Asymmetric Total Syntheses and Biological Studies of Tuberostemoamide and Sessilifoliamide A

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I. General Information

All reactions were performed in oven-dried glassware fitted with rubber septa under an argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Methylene chloride (CH₂Cl₂) was distilled immediately before use from calcium hydride. Diethyl ether and tetrahydrofuran (THF) was distilled immediately before use from sodium-benzophenone ketyl. All other solvents were processed through the reference *Purification of Laboratory Chemicals (Seventh Edition)*. External bath temperatures were used to record all reaction temperatures. Silica gel (300~400 mesh) and petroleum ether, EtOAc, CH₂Cl₂ and MeOH are used for product purification by flash column chromatography. NMR spectra were recorded on Bruker 400 MHz (400 MHz for ¹H NMR and 101 MHz for ¹³C NMR) spectrometers. Proton chemical shifts are reported relative to a residual solvent peak (CDCl₃ at 7.26 ppm) and carbon chemical shifts are reported relative to a residual solvent peak (CDCl₃ at 77.0 ppm) in order to compare with natural products conveniently. The following abbreviations were used to designate multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = multiplet, br = broad. High-resolution mass spectra (HRMS) were measured on a BruckerDaltonics Apex II 47e Specification (for HRMS).

II. Experimental Procedures and Spectroscopic Data of Compounds

S1: To a stirred mixture of 8 (3.2 g, 14.0 mmol, 1.0 equiv) and 9 (4.4 g, 18.2 mmol, 1.3 equiv) in DMF (64.4 mL) was added KHMDS (1M in THF, 21.0 mL, 21.0 mmol, 1.5 equiv) at -15 °C under Ar atmosphere. The resulting mixture was stirred at that temperature for 40 min, and then was warmed to room temperature and stirred for another 3h. After quenching with aqueous saturated NH₄Cl solution (50 mL), diluted with water (200 mL), the organic layer was separated. Then the aqueous layer was extracted with EtOAc (3 × 50 mL) and the combined organic phase was washed with water (20 mL) and brine (3 × 15 mL), dried over anhydrous Na₂SO₄, filtered, and evaporated under vacuum. The residue so obtained was purified by flash column chromatography with EtOAc/petroleum ether (1:1) to give the TBS-ether product S1 (4.2 g, 87%) as a colorless oil. \([\alpha]_D^{23.5} +5.00 (c = 2.0 \text{ in CH}_2\text{Cl}_2)\) [Lit.¹ for the observed specific rotation of the compound with similar structure: \([\alpha]_D^{23.5} = +5.76 (c = 1.0 \text{ in CHCl}_3)\)]. ¹H NMR (400 MHz, CDCl₃) δ 4.36 (t, J = 5.2 Hz, 1H), 3.72 – 3.54 (m, 4H), 3.31 (s, 6H), 3.04 – 2.95 (m, 1H), 2.50 – 2.38 (m, 1H), 2.33 – 2.24 (m, 1H), 2.11 – 2.00 (m, 1H), 1.87 – 1.78 (m, 1H), 1.68 – 1.49 (m, 4H), 0.87 (s, 9H), 0.04 (d, J = 2.3 Hz, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 175.44, 104.22, 63.86, 58.84, 53.04, 52.91, 40.35, 30.43, 29.81, 25.74, 22.48, 21.48, 18.10. IR (KBr, ν / cm⁻¹) 2954, 2932, 2859, 1689, 1463, 1422, 1254, 1128, 1079. HRMS (ESI, m/z): [M + Na]⁺ calcd for C₁₇H₂₇NO₄SiNa⁺ 368.2228, found 368.2249.
(S)-1-(4,4-dimethoxybutyl)-5-(hydroxymethyl)pyrrolidin-2-one 7: The TBS-ether product (3.2 g, 9.3 mmol, 1 equiv) in THF (46.4 mL) was added TBAF (1M in THF, 10.2 mL, 10.2 mmol, 1.1 equiv) at 0 °C stirred for 10 min before stirred at room temperature for 2h. The mixture was directly purified by flash column chromatography with CH$_2$Cl$_2$/MeOH (30:1) to give 7 (1.83 g, 85%) as a colorless oil. \([\alpha]_D^{24.1} = +5.0 (c = 2.0 \text{ in CHCl}_3), \) [Lit.\(^1\) for the observed specific rotation of the compound with similar structure: \([\alpha]_D^{20} = +6.40 (c = 1.0 \text{ in CHCl}_3)]. \)\(^{1H} \text{NMR (400 MHz, CDCl}_3) \delta 4.34 (t, J = 5.1 \text{ Hz, } 1H), 3.82 – 3.75 (m, 1H), 3.69 – 3.52 (m, 3H), 3.29 (d, J = 2.1 \text{ Hz, } 6H), 3.07 – 2.98 (m, 1H), 2.50 – 2.38 (m, 1H), 2.33 – 2.22 (m, 1H), 2.11 – 2.00 (m, 1H), 2.00 – 1.90 (m, 1H), 1.66 – 1.45 (m, 4H). \(^{13}C \text{NMR (101 MHz, CDCl}_3) \delta 175.95, 104.12, 62.83, 59.10, 53.26, 52.87, 40.40, 30.46, 29.67, 22.46, 21.08. \) IR (KBr, \(\nu / \text{cm}^{-1}\)) 3401 (br), 2947, 2835, 1664, 1461, 1424, 1129, 1068. HRMS (ESI, m/z): [M + Na]\(^+\) calcd for C$_{11}$H$_{21}$NO$_3$Na$^+$ 254.1363, found 254.1367.

(S)-methyl 2-((1-(4,4-dimethoxybutyl)-5-oxopyrrolidin-2-yl)methylene)butanoate 10: To a stirred solution of oxalyl chloride (2.9 mL, 33.8 mmol, 2.6 equiv) in CH$_2$Cl$_2$ (32.5 mL) was slowly added DMSO (5.0 mL, 77.9 mmol, 6.0 equiv) at -78 °C and the solution was stirred for 10 min. A solution of 7 (3.0 g, 13.0 mmol, 1 equiv) in CH$_2$Cl$_2$ (26.0 mL) was added, and the mixture was stirred at the same temperature for 30 min. To this solution, Et$_3$N (13.5 mL, 103.9 mmol, 8.0 equiv) was added and stirred for another 10 min before quenched with H$_2$O. Subsequently, the mixture was warmed to room temperature and stirred for 5 min. The mixture was extracted with DCM (3 × 50 mL) and aqueous saturated NaCl solution (200 mL). The combined organic extracts were washed with brine (3 × 15mL), dried over Na$_2$SO$_4$, concentrated. Then the mixture was concentrated under reduced pressure and the crude S2 product was subjected to the Wittig reaction conditions as soon as possible without further purification by flash column chromatography. To a stirred solution of the crude aldehyde S2 in DCM (65.0 mL) was added methyl 2-(triphenylphosphoranylidene)butanoate reagent A (7.0 g, 19.5 mmol, 1.5 equiv), and the resulting mixture was stirred at room temperature for 12 h. Then the mixture was purified by flash column chromatography (petroleum ether/ EtOAc, 1:2) to give 10 (2.9 g, 72% for 2 steps) as a colorless oil. \([\alpha]_D^{22.2} = +10.00 (c = 3.0 \text{ in CHCl}_3), \) [Lit.\(^1\) for the observed specific rotation of the compound with similar structure: \([\alpha]_D^{20} = +5.30 (c = 0.9 \text{ in CHCl}_3)]. \)\(^{1H} \text{NMR (400 MHz, CDCl}_3) \delta 6.49 (d, J = 9.8 \text{ Hz, } 1H), 4.52 – 4.40 (m, 1H), 4.32 (t, J = 4.9 \text{ Hz, } 1H), 3.75 (s, 3H), 3.60 – 3.50 (m, 1H), 3.28 (s, 6H), 2.99 – 2.70 (m, 1H), 2.52 – 2.18 (m, 5H), 1.81 – 1.69 (m, 1H), 1.61 – 1.41 (m, 4H), 1.05 (t, J = 7.5 Hz, 3H). \(^{13}C \text{NMR (101 MHz, CDCl}_3) \delta 174.63, 167.26, 139.87, 136.65, 104.11, 55.34, 52.97, 52.93, 51.99, 40.63, 30.13, 29.79, 25.24, 22.51, 20.28, 14.50. \) IR (KBr, \(\nu / \text{cm}^{-1}\)) 2952, 2835, 1716, 1690, 1439, 1415, 1306, 1239, 1163, 1128, 1072, 1049. HRMS (ESI, m/z): [M + Na]\(^+\) calcd for C$_{16}$H$_{27}$NO$_3$Na$^+$ 336.1781, found 336.1762.
Table S1. Optimization of the reaction conditions to get Z isomer of 10

<table>
<thead>
<tr>
<th>entry</th>
<th>condition</th>
<th>yield</th>
<th>Z : E</th>
</tr>
</thead>
<tbody>
<tr>
<td>1[a]</td>
<td>reagent B (1.4 equiv), KHMDS (1.5 equiv), 18-crown-6 (7.0 equiv), THF, -78 °C</td>
<td>74%</td>
<td>61.3 : 28.7</td>
</tr>
<tr>
<td>2</td>
<td>reagent C (1.4 equiv), KHMDS (1.5 equiv), 18-crown-6 (7.0 equiv), THF, -78 °C</td>
<td>43%</td>
<td>26.9 : 73.1</td>
</tr>
<tr>
<td>3[b]</td>
<td>reagent C (1.4 equiv), NaH (1.4 equiv), THF, 0 °C</td>
<td>85%</td>
<td>94.6 : 5.4</td>
</tr>
</tbody>
</table>


S3: To a stirred solution of oxalyl chloride (1.5 mL, 16.9 mmol, 2.6 equiv) in CH₂Cl₂ (17 mL) was added DMSO (2.5 mL, 39 mmol, 6 equiv) at -78 °C and the solution was stirred for 10 min. A solution of 7 (1.5 g, 6.5 mmol, 1 equiv) in CH₂Cl₂ (13 mL) was added, and the mixture was stirred at the same temperature for 30 min. To this solution, Et₃N (6.7 mL, 52.0 mmol, 8.0 equiv) was added and stirred for another 5 min before quenched with H₂O. Subsequently, the mixture was warmed to room temperature and stirred for 10 min. The mixture was extracted with DCM and aqueous saturated NaCl solution. The combined organic extracts were washed with brine, dried over Na₂SO₄, concentrated. The residue was subjected to the modified Ando’s conditions as soon as possible after further purification by very flash column chromatography.

To a stirred solution of reagent C (3.3 g, 9.11 mmol, 1.4 equiv) in THF (45.6 mL) was added NaH (234 mg, 9.76 mmol, 1.5 equiv) at 0 °C. After being stirred for 15 min at this temperature, the above aldehyde S2 (1.5 g, 6.51 mmol, 1.0 equiv) was added to the mixture. Three hours later, the mixture was quenched with saturated aqueous NH₄Cl solution (20 mL) and diluted with water (100 mL), the organic layer was separated. Then the aqueous layer was extracted with EtOAc (3 × 40 mL), the combined organic phase was washed with brine (20 mL), dried over anhydrous Na₂SO₄, filtered, and evaporated under vacuum. The residue was purified by flash column chromatography (CH₂Cl₂ /MeOH = 30:1) to give product S3 (1.7 g, 82% for 2 steps) as a colorless oil. [α]D²⁴³ = +23.3 (c = 3.0 in CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃) δ 5.66 (d, J = 9.3 Hz, 1H), 4.95 – 4.79 (m, 1H), 4.33 (t, J = 4.8 Hz, 1H), 3.77 (s, 3H), 3.56 – 3.44 (m, 1H), 3.29 (s, 6H), 2.96 – 2.84 (m, 1H), 2.48 – 2.25 (m, 5H), 1.74 – 1.62 (m, 1H), 1.58 – 1.44 (m, 4H), 1.04 (t, J = 7.4 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 175.09, 167.95, 139.14, 137.12, 104.45, 56.57, 53.20, 53.02, 51.96, 40.94, 30.42, 30.11, 27.43, 25.74, 22.88, 13.41. IR (KBr, v /
Radical cyclization product 11a/11b: A mixture of 10 (2.2 g, 7.0 mmol, 1.0 equiv) and p-TsOH·H2O (532 mg, 2.8 mmol, 0.4 equiv) in acetone (46.7 mL) was stirred for 8 h at ambient temperature before quenching with aqueous saturated NaHCO3 solution (20 mL). The acetone was removed in vacuo, the residue was diluted with water (60 mL) and extracted with EtOAc (3 × 30 mL). The combined organic extracts were washed with with brine, dried over Na2SO4, filtered, concentrated and evaporated under vacuum. The residue so obtained was purified by flash column chromatography (EtOAc/petroleum ether = 20:1 → EtOAc) as soon as possible to give the aldehyde 6 (1.68 g, 90%).

