

## Biosynthesis of Homoaporphines

By A. R. BATTERSBY,\* P. BÖHLER, M. H. G. MUNRO, and R. RAMAGE

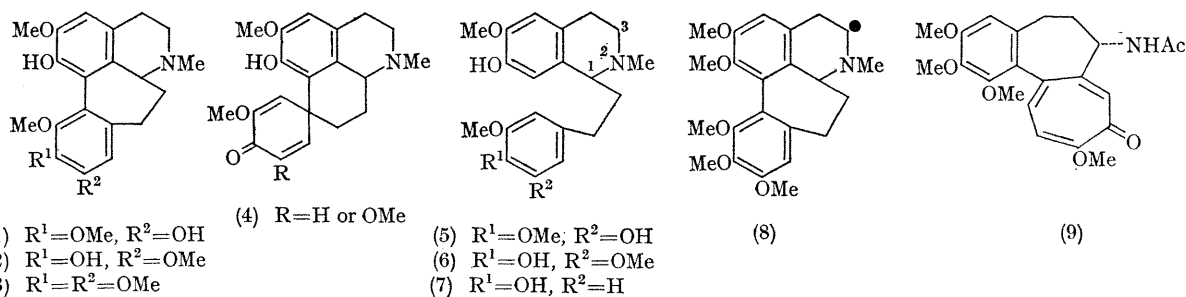
(The Robert Robinson Laboratories, University of Liverpool, Liverpool L69 3BX)

**Summary** The homoaporphine alkaloids [*e.g.* (1)] of *Kreysigia multiflora* are shown to be derived *in vivo* from autumnaline (5).

THE structures of floramultine, multifloramine, and kreysigine from *Kreysigia multiflora* have been shown<sup>1,2</sup>

arise naturally by way of homoproaporphines [*e.g.* (4)] or by direct coupling *e.g.* of autumnaline (5).

In order to distinguish between these possibilities, the [<sup>3-<sup>14</sup>C</sup>]diphenols (5), (6), and (7) were administered to *Kreysigia multiflora* shoots. Diazomethane methylation of the total alkaloids extracted from the shoots converted



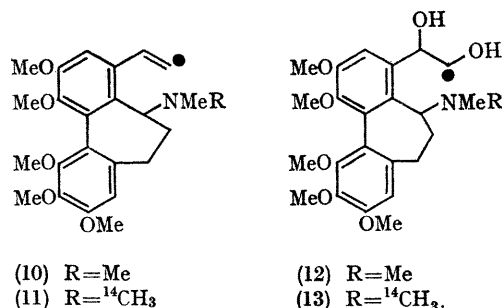
respectively, to be (1), (2), and (3) based upon the homoaporphine skeleton. By analogy with the biosynthesis of several aporphine alkaloids,<sup>3-5</sup> the homoaporphines could

the homoaporphines (1), (2), and (3) into *O*-methylkreysigine (8) which was isolated by dilution with inactive carrier. The good incorporation (1.6%) of autumnaline

(5) compared to the very low efficiency ( $<0.014\%$ ) of the diphenol (6) is in accord with a mechanism involving direct coupling. These results imply that floramultine (1) is the first homooporphine alkaloid to be formed. The incorporation (0.21%) of (7) is presumably by conversion into autumnaline (5) as occurs in the biosynthesis of colchicine<sup>6,7</sup> (9).

Proof that the incorporation of autumnaline (5) was specific was obtained by conversion of the labelled *O*-methylkreysigine (8) into its methiodide, followed by Hofmann degradation to the methine (10). The spectroscopic data for (10) proved this structure and eliminated the possible alternative one. The corresponding diol (12), prepared from (10) with osmium tetroxide, was cleaved by periodate to yield formaldehyde isolated as its dimedone derivative. The specific activity of this derivative showed that at least 85% of the total activity of (8) is located at the position shown. The slightly low value found is a result of dilution by radio-inactive formaldehyde arising from an *N*-methyl group. The source of dilution was determined by repeating the degradative sequence on radio-inactive (8)

but using [<sup>14</sup>C]methyl iodide to yield the labelled methine (11) and diol (13) and, finally, radioactive formaldehyde dimethone.



These results demonstrate the specific formation of the homooporphine system from autumnaline (5); the detail of the process is under current investigation.

(Received, August 6th, 1969; Com. 1211.)

<sup>1</sup> A. R. Battersby, R. B. Bradbury, R. B. Herbert, M. H. G. Munro, and R. Ramage, *Chem. Comm.*, 1967, 450.

<sup>2</sup> A. R. Battersby, E. McDonald, M. H. G. Munro, and R. Ramage, *Chem. Comm.*, 1967, 934.

<sup>3</sup> D. H. R. Barton, D. S. Bhakuni, G. M. Chapman, and G. W. Kirby, *J. Chem. Soc. (C)*, 1967, 2134.

<sup>4</sup> A. R. Battersby, T. J. Brocksom, and R. Ramage, *Chem. Comm.*, 1969, 464.

<sup>5</sup> G. Blaschke, *Arch. Pharm.*, 1968, **301**, 432.

<sup>6</sup> A. R. Battersby, R. B. Herbert, E. McDonald, R. Ramage, and J. H. Clements, *Chem. Comm.*, 1966, 603.

<sup>7</sup> A. C. Barker, A. R. Battersby, E. McDonald, R. Ramage, and J. H. Clements, *Chem. Comm.*, 1967, 390.