

Photolysis of 4,5-Epoxycholest-2-enes

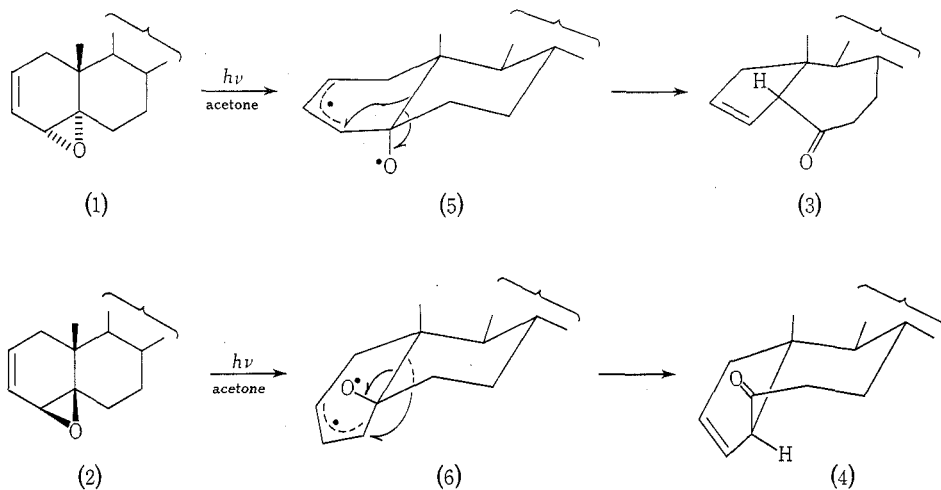
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Abstract

Photolysis of 4 α ,5-epoxy-5 α - and 4 β ,5-epoxy-5 β -cholest-2-enes in acetone (3000-Å lamps) effects molecular rearrangement to A-nor-B-homo-5 β - and -5 α -cholest-2-en-6-ones respectively.

The photolysis of α,β -epoxy olefins has received relatively little attention.¹ We now report the photolysis of two steroid epoxy alkenes of this type. The epoxides, 4 α ,5-epoxy-5 α - and 4 β ,5-epoxy-5 β -cholest-2-enes (1) and (2), were prepared by solvolysis of 4 α ,5-epoxy-5 α -cholestan-3 α -yl tosylate in collidine and 4 β ,5-epoxy-5 β -cholestan-3 β -yl tosylate by heating with Li₂CO₃-dimethylformamide respectively.²



The α -epoxide (1) was irradiated at 3000 Å for 10 h and gave a good yield (60%) of A-nor-B-homo-5 β -cholest-2-en-6-one (3). The identity of this compound follows from the infrared carbonyl absorption at ν_{\max} 1709 cm⁻¹, from the absence of a conjugated chromophore as shown by the ultraviolet spectrum, and from the p.m.r. spectrum which shows two vinyl protons and C 5-H deshielded by alkene and carbonyl moieties.

¹ Bauer, D. von, Iizuka, T., Schaffner, K., and Jeger, O., *Helv. Chim. Acta*, 1972, **55**, 852; Kristinsson, H., Mateer, R. A., and Griffin, G. W., *Chem. Commun.*, 1966, 415; Becker, R. S., Bost, R. O., Kolc, J., Bertoniere, N. R., Smith, R. L., and Griffin, G. W., *J. Am. Chem. Soc.*, 1970, **92**, 1302.

² Coxon, J. M., Garland, R. P., Hartshorn, M. P., and Lane, G. A., *Tetrahedron*, 1970, 1533.

The structure was further established by hydrogenation to A-nor-B-homo-5 β -cholestan-6-one, a known compound.³

