Conversion of the Acetal to 2,3-Dimethyl-cyclopentene Aldehyde.—Five g. of magnesium turnings was added during the course of four hours to 50 g. of the bromo-acetal dissolved in 75 g. of ether, the temperature being maintained so that continual refluxing occurred. After this mixture had been heated for another four hours, and then cooled, sufficient water was added to decompose the thick, pasty, lower layer, and then about 15 cc. of sulfuric acid (1:1) until the solution was distinctly acid. The ether was removed, the aqueous solution refluxed for two hours, the product distilled with steam and the distillate extracted with ether. The ether solution was dried over calcium chloride and fractionated, yielding 2.6 g. (20%) of an oil boiling between 160° and 170°, which possessed the pungent odor of 2,3-dimethyl-cyclopentene aldehyde. This corresponded in all of its properties with the product obtained by the electrolytic reduction of crotonaldehyde.[3] The semicarbazone melted at the same temperature (184–186°) and a mixture of the two produced no alteration in the melting point.

Analysis of the semicarbazone. Subs., 0.1267: 26.1 cc. of N_2 (over water, 19°, 747 mm.). Calc. for $C_9H_{15}ON_3$: N, 23.2. Found: 23.4.

The attempt to substitute the corresponding chlorobutyraldehyde diethyl acetal[4] for the bromo derivative in the above reaction was not successful.

Summary

2,3-Dimethyl-cyclopentene aldehyde has been synthesized and shown to be identical with the unsaturated aldehyde obtained by the electrolytic reduction of crotonaldehyde.

NEW HAVEN, CONNECTICUT

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

STUDIES ON THE REACTIONS RELATING TO CARBOHYDRATES AND POLYSACCHARIDES

X. SYNTHESIS AND RELATIVE STABILITY OF CYCLIC ACETALS FROM 1,2- AND 1,3-GLYCOLS

BY HAROLD HIBBERT AND JOHN ARREND TIMM[1,2]

RECEIVED FEBRUARY 9, 1924

In a previous communication[3] it was shown that on treating a mixture of one molecular equivalent each of a 1,2- and a 1,3-glycol with one equivalent of acetylene in the presence of small amounts of sulfuric acid and a mercury salt as catalyst, a partition of the acetylene takes place resulting in the formation of a mixture of cyclic acetals, namely, of a 5- and a 6-membered derivative, the latter always in the larger amount.

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[3] Part VIII. THIS JOURNAL, **46**, 997 (1924).

[4] Wohl and Frank, *Ber.*, **35**, 1905 (1902).

[1] This paper is constructed from Part I of a dissertation presented by John Arrend Timm in June, 1922, to the Faculty of the Graduate School of Yale University, in candidacy for the degree of Doctor of Philosophy. The thesis contains a review of the literature on cyclic acetal formation.

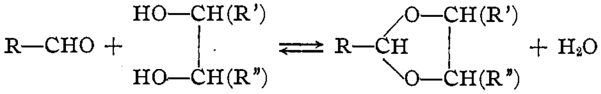
[2] Communicated to the Cellulose Section, American Chemical Society, Birmingham, Alabama, April, 1922.

[3] THIS JOURNAL, **45**, 3117 (1923).

Apart from the acetylene process for the synthesis of cyclic acetals,[4] these products are usually obtained by one of two processes: (a) heating together the polyhydroxy derivative and aldehyde in a sealed tube at an elevated temperature;[5] or, better, (b) heating together the two components under atmospheric pressure in the presence of a catalyst[6] such as sulfuric[7] or phosphoric[8] acid or with a small quantity of iodine.[9]

The fact that small quantities of acids catalyze the ring formation to a remarkable extent, together with the possibility that the cyclic acetal groupings present in the manifold products of the plant world are probably synthesized by the plant in a similar manner,[10] indicated the advisability of first applying the partition principle to an intermolecular reaction between a 1,2- and a 1,3-glycol with simple aldehydes before proceeding to investigate the more complex changes involving intramolecular reactions such as occur, for example, in the various carbohydrates and polysaccharides. With these latter derivatives very little is known as to the relative stability of the cyclic acetal rings present in their molecules.

