

15. Reactions of Furan Compounds. Part II. Fission of the Tetrahydrofuran and the Tetrahydropyran Ring.

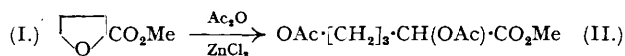
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Various tetrahydrofuran compounds and tetrahydropyran with reagents such as acetic anhydride or hydrogen bromide give open-chain butane or pentane derivatives.

The fission reaction has been applied to tetrahydrofuran, tetrahydrofurfuryl alcohol, its acetate, chloride and bromide, methyl tetrahydrofuroate, acetotetrahydrofurfurylamide, and tetrahydropyran. Simple methods of preparation of the following compounds have been devised: 1 : 2 : 5-triacetoxy-, 1 : 2 : 5-trihydroxy-, 1 : 2 : 5-tribromo-, 1-bromo-5-acetoxy-, and 1 : 5-dibromo-*n*-pentane, 1 : 4-dibromobutane, 1-bromo- Δ^4 -pentene, and 3-bromopropylethylene oxide.

PAUL (*Bull. Soc. chim.*, 1933, **53**, 417; 1941, **8**, 369; *Compt. rend.*, 1939, **208**, 587) appears to have carried out the first systematic experiments on the splitting of the ether linkages in the tetrahydro-furan and -pyran rings, and the present work is supplementary to his. The discussion is divided into sections according to the fission reagent.

Fission by Acetic Anhydride.—Paul (*loc. cit.*, 1933) investigated the reaction of tetrahydrofuran derivatives with acetic anhydride in the presence of zinc chloride as catalyst by heating the reactants in a sealed tube to 190–200°. He showed, *e.g.*, that tetrahydrofurfuryl alcohol is converted into 1 : 2 : 5-triacetoxypentane, but we find that use of a sealed tube is not always necessary, refluxing at atmospheric pressure for some time being sufficient with both tetrahydrofurfuryl alcohol and methyl tetrahydrofuroate (I). The latter gave a compound derived from methyl $\alpha\delta$ -diacetoxyvalerate (II).



Other compounds examined did not react well. Tetrahydrofurfuryl methyl ether gave methyl acetate and triacetoxypentane. Acetotetrahydrofurfurylamide was unaffected, but tetrahydrofuronitrile readily lost hydrogen cyanide and produced tarry material. Tetrahydrofurfuryl chloride and bromide gave complex mixtures containing mono-, di-, and tri-halides.

In these reactions it is likely that zinc chloride forms with acetic anhydride a complex which possesses a considerably enhanced tendency to lose a positively charged acetyl group. This group can then become attached to the ether oxygen atom and the oxonium compound produced, $\text{>O}^+\text{Ac} \left\{ \text{ZnCl}_2\text{OAc} \right\}^-$, undergoes degradation.

The intervention of an ionic complex is supported by the absence of reaction if the vapours of tetrahydrofurfuryl alcohol and acetic anhydride are passed at a high temperature over a catalyst containing zinc chloride. Under these conditions, in the absence of solvent, ionisation is undoubtedly suppressed and reaction cannot occur.

Fission by Hydrogen Halides.—Paul (*loc. cit.*, 1933) saturated tetrahydrofurfuryl alcohol with gaseous hydrogen bromide at 100° and obtained what he considered to be a mixture of isomeric dibromohydrins (III) and $\text{OH} \cdot [\text{CH}_2]_3 \cdot \text{CHBr} \cdot \text{CH}_2\text{Br}$ (III*a*). We have further examined this reaction. Analysis of the crude product established the presence of two bromine atoms. It distilled in a vacuum with slight loss of hydrogen bromide, but when fractionation was attempted in the presence of stainless-steel Lessing rings, hydrogen bromide was rapidly evolved, and tetrahydrofurfuryl bromide (b. p. 56–58°/12 mm.) produced.

The crude dibromohydrin showed but little reaction with zinc, indicating the absence of the 4 : 5-dibromo-

(500 c.c.) for 3 hrs., and acetic acid then removed by steam-distillation. The residue was distilled in a vacuum, giving 1 : 2 : 5-trihydroxypentane as a viscous liquid, b. p. 180—182°/6 mm.; yield 60%. If steam-distillation was omitted, the product had b. p. 170—174°/10 mm. and saponification showed that it contained the equivalent of 70% of the mono-acetoxy-compound.

