X
R₁
HOCH₂

$$R_2$$

HOCH₂
 R_2
 CH_2OH
I
I.a. R₁ = R₂ = CH₂OH; X = OH
b. R₁ = CH₂OH; R₂ = CH₃; X = OH
c. R₁ = R₂ = CH₄; X = OH
d. R₁ = R₂ = CH₂OH; X = H

It has now been found that a similar reaction takes place in a 1,3-bis(methylene) system activated by terminal aldehyde groups rather than by a central ketone function. The exhaustive hydroxymethylation of glutaraldehyde gives the previously unreported tetrahydro-3,3,5,5-tetrakis(hydroxymethyl)-pyran (Id). A general reaction mechanism would seem to apply to all of the above cases. The following scheme is proposed for the glutaraldehyde-formaldehyde reaction and is analogous to that suggested for the formation of dipentaerythritol in the preparation of pentaerythritol from acetaldehyde and formaldehyde.³



The tetraacetate, dibenzylidene acetal, and diisopropylidene ketal derivatives of Id were prepared.

EXPERIMENTAL⁴

Tetrahydro-3,3,5,5-tetrakis(hydroxymethyl)pyran (Id). To 236 g. (3.30 moles) of 42% aqueous formaldehyde solution adjusted to pH 11.0 by addition of 50% sodium hydroxide solution was added 200 g. (0.50 mole) of 25% aqueous glutaraldehyde (Union Carbide Chemicals Co.) at 40-45° over a 1-hr. period. Thereafter, the temperature of the mixture was held at 50, 60, and 70° for 4, 3, and 2 hr., respectively. pH 11.0 was maintained throughout by intermittent addition of base. Theoretical base consumption was observed following the complete heating period. Deionization of the total crude reaction solution by passage through columns of Dowex 50 and Dowex 1 exchange resin, in that order, gave 60.6 g. of crystalline to semicrystalline product in the initial portions of effluent. Further rinsing gave an additional 10.3 g. of oily by-product considered to represent lower condensation products. The major portion of the latter material was absorbed by the exchange resin and not recovered. The main product contained 55.5% Id (32.6% yield) as determined by quantitative isolation of its dibenzylidene derivative. Preparation of an analytical sample of Id by water recrystallization gave a white crystalline solid; m.p. 176.5°.

(3) S. Wawzonek and D. A. Rees, J. Am. Chem. Soc., 70, 2433 (1948).

(4) All melting points are uncorrected.

NOTES

Anal. Calcd. for $C_9H_{18}O_6$: C, 52.41; H, 8.80; OH, 32.99; mol. wt., 206.23. Found: C, 52.64, 52.51; H, 8.80, 8.96; OH (acetylation), 32.3, 31.9; mol. wt. (cryoscopic in ethanol), 206, 206.

Derivatives of tetrahydro-3,5,5,5-tetrakis(hydroxymethyl)pyran (Id). (1) Tetraacetate. A mixture of 10 g. (0.049 mole) of Id, 40 g. (0.39 mole) of acetic anhydride, and 4 ml. of glacial acetic acid was heated under reflux for 1 hr., allowed to stand overnight, and then poured into 100 ml. of water. The crystalline white solid which separated amounted to 7.8 g. (43% yield), m.p. 91-95°, recrystallized from *n*-hexane, 94°.

Anal. Calcd. for $C_{17}H_{26}O_9$: C, 54.54; H, 7.00; mol. wt., 374.38; Sapon. No., 599.48. Found: C, 54.81, 55.00; H, 7.09, 7.17; mol. wt. (Rast), 386, 381; Sapon. No., 604.

(2) Dibenzylidene acetal. A mixture of 5.0 g. (0.024 mole) of impure Id, 25 ml. of water, 25 ml. of methanol, and 5 ml. of concd. hydrochloric acid was reacted with 10 ml. of benzaldehyde for 45 min. at steam bath temperature. There was obtained 8.14 g. (89% yield) of crude white solids which upon recrystallization from butyl acetate melted at 232-234°.

Anal. Calcd. for $C_{23}H_{26}O_5$: C, 72.22; H, 6.85; mol. wt., 382.43. Found: C, 72.37, 72.47; H, 7.01, 7.02; mol. wt. (Rast), 388, 403.

Tests with pure Id showed the dibenzylidene reaction to be quantitative and applicable to the determination of Id in mixtures, or compounds hydrolyzed under the reaction conditions.

(3) Diisopropylidene ketal. A mixture of 10 g. (0.048 mole) of Id, 150 ml. of acetone, 5 drops of concd. sulfuric acid, and 15 g. of 2,2-dimethoxypropane (Dow Chemical Co.) was heated under reflux overnight. Concentration of the reaction mixture gave 11.6 g. (91.4% yield) of white crystals. Recrystallization from acetone gave a melting point of 201-205°.

