longer contained the bands at 1719 and 2735 cm.$^{-1}$ attributable to the aldehyde function.

These results lead to the unequivocal conclusion that the olefinic double bond in gelsemine is present in a vinyl side chain, and not in an exocyclic methylene group as had heretofore been assumed.

THE DIVISION OF PURE CHEMISTRY
NATIONAL RESEARCH COUNCIL OF CANADA
OTTAWA, CANADA
LÉO MARION
K. SARGEANT

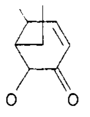
RECEIVED AUGUST 22, 1956

CODEINONE DIMETHYL KETAL AND ITS CONVERSION TO THEBAINE

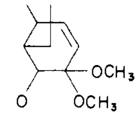
Sir:

Thebaine is prodigious among morphine alkaloids for the number and variety of its transformation products.[1] However, no morphine derivative as yet has been converted to thebaine, and it is this conversion we now wish to report.

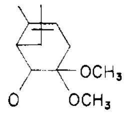
Ketalization of codeinone (I) with trimethyl orthoformate, methanol, and sulfuric acid was expected to give codeinone dimethyl ketal (II) or neopinone dimethyl ketal (III), but the only isolable product was 8-methoxy-Δ^6-dihydrothebaine (IV) [m.p. 190–191°; $[\alpha]^{25}\mathrm{D}$ $-133°$ (c, 0.9, ethanol); *anal.* Calcd. for $C_{20}H_{25}O_4N$: C, 70.0; H, 7.3; OCH_3, 27.1. Found: C, 70.2; H, 7.1; OCH_3, 27.5]. The structure of IV was established as follows. Degradation of the *methiodide* [m.p. 212–213°; $[\alpha]^{25}\mathrm{D}$ $-86°$ (c, 1, ethanol); *anal.* Calcd. for $C_{21}H_{28}O_4NI \cdot H_2O$: C, 50.1; H, 6.0; I, 25.2. Found: C, 50.3; H, 5.8; I, 24.8] gave a *methine* [m.p. 124–125°, $[\alpha]^{25}\mathrm{D}$ $-119°$ (c, 0.9, ethanol); *anal.* Calcd. for $C_{21}H_{27}O_4N$: C, 70.6; H, 7.6; OCH_3, 26.0. Found: C, 70.4; H, 7.5; OCH_3, 25.6] which was stable to all attempts at alkaline isomerization, indicating the alicyclic double bond was not Δ^7. With cyanogen bromide an *N-cyanonor* compound [m.p. 228–231°; $[\alpha]^{25}\mathrm{D}$ $-185°$ (c, 1, pyridine); *anal.* Calcd. for $C_{20}H_{22}O_4N_2$: C, 67.8; H, 6.3; N, 7.9. Found: C, 68.0; H, 6.4; N, 7.9] was obtained, indicating the double bond was not Δ^8. Acid hydrolysis gave a mixture of codeinone and 8-methoxydihydrocodeinone [m.p. 195–197°; *anal.* Calcd. for $C_{19}H_{23}O_4N$: C, 69.3; H, 7.0; OCH_3, 18.9. Found: C, 69.4; H, 6.8; OCH_3, 19.4], and hydroxylation with osmium tetroxide gave 7-hydroxy-8-methoxydihydrocodeinone, characterized as the *oxime* [m.p. 251–253°; $[\alpha]^{25}\mathrm{D}$ -204 (c, 1, pyridine); *anal.* Calcd. for $C_{19}H_{24}O_5N_2$: C, 63.3; H, 6.7; N, 7.8; OCH_3, 17.2. Found: C, 62.9; H, 6.9; N, 7.9; OCH_3, 16.9].