The reaction between an aldehyde and a glycol, namely,



$$\mathrm{R{-}CHO} + \begin{array}{l}\mathrm{HO{-}CH(R')}\\ \quad\ \ |\\ \mathrm{HO{-}CH(R'')}\end{array} \rightleftharpoons \mathrm{R{-}CH}\begin{array}{l}\diagup\mathrm{O{-}CH(R')}\\ \qquad\quad |\\ \diagdown\mathrm{O{-}CH(R'')}\end{array} + \mathrm{H_2O}$$

is a reversible one, as indicated in the experimental part, so that the attempt to prepare cyclic acetals by the use of a small amount of acid as a catalyst always results in the establishment of an equilibrium between the glycol and the aldehyde on the one hand, and the cyclic acetal and water on the other. A determination of the equilibrium constant should thus provide an accurate measure of the relative ease of hydrolysis of the acetal in question. Unfortunately, the reactions between the simple glycols and

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[4] THIS JOURNAL, **45**, 3108 (1923).

[5] Lochert, *Ann., chim. phys.*, [6] 16, 26 (1889).

[6] The action of the catalyst varies in a marked manner with the nature of the two components. Thus formaldehyde (polyoxymethylene) may be readily condensed with ethylene glycol by the use of phosphoric acid as catalyst but it was not found possible to replace the latter by sulfuric acid. Chloral reacts readily with glycols but the isolation of the condensation products has not as yet been accomplished. The question of the mechanism by which the acid functions as catalyst is under investigation.

[7] Fischer and Giebe, *Ber.*, **30**, 3053 (1897).

[8] Verley, *Bull. soc. chim.*, [3] **21**, 276 (1899).

[9] Hibbert, THIS JOURNAL, **37**, 1748 (1915).

[10] Thus Bergmann and Miekeley [*Ber.*, **55**, 1391 (1922)] have shown that a concentration of 0.0005 *N* HCl is sufficient to effect acetalization in the case of δ-aceto-*n*-butyl alcohol. The recent researches of Bergmann and co-workers [*Ber.*, **54**, 440, 1564, 2150 (1921); **55**, 158, 1390 (1922)] on hydroxy ketones and related compounds, and the pioneer work of Helferich and co-workers [*Ber.*, **52**, 1123, 1800 (1919); **54**, 930, 2640 (1921); **55**, 702, 3348 (1922)] on γ- and δ-hydroxy-aldehydes, are opening up new fields in carbohydrate and polysaccharide chemistry which will doubtless necessitate a revision of a number of the commonly accepted structural theories.

the more common aldehydes give rise to heterogeneous mixtures, in which two liquid phases are present, thus rendering an exact determination of the equilibrium constants difficult of accomplishment.

Nevertheless, the fact that the properties of the acetals resulting from the condensation of simple glycols with various unsubstituted aldehydes have much in common as regards solubility relations and other properties, indicates that the partition coefficient between a mixture of a 1,2- and a 1,3-glycol and a given aldehyde should provide evidence as to the ease of formation and stability of the 5- and 6-membered rings, respectively. It is of interest that the results found actually do run parallel to those obtained on the relative ease of formation by "the acetylene partition method."[3] Thus if a mixture of one molecular equivalent each of a 1,2- and a 1,3-glycol is heated on the steam-bath with one equivalent of an aldehyde and a small amount of dil. sulfuric acid, as catalyst, and if the products are agitated vigorously *until equilibrium is established*, the reaction products invariably contain a higher percentage of the 6- than of the 5-membered cyclic acetal,[11] thus indicating the greater tendency toward formation and the smaller tendency toward hydrolysis of the former.[12] Thus a mixture of one molecular equivalent each of ethylene and trimethylene glycol with one equivalent of paracetaldehyde, *n*-butyraldehyde, *n*-heptaldehyde and benzaldehyde, respectively, gave a partition ratio of 1:1.8, 1:6.6, 1:7.3, and 1:2.1, respectively, in favor of the 6- as compared with the 5-membered acetal. (Tables I and II.) Under the experimental conditions the 6-membered acetal is evidently more stable than the 5-, the proportion of the former increasing rapidly with increase in the molecular weight of the aldehyde up to *n*-heptaldehyde. In the case of benzaldehyde there is only a slight increase.