To a stirred solution of the aldehyde 6 (1.21 g, 4.53 mmol, 1.0 equiv) in THF (157 mL) in the presence of MeOH (0.92 mL, 22.7 mmol, 5.0 equiv) was added SmI2 (0.1M in THF, 145 mL, 14.5 mmol, 3.2 equiv) at 0 °C under argon. After being stirred for 1 h at this temperature, the resulting mixture was quenched with saturated aqueous NH4Cl solution (400 mL). The organic layer was separated and the aqueous layer extracted with EtOAc (5 × 80 mL). The combined organic layers were washed with saturated aqueous Na2S2O3 (30 mL) and brine (3 × 20 mL), filtered, dried over Na2SO4, and evaporated. The residue was purified by flash column chromatography (EtOAc → EtOAc /MeOH = 5:1) to give products 11a/11b (654.9 mg, 61%) as white solids. CCDC 1874368 contains the supplementary crystallographic data of 11a/11b. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Plausible mechanism of SmI2-induced radical cyclization:

Although the precise reaction mechanism of SmI2-induced radical cyclization remained unclear, the observed stereoselectivity would be rationalized by assuming that: the first single-electron reduction of aldehyde 6 with SmI2 gives a ketyl radical (transition state I), then a facial selective 1,4-addition reaction of the newly formed radical proceeds to give transition state II. The radical in II is reduced by SmI2 again and then quenched by MeOH to give 11a or 11b. (see ref. Honda, T., Matsukawa, T. & Takahashi, K. Org. Biomol. Chem. 9, 673-675, (2011); Kimura, T. & Nakata, T. Tetrahedron: Asymmetry 21, 1389-1395, (2010); Wang, X. D., Wang, H. H., Wu, X., Yu, T. Q., Gao, W. W, Shi, T., Peng, X., He, D. & Wang, Z. Synlett 28, 1660-1662, (2017).)
(3aR,10aS)-1-ethyl-3a,4,5,6,10,10a-hexahydro-2H-furo[3,2-c]pyrrolo[1,2-a]azepine-2,8(9H)-dione 12: To a stirred solution of 11a/11b (1.62 g, 6.83 mmol, 1.0 equiv) in THF (68 mL) was added LiHMDS (1.0 in THF, 10.2 mL, 10.25 mmol, 1.5 equiv) at -78 °C under argon atmosphere. After being stirred at the same temperature for 1 h, N-bromosuccinimide (1.81 g, 10.25 mmol, 1.5 equiv) in THF (30 mL) was added. The resulting mixture was slowly warmed to room temperature. After being quenched with saturated aqueous NH₄Cl solution, the organic layer was separated and the aqueous layer extracted with EtOAc (3 × 60 mL). The combined organic layers were washed with brine, filtered and dried over Na₂SO₄, and concentrated under reduced pressure to leave the residue, which was then purified by column chromatography (EtOAc → CH₂Cl₂/MeOH = 30:1) to give the bromo intermediate. Then the intermediate was dissolved in toluene (136 mL) followed by a subsequent addition of 1,8-Diazabicyclo[5.4.0]undec-7-ene (3.12 g, 20.49 mmol, 3 equiv). After stirred at 80 °C for 2 h, the mixture was quenched with saturated aqueous NH₄Cl solution (100 mL). The organic layers were separated, and the aqueous layer was extracted with EtOAc (3 × 40 mL). The combined organic layer was washed with brine and dried over Na₂SO₄, filtered and concentrated under reduced pressure to leave a residue, which was subjected to column chromatography on silica gel (EtOAc → CH₂Cl₂/MeOH = 30:1) to afford 12 (1.36 g, 85% for two steps) as a white solid: mp 163–165 °C. (Lit.² 127–129 °C; Lit.³ 166–167 °C; Lit.⁴ 168–170 °C). [α]D²⁴ = -240.0 (c = 1.0 in CH₂Cl₂), [the observed specific rotation of the reported compound with similar structure: Lit.¹ [α]D = -204.0 (c = 0.4 in CHCl₃); Lit.² [α]D²⁷ = -246.3 (c = 0.63 in MeOH); Lit.⁴ [α]D²⁴ = -261.1 (c = 1.33 in MeOH); Lit.⁵ [α]D²⁷ = -261.1 (c = 0.33 in MeOH)). ¹H NMR (400 MHz, CDCl₃) δ 4.87 (dd, J = 11.6, 3.1 Hz, 1H), 4.79–4.73 (m, 1H), 4.31–4.22 (m, 1H), 2.56–2.44 (m, 5H), 2.35–2.23 (m, 2H), 1.92–1.60 (m, 3H), 1.38–1.22 (m, 1H), 1.14 (t, J = 7.6 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 174.14, 172.68, 164.18, 129.26, 80.88, 57.31, 43.32, 34.95, 30.13, 26.61, 25.62, 17.46, 12.55. IR (KBr, ν / cm⁻¹) 2939, 2881, 1750, 1690, 1444, 1415, 1359, 1320, 1258, 1163, 1109, 1027. HRMS (ESI, m/z): [M + Na]⁺ calcd for C₁₃H₁₇NO₃Na⁺ 258.1101, found 258.1105. CCDC 1874370 contains the supplementary crystallographic data of 12. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
Reduction of C=C bond in 12

![Chemical structures](image)

Table S2. Optimization of the Stereoselective Reduction of Double-Bond in Unsaturated Ester 12.

<table>
<thead>
<tr>
<th>entry</th>
<th>conditions[a]</th>
<th>4:11a ratio[b]</th>
<th>4/11a yield (%)[c]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NaBH₄, NiCl₂·6H₂O, r.t.</td>
<td>1.12 : 1</td>
<td>90</td>
</tr>
<tr>
<td>2</td>
<td>NaBH₄, NiCl₂·6H₂O, -30 °C</td>
<td>1.50 : 1</td>
<td>82</td>
</tr>
<tr>
<td>3</td>
<td>NaBH₄, anhydrous NiCl₂, -30 °C, 16h</td>
<td>1.92 : 1</td>
<td>57</td>
</tr>
<tr>
<td>4</td>
<td>NaBH₄, CuCl, r.t., 36h</td>
<td>N.R.[f]</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>NaBH₄, CeCl₃·7H₂O, r.t., 36h</td>
<td>N.R.[f]</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>Mg, 80 °C, 1 h</td>
<td>2.02 : 1</td>
<td>89</td>
</tr>
<tr>
<td>7</td>
<td>Mg, 40 °C, 2 h</td>
<td>2.18 : 1</td>
<td>99</td>
</tr>
<tr>
<td>8</td>
<td>Mg, 0 °C</td>
<td>2.80 : 1</td>
<td>83</td>
</tr>
<tr>
<td>9</td>
<td>Mg, -10 °C</td>
<td>3.30 : 1</td>
<td>99</td>
</tr>
<tr>
<td>10</td>
<td>Mg, -20 °C</td>
<td>3.7 : 1</td>
<td>99</td>
</tr>
<tr>
<td>11</td>
<td>Mg, -30 °C</td>
<td>6 : 1</td>
<td>99</td>
</tr>
<tr>
<td>12</td>
<td>Mg, -40 °C, 36h</td>
<td>10 : 1</td>
<td>99</td>
</tr>
<tr>
<td>13</td>
<td>Mg, -50 °C, 3 days</td>
<td>N.R.[f]</td>
<td>-</td>
</tr>
</tbody>
</table>

[a] Reactions were carried out in MeOH (0.05 M) at the indicated temperatures under argon atmosphere. [b] 10 equiv of NaBH₄ and 0.25 equiv NiCl₂·6H₂O or anhydrous NiCl₂ or CuCl or CeCl₃·7H₂O were used. [c] 30 equiv of Mg was used after washed with 3M HCl and sanded with sandpaper. [d] Determined by ¹H NMR spectroscopic analysis of the inseparable mixture of 4/11a after purification. [e] Yield of a pure mixture of 4/11a isolated by aqueous workup followed by flash silica column chromatography. [f] No consumption of 12 was observed.
Reduction of 12 using NaBH₄/ NiCl₂·6H₂O:

Butenolide 12 (517 mg, 2.20 mmol, 1 equiv) and NiCl₂·6H₂O (131 mg, 0.55 mmol, 0.25 equiv) was dissolved in anhyd MeOH (27.5 mL). After cooling to -30 °C, one portion of NaBH₄ (250 mg, 6.60 mmol, 3 equiv) was added. The resulting mixture was stirred at -30 °C for 20 min followed by addition of another portion of NaBH₄ (250 mg, 6.60 mmol, 3 equiv). After stirring at this temperature for 6 h, 1M HCl (30 mL) was added to quench the reaction, and continuously stirred until the solution became clear. Then MeOH was evaporated under reduced pressure. The aqueous layer was extracted with CH₂Cl₂ (3 × 20 mL) and the combined organic layers were washed with saturated aqueous NaHCO₃ solution (10 mL), dried (anhyd Na₂SO₄), filtered and concentrated. The residue was purified by silica column chromatography (CH₂Cl₂/MeOH = 15:1) to give 4 and 11a with a ratio of 1.5:1 (457 mg, 87.6 %). **ethylstenoamide 4 : mp 179-181 °C.** (mp of the reported compound with similar structure: Lit.¹ 184–185 °C; Lit.²–³ 187–188 °C; Lit.⁴ 186–187 °C; Lit.⁵ 181-183 °C; Lit.⁶ 185–186 °C; Lit.⁷ 185–186 °C; Lit.⁸ 190-191 °C; Lit.⁹ 182-183 °C; Lit.¹⁰ 190-191 °C). [α]D²³.⁹ = -160.0 (c = 1.0 in MeOH), [the observed specific rotation of the reported compound with similar structure: Lit.¹ [α]D²⁰ = -138.0 (c = 0.2 in MeOH); Lit.²–³ [α]D³⁰ = -219.3 (c = 0.5 in MeOH); Lit.⁴ [α]D⁵⁵ = -183.6 (c = 1.36 in MeOH); Lit.⁵ [α]D⁵⁷ = -151.58 (c = 0.46 in MeOH); Lit.⁶ [α]D²⁵ = -187.0 (c = 0.5 in MeOH); Lit.⁷ [α]D²⁵ = -191.6 (c = 0.5 in MeOH); Lit.⁸ [α]D³⁰ = -213.1 (c = 0.5 in MeOH); Lit.⁹ [α]D²⁰ = -141 (c = 0.3 in MeOH); Lit.¹⁰ [α]D²⁶ = -141 (c = 0.19 in MeOH) and -181 (c 0.89 in MeOH)).¹H NMR (400 MHz, CDCl₃) δ 4.22 – 4.07 (m, 2H), 4.05 – 3.94 (m, 1H), 2.71 – 2.61 (m, 1H), 2.57 – 2.45 (m, 2H), 2.44 – 2.32 (m, 3H), 2.07 – 1.99 (m, 1H), 1.93 – 1.80 (m, 2H), 1.78 – 1.47 (m, 4H), 1.03 (t, J = 7.5 Hz, 3H).¹³C NMR (101 MHz, CDCl₃) δ 176.86, 174.00, 77.34, 56.32, 50.16, 43.33, 40.19, 34.71, 30.57, 25.47, 22.78, 22.58, 11.35. IR (KBr, v / cm⁻¹) 2939, 2963, 2891, 1767, 1679, 1461, 1422, 1325, 1277, 1187, 1016. HRMS (ESI, m/z): [M + Na]⁺ calcd for C₁₉H₂₈NO₄Na⁺ 260.1257, found 260.1254. CCDC 1883782 contains the supplementary crystallographic data of 4. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

**9,10-bis-epi-ethylstenoamide 11a : mp 170-172 °C.** [α]D²³.⁷ = -150.0 (c = 1.0 in MeOH); [Lit.¹¹ for the observed specific rotation of the reported compound with similar structure: [α]D²¹ = -63.3 (c = 1.69 in MeOH)].¹H NMR (400 MHz, CDCl₃) δ 4.67 – 4.59 (m, 1H), 4.16 – 4.06 (m, 1H), 3.69 – 3.60 (m, 1H), 2.87 – 2.78 (m, 1H), 2.56 – 2.38 (m, 3H), 2.37 – 2.18 (m, 2H), 2.12 – 1.95 (m, 2H), 1.94 – 1.73 (m, 4H), 1.66 – 1.54 (m, 1H), 1.04 (t, J = 7.4 Hz, 3H).¹³C NMR (101 MHz, CDCl₃) δ 177.42, 174.68, 80.34, 58.86, 47.61, 46.02, 43.73, 29.82, 28.79, 24.68, 23.06, 22.24, 10.89. IR (KBr, v / cm⁻¹) 2935, 1765, 1679, 1461, 1426, 1385, 1286, 1260, 1187, 1139, 1016. HRMS (ESI, m/z): [M + Na]⁺ calcd for C₁₃H₁₈NO₄Na⁺ 260.1257, found 260.1262. CCDC 1883803 contains the supplementary crystallographic data of 11a. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
Reduction of 12 using Mg/MeOH:
To a stirred solution of butenolide 12 (240 mg, 1.02 mmol, 1 equiv) in anhyd MeOH (20.4 mL) was added Mg ribbon chips (734 mg, 30.6 mmol, 30 equiv) and the mixture was continually stirred at -40 °C. After 36h, the reaction was completed and 5 N HCl was added to quench the reaction and the aqueous layer, then MeOH was evaporated under reduced pressure. The aqueous layer was extracted with CH₂Cl₂ (3 × 20 mL), washed with brine, dried (anhyd Na₂SO₄) and concentrated. The residue was purified by silica column chromatography (CH₂Cl₂/MeOH = 15:1) to a mixture of give 4 and 11a with a ratio of 10:1 (239 mg, 99%).

Reduction of 12 using Pd/C catalyzed hydrogenation:
Butenolide 12 (340 mg, 1.45 mmol, 1 equiv) and 10% Pd/C (769 mg, 0.72 mmol, 0.5 equiv) were dissolved in anhyd MeOH (7.3 mL) and the mixture was continually stirred under hydrogen atmosphere (120 atm) at 70 °C for 5 days. Then the mixture was filtered, and the filtrate was evaporated under reduced pressure. The residue was directly purified by silica column chromatography (CH₂Cl₂/MeOH = 15:1) to a mixture of give 13 and 11a with a ratio of 1:1.2 (309 mg, 90%).

A mixture of 13 and 11a (309 mg, 1.31 mmol, 1.0 equiv) was dissolved in MeOH (13.1 mL), and treated with K₂CO₃ (1.8 g, 13.1 mmol, 10.0 equiv). The resulting reaction mixture was stirred at room temperature for 24 h and concentrated. The residue was then treated with water, neutralized with 10% aqueous HCl solution, and extracted with CH₂Cl₂ (3 × 20 mL). The organic layers were isolated, dried over anhydrous Na₂SO₄, and concentrated in vacuo. The residue was purified by flash column chromatography (CH₂Cl₂/MeOH = 15:1) to give 11a (263 mg, 85%) as the only detectable product.

