9.01 (w), 9.32 (m), 9.51 (s), 9.77 (m), 11.17 (w), 11.75 (w), 12.80 (w), 13.42 (s), 14.55 (w).

Anal. Found: C, 55.01; H, 3.09; O, 21.78; Ag, 8.85; I, 9.74.

A portion of the oligmer (0.191 g.) was hydrolyzed with base to salicylic acid (0.111 g.).

Acknowledgment.—The author expresses thanks for technical assistance to Mrs. Jean Whittaker and Mr. Eugene White and for encouraging and stimulating discussions to Prof. Cheves Walling, Dr. Archibald P. Stuart, and Dr. Howard P. Angstadt.

Fate of the Carbinol Carbon in the Conversion of Tetrahydrofurfuryl Alcohol to Dihydropyran

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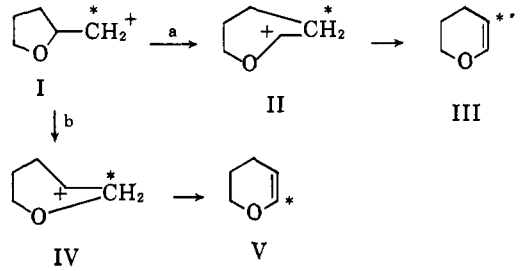
Tetrahydrofurfuryl alcohol with carbon-14 in the exocyclic carbon atom was prepared by carbonating furyllithium with radioactive carbon dioxide and reducing the resulting furoic(^{14}COOH) acid. Lithium aluminum hydride converted the acid to furfuryl alcohol. Hydrogen over Raney nickel then saturated the ring to give the labeled tetrahydrofurfuryl alcohol. Passing the labeled alcohol over hot alumina produced radioactive dihydropyran. Ozonization cleaved the dihydropyran to formic acid and 4-hydroxybutanal, while nitric acid oxidation of the dihydropyran gave glutaric acid which with hydrazoic acid was degraded to 1,3-diaminopropane. The results of radioactivity assays on these materials showed that the carbon-14 in dihydropyran was located in the 2- and 6-positions. The relations of this distribution to postulated reaction pathways is discussed.

When tetrahydrofurfuryl alcohol is passed over alumina at 350°, dehydration and ring expansion occur to give dihydropyran.[1,2] Although the reaction has been examined and improved by several groups,[3-5] only little evidence useful in defining a mechanism has been obtained. We wish to report work bearing on this aspect of the tetrahydrofurfuryl alcohol–dihydropyran conversion.

In the first stages of the reaction, alumina may be taken to coordinate with one or both of the oxygen atoms in tetrahydrofurfuryl alcohol. We assumed as a working hypothesis that the hydroxyl oxygen is the one involved and, therefore, that the exocyclic carbon atom becomes electron deficient. This presents two rearrangement possibilities, which are formulated here—in terms of the limiting carbonium ion-form I[6]—as paths a and b. Path a proceeds through a Wagner–Meerwein rearrangement with ring expansion (see II) and loss of proton to give the dihydropyran product III. A close analogy may be found in the alumina dehydration of cyclopentylcarbinol to cyclohexene.[10] An added favorable feature is the possibility of delocalization of the positive charge in II to oxygen.[11] Path b has the ring oxygen migrating to the external methylene group to give IV, which on loss of a proton becomes dihydropyran V. An ethylene oxide ring derived from IV could be involved in the rearrangement just as in the conversion of 2-methoxy-2-methylpropyl *p*-bromobenzenesulfonate to isobutyraldehyde.[12] A basis of choice between paths a and b lay in the fact that the former places the exocyclic carbon atom of tetrahydrofurfuryl alcohol at the dihydropyran 3-position (*cf.* III), while the latter places it at the dihydropyran 2-position (*cf.* V). With this in mind, we proceeded to prepare tetrahydrofurfuryl alcohol with carbon-14 in the exocyclic methylene group, to carry out the dehydration–rearrangement, and to locate the carbon-14 in the derived dihydropyran.



