



TWO PYRIDINE-2,6(1*H*,3*H*)-DIONE ALKALOIDS FROM *SPERANSKIA TUBERCULATA*

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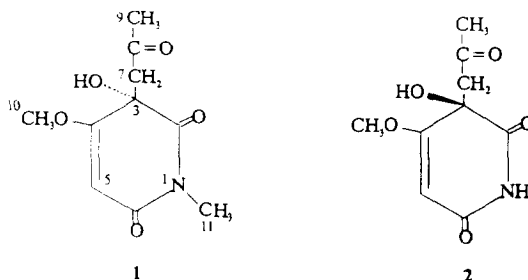
Abstract—Two new pyridine-2,6(1*H*,3*H*)-dione alkaloids, designated as speranskatines A and B, were isolated from an acetone extract of dried whole plants of *Speranskia tuberculata*. Their structures were determined by means of spectroscopic and X-ray crystallographic analysis.

INTRODUCTION

Speranskia tuberculata is distributed in the Gan-Su, Ji-Ling, He-Bei, Shan-Dong and An-Hui Provinces of the People's Republic of China. It has been used for the treatment of rheumatic arthritis, constricture, sores, swelling, pain and inflammatory diseases [1]. No previous phytochemical work has been reported on this genus. In the continuation of our investigations on the constituents of the Euphorbiaceae [2–5], we have now isolated two new pyridine-2,6(1*H*,3*H*)-dione alkaloids from an acetone extract of dried whole plants of *S. tuberculata* and determined their structures. This paper describes the structural elucidation of the alkaloids based on spectroscopic and X-ray crystallographic analysis. It is of interest, that only known natural pyridine-2,6(1*H*,3*H*)-dione alkaloid, hermidin, was isolated from *Mercurialis perennis*, which also belongs to the Euphorbiaceae [6, 7].

RESULTS AND DISCUSSION

The acetone extract of dried whole plants of *S. tuberculata* was repeatedly chromatographed on silica gel to afford two new alkaloids, named speranskatines A (1) and B (2). The EI mass spectrum of 1 showed a $[M]^+$ at m/z 227 and the molecular formula $C_{10}H_{13}NO_5$ was assigned on the basis of elemental analysis and HR mass spectrometry. The strong UV and IR absorption (λ_{max}^{MeOH} nm: 261, 225; ν_{max}^{KBr} cm^{-1} : 3327, 1716, 1695, 1673, 1633, 843) in combination with 1H NMR data [δ 3.78 (OMe), 3.22 (NMe), each 3H, s; 5.45, 1H, s] suggested a parent structure for 1 of 1-methylpyridine-2,6(1*H*,3*H*)-dione [7–9] and the presence of a hydroxyl



group and a methoxyl group. In the EI mass spectrum, the fragment peaks at m/z 170 $[M - CH_2COCH_3]^+$, 57 $[CH_2COCH_3]^+$ and 43 $[COCH_3]^+$ indicate that there was a 2-oxopropyl group in 1, which was confirmed by 1H NMR (δ 2.15, 3H, s; 3.28, 2H, s) and ^{13}C NMR [δ 205.5 (s), 50.0 (t), 30.6 (q)] spectra. The chemical shift of C-3 (δ 70.8) in the ^{13}C NMR spectrum showed that the 2-oxopropyl group, along with the hydroxyl or methoxyl group, was attached to C-3. A COLOC experiment (Fig. 1) established unambiguously the attachment of the

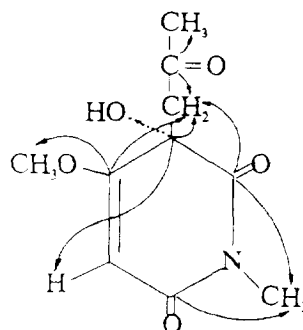


Fig. 1. COLOC correlations for compound 1.