Further "partition experiments" carried out between one molecular equivalent of ethylene glycol and a mixture of one equivalent of benzaldehyde with one of paracetaldehyde, *n*-butyraldehyde and *n*-heptaldehyde, respectively, gave ratios of 1: 3.6, 1: 1.2, and 1: 0.7 of the cyclic acetals formed from benzaldehyde and the aliphatic aldehyde, respectively (Table III).

Substituting trimethylene glycol for ethylene glycol, the corresponding ratios were found to be 1:6.2, 1:4.4 and 1:2.0, respectively (Table IV).

The proportion of cyclic acetal formed from the aliphatic aldehydes thus decreases rapidly with increase in molecular weight from acetaldehyde to heptaldehyde; in other words, the stability of the ring diminishes.

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[11] The amount of each present at equilibrium was determined by submitting the reaction-product to fractional distillation.

[12] While "tendency toward formation" doubtless runs parallel to "resistance towards hydrolysis" the former is not to be confused with "reaction-velocity."

Behavior of Cyclic Acetals towards Chemical Reagents

In agreement with the previous work of Lochert[5] it was found that the cyclic acetals obtained in the present investigation are very unstable toward dilute acids. Boiling with a considerable volume of water for several hours is sufficient to accomplish nearly complete hydrolysis in many cases.

They are much more stable toward dilute alkali and are remarkably stable in acetone solution toward boiling alkaline permanganate. This behavior is in harmony with the unexpected stability shown by diacetone glucose, fructose and mannitol toward the same reagent, as found by Karrer.[13]

Experimental Part

Preparation of the Cyclic Acetals from Ethylene Glycols and Trimethylene Glycols.—The following general procedure was found to give a satisfactory yield and product.

One-half mole of the glycol was mixed with one-half mole of the aldehyde in a flask fitted with a reflux condenser, about 0.25 g. of 40% sulfuric acid was added, and the mixture, vigorously agitated, was heated on a steam-bath at 100° for ten hours. In general, two layers formed, the upper of which contained the acetal and some unchanged

Table I

Cyclic Acetals from Ethylene and Trimethylene Glycols

				Properties
Glycol	Reagents	B. p. °C.	Yield %	Remarks
Ethylidene ethylene[14]	Ethylene glycol, paracetaldehyde	83–85	87	....
Butylidene ethylene	Ethylene glycol, *n*-butyraldehyde	132–136	50	Colorless, mobile; sl. unpleasant odor; sl. sol. in water; miscible in ether[a]
Heptylidene ethylene[5]	....	198–202	50	....
Benzylidene ethylene[15]	....	225	80–85	Colorless; pleasant arom. odor; insol. in water; readily sol. in ether[b]
Ethylidene trimethylene[5]	....	110–112	90	....
Butylidene trimethylene	....	154–157	55	Colorless; ethereal odor; insol. in water; sol. in ether[c]
Heptylidene trimethylene[5]	....	215	51	....
Benzylidene trimethylene[16]	....	252–254	75	....

[a] *Analysis.* Calc. for $C_6H_{12}O_2$: C, 62.06; H, 10.35. Found: C, 61.83, 61.87; H, 10.67, 10.71.

[b] *Analysis.* Calc. for $C_9H_{10}O_2$: C, 71.96; H, 6.67. Found: C, 71.81, 71.83; H, 6.87; 6.69.

