

RADICAL DEOXYGENATION OF TERTIARY ALCOHOLS

Derek H.R. Barton, Wolfgang Hartwig, Robyn S. Hay Motherwell,
William B. Motherwell* and Andreas Stange.

(Institut de Chimie des Substances Naturelles, C.N.R.S.,
91190 Gif-sur-Yvette, France)

ABSTRACT - The thioformates of tertiary alcohols are smoothly reduced by tributyl tin hydride to the corresponding hydrocarbon in a radical chain reaction.

Radical deoxygenation of secondary alcohols by tin hydride reduction of appropriate thiocarbonyl derivatives is a preparatively useful reaction, especially for complex molecules¹. Primary alcohols can also be deoxygenated by this method, but at considerably higher temperature².

The extension of this radical reaction to tertiary alcohols is desirable because the configuration at a neighbouring β -centre would not be put at risk as it is in the methods at present employed, which often involve elimination of water followed by hydrogenation. However, it is more difficult to effect radical deoxygenation because the type of thiocarbonyl derivative which works well for primary or secondary alcohols, is too unstable thermally and eliminates to olefin faster than it is reduced. There are several examples of radical reduction of tertiary benzoates where extra activation by a carbonyl group is present³. A more promising method (one example so far) is the tin hydride reduction of the phenylselenocarbonate of a tertiary alcohol⁴.

Our own approach to this problem was to suppose that a thioformate would have the correct combination of relative thermal stability and relative ease of reductive elimination (Scheme 1). The thioformates of secondary alcohols are usually reduced without fission, except when several oxygen- β -carbon bonds

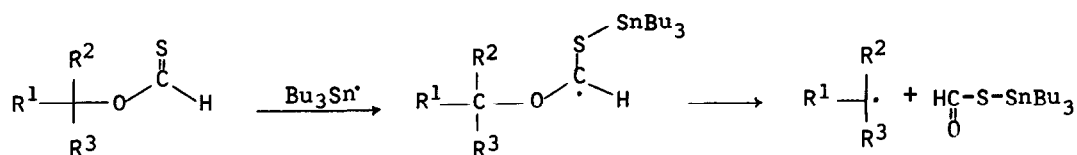
are present⁵. However, the carbon-oxygen bond in a tertiary alcohol derivative should be weaker, because of the increased stability of the tertiary radical formed. In the event, we have been able to show that this conception is correct.

The lack of suitable thioformyl transfer reagents led us to study the use of isonitriles as precursors to thioformates (Scheme 2). The alcohol (1) was selected as a suitable crystalline tert-alcohol (m.p. 45.5°C). It was readily prepared from methyl stearate and MeMg I. This alcohol did not react with cyclohexylisocyanide in the presence of CuO⁶, but it did react smoothly with p-methoxyphenylisocyanide⁷ at 80° under argon (no solvent). Treatment of the derived iminoether (2) with H₂S gave the desired thioformate (3) in poor yield (20-40%). Consideration of the need to protonate the departing amine function in the Vilsmeier synthesis of thiocarbonyl esters⁸ (see (4), (a) versus (b)) suggested that p-dimethylaminophenylisocyanide⁷ should provide a better departing group than p-methoxyphenylanilino (see (5)). In the event using a 10% excess of reagent at 85° in presence of CuO gave a 90% yield of derivative (6). On treatment in dry pyridine containing hydrogen sulphide (excess) and 100% H₂SO₄ (several equivalents) at -10-0° this gave the desired thioformate (3) in good yield (90%). Reduction of this compound in benzene under reflux with tributyltin hydride in the usual way¹ gave without difficulty the saturated hydrocarbon (7) (83%). Similarly the alcohol (8) was converted to its thioformate (9) (85%) and thence into the saturated hydrocarbon (10) (71%).

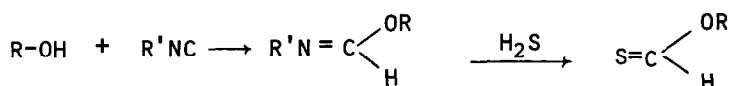
We have also explored several other possible methods of radical deoxygenation of tertiary alcohols. Reaction of the alcohol (1) with butyl lithium followed by treatment with dry COS (excess) and then with MeI gave the thiocarbonate (11). Reduction of this compound with tributyltin hydride at 130° gave the hydrocarbon (56%) as well as olefins (21%).

The alcohol (1) was easily converted into its thiomethylmethyl ether (12) by the method of Pojer and Angyal⁹. We hoped¹⁰ that reduction to the radical (13) would provoke elimination of formaldehyde. Various tin hydrides did not reduce (12), but tributylgermanium hydride at 110° (toluene) reduced it cleanly to the methyl ether (14), without fragmentation.

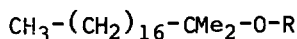
Despite the known propensity for phosphoranyl radicals to undergo β scission¹¹, it was interesting to note that the derivative (15) did not react with tributyltin hydride at 110° (toluene).



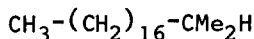
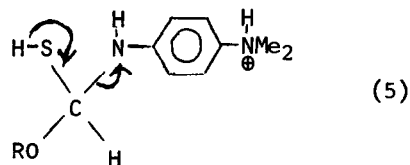
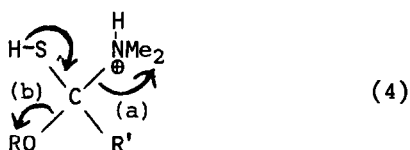
SCHEME 1



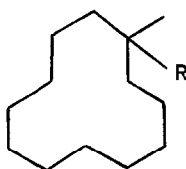
SCHEME 2



- (1) R = H
- (2) R = CH = N-C₆H₄-OMe-p
- (3) R = CH = S
- (6) R = CH = N-C₆H₄-NMe₂-p
- (11) R = COSMe
- (12) R = CH₂-SMe
- (13) R = CH₂'
- (14) R = Me
- (15) R = Ph₂P = S



(7)



- (8) R = OH
- (9) R = O-CHS
- (10) R = H

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10. Cf. A.R. Forrester, M. Gill, E.M. Johansson, C.J. Meyer and R.H. Thomson, Tet. Letts., 3601 (1977).
11. For a detailed discussion of the formation and breakdown of phosphoranyl radicals see : W.G. Bentrude in "Free Radicals", Vol. II, p. 595. Ed. J.K. Kochi, Wiley Interscience, New York, 1973.

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