Highly Enantio- and Diastereoselective One-pot Methods for the Synthesis of Halocyclopropyl Alcohols

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Supporting Information

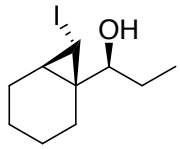
Table of Contents **Page**

General Methods. All reactions were carried out under a nitrogen atmosphere with oven-dried glassware. The progress of all reactions was monitored by thin-layer chromatography to ensure the reactions had reached completion. All manipulations involving dialkylzinc reagents were carried out an inert atmosphere in a Vacuum Atmosphere drybox with an attached MO-40 Dritrain or by using standard Schlenk or vacuum line techniques. Dialkylzinc compounds, except dimethyl- and diethylzinc, which are commercially available, were prepared by literature methods.[1-2] Dichloromethane and hexanes were dried through alumina columns. All aldehydes were distilled prior to use and stored under N_2. Unless otherwise specified, all chemicals were obtained from Aldrich, Acros, or GFS chemicals, and all solvents were purchased from Fischer Scientific. The ^{1}H NMR and ^{13}C NMR spectra were obtained on Bruker 500 or 300 MHz Fourier transform spectrometers at the University of Pennsylvania NMR facility. Chemical Shifts are reported in units of parts per million downfield from tetramethylsilane, and all coupling constants are reported in Hertz. The infrared spectra were obtained using a Perkin-Elmer 1600 series spectrometer. Thin-layer chromatography was performed on Whatman precoated silica gel 60 F-254 plates and visualized by ultra-violet light or by staining with ceric ammonium molybdate stain. Silica gel (230-400 mesh, Silicycle) was used for air-flashed chromatography. Deactivated silica gel was prepared by combining silica gel with 2.5 wt% NEt_3.

Cautionary Note: Dialkylzinc reagents are highly reactive compounds and require extreme caution.

Substrates and Products from Table 2.

General Procedure A.

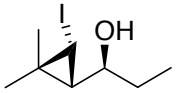


1a

1-(7-iodobicyclo[4.1.0]heptan-1-yl)propan-1-ol

A 10 mL Schlenk flask was charged with (–)-MIB (4.7 mg, 0.02 mmol, 4 mol %) and 1.0 mL hexanes and cooled to 0 °C. A solution of Et_2Zn (1.0 mL, 1.0 M in hexanes, 1.0 mmol) was added, followed by dropwise addition of 1-cyclohexene carboxaldehye (57 μL, 0.5 mmol). The solution was stirred at 0° C until alkyl addition was complete by TLC (8 h). A solution of Et_2Zn (1.0 mL, 1.0 M in hexanes, 1.0 mmol) and neat CF_3CH_2OH (72 μL, 1.0 mmol) were added slowly at 0 °C. After stirring at 0 °C for 10 min, iodoform (394 mg, 1.0 mmol) dissolved in 3.0 mL dichloromethane and 4 Å molecular sieves were added. The Schlenk flask was wrapped in aluminum foil to exclude light and stirring was continued at room temperature for 24 h, after which the reaction mixture was then quenched with saturated solution of NH_4Cl (15 mL). The organic and aqueous layers were separated, and the aqueous layer was extracted with 3X20 mL dichloromethane. The combined organic layers were then washed with saturated aqueous $Na_2S_2O_3$ followed by saturated aqueous $NaHCO_3$ and then dried over $MgSO_4$. The filtrate was concentrated *in vacuo* and the residue was chromatographed on deactivated silica (10% ethyl acetate in hexanes) to afford the title compound as a light yellow oil in 66% yield. $[\alpha]_D^{20}$ = +15.85 (c = 0.65, $CHCl_3$); ^1H NMR (C_6D_6, 500 MHz): δ 0.87 (m, 1H), 1.00 (t, 3H, *J* = 7.5 Hz), 1.02 (m, 2H), 1.06 (m, 1H), 1.39 (m, 5H), 1.73 (m, 1H), 1.87 (br s, 1H), 2.05 (m, 1H,), 2.22 (d, 1H, *J* = 4.9 Hz), 3.29 (m, 1H) ppm.; $^{13}C\{^1H\}$ NMR (C_6D_6, 75 MHz,): δ 4.52, 11.19, 20.79, 21.79,

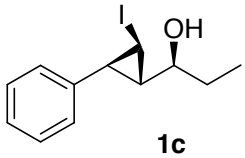
22.30, 23.06, 26.82, 27.55, 30.37, 82.96 ppm; IR (neat): 3396 (OH), 2927, 2855, 1454, 1102, 1020, 970, 790, 630 cm^{-1}; HRMS-CI m/z 263.0285 [$(M\text{-}OH)^+$; calcd for $C_{10}H_{16}I$: 263.0297].



