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 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-cryptaustoline 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 dehydro-
laudanosoline.

II. Experimental

Melting points are uncorrected. Analyses are by Dr. K. W. Zimmerman, C.S.I.R.O. Micro-
analytical 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\(^\circ\)C (Pictet and Athanasescu give m.p. 120\(^\circ\)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\(^\circ\)C,
\( \delta\_{lD}^{12} = -110\pm 4^\circ \) (c, 0·3 in ethanol). Pictet and Athanasescu reported \( \delta\_{lD}^{15} = -105^\circ \) (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\(^\circ\)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\(^\circ\)C, \( \delta\_{D}^{24} = +107\pm 4^\circ \) (c, 0·3 in ethanol). Pictet and
Athanasescu reported \( \delta\_{D}^{15} = +106^\circ \) (c, 1·6 in ethanol) for the natural and \( \delta\_{D}^{15} = +87·7^\circ \) (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\(^\circ\)C, \( \delta\_{D}^{24} = +48\pm 3^\circ \) (c, 0·3 in water) and
m.p. 125-127\(^\circ\)C, \( \delta\_{D}^{24} = -47·5\pm 3^\circ \) (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. \( d \)-Laudano-
soline 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\(^\circ\)C, \( \delta\_{D}^{24} = -184\pm 4^\circ \) (c, 0·4 in water). Authentic \( O \)-methylicryptaustoline iodide recrystallized and dried in the same manner had m.p. 80-84 \( ^\circ\)C, \( \delta\_{D}^{28} = -186\pm 4^\circ \)
(c, 0·4 in water).

The methine-I from the synthetic product formed colourless needles from ethanol, m.p. 101\(^\circ\)C,
\( \delta\_{D}^{28} = -213\pm 5^\circ \) (c, 0·1 in ethanol) (Found: C, 71·0; H, 7·0; N, 3·9%). Calc. for \( C_{21}H_{24}O_{7}N \):
C, 71·0; H, 7·0; N, 3·9%. The methine-I from the natural product had m.p. 101\(^\circ\)C, alone
or mixed with the above, \( \delta\_{D}^{24} = -215\pm 5^\circ \) (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\(^\circ\)C, \( \delta\_{D}^{24} = +184\pm 4^\circ \) (c, 0·4
in water). The related methine-I had m.p. 101\(^\circ\)C, \( \delta\_{D}^{26} = 212\pm 5^\circ \) (c, 0·1 in ethanol) (Found:
C, 70·8; H, 6·8; N, 3·9%). Calc. for \( C_{21}H_{24}O_{7}N \): 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 \( ^\circ\)C, \( \delta\_{D}^{24} = 0^\circ \) (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 \( ^\circ\)C, \( \delta\_{D}^{26} = 0^\circ \) (c, 0·1 in ethanol)
was obtained from \( l \)-methine-I, \( d \)-methine-I, \( O \)-methylicryptaustoline methine-I, and
tetra-methyldehydrolaudanosoline methine-I.
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IV. REFERENCES