Supporting Information

Enantioselective construction of substituted pyridine and seven-membered carbocyclic skeleton: Biomimetic synthesis of (-)-rupestine D, (-)-guaipyridine, (-)-epiguaipyridine, (-)-cananodine and their stereoisomers

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1. General Information

All reactions were performed in round-bottomed flasks or test tubes. All reagents were purchased from commercial suppliers and used without further purification unless otherwise noted. Solvent purification was conducted according to Purification of Laboratory Chemicals 2nd edn (Perrin, D. D., Armarego, W. L. F. and Perrin, D. R., Pergamon Press: Oxford, 1980). The solvents for reactions without water and oxygen were degassed in flame-dried glassware via syringe needle under Ar for 30 min. Reactions were monitored by thin layer chromatography (TLC, Silica gel 60 HF254) supplied by Merk KGaA (Germany). Visualization was accomplished with UV light, exposure to iodine, stained with ethanolic solution of phosphomolybdic acid or basic solution of KMnO4. The products were purified by flash column chromatography on silica gel (200 – 300 meshes) from the Shanghai Titan Scientific Ci.,Ltd (China). Melting points were determined on a Buchi M-560. Infrared (IR) spectra were recorded on a Thermo Scientific Nicolet 6700 spectrometer. Optical rotation was obtained from Rudolph Research Analytical Autopol IV automatic polarimeter. 1H NMR and 13C NMR spectra were recorded on Varian INOVA-400MHz instruments and calibrated by using residual undeuterated chloroform (δ, 1H NMR = 7.260, 13C NMR = 77.00). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, dd = doublet of doublets, ddd = doublet of doublet of doublet, dt = triplet of doublet, t = triplet, q = quartet, m = multiplet, br = broad and coupling constants (J) are reported in Hertz (Hz). High-resolution mass spectra (HRMS) were recorded on a UHPLC-Q-orbitrap-MS (Thermo, Bremen, Germany).
2. Experimental Procedures and Characterization Data

Preparation of S1: (R)-(−)-citronellene (41.0 g, 297 mmol, 1 equiv) in 0.6 L of CH$_2$Cl$_2$ was added dropwise to a solution of SeO$_2$ (3.30 g, 49.5 mmol) and TBHP (42.0 g, 70% wt% in water, 326 mmol) at room temperature. Stirring was continued for an additional 30 min at 0 °C after this mixture was stirred at room temperature for 2 h, then, the reaction was quenched by an aqueous sat. Na$_2$S$_2$O$_3$ solution. The solution was extracted with MTBE (3×600 mL) and combined organic layers were washed with brine, then, the organic layers were dried over Na$_2$SO$_4$. The solvent was evaporated under reduced pressure.

A magnetically stirred solution of the mixture of the previous step and CeCl$_3$·7H$_2$O (55.2 g, 148 mmol) in MeOH (200 mL) was cooled to 0 °C and then treated, in portions, with sodium borohydride (5.61 g, 148 mmol) (CAUTION: EVOLUTION OF HYDROGEN GAS). The resulting mixture was stirred at 0 °C for 1 h before being quenched with water (50 mL) and then concentrated under reduced pressure. The residue so-formed was extracted with MTBE (3×100 mL) and combined organic layers were washed with brine, then, the combined organic phases were dried over Na$_2$SO$_4$, then purified by flash chromatography on silicagel (PE/EA, 15:1) to give a colorless liquid product S1 (32.0 g, 207 mmol 70%).

$[\alpha]_D^{20} = +9$ (c 0.10, MeOH);

$^1$H NMR (400 MHz, CDCl$_3$) δ 5.67 (ddd, $J = 17.5, 10.3, 7.5$ Hz, 1H), 5.38 – 5.34 (m, 1H), 4.96 – 4.88 (m, 2H), 3.95 (d, $J = 6.0$ Hz, 2H), 2.14 – 2.07 (m, 1H), 2.05 – 1.92 (m, 3H), 1.63 (s, 2H), 1.32 (qd, $J = 7.2, 1.5$ Hz, 2H), 0.97 (d, $J = 6.8$ Hz, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 144.41, 134.59, 126.12, 112.63, 68.75, 37.33, 25.24, 20.09, 13.56. 

IR(KBr) 3334, 3077, 2961, 2914, 2863, 1639, 1455, 995, 910 cm$^{-1}$;

HRMS (ESI): $m/z$ calcd. for C$_{10}$H$_{18}$O [M + H]$^+$ 155.1436, found 155.1428.

Preparation of 9: To a stirred mixture of Ti(OiPr)$_4$ (3.39 g, 11.9 mmol), CaH$_2$ (20 mg), silica gel (20
mg) and 4 Å molecular sieves (20 mg) in 80 mL of dry CH₂Cl₂ was added D-(-)-diisopropyl tartrate (DIPT) (2.78 g, 11.9 mmol) in 80 mL of dry CH₂Cl₂ at −20 °C under N₂ and stirred for 10 min. A solution of compound S1 (15.3 g, 99.3 mmol) in 40 mL of dry CH₂Cl₂ was injected and stirred for another 10 min. Then the mixture was cooled to −50 °C, 45.8 mL of anhydrous TBHP (2.6 M in toluene,119 mmol) was injected slowly. After addition, the mixture was allowed to warm to −20 °C, stirred for 2 h and monitored by TLC. The reaction mixture was quenched by 100 mL of 10% aqueous tartaric acid, warmed to room temperature, and stirring was continued until the aqueous layer became clear. The reaction mixture was extracted with ethyl acetate, washed successively with 5% aqueous NaOH, saturated aqueous NaHCO₃, water and brine, dried (Na₂SO₄), and concentrated in vacuo. The residue was purified by silica gel chromatography (PE/EA–6:1) to give epoxide 9 (15.2 g, 89.3 mmol, 90%).

\[ \alpha ]^D_{D20} = +7 (c 0.10, MeOH);

\( ^1H \) NMR (400 MHz, CDCl₃) δ 5.68 (ddd, \( J = 17.5, 10.3, 7.5 \) Hz, 1H), 5.00 – 4.93 (m, 2H), 3.67 (ddd, \( J = 12.2, 4.5 \) Hz, 1H), 3.57 (dd, \( J = 12.2, 8.5 \) Hz, 1H), 3.02 (t, \( J = 5.9 \) Hz, 1H), 1.60 – 1.48 (m, 3H), 1.27 (s, 3H), 1.01 (d, \( J = 6.7 \) Hz, 3H).

\( ^13C \) NMR (100 MHz, CDCl₃) δ 143.99, 113.10, 65.29, 60.91, 37.53, 33.01, 25.85, 20.09, 14.22.

IR(KBr) 3393, 2919, 2849, 1644, 1469, 1278, 1103 cm⁻¹;

HRMS (ESI): \( m/z \) calcd. for C₁₀H₁₈O₂ [M + H]^+ 171.1385, found 171.1376.