Sessilifoliamide A 2: To a stirred solution of (R)-tert-butyl(4-iodo-2-methylbutoxy)diphenylsilane 14 (370 mg, 0.84 mmol, 2 equiv) in Et₂O (8 mL) was added t-BuLi (1.3 in pentane, 1.3 mL, 1.64 mmol, 3.9 equiv) dropwise at -78 °C and the solution was stirred at -78 °C for 15 min. The mixture was then warmed to -50 °C and stirred for another 15 min followed by addition of 4 (100 mg, 0.42 mmol, 1 equiv) in Et₂O and toluene (4.2 mL, V/V=1:5) at -78 °C. After stirring for 3 h, the reaction was quenched by saturated aqueous NH₄Cl solution (5 mL), then diluted with water (40 mL). The organic layer was separated and extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with brine, dried (anhyd Na₂SO₄) and concentrated. The residue was purified by silica column chromatography (petroleum ether/EtOAc = 1:1 → EtOAc) to give the protected product. To a solution of the above crude product in THF (2.1 mL) was added TBAF (1M in THF, 0.55 mL, 0.55 mmol, 1.3 equiv) in one portion at room temperature and the resultant mixture was stirred for 10 min. Directly purified by flash column chromatography on neutral silica gel (CH₂Cl₂/MeOH, 30:1→ 15:1) gave product 15.
Product 15, KBr (54.7 mg, 0.46 mmol, 1.1 equiv), NaHCO₃ (352.8 mg, 4.2 mmol, 10.0 equiv) and TEMPO (27 mg, 0.17 mmol, 0.4 equiv) was dissolved in DCM (4.2 mL) and stirred at 0 °C. Then to the mixture was added commercially available disinfectant NaOCl (0.12 mL, 1.68 mmol, 4 equiv). After stirring for another 15 min, the mixture was added NaOCl (0.12 mL, 1.68 mmol, 4 equiv) again and stirred for another 15 min followed by the last portion of NaOCl (0.06 mL, 0.84 mmol, 2 equiv). After stirring for 6 h, the aqueous layer was quenched with saturated aqueous Na₂SO₃ solution (5 mL), diluted with water (10 mL) and extracted with CH₂Cl₂ (3 × 10 mL). The combined organic layers were dried over Na₂SO₄ and concentrated. The residue was purified by silica column chromatography (CH₂Cl₂/MeOH, 30:1 → 15:1) to give a single natural product sessilifoliamide A 2 (93 mg, 72% for 3 steps) as a white solid. mp: 162-164 °C. (Lit.¹² 166-168 °C); [α]D²⁹ = −145.0 (c = 2.0 in CHCl₃); [Lit.¹² for the observed specific rotation of reported sessilifoliamide A: [α]D²⁹ = -128 (c = 0.35 in CHCl₃)). ¹H NMR (400 MHz, CDCl₃) δ 4.09 – 3.97 (m, 2H), 3.94 – 3.85 (m, 1H), 3.01 – 2.88 (m, 1H), 2.65 (t, J = 13.2 Hz, 1H), 2.57 – 2.48 (m, 1H), 2.44 – 2.31 (m, 3H), 2.14 – 2.06 (m, 1H), 2.03 – 1.91 (m, 3H), 1.77 – 1.66 (m, 2H), 1.66 – 1.42 (m, 4H), 1.26 (d, J = 7.2 Hz, 3H), 1.02 (t, J = 7.6 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 178.80, 173.86, 114.55, 79.75, 56.34, 52.02, 49.36, 40.25, 38.83, 36.09, 34.52, 30.76, 25.61, 22.10, 21.24, 15.17, 12.93. IR (KBr, v / cm⁻¹) 2932, 1774, 1687, 1459, 1422, 1323, 1275, 1202, 1170, 1139, 965, 924. HRMS (ESI, m/z): [M + Na⁺] calcd for C₁₇H₂₃NO₄Na⁺ 330.1676, found 330.1667. CCDC 1883815 contains the supplementary crystallographic data of 2. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

13-epi-sessilifoliamide A 20: To a stirred solution of (S)-tert-butyl(4-iodo-2-methylbutoxy)diphenylsilane 17 (184 mg, 0.42 mmol, 2 equiv) in Et₂O (4 mL) was added t-BuLi (1.3M in pentane, 0.63 mL, 0.82 mmol, 3.9 equiv) dropwise at -78 °C and the solution was stirred at -78 °C for 15 min. The mixture was then warmed to -50 °C and stirred for another 15 min followed by addition of 4 (50 mg, 0.21 mmol, 1 equiv) in Et₂O and toluene (2.1 mL, V/V=1:5) at -78 °C. After stirring for 3 h, saturated aqueous NH₄Cl solution was employed to quench the reaction and EtOAc was used to extract the aqueous layer. The combined organic layers were washed with brine, dried (anhyd Na₂SO₄) and concentrated. The residue was purified by silica column chromatography (petroleum ether/EtOAc = 1:1 → EtOAc) to give the protected product, THF (1.1 mL) solution of which was added TBAF (1M in THF, 0.27 mL, 0.27mmol, 1.3 equiv) in one portion at room temperature and the resultant mixture was stirred for 10 min. Directly silica flash chromatography (CH₂Cl₂/MeOH, 30:1 → 15:1) gave product 18.

Product 18, KBr (27.5 mg, 0.23mmol, 1.1 equiv), NaHCO₃ (176 mg, 2.1 mmol, 10 equiv) and TEMPO (13 mg, 0.08 mmol, 0.4 equiv) was dissolved in DCM (2.1 mL) and stirred at 0 °C. Then to the mixture was added commercially available disinfectant NaClO (0.06 mL, 0.84 mmol, 4 equiv). After stirring for another 15 min, the mixture was added NaClO (0.06 mL, 0.84 mmol, 4 equiv) again and stirred for another 15 min followed by the
last portion of NaClO (0.03 mL, 0.42 mmol, 2 equiv). After stirring for 6 h, the aqueous layer was quenched with saturated aqueous Na₂S₂O₃ solution and extracted with CH₂Cl₂. The combined organic layers were washed with brine, dried over Na₂SO₄ and concentrated. The residue was purified by silica column chromatography (CH₂Cl₂/MeOH, 30:1 →15:1) to give lactonization products 19 (42 mg, 65% for 3 steps) as a colorless solid. mp: 148-150 °C. (Lit₁² 166-168 °C); [α]₁₀¹°D = -122.0 (c = 5.0 in CHCl₃); [Lit.₁² for the observed specific rotation of reported sessilifoliamide A: [α]²⁷ = -128 (c = 0.35 in CHCl₃)). ¹H NMR (400 MHz, CDCl₃) δ 4.09 – 3.88 (m, 3H), 2.78 – 2.61 (m, 2H), 2.59 – 2.49 (m, 2H), 2.45 – 2.35 (m, 2H), 2.18 – 2.10 (m, 1H), 2.03 – 1.93 (m, 3H), 1.78 – 1.66 (m, 2H), 1.65 – 1.42 (m, 4H), 1.36 (d, J = 7.4 Hz, 3H), 1.02 (t, J = 7.6 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 178.63, 173.84, 115.92, 79.98, 56.34, 51.75, 50.74, 40.28, 37.93, 36.10, 35.78, 30.78, 25.64, 22.11, 20.98, 17.39, 12.92. IR (KBr, ν / cm⁻¹) 2961, 2917, 2853, 1769, 1687, 1459, 1422, 1321, 1273, 1204, 960, 923. HRMS (ESI, m/z): [M + Na]⁺ calcd for C₁₇H₂₅NO₄Na⁺ 330.1676, found 330.1680. CCDC 1883806 contains the supplementary crystallographic data of 19. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif

Table S3. Optimization of the acid-catalyzed chiral inversion of spirocenter in sessilifoliamide 2.

<table>
<thead>
<tr>
<th>entry</th>
<th>conditions</th>
<th>result[a]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>TFA, DCM, 0 °C</td>
<td>trace</td>
</tr>
<tr>
<td>2</td>
<td>TFA, DCM, r.t.</td>
<td>trace</td>
</tr>
<tr>
<td>3</td>
<td>TFA, DCM, 40 °C</td>
<td>trace</td>
</tr>
<tr>
<td>4</td>
<td>(R)-reagent D, DCM, r.t.</td>
<td>trace</td>
</tr>
<tr>
<td>5</td>
<td>(R)-reagent D, DCM, 40 °C</td>
<td>trace</td>
</tr>
<tr>
<td>6</td>
<td>(S)-reagent D, DCM, 40 °C</td>
<td>trace</td>
</tr>
<tr>
<td>7</td>
<td>(R)-reagent E, toluene, 40 °C</td>
<td>trace</td>
</tr>
<tr>
<td>8</td>
<td>(S)-reagent E, toluene, 40 °C</td>
<td>trace</td>
</tr>
<tr>
<td>9</td>
<td>MgSO₄, toluene, 80 °C</td>
<td>slow degradation</td>
</tr>
<tr>
<td>10</td>
<td>ZnCl₂, DCM, r.t.</td>
<td>slow degradation</td>
</tr>
<tr>
<td>11</td>
<td>AcOH[b]</td>
<td>trace</td>
</tr>
<tr>
<td>12</td>
<td>PPTS</td>
<td>trace</td>
</tr>
<tr>
<td>13</td>
<td>p-TsOH, DCM, r.t.</td>
<td>trace</td>
</tr>
<tr>
<td>14</td>
<td>CSA, DCM, r.t.</td>
<td>&lt;5%</td>
</tr>
</tbody>
</table>

[a] Reactions was obtained by ¹HNMR.

[b] directly used as solvent.
11-epi-Sessilifoliamide A 16: To a stirred solution of sessilifoliamide A 2 (110 mg, 0.36 mmol, 1.0 equiv) in CH2Cl2 (5 mL) was added camphorsulfonic acid (CSA) (16 mg, 0.072 mmol, 0.2 equiv) and the solution was stirred at room temperature for 12 h. Then the mixture was quenched with saturated aqueous NaHCO3 solution (10 mL) and extracted with CH2Cl2 (3 × 8 mL). The combined organic layers were washed with brine, dried over Na2SO4 and concentrated. The residue was purified by silica column chromatography (EtOAc /petroleum ether = 10:1 → EtOAc) to give 16 (3.3 mg, 3%, 25% brsm, brsm = based on recovered starting material) as a amorphous solid and the recovered 2 (97 mg, 88%) was. mp: 156-158 °C. (Lit.12 166-168 °C): [α]D22.2 = −132.0 (c = 2.0 in CHCl3); [Lit.12 for the observed specific rotation of reported sessilifoliamide A: [α]D = −128 (c = 0.35 in CHCl3)).1H NMR (400 MHz, CDCl3) δ 4.15 – 4.06 (m, 1H), 4.03 – 3.89 (m, 2H), 2.77 – 2.51 (m, 3H), 2.43 – 2.30 (m, 2H), 2.27 – 2.14 (m, 2H), 2.13 – 1.88 (m, 4H), 1.83 – 1.68 (m, 2H), 1.59 – 1.37 (m, 4H), 1.29 – 1.24 (m, 2H), 0.97 (t, J = 7.3 Hz, 3H).13C NMR (101 MHz, CDCl3) δ 178.43, 174.43, 116.33, 78.50, 57.47, 53.62, 50.00, 40.31, 35.84, 35.61, 34.22, 30.69, 25.65, 25.50, 22.81, 16.91, 11.68. IR (KBr, ν / cm−1): 2967, 2941, 2879, 1776, 1687, 1459, 1422, 1323, 1273, 911. HRMS (ESI, m/z): [M + Na]+ calcd for C17H25NO4Na+ 330.1676, found 330.1682.

