SUPPLEMENTARY MATERIAL

Three new polyketides from the marine sponge-derived fungus *Trichoderma* sp. SCSIO41004

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Abstract

Three new polyketides named trichbenzoisochromen A (**1**), 5,7-dihydroxy-3-methyl -2-(2-oxopropyl)naphthalene-1,4-dione (**2**), and 7-acetyl-1,3,6-trihydroxyanthracene-9,10-dione (**3**) together with six known compounds (**4**–**9**) were isolated from a sponge-derived fungus *Trichoderma* sp. SCSIO41004. The structures of three new polyketides (**1**–**3**) were determined by the extensive spectroscopic analysis, including 1D, 2D-NMR, HRESIMS data. The absolute configuration of compound **1** was confirmed by the specific optical rotation value and CD spectra analyses. Compound **4** exhibited significant inhibitory activity against EV71 with the IC_{50} value of 25.7 μM.

Keywords: *Trichoderma* sp. SCSIO41004, sponge-derived fungus, antiviral

Table S1 ^{1}H and ^{13}C NMR data for compound **1**(500, 125 MHz, TMS, δ ppm)

Position	δ_C [a]	δ_C [b]	δ_H [a] (mult, *J* in Hz)	δ_H [b] (mult, *J* in Hz)
1	70.8	69.2	4.57 (1H, d, 12.0)	4.38 (1H, d, 11.5)
			3.82 (1H, d, 12.0)	3.82 (1H, d, 11.5)
3	157.7	155.8		
4	100.9	100.1	5.45 (1H, s)	5.42 (1H, s)
4a	139.0	138.1		
5	115.8	113.7	5.99 (1H, s)	6.00 (1H, s)
5a	142.8	141.3		
6	108.7	107.4	6.15 (1H, d, 2.0)	6.19 (1H, brs)
7	168.3	166.7		
8	101.5	100.2	6.07 (1H, d, 2.0)	6.06 (1H, brs)
9	167.8	165.7		
9a	106.5	104.9		
10	199.6	198.6		
10a	66.4	64.4		
11	20.0	19.8	1.93 (3H, s)	1.87 (3H, s)
OH-9				12.28 (1H, s)

[a]NMR spectra measured in CD_3OD

[b]NMR spectra measured in DMSO-d_6

Table S2 ^{1}H and ^{13}C NMR data for compounds **2** and **3** (700, 175 MHz, TMS, δ ppm)

2			**3**		
Position	δ_C[a]	δ_H[a] (mult, *J* in Hz)	Position	δ_C[b]	δ_H[b] (mult, *J* in Hz)
1	183.4		1	164.70	
2	140.9		2	108.08	6.62 (d, 2.8)
3	146.0		3	164.99	
4	187.8		4	108.33	7.13 (d, 2.8)
4a	133.7		4a	135.17	
5	164.1		4b	137.18	
6	106.9	6.51 (1H, d, 2.1)	5	115.32	7.62 s
7	164.8		6	163.19	
8	107.8	6.99 (1H, d, 2.1)	7	124.21	
8a	108.6		8	130.17	8.45 s
9	41.0	3.85 (2H, s)	8a	127.75	
10	205.3		8b	109.41	
11	28.7	2.29 (3H, s)	9	184.88	
12	11.2	2.08 (3H, s)	10	181.47	
			11	200.5	
			12	30.25	2.69 (3H, s)
			OH-1		12.89 (1H, s)

[a]NMR spectra measured in CD_3OD

[b]NMR spectra measured in DMSO-d_6

Table S3 The in vitro cytotoxic activities and antiviral activities of compounds **1, 2** and **4**–**7**

Compounds	Three selected tumor cell lines						Two selected virus			
	K562		MCF-7		SGC7901		enterovirus 71		influenza virus H3N2	
	Cell viability % (30μM)	IC_{50}	Cell viability % (30μM)	IC_{50}	Cell viability % (30μM)	IC_{50}	Inhibition rate% (30μM)	IC_{50} (μM)	Inhibition rate% (30μM)	IC_{50}
1	107.93	ND	111.24	ND	104.19	ND	25.18	ND	22.8	ND
2	110.11	ND	116.64	ND	94.74	ND	9.01	ND	3.9	ND
4	89.93	ND	80.56	ND	73.19	ND	63.93	25.7	14.3	ND
5	103.96	ND	114.91	ND	100.46	ND	29.18	ND	0.4	ND
6	83.17	ND	92.51	ND	100.38	ND	20.30	ND	13.4	ND
7	90.92	ND	71.84	ND	97.99	ND	16.84	ND	-1.9	ND

ND: no detected

The physicochemical data of the known compounds 4–9

ZSU-H85 A (**4**): Yellow powder; ^{1}H NMR (500 MHz, CD_3OD): δ_H 8.26 (1H, s, H-5), 7.44 (1H, s, H-8), 7.06 (1H, d, *J* = 2.5 Hz, H-1), 6.48 (1H, d, *J* = 2.5 Hz, H-3), 5.20 (1H, q, *J* = 6.5 Hz, H-15), 1.49 (d, 6.5 Hz, H-16). ^{13}C NMR (125 MHz, CD_3OD): δ_C 187.3 (C-10), 183.8 (C-9), 166.4 (C-2), 166.1 (C-4) , 161.0 (C-7), 140.9 (C-6), 136.6 (C-11), 135.3 (C-13), 126.8 (C-14), 126.4 (C-5),113.5 (C-8), 110.8 (C-12), 109.3 (C-1), 108.9 (C-3), 65.9 (C-15), 23.7 (C-16).

1, 3, 6-Trihydroxy-8-methytanthraquinone (**5**) : Yellow powder; ^{1}H NMR (500 MHz, CD_3OD): δ_H 7.46 (1H, brs, H-5), 7.08 (1H, brs, H-4), 6.94 (1H, brs, H-7), 6.53 (1H, brs, H-2). ^{13}C NMR (125 MHz, CD_3OD): δ_C 189.74 (C-9), 184.35 (C-10), 166.28 (C-3), 165.43 (C-1), 163.19 (C-6), 146.70 (C-8), 138.46 (C-14), 136.03 (C-12), 125.65 (C-7), 124.41 (C-13), 113.32 (C-5), 111.71 (C-11), 109.33 (C-2), 108.22 (C-4), 24.18 (C-15).

2,5-Dimethyl-7-hydroxy-chromone (**6**) : Yellow powder; ^{1}H NMR (500 MHz, CD_3OD): δ_H 6.62 (2H, brs, H-6, 8), 5.99 (1H, s, H-3), 2.70 (3H, s, 5-CH_3), 2.31 (3H, s, 2-CH_3). ^{13}C NMR (125 MHz, CD_3OD): δ_C 182.0 (C-4), 166.6 (C-2), 163.0 (C-7), 161.4 (C-8a), 143.6 (C-5), 118.0 (C-3), 115.6 (C-4a), 111.4 (C-6), 101.6 (C-8), 23.1 (5-CH_3), 19.8 (2-CH_3).

7-Hydroxy-2-(2'S-hydroxypropyl)-5-methylchromone (**7**) : Yellow powder; ^{1}H NMR (500 MHz, CD_3OD): δ_H 6.68 (1H, d, *J* = 2.0 Hz, H-8), 6.66 (1H, *brs*, H-6), 6.08 (1H, *s*, H-3), 4.21 (1H, m, H-10), 2.74 (3H, s, 12-CH_3), 2.74 (1H, dd, *J* = 14.0, 5.0 Hz, H-9), 2.67 (1H, dd, *J* = 14.5, 8.0 Hz, H-9), 1.29 (3H, d, *J* = 6.5 Hz, 11-CH_3). ^{13}C NMR (125 MHz, CD_3OD): δ_C 181.9 (C-4), 167.0 (C-2), 163.0 (C-7), 161.4 (C-8a), 143.5 (C-5), 118.0 (C-6), 115.7 (C-4a), 112.4 (C-3), 101.7 (C-8), 66.3 (C-10), 44.2 (C-9), 23.5 (C-11), 23.1 (C-12).

Cyclonerotriol (**8**) : Yellow powder; ^{1}H NMR (500 MHz, CD_3OD): δ_H 5.40 (1H, t, *J* = 6.5 Hz, H-10), 3.91 (2H, s, H_2-12), 2.09 (2H, m, H-9a, 9b), 1.83 (3H, m, H-5a, 5b, 6), 1.66 (3H, s, 14-CH_3), 1.54-1.64 (3H, m, H-2, 4a, 5b)**,** 1.43-1.54 (3H, m, H-4b, 8a, 8b), 1.13 (3H, s, 13-CH_3), 1.22 (3H, s, 14-CH_3), 1.01 (1H, d, *J* = 6.5 Hz, H-1). ^{13}C NMR (125 MHz, CD_3OD): δ_C 135.7 (C-11), 127.1 (C-10), 82.1 (C-3), 75.5 (C-7), 69.0 (C-12), 55.4 (C-6), 45.5 (C-2), 41.6 (C-8), 41.4 (C-4), 26.1 (C-13), 25.1 (C-14), 24.6 (C-5), 23.3 (C-9), 15.4 (C-1),13.7 (C-15).

