotonic aldehydes form the corresponding 1,3-dioxolanes in yields of 22%.[24]

Unsaturation in the glycol reactant seems to favor 1,3-dioxolane formation. Thus condensation of 4,5-dihydroxy-2,6-octadiene (dipropenyl glycol) with various saturated aldehydes with sulfuric acid as catalyst gave the following yields of 1,3-dioxolanes.[25]



R =	
CH_3	90%
C_2H_5	90%
n-C_3H_7	92%
n-C_6H_{13}	85%



R =	
CH_3	87%
n-C_3H_7	50%
n-C_6H_{13}	50%
C_6H_5	85%

[22] Dworzak and Herrmann, *Monatsh.*, **52**, 83 (1929).

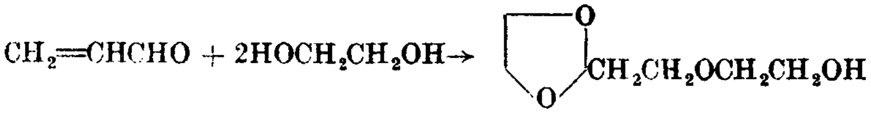
[23] Hibbert and Whelen, *J. Am. Chem. Soc.*, **51**, 3115 (1929).

[24] Hibbert, Houghton, and Taylor, *J. Am. Chem. Soc.*, **51**, 611 (1929).

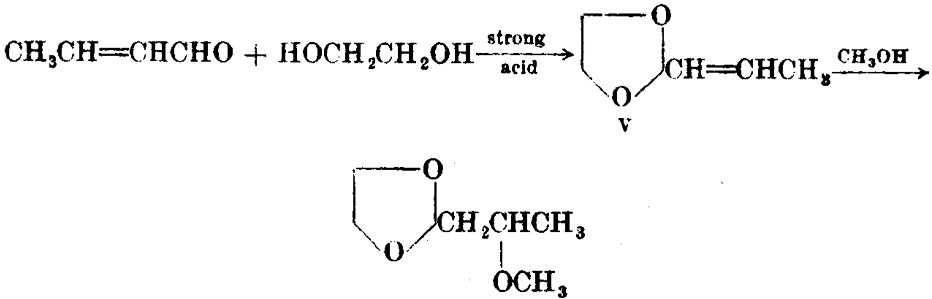
[25] Burt and Howland, *J. Am. Chem. Soc.*, **52**, 217 (1930).

The yields of dioxolane from dipropenyl glycol are in general higher than those reported for analogous compounds from ethylene glycol.[26] However, chloral, benzaldehyde, cinnamic aldehyde, and crotonic aldehyde failed to give a dioxolane with dipropenyl glycol.

According to the patent literature,[27] when a mixture of ethylene glycol and acrolein is treated with hydrogen chloride and allowed to stand for 2 hr. at 40–50°, a vinyl-1,3-dioxolane is formed which then adds a second molecule of ethylene glycol to the side-chain double bond to give III. In an analogous reaction IV is formed by addition of methanol to the dioxolane (V) from crotonic aldehyde and ethylene glycol.[28]



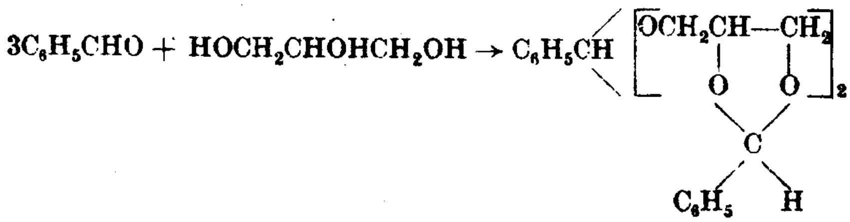
III



V

IV

When benzaldehyde is heated with ethylene glycol or 2,3-dihydroxybutane at 140–150° in the presence of a sulfonated phenolic resin as a catalyst the appropriate dioxolanes are formed.[28a] With glycerol under comparable conditions the reaction is more complicated.



A variant of the above general syntheses leads to 2-ethoxy-1,3-dioxolane.[29]

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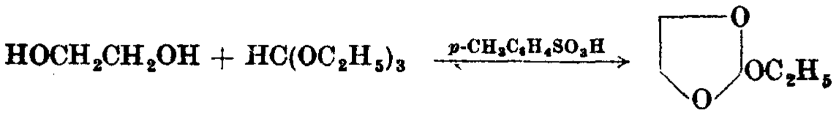
[26] Hibbert and Timm, *J. Am. Chem. Soc.*, **46**, 1283 (1924).

