# Constituents of *Trigonostemon chinensis*

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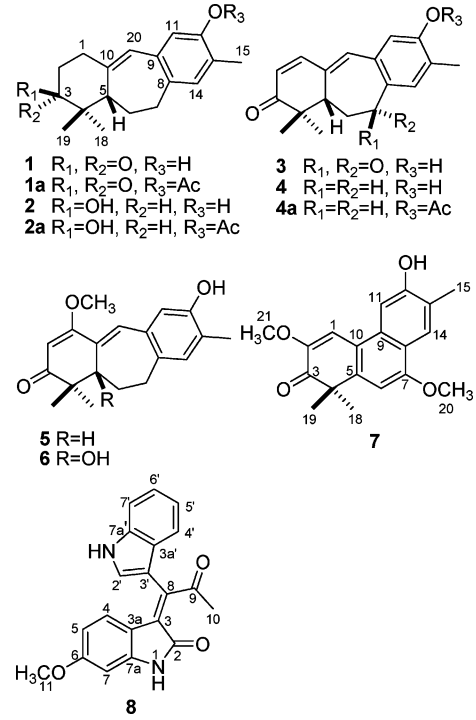
Phytochemical investigation on the stem bark and wood of *Trigonostemon chinensis* led to the isolation of four new dinorditerpenoids, trigonostemons A−D (**1**, **3**, **5**, **6**), a new phenanthrenone, trigonostemon E (**7**), and a new bisindole alkaloid, trigonostemon F (**8**). The structures were established by extensive spectroscopic methods. The absolute configurations of **1**−**6** were determined by X-ray crystallography, circular dichroism, quantum chemical TDDFT calculations, and chemical transformations. The relative configuration of **8** was confirmed by X-ray diffraction analysis.

The genus *Trigonostemon* consists mostly of shrubs that are widely distributed in Southeast Asia. *Trigonostemon reidioides* has been used in Thai medicine as an antidote, expectorant, and laxative agent. Previous phytochemical studies on this plant resulted in the isolation of a phenanthrenone (trigonostemone[1]), a flavonoidal indole alkaloid (lotthanongine[2]), and seven modified daphnane diterpenoids (rediocides A−G.[3−6]). Yue et al. reported 3,4-*seco*-cleistanthanic diterpenoids[7] from a *Trigonostemon chinensis* collected in Hainan Province, and two daphnane diterpenoids[8] were isolated from the same species collected in Yunnan Province. Carboline alkaloids[9] and phenanthrenes[10] were from *Trigonostemon lii*, another species collected in Yunnan Province.

In this paper, we report results of an investigation of the stem bark and wood of *T. chinensis* Merr. (Euphorbiaceae) collected from Guangxi Province, People's Republic of China. Four new dinorditerpenoids (**1**, **3**, **5**, **6**), a new phenanthrenone (**7**), a new bisindole derivative (**8**), and five known compounds were isolated. Structures of the new compounds were elucidated by extensive spectroscopic methods and X-ray diffraction analyses. The known compounds, compared with literature data, were identified as 1,2-dihydroheudelotinol (**2**),[11] heudelotinone (**4**),[11] 6,9-*O*-dedimethyltrigonostemone (**9**),[10] trigonostemone (**10**),[1] and trigonochinene E (**11**).[7] X-ray crystallography, circular dichroism, quantum chemical TDDFT calculations, and chemical transformations allowed assignment of absolute configurations to compounds **1**−**6**.




## Results and Discussion

Compound **1** crystallized from acetone as colorless needles and had the molecular formula $C_{18}H_{22}O_2$, as deduced from its HREIMS, requiring eight degrees of unsaturation. IR absorptions at 3442, 1691, and 1639 $cm^{-1}$ showed the presence of an OH group, a carbonyl group, and a double bond, respectively. IR absorptions at 1562 and 1502 $cm^{-1}$ suggested the presence of an aromatic ring, and this was supported by a UV maximum at 302 nm. The $^1H$ NMR spectrum (Table 1) displayed signals of three low-field singlets at $\delta_H$ 6.80, 6.60, and 6.40 and three tertiary methyl signals at $\delta_H$ 2.20, 1.15, and 1.00. The $^{13}C$ NMR spectrum (Table 2) indicated 18 resonances ascribed to one carbonyl group, one aromatic ring, one double bond, and one tertiary, one methine, four methylene, and three methyl carbons. As six of eight degrees of unsaturation were accounted for, the two remaining suggested another two rings in this structure. The $^1H$ and $^{13}C$ NMR data of **1** were similar to those of heudelotinone (**4**), a dinorditerpenoid compound derived from an abietane-type skeleton. The MS data revealed that **1** contained two more protons than **4**, and correspondingly two methylene carbons ($\delta_C$ 37.1, 38.2) instead of two $sp^2$ carbons ($\delta_C$ 137.8, 149.6) in **4** were evident in the $^{13}C$ NMR spectrum. HMBC correlations of the two methylene protons ($\delta_H$ 2.70 (2H, m, H-1), 2.64 (1H, m, H-2a), 2.45 (1H, m, H-2b)) with C-3 ($\delta_C$ 215.0) provided further evidence that **1** was a 1,2-dihydro derivative of **4**. The full structure of **1**, named trigonostemon A, was confirmed through an improved X-ray diffraction experiment (Figure 1).

