The Dehydrogenation of Lanosterol Derivatives by 2,3-Dichloro-5,6-dicyanobenzoquinone

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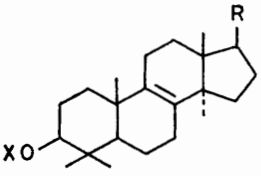
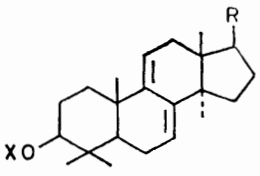
The dehydrogenation of 3β-acetoxylanost-8-ene (1a) by 2,3-dichloro-5,6-dicyanobenzoquinone to give, after hydrolysis, 3β-hydroxylanosta-7,9(11)-diene (2b), 3-hydroxy-19(10→5)*abeo*-4,5-secolanosta-4(30),5,7,9,11-pentaene (3a), and 19(10→5)*abeo*-4,5-secolanosta-5,7,9,11-tetraen-3-one (4) is described. Similarly 3β-hydroxylanost-8-ene (1b) is also dehydrogenated to a mixture of (2b) and (4).

While 2,3-dichloro-4,5-dicyanobenzoquinone(DDQ) has been frequently used to dehydrogenate unsaturated ketones and hydroaromatic compounds there are few examples where the substrate contains a single isolated double-bond.[1] We now report that DDQ reacts readily with 3β-hydroxylanost-8-ene (1b) and with the 3β-acetoxy-derivative (1a), both of which have only one tetrasubstituted double-bond.

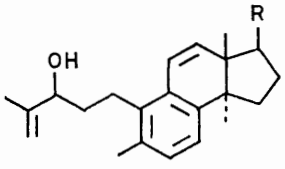


(1)

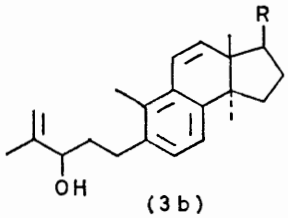


(2)

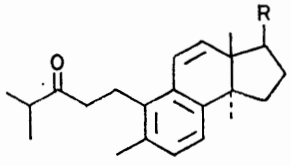
a; X = Ac
b; X = H



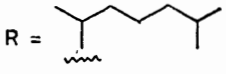
(3a)



(3b)



(4)



Heating 3β-acetoxylanost-8-ene (1a) with DDQ under reflux for 24 h gave an apparently homogeneous product that exhibited a complex n.m.r. spectrum. Separation of the product into three components was effected by basic hydrolysis followed by preparative layer chromatography. The major product was 3β-hydroxylanosta-7,9(11)-diene (51%) (2b), identified by comparison with authentic material.[2] Two other compounds (3) (19%) and (4) (6%) of unknown structure were isolated as gums.

Analysis of the n.m.r. spectrum of (3) showed signals indicative of a terminal methylene (δ 4.90 and 5.00) and a methyl attached to a double-bond (δ 1.72), which showed long-range coupling with the terminal methylene. The presence of these groups, together with resonances for an aromatic methyl (δ 2.28) and two aromatic protons (δ 6.76 and 7.00) implied a structure with a secolanostane skeleton containing an aromatic ring. The n.m.r. evidence for an aromatic ring and two double-bonds (*i.e.* an additional four double-bond equivalents) and the molecular formula $C_{30}H_{46}O$ (*m/e* 422.354 8), which showed (3) to have six protons less than the starting material, confirmed the secolanostane structure. The chemical shift (δ 4.10) of the hydrogen on the hydroxy-bearing carbon indicated that an allylic alcohol function was present in (3). These data suggested the structure for (3) to be either (3a or b). A decision between these possibilities was made by an n.m.r. experiment with the paramagnetic shift reagent tris(dipivalomethanato)-europium. The shift reagent caused a downfield shift of the doublet assigned to 11-H (δ 6.60) while the doublets for the aromatic hydrogens (δ 6.76 and 7.00) were not affected. This clearly demonstrated (3a) was the correct structure because a shift of the aromatic and not the vinylic resonances would be expected for structure (3b).

A comparison of the spectra of (3a) and (4) showed compound (4) to have a saturated ketone function in place of the allylic alcohol group of (3a), the remainder of the structure being the same.

