Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Concise asymmetric total synthesis of (-)-patchouli alcohol

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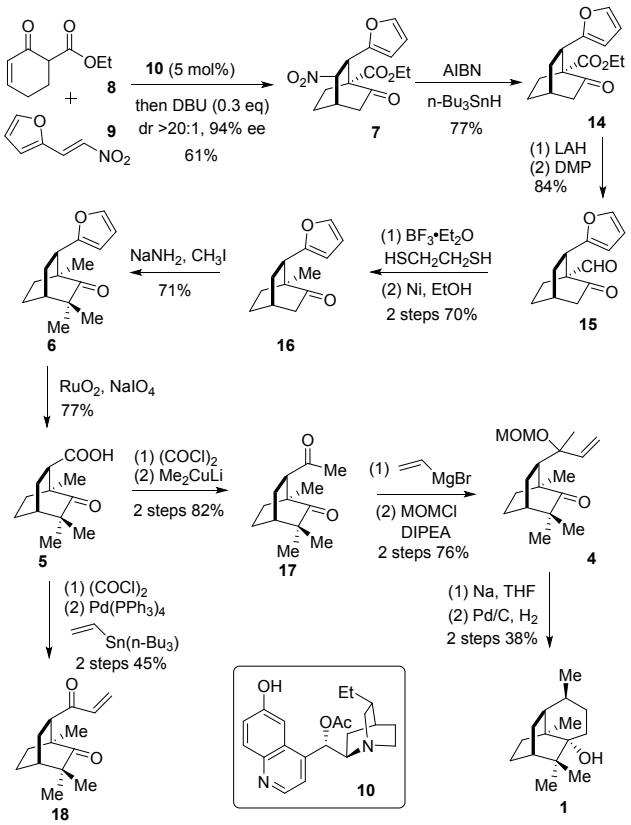
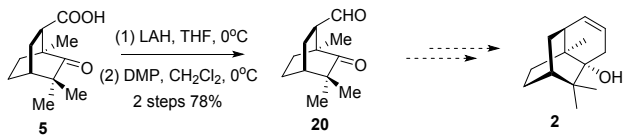
General Information

All non-aqueous reactions were run under a positive pressure of nitrogen. Anhydrous solvents

were obtained using standard drying techniques. Commercial grade reagents were used without further purification unless stated otherwise. Flash chromatography was performed on 300-400 mesh silica gel with the indicated solvent systems. ^{1}H NMR were recorded on a Bruker 400 (400 MHz) spectrometer and chemical shifts are reported in ppm down field from TMS, using TMS (0.00 ppm) or residual chloroform (7.26 ppm) as an internal standard. Data are reported as: (s = singlet, br = broad, d = doublet, t = triplet, q = quartet, quint = quintuplet, hept = heptalet, m = multiplet; *J* = coupling constant in Hz, integration.). ^{13}C NMR spectra were recorded on a Bruker 400 (100 MHz) spectrometer, using proton decoupling unless otherwise noted. Chemical shifts are reported in ppm down field from TMS, using the central resonance of $CDCl_3$ (77.00 ppm) as the internal standard. $[\alpha]_D$ values were given in 10^{-1} deg cm^2 g^{-1}. HRMS were recorded by using either FTMS-7 or IonSpec 4.7 spectrometers.



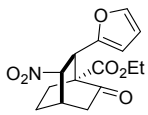
Scheme 1 Total synthesis of (-)-patchouli alcohol (1)



Scheme 2 Formal synthesis of (-)-norpatchoulenol (2)

Compound 7

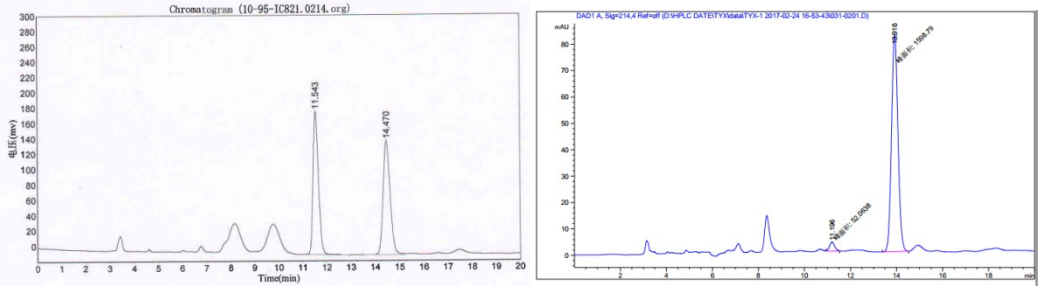
Ethyl(1R,2S,3S,4S)-2-(furan-2-yl)-3-nitro-6-oxobicyclo[2.2.2]octane-1-carboxylate



7

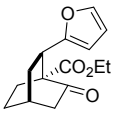
To a solution of CAT **10** (128 mg, 0.37 mmol) and the nitroolefin **9** (3.1 g, 22.3 mmol) in 10 mL anhydrous CH_2Cl_2 at room temperature was added enone **8** (1.8 g, 10.7 mmol). The resulting mixture was stirred at the same temperature until enone **8** is consumed as indicated by TLC. Then DBU (0.34 mL, 3.20 mmol) was added and the mixture was allowed to stir at ambient temperature until completion as indicated by TLC. The solution was concentrated in vacuo and purified by flash chromatography on silica gel (Hexane / EtOAc = 20 / 1) to give **7** (2 g, 61% yield) as a yellow solid. $[\alpha]_D^{23}$ 28.0 (*c* = 1.0, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.29 (d, *J* = 0.8 Hz, 1H), 6.27 (dd, *J* = 2.0 Hz, *J* = 3.2 Hz, 1H), 6.14 (d, *J* = 4.0 Hz, 1H), 4.93 (m, 1H), 4.57 (d, *J* = 4.4 Hz, 1H), 4.11 (m, 2H), 3.04-3.02 (m, 1H), 2.80-2.75 (m, 1H), 2.60-2.54 (m, 1H), 2.33-2.29 (m, 1H), 1.88-1.72 (m, 2H), 1.33-1.23 (m, 1H), 1.21 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 204.1, 168.7, 151.8, 142.5, 110.5, 108.1, 88.3, 61.3, 56.3, 42.0, 40.8, 33.7, 26.9, 19.2, 13.8. **IR** (thin film): 3435, 3141, 3120, 2996, 2959, 1715, 1653, 1621, 1557, 1505, 1473, 1443, 1408, 1371, 1336, 1301, 1336, 1301, 1270, 1236, 1142, 1120, 1083, 1062, 1074, 1045, 1045, 1011, 996, 960, 930, 892, 884, 867, 803, 753, 628, 600, 508, 436 cm^{-1}. **LRMS** (ESI): 308.0 $(M+H)^+$, 330.0 $(M+Na)^+$. **HRMS** (ESI): calcd for $C_{15}H_{18}O_6N$ $(M+H)^+$: 308.1129. Found: 308.1130. **Melting point**: 117-118 °C.

HPLC for **7**



Compound 14

Ethyl(1R,2R,4R)-2-(furan-2-yl)-6-oxobicyclo[2.2.2]octane-1-carboxylate



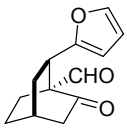
14

A solution of **7** (1.16 g, 3.78 mmol), tributyltin hydride (3.8 mL, 18.9 mmol) and AIBN (61 mg, 0.38 mmol) in 18 mL anhydrous mesitylene was heated at 150°C for 20 min under an Ar atmosphere. Then the solution was purified by flash

chromatography on silica gel (Hexane / EtOAc = 20 / 1) to give **14** (759 mg, 77% yield) as a colorless oil. **[α]**$_D^{24}$ -69.6 (*c* = 1.0, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.26 (d, *J* = 0.8 Hz, 1H), 6.22 (dd, *J* = 2.0 Hz, *J* = 3.6 Hz, 1H), 5.96 (d, *J* = 2.8 Hz, 1H), 4.06 (m, 2H), 3.55 (dd, *J* = 11.2 Hz, *J* = 4.8 Hz, 1H), 2.66-2.62 (m, 1H), 2.43-2.39 (m, 1H), 2.31-2.17 (m, 4H), 1.90-1.62 (m, 3H), 1.10 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 208.3, 170.5, 156.5, 141.1, 110.0, 105.7, 60.7, 57.1, 45.0, 38.2, 32.9, 28.4, 27.5, 24.6, 13.9. **IR** (thin film): 3528, 3117, 2955, 2929, 2871, 1732, 1598, 1505, 1464, 1417, 1366, 1336, 1262, 1148, 1097, 1077, 1058, 1011, 959, 924, 902, 864, 805, 742, 689, 598, 515 cm^{-1}. **LRMS** (ESI): 263.2 $(M+H)^+$ **HRMS** (ESI): calcd for $C_{15}H_{19}O_4$ $(M+H)^+$: 263.1279. Found: 263.1278.

Compound 15

(1S,2R,4R)-2-(furan-2-yl)-6-oxobicyclo[2.2.2]octane-1-carbaldehyde



15

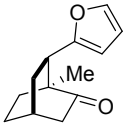
To a solution of **14** (319 mg, 1.22 mmol) in 6 mL anhydrous Et_2O under an Ar atmosphere was added $LiAlH_4$ (58 mg, 1.53 mmol). The solution was stirred for 2 h at 0°C. It was then quenched with water. The organic layer was removed and the aqueous phase was extracted with dichloromethane for three times. The combined organic extracts were dried over anhydrous Na_2SO_4 and evaporated under reduced pressure.

