Gold-Catalyzed Synthesis of Substituted Tetrahydronaphthalenes

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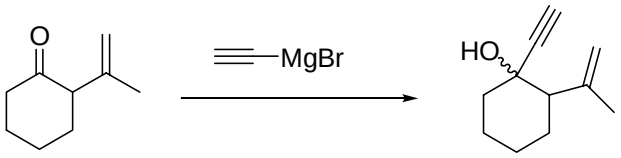
Experimental

General information :

All reactions were performed under nitrogen or argon atmosphere in flame-dried glassware equipped with a magnetic stir bar and a rubber septum, unless otherwise indicated. All solvents were freshly distilled prior to use; diethyl ether and THF over sodium and benzophenone; acetonitrile and DCM over calcium hydride. Silver trifluoromethanesulfonate (AgOTf) was obtained from Aldrich Chemical Company. Silver tetrafluoroborate ($AgBF_4$), silver hexafluoroantimonate ($AgSbF_6$), gold (III) chloride, gold (I) chloride were purchased from Strem Chemicals. Triphenylphosphinegold(I)chloride ($Au(PPh_3)Cl$) was obtained from Aldrich and Strem. All other commercial reagents were used without purification, unless otherwise noted.

Reactions were monitored by thin layer chromatography (TLC) analysis of aliquots using glass sheets pre-coated (0.2 mm layer thickness) with silica gel 60 F_{254} (E. Merck). Thin layer chromatography plates were viewed under UV light and stained with phosphomolybdic acid or *p*-anisaldehyde staining solution. Column chromatographies were carried out with silica gel 60 (230-400 mesh, Merck). ^1H and ^{13}C NMR spectra were recorded in deuterated solvents, on Bruker Avance 300 MHz, Bruker Avance 400 MHz and Bruker Avance 500 MHz spectrometers. IR spectra were recorded with a Bomem Michaelson 100 FTIR spectrometer. HRMS were obtained on a Kratos Analytical Concept instrument (University of Ottawa Mass Spectrum Centre). Melting points were recorded on a Gallenkamp melting point machine apparatus P 1106G.

Preparation of substrate 1 :



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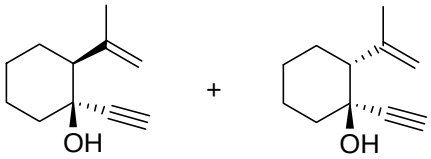
1-Ethynyl-2-isopropenyl-cyclohexanol (1)



[1S,2S] [1S, 2R]

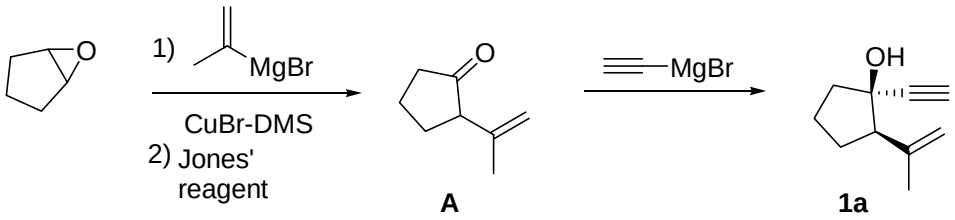
To a solution of 2-isopropenyl-cyclohexanone[1] (7.56 g, 55 mmol) in THF (12 mL) at 0 °C was added dropwise ethynylmagnesium bromide (273.5 mL, 137 mmol). The

solution was warmed to room temperature and stirred 3 hours. The mixture was cooled to 0 °C and quenched with NH_4Cl (sat. aq.). The mixture was extracted with ether (3X). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated. Flash chromatography (5 % hexane in benzene to 10 % ethyl acetate in hexanes) afforded alcohol **1** as mixture of diastereoisomer (*60:40*) as a yellow oil (8.36 g, 93 %).

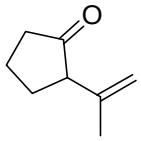
Major (±)-[1S,2S] : IR (neat, cm^{-1}) 3548 (m), 3468 (br), 3307 (s), 3079 (w), 2938 (s), 2856 (s), 1639 (m), 1447 (m), 1071 (m), 972 (s); ^1H NMR ($CDCl_3$, 300 MHz) δ 4.95 (s, 1H), 4.79 (s, 1H), 2.37 (s, 1H), 2.23 (s, 1H), 2.18-2.08 (m, 2 H), 1.92 (s, 3H), 1.72-1.37 (m, 6H), 1.28-1.12 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 148.4 (C_4), 112.8 (CH_2), 89.0 (C_4), 71.7 (CH), 67.4 (C_4), 52.8 (CH), 40.1 (CH_2), 27.0 (CH_2), 26.1 (CH_3), 26.1 (CH_2), 20.8 (CH_2); HRMS (EI) m/z calcd for $C_{11}H_{14}$ [$(M-H_2O)^+$] 146.1095, found 146.1095.

Minor (±)-[1S,2R]: IR (neat, cm^{-1}) 3450 (br), 3305 (s), 2935 (s), 2859 (m), 1634 (w), 1448 (m), 1063, (m), 1015 (m); ^1H NMR ($CDCl_3$, 500 MHz) δ 4.97 (s, 1H), 4.90 (s, 1H), 2.72 (s, 1H), 2,45 (s, 1H), 2.13-2.07 (m, 2H), 1.86 (s, 3H), 1.74-1.69 (m, 2H), 1.68-1.63 (m, 3H), 1.47 (dt, J = 3.9 Hz, J=12.9 Hz, 1H), 1.29-1.14 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 145.7 (C_4), 115.5 (CH_2), 86.3 (C_4), 74.8 (CH), 70.1 (C_4), 56.3 (CH), 40.8 (CH_2), 28.7 (CH_2), 25.9 (CH_2), 24.1 (CH_2), 21.2 (CH_3); HRMS (EI) m/z calcd for $C_{11}H_{16}O$ (M^+) 164.1201, found 164.1205.

Preparation of substrate 1a :



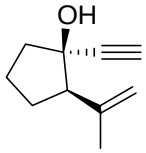
2-Isopropenyl-cyclopentanone (A)



A dry round bottom flask was charged with CuBr·DMS (0.733 g, 3.57 mmoles) and THF (100 mL). The solution was cooled to -30 °C, followed by the addition of isopropenylmagnesium bromide (92.7 mL, 46.4 mmoles). The mixture was stirred for 20 minutes, at which point cyclopentene oxide (3.11 mL, 36.0 mmoles) was added and the solution was stirred to room temperature. The reaction was followed by TLC and quenched with NH_4Cl (sat. aq.) upon completion. The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The residue was re-dissolved in diethyl ether (50 mL) and Jones' reagent (20.6 mL, 53.5 mmoles) was slowly added at 0 °C. The reaction was allowed to reach room temperature. Upon completion, as observed by TLC analysis, the reaction was quenched with NH_4Cl (sat. aq.). The mixture was extracted with diethyl ether (3x) and

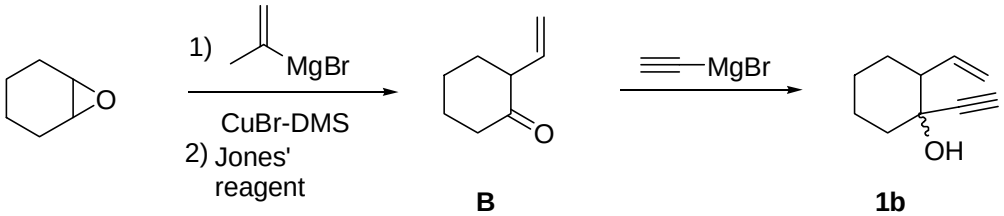
the combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (15% ethyl acetate in hexanes) afforded **A** (2.145 g, 48%) as a yellow oil. Characterisation data is available through the literature.[2]

1-Ethynyl-2-isopropenyl-cyclopentanol (1a)



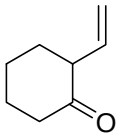
To a solution of ketone **A** (5.30 g, 38.2 mmol) in THF (8.5 mL) at 0 °C was added dropwise ethynylmagnesium bromide (191 mL, 95.5 mmol). The reaction was warmed to room temperature and stirred until completion by TLC, at which point it was quenched with NH_4Cl (sat. aq.). The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (5 % ethyl acetate in hexanes) afforded the **1a** as a yellow oil (1.00 g, 18%). IR (neat, cm^{-1}) 3496 (br), 3305 (s), 3085 (w), 2969 (s), 2923 (m), 2875 (m), 1640 (m), 1450 (m), 1376 (m), 1019 (m), 896 (m), 649 (m); ^1H NMR ($CDCl_3$, 300 MHz) δ 5.03 (s, 1H), 4.89 (s, 1H), 2.60 (m, 1H), 2.41 (s, 1H), 2.19-1.97 (m, 3H), 1.92 (s, 3H), 1.85-1.53 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 143.9 (C_4), 113.5 (CH_2), 87.9 (C_4), 73.2 (C_4), 71.8 (CH), 57.9 (CH), 42.2 (CH_2), 28.4 (CH_2), 25.2 (CH_3), 21.8 (CH_2); HRMS (EI) m/z calcd for $C_{10}H_{14}O$ (M^+) 150.1045, found 150.1016.

Preparation of substrate 1b :



B **1b**

2-Vinyl-cyclohexanone (B)



A dry round bottom flask was charged with CuBr·DMS (1.256 g, 6.11 mmoles) and THF (150 mL). The solution was cooled to -30 °C, followed by the addition of vinylmagnesium bromide (99.3 mL, 79.4 mmoles). The mixture was stirred for 20 minutes, at which point cyclohexene oxide (6.18 mL, 61.1 mmoles) was added and the solution was stirred to room temperature. The reaction was followed by TLC and quenched with NH_4Cl (sat. aq.) upon completion. The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The residue was re-dissolved in diethyl ether (100 mL) and Jones' reagent (70.5 mL, 91.7 mmoles) was slowly added at 0 °C. The reaction was allowed to reach

room temperature. Upon completion, as observed by TLC analysis, the reaction was quenched with NH_4Cl (sat. aq.). The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (15% ethyl acetate in hexanes) afforded **B** (3.210 g, 42%) as a yellow oil. Characterisation data is available through the literature.[3]

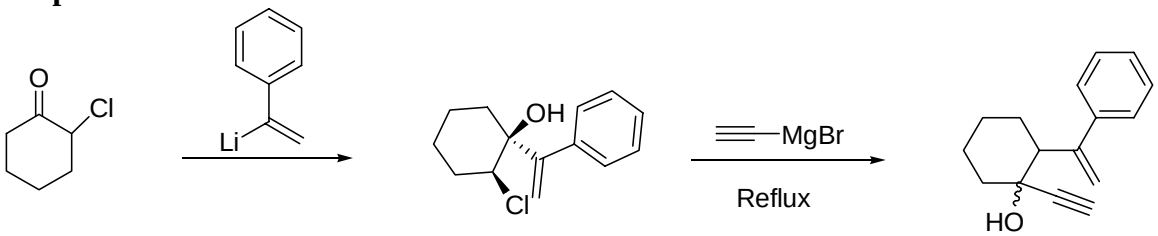
1-Ethynyl-2-vinyl-cyclohexanol (1b)

[1S,2S] [1S, 2R]

To a solution of ketone **B** (0.312 g, 2.52 mmol) in THF (10 mL) at 0 °C was added dropwise ethynylmagnesium bromide (10.1 mL, 5.04 mmol). The reaction was warmed to room temperature and followed to completion by TLC, at which point it was quenched with NH_4Cl (sat. aq.). The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (10 % ethyl acetate in hexanes) afforded both diastereoisomers (60*:40*) as yellow oils (163.5 mg, 43 %).

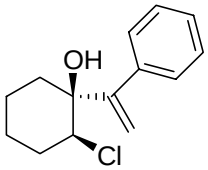
Major (±)-[1S,2S] : IR (neat, cm^{-1}) 3464(br), 3303 (m), 2935 (s), 2861 (m), 1730 (w), 1640(w), 1445 (m), 1082 (m); ^1H NMR ($CDCl_3$, 400 MHz) δ 6.16 (ddd, J=17.3, 10.7, 6.5 Hz, 1H), 5.22 (ddd, J=10.6, 1.6, 1.3 Hz, 1H), 5.15 (ddd, J=17.4, 1.6, 1.6 Hz, 1H), 2.43 (s, 1H), 2.34-2.29 (m, 1H), 2.15-1.99 (m, 2H), 1.84 (d, J=1.1 Hz, 1H), 1.73-1.49 (m, 4H), 1.42 (s, 1H), 1.34-1.19 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.7 (CH), 118.4 (CH_2), 88.2 (C_4), 71.8 (CH), 68.3 (C_4), 49.1 (CH), 38.8 (CH_2), 25.5 (CH_2), 24.6 (CH_2), 21.0 (CH_2); HRMS (EI) m/z calcd for $C_{10}H_{14}O$ [M^+] 150.1045, found 150.1032.
Minor (±)-[1S,2R]: IR (neat, cm^{-1}) 3441 (br), 3302 (m), 3080 (w), 2935 (s), 2859 (m), 2106 (w), 1640 (w), 1447 (m), 1051 (m), 642 (m); ^1H NMR ($CDCl_3$, 400 MHz) δ 5.90-5.81 (m, 1H), 5.20-5.14 (m, 2H), 2.48 (s, 1H), 2.45 (s, 1H), 2.08-2.00 (m, 2H), 1.75-1.42 (m, 6H), 1.28-1.16 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.3 (CH), 117.4 (CH_2), 85.1 (C_4), 74.2 (CH), 71.0 (C_4), 53.7 (CH), 39.4 (CH_2), 30.2 (CH_2), 25.4 (CH_2), 24.0 (CH_2); HRMS (EI) m/z calcd for C_8H_{11} [$M-C_2H_3O^+$] 107.0855, found 107.0801.

Preparation of substrate 1c :



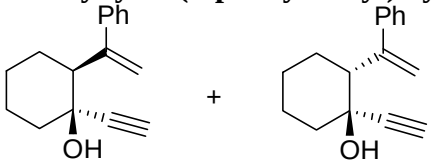
C **1c**

(±)-(1S, 2S)-2-Chloro-1-(1-phenyl-vinyl)-cyclohexanol (C)



To a -90 °C solution of α-bromostyrene (1.27 mL, 8.76 mmol) in ether (36 mL) was added t-BuLi (8.24 mL, 14.02 mmol) dropwise. The solution was protected from light and stirred for 75 min. at -90 to -100 °C. After cannulation of 2-chlorocyclohexanone (0.500 mL, 4.38 mmol) in ether (8 mL), the mixture was slowly warmed to -60 °C and followed to completion by TLC. The reaction mixture was cooled to -90 °C and quenched with a saturated solution of ammonium chloride. The mixture was extracted with diethyl ether (3x) and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (5% ethyl acetate in hexanes) afforded **C** as a yellow oil (867.6 mg, 84 %). IR (neat, cm^{-1}) 3555 (br), 3080 (w), 3054 (w), 2940 (s), 2862 (m), 1191 (m), 1445 (m), 1285 (m), 1069 (s), 986 (s), 701 (s); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.29 (s, 5H), 5.57 (d, J=1.5 Hz, 1H), 5.02 (d, J=1.5 Hz, 1H), 4.02 (dd, J=11.2, 5.8 Hz, 1H), 2.27 (d, J=2.3 Hz, 1H), 2.03-1.93 (m, 3H), 1.72-1.64 (m, 3H), 1.47-1.42 (m, 1H), 1.26-1.05 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 155.2 (C_4), 140.8 (C_4), 129.2 (CHx2), 128.0 (CHx2), 127.4 (CH), 115.2 (CH_2), 76.5 (C_4), 66.2 (CH), 36.9 (CH_2), 32.5 (CH_2), 25.9 (CH_2), 20.6 (CH_2); HRMS (EI) m/z calcd for $C_{14}H_{17}ClO$ [M^+] 236.0968, found 236.0950.

1-Ethynyl-2-(1-phenyl-vinyl)-cyclohexanol (1c)



[1S,2S] [1S, 2R]

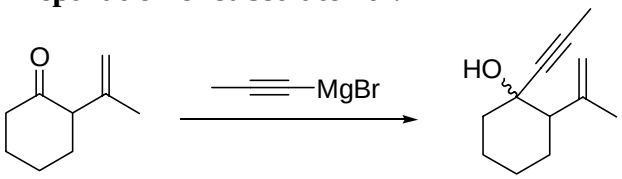
To a solution of ketone **C** (0.223 g, 0.943 mmol) in THF (3.7 mL) was added dropwise ethynylmagnesium bromide (5.7 mL, 2.83 mmol). The reaction was heated to reflux and stirred until completion by TLC (5 hours), at which point it was cooled to room temperature and quenched with NH_4Cl (sat. aq.). The mixture was extracted with diethyl ether (3x) and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (10 % ethyl acetate in hexanes) afforded both diastereoisomer (*54:46*) of **1c** as yellow oils (134.0 mg, 63 %).

Major (±)-[1S,2S]: IR (neat, cm^{-1}) 3553 (br), 3292 (m), 2936 (s), 2857 (m), 1493 (m), 1444 (m), 1143 (w), 1067 (m), 971 (m); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.41-7.38 (m, 2H), 7.31-7.21 (m, 3H), 5.40 (d, J=0.8 Hz, 1H), 5.28 (s, 1H), 2.87 (dd, J=12.4, 3.5 Hz, 1H), 2.20 (d, J=1.6 Hz, 1H), 2.15-2.11 (m, 1H), 2.07 (s, 1H), 1.87-1.59 (m, 6H), 1.40-1.29 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 151.6 (C_4), 144.4 (C_4), 128.2 (CHx2), 127.3 (CH), 127.1 (CHx2), 115.4 (CH_2), 88.1(C_4), 72.1 (CH), 67.4 (C_4), 51.0 (CH), 40.0 (CH_2),

28.0 (CH_2), 26.0 (CH_2), 20.6 (CH_2); HRMS (EI) m/z calcd for $C_{16}H_{18}O$ [M^+] 226.1358, found 226.1351.

