TABLE II

SULFIDES

Compound	M. p., °C.	B. p., °C.	% S Calcd.	% S Found
Ethyl cetyl sulfide	19	201–205 (12 mm.)	11.19	11.34
Ethyl lauryl sulfide	−6 to −5	167–171 (18 mm.)	13.91	14.14
Mercuric Halide Addition Compounds				
Ethyl cetyl sulfide mercuric chloride	75.5		5.75	5.17
Ethyl cetyl sulfide mercuric bromide	58		4.95	5.21
Sulfones				
Ethyl cetyl	88		10.06	10.18
Ethyl lauryl	78.5		12.22	12.24
Sulfonium Nitrate				
Methyl ethyl cetyl	61		8.82	8.75
Sulfonium Halides			% Halogens	
Methyl ethyl cetyl sulfonium iodide	73		29.62	29.61
Methyl ethyl cetyl sulfonium bromide	77		20.95	20.68
Methyl ethyl lauryl sulfonium iodide	65		34.08	33.92

Summary

1. Two new unsymmetrical dialkyl sulfides have been prepared and characterized by their sulfones and mercuric halide addition products.

2. These sulfides readily form sulfonium salts under suitable conditions.

3. Methanol was found to be the best solvent for sulfonium halide formation.

4. In general, with the exception of nitrobenzene, solvents possessing a high dielectric constant favor the reaction for sulfonium halide formation, from the standpoint of yield, purity of product and ease of isolation. The paradoxical behavior of acetic acid in this connection is also noted.

CHAPEL HILL, NORTH CAROLINA

RECEIVED MARCH 4, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

The Synthesis of Certain Trisaccharides and a Study of their Behavior in Alkaline Solution[1,2]

BY SAMUEL H. NICHOLS, JR.,[3a] WM. LLOYD EVANS AND HAROLD D. McDOWELL[3b]

In an aqueous solution of potassium hydroxide maltose is converted into approximately one-half as much lactic acid as an equivalent solution of *d*-glucose under the same experimental conditions.[4]

To explain this difference in yields, Evans and Benoy advanced the following suggestions. (a) The reducing section of the maltose molecule is degraded with the formation of either formaldehyde or glycol aldehyde, and either 3-glucosido-arabinose or 2-glucosido-erythrose, respectively. (b) The 3-glucosido-arabinose may also undergo fragmentation to formaldehyde and 2-glucosido-erythrose. (c) The final 2-glucosido-erythrose was then believed to undergo alkaline hydrolysis to erythrose and glucose. (d) Since formaldehyde, glycol aldehyde and erythrose produce no lactic acid under our experimental conditions and, on the other hand, glucose does, it is evident that only one-half of the maltose molecule is yielding lactic acid, and that that half is the glucosido section, that is, the non-reducing section of the molecule. The investigations of Evans and co-workers[5] were extended to other disaccharides and to oligosaccharides in the dihydroxyacetone series in order to find further evidence for the above suggested mechanism.

(1) The material of this paper has been abstracted from a thesis submitted by Samuel Harding Nichols, Jr., to the Graduate School of The Ohio State University in partial fulfillment of the requirements for the degree of Doctor of Philosophy, 1939.

(2) An abstract of this paper was presented at the Baltimore meeting of the American Chemical Society in 1939.

(3) (a) Present address: Department of Chemistry, University of Vermont, Burlington, Vermont. (b) The Ohio State University W. P. A. Project 18062.

(4) W. L. Evans and M. P. Benoy, THIS JOURNAL, **52**, 294 (1930).

(5) H. Gehman, L. C. Kreider and W. L. Evans, *ibid.*, **58**, 2388 (1936).

The trisaccharides used in these studies were the hendekaacetates of 6-cellobiosido-glucose, 6-maltosido-glucose, 6-cellobiosido-mannose and 6-maltosido-mannose. Since only the first of these four compounds had been prepared previously as a crystalline material,[6] it was found necessary to synthesize the other three hendekaacetates. It is obvious that potassium hydroxide solutions would deacetylate these trisaccharide derivatives with the accompanying formation of potassium acetate. The free carbohydrates thus formed would then undergo degradation into fragments containing a smaller number of carbon atoms as indicated above. To ascertain whether these trisaccharides would behave in accordance with the above postulates was the principal objective of this work.