**Preparation of S2**: To a magnetically stirred solution of epoxide 9 (20 mg, 0.117 mmol) in dry THF was added (R)-(+)-α-methoxy-α-trifluoromethylphenylacetic acid (41.2 mg, 0.176 mmol), DCC (36.3 mg, 0.176 mmol) and DMAP (7.2 mg, 0.058 mmol). The resultant mixture was stirred at room temperature for 2 h. The reaction mixture was slowly quenched with aqueous saturated NH₄Cl solution (10 mL), then concentrated under reduced pressure. The residue so-formed was extracted with MTBE (3×20 mL) and combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, PE/EA–20:1) afforded the product S2 (39.3 mg, 0.101 mmol, 87%) as a colorless oil. (89% de, determined by \( ^1H \) NMR analysis of its Mosher ester S2).
Preparation of S3: Magnesium turnings (16.3 g, 670 mmol) and spiked with I₂ (trace) were added to a flame dried three-neck 2 L round-bottom flask assembled with a constant pressure funnel, which had been previously flame dried and allowed to cool under a stream of nitrogen and then, anhydrous THF (200 mL) was added in using syringe. Freshly distilled THF (1 L) mixed with 3-chloro-2-methylpropene (55.1 g, 609 mmol) in the constant pressure funnel were slowly added to the flask and heated to a slight boiling to initiate the reaction. After several minutes, the reaction mixture turned from yellow to turbid gray. After dropping was finished, the reaction was stirred for 3 hours at the room temperature.

To epoxide 9 (20.7 g, 122 mmol) in anhydrous THF (100 mL) at room temperature under N₂ were treated with newly prepared Grignard reagent at 0°C. The resultant mixture was stirred at 0°C for 2 h. The reaction mixture was slowly quenched with aqueous saturated NH₄Cl solution (200 mL), then concentrated under reduced pressure. The residue so-formed was extracted with MTBE (3×200 mL) and combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, PE/EA–6:1) afforded the product S3 (25.3 g, 112 mmol, 92%) as a colorless oil.

\[\alpha \]^{20}_D = -25 (c 0.10, MeOH);

\(^1\)H NMR (400 MHz, CDCl₃) δ 5.68 (ddd, \(J = 17.4, 10.2, 7.5\) Hz, 1H), 4.95 – 4.87 (m, 2H), 4.75 (s, 2H), 3.54 (d, \(J = 11.1\) Hz, 1H), 3.38 (d, \(J = 11.1\) Hz, 1H), 2.37 (brs, 2H), 2.10 – 2.02 (m, 2H), 1.90 – 1.84 (m,
1H), 1.73 (s, 3H), 1.69 – 1.52 (m, 2H), 1.41 – 1.25 (m, 2H), 1.14 – 1.08 (m, 1H), 1.07 (s, 3H), 0.96 (d, J = 6.8 Hz, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 145.58, 144.75, 112.39, 111.68, 75.94, 68.25, 42.68, 39.67, 38.23, 36.17, 27.77, 22.37, 20.07, 19.91.

IR(KBr) 3404, 3074, 2968, 2933, 1645, 1456, 1374, 1042, 994, 909, 888 cm$^{-1}$;

HRMS (ESI): m/z calcd. for C$_{14}$H$_{26}$O$_2$ [M + H]$^+$ 227.2011, found 227.2002.

Preparation of 11: Compound S3 (51.1 g, 226 mmol) was reacted with acetone (450 mL) in the presence of p-TsOH·H$_2$O (4.30 g, 22.6 mmol cat.) under a N$_2$ atmosphere at room temperature over 2 h. The reaction mixture was quenched with aqueous saturated NaHCO$_3$ solution (100 mL), then concentrated under reduced pressure. The residue so-formed was extracted with MTBE (3×100 mL) combined organic layers were washed with brine, dried over anhydrous Na$_2$SO$_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, PE/EA–20:1) afforded the product 11 (58.3 g, 219 mmol, 97%) as colorless oil.

[α]$^D_{20} = -21$ (c 0.10, MeOH);

$^1$H NMR (400 MHz, CDCl$_3$) δ 5.69 (ddd, J = 17.5, 10.3, 7.4 Hz, 1H), 4.95 – 4.87 (m, 2H), 4.73 (d, J = 8.7 Hz, 2H), 3.77 (d, J = 8.5 Hz, 1H), 3.68 (d, J = 8.4 Hz, 1H), 2.03 – 2.10 (m, 1H), 1.97 – 1.84 (m, 2H), 1.72 (s, 3H), 1.70 – 1.66 (m, 1H), 1.64 – 1.50 (m, 1H), 1.40 (s, 3H), 1.38 – 1.25 (m, 5H), 1.21 – 1.13 (m, 4H), 0.96 (d, J = 6.7 Hz, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 144.90, 144.39, 112.20, 112.07, 108.59, 84.43, 73.75, 44.28, 40.76, 38.00, 35.56, 28.14, 27.55, 26.89, 22.23, 21.36, 19.85.

IR(KBr) 3075, 2981, 2934, 2864, 1643, 1455, 1377, 1253, 1059, 908, 890 cm$^{-1}$;

HRMS (ESI): m/z calcd. for C$_{17}$H$_{30}$O$_2$ [M + H]$^+$ 267.2324, found 267.2314.

Preparation of 7: A solution of diene 11 (6.00 g, 23.0 mmol) in CH$_2$Cl$_2$ (1.5 L, 0.015 M) was treated
with Grubbs second generation catalyst (2.40 g, 2.39 mmol), and the reaction mixture was refluxed for 2 h. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (silica gel, PE:EA-50:1) afforded the product 7 (4.56 g, 19.2 mmol 85%) as colorless crystals.

The single crystal of the A08 was cultivated from a mixture of n-hexane and MTBE. X-ray crystallographic data: see S37.

\[ \begin{align*}
\text{mp } & 40.5-42.5^\circ C; \\
\text{\^{1}H NMR (400 MHz, CDCl}_3 \text{)} & \delta 5.20 (s, 1H), 3.83 (d, \text{ } J = 8.3 \text{ Hz}, 1H), 3.70 (d, \text{ } J = 8.3 \text{ Hz}, 1H), 2.33 (s, 1H), 2.17 – 1.98 (m, 2H), 1.93 – 1.79 (m, 1H), 1.77 – 1.71 (m, 1H), 1.68 (s, 3H), 1.58 – 1.63 (m, 2H), 1.52 – 1.42 (m, 1H), 1.41 (s, 3H), 1.38 (s, 3H), 1.20 (s, 3H), 0.97 (d, \text{ } J = 7.2 \text{ Hz}, 3H). \\
\text{\^{13}C NMR (100 MHz, CDCl}_3 \text{)} & \delta 135.15, 131.77, 109.08, 84.17, 73.43, 44.76, 34.57, 33.25, 31.74, 27.41, 27.30, 27.08, 27.04, 23.14, 21.31. \\
\text{IR(KBr)} & 2982, 2933, 2856, 1455, 1377, 1368, 1060 \text{ cm}^{-1}; \\
\text{HRMS (ESI)}: m/z \text{ calcd. for C}_{15}\text{H}_{26}\text{O}_2 [M + H]^+ 239.2011, \text{ found } 239.2001.
\end{align*} \]

