Chemistry of Natural Compounds, Vol. 46, No. 4, 2010

CONVOLININE, A NEW ALKALOID FROM *Convolvulus subhirsutus* OF UZBEKISTAN FLORA

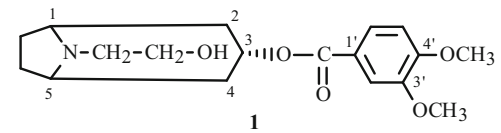
A. M. Gapparov, S. F. Aripova,* B. Tashkhodzhaev, M. G. Levkovich, and O. Aripov

UDC 957.944/945

Several alkaloids of known structure and the new base convolinine were isolated from total alkaloids from the aerial part of Convolvulis subhirsutus *growing in Uzbekistan. It has been established that convolinine is an* N*-hydroxyethyl derivative of convolvine and has the structure (±)-3α-(3,4-dimethoxybenzoyl)-*N*-hydroxyethylnortropane based on spectral data and an x-ray crystal structure.*

Keywords: *Convolvulus subhirsutus*, alkaloids, convolinine, (±)-3α-(3,4-dimethoxybenzoyl)-*N*-hydroxyethylnortropane (*N*-hydroxyethylconvolvine).

Ten alkaloids (convolvine, convolamine, convolidine, phyllalbine, convolvidine, convolicine, convoline, phyllalbine *N*-oxide, nortropine, conpropine) were isolated from the aerial part of *Convolvulus subhirsutus* growing in Uzbekistan [1, 2]. In continuation of the study of *C. subhirsutus* roots collected in Tashkent Oblast, a new alkaloid (mp 128–129°C, $[\alpha]_D$ 0°) was isolated from total alkaloids of the non-phenolic part after isolation of convolvine and convolamine by column chromatography over Al_2O_3 of the mother liquor of the non-phenolic part of total bases from the benzene:$CHCl_3$ fractions. The physicochemical properties and chromatographic mobility differed from those described in the literature for tropane bases. We called it convolinine (**1**).



1

The alkaloid had the formula $C_{18}H_{25}NO_5$. The IR spectrum of the base contained absorption bands for active H at 3290 cm^{-1}; ester carbonyl, at 1749; 3,4-disubstituted benzene, at 1601, 1516, 878, and 821; stretching and bending vibrations of CH_3–, CH_2–, and CH–, at 2922, 2854, 1463, 1419, 1284, and 1274; and ether –C–O–C–, at 1074 and 1021.

The PMR spectrum exhibited resonances for protons of two aromatic methoxyls as two 3H singlets at 3.87 and 3.89 ppm. An 8H multiplet was found in the range 1.85–2.85 that is characteristic of tropane bases for four CH_2 groups of a tropane ring in the C-2, C-4, C-6, and C-7 positions. A 2H multiplet probably for CH_2 protons bound to a N atom was observed at 3.77. A 2H multiplet for two methine protons of C-1 and C-5 in a tropane ring that is characteristic of tropane alkaloids occurred at 3.59. A ^1H triplet for $H_{3\beta}$ that is diagnostic for tropane bases esterified on the C-3 hydroxyl was located at 5.23. Resonances for three aromatic protons with characteristic structure of *meta*- and *para*-substitution were seen at 7.60–6.80. The isolated α-proton appeared as a doublet with J = 2.0 Hz at 7.50. The other aromatic -proton gave a doublet of doublets (meta-constant J = 2.0 Hz and ortho-constant J = 8.5 Hz) at 7.58. Finally, the β-proton resonated at 6.84 as a doublet (J = 8.5 Hz). A 2H multiplet for protons of CH_2 bonded to oxygen was noted at 2.75.

Based on these spectral characteristics, IR spectra (absorption bands for active H), PMR spectra, and taking into account the molecular weight of the alkaloid (M^+ 335) with an unsubstituted *N*-containing tropane core, it can be hypothesized that convolinine has a substituted N atom and that the substituent is $–C_2H_4OH$. The PMR spectra suggest that this could be a $–CH_2–CH_2–OH$ group on the N atom.

S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, Tashkent, fax: (99871) 120 64 75, e-mail: salima_aripova@mail.ru. Translated from Khimiya Prirodnykh Soedinenii, No. 4, pp. 497–498, July–August, 2010. Original article submitted January 4, 2010.

 0009-3130/10/4604-0590

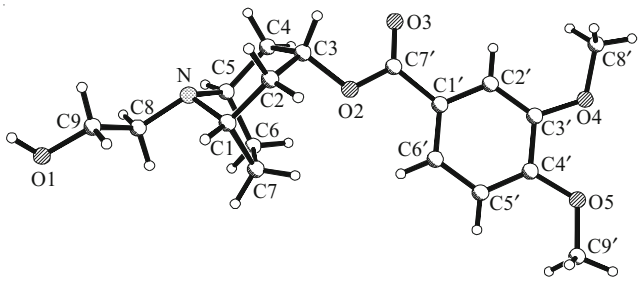


Fig. 1. Molecular structure of **1**.

