Supplementary Information (SI) for Chemical Communications. This journal is © The Royal Society of Chemistry 2024

# **Supporting Information**

### Enantioselective Total Synthesis of Atisane Diterpenoids: (+)-Sapinsigin H, (+)-Agallochaol C, and (+)-16α, 17-dihydroxy-atisan-3-one

Dattatraya H. Dethe\*, Nitin Sharma, Sakshi Juyal, Prabhakar Singh, Salman A. Siddiqui

Department of Chemistry, Indian Institute of Technology Kanpur, Kanpur - 208016, India. Tel: +91-512-2596537, fax: +91-512-2597436 Email: <u>ddethe@iitk.ac.in</u>

30 July 2024

**Note added after first publication:** This supplementary information file replaces that originally published on 03 June 2024. The original version contained mirror images of the molecular structures in error. The structures have been corrected in this updated version.

## Contents

General Information	3
Experimental Procedures:	5
Synthesis of triflate 13:	5
Synthesis of ester 12 using Heck reaction:	5
Saponification to acid 16:	6
Benzannulation reaction to phenyl propionate 17:	7
Synthesis of compound 10 using DAR:	7
Synthesis of ketone 16:	8
Synthesis of <b>19</b> using hydrogenation:	9
Synthesis of <b>19a</b> using wittig olefination:	9
Synthesis of hydroxy compound 19b:	10
Synthesis of <b>9</b> using DMP oxidation:	11
Synthesis of 22 and 23:	11
Synthesis of (+)-16α, 17-dihydroxy-atisan-3-one:	13
Synthesis of (+)-Sapinsigin H:	13
Baeyer–Villiger oxidation to <b>24</b> :	14
Synthesis of acid <b>24a</b> :	14
Synthesis of (+)-agallochaol C:	15
<sup>1</sup> H and <sup>13</sup> C NMR comparison	16
Crystallographic Data for Single Crystal X-Ray Structure of Compound 9	19
NMR Spectra	

#### **General Information**

**General Aspects:** All reactions were carried out under nitrogen atmosphere with dry solvents under anhydrous conditions, unless otherwise mentioned. All the chemicals were purchased commercially, and used without further purification. Anhydrous THF and diethyl ether were distilled from sodium benzophenone, and dichloromethane was distilled from calcium hydride. Yields refer to chromatographically pure compounds, unless otherwise stated. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm Merck silica gel plates (60F-254) using UV light as a visualizing agent and an p-anisaldehyde or ninhydrine stain, and heat as developing agents. Merck silica gel (particle size 100-200 and 230-400 mesh) was used for flash column chromatography. Neat compounds were used for record IR spectra. NMR spectra were recorded on either a Bruker Avance 400 (<sup>1</sup>H, 400 MHz; <sup>13</sup>C, 100 MHz), Bruker Avance 500 (<sup>1</sup>H, 500 MHz; <sup>13</sup>C, 125 MHz), or JEOL DELTA (ECX) 500 (<sup>1</sup>H, 500 MHz; <sup>13</sup>C, 125 MHz). Mass spectrometric data were obtained using Agilent-Premier-APCI-MS instruments and IR data recorded from PerkinElmer, FT-IR spectrometer. Optical rotations were measured using a Polarimeter (AUTOPOL II) at 20 °C.

The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublet, ddd = doublet of a doublet of a doublet, dt = doublet of a triplet, td = triplet of a doublet, m = multiplet, br = broad.



Total Synthesis of (+)-16a, 17-dihydroxy-atisan-3-one, (+)-sapinsigin H and (+)-agallochaol Ca

<sup>a</sup>Yields of material isolated by silica gel chromatography.

#### **Experimental Procedures:**

Synthesis of triflate 13:



Ketone **15** (14.76 mmol, 5 g, 1.0 equiv) was dissolved in dry THF (150 ml) under nitrogen. The resulting mixture was cooled to -78 °C and a 1.9 M solution of NaHMDS (16.24 mmol, 8.5 ml, 1.1 equiv) in THF was added dropwise. The resulting yellow solution was stirred at -78 °C for 2 h. Then PhNTf<sub>2</sub> (16.24 mmol, 5.8 g, 1.1 equiv) dissolved in 30 ml THF was added at -78 °C and the reaction mixture was allowed to slowly warm to rt overnight. The reaction mixture was quenched by addition of saturated aqueous NH<sub>4</sub>Cl solution (100 ml) and the aqueous phase was extracted with Et<sub>2</sub>O (3 × 100 ml). The combined organic phases were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated. The residual red oil was purified by column chromatography on silica gel to give triflate **13** (6.5 g, 95%) as a colorless oil.

 $\mathbf{R}_{\mathbf{f}} = 0.5$  (2% EtOAc in hexanes)

 $[\alpha]_D^{23} = +21.5 \ (c = 0.5, \text{CHCl}_3)$ 

<sup>1</sup>**H NMR (400 MHz, CDCl<sub>3</sub>)** δ 3.23 – 3.14 (m, 1H), 2.17 (m, *J* = 24.4 Hz, 2H), 1.79 (dt, *J* = 13.1, 3.4 Hz, 1H), 1.70 (s, 3H), 1.62-1.54 (m, 2H), 1.54-1.44 (m, 2H), 1.41 – 1.31 (m, 1H), 1.22-1.19 (m, 1H), 1.13 (s, 3H), 0.92 (s, 3H), 0.88 (s, 9H), 0.78 (s, 3H), 0.03 (d, *J* = 4.2 Hz, 6H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ151.69, 124.46, 118.81 (q, *J* = 320 Hz), 78.86, 51.87, 39.32, 39.22, 33.03, 32.23, 28.51, 27.51, 25.93, 18.92, 18.28, 18.15, 17.45, 16.01, -3.76, -4.94.

<sup>19</sup>F NMR (373 MHz, CDCl<sub>3</sub>) δ -73.06 (s).

**HRMS (EI)** calculated for  $C_{21}H_{37}F_3NaO_4SSi [M+Na]^+$ : m/z 493.2032, found: 493.2036

**IR**: 3427, 2955, 2930, 2857, 1706, 1401, 1209, 1140, 885, 607 cm<sup>-1</sup>.

Synthesis of ester **12** using Heck reaction:



Triflate **13** (28.4 mmol, 13.38 g, 1.0 equiv), methyl acrylate (0.284 mol, 25.7 ml, 10.0 equiv), Et<sub>3</sub>N (0.284 mol, 39.6 ml, 10.0 equiv), PPh<sub>3</sub> (2.84 mmol, 0.74 g, 0.1 equiv) and DMA (60 ml) were added to a Schlenk flask. The resulting solution was degassed by three cycles of freeze/pump/thaw technique before  $Pd(OAc)_2$  (2.84 mmol, 0.638 g, 10 mol %) was added. The flask was sealed and the reaction mixture was stirred at 95 °C overnight. The resulting suspension was diluted with EtOAc and filtered

through cotton. The filtrate was extracted with aqueous 1 M HCl and  $H_2O$ , dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated. The residual yellow oil was purified by column chromatography on silica gel to give ester **12** (10.9 g, 95%) as a light-yellow oil.

 $\mathbf{R}_{\mathbf{f}} = 0.5$  (5% EtOAc in hexanes)

 $[\alpha]_D^{23} = +17.6 (c = 0.4, CHCl_3)$ 

<sup>1</sup>**H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.27 (d, *J* = 16.0 Hz, 1H), 5.71 (d, *J* = 16.0 Hz, 1H), 3.73 (s, 3H), 3.17 (dd, *J* = 11.1, 4.8 Hz, 1H), 1.66 (s, 3H), 1.60-1.45 (m, 5H), 1.25 – 1.06 (m, 4H), 1.03 (s, 3H), 0.90 (s, 3H), 0.86 (s, 9H), 0.76 (s, 3H), 0.00 (s, 6H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 167.48, 144.69, 139.04, 132.38, 122.57, 79.20, 51.50, 50.45, 39.62, 37.78, 36.36, 34.24, 28.46, 28.07, 25.97, 21.24, 20.43, 18.62, 18.18, 15.94, -3.73, -4.90.

**HRMS (EI)** calculated for  $C_{24}H_{42}NaO_3Si [M+Na]^+$ : m/z 429.6718, found: 429.6719.

IR: 3440, 2949, 2932, 2855, 1723, 1633, 1306, 1256, 1105, 884 cm<sup>-1</sup>.

