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Two Polyoxygenated Pyrrolylpyridine and Bipyrrole Alkaloids from *Speranskia tuberculata*

Jian Gong SHI[1,*], Wen Yan HU[1], Guang Xiong ZHOU[1], Yong Chun YANG[1], Han Qing WANG[2,*], Min WANG[2]

[1]*Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Bejing 100050*
[2]*Lanzhou Institute of Chemical Physics, Chinese Academy of Sciences, Lanzhou 730000*

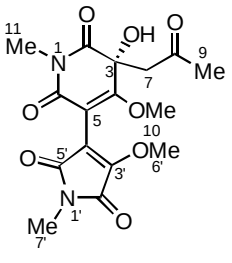
Abstract: Two novel polyoxygenated pyrrolylpyridine and bipyrrole alkaloids, speranskilatine A **1,** and speranberculatine A **2**, have been isolated from *Speranskia tuberculata*. Their structures were elucidated by spectroscopic methods including 2D NMR techniques and X-ray crystallographic analysis.

Keywords: *Speranskia tuberculata*, Euphorbiaceae, pyrrolylpyridine and bipyrrole alkaloids, speranskilatine A, speranberculatine A.

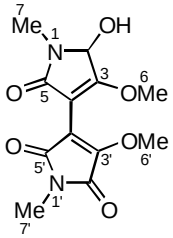
Speranskia tuberculata (Bge.) Ball (Euphorbiaceae) is used as a folk medicine (Tou Gu Cao) for the treatment of rheumatic arthritis, constracture, sores, swelling, pain and inflammatory diseases in China[1]. No chemical constituent was described for this genus before we reported two optical active pyridine-2, 6 (1*H*, 3*H*)-dione alkaloids speran-skatines A, B[2] and two bipyridine-2, 6 (1*H*, 3*H*)-dione, speranculatines A and B[3] in previous papers. We report here the structural elucidation of two novel polyoxygenated pyrrolylpyridine and bipyrrole alkaloids named speranskilatines A **1** and speranberculatine A **2** from the same plant.

Speranskilatine A **1**, mp 166-167 °C, $[\alpha]_D^{18}$ + 3.8 (*c* 1.30, MeOH), was obtained as colorless prisms from $CHCl_3$. The IR spectrum of **1** showed the presence of hydroxyl (3381 cm^{-1}), carbonyl (1715 cm^{-1}) and lactam carbonyl (1780, 1680, 1657 cm^{-1}) groups. The EIMS and positive ion FABMS spectra exhibited a molecular ion peak at *m/z* 366 $[M]^+$ and a quasi-molecular ion peak at *m/z* 367 $[M+H]^+$, respectively. The molecular formula $C_{16}H_{18}N_2O_8$ was determined by HRFABMS *m/z* 367.1154 (calcd for $C_{16}H_{19}N_2O_8$ 367.1141). The ^1H and ^{13}C NMR data of **1** (**Table 1**) showed characteristic signals for 3-hydroxy-4-methoxy-3-(2-oxopropyl)-1-methylpyridine-2,6(1*H*, 3*H*)-dione-5-yl. The remaining NMR signals were unambiguously attributed to a 3'-methoxy-2', 5'-dioxo-1'-methylpyrrol-4'-yl moiety based on the HMBC cross-peaks from H_3-7' to C-2',

C-5', and from H_3-6' to C-3'.