11,13-bis-epi-sessilifoliamide A 20: To a stirred solution of 19 (220 mg, 0.72 mmol, 1 equiv) in CH2Cl2 (7.2 mL) was added trifluoromethanesulfonic acid (TFA) (22 mg, 0.14 mmol, 0.2 equiv) and the solution was stirred at room temperature for 2 h. Then the mixture was quenched with saturated aqueous NaHCO3 solution and extracted with CH2Cl2 (3 × 20 mL). The combined organic layers were washed with brine, dried over Na2SO4 and concentrated. The residue was purified by silica column chromatography (EtOAc /petroleum ether = 10:1 → EtOAc) to give 20 (134.8 mg, 61%, 87% brsm) as a white solid and the recovered 19 (65 mg, 30%). mp: 150-152 °C. (Lit.12 166-168 °C): [α]D22.2 = −135.0 (c = 2.0 in CHCl3); [Lit.12 for the observed specific rotation of reported sessilifoliamide A: [α]D = −128 (c = 0.35 in CHCl3)).1H NMR (400 MHz, CDCl3) δ 4.13 – 4.06 (m, 1H), 3.99 – 3.88 (m, 2H), 3.01 – 2.86 (m, 1H), 2.66 (t, J = 12.7 Hz, 1H), 2.42 – 2.29 (m, 3H), 2.26 – 2.15 (m, 2H), 2.13 – 1.92 (m, 4H), 1.81 – 1.71 (m, 2H), 1.61 – 1.35 (m, 2H), 1.30 – 1.16 (m, 4H), 0.97 (t, J = 7.3 Hz, 3H).13C NMR (101 MHz, CDCl3) δ 178.52, 174.41, 114.81, 78.11, 57.49, 53.71, 49.11, 40.27, 37.72, 34.93, 34.09, 30.66, 25.64, 24.85, 22.76, 14.82, 11.58. IR (KBr, ν / cm−1): 2967, 2941, 2879, 1776, 1687, 1452, 1422, 1321, 1295, 1273, 1251, 1215, 1165, 1137, 1049, 1019, 960, 919. HRMS (ESI, m/z): [M + Na]+ calcd for C17H25NO4Na+ 330.1676, found 330.1673. CCDC 1883804 contains the supplementary crystallographic data of 20. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
Tuberostemoamide 1 : To a stirred solution of 2 or 19 (950 mg, 3.09 mmol, 1.0 equiv) in THF (31 mL) was added LiHMDS (1.0 in THF, 4.64 mL, 4.64 mmol, 1.5 equiv) at -78 °C. After being stirred at the same temperature for 1h, N-bromosuccinimide (821 mg, 4.64 mmol, 1.5 equiv) in THF (14 mL) was added. The resulting mixture was stirred for another 4h at -30 oC, then warmed to room temperature and stirred for 10 min. After being quenched with saturated aqueous NH₄Cl solution and extracted with EtOAc (3 × 50 mL), the organic layer was washed with brine and dried over Na₂SO₄, and concentrated under reduced pressure to leave the residue, which was then purified by column chromatography (EtOAc → CH₂Cl₂/MeOH = 30:1) to give the bromo intermediate. Then the bromo intermediate was dissolved in toluene (62 mL) followed by a subsequent addition of 1,8-Diazabicyclo[5.4.0]undec-7-ene (1.41 g, 9.27 mmol, 3.0 equiv). After stirred at 80 °C for 2 h, the mixture was quenched with saturated aqueous NH₄Cl solution and the organic layer was separated. Then the aqueous layer was extracted with EtOAc (3 × 50 mL) and the combined organic phase was washed with brine, dried over anhydrous Na₂SO₄, filtered, and evaporated under vacuum. which was subjected to column chromatography on silica gel (EtOAc → CH₂Cl₂/MeOH = 30:1) to afford tuberostemoamide 1 (754 mg, 80% for 2; 707 mg, 75% for 19) as a white solid. mp: 150-152 °C. (Lit. 13-14 155-157 °C); [α]D24.8° = −90.0 (c = 0.08 in MeOH); [Lit. 13-14 for the observed specific rotation of reported tuberostemoamide]: [α]D = -94 (c = 0.06 in MeOH). ¹H NMR (400 MHz, CDCl₃) δ 6.65 (q, J = 1.4 Hz, 1H), 4.11 – 3.97 (m, 3H), 2.77 – 2.57 (m, 2H), 2.44 – 2.36 (m, 2H), 2.19 – 2.11 (m, 2H), 2.04 – 1.96 (m, 1H), 1.94 (d, J = 1.6 Hz, 3H), 1.81 – 1.59 (m, 3H), 1.54 – 1.34 (m, 3H), 0.89 (t, J = 7.6 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 173.73, 171.18, 143.87, 134.05, 113.53, 80.60, 56.02, 51.69, 49.56, 40.18, 35.68, 30.66, 25.48, 21.99, 20.19, 12.82, 10.50. IR (KBr, ν / cm⁻¹) 3055, 2926, 2855, 1765, 1681, 1459, 1446, 1321, 1265, 973, 874, 736, 703. HRMS (ESI, m/z): [M + Na]⁺ calcd for C₁₁H₂₃NO₄Na⁺ 328.1519, found 328.1527. CCDC 1874369 contains the supplementary crystallographic data of 1. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
**11-epi-tuberostemoamide 21:** To a stirred solution of 20 (475 mg, 1.55 mmol, 1.0 equiv) in THF (15 mL) was added LiHMDS (1.0 in THF, 2.33 mL, 2.33 mmol, 1.5 equiv) at -78 °C. After being stirred at the same temperature for 1h, N-bromosuccinimide (415 mg, 2.33 mmol, 1.5 equiv) in THF (7 mL) was added. The resulting mixture was stirred for another 4h at - 30 °C, then warmed to room temperature and stirred for 10 min. After being quenched with saturated aqueous NH₄Cl solution and extracted with EtOAc, the organic layer was washed with brine and dried over Na₂SO₄, and concentrated under reduced pressure to leave the residue, which was then purified by column chromatography (EtOAc → CH₂Cl₂/MeOH = 30:1) to give the bromo intermediate. Then the bromo intermediate was dissolved in toluene (30 mL) followed by a subsequent addition of 1,8-Diazabicyclo[5.4.0]undec-7-ene (707 mg, 4.65 mmol, 3.0 equiv). After stirred at 80 °C for 2 h, the mixture was quenched with saturated aqueous NH₄Cl solution and the organic layer was separated. Then the aqueous layer was extracted with EtOAc (3 × 50 mL) and the combined organic phase was washed with water (20mL) and brine (3 × 15 mL), dried over anhydrous Na₂SO₄, filtered, and evaporated under vacuum. which was subjected to column chromatography on silica gel (EtOAc → CH₂Cl₂/MeOH = 30:1) to afford 21 (345 mg, 73%) as a white solid. mp: 147-149 °C. (Lit.¹³-¹⁴ 155-157 °C); [α]D²⁴.⁷ = −101.0 (c = 0.08 in MeOH); [Lit.¹³-¹⁴ for the observed specific rotation of reported tuberostemoamide: [α]D = −94 (c = 0.06 in MeOH)]. ¹H NMR (400 MHz, CDCl₃) δ 6.76 (q, J = 1.7 Hz, 1H), 4.16 – 4.08 (m, 2H), 3.99 – 3.91 (m, 1H), 2.66 (m, 1H), 2.42 – 2.32 (m, 3H), 2.26 – 2.16 (m, 2H), 2.10 – 1.92 (m, 5H), 1.71 – 1.35 (m, 5H), 0.93 (t, J = 7.4 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 174.29, 170.89, 142.39, 133.72, 114.15, 80.58, 57.18, 54.55, 50.92, 40.29, 34.38, 30.61, 26.43, 25.54, 22.87, 12.15, 10.63. IR (KBr, v / cm⁻¹) 2933, 2874, 1765, 1687, 1448, 1422, 1318, 1293, 1273, 1172, 1103, 1023, 993, 956, 926, 760. HRMS (ESI, m/z): [M + Na]⁺ caleed for C₁₇H₂₅NO₄Na⁺ 328.1519, found 328.1533. CCDC 1883814 contains the supplementary crystallographic data of 21. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

**Transformation of Tuberostemoamide (1) to sessilifoliamide A (2):** Tuberostemoamide 1 (12 mg, 0.0393 mmol, 1.0 equiv) was dissolved in EtOAc (1 mL) and 10% Pd/C (12.5 mg, 0.0118 mmol, 0.3 equiv) was added under argon atmosphere, then argon was replaced with H₂ (in a balloon). The reaction mixture was stirred at room temperature for 12 h. After completion of the reaction, H₂ atmosphere was removed. The mixture was passed through Celite-sintered glass funnel, and the filtrate was evaporated under reduced pressure. The residue was directly purified by silica column chromatography (CH₂Cl₂/MeOH = 15:1) to give a mixture of sessilifoliamide A 2 and its epimer 13-epi-sessilifoliamide A 19 with a ratio of 5.5: 1 (10.9 mg, 90%).

According to the experimental results in Mg/MeOH reduction, we considered that the mechanism of the reduction process may be as follows (Scheme S1): compound 12 suffered from two subsequent reduction reactions by Mg and formed anion S6. S6 could spontaneously maintain the thermodynamically more stable configuration under thermodynamic control, then the thermodynamically more stable configuration of S6 was quenched by proton arised from MeOH to give two isomers S7 and S8 with a certain degree of stereoselectivity. When the temperature was lower, the above mentioned proton quench process was prior to be under kinetic control to give the kinetically more stable configuration S7 as the major product, while S8 as the minor product. So C9 position was not only under thermodynamic control but also under kinetic control. With stereochemistry at C9 determined, 4 and 11a with the determined stereochemistry at C10 were respectively obtained as the only product of the stereoselective proton quench of S7 and S8 under thermodynamic control. In other words, C10 position was under thermodynamic control.

Based on the experimental results in NaBH₄/NiCl₂•6H₂O reduction, we considered that the mechanism of the reduction process may be as follows (Scheme S2): hydrogen anion was added to C9 position with a certain degree of stereoselectivity to afford two enol anions S9 and S10. When the temperature was lower, the above
mentioned proton quench process was prior to be under kinetic control to give the kinetically more stable configuration S9 as the major product, while S10 as the minor product. The two enol anions were then suffered from the similar process as those of S7 and S8 to respectively give product 4 and 11a as the single product. As analyzed above, the whole processes in both NaBH₄/NiCl₂•6H₂O and Mg/MeOH reduction were greatly similar to each other, and the mechanism was stereoselective hydrogen addition one by one to the C=C bond. In conclusion, C9 position may be not only under thermodynamic but also under kinetic control; in the premise that stereochemistry of C9 was confirmed, C10 position may be under thermodynamic control, only in this way could a single product with the thermodynamically most stable configuration be obtained in the last quench step.

On the basis of the experimental result in Pd/C reduction, we considered that the mechanism of the reduction process may be as follows (Scheme S3): under catalysis of Pd/C, cis-hydrogenation from the least hindered back face of C=C bond in 12 was happened to form 9-epi-ethylstemoamide 13. 13 was then transformed into 9,10-bis-epi-ethylstemoamide 11a under this harsh condition, which led to the consequence that a mixture of 13 and 11a with a ratio of 1:1.2 was considered as the ultimate product of Pd/C catalyzed hydrogenation. The facile epimerization at C10 of 13 to 11a is in good accordance with the fact that α-Me isomer is thermodynamically more stable than β-Me isomer (MM2 calculations) in the synthesis of 9,10-bis-epi-stemoamide.⁴ Different from the one by one hydrogen addition to the C=C bond, Pd/C catalyzed hydrogenation was a facial selective cis-addition of a pair of hydrogens to the least hindered α-face of C=C bond, so the process was under kinetic control.

### Scheme S3. Proposed Mechanism for Pd/C catalyzed hydrogenation

![Scheme S3](image-url)
IV. Comparison of NMR of Natural and Synthetic Tuberoestemoamide, Sessilifoliamide A and Their Epimers.

Table S4. Comparison of $^1$H NMR data assignment of natural and synthetic sessilifoliamide A (2).

<table>
<thead>
<tr>
<th>$^1$H position</th>
<th>Natural $^{2,\text{a, c}}$</th>
<th>Synthetic $^{2,\text{b, c}}$ (deviation)$^{2,\text{d, e}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.67 (m)</td>
<td>1.66 – 1.42 (m)</td>
</tr>
<tr>
<td></td>
<td>1.98 (m)</td>
<td>2.03 – 1.91 (m)</td>
</tr>
<tr>
<td>2</td>
<td>2.37 (m)</td>
<td>2.44 – 2.31 (m)</td>
</tr>
<tr>
<td></td>
<td>2.64 (brt, 12.4)</td>
<td>2.65 (t, 13.2)</td>
</tr>
<tr>
<td>5</td>
<td>3.61 (brd, 14.0)</td>
<td><strong>3.94 – 3.85 (m)</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(-0.33 – 0.24)</td>
</tr>
<tr>
<td>6</td>
<td>1.44 (m)</td>
<td>1.66 – 1.42 (m)</td>
</tr>
<tr>
<td></td>
<td>1.69 (m)</td>
<td>1.77 – 1.66 (m)</td>
</tr>
<tr>
<td>7</td>
<td>1.53 (m)</td>
<td>1.77 – 1.66 (m)</td>
</tr>
<tr>
<td></td>
<td>2.09 (m)</td>
<td>2.14 – 2.06 (m)</td>
</tr>
<tr>
<td>8</td>
<td>3.90 (dd, 2.6, 9.9, 10.6)</td>
<td>4.09 – 3.97 (m)</td>
</tr>
<tr>
<td>9</td>
<td>2.52 (m)</td>
<td>2.57 – 2.48 (m)</td>
</tr>
<tr>
<td>9a</td>
<td>4.00 (m)</td>
<td>4.09 – 3.97 (m)</td>
</tr>
<tr>
<td>10</td>
<td>1.93 (m)</td>
<td>2.03 – 1.91 (m)</td>
</tr>
<tr>
<td></td>
<td>1.97 (m)</td>
<td>2.03 – 1.91 (m)</td>
</tr>
<tr>
<td>12</td>
<td>2.36 (m)</td>
<td>2.44 – 2.31 (m)</td>
</tr>
<tr>
<td></td>
<td>2.93 (m)</td>
<td>3.01 – 2.88 (m)</td>
</tr>
<tr>
<td>13</td>
<td>2.93 (m)</td>
<td>3.01 – 2.88 (m)</td>
</tr>
<tr>
<td>15</td>
<td>1.25 (d, 7.2)</td>
<td>1.26 (d, 7.2)</td>
</tr>
<tr>
<td></td>
<td>1.56 (m)</td>
<td>1.66 – 1.42 (m)</td>
</tr>
<tr>
<td>17</td>
<td>1.01 (t, 7.7)</td>
<td>1.02 (t, 7.6)</td>
</tr>
</tbody>
</table>

$^a$ Recorded in CDCl$_3$, 300 MHz. $^b$ Recorded in CDCl$_3$, 400 MHz. $^c$ Multiplicity and $J$ values in Hz are given in parentheses. $^d$ Deviations (given in parentheses) = Natural - Synthetic. $^e$ Distinct $^1$H NMR deviations was marked with red.
Table S5. Comparison of $^1$H NMR data assignment of natural and synthetic sessilifoliamide A (2) and its epimers.

<table>
<thead>
<tr>
<th>$^1$H Position</th>
<th>Natural $^{2,5}$ (deviation)$^{6,5}$</th>
<th>Synthetic $^{2,5}$ (deviation)$^{6,5}$</th>
<th>Synthetic $^{16,5}$ (deviation)$^{6,5}$</th>
<th>Synthetic $^{19,5}$ (deviation)$^{6,5}$</th>
<th>Synthetic $^{20,5}$ (deviation)$^{6,5}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>2.64 (brt, 12.4)</td>
<td>2.65 (t, 13.2)</td>
<td>2.77 – 2.51 (m)</td>
<td>2.78 – 2.61 (m)</td>
<td>2.66 (t, 12.7)</td>
</tr>
<tr>
<td></td>
<td>3.61 (brd, 14.0)</td>
<td>(−0.48 ~ −0.36)</td>
<td>4.03 – 3.89 (m)</td>
<td>(−0.42 ~ −0.28)</td>
<td>3.99 – 3.87 (m)</td>
</tr>
<tr>
<td>15</td>
<td>1.25 (d, 7.2)</td>
<td>1.26 (d, 7.2)</td>
<td>1.59 – 1.37 (m)</td>
<td>1.36 (d, 7.4)</td>
<td>1.29 – 1.17 (m)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(−0.34 ~ −0.12)</td>
<td></td>
<td>(−0.11)</td>
</tr>
</tbody>
</table>

$^a$ Recorded in CDCl$_3$, 300 MHz. $^b$ Recorded in CDCl$_3$, 400 MHz. $^c$ Multiplicity and J values in Hz are given in parentheses. $^d$ Deviations (given in parentheses) = Natural - Synthetic. $^e$ Distinct $^1$H NMR deviations was marked with red.

Comparison of $^1$H NMR spectra of synthetic sessilifoliamide A (2) and its epimers.
Table. S6 Comparison of $^{13}$C NMR data assignment of natural and synthetic sessilifoliamide A (2) and its epimers.