1b

1-(3-Iodo-2,2-dimethylcyclopropyl)propan-1-ol

The product was prepared by General Procedure A using 3-methyl-2-butenal (48 μL, 0.5 mmol). The crude product was purified by column chromatography on deactivated silica (5% ethyl acetate in hexanes) to afford the title compound as a light yellow oil in 62% yield. $[\alpha]_D^{20}$ = +26.80 (c = 1.00, $CHCl_3$); ^1H NMR (C_6D_6, 300 MHz): δ 0.36 (dd, 1H, *J* = 7.8, 10.5 Hz), 0.71 (s, 3H), 0.92 (s, 3H), 0.95 (t, 3H, *J* = 7.5 Hz), 1.42 (m, 1H), 1.58 (m, 1H), 1.89 (br s, 1H), 2.24 (d, 1H, *J* = 7.8 Hz), 3.30 (m. 1H) ppm; $^{13}C\{^1H\}$ NMR (C_6D_6, 125 MHz,): δ 9.27, 10.06, 19.91, 21.76, 26.64, 29.73, 33.38, 74.35 ppm; IR (neat): 3415 (OH), 2959, 2932, 2876, 1455, 1375, 1236, 1191, 1102, 1016, 961, 740, 620 cm^{-1}; HRMS-CI m/z 237.0147 [$(M\text{-}OH)^+$; calcd for $C_8H_{14}I$: 237.0140].



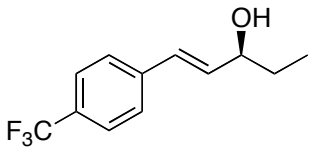
1c

1-(2-Iodo-3-phenylcyclopropyl)propan-1-ol

The product was prepared by General Procedure A using *trans*-cinnamaldehyde (63 μL, 0.5 mmol). The crude product was purified by column chromatography on deactivated silica (5% ethyl acetate in hexanes) to afford the title compound as a light yellow oil in 70% yield. $[\alpha]_D^{20}$ = +7.43 (c = 0.70, $CHCl_3$); ^1H NMR (C_6D_6, 300 MHz): δ 0.83 (t, 3H, *J* = 7.4 Hz), 1.34 (m, 2H), 1.56 (m, 1H), 1.64 (dd, 1H, *J* = 8.2, 6.4 Hz), 2.68 (dd, 1H, *J* = 8.2, 4.9 Hz), 2.85 (m, 1H), 7.09 (m, 2H), 7.16 (m, 3H) ppm; $^{13}C\{^1H\}$ NMR (C_6D_6, 75 MHz,): δ 4.03, 7.96, 23.69, 27.99, 32.21, 71.86,

125.04, 126.91, 127.17, 133.95 ppm; IR (neat): 3394 (OH), 3120, 3100, 2962, 2927, 2874, 1498,1456, 1109, 650 cm^{-1}; HRMS-CI m/z 284.0051 [$(M-H_2O)^+$; calcd for $C_{12}H_{13}I$: 284.0062].

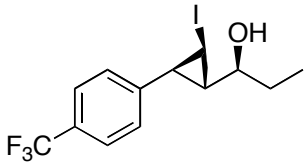
General Procedure A1.



(*E*)-1-(4-(trifluoromethyl)phenyl)pent-1-en-3-ol

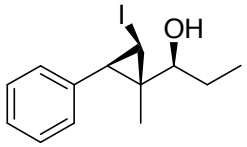
A 10 mL Schlenk flask was charged with (–)-MIB (2.3 mg, 0.01 mmol, 4 mol %) and 0.5 mL hexanes and cooled to 0 °C. A solution of Et_2Zn (0.5 mL, 1.0 M in hexanes, 0.5 mmol) was added, followed by dropwise addition of *p*-trifluoromethylcinnamaldehyde (50 mg, 0.25 mmol dissolved in 0.5 mL toluene). The solution was stirred at 0 °C until alkyl addition was complete by TLC (8 h). The reaction mixture was then quenched with saturated solution of NH_4Cl (15 mL). The organic and aqueous layers were separated, and the aqueous layer was extracted with 3X20 mL dichloromethane. The combined organic layers were then washed with brine and then dried over $MgSO_4$. The filtrate was concentrated *in vacuo* and the residue was chromatographed on deactivated silica (10% ethyl acetate in hexanes) to afford the title compound as a light yellow oil in 72% yield. $[\alpha]_D^{20}$ = - 1.019 (c = 0.03, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz): δ 0.99 (t, 3H, *J* = 7.3 Hz), 1.68 (m, 3H), 4.26 (m, 1H), 6.32 (dd, 1H, J_1 = 6.2; J_2= 14.2 Hz), 6.62 (d, 1H, *J* = 14.5 Hz), 7.47 (d, 2H, *J* = 8.4 Hz), 7.58 (d, 2H, *J* = 8.4 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz,): δ 9.92, 30.43, 74.24, 125.73, 125.78, 126.80, 129.06, 135.15 ppm; $^{19}F\{^1H\}$ NMR ($CDCl_3$, 282 MHz): δ -63.65 (s) ppm; IR (neat): 3350 (OH), 3043, 2970, 2934, 2879, 2645, 2322, 2083, 1918, 1796, 1653, 1615, 1579, 1516, 1462, 1414, 1379, 1326, 1264, 1206, 1163,

1126, 1068, 1016, 968, 899, 863, 837, 818 cm^{-1}; HRMS-CI m/z 231.1001 $[(MH)^+$; calcd for $C_{12}H_{14}OF_3$: 231.0997].



