

THE TETRAHYDROPYRAN-2-OLS

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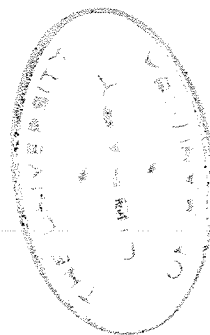
THEIR DERIVATIVES

by

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REACTIONS OF SOME HALOGEN DERIVATIVES OF
TETRAHYDROPYRAN-2-OL

By E. H. CHARLESWORTH AND A. GIESINGER

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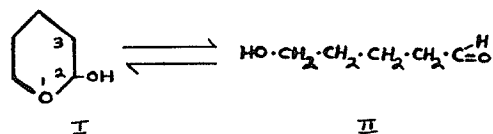
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ABSTRACT

The 3-halotetrahydropyran-2-ols have been found to readily give derivatives of tetrahydrofurfural in aqueous alcohol under weakly basic or acidic conditions. In strongly alkaline solution tetrahydropyran-2,3-diol and its anhydro-polymers were formed. 3,3-Dichlorotetrahydropyran-2-ol and 2,3,3-trichlorotetrahydropyran have been converted by aqueous alkali to viscous sirups which appear to contain 2-hydroxytetrahydropyran-3-one and its tautomers. On oxidation with permanganate these sirups have yielded succinic acid.

INTRODUCTION

The aldehydic properties of tetrahydropyran-2-ol (I) were explained by Paul (7, 9) on the assumption that it existed in equilibrium with δ -hydroxyvaleric aldehyde (II). Paul's view has since been confirmed by other workers,



particularly Schniepp and Geller (14) and Woods and Sanders (17). The latter authors obtained a crystalline 2,4-dinitrophenylhydrazone.

The 3-halotetrahydropyran-2-ols (IV), readily prepared by the hydrolysis of the corresponding 2,3-dihalides (III) in the presence of mild alkaline reagents, have been reported by Paul (8, 10, 11), by I.G. Farben (5), and by Hawkins and Bennett (1, 2). As these possess some aldehydic properties, it has been assumed that they exist in equilibrium with a δ -hydroxyvaleric aldehyde form (V). Crystalline derivatives, however, are not reported, although Paul (11) did isolate a liquid oxime of tetrahydrofurfural following the hydrolysis of the 2,3-dichloride. Paul (9) found that 3-bromotetrahydropyran-2-ol reacted rapidly with phenylhydrazine, but gave only crystals of phenylhydrazine hydrobromide. This latter reaction suggests that in the presence of an organic base the bromohydrin loses hydrogen bromide more rapidly than it acts as an aldehyde.

In view of their undoubted aldehyde properties, it seemed desirable to prepare crystalline derivatives of these halotetrahydropyrans and thus to determine the nature of the aldehydic substances derived from them. Both the chloro- and bromo-tetrahydropyranol were found to react with substituted phenylhydrazines to yield the same halogen-free derivatives, namely,

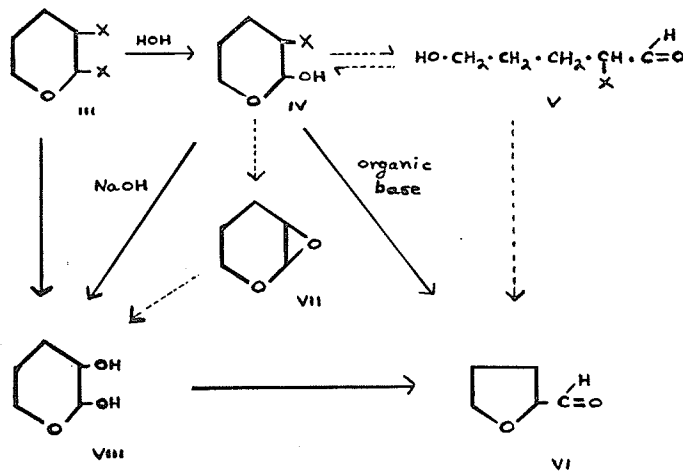
- (i) a 2,4-dinitrophenylhydrazone, m.p. 133-134°;
- (ii) a 2,4-dinitrophenylosazone, m.p. 242°;

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- (iii) a *p*-nitrophenylhydrazone, m.p. 146°;
 (iv) a *p*-nitrophenylosazone, m.p. 246°;
 (v) a *p*-benzylphenylhydrazone, m.p. 74–75°.