The formation of (3a) and (4) presumably proceeds *via* the diene (2) since treatment of (2a) with DDQ, under the same conditions as (1a), also gave a mixture of (3a) and (4). Use of a large excess of DDQ provided a more complete conversion of (1a) to (3a) and (4). Reaction of (1a) with chloranil afforded only starting material. A pathway to these products is suggested in the Scheme.

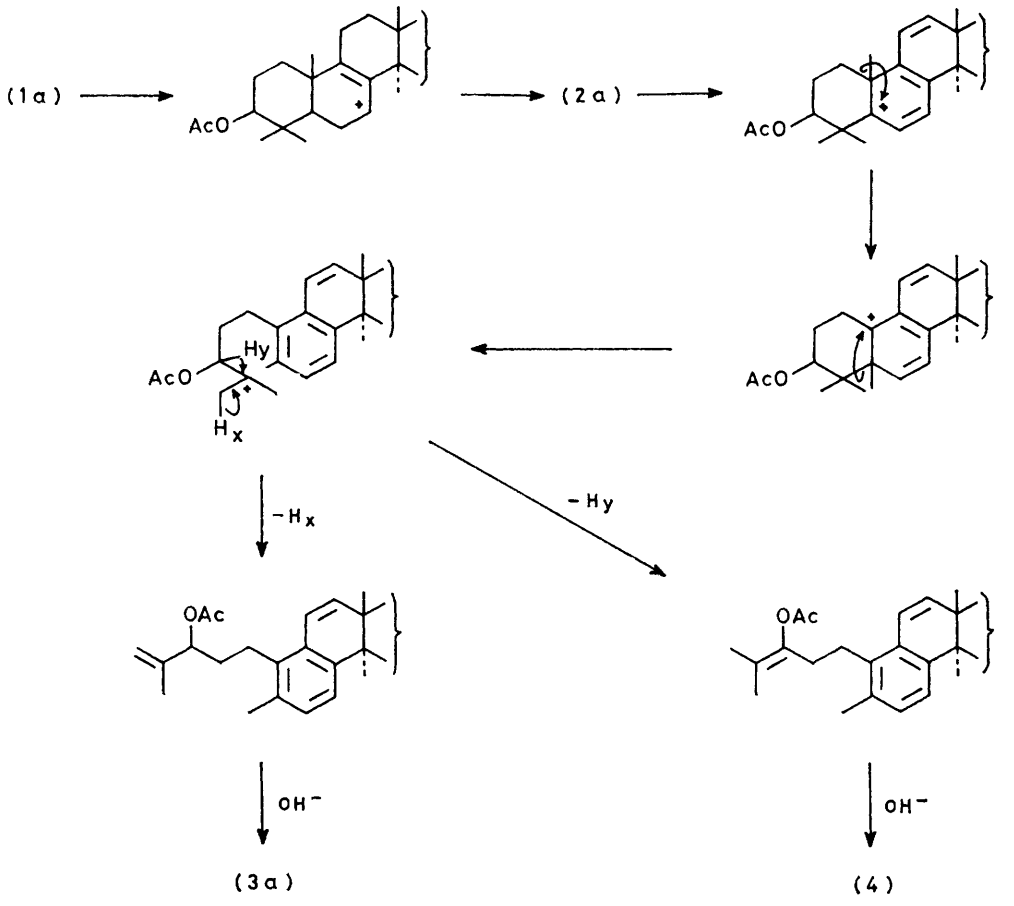
When 3β-hydroxylanost-8-ene (1b) was heated with DDQ under reflux for 24 h the diene 2b (20%) and the tetraenone (4) (24%) were formed. Thus only the pathway involving loss of H_y in the Scheme was followed by this compound.

Related rearrangements have been observed by Nijs and Speckamp [3] when steroidal azoester adducts were treated with acid. Aromatisation of ring B in triterpene 7,9(11)-dienes with acid [4] and other reactions leading

to ring B aromatic lanostanes have been described recently.[5]

EXPERIMENTAL

I.r. spectra were determined on a Perkin-Elmer 397 instrument and u.v. spectra in ethanol on a Beckman Acta CV spectrophotometer. N.m.r. spectra for deuteriochloroform solutions with tetramethylsilane as internal standard were recorded on a Varian EM-360 instrument and mass spectra on AEI MS30 and MS902 instruments. Microanalyses were determined by Professor A. D. Campbell, University of Otago, New Zealand.