Experimental Part

Part A. Preparation of Trisaccharides

1. 6-β-Cellobioside-β-d-glucose Hendecaacetate.—This compound was prepared by the Königs and Knorr condensation of acetobromocellobiose and β-d-glucose-1,2,3,4-tetraacetate in a manner similar to the procedure used by Helferich and Schäfer,[6] except that certain improvements were made by employing Drierite as an internal desiccant, a technique introduced by Kreider and Evans.[7]

In a typical experiment, 20 g. of β-d-glucose-1,2,3,4-tetraacetate, prepared according to the method of Helferich and Klein[8] with the modifications of Reynolds and Evans,[9] was mixed with 15 g. of silver oxide[8] and 50 g. of "Drierite" which had been previously heated for several hours at 225°. This mixture was suspended in 150 ml. of alcohol-free anhydrous chloroform contained in a three-necked flask (500 ml.) equipped with a drying tube, a dropping funnel and a mechanical stirrer connected through a mercury seal. After the mixture was stirred one hour in order to assure complete removal of moisture, 3 g. of iodine was added as a catalyst. Then 40 g. of acetobromocellobiose, prepared by the method of Zemplén,[10] except that the acetic acid solution of cellobiose octaacetate and hydrogen bromide was allowed to stand in the icebox during the reaction,[11] was dissolved in 100 ml. of absolute alcohol-free chloroform, and this solution was added dropwise over the period of one hour, after which stirring was continued for twenty-four hours.

At the end of this time, the mixture was filtered once, treated with carboraffin, and filtered twice more. The solution was then concentrated by evaporation at reduced pressure. The resulting thick sirup was crystallized on stirring with absolute ethanol. It was heated with 350 ml. of 95% ethanol, cooled and filtered. The product was dried for eight hours in a vacuum oven at 40°, after which it weighed 25.2 g. (45.4%). After recrystallization from alcohol, its melting point was 246.5° (cor.). Its rotation was observed to be $[\alpha]^{24}D$ −10.9°, ($CHCl_3$), l = 2 dm., obsd. −0.74°, concn. 0.03372 g. per ml. Helferich and Schäfer[6] had reported −10.3° for this compound. It should be noted that the expedient of using an internal desiccant nearly doubled the reported yield of Helferich and Schäfer (24.8%).

2. 6-Maltosido-β-d-glucose Hendecaacetate.—This compound was prepared in a manner similar to the foregoing, using 10 g. of β-d-glucose-1,2,3,4-tetraacetate, 15 g. of silver oxide and 50 g. of "Drierite," except that the acetobromomaltose[12] prepared from 10 g. of maltose octaacetate[13] was not isolated, but the sirup was added dropwise in the dry chloroform solution in which it was prepared, but which for convenience was concentrated to a volume of 100 ml. Three grams of iodine was added as before.

After twenty-four hours, the 6-maltosido glucose hendecaacetate solution was filtered, treated with carboraffin, filtered twice more and concentrated to a thick sirup. It crystallized on the addition of alcohol. The yield of product, dried for several hours in the vacuum oven at 50°, was 17.06 g., or 59.9%. The product was recrystallized three times from 1500-ml. portions of 95% ethanol, after which it had a constant melting point of 235.5–236° (uncor.), or 242.2–242.7° (cor.); $[\alpha]^{24}D$ +42.5°; ($CHCl_3$), concn. 0.0192 g. per ml., l = 2 dm. The rotation of this compound calculated on the basis of the molecular rotation of 6-cellobiosido glucose hendecaacetate and Hudson's[14] "B" value for cellobiose octaacetate and maltose octaacetate is +43.3°.