The HREIMS of **3** afforded the molecular formula $C_{18}H_{18}O_3$ and indicated 10 degrees of unsaturation. The NMR data of **3** were again similar to those of **4**, except that a carbonyl ($\delta_C$ 199.5) in **3** replaced a methylene in **4**. This carbonyl carbon was assigned as C-7 by the HMBC correlation of H-14 ($\delta_H$ 7.78, s) to C-7 ($\delta_C$

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**Table 1.** $^1$H NMR Data of Compounds **1**, **3**, **5**, **6**, and **7** (300 MHz, $\delta$ in ppm, $J$ in Hz)

| no. | **1**[a] | **3**[a] | **5**[a] | **6**[b] | **7**[c] |
|---|---|---|---|---|---|
| 1 | 2.70 (2H, m) | 7.10 (d, 9.8) | | | 7.22 (s) |
| 2 | 2.45 (m) | 6.05 (d, 9.8) | 5.40 (s) | 5.38 (s) | |
| | 2.64 (m) | | | | |
| 5 | 2.60 (m) | 3.10 (d, 13.0) | 2.76 (m) | | |
| 6 | 2.15 (m) | 2.90 (2H, m) | 2.28 (m) | 2.20 (dd, 14.1, 8.1) | 6.60 (s) |
| | 1.69 (m) | | 1.72 (m) | 1.80 (dd, 14.1, 11.3) | |
| 7 | 2.66 (2H, m) | | 2.72 (m) | 2.80 (dd, 15.1, 11.3) | |
| | | | 2.60 (m) | 2.60 (dd, 15.1, 8.1) | |
| 11 | 6.60 (s) | 7.40 (s) | 6.78 (s) | 6.78 (s) | 7.38 (s) |
| 14 | 6.80 (s) | 7.78 (s) | 6.90 (s) | 6.82 (s) | 7.90 (s) |
| 15 | 2.20 (3H, s) | 2.30 (3H, s) | 2.23 (3H, s) | 2.18 (3H, s) | 2.42 (3H, s) |
| 18 | 1.00 (3H, s) | 1.05 (3H, s) | 0.98 (3H, s) | 0.95 (3H, s) | 1.58 (3H, s) |
| 19 | 1.15 (3H, s) | 1.35 (3H, s) | 1.20 (3H, s) | 1.18 (3H, s) | 1.58 (3H, s) |
| 20 | 6.40 (s) | 6.66 (s) | 7.36 (s) | 7.28 (s) | 4.05 (3H, s) |
| 21 | | | 3.82 (3H, s) | 3.80 (3H, s) | 3.92 (3H, s) |

[a] In $CDCl_3$. [b] In $CD_3OD$. [c] In $CDCl_3$ + $CD_3OD$.

**Table 2.** $^{13}$C NMR Data of Compounds **1**, **3**, **5**, **6**, and **7** (100 MHz, $\delta$ in ppm)

| no. | **1**[a] | **3**[a] | **5**[a] | **6**[b] | **7**[c] |
|---|---|---|---|---|---|
| 1 | 37.1 $CH_2$ | 147.2 CH | 169.8 qC | 171.8 qC | 112.9 CH |
| 2 | 38.2 $CH_2$ | 125.2 CH | 100.0 CH | 100.5 CH | 147.2 qC |
| 3 | 215.0 qC | 202.8 qC | 205.2 qC | 207.0 qC | 200.0 qC |
| 4 | 49.2 qC | 45.7 qC | 46.0 qC | 53.5 qC | 49.3 qC |
| 5 | 52.0 CH | 42.5 CH | 50.0 CH | 81.2 qC | 142.6 qC |
| 6 | 31.4 $CH_2$ | 42.8 $CH_2$ | 31.3 $CH_2$ | 36.4 $CH_2$ | 99.9 CH |
| 7 | 32.0 $CH_2$ | 199.5 qC | 32.3 $CH_2$ | 29.4 $CH_2$ | 155.5 qC |
| 8 | 134.4 qC | 130.1 qC | 134.5 qC | 127.9 qC | 114.3 qC |
| 9 | 134.5 qC | 134.6 qC | 133.5 qC | 137.6 qC | 131.3 qC |
| 10 | 139.9 qC | 139.3 qC | 132.7 qC | 134.6 qC | 119.1 qC |
| 11 | 116.5 CH | 118.8 CH | 118.1 CH | 120.9 CH | 103.8 CH |
| 12 | 151.9 qC | 157.8 qC | 152.4 qC | 155.2 qC | 155.5 qC |
| 13 | 121.9 qC | 125.3 qC | 124.5 qC | 127.9 qC | 126.2 qC |
| 14 | 130.7 CH | 125.2 CH | 131.2 CH | 132.3 CH | 123.7 CH |
| 15 | 15.4 $CH_3$ | 15.4 $CH_3$ | 15.6 $CH_3$ | 16.5 $CH_3$ | 16.3 $CH_3$ |
| 18 | 20.8 $CH_3$ | 21.6 $CH_3$ | 20.3 $CH_3$ | 17.8 $CH_3$ | 28.1 $CH_3$ |
| 19 | 22.6 $CH_3$ | 22.8 $CH_3$ | 24.6 $CH_3$ | 25.0 $CH_3$ | 28.1 $CH_3$ |
| 20 | 127.6 CH | 137.2 CH | 132.3 CH | 135.2 CH | 55.3 $CH_3$ |
| 21 | | | 56.0 $CH_3$ | 57.3 $CH_3$ | 55.1 $CH_3$ |

[a] In $CDCl_3$. [b] In $CD_3OD$. [c] In $CDCl_3$ + $CD_3OD$.

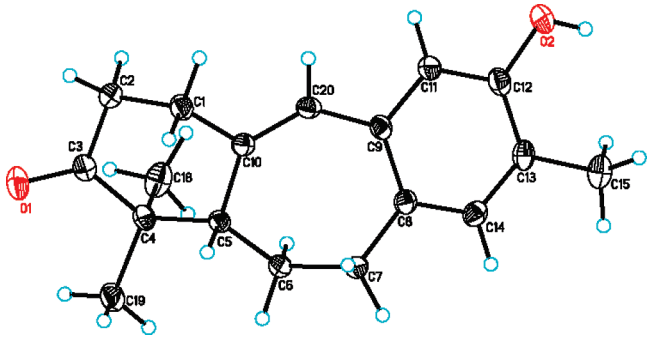


**Figure 1.** Perspective ORTEP drawing for **1**.

199.5), and this was supported by the downfield chemical shift of H-14 due to the deshielding effect of the C-7 carbonyl group. Thus, **3** (trigonostemon B) was deduced to be heudelotin-3,7-dione.

