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THE STEREOCHEMISTRY OF ETHYLENEIMINES FUSED TO SIX-MEMBERED RINGS

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BY studying the reactions of a number of steroidal epoxides, Barton has formulated the "rule of diaxial opening" which has come to be one of the fundamental tenents of conformational analysis.[1,2] Comparatively little effort has been expended, however, toward the elucidation of the stereochemistry of ring opening of analogous ethyleneimines. It has been shown that ethyleneimines undergo ring opening in a trans manner,[3,4,5] but it remains to be shown whether or not this ring system opens in a diaxial manner when fused to a six-membered ring.

We would now like to report the first synthesis of a steroidal ethyleneimine and evidence that the ring does indeed open in a trans-diaxial manner. 2-Cholestene was converted into an iodo-isocyanate I, m.p. 110.5-112°, ν_{max} 2260 cm^{-1}, in 90% yield upon treatment with iodine isocyanate in ether solution.[6,7] The structure of this compound is inferred from the fact that iodine isocyanate is known to add to olefins in a trans manner[7] and from the structure of the products in the reaction sequence. Compound

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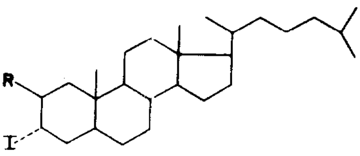
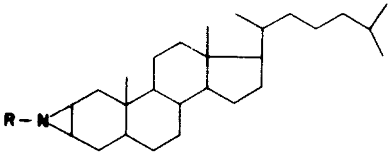
[1] G. Alt and D. H. R. Barton, J. Chem. Soc. 4284 (1954)
[2] D. H. R. Barton and R. Cookson, Quart. Revs. 10, 67 (1956)
[3] R. Ghirardelli and H. Lucas, J. Amer. Chem. Soc. 77, 106 (1955)
[4] F. Winternitz, M. Mousseron, R. Dennilauler, Bull. Soc. Chim. Fr. 1956, 382
[5] O. Paris and P. Fanta, J. Amer. Chem. Soc. 74, 3007 (1952)
[6] L. Birckenbach and M. Lindhard, Chem. Ber. 64, 961 (1931)
[7] G. Drefahl and K. Ponsold, Chem. Ber. 93, 519 (1960)

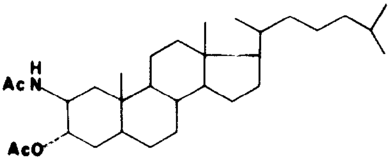
I formed a methyl ureathan (II, m.p. 160-162°, ν_{max} 3430, 1730, and 1495 cm^{-1}) in 90% yield on refluxing with methanol. Ureathan II was cyclized in 88% yield by refluxing with alcoholic potassium hydroxide to the 2β,3β-iminocholestane IV, m.p. 105-106.5°, ν_{max} 3300, 1420, and 800 cm^{-1} (phenylurea V, m.p. 145-146°). Ethyleneimine IV was also obtained by hydrolyzing the isocyanate I with hydroiodic acid in aqueous acetone to the iodoamine hydroiodide III, m.p. 197-198° dec, ν_{max} 3080, 1880, and 1570 cm^{-1}, and cyclizing III to IV in 65% yield with alcoholic potassium hydroxide at room temperature.



I R:NCO;
II R:$NHCO_2CH_3$;
III R:$NH_3^+I^-$



IV R:H
V R:$CONHC_6H_5$



VI

When the ethyleneimine IV was heated briefly with glacial acetic acid and the product was acetylated, amido acetate VI, m.p. 191-192°, ν_{max} 3300, 3080, 1740, 1640, 1555, and 1240 cm^{-1}, was obtained in 75% yield. The structure of VI was proved by unequivocal synthesis from 2α,3α-oxidocholestane and aqueous-alcoholic ammonia at 100° for 10 hours, since epoxides are known to undergo ammonolysis in a trans-diaxial manner.[8] Thus, ethyleneimine IV must be opened in a trans-

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[8] J. Sicher, F. Sipos and M. Tichy, Coll. Czech. Chem. Commun., 26 847 (1961)

diaxial fashion in order to give 2β-acetamido-3α-cholestanyl acetate VI. Similarly, ethyleneimine IV is opened diaxially by hydrochloric acid or by hydroiodic acid to yield 2α-chloro-3β-aminocholestane hydrochloride (85%) or 2α-iodo-3β-aminocholestane hydroiodide III (98%) respectively. That the ring opening does not proceed by way of carbonium ions but requires a strong nucleophile is further indicated by the fact that ethyleneimine IV is not affected by perchloric acid in methanol. The structural assignments presented are in agreement with the assumption that iodine isocyanate adds diaxially to 2-cholestene.

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