Tetrahedron Letters,Vol.24,No.11,pp 1189-1190,1983 0040-4039/83/111189-02$03.00/0
Printed in Great Britain

A NEW METHOD FOR CLEAVING METHYL AND METHYLTHIOMETHYL ETHERS

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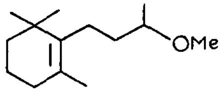
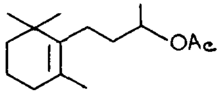
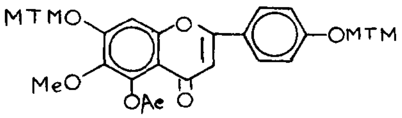
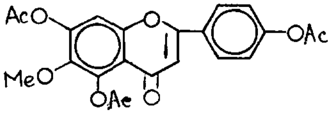
Summary: Chlorotrimethylsilane (CTMS) and acetic anhydride has been shown to cleave methyl and methylthiomethyl ethers to furnish the corresponding acetates in excellent yield. Tertiary alcohols can be acetylated efficiently with this reagent combination.

Trimethylsilyl-derived reagents find an immense application in organic synthesis[1]. We argued that a combination of chlorotrimethylsilane and acetic anhydride would generate acylonium ion ($CH_3C^+= O$) capable of reacting with nucleophilic species. This was proved to be the case indeed when the reaction of cholest-5-en-3 β-ol methyl ether with CTMS/Ac_2O furnished 3 β-acetoxycholest-5-ene (entry 1 Table I) in 90% yield. The corresponding acetate is formed with retention of configuration has been proved through examples given at entry 1, 2 and 3 of Table I. Under similar reaction conditions methyl ethers of phenols

Table-I. Cleavage of methyl and methylthiomethyl ethers[a]

Entry	Substrate	Time in min/rt	Product	yield[b] (%)
1	Cholest-5-en-3β-ol methyl ether[c]	20	3β-Acetoxycholest-5-ene	90
2	Cholestan-3β-ol methyl ether[c]	15	3β-Acetoxy-5α-Cholestane	95
3	Cholestan-3β,5α-diol 3-methyl ether[c]	30	Cholestan-3β,5α-diol diacetate	70
4	Carveol methyl ether	25	Carveol acetate	90
5		30		85
6	Cholest-5-en-3β-ol methylthiomethyl ether	10	3β-Acetoxycholest-5-ene	60
7	Cholestan-3β-ol methylthiomethyl ether	15	3β-Acetoxy-5α-Cholestane	70
8	$CH_3(CH_2)_{14}$ CH_2O MTM	10	$CH_3(CH_2)_{14}$ CH_2OAc	65
9		25		95
10	Linalool	10	Linalyl acetate	90

[a] All compounds mentioned in Table I gave satisfactory analysis, IR, NMR and Mass spectral data.

[b] Yields of the isolated products of $\rangle$ 90% purity as determined by t.l.c., IR and NMR spectroscopy.

[c] The corresponding propionate and butyrate was obtained when Ac_2O was replaced with propionic and butyric anhydride respectively.

remain uneffected[2]. However it was further discovered that methylthiomethyl(MTM) ethers of aliphatic and aromatic alcohols are cleaved efficiently with this reagent combination (entry 6-9 Table I). MTM is a useful protective group for aliphatic and aromatic hydroxyl groups but the reaction conditions described for its deprotection may not be universally applicable[4-7]. BF_3/Ac_2O - an alternative to our method leads to a mixture of the corresponding epimeric acetates and elimination products with completely saturated steroidal methyl ethers[8].

It was found that the combination of acetyl chloride and acetic anhydride was ineffective for the above mentioned cleavage reactions. However, evidence in support of acylonium ion generation in the reaction medium was forthcoming from the observation that tert-alcohols undergo acetylation under the reaction conditions (entry 3 & 10 Table I)[9]. It would therefore be a useful method for the acetylation of a tertiary hydroxyl group.

In a typical experiment a solution of the substrate (0.5 mmol) in acetic anhydride (2 ml) is treated with chlorotrimethylsilane (2.0 mmol) with stirring at rt, monitoring the reaction by TLC. A few drops of dry dichloromethane were added when the substrate was not soluble in Ac_2O.

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9. The mechanistic details of the reaction are under investigation and will be given in a full publication.

(Received in UK 17 November 1982)