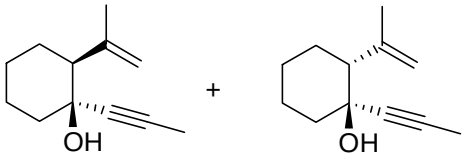
Minor (±)-[1S,2R]: IR (neat, cm^{-1}) 3566 (br), 3443 (br), 3297 (m), 2935 (s), 2859 (m), 1622 (w), 1444 (m), 1321 (w), 1059 (s), 998 (m); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.44-7.43 (m, 2H), 7.35-7.21 (m, 3H), 5.56 (s, 1H), 5.47 (d, J=0.5 Hz, 1H), 2.70 (dd, J=12.4, 2.9 Hz, 1H), 2.59 (s, 1H), 2.22 (s, 1H), 2.16-2.10 (m, 1H), 1.92-1.63 (m, 6H), 1.44-1.33 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.3 (C_4), 144.2 (C_4), 128.5 (CHx2), 127.5 (CH), 126.9 (CHx2), 115.8 (CH_2), 85.3 (C_4), 75.3 (CH), 73.5 (C_4), 52.8 (CH), 41.2 (CH_2), 30.9 (CH_2), 26.1 (CH_2), 24.0 (CH_2); HRMS (EI) m/z calcd for $C_{16}H_{18}O$ [M^+] 226.1358, found 226.1353.

Preparation of substrate 1d :



1d

2-Isopropenyl-1-prop-1-ynyl-cyclohexanol (1d)



[1S,2S] [1S, 2R]

To a solution of 2-isopropenyl-cyclohexanone[1] (0.608 g, 4.40 mmol) in THF (7.8 mL) at 0 °C was added dropwise 1-propynylmagnesium bromide (17.6 mL, 8.81 mmol). The reaction was warmed to room temperature and stirred until completion by TLC, at which point it was quenched with NH_4Cl (sat. aq.). The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (10 % hexanes in benzene) afforded both diastereoisomers (*71:29*) of **1d** as yellow oils (0.486 g, 62 %).

Major (±)-[1S,2S] : IR (neat, cm^{-1}) 3549 (br), 3079 (w), 2936 (s), 2855 (s), 1639 (m), 1447 (m), 1370 (m), 1286 (m), 969 (s), 893 (m); ^1H NMR ($CDCl_3$, 300 MHz) δ 4.89 (s, 1H), 4.73 (s, 1H), 2.11 (s, 1H), 2.10-1.99 (m, 2H), 1.88 (s, 3H), 1.71 (s, 3H), 1.66-1.21 (m, 6H), 1.22-1.06 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 148.5 (C_4), 111.9 (CH_2), 84.2 (C_4), 78.7 (C_4), 66.8 (C_4), 52.6 (CH), 39.8 (CH_2), 26.5 (CH_2), 25.6 (CH_2), 25.6 (CH_3), 20.4 (CH_2), 3.1 (CH_3); HRMS (EI) m/z calcd for $C_{12}H_{18}O$ (M^+) 178.1358, found 178.1361

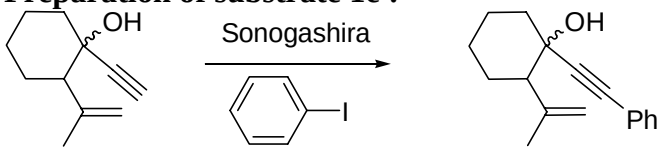
Minor (±)-[1S,2R] : IR (neat, cm^{-1}) 3450 (br), 2933 (s), 2857 (m), 2236 (w), 1639 (w), 1446 (m), 1373 (m), 1061 (m), 1012 (m); ^1H NMR ($CDCl_3$, 500 MHz) 4.96-4.95 (m, 1H), 4.88 (d, J=1.7Hz, 1H), 2.63 (s, 1H), 2.10-1.98 (m, 2H), 1.84-1.83 (m, 6H), 1.73-1.59 (m, 5H), 1.47-1.42 (m, 1H), 1.27-1.18 (m, 1H);^{13}C NMR ($CDCl_3$, 75 MHz) δ 145.8 (C_4), 114.7 (CH_2), 81.9 (C_4), 81.0 (C_4), 69.7 (C_4), 56.2 (CH), 40.6 (CH_2), 28.5 (CH_2), 25.6

(CH_2), 23.9 (CH_2), 20.7 (CH_3), 3.5 (CH_3); HRMS (EI) m/z calcd for $C_{12}H_{17}$ [$(M\text{-}OH)^+$] 161.1325, found 161.1328.

General procedure for Sonogashira coupling[4]

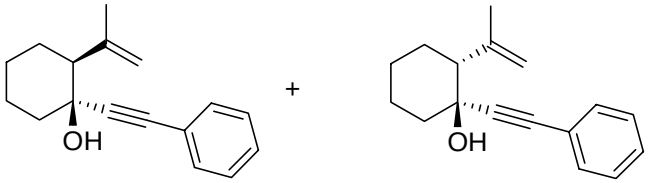
$PdCl_2(PPh_3)_2$ (5 mol %) and CuI (5 mol %) were weighed in the glovebox. A solution of the alkyne (1.0 eq.) in acetonitrile (0.07 M) was cannulated. Following the addition of the appropriate coupling partner (1.1 eq.), the resulting solution was degassed with argon for 10 min. Then, freshly distilled diisopropylethylamine (5.0 eq) was added and the mixture was stirred at room temperature. Upon completion by TLC, the reaction mixture was concentrated and loaded directly onto a silica gel column for purification.

Preparation of substrate 1e :



1 **1e**

2-Isopropenyl-1-phenylethynyl-cyclohexanol (1e)



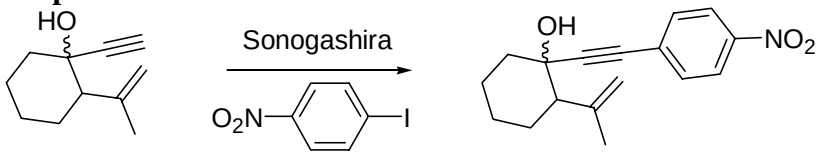
[1S,2S] [1S, 2R]

Using the general procedure for Sonogashira, alcohol **1** (128.1 mg, 0.781 mmol) was coupled with iodobenzene (0.096 mL, 0.859 mmol). Purification by flash chromatography (10 % ethyl acetate/90 % hexanes) gave compounds **1e** as yellow oils (113.5 mg, 61 %).

Major (±)-[1S,2S] : IR (neat, cm^{-1}) 3550 (br), 3463 (br), 3079 (m), 2936 (s), 2855 (s), 2226 (w), 1638 (m), 1490 (s), 1444 (s), 1287 (m), 969 (s), 756 (s); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.39-7.36 (m, 2H), 7.28-7.26 (m, 3H), 5.02 (dd, J=1.5, 1.5 Hz, 1H), 4.88 (s, 1H), 2.32-2.28 (m, 2H), 2.25-2.20 (m, 1H), 2.04 (s, 3H), 1.79-1.59 (m, 4H), 1.55-1.47 (m, 2H), 1.34-1.22 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.4 (C_4), 131.6 (CHx2), 128.2 (CHx2), 128.1 (CH), 123.0 (C_4), 112.4 (CH_2), 94.1 (C_4), 83.1 (C_4), 67.4 (C_4), 52.7 (CH), 39.7 (CH_2), 26.8 (CH_2), 26.0 (CH_2), 25.8 (CH_2), 20.7 (CH_3); HRMS (EI) m/z calcd for $C_{17}H_{20}O$ [M^+] 240.1514, found 240.1535.

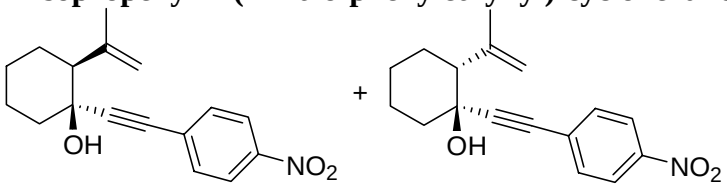
Minor (±)-[1S,2R] : IR (neat, cm^{-1}) 3537 (br), 3448 (br), 3079 (w), 2933 (s), 2857 (m), 1636 (w), 1597 (w), 1490 (m), 1443 (m), 1063 (m), 1013 (m), 756 (s); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.41-7.38 (m, 2H), 7.30-7.26 (m, 3H), 5.00 (dd, J=1.5, 1.5 Hz, 1H), 4.96 (s, 1H), 2.78 (s, 1H), 2.23-2.15 (m, 2H), 1.92 (s, 3H), 1.78-1.66 (m, 5H), 1.60-1.52 (m, 1H), 1.34-1.23 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 145.7 (C_4), 131.6 (CHx2), 128.4 (CHx2), 128.3 (CH), 123.1 (C_4), 115.3 (CH_2), 91.4 (C_4), 86.4 (C_4), 70.4 (C_4), 56.7 (CH), 40.7 (CH_2), 28.8 (CH_2), 25.8 (CH_2), 24.2 (CH_2), 20.9 (CH_3); HRMS (EI) m/z calcd for $C_{17}H_{20}O$ [M^+] 240.1514, found 240.1507.

Preparation of substrate 1f :



1 **1f**

2-Isopropenyl-1-(4-nitro-phenylethynyl)-cyclohexanol (1f)

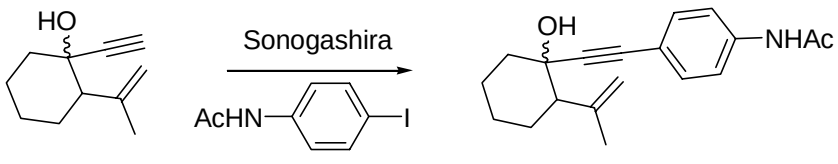


[1S,2S] [1S, 2R]

Using the general procedure for Sonogashira, alcohol **1** (101.1 mg, 0.616 mmol) was coupled with 1-iodo-4-nitrobenzene (172 mg, 0.678 mmol). Purification by flash chromatography (10 % ethyl acetate/90 % hexanes to 20 % ethyl acetate/80 % hexanes) gave compounds **1f** as yellow oils (135.9 mg, 77 %).

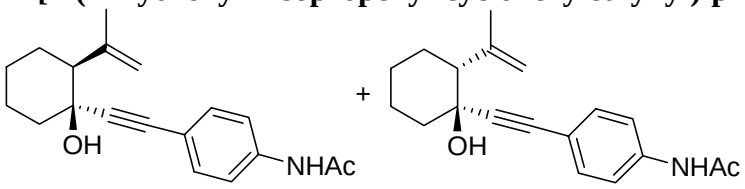
Major (±)-[1S,2S]: IR (neat, cm^{-1}) 3542 (br), 3079 (w), 2937 (s), 2856 (m), 2226 (w), 1638 (w), 1594 (s), 1530 (s), 1345 (s); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.14 (d, J=9.0 Hz, 2H), 7.49 (d, J=9.0 Hz, 2H), 5.03 (dd, J=1.5, 1.5 Hz, 1H), 4.88 (s, 1H), 2.33-2.28 (m, 2H), 2.23-2.19 (m, 1H), 1.99 (dd, J=1.2, 0.8 Hz, 3H), 1.79-1.59 (m, 4H), 1.57-1.49 (m, 2H), 1.34-1.22 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.1 (C_4), 147.1 (C_4), 132.3 (CHx2), 130.1 (C_4), 123.7 (CHx2), 112.8 (CH_2), 99.7 (C_4), 81.8 (C_4), 67.8 (C_4), 52.7 (CH), 39.4 (CH_2), 26.6 (CH_2), 25.9 (CH_2), 25.8 (CH_2), 20.5 (CH_3); HRMS (EI) m/z calcd for $C_{17}H_{19}NO_3$ [M^+] 285.1365, found 285.1364.
Minor (±)-[1S,2R] : IR (neat, cm^{-1}) 3533 (br), 3441 (br), 3078 (m), 2934 (s), 2858 (m), 2223 (w), 1594 (s), 1519 (s), 1345 (s), 855 (s); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.15 (d, J=8.9 Hz, 2H), 7.52 (d, J=8.9 Hz, 2H), 5.02 (dd, J=1.5, 1.5 Hz, 1H), 4.95 (s, 1H), 2.83 (s, 1H), 2.24-2.16 (m, 2H), 1.89 (s, 3H), 1.82-1.54 (m, 6H), 1.36-1.22 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 147.3 (C_4), 145.1 (C_4), 132.4 (CHx2), 130.0 (C_4), 123.7 (CHx2), 115.7 (CH_2), 97.1 (C_4), 84.6 (C_4), 70.5 (C_4), 56.6 (CH), 40.6 (CH_2), 28.8 (CH_2), 25.8 (CH_2), 24.2 (CH_2), 21.0 (CH_3); HRMS (EI) m/z calcd for $C_{17}H_{19}NO_3$ [M^+] 285.1365, found 285.1370.

Preparation of substrate 1g :



1 **1g**

N-[4-(1-Hydroxy-2-isopropenyl-cyclohexylethynyl)-phenyl]-acetamide (1g)

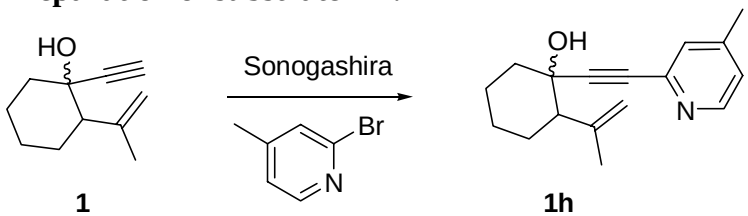


[1S,2S] [1S, 2R]

Using the general procedure for Sonogashira, alcohol **1** (116.0 mg, 0.707 mmol) was coupled with N-(4-Iodo-phenyl)-acetamide[5] (203.0 mg, 0.778 mmol). Purification by flash chromatography (10 % ethyl acetate/90 % dichloromethane) gave compounds **1g** as yellow foams (182.1 mg, 87 %).

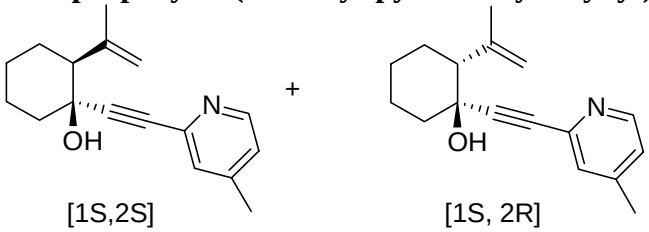
Major (±)-[1S,2S] : IR (neat, cm^{-1}) 3305 (br), 3102 (w), 2934 (s), 2856 (w), 1671 (s), 1597 (s), 1530 (s),, 1512 (s), 1316 (m); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.44-7.42 (m, 3H), 7.31-7.29 (m, 2H), 5.01 (dd, J=1.5, 1.5 Hz, 1H), 4.86 (s, 1H), 2.31-2.26 (m, 2H), 2.22-2.17 (m, 1H), 2.15-2.14 (m, 3H), 2.01 (s, 3H), 1.91 (s, 1H), 1.76-1.46 (m, 5H), 1.29-1.22 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.4 (C_4), 148.5 (C_4), 138.0 (C_4), 132.5 (CHx2), 129.2 (C_4), 119.5 (CHx2), 112.6 (CH_2), 94.0 (C_4), 83.1 (C_4), 67.6 (C_4), 52.9 (CH), 40.0 (CH_2), 26.9 (CH_2), 26.1 (CH_3), 25.9 (CH_2), 24.8 (CH_3), 20.7 (CH_2); HRMS (EI) m/z calcd for $C_{19}H_{23}NO_2$ [M^+] 297.1729, found 297.1721.
Minor (±)-[1S,2R] : IR (neat, cm^{-1}) 3305 (br), 2934 (s), 2857 (m), 1672 (s), 1595 (s), 1530 (s), 1512 (s), 1315 (s), 839 (m); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.45-7.43 (m, 2H), 7.35-7.33 (m, 3H), 5.00 (s, 1H), 4.94 (s, 1H), 2.79 (s, 1H), 2.22-2.16 (m, 5H), 1.91(s, 3H), 1.77-1.52 (m, 6H), 1.31-1.22 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.4 (C_4), 145.7 (C_4), 138.1 (C_4), 132.4 (CHx2), 119.5 (CHx2), 118.8 (C_4), 115.3 (CH_2), 91.0 (C_4), 86.1 (C_4), 70.4 (C_4), 56.8 (CH), 40.7 (CH_2), 28.8 (CH_2), 25.9 (CH_2), 24.9 (CH_3), 24.2 (CH_2), 21.1 (CH_3); HRMS (EI) m/z calcd for $C_{19}H_{23}NO_2$ [M^+] 297.1729, found 297.1738.

Preparation of substrate 1h :



1 **1h**

2-Isopropenyl-1-(5-methyl-pyridin-2-ylethynyl)-cyclohexanol (1h)



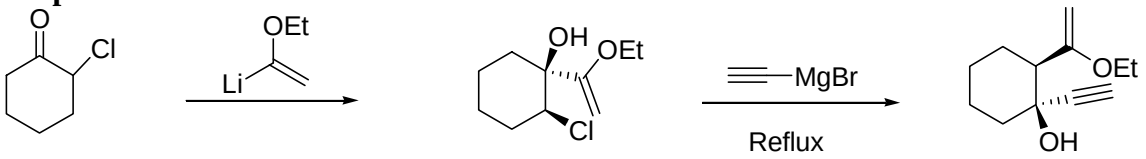
[1S,2S] [1S, 2R]

Using the general procedure for Sonogashira, alcohol **1** (108.2 mg, 0.659 mmol) was coupled with 2-bromo-5-methylpyridine (127.2 mg, 0.725 mmol). Purification by flash chromatography (30 % ethyl acetate/70 % hexanes) gave compounds **1h** as yellow solids (120.5 mg, 72 %).

Major (±)-[1S,2S] : IR (neat, cm^{-1}) 3244 (br), 2928 (s), 2855 (m), 2223 (w), 1642 (m), 1559 (m), 1482 (s), 1141 (m), 977 (m); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.35 (s, 1H), 7.39 (d, J=8.9 Hz, 1H), 7.25 (d, J=7.2 Hz, 1H), 4.99 (dd, J=1.6, 1.6 Hz, 1H), 4.87 (s, 1H), 2.39 (d, J=1.3 Hz, 1H), 2.33-2.29 (m, 1H), 2.32 (s, 3H), 2.25-2.20 (m, 1H), 2.00 (s, 3H), 1.81-1.45 (m, 6H), 1.32-1.20 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 150.5 (CH), 148.3 (C_4), 140.4 (C_4), 136.7 (CH), 132.8 (C_4), 126.9 (CH), 112.7 (CH_2), 93.3 (C_4), 82.9 (C_4), 67.5 (C_4), 53.0 (CH), 39.4 (CH_2), 26.8 (CH_2), 25.9(CH_2), 25.9 (CH_3), 20.6 (CH_2), 18.6 (CH_3); HRMS (EI) m/z calcd for $C_{17}H_{21}NO$ [M^+] 255.1623, found 255.1596; mp = 123.9-128.8 °C.