[c] *Analysis.* Calc. for $C_7H_{14}O_2$; C, 64.61; H, 10.76. Found: C, 64.52, 64.46; H, 10.82; 10.91.

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[13] Karrer, *Helvetica Chim. Acta*, **4,** 728 (1921).

[14] Wurtz, *Compt. rend.*, **53,** 378 (1861); *Ann.*, **120,** 328 (1861).

[15] Verley, *Compt. rend.*, **128,** 317 (1899). In this paper a product boiling at 140° is described as benzylidene ethylene glycol, no analysis being given. No explanation can be offered as to the discrepancy, except the possibility that the material in question was an impure product.

[16] Fischer, *Ber.*, **27,** 1524 (1894).

aldehyde; the lower layer consisted mainly of water and unchanged glycol. Enough solid potassium carbonate was added to neutralize the acid and the acetal layer was separated. The lower layer was extracted with ether and the ether extract added to the upper layer. It was then dried over anhydrous sodium sulfate, the ether removed and the residual oil purified by fractionation through a short column filled with glass beads.

Relative Stability of Five- and Six-membered Cyclic Acetals as Shown by Partition Experiments between an Aldehyde and a Mixture of a 1, 2- with a 1, 3-Glycol

Partition of Heptaldehyde between Ethylene Glycol and Trimethylene Glycol.—Two experiments were first carried out to settle definitely whether an equilibrium is established in the reaction between heptaldehyde and glycols in the presence of dil. sulfuric acid as a catalyst.

EXPERIMENT I.—A mixture of 57 g. of heptaldehyde (0.5 mole) with 31 g. of ethylene glycol (0.5 mole) and 0.25 g. of 40% sulfuric acid was vigorously agitated and heated for ten hours at 100°. The product, which had separated into two layers, was cooled, the upper layer removed, washed with 20 cc. of 10% potassium carbonate solution to remove the acid and any unchanged glycol, dried with sodium sulfate and fractionated; yield, 46 g. or 58%; b. p., 197-202°.

EXPERIMENT II.—A mixture of 39.5 g. of heptylidene ethylene glycol (b. p., 197–202°) with 0.25 g. of 40% sulfuric acid and 4.5 g. of water was vigorously agitated and heated at 100° for ten hours; 23 g. of the acetal was isolated as indicated above; yield, 58%; b. p., 196–202°.

The existence of a definite equilibrium point is thus established.[17]

Partition of Heptaldehyde between Ethylene Glycol and Trimethylene Glycol[17]

A mixture of 26 g. of heptaldehyde (0.25 mole), 16 g. of ethylene glycol, 19 g. of trimethylene glycol (0.25 mole) and 0.12 g. of 40% sulfuric acid was stirred vigorously and heated at 100° for ten hours. The product was cooled, the lower layer extracted with ether, and the ether extract

TABLE II

Expt.		B. p. °C.	Grams obtained	Mole per cent.	Partition ratio
I	Heptylidene ethylene glycol	199–203	2.5	6.4	1
	Heptylidene trimethylene glycol	215–218	20	46	7.2
II	Heptylidene ethylene glycol	198–203	2	5.1	1
	Heptylidene trimethylene glycol	215–219	16.5	38	7.5

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[17] Before proceeding with the partition experiments described above, a special series of experiments was carried out with mixtures of the related 5- and 6-membered cyclic acetals in which it was shown that these could be separated by fractional distillation with an accuracy of 2–5%. Further work is being planned to permit much more accurate determinations of the equilibrium point. A study of the behavior of cyclic acetals from "hydroxy acids" is in progress. In connection with earlier work (Ref. 4) dealing with the "acetylene method" for the preparation of cyclic acetals it was overlooked that a similar process is disclosed in U. S. pat. 1,084,581 granted to Chemische Fabrik Griesheim Elektron, Germany.

added to the upper layer. The combined solution was washed with a small amount of concd. potassium carbonate solution, then with water, dried with sodium sulfate, the ether removed and the residual oil distilled. The fraction boiling between 190° and 230° was carefully redistilled through a fractionating column filled with glass beads.

