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Isolation, structural elucidation, and chemical transformation of interconvertible 8,12-hemiketal germacranolide sesquiterpenoids from *Salvia castanea* Diels f. *tomentosa* Stib.

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ABSTRACT

From the aerial parts of *Salvia castanea* Diels f. *tomentosa* Stib., four new hemiketal germacranolide sesquiterpenoids, castanins C–F (**1**–**4**), were obtained as two pairs of interconvertible forms along with their acetates, **5** and **6**. Their structures were elucidated by spectroscopic methods and X-ray analysis of the uninterconvertible isomeric acetates, **5** and **6**. The computational study explained that the ratios of **1** and **2**, **3** and **4**, and their acetates (**5** and **6**) in the mixtures were 1:1, 1:2, and 1:3, respectively. In addition, the semisynthesis of castanins C (**1**) and D (**2**) was conducted by the photooxidation of castanin B (**8**), the major constituent of this plant. Compounds **5**, **6**, and **8** were also tested for their inhibitory activity toward MCF-7, HeLa, and HepG2 cell lines.

1. Introduction

The genus *Salvia*, belonging to the family Labiatae, is a rich source of diterpenoids, especially abietane and clerodane diterpenoids. Since the first report of a labdane diterpenoid, sclareol, from *Salvia sclarea L.* in 1928,[1] hundreds of diterpenoids including abietanes, clerodanes, icetexanes, labdanes, primranes, and kauranes with different oxygenations and cleavage patterns have been isolated from this genus. However, to the best of our knowledge, only less than twenty sesquiterpenoids were reported, most of which were eudeusmane and germarane sesquiterpenoids.[2–7] Herein, we wish to report our study of sesquiterpenoid constituents from *Salvia castanea* Diels f. *tomentosa* Stib., an herb with castaneous flowers that is distributed in the southwest of China.[8] We have reported two sesquiterpenoids, castanins A and B (**8**),[2] in our previous study of this plant. Continued phytochemical investigation of the aerial parts of this plant led to the isolation of four new hemiketal germacranolide sesquiterpenoids, castanins C–F (**1**–**4**).

The structural determination of these metabolites was complex because they existed as two mixtures of interconvertible isomers, respectively. The two mixtures always behaved like a single compound when examined by TLC (silica gel) and reversed-phase HPLC, respectively. Their ^{1}H and ^{13}C NMR spectra showed doubling of all signals, but the MS spectrum indicated a monomer. Extensive analysis of the NMR spectral data of the mixtures, in combination with the fact that several hemiketal and hemiketal metabolites have been isolated from different sources as interconvertible forms,[9–12] led to the recognition of the mixtures as two interconvertible hemiketal sesquiterpenoids, respectively (Fig. 1). These two pairs of interconvertible isomers, castanins C–F (**1**–**4**), were separated as their uninterconvertible isomeric acetates, **5** and **6**, respectively.

Hemiketal and hemiacetal metabolites, which usually exist as interconverting isomers in different ratio, have been reported from biological sources previously such as enfumafungin,[9] 30-hydroxy-friedelan-3-on-28-al,[13] 3-*epi*-skimmiarepin A,[14] and scutegalin B.[15] It's interesting to note that the ratio of these two pairs of epimeric isomers in our study was nearly 1:1 (for **1** and **2**) and 1:2 (for **3** and **4**), respectively. The computational chemical study about the relative energies of **1**–**4**, and their intermediates at the level of B3LYP/6-31G (d) in acetone using the PCM mode indicated that the ratios of these four compounds in the mixtures were all reasonable. In addition, the computational chemical study also supported the experimental results as the ratio of the acetylation derivatives from the two mixtures, **5** and **6**, was both nearly 1:3.