The molecular formula $C_{19}H_{22}O_3$ of trigonostemon C (**5**), deduced from HREIMS, required nine degrees of unsaturation. NMR data (Tables 1 and 2) revealed that **5** also was also similar in structure to **4**, except for an additional $OCH_3$ group ($\delta_H$ 3.82, 3H, s; $\delta_C$ 56.0). HMBC correlation from the $OCH_3$ protons ($\delta_H$ 3.82, 3H, s) to C-1 ($\delta_C$ 169.8) confirmed that the $OCH_3$ group was located at C-1. Therefore, **5** was determined to be a 1-methoxyl derivative of heudelotinone.

Compound **6** had the molecular formula $C_{19}H_{22}O_4$ (HREIMS). The $^1$H and $^{13}$C NMR data of **6** (Tables 1 and 2) showed some

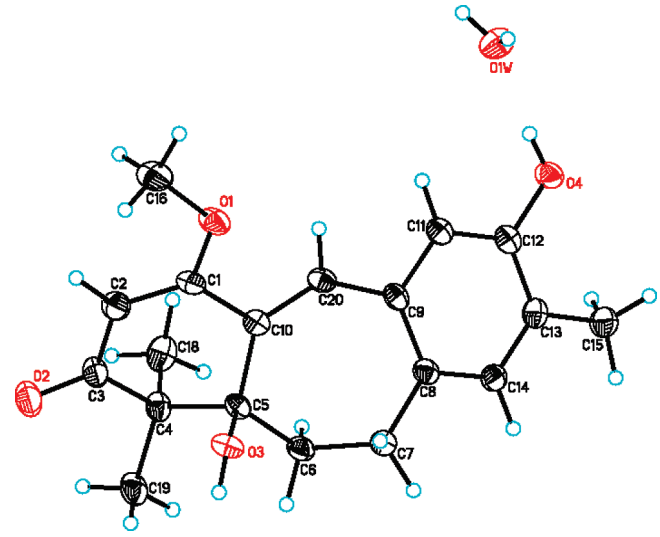


**Figure 2.** Perspective ORTEP drawing for **6**.

similarities to those of **5**, except that an oxygenated tertiary carbon ($\delta_C$ 81.2) in **6** replaced the secondary carbon $\delta_C$ 50.0 (C-5) in **5**. HMBC correlations from $H_3$-18 and $H_3$-19 to the tertiary carbon at $\delta_C$ 81.2 allowed the assignment of C-5. Thus, **6** was deduced to be a 1-methoxy-5-hydroxy derivative of heudelotinone, the first C-5 oxygenated abietane-type dinorditerpene with a skeletal rearrangement 9 (10→20) isolated from a plant. The structure of **6** (trigonostemon D) was confirmed by an X-ray diffraction experiment (Figure 2).

The molecular formula of **7** ($C_{19}H_{20}O_4$) was inferred by its HREIMS. The $^1$H NMR data (Table 1) displayed four aromatic singlets ($\delta_H$ 7.90, 7.38, 7.22, and 6.60), two methoxy ($\delta_H$ 4.05 and 3.92), and three tertiary methyl signals ($\delta_H$ 2.42 and 1.58). The $^{13}$C NMR and DEPT spectra (Table 2) exhibited 19 signals, including five $CH_3$, four CH ($sp^2$ carbons), and 10 quaternary carbons. These NMR data suggested that **7** was similar in structure to the known phenanthrenone trigonostemone,[1] isolated from *T. reidioides*. Two $OCH_3$ groups, rather than three in trigonostemone, were present in **7**. One $OCH_3$ group ($\delta_H$ 3.92) was placed at C-2 on the basis of the HMBC correlation between them. The other $OCH_3$ group was at C-7, as deduced from the NOE difference spectrum, in which H-6 ($\delta_H$ 6.60) was enhanced when the $OCH_3$ at $\delta_H$ 4.05 was irradiated. Thus, **7** was established to be 12-demethyltrigonostemone.

The molecular formula of trigonostemon G (**8**) was determined to be $C_{20}H_{16}N_2O_3$ (HREIMS). The IR spectrum showed absorption bands at 3265 (NH), 1687 (NH-C=O), and 1612 (aromatic ring) $cm^{-1}$. UV absorptions at 272 and 395 nm suggested the presence

**Table 3.** $^1$H (300 MHz) and $^{13}$C NMR (100 MHz) Data of Compound **8** (in $CD_3COCD_3$, $\delta$ in ppm, $J$ in Hz)

| no. | $\delta_C$ | $\delta_H$ |
|---|---|---|
| 1 | | 9.60 (br s) |
| 2 | 169.2 qC | |
| 3 | 144.9 qC | |
| 3a | 115.6 qC | |
| 4 | 125.6 CH | 6.65, d (8.7) |
| 5 | 106.6 CH | 6.25, dd (8.7, 2.4) |
| 6 | 161.6 qC | |
| 7 | 96.8 CH | 6.55, d (2.4) |
| 7a | 122.0 qC | |
| 8 | 143.2 qC | |
| 9 | 203.9 qC | |
| 10 | 28.9 $CH_3$ | 2.38 (3H, s) |
| 11 | 55.4 $CH_3$ | 3.80 (3H, s) |
| 1′ | | 11.10 (br s) |
| 2′ | 127.7 CH | 7.65 (s) |
| 3′ | 109.1 qC | |
| 3a′ | 125.4 qC | |
| 4′ | 121.5 CH | 7.32, dd (7.9, 1.0) |
| 5′ | 120.8 CH | 7.10, ddd (7.9, 7.9, 1.0) |
| 6′ | 123.1 CH | 7.25, ddd (7.9, 7.9, 1.0) |
| 7′ | 112.9 CH | 7.60, dd (7.9, 1.0) |
| 7a′ | 137.7 qC | |