Adenosine (**9**): Lightyellow powder; ^{1}H NMR (500 MHz, DMSO-d^{6}): δ_{H} 8.36 (1H, s, H-8), 8.14 (1H, s, H-2), 5.88 (1H, d, J = 6.0 Hz, H-1'), 5.49 (1H, brs, OH-5'), 5.46 (1H, brs, OH-2'), 5.24 (1H, brs, OH-3'), 4.62 (1H, m, H-2'), 4.15 (1H, brs, H-3'), 3.97 (1H, q, J = 3.5 Hz, H-4'), 3.57 (2H, m, H-5'). ^{13}C NMR (125 MHz, DMSO-d^{6}): δ_{C} 156.2 (C-6), 152.4 (C-2), 149.4 (C-4), 140.0 (C-8),119.4 (C-5), 88.0 (C-1'), 86.0 (C-4'), 73.5 (C-2'), 70.7 (C-3'), 61.7 (C-5').

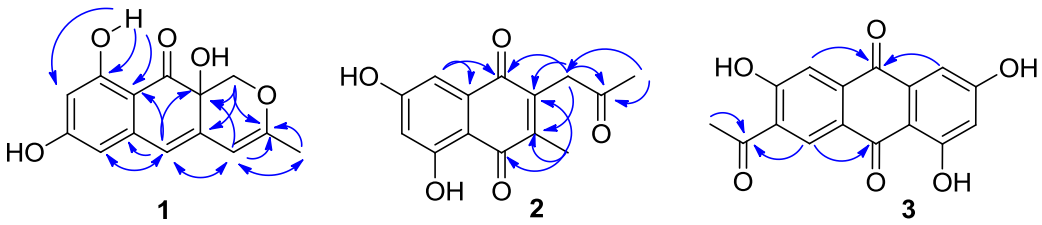

Figure. S1 Key HMBC correlations of compounds **1-3**.