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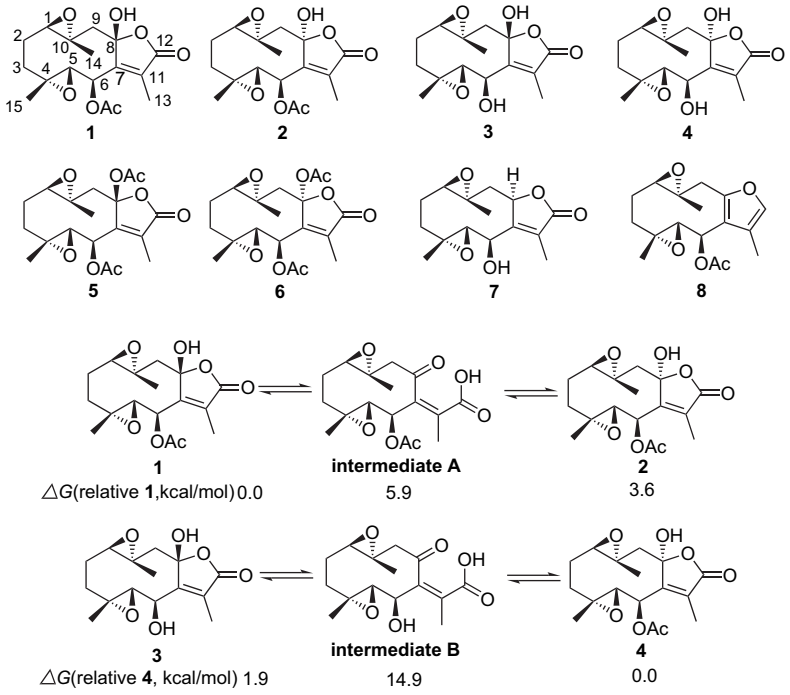

Figure 1. Equilibrium systems and the relative energies of interconvertible isomers and their intermediates at the level of B3LYP/6-31G (d) in acetone using the PCM mode.

Careful comparison of the structural features of **1** and **2** with those of the major constituent of this plant, castanin B (**8**), indicated that the biogenetic pathway of **1** and **2** was started from **8** by an oxidation process. This deduction was confirmed by a photooxidation of **8**, in which the mixture of **1** and **2** was obtained successfully.[16] Reported herein were the isolation, structure elucidation, chemical transformation, and biological activity of these compounds.

2. Results and discussion

The mixture of **1** and **2** was isolated as white powder. Although the mixture presented a single spot on TLC (silica gel) developed in several solvent systems and only one peak in HPLC analysis, its ^{1}H and ^{13}C NMR spectra initially appeared to be unduly complex. Two sets of 17 carbon signals including two acetyl groups, two α,β-unsaturated γ-lactone groups, and four epoxyl groups (Table 1) with the almost equal intensity were observed in the ^{13}C NMR spectrum. In the ESIMS of this mixture, an $[M+Na]^+$ ion peak at *m*/*z* 361 for the molecular formula $C_{17}H_{22}O_7$ was found. These observations indicated this was a 1:1 mixture of two interconverting sesquiterpenoid isomers (Fig. 1). This deduction was rationalized through the separation and identification of **5** and **6**, the acetates of **1** and **2** (Fig. 2). The structures of **5** and **6** were identified by MS and NMR spectroscopic means in combination with the X-ray analysis.

