Conversion of the Alkaloid Atisine into a Compound with the Lycoctonine Skeleton

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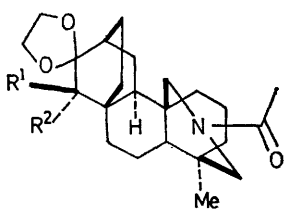
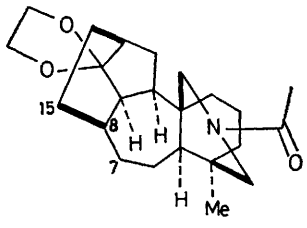
Summary The conversion of atisine into the ketone (**13**), which has a lycoctonine skeleton, and the *X*-ray structure determination of this product is described.

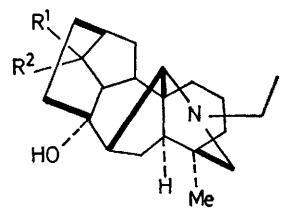
THE skeletal structure of the first C_{20} aconite alkaloid atisine was deduced in 1953,[1] and an *X*-ray analysis later revealed the structure of lycoctonine,[2] the prototype of the rearranged C_{19} alkaloids. As a result of these structural studies a possible biosynthetic transformation of atisine-type starting materials into lycoctonine-type alkaloids by rearrangement, bridging, and the loss of a carbon atom was postulated.[3]



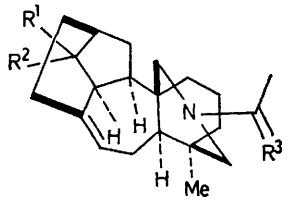
(1) $R^1, R^2 = =O$
(2) $R^1 = OH, R^2 = H$
(3) $R^1 = H, R^2 = OH$
(4) $R^1 = OSO_2C_6H_4Me\text{-}p, R^2 = H$



(7)
(5) $\Delta^{8,15}$ compound
(6) $\Delta^{7,8}$ compound



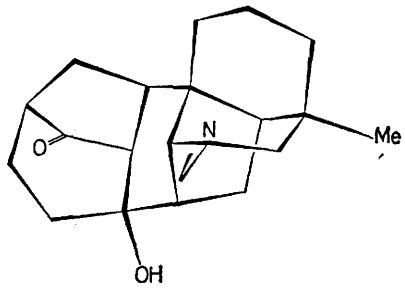
(11) $R^1 = OH, R^2 = H$
(12) $R^1 = H, R^2 = OH$
(13) $R^1, R^2 = =O$



(8) $R^1, R^2 = =O, R^3 = =O$
(9) $R^1 = OH, R^2 = H, R^3 = H_2$
(10) $R^1 = H, R^2 = OH, R^3 = H_2$

We now report the laboratory conversion of atisine into compound (**13**) and the verification of the lycoctonine-like skeleton of this material by *X*-ray crystallography. Reduction ($NaBH_4$) of the acetal-ketone (**1**), prepared from atisine as reported by Johnston and Overton,[4] gave a mixture of the alcohols (**2**) and (**3**) also obtained by these authors.[4] Separation by preparative t.l.c. and crystallization yielded the pure β-isomer (**2**) [m.p. 190—192 °C, τ 6·00 (4H, s, OCH_2CH_2O), 7·90 (3H, s, NCOMe), and 9·13 (3H, s, ≥CMe); ν_{max} 3540 (OH) and 1640 cm^{-1} (amide CO)]. Tosylation of the β-alcohol (**2**) with toluene-*p*-sulphonyl chloride in pyridine gave the amorphous tosylate (**4**) which was homogeneous on t.l.c. [τ 6·57 (4H, m, OCH_2CH_2O) and 7·55 (3H, s, tosyl-Me)].

A solution of this material in Me_2SO with tetramethylguanidine was heated at 180 °C for 24 h. The oily rearranged products (**5**) and (**6**) were separated by preparative t.l.c. in an overall yield of 85%.



FIGURE

The product (**5**) had been previously obtained[4] by pyrolytic rearrangement of a tosyloxy-ketone followed by acetalization, and Professor Overton has kindly established its identity with his own material. The crucial isomer (**6**) showed the following: ν_{max} 1640 cm^{-1} (amide CO); τ 4·66 (1H, t, vinylic-H), 6·03 (4H, s, OCH_2CH_2O), 7·90 (3H, s, NCOMe), and 9·07 (3H, s, CMe).

Hydrogenation of compounds (**5**) and (**6**) gave the same dihydroderivative (**7**), the identity of which was established by t.l.c., and *i.r.*, *n.m.r.*, and mass spectroscopy. Deacetalization of compound (**6**) in aqueous methanolic HCl under reflux yielded the corresponding oily ketone (**8**) [ν_{max} 1760 cm^{-1} (CO)]. Reduction ($LiAlH_4$) of this material gave a mixture of the epimeric hydroxyamines (**9**) and (**10**). These compounds were treated without separation with $Hg(OAc)_2$[5] and the epimeric products (**11**) and (**12**) of this oxidative cyclization were converted into the ketone (**13**) by further oxidation with Jones reagent. Compound (**13**) was recrystallized from ether–pentane to a constant m.p. of 157—159 °C [ν_{max} 3600 and 3450 (OH), and 1751 cm^{-1} (C=O); τ 8·93 (3H, t, *J* 7 Hz, NCH_2Me) and 9·20 (3H, s, CMe)], and subjected to *X*-ray analysis.

Crystals of (**13**) belong to the space group $P2_12_12_1$: $a = 10{\cdot}404$, $b = 22{\cdot}040$, $c = 7{\cdot}666$ Å. The structure was solved by direct phasing methods and refined using a least-squares procedure. The projection of the molecule along the *a* axis is shown in the Figure.

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