of an extensive conjugated system. The $^{13}$C NMR spectrum (Table 3) indicated 20 carbons including two carbonyl [$\delta_C$ 203.9 (C═O) and 169.2 (NH-C═O)], 16 sp$^2$, and two methyl carbons. The $^1$H NMR spectrum (Table 3) showed signals of an ABX aromatic system at $\delta_H$ 6.25 (1H, dd, $J$ = 8.7, 2.4 Hz), 6.55 (1H, d, $J$ = 2.4 Hz), and 6.65 (1H, d, $J$ = 8.7 Hz), an AA′BB′ aromatic system at $\delta_H$ 7.10 (1H, ddd, $J$ = 7.9, 7.9, 1.0 Hz), 7.25 (1H, ddd, $J$ = 7.9, 7.9, 1.0 Hz), 7.32 (1H, dd, $J$ = 7.9, 1.0 Hz), and 7.60 (1H, dd, $J$ = 7.9, 1.0 Hz), two NH protons at 11.10 (1H, br s) and 9.60 (1H, br s), a singlet aromatic proton at $\delta_H$ 7.65, an $OCH_3$ group at $\delta_H$ 3.80, and a methyl at $\delta_H$ 2.38. These data suggested the existence of two indole rings, one $OCH_3$, and one acetyl group. One indole ring was deduced from HMBC correlations of H-4′/C-3′, H-2′/C-3a′, H-7′/C-3a′, and H-2′/C-8, and the other indole ring from the long-range correlations of H-1/C-3a, H-1/C-7a, H-4/C-3, and H-4/C-7a. The $OCH_3$ group was positioned at C-6 from the HMBC cross-peaks between the *O*-methyl and C-6. HMBC correlations from $H_3$-10 to C-8 and C-9 ($\delta_C$ 203.9) suggested that the acetyl group was attached to C-8. Considering the NMR data and degrees of unsaturation, an additional double bond was located between C-3 and C-8. Key ROESY correlations of H-4/H-2′ indicated the *Z*-configuration for the double bond. An X-ray experiment confirmed the structure of **8** (Figure 3). Trigonostemon F (**8**) was a new naturally occurring bis-indole derivative comprised of an indole ring and an oxindole ring.

Trigonostemons A−D (**1**, **3**, **5**, **6**), together with the two known compounds 1,2-dihydroheudelotinol (**2**) and heudelotinone (**4**), are all dinorditerpenoids whose molecules feature a chiral center at C-5. In order to determine the absolute configurations of these six compounds, X-ray diffraction, circular dichroism, chemical transformation, and computational calculation experiments were carried out. The absolute configuration of **1** was determined by an improved X-ray crystallographic diffraction experiment using Cu Kα radiation (Figure 1). The configuration at C-5 was determined to be *S*. The crystal structure of **6** (Figure 2) was also determined. The absolute configuration of **6** at C-5 was *R* (the substitution at C-5 was an OH group in **6** but an H atom in **1**).

The CD spectra of compounds **1**, **5**, and **6** were recorded (Figure 4). Compounds **5** and **6** showed very similar Cotton effects in their spectra, while the Cotton effects of **1** moved to shorter wavelength due to the lack of a double bond between C-1 and C-2. Comparison of their CD spectra confirmed the *S*-configuration at C-5 in **5**.

The planar structures of **2** and **4** were identified by comparison of their observed and reported physical data,[11] but their absolute

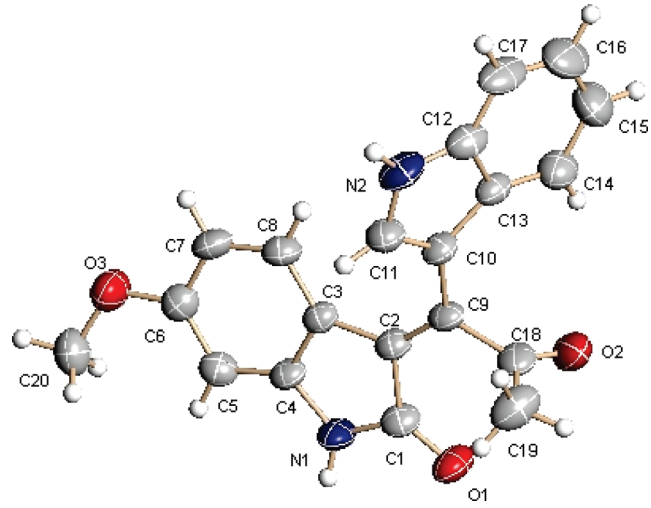


**Figure 3.** Perspective ORTEP drawing for **8**.

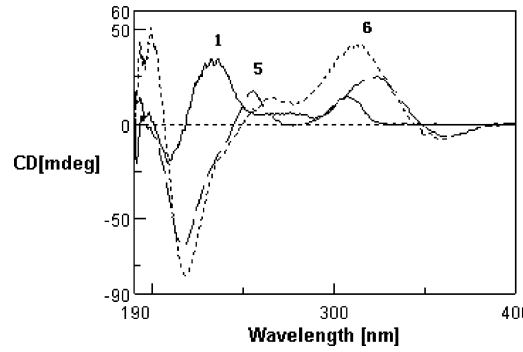


**Figure 4.** CD curves of compounds **1** (solid line), **5** (long dashed), and **6** (dotted).

configurations remained uncertain. Their complete structures were determined unambiguously by chemical conversions. Compound **2** (0.075 mmol) was first monoacetylated to **2a** and then oxidized by pyridinium chlorochromate (PCC) to give 12-acetyl-1,2-dihydroheudelotinone, whose ESIMS, $^1$H NMR, TLC, and CD spectra were identical to **1a**, an acetylated derivative of **1**. Thus, compound **2** was deduced to have an *S*-configuration. In the same way, compound **1a** was oxidized by PCC to afford 12-acetylheudelotinone, whose ESIMS, $^1$H NMR, TLC, and CD spectra were identical to those of **4a**, an acetylated derivative of **4**. Therefore, compound **4** was elucidated as 5*S*-heudelotinone.

