

6-Methylcodeine—A New Opium Alkaloid

Sir:

A new nonphenolic alkaloid has been isolated from the mother liquor produced during the extraction and purification of morphine from opium.¹ It accompanied the codamine fraction during the separation of the minor opium alkaloids by preparative thin-layer chromatography (1), and was separated from codamine by extrac-

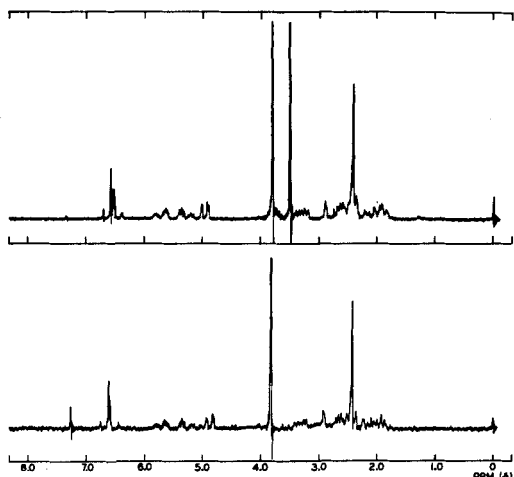


Fig. 1.—NMR spectra of codeine (bottom) and 6-methylcodeine (top).

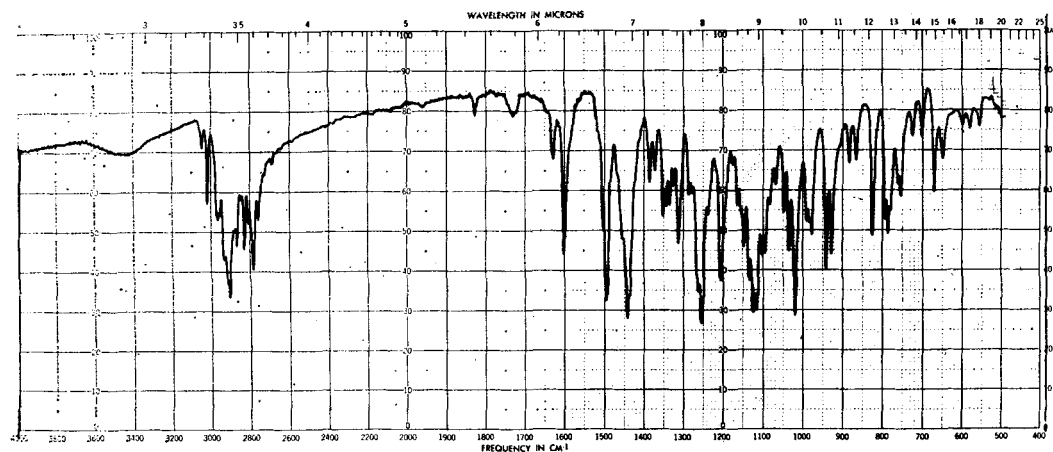


Fig. 2.—I.R. spectrum of 6-methylcodeine, 0.5% in KBr.

tion with ether at pH 13. The alkaloid was purified as the picrate which crystallized from alcohol in long needles, melting at 221°. The base obtained from the picrate crystallized from ether-petroleum ether as prisms, m.p. 140.5–141.5°, $[\alpha]_D^{24} = -188.5^\circ$ ($c = 1.09$ in 95% ethanol). Its purity was demonstrated by gas chromatography on two columns of different

polarity (silicone rubber SE-30 and XE-60). The NMR spectrum of the alkaloid base was very similar to that of codeine except for the presence of two methoxyl groups instead of one (Fig. 1) and a total of 23 hydrogens, indicating that we might be dealing with the methyl ether of codeine. This was confirmed by synthesis of 6-methylcodeine ($C_{19}H_{23}NO_3$) by methylation of codeine-*N*-oxide with dimethyl sulfate in alkaline solution (2). The NMR and I.R. spectra (Fig. 2) of the synthetic product were found to be identical with those of the isolated alkaloid. No melting point depressions were observed with the free bases or the picrates.

Since it was possible that codeine methyl ether might be an artifact formed in the mother liquor during the isolation of morphine, perhaps by reduction of thebaine, a 30-Gm. sample of opium powder U.S.P. was extracted, and the alkaloids were separated and purified as before. Although the opium sample was too small to permit isolation of crystalline methylcodeine, both gas and thin-layer chromatography (two columns and two solvent systems) gave indications of the presence of this alkaloid.

It seems reasonable to expect that methylcodeine may play an important role in the alkaloid production of the opium poppy as a possible intermediate in the conversion of thebaine to codeine. This problem is being investigated.

- (1) Brochmann-Hanssen, E., Nielsen, B., and Utzinger, G., *J. Pharm. Sci.*, to be published.
(2) Mannich, C., *Arch. Pharm.*, **254**, 356(1916).

E. BROCHMANN-HANSEN
B. NIELSEN

Department of Pharmaceutical Chemistry
School of Pharmacy
University of California
San Francisco

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