To a solution of the residue in 6 mL anhydrous CH_2Cl_2 at 0°C was added Dess-Martin periodinane (DMP) (1.18 g, 2.78 mmol). The solution was stirred for 4 h at 0°C. It was then quenched with saturated sodium bicarbonate solution. The organic layer was removed and the aqueous phase was extracted with dichloromethane for three times. The combined organic extracts were dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel (Hexane / EtOAc = 10 / 1) to give **15** (223 mg, 84% yield) as a colorless oil. **[α]**$_D^{24}$ -20.0 (*c* = 1.0, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.88 (s, 1H), 7.28 (d, *J* = 0.8 Hz, 1H), 6.24 (dd, *J* = 2.8 Hz, *J* = 2.0 Hz, 1H), 6.01 (d, *J* = 2.8 Hz, 1H), 3.49 (dd, *J* = 10.8 Hz, *J* = 5.2 Hz, 1H), 2.62-2.57 (m, 1H), 2.42-2.22 (m, 3H), 2.24-1.88 (m, 2H), 1.84-1.76 (m, 2H), 1.76-1.72 (m, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 212.4, 203.2, 154.6, 142.1, 110.2, 106.8, 57.6, 44.8, 37.7, 31.9, 27.5, 24.9, 24.1. **IR** (thin film): 3419, 3117, 2954, 2871, 2747, 1720, 1645, 1578, 1505, 1455, 1403, 1340, 1260, 1147, 1076, 1013, 960, 935, 883, 804, 737, 669, 612, 598, 490 cm^{-1}.

LRMS (ESI): 219.1(M+H) $^{+}$. **HRMS** (ESI): calcd for $C_{13}H_{15}O_3$ (M+H) $^{+}$: 219.1016. Found: 219.1015.

Compound 16

(1S,4R,6R)-6-(furan-2-yl)-1-methylbicyclo[2.2.2]octan-2-one



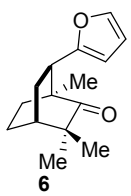
16

To a solution of **15** in 64 mL anhydrous CH_2Cl_2 (2.8 g, 12.8 mmol) was added 1, 2-ethanedithiol (1.17 mL, 14.1 mmol) under an Ar atmosphere. At 0^{o}C, the mixed solution was then added $BF_3{\cdot}Et_2O$ (2 uL). The mixture was stirred at 0 ^{o}C for 10 min and gradually warmed to r.t. for 1 h. The stirred solution was evaporated under reduced pressure.

Freshly prepared Ra-Ni (5g) was added to a solution of the residue in 44 mL anhydrous EtOH under an Ar atmosphere. The mixture was heated under reflux for 10 h, cooled to room temperature and filtered through Celite (CAUTION: Do not let the pyrophoric Raney nickel get dry.) The filter cake is washed several times with ethanol. The filtrate was concentrated in vacuo and purified by flash chromatography on silica gel (Hexane / EtOAc = 10 / 1) to give **16**(1.8 g, 70% yield) as a colorless oil. $[\alpha]_D^{24}$ -47.1 (*c* = 1.0, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.25 (d, *J* = 0.8 Hz, 1H), 6.22 (dd, *J* = 3.6 Hz, *J* = 2.4 Hz, 1H), 5.94 (d, *J* = 3.2 Hz, 1H), 3.05 (dd, *J* = 11.2 Hz, *J* = 6.0 Hz, 1H), 2.52-2.16 (m, 4H), 1.86-1.78 (m, 2H), 1.68-1.60 (m, 2H), 1.02-0.85 (m, 1H), 0.79 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 215.9, 156.6, 141.5, 109.9, 106.0, 46.5, 44.7, 41.7, 32.8, 32.2, 27.7, 25.0, 18.3. **IR** (thin film): 2933, 2870, 1718, 1684, 1653, 1593, 1558, 1540, 1506, 1456, 1403, 1376, 1339, 1239, 1165, 1148, 1088, 1011, 969, 942, 904, 883, 802, 734, 598, 418 cm^{-1}. **LRMS** (ESI): 205.1 (M+H) $^{+}$. **HRMS** (ESI): calcd for $C_{13}H_{17}O_2$ (M+H) $^{+}$:205.1223. Found: 205.1223.

Compound 6

(1S,4R,6R)-6-(furan-2-yl)-1,3,3-trimethylbicyclo[2.2.2]octan-2-one



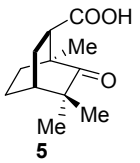
6

To a solution of **16** (10 mg, 0.05 mmol) in 0.4 mL anhydrous Et_2O was added $NaNH_2$ (10 mg, 0.25 mmol) under an Ar atmosphere and the mixture refluxed for 4 h. After cooling, methyl iodide (12 uL, 0.25 mmol) was added and the mixture refluxed overnight. It was then quenched with saturated ammonium chloride

solution. The organic layer was removed and the aqueous phase was extracted with dichloromethane for three times. The combined organic extracts were dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel (Hexane / EtOAc = 20 / 1) to give **6** (8 mg, 71% yield) as a colorless oil. $[\alpha]_D^{24}$ -56.2 (*c* = 1.0, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.17 (d, *J* = 0.8 Hz, 1H), 6.14 (dd, *J* = 3.2 Hz, *J* = 2.0 Hz, 1H), 5.86 (d, *J* = 3.6 Hz, 1H), 2.97 (dd, *J* = 11.6 Hz, *J* = 6.0 Hz, 1H), 2.43-2.36 (m, 1H), 2.18-2.14 (m, 1H), 2.14-1.58 (m, 4H), 1.21-1.18 (m, 1H), 1.14 (s, 3H), 1.12 (s, 3H), 0.70 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 219.0, 157.2, 141.3, 110.0, 105.7, 47.2, 46.1, 42.8, 41.3, 34.2, 33.7, 32.8, 20.5, 18.6, 14.2. **IR** (thin film): 3853, 3649, 3115, 2965, 2927, 1716, 1653, 1593, 1559, 1541, 1506, 1457, 1382, 1359, 1339, 1261, 1237, 1212, 1148, 1072, 1030, 1014, 981, 961, 920, 885, 801, 732, 598 cm^{-1}. **LRMS** (ESI): 233.1 $(M+H)^+$. **HRMS** (ESI): calcd for $C_{15}H_{21}O_2$ $(M+H)^+$: 233.1536. Found: 233.1537.

Compound 5

(1S,2R,4R)-1,5,5-trimethyl-6-oxobicyclo[2.2.2]octane-2-carboxylic acid

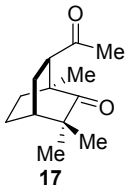


5

The ketone **6** (124 mg, 0.53 mmol) was dissolved in a solution of CH_3CN (9 mL), CCl_4 (6 mL) and H_2O (9 mL). Then $NaIO_4$ (864 mg, 2.67 mmol) was added after the addition of RuO_2 (4 mg, 0.03 mmol). After 30 min of stirring at room temperature, the solution was diluted with dichloromethane, the organic layer was removed and the aqueous phase was extracted with dichloromethane for three times. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by flash chromatography on silica gel to give **5** (87 mg, 77% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.75 (dd, *J* = 11.2 Hz, *J* = 6.4 Hz, 1H), 2.13-1.95 (m, 3H), 1.75-1.59 (m, 3H), 1.45-1.30 (m, 1H), 1.21 (s, 3H), 1.16 (s, 3H), 0.99 (s, 3H). **IR** (thin film): 2932, 2611, 1717, 1458, 1385, 1308, 1214, 1127, 1082, 1032, 985, 845, 799, 737, 701, 578, 508, 484 cm^{-1}. **LRMS** (ESI): 209.2 $(M-H)^-$. **For 5 as a known compound, see：** Subba Rao, G. S. R.; Kaliappan, K. P. *J. Chem. Soc., Perkin Trans.1* **1997**, 1385.

Compound 17

(1S,4R,6R)-6-acetyl-1, 3, 3-trimethylbicyclo[2.2.2]octan-2-one



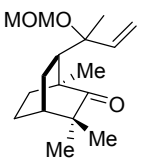
17

The keto acid **5** (22 mg, 0.12 mmol) was dissolved in 0.6 mL anhydrous CH_2Cl_2 solution under an Ar atmosphere. Then, Oxalyl dichloride (21uL, 0.24 mmol) and 1 drop of anhydrous DMF was slowly added at 0 ^oC. The solution was stirred for 12 h at room temperature and excess of oxalyl dichloride were removed by evaporation in vacuo to give the crude acid chloride.