Considering the biogenetic relationships between the dinorditerpenoids isolated from *T. chinensis*, **3** was assumed to have a 5*S*-configuration. As compound **3** had a different CD spectrum and optical rotation from those of the other five dinorditerpenoids, common methods could not provide its absolute configuration. Thus, quantum chemical TDDFT was applied. The ECD spectrum of 5*S*-heudelotin-3,7-dione was calculated and then compared with the experimental ECD spectrum (Figure 5). The results showed that the calculated and experimental CD curves coincided very well, which supported the 5*S*-configuration for compound **3**.

In summary, six rearranged abietane-type dinorditerpenoids (four new and two known) were isolated from *T. chinensis*, and their absolute configurations were determined. The configuration at C-5 in these compounds was consistent, suggesting that these compounds originate from the same biosynthetic pathway.

## Experimental Section

**General Experimental Procedures.** Optical rotations were taken on a Perkin-Elmer 341 polarimeter. IR spectra were recorded on a Nicolet Magna FT-IR 750 spectrophotometer using KBr disks. CD

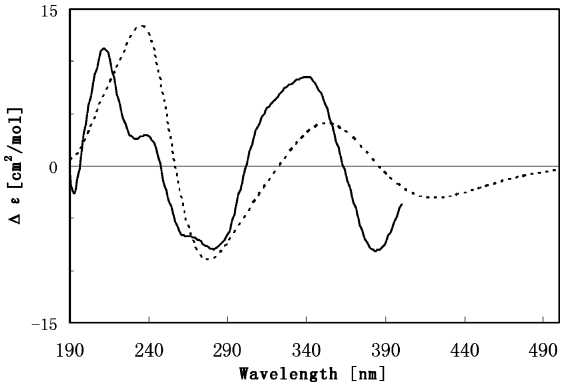


**Figure 5.** Experimental ECD spectrum (solid line) and conformationally averaged ECD spectrum (dotted) of compound **3** (by relative Gibbs free energy, $\Delta G$, $\sigma = 0.2$).

spectra were obtained on a JASCO 810 spectrometer. UV spectra were recorded on a Shimadzu UV-2550 spectrophotometer. NMR spectra were recorded on Bruker AM-400 and INVOR-600 NMR spectrometers. The chemical shift ($\delta$) values are given in ppm with TMS as internal standard, and coupling constants ($J$) are in Hz. EIMS and HREIMS spectra were recorded on a Finnigan MAT-95 mass spectrometer or on a Micromass LC-MS-MS mass spectrometer. Silica gel was used for flash chromatography (Qingdao Marine Chemical Industrials). MCI gel CHP20P (75−150 $\mu$m, Mitsubishi Chemical Industries, Japan) and Sephadex LH-20 (Pharmacia Biotech AB, Uppsala, Sweden) were also used as column packing materials. TLC was carried out on precoated silica gel GF254 plates (Yantai Chemical Industrials), and the TLC spots were viewed at 254 nm after spraying with 5% sulfuric acid in alcohol containing 10 mg/mL vanillin. X-ray crystallographic analysis was carried out on an Oxford Diffraction CCD diffractometer with Cu Kα radiation ($\lambda = 1.54178$ Å) and a Bruker Smart Apex CCD diffractometer with graphite-monochromated Mo Kα radiation ($\lambda = 0.71073$ Å).

**Plant Material.** Stem bark and wood of *T. chinensis* were collected in Riyang County in Guangxi Province, China, and identified by Professor Shouyang Liu, from Guangxi Institute of Traditional Chinese Medicine. A voucher (20070502) was deposited at the herbarium of Shanghai Institute of Materia Medica, Chinese Academy of Sciences.