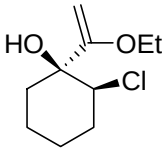
Minor (±)-[1S,2R] : IR (neat, cm^{-1}) 3290 (br), 2932 (s), 2857 (m), 2223 (w), 1642 (m), 1595 (m), 1561 (m), 1478 (s), 1067 (m); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.38 (s, 1H), 7.41 (dd, J=8.0, 2.5 Hz, 1H), 7.27 (d, J=8.0 Hz, 1H), 4.99 (dd, J=1.6, 1.6 Hz, 1H), 4.95 (s, 1H), 2.88 (s, 1H), 2.30 (s, 3H), 2.22-2.18 (m, 2H), 1.92 (s, 3H), 1.78-1.74 (m, 5H), 1.61-1.52 (m, 1H), 1.27-1.23 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 150.7 (CH), 145.7 (C_4), 140.5 (C_4), 136.8 (CH), 132.8 (C_4), 126.7 (CH), 115.3 (CH_2), 90.9 (C_4), 85.9 (C_4), 70.5 (C_4), 56.6 (CH), 40.6 (CH_2), 28.7 (CH_2), 25.8 (CH_2), 24.1 (CH_2), 21.1 (CH_3), 18.6 (CH_3); HRMS (EI) m/z calcd for $C_{17}H_{21}NO$ [M^+] 255.1623, found 255.1603; mp = 102.6-106.1 °C.

Preparation of substrate 1i :



D **1i**

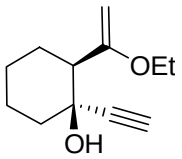
(±)-[1S,2S]-2-Chloro-1-(1-ethoxy-vinyl)-cyclohexanol (D)



To a -78 °C solution of ethyl vinyl ether (3 mL, 31.5 mmol) in THF (1.5 mL) was added t-BuLi (5.50 mL, 8.76 mmol) dropwise. The solution was protected from light and stirred for 30 min. at -78 °C. The resulting black solution was warmed to 0 °C for 10 min. then cooled back to -78 °C. After cannulation of 2-chlorocyclohexanone (0.250 mL, 2.19 mmol) in THF (15 mL), the mixture was stirred at -78 °C and followed to completion by TLC (45 min.). The reaction mixture was quenched with isopropanol followed by water. The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (5% ethyl acetate in hexanes with triethylamine) afforded **D** as a yellow oil (370.4 mg, 83

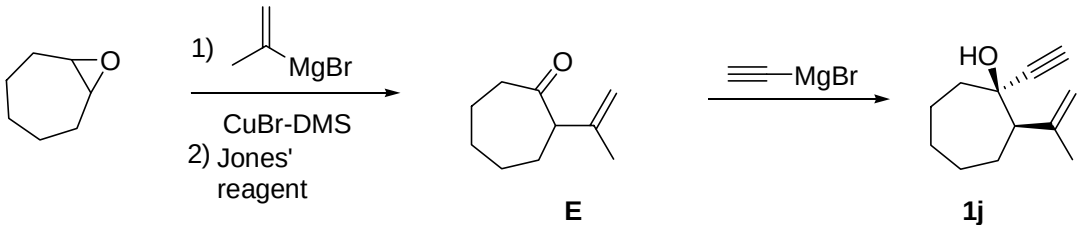
%). IR (neat, cm^{-1}) 3561 (br), 2978 (m), 2940 (s), 2863 (w), 1623 (m), 1446 (m), 1286 (m), 1248 (s), 1139 (s), 1074 (s); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.41-4.35 (m, 2H), 3.96 (d, J=2.4 Hz, 1H), 3.71 (q, J=7.0 Hz, 2H), 2.31 (s, 1H), 1.99-1.83 (m, 2H), 1.76-1.53 (m, 4H), 1.46-1.31 (m, 2H), 1.25 (t, J=7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.7 (C_4), 80.3 (CH_2), 75.1 (C_4), 65.0 (CH), 63.4 (CH_2), 35.9 (CH_2), 32.0 (CH_2), 26.1 (CH_2), 20.4 (CH_2), 14.5 (CH_3); HRMS (EI) m/z calcd for $C_{10}H_{17}O_2Cl$ [M^+] 204.0917, MS is unavailable because of compound volatility.

(±)-[1S,2S]-2-(1-Ethoxy-vinyl)-1-ethynyl-cyclohexanol (1i)



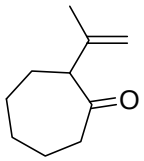
To a solution of ketone **D** (0.370 g, 1.81 mmol) in THF (7.1 mL) was added dropwise ethynylmagnesium bromide (10.9 mL, 5.43 mmol). The reaction was heated to reflux and stirred until completion by TLC (5 hours), at which point it was cooled to room temperature and quenched with NH_4Cl (sat. aq.). The mixture was extracted with diethyl ether (3x) and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (10 % ethyl acetate in hexanes with triethylamine) afforded **1i** as a yellow oil (145.1 mg, 41 %). IR (neat, cm^{-1}) 3531 (s), 3292 (m), 2940 (s), 2856 (m), 1659 (m), 1617 (m), 1292 (s), 1072 (s), 973 (s); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.95 (s, 2H), 3.86 (d, J=2.2 Hz, 1H), 3.82-3.65 (m, 2H), 2.35 (s, 1H), 2.25 (dd, J=12.8, 3.5 Hz, 1H), 2.08-1.99 (m, 1H), 1.94-1.79 (m, 1H), 1.74-1.38 (m, 6H), 1.26 (t, J=7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 163.9 (C_4), 88.2 (C_4), 84.0 (CH_2), 70.6 (CH), 68.5 (C_4), 63.4 (CH_2), 52.1 (CH), 38.8 (CH_2), 26.1 (CH_2), 25.4 (CH_3), 20.3 (CH_2), 14.5 (CH_3); HRMS (EI) m/z calcd for $C_{12}H_{18}O_2$ [M^+] 194.1307, found 194.1282.

Preparation of substrate 1j :



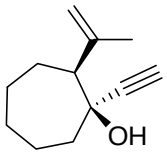
E **1j**

2-Isopropenyl-cycloheptanone (E)



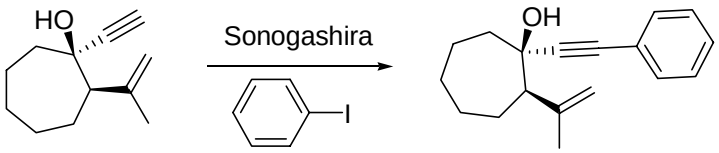
A dry round bottom flask was charged with CuBr·DMS (0.428 g, 2.08 mmoles) and THF (54 mL). The solution was cooled to -30 °C, followed by the addition of isopropenylmagnesium bromide (54.1 mL, 27.0 mmoles). The mixture was stirred for 20 minutes, at which point cycloheptene oxide[6] (2.33 g, 20.8 mmoles) was added and the solution was stirred to room temperature. The reaction was followed by TLC and quenched with NH_4Cl (sat. aq.) upon completion. The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The residue was re-dissolved in diethyl ether (30 mL) and Jones' reagent (11.7 mL, 31.2 mmoles) was slowly added at 0 °C. The reaction was allowed to reach room temperature. Upon completion, as observed by TLC analysis, the reaction was quenched with NH_4Cl (sat. aq.). The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (10% ethyl acetate in hexanes) afforded **E** (1.14 g, 36 %) as a yellow oil. IR (neat, cm^{-1}) 3084 (w), 2930 (s), 2856 (m), 1703 (s), 1642 (m), 1454 (m), 889 (m); ^1H NMR ($CDCl_3$, 300 MHz) δ 4.83 (dd, J=1.4, 1.4 Hz, 1H), 4.72 (s, 1H), 3.00 (dd, J=11.4, 3.5 Hz, 1H), 2.60-2.51 (m, 1H), 2.41-2.33 (m, 1H), 1.93-1.83 (m, 4H), 1.68 (s, 3H), 1.65-1.57 (m, 1H), 1.54-1.38 (m, 1H), 1.37-1.24 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 214.1 (C_4), 144.5 (C_4), 112.1 (CH_2), 60.4 (CH), 42.4 (CH_2), 30.2 (CH_2), 29.6 (CH_2), 28.4 (CH_2), 25.5 (CH_2), 21.9 (CH_3); HRMS (EI) m/z calcd for $C_{10}H_{16}O$ [M^+] 152.1201, found 152.1188.

(±)-[1S,2S]-1-Ethynyl-2-isopropenyl-cycloheptanol (1j)



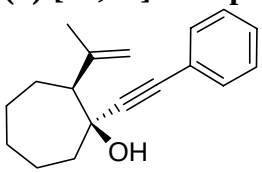
To a solution of ketone **E** (0.565 g, 3.71 mmol) in THF (6 mL) at 0 °C was added dropwise ethynylmagnesium bromide (18.6 mL, 9.28 mmol). The reaction was warmed to room temperature and stirred until completion by TLC, at which point it was quenched with NH_4Cl (sat. aq.). The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (5 % ethyl acetate in hexanes) afforded the alcohol **1j** as a yellow oil (0.524 g, 79 %). IR (neat, cm^{-1}) 3533 (br), 3307 (m), 3073 (w), 2931(s), 2862 (m), 1641 (w), 1444 (m), 1065 (w); ^1H NMR ($CDCl_3$, 300 MHz) δ 5.00 (dd, J=1.5, 1.5 Hz, 1H), 4.78 (s, 1H), 2.42-2.37 (m, 3H), 2.19 (dd, J=14.5, 9.5 Hz, 1H), 1.95 (t, J=0.5 Hz, 3H), 1.89-1.69 (m, 5H), 1.52-1.30 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 149.7 (C_4), 113.9 (CH_2), 90.0 (C_4), 70.7 (CH), 70.0 (C_4), 56.8 (CH), 42.1 (CH_2), 29.5 (CH_2), 29.3 (CH_2), 28.7 (CH_2), 25.5 (CH_3), 21.5 (CH_2); HRMS (EI) m/z calcd for $C_{12}H_{18}O$ [M^+] 178.1358, found 178.1349.

Preparation of substrate 1k:



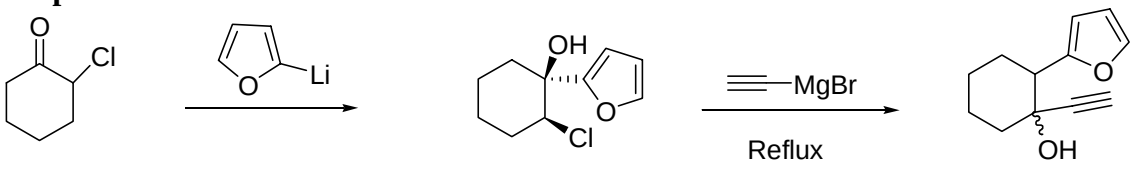
1j **1k**

(±)-[1S,2S]-2-Isopropenyl-1-phenylethynyl-cycloheptanol (1k)



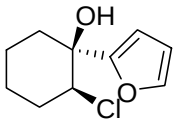
Using the general procedure for Sonogashira, alcohol **1j** (109.2 mg, 0.613 mmol) was coupled with iodobenzene (0.075 mL, 0.674 mmol). Purification by flash chromatography (5 % ethyl acetate/95 % hexanes) gave compound **1k** as a yellow oil (120.5 mg, 77 %). IR (neat, cm^{-1}) 3526 (br), 3077 (w), 2927 (s), 2857 (m), 1638 (w), 1490 (m), 1443 (m), 755 (s), 691 (m); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.39-7.36 (m, 2H), 7.28-7.26 (m, 3H), 5.05 (s, 1H), 4.84 (s, 1H), 2.52 (d, J=10.5 Hz, 1H), 2.51 (s, 1H), 2.30 (dd, J=14.3, 9.8 Hz, 1H), 2.03 (s, 3H), 1.99-1.72 (m, 5H), 1.58-1.37 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 149.9 (C_4), 131.6 (CHx2), 128.3 (CHx2), 128.2 (CH), 123.1 (C_4), 113.9 (CH_2), 95.4 (C_4), 82.6 (C_4), 70.4 (C_4), 57.1 (CH), 42.1 (CH_2), 29.5 (CH_2), 29.3 (CH_2), 28.8 (CH_2), 25.6 (CH_3), 21.7 (CH_2); HRMS (EI) m/z calcd for $C_{18}H_{22}O$ [M^+] 254.1671; found 254.1686.

Preparation of substrate 9 :



F **9**

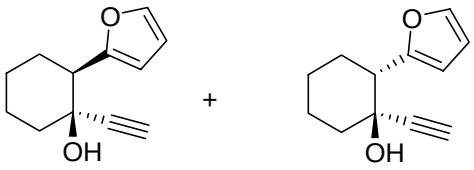
(±)-[1S,2S]-2-Chloro-1-furan-2-yl-cyclohexanol (F)



To a 0 °C solution of furan (0.287 mL, 3.95 mmol) in THF (17 mL) was added n-BuLi (2.63 mL, 4.21 mmol) dropwise. The solution was stirred for 90 min. then cooled to -78 °C. After cannulation of 2-chlorocyclohexanone (0.300 mL, 2.63 mmol) in THF (5 mL), the mixture was stirred at -78 °C and followed to completion by TLC (45 min.). The reaction mixture was quenched with a saturated solution of ammonium chloride. The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (10 % ethyl acetate in hexanes) afforded **F** as a yellow oil (439.8 mg, 83 %). IR (neat, cm^{-1}) 3545 (br), 2941 (s), 2863 (m), 1505 (m), 1447 (m), 1347 (w), 1293 (m), 1155 (s), 986 (s), 739 (s); ^1H NMR ($CDCl_3$, 300 MHz) 7.33 (dd, J=0.9, 0.8 Hz, 1H), 6.32-6.28 (m, 2H), 4.46 (dd,

J=8.0, 6.2 Hz, 1H), 2.65-2.61 (m, 1H), 2.07-2.00 (m, 3H), 1.86-1.64 (m, 3H), 1.52-1.31 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 158.5 (C_4), 141.6 (CH), 110.3 (CH), 105.6 (CH), 73.4 (C_4), 66.7 (CH), 37.2 (CH_2), 32.2 (CH_2), 25.6 (CH_2), 20.6 (CH_2); HRMS (EI) m/z calcd for $C_{10}H_{13}O_2Cl$ [M^+] 200.0604, found 200.0607.

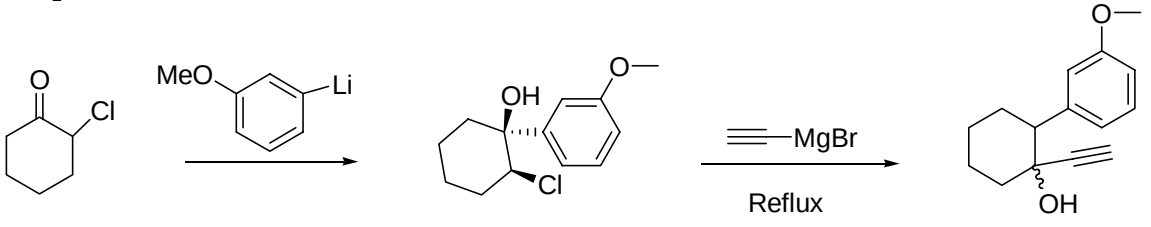
1-Ethynyl-2-furan-2-yl-cyclohexanol (9)



[1S,2S] [1S, 2R]

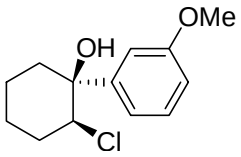
To a solution of ketone **F** (0.439 g, 2.19 mmol) in THF (8.6 mL) was added dropwise ethynylmagnesium bromide (13.1 mL, 6.57 mmol). The reaction was heated to reflux and stirred until completion by TLC (3 hours), at which point it was cooled to room temperature and quenched with NH_4Cl (sat. aq.). The mixture was extracted with diethyl ether (3x) and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (10 % ethyl acetate in hexanes) afforded both diastereoisomers of **9** (54:46) as yellow foams (353.7 mg, 85 %).
Major (±)-[1S,2S] : IR (neat, cm^{-1}) 3558 (br), 3292 (s), 2938 (s), 2861 (m), 1590 (w), 1503 (m), 1447 (m), 972 (s); ^{1}H NMR ($CDCl_3$, 300 MHz) 7.35 (s, 1H), 6.33 (s, 1H), 6.18 (d, J=3.0Hz, 1H), 2.97 (dd, J=12.3, 3.8 Hz, 1H), 2.39 (s, 1H), 2.35 (s, 1H), 2.16-2.09 (m, 1H), 2.02-1.85 (m, 1H), 1.79-1.51 (m, 5H), 1.39-1.23 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.0 (C_4), 141.7 (CH), 110.3 (CH), 107.1 (CH), 87.7 (C_4), 71.7 (CH), 68.3 (C_4), 46.6 (CH), 38.8 (CH_2), 26.5 (CH_2), 25.2 (CH_2), 20.5 (CH_2); HRMS (EI) m/z calcd for $C_{12}H_{14}O_2$ [M^+] 190.0994, found 190.0976.
Minor (±)-[1S,2R] : IR (neat, cm^{-1}) 3557 (br), 3291 (s), 2937 (s), 2862 (m), 1589 (w), 1503 (m), 1448 (m), 1151 (m), 1058 (s); ^{1}H NMR ($CDCl_3$, 300 MHz) 7.35 (s, 1H), 6.33 (s, 1H), 6.19 (d, J=3.2Hz, 1H), 3.05 (s, 1H), 2.77 (dd, J=12.5, 3.6 Hz, 1H), 2.40 (s, 1H), 2.17-2.03 (m, 1H), 1.95-1.84 (m, 1H), 1.80-1.53 (m, 5H), 1.40-1.23 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.0 (C_4), 141.7 (CH), 110.3 (CH), 106.6 (CH), 84.6 (C_4), 74.5 (CH), 72.1 (C_4), 48.2 (CH), 39.4 (CH_2), 28.0 (CH_2), 25.3 (CH_2), 23.6 (CH_2); HRMS (EI) m/z calcd for $C_{12}H_{14}O_2$ [M^+] 190.0994, found 190.0981.