<table>
<thead>
<tr>
<th>$^{13}$C position</th>
<th>Natural 2 $^a$</th>
<th>Synthetic 2 $^b$ (deviation) $^{c,d}$</th>
<th>Synthetic 16 $^b$ (deviation) $^{c,d}$</th>
<th>Synthetic 19 $^b$ (deviation) $^{c,d}$</th>
<th>Synthetic 20 $^b$ (deviation) $^{c,d}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>22.1</td>
<td>22.1 (0)</td>
<td>25.5 (-3.4)</td>
<td>22.1 (0)</td>
<td>24.9 (-2.8)</td>
</tr>
<tr>
<td>2</td>
<td>30.8</td>
<td>30.8 (0)</td>
<td>30.7 (+0.1)</td>
<td>30.8 (0)</td>
<td>30.7 (+0.1)</td>
</tr>
<tr>
<td>3</td>
<td>174.0</td>
<td>173.9 (+0.1)</td>
<td>174.4 (-0.4)</td>
<td>173.8 (+0.2)</td>
<td>174.4 (-0.4)</td>
</tr>
<tr>
<td>5</td>
<td>40.3</td>
<td>40.3 (0)</td>
<td>40.3 (0)</td>
<td>40.3 (0)</td>
<td>40.3 (0)</td>
</tr>
<tr>
<td>6</td>
<td>25.6</td>
<td>25.6 (0)</td>
<td>25.7 (-0.1)</td>
<td>25.6 (0)</td>
<td>25.6 (0)</td>
</tr>
<tr>
<td>7</td>
<td>36.1</td>
<td>36.1 (0)</td>
<td>35.6 (+0.5)</td>
<td>36.1 (0)</td>
<td>34.9 (+1.2)</td>
</tr>
<tr>
<td>8</td>
<td>79.7</td>
<td>79.8 (-0.1)</td>
<td>78.5 (+1.2)</td>
<td>80.0 (-0.3)</td>
<td>78.1 (+1.6)</td>
</tr>
<tr>
<td>9</td>
<td>52.0</td>
<td>52.0 (0)</td>
<td>53.6 (-1.6)</td>
<td>51.8 (+0.2)</td>
<td>53.7 (-1.7)</td>
</tr>
<tr>
<td>9a</td>
<td>56.4</td>
<td>56.3 (+0.1)</td>
<td>57.5 (-1.1)</td>
<td>56.3 (+0.1)</td>
<td>57.5 (-1.1)</td>
</tr>
<tr>
<td>10</td>
<td>49.4</td>
<td>49.4 (0)</td>
<td>50.0 (-0.6)</td>
<td>50.7 (-1.3)</td>
<td>49.1 (+0.3)</td>
</tr>
<tr>
<td>11</td>
<td>114.6</td>
<td>114.6 (0)</td>
<td>116.3 (-1.7)</td>
<td>115.9 (-1.3)</td>
<td>114.8 (-0.2)</td>
</tr>
<tr>
<td>12</td>
<td>38.9</td>
<td>38.8 (+0.1)</td>
<td>35.8 (+3.1)</td>
<td>37.9 (-1.0)</td>
<td>37.7 (+1.2)</td>
</tr>
<tr>
<td>13</td>
<td>34.5</td>
<td>34.5 (0)</td>
<td>34.2 (+0.3)</td>
<td>35.5 (-1.0)</td>
<td>34.1 (+0.4)</td>
</tr>
<tr>
<td>14</td>
<td>178.8</td>
<td>178.8 (0)</td>
<td>178.4 (+0.4)</td>
<td>178.6 (+0.2)</td>
<td>178.5 (+0.3)</td>
</tr>
<tr>
<td>15</td>
<td>15.2</td>
<td>15.2 (0)</td>
<td>16.9 (-1.7)</td>
<td>17.4 (-2.2)</td>
<td>14.8 (+0.4)</td>
</tr>
<tr>
<td>16</td>
<td>21.2</td>
<td>21.2 (0)</td>
<td>22.8 (-1.6)</td>
<td>21.0 (+0.2)</td>
<td>22.8 (-1.6)</td>
</tr>
<tr>
<td>17</td>
<td>12.9</td>
<td>12.9 (0)</td>
<td>11.7 (+1.2)</td>
<td>12.9 (0)</td>
<td>11.6 (+1.3)</td>
</tr>
</tbody>
</table>

$^a$ Recorded in CDCl$_3$, 300 MHz. $^b$ Recorded in CDCl$_3$, 400 MHz. $^c$ Deviations (given in parentheses) = Natural − Synthetic. $^d$ Deviations exceeding 0.2 were marked with red. $^e$ Multiplicity and $J$ values in Hz are given in parentheses. $^f$ Distinct $^1$H NMR deviations of characteristic positions were marked with red.
Comparison of $^{13}$C NMR spectra of synthetic sessilifoliamide A (2) and its epimers.
Table S7. Comparison of $^{13}$C NMR data assignment of tuberostemoamide (1) and its epimers.

<table>
<thead>
<tr>
<th>$^{13}$C Position</th>
<th>Natural 1&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Synthetic 1&lt;sup&gt;b&lt;/sup&gt; (deviation)&lt;sup&gt;4,†&lt;/sup&gt;</th>
<th>Synthetic 21&lt;sup&gt;b&lt;/sup&gt; (deviation)&lt;sup&gt;4,†&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>34.6</td>
<td>30.7 (4.9)&lt;sup&gt;g&lt;/sup&gt;</td>
<td>30.6 (4.0)</td>
</tr>
<tr>
<td>2</td>
<td>35.7</td>
<td>35.7 (0)</td>
<td>34.4 (1.3)</td>
</tr>
<tr>
<td>3</td>
<td>173.8</td>
<td>173.7 (0.1)</td>
<td>174.3 (-0.5)</td>
</tr>
<tr>
<td>5</td>
<td>40.2</td>
<td>40.2 (0)</td>
<td>40.3 (-0.1)</td>
</tr>
<tr>
<td>6</td>
<td>22.0</td>
<td>22.0 (0)</td>
<td>25.5 (-3.5)</td>
</tr>
<tr>
<td>7</td>
<td>25.5</td>
<td>25.5 (0)</td>
<td>26.4 (-0.9)</td>
</tr>
<tr>
<td>8</td>
<td>80.6</td>
<td>80.6 (0)</td>
<td>80.6 (0)</td>
</tr>
<tr>
<td>9</td>
<td>49.6</td>
<td>49.6 (0)</td>
<td>50.9 (-1.3)</td>
</tr>
<tr>
<td>9a</td>
<td>56.1</td>
<td>56.0 (0.1)</td>
<td>57.2 (-1.1)</td>
</tr>
<tr>
<td>10</td>
<td>51.7</td>
<td>51.7 (0)</td>
<td>54.6 (-2.9)</td>
</tr>
<tr>
<td>11</td>
<td>113.5</td>
<td>113.5 (0)</td>
<td>114.2 (-0.7)</td>
</tr>
<tr>
<td>12</td>
<td>143.9</td>
<td>143.9 (0)</td>
<td>142.4 (+1.5)</td>
</tr>
<tr>
<td>13</td>
<td>134.0</td>
<td>134.1 (-0.1)</td>
<td>133.7 (+0.3)</td>
</tr>
<tr>
<td>14</td>
<td>171.1</td>
<td>171.2 (-0.1)</td>
<td>170.9 (+0.2)</td>
</tr>
<tr>
<td>15</td>
<td>10.4</td>
<td>10.5 (-0.1)</td>
<td>10.6 (-0.2)</td>
</tr>
<tr>
<td>16</td>
<td>20.2</td>
<td>20.2 (0)</td>
<td>22.9 (-2.7)</td>
</tr>
<tr>
<td>17</td>
<td>12.7</td>
<td>12.8 (-0.1)</td>
<td>12.2 (+0.5)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Recorded in CDCl<sub>3</sub>, 300 MHz.  
<sup>b</sup> Recorded in CDCl<sub>3</sub>, 400MHz.  
<sup>c</sup> Multiplicity and $J$ values in Hz are given in parentheses.  
<sup>d</sup> Deviations (given in parentheses) = Natural - Synthetic.  
<sup>†</sup> Distinct $^1$H NMR deviations of characteristic positions were marked with red.  
<sup>‡</sup> $^{13}$C NMR deviations exceeding 0.2 were marked with red.  
<sup>g</sup> We are especially grateful to Prof. Wenhan Lin for providing the original $^{13}$C NMR spectrum of tuberostemoamide (1) when our work was about to be submitted. We found that $^{13}$C NMR spectrum of our synthetic sample was in good accordance with the original spectrum of the natural sample, maybe the wrong $^{13}$C NMR data at C1 position in reported literature was caused by writing error.
Comparison of $^1$H NMR spectra of tuberostemoamide (1) and its epimers.
Comparison of $^{13}$C NMR of tuberostemoamide (1) and its epimers.
V. $^1$H and $^{13}$C NMR Spectra of Compounds

$^1$H NMR Spectrum of S1 (400 MHz, CDCl$_3$)

![NMR Spectrum Diagram]

[Diagram showing NMR spectrum of S1 with peak assignments and chemical shifts]
$^{13}$C NMR Spectrum of S1 (101 MHz, CDCl$_3$)
$^1$H NMR Spectrum of 7 (400 MHz, CDCl$_3$)

[Image of the NMR spectrum with peaks at various ppm values]
$^{13}$C NMR Spectrum of 7 (101 MHz, CDCl$_3$)
$^1$H NMR Spectrum of 10 (400 MHz, CDCl$_3$)
\[ ^{13}\text{C} \text{NMR Spectrum of 10 (101 MHz, CDCl}_3) \]
$^1$H NMR Spectrum of S3 (400 MHz, CDCl$_3$)

S3
Z isomer of 10
$\text{C NMR Spectrum of S3 (101 MHz, CDCl}_3$)

S3
Z isomer of 10
$^{1}H$ NMR Spectrum of 12 (400 MHz, CDCl$_3$)
$^{13}$C NMR Spectrum of 12 (101 MHz, CDCl$_3$)
$^1$H NMR Spectrum of 4 (400 MHz, CDCl$_3$)
$^{13}$C NMR Spectrum of 4 (101 MHz, CDCl$_3$)
$^1$H NMR Spectrum of 11a (400 MHz, CDCl$_3$)

![NMR Spectra](image)
\(^{13}\)C NMR Spectrum of 11a (101 MHz, CDCl\(_3\))

11a
$^1$H NMR Spectrum of 2 (400 MHz, CDCl$_3$)

2: sessilifoliamide A
$^{13}$C NMR Spectrum of 2 (101 MHz, CDCl$_3$)

2: sessilifoliamide A
$^1$H NMR Spectrum of 19 (400 MHz, CDCl$_3$)

19: 13-epi-sessilifoliamide A
$^{13}$C NMR Spectrum of 19 (101 MHz, CDCl$_3$)

19: 13-epi-sessilfoliamide A
$^1$H NMR Spectrum of 16 (400 MHz, CDCl$_3$)

\[ \text{16: 11-epi-sessilifoliamide A} \]
$^{13}$C NMR Spectrum of 16 (101 MHz, CDCl$_3$)

16: 11-epi-sessilifoliamide A
$^1$H NMR Spectrum of 20 (400 MHz, CDCl$_3$)

H$_2$C

20: 11,13-bisepi-sessilifoliamide A
$^{13}$C NMR Spectrum of 20 (101 MHz, CDCl$_3$)

20: 11,13-bisepi-sessilifoliamide A
$^1$H NMR Spectrum of 1 (400 MHz, CDCl$_3$)
$^{13}$C NMR Spectrum of 1 (101 MHz, CDCl$_3$)

1: tuberostemoamide
21: 11-epi-tuberostemoamide

$^1$H NMR Spectrum of 21 (400 MHz, CDCl$_3$)
13C NMR Spectrum of 21 (101 MHz, CDCl₃)

21: 11-epi-tuberosethoamide
VI. Biological Studies

Employing the developed synthetic technologies in this research program, we were able to evaluate biological activities of several compounds (1, 2, 4, 12, 11a, 19, 20, 21) possessed the similar 5/7/5 tricycle-skeleton with stemoamide (5).

In Vitro Cytotoxicity Assay.

Anti-proliferative activities against HepG2, SMMC-7721, LoVo, HL-60 and WI38 cell lines were determined by MTT method (Table S8). Except the compound 20, which exhibited potential anti-proliferative activity on HepG2 cell line (IC$_{50}$ = 99.02 ± 3.60 μM), other seven compounds showed nearly no toxicities to all other tumor cell lines and normal cell line (all IC$_{50}$ > 200 μM).

Cells were plated in 96-well microtiter plates at a density of 5×10^4/well and incubated in a humidified atmosphere with 5% CO$_2$ at 37 °C for 24 h. Tested compounds were added onto triplicate wells with different concentrations and 0.1% DMSO for the control. After they had been incubated for 24 h, 10 μL of MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) solution (5 mg/mL) was added to each well, and the plate was incubated for an additional 4 h. The formazan was dissolved in 100 μL of DMSO. All experiments were performed three times.

Table S8. In vitro antiproliferative activity of selected compounds and DDP.

<table>
<thead>
<tr>
<th>Compd.</th>
<th>IC$_{50}$<a href="%CE%BCM">a</a></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HePG2</td>
</tr>
<tr>
<td>1</td>
<td>&gt;200</td>
</tr>
<tr>
<td>2</td>
<td>&gt;200</td>
</tr>
<tr>
<td>4</td>
<td>&gt;200</td>
</tr>
<tr>
<td>12</td>
<td>&gt;200</td>
</tr>
<tr>
<td>11a</td>
<td>&gt;200</td>
</tr>
<tr>
<td>19</td>
<td>&gt;200</td>
</tr>
<tr>
<td>20</td>
<td>99.02±3.60</td>
</tr>
<tr>
<td>21</td>
<td>&gt;200</td>
</tr>
<tr>
<td>DDP</td>
<td>25.56±2.79</td>
</tr>
</tbody>
</table>

[a] Results expressed as the mean ± SD deviation of at least three separate determinations. DDP = cis-dichlorodiammine platinum.

Cholinesterase Inhibitory Assays

In addition of the anti-proliferative activity, Stemonaceae plants also have acetylcholinesterase (AChE) inhibitory activities and anti-inflammatory activities. Unfortunately, the selected compounds showed no any EeAChE inhibitory activities (all IC$_{50}$ > 250 μM) (Table S9). Inhibitory activity studies on butyrylcholinesterase (eqBChE) demonstrated that 11,13-bis-epi-sessilifoliamide A (20) showed selective inhibitory activity on eqBChE (IC$_{50}$ = 26.42 ± 3.43 μM) (Table S9). Plots of initial velocity versus enzyme concentration (Figure S1) revealed that 20 may be the reversible inhibitor of eqBChE. Thus, 11,13-bis-epi-sessilifoliamide A 20 was expected to be a potential drug for treatment of neurodegenerative diseases after further modification.
Acetylthiocholine iodide, butyrylthiocholine iodide and 5,5-dithiobis-(2-nitrobenzoic) acid (DTNB) were purchased from Sigma Aldrich. EeAChE (E.C. 3.1.1.7, type V-S, purified from E. electricus) and eqBuChE (E.C. 3.1.1.8, purified from equine serum) were diluted in 20 mM HEPES buffer pH 7.2-7.4, phosphate buffer pH 7.4 such as to have enzyme solution with 0.25 units/mL enzyme activity. In the procedure, 25 μL of compound solution (10×final concentration) or 25 μL of sodium phosphate buffer (pH 7.2-7.4) were added to plate wells containing 10 μL of enzyme (0.01-0.05 IU/mL final) and 65 μL of sodium phosphate buffer (pH 7.2-7.4). After 10 min of preincubation, 100 μL of 0.3 mM DTNB dissolved in phosphate buffer (pH 7.2-7.4) and 50μL of substrate (acetylthiocholine or butyrylthiocholine iodide, 1 mM final) were added and the plate was read at 405 nm for 10 min. All experiments were run in triplicate and performed at least twice. Tested compounds were dissolved at 0.1 M in DMSO and diluted in phosphate buffer to the required concentrations just before use. Galanthamine was used as reference standard. The final concentrations of DMSO (<0.4% v.v.) did not affect enzyme activity.