Preparation of S4: Compound 7 (10.0 g, 42.0 mmol) in 100 mL of CH₂Cl₂ was added dropwise to a solution of SeO₂ (466 mg, 4.2 mmol) and TBHP (5.13 g, 70% wt% in water, 46.2 mmol) at room temperature, stirring was continued for an additional 30 min at 0 °C, then this mixture was stirred at room temperature for 2 h, the reaction was quenched by an aqueous sat. Na₂S₂O₃ solution. The solution was extracted with MTBE (3×150 mL) and combined organic layers were washed with brine. The organic layers were dried over Na₂SO₄, the solvent was evaporated under reduced pressure.

A magnetically stirred solution of the mixture of the previous step and CeCl₃·7H₂O (7.82 g, 21 mmol) in MeOH (30 mL) was cooled to 0 °C and then treated, in portions, with sodium borohydride (794 mg, 21 mmol) (CAUTION: EVOLUTION OF HYDROGEN GAS). The resulting mixture was stirred at 0 °C for 1 h before being quenched with water (50 mL) and then concentrated under reduced pressure. The residue so-formed was extracted with MTBE (3×100 mL) and combined organic layers were washed with brine. The combined organic phases were dried over Na₂SO₄, then purified by flash chromatography.
chromatography on silicagel (PE/EA, 15:1) to give a colorless liquid product S4 (6.94 g, 27.3 mmol 65%).

\[
\left[\alpha\right]_{D}^{20} = -37 \text{ (c 0.10, MeOH)};
\]

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 5.47 (s, 1H), 3.92 (d, \(J = 4.4\) Hz, 2H), 3.85 (d, \(J = 8.4\) Hz, 2H), 3.70 (d, \(J = 8.4\) Hz, 2H), 2.38 (s, 1H), 2.17 – 1.80 (m, 4H), 1.71 – 1.44 (m, 4H), 1.39 (s, 3H), 1.37 (s, 3H), 1.20 (s, 3H), 1.00 (d, \(J = 7.2\) Hz, 3H).

\(^1\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 138.74, 133.29, 109.10, 84.18, 73.38, 69.46, 45.20, 32.68, 32.03, 29.91, 27.26, 27.11, 27.06, 22.55, 21.13.

IR (KBr) 3425, 2985, 2933, 2867, 1455, 1377, 1250, 1201, 1058 cm\(^{-1}\);
HRMS (ESI): \(m/z\) calcd. for C\(_{15}\)H\(_{26}\)O\(_3\) [M + H]\(^+\) 255.1960, found 255.1953.

Preparation of 12: To a stirred mixture of Ti(OiPr)\(_4\) (1.34 g, 4.72 mmol), CaH\(_2\) (10 mg), silica gel (10 mg) and 4 Å molecular sieves (10 mg) in 10 mL of dry CH\(_2\)Cl\(_2\) was added D-(‒)-diisopropyl tartrate (DIPT) (1.10 g, 4.72 mmol) in 20 mL of dry CH\(_2\)Cl\(_2\) at \(-20\) °C under N\(_2\) and stirred for 10 min. A solution of compound S4 (10.0 g, 39.3 mmol) in 30 mL of dry CH\(_2\)Cl\(_2\) was injected and stirred for another 10 min. Then the mixture was cooled to \(-50\) °C, 18.17 mL of anhydrous TBHP (2.6 M in toluene,119 mmol) was injected slowly. After addition, the mixture was allowed to warm to \(-20\) °C, stirred for 2 h and monitored by TLC. The reaction mixture was quenched by 50 mL of 10% aqueous tartaric acid, warmed to room temperature, and stirring was continued until the aqueous layer became clear. The reaction mixture was extracted with ethyl acetate, washed successively with 5% aqueous NaOH, saturated aqueous NaHCO\(_3\), water and brine, dried (Na\(_2\)SO\(_4\)), and concentrated in vacuo. The residue was purified by silica gel chromatography (PE/EA–3:1) to give epoxide 12 (9.56 g, 35.4 mmol, 90%).

\[
\left[\alpha\right]_{D}^{20} = +4 \text{ (c 0.10, MeOH)};
\]

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 3.81 (d, \(J = 8.3\) Hz, 1H), 3.72 (d, \(J = 8.3\) Hz, 1H), 3.61 (dd, \(J = 12.1, 5.3\) Hz, 1H), 3.51 (dd, \(J = 12.1, 7.6\) Hz, 1H), 3.07 (d, \(J = 5.1\) Hz, 1H), 2.44 – 2.41 (m, 1H), 1.90 – 1.75
Preparation of S5: To epoxide 12 (14.0 g, 51.8 mmol) and copper iodide (990 mg, 5.20 mmol) in anhydrous THF (100 mL) at room temperature under N₂ were treated with allylmagnesium bromide (129 mL, 129 mmol 1 M in ether) in THF at 0°C. The resultant mixture was stirred at 0 °C for 2 h. The reaction mixture was slowly quenched with aqueous saturated NH₄Cl solution (20 mL), then concentrated under reduced pressure. The residue so-formed was extracted with MTBE (3×100 mL) and combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, PE/EA–1:1) afforded the product S5 (14.9 g, 47.7 mmol, 92%) as colorless oil.

\[ \alpha ]^D_{D20} = +37 \text{ (c 0.10, MeOH);} \]

**1H NMR** (400 MHz, CDCl₃) δ 5.83 (ddddd, \( J = 17.0, 10.0, 8.1, 5.8 \text{ Hz, 1H} \)), 5.07 (dd, \( J = 17.1, 1.5 \text{ Hz, 1H} \)), 4.99 (dd, \( J = 10.1, 0.9 \text{ Hz, 1H} \)), 3.82 (d, \( J = 8.3 \text{ Hz, 1H} \)), 3.69 (d, \( J = 8.3 \text{ Hz, 1H} \)), 3.53 (dd, \( J = 11.2, 4.2 \text{ Hz, 1H} \)), 3.33 (dd, \( J = 11.1, 6.6 \text{ Hz, 1H} \)), 2.42 (dddd, \( J = 10.9, 7.0, 5.6, 1.5 \text{ Hz, 1H} \)), 2.27 – 2.16 (m, 1H), 2.13 (s, 1H), 2.04 – 1.94 (m, 2H), 1.90 – 1.82 (m, 2H), 1.65 (s, 1H), 1.63 – 1.48 (m, 2H), 1.45 – 1.41 (m, 1H), 1.40 (s, 3H), 1.37 (s, 3H), 1.28 – 1.17 (m, 2H), 1.16 (s, 3H), 0.95 (d, \( J = 7.0 \text{ Hz, 3H} \)).