(b) *Methyl tetrahydrofuroate*. The ester (22.8 g.), acetic anhydride (65 g.), and zinc chloride (anhydrous, 0.5 g.) were refluxed for 15 hrs. The product was distilled in a vacuum, giving unchanged ester, b. p. 70°/13 mm. (7.5 c.c.), and a product, b. p. 115—160°/13 mm. (9.0 c.c.). The latter was shaken with aqueous sodium carbonate until neutral, and redistilled. Most of the distillate had b. p. 142—143°/14 mm.; it was saturated to bromine in aqueous acetic acid solution, and contained acetoxy and carbomethoxy groups. Carbon monoxide was evolved with warm concentrated sulphuric acid. Analysis (Found: C, 49.2; H, 6.9; Ac, 24.9; equiv., by saponification, 72. Calc. for $C_8H_{14}O_5$: C, 50.5; H, 7.4; Ac, 22.6%; equiv., 95) suggests the product was essentially a methyl hydroxyacetoxyvalerate. It is probable that the sodium carbonate treatment caused some hydrolysis of the diacetoxy-compound formed initially (Paul, *loc. cit.*, 1941).

(c) *Tetrahydrofuronitrile*. The nitrile (8.6 g.) was refluxed with acetic anhydride (15 g.) and zinc chloride (anhydrous, 0.2 g.). Hydrogen cyanide was rapidly evolved, and tarry material formed. Attempted distillation gave a small amount of a solid, b. p. 120—130°/12 mm., m. p. 74—76° [Found: C, 47.7; H, 7.1; N (Rast), 106. Calc. for $C_4H_7O_2N$: C, 47.5; H, 6.9%; *M*, 101], shown by hydrolysis to be diacetamide.

II. *Fission with Hydrogen Chloride*.—(a) *Tetrahydrofurfuryl alcohol*. The alcohol (48.5 c.c.) was heated to 150° and saturated with gaseous hydrogen chloride. After 9 hrs. the product contained unreacted alcohol (about 25%) together with variable amounts (12—25% of the theoretical) of tetrahydrofurfuryl chloride, b. p. 40°/14 mm. The rest of the product consisted largely of a liquid, b. p. 110—140°/10 mm. (20—25% of product by weight).

(b) *Acetotetrahydrofurfurylamide*. The acetyl compound (28.6 g.), acetic anhydride (35 g.), and zinc chloride (anhydrous, 0.5 g.) were refluxed for 15 hrs. whilst hydrogen chloride (10 g.) was passed into the mixture. Distillation gave a product (6.8 g.), b. p. 160—190° (Found: N, 7.6; Cl, 14.5. $C_9H_{16}O_3NCl$ requires N, 6.3; Cl, 16.0%), probably mainly *aceto*-[2(or 5)-*chloro*-5(or 2)-*acetoxy*-*n*-*amyl*]amide. This, like the corresponding bromo-compound, was miscible with water in all proportions.

III. *Fission with Hydrogen Bromide*.—(a) *Tetrahydrofuran*. Tetrahydrofuran (72 g., 80 c.c., 1 g.-mol.), b. p. 64—66.5°, was added slowly to a cold mixture of hydrobromic acid (50%, 972 g., 6 g.-mols.) and concentrated sulphuric acid (50 c.c.), and the mixture refluxed for 3 hrs. The product was steam-distilled, and the lower layer dried over calcium chloride followed by phosphoric oxide. Tetramethylene dibromide, thus obtained in 82% yield, had b. p. 198—201° (Found: C, 22.8; H, 3.8; Br, 72.35. Calc. for $C_4H_8Br_2$: C, 22.2; H, 3.7; Br, 74.0%).

(b) *Tetrahydrofuran*. The cyclic ether (17.2 g.) was treated as described in (a). The pentamethylene dibromide, obtained in 78% yield, had b. p. 106—108°/19 mm.

Tetrahydrofurfuryl alcohol and methyl tetrahydrofuroate did not undergo fission under similar conditions.

(c) *Tetrahydrofurfuryl alcohol and gaseous hydrogen bromide*. The alcohol (48.5 c.c.) was heated to 100°, and hydrogen bromide passed in until the increase in weight was 80—85 g. (6 hrs.). The product was poured into water, and the lower layer (100—115 g.) separated (Found: Br, 56.6%). About 90 g. of this distilled with slight decomposition at 120—140°/12 mm. A dibromohydroxypentane would require Br, 65%, and a bromodihydroxypentane Br, 43.7%.

The crude dibromohydrin was mixed with zinc in the presence of methyl alcohol. Very little reaction occurred in the cold, and heating under reflux produced only a slow evolution of hydrogen, indicating the absence of appreciable amounts of the 1 : 2-dibromo-compound.