Anal. Calcd. for $C_{18}H_{21}O_5(OAc)_{16}$: acetyl,[15] 11.387 cc. of 0.1 *N* sodium hydroxide for 100 mg.; C, 49.67; H, 5.63; mol. wt., 966. Found: 11.38 and 11.33 cc. of base; C (micro), 49.15 and 48.88; H (micro), 5.62 and 5.57; mol. wt. (Rast),[16] 994 and 1076.

The compound was prepared as a white solid, crystallizing in very fine needles. It is insoluble in water and petroleum ether, rather difficultly soluble in ether and cold alcohol and very soluble in chloroform and acetone.

3. 6-Cellobiosido-β-d-mannose Hendecaacetate.—This compound was prepared in a manner similar to the foregoing by using 21 g. (slight excess) of β-d-mannose-1,2,3,4-tetraacetate,[17] 15 g. of silver oxide and 50 g. of "Drierite" and 2 g. of iodine suspended in 150 ml. of absolute chloroform. A solution of 40 g. of acetobromocellobiose in 150 ml. of chloroform was added dropwise for one hour. The stirring was continued for twenty-four hours, after which the solution was clarified and filtered, and then concentrated to a thick sirup. It could not be crystallized on the addition of alcohol. It was dissolved in 75 ml. of absolute ethanol and water was added dropwise to incipient turbidity. Then the solution was added dropwise to one liter of distilled water externally cooled by an

(6) B. Helferich and W. Schäfer, *Ann.*, **450**, 229 (1926).
(7) L. C. Kreider and W. L. Evans, THIS JOURNAL, **58**, 797 (1936).
(8) B. Helferich and W. Klein, *Ann.*, **450**, 219 (1926).
(9) D. D. Reynolds and W. L. Evans, THIS JOURNAL, **60**, 2559 (1938).
(10) G. Zemplén, *Ber.*, **61**, 930 (1928).
(11) V. A. Miller, Ph.D. Dissertation, Ohio State University, 1938.
(12) D. H. Brauns, THIS JOURNAL, **51**, 1820 (1929).
(13) K. Freudenberg, H. V. Hochstetter and H. Engels, *Ber.*, **58**, 666 (1925).
(14) C. S. Hudson, "Bureau of Standards Scientific Paper No. 533," Washington, D. C., 1926.
(15) A. Kunz and C. S. Hudson, THIS JOURNAL, **48**, 1978 (1926).
(16) K. Rast, *Ber.*, **55**, 1051 and 3727 (1922).
(17) B. Helferich and J. F. Leete, *ibid.*, **62**, 1549 (1929).

ice-bath and mechanically stirred. The precipitate was filtered and dried in the vacuum oven at 40° for eight hours. The yield was 42 g. (76%).

Since the substance could not be crystallized or purified owing to the presence of an impurity which was identified as cellobiose heptaacetate, the mixture was acetylated with acetic anhydride in pyridine solution, thus converting the cellobiose heptaacetate to the less soluble octaacetate. The acetylated mixture was precipitated in water, filtered and dried. It was dissolved in sufficient hot 95% ethanol from which 8 g. of cellobiose octaacetate was separated out of 38.1 g. of the original dry mixture. The remaining 6-cellobiosido mannose hendecaacetate was further purified by pouring its alcoholic solution dropwise into distilled water. This process was repeated twice, after which the dry weight of product was 21.8 g. The softening point of the amorphous compound is 120–126° (cor.); $[\alpha]^{23}D$ −18.4° ($CHCl_3$); obsd. −0.87°; concn. 0.0118 g. per ml., l = 4 dm. The specific rotation as calculated by the method of molecular epimeric difference of the rotation values for 6-cellobiosido glucose hendecaacetate, β-glucose-1,2,3,4-tetraacetate and β-mannose-1,2,3,4-tetraacetate is −22.7°. The discrepancy between the calculated and observed specific rotations may be attributed to the fact that the compound is amorphous. Moreover, mannose compounds sometimes show a deviation from the values calculated by Hudson's rules of iso-rotation.