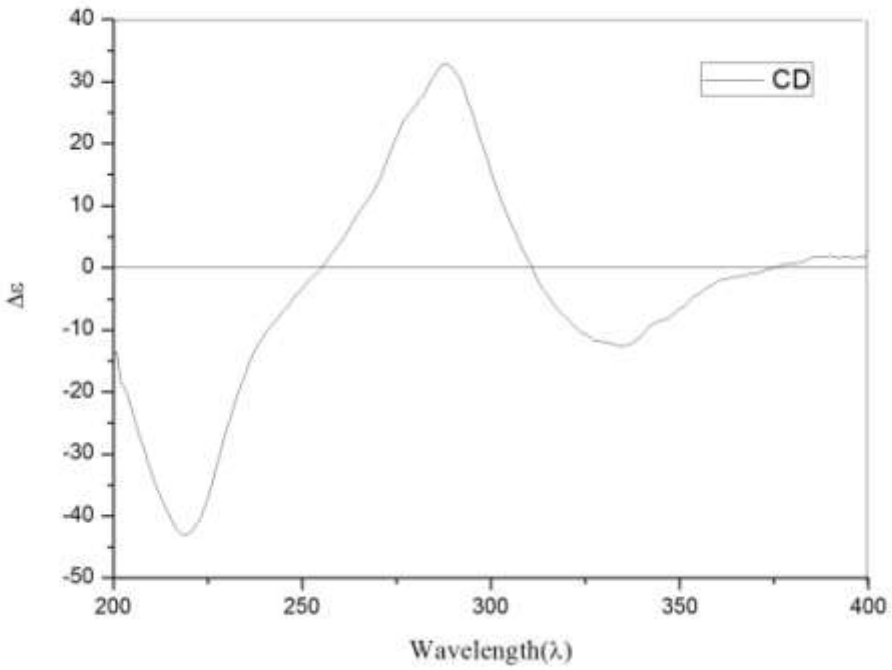

Figure. S2 The experimatal CD curve of compound **1**

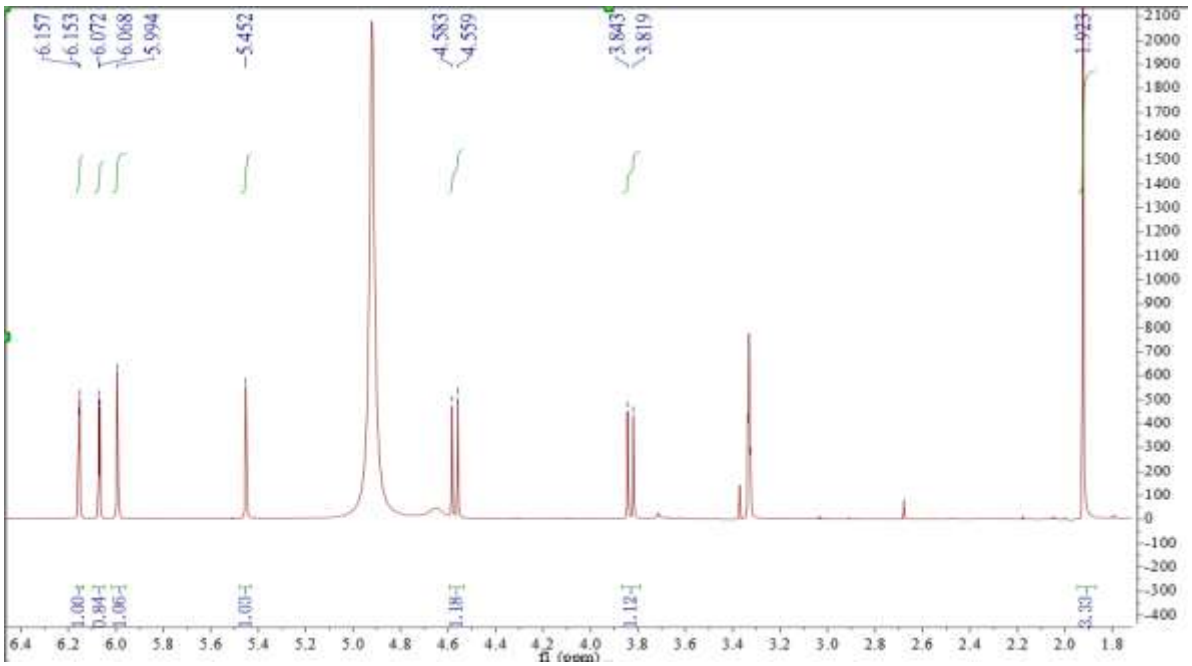

Figure. S3 ^{1}H NMR (500 MHz, CD_3OD) of the new compound **1**

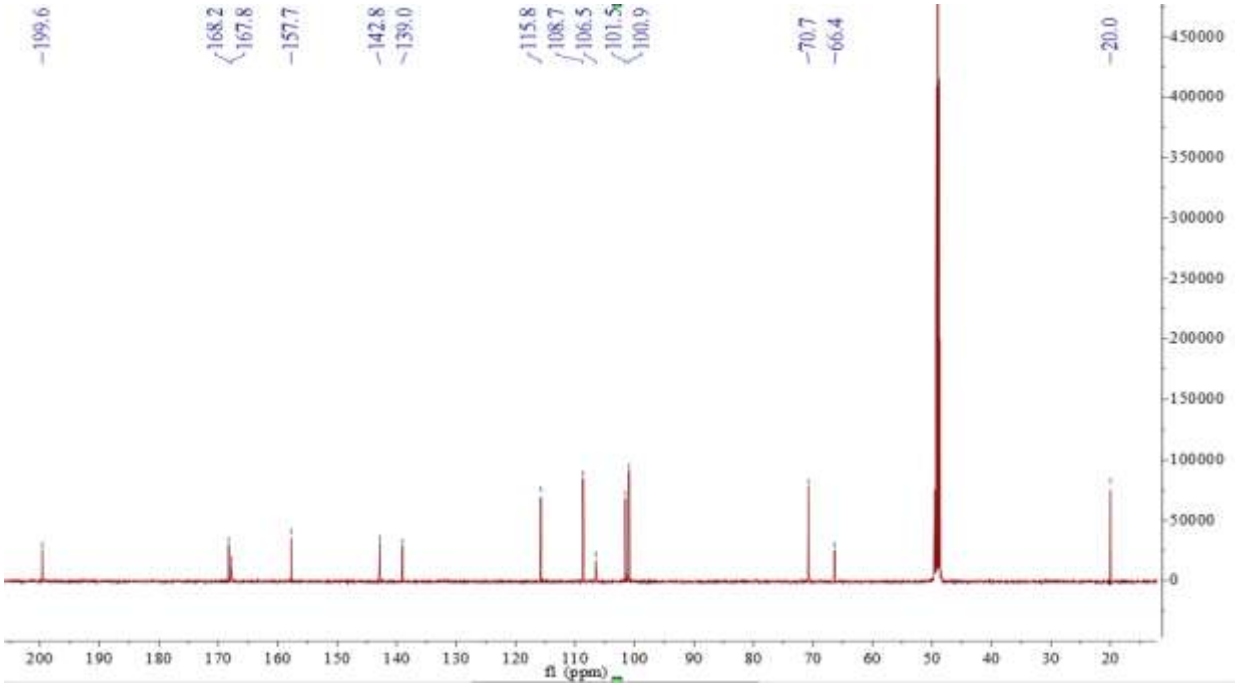

Figure. S4 ^{13}C NMR (125 MHz, CD_3OD) of the new compound **1**

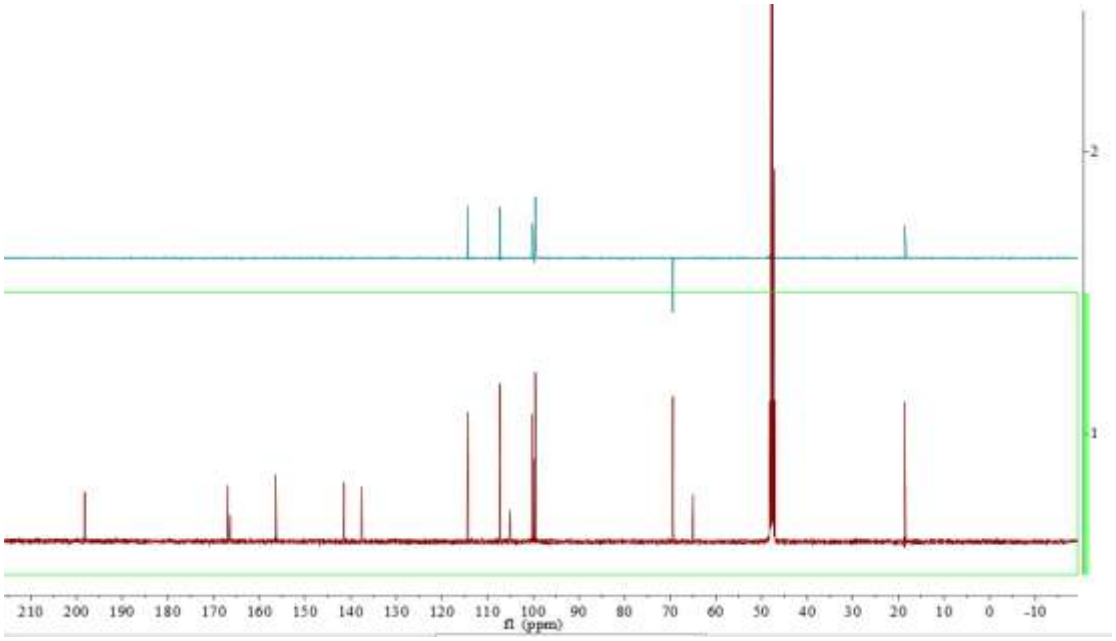

Figure. S5 ^{13}C NMR(DEPT) (125 MHz, CD_3OD) of the new compound **1**

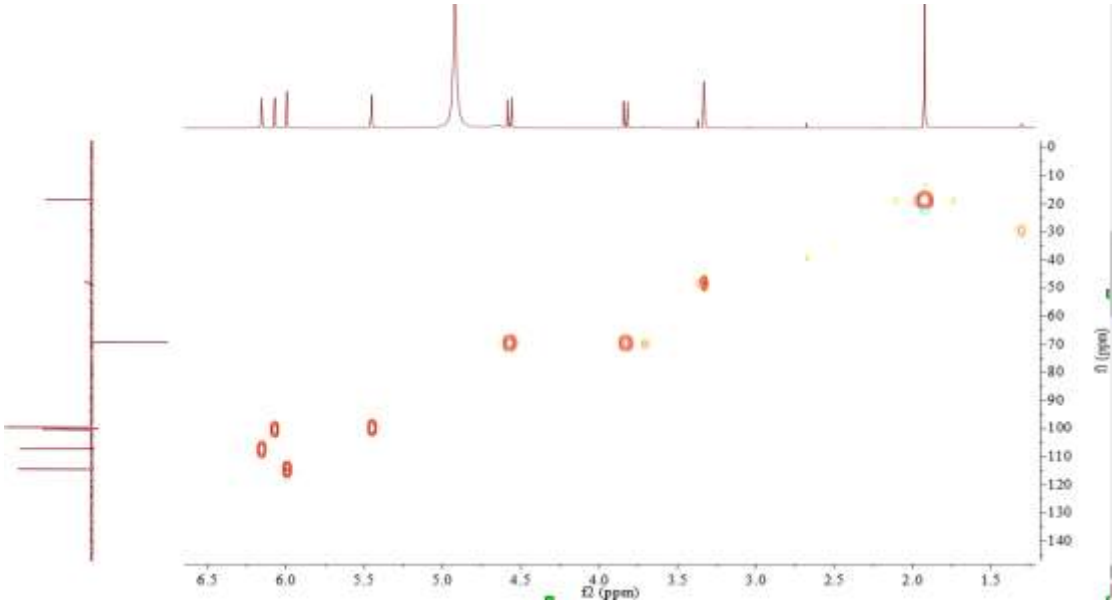

Figure. S6 HMQC (500 MHz, CD_3OD) of the new compound **1**

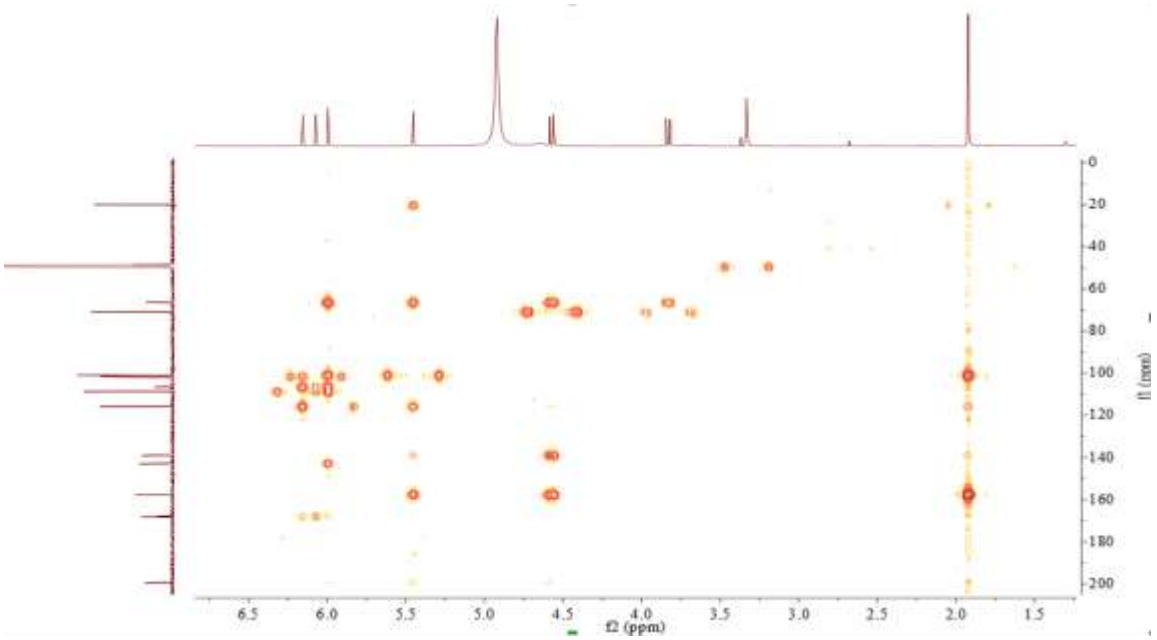