The results led to the conclusion that convolinine was apparently an *N*-hydroxyethyl derivative of convolvine.

A single-crystal x-ray structure analysis (XSA) was performed for the final proof of the structure of convolinine. The alkaloid crystallized in centrosymmetric space group Pbca. Therefore, the crystal contained both enantiomers. Figure 1 shows the molecular structure of **1** from the XSA. The XSA confirmed the structure that was hypothesized from the spectral data and enabled the relative configuration at C3 to be established. The substituent on C3, a veratroyloxy group, had the α-axial orientation relative to the tropane core and deviated from the symmetry plane of the tropane core. The C4C3O2C1′ torsion angle was 84.3°. The planar fragments, the aromatic ring with *p*- and *m*-methoxyls and the ester, were slightly twisted relative to each other. The C3′C2′C1′O3 torsion angle was 12.9°. In general, the orientation and placement of the substituent in the C3 position were similar to those observed for *o*-benzoyltropine hydrochloride [3].

The seven-membered ring adopted the boat conformation. The five-membered heterocycle was an N-envelope. The aromatic ring was planar within ±0.008 Å. The bond distances and angles were normal [4] except for the C8–C9 distance of 1.421(8) Å (due to high thermal motion of C9).

The crystal included O–H...N H-bonds between O1–H of the initial molecule and the N atom of that transformed by a 2_1 axis (x, 0.25, 0). The parameters of the H-bonds were N...O, 2.867 Å; H...N, 0.82; O–H...N, 142°. An infinite chain along the crystallographic *a* axis was formed by these H-bonds.

Thus, the results enabled convolinine to be identified as (±)-3α-(3,4-dimethoxybenzoyl)-*N*-hydroxyethylnortropane.

EXPERIMENTAL

IR spectra were taken (mineral oil) on a Perkin–Elmer model 2000 Fourier IR-spectrometer; NMR spectra, on a Unity-400$^+$ instrument at operating frequency 400 MHz (CD_3OD solvent, HMDS internal standard, δ-scale); mass spectra, in an HP 6890/5973 GC/MS.

Isolation and separation of total alkaloids have been reported [1, 2].

Isolation of Convolinine. Mother liquor of the non-phenolic part of total alkaloids from roots after isolation of the major alkaloids convolvine and convolamine was dried, mixed with an equal volume of silica gel, and placed on a column of silica gel in a 1:25 ratio. The column was eluted by hexane:benzene (1:1), benzene, and benzene:acetone (3:1). Crystals with mp 128–129°C (20 mg) and R_f 0.45 ($CHCl_3$:MeOH, 2:0.1) were isolated from the benzene:acetone fractions.

X-ray structure analysis (XSA) was performed on an Xcalibur diffractometer (Oxford Diffraction, 298 K, Ruby CCD detector, graphite monochromator, ω/2θ-scanning, CuK_α-radiation). The crystals were transparent needles with approximate sizes 0.45 × 0.06 × 0.08 mm. A minor amount of the isolated compound did not produce single crystals of the required quality and size for XSA. Therefore, an adequate data set of experimental reflections could not be collected.

The crystallographic data and principal refinement parameters for **1** were $C_{18}H_{25}NO_5$, MW = 335.39, orthorhombic system, space group Pbca, a = 8.367(2), b = 10.783(2), c = 38.427(8) Å, V = 3466.9(12) Å^3, Z = 8, d_{calcd} = 1.266 g/cm^3, μ_{exp} = 0.093 mm^{-1}, 2θ scan range ≤ 110.67°, number of measured reflections 2126, number of reflections with $I \geq 2\sigma(I)$ 1388, number of refined parameters 220, R_1 [$I \geq 2\sigma(I)$] = 0.0791, wR_2 = 0.1821 (over all reflections), GOOF = 1.103. Absorption corrections were applied using the Multi-scan method.

The structure was solved by direct methods using the SHELXS-97 programs and was refined using the SHELXL-97 program. All nonhydrogen atoms were refined by full-matrix anisotropic least-squares methods (over F^2). Positions of H

atoms were calculated geometrically and were refined using a rider model. The hydroxyl H atom was found from a difference electron-density synthesis and refined isotropically by fixing it to the corresponding O atom.

The XSA data were deposited as a CIF file in the Cambridge Crystallographic Data Centre (CCDC W = 758625).

REFERENCES

1. A. M. Gapparov, N. A. Razzakov, and S. F. Aripova, *Khim. Prir. Soedin.*, 242 (2007) [*Chem. Nat. Comp.*, **43**, 3, 291 (2007) (Engl. transl.)].
2. A. M. Gapparov, S. F. Aripova, N. A. Razzakov, and V. U. Khuzhaev, *Khim. Prir. Soedin.*, 601 (2008) [*Chem. Nat. Comp.*, **44**, 6, 743 (2008) (Engl. transl.)].
3. T. A. Hamor, *J. Chem. Soc., Perkin Trans. 2*, 1359 (1976).
4. F. N. Allen, O. Kennard, and D. G. Watson, *J. Chem. Soc., Perkin Trans. 2*, **12**, S1 (1987).