**13C NMR** (100 MHz, CDCl₃) δ 140.57, 114.98, 109.07, 84.19, 75.81, 73.81, 69.33, 50.07, 39.28, 38.63, 30.54, 30.33, 28.17, 27.72, 27.49, 27.10, 22.17, 20.77.

**IR(KBr)** 3454, 2984, 2933, 2867, 1455, 1378, 1212, 1057 cm⁻¹;

**HRMS (ESI):** \( m/z \) calcd. for C₁₅H₂₂O₄ [M + H]⁺ 271.1909, found 271.1901.
**Preparation of 13:** To a solution of S5 (20.0 g, 64.1 mmol) in a 20:1 mixture of THF (100 mL) and water (5 mL) was added NaIO₄ (16.5 g, 76.9 mmol) at room temperature, and the resulting mixture was stirred at room temperature for 2 h. The reaction mixture was slowly quenched with aqueous saturated Na₂S₂O₃ solution (20 mL). The aqueous layer was back-extracted with MTBE (3×100 mL). The combined organic extracts were washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, PE/EA–15:1) afforded the product 13 (17.1 g, 60.9 mmol, 95%) as colorless oil.

\[
\left[\alpha\right]^{20}_D = +72 \text{ (c 0.10, MeOH)};
\]

\(^1\text{H NMR}\) (400 MHz, CDCl₃) δ 5.65 (dddd, \(J = 16.1, 10.0, 8.1, 5.8\) Hz, 1H), 5.00 – 4.93 (m, 2H), 3.75 (d, \(J = 8.6\) Hz, 1H), 3.62 (d, \(J = 8.6\) Hz, 1H), 2.89 (td, \(J = 7.1, 2.3\) Hz, 1H), 2.58 – 2.42 (m, 1H), 2.34 (dt, \(J = 17.4, 2.8\) Hz, 1H), 2.21 – 1.86 (m, 5H), 1.84 – 1.68 (m, 2H), 1.37 (s, 3H), 1.35 (s, 3H), 1.24–1.14 (m, 4H), 0.72 (d, \(J = 7.3\) Hz, 3H).

\(^{13}\text{C NMR}\) (100 MHz, CDCl₃) δ 212.32, 136.70, 116.36, 109.27, 83.42, 72.63, 54.32, 47.16, 43.81, 37.05, 33.68, 33.11, 27.27, 27.08, 24.95, 21.05, 13.65.

\(\text{IR(KBr)}\) 2983, 1699, 1379, 1058, 993, 912 cm\(^{-1}\);

\(\text{HRMS (ESI)}\): \(m/z\) calcd. for C₁₇H₂₈O₃ \([M + Na]^+\) 303.1936, found 303.1921.

**Preparation of S6:** A solution of grubbs second generation catalyst (1.82 g, 2.14 mmol) in 50 mL of anhydrous CH₂Cl₂ was added to a solution of 2-(1-methylethenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (9.00 g, 53.5 mmol) under a nitrogen atmosphere. The reaction mixture was brought to reflux. A solution of 13 (3.00 g, 10.7 mmol) in 100 mL of CH₂Cl₂ was slowly added 2 h via a syringe pump. The solvent was concentrated under reduced pressure. Purification by flash column chromatography (silica gel, PE/EA–15:1) afforded S6 (7.00 g, 60.9 mmol, 95%) as colorless oil.
chromatography (silica gel, PE/EA–20:1) afforded the product S6 (3.38 g, 8.03 mmol, 75%) as colorless oil.

\[ \alpha_{D}^{20} = +41 \text{ (c 0.10, MeOH);} \]

\( ^{1} \text{H NMR} \ (600 \text{ MHz, CDCl}_3 \) \( \delta \) 6.15 – 6.12 (m, 1H), 3.79 (d, \( J = 8.6 \) Hz, 1H), 3.65 (d, \( J = 8.5 \) Hz, 1H), 2.97 (ddd, \( J = 8.1, 6.1, 2.2 \) Hz, 1H), 2.53 – 2.43 (m, 1H), 2.39 (ddd, \( J = 17.7, 3.8, 2.1 \) Hz, 1H), 2.25 – 2.20 (m, 1H), 2.18 – 2.13 (m, 1H), 2.09 – 2.00 (m, 2H), 1.95 (dt, \( J = 14.0, 2.8 \) Hz, 1H), 1.86 – 1.73 (m, 2H), 1.69 (s, 3H), 1.41 (s, 3H), 1.39 (s, 3H), 1.25 (s, 13H), 1.20 (s, 3H), 0.77 (d, \( J = 7.2 \) Hz, 3H).

\( ^{13} \text{C NMR} \ (100 \text{ MHz, CDCl}_3 \) \( \delta \) 212.57, 143.66, 109.28, 83.46, 83.14, 72.68, 54.22, 47.10, 43.82, 37.08, 33.27, 28.58, 27.34, 27.07, 25.04, 24.81, 24.77, 21.02, 14.09, 13.70.

\( \text{IR(KBr)} \ 2980, 1698, 1378, 1369, 1146, 1058, 860, 670 \text{ cm}^{-1}; \)

\( \text{HRMS (ESI)}: m/z \) calcd. for C24H41BO5 [M + Na]⁺ 443.2945, found 443.2939.

**Preparation of 14:** To a solution of S6 (1.60 g, 3.81 mmol) in 5:1 mixture of THF (10 mL) and water (2 mL) was added NaBO₃·4H₂O (1.75 g, 11.4 mmol) at room temperature, and the resulting mixture was stirred at room temperature for 1 h. The reaction mixture was slowly quenched with aqueous saturated Na₂S₂O₃ solution. The aqueous layer was back-extracted with MTBE (3×10 mL). The combined organic extracts were washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, PE/EA–15:1) afforded the product 14 (1.09 g, 3.50 mmol, 92%) as a pale colorless oil.

\[ \alpha_{D}^{20} = +43 \text{ (c 0.10, MeOH);} \]

\( ^{1} \text{H NMR} \ (600 \text{ MHz, CDCl}_3 \) \( \delta \) 3.79 (d, \( J = 8.6 \) Hz, 1H), 3.66 (d, \( J = 8.6 \) Hz, 1H), 3.79 (d, \( J = 8.6 \) Hz, 1H), 2.88 (ddd, \( J = 9.6, 4.4, 2.4 \) Hz, 1H), 2.45 (ddd, \( J = 17.2, 8.7, 5.9 \) Hz, 1H), 2.37 (ddd, \( J = 17.7, 4.0, 2.3 \) Hz, 1H), 2.26 (ddd, \( J = 17.2, 8.5, 6.3 \) Hz, 1H), 2.17 (dd, \( J = 17.7, 12.3 \) Hz, 1H), 2.11 (s, 4H), 2.09 – 1.97 (m, 2H), 1.92 (d, \( J = 14.6 \) Hz, 1H), 1.86 – 1.73 (m, 2H), 1.49 (ddddd, \( J = 13.4, 8.7, 6.3, 4.3 \) Hz, 1H), 1.39 (s, 3H), 1.21 (s, 4H), 0.76 (d, \( J = 7.3 \) Hz, 3H).

