



Tremulane sesquiterpenes from cultures of the basidiomycete *Irpex lacteus*

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ABSTRACT

Five new tremulane sesquiterpenes, named irlactins F–J (1–5), were isolated from cultures of the basidiomycete *Irpex lacteus* together with two known analogues (6 and 7). Structures and relative configurations of compounds 1–5 were elucidated by spectroscopic data analysis. Compound 4 exhibited moderate cytotoxicities on HL-60, SMMC-7721, A-549, MCF-7, and SW480 cells with IC₅₀ values of 16.23, 20.40, 25.55, 19.05, and 18.58 μM, respectively.

1. Introduction

The basidiomycete *Irpex lacteus* is a white rot fungus of the family Polyporaceae distributed throughout temperate areas of the world [1]. Our previous investigations of this fungus have reported four novel sesquiterpenoids with a rearranged 6/6 bicyclic system and their biosynthetic precursor, a tremulane sesquiterpene [2]. In a continuing phytochemical study of this fungus, five new tremulane sesquiterpenes, irlactins F–J (1–5), along with two known analogues (6 and 7), were isolated from cultures of the fungus *Irpex lacteus* from its scale-up cultures Fig. 1. The structures were established by extensive spectroscopic data analysis. Meanwhile, all compounds were evaluated for their cytotoxicities against five human cancer cell lines, and for inhibitory effects on isozymes of 11β-hydroxysteroid dehydrogenases which catalyze the interconversion of active cortisol and inactive cortisone.

2. Results and discussion

2.1. Structure elucidation

Compound 1 was obtained as a colorless oil with the molecular formula of C₁₄H₂₂O₂ based on the HRESIMS at *m/z* 245.1519 [M + Na]⁺ (calcd 245.1517 for C₁₄H₂₂O₂Na), indicating four degrees of unsaturation. The IR absorption bands at 3440, 1725 cm⁻¹ indicated the presence of OH and CO groups. The ¹H NMR spectrum exhibited signals due to two tertiary methyls (δ_H 1.16, 0.97), a secondary methyl (δ_H 0.75), and an oxymethylene group (δ_H 4.28). The ¹³C and DEPT NMR spectra (Table 2) displayed 14 carbons, including a ketone carbonyl group (δ_C 205.3), three quaternary carbons (two olefinic carbons

at δ_C 164.8 and 135.8 and a sp³ quaternary carbon resonance at δ_C 37.5), two methines, five methylenes (oxygenated one at δ_C 61.1), and three methyls (δ_C 16.5, 27.1, 28.6). The above-mentioned data exhibited similarities with those of ceriponol B [3], which suggested that compound 1 also possessed the 12-nortremulane skeleton. The major difference was the absence of a hydroxyl group at C-5 in 1. This assignment was confirmed by HMBC correlations from H-5 to C-3, H-7 and H-13 to C-5 (Fig. 2). In the ROESY spectrum, the key correlations of H-7 with H-6 and Me-14 suggested that H-6, H-7, and Me-14 were in the same side and randomly assigned as β-orientations. The structure of compound 1 was elucidated as 12-nor-3-oxo-11-hydroxy-1-tremulene, and named irlactin F.

Compound 2 was assigned the molecular formula C₁₆H₂₄O₃ by HRESIMS (found [M + Na]⁺ 287.1629, calcd for 287.1623). The ¹³C and DEPT NMR spectra (Table 2) of 2 revealed 16 carbon resonances, including three sp² quaternary carbons (δ_C 171.4, 133.9 and 190.3), three methylene carbons (δ_C 42.1, 46.6, and 28.7), four methyl carbons (δ_C 12.3, 26.4, 28.7, and 58.2), five methine carbons (δ_C 44.1, 41.3, 35.8, 84.7 and 102.7), and one quaternary carbon (δ_C 37.5). The above-mentioned data exhibited similarities with those of conocenol D [4]. The key difference was that an oxymethylene at C-2 in conocenol D was oxygenated into an aldehyde, which was confirmed by HMBC correlations of H-3 with C-11, and H-11 with C-2 and C-3. The relative configuration of 2 was determined by the ROESY correlations of H-6 with H-7, H-7 with H-12, Me-14 with H-7, Me-13 with H-5, indicating that H-6, H-7, H-12, and Me-14 were β-oriented, while H-3, H-5, Me-13 and Me-15 were α-oriented. Therefore, compound 2 was established to be irlactin G.