Preparation of substrate 11 :



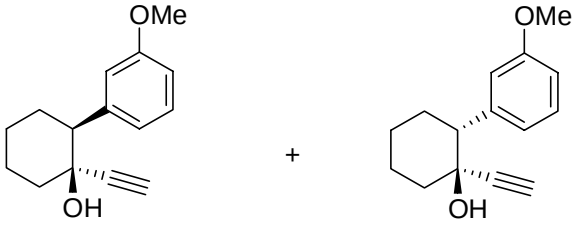
G **11**

(±)-[1S,2S]-2-Chloro-1-(3-methoxy-phenyl)-cyclohexanol (G)



To a -78 °C solution of 3-bromoanisole (0.984 mL, 5.26 mmol) in THF (17 mL) was added n-BuLi (2.96 mL, 4.73 mmol) dropwise. The white heterogeneous mixture was stirred for 30 min. After cannulation of 2-chlorocyclohexanone (0.300 mL, 2.63 mmol) in THF (5 mL), the mixture was stirred at -78 °C and followed to completion by TLC (45 min.). The reaction mixture was quenched with a saturated solution of ammonium chloride. The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (10 % ethyl acetate in hexanes) afforded **G** as a clearless oil (577.8 mg, 91 %). IR (neat, cm^{-1}) 3542 (br), 2940 (s), 2861 (m), 1721 (w), 1602 (s), 1584 (s), 1485 (s), 1447 (s), 1433 (s), 1285 (s), 1250 (s), 1165 (m), 1067 (s), 985 (s); ^{1}H NMR ($CDCl_3$, 300 MHz) 7.23 (dd, J=7.9, 8.0 Hz, 1H), 7.00 (t, J=2.1 Hz, 1H), 6.95 (d, J=7.7 Hz, 1H), 6.76 (dd, J=8.1, 2.5 Hz, 1H), 4.43 (dd, J=10.1, 6.4 Hz, 1H), 3.77 (s, 3H), 2.47 (d, J=2.4 Hz, 1H), 2.13-2.05 (m, 2H), 1.99-1.93 (m, 1H), 1.85-1.35 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 159.7 (C_4), 148.5 (C_4), 129.4 (CH), 116.8 (CH), 112.1 (CH), 111.0 (CH), 75.8 (C_4), 68.0 (CH), 55.3 (CH_3), 40.5 (CH_2), 32.8 (CH_2), 26.3 (CH_2), 21.0 (CH_2); HRMS (EI) m/z calcd for $C_{13}H_{17}O_2Cl$ [M^+] 240.0917, found 240.0921.

1-Ethynyl-2-(3-methoxy-phenyl)-cyclohexanol (11)



[1S,2S] [1S, 2R]

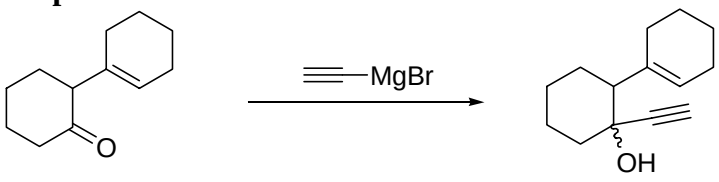
To a solution of ketone **G** (0.414 g, 1.72 mmol) in THF (6.8 mL) was added dropwise ethynylmagnesium bromide (10.3 mL, 5.16 mmol). The reaction was heated to reflux and stirred until completion by TLC (10 hours), at which point it was cooled to room temperature and quenched with NH_4Cl (sat. aq.). The mixture was extracted with diethyl ether (3x) and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (10 % ethyl acetate in hexanes) afforded both diastereoisomers (56:44) of **11** (186.6 mg, 47 %).

Major (±)-[1S,2S] : (Yellow oil) IR (neat, cm^{-1}) 3471 (br), 3285 (m), 2937 (s), 2858 (m), 1600 (s), 1583 (s), 1487 (m), 1260 (s), 1049 (m), 973 (m); ^{1}H NMR ($CDCl_3$, 500 MHz) 7.24-7.21 (m, 1H), 6.92-6.89 (m, 2H), 6.81 (ddd, J=8.2, 2.6, 0.9 Hz, 1H), 3.80 (s, 3H), 2.75 (dd, J=13.0, 3.6 Hz, 1H), 2.35 (s, 1H), 2.22-2.17 (m, 1H), 2.03 (dddd, J=13.2,

13.2, 13.2, 3.7 Hz, 1H), 1.85-1.52 (m, 6H), 1.44-1.32 (m, 1H);^{13}C NMR ($CDCl_3$, 125 MHz) δ 159.3 (C_4), 143.1 (C_4), 129.0 (CH), 121.7 (CH), 115.5 (CH), 112.4 (CH), 88.3 (C_4), 72.8 (CH), 68.9 (C_4), 55.3 (CH_3), 52.5 (CH), 39.9 (CH_2), 26.9 (CH_2), 26.0 (CH_2), 20.8 (CH_2); HRMS (EI) m/z calcd for $C_{15}H_{18}O$ [M^+] 230.1307, found 230.1314.

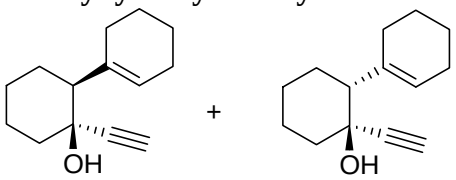
Minor (±)-[1S,2R]: (White solid) IR (neat, cm^{-1}) 3459 (br), 3284 (m), 2934 (s), 1601 (m), 1492 (m), 1257 (m), 1054 (m); ^{1}H NMR ($CDCl_3$, 500 MHz) 7.22 (dd, J=7.9, 7.9 Hz, 1H), 6.95-6.93 (m, 2H), 6.81 (ddd, J=8.2, 2.5, 1.0Hz, 1H), 3.78 (s, 3H), 2.61 (dd, J=13.0, 3.1 Hz, 1H), 2.52 (s, 1H), 2.21 (s, 1H), 2.17-2.13 (m, 1H), 1.97 (dddd, J=13.0, 13.0, 13.0, 3.5 Hz, 1H), 1.83-1.59 (m, 5H), 1.39-1.25 (m, 1H);^{13}C NMR ($CDCl_3$, 125 MHz) δ 159.4 (C_4), 141.9 (C_4), 129.1 (CH), 122.1 (CH), 115.2 (CH), 112.7 (CH), 85.1 (C_4), 75.6 (CH), 66.7 (C_4), 55.3 (CH_3), 54.8 (CH), 40.4 (CH_2), 30.0 (CH_2), 26.1 (CH_2), 24.1 (CH_2); HRMS (EI) m/z calcd for $C_{15}H_{18}O$ [M^+] 230.1307, found 230.1324; mp = 123.4-127.2 °C.

Preparation of substrate 14a :



14a

2-Ethynyl-bicyclohexyl-1'-en-2-ol (14a)



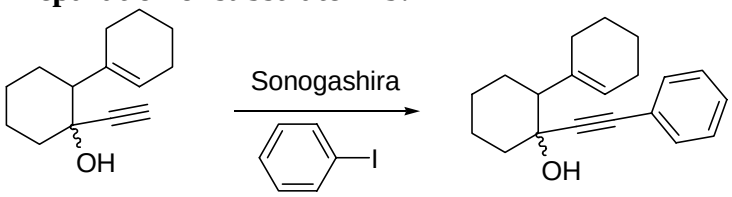
[1S,2S] [1S, 2R]

To a solution of 2-(1-cyclohexenyl)-cyclohexanone (0.500 g, 2.80 mmol) in THF (4 mL) at 0 °C was added dropwise ethynylmagnesium bromide (14 mL, 7.0 mmol). The reaction was warmed to room temperature and stirred until completion by TLC, at which point it was quenched with NH_4Cl (sat. aq.). The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (5% ethyl acetate in hexanes) afforded both diastereoisomers (*60:40*) of **14a** as white solids (486.3 mg, 85 %).

Major (±)-[1S,2S]: IR (neat, cm^{-1}) 3439 (br), 3253 (m), 2939 (w), 1642 (m); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.53 (s, 1H), 2.51-2.40 (m, 1H), 2.34 (s, 1H), 2.25 (s, 1H), 2.13-2.06 (m, 1H), 2.04-1.89 (m, 4H), 1.71-1.32 (m, 10H), 1.26-1.11 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) 140.8 (C_4), 123.8 (CH), 89.4 (C_4), 71.4 (CH), 67.6 (C_4), 53.0 (CH), 39.9 (CH_2), 32.3 (CH_2), 26.8 (CH_2), 26.3 (CH_2), 25.7 (CH_2), 23.4 (CH_2), 22.8 (CH_2), 20.9 (CH_2); HRMS (EI) m/z calcd for $C_{14}H_{20}O$ (M^+) 204.1514, found 204.1498; m.p. 77.5-78.3 °C.

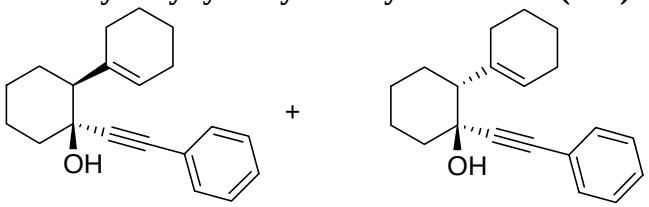
Minor (±)-[1S,2R]: IR (neat, cm^{-1}) 3305 (br), 3224 (s), 2930 (s), 2863 (s), 2098 (m), 1652 (w), 1446 (s), 1328 (m), 1135 (m), 1064 (s), 1033 (s), 952 (w); ^1H NMR ($CDCl_3$, 300 MHz) δ 5.62 (s, 1H), 2.78 (s, 1H), 2.43-2.36 (m, 2H), 2.09-1.88 (m, 5H), 1.77-1.39 (m, 10H), 1.29-1.15 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 137.4 (C_4), 127.0 (CH), 86.5 (C_4), 74.2 (CH), 69.8 (C_4), 57.0 (CH), 40.5 (CH_2), 28.0 (CH_2), 26.3 (CH_2), 25.9 (CH_2), 25.5 (CH_2), 23.9 (CH_2), 23.0 (CH_2), 22.5 (CH_2); HRMS (EI) m/z calcd for $C_{14}H_{20}O$ [M^+] 204.1514, found 204.1532; mp = 83.0-86.7 °C.

Preparation of substrate 14b:



14a **14b**

2-Phenylethynyl-bicyclohexyl-1'-en-2-ol (14b)



[1S,2S] [1S, 2R]

Using the general procedure for Sonogashira, alcohol **14a** (98.8 mg, 0.484 mmol) was coupled with iodobenzene (0.060 mL, 0.532 mmol). Purification by flash chromatography (5 % ethyl acetate/95 % hexanes) gave compounds **14b** as yellow oils (116.1 mg, 86 %).

Major (±)-[1S,2S]: IR (neat, cm^{-1}) 3545 (br), 2931 (s), 2855 (w), 1598 (w), 1489 (m), 1443 (m), 1063 (w), 968 (m); ^1H NMR ($CDCl_3$, 500 MHz) 7.36-7.34 (m, 2H), 7.28-7.26 (m, 3H), 5.59 (s, 1H), 2.59-2.56 (m, 1H), 2.30 (d, J=1.9 Hz, 1H), 2.22-2.18 (m, 1H), 2.13 (dd, J=13.0, 3.6 Hz, 1H), 2.07-2.00 (m, 3H), 1.75-1.43 (m, 10H), 1.28-1.24 (m, 1H);^{13}C NMR ($CDCl_3$, 125 MHz) δ 140.8 (C_4), 131.7 (CHx2), 128.4 (CHx2), 128.2 (CH), 123.5 (CH), 123.3 (C_4), 94.6 (C_4), 83.0 (C_4), 67.9 (C_4), 53.2 (CH), 39.6 (CH_2), 32.1 (CH_2), 26.6 (CH_2), 26.2 (CH_2), 25.6 (CH_2), 23.4 (CH_2), 22.7 (CH_2), 20.8 (CH_2); HRMS (EI) m/z calcd for $C_{20}H_{24}O$ [M^+] 280.1827; found 280.1812.

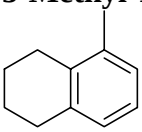
Minor (±)-[1S,2R] (characterized as a mixture of trans and cis): IR (neat, cm^{-1}) 3538 (br), 2931 (s), 2856 (m), 1597 (w), 1489 (m), 1443 (m), 1059 (m), 755 (s), 650 (m); ^1H NMR ($CDCl_3$, 500 MHz) 7.38-7.37 (m, 2H), 7.29-7.26 (m, 3H), 5.68 (s, 1H), 2.83 (s, 1H), 2.49-2.46 (m, 1H), 2.29-2.11 (m, 2H), 2.08-1.95 (m, 3H), 1.82-1.43 (m, 10H), 1.30-1.22 (m, 1H);^{13}C NMR ($CDCl_3$, 125 MHz) δ 137.7 (C_4), 131.6 (CHx2), 128.4 (CHx2), 128.1 (CH), 127.0 (CH), 123.3 (C_4), 91.9 (C_4), 86.0 (C_4), 70.4 (C_4), 57.5 (CH), 40.6

(CH_2), 28.3 (CH_2), 26.4 (CH_2), 26.0 (CH_2), 25.6 (CH_2), 24.2 (CH_2), 23.1 (CH_2), 20.8 (CH_2); HRMS (EI) m/z calcd for $C_{20}H_{24}O$ [M^+] 280.1827, found 280.1807.

General procedure for gold(I)-catalyzed benzannulation of 5-hydroxy-1,4-enynes

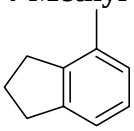
AgOTf (2.5 mol %) and Au(PPh_3)Cl (2.5 mol %) were weighed in the glovebox and transferred to a flame-dried flask with a magnetic stirrer. Then, a solution of the substrate in dichloromethane (0.1 M based on the alcohol) was cannulated. The resulting dark solution was stirred for 15-18 hours until completion by TLC. The reaction mixture was filtered through celite and evaporated *in vacuo*. Purification by flash chromatography yielded the desired benzannulated products.

5-Methyl-1,2,3,4-tetrahydro-naphthalene (2)



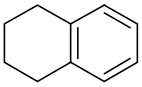
Purification by flash chromatography (5 % ethyl acetate/hexanes) afforded tetrahydronaphthalene **2** (40.2 mg, 84 %) as a yellow oil. Characterization is available through the literature.[7]

4-Methyl-indan (2a)



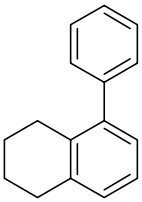
Purification by flash chromatography (5 % ethyl acetate/hexanes) afforded indan **2a** (11.3 mg, 28 %) as a yellow oil. Characterization is available through the literature.[7]

1,2,3,4-Tetrahydro-naphthalene (2b)



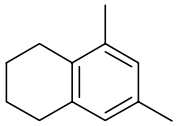
Purification by flash chromatography (2 % ethyl acetate/hexanes) afforded tetrahydronaphthalene **2b** (11.2 mg, 10 %) as a yellow oil. Characterization is available through the literature.[8]

5-Phenyl-1,2,3,4-tetrahydro-naphthalene(2c)



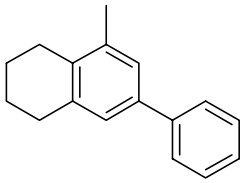
Purification by flash chromatography (5 % ethyl acetate/hexanes) afforded tetrahydronaphthalene **2c** (46.4mg, 84 %) as a yellow oil. Characterization is available through the literature.[8]

5,7-Dimethyl-1,2,3,4-tetrahydro-naphthalene (2d)



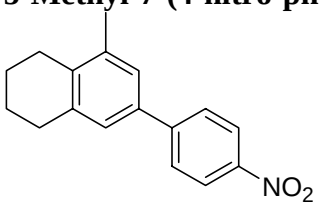
Purification by flash chromatography (5 % ethyl acetate/hexanes) afforded tetrahydronaphthalene **2d** (48.2 mg, 77 %) as a yellow oil. Characterization is available through the literature.[8]

5-Methyl-7-phenyl-1,2,3,4-tetrahydro-naphthalene (2e)



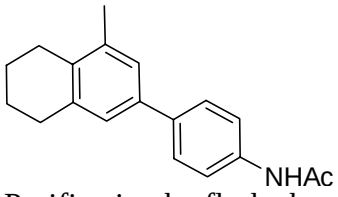
Purification by flash chromatography (5 % ethyl acetate/hexanes) afforded tetrahydronaphthalene **2e** (28.7 mg, 86 %) as a yellow oil.[9] IR (neat, cm^{-1}) 3030 (m), 2927 (s), 1599 (m), 1568 (m), 1473 (s), 1437 (m), 867 (m), 760 (s), 697 (s); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.58-7.55 (m, 2H), 7.42 (d, J=7.3 Hz, 1H), 7.39 (d, J=7.8 Hz, 1H), 7.32-7.17 (m, 3H), 2.83 (dd, J=6.0, 6.0 Hz, 2H), 2.67 (dd, J=6.0, 6.0 Hz, 2H), 2.28 (s, 3H), 1.91-1.76 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 141.5 (C_4), 138.2 (C_4), 137.6 (C_4), 137.2 (C_4), 134.9 (C_4), 128.7 (CHx2), 127.1 (CHx2), 126.9 (CH), 126.0 (CH), 125.7 (CH), 30.4 (CH_2), 26.7 (CH_2), 23.5 (CH_2), 23.0 (CH_2), 19.8 (CH_3); HRMS (EI) m/z calcd for $C_{17}H_{18}$ [M^+] 222.1409, found 222.1397.