[27] Ger. pat. 669,805 [*C. A.*, **33**, 5414 (1939)].

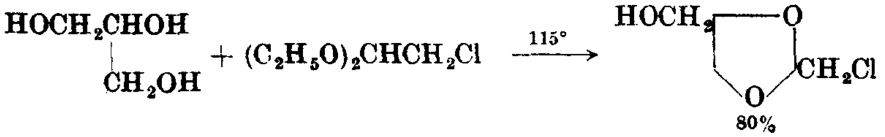
[28] Ger. pat. 664,271 [*C. A.*, **33**, 1344 (1939)].

[28a] Mastagli, Zafiriadis, and Lagrange, *Compt. rend.*, **237**, 187 (1953).

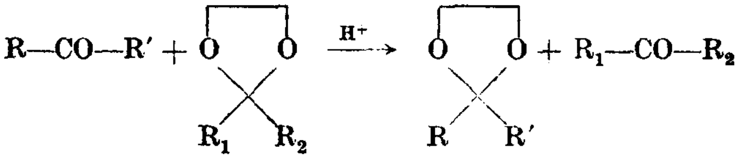
[29] Mkhitaryan, *J. Gen. Chem.* (*U.S.S.R.*), **10**, 66' (1940) [*C. A.*, **34**, 7859 (1940)].



Similar to the above reaction is the preparation of 1,3-dioxolanes from open chain acetals, e.g.,[30, 30a]



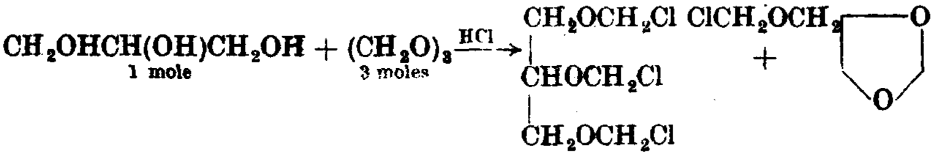
It is also possible and, in certain instances, desirable to prepare dioxolanes by exchange dioxolanation, e.g.,



$R_1 = CH_3$
$R_2 = CH_3$ or C_2H_5

This method takes advantage of the equilibrium nature of the reaction by removing the more volatile ketone component from the reaction mixture. It has been of particular advantage in blocking steroid ketones.[30b,c] Exchange dioxolanation appears to be more subject to steric and electronic effects than direct dioxolanation, and yields are comparable or, in most instances, superior to those obtained by the direct method. With steroidal ketones the order of reactivity is: saturated 3- or 20-ketones $>$ α,β-unsaturated 3- and 20-ketones $>$ 2- or 4-monobromo-3-ketones $\gg$ (no reaction) 17-ketones and 2,4-dibromo-3-ketones.

It has been noted that in the presence of excess hydrogen chloride the yield of 1,3-dioxolane-4-methanol from glycerol and formaldehyde is very low. When hydrogen chloride is passed into a mixture of the reactants with strong cooling until no more is absorbed, the major products isolated are those resulting from chloromethylation.[31]



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[29] Hallonquist and Hibbert, *Can. J. Research*, **8**, 129 (1933).

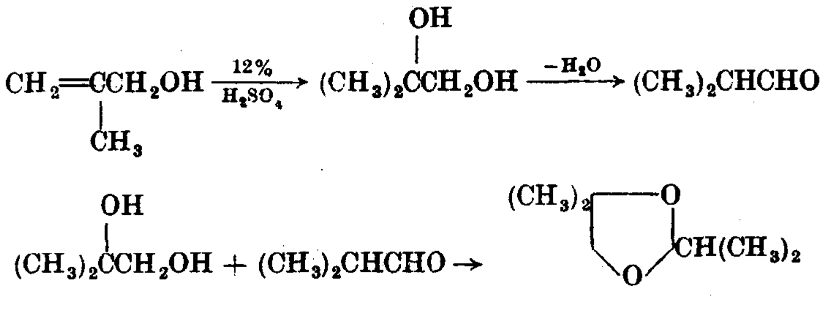
[30a] Blicke and Anderson, *J. Am. Chem. Soc.*, **74**, 1733 (1952).

