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ONE STEP CONVERSION OF ALDEHYDES TO ESTERS

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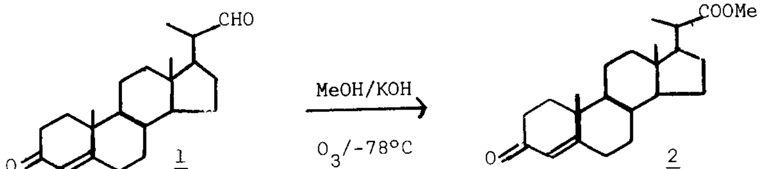
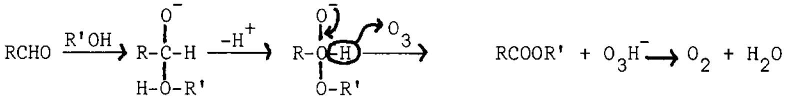
The ozonization of aldehydes[2] has been studied by several groups mainly from a mechanistic point of view. In 1971 Deslongchamps and co-workers[3] reported the oxidation of acetals to the corresponding esters and alcohols with ozone: $RCH(OR')_2 + O_3 \rightarrow RCOOR' + R'OH + O_2$. The reaction constitutes a novel two-step method for converting an aldehyde into an ester. While studying the ozonolysis of enols in our laboratory we encountered an interesting oxidation reaction, which led to the examination of the oxidation of aldehydes in basic media. As shown below, a set of reaction conditions was found that resulted in a feasible one-step conversion of aldehydes to esters. Aside from its intrinsic mechanistic interest this reaction may also be of synthetic utility in certain instances.

In a typical experiment the steroidal aldehyde 1[4] (0.5 g) was dissolved in 75 ml of 10% methanolic potassium hydroxide solution and cooled to -78°C. Ozone was passed through the solution for 90 mins to yield upon work up (dilution with water and ether extraction) 85% of methyl 3-oxo-bisnor-4-cholenate (2). The generality of this reaction was confirmed (Table 1) by obtaining similar results with other representative aldehydes. Ethanol could be substituted for methanol to provide the corresponding ethyl ester. In our attempts to extend this reaction to higher alcohols we were faced with practical problems, the major one being the insolubility of potassium hydroxide in these alcohols at -78°C. This could be overcome by adding the aldehyde to a solution of lithium alkoxide in tetrahydrofuran at -78°C and passing ozone through the mixture for 90 mins. Typical examples and yields are summarized in Table 1, showing that secondary and neopentyl esters can be prepared by this procedure. α,β-Unsaturated aldehydes, such as cinnamaldehyde, are unsuitable since they suffer initial retroaldolization followed by oxidation (e.g. cinnamaldehyde → methyl benzoate).



The mechanism probably resembles that of the Cannizaro and Tischenko[5] reactions, the oxidation step being the transfer of hydride ion to the electrophilic ozone. Control experiments showed that KOH or lithium alkoxide and continuous passage of O_3 is necessary for oxidation to occur. (An alternative mechanism[6] involving O_3 attack on the C-H bond of the hemiacetal with the production of a hydrotrioxide (A)[3] decomposing into acid and ester cannot be excluded).



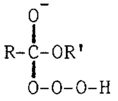


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Table 1. Oxidation of Aldehydes to Esters with Ozone in Basic Media

Aldehyde (R-CHO)	Alcohol (R'-OH)	Solvent	Esters*(yield %)
Cyclohexyl	MeOH	MeOH/KOH	RCO_2Me (58)
	EtOH	EtOH/KOH	RCO_2Et (60)
	MeOH/MeLi	THF	RCO_2Me (63)
	EtOH/MeLi	THF	RCO_2Et (56)
Phenyl	MeOH	MeOH/KOH	RCO_2Me (66)
	EtOH	EtOH/KOH	RCO_2Et (60)
	MeOH/MeLi	THF	RCO_2Me (57)
	EtOH/MeLi	THF	RCO_2Et (37)
3-Oxo-bisnor-4-cholenyl	MeOH	MeOH/KOH	RCO_2Me (85)
	EtOH	EtOH/KOH	RCO_2Et (87)
	$(CH_3)_2CHOH$/MeLi	THF	$RCO_2CH(CH_3)_2$ (42)
	$CH_3(CH_2)_5OH$/MeLi	THF	$RCO_2(CH_2)_5CH_3$ (42)
	$CH_3CH_2C(CH_3)_2CH_2OH$/MeLi	THF	$RCO_2CH_2C(CH_3)_2CH_2CH_3$ (63)
n-Heptyl	MeOH/MeLi	THF	RCO_2Me (66)
	EtOH/MeLi	THF	RCO_2Et (58)
	$(CH_3)_2CHOH$/MeLi	THF	$RCO_2CH(CH_3)_2$ (36)

*The other product of this reaction is the corresponding acid. Esters are not hydrolyzed to the acids under the reaction conditions (-78°C, 90 min).

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