Pergamon

Tetrahedron Letters 43 (2002) 163–165

TETRAHEDRON LETTERS

Erectones A and B, two dome-shaped polyprenylated phloroglucinol derivatives, from *Hypericum erectum*

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Received 24 September 2001; revised 26 October 2001; accepted 5 November 2001

Abstract—Examination of the whole plant of the Chinese herbal medicine *Hypericum erectum* yielded two novel metabolites, erectones A and B (**1** and **2**), which were characterized by their 2,2a,3,3a,6,6a,8b,8c-octahydro-1-oxa-cyclopenta[*bc*]acenaphthylen-7-one cores with isoprenyl and geranyl substituents. Their structures were established using extensive spectroscopic methods.

In recent years the antidepressant activity of *Hypericum perforatum* (St. John's wort) has resulted in the widespread interest in the study of the *Hypericum* genus (Guttiferae).[1] *H. erectum*, a traditional Chinese herb used as an anti-haemorrhagic agent and as an astringent and antibiotic agent,[2] has been reported to contain some antiviral prenylated phloroglucinol derivatives[3] and two anti-haemorrhagic compounds, otogirin and otogirone.[4] In continuation of our phytochemical work on the plants of the *Hypericum* genus,[1,5,6] we have examined the petroleum ether extract of the whole plant of *H. erectum* and succeeded in isolating two compounds, named erectones A and B (**1**, **2**) (Fig. 1), possessing the novel tetracyclic octahydro-1-oxa-cyclopenta[*bc*]acenaphthylen-7-one skeleton, probably formed by cycloaddition and complex cyclizations involving prenylated groups. The structures of these rigid tetracyclic compounds were elucidated by extensive spectroscopic studies.

Erectone A (**1**) (3.4 mg, 7.5×10^{-6} %) was isolated as an optically active colourless oil, $[\alpha]_D^{25}$ −6° (*c* 0.23, $CHCl_3$), with the following spectroscopic characteristics: IR (film) ν_{max}: 3432 (OH), 1634 (conjugated carbonyl); UV (MeOH) λ_{max} (log ε): 273 (3.99) nm; HREIMS *m*/*z* 480.3227 (calcd for $C_{31}H_{44}O_4$, 480.3239); NMR data see Table 1.

The molecular formula of (**1**), $C_{31}H_{44}O_4$, indicated the presence of 10 degrees of unsaturation. ^{13}C and ^1H NMR spectroscopic data showed the presence of a β-oxygenated substituted conjugated carbonyl moiety ($C_7/C_8/C_{8a}/O$), one trisubstituted unconjugated olefinic moiety (C_4, C_5), one isoprenyl group (C_9 to C_{13}) attached to a chiral carbon, and one geranyl group (C_{14} to C_{23}). ^{13}C NMR and DEPT spectra of **1** also showed the presence of three other methyl groups (C_{24}, C_{25}, C_{26}), the last two are geminal, two methylene carbons (C_6, C_3), two methine carbons (C_{3a}, C_{2a}) and four

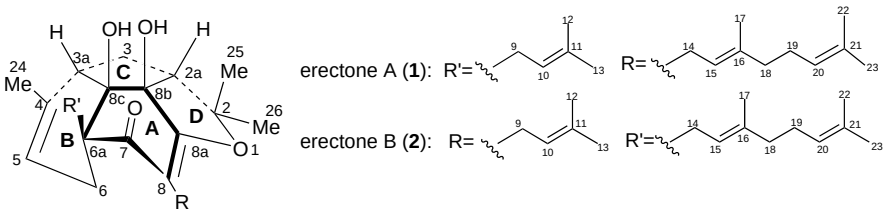

Figure 1. Structures of erectones A and B.

Keywords: erectone; phloroglucinol; *Hypericum erectum*; Guttiferae.
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0040-4039/02/$ - see front matter
PII: S0040-4039(01)02118-9

Table 1. ^{13}C NMR ($CDCl_3$, 100 Hz), ^{1}H NMR ($CDCl_3$, 400 Hz) and HMBC spectral data for compounds **1** and **2**