\( ^{13} \text{C NMR} \ (100 \text{ MHz, CDCl}_3 \) \( \delta \) 212.54, 208.67, 109.32, 83.41, 72.51, 54.01, 47.27, 43.65, 41.78, 36.98, 34.91, 29.86, 27.29, 27.07, 24.89, 24.17, 21.30, 13.97.

\( \text{IR(KBr)} \ 2932, 2874, 1715, 1698, 1378, 1368, 1057 \text{ cm}^{-1}; \)

\( \text{HRMS (ESI)}: m/z \) calcd. for C18H30O4 [M + Na]⁺ 333.2042, found 333.2035.
Preparation of 15: To a solution of 14 (1.50 g, 4.84 mmol) in EtOH (10 mL) was added Cu(OAc)$_2$ (1.06 g, 5.81 mmol) and NH$_4$OAc (447 mg, 5.81 mmol). The reaction mixture was stirred for 12 h at room temperature and then filtered over a pad of Celite and concentrated in vacuo. The residue was diluted with water (20 mL) and extracted with MTBE (3×20 mL), and the combined organic layer was washed with water and brine, dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. The residue was purified by silica column chromatography (PE/EA–5:1) to give product 15 as colorless oil (1.19 g, 4.11 mmol, 85%).

$[\alpha]_D^{20} = +21$ (c 0.10, MeOH);

$^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.28 (d, $J = 7.7$ Hz, 1H), 6.91 (d, $J = 7.6$ Hz, 1H), 4.03 (d, $J = 8.5$ Hz, 1H), 3.85 (d, $J = 8.5$ Hz, 1H), 3.03 – 2.95 (m, 1H), 2.95 – 2.81 (m, 2H), 2.47 (s, 3H), 2.04 (d, $J = 13.4$ Hz, 1H), 1.81 – 1.71 (m, 3H), 1.61 – 1.51 (m, 1H), 1.40 (s, 3H), 1.34 (s, 3H), 1.29 (d, $J = 7.3$ Hz, 3H), 1.24 (s, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 158.60, 154.58, 137.15, 136.41, 121.02, 109.13, 84.30, 74.49, 45.39, 41.60, 37.58, 33.41, 27.38, 27.19, 25.26, 23.81, 19.99, 18.29.

IR(KBr) 2932, 2866, 1462, 1377, 1208, 1058 cm$^{-1}$;

HRMS (ESI): $m/z$ calcd. for C$_{18}$H$_{27}$NO$_2$ [M + H]$^+$ 290.2120, found 290.2111.

Preparation of 16: To a stirred solution of compound 15 (1.50 g, 5.18 mmol) in THF (5 mL) was added aqueous 3 M HCl (5 mL) at room temperature. After stirring for 6 hours at room temperature. The reaction mixture was slowly quenched with aqueous saturated NaHCO$_3$ solution, then mixture was extracted with MTBE (3×20 mL). The combined organic layer was dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. The residue was purified by silica column chromatography (CH$_2$Cl$_2$/MeOH–15:1) to afford product 16 (1.20 g, 4.82 mmol, 93%) as a colorless oil.
Preparation of 17: To a solution of 16 (1.50 g, 6.02 mmol) in 5:1 mixture of THF (5 mL) and water (1 mL) was added NaIO₄ (1.54 g, 7.23 mmol) at room temperature, and the resulting mixture was stirred at room temperature for 30 minutes. The reaction mixture was slowly quenched with aqueous saturated Na₂S₂O₃ solution (20 mL). The aqueous layer was back-extracted with MTBE (3×10 mL). The combined organic extracts were washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, PE/EA–1:1) afford product 17 (1.18 g, 5.42 mmol, 90%) as a colorless oil.

$\alpha^{20}_D = +20$ (c 0.10, MeOH);

$^1$H NMR (400 MHz, CDCl₃) δ 7.36 (d, $J = 7.7$ Hz, 1H), 6.99 (d, $J = 7.7$ Hz, 1H), 3.50 (d, $J = 11.8$ Hz, 1H), 3.21 (d, $J = 11.7$ Hz, 1H), 3.17 – 2.97 (m, 3H), 2.47 (s, 3H), 1.95 – 1.78 (m, 2H), 1.74 – 1.61 (m, 1H), 1.55 – 1.41 (m, 1H), 1.31 (d, $J = 6.9$ Hz, 3H), 1.09 (s, 3H), 1.05 – 0.84 (m, 1H).

$^{13}$C NMR (100 MHz, CDCl₃) δ 158.62, 154.24, 136.24, 134.35, 121.43, 73.50, 65.32, 43.67, 35.39, 34.11, 25.09, 23.49, 23.21, 18.74.

IR (KBr) 3400, 2928, 1592, 1463, 1375, 830 cm⁻¹;

HRMS (ESI): m/z calcd. for C₁₅H₂₃NO₂ $[M + H]^+$ 250.1807, found 250.1799.
Preparation of 5: To a solution of 17 (250 mg, 1.15 mmol) in 10:1 mixture of THF (5 mL) and water (0.5 mL) was added KOH (130 mg, 2.30 mmol) at reflux for 3 h. The reaction mixture was slowly quenched with aqueous saturated NH₄Cl solution (10 mL). The aqueous layer was back-extracted with MTBE (3×10 mL). The combined organic extracts were washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, PE/EA–1:1) afforded the 17 and 5 (238 mg, 1.09 mmol, 95%) as a pale yellow solid.