Compound **5** was isolated as colorless needles. Its molecular formula, $C_{19}H_{24}O_8$, was deduced by the positive HR-ESIMS (*m*/*z* 321.1348, $[M-OAc]^+$, calcd 321.1338) together with the NMR data (Tables 1 and 2). The IR spectrum of **5** showed the presence of α,β-unsaturated γ-lactone and acetyl groups at 1784 and 1757 cm^{-1}. The NMR data indicated that **5** contained two AcO groups, an α,β-unsaturated γ-lactone, three Me, three CH_2, and three oxygenated CH groups, as well as three quaternary C-atoms (including a dioxygenated one and two oxygenated ones). Considering the characteristic ^{13}C NMR signals at δ_C 9.4 (q), 18.5 (q), and 19.0 (q) due to C-13, C-14, and C-15, two epoxyl groups at δ_C 65.7 (d, C-1), 57.9 (s, C-10), 63.8 (s, C-4), and 63.2 (d, C-5), together with the α,β-unsaturated γ-lactone group at δ_C 151.9 (s, C-7), 134.2 (s, C-11), and 169.2 (s, C-12), compound **5** was deduced to be a 1,10:4,5-diepoxy glechoman-8,12-olide sesquiterpenoid.[17–20] A side-by-side comparison of NMR data of **5** with those of 1β,10α:4α,5β-diepoxy-6β-hydroxy glechoman-8α,12-olide (**7**) indicated that they are closely related except for the appearance of one more acetoxyl and an additional acetyl groups in **5**.[18] One acetoxyl group of compound **5** was attached to C-6 based on the HMBC correlation from H–6 (δ_H 6.70, s, 1H) to C-5 (δ_C 63.2, d), C-7 (151.9, s), C-8 (106.1, s), C-11 (134.2, s), and the acetyl carbonyl carbon at δ_C 169.2 (s). The other one was located at C-8 on the basis of HMBC correlations between the methyl of acetyl group at δ_H 2.15 (br s, 3H) and C-8 (δ_C 106.1, s). The single crystal X-ray analysis (Fig. 3) confirmed the planar structure of **5** furthermore and established the α-orientation of H-1, H-5, and H-6, together with the β-orientation of Me-14, Me-15,

Table 1
^{13}C NMR spectroscopic data of compounds **1**–**6**[a]

	1	2	3	4	5	6
1	68.1 (d)	69.1 (d)	69.1 (d)	69.7 (d)	67.5 (d)	68.9 (d)
2	25.0 (t)	23.0 (t)	25.7 (t)	23.7 (t)	24.8 (t)	22.7 (t)
3	37.9 (t)	37.6 (t)	38.4 (t)	38.3 (t)	38.1 (t)	37.4 (t)
4	63.8 (s)	60.0 (s)	64.3 (s)	61.4 (s)	63.8 (s)	59.7 (s)
5	62.9 (d)	59.7 (d)	65.7 (d)	62.5 (d)	63.2 (d)	59.4 (d)
6	67.4 (d)	66.8 (d)	67.5 (d)	66.5 (d)	66.8 (d)	65.9 (d)
7	153.0 (s)	152.8 (s)	158.2 (s)	158.2 (s)	151.9 (s)	150.5 (s)
8	106.5 (s)	107.0 (s)	108.9 (s)	106.5 (s)	106.1 (s)	106.5 (s)
9	50.2 (t)	46.0 (t)	51.0 (t)	46.7 (t)	49.4 (t)	44.3 (t)
10	58.7 (s)	56.4 (s)	59.4 (s)	56.9 (s)	57.9 (s)	55.7 (s)
11	131.5 (s)	129.0 (s)	130.5 (s)	130.0 (s)	134.2 (s)	132.3 (s)
12	168.9 (s)	170.2 (s)	170.6 (s)	172.0 (s)	169.2 (s)	170.2 (s)
13	9.1 (q)	11.0 (q)	9.4 (q)	11.2 (q)	9.4 (q)	11.0 (q)
14	18.0 (q)	17.0 (q)	17.4 (q)	19.4 (q)	18.5 (q)	16.9 (q)
15	19.4 (q)	16.3 (q)	18.8 (q)	16.7 (q)	19.0 (q)	16.1 (q)
OAc-6	168.8 (s)	168.0 (s)			169.2 (s)	168.2 (s)
	20.3 (q)	20.6 (q)			20.6 (q)	19.9 (q)
OAc-8					168.7 (s)	168.4 (s)
					22.0 (q)	21.4 (q)

[a] Data were recorded at 100 MHz on a Bruker AM-400 MHz spectrometer in acetone-d_6, chemical shift values δ are in parts per million.