I II III IV V

In order to obtain the labeled starting alcohol, furyllithium was carbonated with radioactive carbon dioxide. Lithium aluminum hydride converted the resulting furoic(^{14}COOH) acid (VI) to furfuryl alcohol,

(1) The formal names for this compound and its derivatives are cumbersome and unfamiliar. Thus, for the parent compound we have our choice of 5,6(or 2,3)-dihydro-4*H*-pyran, 5,6(or 2,3)-dihydro-γ-pyran, or 5,6(or 2,3)-dihydro-1,4-oxin. For convenience, we have based the naming here on Δ²-dihydropyran and, wherever possible, have dropped the Δ². Note that this scheme automatically places the double bond at the 2,3- rather than the 5,6-position.

(2) R. Paul, *Bull. soc. chim.*, [4] **53**, 1489 (1933).

(3) R. L. Sawyer and D. W. Andrus, *Org. Syn.*, **23**, 25 (1943).

(4) L. E. Schniepp and H. H. Geller, *J. Am. Chem. Soc.*, **68**, 1646 (1946).

(5) C. H. Kline and J. Turkevich, *ibid.*, **67**, 498 (1945).

(6) The tetrahydrofurfuryl cation has been suggested before as a key intermediate: *cf.* Paul,[7] who interpreted his reaction in terms of something resembling the cation, Wilson,[8] and Fried.[9]

(7) R. Paul, *Bull. soc. chim.*, [5] **2**, 745 (1935).

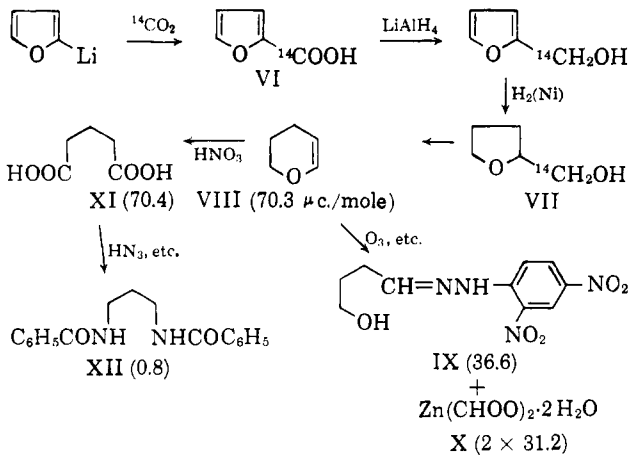
(8) G. J. Baumgartner and C. L. Wilson, *J. Am. Chem. Soc.*, **81**, 2440 (1959); H. P. Thomas and C. L. Wilson, *ibid.*, **73**, 4803 (1951).

(9) J. Fried, "Heterocyclic Compounds," Vol. I, R. C. Elderfield, Ed., John Wiley and Sons, Inc., New York, N. Y., 1950, p. 348.

(10) H. S. Turner and R. J. Warne, *J. Chem. Soc.*, 789 (1953).

(11) Other pertinent analogies involving a carbon shift to the adjacent electron-deficient carbon may be cited. These include diazotization of cyclopentylmethylamine to cyclohexanol [P. A. S. Smith, D. R. Baer, and S. N. Ege, *J. Am. Chem. Soc.*, **76**, 4564 (1954)], of 2-(aminomethyl)-tetrahydrofuran to an "oxidation product" of 5-hydroxypentanal [N. V. Williams, *Chem. Abstr.*, **26**, 3253 (1932); *Bull. acad. sci. USSR, Classe sci. math. nat.*, 1117 (1931)], and of 2-(aminomethyl)-tetrahydropyran to 6-hydroxyhexanal [J. Colonge and P. Corbet, *Bull. soc. chim. France*, 287 (1960); *Compt. rend.*, **247**, 2144 (1958)]. The rearrangement of pinacol to pinacolone over alumina at 320° [W. N. Ipatieff and W. Leontowitsch, *Chem. Zentr. II*, **77**, 87 (1906); *J. Russ. Phys. Chem. Soc.*, **35**, 606 (1903)], the conversion of 4-hydroxy-2,4,6-trimethyl-2,5-cyclohexadienone to trimethylhydroquinone with dilute acid [E. Bamberger and A. Rising, *Ber.*, **33**, 3636 (1900)], and the transformation of 3-ethoxy-2-methyl-2-heptanol to 2,2-dimethylhexaldehyde in hot formic acid [I. Elphimoff-Felkin, *Bull. soc. chim. France*, 497 (1950)] are also related.

