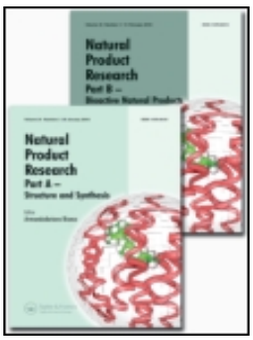

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iso-N-FORMYL-5-EN-CHONEMORPHINE, A STEROIDAL ALKALOID FROM *SARCOCOCCA ZEYLANICA*

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Abstract: Chemical investigation of the non-quaternary alkaloidal fraction of the aerial parts of *Sarcococca zeylanica* of the family Buxaceae furnished a steroidal alkaloid *iso-N*-formyl-5-en-chonemorphine, which has not been previously reported as a natural product. The structure of this alkaloid was established on the basis of spectroscopic evidence.

Key Words: *Sarcococca zeylanica*, Buxaceae, *iso-N*-formyl-5-en-chonemorphine, steroidal alkaloids.

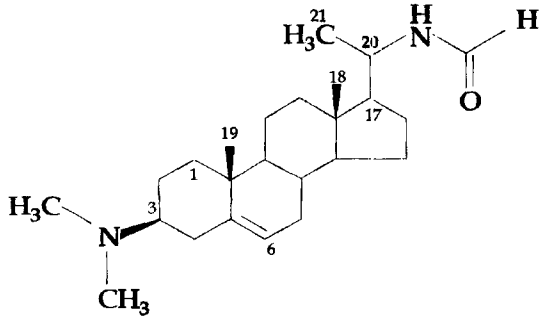
INTRODUCTION

The family Buxaceae comprises nearly 5 genera and about 100 species[1]. Several members of the family Buxaceae have been used in folk medicine[2]. It has been reported that the Sri Lankan flora comprise only two species of the family Buxaceae, *Sarcococca zeylanica* and *S. brevifolia*, both being endemic to the island[3]. *S. zeylanica* is an evergreen shrub growing in the mid island region of Sri Lanka.

A preliminary survey had indicated the presence of alkaloids in the leaves and twigs of the plant[4]. A number of pregnane type alkaloids have been reported from the several species of *Sarcococca*[5-9]. In this paper we report the isolation and structure elucidation of a steroidal alkaloid *iso-N*-formyl-5-en-chonemorphine (**1**) from the aerial parts of *Sarcococca zeylanica,* which has not been previously reported as a natural product.

RESULTS AND DISCUSSION

Chromatographic separation of the crude non-quaternary alkaloid fraction over a column of silica gel followed by PTLC furnished compound **1**. It showed a positive response with Dragondorff's reagent indicating its alkaloidal nature.



1

The positive mode FABMS of **1** showed a peak at *m/z* 373 for $[M+H]^+$. The high-resolution mass spectrum of **1** showed the $[M]^+$ at *m/z* 372.3133 which is consistent with the molecular formula $C_{24}H_{40}N_2O$ (calc. 372.3143), indicating the presence of six degrees of unsaturation in the molecule. Four of these were accounted for by the tetracyclic structure of the pregnene type steroid and the remaining ones by the amidic carbonyl group. The base peak at *m/z* 84.0831