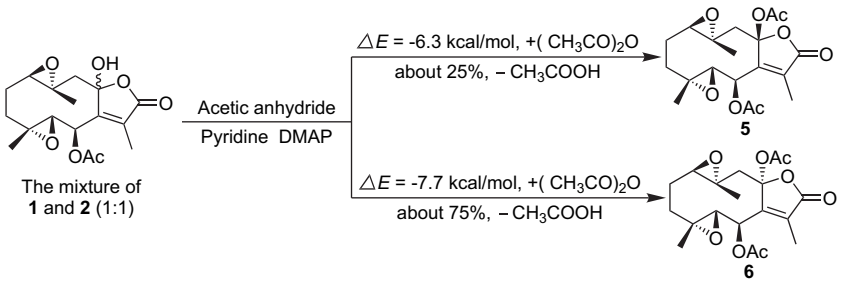

Figure 2. The acetylation of **1** and **2** together with the computational reaction energies of forming **5** and **6**.

Table 2
^{1}H NMR spectroscopic data of **1**–**6**[a]

	1	2	3	4	5	6
1	2.94 (m)	2.94 (m)	2.95 (m)	2.95 (m)	2.95 (dd, 2.3, 11.1)	3.00 (d, 10.8)
2a	1.49 (m)	1.49 (m)	1.47 (m)	1.47 (m)	1.59 (m)	1.53 (m)
2b	2.08 (m)	1.95 (m)	2.03 (m)	2.03 (m)	2.05 (m)	1.96 (m)
3a	1.26 (m)	1.29 (m)	1.32 (m)	1.32 (m)	1.28 (m)	1.36 (m)
3b	2.12 (m)	2.12 (m)	2.20 (m)	2.20 (m)	2.11 (m)	2.22 (m)
5	3.03 (br s)	3.47 (d, 5.8)	3.93 (br s)	3.52 (d, 5.3)	3.12 (br s)	3.60 (d, 5.8)
6	6.26 (br s)	6.22 (d, 5.8)	5.52 (br s)	5.52 (d, 5.3)	6.70 (br s)	6.17 (d, 5.8)
9a	1.52 (m)	1.97 (m)	1.47 (m)	2.02 (m)	1.59 (d, 14.9)	2.22 (d, 15.1)
9b	2.94 (m)	2.94 (m)	3.00 (m)	3.00 (m)	3.15 (d, 14.9)	3.27 (d, 15.1)
13	1.88 (br s)	1.99 (br s)	1.84 (br s)	2.03 (br s)	2.00 (br s)	2.13 (br s)
14	1.56 (br s)	1.04 (br s)	1.66 (br s)	1.07 (br s)	1.62 (br s)	1.13 (br s)
15	1.59 (br s)	1.34 (br s)	1.61 (br s)	1.43 (br s)	1.55 (br s)	1.44 (br s)
OAc-6	2.05 (br s)	2.11 (br s)			2.09 (br s)	2.09 (br s)
OAc-8					2.15 (br s)	2.17 (br s)

[a] Data were recorded at 400 MHz on a Bruker AM-400 MHz spectrometer in acetone-d_6, chemical shift values δ are in parts per million, and the coupling constant J is in hertz (in parentheses).

