A New Method for the Deoxygenation of Tertiary and Secondary Alcohols

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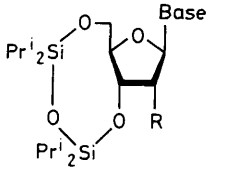
The derivatisation of alcohols as their methyl oxalyl esters is shown to be a convenient and selective method for deoxygenation by stannyl radicals.

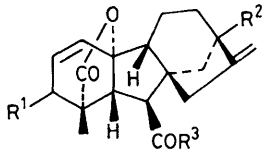
There are now many methods in the literature[1,2] for the deoxygenation of alcohols by photochemical or stannane reduction of suitable derivatives. More recently Barton and others have employed thiobenzoates,[3,4] *S*-methyl dithiocarbonates,[3,5] thiocarbonylimidazolides,[6] and cyclic thiocarbonates[3,5] for the deoxygenation of secondary alcohols. Robins *et al.*,[7,8] in a similar procedure, reported a mild method for functionalisation of the 2′-hydroxy group of the nucleoside (**1**) as the *O*-phenylthiocarbonate derivative (**2**) which overcame the problems associated with a strong base. Barton and McCombie also reported[3] a general synthesis of *O*-alkyl thioesters under essentially neutral conditions. We now describe a new method for the efficient and selective removal of secondary and tertiary alcohols which employs methyl oxalyl esters prepared under mild conditions without added base.



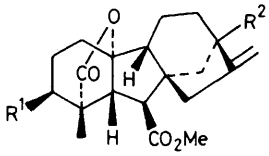
R

(**1**) OH

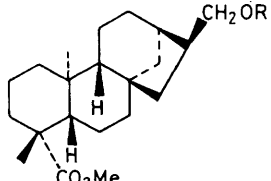
(**2**) OCSOPh



	R^1	R^2	R^3
(**3**)	OAc	OX	Me
(**4**)	OAc	OH	Me
(**5**)	OAc	H	Me
(**6**)	OAc	OH	OH
(**7**)	OAc	OX	Cl
(**8**)	OAc	OX	OH
(**9**)	OAc	H	OH
(**10**)	OH	OH	OH
(**11**)	OH	H	OH



	R^1	R^2
(**12**)	OAc	OH
(**13**)	OAc	H
(**14**)	OAc	OX
(**15**)	OX	H
(**16**)	OH	H
(**17**)	H	H
(**18**)	OX	OAc
(**19**)	OH	OAc
(**20**)	H	OAc
(**21**)	$OCOCO_2H$	H
(**22**)	$OCOCO_2H$	OAc

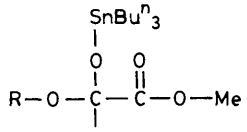


R

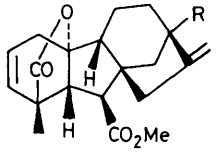
(**25**) OX

(**26**) H

(**27**) $COCO_2H$



(**28**)



R

(**23**) H

(**24**) OAc

OX = $OCOCO_2Me$

We find that methyl oxalyl esters are readily preparable from primary, secondary, and tertiary alcohols, from either oxalyl chloride (stirring at room temperature in an aprotic solvent) with methanolysis on work-up, or from methyl oxalyl chloride in an aprotic solvent such as tetrahydrofuran under refluxing conditions. For example, the methyl oxalyl ester (**3**) was prepared from gibberellin A_3 (GA_3) methyl ester 3-acetate (**4**) and methyl oxalyl chloride. With tri-n-butylstannane and 2,2′-azo(2-methylpropionitrile) in refluxing toluene the oxalyl ester (**3**) gave GA_7 methyl ester 3-acetate (**5**) as the sole product in an overall yield of 65%. No reaction occurred in the absence of initiator or tri-n-butylstannane or after prolonged irradiation at 356 nm. When applied to GA_3 3-acetate (**6**), reaction with methyl oxalyl chloride gave the 13-methyl oxalate derivative of the acid chloride (**7**) which was readily hydrolysed on work-up to the free acid (**8**). Reduction of the oxalate (**8**) followed by hydrolysis of the 3-acetate (**9**) provided an efficient 4-step conversion of GA_3 (**10**) into GA_7 (**11**) in an overall yield of 50%. Gibberellin A_1 methyl ester 3-acetate (**12**) was also converted into GA_4 methyl ester 3-acetate (**13**) *via* the oxalyl ester (**14**).

The ease of preparation of the methyl oxalyl esters (**3**) and (**14**) is noteworthy, in contrast to our experienced difficulty in forming the corresponding thiocarbonate[3] and thiobenzoate[3] derivatives. Robins *et al.*[7,8] have prepared *O*-phenyl thiocarbonates from hindered secondary alcohols with *O*-phenyl chlorothiocarbonate and 4-dimethylaminopyridine in acetonitrile. However, GA_3 methyl ester 3-acetate (**4**) gave only starting material.

The secondary methyl oxalate (**15**) of GA_4 methyl ester (**16**) gave GA_9 methyl ester (**17**) and a small amount of GA_4 methyl ester (**16**), when refluxed in toluene in the presence of tri-n-butylstannane and 2,2′-azo(2-methylpropionitrile). Similarly the methyl oxalate (**18**) of GA_1 methyl ester 13-acetate (**19**) gave GA_{20} methyl ester 13-acetate (**20**) and a small amount of (**19**). In both cases abstraction of a *cis*(β)-proton did not occur since the $\Delta^{2,3}$-products (**23**) and (**24**) respectively were not observed. Reduction of the primary oxalate (**25**) gave mainly the primary alcohol (**26**). In the reduction of (**15**), (**18**), and (**25**) small amounts of the acids (**21**), (**22**), and (**27**) were respectively formed, and in each case were identified by methylation with diazomethane to give the original methyl oxalyl esters.

No detailed study of the mechanism of the reduction of the oxalyl esters has been undertaken. Whether the intermediate formed from the initial attack of stannyl radical on the oxalate is an adduct or a radical anion[9] of the form $[RO_2C–CO_2Me]^{\bullet-}$ is not known. When R is tertiary β-scission of the alkyl–oxygen bond predominates to give the alkane. The yield of ROH increases as the stability of R$^\bullet$ decreases, possibly *via* a two-step process involving hydrogen capture to give inter-

mediate (**28**) and hydrolysis on work-up (as proposed by Barton and McCombie[3] for primary thiocarbonates).

The formation of small amounts of the acids (**21**), (**22**), and (**27**) is hard to explain. It may be that as the stability of R· becomes comparable to CH_3· steric constraints favour some *O*-alkyl homolysis at the least hindered end of the oxalate.

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