Selective Hydroboration of $\Delta^{20(21)}$-Steroids

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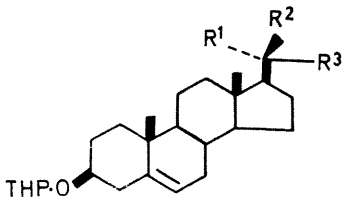
Summary A stereoselective synthesis of 21-hydroxy-steroids of the (20*S*) series including the preparation of 3β,21-dihydroxy-(20*S*)-cholest-5-ene and its conversion into 20-isocholesterol, is described.

THE stereoselective synthesis of alcohols in the steroid series through hydroboration of double bonds in the ring system is well known.[1] However, this reaction has not yet been applied systematically to olefinic side-chains. We have

found that, under carefully controlled conditions, hydroboration of Δ^{21} olefins of the type (1) leads to (20*S*)-21-hydroxy-steroids in good yield.

For instance, the tetrahydropyranyl (THP) derivative (1) when treated with an excess (1 : 5) of disiamylborane[2] at room temperature for 4 h, and then 30% hydrogen peroxide and 10% sodium hydroxide at 0° gives a 45% yield (4x recryst., ether–hexane) of the (20*S*)-alcohol (2), identical in all respects with an authentic sample.[3] The use of the calculated amount of diborane leads to a 40 : 60 mixture of the (20*R*) and (20*S*) isomers.



	R^1	R^2	R^3
(1)	CH_2		Me
(2)	H	CH_2OH	Me
(3)	O		C_6H_{13}
(4)	O		$CH_2.CO_2Me$
(5)	CH_2		C_6H_{13}
(6)	H	CH_2OH	C_6H_{13}
(7)	H	Me	C_6H_{13}

The tetrahydropyranyl derivative of 20-oxo-21-norcholesterol (3) was prepared, either according to the Kurath and Capezzuto procedure (4), or, more conveniently, from the β-keto-ester (4). The latter compound, readily obtained from pregnenolone,[5] was alkylated by isopentyl bromide and the product decarboxylated.

Finally a Wittig reaction[6] using Sondheimer's[6] or Corey's[7] procedure gives the tetrahydropyranyl ether of 3β-hydroxycholesta-5,20(21)-diene (5).

Hydroboration, using disiamylborane, of the latter olefin was more stereoselective than that described above; the pure primary alcohol (6) was easily isolated, and there was no evidence that any other isomer was present (t.l.c., n.m.r.).

The structure of compound (6) was proved by reduction of its tosylate with $LiAlH_4$[8] in ether, which afforded compound (7) m.p. 149—151° (methanol–methylene chloride), $[\alpha]_D^{25}$ −22·1° ($CHCl_3$).

These data agree well with those for the THP derivative of cholesterol[9]: m.p. 154—155, $[\alpha]_D^{25}$ −23·5° ($CHCl_3$). The i.r. spectra of these compounds are superimposable. However the mixed m.p. shows considerable depression (*ca.* 25° for a 1 : 1 mixture).

Treatment of (7) by ethanol–hydrochloric acid gives 3β-hydroxy-(20*S*)-cholest-5-ene, m.p. 158—160°.[6]

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[1] F. Sondheimer and M. Nussim, *J. Org. Chem.*, 1961, **26**, 630.
[2] H. C. Brown and B. C. Subba Rao, *J. Amer. Chem. Soc.*, 1959, **81**, 6423.
[3] We thank Dr. P. Crabbé for supplying us with this sample.
[4] P. Kurath and M. Capezzuto, *J. Amer. Chem. Soc.*, 1956, **68**, 3527.
[5] V. H. Wallingford, A. H. Homeyer, and D. M. Jones, *J. Amer. Chem. Soc.*, 1941, **63**, 2252.
[6] F. Sondheimer and R. Mechoulam, *J. Amer. Chem. Soc.*, 1958, **80**, 3087.
[7] E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, 1962, **84**, 866; 1965, **87**, 1347.
[8] H. Schmid and P. Karrer, *Helv. Chim. Acta*, 1949, **32**, 1371.
[9] A. C. Ott, M. F. Murray, and R. L. Pederson, *J. Amer. Chem. Soc.*, 1952, **74**, 1239.