91. Formation of (+)Dihydrocodeine and (+)Dihydromorphine from Sinomenine.

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To reduce the ketonic group of (+)dihydrocodeinone¹⁾ (I), without opening the oxyde linkage, several trials were made without marked results. Thus sodium-amalgam in water or in acidic medium invariably opens the oxyde linkage. The reduction with sodium isopropylate²⁾, just like the catalytic reduction under ordinary condition using palladium as catalyst, left the substance untouched. The experiment of Mannich and Löwenheim³⁾, who reported that they could reduce (–)dihydrocodeinone to (–)dihydrocodeine by Clemmensen's zinc-amalgam, could not be verified by the present author, although the reduction was carried out under varying conditions. T. Hill's⁴⁾ report that he could reduce codeinone to codeine by hydrazine or by sodium hydro-sulphite seems after our experiments to be inapplicable to (+)dihydrocodeinone. At last, the katalytic reduction of the substance with platinum oxide and hydrogen in pyridine solution⁵⁾ gave the desired (+)dihydrocodeine (II) in an almost calculated yield⁶⁾.

(+)Dihydrocodeine is precipitated at first oily from its dilute hydrochloric acid solution by caustic alkali, but crystallises after several minutes. Dried on porous plate, it melts at 88°, but the melting point could be elevated to 110° by recrystallisation from 80 proc. methanol. Ferric chloride reaction negative. Diazo-reaction very faint. $[\alpha]_D + 146.4^\circ$. The iodomethylate melts at 257°: $[\alpha]_D + 80.1^\circ$. All these properties coincide with those of (–)dihydrocodeine, prepared by the

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- 1) K. Goto: *Liebigs Annalen*, **489**, 95 (1931).
 - 2) Compare Lund: *Ber.*, **70**, 1520 (1937).
 - 3) *Arch. Pharm.*, **258**, 295 (1920).
 - 4) Dissertation, Frankfurt a. M. (1925).
 - 5) Compare, Wieland: *Liebig's Ann.*, **473**, 114 (1928).
 - 6) Schöpf, Hirsch: *Liebigs Ann.*, **489**, 224 (1931). These authors give another method, but was not tried in the present work.

catalytic reduction of codeine¹⁾, except the sign of rotation. Moreover, the racemisation of these two dihydrocodeines and the demthylation of the (+)dihydrocodeine to (+)dihydromorphine (III) establishes the fact that we have here actually (+)dihydrocodeine.

d, 1-Dihydrocodeine crystallises in prisms and melts at 105° : $[\alpha]_D \pm 0$. d, 1-Dihydrocodeine-iodomethylate melts at 257° : $[\alpha]_D \pm 0$.

(+)Dihydrocodeine was demthylated after Mannich and Löwenheim²⁾. It gave (+)dihydromorphine of m.p. $158 \sim 159^{\circ}$. Ferric chloride reaction positive. Diazo-reaction visible up to 2,000,000th dilution. $[\alpha]_D + 151,5^{\circ}$. The iodomethylate melts 245° : $[\alpha]_D + 74,9^{\circ}$. Melting point of hydroiodide 285° : $[\alpha]_D + 87,9^{\circ}$. (-)Dihydromorphine shows the same properties, only rotating the polarized light in opposite sense.

d, 1-Dihydromorphine was prepared from the above two dihydromorphines. M.p. 154° : $[\alpha]_D \pm 0$. The racemic iodomethylate melts at 267° : $[\alpha]_D \pm 0$. The hydro-iodides were also racemised. M.p. 261° : $[\alpha]_D \pm 0^{\circ}$.

The physiological action of (+)dihydrocodeine and (+)dihydromorphine against (-)derivatives will be reported later on.

The details of the present work will be published elsewhere.

1) Oldenburg: *Frđl.* **11**, 996.

2) *Arch. Pharm.*, **258** (1920), 305.