Steroids and Related Studies. Part XXXIII.[1] Some Steroidal Tetrazoles

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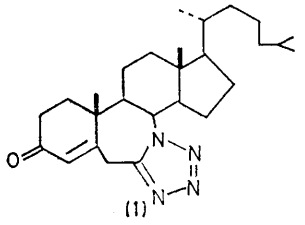
A Schmidt reaction with 7a-aza-B-homocholest-4-eno[7a,7-*d*]tetrazol-3-one (1) gave two of the eight possible products: 4,7a-diaza-AB-bishomocholest-4a-eno[7a,7-*d*]tetrazol-3-one (3) and either 3,7a-diaza-AB-bishomocholest-4a-eno[3,4-*d*][7a,7-*d*]bistetrazole (6) or the Δ^5-isomer (8).

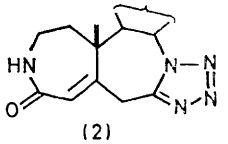
DURING our studies on steroidal tetrazoles we obtained 7a-aza-B-homocholest-5-eno[7a,7-*d*]tetrazol-3β-yl acetate, the hydrolysis products of which on Oppenauer oxidation yielded 7a-aza-B-homocholest-4-eno[7a,7-*d*]tetrazol-3-one (1).[2] We envisaged that treatment of



(1)

the latter under Schmidt reaction conditions could lead to any of several products, *viz.* four lactams and four bistetrazoles.

The $\alpha\beta$-unsaturated ketone (1) was treated with a nearly unimolecular quantity of sodium azide, with polyphosphoric acid as solvent and catalyst. Only one product was isolated, $C_{27}H_{43}N_5O$, in 39% yield showing lactam carbonyl absorption at 1667 cm^{-1}, for which the four possible isomeric structures (2)—(5) were considered. It showed a u.v. maximum at 246 nm, which does not favour structure (2) since an $\alpha\beta$-unsaturated lactam would be expected to absorb around 220 nm.[3] The n.m.r. spectrum showed a one-proton doublet (J 6 Hz)



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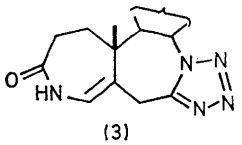

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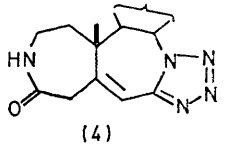

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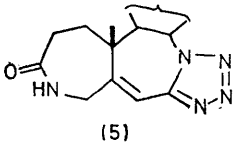
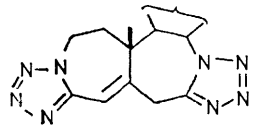


(5)

centred at δ 5·81 and a one-proton diffuse doublet at δ 7·17. On deuterium exchange the former collapsed to a singlet and the latter disappeared, indicating that the signals were due to an olefinic and an NH proton, respectively. The size of the coupling constant favoured a vicinal relationship NH·CH:C as in structure (3) and excluded the other possible structures. A two-proton singlet at δ 3·68 corresponding to the C-6 methylene group also supported structure (3).

Compound (1) was then treated with an excess of hydrazoic acid, with boron trifluoride as catalyst. The product, $C_{27}H_{42}N_8$ (32% yield), was a bistetrazole, for which structures (6)—(9) were possible. It showed a u.v. maximum at 244 nm. Structures (7) and (9) were excluded since there was no n.m.r. signal at δ *ca.* 3·0 corresponding to C-2 methylene protons.[4,5] Of the structures (6) and (8), the former would be favoured only if we assume that a double-bond shift does not take place



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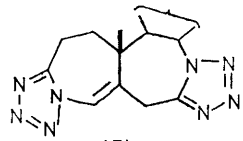

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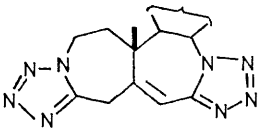

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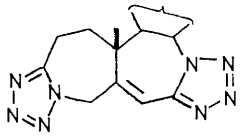

(9)

during the reaction, by analogy with the formation of compound (3) from (1). The bistetrazole showed a three-proton n.m.r. multiplet at δ 4·56 assignable to the C-2 methylene and the C-8 methine in structure (6).[2,5] The vinylic proton singlet was at δ 6·68, and the C-6 methylene singlet at δ 4·04.