Based on the HRESIMS at *m/z* 315.1568 [M + Na]⁺, compound 3

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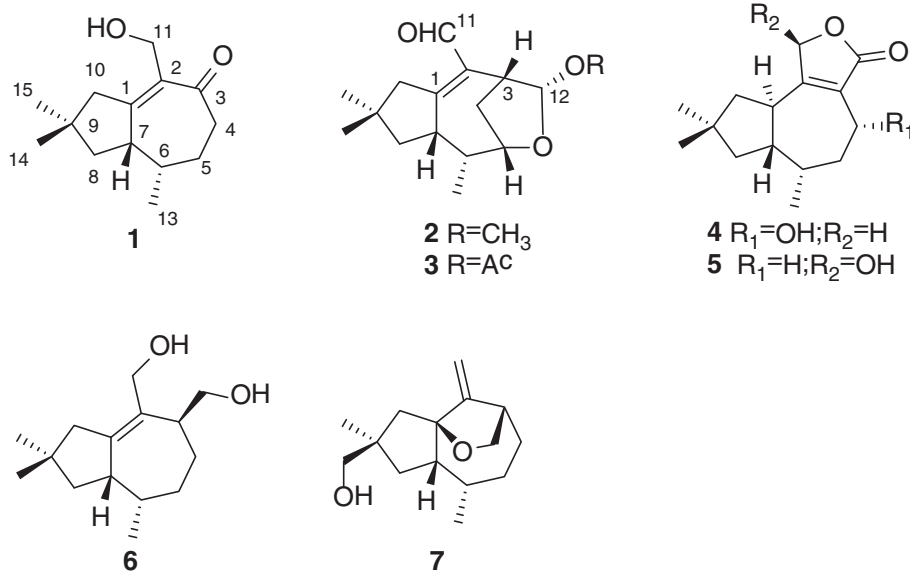
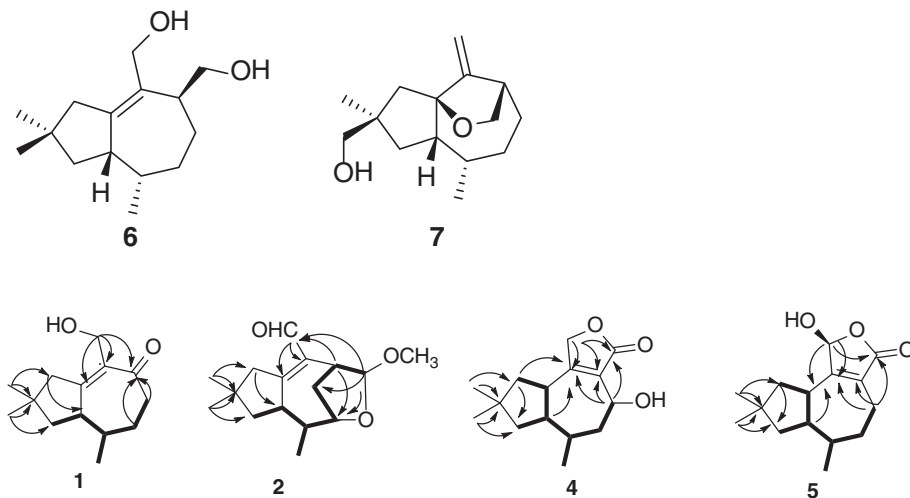
Fig. 1. Structures of 1–7 from the fungus *Irpex lacteus*.

Fig. 2. Selected HMBC (H → C) and COSY (—) correlations of compounds 1, 2, 4, and 5.

Table 1
¹H NMR data of compounds 1–5 (CDCl₃, δ in ppm and *J* in Hz).