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methoxyl group to C-4. The above spectral evidence thus revealed that **1** was 3-hydroxy-4-methoxy-3-(2-oxopropyl)-1-methylpyridine-2,6(1*H*,3*H*)-dione. In order to confirm the complete structure and determine the rela-

tive configuration at C-3, **1** was subjected to single crystal X-ray diffraction analysis. The ORTEP drawing is shown in Fig. 2. As a result, the 2-oxopropyl and *N*-methyl groups occurred on different sides of the ring, such that

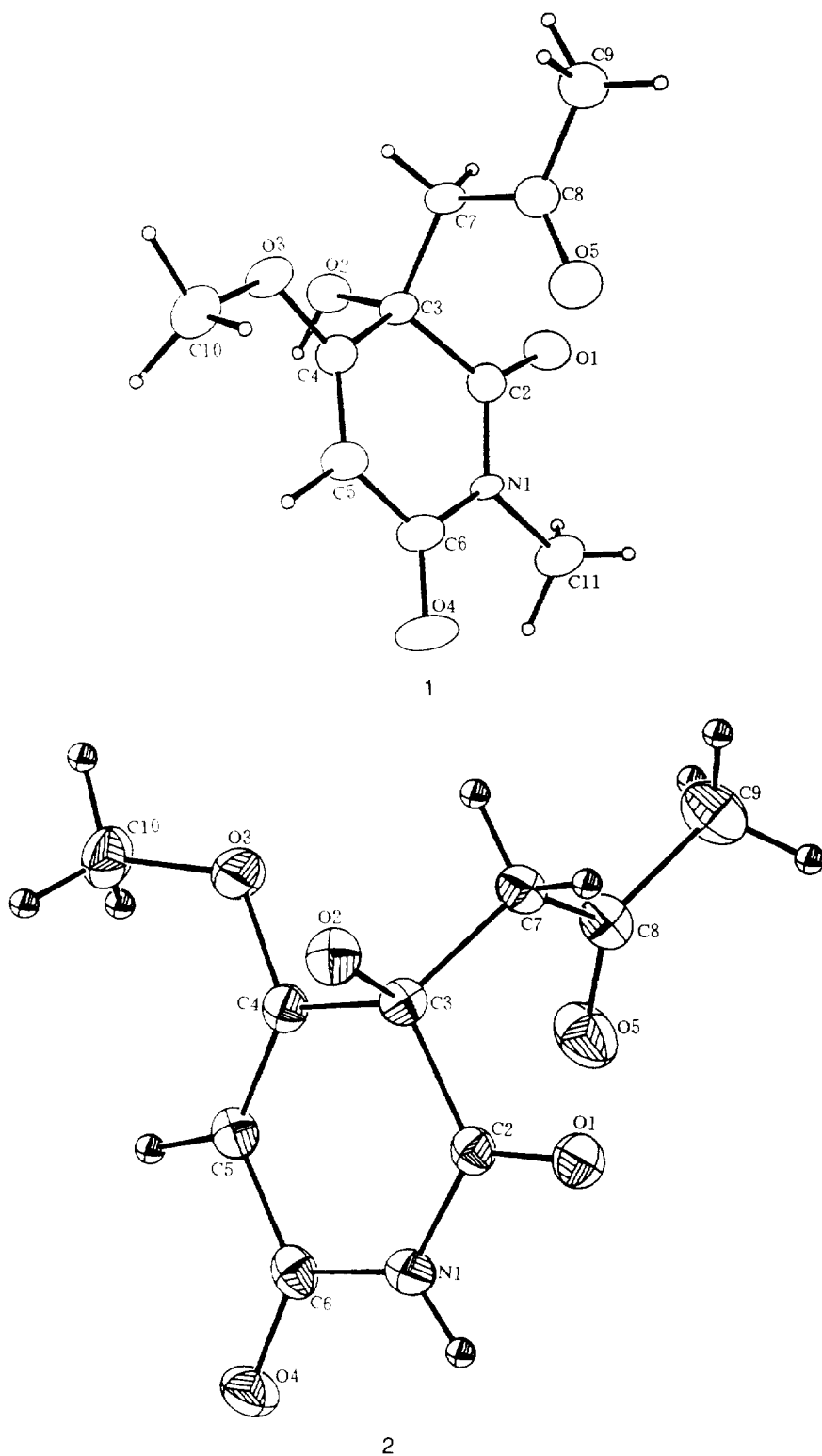


Fig. 2. ORTEP drawings of compounds **1** and **2**.

the 2-oxopropyl group attached to the asymmetric centre at C-3 could rotate freely in solution; this led to an explanation for the singlet for the methylene protons in the ^1H NMR spectrum of **1**.