(12) S. Winstein, C. R. Lindegren, and L. L. Ingraham, *J. Am. Chem. Soc.*, **75**, 155 (1953). Other examples of the migration of oxygen to an adjacent electron-deficient carbon atom may be found in the solvolysis of tetrahydrofurfuryl tosylate and bromide to 3-hydroxytetrahydropyran [D. Gagnaire, *Bull. soc. chim. France*, 1813 (1960)] and in the isomerization of tetrahydrofurfuryl acetate to 3-acetoxytetrahydropyran in the presence of zinc chloride [D. Gagnaire and A. Butt, *ibid.*, 309 (1961)].



which on hydrogenation over Raney nickel[13] gave the radioactive tetrahydrofurfuryl alcohol VII. Passing this material over hot alumina furnished labeled dihydropyran VIII.

Ozonolysis afforded a convenient way of separating the carbon atoms of positions 2 and 3 of the dihydropyran. The carbon at position-2 emerged as formic acid (collected in the form of the zinc salt X) while the carbon at position 3 emerged as part of 4-hydroxybutanal (collected in the form of its 2,4-dinitrophenylhydrazone IX). Assay showed that the activity of the dihydropyran VIII (70.3 μc./mole) was divided between the two cleavage fragments X and IX (2 × 31.2 and 36.6 μc./mole), respectively. This result was consistent with the operation of path a *and* path b to roughly the same extent.

However, this conclusion was premature. When the radioactive glutaric acid (XI) derived from dihydropyran (VIII) by oxidation was decarboxylated with hydrazoic acid, the 1,3-diaminopropane product (collected as the dibenzoyl derivative XII) was practically devoid of activity.[14] Since the original 3-position of dihydropyran is carried by the dibenzoyl derivative XII, the 3-position cannot be active. Thus, the activity of the 4-hydroxybutanal (as in IX) is seen to reside not at the aldehydic carbon, but instead at the hydroxy end of the C_4 chain, and the activity of dihydropyran VIII is divided not between positions 2 and 3, but instead between positions 2 and 6.

The accompanying diagram summarizes the distribution in terms of per cent activities.[15] Reaction

pathway a is clearly excluded. Pathway b is still admissable but only with modification, for as it stands, it fails to account for the appearance of the exocyclic carbon of tetrahydrofurfuryl alcohol at the dihydropyran 6-position. Possibly path b furnishes dihydropyran-2-^{14}C (V), which subsequently rearranges to a mixture of dihydropyran-2-^{14}C and dihydropyran-6-^{14}C. Work in this area is being continued.

Experimental[16]

Furoic(^{14}COOH) Acid (VI).—Butyllithium was prepared[17] under nitrogen from 27.5 g. (0.20 mole) of dry, redistilled butyl bromide, 3.9 g. (0.56 g.-atom) of lithium wire, and 140 ml. of ether freshly distilled from lithium aluminum hydride. The filtered butyllithium solution was titrated,[18] and 73 ml. containing 0.10 mole of reagent was taken for the metalation of furan.

Furan (34 g., 0.50 mole) was distilled directly into the ethereal butyllithium solution from a mixture of furan and lithium aluminum hydride. A 300-ml., round-bottomed, 3-necked flask provided with a water-cooled condenser, served as the reaction vessel. So far as possible, dry nitrogen blanketed the reaction mixture. After the reaction mixture was diluted with 30 ml. of ether distilled directly from ethereal lithium aluminum hydride, metalation was allowed to proceed at room temperature with occasional short periods of boiling.

The reaction flask, fitted with an efficient induction stirrer,[19] was attached to a vacuum manifold.[19] Carbon dioxide was generated in the line over a 20-min. period by adding 50 ml. of concentrated sulfuric acid to 20.0 g. of dry barium carbonate containing 24.4 μc. of carbon-14. The gas was passed into the stirred furyllithium solution at −60°. Careful warming of the sulfuric acid mixture released all residual carbon dioxide. After a total carbonation time of 40 min., 20 ml. of water was added by drops followed by 30 ml. of 6 *N* sulfuric acid. The mixture was stirred at room temperature for 1 hr., the uncombined carbon dioxide was collected at liquid-nitrogen temperatures, and the flask was removed from the line.