Anal. Calcd.: acetyl,[15] 11.387 cc.; C, 49.67; H, 5.63; mol. wt., 966. Found: acetyl,[15] 11.37 and 11.37 cc.; C (micro), 48.97 and 48.73; H (micro), 5.67 and 5.65; mol. wt. (Rast),[16] 888 and 924.

4. 6-Maltosido-β-*d*-mannose Hendecaacetate.—This compound was prepared by the condensation of 10 g. of β-*d*-mannose-1,2,3,4-tetraacetate and the acetobromomaltose prepared from 20 g. of maltose octaacetate. This reaction was carried out in 200 ml. of absolute chloroform in the presence of 15 g. of silver oxide, 50 g. of "drierite," and 2 g. of iodine. Twenty-four hours were allowed for the completion of the reaction, after which the solution was filtered, clarified and concentrated as before. The resulting sirup was stirred with alcohol, but it could not be crystallized. It was taken up in 75 ml. of absolute ethanol and evaporated to dryness at reduced pressure in order to remove the last traces of chloroform. Then it was redissolved in alcohol, and water was added dropwise until the solution just became turbid. Then the whole solution was added dropwise to one liter of distilled water, mechanically stirred and cooled by a surrounding ice-bath. The precipitate, after filtration and drying in the vacuum oven for eight hours at 40°, weighed 21.7 g. (76%).

The crude 6-maltosido mannose hendecaacetate resisted all attempts to crystallize it, but when it was dissolved in ether and the solution allowed to evaporate slowly, a certain amount of crystalline maltose heptaacetate was separated. After as much of this substance as possible had been removed, it was decided to acetylate the mixture. Accordingly, 49 g. of the crude, oven-dried substance was dissolved in pyridine and treated with acetic anhydride. After twelve hours the solution was added dropwise to water. The product was filtered and dissolved in 200 ml. of hot 95% ethanol. This solution was seeded with crystals of maltose octaacetate and placed in the ice box, but only a little of this substance crystallized out. After filtration, the solution was added dropwise to cold water, stirred for several hours and again filtered. This process was repeated twice. After this fractional precipitation, the 6-maltosido mannose hendecaacetate weighed, oven-dried, 28.3 g. It has a softening point of 110–115° (uncor.); $[\alpha]^{25}D$ +58.6° ($CHCl_3$); obsd. +4.59°; concn. 0.0196 g. per ml.; l = 4 dm. The rotation calculated by epimeric difference is +30.8°. Again, this discrepancy may be attributed to the fact that the substance is amorphous, or to the fact that mannose compounds often show anomalous rotations. *Anal.* Calcd. for $C_{18}H_{21}O_5(OAc)_{11}$: acetyl,[15] 11.387 cc. of 0.1 *N* alkali; C, 49.67; H, 5.63; mol. wt., 966. Found: acetyl,[15] 11.38 and 11.44 cc.; C (micro), 49.19 and 49.19; H, 5.70 and 5.71; mol. wt. (Rast),[16] 894 and 910. The product is a white amorphous solid. It is very soluble in chloroform, acetone and alcohol. It is moderately soluble in ether, but sparingly soluble in water and petroleum ether.

Part B. Alkaline Degradation of Compounds.—The experimental methods employed in this work were the same as those used by Nadeau, Newlin and Evans.[18] As the materials to be used in this work were somewhat difficult to obtain in large amounts, it was decided to employ 25 ml. of potassium hydroxide solution and a sufficient weight of the trisaccharide hendecaacetate to give a 0.125 molar solution (3.02 g.). The alkali used was approximately from 3 to 8 normal. The use of acetylated sugars necessitated a normality correction owing to the reduction of alkaline strength due to deacetylation. A correction also was made for volume expansion.

