Acid-catalysed Backbone Rearrangement involving the C–D Ring Junction in Normal Steroid Series

By **Mario Anastasia,* Ada Manzocchi Soave,** and **Antonio Scala,** Institute of Chemistry, School of Medicine, University of Milan, I–20133 Milan, Italy

Protic and Lewis acids cause partial backbone rearrangement involving the C–D ring junction in the normal steroid series with ring contraction and formation of 12,14α-cyclo-12,13-seco-5α-cholest-13(17)-ene compounds. 12-Methylene rather than 13-methyl rearrangement is suggested and a revision of a previously proposed structure is given.

DOUBLE bond isomerizations in the steroid series involving the 7, 8(9), and 8(14) positions to yield 14-ene steroids are well known.[1,2] In contrast few data have been reported about backbone rearrangements involving the same positions. 3β-Acetoxy-12,14α-cyclo-12,13-seco-5α-cholest-13(17)-ene (1a) † was obtained in moderate yield when 3β-acetoxy-5α-cholest-14-ene (2a) was treated with BF_3–ether in benzene and acetic anhydride for 170 h.[3] Treatment of 5α-cholest-8(14)-ene (3b) with anhydrous toluene-*p*-sulphonic acid yielded a tetrasubstituted olefin which was attributed a structure of type (7).[4] In a recent paper we reported that 3β-acetoxy-14-chloro-5α,14β,17α-cholestane (5) can be obtained from 3β-acetoxy-5α-cholest-7-ene (4a), -8(14)-ene (3a), and -14-ene (2a) by the action of HCl at −60 °C.[5] The side chain epimerization may involve the intermediate formation of the spiro compound (1a). In this case, the protic acid HCl behaves in the same manner as the Lewis acid BF_3 and not as the protic toluene-*p*-sulphonic acid.

In order to clarify the behaviour of 7, 8(14), and 14-ene steroids towards Lewis and protic acids, we examined the reaction of BF_3–ether with acetates (2a)—(4a) and olefins (2b)—(4b) under the conditions reported for (2a)[3] or in anhydrous chloroform for 30 min. An oily product was obtained from the acetates after chromatography with properties identical to those reported for (1a). However, the mass spectrum of our product did not show a strong peak at *m/e* 315 attributable to the loss of the side chain reported as characteristic for (1a).[3] In contrast, two very intense peaks were observed at *m/e* 206 and 121. The former originated from the molecular ion (*m/e* 428, *m** 99.15) probably due to the fission of 8(14) and 11(12) bonds. The latter originated from the ion at *m/e* 206 (*m** 71.07) corresponding to the fission of the 20(22) bond. On the other hand loss of the side chain was observed in the mass spectrum of (2a), the starting material.[3]

The oily spiro compound (1b) was obtained from the olefins (2b)—(4b). The mass spectrum of (1b) showed intense peaks at *m/e* 206 and 121; the ^1H n.m.r. spectrum showed δ 1.47 (t, *J* 0.7 Hz) attributable to a methyl group attached to a 13(17) double bond. Ozonolysis of (1b) gave the seco-diketone (6), δ 2.1 due to the newly formed acetyl group; the 21-CH_3 protons appeared as a doublet centred at δ 1.05 (*J* 10 Hz) which collapsed to a singlet by irradiation at δ 2.52.

The same spiro compounds (1a and b) were obtained from acetates (2a)—(4a) or olefins (2b)—(4b), respectively, by the action of toluene-*p*-sulphonic acid in the solvent system reported for (2b),[4] or better in boiling benzene. These findings clearly indicate that the proposed structure [4] of type (7) should be rejected.

Our results demonstrate that the spiro olefins of type (1) are the products of backbone rearrangement promoted by either protic or Lewis acids on steroids of

† The stereochemistry of this compound is based on mechanistic arguments only.