	Compound **1**			Compound **2**		
Position	δ_H	δ_C	HMBC[a]	δ_H	δ_C	HMBC[a]
2		90.2 s			90.3 s	
2a	2.45 dd, 11.3, 7.4	52.0 d	2, 3, 25, 8a, 8b	2.41 dd, 11.3, 7.4	52.0 d	2, 3, 25, 8a, 8b
3	β: 1.95 m	29.4 t	8b, 8c	β: 1.95 m	29.4 t	8b, 8c
	α: 1.07 m		2, 2a, 3a, 4	α: 1.07 m		2, 2a, 3a, 4
3a	2.56 m	51.6 d	4, 6a, 8c, 24	2.57 m	51.6 d	4, 6a, 8c, 24
4		134.5 s			134.4 s	
5	5.34 m	121.3 d	4, 24	5.35 m	121.4 d	4, 24
6	β: 2.53 m	31.1 t	4, 7, 6a, 8c	β: 2.54 m	31.3 t	4, 7, 8c, 14
	α: 1.98 m			α: 1.95 m		
6a		52.3 s			52.3 s	
7		198.9 s			199.1 s	
8		117.7 s			117.9 s	
8a		170.6 s			170.6 s	
8b		84.6 s			84.7 s	
8c		79.0 s			79.1 s	
9	2.53 m	35.2 t	6, 6a, 11	2.85 m	22.0 t	7, 8, 8a, 11
	2.25 m		6a, 7, 11			
10	5.03 m	122.3 d	9, 12, 13	5.02 m	121.6 d	12, 13
11		136.7 s			131.7 s	
12	1.58 s	25.9 q	10, 13	1.51 s	25.8 q	10, 13
13	1.63 s	18.2 q	10, 12	1.60 s	17.9 q	10, 12
14	2.87 m	21.8 t	7, 8, 8a, 16	2.54 m	35.2 t	6, 6a, 16
				2.24 m		6a, 7, 8c, 16
15	5.01 t, 7.5	121.2 d	17, 18	5.05 m	122.2 d	17, 18
16		135.4 s			140.3 s	
17	1.60 s	16.1 q	15, 18	1.60 s	16.7 q	15, 18
18	1.85 m	39.8 t	15, 17, 20	1.92 m	40.0 t	15, 19, 20
19	1.95 m	26.9 t	16, 18, 21	1.97 m	26.4 t	16, 18, 21
20	4.98 m	124.4 d	18, 22, 23	4.96 m	123.7 d	18, 22, 23
21		131.2 s			132. 1 s	
22	1.60 s	25.6 q	20, 23	1.55 s	25.7 q	20, 23
23	1.50 s	17.0 q	20, 22	1.60 s	17.5 q	20, 22
24	1.45 s	19.9 q	3a, 5	1.45 s	20.0 q	3a, 5
25	1.60 s	27.2 q	2, 2a, 26	1.60 s	27.2 q	2a, 2, 26
26	1.30 s	25.0 q	2, 2a, 25	1.30 s	25.0 q	2a, 2, 25
OH-8b	3.37 br			3.36 br		
OH-8c	3.37 br			3.36 br		

[a] Carbons that correlate with the proton resonance.

quaternary carbons (C_{6a}, C_{8b}, C_{8c}, C_2), among which the last three were oxygenated. Based on its molecular formula and NMR data, compound **1** should be a tetracyclic derivative with two hydroxyl groups. The structure of the tetracyclic core and the positions of attachment of the substituents were determined by tracing the following important connectivities shown in the HMBC spectrum.

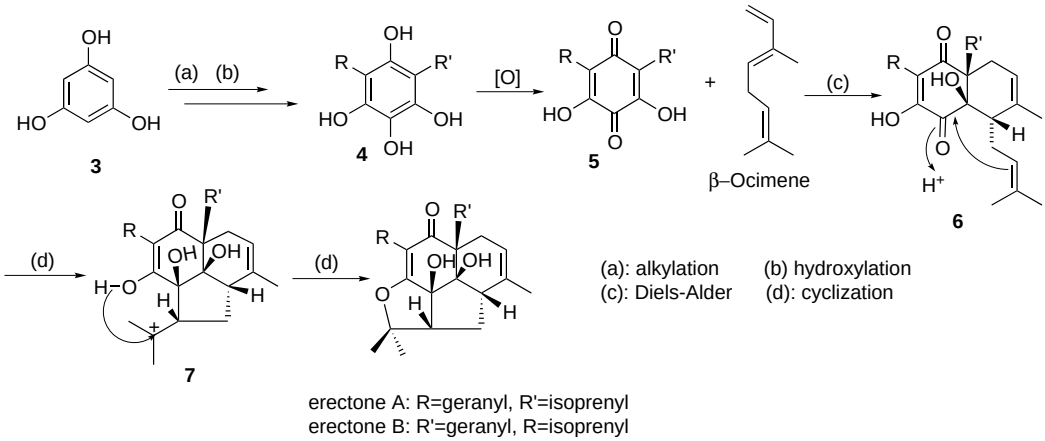
Cross peaks were observed between the methylene protons of C_6 and the quaternary carbon at δ 52.3 (C_{6a}), the oxygenated quaternary carbon at δ 79.0 (C_{8c}), and the olefinic carbon at δ 134.5 (C_4). Moreover, the methine proton of C_{3a} was correlated with C_{6a} and C_4, and the methine olefinic proton of C_5 was correlated with C_4 and the methyl carbon C_{24}. Therefore, carbons 3a, 4, 5, 6, 6a, and 8c formed ring **B**, with a methyl group at C_4.

