Stepwise Side-chain Shortening of Cholanic Aldehydes

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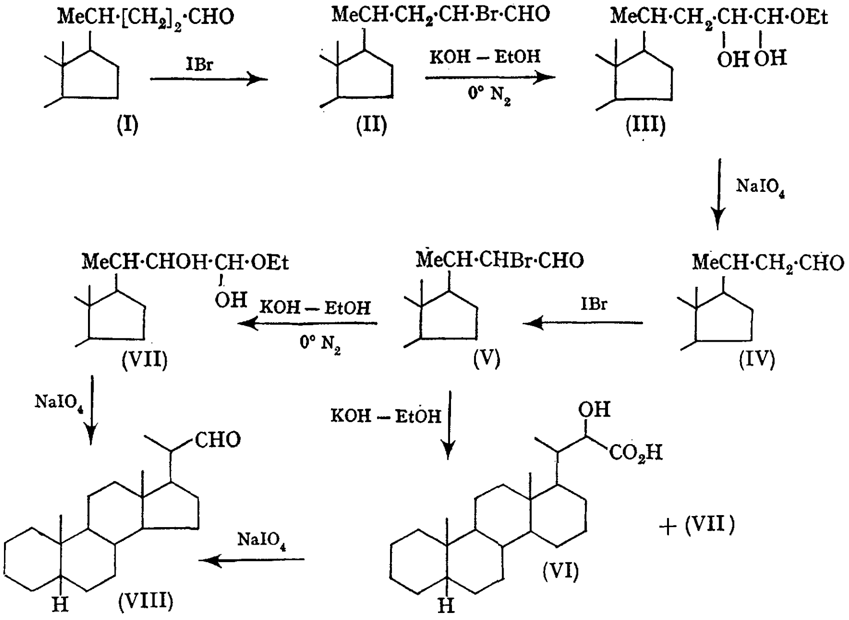
Iodine bromide was shown to selectively effect monobromination of cholanic aldehydes in very high yields.[1] We report a new method for the stepwise degradation of the side-chain in cholanic aldehydes, in which one carbon is eliminated each time:

When 23-bromocholanal[1] (II) is stirred with potassium hydroxide in ethanol (2%) under nitrogen at 0°, the resulting product is the corresponding hydroxy-semiacetal (III). Its spectrum shows absorption at 1062, 1100, 1120, and 1165 cm.$^{-1}$ (semiacetal) but is transparent at 2700 and



1720 cm.$^{-1}$ (–CHO). If (III) is treated with sodium periodate in a 4 : 2 : 1 mixture of acetone: acetic acid : water at 40—50° for 2 hr., it gives norcholanal (IV) in quantitative yield, m.p. 138—139°, $[\alpha]_D^{20}$ $+11{\cdot}3°$ ($CHCl_3$, 1%) (lit.[2] m.p. 133—135°, $[\alpha]_D^{27}$ $+8{\cdot}0$).

Likewise, 22-bromonorcholanal (V), produced from the reaction of (IV) with iodine bromide, hydrolyses to the respective hydroxy-semiacetal (VII) which is then cleaved by sodium periodate to give in almost quantitative yield the hitherto unknown bisnorcholanal (VIII), m.p. 97—100°, $[\alpha]_D^{20}$ $+13°$ ($CHCl_3$, 1·5%), i.r. (KBr) : 2700 and 1730 cm.$^{-1}$ (–CHO).

The n.m.r. spectrum of (VIII) in CH_2Cl_2 exhibits a doublet centred at 576 c./sec. with J 3·5 c./sec., attributable to one aldehydic proton, a doublet at 65·5 c./sec. with $J = 7$ c./sec. (C-21 methyl), and two singlets at 56 and 41·5 c./sec. attributable to C-19 and C-18 methyls, respectively.

The hydrolysis stages (II → III and V → VII) were found to be sensitive to atmospheric oxygen.[3] For example, when the hydrolysis of (V) is carried out at normal temperature and pressure, a 1 : 1-mixture of (VI) and (VII) is obtained. 22-Hydroxynorcholanic acid (VI) had m.p. 215—220° $[\alpha]_D^{20}$ $+23{\cdot}6°$ (EtOH, 2%), i.r. (Nujol), 3440, 3350, 1735, 1720, 1132, and 1097 cm.$^{-1}$; n.m.r.† (in c./sec.) singlet at 44 (C-18, 3H), singlet at 59 (C-19, 3H), doublet with J 9 c./sec. at 246 (22-OH, 1H), multiplet at 357 (COOH, 1H). Periodate cleavage of (VI) by the method described[2] afforded bisnorcholanal (VIII) in 90% yield.

This method complements an earlier method,[2] and the two combined, afford a useful tool for the formation and degradation of steroidal aldehydes derived from bile acids.

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† The n.m.r. spectrum was run with dimethylformamide as internal reference. See N. S. Bhacca, D. P. Hollis, L. F. Johnson, E. A. Pier, and J. N. Shoolery, "NMR Spectra Catalog", Varian Associates, Vol. 1 and 2, 1962 and 1963.

[1] Y. Yanuka, R. Katz, and S. Sarel, preceding paper.

[2] Y. Yanuka, R. Katz, and S. Sarel, *Tetrahedron Letters*, 1968, 1725.

[3] *Cf.* (*a*) A. Kirrmann, P. Chancel, M. Vignalon, and P. Federlin, *Bull. Soc. chim. France*, 1950, 707; (*b*) A. Kirrmann and P. Chancel, *ibid.*, p. 711; (*c*) P. Chancel, *ibid.*, p, 714; (*d*) P. Federlin and A. Krattiger, *ibid.*, 1954, 1293.