[30b] Dauben, Jr., Löken, and Ringold, *J. Am. Chem. Soc.*, **76**, 1359 (1954). In this paper an excellent review of methods of blocking steroid ketones by direct dioxolanation is given.

[30c] Rosenkranz, Velasco, and Sondheimer, *J. Am. Chem. Soc.*, **76**, 5024 (1954).

[31] Lichtenberger and Martin, *Bull. soc. chim. France*, **1947**, 468.

A synthesis of 2-isopropyl-4,4-dimethyl-1,3-dioxolane from β-methylallyl alcohol probably falls into this same category and can be pictured as proceeding through the following steps.[32]



$$CH_2{=}\underset{\displaystyle CH_3}{C}CH_2OH \xrightarrow[H_2SO_4]{12\%} (CH_3)_2\overset{\displaystyle OH}{C}CH_2OH \xrightarrow{-H_2O} (CH_3)_2CHCHO$$

When an opportunity presents itself for the formation of either a 1,3-dioxolane or a 1,3-dioxane, as in reactions with glycerol, both compounds may be formed. This point is discussed in detail on p. 37.

From Ketones and 1,2-*Glycols.* Ketones in general are not so reactive in the formation of 1,3-dioxolanes as are aldehydes. Thus with 0.25–1% of sulfuric or hydrochloric acid as a catalyst, ethylene glycol condenses with acetone, methyl ethyl ketone, and di-*n*-propyl ketone to give 8%, 15%, and 30% of the respective 2,2-dialkyl-1,3-dioxolanes. However, in the presence of dehydrating agents better yields result. Thus glycerol on treatment with acetone in the presence of 1% of hydrogen chloride and ignited sodium sulfate gives 78% of 2,2-dimethyl-1,3-dioxolane-4-methanol,[33] and 60% of the carbinol results when the reactants (excess acetone) are stirred with anhydrous copper sulfate at room temperature for 123 hr.[34]

The 4-carboxylic and 4,5-dicarboxylic esters of 2,2-dimethyl-1,3-dioxolane are prepared from acetone and glyceric and tartaric acid esters, respectively. From methyl glycerate with zinc chloride 44% of methyl 2,2-dimethyl-1,3-dioxolane-4-carboxylate results; with ethyl glycerate the yield is 29%. Either ester when shaken with acetone and cupric sulfate gives 79% of the dioxolane ester.[35] Acetone and dimethyl or diethyl tartrate give 47% yields of the dioxolane-4,5-dicarboxylic esters on boiling for 36 hr. with anhydrous cupric sulfate.[11, 36]

Glyceric aldehyde reacts with acetone to give 2,2-dimethyl-1,3-dioxolane-4-aldehyde only in a room free of acid vapors.[37] However, the

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[32] Hearne, Tamele, and Converse, *Ind. Eng. Chem.*, **33**, 805 (1941).

[33] Fischer and Pfähler, *Ber.*, **53**, 1606 (1920).

[34] Hibbert and Morazain, *Can. J. Research*, **2**, 35 (1930).

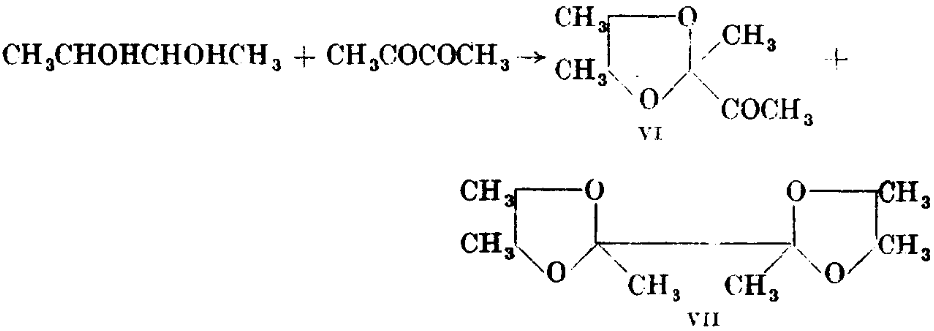
[35] Ott and Kramer, *J. prakt. Chem.*, [2] **137**, 255 (1933).

[36] Tsuzuki, *Bull. Chem. Soc. Japan*, **10**, 255 (1935).