To a solution of copper iodide (16 mg, 0.084 mmol) in 0.4 mL anhydrous Et_2O under an Ar atmosphere was added a solution of MeLi (0.53 uL, 0.53 mmol) at 0^oC. After 5 min, the reaction mixture was cooled to -78^oC and the crude acid chloride was added slowly. After 15 min, the reaction mixture was quenched with saturated ammonium chloride solution. The organic layer was removed and the aqueous phase was extracted with diethyl ether for three times. The combined organic extracts were dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel (Hexane / EtOAc = 10 / 1) to give **17** (15 mg, 82% yield) as a white solid. $[\alpha]_D^{24}$ -41.4 (*c* = 1.0, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.98 (t, *J* = 9.2 Hz, 1H), 2.14 (s, 3H), 2.02-1.95 (m, 3H), 1.73-1.69 (m, 2H), 1.69-1.52 (m, 2H), 1.17 (s, 3H), 1.14 (s, 3H), 0.93 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 219.3, 210.6, 54.7, 45.8, 44.2, 38.1, 31.7, 31.2, 27.3, 25.4, 23.6, 22.3, 18.6. **IR** (thin film): 3394, 3056, 2968, 1716, 1486, 1461, 1422, 1382, 1266, 1216, 1174, 1144, 1126, 1109, 1062, 1035, 1018, 982, 964, 941, 920, 839, 820, 801, 736, 702, 636, 605, 584, 554, 532, 495, 476, 432 cm^{-1}. **LRMS** (ESI): 209.1 $(M+H)^+$. **HRMS** (ESI): calcd for $C_{13}H_{21}O_2$ $(M+H)^+$: 209.1536. Found: 209.1536. **Melting point**: 54-55^oC

Compound 4

(1S,4R,6R)-6-(2-(methoxymethoxy)but-3-en-2-yl)-1,3,3-trimethylbicyclo[2.2.2] octan-2-one



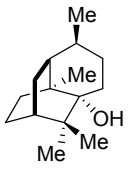
4

To a solution of diketone **17** (75 mg, 0.36 mmol) in 1.8 mL anhydrous THF under an Ar atmosphere was added a solution of vinylmagnesium bromide (0.43 mL, 0.43 mmol) at 0^oC and the mixture stirred for 1 h at the same temperature. The reaction was quenched with saturated ammonium chloride solution and extracted with dichloromethane for three times. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (Hexane / EtOAc = 20 / 1) to give a 1:1 epimeric mixture of the tertiary allyl alcohol (75 mg, 88% yield) as a colorless oil.

To a solution of the alcohol (40 mg, 0.17 mmol) in 0.85 mL anhydrous DMF at 0°C were added methoxymethyl chloride (26 uL, 0.34 mmol) and diisopropylethylamine (DIPEA) (73 uL, 0.43 mmol) slowly. The reaction mixture was stirred for 24 h at room temperature. It was then diluted with water and extracted with dichloromethane for three times. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (Hexane / EtOAc = 10 / 1) to give the ether **4** (41 mg, 86% yield) as a colorless oil. $[\alpha]_D^{23}$ -65.7 (*c* = 0.8, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.71 (m, 1H), 5.16 (m, 2H), 4.63(t, *J* = 6.8 Hz, 2H), 3.35 (s, 3H), 2.17-2.06 (m, 1H), 1.91-1.85 (m, 1H), 1.75-1.71 (m, 1H), 1.66-1.51 (m, 5H), 1.25 (s, 3H), 1.18 (s, 3H), 1.10 (s, 3H), 1.07 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 222.8, 222.5, 142.5, 139.9, 118.0, 115.2, 91.7, 91.4, 82.7, 82.3, 56.1, 55.7, 51.4, 50.6, 46.8, 46.7, 45.7, 37.7, 37.6, 35.0, 34.9, 28.1, 27.4, 26.0, 23.2, 23.1, 21.8, 21.7, 20.9, 20.8. **IR** (thin film): 3404, 3084, 3930, 2820, 2777, 2250, 1716, 1641, 1467, 1414, 1384, 1359, 1340, 1317, 1282, 1219, 1196, 1143, 1101, 1081, 1024, 974, 921, 885, 853, 828, 807, 733, 647, 485 cm^{-1}. **LRMS** (EI): 210, 178, 137, 115, 81, 45. (ESI): $(M-H)^+$ 279. **HRMS** (EI): calcd for $C_{17}H_{28}O_3$ $(M)^+$: 280.2038. Found: 280.2049.

(-)-Patchouli alcohol

(4S,8aS)-4,8a,9,9-tetramethyloctahydro-1,6-methanonaphthalen-1(2H)-ol



(-)-patchouli alcohol (1)

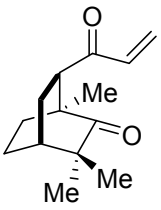
To a solution of **4** (10 mg, 0.036 mmol) in 0.5 mL anhydrous THF under an Ar atmosphere was added freshly cut sodium metal (10 mg, 0.42 mmol) at room temperature. After the mixture had been refluxed for 24 h, excess of sodium metal was quenched carefully with ethanol at 0°C, diluted with water and extracted with diethyl ether. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (Hexane / EtOAc = 50 / 1) to give the alcohol (3 mg) as a colorless oil.

To a solution of the alcohol (3 mg, 0.014 mmol) in 0.3 mL anhydrous EtOH was added 10% Pd/C (2 mg) and the reaction stirred at room temperature in a hydrogen atmosphere for 12 h. The catalyst was then removed by filtration through Celite and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography on silica gel (Hexane / EtOAc = 50 / 1) to give Patchouli alcohol **1** (3 mg, 38% yield) as a colorless oil. $[\alpha]_D^{24}$ -95.0 (*c* = 0.4, $CHCl_3$). **^{1}H NMR**

(400 MHz, $CDCl_3$): δ 2.01-1.93 (1H, m), 1.93-1.80 (2H, m), 1.75-1.55 (1H, m), 1.55-1.40 (5H, m), 1.40-1.15 (4H, m), 1.08 (3H, s), 1.07 (3H, s), 1.06 (1H, brs, OH), 0.85 (3H, s), 0.79 (d, *J* = 6.8 Hz, 3H).**^{13}C NMR** (100 MHz, $CDCl_3$): δ 75.6, 43.7, 40.1, 39.1, 37.7, 32.7, 28.8, 28.6, 28.1, 26.9, 24.6, 24.3, 20.7, 18.6. **IR** (thin film): 3478, 2990, 2949, 2869, 1466, 1386, 1375, 1365, 1327, 1280, 1216, 1189, 1101, 1052, 1039, 1009, 998, 983, 967, 958, 932, 890, 855, 814, 776, 737, 647, 568, 493 cm^{-1}. **LRMS** (EI): 222 (M^+). **HRMS** (EI): calcd for $C_{15}H_{26}O$ (M) $^+$: 222.1984. Found: 222.1983.

Compound 18

(1S,4R,6R)-6-acryloyl-1,3,3-trimethylbicyclo[2.2.2]octan-2-one



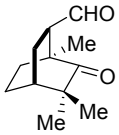
18

The keto acid **5** (22 mg, 0.12 mmol) was dissolved in 0.6 mL anhydrous CH_2Cl_2 solution under an Ar atmosphere. Then, Oxalyl dichloride (21uL, 0.24 mmol) and 1 drop of anhydrous DMF was slowly added at 0 ^oC. The solution was stirred for 12 h at room temperature and excess of oxalyl dichloride were removed in vacuo to give the crude acid chloride.

To a solution of the crude acid chloride (23 mg, 0.12 mmol) in 0.6 mL anhydrous THF were added $Pd(PPh_3)_4$ (1 mg, 0.001 mmol) and Tributyl (vinyl) tin (37 uL, 0.13 mmol) under an Ar atmosphere. The reaction mixture was stirred for 2 h at 70 ^oC. It was then diluted with water and extracted with dichloromethane for three times. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (Hexane / EtOAc = 10 / 1) to give the **18** (10 mg, 45% yield) as a colorless oil. **$[\alpha]_D^{24}$** -54.5 (*c* = 0.1, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 6.34 (dd, *J* = 10.0 Hz, *J* = 17.2 Hz, 1H), 6.23 (d, *J* = 16.8 Hz, 1H), 5.83 (dd, *J* = 10.4 Hz, *J* = 1.2 Hz, 1H), 3.27 (dd, *J* = 11.2 Hz, *J* = 6.8 Hz, 1H), 2.05-1.98 (m, 4H), 1.75-1.63 (m, 3H), 1.20 (s, 3H), 1.16 (s, 3H), 0.89 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 219.3, 202.5, 136.6, 129.0, 50.8, 45.8, 44.4, 38.2, 31.8, 27.9, 25.4, 23.7, 22.4, 18.8. **IR** (thin film): 3412, 3088, 2965, 2925, 2862, 1954, 1716, 1691, 1667, 1608, 1459, 1401, 1382, 1337, 1316, 1262, 1214, 1200, 1092, 1031, 982, 947, 924, 861, 843,800, 741, 701, 667, 562, 239, 495 cm^{-1}. **LRMS** (EI): 220 (M) $^+$ **HRMS** (EI): calcd for $C_{14}H_{20}O_2$ (M) $^+$: 220.1463, found: 220.1474.

Compound 20

(1S,2R,4R)-1,5,5-trimethyl-6-oxobicyclo[2.2.2]octane-2-carbaldehyde



20

To a solution of **5** (106 mg, 0.5 mmol) in 2.5 mL anhydrous THF under Ar atmosphere was added Borane-tetrahydrofuran complex (1.0 M, 1.1 mL, 1.1 mmol) at 0°C. The solution was stirred for 2 h. It was then quenched with water. The organic layer was removed and the aqueous phase was extracted with dichloromethane for three times. The combined organic extracts were dried over anhydrous Na_2SO_4 and evaporated under reduced pressure.