Saponification to acid **16**:



Solid LiOH (15.5 mmol, 6.5 g, 6.0 equiv) was added to a solution of ester **12** (25.8 mmol, 10.5 g, 1.0 equiv) in THF/MeOH/H<sub>2</sub>O (v/v/v, 3:1:2; 60.0 ml), and the resultant suspension was stirred at room temperature for 12 h. The reaction mixture was diluted with 1 M HCl and acidified to pH=0. The aqueous phase was then extracted using CH<sub>2</sub>Cl<sub>2</sub>, and the combined organic phases were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated. The residue was purified by column chromatography on silica gel to give dienoic acid **16** (0.293 g, 88%) as a white solid.

 $\mathbf{R}_{\mathbf{f}} = 0.5$  (30% EtOAc in hexanes)

 $[\alpha]_{D}^{23} = +16 \ (c = 0.1, \text{ CHCl}_{3})$ 

<sup>1</sup>**H NMR (400 MHz, CDCl<sub>3</sub>)** δ 7.39 (d, *J* = 16.0 Hz, 1H), 5.74 (d, *J* = 16.0 Hz, 1H), 3.18 (m, 1H), 2.13 (bs, 2H), 1.71-1.68 (m, 2H), 1.69 (s, 3H), 1.62-1.44 (m, 3H), 1.24 (d, 2H), 1.11 (d, 1H), 1.05 (s, 3H), 0.91 (s, 3H), 0.87 (s, 9H), 0.76 (s, 3H), 0.01 (s, 6H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 172.53, 147.01, 138.94, 133.63, 122.02, 79.15, 50.44, 39.63, 37.83, 36.34, 34.39, 28.47, 28.07, 25.98, 21.33, 20.49, 18.59, 18.18, 15.95, -3.73, -4.89.

**HRMS (EI)** calculated for  $C_{23}H_{41}O_3Si [M+H]^+$ : *m/z* 393.2825, found: 393.2806.

**IR**: 2938, 1697, 1643, 1355, 1240, 1047, 1001, 892, 881 cm<sup>-1</sup>.

Benzannulation reaction to phenyl propionate 17:



Dienoic acid **16** (9.93 mmol, 3.9 g, 1.0 equiv) was dissolved in propionic anhydride (80 ml) and then sealed in a Schlenk flask and heated to 180 °C for 2 days. The resulting yellow suspension was concentrated and purified by column chromatography on silica gel to give tricyclic compound **17** (2.9 g, 80%) as a yellow oil.

 $\mathbf{R}_{\mathbf{f}} = 0.5 \ (15\% \ \text{EtOAc in hexanes})$ 

 $[\alpha]_D^{23} = +14.5 \ (c = 0.45, \text{CHCl}_3)$ 

<sup>1</sup>**H** NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.19 (d, J = 8.6 Hz, 1H), 6.81 (dd, J = 8.6, 2.5 Hz, 1H), 6.74 (d, J = 2.5 Hz, 1H), 4.55 (dd, J = 11.5, 4.7 Hz, 1H), 2.96-2.79 (m, 2H), 2.54 (q, J = 7.6 Hz, 2H), 2.34 (q, J = 7.6 Hz, 2H), 2.28 (dt, J = 13.2, 3.4 Hz, 1H), 1.89-1.79 (m, 2H), 1.79-1.72 (m, 2H), 1.63-1.58 (m, 2H), 1.39 (dd, J = 12.2, 2.3 Hz, 1H), 1.23 (t, J = 7.6 Hz, 3H), 1.19 (s, 3H), 1.15 (t, J = 7.5 Hz, 3H), 0.96 (s, 3H), 0.93 (s, 3H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 174.28, 173.23, 148.39, 146.56, 136.50, 125.61, 121.30, 118.92, 80.26, 77.41, 77.09, 76.77, 49.83, 38.06, 37.41, 36.66, 30.54, 28.21, 28.12, 27.84, 25.03, 24.41, 18.65, 16.61, 9.40, 9.18.

**HRMS (EI)** calculated for  $C_{23}H_{32}NaO_4$  [M+Na]<sup>+</sup> : m/z 395.2198, found: 395.2190.

**IR**: 2971, 2945, 2880, 1760, 1731, 1493, 1193, 1156, 809 cm<sup>-1</sup>.

#### Synthesis of compound **10** using DAR:



To a solution of **17** (2.63 mmol, 979 mg, 1.0 equiv) in MeOH (130 ml) at -7 °C was added 1,1,3,3tetramethylguanidine (2.76 mmol, 0.347 ml, 1.05 equiv) and the resulting solution was stirred for 2 h at -7 °C. Then PhI(OAc)<sub>2</sub> (6.31 mmol, 2.03 g, 2.4 equiv) was added at -7 °C and the reaction mixture was stirred for 2 h. The resulting yellow reaction mixture was quenched by addition of solid NaHCO<sub>3</sub> at -7 °C and filtered through a plug of celite, thoroughly washing the filter cake with EtOAc (200 ml). The filtrate was concentrated and the residual yellow oil was purified by column chromatography on silica gel to give inseperable compound **11** and **18** (826 mg) as a yellow oil.

 $\mathbf{R}_{\mathbf{f}} = 0.30$  (5% EtOAc in hexanes)

A solution of the inseperable compound **11** and **18** (826 mg) in toluene (15 ml) was sealed in a Parr high-pressure bomb and pressurized ethylene to 30 bar. The reaction mixture was heated to 110 °C (pressure raised to 40 bar) and held at this temperature for 24 h and then concentrated in vacuo. The resulting yellow residue was purified by column chromatography on silica gel to give cycloadduct **10** (446 mg, 42% from **17**) and **18** (346 mg, 38%) as a yellow oil.

 $\mathbf{R_f} = 0.7$  (5% EtOAc in hexanes)

 $[\alpha]_D^{23} = +24.3 \ (c = 0.37, \text{CHCl}_3)$ 

<sup>1</sup>**H NMR (400 MHz, CDCl<sub>3</sub>)** δ 5.72 (d, *J* = 6.8 Hz, 1H), 4.48 (dd, *J* = 11.5, 4.6 Hz, 1H), 3.40 (s, 3H), 3.39 (s, 3H), 3.03 (m, 1H), 2.30 (qd, *J* = 7.6, 1.2 Hz, 2H), 2.25-2.19 (m, 1H), 1.91-1.86 (m, 2H), 1.83-1.78 (m, 1H), 1.74-1.69 (m, 3H), 1.67-1.64 (m, 1H), 1.58-1.45 (m, 4H), 1.39-1.35 (m, 1H), 1.13 (t, *J* = 7.6 Hz, 3H), 1.10 (s, 3H), 0.92 (s, 3H), 0.86 (s, 3H).

<sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 203.83, 174.34, 160.80, 115.31, 96.23, 80.54, 56.09, 52.15, 48.23, 48.18, 46.86, 38.10, 38.10 36.42, 31.04, 28.14, 27.99, 26.53, 24.42, 24.04, 22.69, 18.47, 16.55, 9.43.

**HRMS (EI)** calculated for  $C_{24}H_{36}NaO_5 [M+Na]^+$ : m/z 427.2460, found: 427.2459.

**IR**: 3444, 2925, 2854, 1731, 1462, 1100, 1151, 1075, 773 cm<sup>-1</sup>.

Synthesis of ketone **16**:



To a solution of **10** (1.1 mmol, 446 mg, 1 equiv) in THF (5 ml) and MeOH (1 ml) was added freshly prepared SmI<sub>2</sub> until there was no disappearance of the blue color at room temperature. After 30 minutes, the resulting mixture was quenched with saturated aqueous NaHCO<sub>3</sub> (10 ml) and diluted with EtOAc (10 ml). The layers were separated, and the aqueous phase was extracted with EtOAc (15 ml  $\times$  3). The combined organic extracts were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated to give the residue, which was purified by flash chromatography on silica gel to give **10a** (322 mg, 85%).

 $\mathbf{R}_{\mathbf{f}} = 0.4 \ (10\% \ \text{EtOAc in hexanes})$ 

 $[\alpha]_D^{23} = +62.0 \ (c = 0.73, \text{CHCl}_3)$ 

<sup>1</sup>**H NMR (400 MHz, CDCl<sub>3</sub>)** δ 5.69 (d, *J* = 6.7 Hz, 1H), 4.42 (dd, *J* = 11.1, 4.7 Hz, 1H), 3.08 (m, 1H), 2.30 (q, *J* = 7.4 Hz, 2H), 2.02-1.96 (m, 2H), 1.81 – 1.63 (m, 8H), 1.61-1.49 (m, 4H), 1.32 – 1.23 (m, 1H), 1.12 (t, *J* = 7.6, 1.0 Hz, 3H), 1.11 (s, 3H), 0.96 (s, 3H), 0.80 (s, 3H).