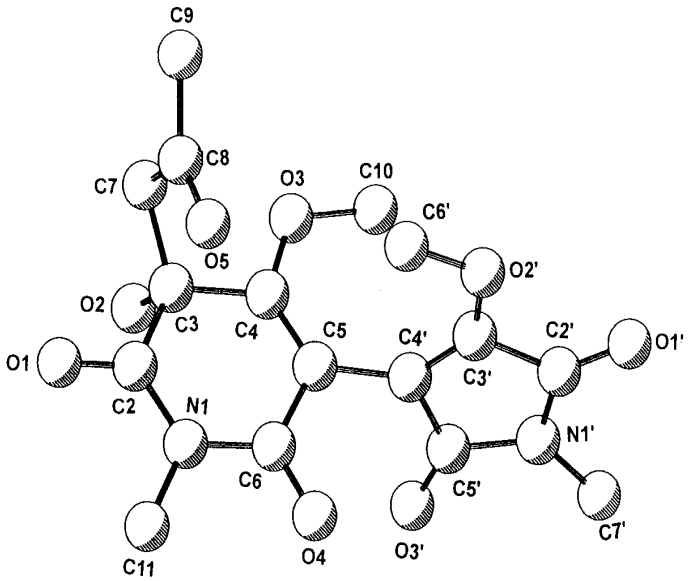
1



2

The single crystal X-ray diffraction analysis indicated that the pyridine-2,6 (1*H*, 3*H*)-dione ring possessed an envelope conformation as that observed for speranskatines A, B and speranculatines A, B. All atoms of the 2',5'-dioxo-1'-methylpyrrolyl ring were on one plane, the nitrogen was in the sp^2 hybrid mode. The dihedral angle between the two ring planes was 77.80° in the solid-state. The ORTEP drawing, with the atom numbering scheme indicated, is shown in **Figure 1**. Therefore, the structure of speranskilatine A **1** was established to be *rel*-(3*R**)-(+)-3-hydroxy-4-methoxy-3-(2-oxopropyl)-5-(3'-methoxy-2',5'-dioxo-1-methyl pyrrol-4'-yl)-1-methyl-pyridine-2,6(1*H*, 3*H*)-dione.

Figure 1. ORTEP diagram of **1**



Speranberculatine A **2**, a pale yellow gum, $[\alpha]_D^{18}$ - 14.8 (*c* 0.50, MeOH), displayed IR absorption bands of hydroxyl (3283 cm^{-1}), and lactam carbonyl (1778, 1714, 1700 cm^{-1}) groups. The EIMS and positive ion FABMS spectra exhibited a molecular ion peak at *m/z* 282 $[M]^+$ and a quasi-molecular ion peak at *m/z* 283 $[M+H]^+$, respectively. The molecular formula was determined as $C_{12}H_{14}N_2O_6$ on the basis of HRFABMS *m/z* 283.0918 (calcd for $C_{12}H_{15}N_2O_6$ 283.0930). The ^1H and ^{13}C NMR data of **2** (**Table 1**) showed signals similar to those for 3'-methoxy-2',5'-dioxo-1'-methylpyrrol-4'-yl moiety observed in NMR spectra of **1**. Therefore, the composition of the remaining moiety of **2** is $C_6H_8NO_3$. Comparison of the NMR spectral data of **2** with those of **1** indicated that an oxymethine of **2** (δ_H 5.22, 1H, s; δ_C 81.3 d) replaced the 2-oxopropyl group and C-3 of **1**. Furthermore, the ^{13}C NMR spectrum of **2** showed three lactam carbonyl signals instead of four lactam carbonyl signals of **1**. The HMBC spectrum of **2** exhibited cross-peaks from the oxymethine proton to C-4, C-5, from H_3-7 to C-2, C-5, and from H_3-6 to C-3, but no cross-peak from the oxymethine proton to C-4' was observed. These evidences proved that the upper moiety of **2** was a 2-hydroxy-3-methoxy-1-methylpyrrol-5 (2*H*)-one-4-yl. Accordingly, the structure of speranberculatine A **2** was elucidated to be (-)-2-hydroxy-3, 3'-dimethoxy-1, 1'-dimethyl-4, 4'-bipyrrole-5, 2',5'-(2*H*)-trione.

Table 1. NMR Data for Speransilatine A **1** and Speranberculatine A **2** [a]

	1		**2**	
No.	H	C	H	C
2	-	171.8 s	5.22 s	81.3 d
3	-	71.3 s	-	170.2 s
4	-	167.1 s	-	96.0 s
5	-	102.9s[b]	-	169.3 s
6	-	164.6 s	3.99 s	58.6 q
7a	3.56 d (17.8)	50.3 t	2.94 s	26.0 q
7b	3.35 d (17.8)	-	-	-
8	-	205.7 s	-	-
9	2.12 s	29.8 q	-	-
10	3.89 s	60.6 q	-	-
11	3.24 s	27.4 q	-	-
2'	-	171.4 s	-	171.2 s
3'	-	156.1 s	-	156.2 s
4'	-	101.4 s[b]	-	101.1 s
5'	-	165.4 s	-	165.5 s
6'	3.96 s	59.5 q	4.08 s	59.2 q
7'	3.03 s	24.0 q	3.00 s	24.0 q

[a] Measured in $CDCl_3$ at 100.62 MHz, δ in ppm. Assignments and multiplicity were based on HMQC, HMBC and DEPT experiments. [b] Values in same column may be interchanged.

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