Similar partition experiments were carried out with paracetaldehyde, *n*-butyraldehyde and benzaldehyde, the results obtained being shown in Table III.

TABLE III

Expt.	Aldehyde	Wt. taken G.	Wt. 5-membered acetal	B. p. °C.	Wt. 6-membered acetal	B. p. °C.	Mole per cent. 5^a	Mole per cent. 6^a	Partition ratio 5	Partition ratio 6
3a	$(CH_3CHO)_3$	22 (0.5 mole)	12	83–86	28	108–110	28	47	1	1.7
3b		22	14	83–86	31	107–110	32	63	1	1.9
4a	$C_3H_7CHO(n)$	36 (0.5 mole)	6	132–137	48	154–157	11	75	1	6.8
4b		36	4.5	133–135	33	154–157	8	51	1	6.4
5a	C_6H_5CHO	53 (0.5 mole)	10	224–228	25	249–251	13	31	1	2.3
5b		53	11	224–228	23	249–251	15	28	1	1.9
5c		53	15.5	224–228	36	249–251	21	44	1	2.1

[a] The numbers 5 and 6 refer to 5- and 6-membered rings, respectively.

Partition of a Glycol between Two Aldehydes

The mixture of two aldehydes and a glycol in equimolecular proportions was agitated and heated with 0.25 g. of sulfuric acid at 100° for ten

TABLE IV

EXPERIMENTS WITH ETHYLENE GLYCOL AND A MIXTURE OF BENZALDEHYDE AND AN ALIPHATIC ALDEHYDE

Expt.	Glycol moles	Ethylene glycol formed	B. p. °C.	Wt. acetal G.	Mole per cent.	Partition ratio
6a	0.5	Ethylidene	82–87	27	61.4	3.5
		Benzylidene	220–225	13	17.3	1
6b	.5	Ethylidene	82–87	22	50	3.8
		Benzylidene	220–225	10	13	1
7a	.25	Butylidene	132–136	10	34.5	1.1
		Benzylidene	222–225	12	32	1
7b	.25	Butylidene	132–136	13	45	1.3
		Benzylidene	222–225	12.5	33	1
8	.25	Heptylidene	199–202	10.5	26.6	0.7
		Benzylidene	225–227	14	38	1

TABLE V

EXPERIMENTS WITH TRIMETHYLENE GLYCOL AND A MIXTURE OF BENZALDEHYDE AND AN ALIPHATIC ALDEHYDE

Expt.	Glycol moles	Trimethylene glycol formed	B. p. °C.	Wt. acetal G.	Mole per cent.	Partition ratio
9a	0.5	Ethylidene	108–110	25	49	6.1
		Benzylidene	249–251	6.5	8	1
9b	.5	Ethylidene	108–111	30.5	60	6.3
		Benzylidene	248–251	8	9.5	1

Table V (*Continued*)

Expt.	Glycol moles	Trimethylene glycol formed	B. p. °C.	Wt. acetal G.	Mole per cent.	Partition ratio
10a	.25	Butylidene	150–155	14	42	4.3
		Benzylidene	248–252	4	9.8	1
10b	.25	Butylidene	150–155	15.5	47.5	4.5
		Benzylidene	248–252	4.5	10.5	1
11	.25	Heptylidene	215–218	15	35	2
		Benzylidene	251–253	7.5	18	1

In experiments 6a, 6b, 9a and 9b, 0.5 mole of ethylene glycol was employed with 0.5 mole of benzaldehyde and paracetaldehyde. In 7a, 7b, 10a, 10b, the latter was replaced by *n*-butyraldehyde and in 8 and 11 by *n*-heptaldehyde, 0.25 molar quantity being used.

hours and the reaction product then treated as above, the acetals being finally separated by careful fractionation.