<sup>13</sup>C NMR (400 MHz, CDCl<sub>3</sub>) δ 213.18, 174.17, 160.70, 115.61, 80.36, 49.19, 46.97, 46.65, 39.79, 38.77, 37.80, 35.96, 33.70, 30.41, 28.08, 27.33, 23.78, 22.93, 22.76, 17.70, 15.93, 9.38.

**HRMS (EI)** calculated for  $C_{22}H_{33}O_3$  [M+H]<sup>+</sup> : m/z 345.2430, found: 345.2423

**IR**: 2936, 2879, 1760, 1723, 1373, 1088, 826 cm<sup>-1</sup>.

Synthesis of **19** using hydrogenation:



Compound **10a** (0.934 mmol, 322 mg) was dissolved in anhydrous EtOAc (8 ml) and the 10% Pd/C was added. The reaction mixture was stirred at rt for overnight under an H<sub>2</sub> balloon. After filtration through the celite pad, the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel to provide **19** (297 mg, 92%).

 $\mathbf{R}_{\mathbf{f}} = 0.5 \ (10\% \ \text{EtOAc in hexanes})$ 

 $[\alpha]_D^{23} = +37.8 \ (c = 0.4, \text{CHCl}_3)$ 

<sup>1</sup>**H NMR (400 MHz, CDCl<sub>3</sub>)** δ 4.48 (dd, *J* = 10.3, 6.0 Hz, 1H), 2.34-2.28 (m, 3H), 2.06-2.01 (m, 1H), 1.87-1.71 (m, 4H), 1.65-1.52 (m, 8H), 1.31-1.24 (m, 3H), 1.13 (t, *J* = 7.6 Hz, 3H), 1.03 (s, 3H), 0.87 (s, 3H), 0.86 (s, 3H).

<sup>13</sup>C NMR (400 MHz, CDCl<sub>3</sub>) δ 217.42, 174.27, 80.43, 60.45, 56.02, 55.31, 51.80, 43.10, 38.60, 37.84, 37.42, 37.32, 36.11, 28.11, 27.63, 25.27, 23.80, 23.20, 18.28, 16.70, 14.08, 9.38.

**HRMS (EI)** calculated for  $C_{22}H_{35}O_3 [M+H]^+$ : m/z 347.2586, found: 347.2581

**IR**: 3444, 2924, 2851, 1729, 1643, 1462, 1191, 1034, 980, 652 cm<sup>-1</sup>.

Synthesis of **19a** using wittig olefination:



To a suspension of  $Ph_3PCH_3Br$  (0.865 mmol, 309 mg, 3 equiv) in THF (10 ml) was added KO'Bu (65 mg, 0.57 mmol, 2 equiv) at 0 °C. After 30 minutes, a solution of **19** (0.288 mmol, 100 mg, 1 equiv) in THF (5 ml) was added dropwise and the mixture was warmed to room temperature. The reaction mixture was stirred at this temperature for 2 h then quenched with sat. NH<sub>4</sub>Cl aqueous (10 ml). The aqueous layer was extracted with EtOAc (10 ml ×3) and the combined organic layers were dried over

anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel to provide **19a** (90.2 mg, 91%).

 $\mathbf{R}_{\mathbf{f}} = 0.8$  (10% EtOAc in hexanes)

 $[\alpha]_D^{23} = +2.4 \ (c = 1.0, \text{CHCl}_3)$ 

<sup>1</sup>**H** NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  4.70 (d, J = 2 Hz, 1H), 4.54 (d, J = 2 Hz, 1H), 4.48-4.44 (m, 1H), 2.29 (q, J = 7.6 Hz, 2H), 2.19 (m, 1H), 2.01-2.00 (m, 1H), 1.88-1.84 (m, 2H), 1.61-1.50 (m, 6H), 1.44 – 1.34 (m, 4H), 1.29-1.20 (m, 4H), 1.11 (t, J = 7.5 Hz, 3H), 1.02-0.97 (m, 1H), 0.96 (s, 3H), 0.84 (s, 3H), 0.83 (s, 3H).

<sup>13</sup>C NMR (400 MHz, CDCl<sub>3</sub>) δ 174.35, 152.71, 104.68, 80.81, 55.46, 52.62, 48.12, 39.33, 37.85, 37.43, 37.31, 36.45, 33.38, 28.66, 28.58, 28.15, 28.15, 27.33, 23.33, 18.45, 16.74, 14.08, 9.42.

HRMS (EI) calculated for C<sub>23</sub>H<sub>36</sub>NaO<sub>2</sub> [M+Na]<sup>+</sup> : *m/z* 367.2613, found: 367.2607

**IR**: 2937, 2858, 1722, 1446, 1468, 1345, 1206, 1077, 871 cm<sup>-1</sup>.

Synthesis of hydroxy compound 19b:



To a solution of the ester **19a** (0.261 mmol, 90.2 mg, 1 equiv) in THF (10 ml) was added LAH (9.9 mg, 0.261 mmol, 1 equiv) at 0 °C. The resulting mixture was then stirred at rt for 1 h. After completion of the reaction (TLC monitoring) the excess LAH was quenched with ice water. After stirring for 10 min at room temperature the whole mixture was extracted with EtOAc (3 x 10 ml). The combined organic extracts were washed with NaHCO<sub>3</sub>, brine and dried (Na<sub>2</sub>SO<sub>4</sub>). Solvent was removed in vacuo and purification was done by flash chromatography on silica gel to yield **19b** (71.5 mg, 95%) as a clear, colorless oil.

 $\mathbf{R}_{\mathbf{f}} = 0.5$  (20% EtOAc in hexanes)

 $[\alpha]_D^{23} = +31.3 \ (c = 0.5, \text{CHCl}_3)$ 

<sup>1</sup>**H NMR (400 MHz, CDCl**<sub>3</sub>) δ 4.70 (dd, *J* = 4.2, 2.0 Hz, 1H), 4.54 (dd, *J* = 4.2, 2.0 Hz, 1H), 3.21 – 3.16 (m, 1H), 2.20 (m, 1H), 2.03 (d, *J* = 16.6 Hz, 1H), 1.88-1.84 (m, 2H), 1.59-1.53 (m, 8H), 1.42-1.34 (m, 4H), 1.12 – 1.07 (m, 2H), 0.96 (s, 3H), 0.94 (s, 3H), 0.77 (s, 3H), 0.73-0.71 (m, 1H).

<sup>13</sup>C NMR (400 MHz, CDCl<sub>3</sub>) δ 152.85, 104.58, 79.25, 55.40, 52.74, 48.18, 39.47, 38.83, 37.68, 37.53, 36.50, 33.37, 28.66, 28.60, 28.18, 27.33, 26.97, 18.57, 15.56, 14.02.

**HRMS (EI)** calculated for  $C_{20}H_{33}O[M+H]^+$ : *m/z* 289.2531, found: 289.2539.

**IR**: 3316, 2929, 2864, 1646, 1442, 1364, 1024, 872, 747 cm<sup>-1</sup>.

Synthesis of 9 using DMP oxidation:



To a solution of **19b** (0.247 mmol, 71.5 mg, 1 equiv) in  $CH_2Cl_2$  (10 ml) was added NaHCO<sub>3</sub> (1.982 mmol, 166.5 mg, 8 equiv) and Dess-Martin periodinane (0.297 mmol, 126.1 mg, 1.2 equiv) at room temperature. The reaction mixture was stirred at this temperature for 1 h then quenched with saturated aqueous Na<sub>2</sub>SO<sub>3</sub> (5 ml) and diluted with  $CH_2Cl_2$  (5 ml). The layers were separated and the aqueous phase was extracted with  $CH_2Cl_2$  (10 ml × 3). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated to afford crude product, which was purified by flash chromatography on silica gel to give **9** (67.2 mg, 95%) as clear oil. This oil fully crystallized in RB within 12 hours.