Furoic acid was recovered by batch and continuous extractions with ether. The acid was partially purified by transferring it from the ether solution to aqueous sodium hydroxide and then after acidification back to ether. This ether solution was dried with calcium sulfate and treated with a small amount of activated alumina gel plus 2 g. of decolorizing carbon. Filtration gave a clear, almost colorless solution, from which solvent was stripped by first warming the solution at 50–60° and then drying the residue in a desiccator over phosphorus pentoxide. The solvent-free solid (9.3 g., m.p. 128–130°, neut. equiv. 112–113) was crystallized first from water (decolorizing carbon was used here) and then from carbon tetrachloride to give pure furoic(^{14}COOH) acid (VI) that weighed 8.6 g. (76% based on carbon dioxide) and melted at 133° (cor.).

Anal. Calcd. for $C_5H_4O_3$: C, 53.38; H, 3.6; neut. equiv., 112.1. Found: C, 53.73, 53.61; H, 3.50, 3.56; neut. equiv., 112.3; radioactivity, 242, 247 (av. 245) μc./mole.

The *p*-nitrobenzyl ester[20] of this furoic(^{14}COOH) acid (VI) melted after two recrystallizations from 95% ethyl alcohol at 134–134.5°.

Anal. Calcd. for $C_{12}H_9O_5N$: C, 58.30. Found: C, 58.24, 58.35; radioactivity, 255 μc./mole.

A small sample of the radioactive furoic acid VI was decarboxylated[21] by boiling a mixture of the acid (0.35 g.), copper powder (0.35), and freshly distilled quinoline (4 ml.) for several minutes. The furan in the evolved gases was collected and,

(13) G. Hilly, *Bull. soc. chim.*, [5] **4**, 1630 (1937).

(14) The measured counts per minute was just over the background.

(15) For the purposes of this distribution, the molar activity of the dihydropyran was taken as 69.6 and was arrived at by averaging the molar activities of dihydropyran VIII, glutaric acid XI, and the 2,4-dinitrophenylhydrazone of the derived 5-hydroxypentanal (see Experimental section). If the distribution of activity between positions 2 and 6 of the dihydropyran is based on the activities of zinc formate (X), 1,3-dibenzamidopropane (XII), and dihydropyran (VIII), the distribution comes to 45% at the 2-position and 54% at the 6-position. If the distribution is based in the activities of 4-hydroxybutanal (*cf.* IX), 1,3-dibenzamidopropane (XII), and dihydropyran (VIII), the values come to 48% at the 2-position and 51% at the 6-position. With assay standard deviations of 2–3%, the activity distribution in the dihydropyran 2- and 6-positions is either very close to or is indistinguishable from 1:1.

(16) Melting points are uncorrected unless otherwise indicated. Some of the elementary analyses were performed by C. K. Fitz, 115 Lexington Avenue, Needham Heights 94, Mass.

(17) H. Gilman, J. A. Beel, C. G. Brannen, M. W. Bullock, G. E. Dunn, and L. S. Miller, *J. Am. Chem. Soc.*, **51**, 1499 (1949).

(18) H. Gilman and A. H. Haubein, *ibid.*, **66**, 1515 (1944).

(19) M. Calvin, C. Heidelberger, J. C. Reid, B. M. Tolbert, and P. F. Yankwich, "Isotopic Carbon," John Wiley and Sons, Inc., New York, N. Y., 1949.

(20) R. L. Shriner and R. C. Fuson, "Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1948, p. 157.

(21) *Cf.* E. C. Wagner and J. K. Simons, *J. Chem. Educ.*, **13**, 265 (1936); H. Gilman and M. B. Louisinian, *Rec. trav. chim.*, **52**, 156 (1933); W. G. Dauben and P. Coad, *J. Am. Chem. Soc.*, **71**, 2928 (1949).

after mixing with maleic anhydride (0.25 g.) and ether (3 ml.), was set aside for 2 days.[22] The precipitated hard, white crystals were collected, rinsed with ether, and dried to give 0.34 g. (68%) of 3,6-endoxy-1,2,3,6-tetrahydrophthalic anhydride, m.p. 124–125° dec.

Anal. Calcd. for $C_8H_6O_4$: C, 57.83; H, 3.64. Found: C, 58.19; H, 3.71; radioactivity, 0.0 μc./mole.

