Isomerisation of Epoxides

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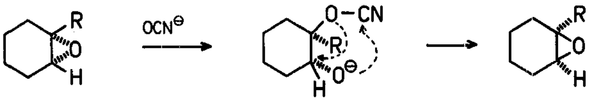
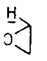
Epoxides of various types can be isomerised by treatment with potassium cyanate in 50% aqueous ethanol. We carried out the reaction at room temperature or in the boiling solvent and obtained the isomerised products in yields of 20–48%. It was observed[1] that the reaction takes place only if the intermediary ring-opening product can be converted into the diequatorial form:



It has been reported[2,3] that the ring opening of steroid epoxides leads to products possessing a *trans*-diaxial structure and that interconversion is impossible. Thus, in the case of 5α,6α-epoxysteroids and also in the case of 2,3-epoxynorbornane no isomerisation products could be obtained.

Table 1. Isomerisation of Epoxysteroids

Starting Epoxide	Yield of isomerised product	N.M.R. Data		
			$17\text{-CO-C}\underline{\text{H}}_3$	$L\frac{h}{2}$ 10-CH_3
5α, 6α—epoxypregnenolone	0	2.85	2.12	1.2 cps
5β, 2β—epoxypregnenolone	21	2.99	2.19	0.5
5α, 6α—epoxypregnenolone acetate	0	2.92	2.16	1.3
5β, 6β—epoxypregnenolone acetate	24	3.02	2.11	0.7
5α, 6α—epoxycholesterol	0	2.89	—	—
5β, 6β—epoxycholesterol	22	2.94	—	—
5α, 6α—epoxycholesterol acetate	0	2.93	—	1.6
5β, 6β—epoxycholesterol acetate	48	3.17	—	0.4
16α, 17α—epoxypregnenolone	31	3.66	2.15	—
16β, 17β—epoxypregnenolone	—	3.39	2.08	—
16α, 17α—epoxypregnenolone acetate	20	3.70	2.17	—
16β, 17β—epoxypregnenolone acetate	0	3.52	2.12	—
16α, 17α—epoxyprogesterone	28	3.72	2.19	—
16β, 17β—epoxyprogesterone	0	3.51	2.04	—

However, 5β,6β-epoxysteroids can be isomerised to the 5α,6α-forms via the *trans*-equatorial ring-opening reaction formulated above. Analogously, 16α,17α-epoxysteroids may be converted into the 16β,17β-isomers in 20–31% yield, due to the relatively low rigidity of the steroidal ring D.

The isomerisation was proved by N.M.R. spectrometry (Table 1). The 5α,6α-epoxides show the signal of the oxirane proton at 2.8–2.9 ppm; the 5β, 6β-epoxides show the corresponding signal at 3.0–3.3 ppm. For 16α,17α-epoxysteroids, the signal is at 3.6–3.7 ppm, and for 16β,17β-epoxysteroids at 3.3–3.5 ppm[3,4]. The signals for 17α- and 17β-acetyl groups are found at ~2.15 and ~2.08 ppm, respectively[5]. The percentage of isomeric epoxide was calculated from the N.M.R. spectra (10%, $CDCl_3$) obtained using a Varian A-60 apparatus.

Procedure: The epoxide (1 mol) is added in 2 portions to a solution of potassium cyanate in water/ethanol (1+1); the resultant solution is stirred vigorously for 30 min. at reflux temperature and for 36—48 hr at room temperature. The epoxide is extracted with ether or chloroform. The extract is washed with saturated sodium chloride solution and dried over sodium sulfate. The solvent is removed in vacuo and the residue recrystallized from ethanol.

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