Conversion of the dibromohydrin (III) into tetrahydrofurfuryl bromide (IV). The crude dibromohydrin was heated in a vacuum in a Claisen flask having a 4" fractionating column packed with stainless-steel rings. The distillate was redistilled, giving tetrahydrofurfuryl bromide (34 g.), b. p. 57—64°/12 mm. The yield calculated on the alcohol used (51 g.) was 41%. In another experiment the fractionating column was omitted but a few of the metal rings were added to the crude dibromohydrin (37 g.). The product consisted of tetrahydrofurfuryl bromide, b. p. 56—58°/12 mm., 16 g., 64% (Found: C, 36.8; H, 5.6; Br, 47.7. Calc. for C_5H_8OBr : C, 36.4; H, 5.5; Br, 48.5%), and a liquid, b. p. 130—140°/12 mm., which, from its vigorous reaction with zinc and its bromine content (75.0%), was mainly 1 : 2 : 5-tribromopentane (Br, 77.7%).

Conversion of dibromohydrin (III) into 1 : 2 : 5-tribromopentane. The crude dibromohydrin was treated with phosphorus pentabromide suspended in carbon tetrachloride (cf. *Org. Synth.*, 1933, 13, 21). When hydrogen bromide ceased to be evolved the product was decomposed carefully with water and distilled. 1 : 2 : 5-Tribromopentane, b. p. 130—132°/16 mm., was obtained in 46.2% yield calculated on the alcohol taken. Von Braun and Köhler (*Ber.*, 1918, 51, 93) give b. p. 128—132°/11 mm.

1-Bromo- Δ^4 -pentene from tribromopentane. The tribromo-compound (126 g.) was added slowly to zinc (needles, 34.1 g.) covered with methyl alcohol (50 c.c.). The very vigorous reaction was completed by refluxing with external heating for 0.5 hr. Water was added, and the lower layer distilled after drying over calcium chloride; b. p. 127—129°/770 mm. (41.4 g., 71.2%). The zinc consumed (24.8 g.) corresponded with a 72% yield of 1-bromo- Δ^4 -pentene (Found: Br, 53.0. Calc. for C_5H_8Br : Br, 53.6%). Von Braun and Köhler (*loc. cit.*) give b. p. 110°, obviously in error, since 127—129° agrees with Gaubert, Linstead, and Rydon's b. p. (J., 1937, 1972).

Reaction between dibromohydrin (III) and potassium hydroxide. (i) No solvent. The crude dibromohydrin (89 g.) was cooled in ice and stirred while powdered potassium hydroxide (30 g.) was added in small portions so that the temperature did not rise above 30°. Stirring was continued for 1 hr. and then for a further 0.5 hr. after addition of water (30 c.c.). More water was added, and the organic layer separated and distilled. Two fractions were obtained: (1) b. p. 78—82°/17 mm. (47 g.); (2) b. p. 110—140°/18 mm. (2.5 g.). The latter reacted violently with zinc and was probably mainly 1 : 2 : 5-tribromopentane. A portion (36 g.) of fraction (1) was shaken with hydrochloric acid (15%); much heat was evolved, and the product was washed with water and distilled, giving: (a) b. p. 65—67°/18 mm. (13.6 g.; tetrahydrofurfuryl bromide); (b) b. p. 113—120°/18 mm. (slight decomp.; 7.6 g.); (c) b. p. 126—135°/17 mm. (7.7 g.). Fractions (b) and (c) were treated with powdered potassium hydroxide, and the product washed with water and distilled. It gave tetrahydrofurfuryl chloride, b. p. 51—56°/17 mm. (5.5 g.), and a compound, b. p. 75—80°/17 mm. (2.7 g.), which again became hot on treatment with hydrochloric acid.

(ii) In dioxan. The above reaction of the crude dibromohydrin (90 g.) with potassium hydroxide was repeated in the presence of dry dioxan (100 c.c.). The product, b. p. 75—82°/17 mm. (50 g.), was treated with cold hydrobromic acid (50%), and distillation afforded 3.0 g., b. p. 61—64°/17 mm. (tetrahydrofurfuryl bromide), and 16.5 g., b. p. 120—140°/12 mm. (slight decomp.).

A large amount of the product obtained by reaction of the crude dibromohydrin with potassium hydroxide was fractionated through a 10" column packed with stainless-steel rings, giving (a) b. p. 56—58°/12 mm., tetrahydrofurfuryl bromide, and (b) b. p. 74—76°/13.5 mm., which by its analysis (Found: C, 36.2; H, 5.35; Br, 48.4. C_5H_8OBr requires C, 36.4; H, 5.5; Br, 48.5%) and reactions with aqueous acids is considered to be 3-bromopropylethylene oxide.

