and H_2O, then concentrated *in vacuo*. The residue was subjected to PLC and developed with solvent system A. A band (*Rf* 0.44) was visualized under a UV lamp, scraped off and extracted with $CHCl_3$ to give a mixture of IIb and IIIb (a pale yellow oil, 146 mg, 78.1% from Ia). The MS and ^{1}H-NMR data of the mixture agreed with those of Petrzilka and Demuth.[4]

8α,9α-Epoxyhexahydrocannabinol (IIa)——A mixture of IIb and IIIb (140 mg) in dry ether (10 ml) was treated with an equimolar amount of $LiAlH_4$ (14.3 mg). It was stirred at room temperature for 30 min, then $LiAlH_4$ was filtered off and the filtrate was evaporated *in vacuo* under an N_2 stream. The residue was dissolved in a small amount of $CHCl_3$, and resubjected to PLC, developing twice with solvent system B. A band (*Rf* 0.52) was scraped off and extracted with $CHCl_3$, giving a pale yellow oil in a yield of 27.3% from Ia (48 mg). $[\alpha]_D^{20} = -188°$ (c=0.38, EtOH). UV λ_{max}^{EtOH} nm (ε): 211 (38100), 230 (sh), 277 (1170), 284 (1220). GC–MS and ^{1}H-NMR data are given in Tables I and II, respectively.

8β,9β-Epoxyhexahydrocannabinol (IIIa)——On the PLC plates for the preparation of IIa, a band located at *Rf* 0.63 was scraped off and extracted with $CHCl_3$, giving a pale yellow oil in a yield of 18.2% from Ia (32 mg). $[\alpha]_D^{20} = -191°$ (c=0.42, EtOH). UV λ_{max}^{EtOH} nm (ε): 211 (37400), 230 (sh), 277 (1270), 284 (1360). GC–MS and ^{1}H-NMR data are given in Tables I and II, respectively.

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Isolation of O-Methylmaritidine from Bulbs of *Narcissus tazetta* L.

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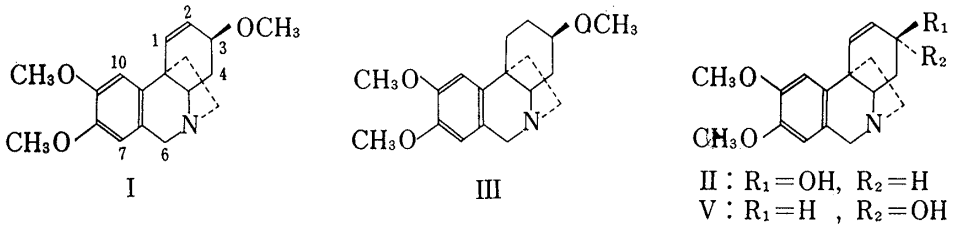
A new alkaloid, O-methylmaritidine, from *Narcissus tazetta* L. (Amaryllidaceae) has been assigned the structure (I) on the basis of the close correspondences of infrared, nuclear magnetic resonance, optical rotatory dispersion, ultra violet, and mass spectra to those of alkaloids of known structures.

Keywords——O-methylmaritidine; *Narcissus tazetta* L.; Amaryllidaceae; maritidine; buphanisine; dihydro-O-methylmaritidine

The alkaloid constituents of *Narcissus tazetta* L. (Amaryllidaceae) have been studied extensively.[1] We report in this paper the isolation of a new minor alkaloid, which was named O-methylmaritidine, from the bulbs of *N. tazetta* L.

The two alkaloidal fractions, chloroform-insoluble and chloroform-soluble, were obtained

from the ethanol extract of the fresh bulbs. Lycorine and pseudolycorine were isolated from the chloroform-insoluble fraction. The chloroform-soluble fraction gave tazettine, homolycorine, O-methylmaritidine (I), demethylhomolycorine, and pretazettine.