Table S9. Inhibitory activity of all selected compounds on butyrylcholinesterase.

<table>
<thead>
<tr>
<th>Compound</th>
<th>EqBuChEIC₅₀ (μM)</th>
<th>Compound</th>
<th>EeAChEIC₅₀ (μM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&gt;250</td>
<td>1</td>
<td>&gt;250</td>
</tr>
<tr>
<td>2</td>
<td>&gt;250</td>
<td>2</td>
<td>&gt;250</td>
</tr>
<tr>
<td>4</td>
<td>&gt;250</td>
<td>4</td>
<td>&gt;250</td>
</tr>
<tr>
<td>12</td>
<td>&gt;250</td>
<td>12</td>
<td>&gt;250</td>
</tr>
<tr>
<td>11a</td>
<td>&gt;250</td>
<td>11a</td>
<td>&gt;250</td>
</tr>
<tr>
<td>19</td>
<td>&gt;250</td>
<td>19</td>
<td>&gt;250</td>
</tr>
<tr>
<td>20</td>
<td>26.42±3.43</td>
<td>20</td>
<td>&gt;250</td>
</tr>
<tr>
<td>21</td>
<td>&gt;250</td>
<td>21</td>
<td>&gt;250</td>
</tr>
<tr>
<td>Galanthamine</td>
<td>2.82±0.03</td>
<td>Galanthamine</td>
<td>0.14±0.01</td>
</tr>
</tbody>
</table>

Figure. S1. Plots of initial velocity versus enzyme concentration for the inhibition activity of compound 20 on the hydrolysis of butyrylcholinesterase

Anti-inflammatory assay

The inhibitory effects of the synthetic compounds on LPS-induced pro-inflammatory mediators, including NO, TNF-α, and IL-6 production in RAW264.7 macrophage were then studied. On the basis of determining the effective concentrations of anti-inflammatory tests, LPS-activated macrophages were applied to evaluate the anti-inflammatory activities. As shown in Figure S2, all tested compounds attenuated the production of
LPS-induced pro-inflammatory mediators in RAW264.7 macrophage. Among them, compound 2 inhibited the release of NO, TNF-α, and IL-6. These results suggested that the anti-inflammation activity in vitro of Stemonaceae plants probably was accomplished by the decreased release of NO, TNF-α and IL-6, and the activities of epimers were different from each other and sessilifoliamide A (2) may be a part of the anti-inflammatory substances in Stemonaceae plants.

(1) Cell viability

In order to obtain more accurate results of anti-inflammatory experiments, eliminate the effects of cell death caused by tested compounds on the results as far as possible, macrophages were exposed for 24 h to the selected compounds (12.5, 25, 50, 100 and 200 μM), then the cell viability was measured using MTT method. As shown in Figure S3, none of the tested compounds at concentrations ranging from 12.5 μM to 200μM had any significant effect on cell viability, this also suggested the compounds at the range of 12.5-50 μM are acceptable and effective in anti-inflammatory tests.

Figure S2. The effect of some selected compounds on lipopolysaccharide (LPS)-induced NO, TNF-α, and IL-6 production in RAW264.7 macrophage. Each bar represents the mean ± SD of three independent experiments. # p< 0.05, ** p < 0.01 vs. control. * p < 0.05, ** p < 0.01, vs. LPS-treated cells.

Figure S3. Effect of selected compounds on cell viability. Data represent percent viability as mean ± SD of 3 replicates per concentration of each compound.

(2) NO production assay

Nitrite level, an index for NO production, was measured in the supernatant of RAW264.7 cells by the Griess method.²¹ RAW264.7 cells were inoculated to 6-well plates at the density of 5×10⁵ cells per well and cultured...
for 18 h. Different compounds were added to each well, to which was additionally added LPS (1000 ng/mL) and incubated at 37 °C for 24 h. After stimulated for 24 h by LPS, the supernatant of the cell culture medium and the same volume of Griess reagent (1% sulfanilamide and 0.1% naphthyl ethylenediamine dihydrochloride in 5% phosphoric acid) were added to a 96-well plate for 10 min, and nitrite was measured at 540 nm (OD₅₄₀) using a microplate reader (Bio-Rad Laboratories, CA, USA). Meanwhile, the results were evaluated from three independent experiments.

(3) Cytokines Measurement

Production of the pro-inflammatory cytokines was evaluated by an enzyme-linked immunosorbent assay (ELISA). RAW264.7 cells (5 x 10⁵ cells/well) were pretreated with or without compounds in 6-well plates and the cells were stimulated with 1000 ng/mL LPS at the same time then cultured for 24 h to assay TNF-α and IL-6 production. The levels of TNF-α, IL-6 in cell culture supernatant were measured using a specific ELISA kit (TNF-α: Elabscience, E-EL-M0959c; IL-6: Shanghai Enzyme-linked Biotechnology Co., Ltd, ml063160) according to the manufacturer's instructions, and were read at 450 nm (OD₄₅₀) in a microplate reader. LPS was used as the positive control in parallel experiments. The results were calculated from two independent experiments.
VII. Reference

VIII. A Map Of Structural relationship of Some Stemona Alkaloids

After carefully analyzing the structures of stemoamide-group alkaloids, we think there are highly structural correlations among them. Stemoamide and ethylstemoamide may be the main parent molecules of them and may play significant roles in accomplishing possible biotransformations of more stemoamide-group alkaloids.

**Figure S4.** “Stemoamide type” stemoamide-group alkaloids.

**Figure S5.** “Ethylstemoamide type” stemoamide-group alkaloids.
Crystal Data and Cif Check Report for compound 11a/11b (CCDC: 1874368)

11a: R=α-H
11b: R=β-H

ORTEP of 11a/11b
checkCIF/PLATON report

Structure factors have been supplied for datablock(s) wangzhen-02

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No syntax errors found. CIF dictionary Interpreting this report

Datablock: wangzhen-02

Bond precision: C-C = 0.0052 Å Wavelength=1.5418 Å

Cell: a=11.9688(7) b=8.2429(5) c=13.4357(10)
alpha=90 beta=110.327(8) gamma=90

Temperature: 295 K

Calculated Reported
Volume 1242.99(15) 1242.98(15)
Space group P 21/c P 1 21/c 1
Hall group -P 2ybc -P 2ybc
Moiety formula C13 H19 N O3 C13 H19 N O3
Sum formula C13 H19 N O3 C13 H19 N O3
Mr 237.29 237.29
Dx,g cm-3 1.268 1.268
Z 4 4
Mu (mm-1) 0.729 0.729
F000 512.0 512.0
F000’ 513.58
h,k,lmax 14,9,15 14,9,15
Nref 2190 2183
Tmin,Tmax 0.877,0.916 0.576,1.000
Tmin’ 0.877

Correction method= # Reported T Limits: Tmin=0.576 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.997 Theta(max)= 66.590
R(reflections)= 0.0890(1903) wr2(reflections)= 0.2779(2183)
S = 1.105 Npar= 182

The following ALERTS were generated. Each ALERT has the format test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.
Alert level C

The maximum difference density is > 0.1*ZMAX*0.75
The relevant atom site should be identified.

DIFMX02_ALERT_1_C  The maximum difference density is > 0.1*ZMAX*0.75
PLAT084_ALERT_3_C  High wR2 Value (i.e. > 0.25) ................. 0.28 Report
PLAT097_ALERT_2_C  Large Reported Max. (Positive) Residual Density 0.71 eA-3
PLAT234_ALERT_4_C  Large Hirshfeld Difference C1 --C2  0.16 Ang.
PLAT241_ALERT_2_C  High ‘MainMol’ Ueq as Compared to Neighbors of
                   O2 Check
PLAT241_ALERT_2_C  High ‘MainMol’ Ueq as Compared to Neighbors of
                   C1 Check
PLAT241_ALERT_2_C  High ‘MainMol’ Ueq as Compared to Neighbors of
                   C7 Check
PLAT242_ALERT_2_C  Low ‘MainMol’ Ueq as Compared to Neighbors of
                   C6 Check
PLAT242_ALERT_2_C  Low ‘MainMol’ Ueq as Compared to Neighbors of
                   C9 Check
PLAT242_ALERT_2_C  Low ‘MainMol’ Ueq as Compared to Neighbors of
                   C11 Check
PLAT260_ALERT_2_C  Large Average Ueq of Residue Including
                   O1  0.082 Check
PLAT340_ALERT_3_C  Low Bond Precision on C-C Bonds .............. 0.00525 Ang.
PLAT360_ALERT_2_C  Short C(sp3)-C(sp3) Bond C7 - C8  1.40 Ang.
PLAT411_ALERT_2_C  Short Inter H...H Contact H2BA ..H8A  2.02 Ang.
                   x,-1/2-y,1/2+z = 4_556 Check
PLAT790_ALERT_4_C  Centre of Gravity not Within Unit Cell: Resd. #
                   1 Note
                   C13 H19 N O3
PLAT906_ALERT_3_C  Large K Value in the Analysis of Variance ...... 3.405 Check
PLAT911_ALERT_3_C  Missing FCF Refl Between Thmin & STh/L= 0.595 7 Report
PLAT913_ALERT_3_C  Missing # of Very Strong Reflections in FCF .... 5 Note

Alert level G

PLAT003_ALERT_2_G  Number of Uiso or Uij Restrained non-H Atoms ... 5 Report
PLAT072_ALERT_2_G  SHELXL First  Parameter in WGHT Unusually Large 0.16 Report
PLAT186_ALERT_4_G  The CIF-Embedded .res File Contains ISOR Records 1 Report
PLAT230_ALERT_2_G  Hirshfeld Test Diff for O2 --C4  5.2 s.u.
PLAT230_ALERT_2_G  Hirshfeld Test Diff for C1 --C2B  6.3 s.u.
PLAT300_ALERT_4_G  Atom Site Occupancy of C2 Constrained at 0.5 Check
PLAT300_ALERT_4_G  Atom Site Occupancy of C2B Constrained at 0.5 Check
PLAT300_ALERT_4_G  Atom Site Occupancy of C3 Constrained at 0.5 Check
PLAT300_ALERT_4_G  Atom Site Occupancy of C3B Constrained at 0.5 Check
PLAT300_ALERT_4_G  Atom Site Occupancy of C4 Constrained at 0.55 Check
PLAT300_ALERT_4_G  Atom Site Occupancy of C4B Constrained at 0.45 Check
PLAT300_ALERT_4_G  Atom Site Occupancy of H1AA Constrained at 0.5 Check
PLAT300_ALERT_4_G  Atom Site Occupancy of H1AB Constrained at 0.5 Check
PLAT300_ALERT_4_G  Atom Site Occupancy of H1AC Constrained at 0.5 Check
PLAT300_ALERT_4_G  Atom Site Occupancy of H2 Constrained at 0.5 Check
PLAT300_ALERT_4_G  Atom Site Occupancy of H2B Constrained at 0.5 Check
PLAT300_ALERT_4_G  Atom Site Occupancy of H2BC Constrained at 0.5 Check
PLAT300_ALERT_4_G  Atom Site Occupancy of H3A Constrained at 0.5 Check
PLAT300_ALERT_4_G  Atom Site Occupancy of H3B Constrained at 0.5 Check
PLAT300_ALERT_4_G  Atom Site Occupancy of H4 Constrained at 0.55 Check
PLAT300_ALERT_4_G  Atom Site Occupancy of H4B Constrained at 0.45 Check
PLAT300_ALERT_4_G  Atom Site Occupancy of H5A Constrained at 0.55 Check
PLAT300_ALERT_4_G  Atom Site Occupancy of H5B Constrained at 0.45 Check
PLAT301_ALERT_3_G  Main Residue Disorder ..............(Resd 1 ) 18% Note
PLAT720_ALERT_4_G  Number of Unusual/Non-Standard Labels ........ 8 Note
PLAT779_ALERT_4_G  Model has Chirality at C4 (Centro SPGR) R Verify
PLAT779_ALERT_4_G  Model has Chirality at C6 (Centro SPGR) S Verify
PLAT779_ALERT_4_G  Model has Chirality at C10 (Centro SPGR) R Verify
PLAT779_ALERT_4_G  Model has Chirality at C4B (Centro SPGR) S Verify
PLAT860_ALERT_3_G  Number of Least-Squares Restraints ............ 30 Note
PLAT909_ALERT_3_G  Percentage of I>2sig(I) Data at Theta(Max) Still 72% Note
PLAT910_ALERT_3_G  Missing # of FCF Reflection(s) Below Theta(Min). 1 Note
It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

**Publication of your CIF in IUCr journals**

A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica, Journal of Applied Crystallography, Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *ICrData*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

**Publication of your CIF in other journals**

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

**PLATON version of 06/01/2019; check.def file version of 19/12/2018**
Crystal Data and Cif Check Report for Compound 12
(CCDC: 1874370)
checkCIF/PLATON report

Structure factors have been supplied for datablock(s) wangzhen-04

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No syntax errors found.  