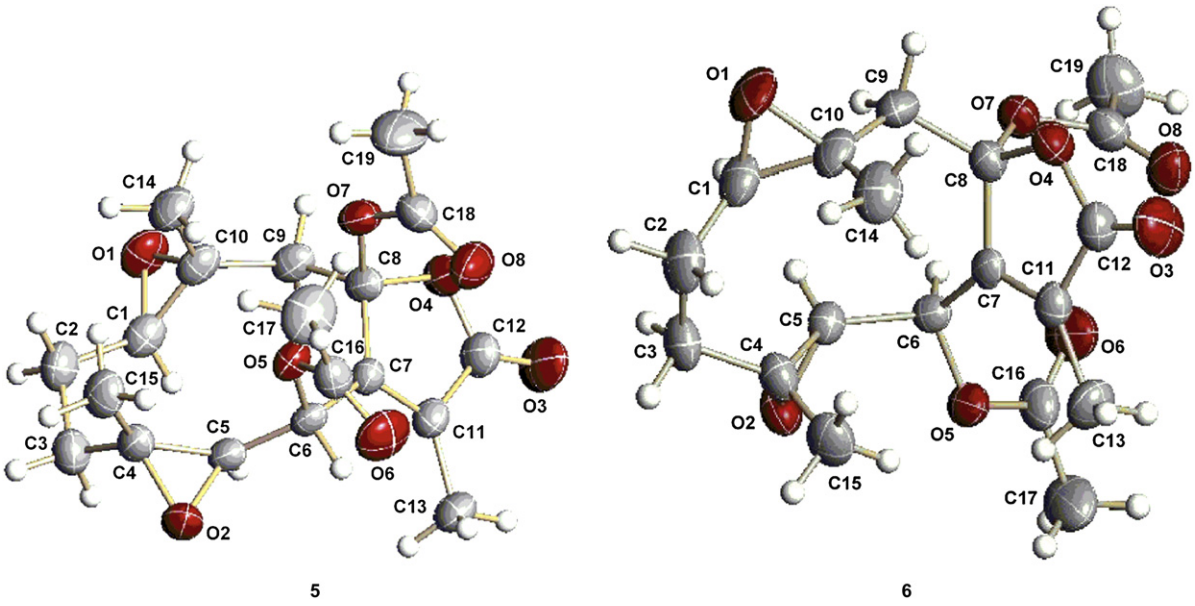

Figure 3. X-ray crystal structures of **5** and **6**.

and the acetoxyl group on C-8, respectively. Then, the structure of **5** was elucidated as 1β,10α:4α,5β-diepoxy-6β,8β-diacetoxy glechomanolide.

The molecular formula of the other acetate (**6**), $C_{19}H_{24}O_8$, was deduced by the positive HR-ESIMS (321.1341, $[M-OAc]^+$, calcd 321.1338). Extensive comparison of the 1D NMR (Tables 1 and 2) and 2D NMR data of **6** and **5** indicated that they were two stereoisomers. This conclusion was confirmed by the X-ray analysis of **6** (Fig. 3), which indicated **6** was the 8-epimer of **5**. Accordingly, compound **6** can be presented as 1β,10α:4α,5β-diepoxy-6β,8α-diacetoxy glechomanolide.

In the HMBC spectrum of the mixture of **1** and **2**, obviously correlations from H-6 (δ_H 6.26, br s, 1H, for **1**; and 6.22, d, J=5.8 Hz, 1H, for **2**) to the two acetyl carbonyl carbons at δ_C 168.8 (s, for **1**) and 168.0 (s, for **2**) can be found, which indicated the acetyl group of **1** and **2** was located at C-6. So, compounds **5** and **6** can be

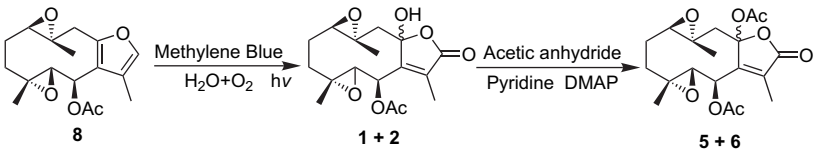

Figure 4. Semisynthesis of **1** and **2** by photooxidation of **8**.

determined as the 8-acetyl derivative of **1** and **2**, respectively. The ^{1}H NMR and ^{13}C NMR spectral data of **1** and **2** (Tables 1 and 2) were assigned by the HMBC experiment of the mixture in combination with the carefully comparison with those of **5** and **6**. Therefore, the structures of **1** (castanin C) and **2** (castanin D) were established as 1β,10α:4α,5β-diepoxy-6β-acetoxy-8β-hydroxy glechomanolide (**1**) and 1β,10α:4α,5β-diepoxy-6β-acetoxy-8α-hydroxy glechomanolide (**2**), respectively.