Figure. S7 HMBC (500 MHz, CD_3OD) of the new compound **1**

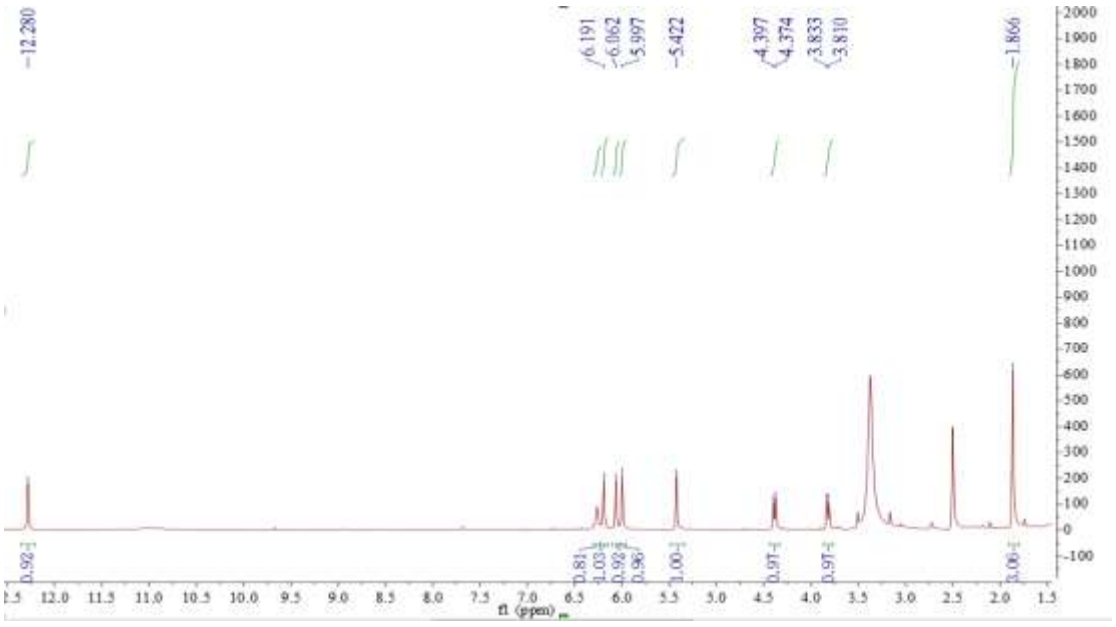

Figure. S8 ^{1}H NMR (500 MHz, DMSO-d_6) of the new compound **1**

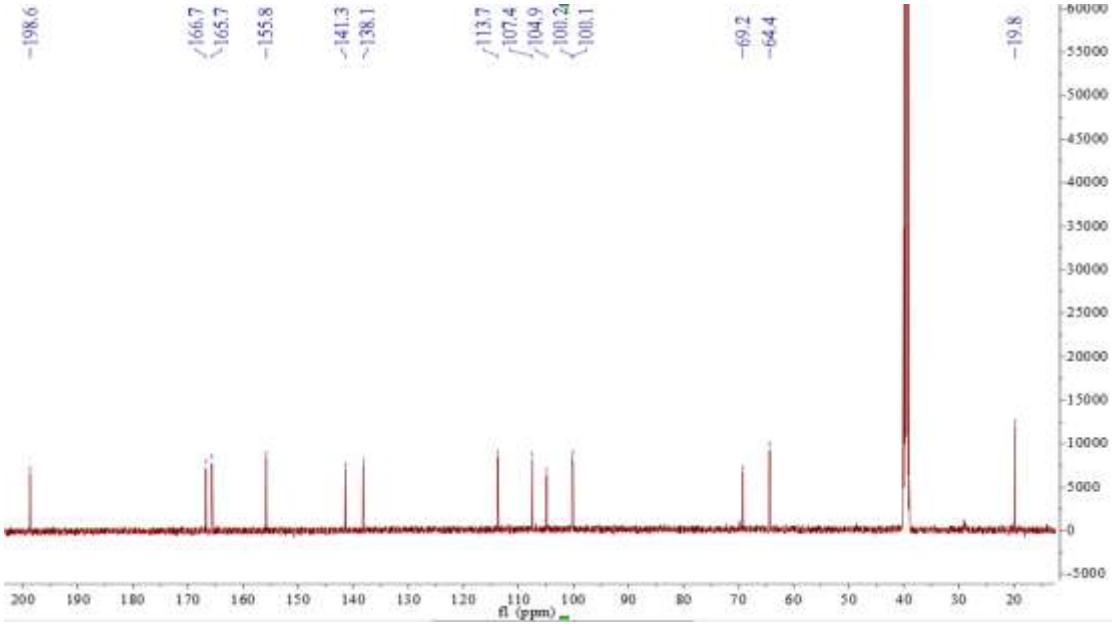

Figure. S9 ^{13}C NMR (125 MHz, DMSO-d_6) of the new compound **1**

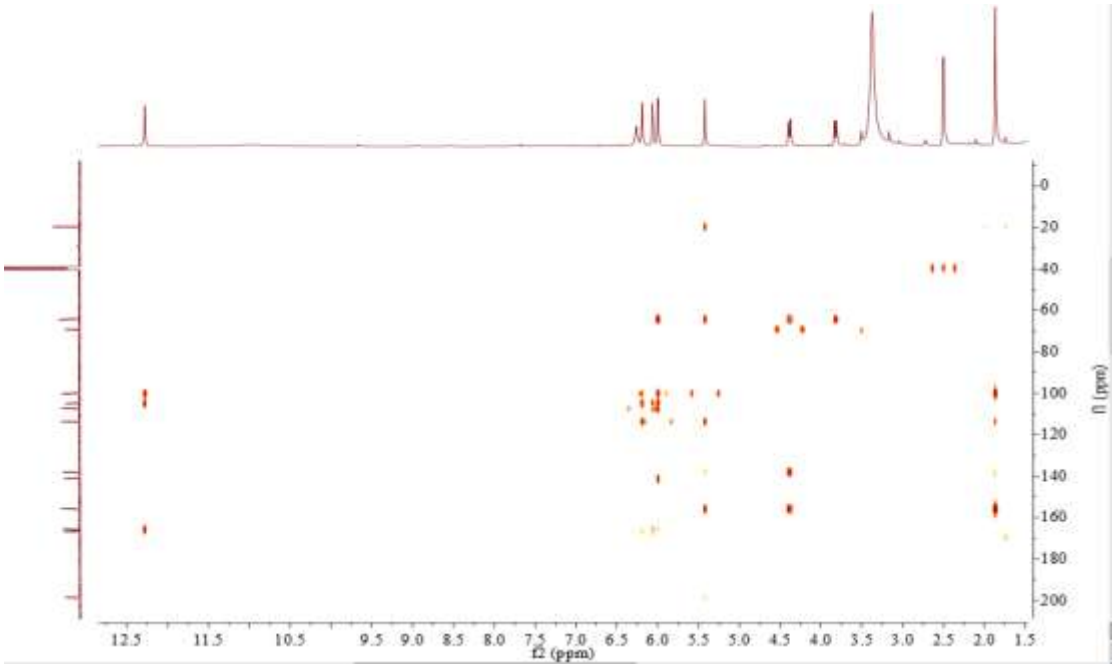

Figure. S10 HMBC (500 MHz, DMSO-d_6) of the new compound **1**

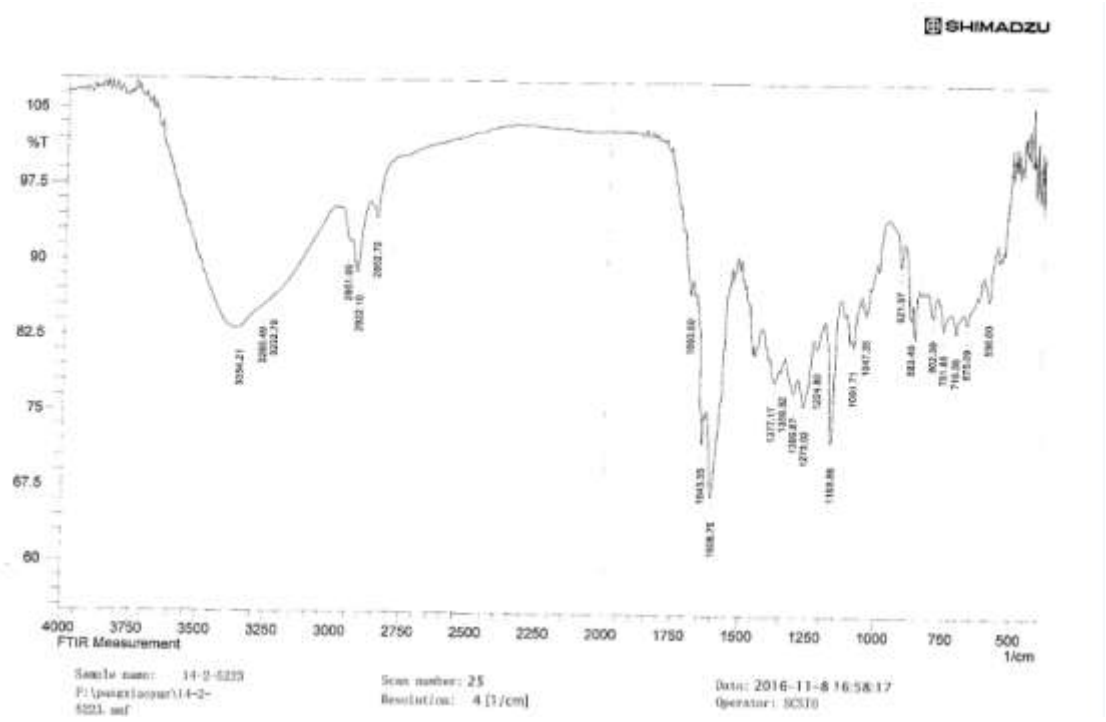

Figure. S11 IR of the new compound **1**

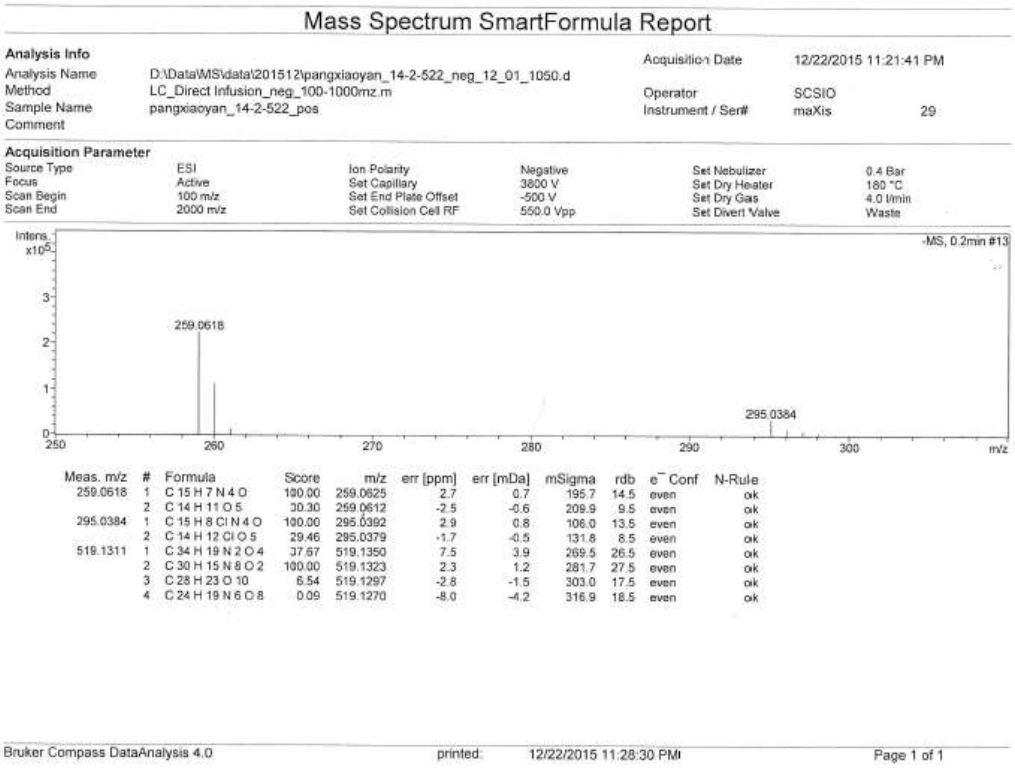

Figure. S12 HR-ESIMS of the new compound **1**