Tetrahydrofurfuryl Alcohol (VII) from Furoic(carboxyl-^{14}C) Acid (VI).—A saturated solution of furoic(carboxyl-^{14}C) acid (5.6 g. or 0.050 mole) in 25 ml. of absolute ether was added dropwise to a stirred mixture of 2.3 g. (0.061 mole) of lithium aluminum hydride in 100 ml. of ether.[23] Two 25-ml. portions of ether served to rinse all the furoic acid into the reaction mixture. The addition required 15 min., after which time the mixture was boiled for 1 hr.

Aqueous sodium hydroxide solution (30 ml. containing 4 g. of base) was added cautiously to the stirred reaction mixture. After removal of the two liquid layers, the white residual solid was shaken with three 10-ml. portions of ether. The combined ether layers were separated and washed several times with 10-ml. portions of water until the washings were neutral. The combined aqueous layer and washings were extracted continuously for 5.5 hr., and the ether extract, after several washings with small portions of water, was combined with the first ether portion. The ether solution, dried at 0° with magnesium sulfate, was carefully concentrated to obtain pale yellow, oily, furfuryl alcohol.

A teaspoonful of Raney nickel[13] wet with methanol was added to a glass vessel containing the furfuryl alcohol in about 5 ml. of ether. Two milliliters of methanol was used to rinse down the Raney nickel. The mixture at 50° was shaken with hydrogen at a pressure of 1300 lb. for 5.5 hr. The hydrogenation mixture was filtered, and the filtrate after concentration was distilled through a 4-in. vacuum-jacketed Vigreux column. Water-white tetrahydrofurfuryl alcohol (VII), boiling at 78–79° (18 mm.), was obtained in a yield of 3.9 g. (77%).

Anal. Calcd. for $C_5H_{10}O_2$: C, 58.80; H, 9.87. Found: C, 58.0; H, 9.60; radioactivity, 241, 241, 245 (av. 242) μc./mole.

Dihydropyran (VIII) from Tetrahydrofurfuryl Alcohol (VII).—The procedure was adapted from Sawyer and Andrus.[3] A glass tube $^3/_8$ in. in diameter was filled for about 60 cm. of its 70-cm. length with Alcoa activated alumina (Grade F-1, 8–14 mesh). The tube, slanted about 20° from the horizontal, was held in a 65-cm. furnace. The upper end of the catalyst tube was fitted with a 3-ml. dropping funnel provided with an inlet for nitrogen and a pressure-equalizing side arm. The lower end of the catalyst tube could be attached to two small cold traps in series.

The catalyst was pretreated[4] by slowly dropping 125 ml. of ordinary dihydropyran through the tube at 100°. Then, at a temperature of approximately 340° (maximum 366°), nitrogen was passed through very slowly for several hours. Finally, 14 ml. of ordinary tetrahydrofurfuryl alcohol was added to the 340° catalyst at a rate of 1 drop every 6 sec. Nitrogen (*ca.* 1 bubble per second) was passed through the hot tube during the addition, which required 0.5 hr., and for 2 hr. thereafter. Emergent material was discarded.

The collecting traps were attached to the end of the pyrolysis tube and were cooled with Dry Ice–acetone. The first trap contained 2 g. of dry potassium carbonate. Radioactive tetrahydrofurfuryl alcohol (VII, 3.81 g.) was added a a rate of 1 drop per second. When almost all had been added, 2.0 ml. of ordinary tetrahydrofurfuryl alcohol was placed in the dropping funnel, and the addition was continued. This rinsing process was repeated with another 2.0-ml. portion and finally with a 0.50-ml. portion of ordinary tetrahydrofurfuryl alcohol. The slow current of nitrogen was maintained during, and for 80 min. after, the addition.

No condensate was found in the second trap. The first trap was warmed to 0°, and the green upper layer of product was transferred to a small vacuum-jacketed Vigreux flask. The lower, aqueous layer was shaken with 0.50 ml. of ordinary dihydropyran, which was then added to the Vigreux flask. The dihydropyran was distilled (b.p. 65–86°) and condensed directly into a cold, 10-ml. distilling flask provided with a short Vigreux column and a fraction cutter. Approximately 40 mg. of lithium aluminum hydride was carefully added to the wet dihydropyran. After standing for 2 hr., the product was distilled. Radioactive dihydropyran (VIII, 5.52 g.) with $n^{21}D$ 1.4399 was collected at b.p. 83.5–84°.

