A SYNTHESIS OF *O*-METHYLCRYPTAUSTOLINE IODIDE

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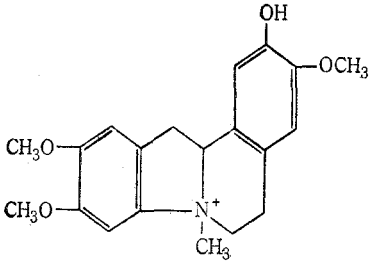
Summary

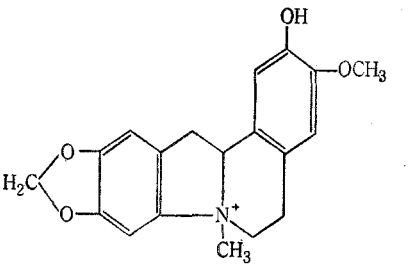
Two optically active forms of *O*-methylcryptaustoline iodide, one of them identical with the methyl ether of the natural alkaloid, have been synthesized.

I. INTRODUCTION

In a previous communication (Ewing *et al.* 1953) it was shown that cryptaustoline (I) and cryptowoline (II), the alkaloids of the bark of *Cryptocarya bowiei* (Hook.) Druce, were laevorotatory forms of simple ethers of dehydrolaudanosoline. Dehydrolaudanosoline itself was originally obtained by Robinson and Sugasawa (1932) and by Schöpf and Thierfelder (1932) by the oxidation of optically inactive laudanosoline and it should be noted that in the ring closure the nitrogen atom becomes asymmetric. The latter authors remarked that the oxidation proceeded so readily and smoothly that derivatives of dehydrolaudanosoline could reasonably be expected to occur naturally. It was therefore of



(I)



(II)

interest to examine the oxidation of *d*- and *l*-laudanosolines. It was found that *d*-laudanosoline hydrobromide obtained from *d*-laudanosine, gave on oxidation and complete methylation, optically pure *l*-cryptaustoline methyl ether, identical with the substance obtained from the natural alkaloid, whilst *l*-laudanosoline gave optically pure *d*-cryptoaustoline methyl ether. It is evident that in the ring closure the configuration of the asymmetric carbon atom determines the configuration of the nitrogen atom in the dehydrolaudanosoline, and this provides some support for Schöpf and Thierfelder's conjecture.

The identity of the synthetic product was established by comparison with material prepared from the natural alkaloid and by degrading each to the same

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laevorotatory methine-I and to the same optically inactive methine-II. Further an equimolecular mixture of the synthetic *d*- and *l*-methine-I was optically inactive and identical with methine-I prepared from optically inactive dehydrolaudanosoline.

II. Experimental

Melting points are uncorrected. Analyses are by Dr. K. W. Zimmerman, C.S.I.R.O. Microanalytical Laboratory.

(*a*) *Resolution of* dl-*Laudanosine*.—The base, synthesized by standard methods, was resolved by a modification of the method of Pictet and Athanasescu (1900). Laudanosine (14·1 g) and *l*-quinic acid (7·9 g) were dissolved in ethanol (15 c.c.) and ether added until a faint turbidity developed. On standing, and more readily on seeding, *l*-laudanosine quinate separated in clusters of leaflets. After three recrystallizations from ethanol-ether the product (7·1 g) had m.p. 132 °C (Pictet and Athanasescu give m.p. 120 °C). By decomposition with alkali in the usual way *l*-laudanosine was obtained and recrystallized from aqueous alcohol. It (4·1 g) had m.p. 89 °C, $[\alpha]_D^{24}$ −110±4° (*c*, 0·3 in ethanol). Pictet and Athanasescu recorded $[\alpha]_D^{15}$ −105° (*c*, 3 in ethanol).

By the addition of more ether to the mother liquor the salt of the *d*-base was obtained as long fibrous needles, which after two recrystallizations from ethanol-ether had m.p. 81–82 °C (yield 7·5 g). This salt was deliquescent, losing its crystalline form and changing to a clear glass on standing in air. Pictet and Athanasescu did not obtain it crystalline. On decomposition it gave *d*-laudanosine (4·4 g), m.p. 89 °C, $[\alpha]_D^{24}$ +107±4° (*c*, 0·3 in ethanol). Pictet and Athanasescu reported $[\alpha]_D^{15}$ +106° (*c*, 1·6 in ethanol) for the natural and $[\alpha]_D^{15}$ +98·7° (*c*, 1·86 in ethanol) for the synthetic base.

(*b*) d- *and* l-*Laudanosoline Hydrobromides*.—*d*- and *l*-Laudanosines were demethylated with hydrobromic acid (Schöpf and Thierfelder 1932). The hydrobromides dried overnight at 20 mm over calcium chloride (m.p. 125–128 °C, $[\alpha]_D^{24}$ +48±3° (*c*, 0·3 in water) and m.p. 125–127 °C, $[\alpha]_D^{24}$ −47·5±3° (*c*, 0·3 in water)) were evidently hydrated and were not analysed.

(*c*) d- *and* l-*Tetramethyldehydrolaudanosoline Iodides*.—The oxidations were effected with chloranil (Robinson and Sugasawa 1932) and the crude products methylated directly. *d*-Laudanosoline hydrobromide yielded *l*-tetramethyldehydrolaudanosoline iodide (40% overall) which crystallized from water in colourless rods. After drying overnight at 20 mm over calcium chloride the product had m.p. 80–84 °C, $[\alpha]_D^{28}$ −184±4° (*c*, 0·4 in water). Authentic *O*-methylcryptaustoline iodide recrystallized and dried in the same manner had m.p. 80–84 °C, $[\alpha]_D^{28}$ −186±4° (*c*, 0·4 in water).

The methine-I from the synthetic product formed colourless needles from ethanol, m.p. 101 °C, $[\alpha]_D^{26}$ −213±5° (*c*, 0·1 in ethanol) (Found : C, 71·0 ; H, 7·0 ; N, 4·0%. Calc. for $C_{21}H_{25}O_4N$: C, 71·0 ; H, 7·0 ; N, 3·9%). The methine-I from the natural product had m.p. 101 °C, alone or mixed with the above, $[\alpha]_D^{26}$ −215±5° (*c*, 0·1 in ethanol).

d-Tetramethyldehydrolaudanosoline iodide formed by oxidation of *l*-laudanosoline followed by methylation separated as colourless rods from water, m.p. 80–84 °C, $[\alpha]_D^{28}$ +184±4° (*c*, 0·4 in water). The related methine-I had m.p. 101 °C, $[\alpha]_D^{26}$ +212±5° (*c*, 0·1 in ethanol) (Found : C, 70·8 ; H, 6·8 ; N, 3·9%. Calc. for $C_{21}H_{25}O_4N$: C, 71·0 ; H, 7·0 ; N, 3·9%). When equal quantities of this and the above methine-I from synthetic *l*-tetramethyldehydrolaudanosoline iodide were crystallized from ethanol colourless leaflets, m.p. 126–127 °C, $[\alpha]_D^{26}$ 0° (*c*, 0·1 in ethanol) were obtained, identical with an authentic specimen prepared from optically inactive laudanosine.

The same methine-II, pale lemon prisms from ethanol, m.p. 108 °C, $[\alpha]_D^{26}$ 0° (*c*, 0·1 in ethanol) was obtained from *l*-methine-I, *d*-methine-I, *O*-methylcryptaustoline methine-I, and tetramethyldehydrolaudanosoline methine-I.

III. Acknowledgments

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