To a solution of the residue in 3 mL anhydrous CH_2Cl_2 at 0°C was added Dess-Martin periodinane (DMP) (522 mg, 1.23 mmol). The solution was stirred for 2 h at 0°C. It was then quenched with the saturated sodium bicarbonate solution. The organic layer was removed and the aqueous phase was extracted with dichloromethane for three times. The combined organic extracts were dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel (Hexane / EtOAc = 10 / 1) to give **20** (76 mg, 78% yield) as a colorless oil. $[\alpha]_D^{21}$ -65.1 (*c* = 1.0, $CHCl_3$). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.49 (s, 1H), 2.65 (dd, *J* = 11.6 Hz, *J* = 6.0 Hz, 1H), 2.18-2.15 (m, 1H), 2.12-1.99 (m, 1H), 1.82-1.74 (m, 2H), 1.76-1.75 (m, 1H), 1.69-1.65 (m, 2H), 1.16 (s, 3H), 1.13 (s, 3H), 1.07(s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 220.0, 201.8, 53.9, 45.9, 44.4, 37.8, 31.7, 24.9, 23.4, 23.2, 22.2, 18.4. **IR** (thin film): 3421, 2965, 2927, 2725, 1717, 1459, 1383, 1360, 1340, 1318, 1260, 1214, 1106, 1025, 801 cm^{-1}. **LRMS** (ESI): 195.2 $(M+H)^+$. **HRMS** (ESI): calcd for $C_{12}H_{19}O_2$ $(M+H)^+$:195.1380, found: 195.1380.

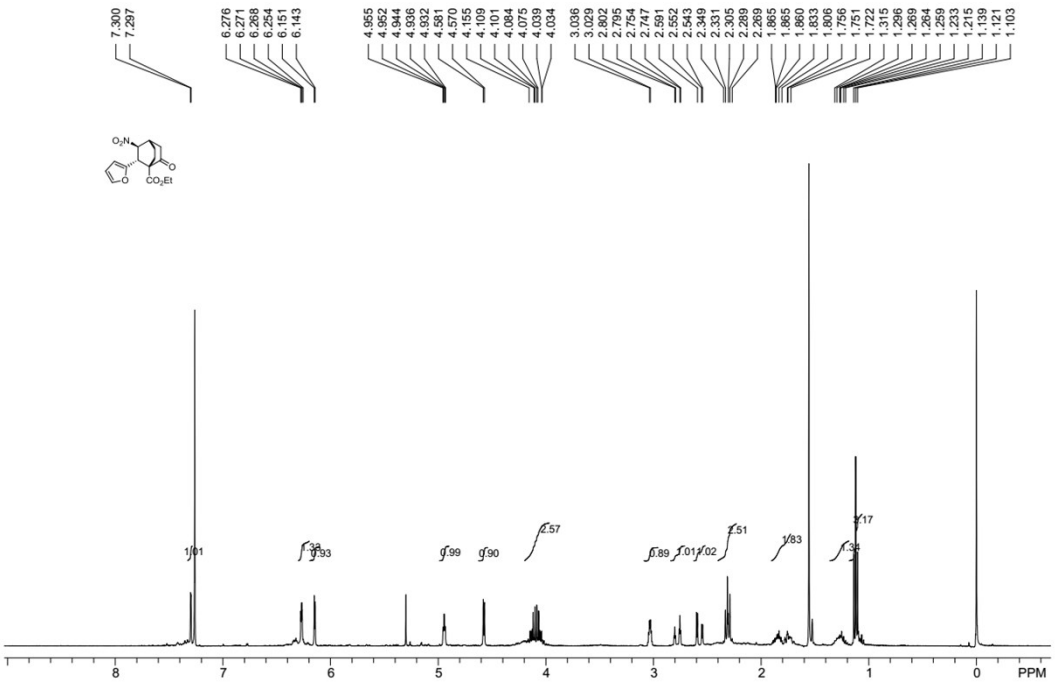
Table 1 Comparison of NMR Data of patchouli alcohol

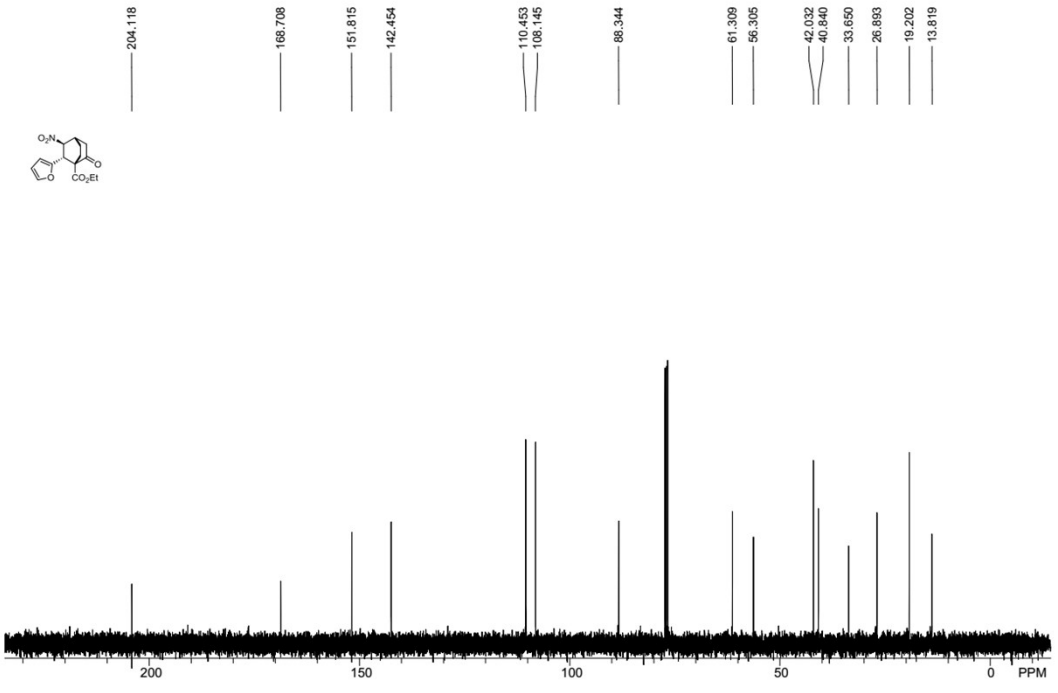
	^{1}H NMR by Srikrishna (300MHz, $CDCl_3$+CCl_4)	^{1}H NMR by this paper (400MHz, $CDCl_3$)	^{13}C NMR by Srikrishna (75 MHz, $CDCl_3$+CCl_4)	^{13}CNMR by this paper (400MHz, $CDCl_3$)
1	2.00-1.80 (3H, m)	2.01-1.93 (1H, m)	75.2	75.6
2		1.93-1.80 (2H, m)	43.7	43.7
3	1.75-1.55 (1H, m)	1.75-1.55 (1H, m)	40.1	40.1
4	1.55-1.15 (9H, m)	1.55-1.40 (5H, m)	39.1	39.1
5		1.40-1.15 (4H, m)	37.6	37.7
6	1.06 (3H, s)	1.08 (3H, s)	32.8	32.7
7	1.04 (3H, s)	1.07 (3H, s)	28.8	28.8
8	1.16 (1H, brs, OH)	1.06 (1H, brs, OH)	28.6	28.6
9	0.82 (3H, s)	0.85 (3H, s)	28.1	28.1
10	0.78 (3H, d, *J*=6.6 Hz)	0.79 (3H, d, *J*=6.8 Hz)	26.9	26.9
11			24.6	24.6
12			24.4	24.3
13			20.7	20.7
14			18.7	18.6

A.Srikrishna, *Tetrahedron:Asymmetry*, **2005**, *16*, 3992.