(1*S*)-1-((1*S*,3*S*)-2-iodo-3-(4-(trifluoromethyl)phenyl) cyclopropyl)propan-1-ol

The product was prepared by General Procedure A using of *p*-trifluoromethylcinnamaldehyde (50 mg, 0.25 mmol dissolved in 0.5 mL toluene). The crude product was purified by column chromatography on deactivated silica (5% ethyl acetate in hexanes) to afford the title compound as a light yellow oil in 75% conversion. $[\alpha]_D^{20}$ = +8.200 (c = 0.027, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz): δ 1.03 (t, 3H, *J* = 9.0 Hz), 1.73 (m, 3H), 2.13 (dd, 1H, J_1 = 8.1; J_2= 6.3 Hz), 3.03 (dd, 1H, J_1 = 4.8; J_2= 8.1 Hz), 3.50 (m, 1H), 7.30 (d, 2H, *J* = 9.0 Hz), 7.59 (d, 2H, *J* = 9.0 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz,): δ -3.77, 10.01, 25.58, 30.32, 34.63, 74.45, 125.22, 125.26, 129.35, 129.45 ppm; $^{19}F\{^1H\}$ NMR ($CDCl_3$, 282 MHz): δ -62.83 (s) ppm; IR (neat): 3389 (OH), 2964, 2924, 1916, 1709, 1618, 1461, 1411, 1310, 1124, 1068, 1016, 972 cm^{-1}; HRMS-CI m/z 353.0017 $[(M-OH)^-$; calcd for $C_{13}H_{13}F_3I$: 353.0014].



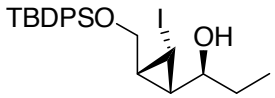
1d

1-(2-Iodo-1-methyl-3-phenylcyclopropyl)propan-1-ol

The product was prepared by General Procedure A using 2-methyl-trans-cinnamaldehyde (70 μL, 0.5 mmol). The crude product was purified by column chromatography on deactivated silica (5% ethyl acetate in hexanes) to afford the title compound as a light yellow oil in 56% yield. $[\alpha]_D^{20}$ = +2.50 (c = 0.40, $CHCl_3$); ^1H NMR (C_6D_6, 300 MHz): δ 0.85 (t, 3H, *J* = 7.4 Hz), 1.00 (s, 3H), 1.36 (m, 2H), 1.65 (d, 1H, *J* = 8.4 Hz), 2.65 (m, 1H), 2.85 (d, 1H, *J* = 8.4 Hz), 7.10 (m, 1H), 7.19 (m, 2H), 7,24 (m, 2H)

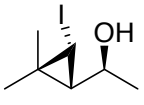
ppm; $^{13}C\{^1H\}$ NMR (C_6D_6, 75 MHz,): δ 8.31, 11.06, 17.77, 27.64, 27.77, 29.32, 79.25, 127.06, 128.53, 131.05, 136.99 ppm; IR (neat): 3411 (OH), 3025, 2974, 2934, 1713, 1495, 1453, 1374, 972, 748, 695, cm^{-1}; HRMS-CI m/z 299.0283 [$(M\text{-}OH)^+$; calcd for $C_{13}H_{16}I$: 299.0297].

1-[2-(tButyl-diphenyl-silanyloxymethyl)-3-iodo-cyclopropyl]-propan-1-ol



1e

The product was prepared by General Procedure A using a solution of 4-(^{t}butyl-diphenyl-sialnyoxy)-but-2-enal (0.5 mL, 1.0 M in toluene, 0.5 mmol). The crude product was purified by column chromatography on deactivated silica (5% ethyl acetate in hexanes) to afford the title compound as a light yellow oil in 74% yield. $[\alpha]_D^{20}$ = +6.00 (c = 2.30, $CHCl_3$); ^1H NMR (C_6D_6, 300 MHz): δ 0.57 (m, 1H), 0.78 (m, 1H), 0.95 (t, 3H, *J* = 7.4 Hz), 1.18 (s, 9H), 1.61 (m, 1H), 1.78 (br s, 1H), 2.29 (dd, 1H, *J* = 7.6, 7.4 Hz), 3.38 (m, 1H), 3.82 (d, 2H, *J* = 7.2 Hz), 7.24 (m, 6H), 7.79 (m, 4H) ppm; $^{13}C\{^1H\}$ NMR (C_6D_6, 75 MHz,): δ -1.54, 10.37, 19.50, 21.75, 25.92, 27.22, 29.95, 66.11, 73.86, 128.30, 130.30, 136.11, 136.22 ppm; IR (neat): 3422 (OH), 3069, 2959, 2930, 2857, 1467, 1428, 1390, 1232, 1110, 823, 703, 610 cm^{-1}; HRMS-CI m/z 477.1100 [$(M\text{-}OH)^+$; calcd for $C_{23}H_{30}O_1SiI$: 477.1111].