Anal. Calcd. for C_5H_8O: C, 71.39; H, 9.58. Found: C, 70.7; H, 10.0; radioactivity, 70.3 μc./mole.

The 2,4-dinitrophenylhydrazone[24] of 5-hydroxypentanal was prepared by first hydrolyzing dihydropyran (0.11 ml.) in 1 ml. of water containing 1 drop of concentrated hydrochloric acid. The homogeneous solution obtained after 15 min. of shaking by hand and 5 hr. of standing was treated with a freshly prepared solution of 2,4-dinitrophenylhydrazine (0.30 g.), 2.5 ml. of water, 8.0 ml. of absolute alcohol, and 1.5 ml. of concentrated sulfuric acid. The mixture was warmed briefly on the steam bath, set aside overnight at room temperature, and then cooled. The collected solid, on recrystallization from 95% alcohol, afforded bright yellow crystals (0.25 g.) of the 2,4-dinitrophenylhydrazone of 5-hydroxypentanal, m.p. 109.5–110°.

Anal. Calcd. for $C_{11}H_{14}N_4O_5$: C, 46.81; H, 5.00. Found: C, 46.8; H, 5.0; radioactivity, 68.2 μc./mole.

Cleavage of Dihydropyran VIII by Ozonolysis.—Over a period of 0.5 hr., 0.010 mole of ozone in oxygen was bubbled into a −10° solution of 0.91 ml. (0.010 mole) of radioactive dihydropyran (VIII) in 40 ml. of dry, freshly distilled methylene chloride. The reaction tube was then held in a bath at 25° while a stream of nitrogen directed at the surface of the solution removed volatile materials. Zinc dust (3.7 g. or 0.05 g.atom) and water (10 ml.) were added, and the mixture was stirred overnight at room temperature. The mixture was then heated on the steam bath under a reflux condenser for 2 hr. Filtration gave a clear solution, which was extracted continuously for 2 days with *ca.* 300 ml. of ether.

The aqueous layer was separated, placed on the steam bath, and concentrated under a jet of nitrogen to a volume of 15 ml. Filtration removed a small amount of white solid, and the resulting clear filtrate was concentrated further to 2–3 ml. Addition of 20 ml. of absolute alcohol gave an immediate precipitate of zinc formate dihydrate (X), which was collected after allowing the mixture to stand for 8 days at −10°. The pure white product, washed on the funnel with absolute alcohol and then dried in the air, weighed 0.60 g. (63%).

Anal. Calcd. for $Zn(CHO_2)_2 \cdot 2H_2O$: C, 12.55; H, 3.16; ZnO, 42.5. Found: C, 12.8, 13.15; H, 3.35, 3.3; ash, 42.3, 42.50; radioactivity, 62.1, 62.6, 62.5 (av. 2 × 31.2) μc./mole.

The ether solution from the continuous extraction was concentrated under slightly reduced pressures. To the pale yellow residual oil dissolved in 20 ml. of 95% alcohol was added a freshly prepared solution of 1.2 g. (0.0061 mole) of 2,4-dinitrophenylhydrazine, 6 ml. of concentrated sulfuric acid, 9 ml. of water, and 30 ml. of 95% alcohol. The clear solution was warmed for a short time on the steam and then set aside in the cold for 10 hr. The precipitate was collected and was crystallized first from 95% alcohol and then from aqueous alcohol. The fine, yellow crystals of 4-hydroxybutanal 2,4-dinitrophenylhydrazone (IX), after drying *in vacuo* for 20 hr., weighed 0.74 g. (27%) and melted at 116.5–117°.

Anal. Calcd. for $C_{10}H_{12}N_4O_5$: C, 44.78; H, 4.51. Found: C, 44.75, 44.7; H, 4.61, 4.43; radioactivity, 35.3, 36.8, 37.2, 37.2, 36.6 (av. 36.6) μc./mole.

Glutaric Acid (XI) from Dihydropyran (VIII).[25]—A mixture of 2.5 ml. of water, 1 drop of concentrated nitric acid, and 1.0 g. (0.012 mole) of radioactive dihydropyran (VIII) was shaken for 15 min. The resulting homogeneous solution, after 2 hr. at room temperature, was added dropwise over a 2-hr. period to a cold (0°), stirred mixture of 4.8 g. of concentrated nitric acid and 0.04 g. of sodium nitrite. Stirring was continued for 2.5 hr. at 0°, and thereafter for 7 hr. at room temperature.

