## Communications to the Editor

*UDC 547.944.6*

### Synthesis of Colchicine from Hexahydrodemethoxydeoxycolchicine

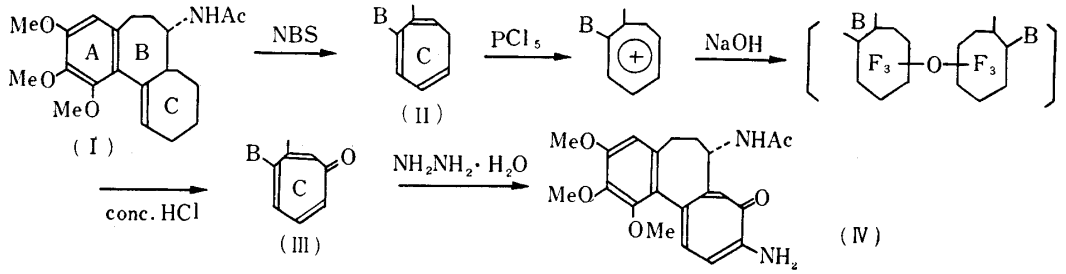
Total synthesis of colchicine was finally achieved by Eschenmoser, *et al.*[1] and by van Tamelen, *et al.*[2] in 1959. The present writer synthesized colchiceineamide (IV) from hexahydrodemethoxydeoxycolchicine[3] (I). Partial synthesis of colchicine from (IV) has already been reported.[4]

In order to change the C-ring in (I) to a tropilidene ring, two moles of N-bromosuccinimide[5] was reacted with (I), the product was dehydrobrominated with collidine, and a new substance (II) of m.p. 207° was obtained (*Anal.* Calcd. for $C_{21}H_{25}O_4N$: C, 70.96; H, 7.09; N, 3.94. Found: C, 71.03; H, 6.91; N, 4.23. UV: $\lambda_{max}^{EtOH}$ 284 mμ (log ε 3.97); IR: $\lambda_{max}^{Nujol}$ 3.02, 6.12 μ; $[\alpha]_D^{27}$ −198°(c=0.80, EtOH)).

Colchicine does not react with N-bromosuccinimide under the same condition. The infrared spectrum of (II) does not show any absorption in the shorter wave-length region below 6.12 μ. Therefore, the newly introduced double bond is thought to be in the C-ring.

In order to change the tropilidene ring in (II) to a tropone ring, (II) was first treated with phosphorus pentachloride to form the tropilium ion[6] and derived to the ether with alkali. The ether was converted to the tropone compound (III) (UV: $\lambda_{max}^{EtOH}$ 343 mμ (log ε 3.76)) with conc. hydrochloric acid.[7] (III) is a weak base, dissolves in dil. hydrochloric acid, and extracted from it with methylene dichloride. (III) is a mixture of ketone compounds which forms a precipitate with 2,4-dinitrophenylhydrazine but it could not be purified.

Amination of (III) by the hydrazine process[8] afforded, from basic portion of the product, crystals (IV) of m.p. 254°(*Anal.* Calcd. for $C_{21}H_{24}O_5N_2$: C, 65.61; H, 6.29; N, 7.29. Found: C, 65.66; H, 6.22; N, 7.38. UV $\lambda_{max}^{EtOH}$ mμ (log ε): 246(4.51), 354(4.32), 370(4.27), 400(4.07); IR $\lambda_{max}^{Nujol}$ μ: 2.65, 2.95, 3.20, 6.02, 6.80, 6.88, 7.05, 7.13, 7.42, 7.57, 8.73, 9.08, 9.52, 9.90, 11.85. $[\alpha]_D^{27}$ −140°(c=1.01, $CHCl_3$)). This substance showed no depression in the melting point on admixture with colchiceineamide and (IV) was therefore identified as colchiceineamide.