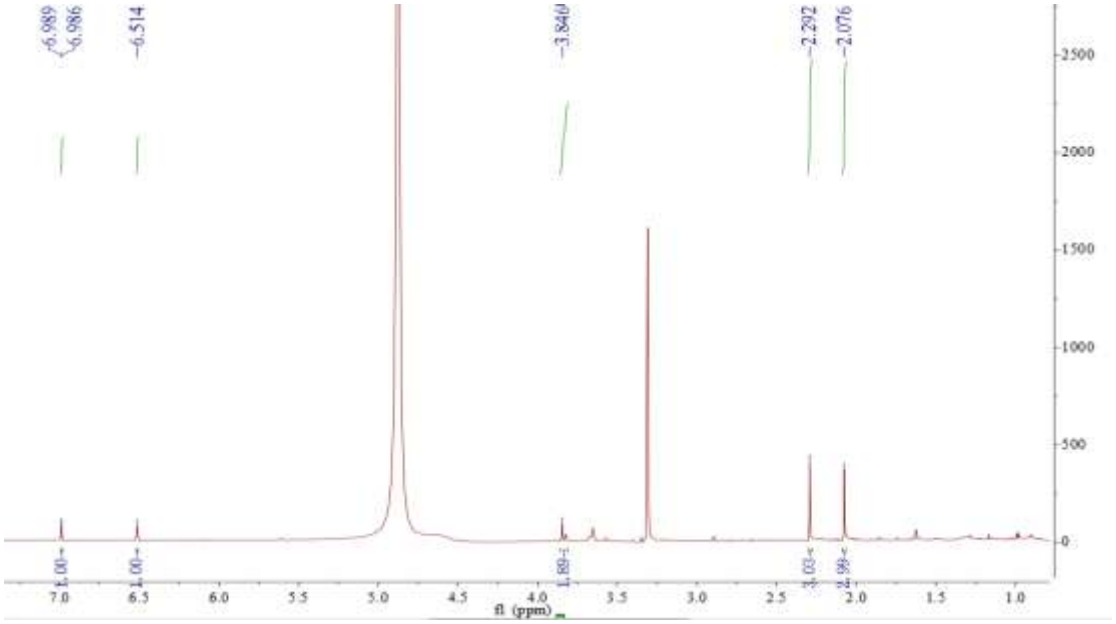

Figure. S13 ^{1}H NMR (700 MHz, CD_3OD) of the new compound **2**

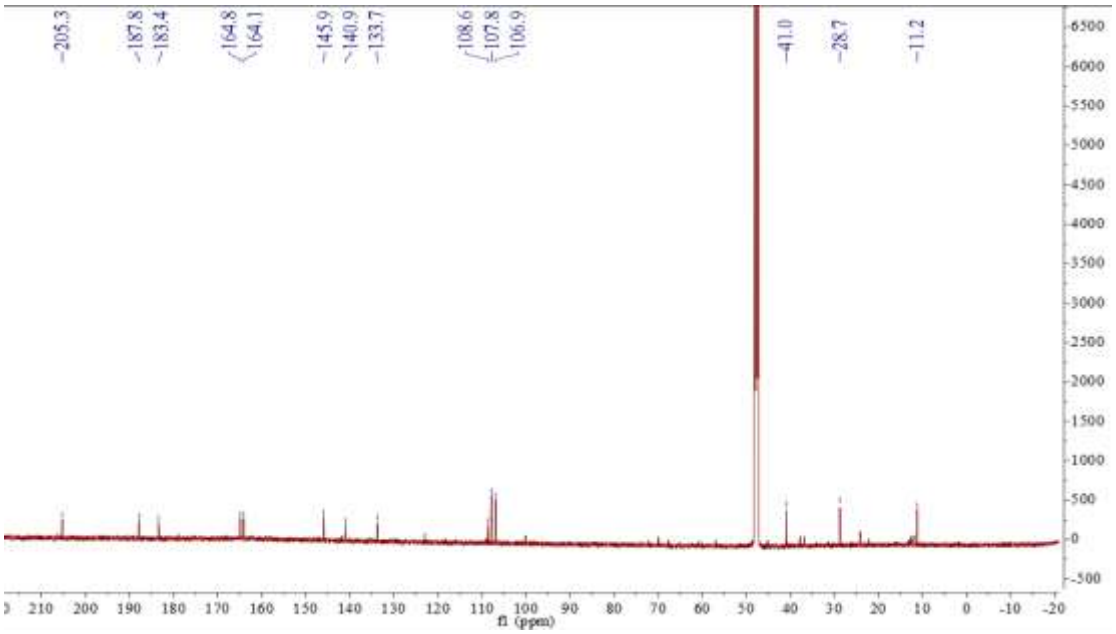

Figure. S14 ^{13}C NMR (175 MHz, CD_3OD) of the new compound **2**

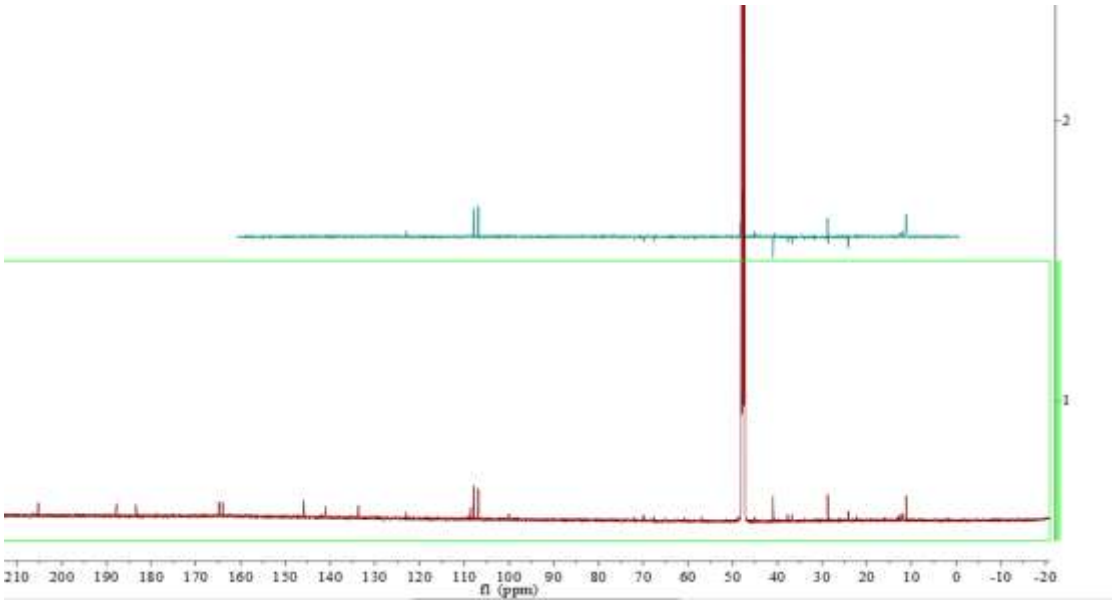

Figure. S15 ^{13}C NMR(DEPT) (175 MHz, CD_3OD) of the new compound **2**

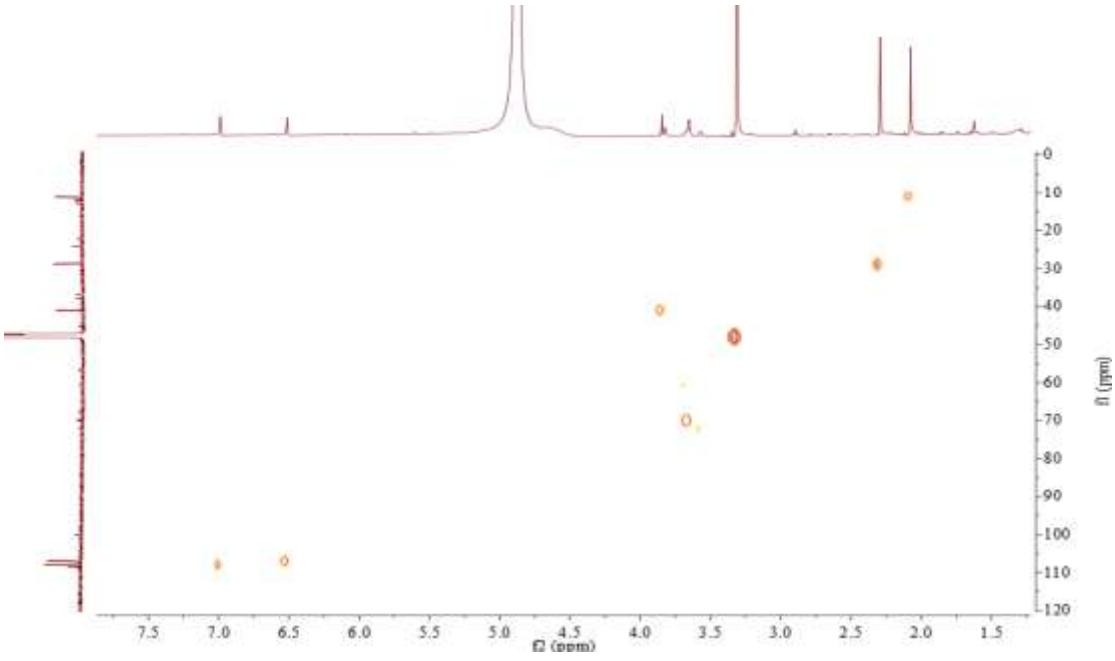

Figure. S16 HMQC (700 MHz, CD_3OD) of the new compound **2**

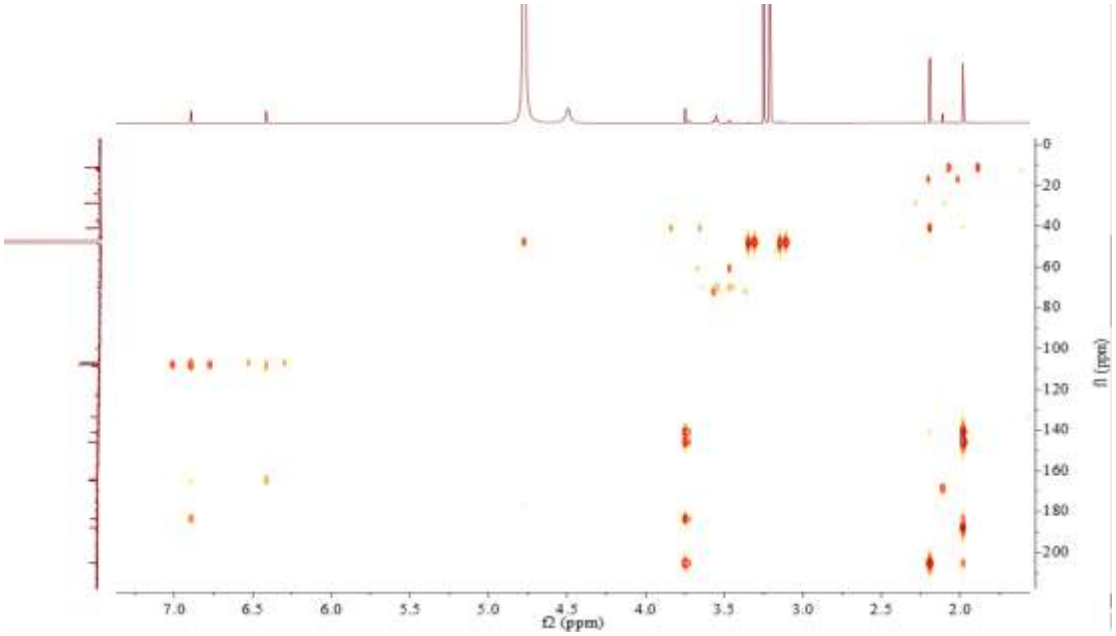

Figure. S17 HMBC (700 MHz, CD_3OD) of the new compound **2**