Irradiation of the β -epoxide (2) was less efficient and gave A-nor-B-homo-5 α -cholest-2-en-6-one (4), which proved difficult to purify and was not obtained in a crystalline form. The identity of this product follows from the carbonyl absorption in the infrared spectrum at ν_{\max} 1709 cm^{-1} , the p.m.r. spectrum which showed two olefinic protons and C 5-H deshielded by the alkene and ketone groups and by conversion into the known A-nor-B-homo-5 α -cholestan-6-one by hydrogenation. The ketone produced was impure, and attempts to purify it resulted in epimerization to the equilibrium mixture of 5 α - and 5 β -isomers. The crystalline 5 β -isomer was treated with aqueous sulphuric acid in dioxan to produce an equilibrium mixture (c. 4 : 1) of 5 α - and 5 β -ketones. These molecular rearrangements are not without precedent and 2,5-dimethyl-4,5-epoxyhex-2-ene has been reported⁴ to give 3,5-dimethylhex-4-en-2-one. The yield of A-nor-B-homo-5 β -cholest-2-en-6-one from irradiation of 4 α ,5-epoxy-5 α -cholest-2-ene makes this a viable route to C 3- and in particular C 2-substituted A-nor-B-homo C 6-ketones. The reactions are believed to occur by acetone-sensitized excitation of the starting epoxides followed by C-O bond cleavage to give allylic oxygen biradicals (5) and (6) respectively. Stereospecific migration of the C 10-C 5 bond to C 4 for each compound results in the formation of ketones (3) and (4).

Experimental

Infrared spectra were recorded on a Shimadzu IR27G spectrophotometer, ultraviolet spectra on a Shimadzu MPS-50L instrument and n.m.r. spectra on a Varian A60 or T60 spectrometer for CDCl_3 solutions with CHCl_3 and SiMe_4 as internal standards. Optical rotatory dispersion measurements were recorded on a Jasco ORD/UV-5. Mass spectra were recorded on an A.E.I. MS902 spectrometer. Alumina used for chromatography was Spence grade H deactivated by the addition of 5% v/v of 10% acetic acid. Photolyses were carried out in a Rayonet photochemical reactor.

Photolysis

(A) 4 α ,5-Epoxy-5 α -cholest-2-ene.—A solution of 4 α ,5-epoxy-5 α -cholest-2-ene (177 mg) in dry degassed acetone in a nitrogen atmosphere was irradiated (3000 Å) in a Pyrex container for 10 h. After removal of solvent the residue was adsorbed onto alumina (20 g). Elution with light petroleum-ether (100 : 2) gave a trace of starting epoxide (10 mg) and A-nor-B-homo-5 β -cholest-2-en-6-one (108 mg) crystallized as plates from methanol, m.p. 83–84°, ν_{\max} 1709 cm^{-1} , λ^{MeOH} 230 nm (ϵ 20), 240 (20). P.m.r. δ 0.72 (C 18-H₃), 0.82 and 0.90 (side chain methyls), 1.15 (C 19-H₃), 3.58 ($W_{h/2}$ 6 Hz, C 5-H), 5.55 and 5.90 ($W_{h/2}$ 8 Hz, C 2-H and C 3-H). Double irradiation at C 2-H, C 3-H or C 5-H led to sharpening of the signals due to the other two protons. O.r.d. (in ethanol) $[\Phi]_{350}$ -1954, $[\Phi]_{335}$ -2490, $[\Phi]_{325}$ -3352, $[\Phi]_{315}$ -4501, $[\Phi]_{307}$ -5364, $[\Phi]_{300}$ -4884, $[\Phi]_{290}$ -2298, $[\Phi]_{281}$ 0, $[\Phi]_{278}$ +575, $[\Phi]_{275}$ +1053, $[\Phi]_{269}$ +1244, $[\Phi]_{265}$ +1149, $[\Phi]_{260}$ +575, $[\Phi]_{256}$ 0 (Found: C, 84.3; H, 11.5; M^+ 384.3403. $\text{C}_{27}\text{H}_{44}\text{O}$ requires C, 84.4; H, 11.5%; M^+ 384.3392).

Hydrogenation of A-nor-B-homo-5 β -cholest-2-en-6-one (30 mg) was effected by agitation in a hydrogen atmosphere of a solution of the compound in pentane containing palladium on carbon (20 mg; 5%) as catalyst. Isolation of the product in the usual manner and recrystallization from methanol gave A-nor-B-homo-5 β -cholestan-6-one (22 mg) as needles, m.p. 93–94°, ν_{\max} 1709 cm^{-1} . P.m.r. δ 0.70 (C 18-H₃), 0.82 and 0.90 (side chain methyls), 1.07 (C 19-H₃), 3.02 ($J_{3,5}$ 8 Hz, $J_{3,4}$ 5 Hz, C 5-H). O.r.d. (in ethanol) $[\Phi]_{350}$ -1055, $[\Phi]_{340}$ -1266, $[\Phi]_{330}$ -1477, $[\Phi]_{320}$ -2215, $[\Phi]_{310}$ -3165, $[\Phi]_{303}$ -3480, $[\Phi]_{300}$ -3375, $[\Phi]_{290}$ -1582, $[\Phi]_{284}$ 0, $[\Phi]_{280}$ +1371, $[\Phi]_{270}$ +3271, $[\Phi]_{260}$

³ Nussim, M., and Mazur, Y., *Tetrahedron*, 1968, 5337.

