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A New *Epi*dithiodioxopiperazine Metabolite Isolated from *Gliocladium roseum* YMF1.00133

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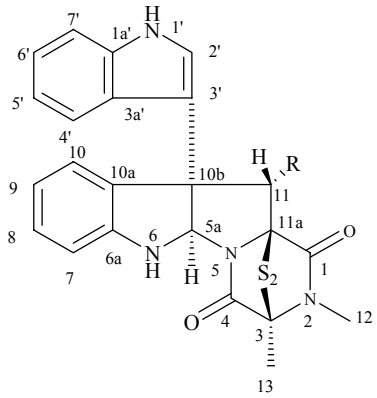
Abstract: Glioclatine, a novel *epi*dithiodioxopiperazine was isolated from wheat solid-substrate fermentation of *Gliocladium roseum* YMF1.00133. Its structure was elucidated by HRESI-MS and NMR spectra.

Keywords: Glioclatine, *epi*dithiodioxopiperazine, *Gliocladium roseum*.

As part of our going search for new nematicidal materials from fresh water fungi, we have found that nematicidal compounds, gliocladine A-E, verticillin A, 11'-deoxyverticillin A, sch52900 and sch52901, belonging to a series of *epi*polythiodioxopiperazines, were produced by a strain of *Gliocladium roseum* YMF1.00133 isolated from the submerged woody substrate collected in freshwater habitat in Yunnan province[1,2]. In continuation of our investigation on *epi*polythiodioxopiperazines from this fungus, here we describe the structural elucidation of one new *epi*dithiodioxopiperazine metabolite, glioclatine **1** (**Figure 1**).

Figure 1 The structures for compounds **1** and **2**



Glioclatine (**1**): R=H
Gliocladine C (**2**): R=OH

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Compound **1** was isolated as a white amorphous powder. Its HRESIMS showed an $[M+H]^+$ ion at *m/z* 449.1136 (calcd. 449.1133), corresponding to the molecular formula $C_{23}H_{20}N_4O_2S_2$ which contained one oxygen atom less than that of gliocladine C **2**[2] (**Figure 1**). The NMR data of **1** were very similar to that of **2**. The most striking differences in the NMR data of **1** compared to that of **2** were the replacement of the hydroxymethine at δ_C 83.5 d with an methylene carobon at δ_C 45.0 t. The difference of chemical shift of the ^{13}C NMR signals for C-10a, C-10b, C-11a, C-3', C-5a of **1** relative to those of **2** also revealed that the methylene carbon was assigned to C-11. In addition, the C-11 oxygenated methine unit (δ_H 6.68 s) in the ^1H NMR spectra of **2** was also replaced by the two additional one-proton singlets at δ_H 3.45 d and 4.45 d with the same coupling constants (*J*=15.0 Hz) of **1**, which were in correspondence with the carbon signal at δ_C 45.0 t in the ^{13}C NMR spectra based on the HMQC experiment. And two hydrogens at δ_H 4.45 d and 3.45 d were assigned to be in α and β configurations, respectively, from the HMBC experiment, in which long--range correlations were observed from δ_H 4.45 to δ_C 133.6 (C-10a), 56.2 (C-10b), 75.1 (C-11a), 166.6 (C-1), 117.4 (C-3') and from δ_H 3.45 to δ_C 84.2 (C-5a), 133.6 (C-10a), 56.2 (C-10b), and 75.1

Table 1 The NMR data of compound **1** and **2** in pyridine-d_5[a] (δ ppm, JHz)

No.	**1**			**2**	
	δ_H	δ_C	HMBC	δ_H	δ_C
1	\	166.6 s	\	\	166.1 s
3	\	74.3 s	\	\	74.5 s
4	\	163.1 s	\	\	163.0 s
5a	6.44 (s)	84.2 d	C-6a, C-10a, C-10b, C-11,C-11, C-3'	5.98 (s)	83.5 d
6a	\	149.9 s		\	148.7 s
7	6.93 (d, 7.7)	110.0 d	C-9, C-10a	6.64 (d, 8.0)	110.5 d
8	7.23 (m)	129.3 d	C-6a, C-10	6.90 (t, 7.6)	129.2 d
9	6.89 (t, 7.4, 7.5)	119.3 d	C-7, C-10a	6.57 (t, 7.4)	119.4 d
10	7.45 (d, 7.6)	124.6 d	C-8, C-6a, C-10b	7.56 (d, 7.5)	124.6 d
10a	\	133.6 s	\	\	133.3 s
10b	\	56.2 s	\	\	62.4 s
11	βH: 3.45 (d, 15.0), αH: 4.45 (d, 15.0)	45.0 t	C-5a, C-10a, C-10b, C-11a C-10a, C-10b, C-11a, C-1, C-3'	6.68 (s)	80.6 d
11a	\	75.1 s	\	\	78.8 s
12	2.99 (s)	27.3 q	C-1, C-3	2.69 (s)	27.1 q
13	1.98 (s)	18.1 q	C-3, C-4	1.72 (s)	17.9 q
1'a	\	138.7 s	\	\	138.3 s
2'	7.42 (br s, 2.5)	123.7 d	C-3', C-3a', C-1a', C-10b	7.49 (s)	123.5 d
3'	\	117.4 s	\	\	115.6 s
3'a	\	126.0 s	\	\	126.9 s
4'	7.94 (d, 8.0)	122.2 d	C-3', C-1a', C-3a	8.25 (d, 7.1)	122.0 d
5'	7.08 (t, 7.9)	120.0 d	C-7', C-3a'	7.09 (m)	119.6 d
6'	7.23 (m)	123.0 d	C-5', C-1a'	7.09 (m)	121.9 d
7'	7.56 (d, 8.0)	112.6 d	C-3a', C-5'	7.42 (d, 7.2)	112.3 d

[a]The NMR data for compound **1** were recorded on Bruker AM-400MHz.

(C-11a). This was also confirmed by the NOE correlations between δ_H 3.45 d and H-10 observed in the NOESY spectrum of **1** which implied that H_β-11 and the C-10a-C-10b bond are also oriented in *trans* to H-5a[3]. Hence it was clear that the oxomethine carbon at C-11 in **2** is deoxygenated to a methylene group in **1**. Thus, the structure of **1** was identified as shown in **Figure 1**, and named glioclatine.

Compound **1**: White amorphous powder; $[\alpha]_D^{17.8}$ +487.2 (*c* 0.39, pyridine); UV (pyridine) λ_{max} (ε) 290.2 (0.1095), 283.0 (0.1084), 205.4 (0.7975) nm; IR (film) ν 3442, 1675, 1611, 1550, 1483, 1468, 745 cm^{-1}; FABMS *m/z* (rel. int): 449$[M+H]^+$(2), 385$[MH-2S]^+$ (5), 328 (4), 232 (18), [bis-indol-3-yl), 176 (4), 159 (3), 97 (7), 80 (100); HRESI-MS *m/z*: 449.1136$[M+H]^+$ (calcd. for $C_{23}H_{21}N_4O_2S_2$ 449.1106); The NMR spectral data see **Table 1**.

Acknowledgments

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