

A New Method for the Radical Deoxygenation of Tertiary Alcohols

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Tertiary alcohols can be deoxygenated in a radical chain reaction based on their mixed oxalate esters with *N*-hydroxy-2-thiopyridone, these esters being obtained directly from the alcohols and oxalyl chloride *etc.* or *via* their trimethylsilyl derivatives.

The deoxygenation of secondary alcohols¹ by a radical chain reaction using tin hydrides has become commonplace.² It is an especially useful reaction for complex natural products.³ At higher temperatures primary alcohols are also deoxygenated.⁴

Two methods for the radical deoxygenation of tertiary alcohols have been reported. The first involves the tin hydride reduction of phenylselenocarbonates⁵ and involves the chloro-carbonate of the tertiary alcohol as intermediate. The second method is the reduction of thioformates.⁶

We now report an improved method of radical deoxygenation which takes advantage of our recent work on the radical

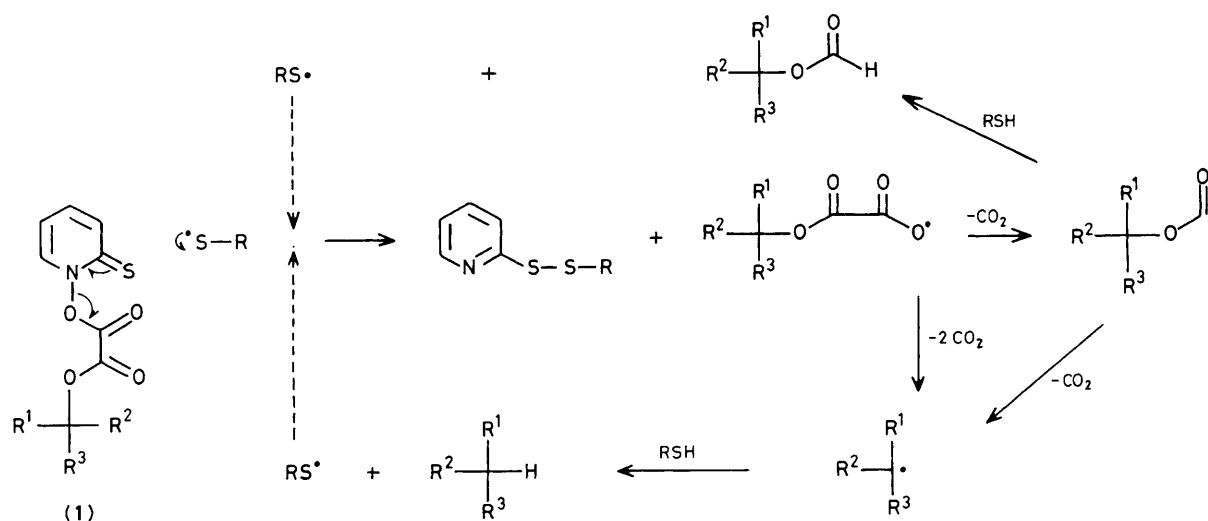
chemistry of thiohydroxamic-*O*-esters.⁷ We conceived that half-oxalate esters of type (1) would show similar radical chemistry⁸ thus permitting the generation, and reduction by hydrogen transfer, of tertiary radicals (Scheme 1). This we have been able to accomplish.

Reaction of the known⁶ alcohol (3) with oxalyl chloride gave the half acid chloride. This was added to benzene under reflux containing the reagent (2b), 4-*N,N*-dimethylaminopyridine (DMAP) (trace), and excess of *t*-butyl thiol (9). After 1 hour, the expected alkane (4) and disulphide (6) were formed in reasonable yield. The principal by-product

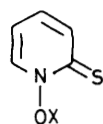
Table 1. Deoxygenation of alcohols.^a

Entry	Substrate	Temp./°C	Thiol (mol)	Products (% Yield)
1	(3)	80	(9) (4)	(4) (63), (5) (25), (6) (62)
2	(3)	80	(10) (2)	(4) (60), (7) (52), (8) (31)
3	(3)	80	(11) (2)	(4) (50)
4	(3)	80	(9) ^b (4)	(4) (69), (5) (6), (6) (75)
5	(3)	80	(12) (2)	(4) (81), (19) (72)
6	(13)	80	(9) (4)	(14) (55)
7	(15)	80	(9) (8)	(16) (90)
8	(17)	80	(9) (5)	(18) (67)
9	(13)	80	(12) (2)	(14) (70), (19) (67)
10	(20) ^f	80	(12) (2)	(4) (76), (19) (82)
11	(21) ^f	80	(12) (2)	(24) (80), (19) (86)
12	(23) ^f	80	(12) (2)	(24) (79), (19) (65)
13	(26) ^f	80	(12) (2)	(27) (77)
14	(28)	132 ^c	(12) (2)	(30) (43), (29) (15), (19) (51)
15	(28)	152 ^d	(12) (2)	(30) (53), (29) (37), (19) (34)
16	(28)	178 ^e	(12) (2)	(30) (40), (29) (40)

^a All new products gave satisfactory spectroscopic and microanalytical data. ^b Use of reagent (2a) and pyridine in place of reagent (2b). ^c Refluxing chlorobenzene. ^d Refluxing cumene. ^e Refluxing *o*-dichlorobenzene. ^f *O*-SiMe₃ ethers were prepared by brief treatment of the alcohol in dichloromethane with a commercial mixture of trimethylsilylchloride, *O,N*-bis(trimethylsilyl)acetamide, and trimethylsilylimidazole (Tri-Sil TBT).