5-Methyl-7-(4-nitro-phenyl)-1,2,3,4-tetrahydro-naphthalene (2f)



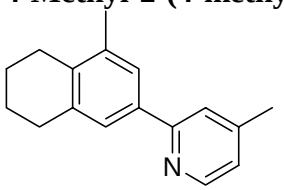
Purification by flash chromatography (5 % ethyl acetate/hexanes) afforded tetrahydronaphthalene **2f** (29.2 mg, 73 %) as a yellow solid. IR (neat, cm^{-1}) 2930 (m), 2858 (w), 1593 (m), 1514 (s), 1341 (s), 1109 (w), 845 (m); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.24 (d, J=8.9 Hz, 2H), 7.70 (d, J=8.9 Hz, 2H), 7.23 (s, 1H), 7.19 (s, 1H), 2.84 (dd, J= 6.2, 6.2 Hz, 2H), 2.66 (dd, J=6.2, 6.2 Hz, 2H), 2.28 (s, 3H), 1.90-1.77 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 148.1 (C_4), 146.9 (C_4), 138.2 (C_4), 137.8 (C_4), 137.1 (C_4), 135.7 (C_4), 127.6 (CHx2), 126.1 (CH), 126.0 (CH), 124.2 (CHx2), 30.4 (CH_2), 26.8 (CH_2), 23.4 (CH_2), 22.9 (CH_2), 19.8 (CH_3); HRMS (EI) m/z calcd for $C_{17}H_{17}NO_2$ [M^+] 267.1259, found 267.1298; mp = 65.7-68.5 °C.

N-[4-(4-Methyl-5,6,7,8-tetrahydro-naphthalen-2-yl)-phenyl]-acetamide (2g)



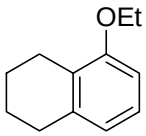
Purification by flash chromatography (60 % ethyl acetate/hexanes) afforded tetrahydronaphthalene **2g** (31.8 mg, 66 %) as a white solid. IR (neat, cm^{-1}) 3251 (m), 2928 (m), 1663 (s), 1605 (m), 1543 (m), 830 (s); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.55 (s, 4H), 7.40 (br, 1H), 7.17 (s, 1H), 7.12 (s, 1H), 2.81 (dd, J=5.9, 5.9Hz, 2H), 2.64 (t, J=6.1, 6.1 Hz, 2H), 2.25 (s, 3H), 2.18 (s, 3H), 1.85-1.75 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 168.5 (C_4), 137.7 (C_4), 137.5 (C_4), 137.5 (C_4), 137.2 (C_4), 136.9 (C_4), 134.9 (C_4), 127.5 (CHx2), 125.8 (CH), 125.4 (CH), 120.2 (CHx2), 30.3 (CH_2), 26.6 (CH_2), 24.8 (CH_3), 23.5 (CH_2), 23.0 (CH_2), 19.8 (CH_3); HRMS (EI) m/z calcd for $C_{19}H_{21}NO$ [M^+] 279.1623, found 279.1621; mp = 137.7-141.1 °C.

4-Methyl-2-(4-methyl-5,6,7,8-tetrahydro-naphthalen-2-yl)-pyridine(2h)



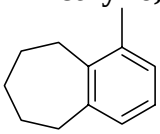
A modified procedure was applied in the case of alcohol **2h** : To a solution of alcohol **1h** (13.5 mg, 0.053 mmol) in dichloromethane (1 mL) was added PTSA (15.1 mg, 0.080 mmol). The mixture was stirred for 2 hours followed by cannulation of a mixture of AgOTf (1.4 mg, 0.0053 mmol) and $Au(PPh_3)Cl$ (2.6 mg, 0.0053 mmol) in dichloromethane (1 mL). The reaction mixture was stirred for 4 days and quenched with a saturated solution of sodium bicarbonate. The mixture was extracted with dichloromethane (3x) and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (30 % ethyl acetate in hexanes) afforded **2h** as white solid (9.4 mg, 75 % yield). IR (neat, cm^{-1}) 2926 (s), 2857 (m), 1598 (w), 1561 (w), 1469 (s), 1375 (w), 1027 (w), 828 (m); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.47 (s, 1H), 7.59-7.55 (m, 2H), 7.51-7.49 (m, 2H), 2.83 (dd, J=6.3, 6.3 Hz, 2H), 2.64 (t, J=6.3, 6.3 Hz, 2H), 2.33 (s,3H), 2.27 (s, 3H), 1.87-1.82 (m, 2H), 1.80-1.74 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 155.3 (C_4), 150.0 (CH), 137.7 (C_4), 137.4 (CH), 137.1 (C_4), 136.5 (C_4), 136.3 (C_4), 131.3 (C_4), 125.4 (CH), 125.2 (CH), 120.0 (CH), 30.4 (CH_2), 26.9 (CH_2), 23.6 (CH_2), 23.1 (CH_2), 19.8 (CH_3), 18.3 (CH_3); HRMS (EI) m/z calcd for $C_{17}H_{19}N$ [M^+] 237.1517, found 237.1497; mp = 88.6-91.7 °C.

5-Ethoxy-1,2,3,4-tetrahydro-naphthalene(2i)



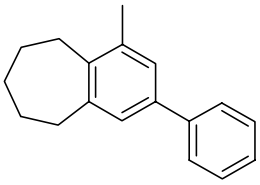
Purification by flash chromatography (10 % ethyl acetate/hexanes) afforded tetrahydronaphthalene **2i** (4.2 mg, 12 %) as a yellow oil.[10] IR (neat, cm^{-1}) 2928 (s), 1586 (m), 1461 (s), 1335 (w), 1252 (s), 1086 (m); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.02 (dd, J=7.9, 7.9 Hz, 1H), 6.65 (d, J=7.5 Hz, 1H), 6.61 (d, J=7.9 Hz, 1H), 3.99 (q, J=7.0 Hz, 2H), 2.73 (dd, J=6.2, 6.2 Hz, 2H), 2.64 (dd, J=5.9, 5.9 Hz, 2H), 1.79-1.71 (m, 4H), 1.39 (t, J=7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 156.6 (C_4), 138.3 (C_4), 125.9 (C_4), 125.4 (CH), 121.0 (CH), 107.6 (CH), 63.2 (CH_2), 29.5 (CH_2), 23.0 (CH_2), 22.7 (CH_2), 22.7 (CH_2), 14.8 (CH_3); HRMS (EI) m/z calcd for $C_{12}H_{16}O$ [M^+] 176.1201, found 176.1208.

1-Methyl-6,7,8,9-tetrahydro-5H-benzocycloheptene (2j)



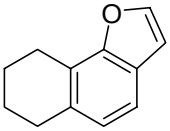
Purification by flash chromatography (5 % ethyl acetate/hexanes) afforded benzannulated product **2j**(16.0 mg, 51 %) as a yellow oil.[11] IR (neat, cm^{-1}) 3066 (w), 3019 (w), 2920 (s), 2849 (s), 1587 (w), 1466 (m), 1445 (m), 957 (w), 771 (m), 743 (m); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.05-6.85 (m, 3H), 2.80-2.75 (m, 4H), 2.29 (s, 3H), 1.83-1.77 (m, 2H), 1.65-1.53 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 144.0 (C_4), 142.0 (C_4), 135.1 (C_4), 128.2 (CH), 127.1 (CH), 125.5 (CH), 36.6 (CH_2), 32.7 (CH_2), 29.9 (CH_2), 28.4 (CH_2), 27.2 (CH_2), 20.8 (CH_3); HRMS (EI) m/z calcd for $C_{12}H_{16}$ [M^+] 160.1252, found 160.1261.

1-Methyl-3-phenyl-6,7,8,9-tetrahydro-5H-benzocycloheptene (2k)



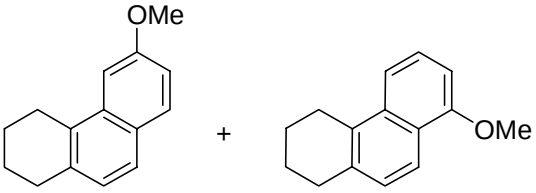
Purification by flash chromatography (5 % ethyl acetate/hexanes) afforded tetrahydronaphthalene **2k** (31.1 mg, 65 %) as a yellow oil. IR (neat, cm^{-1}) 2919 (s), 2850 (m), 1603 (w), 1568 (w), 1474 (m), 1443 (m), 875 (m), 757 (s), 694 (m); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.60-7.57 (m, 2H), 7.43-7.39 (m, 2H), 7.33-7.28 (m, 1H), 7.24 (s, 1H), 7.21 (s, 1H), 2.89-2.84 (m, 4H), 2.39 (s, 3H), 1.90-1.84 (m, 2H), 1.72-1.62 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 144.6 (C_4), 141.4 (C_4), 141.1 (C_4), 138.4 (C_4), 135.6 (C_4), 128.7 (CHx2), 127.1 (CHx2), 126.9 (CHx2), 125.9 (CH), 36.8 (CH_2), 32.7 (CH_2), 29.8 (CH_2), 28.4 (CH_2), 27.3 (CH_2), 20.9 (CH_3); HRMS (EI) m/z calcd for $C_{18}H_{20}$ [M^+] 236.1565, found 236.1579.

6,7,8,9-Tetrahydro-naphtho[1,2-b]furan(10)



Purification by flash chromatography (5 % ethyl acetate/hexanes) afforded tetrahydronaphthalene **10** (18.6 mg, 57 %) as an orange oil.[12] IR (neat, cm^{-1}) 2930 (s), 2857 (m), 1492 (m), 1312 (s), 1129 (m), 1031 (m), 803 (s), 733(s); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.55 (d, J=2.1 Hz, 1H), 7.31 (d, J=7.9 Hz, 1H), 6.96 (d, J=7.9Hz, 1H), 6.69 (d, J=2.1 Hz, 1H), 2.98 (dd, J=11.0, 11.0 Hz, 2H), 2.85 (t, J=10.6, 10.6 Hz, 2H), 1.90-1.75 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 153.8 (C_4), 144.1 (CH), 133.5 (C_4), 124.3 (C_4), 124.2 (CH), 121.2 (C_4), 117.9 (CH), 106.7 (CH), 29.3 (CH_2), 23.4 (CH_2), 22.9 (CH_2), 22.6 (CH_2); HRMS (EI) m/z calcd for $C_{12}H_{12}O$ [M^+] 172.0888, found 172.0887.

6-Methoxy-1,2,3,4-tetrahydro-phenanthrene (12) and 8-Methoxy-1,2,3,4-tetrahydro-phenanthrene(13)



12 **13**

The typical procedure was followed however the reaction mixture was heated to reflux for 18 hours in order for the reaction to go to completion. Purification by flash chromatography (2.5 % ethyl acetate/hexanes) afforded tetrahydrophenanthrenes **12** and **13** (**12**:**13** is 1.5:1) as a yellow oil (24.8 mg, 76 %).[13]

Characterized as a mixture of both isomers :

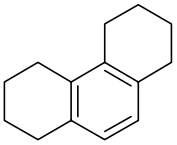
IR (neat, cm^{-1}) 2930 (s), 2857 (m), 1626 (m), 1512 (m), 1391 (m), 1223 (s), 832 (m), 783 (m);

Major (12): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.69 (d, J=8.9 Hz, 1H), 7.53 (d, J=8.6 Hz, 1H), 7.21 (d, J=2.4 Hz, 1H), 7.09 (dd, J=8.9, 2.5 Hz, 1H), 7.06 (d, J=8.3 Hz, 1H), 3.91 (s, 3H), 3.03 (dd, J=6.3, 6.3 Hz, 2H), 2.90 (dd, J=6.0, 6.0 Hz, 2H), 1.99-1.83 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 157.9 (C_4), 135.1 (C_4), 133.8 (C_4), 130.4 (C_4), 130.0 (CH), 127.5 (C_4), 126.1 (CH), 125.5 (CH), 116.8 (CH), 102.1 (CH), 55.4 (CH_3), 30.7 (CH_2), 26.0 (CH_2), 23.5 (CH_2), 23.1 (CH_2);

Minor (13): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.04 (d, J=8.6 Hz, 1H), 7.53 (d, J=8.6 Hz, 1H), 7.38 (dd, J=8.6, 7.7 Hz, 1H), 7.18 (d, J=8.7 Hz, 1H), 6.78 (d, J=7.7 Hz, 1H), 3.98 (s, 3H), 3.08 (t, J=5.7 Hz, 2H), 2.90 (t, J=6.0Hz, 2H), 1.99-1.83 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 156.0 (C_4), 135.0 (C_4), 133.8 (C_4), 131.4 (C_4), 127.6 (CH), 125.9 (CH), 124.1 (C_4), 119.5 (CH), 115.4 (CH), 103.2 (CH), 55.7 (CH_3), 30.6 (CH_2), 26.2 (CH_2), 23.5 (CH_2), 23.0 (CH_2);

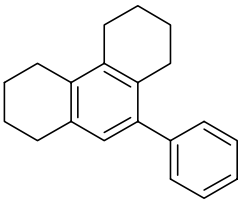
HRMS (EI) m/z calcd for $C_{15}H_{16}O$ [M^+] 212.1201, found 212.1198.

1,2,3,4,5,6,7,8-Octahydro-phenanthrene (15a)



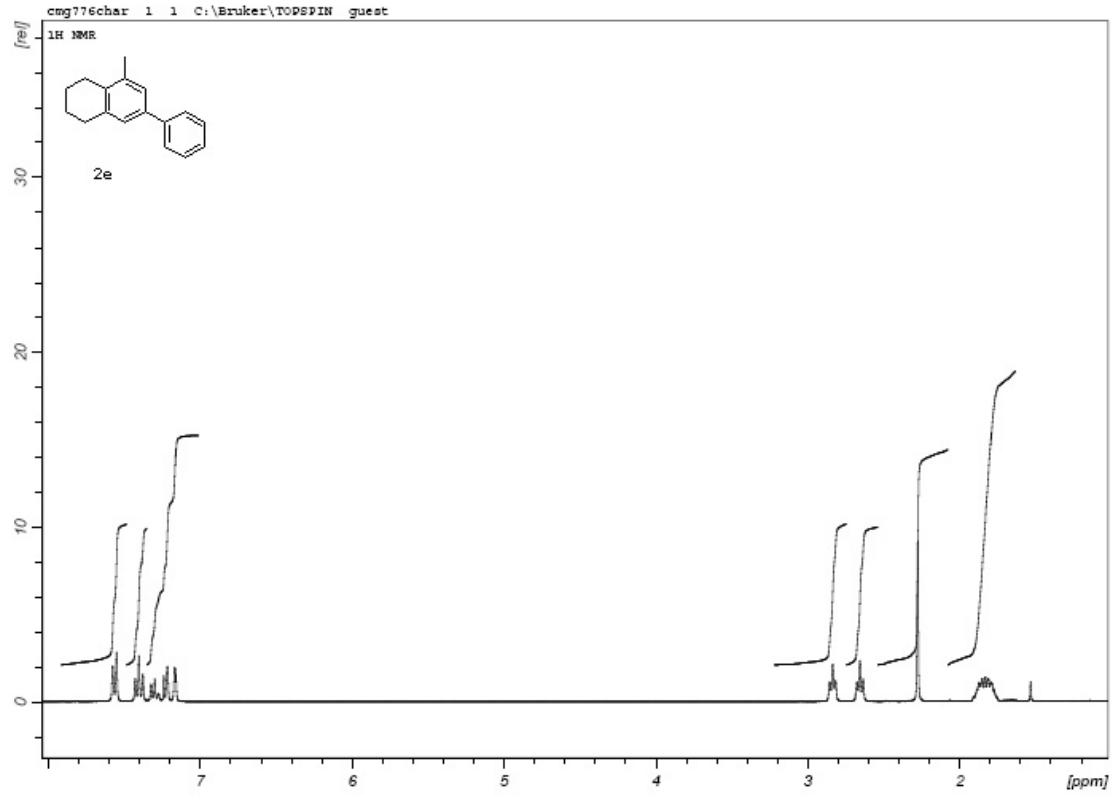
Purification by flash chromatography (5 % ethyl acetate/hexanes) afforded tetrahydronaphthalene **15a** (33.3 mg, 70 %) as a yellow oil. Characterization is available through the literature.[14]

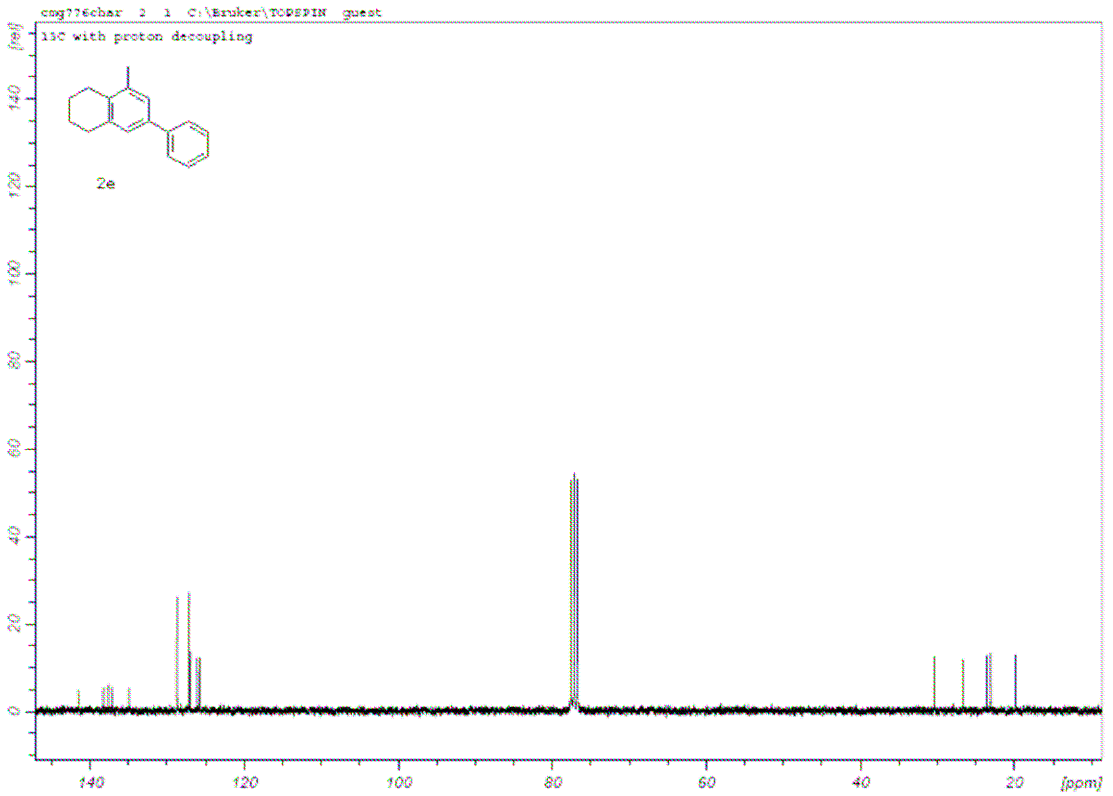
9-Phenyl-1,2,3,4,5,6,7,8-octahydro-phenanthrene (15b)