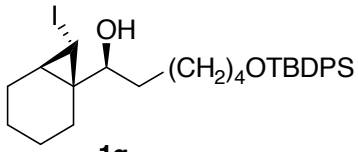
1f

1-(3-Iodo-2,2-dimethylcyclopropyl)ethanol

The product was prepared by General Procedure A using (–)-MIB (7.2 μg, 0.03 mmol), 1.0 mL Me_2Zn (1.2 mmol, 1.2 M in toluene) and 29 μL 3-methyl-2-butenal (0.3 mmol). The reaction was stirred at room temperature. The crude product was purified by column chromatography on deactivated silica (5% ethyl acetate in

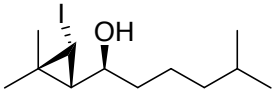
hexanes) to afford the title compound as a light yellow oil in 78% yield. $[\alpha]_D^{20}$ = -2.50 (c = 0.50, $CHCl_3$); ^1H NMR (C_6D_6, 300 MHz): δ 0.31 (dd, 1H, *J* = 9.4, 7.8 Hz), 0.67 (s, 3H), 0.87 (s, 3H), 1.14 (d, 3H, *J* = 6.3 Hz), 1.66 (br s, 1H), 2.21 (d, 1H, *J* = 7.8 Hz), 3.46 (m, 1H) ppm; $^{13}C\{^1H\}$ NMR (C_6D_6, 125 MHz,): δ 9.33, 19.94, 21.21, 22.17, 16.64, 34.66, 69.74 ppm; IR (neat): 3386, 2927, 2855, 1454, 1102, 1020, 970, 628 cm^{-1}; HRMS-CI m/z 222.9979 [(M-OH)$^+$; calcd for $C_8H_{14}I$: 222.9984].

6-(tert-Butyl-diphenyl-silanyloxy)-1-(7-iodo-bicyclo[4,1,0]hept-1-yl)-hexan-1-ol



1g

The product was prepared by General Procedure A using 57 μL 1-cyclohexenecarboxaldehyde (0.5 mmol) and 1.0 mL dialkylzinc (1.0 mmol, 1.0 M in hexanes). The addition reaction was stirred at room temperature. The crude product was purified by column chromatography on deactivated silica (5% ethyl acetate in hexanes) to afford the title compound as a light yellow oil in 70% yield. $[\alpha]_D^{20}$ = +5.54 (c = 1.50, $CHCl_3$); ^1H NMR (C_6D_6, 500 MHz): δ 0.63 (m, 1H), 0.74 (m, 1H), 0.81 (m, 1H), 0.89 (s, 9H), 1.14 (m, 2H), 1.24 (m, 5H), 1.33 (m, 2H), 1.41 (m, 2H), 1.61 (m, 2H), 1.74 (br s, 1H), 1.93 (m, 1H), 2.11 (d, 1H, *J* = 4.85 Hz), 3.16 (m, 1H), 3.70 (t, 2H, *J* = 6.5 Hz), 7.40 (m, 6H), 7.75 (m, 4H) ppm; $^{13}C\{^1H\}$ NMR (C_6D_6, 125 MHz,): δ 4.50, 10.59, 15.36, 20.59, 21.58, 22.84, 23.72, 24.42, 26.61, 26.74, 27.37, 30.37. 33.06, 66.50, 83.50, 127.65, 129.86, 136.62, 139.87 ppm; IR (neat): 3481 (OH), 3069, 2957, 2857, 1458, 1232, 1162, 1076, 1008, 960, 700, 623 $cm^{-1;}$ HRMS-CI m/z 559.1899 [(M-OH)$^+$; calcd for $C_{29}H_{40}O_1SiI$: 559.1893].



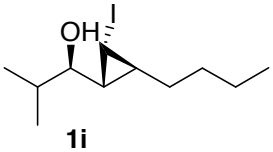
1h

1-(3-Iodo-2,2-dimethylcyclopropyl)-5-methylhexan-1-ol

The product was prepared by General Procedure A using 3-methyl-2-butenal (48 μL 0.5 mmol). The crude product was purified by column chromatography on deactivated silica (5% ethyl acetate in hexanes) to afford the title compound as a light yellow oil in 60% yield. $[\alpha]_D^{20}$ = -0.20 (c = 0.50, $CHCl_3$); ^{1}H NMR (C_6D_6, 500 MHz): δ 0.40 (dd, 1H, *J* = 9.3, 7.8 Hz), 0.74 (s, 3H), 0.89 (s, 3H), 0.90 (s, 3H), 0.98 (s, 3H), 1.18 (m, 2H), 1.41 (m, 2H), 1.52 (m, 2H), 1.64 (m, 1H), 1.79 (br s, 1H), 2.26 (d, 1H, *J* = 7.8 Hz), 3.42 (m, 1H) ppm; ^{13}C{^{1}H} NMR (C_6D_6, 125 MHz,): δ 9.28, 19.92, 21.75, 22.68, 22.79, 23.70, 26.70, 28.29, 33.77, 37.23, 39.37, 73.27 ppm; HRMS-CI m/z 293.0775 [$(M\text{-}OH)^+$; calcd for $C_{12}H_{22}I$: 293.0766].

Substrates and Products from Table 3.

General Procedure B.