Similar to **1** and **2**, the other pair of interconvertible epimeric sesquiterpenoids (**3** and **4**) was also isolated as a mixture and had the same homogeneous behavior in the TLC and HPLC experiments. The EIMS of the mixture revealed the $[M]^{+}$ ion peak at *m*/*z* 296, corresponding to the molecular formula $C_{15}H_{20}O_6$. The ^{1}H and ^{13}C NMR spectra displayed 2 sets of 15 carbon signals with the abundance of 1:2, which indicated the mixture was composed of a two interconverting sesquiterpenoids isomers with the abundance of 1:2. The prominent features distinguished **3** and **4** from **1** and **2** observed in the NMR spectra was the absence of two acetyl groups at C-6 in **3** and **4**. Fortunately, acetylation of the mixture of **3** and **4** affords the same acetates with those of **1** and **2**, **5** and **6** (Fig. 1), which undoubtedly established the structures of **3** and **4** as 1β,10α:4α,5β-diepoxy-6β,8β-dihydroxy glechomanolide (castanin E, **3**), and 1β,10α:4α,5β-diepoxy-6β,8α-dihydroxy glechomanolide (castanin F, **4**), respectively. The assignment of the 1D NMR spectral data of **3** and **4** (Tables 1 and 2) was fulfilled by the careful comparison with those of **5** and **6** in combination with the abundance (1:2) of **3** and **4** in the mixture.

It was noteworthy that the ratio of **1** and **2** in the NMR experiment carried out in acetone-d_6 was nearly 1:1, whereas the ratio of **3** and **4** was 1:2. In order to explain the interesting phenomena, we carried out a computational chemistry study. The results indicated that the solvation free energy difference between epimers **1** and **2** is small (3.6 kcal/mol) and the computed solvation free energy of the intermediate **A** is only 5.9 kcal/mol higher than that of **1** in acetone (Fig. 1), which means that its possible to occur in the solution for such an isomerization, and it is also in agreement with the ratio of 1:1 as found experimentally in the isomeric equilibrium at room temperature. For epimers **3** and **4**, the isomerization between them goes through an intermediate **B**. Though the solvation free energy of **4** is only 1.9 kcal/mol lower than that of **3**, it needs the free energy of 14.9 kcal/mol in order to pass through the intermediate **B**. The value is over twice more than the former (intermediate **A**), which explains the experimental results that the ratio of **3** and **4** is nearly 1:2.

In addition, in the acetylation of the two mixtures, the ratio of obtained acetates **5** and **6** was both nearly 1:3 in the two experiments (see Section 3.3.1). Computational results indicated that in the acetylation reactions from **1** and **2** to **5** and **6** (Fig. 2), compound **1** gave out the energy of 6.3 kcal/mol to form **5**, which was smaller than that of the reaction from **2** to **6** (7.7 kcal/mol). This means **6** can be easier to be obtained, which was also agreed with the experimental results.

From a biogenetic view, the structures of the four glechomanolide sesquiterpenoids (**1**–**4**) were closely related to a glechomafuran sesquiterpenoid, castanin B (**8**), which was also the major constituent of this plant. The co-occurrence of compounds **1**–**2** and **8** in the same plant suggests that **1** and **2** may be biosynthesized from **8**. So, we try to synthesized **1** and **2** from **8**. The photooxidation of **8** gave a mixture of two interconverting hemiketal sesquiterpenoids, which was proved to be compounds **1** and **2** by its acetylation to afford **5** and **6**, respectively (Fig. 4).[16]

The cytotoxicity of compounds **5**, **6**, and **8** was tested against MCF-7, HeLa, and HepG2 cell lines in vitro using the method described previously.[21] All these compounds showed weak inhibitory activities with IC_{50}>150 μg/mL.