(calc. 84.0814, $C_5H_{10}N$) represented the cleavage of ring A along with the $N(CH_3)_2$ substituent in the ring A. An intense peak observed at *m/z* 72.0432 (calc. 72.04498, C_3H_6NO) representing *N*-formylmethyliminium cation, CH_3-CH=N^+HCHO arose by the cleavage of the ring D side chain. Other intense peaks observed at *m/z* 44.0458 (calc. 44.05001, $N(CH_3)_2$) and 328.2587 (calc. 328.26422, $C_{22}H_{24}NO$, [M^+-$N(CH_3)_2$]) arose by the cleavage of the $N(CH_3)_2$ group attached to C-3. The ^{1}H NMR ($CDCl_3$, 500 MHz) of compound **1** showed two sharp singlets at δ 0.74 and 1.00 corresponding to the C-18 and C-19 methyl groups respectively. A three-proton doublet centered at δ 1.19 (J = 6.7 Hz) was assigned to the C-21 secondary methyl protons. A one proton multiplet at δ 4.10 was due to the C-20 methine proton, which showed coupling with the C-21 methyl group. Another one proton multiplet observed at δ 5.28 was characteristic of H-6[10]. A six proton signal observed at δ 2.58 was assigned to two Me groups on N_a. A multiplet at δ 3.40 was assigned to H-3α. A singlet observed at δ 8.08 accompanied by another low intensity singlet at δ 8.07 represented the N_b formyl proton as a result of rotational isomerism[11]. Thus compound **1** was identified as *iso-N*-formyl-5-en-chonemorphine. Structurally related compounds *N*-formylchonemorphine and *iso-N*-formylchonemorphine have been reported from *Chonemorpha macrophylla*[12] and *Sarcococca brevifolia*[9] respectively. This is the first report of compound **1** as a natural product. It has been previously synthesized by Corey and Hertler[13].

EXPERIMENTAL

Mps were determined using a Gallenkamp apparatus and are uncorrected. Optical rotations were measured using a HORIBA Model SEPA-200 polarimeter at 22°. IR spectra were obtained from a JASCO 302-A spectrometer. EI and HREIMS were recorded on JMS HX100 and JMS-DA 500 mass spectrometers.

^{1}HNMR spectra were recorded on a Bruker AMX 500 spectrometer in $CDCl_3$ solution with tetramethylsilane as an internal reference.

Plant Material: Aerial parts of *S. zeylanica*, were collected from the Uva Province of Sri Lanka in September 1995. A voucher specimen is deposited at the Institute of Fundamental Studies, Kandy, Sri Lanka.

Extraction and Isolation: The dry ground mature aerial parts of *Sarcococca zeylanica* (3kg) were extracted with MeOH. Evaporation of the MeOH gave a dark brown solid (460g). This solid (450g) was partitioned between 2N HCl and CH_2Cl_2. The aqueous fraction was washed with CH_2Cl_2. The acidic fraction was basified with 20% NH_4OH and the alkaloids were extracted in to CH_2Cl_2. Evaporation of the solvent gave the total non-quaternary alkaloids as a brownish solid (6.5g). Separation of alkaloids (6.4 g) on a column of silica gel (Merck Art. 7734) with $CHCl_3$-MeOH as eluting solvent, followed by preparative layer chromatography (eluent: 5% MeOH - $CHCl_3$, chamber saturated with NH_3 vapor) gave alkaloid **1** (15mg).

iso-N-formyl-5-en-chonemorphine: mp 220-222°; $[\alpha]_D^{22}$ = 2.1° (c = 2.9 x 10^{-3}, $CHCl_3$); UV (MeOH) λ_{max} 194 nm; IR($CHCl_3$)υ_{max}: 3651, 3325, 1660, 1630, 1490 cm^{-1}; ^{1}HNMR($CDCl_3$, 500 MHz) :δ 0.74 (3H, *s*, Me-18), 1.00 (3H, *s*, Me-19), 1.19 (3H, *d*, J = 6.7 Hz, Me-21), 2.58 (6H, *s*, $N_a(Me)_2$), 3.40(1H, *m*, H-3α), 4.10 (1H, *m*, H-20), 5.28 (1H, *m*, H-6), 8.08/8.07 (1H, *s*, N_b-C<u>H</u>O); FABMS(+)*m/z*: 373 $[M+H]^+$; HREIMS *m/z*: 372.3133 (M^+, $C_{24}H_{40}ON$), 84.0831 ($C_5H_{10}N^+$), 72.0432 ($C_3H_6ON^+$), 44.0458 ($N(CH_3)_2$), 328.2587 ($[M^+-N(CH_3)_2]$); EIMS *m/z* (rel. int. %): 44 (5), 72 (15), 84 (100), 100 (15), 133 (5), 239 (2), 295 (10), 372 (35).

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