

The Absolute Configuration of Cryptopleurine and Tylocrebrine*

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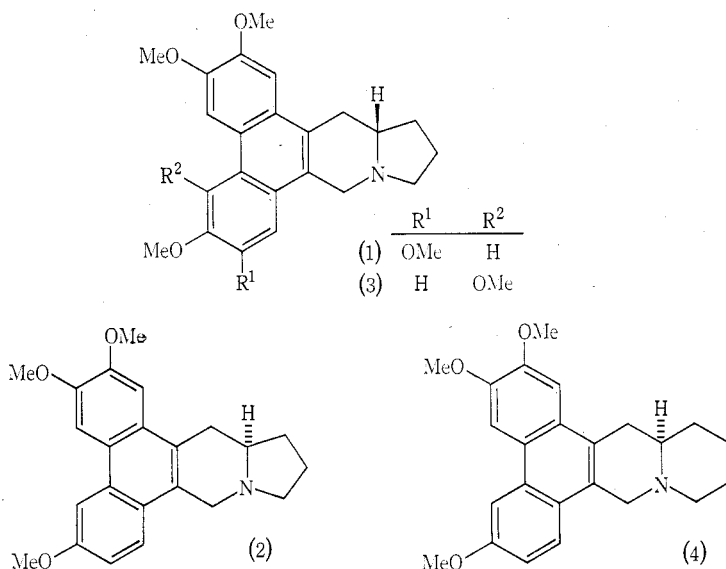
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Abstract

The absolute configurations of cryptopleurine and (–)-tylocrebrine have been established as *R* and *S* respectively by comparison of their optical rotatory dispersion and circular dichroism spectra with those of tylophorine.

A recent publication¹ established the absolute configuration of the phenanthro-indolizidine alkaloid tylophorine (1) as *S*, i.e. corresponding to L-proline. This is of interest because the only alkaloid of this class for which the absolute configuration had been determined earlier² was antofine (2), shown to have the *R*-configuration by the isolation, on ozonolysis, of proline identified as the D-isomer by reaction with D-amino acid oxidase.



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¹ Govindachari, T. R., Rajagopalan, T. G., and Viswanathan, N., *J. Chem. Soc., Perkin Trans. 1*, 1974, 1161.

² Wiegrebe, W., Faber, L., and Breyhan, T., *Arch. Pharm. (Weinheim, Ger.)*, 1971, 304, 188.

We wish to report the absolute configuration of the major phenanthroindolizidine alkaloid from *Tylophora crebriiflora*,³ tylocrebrine (3), and of the closely related phenanthroquinolizidine compound^{4,5} cryptopleurine (4), as determined by optical rotatory dispersion (o.r.d.) and circular dichroism (c.d.).

The main Cotton effect of (1), (3) and (4) is seen (Fig. 1) to be in the 240–260 nm region, in agreement with the u.v. absorption of the polyoxygenated phenanthrene system present in these alkaloids.^{3,5,6} The o.r.d. curve obtained by us for tylophorine base (1) is in good agreement with that reported¹ for the hydrochloride, both showing a negative Cotton effect centered around 255 nm.

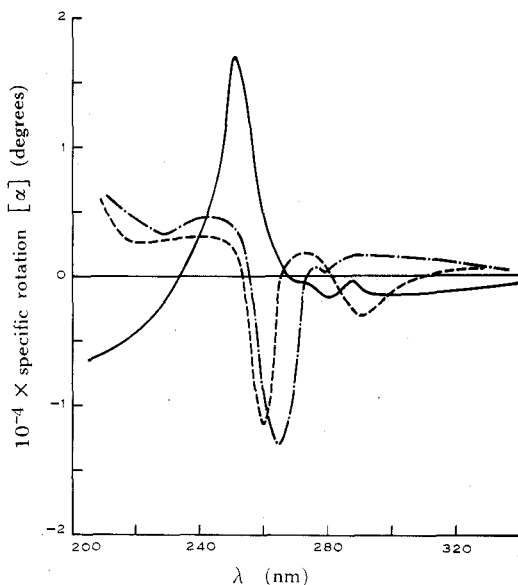


Fig. 1. Optical rotatory dispersion in 95% ethanol.
— Cryptopleurine (4);
--- (–)-tylophorine (1);
- · - (–)-tylocrebrine (3).

