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 alcohols[1] 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 phenylselenocarbonates[5] and involves the chlorocarbonate of the tertiary alcohol as intermediate. The second method is the reduction of thioformates.[6]

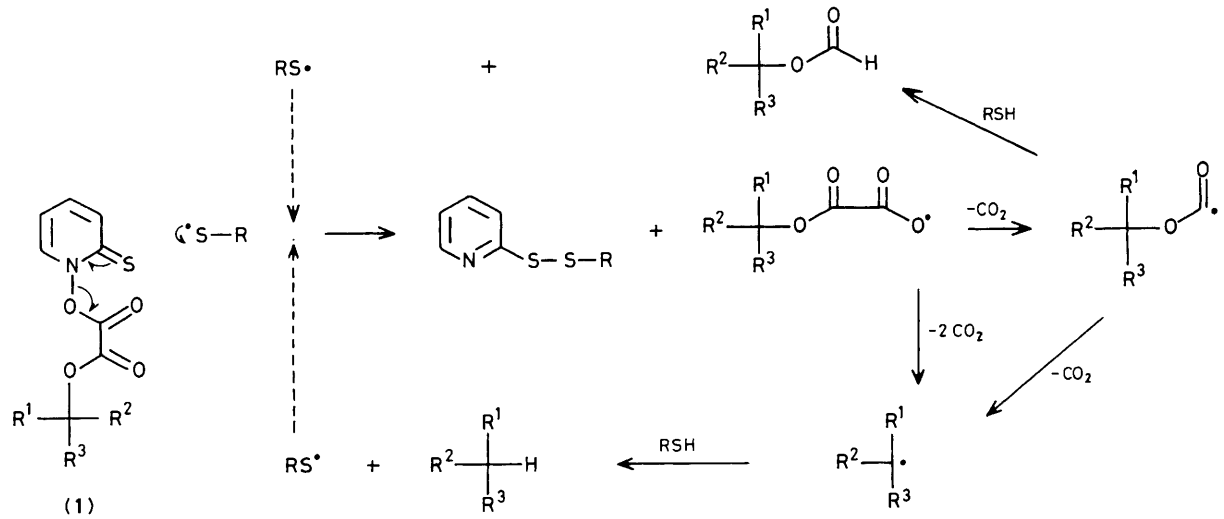
We now report an improved method of radical deoxygenation which takes advantage of our recent work on the radical chemistry of thiohydroxamic-*O*-esters.[7] We conceived that half-oxalate esters of type (**1**) would show similar radical chemistry[8] thus permitting the generation, and reduction by hydrogen transfer, of tertiary radicals (Scheme 1). This we have been able to accomplish.

Reaction of the known[6] 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

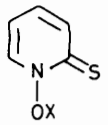
Table 1. Deoxygenation of alcohols.[a]

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*-$SiMe_3$ ethers were prepared by brief treatment of the alcohol in dichloromethane with a commercial mixture of trimethylsilychloride, *O*-*N*-bis(trimethylsilyl)acetamide, and trimethylsilylimidazole (Tri-Sil TBT).



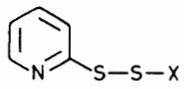
Scheme 1



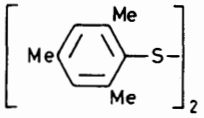
(2a) X = H
(2b) X = Na

$Me[CH_2]_{16}CMe_2X$

(3) X = OH
(4) X = H
(5) X = OCOCOSBu^t
(8) X = $OCOCOSC_6H_2Me_3$-1,3,5
(20) X = O—$SiMe_3$

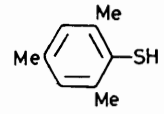


(6) X = Bu^t
(19) X = CEt_3



(7)

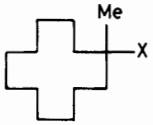
Bu^tSH (9)

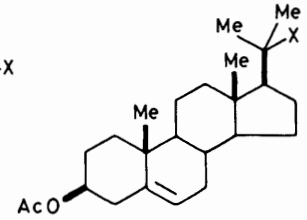


(10)

Ph_3CSH (11)

Et_3CSH (12)





(13) X = OH
(14) X = H

(15) X = OH
(16) X = H

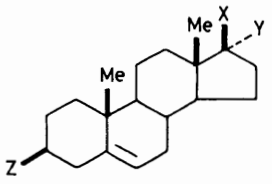
(5) resulted from the competitive nucleophilic attack of the t-butyl thiol on the half-oxalyl chloride. These (entry 1), and other results, are summarised in Table 1.

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 prepared[9] compound afforded an 81% yield (entry 5). It also has the advantage over t-butyl thiol of having little odour.

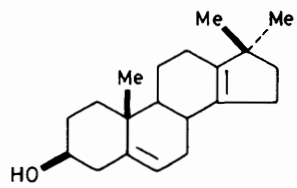
Application (entries 6 and 7) of the reaction (using t-butyl thiol) to the more hindered alcohols (**13**) and (**15**) gave (**14**)[10] and (**16**)[11] respectively in satisfactory yields. The same procedure applied (entry 8) to the alcohol (**17**)[12] gave the known rearranged compound (**18**).[13] 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).

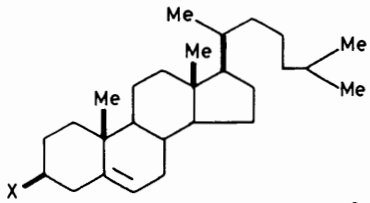
Trimethylsilyl derivatives were also used in the other reductions with thiol (**12**) (see entries 10, 11, and 12). As expected the second product was the disulphide (**19**).



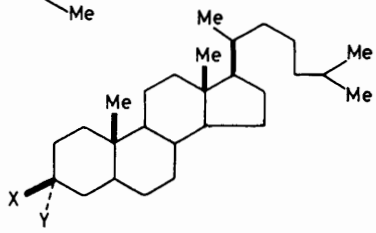
(17) X = Z = OH, Y = Me
(25) X = OH, Z = OAc, Y = Me
(26) X = $OSiMe_3$, Z = OAc, Y = Me
(27) X = Me, Y = H, Z = OAc



(18)



(28) X = OH
(29) X = OCHO
(30) X = H



(21) X = $OSiMe_3$, Y = Me
(22) X = Me, Y = OH
(23) X = Me, Y = $OSiMe_3$
(24) X = Me, Y = H

It is interesting to examine whether the fragmentation of the radical half oxalate loses two moles of CO_2 concertedly or two separate moles of CO_2 (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 CO_2 are not eliminated in a concerted process.

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