The acid mixture in a small evaporating dish was exposed to a current of air overnight. The light brown concentrate (2–3 ml.) was diluted with 5 ml. of water and evaporated on the steam bath in a current of air. The dilution and evaporation was repeated three times. Benzene (20 ml.) plus ether (2 ml.) were added to the last concentrate, and solvent was slowly distilled. Addition of benzene–ether as needed kept the volume of the boiling solution approximately constant. The almost colorless solution was filtered to remove a trace of insoluble solid. The

(22) O. Diels, K. Alder, and E. Naujoks, *Ber.*, **62**, 554 (1929).

(23) *Cf.* R. F. Nystrom and W. G. Brown, *J. Am. Chem. Soc.*, **69**, 2548 (1947).

(24) *Cf.* C. L. Wilson, *J. Chem. Soc.*, 52 (1945); G. F. Woods and H. Sanders, *J. Am. Chem. Soc.*, **68**, 2111 (1946).

(25) *Cf.* J. English, Jr., and J. E. Dayan, *Org. Syn.*, **30**, 48 (1950).

clear filtrate, after concentration to 15 ml., was cooled to precipitate glutaric acid. Two recrystallizations from benzene gave 1.1 g. (69%) of glutaric acid (XI), m.p. 93–94°. Another crystallization did not change the melting point.

Anal. Calcd. for $C_5H_8O_4$: C, 45.45; H, 6.10; neut. equiv., 66.05. Found: C, 45.57, 45.62; H, 6.04, 6.07; neut. equiv., 66.0; radioactivity, 70.8, 71.4, 69.0, 70.2 (av. 70.4) μc./mole.

1,3-Dibenzamidopropane (XII) from Glutaric Acid (XI).[26]—A mixture of radioactive glutaric acid XII (0.50 g. or 0.0038 mole), sodium azide (1.04 g. or 0.0160 mole) and pure chloroform (25 ml.) was swept with a slow stream of nitrogen. The gases from the reaction mixture were passed up a vertical water-cooled condenser and then into aqueous barium hydroxide. Concentrated sulfuric acid (7 ml. or 0.1 mole) was added by drops to the stirred mixture at *ca.* 64° over a 15-min. period. Stirring and heating were continued for 2 hr.

Aqueous sodium hydroxide (60 ml. of a 15% solution) was added slowly with stirring and cooling. Benzoyl chloride (2.4 g. or 0.017 mole) was added and the mixture was shaken vigorously for 10 min. and intermittently for 5 hr. After an additional 15 hr. at room temperature, the two layers were separated and the organic layer was extracted thoroughly with chloroform. The combined chloroform solutions were dried with magnesium sulfate and boiled to remove all solvent. Two crystallizations of the residual oil from benzene gave 0.63 g. (59%) of 1,3-dibenzamidopropane (XII), m.p. 148.5–149° (cor.).

Anal. Calcd. for $C_{17}H_{18}N_2O_2$: C, 72.32; H, 6.43. Found: C, 72.6, 72.02; H, 6.39, 6.69; radioactivity, 0.8 ± 0.4 μc./mole.

Radioactivity Measurement.[27]—Samples to be analyzed were burned quantitatively to carbon dioxide and water, which were collected and measured manometrically. The carbon dioxide was bled into a Bernstein–Ballentine tube or an ionization chamber for counting. Individual radioactivity determinations have standard deviations of 2–3%.

Acknowledgment.—We are grateful to Research Corporation for a grant that supported much of this work and to R. Christian Anderson and David R. Christman for their help and advice. Some of the research was performed under the auspices of the U. S. Atomic Energy Commission.

(26) *Cf.* H. Wolff, "Organic Reactions," R. Adams, Ed., Vol. 3, John Wiley and Sons, Inc., New York, N. Y., 1946, p. 307; S. Rothchild and M. Fields, *J. Org. Chem.*, **16**, 1080 (1951).

(27) R. C. Anderson, Y. Delabarre, and A. A. Bothner-By, *Anal. Chem.*, **24**, 1298 (1952).