EXPERIMENTAL

U.v. and i.r. spectra were obtained for solutions in ethanol and for potassium bromide discs, respectively. N.m.r. spectra (60 MHz) were recorded for solutions in deuteriochloroform containing tetramethylsilane as internal reference. T.l.c. was carried out on silica gel G (Merck) and plates were developed by exposure to iodine vapour. Anhydrous sodium sulphate was employed as drying agent.

4,7a-*Diaza*-AB-*bishomocholest*-4a-*eno*[7a,7-d]*tetrazol*-3-*one* (3).—Sodium azide (0·1 g) was added to a mixture of compound (1) (0·5 g) and polyphosphoric acid (16 g) at 50 °C

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[2] H. Singh, R. K. Malhotra, and N. K. Luhadiya, *J.C.S. Perkin I*, 1974, 1480.
[3] R. H. Mazur, *J. Org. Chem.*, 1961, **26**, 1289.
[4] G. DiMaio and V. Permutti, *Tetrahedron*, 1966, **22**, 2059.
[5] H. Singh, R. B. Mathur, and P. P. Sharma, *J.C.S. Perkin I*, 1972, 990.

during 45 min. The mixture was stirred occasionally during 10 h at 50—55 °C. Crushed ice was added and the product was extracted with chloroform (3 × 50 ml). The extracts were washed free of acid with water, dried, and evaporated. The brown residue (0·45 g) was chromatographed over alumina (20 g) in benzene; elution with benzene–chloroform (3 : 2) afforded the *product* (3) (0·2 g, 39%), m.p. 280—282°. A sample crystallised from methanol had m.p. 285—287°, $\lambda_{max.}$ 246 nm (log ε 4·09), $\nu_{max.}$ 3226, 3111, 2941, 1667, 1536, 1460, 1418, and 1379 cm^{-1}, δ 0·81 (3H, s), 1·37 (3H, s), 3·68 (2H, s), 4·45 (1H, m), 5·81 (1H, d, *J* 6 Hz), and 7·17 (1H, d, *J* 6 Hz) (Found: C, 71·4; H, 9·55; N, 15·55. $C_{27}H_{43}N_5O$ requires C, 71·5; H, 9·55; N, 15·45%).

The aqueous layer was neutralised with ice-cold 50% potassium hydroxide and re-extracted with chloroform (3 × 50 ml). The usual work-up gave no residue.

Treatment of 7a-*Aza*-B-*homocholest*-4-*eno*[7a,7-d]*tetrazol*-3-*one* (1) *with an Excess of Hydrazoic Acid.*—A solution of compound (1) (1·0 g) in dry chloroform (20 ml) was added to a mixture of boron trifluoride–ether complex (1 ml) and hydrazoic acid solution [5] in chloroform (20 ml) during 4 h at 0 °C. The mixture was kept at 25—30 °C for 24 h, then washed successively with aqueous sodium hydrogen carbonate (10%) and water. The chloroform layer was dried and evaporated, and the brown residue (0·4 g) was crystallised from acetone–petroleum (b.p. 60—80°) to afford the bistetrazole (6) or (8) (0·35 g, 32%), m.p. 185—195° (from benzene), $\lambda_{max.}$ 244 nm (log ε 4·20), $\nu_{max.}$ 2899, 2849, 1653, 1527, 1462, 1449, 1439, and 1379 cm^{-1}, δ 0·85 (3H, s), 1·51 (3H, s), 4·04 (2H, s), 4·56 (3H, m), and 6·68 (1H, s) (Found: N, 23·25. Calc. for $C_{27}H_{42}N_8$: N, 23·4%).

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