 $\mathbf{R}_{\mathbf{f}} = 0.5 \ (10\% \ \text{EtOAc in hexanes})$ 

 $[\alpha]_{D}^{23} = +21.5 (c = 2.6, CHCl_3)$ 

<sup>1</sup>**H NMR (400 MHz, CDCl<sub>3</sub>)**  $\delta$  4.69 (d, J = 2.1 Hz, 1H), 4.53 (d, J = 1.9 Hz, 1H), 2.58-2.49 (m, 1H), 2.30-2.24 (m, 1H), 2.22-2.20 (m, 1H), 2.03 (d, J = 16.7 Hz, 1H), 1.93-1.83 (m, 2H), 1.80-1.74 (m, 1H), 1.64 – 1.50 (m, 3H), 1.46-1.37 (m, 4H), 1.32-1.22 (m, 3H), 1.17-1.12 (m, 2H), 1.08 (s, 3H), 1.03 (s, 3H), 1.00 (s, 3H), 0.98-0.97 (m, 1H).

<sup>13</sup>C NMR (400 MHz, CDCl<sub>3</sub>) δ 217.28, 152.15, 105.00, 55.74, 51.89, 48.00, 47.69, 38.79, 38.17, 37.27, 36.36, 34.11, 33.35, 28.50, 28.50, 27.21, 26.20, 21.68, 19.73, 13.51.

**HRMS (EI)** calculated for  $C_{20}H_{31}O[M+H]^+$ : *m/z* 287.2375, found: 287.2369

**IR**: 3438, 2971, 2933, 2864, 1703, 1644, 1446, 1110, 873 cm<sup>-1</sup>.

Synthesis of 22 and 23:



To a solution of **9** (0.516 mmol, 147.8 mg, 1 equiv) in THF/t-BuOH/H<sub>2</sub>O (1/1/0.2 ml) was added NMO (1.032 mmol, 138.2 mg, 2 equiv) and OsO<sub>4</sub> (0.062 mmol, 15.76 mg, 0.63 ml, 2.5% wt in *t*-BuOH, 0.20 equiv) at room temperature. The reaction mixture was stirred at this temperature for 30 h then quenched with saturated aqueous Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> (5 ml) and diluted with EtOAc (10 ml). The layers were separated and

the aqueous phase was extracted with EtOAc ( $10 \text{ ml} \times 3$ ). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated to give the crude product, which was purified by flash chromatography on silica gel to give **20** and **21** as an inseparable mixture (148.8 mg, 90%)

To a solution of **20** and **21** (0.46 mmol, 148.8 mg) in  $CH_2Cl_2$  (15 ml) was added  $Et_3N$  (2.32 mmol, 0.32 ml, 5 equiv) and  $Ac_2O$  (1.3 mmol, 0.13 ml, 3 equiv) at room temperature. The reaction mixture was stirred at this temperature for 24 hours, then quenched with saturated aqueous NaHCO<sub>3</sub> (10 ml) and diluted with  $CH_2Cl_2$  (10 ml). The layers were separated and the aqueous phase was extracted with  $CH_2Cl_2$  (10 ml × 3). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated to afford crude product, which was purified by flash chromatography on silica gel to provide **22** (95 mg, 57%) and **23** (70 mg, 42%).

22:

 $\mathbf{R}_{\mathbf{f}} = 0.5$  (40% EtOAc in hexanes)

 $[\alpha]_D^{23} = +37.0 \ (c = 0.2, \text{CHCl}_3)$ 

<sup>1</sup>**H NMR (400 MHz, CDCl**<sub>3</sub>) δ 4.08 (d, *J* = 11.3 Hz, 1H), 3.93 (d, *J* = 11.4 Hz, 1H), 2.60-2.51 (m, 1H), 2.35-2.28 (m, 1H), 2.08 (s, 3H), 2.05-1.99 (m, 2H), 1.91-1.79 (m, 2H), 1.76-1.75 (m, 1H), 1.60-1.55 (m, 2H), 1.50-1.39 (m, 4H), 1.37-1.27 (m, 2H), 1.24-2.13 (m, 4H), 1.09 (s, 3H), 1.06 (s, 3H), 1.02 (s, 3H), 0.85-0.77 (m, 1H).

<sup>13</sup>C NMR (400 MHz, CDCl<sub>3</sub>) δ 217.34, 171.22, 72.81, 70.31, 55.67, 52.24, 50.65, 47.68, 38.68, 38.01, 37.23, 34.09, 32.83, 32.74, 27.12, 26.27, 23.26, 22.92, 21.68, 20.97, 19.68, 13.56.

HRMS (EI) calculated for C<sub>22</sub>H<sub>34</sub>NaO<sub>4</sub> [M+Na]<sup>+</sup> : *m/z* 385.2355, found: 385.2345

**IR**: 2932, 2853, 1737, 1575,1410, 1320, 1381, 1260, 801 cm<sup>-1</sup>.

23:

 $\mathbf{R}_{\mathbf{f}} = 0.4$  (40% EtOAc in hexanes)

 $[\alpha]_{D}^{23} = +19.0 \ (c = 0.5, \text{CHCl}_3)$ 

<sup>1</sup>**H NMR (400 MHz, CDCl**<sub>3</sub>) δ 4.10 (d, *J* = 11.3 Hz, 1H), 3.93 (d, *J* = 11.4 Hz, 1H), 2.60-2.53 (m, 1H), 2.35-2.28 (m, 1H), 2.10 (s, 3H), 2.15-1.99 (m, 1H), 1.90-186 (m, 1H), 1.83-1.72 (m, 2H), 1.60-1.57 (m, 1H), 1.53-1.39 (m, 4H), 1.39-1.23 (m, 5H), 1.21-1.09 (m, 2H), 1.11 (s, 3H), 1.06 (s, 3H), 1.04 (s, 3H), 0.98-0.94 (m, 1H).

<sup>13</sup>C NMR (400 MHz, CDCl<sub>3</sub>) δ 217.3, 171.3, 73.0, 70.4, 55.8, 52.2, 50.8, 47.8, 38.8, 38.2, 37.2, 34.1, 32.7, 32.6, 27.5, 26.3, 24.7, 21.8, 21.7, 21.1, 19.5, 13.6.

**HRMS (EI)** calculated for  $C_{22}H_{35}O_4 [M+H]^+$ : m/z 363.2535, found: 363.2528

IR: 2939, 2871, 1736, 1690, 1398, 1244, 1086, 1032, 984, 882, 821, 596 cm<sup>-1</sup>.

Synthesis of (+)-16α, 17-dihydroxy-atisan-3-one:



To a solution of **22** (0.068 mmol, 25 mg) in MeOH (5 ml) was added K<sub>2</sub>CO<sub>3</sub> (0.13 mmol, 18.7 mg, 2 equiv) at room temperature. The reaction mixture was stirred at this temperature for one hour then quenched with saturated aqueous NH<sub>4</sub>Cl (10 ml). MeOH was removed under reduced pressure and the aqueous layer was extracted with EtOAc (10 ml  $\times$  3). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated to afford crude product, which was purified by flash chromatography on silica gel to provide (+)-16 $\alpha$ , 17-dihydroxy-atisan-3-one (1) (19.6 mg, 90%).

 $\mathbf{R}_{\mathbf{f}} = 0.40$  (70% EtOAc in hexanes)

 $[\alpha]_{D}^{23} = +32.0 \ (c = 0.05, \text{CHCl}_{3})$ 

<sup>1</sup>**H NMR (400 MHz, CDCl<sub>3</sub>)** δ 3.56 (d, *J* = 11.0 Hz, 1H), 3.42 (d, *J* = 11.0 Hz, 1H), 2.56 (ddd, *J* = 16.1, 12.3, 6.9 Hz, 1H), 2.32 (ddd, *J* = 16.0, 6.1, 3.3 Hz, 1H), 2.02 – 1.94 (m, 1H), 1.92 – 1.74 (m, 3H), 1.66 – 1.54 (m, 1H), 1.50 – 1.37 (m, 4H), 1.34 – 1.26 (m, 2H), 1.26 – 1.15 (m, 4H), 1.13-1.10 (m, 1H), 1.10 (s, 3H), 1.06 (s, 3H), 1.03 (s, 3H), 0.84-0.76 (m, 1H).

<sup>13</sup>C NMR (400 MHz, CDCl<sub>3</sub>) δ 217.50, 74.23, 69.18, 55.82, 52.68, 51.05, 47.79, 38.90, 38.16, 37.37, 34.21, 33.07, 32.32, 27.33, 26.36, 23.37, 23.13, 21.78, 19.81, 13.65.

**HRMS (EI)** calculated for  $C_{20}H_{33}O_3 [M+H]^+$ : m/z 321.2430, found: 321.2415.

IR: 3435, 3924, 2852, 1693, 1650, 1461, 1262, 1080, 1041, 909, 719 cm<sup>-1</sup>.