A Steroidal Internal Displacement Reaction[1]

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Reaction of 3,5-cyclo-6β-methoxy-17β-tosyloxyandrostan-14α-ol with base yields 3,5-cyclo-6β-methoxy-14-androsten-17α-ol instead of fragmentation products. Base treatment of the *p*-toluenesulfonylhydrazone of 3β-acetoxy-14α-hydroxy-5-androsten-17-one affords the rearranged product 13α,14α-oxido-5-androsten-3β-ol.

The 5,10-, 8,9-, and 13,14-seco steroids contain medium sized rings incorporated into the steroid nucleus. It is desirable to synthesize these compounds in order to evaluate this structural variation on biological properties. An attractive route to a 13,14-seco compound involves fragmentation[2] of an appropriately substituted 1,3-diol monotosylate.

Starting with 5-androstene-3β,14α,17β-triol (I),[3] this was converted to the 3,17-ditosylate II. Selective methanolysis of the more reactive 3β-tosylate afforded the 3,5-cyclo derivative III. The necessary stereochemical arrangement of reactive centers is in principle present in III, *e.g.*, the *trans* antiparallel relationship of C-13–C-14 bond and the departing 17β-tosyloxy group to form a seco ketone by bond fragmentation.

Treatment of the 1,3-diol monotosylate III with potassium *t*-butoxide in boiling *t*-butyl alcohol led to the partial recovery of starting material with no detectable seco ketone as evidenced by the infrared spectrum. These conditions were found to be suitable for the fragmentation reaction in other 1,3-diol monotosylates.[2] Reaction of III under more vigorous conditions, with sodium hydride in tetrahydrofuran, which promoted irreversible alkoxide ion formation at C-14 led to a transformation product IV. The substance IV was characterized by the formation of a monoacetate on acetylation with acetic anhydride. The n.m.r. of IV showed the presence of one vinyl proton (4.84 τ).[4]

The transformation of IV to a substance of known structure was accomplished by acetolysis of the 3,5-cyclo steroid to the 3β-acetoxy-Δ^5 compound Va. Oxidation of Va with chromic acid led to the known 17-ketone VI.[3]

The substance V was also isolated from the reaction mixture and is related to IV by the presence of a 3β-hydroxy-Δ5 system generated from the 3,5-cyclo steroid. This change apparently occurred on the acidic alumina employed in the chromatographic separation.

Formation of the 17α-ol IV can be presumed to arise by intermediate formation of the highly strained 14α,17α-oxide compound VII formed by internal displacement, with attendant inversion at C-17, by the C-14 alkoxide ion. The strained intermediate VII undergoes further base-catalyzed elimination to IV.[5]

The absence of seco ketonic material arising from the four-center reaction is probably a result of the non-

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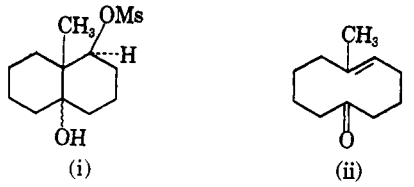
(2) R. B. Clayton, H. B. Henbest, and M. Smith, *J. Chem. Soc.*, 1982 (1957), report the fragmentation of the C-4–C-5 bond on base treatment of 3β-tosyloxy-5α-hydroxycholestane. P. S. Wharton, *J. Org. Chem.*, **26**, 4781 (1961), also has recently reported the facile fragmentation of the bicyclic 1,3-diol monomesylate (i) to (ii).



(i) (ii)

(3)(a) A. F. St. Andre, *et al.*, *J. Am. Chem. Soc.*, **74**, 5506 (1952). The stereochemistry of the hydroxyl at C-14 is alpha in I as demonstrated by (b) S. H. Eppstein, *et al.*, *ibid.*, **80**, 3382 (1958).

(4) The n.m.r. spectrum of 3β-acetoxy-5,14-androstadien-17β-ol showed the C-15 proton signal at 4.81 τ and the C-17α proton signal at 6.0 τ. In compound IV the C-17β proton signal is found at 6.04 τ. We thank Mr. W. V. Anderson for recording the n.m.r. spectra. The spectra were recorded at 60 Mc. on a Varian Associates HR4300 high resolution spectrometer on deuteriochloroform solutions of the steroids.