I III II : R_1=OH, R_2=H
V : R_1=H , R_2=OH

Chart 1

A new base, O-methylmaritidine (I), mp 88—89°C, was assigned the formula $C_{18}H_{23}NO_3$ on the basis of high resolution mass spectrometry and elemental analysis. The ultraviolet (UV) spectrum, having absorption peaks at λ 235 and 287 nm, and the optical rotatory dispersion (ORD) were similar to those of maritidine (II)[2] (see Fig. 1). The infrared (IR) spectrum of (I) showed the presence of olefinic hydrogens (3032 cm^{-1}), an aromatic system (1615 and 1590 cm^{-1}), and ether linkages (1095 and 1068 cm^{-1}). The methylenedioxy group (which occurs frequently in the amaryllis alkaloids), –OH, and –NH groups were absent.[3]

The base (I) absorbed a single mole of hydrogen to form a dihydro derivative (III), mp 195—197°C, $[\alpha]_D^{23}$ +30°. The high resolution mass spectrum was consistent with the formula $C_{18}H_{25}NO_3$. The unaltered UV spectrum, having absorption peaks at λ 235 and 285 nm, shows that the double bond is not conjugated with the aromatic ring in the parent compound.

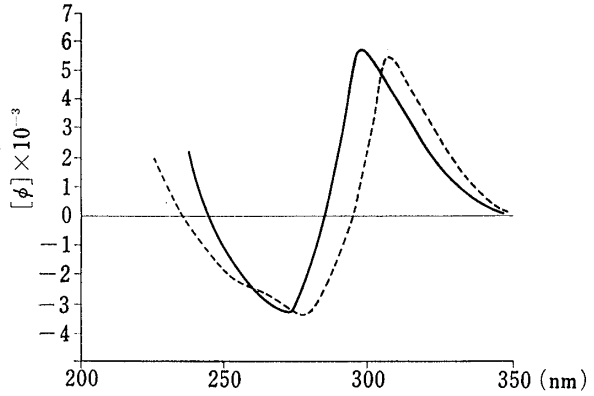


Fig. 1. ORD Spectra of (I) (——) and (II) (----).

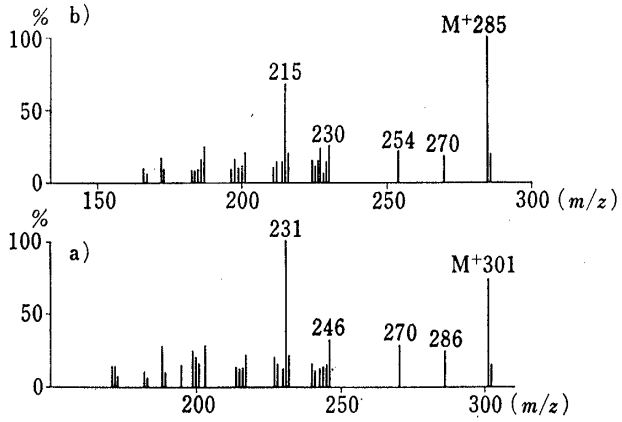
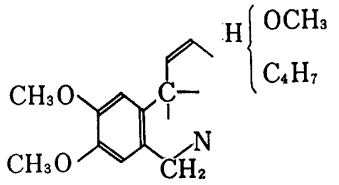


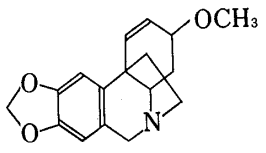
Fig. 2. Mass Spectra of I (a) and IV (b)

Analysis of the nuclear magnetic resonance (NMR) spectrum ($CDCl_3$) now made it possible to assign the structure of (I). The appearance of strong singlet peaks at δ 3.91, 3.88, and 3.40 confirmed the presence of three methoxy groups, two aromatic and one aliphatic. The two aromatic protons each appeared as a singlet peak, δ 6.88 and 6.68. A quartet corresponding to two protons with chemical shifts of δ 4.40 and 4.35 (J=17 Hz), similar to that in the spectra of other amaryllis alkaloids,[4] demonstrated the presence of nonequivalent protons of the benzylic methylene group of the tetrahydroisoquinoline system. Finally, the peaks from the olefinic protons appeared as two groups; that at lower field appeared as a doublet centered at δ 6.55, separated by 10 Hz, while that at higher field appeared as a double doublet, resulting from splitting of a doublet symmetrical to that at δ 6.11 by further coupling of 5 Hz.