SCHEME

Dehydrogenation of 3β-*Acetoxylanost*-8-*ene* (1a).—3β-Acetoxylanost-8-ene (1 g), 2,3-dichloro-5,6-dicyanobenzoquinone (1 g), and benzene (50 ml) were heated under reflux for 24 h. The mixture was cooled, filtered, and the residue was washed with benzene. The combined filtrates were washed with 1% aqueous potassium hydroxide and water and then dried ($MgSO_4$). The solvent was removed and the residue was heated for 1 h on a steam-bath with methanolic potassium hydroxide (0.1M; 30 ml) and dioxan (10 ml). The solution was concentrated *in vacuo*, diluted with water, and extracted with diethyl ether. The extracts were washed with water and dried ($MgSO_4$). The solvent was removed *in vacuo* to yield a solid which was chromatographed on 1 mm thick plates of silica gel. Elution with toluene–ethyl acetate (9 : 1) gave: (a) 3β-hydroxylanosta-7,9(11)-diene (2b) (470 mg) which on acetylation afforded 3β-acetoxylanosta-7,9(11)-diene (2a), m.p. 160—162° (lit.,[2] 164—166°), i.r., n.m.r., and mass spectra identical with those of an authentic sample; [2] (b) 3-*hydroxy*-19(10 → 5)-abeo-4,5-*secolanosta*-4(30),5,7,9,11-*pentaene* (3a) (171 mg) as a gum, $\nu_{max.}$ 3 400, 1 650, 1 050, and 890 cm^{-1}, $\lambda_{max.}$ 274 nm (ε 11 800), δ 0.74 (3 H, s, 18-H_3), 0.83 (6 H, d, *J* 7 Hz, 26-, 27-H_3), 1.10 (3 H, s, 32-H_3), 1.72 (3 H, s, 4-CH_3), 2.28 (3 H, s, 5-CH_3), 4.10 (1 H, t, *J* 7 Hz, 3-H), 4.90br and 5.00br (2 H, 2s, 4-CH_2), 6.35 and 6.60 (2 H, 2d, *J* 10 Hz, 11- and 12-H), and 6.76 and 7.00 (2 H, 2d, *J* 14 Hz, 6- and 7-H) (Found: C, 85.2; H, 11.0%; *m/e*, 422.3560. $C_{30}H_{46}O$ requires C, 85.2; H, 11.0%; *M*, 422.354 8); (c) 19(10 → 5)-abeo-4,5-*secolanosta*-5,7,9,11-*tetraen*-3-*one* (4) (60 mg) as a gum, $\nu_{max.}$ 1 715 cm^{-1}, $\lambda_{max.}$ 274 nm (ε 11 000), δ 0.77 (3 H, s, 18-H_3), 0.88 (6 H, d, *J* 7 Hz, 26-, 27-H_3), 1.10 (6 H, d, *J* 7 Hz, 2 × 4-CH_3), 1.17 (3 H, s, 32-H_3), 2.28 (3 H, s, 5-CH_3), 6.45 (2 H, s, 11- and 12-H), and 6.76 and 7.00 (2 H, 2d, *J* 14 Hz, 6- and 7-H) (Found: C, 84.9; H, 10.9%; *m/e*, 422.355 1. $C_{30}H_{46}O$ requires C, 85.2, H, 11.0%; *M*, 422.354 8).

Dehydrogenation of 3β-*Hydroxylanost*-8-*ene* (1b).—3β-Hydroxylanost-8-ene (0.5 g), 2,3-dichloro-5,6-dicyanobenzoquinone (1 g), and benzene (25 ml) were heated under reflux for 24 h and then worked-up as above (omitting the hydrolysis step). Chromatography gave: (a) 3β-hydroxylanosta-7,9(11)-diene (2b) (95 mg) identical with authentic material,[2] and (b) 19(10 → 5)*abeo*-4,5-secolanosta-5,7,9,11-tetraen-3-one(4) (117 mg) identical with material described above.

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