Synthesis of (+)-Sapinsigin H:



A 10 ml round-bottom flask was charged with ketone 1 (0.017 mmol, 5.6 mg) and *t*-BuOH (2 ml). This solution was then treated with KO<sup>t</sup>Bu (0.12 mmol, 13.7 mg, 7.0 equiv) at room temperature. The flask was vented and back-filled with oxygen (balloon) and the mixture was vigorously stirred under an atmosphere of oxygen. The reaction was quenched by addition of saturated aqueous solution of NH<sub>4</sub>Cl (10 ml). The pH of the mixture was adjusted to ~7 by addition of 1M HCl, and the aqueous layer was extracted with EtOAc (4 x 10 ml). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated to afford crude product, which was purified by flash chromatography on silica gel to provide (+)-Sapinsigin H (**3**) (5.4 mg, 95%).

 $\mathbf{R}_{\mathbf{f}} = 0.40 (70\% \text{ EtOAc in hexanes})$ 

 $[\alpha]_D^{23} = +61.0 \ (c = 0.08, \text{CHCl}_3)$ 

<sup>1</sup>**H NMR (400 MHz, CDCl<sub>3</sub>)** δ 6.24 (s, 1H), 5.96 (s, 1H), 3.59 (d, *J* = 11.0 Hz, 1H), 3.45 (d, *J* = 11.0 Hz, 1H), 2.18 (m, 1H), 1.89-1.88 (bs, 2H), 1.68-1.61 (m, 3H), 1.52-1.49 (m, 2H), 1.48 – 1.46 (m, 2H), 1.39 – 1.35 (m, 1H), 1.29 (s, 3H), 1.25-1.23 (m, 2H), 1.22 (s, 3H), 1.17 (m, 1H), 1.12 (s, 3H), 0.88 – 0.82 (m, 1H).

<sup>13</sup>C NMR (400 MHz, CDCl<sub>3</sub>) δ 201.15, 143.70, 127.85, 74.10, 68.97, 54.14, 52.58, 47.34, 44.08, 38.97, 38.88, 33.49, 32.12, 27.80, 27.04, 23.23, 23.18, 21.86, 18.93, 18.49.

**HRMS (EI)** calculated for  $C_{20}H_{31}O_4 [M+H]^+$ : *m/z* 335.2222, found: 335.2206.

IR: 3439, 2957, 2872, 1694, 1643, 1400, 1386, 1262, 1172, 1044, 686 cm<sup>-1</sup>.

Baeyer–Villiger oxidation to 24:



To a solution of **22** (0.071 mmol, 26 mg) in CH<sub>2</sub>Cl<sub>2</sub> (5 ml) was added NaHCO<sub>3</sub> (0.35 mmol, 30 mg, 5 equiv) and *m*-CPBA (0.1 mmol, 60%, 12 mg, 1.5 equiv) at room temperature. The reaction mixture was stirred at this temperature for 3 h then quenched with saturated aqueous Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> (10 ml). The aqueous layer was extracted by CH<sub>2</sub>Cl<sub>2</sub> (10 ml  $\times$  4) and the combined organic layers were then dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated to give the residue, which was purified by flash chromatography on silica gel to give **24** (17.4 mg, 65%).

 $\mathbf{R}_{\mathbf{f}} = 0.3$  (40% EtOAc in hexanes)

 $[\alpha]_{D}^{23} = +37.0 \ (c = 0.6, \text{CHCl}_3)$ 

<sup>1</sup>**H NMR (400 MHz, CDCl<sub>3</sub>)** δ 4.08 (d, *J* = 11.4 Hz, 1H), 3.93 (d, *J* = 11.4 Hz, 1H), 2.61 (dd, *J* = 7.4, 3.5 Hz, 2H), 2.08 (s, 3H), 2.06 – 2.00 (m, 1H), 1.89 – 1.80 (m, 1H), 1.79 – 1.74 (m, 1H), 1.72 – 1.64 (m, 1H), 1.61-1.54 (d, 3H), 1.50-1.44 (m, 4H), 1.43 (s, 3H), 1.41 (s, 3H), 1.41-1.33 (m, 3H), 1.25-1.16 (m, 4H), 1.14 (s, 3H), 0.87-1.76 (m, 1H).

<sup>13</sup>C NMR (400 MHz, CDCl<sub>3</sub>) δ 175.65, 171.23, 86.51, 72.59, 70.20, 56.16, 52.12, 50.52, 40.63, 38.62, 35.78, 33.30, 32.90, 32.86, 31.72, 26.91, 25.14, 23.52, 23.13, 22.62, 20.97, 14.93.

HRMS (EI) calculated for C<sub>22</sub>H<sub>34</sub>NaO<sub>5</sub> [M+Na]<sup>+</sup> : *m/z* 401.2304, found: 401.2293

IR: 2980, 2939, 1720, 1680, 1510, 1480, 1356, 1211, 996, 756, 692 cm<sup>-1</sup>.

Synthesis of acid **24a**:



Compound 24 (0.045 mmol, 17.4 mg) in CH<sub>2</sub>Cl<sub>2</sub> (10 ml) was added 30 mg of *p*-toluenesulfonic acid. The mixture was stirred at room temperature for 6–8 h. The mixture was diluted with water and extracted with CH<sub>2</sub>Cl<sub>2</sub>. The organic layer was washed with 5% sodium bicarbonate solution, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated. The residue was purified by flash chromatography on silica gel to give 24a (12.7 mg, 75%).

 $\mathbf{R}_{\mathbf{f}} = 0.5$  (50% EtOAc in hexanes)

 $[\alpha]_D^{23} = +26.0 \ (c = 0.37, \text{CHCl}_3)$ 

<sup>1</sup>**H NMR (400 MHz, CDCl**<sub>3</sub>) δ 4.85 (s, 1H), 4.66 (s, 1H), 4.09 (d, *J* = 11.4 Hz, 1H), 3.93 (d, *J* = 11.4 Hz, 1H), 2.34 (ddd, *J* = 33.7, 16.6, 8.3 Hz, 3H), 2.08 (s, 3H), 1.99 – 1.83 (m, 4H), 1.78 – 1.74 (m, 1H), 1.73 (s, 3H), 1.55-1.49 (m, 3H), 1.10-1.30 (m, 3H), 1.20-1.11 (m, 4H), 0.95 (s, 3H), 0.85-0.76 (m, 1H).

<sup>13</sup>C NMR (400 MHz, CDCl<sub>3</sub>) δ 177.81, 171.22, 147.34, 113.61, 73.26, 70.15, 52.10, 50.88, 42.77, 39.68, 38.04, 33.22, 32.93, 32.74, 28.08, 26.98, 24.64, 23.58, 23.18, 22.82, 20.95, 17.80.

HRMS (EI) calculated for C<sub>22</sub>H<sub>34</sub>NaO<sub>5</sub> [M+Na]<sup>+</sup> : *m/z* 401.2304, found: 401.2292

**IR**: 3560, 3000, 1713, 1637, 1398, 1219, 758, 667, 596 cm<sup>-1</sup>.

Synthesis of (+)-agallochaol C:



To a solution of **24a** (0.01 mmol, 4 mg) in MeOH (1.5 ml) was added K<sub>2</sub>CO<sub>3</sub> (0.02 mmol, 2.9 mg, 2 equiv) at room temperature. The reaction mixture was stirred at this temperature for one hour then quenched with saturated aqueous NH<sub>4</sub>Cl (10 ml). MeOH was removed under reduced pressure and the aqueous layer was extracted with EtOAc (10 ml × 4). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated to afford crude product, which was purified by flash chromatography on silica gel (10% CH<sub>2</sub>Cl<sub>2</sub>/MeOH) to provide (+)-agallochaol C (**2**) (3 mg, 90%).

 $R_f = 0.5$  (30% MeOH in CH<sub>2</sub>Cl<sub>2</sub>)

 $[\alpha]_D^{23} = +27.0 \ (c = 0.25, \text{CHCl}_3)$ 

<sup>1</sup>**H NMR (400 MHz, CD<sub>3</sub>OD**) δ 4.85 (s, 1H), 4.70 (s, 1H), 3.49 (d, *J* = 11.4 Hz, 1H), 3.35 (d, *J* = 11.4 Hz, 1H), 2.39 – 2.29 (m, 1H), 2.27-2.22 (m, 1H), 2.03-1.97 (m, 2H), 1.96-1.92 (m, 1H), 1.85-1.80 (m, 2H), 1.76 (s, 3H), 1.68-1.62 (m, 2H), 1.53-1.49 (m, 1H), 1.49-1.42 (m, 2H), 1.30-1.27 (m, 2H), 1.25-1.18 (m, 2H), 1.14 (d, *J* = 13.9 Hz, 1H), 1.06 (dd, J = 13.9, 2.8 Hz, 1H), 0.99 (s, 3H), 0.86-0.80 (m, 1H).