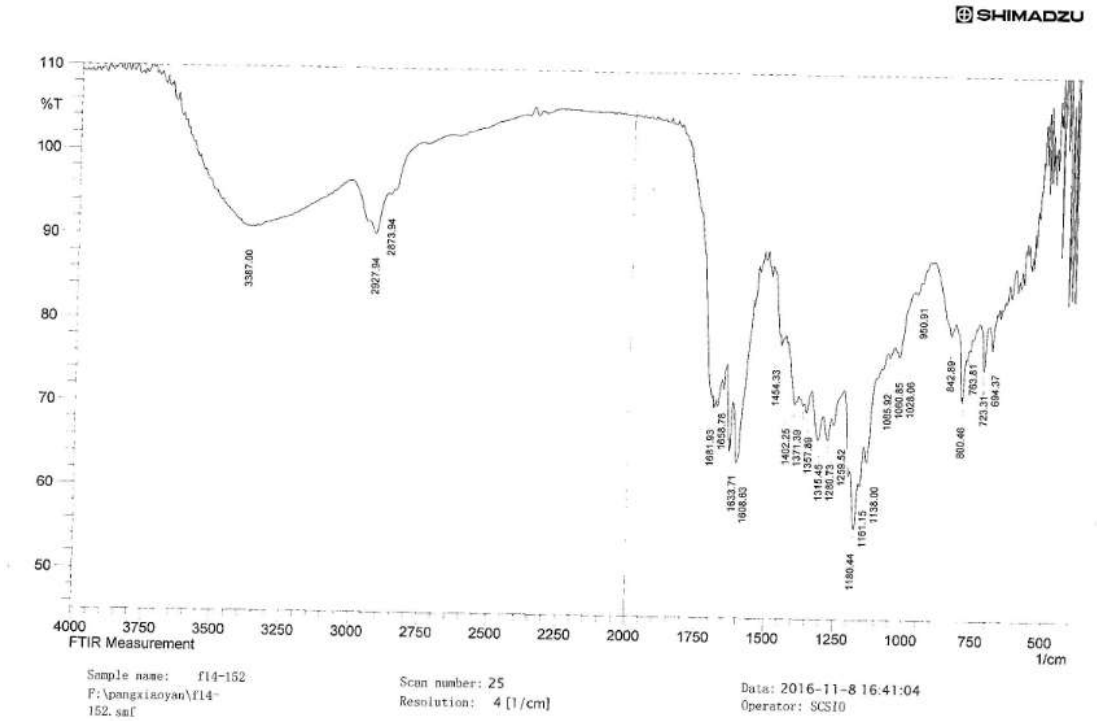

Figure. S18 IR of the new compound **2**

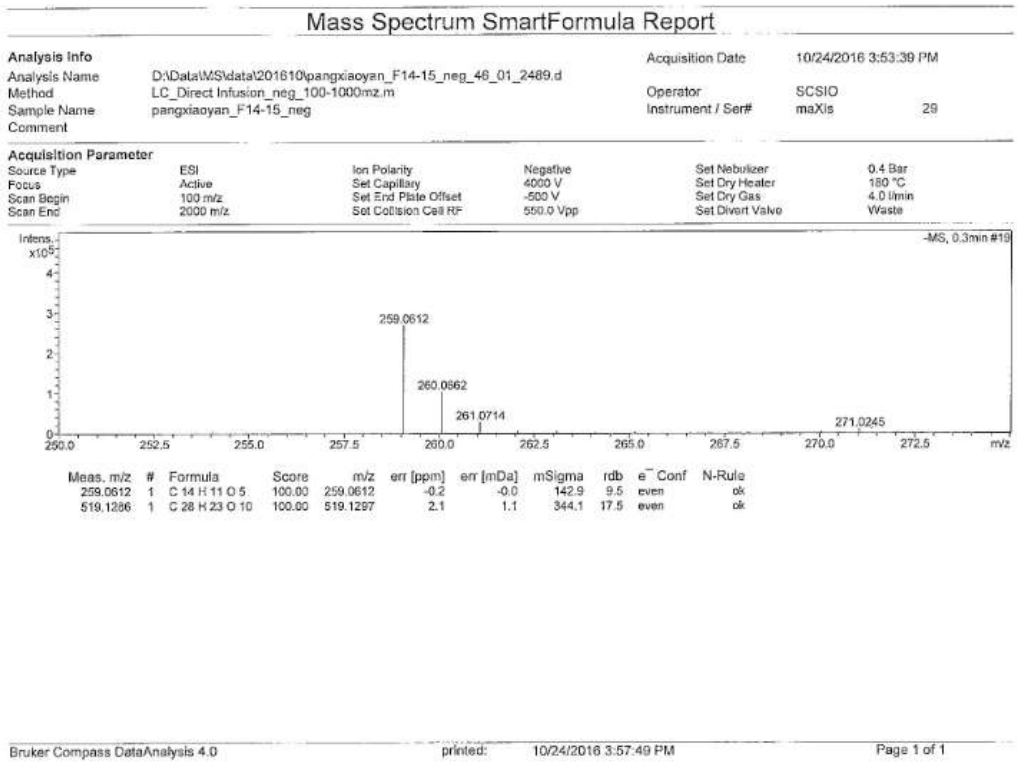

Figure. S19.HR-ESIMS of the new compound **2**

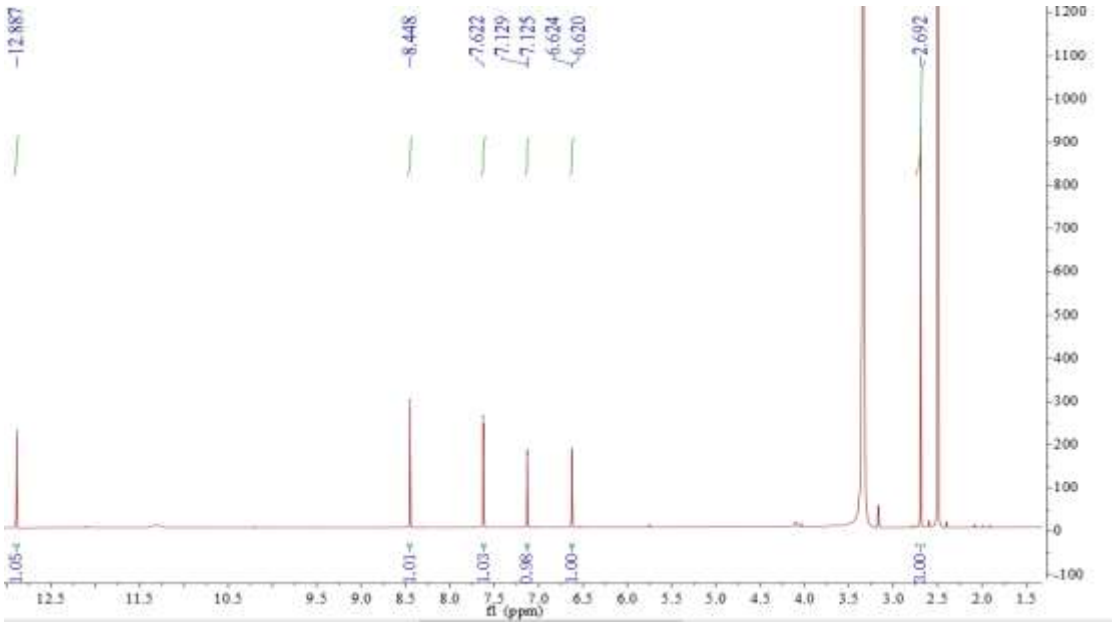

Figure. S20 ^{1}H NMR (700 MHz, DMSO-d_6) of the new compound **3**

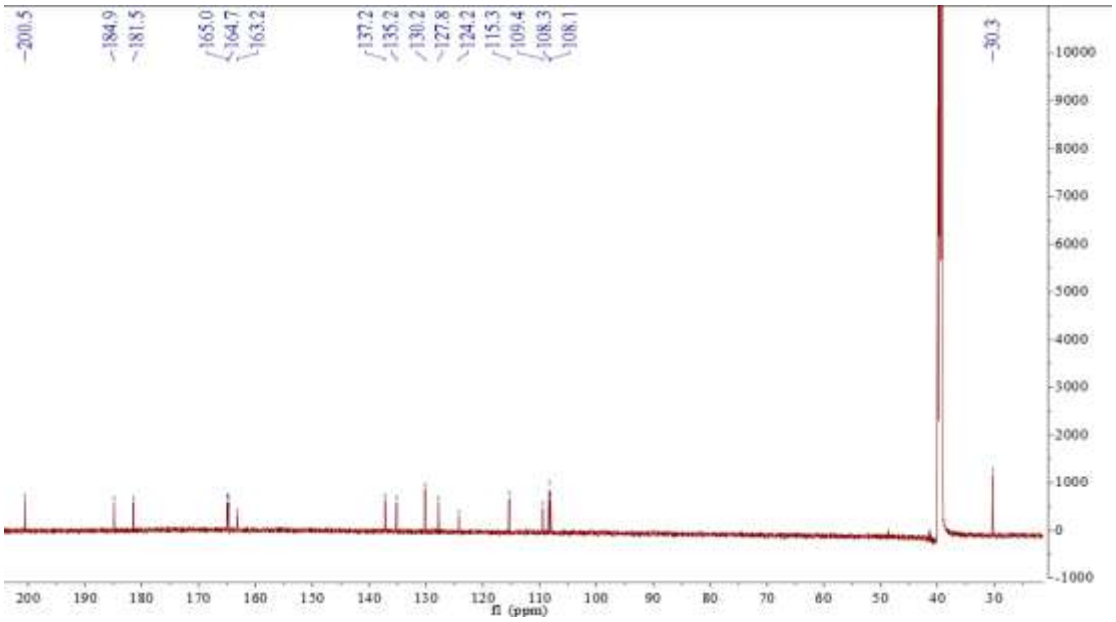

Figure. S21 ^{13}C NMR (175 MHz, DMSO-d_6) of the new compound **3**

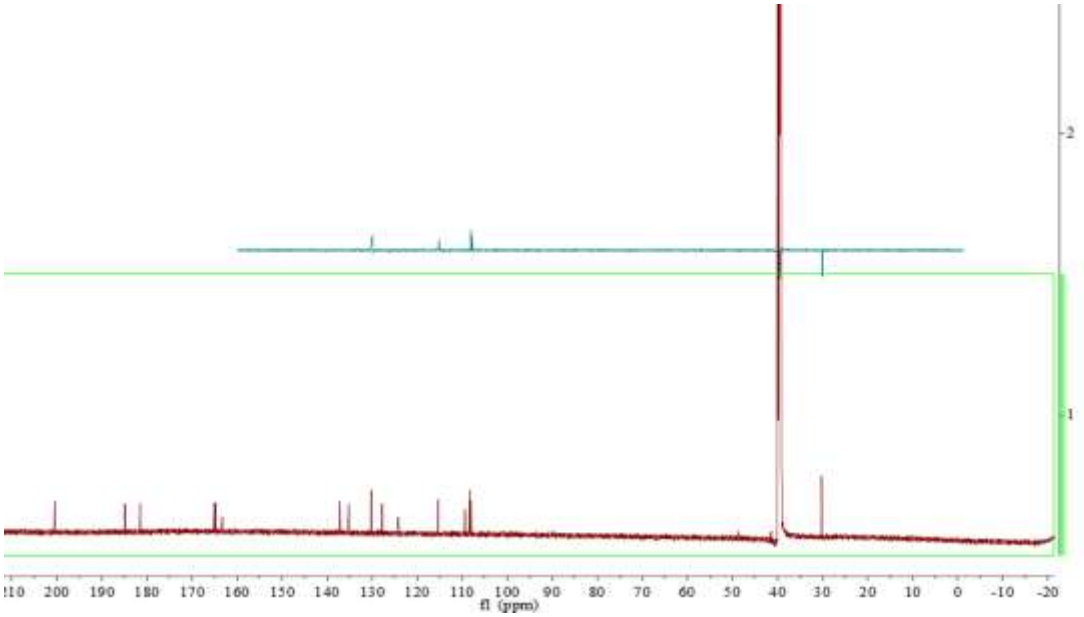

Figure. S22 ^{13}C NMR (DEPT) (175 MHz, DMSO-d_6) of the new compound **3**

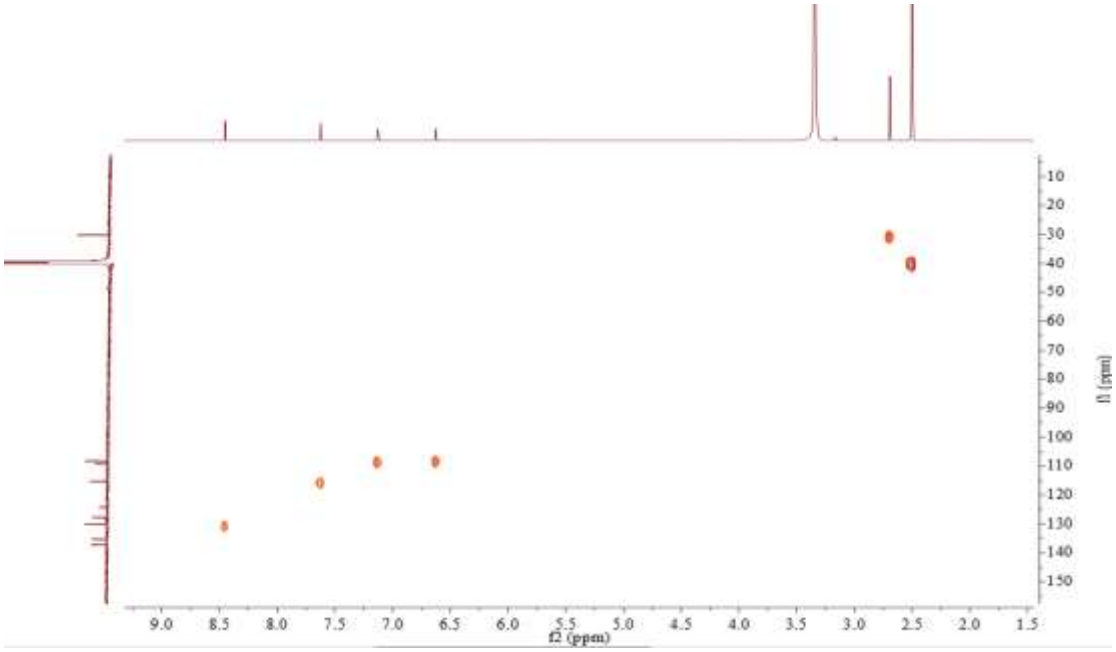

