Absolute Configuration of the Alkaloid Cularine: an *X*-Ray Structure Determination

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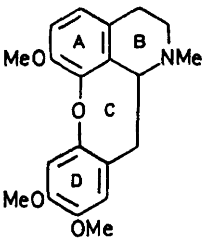
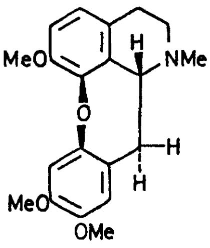
Summary The structure of cularine has been determined by a three-dimensional *X*-ray crystal analysis of the methiodide, and the absolute configuration of the alkaloid has been assigned as (*S*).

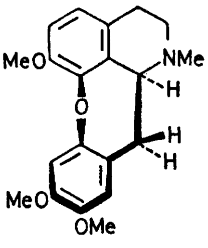
CULARINE, an alkaloid isolated from the genera *Dicentra* and *Corydalis*, was assigned structure (**1**) by Manske[1–3] on the basis of chemical degradation. The alkaloid has a unique feature; the oxygen functions are at the 7,8-positions of the tetrahydroisoquinoline, and a dihydrodibenz[*b,f*]oxepin ring is formed by a biphenyl ether linkage at the 8-position. Its configuration had been shown to be (**2**), *i.e.* (*R*),[4] from both the o.r.d. of the hydrogenolysis product, and the n.m.r. spectrum.[5] However, it was recently reported[6] that the absolute configuration of cularine should be (**3**), *i.e.* (*S*), from chemical correlation.



(1)



(2)



(3)

The present *X*-ray analysis was undertaken in order to determine the absolute configuration definitely, using the methiodide of (**1**).

The crystals are colourless plates. A specimen was sealed in a thin-walled Lindemann glass capillary tube throughout the data collection, since the crystals gradually degraded in air.

Crystal data: $C_{21}H_{26}NO_4I$, m.p. 205°, $M = 483{\cdot}4$, monoclinic, space group $P2_1$, $a = 22{\cdot}31$, $b = 8{\cdot}43$, $c = 11{\cdot}71$ Å, $\beta = 90{\cdot}9°$, $U = 2201{\cdot}9$ Å^3, $D_c = 1{\cdot}53$ g cm^{-3}, D_m 1·52 g cm^{-3} $Z = 4$. Multiple-film equi-inclination Weissenberg photographs were taken using Ni-filtered Cu-K_α radiation about the *b* axis, and intensities of 1312 independent reflexions were measured visually. The structure was solved by the heavy-atom method. The positional and thermal parameters were refined by the least-squares method. The final *R* factor was 0·100 for the observed reflexions.

The absolute configuration was determined using the anomalous dispersion effect of the iodine atom. Significant differences in 14 Bijvoet pairs were observed on oscillation photographs about the *b* axis. The structure factors including the effect of anomalous dispersion by iodine ($\Delta f'' = 7{\cdot}0$ electrons) were calculated using the atomic parameters for molecular configuration (**3**) in a right-handed co-ordinate system. The observed inequalities were in good agreement with those calculated for all 14 pairs. If the configuration (**2**) were correct, the inequalities would have been reversed.

Thus the absolute configuration of cularine is assigned as (*S*). From the chemical studies and the present *X*-ray analysis, it can be concluded that the cularine group of alkaloids[2–8] has the (*S*)-configuration.

The two independent molecules in the asymmetric unit have essentially the same conformation, *i.e.*, the dihydro-oxepin rings are of twist boat-shape, the oxygen atom being the bow. The dihedral angles between the A and D rings in the two molecules are 59·3 and 54·6°.

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