[37] Fischer and Baer, *Ber.*, **63**, 1749 (1930).

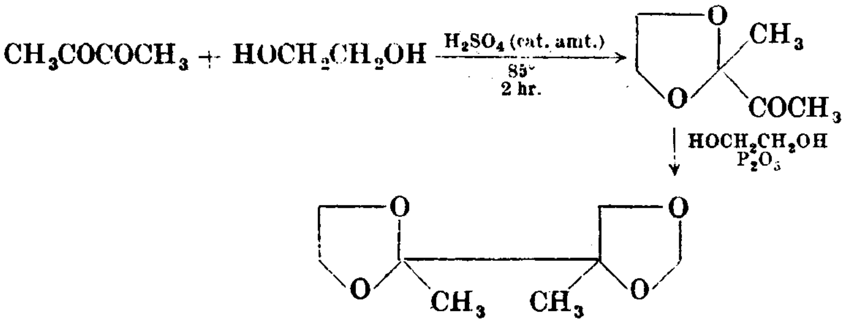
diethyl acetal of glyceric aldehyde readily condenses with acetone in the presence of copper sulfate to give the diethyl acetal of the dioxolane aldehyde.[38]

The reaction between 2,3-butanediol and diacetyl in the presence of hydrochloric or sulfuric acid is of interest. Two products are formed which are assigned the structures VI and VII.[39] Diacetyl with ethylene glycol gives either a mono- or a di-cyclic ketal, depending on the condensing agent.[40]



VI

VII



Tsuzuki[41] condensed a number of aliphatic and alicyclic ketones with dialkyl tartrates with phosphorus pentoxide as condensing agent. Greatly improved yields of 1,3-dioxolanes from a number of glycols including sugars and acetone with phosphorus pentoxide as condensing agent have been reported by Smith and Lindberg.[42]

Just as use of benzene- or *p*-toluene-sulfonic acids as catalysts and azeotropic removal of water results in improved yields of cyclic acetals,

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[38] Fischer, Taube, and Baer, *Ber.*, **60**, 479 (1927).

[39] Backer, *Rec. trav. chim.*, **55**, 1036 (1936); Neish and Macdonald, *Can. J. Research*, **25B**, 70 (1947).

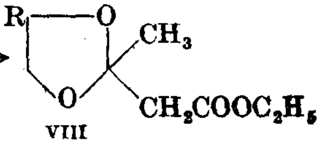
[40] Boëseken and Tellegen, *Rec. trav. chim.*, **57**, 133 (1938).

[41] Tsuzuki, *Bull. Chem. Soc. Japan*, **14**, 19 (1939), and earlier papers.

[42] Smith and Lindberg, *Ber.*, **64**, 505 (1931).

application of this method has also been successful for the preparation of ketals. Salmi[43] succeeded in obtaining the dioxolane VIII (R = H or CH_3) by azeotropic distillation of the water formed from the reactants in the presence of a trace of *p*-toluenesulfonic acid. Preparation of these substances by Smith and Lindberg's method had previously not been successful.[40] 1,3-Dioxolanes were also prepared from cyclopentanone, *l*-methone, and camphor and ethylene glycol. Catechol was condensed with cyclohexanone and *l*-menthone. Many other reports of the preparation of a wide variety of 1,3-dioxolanes have appeared.[44] Particular attention should be called to the semiquantitative study of dioxolane formation and discussion of the effect of structure of the ketone on the reaction reported by Sulzbacker, Bergmann, and Pariser.[45]

$$CH_3COCH_2COOC_2H_5 + HOCH_2CHROH \xrightarrow[\text{benzene}]{\text{dist.}}$$

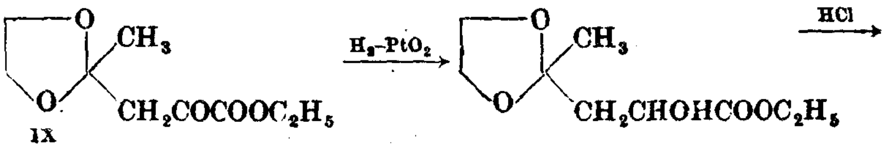


VIII

Maglio and Burger[46] have improved Newman and Renoll's[47] modification of the Fischer and Pfähler synthesis of isopropylidene glycerol to give substantially quantitative yields conveniently. In this procedure glycerol and acetone are boiled with an inert diluent in the presence of calcium carbide and a surface active agent such as a sulfonated petroleum hydrocarbon.