Anal. Calcd. for $C_{15}H_{26}O_5$: C, 62.91; H, 9.15. Found: C, 63.27, 63.25; H, 9.39, 9.29.

The Id content of the recrystallized product was determined by conversion to its dibenzylidene derivative: Calcd., 72.02; found, 71.2. Various samples of Id diisopropylidene ketal melted over a range of 153-206°, suggesting the presence of allotropic crystalline forms.

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Synthesis of Deuterated Biphenyls. II¹

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The synthesis of four deuterated isomers of biphenyl has been reported previously.² To complete the series studied by irradiation³ and mass spectrometry⁴ two new deuterium-substituted bi-

(1) This work was performed under AEC Contract AT(11-1)-GEN-8.

(2) R. I. Akawie, J. M. Scarborough, and J. G. Burr, J. Org. Chem., 24, 946 (1959). Two of these isomers have been reported by A. I. Shatenshtein, G. V. Peregudov, E. A. Izrailevich, and V. R. Kalinachenko, Zhur. Fiz. Khim., 32, 146 (1958); Chem. Abstr., 52, 12554e (1958).

(3) J. G. Burr and J. M. Scarborough, J. Phys. Chem., in press.

(4) J. G. Burr, J. M. Scarborough, and R. H. Shudde, J. Phys. Chem., in press.

phenyls have been prepared: biphenyl-2,2',6,6'- d_4 (I), which has deuterium atoms in the four ortho positions, and biphenyl-2,2',3,3',5,5',6,6'- d_8 (II), which has deuterium atoms in the four ortho and four meta positions. A simpler method has also been developed for the synthesis of biphenyl- d_{10} .



Compounds I and II were each prepared from previously synthesized deuterated biphenyls by the method used for the preparation of biphenyl- $4,4'-d_2$.² Biphenyl-2,2',4,4',6,6'-d₆ was brominated by the method of Buckles and Wheeler⁵ to 4,4'-



dibromobiphenyl-2,2',6,6'-d₄. This was converted by exchange with *n*-butyllithium in ethyl ether to the 4,4'-dilithium compound, which was hydrolyzed with water; the two-step yield of biphenyl-2,2',6,6'-d₄ was 56%. Biphenyl-d₁₀ was similarly converted to biphenyl-2,2',3,3',5,5',6,6'd₈ in 51% yield.

A modification of the method of Leitch⁶ for the preparation of benzene-d₆ was used to synthesize biphenyl-d₁₀ from biphenyl. Exchange between biphenyl and deuterium oxide was carried out over platinum black catalyst by heating to 150° and shaking in a pressure vessel made of stainless steel and copper. The water alone was removed from the reaction mixture and fresh deuterium oxide was added in each successive exchange. After several exchanges⁷ there was obtained biphenyl-d₁₀ of greater isotopic purity than that previously prepared.²

The deuterated biphenyls were found to be free of chemical impurities by gas chromatography. The isotopic content of the products was determined by mass spectrometry at an ionizing voltage high enough to ionize the molecules but too low to remove hydrogen atoms from the molecules.⁸ The values for the isotopic purities are given in Table I. As the deuterium oxide used for the synthesis contained 0.3 atom percent hydrogen, the theoretical maximum purity is given in the last column of Table I.

TABLE I Isotopic Composition of Deuterated Biphenyls		
Compound	Isotopic Composition	Theoretical Maximum Purity
Biphenyl-d ₄	$C_{12}H_6D_6-98.2\%$ $C_{12}H_7D_6-1.6\%$ $C_{12}H_7D_6-0.2\%$	98.8%
Biphenyl-d ₈	$C_{12}H_{1}D_{7} - 0.2\%$ $C_{12}H_{2}D_{6} - 96.0\%$ $C_{12}H_{3}D_{7} - 3.8\%$ $C_{12}H_{4}D_{7} - 0.2\%$	97.6%
Biphenyl-d ₁₀	$\begin{array}{c} C_{12}D_{10} & 96.2\% \\ C_{12}D_{10} & 96.2\% \\ C_{12}HD_{9} & 3.8\% \\ C_{12}H_{2}D_{9} & 0.0\% \end{array}$	97.0%

EXPERIMENTAL⁹

4,4'-Dibromobiphenyl-2,2',6,6'-d₄, m.p. 163.5-164.5°, was prepared from biphenyl-2,2',4,4',6,6'-d₆² by bromination with bromine vapor at room temperature.⁵ A second crop of slightly less pure product, m.p. 162.5-164°, was obtained by concentrating the benzene mother liquor and adding methanol; the total yield was 84%.

