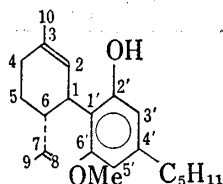


Cannabidiol Monomethyl Ether. A New Neutral Cannabinoid¹⁾

From the various Cannabis about twenty cannabinoids have been isolated and characterized. In this communication, we now report the isolation of cannabidiol monomethyl ether (CBDM) as a new minor cannabinoid, from the domestic hemp "Minamioshihara No. 1".



cannabidiol monomethyl ether (CBDM)

The leaves were percolated with ethanol. The ethanol extract was treated with acetone, and the cannabinoid acid fraction was heated with toluene for 8 hr to afford the neutral cannabinoids. The neutral cannabinoids were subjected to column chromatography on Florisil with benzene as an eluant. The benzene eluate was rechromatographed on silica gel, and a small amount of substance (A) $C_{22}H_{32}O_2$ (Calcd. for $C_{22}H_{32}O_2$: 328.240. Found: 328.241, yield 0.0016

%) was obtained from the hexane-benzene (3:1) eluate as a brownish syrup. The physical constants are as follows, UV $\lambda_{max}^{MeOH} m\mu$ (ϵ): 233 (sh), 273 (1460), 280 (1320), NMR (in $CDCl_3$) ppm: 0.90 (3H, ω - CH_3), 1.68, 1.80 (6H, $C_{3,7}$ - CH_3), 3.70 (3H, C_6' - OCH_3), 4.35, 4.45 (2H, $C_7=CH_2$), 5.60 (1H, C_2 -H), 6.23, 6.30 (2H, $C_{3',5'}$ -H). Mass Spectrum m/e : 328 (M^+), 313, 285, 272, 260, 245 (base peak), 207, 193.

The nuclear magnetic resonance (NMR) spectrum showed the additional singlet peak due to OCH_3 protons at 3.70, besides the signals corresponding to those of cannabidiol (CBD). In the mass spectrum of A, the molecular ion peak and other fragment ion peaks are in close resemblance to those of CBD²⁾ with higher shift of 14 mass unit, indicating that A is a monomethyl ether of CBD.

The identification of A with an authentic sample³⁾ was made by the comparison of ultraviolet, infrared, NMR, and mass spectra and the thin-layer and gas-liquid chromatograms.

Since any neutral cannabinoids have not been detected in the fresh leaves of the hemp, CBDM should exist in nature as the phenol carboxylic acid form that is cannabidiolic acid monomethyl ether (CBDAM). But the attempted isolation of the original acid of CBDM failed due to the low degree of content.

CBDAM is probably formed by the methylation of cannabidiolic acid or the cyclization of the cannabigerolic acid monomethyl ether and these steps suggest the new pathways in the biosynthesis of the cannabinoids.

Faculty of Pharmaceutical Sciences,
Kyushu University
Katakasu, Higashi-ku, Fukuoka

YUKIHIRO SHOYAMA
KEIKO KUBOE
ITSUO NISHIOKA

Faculty of Pharmaceutical Sciences,
Fukuoka University
Nanakuma, Nishi-ku, Fukuoka

TATSUO YAMAUCHI

Received May 22, 1972

- 1) This forms Part VII of "Cannabis." Part VI: Y. Shoyama, R. Oku, T. Yamauchi and I. Nishioka, *Chem. Pharm. Bull.* (Tokyo), **20**, 1927 (1972).
- 2) U. Claussen and F. Korte, *Tetrahedron, supplement* **7**, 89 (1965).
- 3) CBDM was prepared by the partial methylation of CBD with CH_2N_2 in MeOH at 5°.