

irradiation products and their 2,4-dinitrophenylhydrazine derivatives. Circular chromatography¹ of the latter derivatives did, however, reveal an unidentified 2,4-dinitrophenylhydrazone. A small proportion of the tetrahydropyran-2,3-diol remained in the aqueous phase, together with δ -hydroxyvaleric acid and other acids, despite the exhaustive extraction.

Quantitative determination was hampered by the dihydropyran which interferes in methods^{2,3} used to estimate tetrahydropyran-2-ol and the 2,3-diol. However, after its careful removal by distillation the residue was amenable to the standard techniques. The dihydropyran was then determined by its reaction with neutral iodine solutions; bromination⁴ was found unsuitable in the presence of tetrahydropyran-2-ol owing to slow oxidation of the latter in these conditions. The tetrahydropyran-2-ol and -2,3-diol were determined together by using alkaline iodine² and the 2,3-diol was then determined separately by oxidation with periodate.⁵ *G* values for tetrahydropyran-2-ol were 0.61 for the irradiation *in vacuo* and 0.64 in oxygen. Tetrahydropyran-2,3-diol was produced in much greater yield during the irradiation in oxygen (*G* 1.05) than *in vacuo* (*G* 0.46) (in calculating these *G* values the amount of diol in the aqueous phase was included).

Irradiation of an aqueous solution of 2,3-dihydro-2-hydroxymethyl-4*H*-pyran in oxygen gave the 2-hydroxy- and the 2,3-dihydroxy-derivative. More interesting was the finding of tetrahydropyran-2-ol and δ -valerolactone among the products of irradiation of tetrahydropyran in oxygen. The production of tetrahydropyran-2-ol (yield, 8.4%) must involve the addition of the hydroxyl radical at some stage, which was confirmed by irradiating the tetrahydropyran in the presence of hydrogen for the same total dose, which led to only an extremely low yield of both the tetrahydropyran-2-ol (0.36%) and δ -valerolactone. The annexed scheme shows the postulated breakdown of 2,3-dihydro-4*H*-pyran in oxygen.

EXPERIMENTAL

Hydrolysis of 2,3-Dihydro-4H-pyran.—Solutions (0.5% w/v) of dihydropyran in conductivity water were stored at 17° in the presence and absence of washed barium carbonate. The dihydropyran content of centrifuged aliquot parts of these solutions was determined over a period of 7 days by Siggia and Edsberg's method⁶ but without the addition of methanol which precludes the use of "Thyodene" as an indicator. Control mixtures of dihydropyran and tetrahydropyran-2-ol determined in the same way showed no interference by the latter. Only a slight effect was noticeable even when a four-fold excess of the tetrahydropyran-2-ol was present. Hydrolysis of dihydropyran was 20% complete in 24 hr. and 90% complete in 5 days. The rate of hydrolysis in the presence of barium carbonate was negligible during 7 days. Synthetic mixtures of dihydropyran and tetrahydropyran-2-ol (0.5% w/v) were prepared in the presence of barium carbonate. The dihydropyran contents of centrifuged aliquot parts withdrawn at intervals during 7 days were determined.

Irradiation of 2,3-Dihydro-4H-pyran.—Irradiations were carried out, in the presence of oxygen, of dihydropyran solutions (0.5% w/v) prepared in conductivity water previously saturated with oxygen, washed barium carbonate (5 g.) being added to prevent hydrolysis. Irradiation in the absence of oxygen was achieved by degassing a barium carbonate suspension (4 l.) in a 5-l. flask at 0.1 mm. for 3 hr. with frequent shaking. Because of its volatility dihydropyran was then added from a separatory funnel in the side-arm of the flask without allowing air to enter. The flask was shaken to establish equilibrium ($\frac{1}{2}$ hr.) and then placed in a 200-c⁶⁰Co irradiation cell to give a total dose of 4.05 Mrad. Each irradiated solution was extracted continuously with ether for 72 hr. After drying of the ether phase (MgSO₄) and removal of ether by distillation yields were 9.4203 g. (A) from 18.450 g. of dihydropyran (oxygenated irradiation) and 13.854 g. (B) from 18.375 g. (irradiation *in vacuo*). The unchanged dihydropyran was removed by distillation under reduced pressure, yielding A' (3.4061 g., 18.5%) and

¹ Barry and Mitchell, *J.*, 1954, 4020.

² Hirst, Hough, and Jones, *J.*, 1949, 929.

³ Shaffer and Hartmann, *J. Biol. Chem.*, 1921, **45**, 377.

⁴ McCullough and Stone, *Analyt. Chem.*, 1952, **24**, 1206.

⁵ Dyer, *Methods Biochem. Analysis*, 1956, **3**, 111.

⁶ Siggia and Edsberg, *Ind. Eng. Chem.*, 1948, **20**, 762.

