Acid-catalyzed Reaction of Aldehydes and Ketones with Formaldehyde in Non-aqueous Media

BENGT WESSLÉN and LARS OLOF RYRFORS

Institutionen för organisk kemi, Chalmers Tekniska Högskola, Göteborg, Sweden, and Perstorp AB, Perstorp, Sweden

Several examples of acid-catalyzed formation of 1,3-dioxanes from ketones and formaldehyde have been reported in the literature. According to Olsen et al., the reaction between acetone and paraformaldehyde in refluxing acetic acid solution in the presence of sulfuric acid yields compound I. Wöllner et al. report that under similar conditions the bisformals of 2,2,4,4-tetraakis(hydroxymethyl)-3-pentanone (II) and 5-methyl-3,3,5-tris(hydroxymethyl)-4-tetrahydroprpyranol (III) are formed from diethyl ketone and methyl ethyl ketone, respectively. In the latter case, the keto group has undergone reduction.

Similar exhaustive substitution of the π-hydrogen atoms has been observed when cyclohexanone was treated with an excess of paraformaldehyde in the HOOAc–H₂SO₄ system. If an excess of cyclohexanone was used, the bisformal of 2,6- or 2,2-bis(hydroxymethyl)cyclohexanone hydrate (IVa or b) and the formal of 2,2-bis(hydroxymethyl)cyclohexanone were obtained.

Acetophenone has been found to react with formaldehyde in an acidic medium with the formation of 5-benzoyl-1,3-dioxane.

The reaction of propionic aldehyde with paraformaldehyde in HOAc–H₂SO₄ was found by Olsen to give the 1,3-dioxane V in moderate yield. As in the formation of III, reduction of the carbonyl group occurred in this reaction.

In the course of investigations regarding various reactions of formaldehyde in non-aqueous media we have found that aliphatic ketones and aldehydes react readily with trioxane in refluxing chloroform solution in the presence of aluminum chloride, boron trifluoride etherate, or sulfuric acid as catalysts. For example, the reaction of methyl ethyl ketone (1 mole) in 400 ml of chloroform with trioxane (1.33 moles) gave 5-acetyl-5-methyl-1,3-dioxane (VI) in yields of 50 and 75%, based on the amount of ketone used, when aluminum chloride (0.5 mole) and boron trifluoride etherate (0.1 mole), respectively, were added as catalysts. The same reaction product (VI) was obtained in > 90% yield, based on the amount of trioxane added, if methyl ethyl ketone (1 mole) and trioxane (0.5 mole) in 200 ml of chloroform were allowed to react in the presence of sulfuric acid (0.16 mole). Under the latter conditions trioxane reacted with methyl propyl ketone and diethyl ketone to give the 1,3-dioxanes VII, b.p. 76–77°, and VIII, b.p. 67–68°, in yields of 80%. As indicated by v.p.c., the crude reaction mixtures contain only small amounts of volatile by-products.

It is interesting to note that the reaction of 1 mole of the ketone with 3 moles of formaldehyde (= 1 mole of trioxane) to a 1,3-dioxane is greatly favoured, even if only 1.5 moles of formaldehyde (= 0.5 mole of trioxane) are used per mole of ketone. Furthermore, the formation of the 1,3-dioxanes VI or VII indicates that the π-methylene group reacts more readily than the π-methyl group, which is in accordance with the structural course reported for related acid-catalyzed reactions of unsymmetrical ketones.

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The formyl substituted 1,3-dioxanes IX, b.p.$_{84}$ 59—60°, and X, b.p.$_{84}$ 55—56°, were obtained when propionic aldehyde and butyric aldehyde, respectively, were treated with trioxane, boron trifluoride etherate being used as catalyst. In addition to IX, 1-methyl-bicyclo[4.4.0]-3,5,7,9-tetraoxadecane (XI), m.p. 45—46°, was formed from propionic aldehyde, and the corresponding 1-ethyl compound XII, m.p. 25—28°, was obtained in addition to X from butyric aldehyde.


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