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6) D. N. Kursanov, M. E. Vol'pin: Doklady Akad. Nauk. S. S. S. R., **113**, 339(1957).
7) T. Nozoe, T. Ikemi, H. Sugiyama: Paper presented at the 12th Annual Meeting of the Chemical Society of Japan, Kyoto, 1959; Chem. & Ind. (London), **1960**, in press; A. S. Dreiding, *et al.*: Helv. Chim. Acta, **43**, 457(1960).
8) T. Nozoe, T. Mukai, T. Minegishi, T. Fujisawa: Sci. Repts. Tohoku Univ., Series A, **37**, 388 (1953); T. Nozoe, T. Mukai, K. Takase: *Ibid.*, **39**, 164(1956).

The writer expresses his deep gratitude to Prof. T. Nozoe of Tohoku University, Prof. K. Tsuda of the Institute of Applied Microbiology, University of Tokyo, Mr. S. Matsui, Director of this Laboratory, and Dr. G. Sunagawa, Assistant-Director of this Laboratory, for their kind guidance and encouragement throughout the course of the present work.

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August 9, 1960.

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*UDC 547.661.1 : 542.943〔546.717〕*

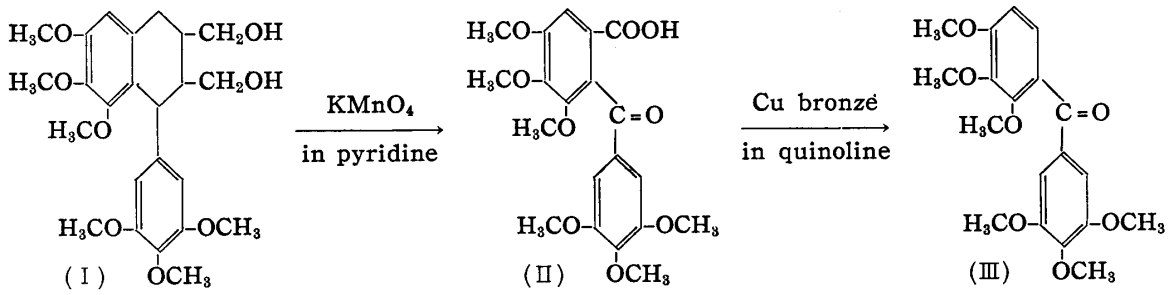
## Decarboxylation of the Permanganate Oxidation Product of Lyoniresinol Dimethyl Ether

In a previous paper[1] it was reported that lyoniresinol dimethyl ether (I) gave a carboxylic acid (II), $C_{20}H_{22}O_9 \cdot 2\frac{1}{2}H_2O$, m.p. 186.7～187°,* by oxidation with potassium permanganate in pyridine and that the molecular formula of (II) agreed with that of galloylgallic acid hexamethyl ether.

A neutral substance (III), m.p. 129.8～130° (*Anal.* Calcd. for $C_{19}H_{22}O_7$: C, 62.97; H, 6.12; O, 30.91. Found: C, 62.71; H, 6.20; O, 31,14. IR $\nu_{CO}^{KBr}$ 1660 $cm^{-1}$), was obtained from (II) by decarboxylation with copper bronze in quinoline and the substance (III) was confirmed as 2,3,4,3′,4′,5′-hexamethoxybenzophenone by comparison with an authentic sample, m.p. 129.9° (*Anal.* Calcd. for $C_{19}H_{22}O_7$: C, 62.97; H, 6.12; O, 30.91. Found: C, 62.78; H, 6.25; O, 30.80. IR $\nu_{CO}^{KBr}$ 1660 $cm^{-1}$), by elemental analysis, mixed melting point determination, and from infrared absorption spectra.

The authentic sample of 2,3,4,3′,4′,5′-hexamethoxybenzophenone[2] was prepared by methylation of the condensation product (2-hydroxy-3,4,3′,4′,5′-pentamethoxybenzophenone) of pyrogallol trimethyl ether and galloyl chloride trimethyl ether.

Thus, it was proved that the two trimethylpyrogallol rings were joined to one another with one carbon atom between them.

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July 16, 1960.

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* All m.p.s were determined by micro-method and are uncorrected.

1) M. Yasue, Y. Kato: Yakugaku Zasshi, **80**, 1013(1960).
2) W. H. Perkin, C. Weizmann: J. Chem. Soc., **89**, 1665(1906).