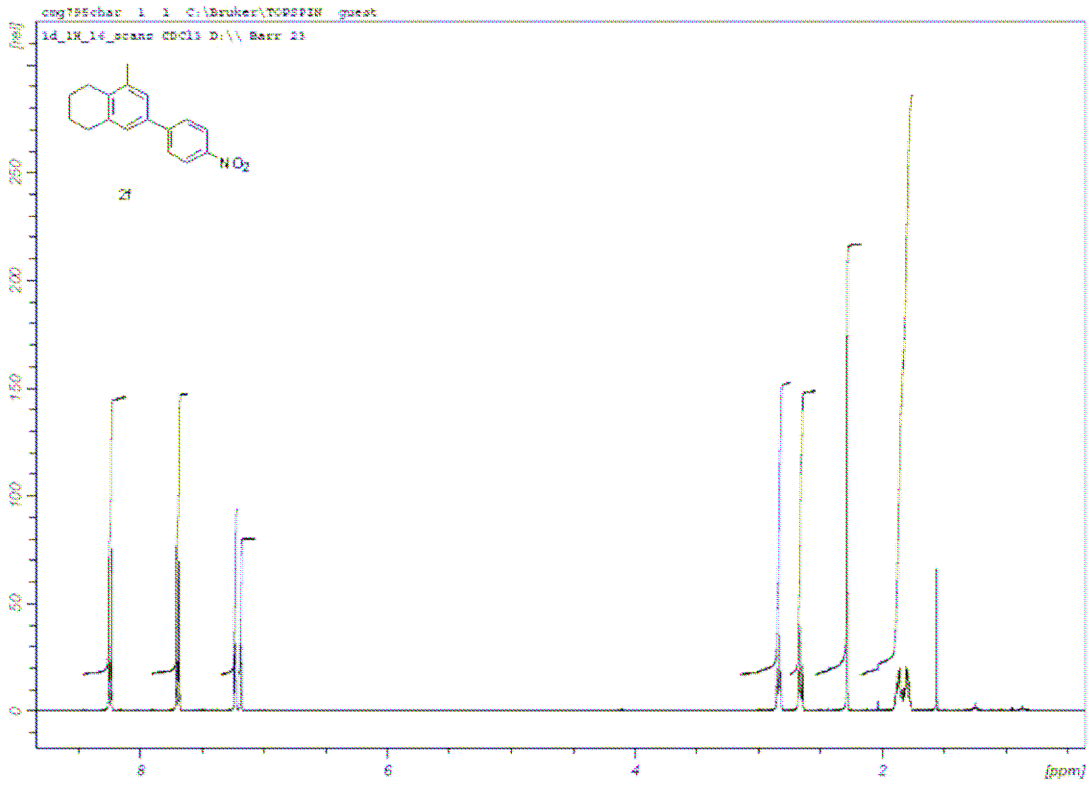


Purification by flash chromatography (5 % ethyl acetate/hexanes) afforded tetrahydronaphthalene **15b** (37.5 mg, 81 %) as a yellow oil.[15] IR (neat, cm^{-1}) 2926 (s), 2857 (m), 1598 (w), 1496 (w), 1441 (w), 695 (m); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.39-7.28 (m, 5H), 6.83 (s, 1H), 2.77 (dd, J=6.2, 6.2 Hz, 2H), 2.65-2.55 (m, 6H), 1.87-1.75 (m, 6H), 1.66-1.61 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 142.4 (C_4), 139.6 (C_4), 135.8 (C_4), 134.8 (C_4), 134.3 (C_4), 132.1 (C_4), 129.5 (CHx2), 128.1 (CH), 128.0 (CHx2), 126.6 (CH), 30.1 (CH_2), 29.0 (CH_2), 27.0 (CH_2), 26.5 (CH_2), 23.7 (CH_2), 23.3 (CH_2), 23.1 (CH_2), 22.9 (CH_2); HRMS (EI) m/z calcd for $C_{20}H_{22}$ [M^+] 262.1721, found 262.1752.

^{1}H and ^{13}C NMR Spectra for compounds **2e-2k**, **10**, **12, 13** and **15b**