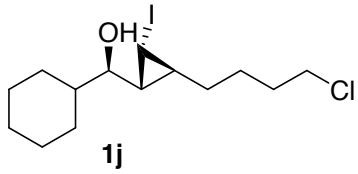


1i

1-(2-butyl-3-iodocyclopropyl)-2-methylpropan-1-ol.

1-Hexyne (58 μL, 0.50 mmol) and diethylborane (0.50 mL, 0.50 mmol, 1.0 M in toluene) were added to a dry flask under nitrogen and stirred at room temperature for 30 min. The reaction flask was then cooled to –78 °C, (–)-MIB (4.7 mg, 0.02 mmol, 4 mol %) was added followed by Et_2Zn (0.3 mL, 2.0 M in dichloromethane). The reaction mixture was then warmed to –10 °C and isobutyraldehyde (46 μL, 0.5 mmol) was added dropwise. The solution was stirred for 8 h at –10 °C until vinyl

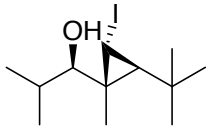
addition was complete by TLC. The volatile materials, including the byproduct Et_3B, were removed *in vacuo* at 0 °C. Hexanes (2.0 mL) was added and the volatile materials were again removed under reduced pressure. This step was repeated two more times to insure removal of Et_3B. Et_2Zn (1.5 mL, 1.5 mmol, 1.0 M in dichloromethane), iodoform (6 equiv. in 5.0 mL dichloromethane, 3.0 mmol) and activated 4 Å molecular sieves were added at 0 °C. The Schlenk flask was covered with aluminum foil to exclude light and the reaction mixture was stirred at room temperature for 24 h. It was then quenched with saturated solution of NH_4Cl (15 mL). The organic and aqueous layers were separated, and the aqueous layer was extracted with 3X20 mL dichloromethane. The combined organic layers were then washed with saturated aqueous $Na_2S_2O_3$ and then saturated aqueous $NaHCO_3$ and dried over $MgSO_4$. The filtrate was concentrated *in vacuo* and the residue was chromatographed on deactivated silica (3% ethyl acetate in hexanes) to afford the title compound as a colorless oil in 64% yield. $[\alpha]_D^{20}$ = 16.66 (c = 0.50, $CHCl_3$); δ ^{1}H NMR ($CDCl_3$, 500 MHz): 2.93 (dd, 1H, *J* = 4.4, 7.8 Hz), 2.57 (dd, 1H, *J* = 5.80, 6.21), 1.73 (m, 1H), 1.52 (br s, 1H), 1.43 (m, 2H), 1.31 (m, 4H), 0.91 (d, 6H, *J* = 6.67), 0.86 (t, 3H, *J* = 7.1), 0.83 (m, 1H), 0.42 (m, 1H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz,): δ 79.02, 34.52, 34.26, 33.85, 30.83, 22.74, 21.08, 18.85, 18.00, 14.30, -3.53 ppm; IR (neat): 3421 (OH), 2958, 2857, 1465, 1379, 1224, 998, 801 cm^{-1}; HRMS-CI m/z 279.0609 [$(M-OH)^+$; calcd for $C_{11}H_{20}I$: 279.0609].



1j

(2-(4-chlorobutyl)-3iodocyclopropyl)(cyclohexyl)methanol. The product was prepared by General Procedure B using 6-chloro-1-hexyne (60 μL, 0.5 mmol) and cyclohexane carboxaldehyde (61 μL, 0.5 mmol). The crude product was purified by column

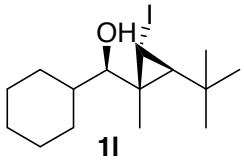
chromatography on deactivated silica (3% ethyl acetate in hexanes) to afford the title compound as a colorless oil in 78% yield. $[\alpha]_D^{20}$ = + 23.78 (c = 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz): δ 3.50 (t, 2H, *J* = 6.7 Hz), 2.94 (dd, 1H, *J* = 5.90, 6.21 Hz), 2.57 (dd, 1H, *J* = 4.4, 7.6 Hz), 1.77 (m, 2H), 1.69 (m, 4H), 1.49 (m, 4H), 1.35 (m, 4H), 1.04 (m, 4H), 0.83 (m, 1H), 0.42 (m, 1H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz,): δ 78.27, 45.19, 44.60, 33.84, 32.59, 29.26, 28.66, 26.71, 26.47, 26.45, 26.36, 25.97, 20.78, -3.68 ppm; IR (neat): 3403 (OH), 2959, 2873, 1465, 1260, 1152, 1100, 1035, 800, 672 cm^{-1}; HRMS-CI m/z 353.0549 $[(M\text{-}OH)^+$; calcd for $C_{14}H_{23}ClI$: 353.0532].