Speranskatine **B** (**2**) had a molecular formula $\text{C}_9\text{H}_{11}\text{NO}_5$ (EI and HR mass spectrometry and elemental analysis). Its UV and IR spectra showed similar absorption bands to those of **1**. Comparing the NMR spectra of **2** with those of **1** (Table 1), the appearance of a N-H and the absence of a N-methyl group in the NMR spectra of **2** suggested that **2** was 3-hydroxy-4-methoxy-3-(2-oxopropyl)-pyridine-2,6(1*H*,3*H*)-dione. However, in the ^1H NMR spectrum of **2**, the methylene protons of the 2-oxopropyl group did not appear as a singlet, as in that of **1**, but as an AB system; this indicated that the asymmetric centre at C-3 of **2** had the opposite configuration to that of **1**. The structure of **2** was also proved by X-ray crystallographic analysis. The ORTEP drawing (Fig. 2) showed that the 2-oxopropyl group and N-H were on the same side of the ring, such that a hydrogen bond could be formed between them and thus, rotation of the 2-oxopropyl group was obstructed in solution. Therefore, the methylene protons appeared as an AB system in the ^1H NMR spectrum of **2**.

The absolute stereostructures of **1** and **2** have not yet been determined.

EXPERIMENTAL

General. Mps: uncorr. Optical rotations: 18° , MeOH. UV: MeOH. IR: KBr. ^1H NMR (400 MHz). ^{13}C NMR (100 MHz) and 2D NMR: TMS as int. standard with CDCl_3 as solvent. HRMS and EIMS: direct inlet, 70 eV. All solvents were redist. prior to use.

Plant material. *Speranskia tuberculata* (Bge.) Ball was collected from Beizai, Gansu Province of the People's Republic of China, in September 1993 and identified by

Prof. Guo-Liang Zhang. A voucher specimen (no. 930911) is deposited in the Herbarium of the Department of Biology (Lanzhou University).

Extraction and isolation. Air-dried and powdered whole plants (10 kg) were extracted with Me_2CO at 30° for 4×24 hr. The concd extract (235 g) was chromatographed on a silica gel (200–300 mesh, 1200 g) column and eluted with a petrol (60– 90°) and Me_2CO (20:1–0:1) gradient (1500 ml each eluent). The fr. (2.7 g) eluted with petrol– Me_2CO (1:1) gave a positive Dragendorff's test and was repeatedly rechromatographed by silica gel CC eluting with petrol–EtOAc (1:3) to yield speranskatines **A** (54 mg) and **B** (18 mg).

Speranskatine A (1). Transparent prisms from EtOAc, mp $158\text{--}160^\circ$. $[\alpha]_{\text{D}}^{25} + 14.8^\circ$ (MeOH; c 0.54). UV λ_{max} nm: 261, 225. IR ν_{max} cm^{-1} : 3327, 3104, 2985, 2947, 1716, 1695, 1673, 1633, 1467, 1438, 1384, 1365, 1311, 1264, 1214, 1192, 1170, 1105, 1052, 1035, 994, 974, 944, 843, 779, 726, 667, 643, 621. EIMS m/z (rel. int.): 227 $[\text{M}]^+$ (7), 199 $[\text{M} - \text{CO}]^+$ (9), 194 (4), 184 $[\text{M} - \text{COCH}_3]^+$ (2), 170 $[\text{M} - \text{CH}_2\text{COCH}_3]^+$ (48), 149 (5), 142 (47), 127 (100), 109 (7), 99 (9), 83 (44), 69 (39), 58 (14), 57 (16), 43 (73). ^1H and ^{13}C NMR: Table 1. HRMS m/z : 227.2184, $\text{C}_{10}\text{H}_{13}\text{NO}_5$ requires 227.2191, analyt.: found: C, 52.84; H, 5.78; N, 6.20, $\text{C}_{10}\text{H}_{13}\text{NO}_5$ requires: C, 52.86; H, 5.77; N, 6.16.

