Gaddum, J. H., Hameed, K. A., Hathaway, D. E. & Stephens, F. F. (1955). *Quart. J. exp. Physiol.*, **40**, 49–74.
Leach, G. D. H. (1956). *J. Pharm. Pharmacol.*, **8**, 501–503.
Leonard, B. E. (1965). *Ibid.*, **17**, 566–576.
Schild, H. O. (1947). *Brit. J. Pharmacol.*, **2**, 189–206.
Schild, H. O. (1957). *Pharmacol. Rev.*, **9**, 242–246.

The preparation of *O*-methylporphyroxine and its detection in opium

SIR,—Pfeifer (1965) has recently reported the detection of papaverrubin B (*O*-methylporphyroxine) in opium, but no experimental details were given. We have prepared *O*-methylporphyroxine and found it to differ from that described by Pfeifer & Teige (1962) in m.p. and infrared absorption spectrum. We have also detected *O*-methylporphyroxine in Japanese opium.

Porphyroxine was isolated from Japanese opium (2 kg) essentially by the method of Pfeifer & Teige (1962), although the later stages of their procedure (precipitation of thebaine hydrogen tartrate and column chromatography) were omitted since porphyroxine could be crystallised from methanol without these steps. Its m.p., 234–236°, was undepressed on admixture with a sample isolated from Indian opium by Genest & Farmilo (1963). The mother liquors were recycled through the extraction procedure until no more porphyroxine could be separated by crystallisation. The final filtrate was shown by thin-layer chromatography to contain, in addition to all the common opium alkaloids, porphyroxine and traces of several other compounds giving a red coloration when heated with phosphoric acid. Crude *O*-methylporphyroxine was separated from this mixture by preparative thin-layer chromatography (0·75 mm silica gel G /0·01N NaOH layers; solvent system, benzene : methanol 8 : 2), a zone of Rf 0·6–0·8 being eluted. Further purification was effected by extraction of an ether solution with aqueous 10% KOH to remove phenolics, crystallisation from methanol to remove the bulk of the narcotine, and countercurrent distribution (20 tubes) between chloroform and 2% aqueous tartaric acid. The material remaining after these treatments, some of which were repeated several times, was freed from residual traces of narcotine by repeated preparative thin-layer chromatography (0·25 mm silica gel G /0·01N NaOH layers; solvent system, benzene : ethyl acetate 75 : 25). A zone between Rf 0·1 and 0·3 was eluted, evaporation affording 2 mg of a light brown gum which could not be crystallised. It was shown to be homogeneous by thin-layer chromatography in six solvent systems (see Table 1), and to be identical with *O*-methylporphyroxine by thin-layer chromatography, colour reaction, infrared and ultraviolet spectra.

Authentic *O*-methylporphyroxine was prepared by methylation of porphyroxine (230 mg) with excess diazomethane in ether : ethanol at 0° for 6 hr. The

TABLE 1. THIN-LAYER CHROMATOGRAPHY OF *O*-METHYLPORPHYROXINE ON SILICA GEL G : 0·01 N NaOH LAYERS

System	Rf	$R_{porphyroxine}$	$R_{narcotine}$
Benzene : methanol 8 : 2	0·70	1·3	1·0
Benzene : diethylamine 95 : 5	0·68	2·1	1·0
Benzene : ethyl acetate 75 : 25	0·23	1·3	0·72
Benzene : ethyl acetate : diethylamine 90 : 5 : 5	0·59	2·4	1·0
Cyclohexane : chloroform : diethylamine 5 : 4 : 1	0·57	2·5	0·98
Cyclohexane : diethylamine 8 : 2	0·24	1·8	0·92

Spray reagents: porphyroxine and *O*-methylporphyroxine, 12% aqueous phosphoric acid; narcotine aqueous potassium iodoplatinate (Genest & Farmilo, 1963).

compound was purified by washing with 10% aqueous KOH, to remove unreacted starting material, and crystallised successively from methanol, ethyl acetate and methanol. Yield 180 mg (76%), m.p. 202–204°. (Pfeifer, 1962, gives m.p. 241–243°). Found: C, 66·1; H, 6·25; N, 3·8; O, 23·9; active H, 0·2, 0·4%; *M* (mass spectrum), 385. Calc. for $C_{21}H_{23}O_6N$: C, 65·5; H, 6·0; N, 3·6; O, 24·9; one active H, 0·3%; *M* 385. The nmr spectrum ($CDCl_3$ solution) has singlets at 6·11, 6·15 and 6·32τ each integrating for three protons, and attributable to three methoxyl groups. In this region, the spectrum of porphyroxine [$(CD_3)_2SO$ solution] has two three-proton singlets (at 6·31 and 6·50τ). Ultraviolet data: *O*-methylporphyroxine in ethanol λ_{max} 285·5, 234 mμ (ϵ_{max} 6,400, 10,580) λ_{min} 258, 225 mμ (ϵ_{min} 1,180, 9,280). *O*-Methylporphyroxine gave the characteristic red coloration when heated with dilute mineral acid.

In the infrared spectrum (see Fig. 1), absorption due to the phenolic OH of porphyroxine (3,420 cm^{-1}) has disappeared, whilst the band at 3,300 cm^{-1}

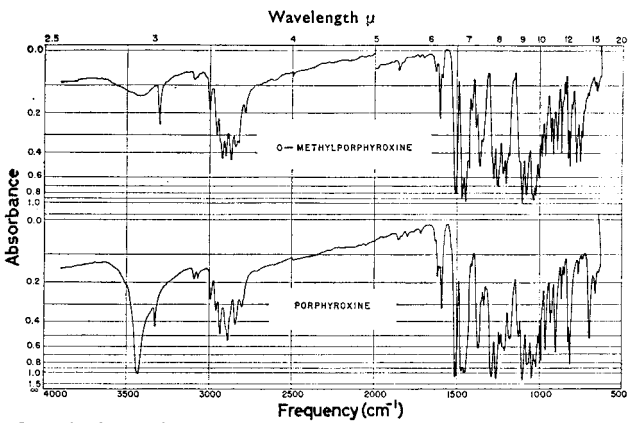

FIG. 1. Infrared absorption spectra of porphyroxine and *O*-methylporphyroxine (potassium bromide discs).

(attributable to :NH) remains. Pfeifer & Teige (1962) have published a spectrum for *O*-methylporphyroxine which differs markedly from ours, but which is identical with the spectrum of our porphyroxine. No analytical data were given for the compound and it seems probable that the conditions used effected change of the porphyroxine from one form to another. Klayman (1956) has reported the isolation of porphyroxine in two polymorphic forms, of m.p. 186–191° and 228–231°.

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References

Genest, K. & Farmilo, C. G. (1963). *J. Pharm. Pharmacol.*, **15**, 197–201.
Klayman, D. L. (1956). Ph.D. thesis, Rutgers University.
Pfeifer, S. & Teige, J. (1962). *Pharmazie*, **17**, 692–705.
Pfeifer, S. (1965). *Ibid.*, **20**, 240.