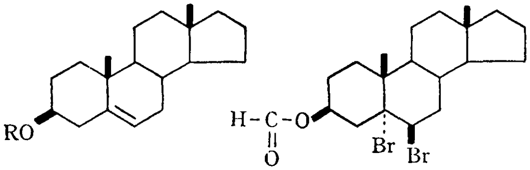
Oxidative Cleavage of Ethers

By I. T. HARRISON and S. HARRISON
(*Syntex Research,* 3401 *Hillview Ave., Palo Alto, California*)

THE protection of aliphatic and alicyclic hydroxyl groups by conversion into the methyl ether is a reaction of limited synthetic utility due to the low yields generally obtained in the subsequent ether-cleavage reactions. We find that anhydrous chromium trioxide[1] in acetic acid converts methyl ethers into the corresponding formate, hydrolysable by base to the alcohol, in yields of about 50—60%.

For example, hexadecyl methyl ether, $Me[CH_2]_{15}$-OMe, (200 mg.) oxidised by a suspension of chromium trioxide (1 g.) in a mixture of acetic acid (10 ml.) and dichloromethane (10 ml.) for 1 hr. at 20° gave, after chromatography of the products on silica gel, a 48% yield of hexadecyl formate, $Me[CH_2]_{15}OCHO$, identified by infrared comparison with an authentic sample, ν_{max} (film) 1730 and 1179 cm.$^{-1}$ and by hydrolysis to hexadecanol m.p. 49—50° not depressed on admixture with an authentic sample. Hexadecanoic acid, m.p. 61—62°, was a minor product of the reaction. A similar oxidation of ethyl hexadecyl ether, $Me[CH_2]_{15}OEt$, gave hexadecanoic acid (55%) as the major product, and hexadecyl acetate (9%), m.p. 25°, not depressed by an authentic sample.

Oxidation of 3β-methoxyandrost-5-ene (I) in acetic acid, after prior protection of the double bond as the dibromide by addition of excess bromine, formed the formate (II). Regeneration of the double bond with zinc dust in acetic acid then gave 3β-formyloxyandrost-5-ene (III), ν_{max} (film) 1721 and 1173 cm.$^{-1}$, which was hydrolysed by alcoholic sodium hydroxide solution to the corresponding alcohol (IV), m.p. and mixed m.p. 133—134°, isolated in 62% overall yield.



(I) R = Me
(III) R = HCO
(IV) R = H

(II)

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[1] L. F. Fieser, *J. Amer. Chem. Soc.*, 1948, **70**, 3237.