The o.r.d. curve of (–)-tylocrebrine (3) (Fig. 1) shows it to have the *S*-configuration like tylophorine, the two curves being almost superimposable between 200 and 280 nm. The negative sign of the Cotton effect was confirmed by a negative c.d. maximum at 252 nm. The slight differences shown in the 280–320 nm region of the o.r.d. spectrum may be ascribed to the different oxygenation pattern, in agreement with the u.v. spectra of these alkaloids.³ It appears that, as in the aporphine series,^{7,8} the sign of the Cotton effect in the 280–320 nm region is substitution-dependent⁷ whereas the sign of the major aromatic Cotton effect in the 240–260 nm region is independent of substitution.⁸

The interpretation of the o.r.d. curves for the phenanthroindolizidine alkaloids relies on the indolizidine ring junction being in the stable *trans* configuration.⁹ In the

³ Gellert, E., Govindachari, T. R., Lakshmikantham, M. V., Ragade, I. S., Rudzats, R., and Viswanathan, N., *J. Chem. Soc.*, 1962, 1008.

⁴ Gellert, E., and Riggs, N. V., *Aust. J. Chem.*, 1954, **7**, 113; Gellert, E., *Aust. J. Chem.*, 1956, **9**, 489.

⁵ Friedrichsons, J., and Mathieson, A. M., *Nature (London)*, 1954, **173**, 732; *Acta Crystallogr.*, 1955, **8**, 761.

⁶ Govindachari, T. R., Pai, B. R., and Nagarajan, K., *J. Chem. Soc.*, 1954, 2801; Govindachari, T. R., *J. Indian Chem. Soc.*, 1973, **50**, 1.

⁷ Djerassi, C., Mislow, K., and Shamma, M., *Experientia*, 1962, **18**, 53.

⁸ Cymerman Craig, J., and Roy, S. K., *Tetrahedron*, 1965, **21**, 395.

⁹ Crabb, T. A., Newton, R. F., and Jackson, D., *Chem. Rev.*, 1971, **71**, 109.

case of cryptopleurine (4), it has already been shown^{4,5} that the phenanthroquinolizidine system is in the *trans* configuration. The o.r.d. measurement can therefore be used for assignment of absolute configuration for cryptopleurine (4) and shows (Fig. 1) that this has the opposite configuration from tylocrebrine and tylophorine. It is therefore, like antofine (2), a member of the *R*-series. The positive Cotton effect was confirmed by a positive c.d. maximum at 233 nm.

Experimental

O.r.d. and c.d. curves were measured with a JASCO ORD/CD5 and a JOUAN Mark II spectropolarimeter at 25° in 95% ethanol. Only c.d. maxima are given, and are recorded in terms of molecular ellipticity¹⁰ $[\theta]$.

Cryptopleurine had m.p. 196.5–197°, $[\alpha]_D^{25} -105^\circ$ (c, 1.0 in CHCl_3); o.r.d. (c, 0.0043 in 95% ethanol); c.d. (c, 0.0085 in 95% ethanol) $[\theta]_{233} +15000$.

Tylophorine had m.p. 282–284°, $[\alpha]_D^{25} -12^\circ$ (c, 0.7 in CHCl_3); o.r.d. (c, 0.0014 in 95% ethanol).

(–)-Tylocrebrine had m.p. 218–220°, $[\alpha]_D^{25} -44^\circ$ (c, 0.7 in CHCl_3); o.r.d. (c, 0.0035 in 95% ethanol); c.d. (c, 0.014 in 95% ethanol) $[\theta]_{252} -4370$.

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¹⁰ Djerassi, C., and Bunnenberg, E., *Proc. Chem. Soc., London*, 1963, 299.