Figure. S23 HMQC (700 MHz, DMSO-d_6) of the new compound **3**

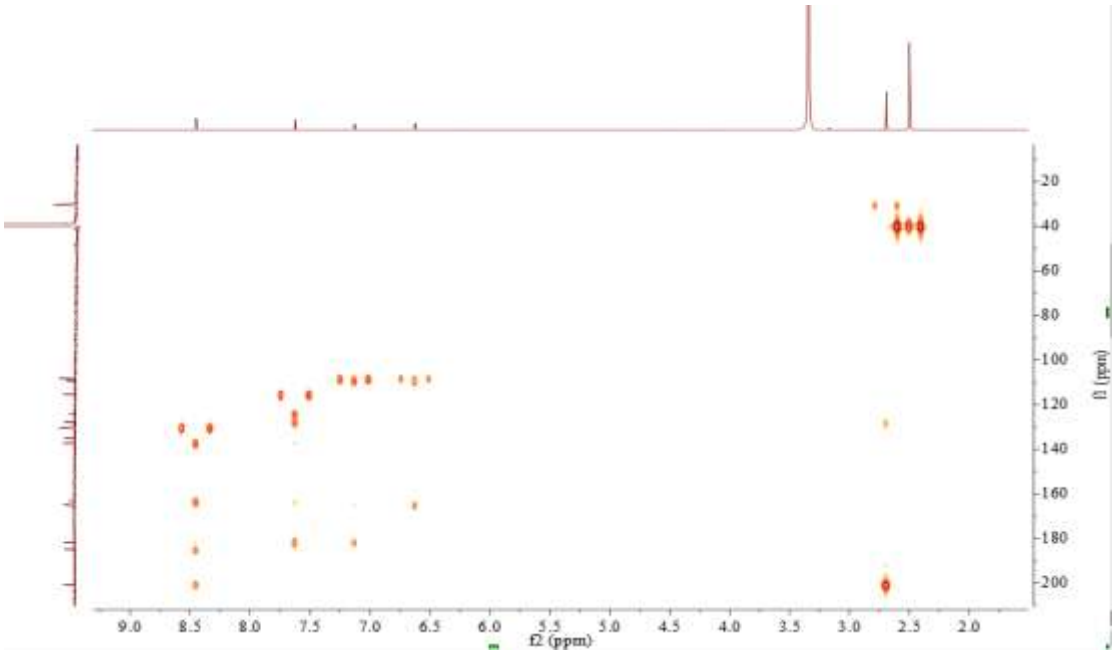

Figure. S24 HMBC (700 MHz, DMSO-d_6) of the new compound **3**

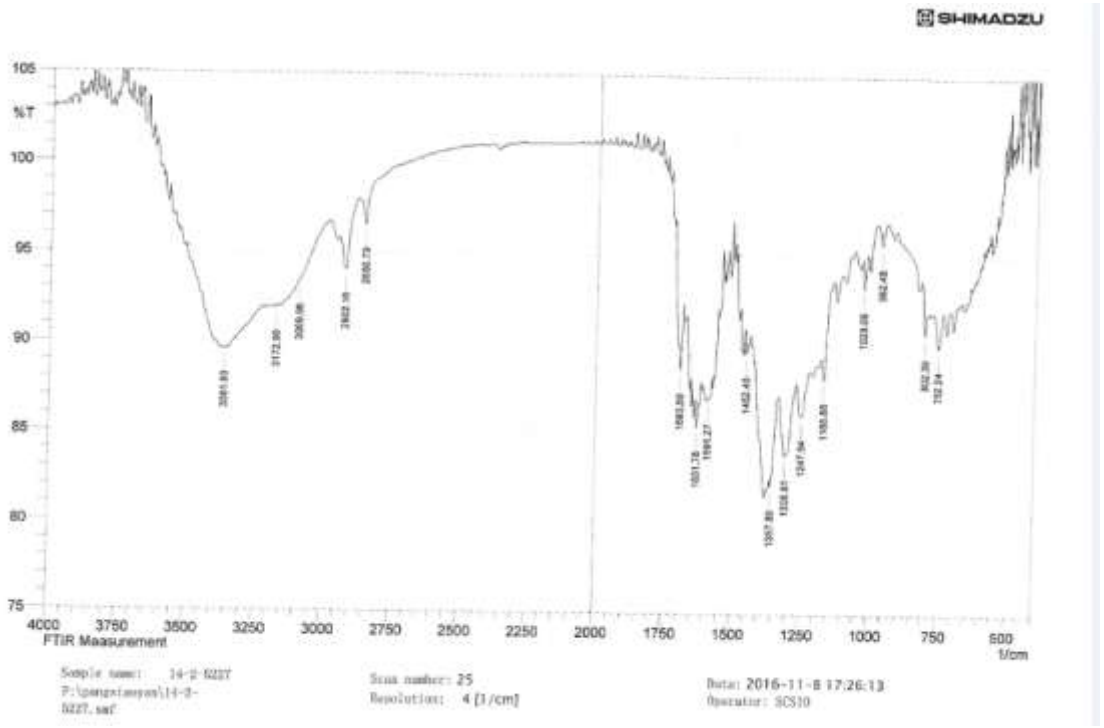

Figure. S25. IR of the new compound **3**

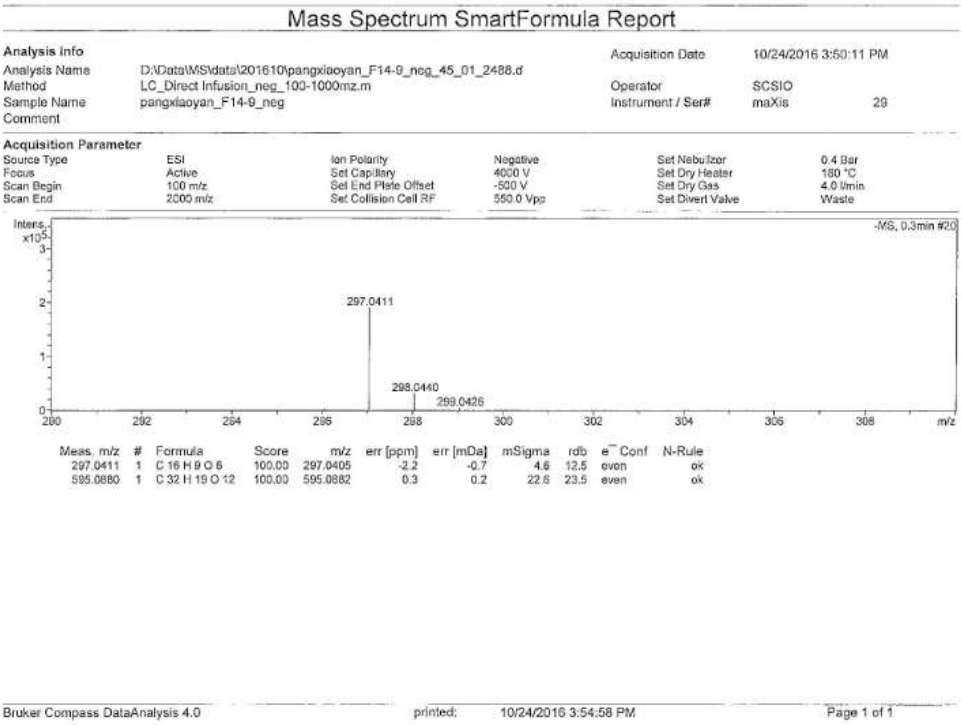

Figure. S26 HR-ESIMS of the new compound **3**

The ITS gene sequence data of *Trichoderma* sp. SCSIO41004

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TCGCAGCCCCGGACCAAGGCGCCCGCCGGAGGACCAACCAAAACTCTTTTTGTATACCCCCTC
GCGGGTTTTTTATAATCTGAGCCTTCTCGGCGCCTCTCGTAGGCGTTTCGAAAATGAATCAAA