<sup>13</sup>C NMR (400 MHz, CD<sub>3</sub>OD) δ 177.91, 149.50, 114.31, 75.48, 70.10, 53.89, 52.65, 44.69, 41.23, 39.98, 35.64, 34.45, 33.71, 30.51, 28.64, 26.43, 24.66, 24.56, 24.50, 18.90.

HRMS (EI) calculated for C<sub>20</sub>H<sub>32</sub>NaO<sub>4</sub> [M+Na]<sup>+</sup> : *m/z* 359.2198, found: 359.2188

**IR**: 3559, 3418, 2930, 1703, 1638, 1445, 1261, 1220, 890, 749 cm<sup>-1</sup>.

## <sup>1</sup>H and <sup>13</sup>C NMR comparison

Comparison of NMR data for natural *ent*-16α, 17-dihydroxy-atisan-3-one with our synthetic (+)-16α, 17-dihydroxy-atisan-3-one.



(+)-16α,17-dihydroxy-atisan-3-one (1)

Natural <i>ent</i> -16α, 17-dihydroxy-atisan-3-one			Synthetic (+)-16α, 17-dihydroxy-atisa			
	400 MHz, CDCl <sub>3</sub>	100 MHz	400 MHz, CDCl <sub>3</sub>	400 MHz	$\Delta \delta_H$	$\Delta \delta_C$
	$\delta_{\!H}$ , ppm, $J$ in $H\!z$	$\delta c$ , ppm	$\delta_{\!H}$ , ppm, $J$ in $H\!z$	$\delta c$ , ppm	ppm	ppm
1	Ha: 1.85, m Hb: 1.38, m	38.0	Ha: 1.92-1.74, m Hb: 1.50-1.37, m	38.1		0.1
2	Ha: 2.58, ddd, 16.0, 12.3, 6.9 Hb: 2.33, ddd, 16.0, 6.0, 3.2	34.0	Ha: 2.55, ddd, 16.1, 12.3, 6.9 Hb: 2.32, ddd, 16.0, 6.1, 3.3	34.2	- 0.03 - 0.01	0.2
3		217.5		217.5		0
4		47.6		47.7		0.1
5	1.30, m	55.6	1.26-1.34, m	55.8	-	0.2
6	Ha: 1.45, m	19.6	Ha: 1.50-137, m	19.8	-	0.2
7	Ha: 1.42, m Hb: 1.18, m	38.7	Ha: 1.50-137, m Ha: 1.50-137, m Hb: 1.26-1.15, m	38.9	-	0.2
8		32.8	,,	33.0		0.2
9	1.32, m	50.8	Ha: 1.34-1.26, m	51.0	-	0.2
10		37.2		37.3		0.1
11	Ha: 2.03, m Hb: 1.24, m	22.9	Ha: 2.02-1.94, m Hb: 1.26-1.15, m	23.1	-	0.2
12	1.82. m	32.1	Ha: 1.92-1.74, m	32.3	-	0.2
13	Ha: 1.63, m Hb: 1.50, m	23.2	Ha: 1.66-154, m Hb: 1.50-1.37, m	23.3	-	0.1
14	Ha: 1.87, m Hb: 0.82, m	27.2	Ha: 1.92-1.74, m Hb: 0.84-0.76, m	27.3	-	0.1
15	Ha: 1.24, m Hb: 1.10, m	52.4	Ha: 1.26-1.15, m Hb: 1.13-1.10, m	52.6	-	0.2
16		74.1		74.2		0.1
17	Ha: 3.57, d, 10.9 Hb: 3.43, d, 10.9	68.9	Ha: 3.56, d, 11.0 Hb: 3.42, d, 11.0	69.1	- 0.01 - 0.01	0.2
18	1.07, s	26.1	1.06, s	26.3	- 0.01	0.2
19	1.04, s	21.6	1.03, s	21.7	- 0.01	0.1
20	1.11, s	13.4	1.10, s	13.6	- 0.01	0.2

2. Comparison of NMR data for natural Sapinsigin H with our synthetic (+)-Sapinsigin H.



sapinsigin H (3)

	Natural sapinsigin H		Synthetic sapinsigin H			
	800 MHz, CDCl <sub>3</sub>	800 MHz	400 MHz, CDCl <sub>3</sub>	400 MHz	$\Delta \delta_{H}$	$\Delta \delta_C$
	$\delta_{\!H}$ , ppm, $J$ in $H\!z$	$\delta c$ , ppm	$\delta_{\!H}$ , ppm, $J$ in $H\!z$	$\delta c$ , ppm	ppm	ppm
1	6.24, s	127.7	6.24, s	127.8	0	0.1
2		143.6		143.7		0.1
3		201.0		201.1		0.1
4		44.0		44.0		0
5	1.68, dd, 11.5, 2.6	54.1	1.68-1.61, unresolved	54.1	-	0
6	Ha: 1.52, m	18.8	Ha: 1.52-1.49, m	18.9	-	0.1
	Hb: 1.48, m		Hb: 1.48-1.46, m		-	
7	Ha: 1.47, m	38.8	Ha: 1.48-1.46, m	38.8	-	0
	Hb: 1.24, m		Hb: 1.26-1.15, m		-	
8		33.4		33.4		0
9	1.62, overlap	47.3	Ha: 1.68-1.61, unresolved	47.3	-	0
10		38.9		38.9		0
11	Ha: 2.19, m	23.1	Ha: 2.18, m	23.1	-	0
	Hb: 1.51, m		Hb: 1.52-1.49, m		-	
12	1.89, m	32.1	1.89-1.88, bs	32.1	-	0
13	Ha: 1.63, m	23.2	Ha: 1.68.1.61, m	23.2	-	0
	Hb: 1.38, m	25.5	Hb: 1.39-1.35, m		-	0.1
14	Ha: 1.88, m	27.7	Ha: 1.89-1.88, bs	27.8	-	0.1
15	Hb: 0.85, m	52.5	Hb: 0.88-82, m	52.5	-	0
15	Ha: 1.25, overlap Hb: 1.16 overlap	52.5	Ha: $1.25 - 1.23$ , m Hb: $1.17$ m	52.5	-	0
16		73.9	110. 1.17, m	74.1	-	0.2
10	Ha: 3 59 dd 10 9 4 3	68.9	Ha: 3 59 d 11 0	68.9	0	0.2
17	Hb: 3 45 dd 10 9 4 3	00.7	Hb: 3.45 d 11.0	00.7	0	0
18	1.22. 8	26.9	1.22. s	27.0	0	0.1
19	1.12. s	21.8	1.12, s	21.8	0	0
20	1.29, s	18.4	1.29, s	18.4	0	0