The reactions described under (a) and (b) above suggest that in the absence of solvent the crude dibromohydrin gives

approximately equal amounts of the furan and the ethylene oxide derivative, whereas in the presence of dioxan the latter preponderates (7.4 : 2). In contrast to the dibromohydrin, the chlorobromohydrin (from the ethylene oxide and hydrochloric acid) on cyclisation with potassium hydroxide gives mainly tetrahydrofurfuryl chloride.

IV. *Fission with Hydrogen Bromide in Acetic Acid.*—The reagent was prepared by saturation of acetic acid at 20° with hydrogen bromide, generated by reaction of bromine with boiling tetralin. It contained 35.9% of hydrogen bromide and had *d* 1.34.

(a) *Tetrahydrofurfuryl alcohol.* The hydrogen bromide solution (175 c.c.) and the alcohol (48.5 c.c.) were mixed with cooling and left for 14 hrs. at room temperature. The product (116 g., 81%), isolated by pouring into water and washing with aqueous alkali, had b. p. 139–144°/11 mm. (Found: C, 29.55; H, 4.4; Br, 54.3, 54.6. $C_7H_{12}O_2Br_2$ requires C, 29.2; H, 4.2; Br, 55.6%), and its analysis, reaction with zinc (below), and method of formation indicate it to be 2 : 5-dibromo-n-amyl acetate.

Reaction with zinc. This compound (39 g.) was added to zinc (10 g.) in methyl alcohol (30 c.c.). There was no perceptible reaction in the cold. On boiling, a very slow evolution of hydrogen ensued, but after 2 hrs. only 1.5 g. of the zinc had been consumed. The product gave on distillation (i) b. p. 170–174°/775 mm., 65–68°/12 mm., 10 g. (Found: Br, 46.7. Calc. for C_5H_9OBr : Br, 48.5%), probably tetrahydrofurfuryl bromide, and (ii) b. p. 143–144°/11 mm., 12.5 g. (Found: C, 29.5; H, 4.3; Br, 54.5%), unchanged dibromoamyl acetate.

(b) *Tetrahydrofurfuryl alcohol at 100°.* The product from the alcohol (48.5 c.c.) and hydrogen bromide in acetic acid was heated to 100°, and a slow stream of hydrogen bromide introduced. After 8 hrs. the product, worked up as above, gave 90 g., b. p. 125–135°/8 mm., which, from its reaction with zinc, contained much tribromopentane. 89 G. of the product were treated with zinc, of which 12 g. reacted in 20 minutes, corresponding with 57 g. of tribromopentane. The product on distillation gave (i) b. p. 128–130°, 25 g. (Found: Br, 50.65. Calc. for C_5H_9Br : Br, 53.7%), essentially 1-bromo- Δ^4 -pentene, and (ii) b. p. 149–153°/17 mm., 11.5 g. (Found: Br, 54.6. Calc. for $C_5H_9OBr_2Ac$: Br, 55.6%), mainly unchanged dibromoamyl acetate. A small intermediate fraction (3.5 g.), b. p. 60–77°/18 mm., may have been tetrahydrofurfuryl bromide.

V. *Fission with Hydrogen Bromide in Acetic Anhydride (Acetyl Bromide).*—The reagent, prepared by saturation of acetic anhydride at 20°, contained 50.9% of hydrogen bromide and had *d* 1.54. It may be considered to be a mixture of acetic anhydride, acetyl bromide, acetic acid, and hydrogen bromide.

(a) *Tetrahydrofurfuryl acetate.* The ester (53 g.) was mixed with the hydrogen bromide solution and kept at room temperature for 18 hrs. Isolated in the usual way, the product (55 g.) had b. p. 140–144°/8 mm. and was a mixture (Found: Br, 45.7. Calc. for $C_5H_9OBrAc_2$: Br, 30.0%. Calc. for $C_5H_9OBr_2Ac$: Br, 55.6%).

(b) *Methyl tetrahydrofuroate.* The ester (31 g.) was mixed under cooling with the acetic anhydride reagent (55 c.c.) and kept at room temperature for 48 hrs. The solution was poured into water, and the lower layer shaken with sodium hydroxide solution (5%) until free from acid. Distillation gave 45 g., b. p. 140–143°/10 mm. (Found: Br, 29.3; Ac, 18.0. $C_8H_{13}O_4Br$ requires Br, 31.6; Ac, 17.0%). In the early stages of the distillation low-boiling material was caught in a Drikold-acetone trap. It contained an acetoxy group and formed a quaternary bromide with pyridine and was, therefore, evidently a mixture of methyl acetate and bromide.