The mixture was added to 10:1 mixture of n-hexane (1 mL) and MTBE (0.2 mL), then reflux and filter, the solution was volatilized naturally and slowly to obtain crystal 5. Then, the mixture was cleaned with n-hexane for three times to afford product 5 (150 mg, 0.69 mmol, 60%) as colorless transparent crystal.

\[^{[\alpha]}_{D}^{20} = -26\] (c 0.10, MeOH);
mp 105.5–107 °C;

\[\text{H NMR} \ (400 \text{ MHz, CDCl}_3) \ \delta \ 7.37 \ (d, J = 7.8 \text{ Hz, } 1\text{H}), \ 6.98 \ (d, J = 7.8 \text{ Hz, } 1\text{H}), \ 3.26 – 3.08 \ (m, \ 2\text{H}), \ 3.00 – 2.90 \ (m, \ 1\text{H}), \ 2.58 – 2.52 \ (m, \ 1\text{H}), \ 2.49 \ (s, \ 3\text{H}), \ 2.21 \ (s, \ 3\text{H}), \ 2.12 – 2.01 \ (m, \ 1\text{H}), \ 1.93 – 1.77 \ (m, \ 2\text{H}), \ 1.33 \ (d, J = 7.3 \text{ Hz, } 3\text{H}), \ 1.30 – 1.21 \ (m, \ 1\text{H}).\]

\[\text{C NMR} \ (100 \text{ MHz, CDCl}_3) \ \delta \ 211.13, \ 159.19, \ 154.46, \ 137.74, \ 132.39, \ 121.12, \ 49.54, \ 39.62, \ 35.02, \ 34.75, \ 32.99, \ 28.48, \ 23.88, \ 20.33.\]

\[\text{IR(KBr)} \ 2916, \ 1706, \ 1463, \ 1357, \ 826 \text{ cm}^{-1};\]

\[\text{HRMS (ESI): } m/z \text{ calcd. for C}_{14}\text{H}_{19}\text{NO} [M + H]^+ 218.1545, \text{ found 218.1536}.\]

The single crystal of the 5 was cultivated from a mixture of n-hexane and MTBE. X-ray crystallographic data: see S39.

Preparation of 19: To compound 17 (50 mg, 0.23 mmol) in anhydrous THF (2 mL) at room temperature under N₂ were treated with methylmagnesium bromide (1M in ether, 0.69 mL) at 0 °C. The resultant mixture was stirred at 0 °C for 30 minutes. The reaction mixture was slowly quenched with aqueous saturated NH₄Cl solution (5 mL). The aqueous layer was back-extracted with MTBE (3×10 mL) and combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica
gel, CH₂Cl₂/MeOH–15:1) afforded the product 19 (49 mg, 0.21 mmol, 92%) as a pale colorless oil.

\[ \alpha \]^20 = +3 (c 0.10, MeOH);

\(^1\)H NMR (400 MHz, CDCl₃) \( \delta \) 7.29 (d, \( J = 7.7 \) Hz, 1H), 6.92 (d, \( J = 7.7 \) Hz, 1H), 3.24 (dd, \( J = 14.6, 4.5 \) Hz, 1H), 3.03 – 2.98 (m, 2H), 2.47 (s, 3H), 1.95 – 1.80 (m, 1H), 1.80 – 1.66 (m, 2H), 1.65 – 1.55 (m, 1H), 1.52 – 1.37 (m, 1H), 1.30 (d, \( J = 7.1 \) Hz, 3H), 1.26 (s, 3H), 1.23 (s, 3H).

\(^1\)C NMR (100 MHz, CDCl₃) \( \delta \) 159.24, 154.57, 136.87, 135.45, 120.96, 73.73, 47.18, 39.31, 36.33, 33.67, 27.34, 26.82, 26.03, 23.85, 18.60.

IR (KBr) 3400, 2924, 1462, 1376, 826 cm\(^{-1}\);

HRMS (ESI): \( m/z \) calcd. for C\(_{14}\)H\(_{19}\)NO \([M + H]^+\) 234.1858, found 234.1851.

**Preparation of 21:** To compound 5 (50 mg, 0.23 mmol) in anhydrous THF (2 mL) at room temperature \( N_2 \) were treated with methylmagnesium bromide (1 M in ether, 0.69 mL) at 0 °C. The resultant mixture was stirred at 0 °C for 30 minutes. The reaction mixture was slowly quenched with aqueous saturated NH₄Cl solution (5 mL). The aqueous layer was back-extracted with MTBE (3×10 mL) and combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, CH₂Cl₂/MeOH–15:1) afforded the product 21 (49.4 mg, 0.21 mmol, 90%) as a pale colorless oil.

\[ \alpha \]^20 = -26 (c 0.10, MeOH);

\(^1\)H NMR (400 MHz, CDCl₃) \( \delta \) 7.33 (d, \( J = 7.9 \) Hz, 1H), 6.92 (d, \( J = 7.9 \) Hz, 1H), 3.23 (d, \( J = 13.3 \) Hz, 1H), 2.99 – 2.91 (m, 1H), 2.90 – 2.80 (m, 1H), 2.46 (s, 3H), 2.08 (dt, \( J = 13.3, 2.5 \) Hz, 1H), 1.88 (d, \( J = 12.9, 4.3 \) Hz, 1H), 1.64 – 1.50 (m, 1H), 1.40 (t, \( J = 11.0 \) Hz, 1H), 1.30 (d, 3H), 1.23 (s, 6H), 0.91 – 0.74 (m, 1H).

\(^1\)C NMR (100 MHz, CDCl₃) \( \delta \) 160.86, 154.00, 137.98, 132.39, 120.64, 73.15, 47.88, 39.29, 36.10, 35.12, 32.71, 27.74, 25.60, 23.63, 20.59.

IR (KBr) 3396, 2920, 1463, 1366, 819 cm\(^{-1}\);

HRMS (ESI): \( m/z \) calcd. for C\(_{14}\)H\(_{19}\)NO \([M + H]^+\) 234.1858, found 234.1852.
Preparation of 3: To a stirred suspension of Nysted reagent (1.57 g, 20 wt% suspension in THF, ca. 0.69 mmol) was added TiCl₄ (87.0 mg, 0.46 mmol) at 0 °C. The resultant mixture was stirred at that temperature for 10 min before a solution of compound 17 (10 mg, 0.046 mmol) in THF (1 mL) was added. The resulting mixture was warmed to room temperature and stirred for 1 h. The reaction mixture was quenched with aqueous saturated NaHCO₃ solution (5 mL), then concentrated under reduced pressure. The residue so-formed was extracted with MTBE (3×20 mL) combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, PE/EA–10:1) afforded the product 3 (6.5 mg, 0.03 mmol 65%) as colorless oil.

\[ \gamma^D = -23 \text{ (c } 0.10, \text{ MeOH}); \]

\(^1\)H NMR (400 MHz, Benzene-\(d_6\)) \( \delta \) 6.97 (d, \( J = 7.6 \text{ Hz, 1H} \)), 6.64 (d, \( J = 7.7 \text{ Hz, 1H} \)), 4.82 (s, 1H), 4.74 (s, 1H), 3.40 (d, \( J = 14.3 \text{ Hz, 1H} \)), 3.26 (dd, \( J = 14.3, 9.6 \text{ Hz, 1H} \)), 2.75 – 2.65 (m, 1H), 2.45 (s, 3H), 2.20 (t, \( J = 10.0 \text{ Hz, 1H} \)), 1.85 – 1.74 (m, 1H), 1.72 (s, 3H), 1.66 – 1.62 (m, 1H), 1.62 – 1.54 (m, 2H), 1.12 (d, \( J = 7.3 \text{ Hz, 3H} \)).