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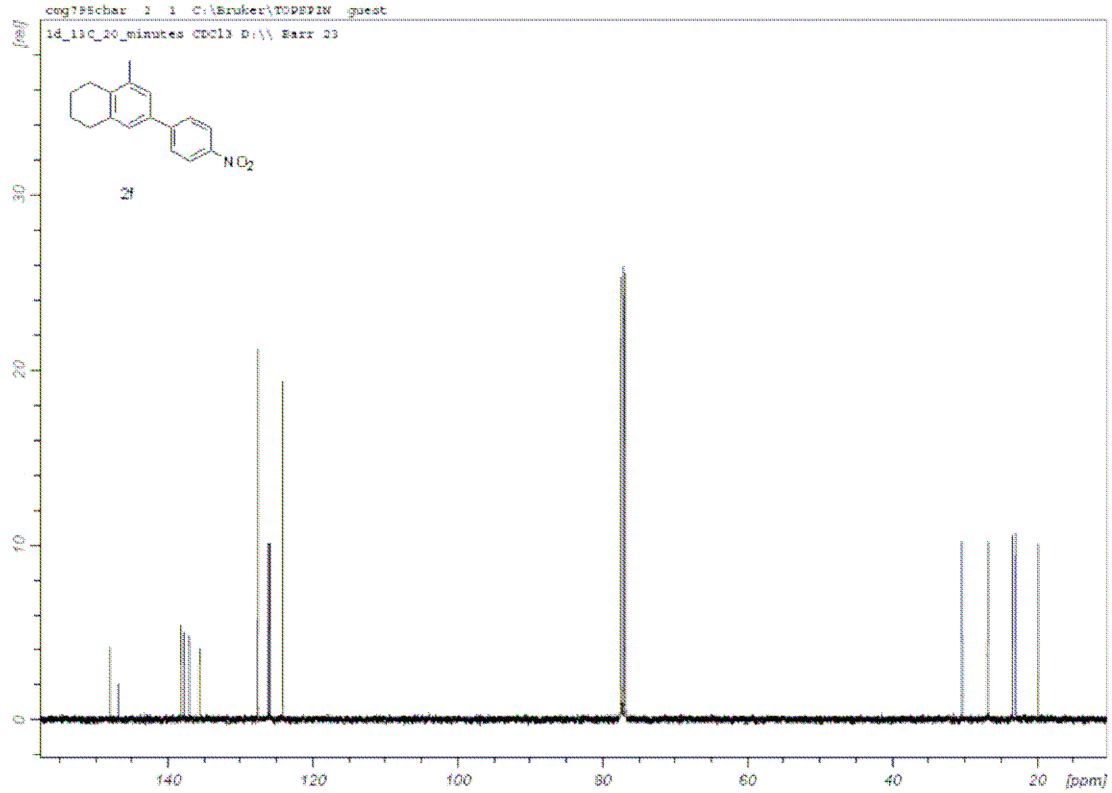
NO2
2f
[rel]
[ppm]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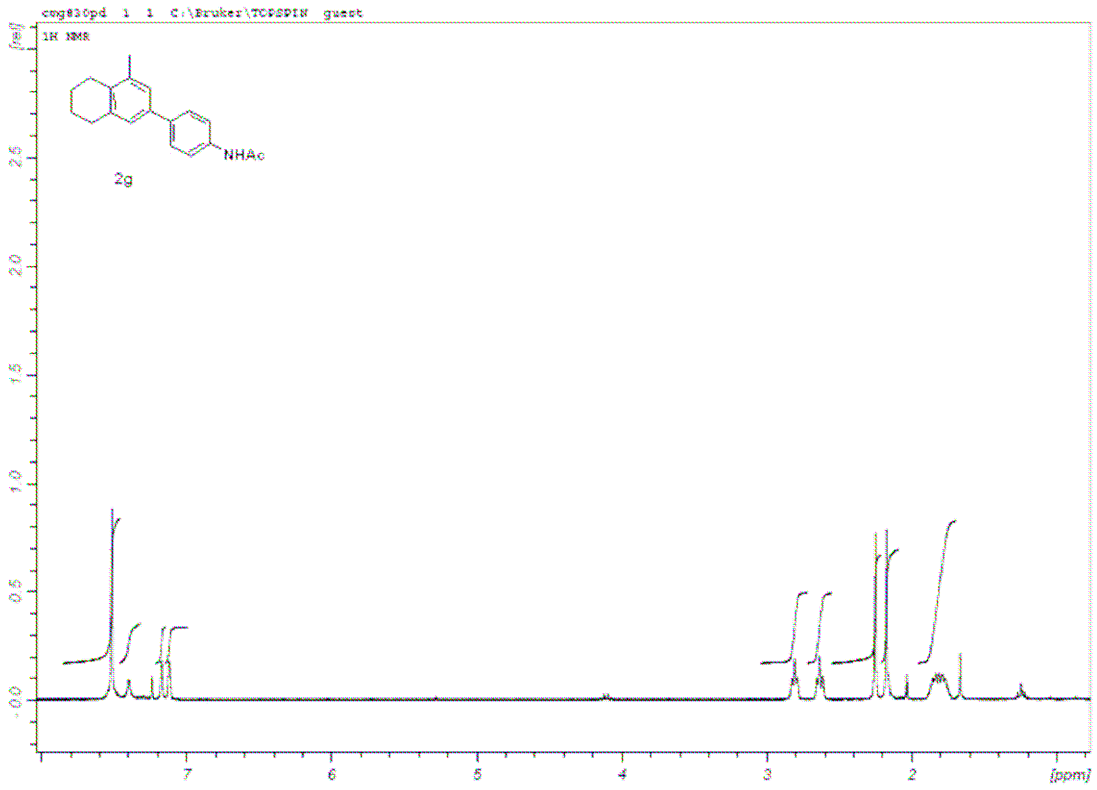
NO2
2f
[rel]
[ppm]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NHAc
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7
6
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4
3
2
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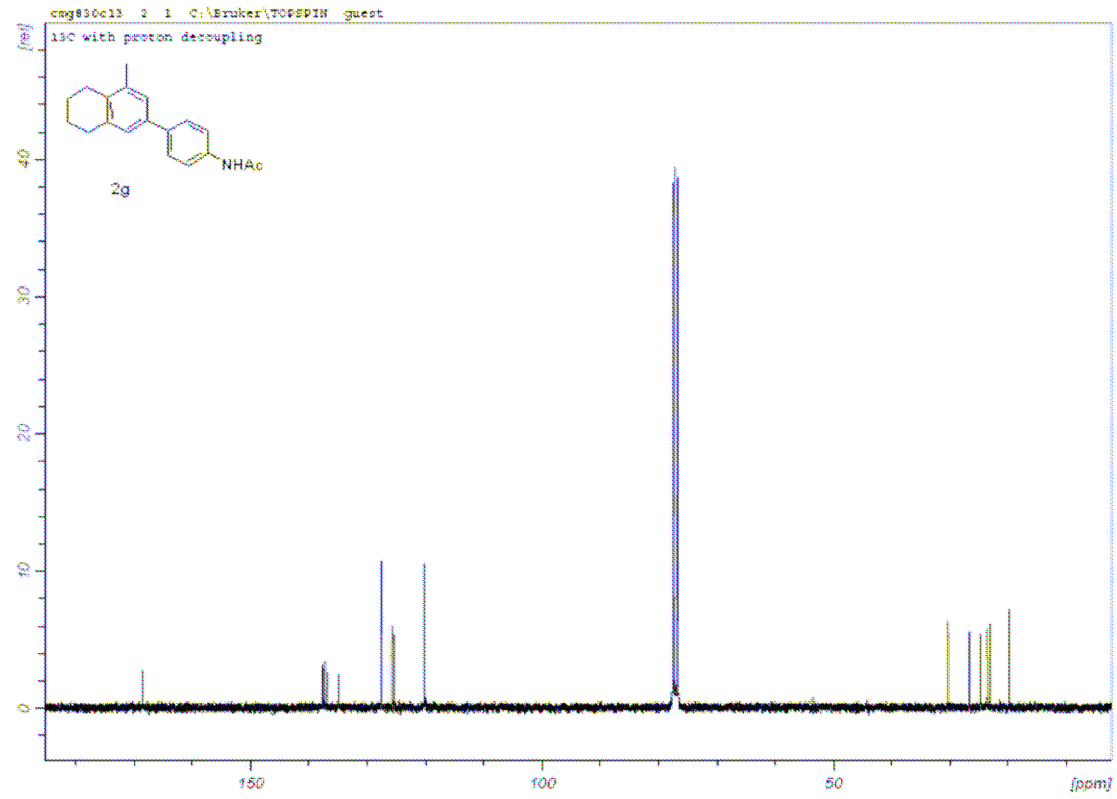
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13C with proton decoupling
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2g
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20
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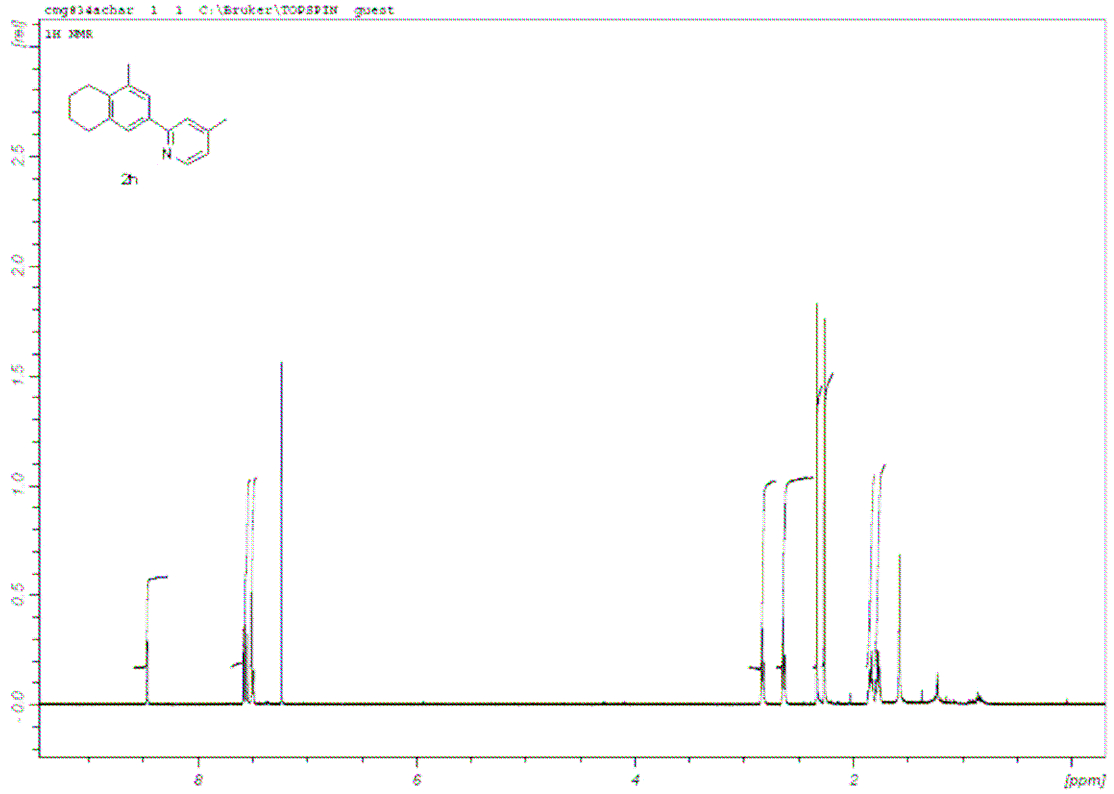
50
[ppm]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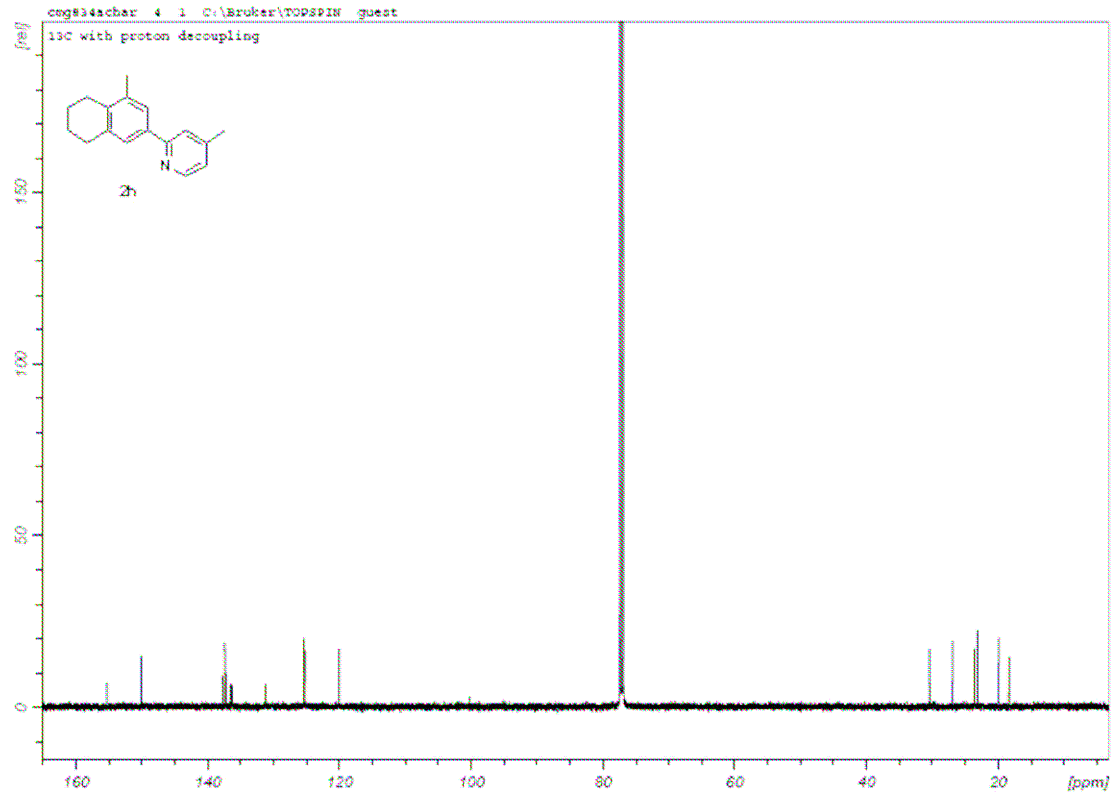
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13C with proton decoupling
2h
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100
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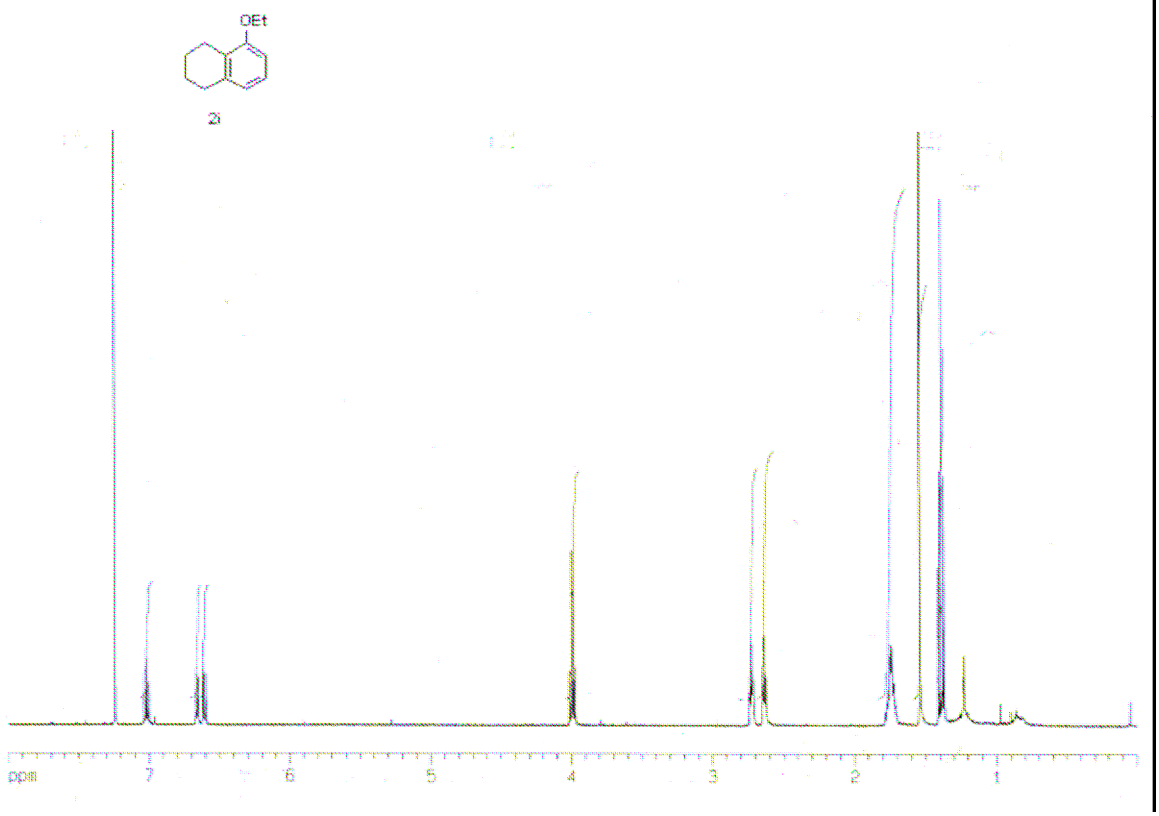
OEt
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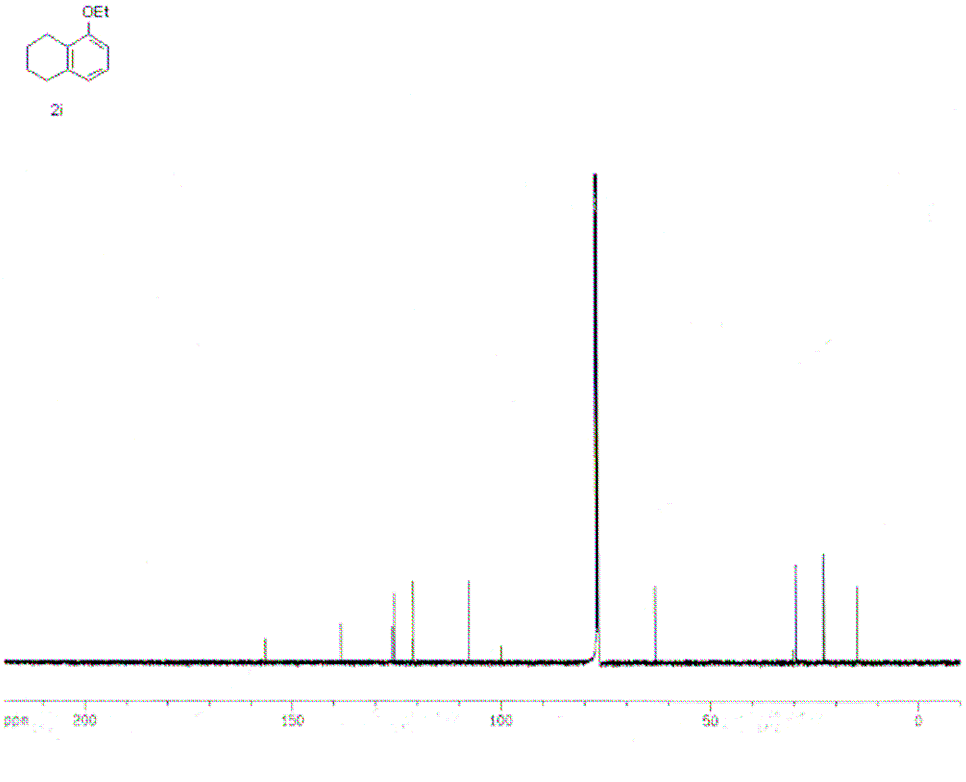
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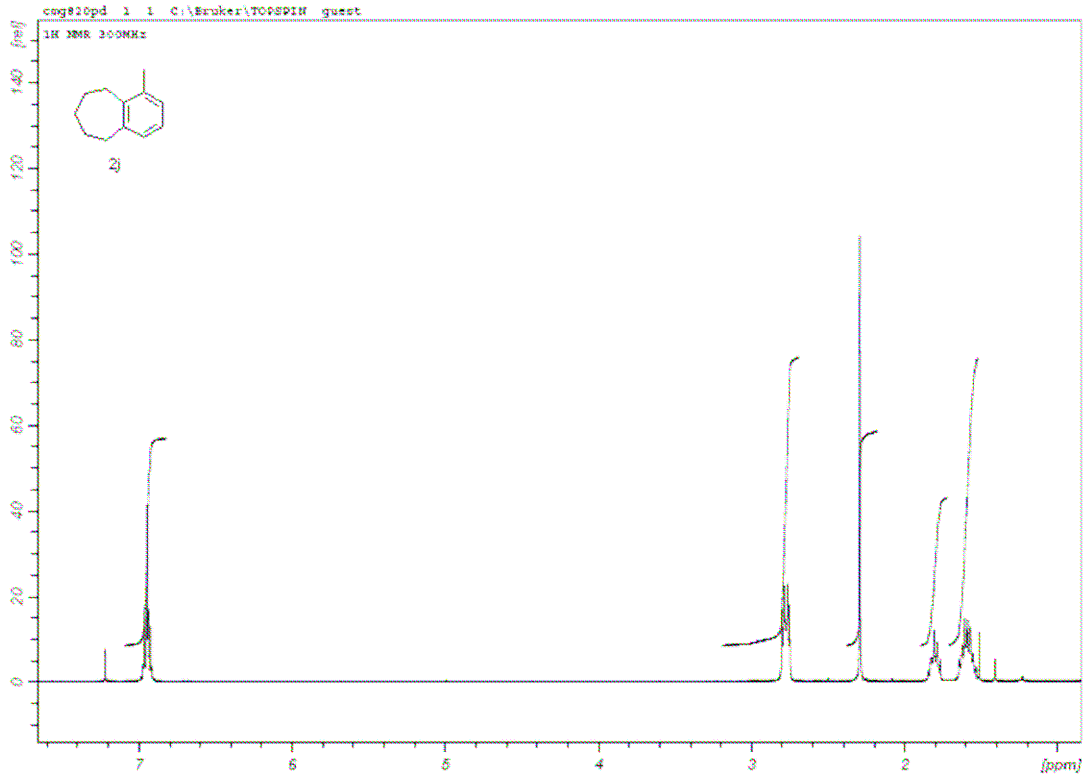
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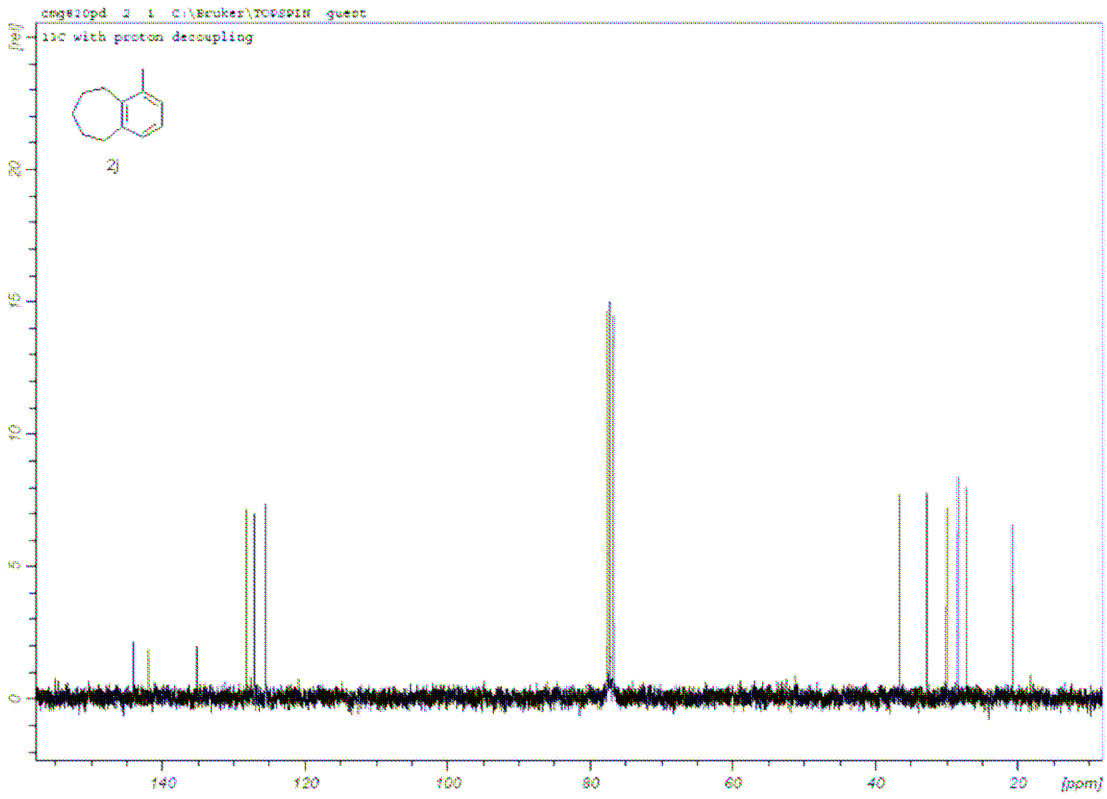
1H NMR 300MHz
2j
[ppm]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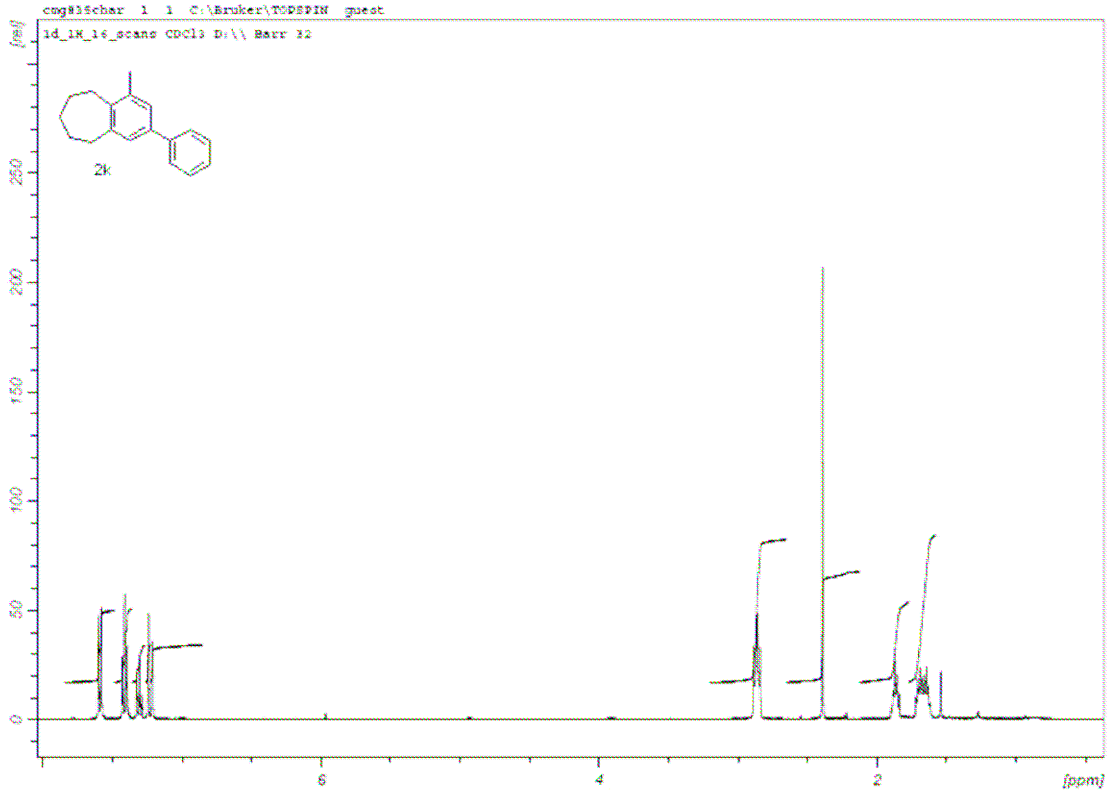
13C with proton decoupling
2j
[ppm]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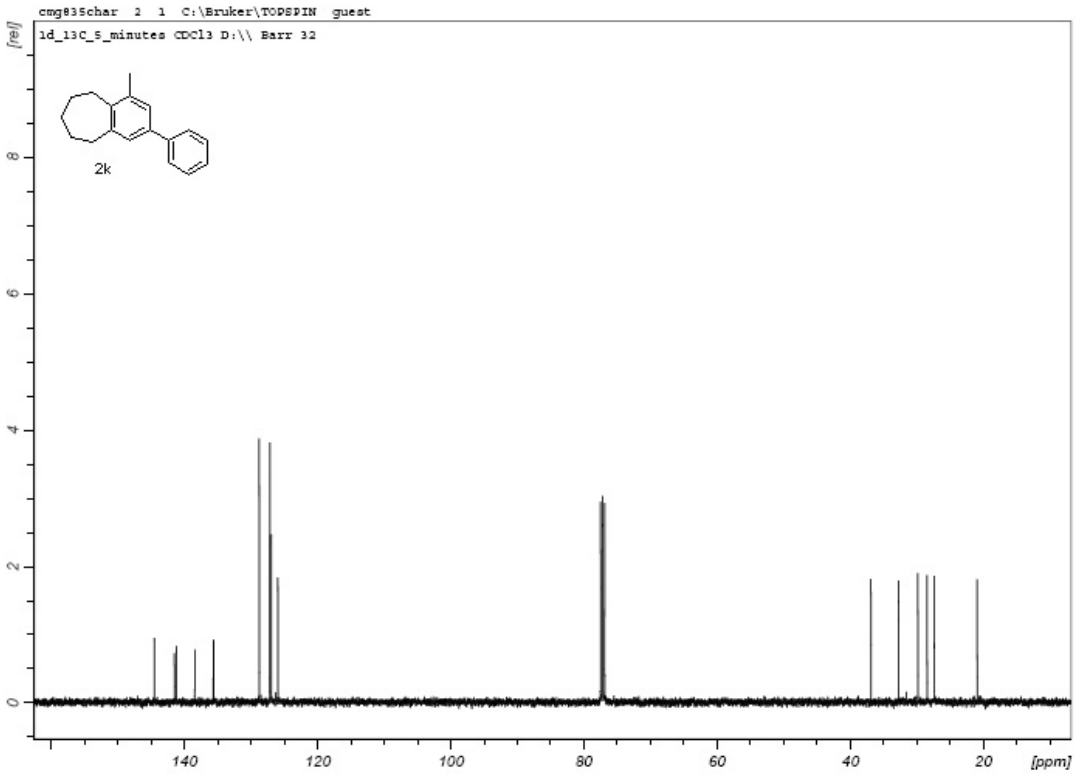
1d_1H_16_scans CDCl3 D:\\ Barr 32
2k
[rel]
250
200
150
100
50
0
6
4
2
[ppm]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2k
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6
4
2
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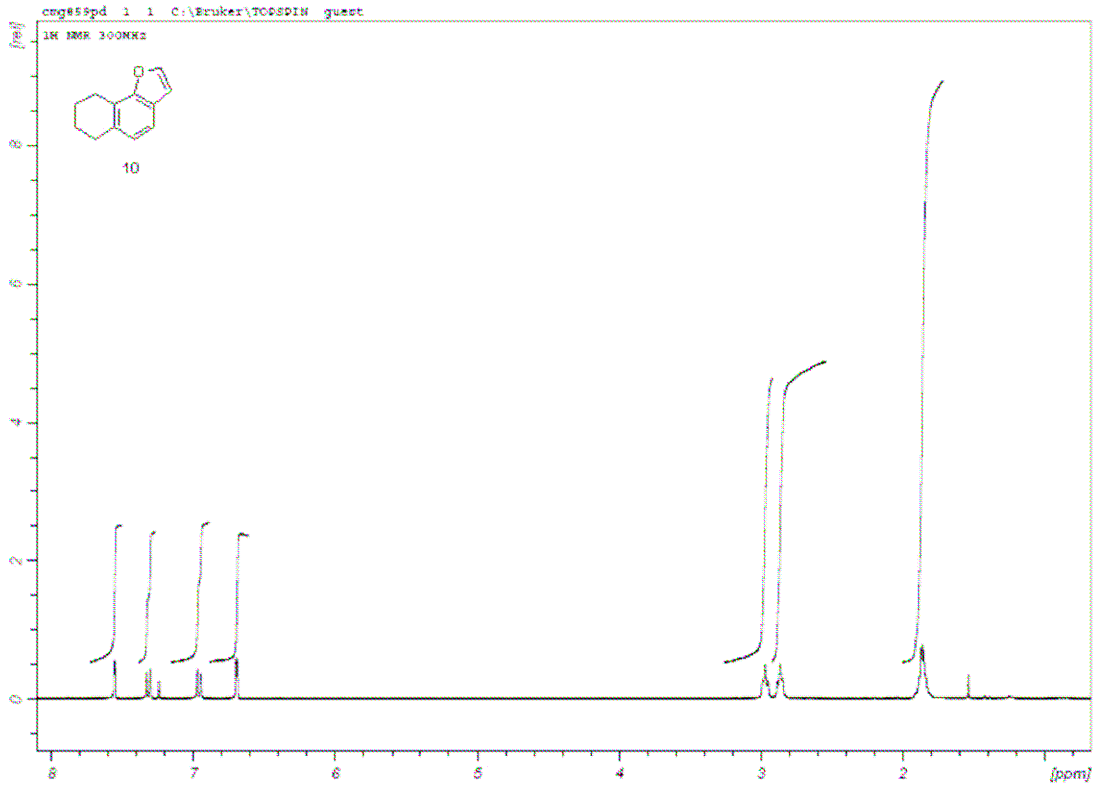
140
120
100
80
60
40
20
[ppm]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10
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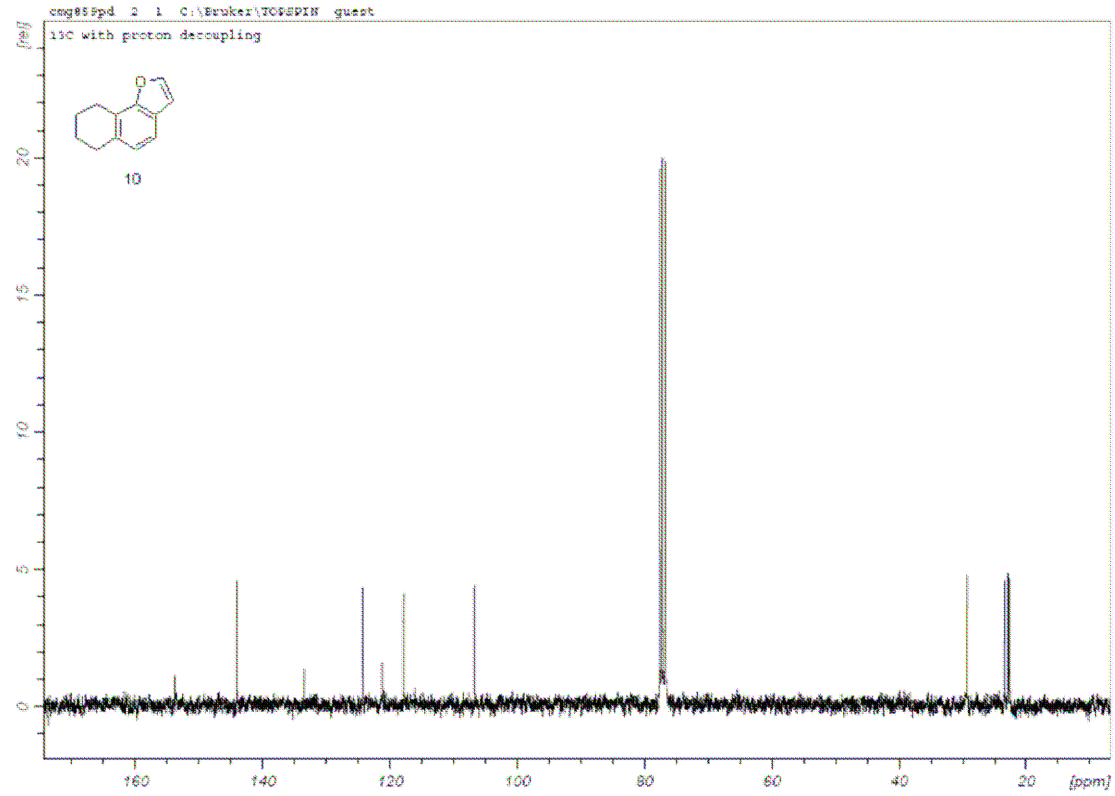
[ppm]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10
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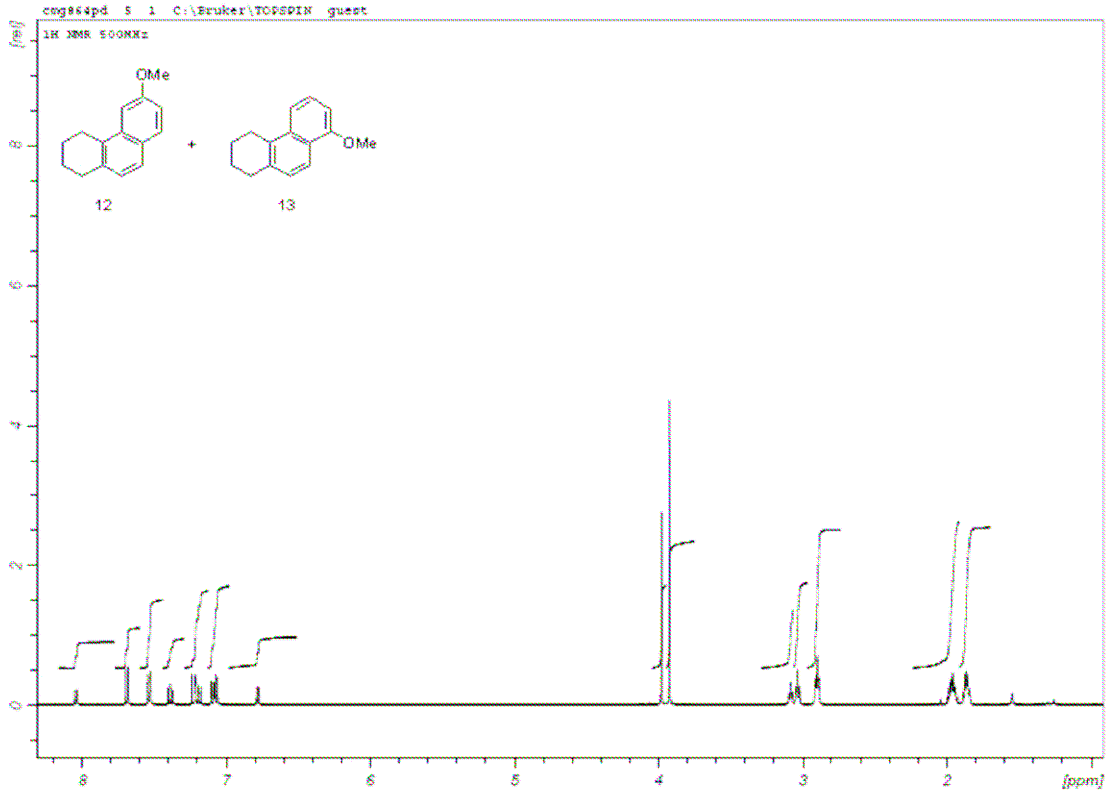
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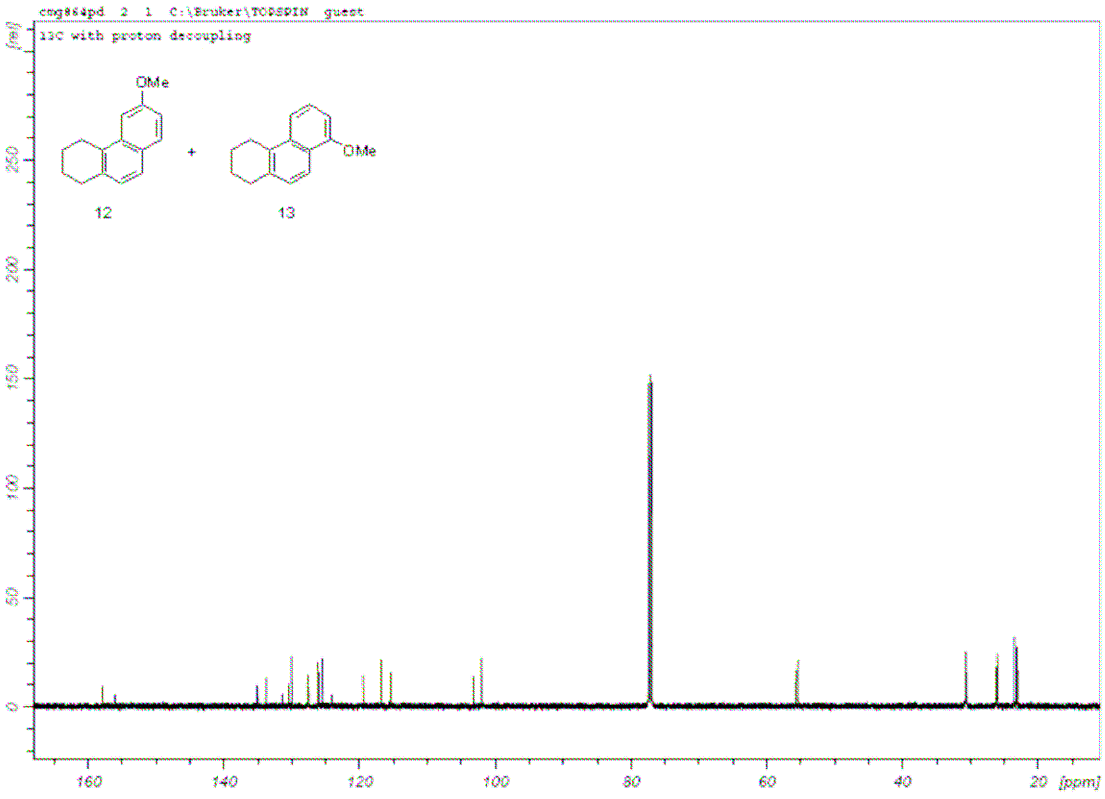
OMe
OMe
12
13
[ppm]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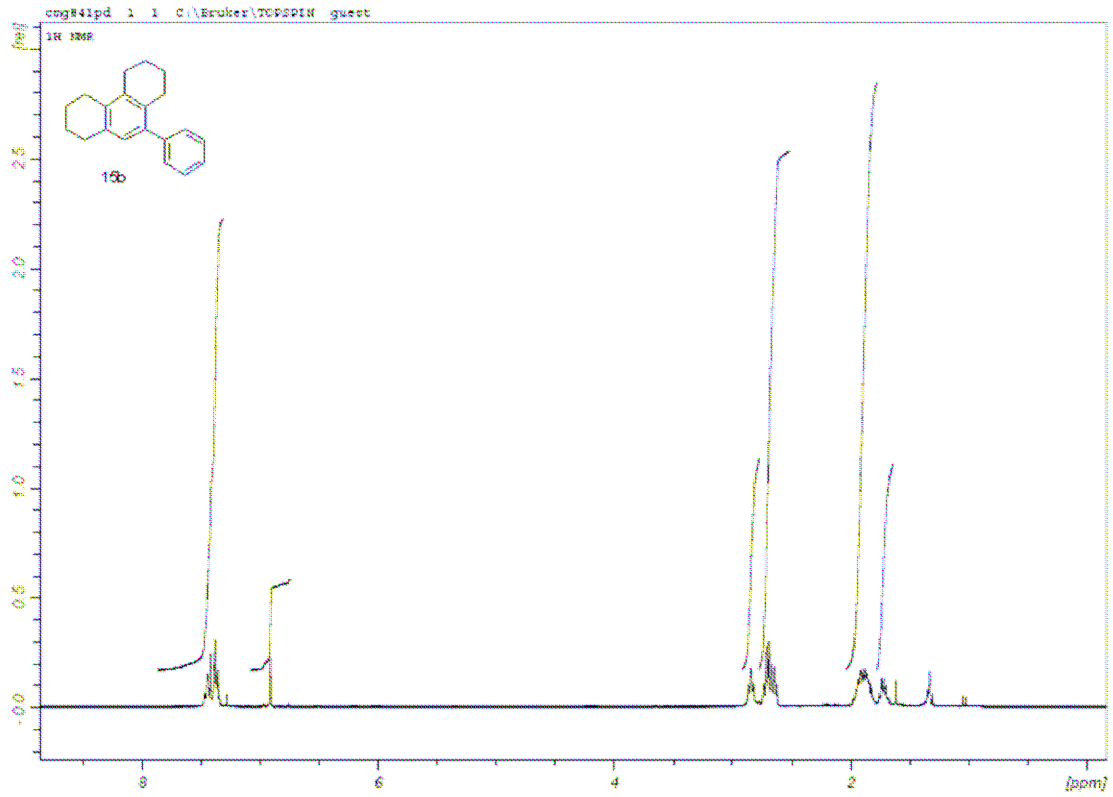
13C with proton decoupling
OMe
OMe
12
13
[ppm]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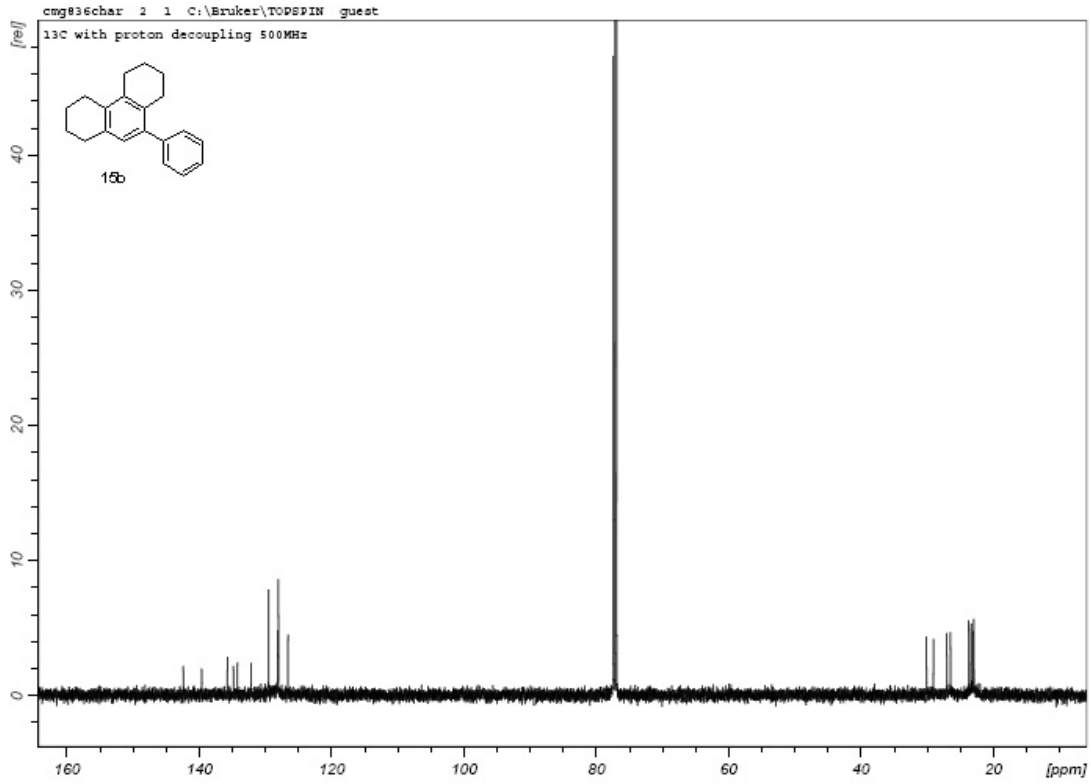
1H NMR
15b
[rel]
[ppm]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13C with proton decoupling 500MHz
15b
[rel]
[ppm]