Biphenyl-2,2',6,6'-d₄ was prepared from 4,4'-dibromobiphenyl-2,2',6,6'-d₄ by the method used to prepare biphenyl-4,4'-d₂.² From 45.8 g. (0.145 mole) of 4,4'-dibromobiphenyl-2,2',6,6'-d₄ and *n*-butyllithium reagent (containing 0.58 mole of total base) there was obtained, after hydrolysis with ordinary water, 15.7 g. of product distilling at 124-128° at 13 mm. Two sublimations *in vacuo* gave 15.3 g. (67%) of white crystals, m.p. 69-70°.

4,4'-Dibromobiphenyl- d_4 , m.p. 163–164°, was prepared from biphenyl- d_{10} in 81% yield by the procedure used for 4,4'-dibromobiphenyl-2,2',6,6'- d_4 .

Biphenyl-2,2',3,3',5,5',6,6'-d₈. From 38.4 g. (0.120 mole) of 4,4'-dibromobiphenyl-d₉ and *n*-butyllithium (containing 0.48 mole of total base) there was obtained, after hydrolysis, distillation at 13 mm., and sublimation at 1 mm., 12.3 g. (63%) of product, m.p. 69-70°.

Biphenyl-d10. The pressure vessel used for the exchanges was a cylinder (capacity 2.4 l.) made of stainless steel and copper which had a bellows valve and a metal thermometer soldered to it. The cylinder was charged with 100 g. of biphenyl, 200 ml. of 99.7% pure deuterium oxide, and 5 g. of platinum black (prepared by reducing platinic oxide with hydrogen). The exchange was carried out at 150° by shaking for 4 days (this may be longer than necessary). The reaction mixture was cooled, filtered with suction, and the solids were returned to the vessel with a fresh batch of deuterium oxide (200 ml.). When the exchanges were completed,⁷ the mixture was cooled and filtered. The product was dissolved in benzene and filtered. After evaporation of the solvent, two sublimations in vacuo gave 40.3 g. of white crystals, m.p. 69-70°. The low yield was partly caused by a small leak in the pressure vessel during exchange.

Gas chromatography. The deuterated biphenyls were analyzed for chemical purity with a Perkin-Elmer model 154B Vapor Fractometer, using a 2 meter column of silicone oil on Celite. Holding the column at different temperatures changed the retention time of biphenyl, and thus made it easy to analyze for chemical impurities either more or less volatile than biphenyl.

(8) D. P. Stevenson and C. D. Wagner, J. Am. Chem. Soc., 72, 5612 (1950).

(9) Melting points and boiling points are uncorrected.

⁽⁵⁾ R. E. Buckles and N. G. Wheeler, Org. Syntheses, 31, 29 (1951).

⁽⁶⁾ L. C. Leitch, Can. J. Chem., 32, 813 (1954).

⁽⁷⁾ The number of exchanges required when the reaction temperature is 150° is not known, as the first two exchanges were carried out at a lower temperature and the biphenyl was partially deuterated before the reaction temperature was changed to 150° .

Mass spectrometry. The mass spectra at low ionizing voltage were determined with a modified Consolidated Electrodynamics Corporation model 21-620 mass spectrometer.

Atomics International

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Allylic Rearrangements. XLVIII. The Absolute Configuration of (+)- α -Methylallyl Alcohol and (+)- α -Methylallyl Chloride¹

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DISCUSSION

In connection with other studies^{3,4} the determination of the relative configurations of optically active α -methylallyl chloride and α -methylallyl alcohol became necessary and this work is described below.

Catalytic hydrogenation of (+)- α -methylallyl alcohol yielded (+)-2-butanol which has the Lconfiguration⁵ and therefore (+)- α -methylallyl alcohol is designated L- in agreement with the work of Wiberg.6,7

Reaction of thionyl chloride with $D-(-)-\alpha$ methylallyl alcohol and tri-n-butylamine in ether yielded (+)- α -methyallyl chloride which was ozonized to (-)- α -chloropropionic acid known to possess the L-configuration.⁸ It follows then that α methylallyl alcohol and α -methylallyl chloride of like sign have like configurations about the asymmetric carbon. The absolute configurations are shown in Fig. 1.

CHO CH=CH2 CH=CH₂ HO►C◀H HOD CI►Ċ◀H CH2OH ĊH L-(-)-Glyceraldehyde⁹ L-(+)-α-Methyl-allyl alcohol $L-(+)-\alpha$ -Methyl-allyl chloride

Fig. 1 Absolute configuration of $(+)-\alpha$ -methylallyl alcohol and chloride

- (3) R. H. DeWolfe and W. G. Young, Chem. Rev., 56, 813 (1956).
- (4) K. L. Olivier and W. G. Young, J. Am. Chem. Soc., 81, 5811 (1959).
- (5) P. A. Levene, A. W. Walti, and H. Haller, J. Biol. Chem., 71, 465 (1927).
 (6) K. B. Wiberg, J. Am. Chem. Soc., 74, 3981 (1952).