Action of Water, Acids and Alkalies

Lochert[5] showed that many of the acetals from aldehydes and the simple glycols are readily hydrolyzed when they are heated with water at 100° and still more readily in the presence of dilute acids. He found, however, that they are remarkably stable towards anhydrous alkalies. In agreement with this it was found that when ethylidene and benzylidene trimethylene glycols were heated with 5 volumes of water at 100° for one hour, 70% of the former was hydrolyzed while with the latter the hydrolysis was complete. Agitation with dil. acid (5 volumes of 2% sulfuric acid) for one hour at room temperature brings about complete hydrolysis in the case of methylene- and benzylidene ethylene glycols and ethylidene- and benzylidene trimethylene glycols.

The acetals are much more stable towards aqueous alkalies. Ten g. of methylene- and benzylidene ethylene glycols and of ethylidene- and benzylidene trimethylene glycols heated for one hour at 100° with 10 cc. of 5% sodium hydroxide hydrolyzed to the extent of 60%, 85%, 75% and 60%, respectively.

Karrer and Hurwitz[13] have shown that acetone sugars which do not contain free primary alcohol groupings in their molecules are stable in acetone solution towards potassium permanganate, even at the boiling point of the solvent. The presence of the acetal ring seems to exert a protective action in preventing the oxidation of the hydroxyl groups attached to the ring carbon atoms.

It is of interest that the cyclic acetals obtained in the present investigation are likewise remarkably stable towards this reagent, in acetone solution, even when heated for several hours at the boiling point of the solvent.

Five g. of methylene ethylene glycol was boiled for two hours with a solution of 7.26 g. of potassium permanganate in 50 cc. of acetone to which a drop of 10% sodium hydroxide solution had been added. From the solution, filtered and freed from acetone, 84% of the acetal was recovered.

Benzylidene- and ethylidene trimethylene glycols showed a similar behavior.

The authors desire to express their thanks to the Committee of the Warren Fund, National Academy of Sciences, for the grant made to them for the purchase of chemicals used in this investigation.

Summary

1. Partition experiments between an aldehyde and a mixture of a 1,2- and a 1,3-glycol, in which a small amount of dil. sulfuric acid is used as a catalyst, indicate that at the equilibrium point there is present a larger proportion of the 6- than of the 5-membered cyclic acetal.

2. It would thus appear that in the cases investigated the 6-membered cyclic acetal rings are more stable towards hydrolysis than the 5- and are also the more easily formed. The results found thus run parallel to those obtained by the acetylene-partition method.[3]

3. With an increase in molecular weight of the aldehyde the amount of 6-membered ring formed increases rapidly over that of the 5-membered ring.

4. Partition experiments between a 1,2- or a 1,3-glycol and a mixture of benzaldehyde and a second aldehyde show that the stability of the cyclic acetal from the latter decreases as the molecular weight of the aldehyde increases.

5. The use of dil. sulfuric acid as a catalyst for the synthesis of cyclic acetals has been shown to be capable of wide application.

6. The following new acetals have been synthesized: butylidene ethylene glycol, butylidene trimethylene glycol and benzylidene ethylene glycol.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF WASHINGTON]

SODIUM HYDROXYLAMINE SULFONATE AS A REAGENT FOR THE PREPARATION OF OXIMES

BY WALDO L. SEMON AND V. RICHARD DAMERELL

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Hydroxylamine, the commonly used reagent for the formation of oximes, is usually prepared from sodium hydroxylamine sulfonate. This latter substance can easily be made by the reduction of sodium nitrite with sodium bisulfite and can be used directly for the preparation of oximes. This not only simplifies the process but is of considerable theoretical and practical importance.

Raschig[1] mentioned that salts of hydroxylamine monosulfonate in

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[1] Raschig, *Ann.*, **241**, 187 (1887).