3. Comparison of NMR data for natural Agallochaol C with our synthetic (+)-Agallochaol C.



(+)-agallochaol C

	Natural agallochaol C		Synthetic agallochaol C			
	$400 \text{ MHz}, \text{CD}_3\text{OD}$	100 MHz	400 MHz, CD <sub>3</sub> OD	400 MHz	$\Delta \delta_H$	$\Delta \delta_C$
	$\delta_H$ , ppm, J in Hz	$\delta c$ , ppm	$\delta_H$ , ppm, J in Hz	$\delta c$ , ppm	ppm	ppm
1	Ha: 1.52-1.48, m	35.5	Ha: 1.53-1.49, m	35.6	-	0.1
	Hb: 1.63, m		Hb: 1.68-1.62, m		-	
2	Ha: 2.27-2.24, m	30.1	Ha: 2.27-2.22, m	30.5	-	0.4
2	Hb: 2.34, m	170.0	Hb: 2.39-2.29, m	170.0	-	0.0
3		1/9.0		1/9.9		0.9
4		149.5		149.5		0
5	2.02-1.98, m	52.6	2.03-1.97, m	52.6	-	0
6	Ha: 1.83-1.80, m	26.4	Ha: 1.85-1.80, m	26.4	-	0
	Hb: 1.30-1.27, m		Hb: 1.30-1.27, m		-	
7	NOT GIVEN	40.0	Ha: 1.30-1.27, m	39.9	-	- 0.1
	Hb: 1.24-1.20, m	24.5	Hb: 1.25-1.18, m	24.4	-	0.1
8	=	34.5		34.4		- 0.1
9	1.47-1.44, m	44.7	Ha: 1.49-1.42, m	44.6	-	- 0.1
10		41.2		41.2		0
11	Ha: 2.02-1.98, m	24.5	Ha: 2.03-1.97, m	24.5	-	0
	Hb: 1.24-1.20, m		Hb: 1.25-1.18, m		-	
12	1.83-1.80, m	33.7	Ha: 1.85-1.80, m	33.7	-	0
13	Ha: 1.67-1.64, m	24.7	Ha: 1.68-162, m	24.6	-	- 0.1
	Hb: 1.47-1.44, m	20.5	Hb: 1.49-1.42, m	20.6	-	0.1
14	Ha: 1.96-1.92, m	28.7	Ha: 1.96-1.92, m	28.6	-	- 0.1
15	Hb: 0.85-0.82, m	52.0	Hb: 0.86-0.80, m	52.0	-	0.1
15	Ha: $1.06$ , dd, $13.7$ , $2.7$	53.9	Ha: 1.06, dd, 13.9, 2.8	53.8	-	- 0.1
1(	HD: 1.10, d, 13.7	75.5	Hb: 1.14, d, 13.9	75 4	-	0.1
16	II 225 1 11 4	/5.5	11 2 25 1 11 4	/5.4	0	- 0.1
17	Ha: $3.35$ , d, 11.4	/0.1	Ha: $3.35$ , d, 11.4	/0.1	0	0
10	Hb: 3.49, d, 11.4	24.6	Hb: 3.49, d, 114	24.5	0	0.1
10	1.70, S	24.0	1./0, S	24.3	0.01	- 0.1
19	Ha: $4.80$ , bs Hb: $4.02$ hs	114.4	Ha: 4.85, s Hb: 4.70	114.3	- 0.01	- 0.1
20		18.0		18.0	- 0.22	0
20	0.99, 8	18.9	0.99, 8	18.9	0	0

Crystallographic Data for Single Crystal X-Ray Structure of Compound 9
Table 1 Crystal data and structure refinement for 10auga_o_0m.

Identification code	10auga_o_0m
Empirical formula	$C_{20}H_{30}O$
Formula weight	286.461
Temperature/K	296.15
Crystal system	triclinic
Space group	P-1
a/Å	6.0028(2)
b/Å	11.2789(3)
c/Å	13.1074(4)
a/°	64.982(1)
β/°	80.954(1)
$\gamma/^{\circ}$	87.690(1)
Volume/Å <sup>3</sup>	793.83(4)
Z	2
$\rho_{calc}g/cm^3$	1.198
$\mu/\text{mm}^{-1}$	0.071
F(000)	316.2
Crystal size/mm <sup>3</sup>	0.21 imes 0.18 imes 0.16
Radiation	Mo K $\alpha$ ( $\lambda = 0.71073$ )
$2\Theta$ range for data collection/°	3.98 to 56.8
Index ranges	$-8 \le h \le 8, -15 \le k \le 15, -17 \le l \le 17$
Reflections collected	17410
Independent reflections	3957 [ $R_{int} = 0.0301$ , $R_{sigma} = 0.0242$ ]
Data/restraints/parameters	3957/0/201
Goodness-of-fit on F <sup>2</sup>	1.053
Final R indexes $[I \ge 2\sigma(I)]$	$R_1 = 0.0390, wR_2 = 0.1013$
Final R indexes [all data]	$R_1 = 0.0424, wR_2 = 0.1040$
Largest diff. peak/hole / e Å <sup>-3</sup>	0.38/-0.20

Table 2 Fractional Atomic Coordinates (×10 <sup>4</sup> ) and Equivalent Isotropic Displacement
Parameters ( $Å^2 \times 10^3$ ) for 10auga_0_0m. U <sub>eq</sub> is defined as 1/3 of the trace of the
orthogonalised U <sub>IJ</sub> tensor.

Atom	x	у	z	U(eq)
01	7194.7(14)	3983.4(8)	6087.6(7)	25.60(19)
C9	6205.7(15)	8115.5(8)	7311.4(7)	10.73(17)
C3	7619.7(16)	4941.1(9)	6234.3(8)	15.27(19)
C8	6928.6(15)	8081.3(9)	8408.6(7)	12.22(18)
C1	6386.9(16)	7264.9(9)	5824.0(8)	13.48(18)
C6	8624.8(16)	5859.0(9)	8711.9(8)	14.90(19)
C16	4802.5(16)	10132.9(9)	8122.3(8)	15.76(19)
C4	8563.0(16)	4797.3(9)	7306.0(8)	13.74(18)
C11	5846.9(16)	9558.8(9)	6484.7(8)	14.20(18)
C5	7635.4(15)	5881.8(9)	7691.7(7)	11.65(17)
C10	7643.9(15)	7301.2(8)	6747.5(7)	10.79(17)
C2	7350.0(17)	6302.2(10)	5335.2(8)	16.26(19)
C12	6335.9(16)	10503.6(9)	7001.3(8)	15.71(19)
C15	5008.1(16)	8707.1(9)	8926.1(8)	15.09(19)
C20	10029.4(15)	7902.1(9)	6189.5(8)	14.62(18)
C13	8794.3(17)	10334.2(9)	7230.7(9)	18.0(2)
C7	7203.3(17)	6666.9(9)	9249.7(8)	15.09(19)
C14	9060.5(16)	8941.7(9)	8157.2(8)	15.45(19)
C17	3441.3(19)	10958.7(11)	8379.6(10)	22.8(2)
C19	11162.4(17)	4823.0(10)	7001.8(9)	18.3(2)
C18	7822(2)	3445.7(9)	8260.9(9)	21.5(2)

Table 3 Anisotropic Displacement Parameters (Å<sup>2</sup>×10<sup>3</sup>) for 10auga\_o\_0m. The Anisotropic displacement factor exponent takes the form: -  $2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+...]$ .

Atom	<b>U</b> 11	$U_{22}$	U33	$U_{12}$	<b>U</b> 13	$U_{23}$
01	34.1(4)	20.3(4)	29.4(4)	0.2(3)	-10.1(3)	-15.4(3)
C9	10.5(4)	10.8(4)	10.8(4)	0.4(3)	-1.8(3)	-4.5(3)
C3	13.4(4)	17.6(4)	16.7(4)	0.7(3)	-0.4(3)	-9.8(4)
C8	13.9(4)	12.3(4)	11.4(4)	1.5(3)	-3.1(3)	-5.6(3)
C1	14.8(4)	14.9(4)	12.1(4)	2.3(3)	-3.9(3)	-6.5(3)
C6	18.8(4)	13.7(4)	12.4(4)	4.1(3)	-5.2(3)	-5.1(3)
C16	16.8(4)	15.5(4)	19.0(4)	1.9(3)	-6.9(4)	-9.8(4)
C4	16.0(4)	12.2(4)	13.7(4)	1.4(3)	-1.8(3)	-6.3(3)
C11	16.2(4)	12.7(4)	13.7(4)	2.0(3)	-4.3(3)	-5.0(3)
C5	12.8(4)	10.7(4)	11.2(4)	0.6(3)	-1.4(3)	-4.6(3)
C10	10.7(4)	11.4(4)	10.2(4)	0.3(3)	-1.4(3)	-4.5(3)
C2	18.7(5)	19.1(5)	13.7(4)	2.1(4)	-3.5(3)	-9.3(4)
C12	18.2(5)	11.5(4)	17.9(4)	1.5(3)	-5.2(4)	-5.9(3)
C15	16.5(4)	16.3(4)	14.7(4)	2.4(3)	-2.8(3)	-8.8(4)
C20	12.2(4)	15.0(4)	15.0(4)	-0.8(3)	0.5(3)	-5.6(3)
C13	16.5(4)	14.7(4)	23.5(5)	-1.9(3)	-3.5(4)	-8.5(4)
C7	20.5(5)	14.2(4)	10.9(4)	2.9(3)	-4.1(3)	-5.2(3)
C14	14.2(4)	16.6(4)	18.7(4)	1.0(3)	-6.0(3)	-9.4(4)
C17	22.8(5)	22.0(5)	29.8(6)	5.4(4)	-7.0(4)	-16.2(5)
C19	16.3(5)	20.7(5)	20.8(5)	5.7(4)	-4.3(4)	-11.6(4)
C18	32.3(6)	12.0(4)	18.4(5)	0.4(4)	-0.5(4)	-5.9(4)

