Metal–Amine Reduction of Sterically Hindered Esters to Alkanes, A New Method for the Deoxygenation of Hindered Alcohols

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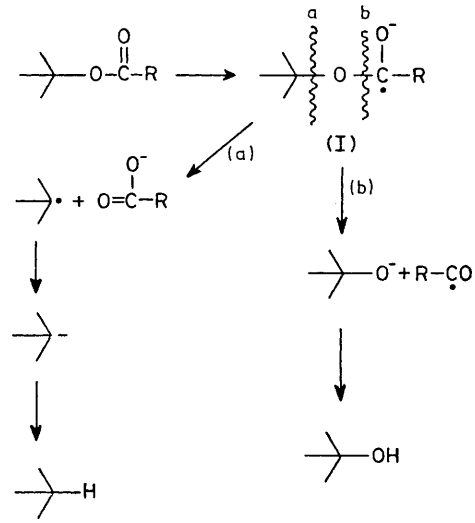
Summary Acetates of sterically hindered secondary alcohols and of tertiary alcohols are reduced by lithium in ethylamine to afford predominantly the corresponding alkanes, rather than the parent alcohols.

THE selective replacement of a hydroxy group by hydrogen (deoxygenation) is a synthetic transformation of considerable importance.[1] We report that sterically hindered alcohols are conveniently and efficiently converted into the corresponding alkanes by metal–amine reduction of the derived esters with carboxylic acids. The only side-reaction is the regeneration of the starting alcohol. Typical examples are summarised in the Table. The readily available acetate esters are admirable substrates. So far, we have mainly used lithium in ethylamine as the reducing system, but other metals (Na, K) and other amines are also effective.

The rapid rearrangement of the 3α,5-cyclo-5α-cholestan-6-yl radical into the more stable cholest-5-en-3-yl radical is well established.[2] Lithium–ethylamine reduction of 3α,5-cyclo-5α-cholestan-6β-yl acetate gave a hydrocarbon fraction (45%) which comprised cholest-5-ene (85%) and



SCHEME

TABLE. Metal-amine reduction of esters.[a]

	Starting material	Product(s) (%)[b]
(1)	3β,6β-Diacetoxy-5α-cholestane	5α-Cholestan-3β-ol (46); 5α-Cholestane-3β,6β-diol (35)
(2)	,,	5α-Cholestan-3β-ol (60); 5α-Cholestane-3β,6β-diol (29)
(3)	3β,6β-Dibenzoyloxy-5α-cholestane	5α-Cholestane-3β,6β-diol (80)
(4)	3β,6β-Diformyloxy-5α-cholestane	5α-Cholestane-3β,6β-diol (86)
(5)	3β,6β-Di-isobutyryloxy-5α-cholestane[c]	5α-Cholestan-3β-ol (16); 5α-Cholestane-3β,6β-diol (55)
(6)	3β,6β-Diformyloxy-5α-cholestane	5α-Cholestan-3β-ol (71); 5α-Cholestane-3β,6β-diol (19)
(7)	3β,6β-Dipropanoyloxy-5α-cholestane	5α-Cholestan-3β-ol (15); 5α-Cholestane-3β,6β-diol (61)
(8)	3β,6β-Dipivaloyloxy-5α-cholestane	5α-Cholestan-3β-ol (79); 5α-Cholestane-3β,6β-diol (9)
(9)	3β,5α-Diacetoxycholestane	5α-Cholestan-3β-ol (66); Cholestane-3β,5α-diol (8)
(10)	3β,5α,6β-Triacetoxycholestane	Cholesterol (81); cholestane-3β,5α,6β-triol (8)
(11)	3β,12α-Diacetoxy-13α-oleanane[d]	13α-Oleanan-3β-ol (85)
(12)	3β,25-Diacetoxy-5α-lanost-8-ene	5α-Lanost-8-en-3β-ol (75); 5α-Lanost-8-ene-3β,25-diol (10)
(13)	Caryolan-1-ol acetate[e]	Caryolane (90)

[a] Reductions were carried out with Li–$EtNH_2$, except for entries (2), (4), (6), and (8) where K–Bu^tNH_2–18-crown-6 was used. Typically, the ester (100 mg) in dry amine was added to a partial solution of lithium (60 mg) in dry amine (10 ml) at 0 °C. The mixture was allowed to reflux for 1 h, then Bu^tOH (5 ml) was added. Normal work-up procedures gave the products indicated. [b] Yields refer to pure, isolated material. [c] Satisfactory analytical and spectroscopic data were obtained for all new compounds reported herein. [d] R. B. Boar, L. Joukhadar, M. de Luque, J. F. McGhie, D. H. R. Barton, D. Arigoni, H. G. Brunner, and R. Giger, *J.C.S. Perkin I*, 1977, 2104. [e] D. H. R. Barton and A. Nickon, *J. Chem. Soc.*, 1954, 4665, and references cited therein.

3α,5-cyclo-5α-cholestane (15%). This result, together with the particular efficiency with which esters of tertiary alcohols are reduced, leads us to favour a mechanism involving radical fragmentation of the initially formed radical anion (I) (Scheme). Mode (a), and thence deoxygenation, evidently becomes the favoured process when cleavage of this C–O bond is attended by a sufficient release of unfavourable steric interactions. Otherwise, mode (b) is preferred, and the alcohol is regenerated.

Under the reaction conditions, reduction of radicals to the corresponding carbanions must be rapid. Thus, the formation of cholesterol by the reduction of 3β,5α,6β-triacetoxycholestane is probably the result of displacement of the acetate group from C-6 by a carbanion at C-5.

The fact that reduction only occurs with esters of sterically hindered alcohols confers upon this method a selectivity not often possible with alternative deoxygenation processes.[1]

Attention is drawn (see Table) to the use of 18-crown-6 as a solubilising agent for reductions with potassium in t-butylamine.

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[2] A. L. J. Beckwith and G. Phillipou, *J.C.S. Chem. Comm.*, 1971, 658, and references therein.