**Extraction and Isolation.** Dried and powdered stem bark and wood of *T. chinensis* (10 kg) was extracted with 95% EtOH (3 × 40 L, 3 days each) at room temperature. After evaporation of solvent, the residue (530 g) was dissolved in water (4 L) and then extracted with petroleum ether (PE), EtOAc, and *n*-BuOH in sequence. The EtOAc extract (90 g) was subjected to column chromatography (CC) over silica gel and eluted with PE/EtOAc (10:1, 5:1, 4:1, 3:1, 2:1, 1:1, 0:1) and MeOH to yield fractions 1−10. Fraction 2 (580 mg) was separated using Sephadex LH-20 ($CHCl_3$/MeOH, 1:1) to yield **1** (180 mg). Fraction 3 (1.3 g) was subjected to Sephadex LH-20 ($CHCl_3$/MeOH, 1:1) to give subfractions 3a−3c. Fraction 3b was purified with Sephadex LH-20 ($CHCl_3$/MeOH, 1:1) to afford two fractions (3b1 and 3b2). Trigonostemone (**10**) (32 mg) was filtered from fraction 3b2 as a yellow gum. Fraction 3c was separated by preparative TLC to yield **4** (50 mg) and **1** (120 mg). Fraction 5 (4 g) was separated on MCI (MeOH/$H_2O$, from 1:1 to 1:0) to give subfractions 5a−5g. Compound **2** (800 mg) was crystallized from fraction 5d. Fraction 5e, eluted with $CHCl_3$/MeOH (1:1), was subjected repeatedly to CC over Sephadex LH-20, and compounds **3** (5 mg) and **5** (68 mg) were obtained. Fraction 6 was subjected to CC (silica gel) eluted with PE/EtOAc (from 6:1, 5:1, 4:1, 3:1, MeOH) to yield fractions 6a−6e. Fraction 6a was purified by Sephadex LH-20 ($CHCl_3$/MeOH, 1:1) to yield **2** (17 mg) and **11** (10 mg). Fraction 7 was purified over MCI eluting with MeOH/$H_2O$ (from 1:1 to 1:0), affording five subfractions, 7a−7e. Compound **7** (35 mg) was obtained from subfraction 7d. Fraction 8 was separated by MCI (MeOH/$H_2O$ from 1:1 to 1:0) to yield subfractions 8a−8j. Fraction 8f was purified by Sephadex LH-20 ($CHCl_3$/MeOH, 1:1) to yield subfractions 8f1−8f3. Fraction 8f2 was separated on Sephadex LH-20 ($CHCl_3$/MeOH, 1:1) to give fractions 8f21−8f22. Fraction 8f22 was subjected to CC eluted with PE/EtOAc (from 5:1, 4:1, 3:1, MeOH) to yield fractions 8f221−8f223. Fraction 8f222 was purified by Sephadex LH-20 eluted with MeOH to give **9** (42 mg). Compound **6** (36 mg) was crystallized from fraction 8f223. Fraction 8 h was subjected to CC eluting with PE/EtOAc (from 2:1, 1:3, MeOH) to yield fractions 8h1−8h3. Compound **8** (203 mg) was obtained after fraction 8h2 was separated on Sephadex LH-20 ($CHCl_3$/MeOH, 1:1).

**Trigonostemon A (1):** white needles (acetone); mp 195.5−198.5 °C; $[\alpha]^{23}_D$ +238 (*c* 0.13, MeOH); UV (MeOH) $\lambda_{max}$ (log $\varepsilon$) 302 (3.21), 264 (3.70) nm; CD (MeOH) $\lambda_{max}$ ($\Delta\varepsilon$) 197 (+1.48), 209 (−6.93), 232 (+12.48), 309 (+5.06) nm; IR (KBr) $\nu_{max}$ 3442, 2939, 1691, 1639, 1562, 1502, 12456, 1161, 1107, 916 $cm^{-1}$; $^1H$ and $^{13}C$ NMR data see Tables 1 and 2; EIMS *m/z* 270 $[M]^+$ (57), 268 (35), 225 (25), 199 (20), 185 (100), 171 (24); HREIMS *m/z* 270.1613 (calcd for $C_{18}H_{22}O_2$ 270.1620).

**Trigonostemon A Acetate (1a):** white powder; $[\alpha]^{24}_D$ +193 (*c* 0.03, MeOH); CD (MeOH) $\lambda_{max}$ ($\Delta\varepsilon$) 208 (−1.98), 230 (+4.17), 263 (+5.10) nm; $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ 6.90 (1H, s, H-14), 6.80 (1H, s, H-11), 6.40 (1H, s, H-20), 2.34 (3H, s, Ac), 2.10 (3H, s, H-15), 1.05 (3H, s, H-19), 0.70 (3H, s, H-18); ESIMS *m/z* 335.2 $[M + Na]^+$.

**5*S*-1,2-Dihydroheudelotinol (2):** white powder; mp 162.0−165.0 °C; $[\alpha]^{24}_D$ +164 (*c* 0.12, MeOH); ESIMS *m/z* 295.0 $[M + Na]^+$; $^1H$ and $^{13}C$ NMR spectroscopic data were identical to those in ref 11.

**5*S*-1,2-Dihydroheudelotinol Acetate (2a):** white powder; mp 158.0−162.0 °C; $[\alpha]^{24}_D$ +206 (*c* 0.10, MeOH); $^1H$ NMR ($CDCl_3$, 300 MHz), $\delta$ 6.85 (1H, s, H-14), 6.75 (1H, s, H-11), 6.25 (1H, s, H-20), 3.40 (1H, dd, $J = 11.6$, 4.3 Hz, H-3), 2.30 (3H, s, Ac), 2.18 (3H, s, H-15), 1.05 (3H, s, H-19), 0.70 (3H, s, H-18); ESIMS *m/z* 337.1 $[M + Na]^+$, 315.1 $[M + H]^+$.

**Trigonostemon B (3):** white powder; $[\alpha]^{23}_D$ −57 (*c* 0.065, MeOH); UV (MeOH) $\nu_{max}$ (log $\varepsilon$) 243 (3.63), 288 (3.94), 353 (2.71) nm; CD (MeOH) $\lambda_{max}$ ($\Delta\varepsilon$) 211 (+11.2), 281 (−7.98), 341 (+8.56), 385 (−8.10) nm; IR (KBr) $\lambda_{max}$ 3305, 2927, 1674, 1649, 1583, 1356, 1296, 1263, 1153, 897, 554 $cm^{-1}$; $^1H$ and $^{13}C$ NMR data, see Tables 1 and 2; EIMS *m/z* 282 $[M]^+$ (15), 256 (20), 149 (27), 129 (27), 111 (41), 97 (70), 83 (76), 69 (75), 57 (100), 55 (86); HREIMS *m/z* 282.1250 (calcd for $C_{18}H_{18}O_3$ 282.1256).

**5*S*-Heudelotinone (4):** yellow powder; $[\alpha]^{23}_D$ +105 (*c* 0.065, MeOH); ESIMS *m/z* 559.1 $[2M + Na]^+$, 269.1 $[M + H]^+$; $^1H$ and $^{13}C$ NMR spectroscopic data were identical to those in ref 11.