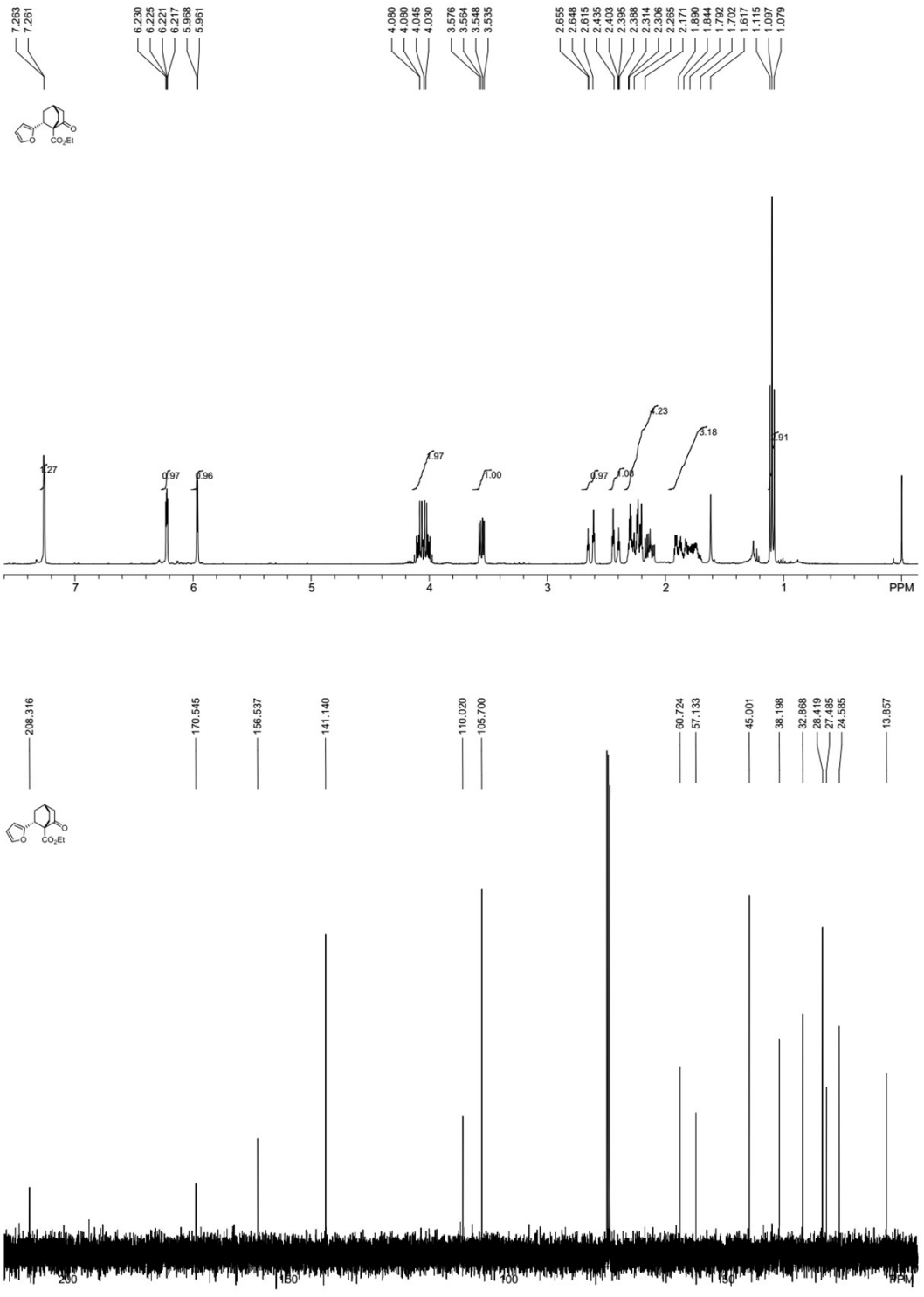
Spectral Data

Compound 7





Compound 14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4.080
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3.564
3.548
3.535
2.655
2.648
2.615
2.435
2.403
2.395
2.388
2.314
2.306
2.265
2.171
1.890
1.844
1.792
1.702
1.617
1.115
1.097
1.079
CO2Et
1.27
0.97
0.96
1.97
1.00
0.97
1.08
3.23
3.18
1.91
7
6
5
4
3
2
1
PPM
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156.537
141.140
110.020
105.700
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45.001
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13.857
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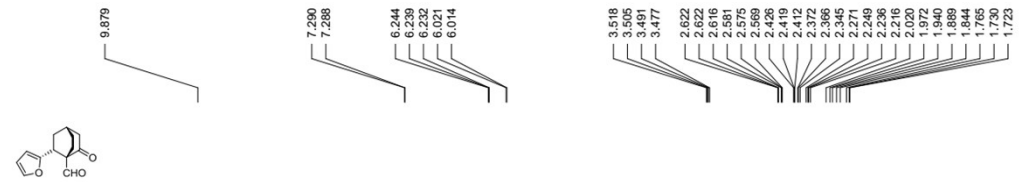
150
100
50
PPM

Compound 15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6.239
6.232
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6.014
3.518
3.505
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2.622
2.616
2.581
2.575
2.569
2.426
2.419
2.412
2.372
2.366
2.345
2.271
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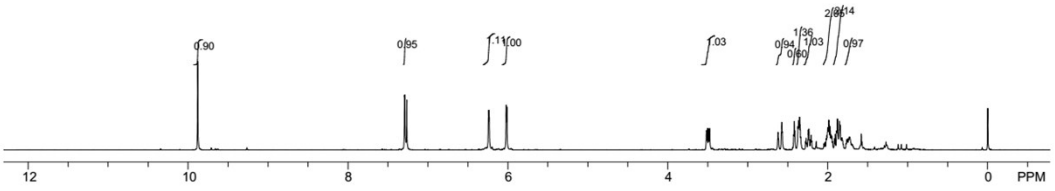
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8
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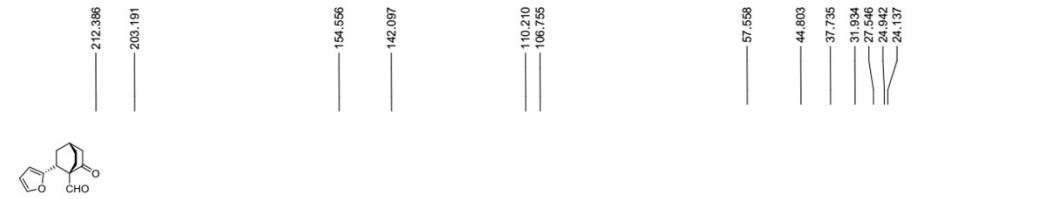
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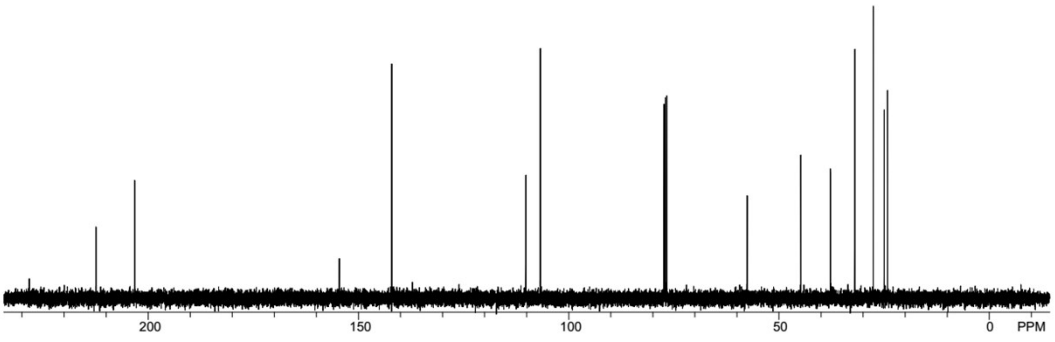
CHO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100
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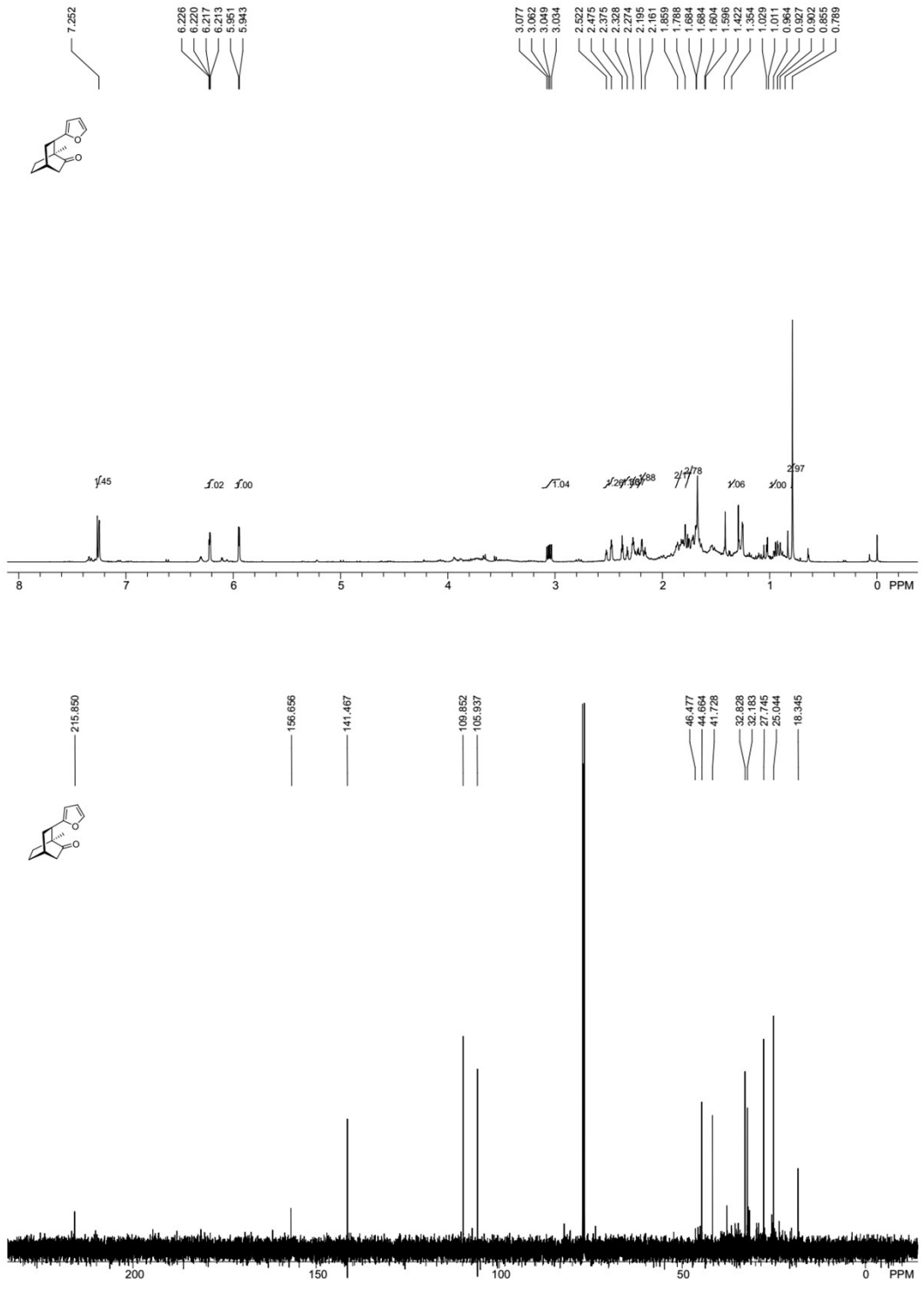
0
PPM