1k

1-(2-tert-butyl-3-iodo-1-methylcyclopropyl)-2-methylpropan-1-ol

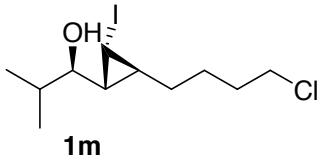
The product was prepared by General Procedure B using 4,4-dimethyl-2-pentyne (67 μL, 0.5 mmol) and isobutyraldehyde (46 μL, 0.5 mmol). The crude product was purified by column chromatography on deactivated silica (3% ethyl acetate in hexanes) to afford the title compound as a colorless oil in 67% yield. $[\alpha]_D^{20}$ = -10.35 (c = 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz): 2.62 (d, 1H, *J* = 9.17 Hz), 2.48 (d, 1H, *J* = 6.72 Hz), 1.77 (m, 1H), 1.50 (br s. 1H), 1.20 (s, 3H), 1.03 (s, 9H), 0.91 (d, 3H, *J* = 6.67 Hz), 0.90 (d, 3H, *J* = 6.67 Hz), 0.75 (d, 1H, *J* = 6.72 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz,): δ 86.22, 35.46, 33.49, 32.24, 30.81, 20.23, 19.24, 18.85, 15.77, 4.71 ppm; IR (neat): 3550 (OH), 2924, 1449, 1363, 1259, 1099, 970, 801, 665 cm^{-1}; HRMS-CI m/z 293.2125 $[(M\text{-}OH)^+$; calcd for $C_{12}H_{22}I$: 293.2121].



1l

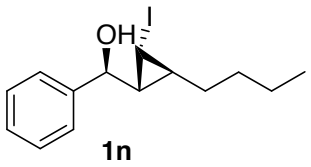
(2-tert-butyl-3-iodo-1-methylcyclopropyl)(cyclohexyl)methanol.

The product was prepared by General Procedure B using 4,4-dimethyl-2-pentyne (67 μL, 0.5 mmol) and cyclohexane carboxaldehyde (61 μL, 0.5 mmol). The crude product was purified by column chromatography on deactivated silica (3% ethyl acetate in hexanes) to afford the title compound as a colorless oil in 70% yield. $[\alpha]_D^{20}$ = -10.35 (c = 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz): 2.59 (d, 1H, *J* = 9.00 Hz), 2.49 (d, 1H, *J* = 6.76 Hz), 1.90 (m, 1H), 1.43 (m, 2H), 1.77 (m, 1H), 1.67 (m, 4H), 1.60 (m, 3H), 1.50 (br s, 1H), 1.19 (s, 3H), 1.03 (s, 9H), 0.71 (d, 1H, *J* = 6.76 Hz), ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz,): δ 85.49, 41.03, 35.49, 33.50, 30.84, 30.78, 30.20, 29.57, 26.60, 26.29, 26.10, 15.76, 4.75 ppm; IR (neat): 3419 (OH), 2953, 2852, 1449, 1363, 1196, 1014, 970, 802 cm^{-1}; HRMS-CI m/z 333.1086 $[(M\text{-}OH)^+$; calcd for $C_{15}H_{26}I$: 333.1079].



1m

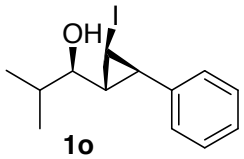
1-(2-(4-chloropropyl)-3-iodocyclopropyl)-2-methylpropan-1-ol. The product was prepared by General Procedure B using 6-chloro-1-hexyne (60 μL, 0.5 mmol) and isobutyraldehyde (46 μL, 0.5 mmol). The crude product was purified by column chromatography on deactivated silica (3% ethyl acetate in hexanes) to afford the title compound as a colorless oil in 80% yield. $[\alpha]_D^{20}$ = + 12.55 (c = 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz): δ 3.50 (t, 2H, *J* = 6.7 Hz), 2.96 (dd, 1H, *J* = 5.93, 6.15 Hz), 2.59 (dd, 1H, *J* = 7.93, 4.49 Hz), 1.78 (m, 2H), 1.71 (m, 1H), 1.53 (m, 2H), 1.50 (br s, 1H), 1.33 (m, 2H), 0.91 (d, 6H, *J* = 6.75 Hz), 0.88 (m, 1H), 0.43 (m, 1H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz,): δ 78.63, 45.16, 34.57, 33.86, 33.77, 32.60, 35.96, 20.73, 18.86, 18.01, -3.77 ppm; IR (neat): 3401 (OH), 2959, 1463, 1260, 1152, 1100, 1035, 800cm^{-1}; HRMS-CI m/z 313.0218 $[(M\text{-}OH)^+$; calcd for $C_{11}H_{19}ClI$: 313.0129].



1n

(2-butyl-3-iodocyclopropyl)(phenyl)methanol.

The product was prepared by General Procedure B using 1-Hexyne (58 μL, 0.50 mmol) and benzaldehyde (51 μL, 0.5 mmol). A solution of Et_2Zn (0.75 mL, 1.5 mmol, 2.0 M in DCM), iodoform (6 equiv. in 3.0 mL dichloromethane. 3.0 mmol) and 4 Å molecular sieves were added at 0 ^oC for iodocyclopropanation (more concentrated condition: 0.24 M -> 0.42 M). The crude product was purified by column chromatography on deactivated silica (5% ethyl acetate in hexanes) to afford the title compound as a colorless oil in 52% yield. $[\alpha]_D^{20}$ = + 5.53 (c = 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz): δ 7.30 (m, 3H), 7.23 (m, 2H), 4.12 (d, 1H, *J* = 8.30 Hz), 3.10 (dd, 1H, *J* = 4.49, 7.73 Hz), 1.90 (br s, 1H), 1.85 (m, 1H), 1.23 (m, 6H), 0.93 (t, 3H, *J* = 6.65 Hz), 0.73 (m, 1H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz,): δ 139.2, 128.5, 127.4, 124.9, 79.10, 34.12, 28.95, 22.78, 18.85, 15.24, 11.11, 9.54 ppm; IR (neat): 3444 (OH), 2929, 2853, 1462, 1252, 1113, 891, 740, 688 cm^{-1}; HRMS-CI m/z 331.0570 [$(MH)^+$; calcd for $C_{14}H_{20}IO$: 331.0559].