**5*S*-Heudelotinone Acetate (4a).** Compound **4** (2.0 mg, 0.007 mmol) was dissolved in dry pyridine (0.5 mL) and treated with acetic anhydride (0.5 mL) for 3 h. Standard workup followed by silica gel CC using petroleum ether/acetone (12:1) gave the acetate **4a** (2.2 mg, 0.007 mmol) as a yellow powder: $[\alpha]^{25}_D$ +210 (*c* 0.05, MeOH); CD (MeOH): $\lambda_{max}$ ($\Delta\varepsilon$) 209 (−13.78), 236 (−6.66), 253 (+11.52), 325 (+11.86), 370 (−5.33) nm; $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ 7.10 (1H, d, $J = 9.8$ Hz, H-1), 7.00 (1H, s, H-14), 6.90 (1H, s, H-11), 6.70 (1H, s, H-20), 5.90 (1H, d, $J = 9.8$ Hz, H-2), 2.35 (3H, s, Ac), 2.20 (3H, s, H-15), 1.20 (3H, s, H-19), 0.95 (3H, s, H-18); ESIMS *m/z* 333.2 $[M + Na]^+$, 311.2 $[M + H]^+$.

**Trigonostemon C (5):** yellow gum; $[\alpha]^{23}_D$ +115.3 (*c* 0.085, MeOH); UV (MeOH) $\lambda_{max}$ (log $\varepsilon$) 318 (3.78), 254 (3.58) nm; CD (MeOH) $\lambda_{max}$ ($\Delta\varepsilon$) 218 (−23.29), 255 (+6.29), 322 (+8.94) nm; IR (KBr) $\nu_{max}$ 3385, 2931, 1610, 1579, 1230, 1186, 1057 $cm^{-1}$; $^1H$ and $^{13}C$ NMR data, see Tables 1 and 2; EIMS *m/z* 298 $[M]^+$ (100), 283 (20), 255 (98), 57 (45); HREIMS *m/z* 298.1571 (calcd for $C_{19}H_{22}O_3$ 298.1569).

**Trigonostemon D (6):** cubic crystals (MeOH); $[\alpha]^{23}_D$ +174.3 (*c* 0.07, MeOH); UV (MeOH) $\lambda_{max}$ (log $\varepsilon$) 332 (3.73), 315 (3.78), 251 (3.59) nm; CD (MeOH) $\lambda_{max}$ ($\Delta\varepsilon$), 218 (−28.88), 271 (+4.43), 314 (+14.93) nm; IR (KBr) $\nu_{max}$ 3423, 1622, 1587, 1230, 1180, 1064, 827 $cm^{-1}$; $^1H$ and $^{13}C$ NMR data, see Tables 1 and 2; EIMS *m/z* 314 $[M]^+$ (70), 296 (24), 229 (100), 147 (18), 57 (26); HREIMS *m/z* 314.1513 (calcd for $C_{19}H_{22}O_4$ 314.1518).

**Trigonostemon E (7):** yellow powder; UV (MeOH) $\lambda_{max}$ (log $\varepsilon$) 409 (3.41), 256 (3.98) nm; IR (KBr) $\nu_{max}$ 3226, 1628, 1591, 1431, 1387, 1209, 1165, 1088, 866 $cm^{-1}$; $^1H$ and $^{13}C$ NMR data, see Tables 1 and 2; EIMS *m/z* 312 $[M]^+$ (43), 269 (26), 101 (75), 83 (100), 57 (34), 55 (84); HREIMS *m/z* 312.1367 (calcd for $C_{19}H_{20}O_4$ 312.1362).

**Trigonostemon F (8):** yellow needles (MeOH); mp 239.5−243.0 °C; UV (MeOH) $\lambda_{max}$ (log $\varepsilon$) 395 (3.37), 272 (3.72) nm; IR (KBr) $\nu_{max}$ 3265, 1687, 1612, 1504, 1452, 1333, 1159, 1103, 748 $cm^{-1}$; $^1H$ and $^{13}C$ NMR data, see Table 3; EIMS *m/z* 332 $[M]^+$ (100), 289 (62), 275 (41), 258 (25), 218 (25); HREIMS *m/z* 332.1169 (calcd for $C_{20}H_{16}N_2O_3$ 332.1161).

**X-ray Crystallographic Data for 1:** $C_{18}H_{22}O_2$, MW 270.36, orthorhombic space group $P2_12_12_1$, $a = 6.146$ Å, $b = 10.07240(10)$ Å, $c = 22.85000(10)$ Å, $V = 1418.694(15)$ Å$^3$, $Z = 4$, $d = 1.266$ g/cm$^3$;

$F(000) = 584$, $\mu = 0.632$ mm$^{-1}$. A single crystal of dimensions 0.40 × 0.35 × 0.30 mm$^3$ was used for X-ray measurements. The data collection was performed on a Gemini R Ultra diffractometer using Cu Kα radiation. Data were collected up to $\theta = 67.59°$ at 120 K. A total of 9178 reflections were collected, of which 2492 independent reflections were measured having an $R_{int}$ of 0.0146. Data collection and reduction was performed with Crysalis (Oxford Diffraction 2007). Crystal structure solution and refinement was achieved using direct methods as implemented in SHELXTL Version 6.10 (Sheldrick, University of Gottingen (Germany), 2000) and visualized using the XP program. A total of 188 parameters were refined using 2492 reflections with $F_o > 4\sigma(F_o)$, giving R1 = 0.0285, wR2 = 0.0757, goodness of fit 1.084, remaining difference electron density 0.180 and −0.190 e$^-$ Å$^{-3}$. The absolute structure was determined giving a Flack parameter of −0.03(19). CCDC 710198 contains the supplementary crystallographic data for this paper.