Compound 16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2.161
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1.684
1.684
1.604
1.596
1.422
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0.927
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0.855
0.789
1.45
1.02
1.00
1.04
0.88
2.78
1.06
2.97
8
7
6
5
4
3
2
1
0 PPM
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109.852
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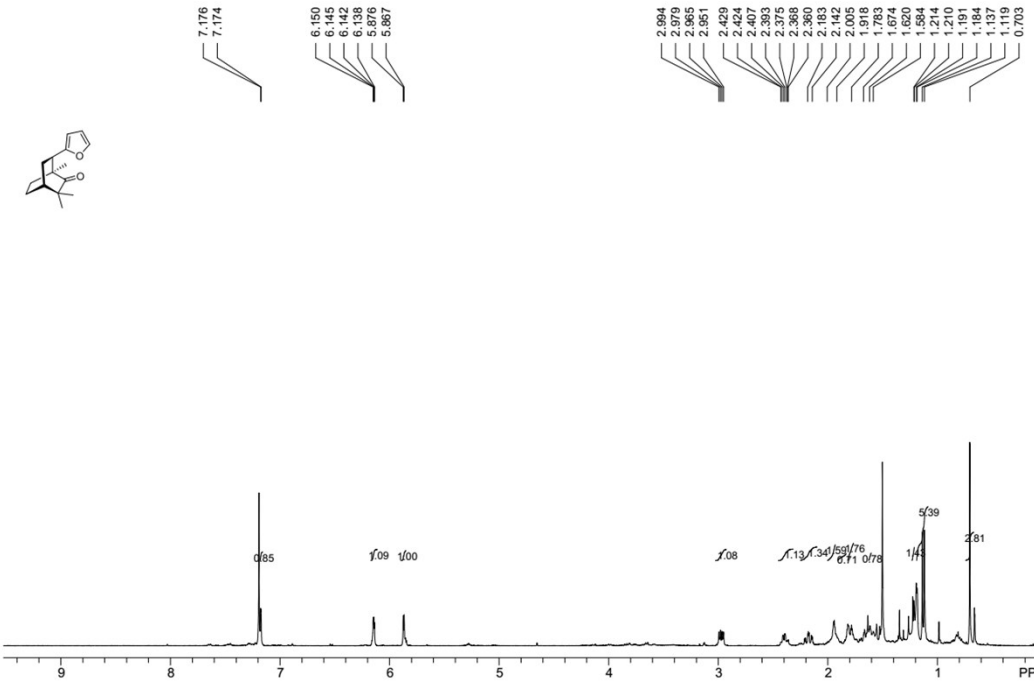
100
50
0 PPM

Compound 6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2.951
2.429
2.424
2.407
2.393
2.375
2.368
2.360
2.183
2.142
2.005
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1.783
1.674
1.620
1.584
1.214
1.210
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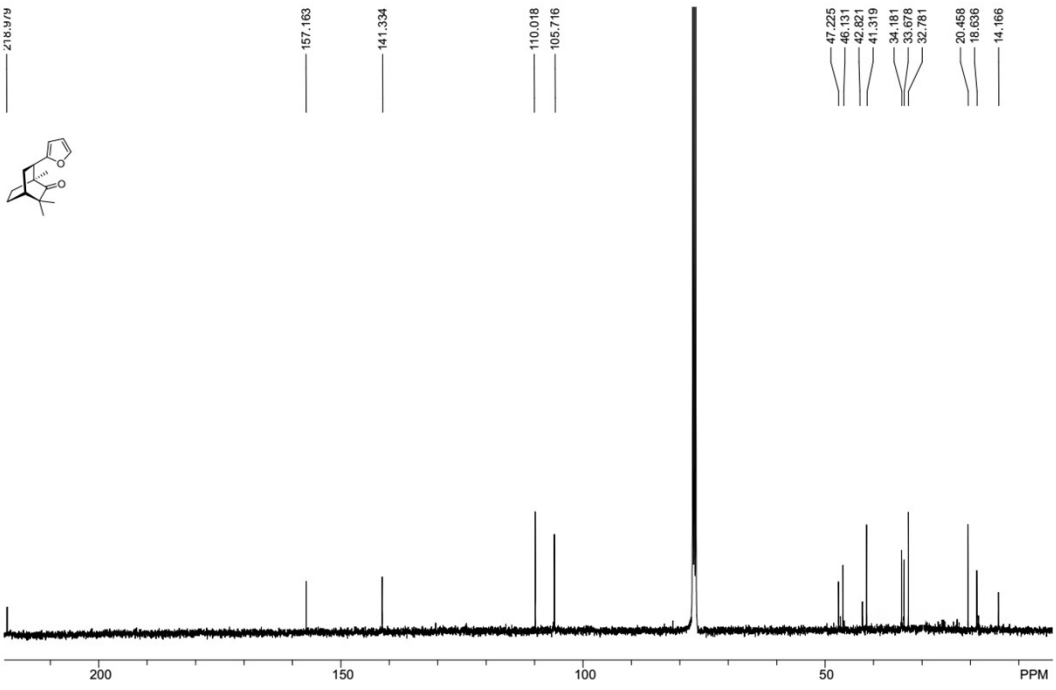
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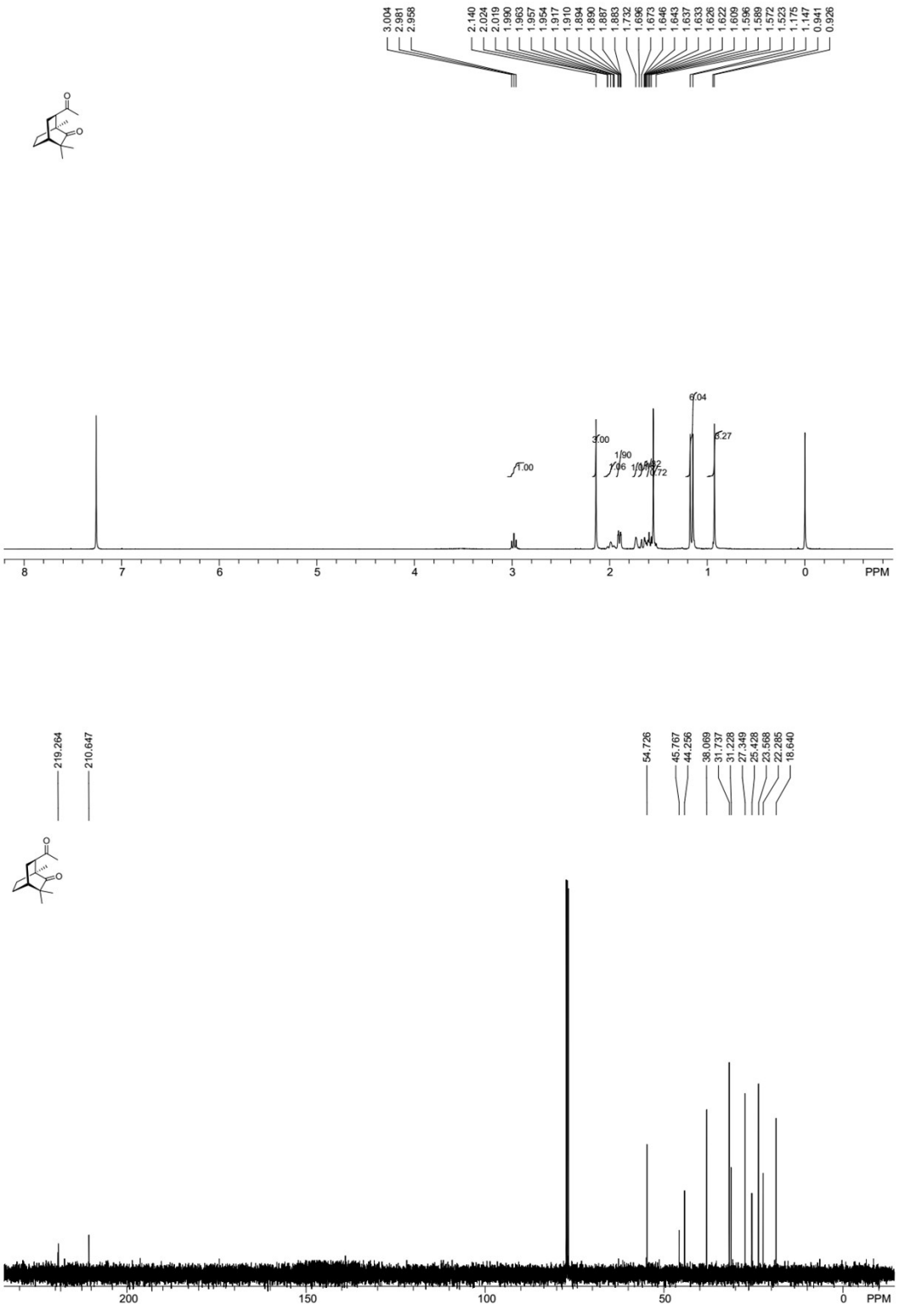
100
50
PPM