I

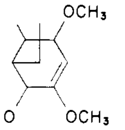


II

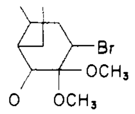


III

An alternative method for preparing codeinone dimethyl ketal was found in the dehydrobromination, using potassium t-amylate, of 7-bromodihydrocodeinone dimethyl ketal (V), itself prepared by methyl hypobromite addition to Δ^6-dihydrothebaine.[2] That the product was codeinone dimethyl ketal (II) [m.p. 138–139°; $[\alpha]^{21}\mathrm{D}$ $-233°$ (c, 0.5, ethanol); *anal.* Calcd. for $C_{20}H_{25}O_4N$: C, 70.0; H, 7.3; OCH_3, 27.1. Found: C, 69.8; H, 7.3; OCH_3, 27.2] derives from the following reactions. Acid hydrolysis gave codeinone, while hydrogenation led to dihydrocodeinone dimethyl ketal [m.p. 122–123°; $[\alpha]^{25}\mathrm{D}$ $-151°$ (c, 0.9, ethanol); *anal.* Calcd. for $C_{20}H_{27}O_4N$: C, 69.6; H, 7.9; OCH_3, 26.9. Found: C, 69.7; H, 8.0; OCH_3, 26.5], identical with the product formed from dihydrocodeinone and trimethyl orthoformate, methanol, and acid. The *methiodide* (m.p. 193–195°) was degraded to a $\Delta^{7,9}$-*methine* [m.p. 71–72°; $[\alpha]^{25}\mathrm{D}$ $-328°$ (c, 0.9, ethanol); $\lambda_{\max}^{\text{ethanol}}$ 274 mμ, ϵ 8,500; *anal.* Calcd. for $C_{21}H_{27}O_4N$: C, 70.6; H, 7.6; OCH_3, 26.0. Found: C, 70.7; H, 7.5; OCH_3, 26.2] which was isomerized with alcoholic alkali to a $\Delta^{8(14),9}$-*methine* [oil; $[\alpha]^{25}\mathrm{D}$ $+301°$ (c, 1.2, ethanol); $\lambda_{\max}^{\text{ethanol}}$ 318 mμ, ϵ 9,000; *anal.* Found: C, 70.6; H, 7.5; OCH_3, 25.8].



IV



V

When codeinone dimethyl ketal was treated with a dried solution of p-toluenesulfonic acid in chloroform, there was obtained a 40% yield of thebaine which after crystallization and sublimation was identical in m.p. and mixed m.p. (192–194°) and ultraviolet spectrum ($\lambda_{\max}^{\text{ethanol}}$ 283 mμ, ϵ 7,500; $\lambda_{\min}$ 256 mμ, ϵ 3,700) with an authentic sample.

In a formal sense, this may be considered to constitute a synthesis of thebaine, since the Δ^6-dihydrothebaine used in the preparation above can be prepared from dihydrocodeinone,[3] and this in turn is easily made from codeine,[1,4] which has been synthesized.[5] Since thebaine recently has been converted to neopine,[6] the latter also may be considered as synthesized.

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(1) L. F. Small and R. E. Lutz, "Chemistry of the Opium Alkaloids," Suppl. 103, Public Health Reports, U. S. Government Printing Office, Washington, D. C., 1932; K. W. Bentley, "The Chemistry of the Morphine Alkaloids," Clarendon Press, Oxford, England, 1954.

(2) We are greatly indebted to Dr. Lyndon F. Small for the details of this reaction. Our bromoketal melted at 116–117°, in agreement with Dr. Small's value.

(3) A. H. Homeyer, *J. Org. Chem.*, **21**, 370 (1956).

(4) H. Rapoport, R. Naumann, E. R. Bissell and R. M. Bonner, *ibid.*, **15**, 1103 (1950).

(5) M. Gates and G. Tschudi, THIS JOURNAL, **78**, 1380 (1956).

(6) H. Conroy, *ibid.*, **77**, 5960 (1955).

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RECEIVED AUGUST 27, 1956

A NEW ALKYLATION OF CARBONYL COMPOUNDS. II[1]

Sir:

We have submitted the new reaction we recently described for the alkylation and acylation of ketones

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(1) Part I: G. Stork, R. Terrell and J. Szmuszkovicz, THIS JOURNAL, **76**, 2029 (1954).