Since it was postulated that only the two terminal hexose sections in the trisaccharides would lead to the formation of lactic acid, it was desired to establish a reference curve using 25 ml. solutions of 0.25 *M* glucose for comparison with 0.125 *M* 6-cellobiosido glucose hendecaacetate and 6-maltosido glucose hendecaacetate, and 0.125 *M* glucose plus 0.125 *M* mannose for comparison with 0.125 *M* 6-cellobiosido mannose hendecaacetate and 6-maltosido mannose hendecaacetate. Since potassium acetate is produced on the deacetylation of the trisaccharide hendecaacetates with potassium hydroxide, the presence of this material with the free sugars might conceivably affect the amount of lactic acid produced. Therefore to attain a condition as nearly like those prevailing in the trisaccharide solutions, a weight of potassium acetate equal to that obtained on the deacetylation of 0.125 *M* trisaccharide hendecaacetate (3.3724 g.) was added to each of the control solutions of the simple hexoses. For the hexose controls, the potassium hydroxide was of such a strength as to approximate that effective upon the trisaccharides after deacetylation. Portions of 25 ml. of the alkali were used and corrections were made in the normalities for expansion in volume of the solution.

Identical techniques were employed for manipulation of the sample, filling the flasks with nitrogen, shaking at 50° for forty-eight hours, determination of density, neutralization with phosphoric acid, concentration, extraction, separation of zinc lactate and ignition to zinc oxide, the substance which is weighed.

(18) G. F. Nadeau, M. R. Newlin and W. L. Evans, THIS JOURNAL, **55**, 4957 (1933).

The experimental data of Tables I and II are typical of the results obtained in these experiments.

TABLE I

LACTIC ACID FROM 0.25 *M* GLUCOSE PLUS (0.125 × 11) MOLE EQUIVALENT OF POTASSIUM ACETATE AT 50° FOR 48 HOURS

Glucose 1.1256 g.; potassium acetate, 3.3724 g.

Corrected *N* KOH	ZnO, g.	Lactic acid, g.	Moles lactic acid per moles sugar
1.7815	0.1256	0.2780	0.2469
2.6970	.1973	.4366	.3879
3.5492	.2344	.5187	.4608
4.4338	.2433	.5384	.4783
5.3062	.2421	.5358	.4760
6.1883	.2443	.5405	.4802

TABLE II

LACTIC ACID FROM 0.125 *M* 6-CELLOBIOSIDO GLUCOSE HENDECAACETATE AT 50° FOR 48 HOURS

Sample, 3.0200 g.; volume alkali, 25 ml.

Corrected *N* KOH	ZnO, g.	Lactic acid, g.	Moles lactic acid per moles sugar producing lactic acid
1.5675	0.0722	0.1598	0.1420
2.3592	.1512	.3346	.2973
3.2592	.2042	.4519	.4015
4.1614	.2097	.4642	.4123
5.9354	.2171	.4804	.4268

The complete data obtained in the study of the behavior of the four saccharides prepared for these experiments are shown in Figs. 1, 2, 3 and 4.

Discussion and Summary

(a) From the graphical data it will be seen that the amount of lactic acid obtained by the action of potassium hydroxide upon 0.125 molar 6-cellobiosido-glucose hendecaacetate Fig. 1 and

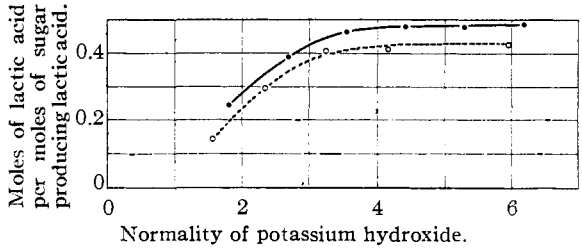


Fig. 1.—Lactic acid from 0.250 *M* glucose + (11 × 0.125) mole equivalents of $KC_2H_3O_2$ ●——● and from 0.125 *M* 6-cellobiosido-glucose hendecaacetate ○- - - -○, at 50° for forty-eight hours.

upon 6-maltosido-glucose hendecaacetate Fig. 2 tends to approach the limiting value of the amount of lactic acid produced from 0.25 molar glucose plus (0.125 × 11) mole of potassium acetate.