Table 4	Bond	Lengths for	10auga o	0m.
			<b>_</b>	

Atom	Atom	Length/Å	Atom	Atom	Length/Å
01	C3	1.2174(12)	C6	C7	1.5320(13)
C9	C8	1.5511(12)	C16	C12	1.5057(14)
C9	C11	1.5568(12)	C16	C15	1.5176(13)
C9	C10	1.5636(12)	C16	C17	1.3291(14)
C3	C4	1.5396(13)	C4	C5	1.5626(12)
C3	C2	1.5105(13)	C4	C19	1.5469(13)
C8	C15	1.5430(12)	C4	C18	1.5344(13)
C8	C7	1.5284(12)	C11	C12	1.5422(13)
C8	C14	1.5443(13)	C5	C10	1.5548(12)
C1	C10	1.5388(12)	C10	C20	1.5409(12)
C1	C2	1.5313(12)	C12	C13	1.5404(13)
C6	C5	1.5365(12)	C13	C14	1.5475(13)

Table	5	Bond	Angles	for	10	au	iga_	0_	<u>0</u> m.	

Aton	1 Aton	1 Atom	Angle/°	Aton	1 Aton	n Atom	Angle/°
C11	C9	C8	109.36(7)	C18	C4	C5	109.37(7)
C10	C9	C8	116.23(7)	C18	C4	C19	107.83(8)
C10	C9	C11	114.92(7)	C12	C11	C9	110.80(7)
C4	C3	01	120.97(9)	C4	C5	C6	113.57(7)
C2	C3	01	120.50(9)	C10	C5	C6	110.86(7)
C2	C3	C4	118.45(8)	C10	C5	C4	117.05(7)
C15	C8	C9	106.16(7)	C1	C10	C9	107.26(7)
C7	C8	C9	110.10(7)	C5	C10	C9	106.34(7)
C7	C8	C15	109.84(7)	C5	C10	C1	107.71(7)
C14	C8	C9	112.63(7)	C20	C10	C9	112.74(7)
C14	C8	C15	105.74(7)	C20	C10	C1	108.85(7)
C14	C8	C7	112.10(8)	C20	C10	C5	113.65(7)
C2	C1	C10	113.74(7)	C1	C2	C3	113.66(7)
C7	C6	C5	110.62(7)	C11	C12	C16	108.77(8)
C15	C16	C12	111.97(8)	C13	C12	C16	108.32(8)
C17	C16	C12	124.00(9)	C13	C12	C11	108.31(8)
C17	C16	C15	124.03(10)	C16	C15	C8	110.21(8)
C5	C4	C3	110.49(7)	C14	C13	C12	109.56(8)
C19	C4	C3	106.16(7)	C6	C7	C8	113.58(7)
C19	C4	C5	114.44(8)	C13	C14	C8	110.61(7)
C18	C4	C3	108.33(8)				

## Table 6 Torsion Angles for 10auga\_o\_0m.

			0	0					
Α	B	С	D	Angle/°	Α	В	С	D	Angle/°
01	C3	C4	C5	-	C3	C2	C1	C10	51.24(9)
				145.28(10)					
01	C3	C4	C19	90.10(10)	C8	C15	C16	C12	6.11(8)
01	C3	C4	C18	-25.49(11)	C8	C15	C16	C17	-173.50(8)
01	C3	C2	C1	141.04(9)	C8	C7	C6	C5	-55.90(8)
C9	C8	C15	C16	-63.91(7)	C8	C14	C13	C12	10.02(8)
C9	C8	C7	C6	48.69(8)	C1	C10	C5	C6	-173.57(7)
C9	C8	C14	C13	50.55(8)	C1	C10	C5	C4	53.98(8)
C9	C11	C12	C16	-58.35(8)	C6	C5	C4	C19	-56.43(8)
C9	C11	C12	C13	59.17(8)	C6	C5	C4	C18	64.65(9)
C9	C10	C1	C2	-169.63(7)	C6	C5	C10	C20	65.76(8)
C9	C10	C5	C6	-58.85(7)	C16	C12	C13	C14	52.63(8)
C9	C10	C5	C4	168.69(6)	C4	C5	C10	C20	-66.69(8)
C3	C4	C5	C6	-176.18(7)	C11	C12	C13	C14	-65.18(8)
C3	C4	C5	C10	-44.96(8)					

Atom	x	у	Z.	U(eq)
H9	4697.3(15)	7697.2(8)	7556.6(7)	12.9(2)
H1a	4813.8(16)	7027.9(9)	6146.0(8)	16.2(2)
H1b	6445.9(16)	8135.5(9)	5207.7(8)	16.2(2)
Нба	8661.8(16)	4962.4(9)	9276.3(8)	17.9(2)
H6b	10160.8(16)	6212.8(9)	8460.8(8)	17.9(2)
H11a	6841.1(16)	9780.9(9)	5766.5(8)	17.0(2)
H11b	4303.2(16)	9652.1(9)	6333.9(8)	17.0(2)
H5	6034.8(15)	5642.4(9)	7983.6(7)	14.0(2)
H2a	8810.4(17)	6638.3(10)	4877.8(8)	19.5(2)
H2b	6360.6(17)	6251.1(10)	4836.0(8)	19.5(2)
H12	6100.7(16)	11410.0(9)	6479.2(8)	18.9(2)
H15a	3595.7(16)	8236.6(9)	9061.9(8)	18.1(2)
H15b	5316.6(16)	8646.3(9)	9650.9(8)	18.1(2)
H20a	9959(2)	8839.2(9)	5843(6)	21.9(3)
H20b	11000(4)	7640(6)	6759.7(14)	21.9(3)
H20c	10615(5)	7602(6)	5618(5)	21.9(3)
H13a	9803.9(17)	10466.2(9)	6534.3(9)	21.6(2)
H13b	9188.6(17)	10980.8(9)	7483.5(9)	21.6(2)
H7a	7904.3(17)	6669.6(9)	9867.0(8)	18.1(2)
H7b	5720.5(17)	6248.4(9)	9574.1(8)	18.1(2)
H14a	9311.4(16)	8995.6(9)	8849.8(8)	18.5(2)
H14b	10362.9(16)	8544.7(9)	7901.0(8)	18.5(2)
H19a	11617.3(19)	4049(4)	6901(7)	27.4(3)
H19b	11643(2)	5583(4)	6309(4)	27.4(3)
H19c	11839.9(17)	4853(8)	7607(3)	27.4(3)
H18a	6221(3)	3422(3)	8497(5)	32.3(3)
H18b	8197(14)	2785.8(12)	7986(2)	32.3(3)
H18c	8583(11)	3284(4)	8897(3)	32.3(3)
H17a	2450(30)	10663(14)	9128(13)	29(4)
H17b	3410(30)	11857(16)	7837(13)	35(4)

Table 7 Hydrogen Atom Coordinates (Å×10<sup>4</sup>) and Isotropic Displacement Parameters (Å<sup>2</sup>×10<sup>3</sup>) for 10auga\_o\_0m.



TfO Me H, отвs Me<sup>Me</sup>Me 13 <sup>19</sup>F NMR (400 MHz, CDCl<sub>3</sub>)

170 150 130 110 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -110 f1 (ppm)





![](_page_29_Figure_0.jpeg)

![](_page_30_Figure_0.jpeg)

![](_page_31_Figure_0.jpeg)

![](_page_32_Figure_0.jpeg)

![](_page_33_Figure_0.jpeg)

-4.50 -4.48 -4.47 -4.46

ſ

![](_page_34_Figure_3.jpeg)

![](_page_34_Figure_4.jpeg)

![](_page_34_Figure_5.jpeg)

![](_page_34_Figure_6.jpeg)

110 100 f1 (ppm) 

![](_page_35_Figure_0.jpeg)

![](_page_36_Figure_0.jpeg)

![](_page_37_Figure_0.jpeg)

110 100 f1 (ppm) 

![](_page_38_Figure_0.jpeg)

120 110 f1 (ppm) 

![](_page_39_Figure_0.jpeg)

![](_page_40_Figure_0.jpeg)

![](_page_41_Figure_0.jpeg)

![](_page_42_Figure_0.jpeg)

![](_page_43_Figure_0.jpeg)