Conversion of Dialdehydes into Cyclic α-Ketols by Thiazolium Salts: Synthesis of Cyclic 2-Hydroxy-2-enones

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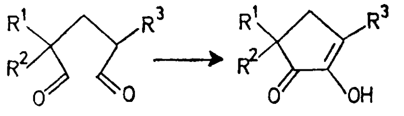
Summary Pentanedials and hexanedials are cyclised by thiazolium salts and triethylamine in acetonitrile into 2-hydroxy-cyclopentanones and -cyclohexanones, easily oxidised to the 2-hydroxy-2-enones.

The thiazolium ion-catalysed dimerisation of aldehydes to acyloins,[1] modelled on the cyanide ion-catalysed benzoin condensation[2] and particularly on reactions catalysed by enzymes containing thiamine,[3] has hardly been used in synthesis, probably because it seems applicable only to symmetrical acyloins.[4] We point out that thiazolium ion-catalysed cyclisation of dialdehydes is a useful synthesis of cyclic α-ketols and thence of 2-hydroxy-2-enones, several of which are important flavouring materials.[5]

Treatment of anhydrous glutaraldehyde (Ia) (4·44 mmol) in acetonitrile with 3-benzyl-4-methylthiazolium chloride (0·44 mmol) and triethylamine (0·88 mmol) at 80 °C gave 2-hydroxycyclopentanone in 78% yield, which was oxidised by copper(II) acetate in a mixture of methanol, water, and acetic acid to 2-hydroxycyclopent-2-en-1-one (IIa) (81%). A range of substituted glutaraldehydes was synthesised by addition of the appropriate $\alpha\beta$-unsaturated aldehyde to an enol ether[6] or preferably enamine[7] and hydrolysis of the resulting dihydropyran. 2-Hydroxy-3-methylcyclopent-2-en-1-one (IIb) ('corylone', 'cyclotene' *etc.*) was prepared in 50% overall yield from prop-2-enal and 1-piperidinopropene as illustrated in the Scheme. The Table records the yields of other hydroxycyclopentenones formed on cyclisation and oxidation of the appropriate dialdehyde.

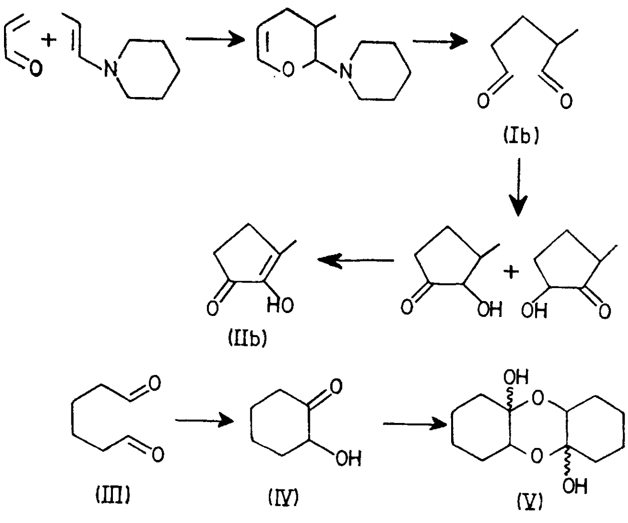


(I) (II)

TABLE

Yields of 2-hydroxycyclopentenones formed on cylisation and oxidation of substituted pentanedials

Pentanedial (I)				% Yield of corresponding 2-hydroxycyclopentenone (II)
	R^1	R^2	R^3	
a	H	H	H	63
b	H	H	Me	63
c	Me	Me	H	88
d	Me	H	Me	74
e	$-CH_2CH{=}CHCH_2CH_2-$		H	68



SCHEME

Unfortunately, the isomeric α-ketols formed in the cyclisation of an unsymmetrical dialdehyde are equilibrated by the triethylamine during the reaction, so that in its present form the thiazolium ion-catalysed cyclisation cannot be used to make one specific isomer. (This does not matter, of course, if the α-diketone is required.)

The thiazolium salt and triethylamine in acetonitrile cyclised hexanedial (III) into 2-hydroxycyclohexanone (IV) in 78% yield which rapidly dimerised to a mixture of the hemi-acetals (V).

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[4] For extension of the reaction to β-addition of aldehydes to acrylic compounds, see H. Stetter and H. Kuhlmann, *Synthesis*, 1975, 379 and refs. there.

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