1o

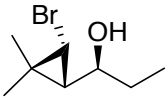
1-(2-iodo-3-phenylcyclopropyl)-2-methylpropan-1-ol.

The product was prepared by General Procedure B using phenylacetylene (55 μL, 0.5 mmol) and isobutyraldehyde (46 μL, 0.5 mmol). A solution of Et_2Zn (0.75 mL, 1.5 mmol, 2.0 M in DCM), iodoform (6 equiv. in 3.0 mL dichloromethane. 3.0 mmol) and 4 Å molecular sieves were added at 0^oC for iodocyclopropanation (more concentrated condition: from 0.24 M to 0.42 M). The crude product was purified by column chromatography on deactivated silica (3% ethyl acetate in

hexanes) to afford the title compound as a colorless oil in 50% yield. $[\alpha]_D^{20}$ = -3.56 (c = 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz): 7.27 (m, 2H), 7.24 (m, 1H), 7.12 (m, 2H), 3.19 (dd, 1H, *J* = 6.22, 6.74 Hz), 2.94 (dd, 1H, *J* = 4.50, 8.23 Hz), 2.0 (dd, 1H, *J* = 6.90, 8.23 Hz), 1.84 (m, 1H), 1.70 (m, 1H), 1.49 (br s, 1H), 0.98 (d, 3H, *J* = 3.23 Hz), 0.97 (d, 3H, *J* = 3.23 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz,): δ 138.97, 129.03, 128.31, 127.17, 78.58, 34.74, 32.38, 29.99, 26.28, 18.87, 18.22 ppm; IR (neat): 3406 (OH), 3058, 2936, 2877, 1498, 1456, 1287, 1073, 966, 743, 623 cm^{-1}; HRMS-CI m/z 298.0238 [$(M-H_2O)^+$; calcd for $C_{13}H_{15}I$: 298.0218].

Substrates and Products from Table 4.

General Procedure C.

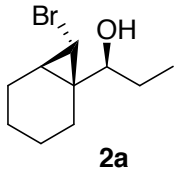


2b

3-Bromo-2,2-dimethylcyclopropyl)propan-1-ol

A 10 mL Schlenk flask was charged with (–)-MIB (4.7 mg, 0.02 mmol, 4 mol %) and cooled to 0 °C. A solution of Et_2Zn (0.50 mL, 1.0 mmol, 2.0 M in DCM) was added, followed by dropwise addition of 3-methyl-2-butenal (48 μL, 0.5 mmol). The reaction was stirred at 0 ºC for 10 h until alkyl addition was complete by TLC. Next, a solution of Et_2Zn (1.25 mL, 2.5 mmol, 2.0 M in DCM) and CF_3CH_2OH (186 μL, 2.5 mmol) were added slowly at 0 ºC. After stirring at 0 °C for 5 min, bromoform (218 μL, 2.5 mmol) was added. The flask was covered with aluminum foil and the solution was stirred at room temperature for 24 h. It was then quenched with saturated solution of NH_4Cl (10 mL). The organic and aqueous layers were separated and the aqueous layer was extracted with 3X15 mL dichloromethane. The combined organic layers were then washed with brine and dried over $MgSO_4$. The filtrate was concentrated *in vacuo* and the residue was

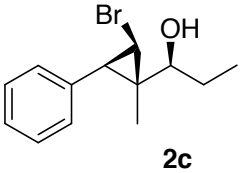
chromatographed on deactivated silica (3% ethyl acetate in hexanes) to afford the title compound as a colorless oil in 75% yield. $[\alpha]_D^{20}$ = + 33.75 (c = 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz): δ 3.48 (m, 1H), 2.97 (d, 1H, *J* = 7.46 Hz), 2.02 (br s, 1H), 1.58 (m, 2H), 1.12 (s, 3H), 1.11 (s, 3H), 0.97 (t, 3H, *J* = 7.65 Hz), 0.89 (dd, 1H, *J* = 7.46, 9.68 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz,): δ 72.29, 35.56, 33.86, 29.81, 27.48, 21.15, 18.38, 10.25 ppm; IR (neat): 3457 (OH), 2930, 1450, 1254, 1169, 1112, 1010, 966, 698 cm^{-1}; HRMS-CI m/z 189.0295 [$(M\text{-}OH)^+$; calcd for $C_8H_{14}Br$: 189.0278].