(b) Similarly, the amount of lactic acid produced from 0.125 molar 6-cellobiosido mannose

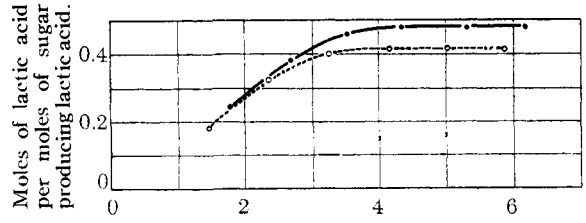


Fig. 2.—Lactic acid from 0.250 *M* glucose + (11 × 0.125) mole equivalents of $KC_2H_3O_2$ ●——● and from 0.125 *M* 6-maltosido-glucose hendecaacetate ○- - - -○, at 50° for forty-eight hours.

hendecaacetate Fig. 3 and 6-maltosido mannose hendecaacetate Fig. 4 tends to approach the amount of lactic acid produced from 0.125 molar glucose plus 0.125 molar mannose plus (0.125 × 11) moles of potassium acetate.

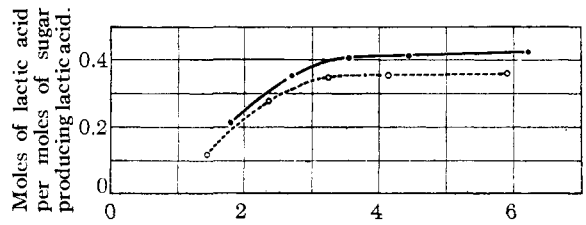
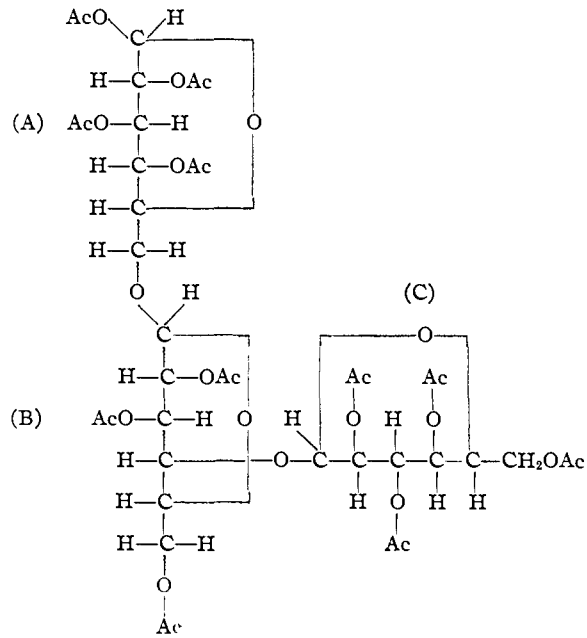


Fig. 3.—Lactic acid from 0.125 *M* glucose + 0.125 *M* mannose + (11 × 0.125) mole equivalents of $KC_2H_3O_2$ ●——● and from 0.125 *M* 6-cellobiosido-mannose hendecaacetate ○- - - -○, at 50° for forty-eight hours.

(c) These observations bear out the postulates of Evans and Benoy as outlined in the introduction



to the effect that only the first and third hexose sections of these trisaccharides will be degraded by the alkali so that lactic acid is a product. The yields of lactic acid are indicative of the general course of these alkaline degradation reactions. As an example, 6-cellobiosidoglucose hendecaacetate is shown in the formula. Sections indicated as (A) and (C) should be sources of lactic acid, while section (B) would be degraded to products other than lactic acid. A similar parallel exists in the case of the other three trisaccharides, all of which produce nearly equal amounts of lactic acid.

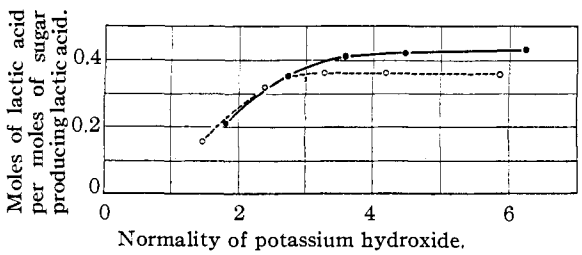


Fig. 4.—Lactic acid from 0.125 *M* glucose + 0.125 *M* mannose + (11 × 0.125) mole equivalents of $KC_2H_3O_2$ ●——● and from 0.125 *M* 6-maltosido-mannose hendecaacetate ○- - - -○, at 50° for forty-eight hours.

