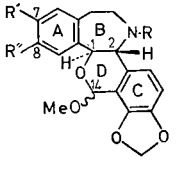
The structure of porphyroxine (papaverrubine D)

SIR,—A few years ago we reported on the isolation and characterisation of porphyroxine (m.p. 192°) from Indian opium (Pfeifer & Teige, 1962). A short time later the alkaloid was also described by Genest & Farmilo (1963), with a differing m.p. (234–236°) and with a molecular formula which we know today to be incorrect.

During our investigations of further alkaloids with the properties of porphyroxine (formation of intensely red coloured solutions when heated with dilute acids) in the genus *Papaver*, we detected a total of six such compounds, which were named papaverrubines A–F (Pfeifer & Banerjee, 1964). Porphyroxine is papaverrubine D. It could be detected in all *Papaver* spp. hitherto investigated.

Later the papaverrubines A and E were isolated from *Papaver rhoeas* L. (Pfeifer & Banerjee, 1965) and B from *Papaver glaucum* Boiss. et Hauskr. (Pfeifer, 1964a). The latter also occurs in opium (Pfeifer, 1965). By mass spectrometry and *N*-methylation it could be shown (Pfeifer, Banerjee, Dolejš & Hanuš, 1965) that A and E are desmethyl bases of the stereoisomeric alkaloids isorhoeadine and rhoeadine, while papaverrubine B is the *N*-desmethyl compound of glaudine, a new papaver alkaloid recently isolated by us (Pfeifer, 1964b; Pfeifer & Mann, 1965). Porphyroxine (papaverrubine D) differs from papaverrubine B only in having a phenolic OH group instead of a methoxyl group and thus represents an *O*-desmethylpapaverrubine B. However, it is not yet clear whether it has the same configuration as papaverrubine B, since the basic structure contains three asymmetric carbon atoms.

We therefore *O*-methylated the porphyroxine with diazomethane in methanol-ether, in which papaverrubine B, m.p. 202–203°, was formed in high yield. Ultraviolet data (methanol): λ_{max} 236, 286 mμ (log ϵ 4·06, 3·86). Infrared data (KBr, cm^{-1}): 3305 (–NH). The identity was proved by thin-layer chromatography with authentic papaverrubine B (silica gel G Merck; solvent system, benzene : acetone : methanol 7 : 2 : 1; Rf 0·64; aluminium oxide G Merck; solvent system, heptane : chloroform : ether 4 : 5 : 1; Rf 0·31). This ensures that porphyroxine (I) has the same configuration as papaverrubine B (II) at the asymmetric carbon atoms 1,2 and 14. Papaverrubine B could also be methylated to glaudine (III) with equimolecular amounts of methyl iodide in tetrahydrofuran.* m.p. 103–105°. Methiodide: m.p. 174–176°. Ultraviolet data (methanol): λ_{max} 237, 287 mμ (log ϵ 4·03, 3·92). Thin-layer chromatography (see above): Rf 0·73, 0·50. Since glaudine has B/D *trans*-configuration (Cross, Mann & Pfeifer, 1966), porphyroxine also belongs to the *trans*-series.



I; R=H; R′=OH; R″=OMe or R′=OMe; R″=OH
porphyroxine (papaverrubine D)

II; R=H; R′=R″=OMe
papaverrubine B

III; R=Me; R′=R″=OMe
glaudine

* Only partial conversion.

By means of acid hydrolysis glaudine can also be transformed into glaucamine (C-14-lactol; B/D *trans*), which can be isomerised to oreogenine (B/D *cis*); oreodine (B/D *cis*) is formed by etherifying this C-14-lactol with methanol (Pfeifer & others, 1965). Both the last-named alkaloids were recently isolated from *Papaver oreophilum* Rupr. (Pfeifer & Mann, 1964). This indicates the following affinity:

$$\text{Porphyroxine (papaverrubine D)} \xrightarrow{O\text{-methylation}} \text{papaverrubine B} \xrightarrow{N\text{-methylation}}$$

$$\text{glaudine} \xrightarrow{\text{hydrolysis}} \text{glaucamine} \xrightarrow{\text{isomerisation}} \text{oreogenine} \xrightarrow{\text{etherification}} \text{oreodine.}$$

The exact position of the OH group of porphyroxine in ring A (C-7 or C-8) has not yet been determined.

Recently, Hughes & Farmilo (1965) also reported on the methylation of porphyroxine. The product obtained by them (m.p. 202–204°) is probably identical with papaverrubine B. The authors remark that we had given no experimental details on papaverrubine B, but they have obviously overlooked my earlier publication (Pfeifer, 1964a). Hence they compare the *O*-methylporphyroxine obtained with a product (m.p. 241–243°) which we had earlier obtained from porphyroxine during methylation experiments (Pfeifer & Teige, 1962). At that time we ourselves already doubted the formation of *O*-methylporphyroxine. After repeated examination by thin-layer chromatography it can now be considered definite that, as rightly presumed by Hughes & Farmilo (1965), only another modification of porphyroxine was formed in this experiment (for this, cf. Klayman, 1956). The m.p. of this form is close to that stated by Genest & Farmilo (1963).

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