Crystal data of speranskatine A (1). $\text{C}_{10}\text{H}_{13}\text{NO}_5$, $M_r = 227.22$, crystal dimensions $0.25 \times 0.18 \times 0.08$ mm³, monoclinic, space group P21/C, $a = 8.588$ (7), $b = 17.461$ (8), $c = 7.893$ (10) Å, $\beta = 113.82$ (1) $^\circ$, $V = 1082.8$ (7) Å³, $Z = 4$, $D = 1.39$ g cm⁻³, CuK_α radiation, $\lambda = 1.5418$ Å, $\mu = 9.166$ cm⁻¹, $F(000) = 480$, room temperature. Intensity data were collected on an Enraf–Nonius CAD 4 diffractometer with graphite-monochromated CuK_α radiation by the ω -2 θ scan technique and were corrected for background by Lorentz, polarization and absorption ($T_{\text{max}} = 0.996$, $T_{\text{min}} = 0.842$) effects. The reflections were collected up to $2\theta = 62^\circ$, of 1886 reflections, 1638 were unique. The structure was solved by direct methods using SDP software and refined by full-matrix least-squares. Final $R = 0.054$, $R_w = 0.055$. The maximum negative and positive peaks in the final difference map were -0.243 eÅ⁻³ and 0.253 eÅ⁻³, respectively.

Speranskatine B (2). Transparent prisms from EtOAc, mp $171\text{--}172^\circ$. $[\alpha]_{\text{D}}^{25} - 30.0^\circ$ (MeOH; c 0.30). UV λ_{max} nm: 256, 216. IR ν_{max} cm^{-1} : 3302, 3197, 3073, 2691, 2924, 2843, 1720, 1709, 1676, 1618, 1446, 1423, 1397, 1309, 1242, 1174, 1098, 1053, 991, 839, 769, 702, 669, 624. EIMS m/z (rel. int.): 213 $[\text{M}]^+$ (10), 185 $[\text{M} - \text{CO}]^+$ (9), 180 (4), 170 $[\text{M} - \text{COCH}_3]^+$ (64), 156 $[\text{M} - \text{CH}_2\text{COCH}_3]^+$ (15), 149 (10), 142 (7), 127 (100), 109 (8), 100 (16), 98 (15), 84 (17), 69 (88), 58 (24), 57 (14), 43 (100). ^1H and ^{13}C NMR: Table 1. HRMS m/z : 213.1932, $\text{C}_9\text{H}_{11}\text{NO}_5$ requires 213.1919, analyt.: found: C, 50.75; H, 5.23; N, 6.61, $\text{C}_9\text{H}_{11}\text{NO}_5$ requires: C, 50.71; H, 5.20; N, 6.57.

Crystal data of speranskatine B (2). $\text{C}_9\text{H}_{11}\text{NO}_5$, $M_r = 213.19$, crystal dimensions $1.2 \times 0.4 \times 0.3$ mm³, monoclinic, space group P21/n, $a = 7.344$ (1), $b = 8.041$ (3), $c = 16.760$ (4) Å, $\beta = 96.39$ (2) $^\circ$, $V = 983.7$ (4) Å³, $Z = 4$, $D = 1.43$ g cm⁻³, MoK_α radiation, $\lambda = 0.71069$ Å,

Table 1. NMR data for compounds **1** and **2** (δ , CHCl_3)*

No.	1		2	
	H	C	H	C
2	—	172.9 s	—	172.7 s
3	—	70.8 s	—	70.5 s
4	—	167.5 s	—	171.7 s
5	5.45 s	94.5 d	5.31 s	94.2 d
6	—	164.6 s	—	165.6 s
7	3.28 s	50.0 t	3.44, 3.34 ABq ($J = 17.5$)	49.5 t
8	—	205.5 s	—	205.9 s
9	2.15 s	30.6 q	2.07 s	30.2 q
10	3.78 s	56.7 q	3.75 s	57.1 q
11	3.22 s	26.6 q	N-H 8.00 s	—

*J (in Hz) in parentheses. Multiplicity of C were determined by DEPT. Assignments were confirmed by ^1H – ^{13}C COSY and COLOC.

$\mu = 1.11 \text{ cm}^{-1}$, $F(000) = 444$, $T = 296 \text{ K}$. Intensity data were collected on a Rigaku AFC-5R diffractometer with graphite-monochromated MoK_α radiation by the θ - 2θ scan technique and were corrected for background by Lorentz, polarization and absorption ($T_{\text{max}} = 1.348$, $T_{\text{min}} = 0.674$) effects. The reflections were collected up to $2\theta = 50^\circ$, of 2009 reflections, 1858 were unique. The structure was solved by direct methods using TEXSAN software and refined by full-matrix least-squares. Final $R = 0.058$, $R_w = 0.071$. The maximum negative and positive peaks in the final difference map were $-0.344 \text{ e}\text{\AA}^{-3}$ and $0.339 \text{ e}\text{\AA}^{-3}$, respectively.

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