Two Novel Poly-Oxygen Bipyridine Alkaloids from *Speranskia tuberculata*

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

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

Abstract: Two novel poly-oxygen bipyridine alkaloids, speranculatines A (**1**) and B (**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, speranculatines A and B.

In a previous paper[1] we reported two optically active pyridine-2, 6 (1H, 3H)-dione alkaloids speranskatines A and B from *Speranskia tuberculata* (Bge.) (Euphorbiaceae) We report here the isolation and structural elucidation of two novel poly-oxygen bipyridine alkaloids named speranculatines A (**1**) and B (**2**) from this plant.

The acetone (or methanol) extract of the air-dried whole plants of *S. tuberculata* was subjected to column chromatography on Si gel to afford a fraction, which demonstrated positive Dragendorf's test. The fraction was further purified to give speranskatines A, B and speranculatines A (**1**) and B (**2**).

Speranculatine A **1**, mp 192-194 ^{o}C, $[\alpha]_D^{18}$ + 21.9, was obtained as colorless prisms from EtOAc. The IR spectrum of **1** showed absorption bands for hydroxy (3370, 3211 cm^{-1}), carbonyl (1716 cm^{-1}) and lactam carbonyl (1671, 1655 cm^{-1}) groups. The EIMS and positive ion FABMS spectra exhibited a molecular ion at *m/z* 452 $[M]^+$ and a quasi-molecular ion at *m/z* 453 $[M+H]^+$. The molecular formula $C_{20}H_{24}N_2O_{10}$ was assigned on the basis of HRFABMS *m/z* 453.14849 (calcd for $C_{20}H_{25}N_2O_{10}$ 453.1509) Both the ^{1}H and ^{13}C NMR spectra contained only half the number of signals expected from the molecular formula, indicating that **1** was a symmetrical dimer. The ^{13}C and DEPT spectra of **1** (Table 1) resembled those of speranskatine A, of which the signals were assigned by COLOC experiment and the structure was confirmed by X-ray crystallography to be *rel*-(*R**)-(+)-3-hydroxy-4-methoxy-3-(2-oxopropyl)-1-methylpyri-dine-2, 6 (1*H*,

3*H*)-dione,[1] except that the olefinic methine carbon at δ 94.5 of speranskatine A was replaced by a quaternary carbon at δ 105.1 in the case of **1**, indicating **1** was a dimer of speranskatine A linked at C-5 and C-5'.

Figure 1. ORTEP diagrams of compounds **1** and **2**

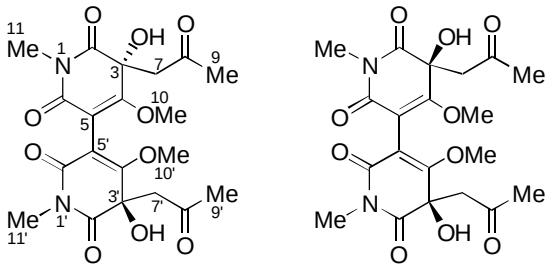

Table 1. NMR Data for Speranculatines A **1** and B **2**[a]

	1		**2**	
No.	H	C	H	C
2	-	172.4 s	-	171.6 s
3	-	71.9 s	-	71.2 s
4	-	167.5 s	-	165.8 s
5	-	105.1 s	-	104.0 s[b]
6	-	166.8 s	-	166.0 s
7a	3.51 d (17.9)	50.4 t	3.57 d (17.8)	49.8 t
7b	3.45 d (17.9)	-	3.37 d (17.8)	-
8	-	207.2 s	-	206.3 s
9	2.16 s	29.7 q	2.13 s	29.8 q
10	3.78 s	60.7 q	3.87 s	60.2 q
11	3.13 s	27.2 q	3.24 s	27.4 q
2'	-	172.4 s	-	171.9 s
3'	-	71.9 s	-	73.1 s
4'	-	167.5 s	-	164.9 s
5'	-	105.1 s	-	102.5 s[b]
6'	-	166.8 s	-	165.9 s
7'a	3.51 d (17.9)	50.4 t	3.25 s	48.4 t
7'b	3.45 d (17.9)	-	3.25 s	-
8'	-	207.2 s	-	206.8 s
9'	2.16 s	29.7 q	2.25 s	31.1 q
10'	3.78 s	60.7 q	3.87 s	60.1 q
11'	3.13 s	27.2 q	3.22 s	27.6 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.

In order to confirm the complete structure and relative stereochemistry, **1** was subjected to a single crystal X-ray diffraction analysis. The ORTEP drawing is shown in **Figure 1**. The two 1-methylpyridine-2, 6 (1*H*, 3*H*)-dione rings possessed an envelope conformation. In each ring, the total of three bond angles from the nitrogen center was 360°, indicating that the nitrogen was in the sp^2 hybrid mode and that the N-methyl group was co-planar with the two lactam carbonyl groups and two olefinc carbons. The dihedral angle between the two ring planes was 88.20° in the solid-state. Consequently, the structure of speranculatine A **1** was assigned as *rel*-(3*R**, 3'*R**)-(+)-3, 3'-dihydroxy-4, 4'-dimethoxy-3, 3'-bis (2-oxopropyl)-1, 1'-dimethyl-5, 5'-bipyridine-2, 2', 6, 6'-(1*H*, 1'*H*, 3*H*, 3'*H*)-tetrone.

Speranculatine B **2**, mp 147-149 °C, $[\alpha]_D^{18}$ + 6.0, colorless prisms (EtOAc), showed almost identical UV, IR, EIMS and FABMS spectral data with those of **1**. The HRFABMS *m/z* 453.1536 (calcd for $C_{20}H_{25}N_2O_{10}$ 453.1509) exhibited the molecular $C_{20}H_{24}N_2O_{10}$, which was identical to that of **1**. The ^1H, ^{13}C NMR and DEPT spectra of **2** (Table 1), the signals of which were assigned by HMQC and HMBC experiments, revealed that **2** was also a dimer of 3-hydroxy-4-methoxy-3-(2-oxopropyl)-1-methylpyridine-2, 6 (1*H*, 3*H*)-dione linked at C-5 and C-5'. The presence of 20 carbon signals in ^{13}C NMR spectrum indicated the asymmetry of **2**, and the only difference between the two monomers of **2** was the configuration of the chiral centers at C-3 and C-3'. An X-ray crystallographic analysis of **2** confirmed the structure and relative stereochemistry assigned from foregoing evidence. The ORTEP drawing is shown in Figure 1. The two rings had similar conformations to those observed in **1**, but the C-3 and C-3' chiral centers showed different configurations. Accordingly, speranculatine B **2** was assigned to be *rel*-(3*S**, 3'*R**)-(+)-3, 3'-dihydroxy-4, 4'-dimethoxy-3, 3'-bis (2-oxopropyl)-1, 1'-dimethyl-5, 5'-bipyridine-2, 2', 6, 6'-(1*H*, 1'*H*, 3*H*, 3'*H*)-tetrone. The optical activity of **2** indicated that the rotation about the central bond connecting the two rings was restricted. Thus, **1** and **2** are diastereomeric atropisomers with relative *S** configurations.

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