In all cases these derivatives are identical with corresponding products made from an authentic sample of tetrahydrofurfural (VI) prepared by the method of Scheibler, Sotscheck, and Friese (13). Hurd and Edwards (3) obtained the same derivatives from tetrahydrofurfural produced by heating tetrahydropyran-2,3-diol (VIII) under reduced pressure.

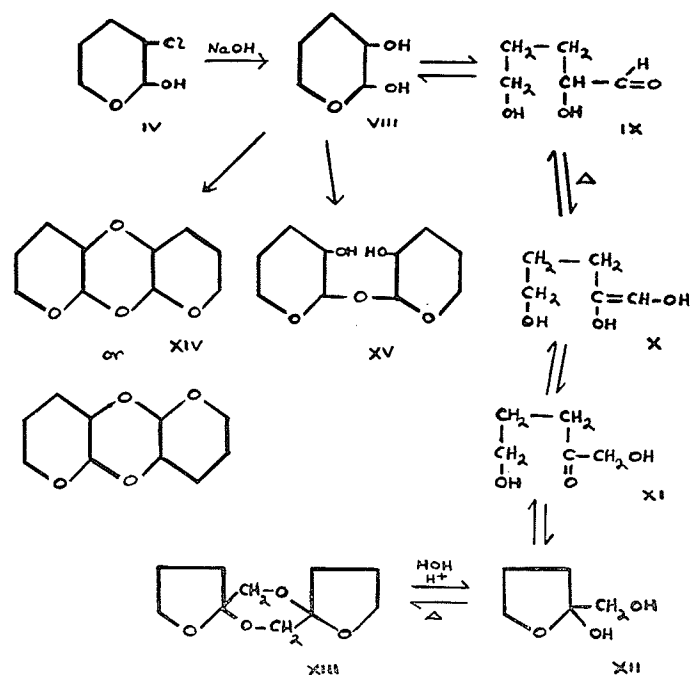


The 3-halotetrahydropyran-2-ols lose hydrogen halide so readily that they can be titrated with aqueous sodium hydroxide. In each case it is possible to isolate a quantitative yield of the sodium halide salt. We had hoped at first to use this method to obtain the oxide (VII). However, in view of the fact that an organic base when extracting hydrogen halide leaves tetrahydrofurfural as a residue, it seemed that the effect of sodium hydroxide might be the same and thus represent a convenient method of preparing tetrahydrofurfural.

The organic product from the reaction proved to be rather elusive. Organic solvents do not extract it in appreciable amounts from the aqueous mixture. Even continuous extraction proved inadequate. The water had to be removed almost completely, either by absorption on drying agents or better by evaporation, before the product could be taken up in organic solvent.

The nature of the product varies somewhat according to the conditions. If the reaction mixture is kept near room temperature throughout the process, a considerable portion of the product is soluble, with some difficulty, in ether. This ether-soluble substance is aldehydic, but it is a higher boiling liquid than tetrahydrofurfural. It gives the same dinitrophenylosazone, m.p. 242°, as tetrahydrofurfural, but not the phenylhydrazone obtainable from that substance. It readily reduces periodic acid to iodate and forms a 3,5-dinitrobenzoate, m.p. 174°. This substance seems to be tetrahydropyran-2,3-diol (VIII), which Hurd and Kelso (4) prepared by hydrogen peroxide oxidation of dihydropyran.

