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4-OXO-1,3-DIOXAN AND ITS METHYL DERIVATIVES

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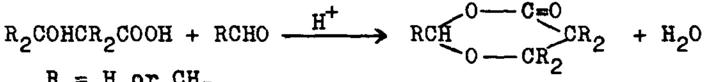
Irrespective of the fact that 1,3-dioxans have been recently intensively studied very little attention has been paid to the preparation of 4-oxo-1,3-dioxans.[1,2] Hennes and Gundiger[2] synthesized some chlorinated derivatives in concentrated sulphuric acid starting from chloral hydrate and a chlorinated 3-hydroxy acid and investigated their herbicidal influences. Kahn, Jr. and Cohen studied the effect of 2,2,6-trimethyl-4-oxo-1,3-dioxan on cation transfer in incubated cold-stored human erythrocytes.[1] Taking into account also their conformationally interesting structure we wish to report the preparation of several methyl-substituted 4-oxo-1,3-dioxans by condensing 3-hydroxy acids with the appropriate aldehydes in slightly acidic media:



(1)

R = H or CH_3

The ethyl esters of 3-hydroxy acids[3] were hydrolysed in methanolic potassium hydroxide solution. The methanol was distilled off and the remaining potassium salts were treated with 20 per cent sulphuric acid to give a pH of 2-3, after which the acids were extracted with ether in a continuous extractor. The ethereal solutions were dried over sodium sulphate and the ether was then removed by distillation. The crude acids were not purified further excepting 2,2-dimethyl-3-hydroxypropanoic acid (m.p. 123-4°C after crystallization from CCl_4), 2,2-dimethyl-3-hydroxybutanoic acid (b.p. 122-128°C/6 torrs, m.p. 33-34°C) and 2,2,3-trimethyl-3-hydroxybutanoic acid (m.p. 152-3°C after crystallization from ligroin b.p. 40-60°C) owing to their relative low stability to heat. The yields of the acids varied from 25 to 89 per cent and the purities exceeded 90 per cent in most cases when checked by NMR spectroscopy. 3-Hydroxybutanoic acid was a purum grade product of Fluka AG.

4-Oxo-1,3-dioxans: One equivalent of a 3-hydroxy acid, 2-3 equivalents of formaldehyde (as paraformaldehyde) or acetaldehyde (as paraldehyde) and a slight amount of *p*-toluenesulphonic acid or 5-6 g of Dowex 50 cation exchange resin were added to dichloromethane and the mixture was boiled in a water entrainment unit. After the theoretical amount of water had been removed, the reaction mixture was filtered and the dichloromethane was distilled off. The residue was then fractionated at reduced pressure. Derivatives with a single methyl substituent on either the 5- or 6-carbon atom are easily decomposed by acidic impurities and heat during purification by distillation. The derivatives having geminal methyl substituents on one or both of these carbon atoms can be distilled without any special precautions.

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Physical constants of the 4-oxo-1,3-dioxans

Methyl subst.	B.p. °C/torr	M.p. °C	d_4^{20}	n_D^{20}	Yield %	Notes
5	58-9/2			1.4470	10	a, b
6	70-1/3			1.4432	39	a
2,5	57-8/2			1.4386	20	a, b, c
2,6	60-1/2				55	a, d
5,5	54-6/2	44-6			43	e
6,6	102-4/12		1.1063	1.4397	54	e
2,5,5	54-6/2	27-8			46	e
2,6,6	102-4/12		1.0519	1.4348	33	e
2,5,6	96-8/10				46	a, f, g
5,6,6	102-4/9	42-3			81	e
5,5,6	79-80/4	38-9			78	e
2,5,6,6	101-5/9			1.4403	70	e, h
2,5,5,6	66-7/4			1.4372	80	e, i
5,6	98-100/10			1.4435	56	a, j
5,5,6,6		101-2			38	e, k
2,5,5,6,6	57-8/2	39-40			54	e

[a] Catalyst Dowex 50. [b] Partly decomposed when distilled. [c,d,f,h,i,j] Isomer ratios 55:45, 95:5, 25:75, 85:15, 95:5 and 70:30, respectively. [e] Catalyst p-toluenesulphonic acid. [g] The smaller component contained still two isomers. [k] Purified by sublimation.

The purities of the prepared compounds were checked by gas chromatography and NMR spectroscopy. Some reactions yielded a mixture of isomers, most of which could be isolated on a preparative gas chromatograph. The properties of these compounds (NMR spectra and kinetic and equilibrium data) will be discussed in other publications. Attempts were also made to carry out condensation reaction (1) with acetone, but they were unsuccessful. Apparently, the reactions are complicated and some modifications of the procedure are needed in the case of this ketone. Likewise, the products formed from 3-hydroxypropanoic acid could not be isolated, although the theoretical amount of water was liberated in the reactions. These reactions are being studied in more detail.

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