ACTTTCAACAACGGATCTCTTGGTTCTGGCATCGATGAAGAACGCAGCGAAATGCGATAAGT
AATGTGAATTGCAGAATTCAGTGAATCATCGAATCTTTGAACGCACATTGCGCCCGCCAGTAT
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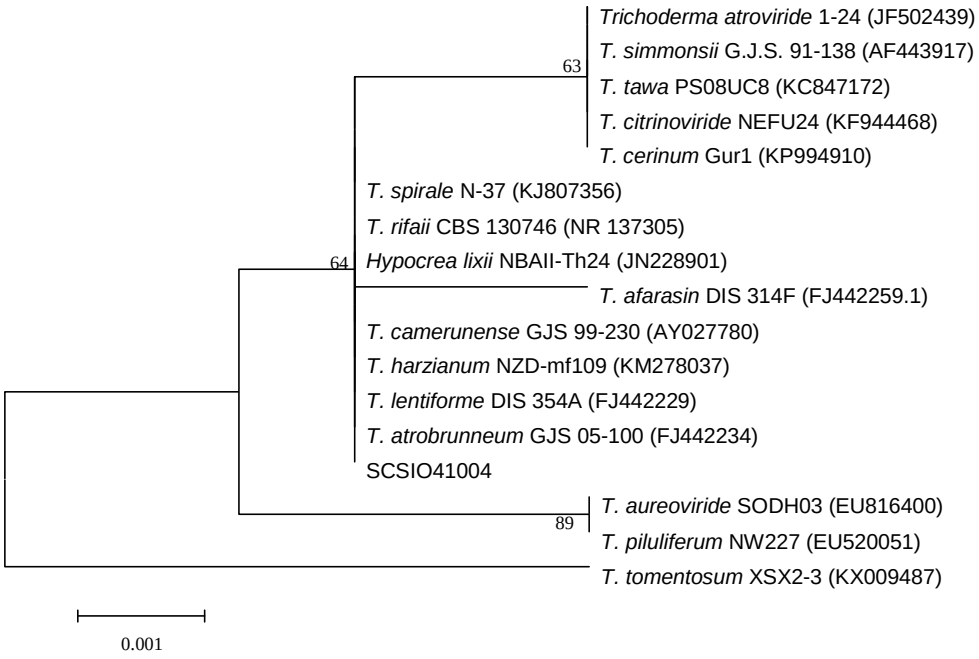

Figure. S27 Neighbor-joining tree based on ITS1-5.8S-ITS2 sequences, showing phylogenetic relationship between strain SCSIO41004 and related *Trichoderma* species. Numbers at nodes indicate bootstrap values from 1000 replicates. GenBank accession numbers are given in *parentheses*. Bar: 0.1% sequence divergence.