B' (3.0751 g., 16.5%) as light brown oils from the mixtures irradiated in oxygen and *in vacuo*, respectively.

The aqueous phase from each ether-extraction was treated with Amberlite IR-120 (H^+) resin and freeze-dried [yields: oxygen irradiation, 0.8603 g. (C) *in vacuo*, 0.2330 g. (D)]. Aqueous solutions of the products were stirred for 12 hr. with Deacidite FF (CO_3^{2-}), and the slurry was poured into a column which was eluted with water (neutral components) and then *N*-ammonium carbonate (acid components). Free acids were recovered from the latter by stirring it with Amberlite IR-120 (H^+). After freeze-drying, C' (0.4822 g.; neutral fraction) and C'' (0.1056 g.; acidic fraction) were obtained from the irradiation in oxygen and D' (0.0721 g.; neutral fraction) and D'' (0.0931 g.; acidic fraction) from the irradiation *in vacuo*.

Chromatographic examination of fractions. Fractions A' and B' were analysed on paper chromatograms irrigated with butan-1-ol-ethanol-water-ammonia (4:1:4.9:0.1). When sprayed with alkaline silver nitrate,⁷ fraction A' showed components with R_F 0.074, 0.16, 0.39, 0.52, 0.54, 0.70, and 0.95; fraction B' contained those with R_F 0.39, 0.54, 0.70, and 0.95. Components with R_F 0.39, 0.54, 0.70, and 0.95 were detectable also with 2,4-dinitrophenylhydrazine,⁸ those with R_F 0.54 and 0.95 with triphenyltetrazolium chloride,⁹ and the component R_F 0.54 with periodate-benzidine.¹⁰ In both fractions A' and B' an additional component with R_F 0.89 was detectable with a hydroxylamine-ferric chloride spray.¹¹ Comparisons with reference compounds suggested the following identities: component R_F 0.95, tetrahydropyran-2-ol; R_F 0.89, δ -valerolactone; R_F 0.54, tetrahydropyran-2,3-diol; R_F 0.4, bistetrahydropyranyl ether.

With the butanol solvent, paper chromatography of the neutral fractions C' and D' revealed that they were mainly tetrahydropyran-2,3-diol with traces of an unidentified component of R_F 0.35.

Paper chromatography of the acidic fractions, C'' and D'' was best achieved in pentan-1-ol-pyridine-water (1:1:1). Spraying with Chlorophenol Red,¹² after evaporation of the formic acid, showed fraction C'' to contain components with R_F 0.18, 0.30, 0.54, 0.70, and 0.88, and fraction D'' only those with R_F 0.08, 0.54, and 0.70. The component of R_F 0.70 corresponded to δ -hydroxyvaleric acid, and this was confirmed by identical mobilities in the butanol solvent used above.

Characterisation of fractions. Distillation of fraction B' (2 g.) gave a product (0.72 g.), b. p. $38^\circ/0.1$ mm., with an infrared spectrum and paper-chromatographic mobility identical with those of tetrahydropyran-2-ol. It was characterised¹³ as its 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 107 — 109° (Found: C, 46.6; H, 4.8; N, 19.8. Calc. for $C_{11}H_{14}N_4O_5$: C, 46.8; H, 5.0; N, 19.8%), and azoate, m. p. and mixed m. p. 65 — 66° (Ladenburg *et al.*¹⁴)

Portions (500 mg.) of fractions A' and B' were separated on a cellulose column and eluted with the butanol solvent (see above) at 25 ml./hr. Analysis of the 10-ml. fractions collected revealed tetrahydropyran-2,3-diol in tubes 51—55. Fraction A' (2 g.) yielded crude diol (650 mg.) which was characterised as the derived 2,4-dinitrophenylsazone, m. p. and mixed m. p. 235 — 237° , and bis-3,5-dinitrobenzoate,¹⁵ m. p. and mixed m. p. 174 — 175° . Fraction B' (3 g.) yielded 300 mg. of diol, moving as a single component on paper chromatograms and ionophoretograms.

Tubes 75—80 from the column fractionation of materials A' or B' contained bistetrahydropyranyl ether. The bulked fractions from both were characterised by heating a concentrated ethanolic solution of the product with 2,4-dinitrophenylhydrazine in hydrochloric acid. Hydrolysis of the "dimer" occurred,¹³ to yield the 2,4-dinitrophenylhydrazone from tetrahydropyran-2-ol, m. p. and mixed m. p. 108 — 109° .

⁷ Trevelyan, Proctor, and Harrison, *Nature*, 1950, **166**, 444.

⁸ Block, Durrum, and Zweig, "A Manual of Paper Chromatography," Academic Press, New York, 1955, p. 344.

⁹ Feingold, Avigad, and Hestrin, *Biochem. J.*, 1956, **64**, 351.