The five-carbon ring **C** was established from the HMBC cross peaks between: (a) the methylene protons of C_3 and the carbons C_4, C_{2a}, and the two oxygenated quaternary carbons C_{8b} and C_{8c}; (b) the methine proton of C_{3a} and the carbons $C_{6a,}$ C_4 and C_{24}.

The cross peaks between the proton of C_{2a} and the oxygenated olefinic carbon C_{8a} and the two oxygenated carbons C_{8b} and C_2 suggested that ring **D** of the tetracyclic core should be a tetrahydrofuran ring, comprising the connectivities of $O/C_2/C_{2a}/C_{8b}/C_{8a}$.

Based on the observation of the above cross peaks, it was evident that the conjugated carbonyl moiety ($C_7/C_8/C_{8a}$) together with the connectivity of $C_{8a}/C_{8b}/C_{8c}/C_{6a}$ formed the ring **A**, with two hydroxyl groups at C_{8b} and C_{8c}, respectively.

The attachment positions of the substituents were established by the following cross peaks: (a) the protons of the isoprenyl methylene C_9 to C_6 and C_7; (b) the protons of the geranyl methylene C_{14} to C_7 and C_{8a}; (c) the protons of the *gem*-dimethyl group C_{25} and C_{26} to each other and to C_2 and C_{2a}.



Scheme 1. Possible biosynthetic pathway to erectones A and B.

The relative configurations of C_{2a}, C_{3a}, C_{6a}, C_{8b} and C_{8c} were deduced from the 2D NOESY spectrum (Fig. 2) and molecular models. The *cis* configuration of H-3a/H-2a and H-3a/H_2-9 (shown in compound **1** as β) was revealed by the 2D NOESY spectrum. Molecular models disclosed that the formation of the tetracyclic core with the *cis* conformations of H-3a/H-2a and H-3a/H_2-9 required the H-3a/OH-8c/OH-8b/H-2a to be *cis*, thereby giving a rigid dome-like structure.

Erectone B (**2**) (3.1 mg, 6.8×10^{-6} %), an optically active colourless oil, $[\alpha]_D^{25}$ −3.4° (*c* 0.21, $CHCl_3$), has the following spectroscopic characteristics: IR (film) ν_{max}: 3430 (OH), 1632 (conjugated carbonyl); UV (MeOH) λ_{max} (log ε): 273 (3.97) nm; HREIMS *m*/*z* 480.3237 (calcd for $C_{31}H_{44}O_4$, 480.3239); NMR data see Table 1.

As shown in Table 1, ^{13}C and ^{1}H NMR spectroscopic data demonstrated the close similarities between compounds **1** and **2**. The only difference revealed by HMBC is that the isoprenyl group was at C_8 and the geranyl group was at C_{6a} in compound **2**.

Erectones A and B are the first pair of polyprenylated octahydro - 1 - oxa - cyclopenta[*bc*]acenaphthylen - 7 - one derivatives. As complex polyprenylated phloroglucinol derivatives occur in many Guttiferous plants, the erectones are presumably biosynthesized from phloroglucinol **3**. Alkylation and hydroxylation of **3** can yield **4**, which may be oxidized to give the 2,6-dihydroxy-*p*-benzoquinone **5**. In the presence of the natural product, β-ocimene, a Diels–Alder addition reaction may occur to form the *cis*-configured product **6**,[7] which subsequently cyclizes to yield the *cis*-configured intermediate **7** which then cyclizes to the novel tetracyclic erectones A and B (Scheme 1).

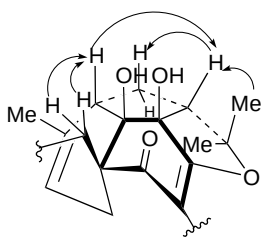


Figure 2. Key NOESY relationship in compounds **1** and **2**.

Antibiotic testing of compounds **1** and **2** was performed against *Staphylococcus aureus*, *Micrococcus lutens*, *Pseudomonas aeruginosa* and *Escherichia coli*. Neither compound showed significant antibiotic activity.

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