3. Experimental

3.1. General

Melting points were measured on Yuhua X-4 apparatus; uncorrected. UV–vis spectral data were obtained using a UV-2401 PC spectrophotometer. Optical rotations were measured on a Horiba SEPA-300 polarimeter. IR spectra were obtained on a Bio-Rad FtS-135 spectrometer. ^{1}H and ^{13}C NMR spectra were obtained on a Bruker AM-400 spectrometer. 2D NMR spectra were recorded on a Bruker DRX-500 NMR instrument. FAB and EIMS: VG Auto Spec-3000 spectrometer; in *m*/*z*. ESI and HR-ESIMS: API Qstar Pulsar instrument.

3.2. Plant material

Plants of *S. castanea* Diels f. *tomentosa* Stib. were collected in Lijiang, Yunnan province, in July 2000, and were identified by Prof. Xi-Wen Li, Kunming institute of Botany. A voucher specimen (no. 200098) was deposited at the Kunming Institute of Botany, Chinese Academy of Sciences, PR China.

3.3. Extraction and isolation

The air-dried and powdered aerial parts (4.1 kg) of *S. castanea* Diels f. *tomentosa* Stib. were extracted with acetone for 24 h at rt (3×10 L). The solvent was removed under vacuum, and the resulting gummy material was subjected to CC (DM-130 porous resin; MeOH/H_2O 1:1 and 9:1). The residue of the 9:1 fraction was partitioned between H_2O and AcOEt (2 L). The org. extract (56 g dry weight) was subjected to CC (SiO_2; petroleum ether/acetone 1:0→0:1). Four fractions (Fr. 1–Fr. 4) were obtained on the basis of TLC analysis. Fr. 3 was re-subjected to CC (SiO_2; petroleum ether/$CHCl_3$/acetone/H_2O 80:15:5:0.5) to yield the mixture of **1** and **2** (540 mg), **3** and **4** (50 mg).

3.3.1. Acetylation of the mixture of interconverting isomers

The mixture of **1** and **2** (100 mg) dissolved in pyridine (3 mL), 0.5 mL acetic acid anhydride was added and then stirred for 48 h. The solvent was removed in vacuum. The powder remained was subjected to preparative HPLC (MeOH/H_2O 45:55) to afford **5** (18 mg) and **6** (55 mg). The acetylation of the mixture of **3** and **4** (50 mg) with the same method also afforded **5** (7 mg) and **6** (19 mg), respectively.

*3.3.2. The mixture of **1** and **2***

White powder; ^{1}H and ^{13}C NMR: see Tables 1 and 2; positive ESIMS for the mixture: *m*/*z* (%): 669 ($[2M+Na]^{+}$, 100), 361

([M+Na]$^+$, 35), 202 (18); positive HR-ESIMS: 361.1261 ([M+Na]$^+$, $C_{19}H_{24}NaO_8^+$; calcd 361.1263).

*3.3.3. The mixture of **3** and **4***

White powder; ^{1}H and ^{13}C NMR: see Tables 1 and 2; EIMS for the mixture: *m*/*z* (%): 296 ([M]$^+$, 8), 278 (25), 260 (45), 232 (23), 217 (30), 205 (29), 175 (34), 163 (30), 124 (78), 109 (45), 97 (63), 82 (50), 67 (91), 53 (100).

*3.3.4. 1β,10α:4α,5β-Diepoxy-6β,8β-diacetoxy glechomanolide (**5**)*

Colorless needles; mp 218–219 °C (MeOH); $[\alpha]_D^{20.1}$ −31.8 (*c* 0.19, MeOH); UV (MeOH): λ_{max} (log ε)=216.2 (3.98) nm; IR (KBr): ν_{max}=2938, 1784, 1757, 1665, 1637, 1461, 1433, 1392, 1374, 1230, 1131.1113, 1025, 978 cm^{-1}; ^{1}H and ^{13}C NMR: see Tables 1 and 2; positive ESIMS: *m*/*z* (%): 403 ([M+Na]$^+$, 45), 321 ([M−OAc]$^+$, 5), 139 (100); positive HR-ESIMS: 321.1348 ([M−OAc]$^+$, $C_{17}H_{21}O_6^+$; calcd 321.1338).