Compound 17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1.622
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1.596
1.589
1.572
1.523
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1.147
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3.00
1.90
1.00
6.27
8
7
6
5
4
3
2
1
0
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44.256
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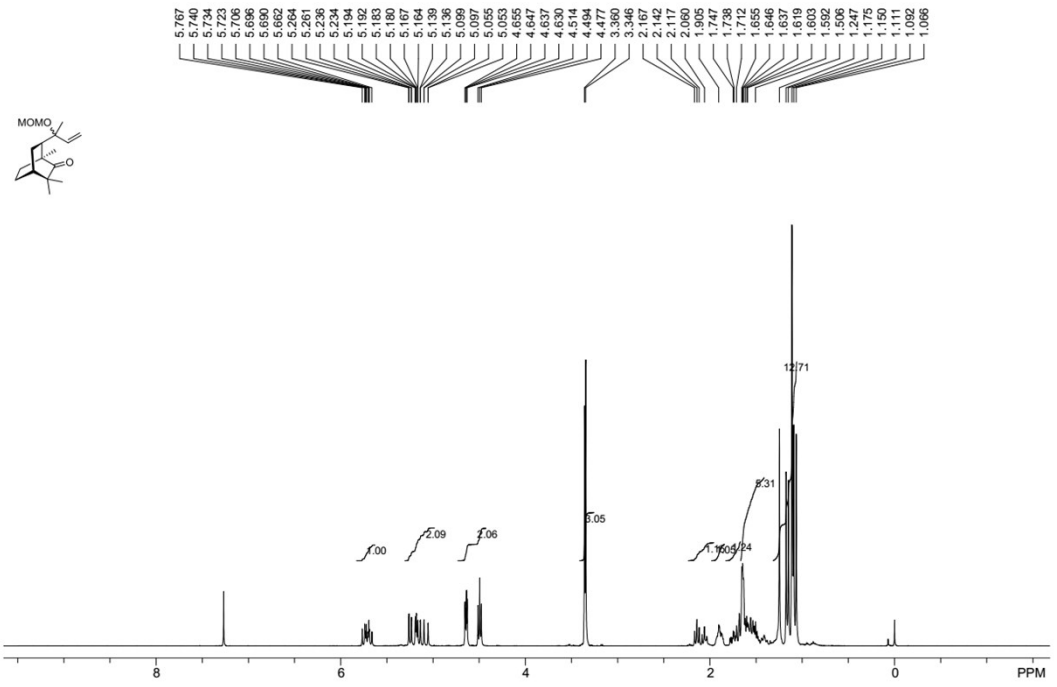
PPM

Compound 4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5.194
5.192
5.183
5.180
5.167
5.164
5.139
5.136
5.099
5.097
5.055
5.053
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4.630
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1.655
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1.637
1.619
1.603
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1.175
1.150
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1.092
1.066
MOMO
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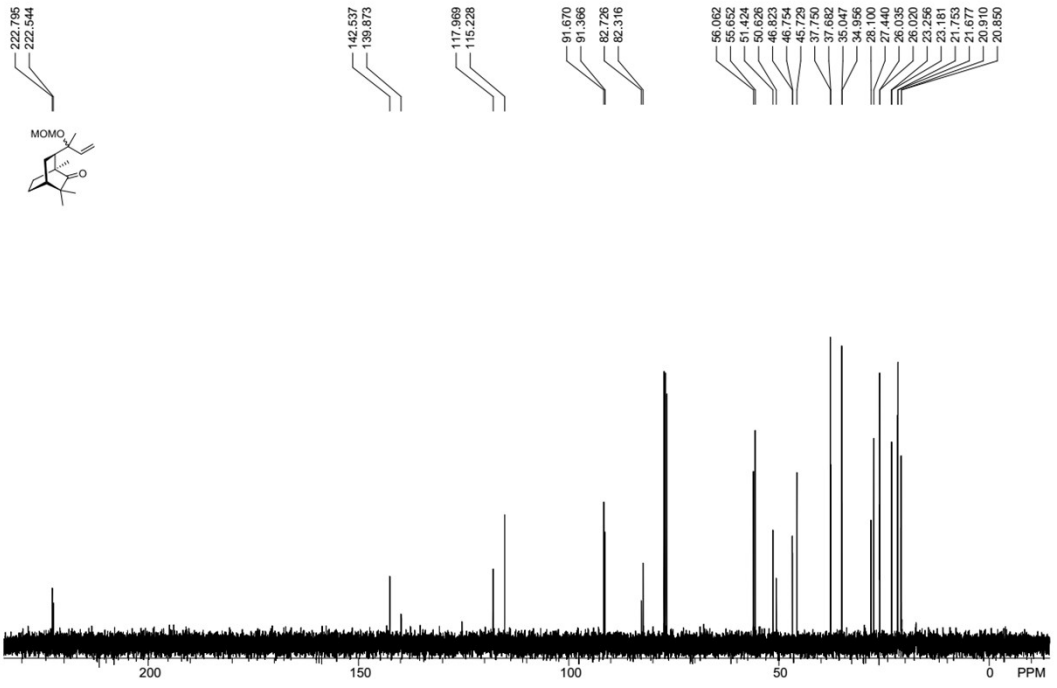
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45.729
37.750
37.682
35.047
34.956
28.100
27.440
26.035
26.020
23.256
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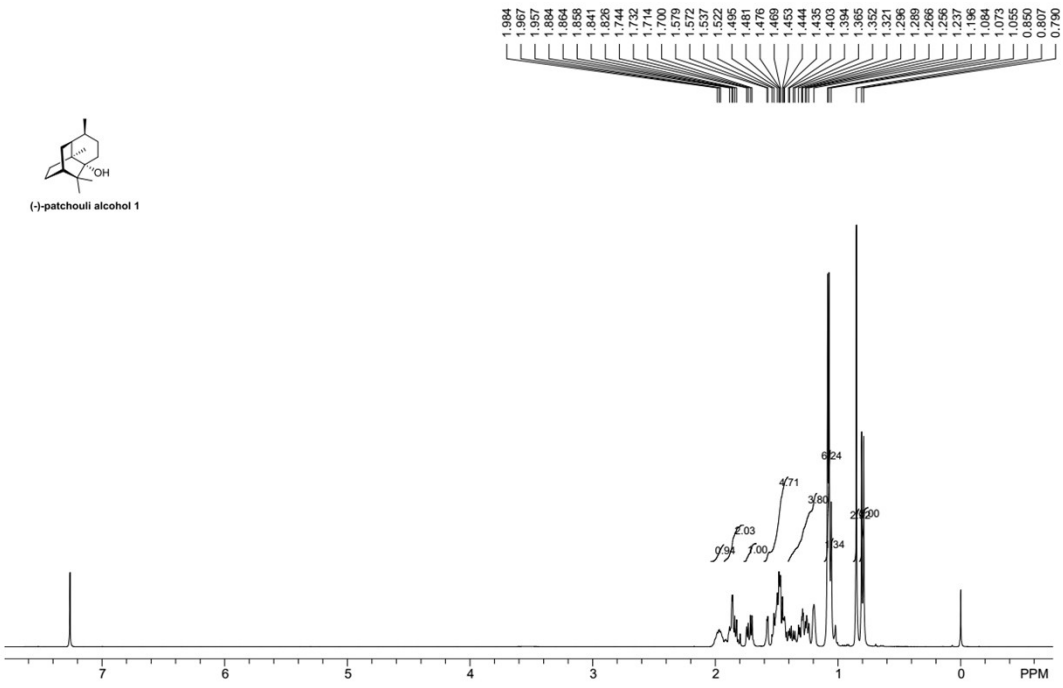
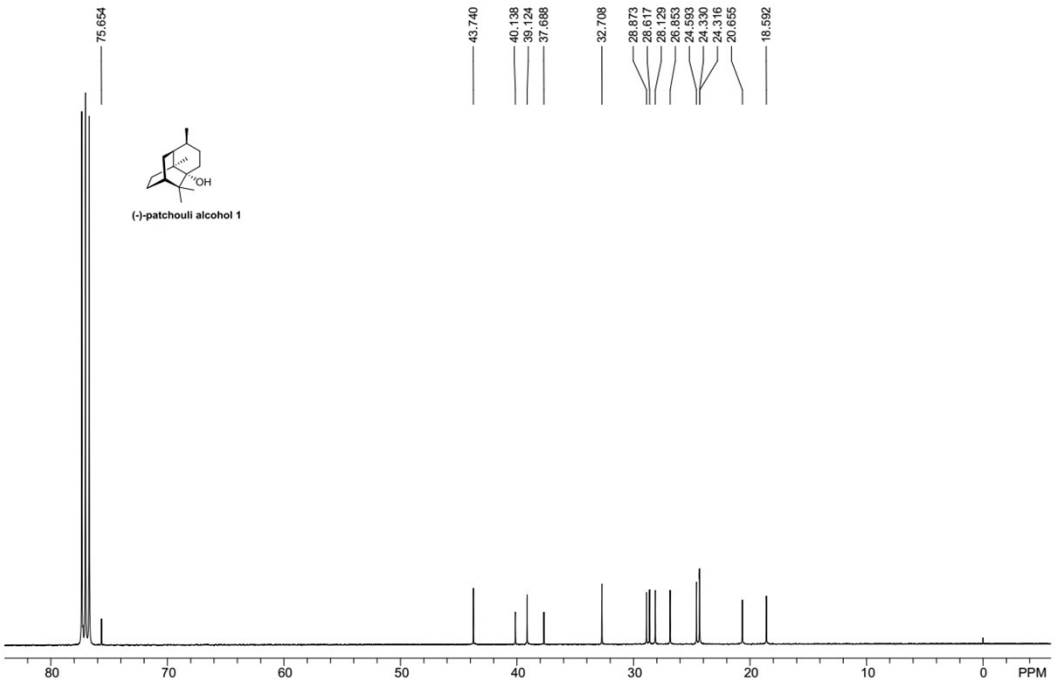
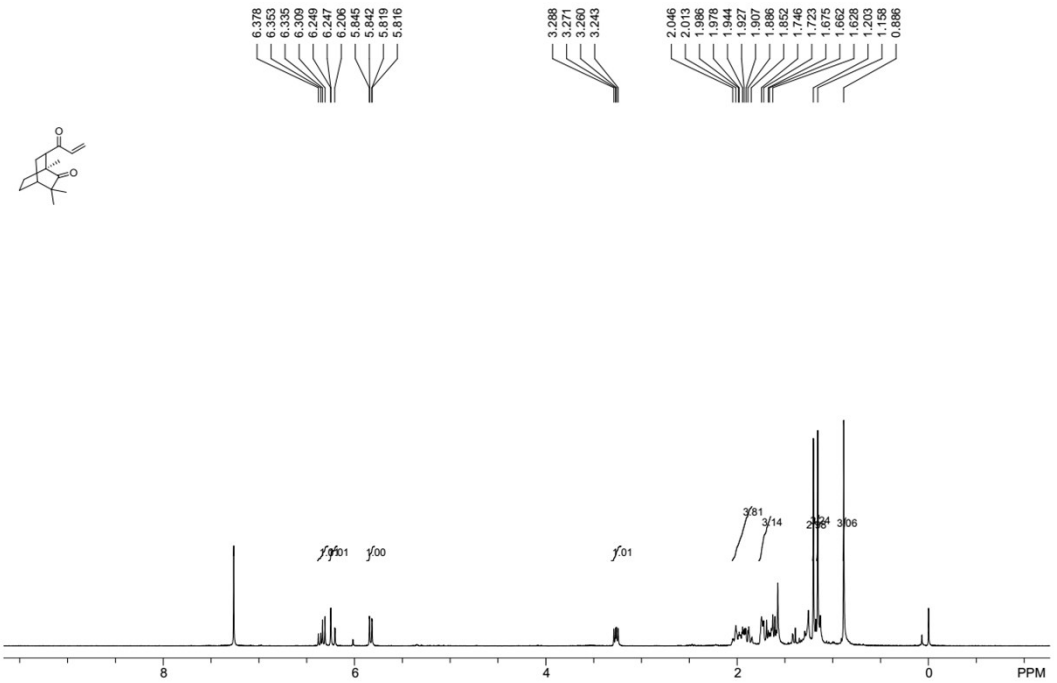
MOMO
O
200
150
100
50
0
PPM