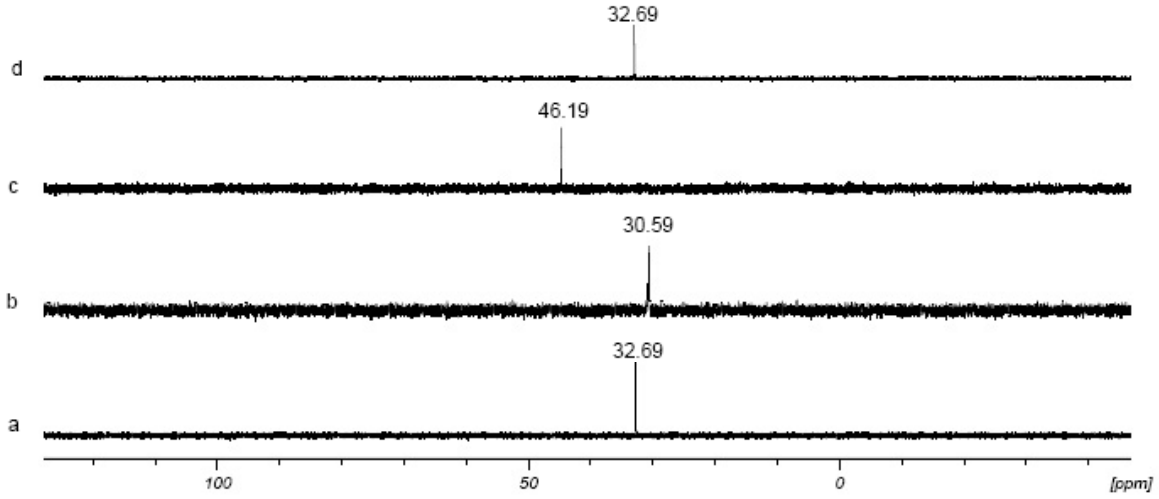

Figure 1. ^{31}P NMR study at 23 °C in $CDCl_3$ (PPh_3 used as a standard at -6.0 ppm). (a) $Au(PPh_3)Cl$; (b) $Au(PPh_3)Cl$ (2.5 mol %) and AgOTf (2.5 mol %) after 16 hours; (c) $Au(PPh_3)Cl$ (2.5 mol %), AgOTf (2.5 mol %) and alcohol **1** (59 % conversion); (d) $Au(PPh_3)Cl$ (5 mol %), TfOH (5 mol %) and alcohol **1** (37 % conversion).

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