Thus, this system could be categorized as (A) (see Chart 2), and it is clear that the partial



A



IV

Chart 2

TABLB I. Comparison of NMR Spectral Data[9]

	I	II	V
δ (H-1)	6.55d	6.66d	6.49dd
δ (H-2)	6.11dd	6.06dd	5.82d
δ (H-3)	~4.3m	~4.3m	~4.4m
$J_{1,2}$	10	10	10
$J_{1,3}$	~0	~0	2
$J_{2,3}$	5	5	~0

structures of (I) can readily be assembled as a derivative of a crinine-type alkaloid. The validity of this inference was substantiated by consideration of the mass spectrum of (I), Fig. 2a, in comparison with that of buphanisine (IV), Fig. 2b.[5,6] From the direct comparison, it is apparent that (I) and (IV) differ in the high mass region by a constant increment of 16 mass units, $C_2H_6O_2$ (62) *vs* CH_2O_2 (46) (see Fig. 2). Thus, the structural identity of the alicyclic moiety with crinine-type carbon skeleton is confirmed, and furthermore, it is clear that (I) is a methyl derivative of maritidine (II) or epimaritidine (V).[7] The assignment of the stereochemistry at C-3 of (I) was made by comparison of the NMR spectral data with those of (II) and (V) (see Table I). The coupling constants of the olefinic hydrogens with the proton at C-3 are consistent with (I) having the same pseudoaxial C-3-OCH_3 as is found in C-3-OH of (II). The same NMR behavior has been observed and explained for derivatives of haemanthamine and crinamine.[8] Thus, the structure (I) corresponds to O-methylmaritidine.

Pseudolycorine (mp 247—248°C), lycorine (mp 243—245°C), tazettine (mp 210—211°C), homolycorine (mp 167—169°C), demethylhomolycorine (mp 213—215°C), and pretazettine (mp 220—221°C as hydrochloride) were identified by direct comparisons with authentic samples.

Experimental

All melting points are uncorrected and were taken on a Yanko micro melting point apparatus, model MP-33. IR spectra were recorded as KBr tablets on a Hitachi 260-30 spectrometer and UV spectra were measured with a Hitachi 323 spectrophotometer. NMR spectra were obtained on a Hitachi R-22 (90 MHz) spectrometer, and the signals are given as chemical shifts in δ value (ppm) with TMS as an internal standard.[9] Mass spectra were obtained with a Hitachi RMU-7 mass spectrometer. Optical rotation was determined with a JASCO DIP-180 spectrometer and ORD was measured with a JASCO ORD/UV-5 spectrometer. Silica gel was used for column chromatography (Silicic acid 2847, Mallinckrodt) and thin layer chromatography (Kieselgel GF_{254}, Merck).

Isolation of Alkaloids from *Narcissus tazetta* L.——Fresh bulbs of this plant were cut into small pieces. The pieces (5 kg) were ground in a mixer and extracted with ethanol at room temperature. Removal of the solvent by evaporation under reduced pressure at 50°C left a residue of 530 g, which was suspended in 5 liters of 3% aqueous citric acid and extracted with 5 liters of ether. The aqueous acid solution was basified to pH 8—9 with solid Na_2CO_3 and extracted with chloroform (5 liters). The chloroform extract was washed with water, dried (Na_2SO_4) and concentrated to *ca.* 400 ml, and 4.48 g of insoluble basic material was removed by filtration. The filtrate was evaporated to dryness to give 6.49 g (total crude alkaloids, 10.97 g, 0.022%) of the chloroform-soluble alkaloids.

The chloroform-insoluble material (4.48 g) was dissolved in 5% aqueous NaOH and 2.3 g of aq. NaOH-insoluble material was removed by filtration. The filtrate was saturated with solid NH_4Cl to give a phenolic alkaloid, pseudolycorine (1.95 g, mp 247—248°C recrystallized from water).[10] The aq. NaOH-insoluble material was recrystallized from ethanol to give lycorine (2.2 g, mp(dp) 243—245°C).[11]

The chloroform-soluble material (6.49 g) was subjected to column chromatography using silica gel (100 g) and eluted successively with $CHCl_3$ (300 ml, fr. 1), $CHCl_3$–C_2H_5OH (97: 3) (510 ml, fr. 2), $CHCl_3$–C_2H_5OH (95: 5) (300 ml, fr. 3), $CHCl_3$–C_2H_5OH (9: 1) (300 ml, fr. 4), $CHCl_3$–C_2H_5OH (4: 1) (690 ml, fr. 5), $CHCl_3$–C_2H_5OH (7: 1) (510 ml, fr. 6), and $CHCl_3$–C_2H_5OH (1: 1) (240 ml, fr. 7).