Position	1	2	3	4	5
1	–	–	–	2.91 dd (8.6, 9.0)	2.82 m
2	–	–	–	–	–
3	–	3.56 d (7.6)	3.66 d (7.6)	–	–
4a	2.64 m	2.07 m	2.07 m	4.76 m	2.48 m
4b	2.56 m	1.68 d (12.5)	1.74 d (12.8)	–	2.37 m
5a	2.14 m	4.62 dd (6.8, 7.4)	4.69 dd (7.1, 7.3)	2.11 m	1.69 m
5b	1.42 m	–	–	1.65 m	–
6	2.10 m	2.17 m	2.23 m	2.15 m	2.10 m
7	3.26 m	3.51 m	3.57 m	2.23 m	2.11 m
8a	1.68 m	1.51 m	1.51 m	1.49 m	1.45 m
8b	1.61 m	–	–	1.46 m	–
9	–	–	–	–	–
10a	2.53 m	3.00 d (16.8)	3.01 d (16.8)	1.75 m	1.99 m
10b	2.24 d (17.4)	2.25 d (16.8)	2.26 d (16.8)	1.37 m	1.42 m
11	4.28 d (6.0)	9.85 s	9.79 s	4.69 br s	5.89 s
12	–	4.86 s	6.04 s	–	–
13	0.75 d (6.7)	0.76 d (7.1)	0.77 d (7.0)	0.96 d (6.5)	0.94d(7.0)
14	0.97 s	0.94 s	0.95 s	1.04 s	1.05 s
15	1.16 s	1.18 s	1.18 s	1.02 s	1.07 s
16	–	3.36 s	–	–	–
17	–	–	2.05 s	–	–

was suggested to possess the molecular formula of C₁₇H₂₄O₄. Compound **3** exhibited spectroscopic features very similar to those of **2**. Detailed comparison of the NMR data (Tables 1 and 2) indicated that **3** was a acetoxy at C-12 substituting a methoxy group in **2**. The assignment was confirmed by the following HMBC correlations: from the H-12 proton signal at δ_H 6.04 (s) to δ_C 170.5 (s, COCH₃). Thus, compound

Table 2
¹³C NMR data of compounds 1–5.

Position	1	2	3	4	5
1	164.8 s	171.1 s	172.0 s	37.3 d	37.9 d
2	135.8 s	136.4 s	135.4 s	167.0 s	130.9 s
3	205.3 s	39.9 d	39.4 d	128.7 s	162.5 s
4	42.0 t	29.0 t	28.7 t	65.6 d	19.9 t
5	30.6 t	84.6 d	85.6 d	42.7 t	33.4 t
6	32.1 d	35.9 d	35.4 d	29.2 d	32.1 d
7	46.6 d	44.2 d	44.1 d	47.8 d	49.0 d
8	44.5 t	42.3 t	42.0 t	43.0 t	44.8 t
9	37.5 s	37.5 s	37.6 s	37.7 s	36.1 s
10	49.3 t	46.6 t	46.7 t	44.0 t	44.5 t
11	61.1 t	190.1 d	189.9 s	71.1 t	96.6 s
12	–	109.3 d	101.6 d	175.3 s	172.0 s
13	16.5 q	12.4 q	12.5 q	15.4 q	11.9 q
14	27.1 q	26.4 q	26.4 q	29.9 q	31.1 q
15	28.6 q	28.6 q	28.8 q	30.3 q	31.4 q
16	–	58.2 q	170.5 s	–	–
17	–	–	21.3 q	–	–

3 was established as irlectin H, as shown.

Compound **4** was isolated as an oil and shown by HREIMS to have molecular formula C₁₅H₂₂O₃. The IR spectrum of **4** showed absorption bands for a hydroxyl (3425 cm⁻¹) and a carboxyl group (1733 cm⁻¹). The ¹H NMR spectra (Table 1) showed the presence of two tertiary methyls (δ_H 1.04, 1.02), a secondary methyl (δ_H 0.96), a oxymethylene (δ_H 4.69) and a oxymethine (δ_H 4.76). The ¹³C NMR and DEPT experiment resolved 15 carbon resonances comprising one carbonyl group at δ_C 175.3, two double bond carbons (δ_C 128.7, 167.0), one oxygenated methylene at δ_C 71.1, one oxygenated methine at δ_C 65.6, three methyls (δ_C 15.4, 29.9, and 30.3), three methylenes (δ_C 42.7, 43.0, and 44.0), three methines (δ_C 37.3, 29.2, and 47.8), and one quaternary carbon at δ_C 37.7. On the whole, the NMR spectral data were in accordance with those of (+)-(1R, 6S, 7S)-tremul-2-ene-12(11)-lactone

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