**X-ray Crystallographic Data for 6:** $C_{19}H_{22}O_4 \cdot H_2O$, MW 332.38, orthorhombic space group $P2_12_12$, $a = 20.00620(10)$ Å, $b = 9.31800(10)$ Å, $c = 9.34860(10)$ Å, $V = 1742.75(3)$ Å$^3$, $Z = 4$, $d = 1.267$ g/cm$^3$; $F(000) = 712$, $\mu = 0.745$ mm$^{-1}$. A single crystal of dimensions 0.50 × 0.25 × 0.20 mm$^3$ was used for X-ray measurements. The data collection was performed on a Gemini R Ultra diffractometer using Cu Kα radiation. Data were collected up to $\theta = 67.64°$ at 120 K. A total of 18 709 reflections were collected, of which 3086 independent reflections were measured having an $R_{int}$ of 0.0813. Data collection and reduction were performed with Crysalis (Oxford Diffraction, 2007). Crystal structure solution and refinement were achieved using direct methods as implemented in SHELXTL Version 6.10 (Sheldrick, University of Gottingen (Germany), 2000) and visualized using the XP program. A total of 237 parameters were refined using 3086 reflections with $F_o > 4\sigma(F_o)$, giving R1 = 0.0431, wR2 = 0.1071, goodness of fit 1.055, remaining difference electron density 0.249 and −0.328 e$^-$ Å$^{-3}$. The absolute structure was determined giving a Flack parameter of 0.01(15). CCDC 710199 contains the supplementary crystallographic data for this paper.

**X-ray Crystal Data for 8:** yellow, needles, $C_{20}H_{16}N_2O_3$, fw 332.35, orthorhombic, crystal size 0.193 × 0.122 × 0.119 mm$^3$, space group $P2_12_12$, $a = 9.2940(14)$ Å, $b = 11.4297(18)$ Å, $c = 15.266(2)$ Å, $V = 1621.6(4)$ Å$^3$, $Z = 4$, $D_{calcd} = 1.361$ g/cm$^3$; $F(000) = 696$, reflections collected 9639, reflection unique 2027 ($R_{int} = 0.0785$), final $R$ indices for $I > 2\sigma(I)$, R1 = 0.0451, wR2 = 0.0653, $R$ indices for all data R1 = 0.0798, wR2 = 0.0734, completeness to 2$\theta$ (27.00) 100.0%, maximum transmission 1.0000, minimum transmission 0.9031. The data collection was performed on a Bruker Smart Apex CCD diffractometer with graphite-monochromated Mo Kα radiation ($\lambda = 0.71073$ Å). The structure was solved by direct methods using the program SHELXS-97. Refinement method was full-matrix least-squares on $F^2$, and goodness-of-fit on $F^2$ is 0.876. The X-ray diffraction material has also been deposited in the Cambridge Crystallographic Data Center (CCCD No. 695260).

**Chemical Conversion of 1 to 4a and 2 to 1a.** Compound **1** (15 mg, 0.0556 mmol) was dissolved in 2 mL of dry pyridine; then 0.5 mL of acetic anhydride was added at room temperature. The reaction mixture was stirred for 3 h to produce **1a** (17 mg, 0.0545 mmol). After removal of solvent, **1a** (17 mg, 0.0545 mmol) was dissolved in 2 mL of $CH_2Cl_2$; then 80 mg of PCC and 80 mg of kieselguhr were added. The mixture was refluxed for 24 h at 60 °C. After workup, the crude reaction mixture was purified by PTLC (petroleum ether/acetone, 3:1) to afford **4a** (2 mg, 0.006 mmol). In the same way, compound **2** (20 mg, 0.075 mmol) was acetylated to **2a** (20 mg, 0.064 mmmol); then **2a** (20 mg, 0.064 mmol) was dissolved in 2 mL of $CH_2Cl_2$ and oxidized using 100 mg of PCC at room temperature for 1 h. The mixture was purified by PTLC (petroleum ether/acetone, 2:1) to afford **1a** (10 mg, 0.032 mmol).

**Conformational Analysis of Compound 3.** The absolute configuration of compound **3** was defined by comparison of quantum chemical TDDFT calculated and experimental ECD spectra. First, conformational analysis of **3** was carried out via Monte Carlo searching with the MMFF94 molecular mechanics force field using the SPARTAN 04 program.[13] The results showed two dominating lowest energy conformers (total Boltzmann distribution over 95%) for compound **3**. Subsequently, the two resulting conformations were reoptimized using DFT at the B3LYP/6-311++G (2d, 2p) level using the GAUSSIAN 03 program.[14] The B3LYP/6-311++G (2d, 2p) harmonic vibrational frequencies were further calculated to confirm their stability. The energies, oscillator strengths, and rotational strengths of the first 30 electronic excitations of the two conformers were calculated using the TDDFT methodology at the B3LYP/6-311++G (2d, 2p) level, and the ECD spectra were then simulated by the overlapping Gaussian function.[15] Finally, the simulated spectra of the two lowest energy conformations were averaged according to their relative Gibbs free energy ($\Delta G$) and the Boltzmann distribution theory (see Supporting Information). The experimental ECD and the calculated spectra both showed negative first, positive second, negative third, and positive fourth Cotton effects in the range 200−500 nm, which revealed the 5*S*-configuration for compound **3** (Figure 5).

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**Supporting Information Available:** $^1$H and $^{13}$C NMR and HMBC spectra for compounds **1**, **3**, **5**, **6**, **7**, and **8**, ROESY spectra for compounds **6** and **8**, NOE difference spectrum for compound **7**, structures of the known compounds **9**−**11**, and computational calculation data of compound **3** are available free of charge via the Internet at http://pubs.acs.org.

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