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[3] H. Izawa, Y. Katada, Y. Sakamoto, and Y. Sato, *Tetrahedron Letters*, 1969, 2947.
[4] R. B. Turner, W. R. Meador, and R. E. Winler, *J. Amer. Chem. Soc.*, 1957, **79**, 4122.
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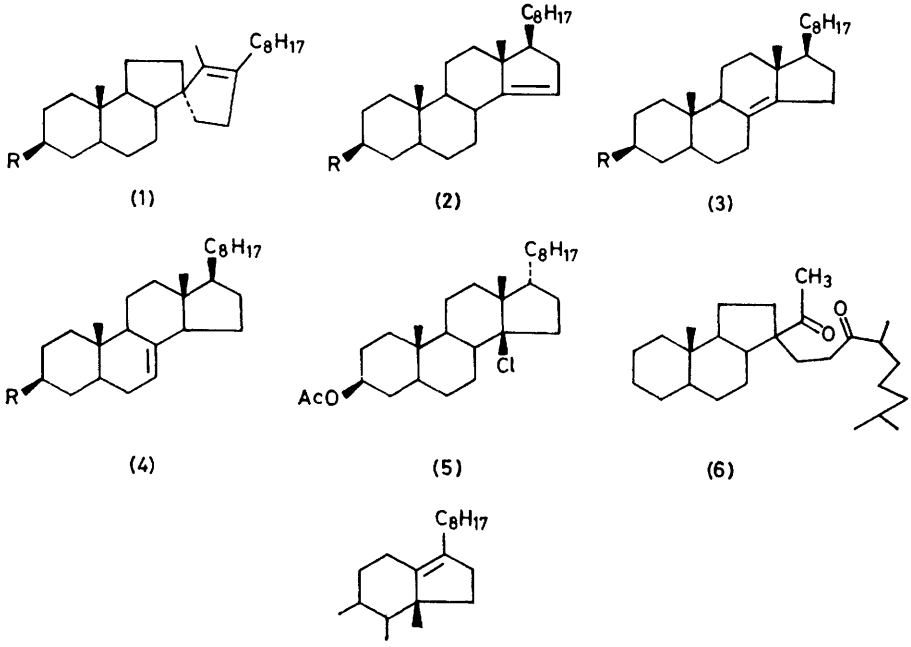
types (2)—(4). The normal backbone structure and stereochemistry of the A–B and B–C ring junctions are retained and a 12-CH_2 shift occurs, possibly originating from a C-14 carbonium ion. In contrast, a 13-CH_3 shift occurs in backbone rearrangement of C-5 carbonium ions in the ' normal ' steroid series,[2] with formation of a 13(17) double bond as present in (7). In this case the A–B and B–C ring junctions suffer inversion of configuration and the rearranged products prefer a $\Delta^{13(17)}$



a; R = OAc
b; R = H

structure providing relief of torsional strain associated with the 17β-side chain.[2] However, examination of molecular models shows that in the case of steroids with a natural B–C ring junction (*i.e.* 8β,9α) a 13(17) double bond is very strained and therefore formation of a compound of type (7) would not be in agreement with the concept that backbone rearrangement leads to the least strained olefin.[6]

EXPERIMENTAL

I.r. spectra were taken for solutions in $CHCl_3$; ^1H n.m.r. spectra were measured with a Varian HA-100 instrument for $CDCl_3$ solutions relative to Me_4Si. Mass spectra were obtained with an LKB 9000 gas chromatograph–mass spectrometer (2 m silanized glass column of 3% SE 30 on Gas Chrom Q, operating at 200—220 °C). Column chromatography was carried out with hexane–benzene on silica gel G–Celite–$AgNO_3$ (1 : 1 : 0.3).

Reactions with Boron Trifluoride–Ether.—A solution of the steroid (300 mg) in chloroform (30 ml) was treated with boron trifluoride–ether (3 ml) for 30 min at room temperature. After the usual work-up the crude residue was chromatographed. From acetates (2a)—(4a), 3β-acetoxy-12,14α-cyclo-12,13-seco-5α-cholest-13(17)-ene (1a) was obtained as a viscous oil (50%), δ 1.46 (3 H, t, *J* 0.7 Hz, 13-Me), 0.93 (3 H, d, *J* 7 Hz, 21-Me, collapsed to s upon irradiation at δ 2.47), 0.84 (6 H, d, *J* 6 Hz, 26- and 27-Me), and 0.80 (3 H, s, 10-Me); *m/e* 428 (M^+), 206, and 121 (Found: C, 81.2; H, 11.2. $C_{29}H_{48}O_2$ requires C, 81.25; H, 11.3%). From olefins (2b)—(4b) 12,14α-cyclo-12,13-seco-5α-cholest-13(17)-ene (1b) was obtained in 50% yield, oil, δ 1.47 (3 H, t, *J* 0.7 Hz, 13-Me), 0.95 (3 H, d, *J* 7, 21-Me, collapsed to s upon irradiation at δ 2.46), 0.84 (6 H, d, *J* 6 Hz, 26- and 27-Me), and 0.76 (3 H, s, 10-Me); *m/e* 380 (M^+), 206, and 121 (Found: C, 87.8; H, 12.6. $C_{27}H_{46}$ requires C, 87.5; H, 12.5%).

*Reactions with Toluene-*p*-sulphonic Acid.*—The steroid (100 mg) was added to a mixture of anhydrous toluene-*p*-sulphonic acid (50 mg) and benzene (25 ml) and heated at reflux for 2 h. After the usual work-up the crude residue was chromatographed. The oil (1a) was obtained in 50% yield from (2a)—(4a) and the oil (1b) in 50% yield from (2b)—(4b).

Ozonolysis of 12,14β-*Cyclo*-12,13-*seco*-5α-*cholest*-13(17)-*ene* (1b).—Compound (1b) (150 mg) in $CHCl_3$ was reacted at −70 °C with a stream of ozonized oxygen. After removal of the solvent, acetic acid (10 ml) and zinc dust (100 mg) were added. The usual work-up gives the slightly impure D-seco-diketone (6), $\nu_{max.}$ 1 710 and 1 695 cm^{-1}; δ 2.1 (3 H, s, 13-Me) and 1.05 (3 H, d, *J* 10 Hz, 21-Me); *m/e* 402 (M^+) and 359.

This research was supported by the Italian Research Council. We thank Professor A. Fiecchi for helpful discussions.

[7/1607 *Received*, 9*th September*, 1977]

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