A lower limit for the rotation of optically pure $L-(+)-\alpha$ -methylallyl chloride of α_D^{25} +61° (for l = 1, neat) has been estimated from comparison of the rotation of the $L-(-)-\alpha$ -chloropropionic acid obtained in this work with that obtained by Lucas^{10a,b} from the degradation of optically pure L-(+)-erythro-3-chloro-2-butanol. This comparison assumes that no racemization occurred during the present ozonization or Lucas' degradations, as the asymmetric centers under consideration were not directly involved in any reactions.

EXPERIMENTAL

dl-a-Methylallyl alcohol was prepared by the method of Delaby¹¹ as modified by Prevost,¹² b.p. 96–97°, $n_{\rm D}^{25}$ 1.4125.

Partial resolution of a-methylallyl alcohol was accomplished by the procedure of Kenyon and Snellgrove.13 The purified alcohol had b.p. 97°, n_D^{25} 1.4121 and α_D^{27} +20.09 ± 0.02° (neat, l 1.0) which is 71.9% of optical purity based on α_D^{30} +13.8 (neat, 1 0.5).⁴ The mother liquors yielded a small amount of (-)- α -methylallyl alcohol of α_D^{25} -8.45° (neat, 1 1.0).

Hydrogenation of (+)- α -methylallyl alcohol. A mixture having $\alpha_{\rm D}^{25}$ +9.78 ± 0.02° (neat, 1 1.0) of 2.21 g. of (+)- α methylallyl alcohol and 2.36 g. of inactive 2-butanol was dissolved in 10 ml. of ether and hydrogenated at atmospheric pressure over 1.41 g. of 5% palladium on barium sulfate. Only about 30% of the theoretical hydrogen was absorbed. The solution was fractionated through a 30-cm. concentric tube column and yielded 1.8 g. of impure (+)-2-butanol in three fractions, the last of which had $\alpha_D^{24} + 1.91 \pm 0.02^{\circ}$ (neat, 1 1.0). The impurity was found to be methylethyl ketone which presumably arose from rearrangement of α -methylallyl alcohol caused by the catalyst. In another hydrogenation with Adam's catalyst, 80% of the theoretical hydrogen was absorbed.

(+)- α -Methylallyl chloride was prepared by dropwise addition of 16.5 g. (0.139 mole) of thionyl chloride over 50 min. to a stirred, ice cooled solution of 10.0 g. (0.139 mole) of $(-)-\alpha$ -methylallyl alcohol and 25.7 g. (0.139 mole) of tri-n-butylamine in 200 ml. of ether. Careful fractionation through a 30-cm. concentric tube column gave 3.3 g. of γ -methylallyl and 7.1 g. of (+)- α -methylallyl chlorides (83% yield).

Ozonization of (+)- α -methylallyl chloride. A solution of 8.39 g. (0.093 mole) of $(+)-\alpha$ -methylallyl chloride, α_{D}^{25} $+5.87 \pm 0.02^{\circ}$ (neat, 1 1.0) and 50 ml. of chloroform was ozonized at 0° with 2-3% ozone. After ozonization was completed, the solution was poured into 25 ml. of water. The mixture was stirred overnight at room temperature and then, after addition of 10 ml. of acetone, was heated cautiously to 50° for 4 hr. When cool, half of the mixture was saturated with magnesium sulfate then treated with 4.9 g. of potassium permanganate in about 100 ml. of water. The mixture was filtered, the filtrate saturated with sodium sulfate and acidified by addition of 2 ml. of concd. sulfuric acid. The colorless solution was extracted with ten portions

⁽¹⁾ This work was supported in part by a National Science Foundation grant.

⁽²⁾ Standard Oil Company of California Predoctoral Fellow, 1952-1954.

⁽⁷⁾ Wiberg designates the (+) stereoisomer as D- and has the vinyl group correspond to the hydroxymethyl group of glyceraldehyde. In the present work the vinyl group corresponds to the carboxaldehyde group of glyceraldehyde and thus the L- designation given here is consistent with Wiberg's **D-** designation.

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⁽⁹⁾ J. J. Bijvoet, A. F. Peerdeman, and A. J. Van Bom-

mel, Nature, 168, 272 (1951). (10) (a) H. J. Lucas and H. K. Garner, J. Am. Chem. Soc., 70, 991 (1948); (b) W. F. Fickett, H. K. Garner, and
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⁽¹³⁾ J. Kenyon and D. Snellgrove, J. Chem. Soc., 127, 1174 (1925).