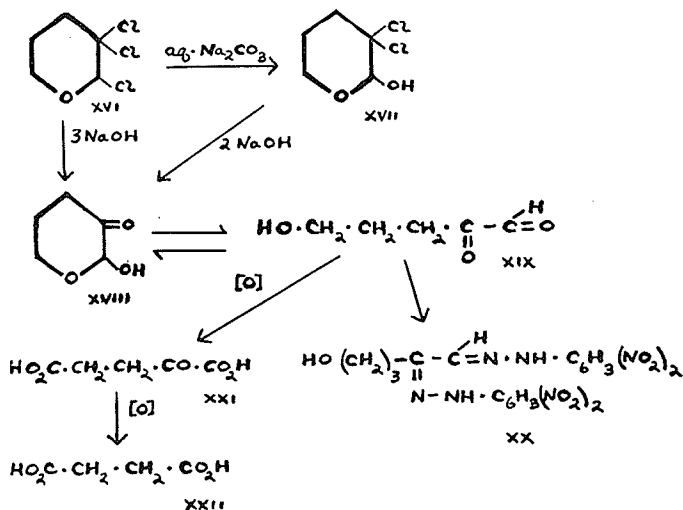
At higher reaction temperatures less of the product is ether-soluble. Small fractions can be extracted with other solvents, but the bulk is soluble only in alcohol and water. Evaporation of the solvent in each case leaves a high boiling sirup which is not easily purified by distillation. In one case a solid, m.p. 190°, precipitated from aqueous solution. In another case a chloroform extract yielded a solid, m.p. 101–102°. The properties of these substances indicate that they are the same $C_{10}H_{16}O_4$ materials as are reported by Hurd and Edwards (3), who obtained them by heating tetrahydropyran-2,3-diol. The lower melting of these two compounds was also obtained by Swadesh and Dunlop (16) from another source. The two groups of workers seem to agree that it has the structure XIII and that it is formed from the diol by the route shown. The structure of the higher melting compound has not been established, but the indications are that it may be XIV. Compound XV has been isolated by Hurd and Kelso (4). Our high boiling sirups are probably mixtures of compounds XIII, XIV, and XV and perhaps more complex structures.



No material was isolated that seemed to be the oxide (VII). If formed at all, it was apparently unstable and hydrolyzed to form the diol (VIII). Other attempts by Paul and Tchelitcheff (12) and by Hurd and Edwards (3) to obtain the oxide have not been too successful.

3,3-Dichlorotetrahydropyran-2-ol (XVII) is mentioned briefly in the literature in a wartime I.G. Farben report (6) and in a German patent (18). We have prepared this substance by warming the 2,3,3-trichloride (XVI) with an equivalent of sodium carbonate solution. It is less aldehydic than the simpler halohydrins discussed earlier, but resembles them in some of its properties. It reduces Fehling's solution when warmed for some time; it

forms the same dinitrophenylosazone, m.p. 242°, but does not form an intermediate hydrazone. When dissolved in warm alcohol, it can be titrated with aqueous sodium hydroxide solution and neutralizes two equivalents of the base. In this reaction the 3,3-dichlorotetrahydropyran-2-ol loses its entire halogen content.



When 2,3,3-trichlorotetrahydropyran (XVI) is warmed and stirred with 3 moles of aqueous sodium hydroxide solution, the organic layer gradually disappears and the alkali is neutralized. A dark red reaction mixture results. The organic product can be isolated by evaporating the water and extracting the residue with alcohol. A quantitative yield of sodium chloride is left behind. On evaporation of the alcohol a viscous dark red halogen-free sirup is left. This material is thought to contain an equilibrium mixture of tetrahydropyranone-3-ol-2 (XVIII) and α-keto-δ-hydroxyvaleric aldehyde (XIX), together with more complex substances. It is aldehydic, reducing Fehling's solution rapidly when warmed. With 2,4-dinitrophenylhydrazine it gives, near room temperature, an almost immediate precipitate of the expected 2,4-dinitrophenylosazone (XX), m.p. 242°. On oxidation with potassium permanganate, both in alkaline and acid solution, succinic acid (XXII) has been obtained. Intermediate compounds such as α-ketoglutaric acid (XXI) have not been isolated as yet from the above oxidations or with milder oxidizing agents.

EXPERIMENTAL

Derivatives of 3-Halotetrahydropyran-2-ols

Both 3-chloro- and 3-bromo-tetrahydropyran-2-ol were prepared by the hydrolysis of the corresponding dihalides with aqueous sodium carbonate solution, following the directions of Hawkins and Bennett (2) for the preparation of 3-chlorotetrahydropyran-2-ol. The methods used for the preparation of the derivatives listed below were essentially those described by Shriner and Fuson (15).