¹⁰ Cifonelli and Smith, *Analyt. Chem.*, 1952, **26**, 1132.

¹¹ Abdel-Akher and Smith, *J. Amer. Chem. Soc.*, 1957, **79**, 5859.

¹² Brown, *Nature*, 1951, **167**, 441.

¹³ Paul, *Bull. Soc. chim. France*, 1934, **1**, 971; Schniepp and Geller, *J. Amer. Chem. Soc.*, 1946, **68**, 1646.

¹⁴ Ladenburg, Fernholz, and Wallis, *J. Org. Chem.*, 1939, **3**, 294.

¹⁵ Hurd and Kelso, *J. Amer. Chem. Soc.*, 1948, **70**, 1484; Swadesh and Dunlop, *J. Org. Chem.*, 1949, **14**, 692.

Quantitative Analysis of the Irradiation Products.—Determination of 2,3-dihydro-4H-pyran was effected by the modified method of Siggia and Edsberg⁶ outlined above. After the irradiation in oxygen, 33% of the initial weight of 2,3-dihydro-4H-pyran was found in the ether extract A and 41% in the ether distillate. For the corresponding irradiation *in vacuo*, 58.6% of the initial weight of dihydropyran was found in the ether extract B and 11.2% in the ether distillate.

Dihydropyran was removed from both extracts A and B by distillation at 20 mm. and a maximum bath-temperature of 30°. The total amounts of tetrahydropyran-2-ol and -2,3-diol present in the residues A' and B' were then determined on aliquot parts (~50 mg.) by using alkaline iodine² and found to be 83.3% and 62.8%, respectively. The concentration of the diol in fractions A' and B' was similarly determined on a sample (~80 mg.) by periodate oxidation⁵ and found to be 52% and 28%, respectively. Hence fractions A' and B' contain 31.1% and 34.8%, respectively, of tetrahydropyran-2-ol.

The amounts of diol and tetrahydropyran-2-ol in the oils obtained from the aqueous phase of the ether extraction were similarly determined. That from irradiation in oxygen contained 56% of the diol and 7.6% of tetrahydropyran-2-ol; that from irradiation *in vacuo* contained 42% of diol and no tetrahydropyran-2-ol.

Irradiation of 2-Hydroxymethyl-2,3-dihydro-4H-pyran.—The enol ether (4 g.) was irradiated for 24 hr. (dose 0.83 Mrad) in water (4 l.) in the presence of barium carbonate under oxygen. The product (1.94 g.) obtained on freeze-drying of the filtered solution was analysed by paper chromatography in butan-1-ol-ethanol-water (4:1:5). Components revealed with alkaline silver nitrate had R_F values of 0.051, 0.13, 0.25, 0.33, 0.52, 0.54, 0.66, and 0.85. The last four of these reacted with 2,4-dinitrophenylhydrazine.⁸ Spraying with 10% aqueous potassium hydroxide suggested that those of R_F 0.52 and 0.54 gave osazones (blue spots) and those of R_F 0.66 and 0.85 gave hydrazones (brown colour). Three of the components (R_F 0.52, 0.54, and 0.66) reacted with periodate-benzidine.¹⁰ Identity in such reactions and in mobility suggested that components of R_F 0.52 and 0.85 were tetrahydro-6-hydroxymethylpyran-2,3-diol and -2-ol, respectively.

Irradiation of Tetrahydropyran.—An aqueous solution (0.1% w/v) of tetrahydropyran was irradiated *in vacuo* to a total dose of 0.8 Mrad, the tetrahydropyran being admitted after degassing of the water. Continuous ether-extraction followed by evaporation of the solvent gave an oil (0.781 g.; 19.5%). Paper chromatography revealed the presence of tetrahydropyran-2-ol and δ -valerolactone. Supporting evidence was obtained from the infrared spectrum of the mixture, the lactone peak observed being similar to that of a mixture of these two components prepared by partial oxidation¹⁶ of tetrahydropyran-2-ol. Determination with alkaline iodine² showed that 43% of the oil was tetrahydropyran-2-ol, its yield corresponding to a G value of 0.94. Tetrahydropyran-2-ol in the irradiation mixture was further characterised as the derived 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 107–108°, and oxime, m. p. 92° (Paul¹³ gives m. p. 92–93°).

Tetrahydropyran (4 g.) was irradiated for 24 hr. (dose 0.83 Mrad) in water (4 l.) under hydrogen. The product (0.102 g.) obtained on freeze-drying of the irradiated solution contained only traces of tetrahydropyran-2-ol, detectable on a paper chromatogram sprayed with 2,4-dinitrophenylhydrazine.⁸ Determination by alkaline iodine² showed 14% of tetrahydropyran-2-ol, corresponding to a G value of 0.046.

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¹⁶ Hight and Williams, *J. Amer. Chem. Soc.*, 1955, **77**, 4399.