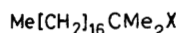


Scheme 1



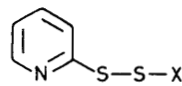
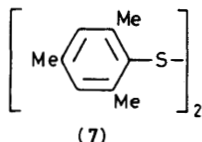
(2a) X = H

(2b) X = Na



(3) X = OH

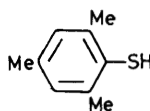
(4) X = H

(5) X = OCOCOSBu^t(8) X = OCOCOSC₆H₄Me₃-1,3,5(20) X = O-SiMe₃(6) X = Bu^t(19) X = CEt₃

(7)



(9)



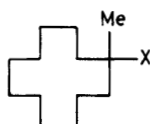
(10)



(11)

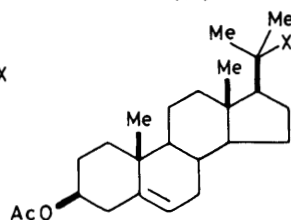


(12)



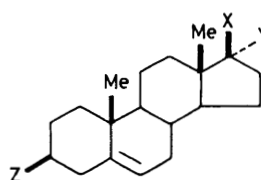
(13) X = OH

(14) X = H



(15) X = OH

(16) X = H

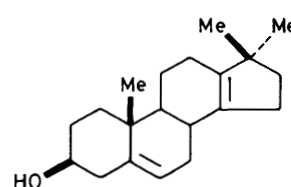


(17) X = Z = OH, Y = Me

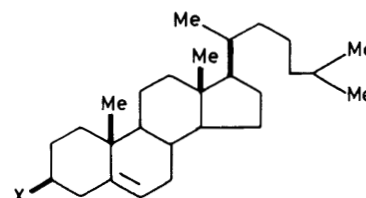
(25) X = OH, Z = OAc, Y = Me

(26) X = OSiMe₃, Z = OAc, Y = Me

(27) X = Me, Y = H, Z = OAc



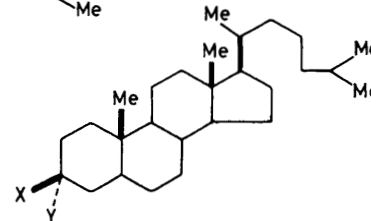
(18)



(28) X = OH

(29) X = OCHO

(30) X = H

(21) X = OSiMe₃, Y = Me

(22) X = Me, Y = OH

(23) X = Me, Y = OSiMe₃

(24) X = Me, Y = H

(5) resulted from the competitive nucleophilic attack of the t-butyl thiol on the half-oxalyl chloride. These (entry 1), and other results, are summarised in Table 1.

In order to diminish this unwanted side reaction we increased the bulk of the thiol (entries 2 and 3) but without improvement in yield and with other complications. The use of reagent (2a) (entry 4) gave a slight improvement, but the solution to the problem was found with the still more bulky thiol (12). This easily prepared⁹ compound afforded an 81% yield (entry 5). It also has the advantage over t-butyl thiol of having little odour.

Application (entries 6 and 7) of the reaction (using t-butyl thiol) to the more hindered alcohols (13) and (15) gave (14)¹⁰ and (16)¹¹ respectively in satisfactory yields. The same procedure applied (entry 8) to the alcohol (17)¹² gave the known rearranged compound (18).¹³ This was clearly an ionic rearrangement product and was formed either by the known proton-catalysed process,¹³ or by an ionic fragmentation of the half oxalate chloride or ester of type (1). We answered this question by converting (17) into its acetate (25) which was trimethylsilylated to (26). This derivative reacted cleanly with oxalyl chloride to give the half-oxalate which was reduced as before using thiol (12) (entry 13). The desired unrearranged deoxy-product (27)¹⁴ was obtained in 77% yield. Hence the problem was the acid-catalysed rearrangement and not the fragmentation of the half-oxalate.

The application of the thiol (12) improved the yield of reduction of (13) to (14) (compare entries 6 and 9).

Trimethylsilyl derivatives were also used in the other reductions with thiol (12) (see entries 10, 11, and 12). As expected the second product was the disulphide (19).

It is interesting to examine whether the fragmentation of the radical half oxalate loses two moles of CO₂ concertedly or two separate moles of CO₂ (see Scheme 1). Reduction of cholesterol (entries 14, 15, and 16) at various temperatures showed that the formate (29) was always formed even at 178 °C. At least then for secondary alcohols two moles of CO₂ are not eliminated in a concerted process.

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