COLUMBUS, OHIO RECEIVED APRIL 20, 1940

[CONTRIBUTION NO. 188 FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, THE UNIVERSITY OF TEXAS]

Synthesis of 5,5-Disubstituted Hydantoins from *sym*-Dialkoxypropanones and Related Compounds

BY BURL G. ROGERS AND HENRY R. HENZE

Certain hydantoins of the monoalkoxymethyl type[1] prepared in this Laboratory have been demonstrated to possess definite hypnotic activity; however, of the derivatives tested thus far few are likely to find clinical use. In an effort to obtain a satisfactory soporific of this type, a study has now been made of the synthesis of 5,5-dialkoxymethylhydantoins and related types. The ketones used for conversion into hydantoins are of the symmetrical type, $ROCH_2COCH_2OR'$, where R and R′ represent the same alkyl grouping, or allyl, and include four compounds which have not been described previously.

Since unsymmetrical dialkoxyacetones, in which the two alkyls are not the same, might be expected to yield hydantoins having greater potentiality of soporific value, attention also has been directed to the preparation of these ketones. The method employed for the attempted syntheses was essentially that previously described by us[2]; however, the products obtained were mixtures of ketones that could not be separated by fractional distillation.

Experimental

Preparation of *sym*-Dialkoxypropanols.—These compounds, of type $ROCH_2CHOHCH_2OR$, were prepared by modification of a method described by Fairbourne and collaborators.[3] Data concerning selected physical properties and analytical results are listed in Table I.

Preparation of *sym*-Dialkoxypropanones.—These ketones, of type $ROCH_2COCH_2OR$, were prepared by the oxidation of the corresponding *sym*-dialkoxypropanols; those not reported previously are listed, together with certain data for characteristic physical properties and analyses, in Table II.

Oxidation of the *sym*-diallyloxypropanol, however, gave a mixture of compounds from which the pure *sym*-diallyloxypropanone could not be separated by repeated distillation. Treatment of a fraction, which on the basis of its molecular refraction appeared to be pure, with 2,4-dinitrophenylhydrazine gave a very impure derivative, which after repeated recrystallizations gave a product that analyzed correctly for the 2,4-dinitrophenylhydrazone of *sym*-diallyloxyacetone and melted at 45–46° (cor.).

Anal. Calcd. for $C_{15}H_{18}N_4O_6$: N, 15.99. Found: N, 15.77.

Although some ketone was obtained, as evidenced by the formation of this derivative, it could not be purified by fractional distillation.

Preparation of *unsym*-Dialkoxypropanols.—These compounds of type $ROCH_2CHOHCH_2OR'$, were synthesized from α-chloro-γ-alkoxypropanols according to a procedure described by Fairbourne, *et al.*[4] Two new examples of this type, namely, the methyl ethyl and the methyl *n*-propyl members, were synthesized and their physical and analytical data are included in Table I.

Attempted Preparation of *unsym*-Dialkoxypropanones.—The procedure employed for the synthesis of these ketones, having the formula $ROCH_2COCH_2OR'$, already has been described for the preparation of the *sym*-dialkoxypropanones. In every case the oxidation of the *unsym*-propanols produced mixtures of ketones from which were obtained mixtures of 2,4-dinitrophenylhydrazones that could not be separated by repeated recrystallizations. Analyses of

(1) Rigler with Henze, THIS JOURNAL, **58**, 474 (1936).
(2) Henze and Rogers, *ibid.*, **61**, 433 (1939).
(3) Fairbourne, Gibson and Stephens, *J. Chem. Soc.*, 445 (1931).
(4) *Ibid.*, 1865 (1932).