*3.3.5. 1β,10α:4α,5β-Diepoxy-6β,8α-diacetoxy glechomanolide (**6**)*

Colorless needles; mp 210–212 °C (MeOH); $[\alpha]_D^{20.0}$ +23.6 (*c* 0.25, MeOH); UV (MeOH): λ_{max} (log ε)=222.0 (3.90) nm; IR (KBr): ν_{max}=2963, 2932, 1783, 1746, 1672, 1630, 1442, 1368, 1291, 1227, 1166, 1125, 1057, 1005, 979 cm^{-1}; ^{1}H and ^{13}C NMR: see Tables 1 and 2; positive FABMS: *m*/*z* (%): 321 ([M−OAc]$^+$, 100), 301 (16), 235 (15), 58 (20); positive HR-ESIMS: 321.1341 ([M−OAc]$^+$, $C_{17}H_{21}O_6^+$; calcd 321.1338).

3.4. Computational experiment

All calculations were carried out using the Gaussian03 program package.[22] The B3LYP hybrid density functional and 6-31G (d) basis set were used.[23,24] For all optimized structures, vibrational spectra were calculated to ensure that no imaginary frequencies for energy minimum were obtained. Zero-point energy (ZPE) corrections were also considered. The crystal data were used to act as the initial optimized structures. The solvation effect was considered by using acetone in the calculations to resemble the experimental condition using the B3LYP/6-31G (d) method. The polarized continuum model (PCM) was used.[25,26] Default parameters for the reaction field cavities were used in the PCM model.

3.5. Photooxidation of 1β,10α:4α,5β-diepoxy-6β-acetoxy-glechomafuran (8)

Compound **8** (200 mg) dissolved in acetone (3 mL), 1.0 mg methylene blue was added and then stirred for 2 days in sunlight. The solvent was removed in vacuum. The residue was subjected to column chromatography over silica gel (petroleum ether/acetone 9:1) to afford the mixture of **1** and **2** (32 mg), which was further acetylated (using the same method discussed above) to yield **5** (5 mg) and **6** (14 mg).

3.6. X-ray crystallographic studies

Crystallographic data for **5**: colorless, transparent needles, $C_{19}H_{24}O_8\cdot CH_3COCH_3$, *M*=380.38, orthorhombic system, space group $P2_12_12_1$, *a*=10.382 (11), *b*=13.397 (14), *c*=13.601 (14) Å; *V*=1891.6 (3) Å^3; *Z*=4; D_x=1.336 g/cm^3, crystal dimensions 0.43×0.26×0.19 mm. The total number of reflections measured was 2353, of which 2349 were unique and 2087 observed, $I>2\sigma(I)$. Final indices: R_f=0.0409, R_w=0.0948 ($w=1/\sigma|F|^2$) for observed reflections, and R_1=0.0456, wR_2=0.1008 for all reflections.

Crystallographic data for **6**: colorless, transparent needles, $C_{19}H_{24}O_8\cdot CH_3COCH_3$, *M*=380.38, orthorhombic system, space group $P2_12_12_1$, *a*=8.518 (8), *b*=12.092 (12), *c*=18.245 (18) Å; *V*=1879.2 (3) Å^3; *Z*=4; D_x=1.344 g/cm^3, crystal dimensions 0.50×0.42×0.19 mm. The total number of reflections measured was 2341, of which 2340 were unique and 1808 observed, $I>2\sigma(I)$. Final indices: R_f=0.0405, R_w=0.0866 ($w=1/\sigma|F|^2$) for observed reflections, and R_1=0.0507, wR_2=0.0900 for all reflections.

Crystallographic data for the structures of **5** and **6** have been deposited in the Cambridge Crystallographic Data Centre (deposition number: CCDC 647120 of **5**, and 647121 of **6**). Copies of this data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB21EZ, UK; fax: +44 1223 336 033; or e-mail: deposit@ ccdc.cam.ac.uk).

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.07.074.

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