(-)-Patchouli alcohol





Compound 18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1.927
1.907
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1.852
1.746
1.723
1.675
1.662
1.628
1.203
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1.01
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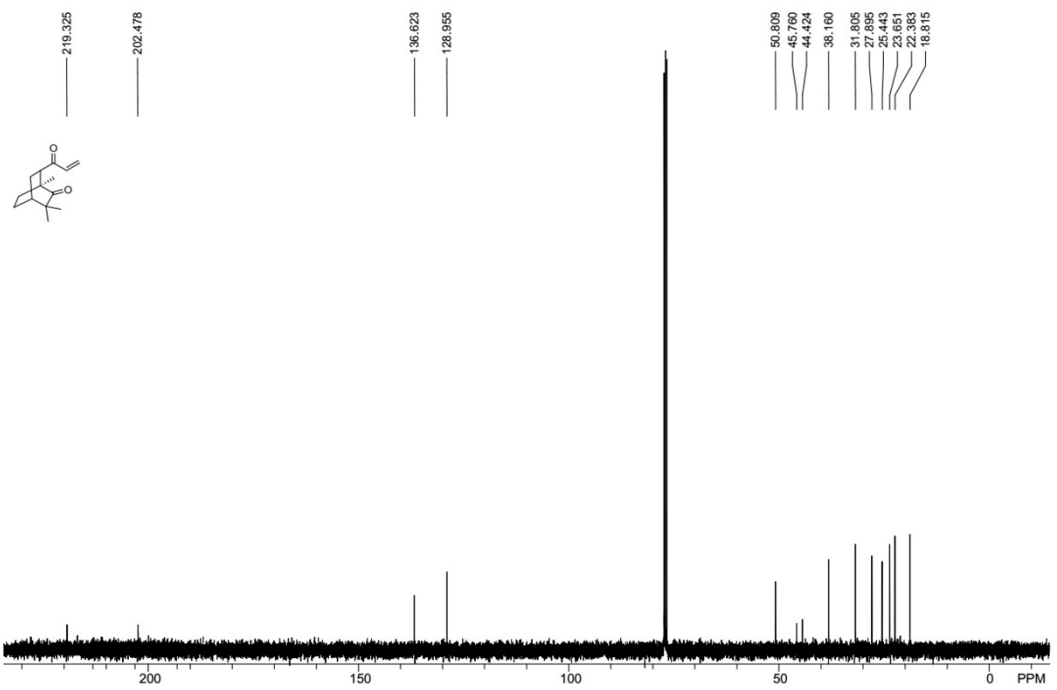
PPM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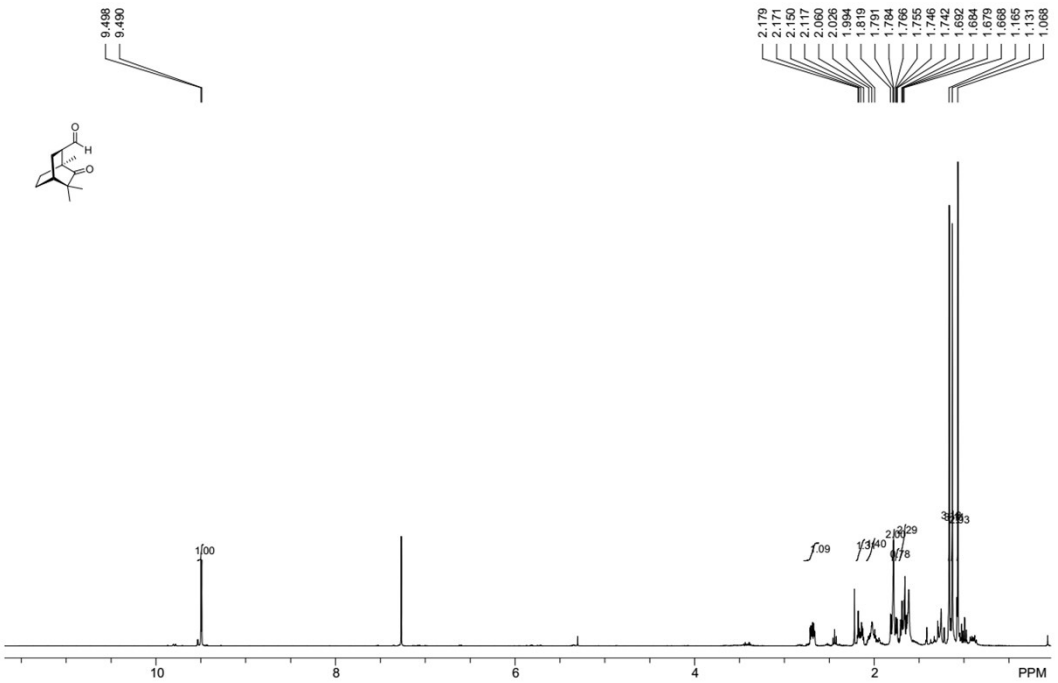
50
0
PPM

Compound 20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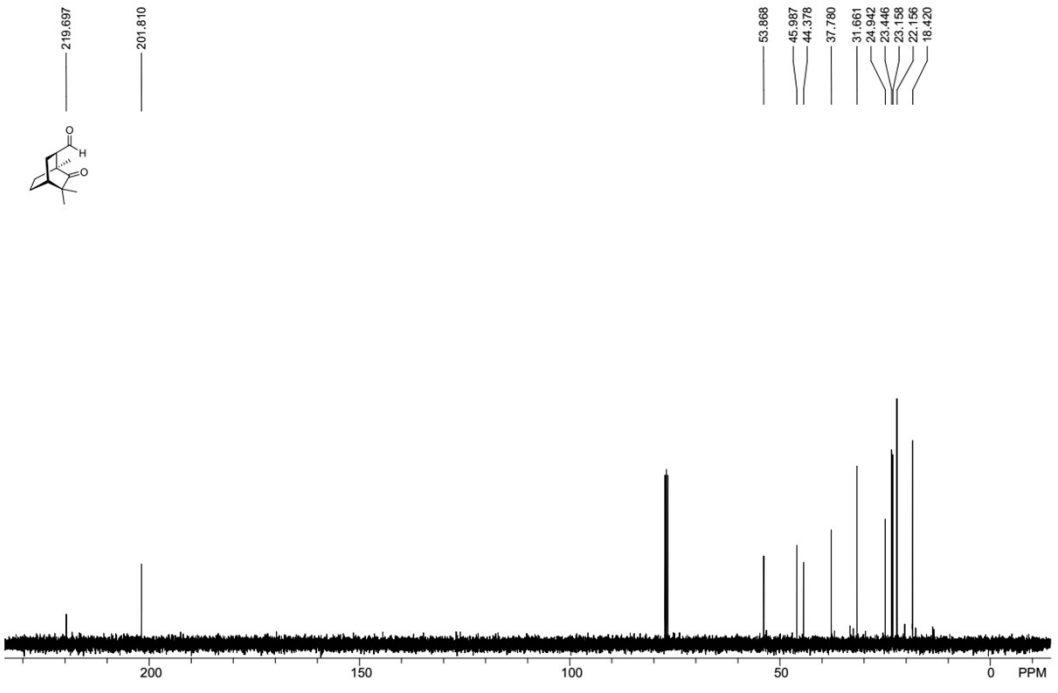
10
8
6
4
2
PPM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PPM