\(^{13}\)C NMR (100 MHz, Benzene-\(d_6\)) \( \delta \) 159.66, 155.05, 151.09, 137.37, 135.93, 120.64, 109.16, 44.66, 44.48, 38.09, 33.54, 31.30, 24.12, 20.91, 18.53.

IR(KBr) 3070, 2961, 2922, 2854, 1644, 1590, 1573, 1460, 886, 821 cm\(^{-1}\);

HRMS (ESI): \( m/z \) calcd. for C\(_{15}\)H\(_{21}\)N [M + H]\(^+\) 216.1752, found 216.1752.

Preparation of 20: To a stirred suspension of Nysted reagent (1.57 g, 20 wt% suspension in THF, ca. 0.69 mmol) was added TiCl₄ (87.0 mg, 0.46 mmol) at 0 °C. The resultant mixture was stirred at that temperature for 10 min before a solution of compound 5 (10 mg, 0.046 mmol) in THF (1 mL) was
added. The resulting mixture was warmed to room temperature and stirred for 1 h. The reaction mixture was quenched with aqueous saturated NaHCO$_3$ solution (5 mL), then concentrated under reduced pressure. The residue so-formed was extracted with MTBE (3×20 mL) combined organic layers were washed with brine, dried over anhydrous Na$_2$SO$_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, PE/EA–10:1) afforded the product 20 (7.2 mg, 0.033 mmol 72%) as colorless oil.

$[\alpha]^{20}_D = -4$ (c 0.10, MeOH);

$^{1}$H NMR (400 MHz, Benzene-$d_6$) δ 7.11 (d, $J = 7.8$ Hz, 1H), 6.72 (d, $J = 7.8$ Hz, 1H), 4.79 (s, 1H), 4.75 (s, 1H), 3.39 (d, $J = 13.3$ Hz, 1H), 3.05 (dd, $J = 13.3$, 10.9 Hz, 1H), 2.70 – 2.59 (m, 1H), 2.48 (s, 3H), 2.14 – 2.01 (m, 1H), 1.89 – 1.77 (m, 1H), 1.68 (s, 3H), 1.65 – 1.48 (m, 2H), 1.19 – 1.00 (m, 4H).

$^{13}$C NMR (100 MHz, Benzene-$d_6$) δ 161.25, 154.68, 151.30, 137.79, 131.80, 120.55, 109.05, 44.76, 44.72, 37.61, 36.76, 35.34, 24.07, 20.74, 20.64.

IR (KBr) 3070, 2961, 2922, 2854, 1644, 1590, 1573, 1460, 886, 821 cm$^{-1}$;

HRMS (ESI): m/z calcd. for C$_{15}$H$_{21}$N [M + H]$^+$ 216.1752, found 216.1752.

3. Comparison of $^1$H NMR and $^{13}$C NMR data of rupestine D (5) and cananodine (3) by table

Table 1. $^1$H NMR comparision

<table>
<thead>
<tr>
<th></th>
<th>natural 5 (CDCl$_3$)</th>
<th>synthetic 5 (CDCl$_3$)</th>
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<td>1.62 - 1.54 (m)</td>
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<td>7α</td>
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9α 3.28 - 3.13 (m) 3.26 - 3.08 (m) 3.41 (br d, J = 14.3) 3.40 (d, J = 14.3)
9β 3.28 - 3.13 (m) 3.26 - 3.08 (m) 3.27 (dd, J = 14.3, 9.8) 3.26 (dd, J = 14.3, 9.6)
13 2.23 (s) 2.21 (m) 1.73 (s) 1.72 (s)
14 2.51 (s) 2.49 (m) 1.35 (d, J = 7.2) 1.33 (d, J = 7.3)
15 4.82 (s) 4.82 (s)
16β 4.75 (1H, br s) 4.74 (s)

Table 2. \(\text{\textsuperscript{13}C NMR comparison}\)

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<th>Rupestone D (CDCl(_3))</th>
<th>5 (CDCl(_3))</th>
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<th>3 (Benzene-(\text{d}_6))</th>
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4. \(\text{\textsuperscript{1}H NMR}, \text{\textsuperscript{19}F NMR and \textsuperscript{13}C NMR spectra of the synthesized compounds}\)

\(\text{\textsuperscript{1}H NMR spectra of S1} (\text{CDCl}_3, 400 \text{ MHz})\)
$\text{C H}_2 \text{C H}_3 \text{C H}_3 \text{O H}$

$^{13}\text{C NMR spectra of S1} \text{ (CDCl}_3, 100 \text{ MHz)}$

$\text{H}_2\text{CCH}_{\text{CH}}\text{CH}_{\text{CH}}\text{OH}$

$^1\text{H NMR spectra of S2} \text{ (CDCl}_3, 400 \text{ MHz)}$
\textbf{C NMR spectra of S2 (CDCl$_3$, 100 MHz)}

\textbf{F NMR spectra of S2 (CDCl$_3$, 376 MHz)}

\textbf{13C NMR spectra of S2 (CDCl$_3$, 100 MHz)}

\textbf{19F NMR spectra of S2 (CDCl$_3$, 376 MHz)}
$^1$H NMR spectra of 9 (CDCl$_3$, 400 MHz)
$^{13}$C NMR spectra of 9 (CDCl$_3$, 100 MHz)

$^1$H NMR spectra of S3 (CDCl$_3$, 400 MHz)
$^{13}$C NMR spectra of S3 (CDCl$_3$, 100 MHz)

$^1$H NMR spectra of 11 (CDCl$_3$, 400 MHz)
$^{13}$C NMR spectra of 11 (CDCl$_3$, 100 MHz)

$^1$H NMR spectra of 7 (CDCl$_3$, 400 MHz)
13C NMR spectra of 7 (CDCl₃, 100 MHz)

1H NMR spectra of S4 (CDCl₃, 400 MHz)
$^{13}$C NMR spectra of S4 (CDCl$_3$, 100 MHz)

$^1$H NMR spectra of 12 (CDCl$_3$, 400 MHz)
13C NMR spectra of 12 (CDCl₃, 100 MHz)

1H NMR spectra of S5 (CDCl₃, 400 MHz)
$^{13}$C NMR spectra of S5 (CDCl$_3$, 100 MHz)

$^1$H NMR spectra of 13 (CDCl$_3$, 400 MHz)
$^{13}$C NMR spectra of 13 (CDCl$_3$, 100 MHz)

$^1$H NMR spectra of S6 (CDCl$_3$, 400 MHz)
**13C NMR spectra of S6 (CDCl₃, 100 MHz)**

**1H NMR spectra of 14 (CDCl₃, 400 MHz)**
$^{13}$C NMR spectra of 14 (CDCl$_3$, 100 MHz)

$^1$H NMR spectra of 15 (CDCl$_3$, 400 MHz)
13C NMR spectra of 15 (CDCl₃, 100 MHz)

1H NMR spectra of 16 (CDCl₃, 400 MHz)
$^{13}$C NMR spectra of 16 (CDCl$_3$, 100 MHz)