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Wavelength=1.5418 Å

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b=10.7437(17) Å  
c=16.569(2) Å  
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|--------|

Temperature:  295 K

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Hall group | P 2ac 2ab  
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Sum formula | C13 H17 N O3  
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Dx, g cm⁻³ | 1.285  
Z          | 4  
Mu (mm⁻¹) | 0.745  
F000      | 504.0  
F000'     | 505.58  
h,k,lmax | 8,12,19  
Nref      | 2146[ 1267]  
Npar       | 155  
Tmin, Tmax | 0.875, 0.901  
Tmin'     | 0.855  
AbsCorr   | MULTI-SCAN  
Correction method= #  
Reported  
T Limits:  Tmin=0.494  
Tmax=1.000  
Data completeness= 1.68/0.99  
Theta(max)= 66.579  
R(reflections)= 0.0503( 1784)  
wR2(reflections)= 0.1397( 2129)  
S = 1.074  

The following ALERTS were generated. Each ALERT has the format  
test-name_ALERT_alert-type_alert-level.  
Click on the hyperlinks for more details of the test.
Alert level C

PLAT241_ALERT_2_C High ‘MainMol’ Ueq as Compared to Neighbors of C9 Check
PLAT340_ALERT_3_C Low Bond Precision on C-C Bonds ............... 0.00575 Ang.
PLAT790_ALERT_4_C Centre of Gravity not Within Unit Cell: Resd. # C13 H17 N O3 Check
PLAT911_ALERT_3_C Missing FCF Refl Between Thmin & STh/L= 0.595 10 Report
PLAT978_ALERT_2_C Number C-C Bonds with Positive Residual Density. 0 Info

Alert level G

PLAT032_ALERT_4_G Std. Uncertainty on Flack Parameter Value High . 0.300 Report
PLAT398_ALERT_2_G Deviating C-O-C Angle From 120 for O2 109.3 Degree
PLAT791_ALERT_4_G Model has Chirality at C4 (Chiral SPGR) S Verify
PLAT791_ALERT_4_G Model has Chirality at C8 (Chiral SPGR) R Verify
PLAT909_ALERT_3_G Percentage of I>2sig(I) Data at Theta(Max) Still 58% Note
PLAT916_ALERT_2_G Hooft y and Flack x Parameter Values Differ by . 0.15 Check
PLAT933_ALERT_2_G Number of OMIT Records in Embedded .res File ... 1 Note

0 ALERT level A = Most likely a serious problem - resolve or explain
0 ALERT level B = A potentially serious problem, consider carefully
5 ALERT level C = Check. Ensure it is not caused by an omission or oversight
7 ALERT level G = General information/check it is not something unexpected

0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
5 ALERT type 2 Indicator that the structure model may be wrong or deficient
3 ALERT type 3 Indicator that the structure quality may be low
4 ALERT type 4 Improvement, methodology, query or suggestion
0 ALERT type 5 Informative message, check

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

Publication of your CIF in IUCr journals

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Publication of your CIF in other journals

Please refer to the Notes for Authors of the relevant journal for any special instructions relating to CIF submission.
Crystal Data and Cif Check Report for ethylstemoamide (4) (CCDC: 1883782)
checkCIF/PLATON report

Structure factors have been supplied for datablock(s) 20181123_houysh_chon01_0m_a

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No syntax errors found. CIF dictionary Interpreting this report

Datablock: 20181123_houysh_chon01_0m_a

Bond precision:  C-C = 0.0017 A  Wavelength=1.54178

Cell:  a=7.7654(2)  b=12.3880(3)  c=24.3967(7)
       alpha=90  beta=90  gamma=90

Temperature:  150 K

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AbsCorr = MULTI-SCAN

Data completeness= 1.000  Theta(max)= 66.586

R(reflections)= 0.0337( 1957)  wr2(reflections)= 0.0836( 2083)

S = 1.054  Npar= 155

The following ALERTS were generated. Each ALERT has the format test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.
**Alert level G**

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<td>Percentage of I&gt;2sig(I) Data at Theta(Max) Still 92% Note</td>
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<td>PLAT913_ALERT_3_G</td>
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0 ALERT level A = Most likely a serious problem - resolve or explain
0 ALERT level B = A potentially serious problem, consider carefully
8 ALERT level G = General information/check it is not something unexpected

1 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
1 ALERT type 2 Indicator that the structure model may be wrong or deficient
2 ALERT type 3 Indicator that the structure quality may be low
4 ALERT type 4 Improvement, methodology, query or suggestion
0 ALERT type 5 Informative message, check

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF.

CheckCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

**Publication of your CIF in IUCr journals**

A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (Acta Crystallographica, Journal of Applied Crystallography, Journal of Synchrotron Radiation); however, if you intend to submit to Acta Crystallographica Section C or E or IUCrData, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

**Publication of your CIF in other journals**

Please refer to the Notes for Authors of the relevant journal for any special instructions relating to CIF submission.

**PLATON version of 06/01/2019; check.def file version of 19/12/2018**
Crystal Data and Cif Check Report for 9,10-bis-epi-ethylstemoamide (11a) (CCDC: 1883803)

11a: 9,10-bis-epi-ethylstemoamide

ORTEP of 11a
checkCIF/PLATON report

Structure factors have been supplied for datablock(s) 20181122_houysh_chon07_0m_a

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No syntax errors found. CIF dictionary Interpreting this report

Datablock: 20181122_houysh_chon07_0m_a

Bond precision: C-C = 0.0032 Å Wavelength=1.54178

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Hall group: -P 2ybc -P 2ybc

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Sum formula: C13 H19 N O3 C13 H19 N O3

Mr: 237.29 237.29

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Mu (mm⁻¹): 0.757 0.757

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</table>

Nref: 2114 2102

Tmin,Tmax:

<table>
<thead>
<tr>
<th>Calculated</th>
<th>Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.879,0.899</td>
<td>0.699,0.753</td>
</tr>
</tbody>
</table>

Tmin: 0.879

Correction method: # Reported T Limits: Tmin=0.699 Tmax=0.753

AbsCorr = MULTI-SCAN

Data completeness: 0.994 Theta(max) = 66.579

R(reflections) = 0.0606(1969) wr2(reflections) = 0.1570(2102)

S = 1.034 Npar= 155

The following ALERTS were generated. Each ALERT has the format test-name_ALERT_alert-type_alert-level.

Click on the hyperlinks for more details of the test.
**Alert level C**

<table>
<thead>
<tr>
<th>Alert ID</th>
<th>Description</th>
<th>Alert Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>DIFMX02_ALERT_1_C</td>
<td>The maximum difference density is &gt; 0.1<em>ZMAX</em>0.75</td>
<td>C</td>
</tr>
<tr>
<td>PLAT094_ALERT_2_C</td>
<td>Ratio of Maximum / Minimum Residual Density</td>
<td>C</td>
</tr>
<tr>
<td>PLAT097_ALERT_2_C</td>
<td>Large Reported Max. (Positive) Residual Density</td>
<td>C</td>
</tr>
<tr>
<td>PLAT906_ALERT_3_C</td>
<td>Large K Value in the Analysis of Variance</td>
<td>C</td>
</tr>
<tr>
<td>PLAT911_ALERT_3_C</td>
<td>Missing FCF Refl Between Thmin &amp; STh/L</td>
<td>C</td>
</tr>
<tr>
<td>PLAT913_ALERT_3_C</td>
<td>Missing # of Very Strong Reflections in FCF</td>
<td>C</td>
</tr>
</tbody>
</table>

**Alert level G**

<table>
<thead>
<tr>
<th>Alert ID</th>
<th>Description</th>
<th>Alert Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLAT793_ALERT_4_G</td>
<td>Model has Chirality at C4</td>
<td>G</td>
</tr>
<tr>
<td>PLAT793_ALERT_4_G</td>
<td>Model has Chirality at C5</td>
<td>G</td>
</tr>
<tr>
<td>PLAT793_ALERT_4_G</td>
<td>Model has Chirality at C6</td>
<td>G</td>
</tr>
<tr>
<td>PLAT793_ALERT_4_G</td>
<td>Model has Chirality at C11</td>
<td>G</td>
</tr>
<tr>
<td>PLAT909_ALERT_3_G</td>
<td>Percentage of I&gt;2sig(I) Data at Theta(Max) Still</td>
<td>G</td>
</tr>
<tr>
<td>PLAT978_ALERT_2_G</td>
<td>Number C-C Bonds with Positive Residual Density.</td>
<td>G</td>
</tr>
</tbody>
</table>

**Alert level A** = Most likely a serious problem - resolve or explain

**Alert level B** = A potentially serious problem, consider carefully

**Alert level C** = Check. Ensure it is not caused by an omission or oversight

**Alert level G** = General information/check it is not something unexpected

0 **ALERT level A** = Most likely a serious problem - resolve or explain

0 **ALERT level B** = A potentially serious problem, consider carefully

6 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight

6 **ALERT level G** = General information/check it is not something unexpected

1 **ALERT type 1** CIF construction/syntax error, inconsistent or missing data

3 **ALERT type 2** Indicator that the structure model may be wrong or deficient

4 **ALERT type 3** Indicator that the structure quality may be low

4 **ALERT type 4** Improvement, methodology, query or suggestion

0 **ALERT type 5** Informative message, check

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

**Publication of your CIF in IUCr journals**

A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (Acta Crystallographica, Journal of Applied Crystallography, Journal of Synchrotron Radiation); however, if you intend to submit to Acta Crystallographica Section C or E or IUCrData, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

**Publication of your CIF in other journals**

Please refer to the Notes for Authors of the relevant journal for any special instructions relating to CIF submission.
Crystal Data and Cif Check Report for

sessilifoliamide A  (2)

(CCDC: 1883815)
checkCIF/PLATON report

Structure factors have been supplied for datablock(s) 20181126_houysh_chon11_0m_a

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

Datablock: 20181126_houysh_chon11_0m_a

Bond precision: C-C = 0.0050 Å
Wavelength=1.54178 Å

Cell:
- a=15.4412(12) Å
- b=8.4857(7) Å
- c=12.4278(9) Å
- alpha=90°
- beta=93.576(3)°
- gamma=90°

Temperature: 150 K

Calculated Reported
Volume 1625.2(2) Å³ 1625.2(2) Å³
Space group P 1 c 1 P -2yc
Hall group P -2yc

Moiety formula C17 H25 N O4, C17 H24 N O4 C17 H25 N O4, C17 H24 N O4
Sum formula C34 H49 N2 O8 C34 H49 N2 O8

Mr 613.75 613.75
Dx,g cm⁻³ 1.254 1.254
Z 2 2

AbsCorr = MULTI-SCAN

Correction method= # Reported T Limits: Tmin=0.677 Tmax=0.753

Data completeness= 1.79/0.90 Theta(max)= 66.582

R(reflections)= 0.0421( 5008) wR2(reflections)= 0.1160( 5133)

S = 1.055 Npar= 400

The following ALERTS were generated. Each ALERT has the format test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.
Alert level C

The maximum difference density is > 0.1*ZMAX*0.75

The relevant atom site should be identified.

Alert level G

PLAT720_ALERT_4_G Number of Unusual/Non-Standard Labels .......... 10 Note

Alert level A

0 ALERT level A = Most likely a serious problem - resolve or explain

0 ALERT level B = A potentially serious problem, consider carefully

9 ALERT level C = Check. Ensure it is not caused by an omission or oversight

17 ALERT level G = General information/check it is not something unexpected

13 ALERT type 1 CIF construction/syntax error, inconsistent or missing data

6 ALERT type 2 Indicator that the structure model may be wrong or deficient

6 ALERT type 3 Indicator that the structure quality may be low

1 ALERT type 4 Improvement, methodology, query or suggestion

0 ALERT type 5 Informative message, check
It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

**Publication of your CIF in IUCr journals**

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**Publication of your CIF in other journals**

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

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**PLATON version of 06/01/2019; check.def file version of 19/12/2018**
Crystal Data and Cif Check Report for
13-epi-sessilifoliamide A (19)
(CCDC: 1883806)

19: 13-epi-sessilifoliamide A

ORTEP of 19
checkCIF/PLATON report

Structure factors have been supplied for datablock(s) 20181119houysh_chon_0m_a

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

Datablock: 20181119houysh_chon_0m_a

<table>
<thead>
<tr>
<th>Bond precision: C-C = 0.0031 A</th>
<th>Wavelength=1.54178</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cell:</td>
<td></td>
</tr>
<tr>
<td>a=9.7149(4)</td>
<td>b=10.9891(4)</td>
</tr>
<tr>
<td>alpha=90</td>
<td>beta=90</td>
</tr>
<tr>
<td>Temperature:</td>
<td></td>
</tr>
<tr>
<td>150 K</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Calculated</th>
<th>Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>1658.53(11)</td>
</tr>
<tr>
<td>Space group</td>
<td>P 2 1 21 21</td>
</tr>
<tr>
<td>Hall group</td>
<td>P 2ac 2ab</td>
</tr>
<tr>
<td>Moiety formula</td>
<td>C17 H25 N O4</td>
</tr>
<tr>
<td>Sum formula</td>
<td>C17 H25 N O4</td>
</tr>
<tr>
<td>Mr</td>
<td>307.38</td>
</tr>
<tr>
<td>Dx,g cm−3</td>
<td>1.231</td>
</tr>
<tr>
<td>Z</td>
<td>4</td>
</tr>
<tr>
<td>Mu (mm−1)</td>
<td>0.708</td>
</tr>
<tr>
<td>F000</td>
<td>664.0</td>
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<tr>
<td>F000’</td>
<td>666.05</td>
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<tr>
<td>h,k,lmax</td>
<td>11,13,18</td>
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<tr>
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<tr>
<td>Tmin,Tmax</td>
<td>0.880,0.919</td>
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<tr>
<td>Tmin’</td>
<td>0.880</td>
</tr>
</tbody>
</table>

Correction method= # Reported T Limits: Tmin=0.645 Tmax=0.753
AbsCorr = MULTI-SCAN

Data completeness= 1.73/1.00 

Theta(max)= 66.584

R(reflections)= 0.0290( 2847) 
wR2(reflections)= 0.0704( 2941)

S = 1.075 

Npar= 201

The following ALERTS were generated. Each ALERT has the format test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.
Alert level G

- PLAT398_ALERT_2_G | Deviating C-O-C Angle From 120 for O2 | 109.9 Degree
- PLAT791_ALERT_4_G | Model has Chirality at C7 | (Chiral SPGR) | R Verify
- PLAT791_ALERT_4_G | Model has Chirality at C8 | (Chiral SPGR) | R Verify
- PLAT791_ALERT_4_G | Model has Chirality at C9 | (Chiral SPGR) | S Verify
- PLAT791_ALERT_4_G | Model has Chirality at C10 | (Chiral SPGR) | S Verify
- PLAT791_ALERT_4_G | Model has Chirality at C11 | (Chiral SPGR) | S Verify
- PLAT791_ALERT_4_G | Model has Chirality at C12 | (Chiral SPGR) | R Verify
- PLAT850_ALERT_4_G | Check Flack Parameter Exact Value 0.00 and s.u. | 0.08 Check
- PLAT909_ALERT_3_G | Percentage of I>2sig(I) Data at Theta(Max) Still | 95% Note
- PLAT978_ALERT_2_G | Number C-C Bonds with Positive Residual Density. | 4 Info