⁴ Paulson, D. R., Korngold, G., and Jones, G., *Tetrahedron Lett.*, 1972, 1723.

+4325, $[\Phi]_{255} + 4429$, $[\Phi]_{250} + 4320$. Lit.³ m.p. 94–95°; ν_{\max} 1705 cm^{-1} ; p.m.r. δ 0.69 and 1.07 (methyls); o.r.d. $a - 63$.

(B) *4 β ,5-Epoxy-5 β -cholest-2-ene*.—A solution of 4 β ,5-epoxy-5 β -cholest-2-ene (140 mg) in acetone was photolysed as above for 12 h and gave a crude reaction product which on rapid chromatography afforded starting material (19 mg) and A-nor-B-homo-5 α -cholest-2-en-6-one (c. 80% pure, 36 mg) as a relatively unstable oil. ν_{\max} 1709 cm^{-1} . P.m.r. δ 0.71 (C 18–H₃), 0.82 (C 19–H₃), 0.82 and 0.90 (side chain methyls), 3.88 ($W_{h/2}$ 6 Hz, C 5–H), 5.80 (C 2–H, C 3–H) (Found: M^+ 384. $\text{C}_{27}\text{H}_{44}\text{O}$ requires M^+ 384).

Hydrogenation of A-nor-B-homo-5 α -cholest-2-en-6-one (30 mg) catalysed by palladium on carbon (5%) for 9 h as above gave A-nor-B-homo-5 α -cholestan-6-one (c. 70% pure). ν_{\max} 1704 cm^{-1} . P.m.r. δ 0.67 (C 18–H₃ and C 19–H₃), 0.82 and 0.90 (side chain methyls), 2.97 ($W_{h/2}$ 15 Hz, C 5–H). O.r.d. $[\Phi]_{350} + 1930$, $[\Phi]_{340} + 2122$, $[\Phi]_{330} + 2894$, $[\Phi]_{320} + 3860$, $[\Phi]_{311} + 4631$, $[\Phi]_{305} + 3860$, $[\Phi]_{295} + 1736$, $[\Phi]_{288} 0$, $[\Phi]_{280} - 1351$, $[\Phi]_{275} - 1925$, $[\Phi]_{270} - 1930$, $[\Phi]_{265} - 1544$, $[\Phi]_{260} - 1351$ (Found: M^+ 386.3551. Calc. for $\text{C}_{27}\text{H}_{46}\text{O}$: M^+ 386.3548). Lit.³ m.p. 86–88°; ν_{\max} 1702 cm^{-1} ; p.m.r. δ 0.67 (methyls); o.r.d. $a + 136$.

Equilibration of A-nor-B-homo-5 β -cholestan-6-one

A mixture of A-nor-B-homo-5 β -cholestan-6-one (50 mg) in dioxan (5 ml) and aqueous sulphuric acid (0.1 ml; 20%) was heated under reflux in a nitrogen atmosphere for 2 h. Isolation of the product in the usual manner gave a mixture (c. 4 : 1) of A-nor-B-homo-5 α - and -5 β -cholestan-6-ones. P.m.r. δ 0.67 (C 18–H₃ and C 19–H₃; 5 α -ketone), 0.82 and 0.90 (side chain methyls), 1.07 (C 19–H₃; 5 β -ketone). O.r.d. $[\Phi]_{350} + 1425$, $[\Phi]_{340} + 1730$, $[\Phi]_{330} + 2341$, $[\Phi]_{320} + 3461$, $[\Phi]_{310} + 4174$, $[\Phi]_{300} + 2850$, $[\Phi]_{290} 0$, $[\Phi]_{285} - 1119$, $[\Phi]_{280} - 2087$, $[\Phi]_{269.5} - 2810$, $[\Phi]_{265} - 2545$, $[\Phi]_{255} - 1934$ (Found: M^+ 386.3544. Calc. for $\text{C}_{27}\text{H}_{46}\text{O}$: M^+ 386.3548). Lit.³ o.r.d. $a + 88$.

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