The reaction of ethyl oxalacetone with ethylene glycol is of interest. Only one ketone group condenses with the glycol, and the structure of the product (IX) has been demonstrated by conversion of IX to *β*-acetylacrylic acid.[48]

$$CH_3COCH_2COCOOC_2H_5 + HOCH_2CH_2OH \xrightarrow{p\text{-}CH_3C_6H_4SO_3H}$$



IX

$$CH_3COCH_2CHOHCOOC_2H_5 \xrightarrow{\text{HCl}} CH_3COCH{=}CHCOOH$$

[43] Salmi, *Ber.*, **71**, 1803 (1938).

[44] Kuhn, *J. prakt. Chem.*, [2] **156**, 103 (1940); Hurd and McAuley, *J. Am. Chem. Soc.*, **70**, 1650 (1948); U. S. pats. 2,377,568 [*C. A.*, **40**, 350 (1946)], 2,419,505 [*C. A.*, **42**, 616 (1948)], Blicke and Schumann, *J. Am. Chem. Soc.*, **74**, 2613 (1952), inter alia.

[45] Sulzbacker, Bergmann, and Pariser, *J. Am. Chem. Soc.*, **70**, 2827 (1948).

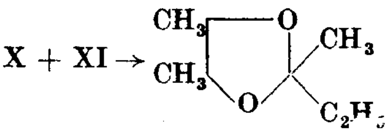
[46] Maglio and Burger, *J. Am. Chem. Soc.*, **68**, 529 (1946).

[47] Newman and Renoll, *J. Am. Chem. Soc.*, **67**, 1621 (1945).

[48] Rossi and Lauchenauer, *Helv. Chim. Acta*, **30**, 1501 (1947).

When 2,3-butanediol (X) is pyrolyzed over alumina at 400°, 2,4,5-trimethyl-2-ethyl-1,3-dioxolane (XII) is formed.[49] Presumably the diol is dehydrated to methyl ethyl ketone (XI), which then reacts with a second molecule of X to give the dioxolane.

$$\underset{\text{X}}{CH_3CHOHCHOHCH_3} \rightarrow CH_3CH{=}COHCH_3 \rightarrow \underset{\text{XI}}{CH_3CH_2COCH_3}$$



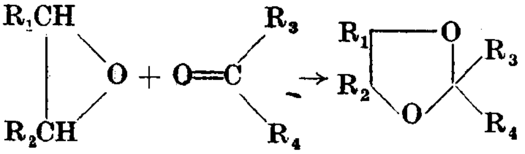
XII

A similar formation of XII in yields of up to 95% when *l*-butanediol-1,3 is heated with sulfuric acid at 85–138° has been reported. Again methyl ethyl ketone is the logical intermediate.[50]

From Ethylene Oxides. After earlier unsuccessful attempts at the direct preparation of 1,3-dioxolanes from ethylene oxides and aldehydes or ketones, Bogert and Roblin[51] noted that, in the presence of metallic chlorides, 1,3-dioxolanes were formed in this manner in yields of 22–32%.

Subsequently this general method has been modified and improved to the extent that yields of 50–75% of a wide variety of 1,3-dioxolanes may be obtained.[30a, 52–54]

The over-all reaction may be expressed as follows.



R_1 = H, alkyl, or aryl; R_2 = H, alkyl, aryl, or CH_2Cl; R_3 = H, alkyl, or aryl; R_4 = alkyl or aryl

The ketone may also be a cyclic ketone. A mechanism which takes into account the specific catalytic effect of the metal chloride has been suggested by Willfang.[53]

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[49] Backer, *Rec. trav. chim.*, **55**, 1036 (1936).

[50] Niesh, Haskell, and Macdonald, *Can. J. Research*, **23B**, 281 (1945).

[51] Bogert and Roblin, *J. Am. Chem. Soc.*, **55**, 3741 (1933).

[52] Bersin and Willfang, *Ber.*, **70**, 2167 (1937).

[53] Willfang, *Ber.*, **74**, 145 (1941).

[54] J. P. Fourneau and Chantalou, *Bull. soc. chim. France*, [5] **12**, 845 (1945).