The alkali wash obtained above was acidified, giving an oil (8 g.) which partly solidified on standing. The liquid portion contained an acetoxy residue but the solid, which crystallised from benzene in colourless plates, m. p. 83–84°, and decomposed at 140° evolving hydrogen bromide, contained bromine but not acetoxy (Found: C, 30.65; H, 4.45; Br, 39.55. $C_8H_{13}O_4Br$ requires C, 30.5; H, 4.6; Br, 40.6%). In view of the reactions and the evidence quoted earlier in discussion, it is highly probable that the ester, acetoxy-acid, and acetoxy-free acid represent successive stages of hydrolysis and are respectively methyl δ -bromo- α -acetoxyvalerate, δ -bromo- α -acetoxyvaleric acid, and δ -bromo- α -hydroxyvaleric acid.

(c) *Acetotetrahydrofurfurylamide.* The acetyl derivative (13.4 c.c., 14.3 g., 0.1 g.-mol.) and hydrogen bromide in acetic anhydride (30 c.c.) were mixed and kept for 2 hrs. The solid product was treated with aqueous sodium hydroxide (30%) with cooling until neutral. The organic layer was separated by ether extraction. Extensive decomposition occurred on attempted distillation, with loss of hydrogen bromide and acetic acid. Analysis of the crude material, however, indicated that the expected fission product, bromoacetoxyacetopentylamide, had been obtained (Found: N, 5.55; Br, 27.05; Ac, 29.6. $C_9H_{16}O_2NBr$ requires N, 5.3; Br, 30.1; 2Ac, 32.3%).

The crude fission product was heated to 100° with excess of silver acetate in glacial acetic acid for 2 hrs. The weight of silver bromide produced indicated that 70% of the bromine had been replaced. The product, distilled with a little decomposition, b. p. 170–193°/3 mm., still contained bromine (Found: Br, 10.8%). Another sample of the crude fission product was heated with silver acetate with stirring for 24 hrs. The product, b. p. 175–185°/3 mm., contained very little bromine (Found: Br, 0.7%) and was mainly 2 : 5-diacetoxyaceto-n-amylamide (Found: Ac, 52.0. $C_{11}H_{19}O_6N$ requires 3Ac, 52.6%). This compound, like the crude bromo-diacetyl derivative, was completely miscible with water although it was readily salted out.

(d) *Tetrahydropyran.* After 5 days at room temperature tetrahydropyran with hydrogen bromide in acetic acid gave a product, b. p. 97–102°/9 mm. (Found: C, 35.2; H, 5.75; Br, 47.95; Ac, 12.9%). The substance being assumed to be a mixture of bromoacetoxy- and dibromo-pentane, the analysis indicates that 29 mols. % of the latter were present.

After 8 days with hydrogen bromide in acetic anhydride, the product contained 13 mols. % of the dibromide (Found: Br, 42.75%). From 48 g. of tetrahydropyran and 60 c.c. of acetic anhydride solution after 6 days the product consisted of unchanged pyran (15 g.), and 5-bromo-n-amyl acetate (1-bromo-5-acetoxy-n-pentane), b. p. 109–110°/15 mm. (Found: Br, 39.1. $C_7H_{13}O_2Br$ requires Br, 38.2%), containing only 2.5 mols. % of dibromide. These are considered to be the best conditions for preparing this acetate.

On heating the pyran in acetic acid under reflux for 6 hrs. whilst hydrogen bromide was passed in, a product was obtained, b. p. 98–99°/10 mm., 61 g. (Found: Br, 67.75%), containing only 6 mols. % of bromoamyl acetate.

Preparation of Tetrahydrofurfuryl Chloride.—Tetrahydrofurfuryl alcohol and phosphorus trichloride either alone or in pyridine failed to afford the chloride. Kirner (*J. Amer. Chem. Soc.*, 1930, **52**, 3251), using thionyl chloride in pyridine, obtained a 75% yield after considerable trouble. Omitting pyridine, we have found that thionyl chloride alone gives a 46% yield. The alcohol (10.2 g., 0.1 g.-mol.) was heated to 100°, and thionyl chloride (80 c.c.) added slowly. The mixture was then distilled in a vacuum, and the product, b. p. <100°, washed with sodium hydroxide solution (15%). Tetrahydrofurfuryl chloride, b. p. 152–154°, was insoluble and could be dried over anhydrous potassium carbonate. The low yield appears to be due to the formation of a chlorosulphite.