$^1$H NMR spectra of 17 (CDCl$_3$, 400 MHz)
$^{13}$C NMR spectra of 17 (CDCl$_3$, 100 MHz)

$^1$H NMR spectra of 5 (CDCl$_3$, 400 MHz)
\[ \begin{align*}
\text{\[^{13}\text{C} \text{ NMR spectra of 5 (CDCl}_3, 100 \text{ MHz})\]}
\end{align*} \]

\[ \begin{align*}
\text{\[^{1}\text{H} \text{ NMR spectra of 19 (CDCl}_3, 400 \text{ MHz})\]}
\end{align*} \]
\[^{13}\text{C} NMR\text{ spectra of 19 (CDCl}_3, 100 \text{ MHz)}\]

\[^{1}\text{H} NMR\text{ spectra of 21 (CDCl}_3, 400 \text{ MHz)}\]
$^{13}$C NMR spectra of 21 (CDCl$_3$, 100 MHz)

$^1$H NMR spectra of 3 (Benzene-D$_6$, 400 MHz)
1^3C NMR spectra of 3 (Benzene-D₆, 100 MHz)

1^H NMR spectra of 20 (Benzene-D₆, 400 MHz)
5. Single Crystal X-ray Data
5.1 X-ray crystallographic data for 7

Structure deposited at the Cambridge Crystallographic Data Center (CCDC 2084871)

Crystal data and structure refinement for CCDC 2084871

<table>
<thead>
<tr>
<th>Identification code</th>
<th>22020929S4S4_0m</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empirical formula</td>
<td>C\textsubscript{15}H\textsubscript{26}O\textsubscript{2}</td>
</tr>
<tr>
<td>Formula weight</td>
<td>238.36</td>
</tr>
<tr>
<td>Temperature/K</td>
<td>160.0</td>
</tr>
<tr>
<td>Crystal system</td>
<td>orthorhombic</td>
</tr>
<tr>
<td>Space group</td>
<td>P\textsubscript{2}\textsubscript{1}2\textsubscript{1}2\textsubscript{1}</td>
</tr>
<tr>
<td>a/Å</td>
<td>6.2068(2)</td>
</tr>
<tr>
<td>b/Å</td>
<td>9.6747(3)</td>
</tr>
<tr>
<td>c/Å</td>
<td>23.6894(6)</td>
</tr>
<tr>
<td>α/°</td>
<td>90</td>
</tr>
<tr>
<td>β/°</td>
<td>90</td>
</tr>
<tr>
<td>γ/°</td>
<td>90</td>
</tr>
<tr>
<td>Volume/Å\textsuperscript{3}</td>
<td>1422.52(7)</td>
</tr>
<tr>
<td>Z</td>
<td>4</td>
</tr>
<tr>
<td>ρ\textsubscript{calc}/g/cm\textsuperscript{3}</td>
<td>1.113</td>
</tr>
<tr>
<td>μ/mm\textsuperscript{-1}</td>
<td>0.555</td>
</tr>
<tr>
<td>F(000)</td>
<td>528.0</td>
</tr>
<tr>
<td>Crystal size/mm\textsuperscript{3}</td>
<td>0.15 × 0.08 × 0.05</td>
</tr>
<tr>
<td>Radiation</td>
<td>CuKα (λ = 1.54178)</td>
</tr>
<tr>
<td>2Θ range for data collection/°</td>
<td>7.464 to 144.952</td>
</tr>
<tr>
<td>Index ranges</td>
<td>-7 ≤ h ≤ 7, -11 ≤ k ≤ 11, -29 ≤ l ≤ 28</td>
</tr>
<tr>
<td>Reflections collected</td>
<td>11340</td>
</tr>
</tbody>
</table>
Independent reflections 2771 \[ R_{int} = 0.0347, R_{\sigma} = 0.0271 \]
Data/restraints/parameters 2771/0/159
Goodness-of-fit on \( F^2 \) 1.050
Final R indexes \[ \|I\| > 2\sigma(I) \] \( R_1 = 0.0310, wR_2 = 0.0733 \)
Final R indexes [all data] \( R_1 = 0.0331, wR_2 = 0.0750 \)
Largest diff. peak/hole / e Å\(^{-3}\) 0.16/-0.12
Flack parameter -0.08(9)

5.2 X-ray crystallographic data for 5

Structure deposited at the Cambridge Crystallographic Data Center (CCDC 2084872)

Crystal data and structure refinement for CCDC 2084872

dentification code cu_220201016_0m
Empirical formula \( \text{C}_{14}\text{H}_{19}\text{NO} \)
Formula weight 217.30
Temperature/K 150.0
Crystal system monoclinic
Space group \( \text{P2}_1 \)
a/Å 4.9824(2)
b/Å 11.7685(5)
c/Å 10.6674(5)
\( \alpha^\circ \) 90
\( \beta^\circ \) 101.617(2)
\( \gamma^\circ \) 90
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<tr>
<th>Property</th>
<th>Value</th>
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<tr>
<td>Volume/Å³</td>
<td>612.67(5)</td>
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<tr>
<td>Z</td>
<td>2</td>
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<tr>
<td>$\rho_{\text{calc}}$/cm³</td>
<td>1.178</td>
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<tr>
<td>$\mu$/mm⁻¹</td>
<td>0.571</td>
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<tr>
<td>F(000)</td>
<td>236.0</td>
</tr>
<tr>
<td>Crystal size/mm³</td>
<td>0.15 × 0.08 × 0.05</td>
</tr>
<tr>
<td>Radiation</td>
<td>CuKα (λ = 1.54178)</td>
</tr>
<tr>
<td>2θ range for data collection/°</td>
<td>8.462 to 136.432</td>
</tr>
<tr>
<td>Index ranges</td>
<td>-5 ≤ h ≤ 5, -13 ≤ k ≤ 14, -12 ≤ l ≤ 12</td>
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<tr>
<td>Reflections collected</td>
<td>10051</td>
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<tr>
<td>Independent reflections</td>
<td>2194 [R$<em>{\text{int}}$ = 0.0486, R$</em>{\text{sigma}}$ = 0.0398]</td>
</tr>
<tr>
<td>Data/restraints/parameters</td>
<td>2194/1/148</td>
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<tr>
<td>Goodness-of-fit on F²</td>
<td>1.073</td>
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<tr>
<td>Final R indexes [I&gt;2σ(I)]</td>
<td>$R_1 = 0.0383$, wR₂ = 0.1012</td>
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<tr>
<td>Final R indexes [all data]</td>
<td>$R_1 = 0.0395$, wR₂ = 0.1025</td>
</tr>
<tr>
<td>Largest diff. peak/hole / e Å⁻³</td>
<td>0.15/-0.19</td>
</tr>
<tr>
<td>Flack parameter</td>
<td>-0.01(15)</td>
</tr>
</tbody>
</table>