

Transannular Hydride Shifts. An Application to the Synthesis of *Lycopodium* Alkaloids

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RECENTLY much interest has been shown in transannular reactions in the bicyclo[3,3,1]nonane system¹⁻⁴ and the occurrence of transannular hydride shifts has been demonstrated.^{2,4} The

driving force in these hydride shifts^{2,4} has been the energy gain associated with the transformation of a disubstituted olefinic system into a trisubstituted one. We now report a case in

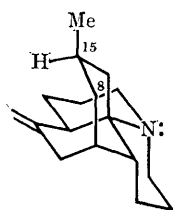
¹ H. Stetter, J. Gartner, and P. Tackle, *Angew. Chem.*, 1965, **4**, 1953.

² H. Dugas, R. A. Ellison, Z. Valenta, K. Wiesner, and C. M. Wong, *Tetrahedron Letters*, 1965, 1279.

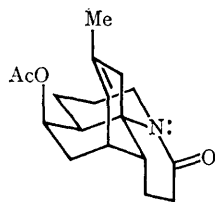
³ M. Eakin, J. Martin, and W. Parker, *Chem. Comm.*, 1965, 206.

⁴ R. A. Appleton and S. H. Graham, *Chem. Comm.*, 1965, 297.

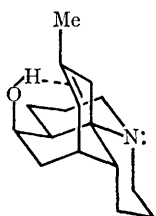
which a trisubstituted olefinic linkage in a bicyclo[3,3,1]nonane system has been saturated at the expense of a secondary alcohol, presumably



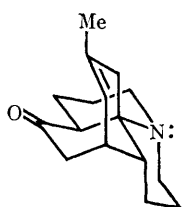
(I)



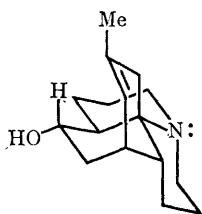
(II)



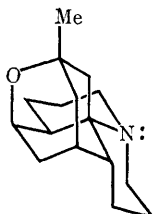
(III)



(IV)



(V)



(VI)

by means of a transannular hydride shift. The reaction is of potential value in the synthesis of *Lycopodium* alkaloids such as lycopodine (I) since it provides a stereospecific method for elaborating the natural configuration at C-15 in these alkaloids.

The starting point for this series of reactions was the unsaturated lactam (II), previously⁵ prepared from lycopodine (I). Reduction of (II) with lithium aluminium hydride afforded the unsaturated alcohol (III),⁶ m.p. 93–94°, ν_{\max} (CCl₄) 3542 (concentration-independent, OH to π -H-bonded hydroxyl?) 1670 cm.⁻¹ (double bond). The alcohol (III) was also obtained by hydrolysis of anhydrolofoline.⁸ Modified Oppenauer oxidation⁹ of (III) yielded the ketone (IV),⁶ m.p. 126–127.5°, ν_{\max} (CCl₄) 1710, 1670 cm.⁻¹, which on reduction with sodium-ammonia-methanol furnished the amorphous alcohol (V)⁶ (m.p. of methiodide 288–289°, ν_{\max} (CCl₄) 3620 (non H-bonded hydroxyl), 1675 cm.⁻¹ (double bond).

The alcohol (V), when dissolved in 75% sulphuric acid,² was transformed into lycopodine (I) in almost quantitative yield. The transformation of a secondary alcohol into a ketone by a transannular hydride shift has previously been observed in the cyclodecane series.¹⁰ As expected,⁵ the alcohol (III) gave only the oxide (VI) when treated with 75% sulphuric acid.

This sequence provides a method for adding a hydrogen to the more hindered side of C-15, a result not easily achieved by other means. Thus, equilibration of a carbonyl function at C-8 yields the 15-epi-series¹¹ (with the bridging ring in the boat conformation¹¹) and we now find that platinum-catalysed hydrogenation of the unsaturated ketone (IV) yields dihydrodeoxyannofoline,¹² the C-15 epimer of dihydrolycopodine (I, carbonyl reduced to axial alcohol).

(Received, September 24th, 1965; Com. 611.)

⁵ W. A. Ayer, D. A. Law, and K. Piers, *Tetrahedron Letters*, 1964, 297.

⁶ Satisfactory microanalytical and/or mass-spectral data were obtained for all new compounds reported, and the nuclear magnetic resonance spectra were completely consistent with the structures formulated.

⁷ K. Nakanishi, "Infrared Absorption Spectroscopy, Practical," Holden-Day, San Francisco, 1962, p. 30.

⁸ R. H. Burnell and D. R. Taylor, *Tetrahedron*, 1961, 15, 173.

⁹ E. W. Warnhoff and P. Reynolds-Warnhoff, *J. Org. Chem.*, 1963, 28, 1431.

¹⁰ V. Prelog and W. Küng, *Helv. Chim. Acta*, 1956, 39, 1394.

¹¹ F. A. L. Anet, *Tetrahedron Letters*, 1960, No. 20, 13.

¹² F. A. L. Anet and N. H. Khan, *Chem. and Ind.*, 1960, 1238.