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THE STEREOSELECTIVE THERMAL ISOMERISATION OF STEROIDAL ISOCYANIDES TO CYANIDES

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Stereoselectivity in the long-known thermal isomerisation of isocyanides to cyanides has recently (1) been demonstrated by conversion of optically active sec-butyl isocyanide into the cyanide with 86% retention of optical activity. Having available in the course of other work a range of cyano and isocyano derivatives of 5α-cholestane, we investigated the steric course of the isomerisation in this series. In every case the cyanide was formed with very high retention of configuration at the relevant ring carbon atom, and, apart from its theoretical interest, the isomerisation provides a useful route to the 6α - and 7β - cyanides, which are unobtainable (except in traces) from the epimeric mesylates with alkali cyanides.

Other steroidal cyanides used in our work were also prepared from the epimeric tosylates by treatment with sodium cyanide in N-methyl-pyrrolidone (2); configurations were confirmed by examination of the half-intensity width of the H-C-CN multiplet in the N.M.R. spectra. Isocyanides were obtained by dehydration of formamides with tosyl chloride in pyridine (3).

The thermal isomerisations were effected by heating the isocyanides under nitrogen to 270° for 20 minutes. Relative proportions of epimeric cyanides formed were determined by high-temperature G.L.C. analysis (4), and the percentages retention of configuration, together with significant physical properties of compounds used in the investigation, are given in the Table. Purification of the solidified melts by chromatography on alumina and recrystallisation gave cyanides of retained configuration in yields up to 70% based on the reactant isocyanides.

TABLE

Properties of Cyano and Isocyano Derivatives of

5α - Cholestane

Derivative.*	m.p., degrees.	CN or NC stretching band,** cm^{-1}.	% Retention of configuration in isomerisation
3α-CN (2)	166 - 168	2247	-
3β-CN (2)	142 - 144	2245	-
6α-CN	138 - 140	2240	-
6β-CN	130 - 132	2237	-
7α-CN	146 - 148	2232	-
7β-CN	100 - 101	2235	-
3α-NC (3)	142	2147	>99
3β-NC	117	2150	94
6α-NC	135	2140	>99
6β-NC	126 - 128	2137	92
7α-NC	144 - 145	2135	>99
7β-NC	96 - 97	2138	92

* Satisfactory analyses have been obtained for all new compounds.

** Measured on Unicam SP 100 infrared spectrometer.

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(4) G.L.C. analyses by courtesy of Prof. J.K. Norymberski, Endocrinological Laboratory, University of Geneva, and Mr. W.R. Dixon, Endocrine Investigation Centre, Jessop's Hospital, Sheffield.