Fr. 1 gave no material. Fr. 2 was subjected to preparative thin layer chromatography (PLC) using silica gel-[$CHCl_3$–C_2H_5OH (10: 3)] to give tazettine (*Rf* 0.44, 260 mg) and homolycorine (*Rf* 0.72, 520 mg). Fr. 3 gave crude demethylhomolycorine (*Rf* 0.44, 780 mg) and O-methylmaritidine (I) (*Rf* 0.57, 330 mg) when subjected to PLC using silica gel-[$CHCl_3$–C_2H_5OH (10: 3)]. Fr. 4 gave pretazettine (1.5 g). The other fractions are under investigation.

O-Methylmaritidine (I)——Colorless prisms from ether (220 mg), mp 88—89°C (243—245°C as hydrochloride, 258—259°C as hydroperchlorate), $[\alpha]_D^{23}$ +30.9° (c=1, $CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3032 (olefinic hydrogen), 1615 and 1590 (aromatic system), 1095 and 1068 (ether linkage). UV $\lambda_{max}^{ethanol}$ nm (log ε): 235 (3.47), 287 (3.30). ORD (c=0.0145, C_2H_5OH) [M]^{23} (nm): +100° (350), +5800° (297) (peak), 0° (285), −3500° (274) (trough). H^1-NMR ($CDCl_3$) δ ppm: 6.88 and 6.68 (each 1H, s, C-7-H and C-10-H), 6.55 (1H, d, J=10 Hz, C-1-H), 6.11 (1H, dd, J=5 Hz, C-2-H), 4.15 (1H, m, C-3-H), 4.40 and 4.35 (each 1H, d, J=17 Hz, AB type of C-6-H_2), 3.91, 3.88, and 3.40 (each 3H, s, C-8-OCH_3, C-9-OCH_3, and C-3-OCH_3), 1.6—2.1 (2H, broad m, C-4-H_2), 2.15—2.25 (2H, broad m, C-11-H_2), 2.8—3.15 (2H, broad m, C-12-H_2). MS m/z: Calcd for $C_{18}H_{23}NO_3$: 301.1676. Found: 301.1645. *Anal.* Calcd for $C_{18}H_{23}NO_3 \cdot HClO_4$: C, 53.79; H, 6.02; N, 3.48. Found: C, 53.59; H, 6.05; N, 3.35.

Dihydro-O-methylmaritidine (III)——(III) was prepared by stirring an ethanol solution of 20 mg of (I) with 20 mg of 5% Pd-C under an atmosphere of hydrogen. The solution was filtered and the solvents were removed under reduced pressure. The residue was chromatographed on silica gel (1 g) with $CHCl_3$–CH_3OH (10: 1). Eluted crude (III) was recrystallized from ethyl acetate to give colorless prisms (15 mg), mp 195—197°C. $[\alpha]_D^{23}$ +30° (c=1.4, $CHCl_3$). UV $\lambda_{max}^{ethanol}$ nm (log ε): 235 (3.86), 285 (3.60). H^1-NMR ($CDCl_3$) δ ppm: 6.75 and 6.64 (each 1H, s, aromatic-H), 4.82 and 4.28 (each 1H, d, J=17 Hz, AB type of C-6-H_2), 3.89 and 3.87 (each 3H, s, aromatic-OCH_3), 3.30 (3H, s, C-3-OCH_3), 1.5—4.0 (12H, m, methylene protons). MS m/z: Calcd for $C_{18}H_{25}NO_3$; 303.1834. Found: 303.1899.

Tazettine——Colorless needles from acetone (250 mg, 0.047%), mp 210—211°C.[11]

Homolycorine——Colorless prisms from ethyl acetate (500 mg, 0.09%), mp 166—168°C.[12]

Demethylhomolycorine——Colorless needles from ethyl acetate (730 mg, 0.147%), mp 213—215°C (259—260°C as picrate).[12]

Pretazettine Hydrochloride——Colorless prisms from ethanol (1.35 g, 0.25%), mp 220—221°C.[13]

Lycorine, pseudolycorine, tazettine, demethylhomolycorine, homolycorine, and pretazettine hydrochloride were identified by comparisons of melting points, IR spectra, and NMR spectra with those of authentic samples.

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