0 ALERT level A = Most likely a serious problem - resolve or explain
0 ALERT level B = A potentially serious problem, consider carefully
0 ALERT level C = Check. Ensure it is not caused by an omission or oversight
10 ALERT level G = General information/check it is not something unexpected

0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
2 ALERT type 2 Indicator that the structure model may be wrong or deficient
1 ALERT type 3 Indicator that the structure quality may be low
7 ALERT type 4 Improvement, methodology, query or suggestion
0 ALERT type 5 Informative message, check

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

Publication of your CIF in IUCr journals

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Publication of your CIF in other journals

Please refer to the Notes for Authors of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 06/01/2019; check.def file version of 19/12/2018
Crystal Data and Cif Check Report for
11,13-bis-epi-sessilifoliamide A (20)
(CCDC: 1883804)
checkCIF/PLATON report

Structure factors have been supplied for datablock(s) 201811222_houysh_chon08_0m_a

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found.  CIF dictionary  Interpreting this report

Datablock: 201811222_houysh_chon08_0m_a

Bond precision:  C-C = 0.0017 A  Wavelength=1.54178

Cell:  
a=15.2941(4)  b=8.0859(2)  c=13.0198(3)
alpha=90  beta=95.659(1)  gamma=90

Temperature:  150 K

Calculated Reported
Volume 1602.27(7) 1602.27(7)
Space group P 21/c  P 1 21/c 1
Hall group -P 2ybc  -P 2ybc
Moiety formula C17 H25 N O4  C17 H25 N O4
Sum formula C17 H25 N O4  C17 H25 N O4
Mr 307.38 307.38
Dx,g cm-3 1.274 1.274
Z 4 4
Mu (mm-1) 0.732 0.732
F000 664.0 664.0
F000’ 666.05

h,k,lmax 18,9,15 18,9,15
Nref 2926 2916
Tmin,Tmax 0.877,0.916 0.688,0.753
Tmin’ 0.877

Correction method= # Reported T Limits: Tmin=0.688 Tmax=0.753
AbsCorr = MULTI-SCAN

Data completeness= 0.997  Theta(max)= 68.283
R(reflections)= 0.0352( 2760)  wR2(reflections)= 0.0898( 2916)
S = 1.038  Npar= 201

The following ALERTS were generated. Each ALERT has the format

    test-name_ALERT_alert-type_alert-level.

Click on the hyperlinks for more details of the test.
It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

### Publication of your CIF in IUCr journals

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### Publication of your CIF in other journals

Please refer to the Notes for Authors of the relevant journal for any special instructions relating to CIF submission.
Crystal Data and Cif Check Report for
tuberostemoamide (1)
(CCDC: 1874369)
checkCIF/PLATON report

Structure factors have been supplied for datablock(s) houysh_0723

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found.  CIF dictionary  Interpreting this report

Datablock: houysh_0723

Bond precision:  C-C = 0.0057 Å  Wavelength=1.54184

Cell:  
\begin{align*}
a &= 7.7103(4) \\
b &= 12.8887(6) \\
c &= 33.1487(17) \\
\alpha &= 90° \\
\beta &= 90° \\
\gamma &= 90° \\
\end{align*}

Temperature:  173 K


\begin{tabular}{l c}
\text{Calculated} & \text{Reported} \\
Volume & 3294.2(3) \\
Space group & P 2 1 2 1 \\
Hall group & P 2ac 2ab \\
Moiety formula & 2(C_{17}H_{23}N_{4}O_{4}), H_{2}O \\
Sum formula & C_{34}H_{48}N_{2}O_{9} \\
Mr & 628.74 \\
Dx,g cm\textsuperscript{-3} & 1.268 \\
Z & 4 \\
Mu (mm\textsuperscript{-1}) & 0.749 \\
F000 & 1352.0 \\
F000’ & 1356.30 \\
h,k,lmax & 9,15,39 \\
Nref & 5810 \[ 3325 \] \\
Tmin,Tmax & 0.887,0.914 \\
Tmin’ & 0.887 \\
\end{tabular}

Correction method= #  Reported T Limits: Tmin=0.847 Tmax=1.000  
AbsCorr = MULTI-SCAN

Data completeness= 1.71/0.98  
\(\Theta\text{(max)}\) = 66.595

\(R(\text{reflections})\) = 0.0489( 4457)  
\(wR2(\text{reflections})\) = 0.1087( 5702)

\(S = 1.004\)  
Npar= 413

The following ALERTS were generated. Each ALERT has the format  
test-name_ALERT_alert-type_alert-level.  
Click on the hyperlinks for more details of the test.
### Alert level C

- **PLAT340_ALERT_3_C** Low Bond Precision on C-C Bonds ............... 0.00572 Ang.
- **PLAT790_ALERT_4_C** Centre of Gravity not Within Unit Cell: Resd. # 1 Note
  - C17 H23 N O4
- **PLAT911_ALERT_3_C** Missing FCF Refl Between Thmin & STh/L= 0.595 21 Report

### Alert level G

- **PLAT907_ALERT_5_G** Number of Unrefined Donor-H Atoms ............... 2 Report
- **PLAT398_ALERT_2_G** Deviating C-O-C Angle From 120 for O2BA 109.5 Degree
- **PLAT398_ALERT_2_G** Deviating C-O-C Angle From 120 for O0BA 109.0 Degree
- **PLAT398_ALERT_2_G** Deviating C-O-C Angle From 120 for O39 109.8 Degree
- **PLAT720_ALERT_4_G** Number of Unusual/Non-Standard Labels ............ 24 Note
- **PLAT790_ALERT_4_G** Centre of Gravity not Within Unit Cell: Resd. # 2 Note
  - C17 H23 N O4
- **PLAT790_ALERT_4_G** Centre of Gravity not Within Unit Cell: Resd. # 3 Note
  - H2 O
- **PLAT791_ALERT_4_G** Model has Chirality at C5BA (Chiral SPGR) S Verify
- **PLAT791_ALERT_4_G** Model has Chirality at C7BA (Chiral SPGR) S Verify
- **PLAT791_ALERT_4_G** Model has Chirality at C1AA (Chiral SPGR) S Verify
- **PLAT791_ALERT_4_G** Model has Chirality at C9 (Chiral SPGR) R Verify
- **PLAT791_ALERT_4_G** Model has Chirality at C9AA (Chiral SPGR) R Verify
- **PLAT791_ALERT_4_G** Model has Chirality at C18 (Chiral SPGR) S Verify
- **PLAT791_ALERT_4_G** Model has Chirality at C29 (Chiral SPGR) S Verify
- **PLAT791_ALERT_4_G** Model has Chirality at C32 (Chiral SPGR) S Verify
- **PLAT791_ALERT_4_G** Model has Chirality at C40 (Chiral SPGR) R Verify
- **PLAT791_ALERT_4_G** Model has Chirality at C45 (Chiral SPGR) R Verify
- **PLAT909_ALERT_3_G** Percentage of I>2sig(I) Data at Theta(Max) Still 56% Note
- **PLAT910_ALERT_3_G** Missing # of FCF Reflection(s) Below Theta(Min). 1 Note
- **PLAT916_ALERT_2_G** Hooft y and Flack x Parameter Values Differ by . 0.25 Check
- **PLAT933_ALERT_2_G** Number of OMIT Records in Embedded .res File ... 2 Note
- **PLAT978_ALERT_2_G** Number C-C Bonds with Positive Residual Density. 1 Info

### ALERT level A = Most likely a serious problem - resolve or explain
### ALERT level B = A potentially serious problem, consider carefully
### ALERT level C = Check. Ensure it is not caused by an omission or oversight
### ALERT level G = General information/check it is not something unexpected

### ALERT type 1 CIF construction/syntax error, inconsistent or missing data
### ALERT type 2 Indicator that the structure model may be wrong or deficient
### ALERT type 3 Indicator that the structure quality may be low
### ALERT type 4 Improvement, methodology, query or suggestion
### ALERT type 5 Informative message, check
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**Publication of your CIF in other journals**

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---

**PLATON version of 06/01/2019; check.def file version of 19/12/2018**
Crystal Data and Cif Check Report for 11-\textit{epi}-tuberostemoamide (21) (CCDC:1883814)
checkCIF/PLATON report

Structure factors have been supplied for datablock(s) 20181123houysh_chon09_0m_a

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

Datablock: 20181123houysh_chon09_0m_a

Bond precision: C-C = 0.0023 Å Wavelength=1.54178

Cell: a=13.5432(6) b=11.4992(5) c=19.8699(9) alpha=90 beta=91.946(2) gamma=90

Temperature: 150 K

Calculated Reported
Volume 3092.7(2) 3092.7(2)
Space group P 21/n P 1 21/n 1
Hall group -P 2yn -P 2yn
Moiety formula C17 H23 N O4 2(C17 H23 N O4)
Sum formula C17 H23 N O4 C34 H46 N2 O8
Mr 305.36 610.73
Dx, g cm-3 1.312 1.312
Z 8 4
Mu (mm-1) 0.759 0.759
F000 1312.0 1312.0
F000’ 1316.11
h,k,lmax 16,13,23 16,13,23
Nref 5463 5428
Tmin,Tmax 0.872,0.913 0.660,0.753
Tmin’ 0.872

Correction method= # Reported T Limits: Tmin=0.660 Tmax=0.753
AbsCorr = MULTI-SCAN

Data completeness= 0.994 Theta(max)= 66.594
R(reflections)= 0.0445( 4727) wr2(reflections)= 0.1138( 5428)
S = 1.081 Npar= 401

The following ALERTS were generated. Each ALERT has the format test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.
## Alert level C

<table>
<thead>
<tr>
<th>ALERT</th>
<th>Description</th>
<th>Alert Code</th>
<th>Percentage</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLAT906_ALERT_3_C</td>
<td>Large K Value in the Analysis of Variance</td>
<td>4.776</td>
<td>Check</td>
<td></td>
</tr>
<tr>
<td>PLAT911_ALERT_3_C</td>
<td>Missing FCF Refl Between Thmin &amp; STh/L= 0.595</td>
<td>35</td>
<td>Report</td>
<td></td>
</tr>
<tr>
<td>PLAT934_ALERT_3_C</td>
<td>Number of (Iobs-Icalc)/SigmaW &gt; 10 Outliers</td>
<td>1</td>
<td>Check</td>
<td></td>
</tr>
</tbody>
</table>

## Alert level G

<table>
<thead>
<tr>
<th>ALERT</th>
<th>Description</th>
<th>Alert Code</th>
<th>Percentage</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLAT042_ALERT_1_G</td>
<td>Calc. and Reported MoietyFormula Strings Differ</td>
<td>Please Check</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PLAT045_ALERT_1_G</td>
<td>Calculated and Reported Z Differ by a Factor</td>
<td>2.00</td>
<td>Check</td>
<td></td>
</tr>
<tr>
<td>PLAT398_ALERT_2_G</td>
<td>Deviating C-O-C Angle From 120</td>
<td>106.9</td>
<td>Degree</td>
<td></td>
</tr>
<tr>
<td>PLAT398_ALERT_2_G</td>
<td>Deviating C-O-C Angle From 120</td>
<td>109.2</td>
<td>Degree</td>
<td></td>
</tr>
<tr>
<td>PLAT720_ALERT_4_G</td>
<td>Number of Unusual/Non-Standard Labels</td>
<td>6</td>
<td>Note</td>
<td></td>
</tr>
<tr>
<td>PLAT793_ALERT_4_G</td>
<td>Model has Chirality at C1' (Centro SPGR)</td>
<td>R</td>
<td>Verify</td>
<td></td>
</tr>
<tr>
<td>PLAT793_ALERT_4_G</td>
<td>Model has Chirality at C2' (Centro SPGR)</td>
<td>R</td>
<td>Verify</td>
<td></td>
</tr>
<tr>
<td>PLAT793_ALERT_4_G</td>
<td>Model has Chirality at C3' (Centro SPGR)</td>
<td>S</td>
<td>Verify</td>
<td></td>
</tr>
<tr>
<td>PLAT793_ALERT_4_G</td>
<td>Model has Chirality at C4' (Centro SPGR)</td>
<td>S</td>
<td>Verify</td>
<td></td>
</tr>
<tr>
<td>PLAT793_ALERT_4_G</td>
<td>Model has Chirality at C5' (Centro SPGR)</td>
<td>R</td>
<td>Verify</td>
<td></td>
</tr>
<tr>
<td>PLAT793_ALERT_4_G</td>
<td>Model has Chirality at C6' (Centro SPGR)</td>
<td>R</td>
<td>Verify</td>
<td></td>
</tr>
<tr>
<td>PLAT793_ALERT_4_G</td>
<td>Model has Chirality at C7' (Centro SPGR)</td>
<td>S</td>
<td>Verify</td>
<td></td>
</tr>
<tr>
<td>PLAT793_ALERT_4_G</td>
<td>Model has Chirality at C8' (Centro SPGR)</td>
<td>S</td>
<td>Verify</td>
<td></td>
</tr>
<tr>
<td>PLAT799_ALERT_4_G</td>
<td>Model has Chirality at C8 (Centro SPGR)</td>
<td>R</td>
<td>Verify</td>
<td></td>
</tr>
<tr>
<td>PLAT909_ALERT_3_G</td>
<td>Percentage of I&gt;2sig(I) Data at Theta(Max) Still</td>
<td>79%</td>
<td>Note</td>
<td></td>
</tr>
<tr>
<td>PLAT913_ALERT_3_G</td>
<td>Missing # of Very Strong Reflections in FCF</td>
<td>2</td>
<td>Note</td>
<td></td>
</tr>
<tr>
<td>PLAT978_ALERT_2_G</td>
<td>Number C-C Bonds with Positive Residual Density</td>
<td>14</td>
<td>Info</td>
<td></td>
</tr>
</tbody>
</table>

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**0 ALERT level A** = Most likely a serious problem - resolve or explain

**0 ALERT level B** = A potentially serious problem, consider carefully

**3 ALERT level C** = Check. Ensure it is not caused by an omission or oversight

**20 ALERT level G** = General information/check it is not something unexpected

**2 ALERT type 1** CIF construction/syntax error, inconsistent or missing data

**5 ALERT type 2** Indicator that the structure model may be wrong or deficient

**5 ALERT type 3** Indicator that the structure quality may be low

**11 ALERT type 4** Improvement, methodology, query or suggestion

**0 ALERT type 5** Informative message, check
It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

**Publication of your CIF in IUCr journals**

A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica, Journal of Applied Crystallography, Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

**Publication of your CIF in other journals**

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

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PLATON version of 06/01/2019; check.def file version of 19/12/2018