2a

1-(7-bromobicyclo[4.1.0]hepan-1-yl)popan-1-ol

The product was prepared by General Procedure C using 1-cyclohexenecarboxaldehyde (54 μL, 0.5 mmol). The crude product was purified by column chromatography on deactivated silica (5% ethyl acetate in hexanes) to afford the title compound as a colorless oil in 70% yield. $[\alpha]_D^{20}$ = +28.10 (c = 1.00, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz); δ 3.35 (m, 1H), 2.84 (d, 1H, *J* = 4.31 Hz), 2.07 (m, 1H), 1.88 (br s, 1H) , 1.64 (m, 2H) 1.61 (m, 2H), 1.43 (m, 1H), 1.31 (m, 2H), 1.18 (m, 1H), 1.06 (m, 2H), 0.97 (t, 3H, *J* = 7.53 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz,): δ 80.00, 33.94, 28.69, 27.11, 26.50, 23.50, 22.09, 21.81, 21.18, 11.25 ppm; IR (neat): 3457 (OH), 2930, 2859, 1450, 1298, 1255, 1112, 966, 802 cm^{-1} HRMS-CI m/z 255.0371 [$(M+Na)^+$; calcd for $C_{10}H_{17}ONaBr$: 255.0360].

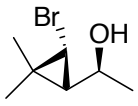


2c

1-(2-bromo-1-methyl-3-phenylcyclopropyl)propan-1-ol.

The product was prepared by General Procedure C using 2-

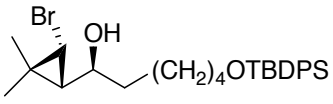
methylcinnamaldehyde (70 μL, 0.5 mmol). The crude product was purified by column chromatography on deactivated silica (10% ethyl acetate in hexanes) to afford the title compound as a colorless oil in 80% yield. $[\alpha]_D^{20}$ = +5.10 (c = 0.45, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz); δ 7.32 (m, 5H), 3.45 (d, 1H, *J* = 8.18 Hz), 3.15 (m, 1H), 2.22 (d, 1H, *J* = 8.18 Hz), 1.77 (br s, 1H), 1.72 (m, 2H), 1.10 (s 3H), 1.08 (t, 3H, *J* = 7.42 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz,): δ 135.49, 131.20, 128.50, 127.06, 80.31, 34.08, 30.14, 28.14, 27.52, 13.25, 11.16 ppm; IR (neat): 3457 (OH), 3025, 2974, 2934, 1713, 1498, 1385, 1315, 832, 699 cm^{-1} HRMS-CI m/z 251.0440 [$(M\text{-}OH)^+$; calcd for $C_{13}H_{16}Br$: 251.0435].



2d

1-(3-bromo-2,2-dimethylcyclopropyl)ethanol.

The product was prepared by General Procedure C using (–)-MIB (012 mg, 0.05 mmol), a solution of Me_2Zn (1.0 mL, 2.0 mmol, 2.0 M in toluene) and 3-methyl-2-butenal (48 μL, 0.5 mmol) for addition step. The addition reaction was stirred at room temperature for 20 hr until addition was complete by TLC. The crude product was purified by column chromatography on deactivated silica (5% ethyl acetate in hexanes) to afford the title compound as a light yellow oil in 70% yield. $[\alpha]_D^{20}$ = - 10.10 (c = 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz); δ 3.76 (m, 1H), 3.00 (d, 1H, *J* = 7.4 Hz), 1.88 (br s, 1H), 1.30 (d, 3H, *J* = 6.26 Hz), 1.17 (s, 3H), 1.13 (s, 3H), 0.85 (m, 1H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz,): δ 67.48, 35.54, 35.12, 27.53, 22.43, 20.85, 17.77 ppm; IR (neat): 3433 (OH), 2926, 1458, 1376, 1260, 1096, 801 cm^{-1} HRMS-CI m/z 176.0131 [$(M\text{-}OH)^+$; calcd for $C_7H_{12}Br$: 176.0122].

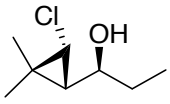


2e

1-(3-Bromo-2,2-dimethyl-cyclopropyl)-6-(tert-butyl-diphenyl-silanyloxy)-hexan-1-ol

The product was prepared by General Procedure C using 3-methyl-2-butenal (48 μL, 0.5 mmol) and a solution of dialkylzinc (1.0 mL, 1.0 mmol, 1.0 M in hexanes). The addition reaction was stirred at room temperature for 15 h until addition was complete by TLC. The crude product was purified by column chromatography on deactivated silica (3% ethyl acetate in hexanes) to afford the title compound as a light yellow oil in 77% yield. $[\alpha]_D^{20}$ = +20.60 (c = 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz); δ 7.61 (m, 4H), 7.33 (m, 6H), 3.61 (t, 2H, *J* = 6.43 Hz), 3.50 (m, 1H), 2.93 (d, 1H, *J* = 7.43 Hz), 1.89 (br s, 1H), 1.55 (m, 4H), 1.38 (m, 4H), 1.09 (s, 3H), 1.06 (s, 3H), 0.99 (s, 9H), 0.80 (m, 1H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz,): δ 135.81, 134.49, 129.73, 127.82, 70.86, 64.11, 36.85, 35.43, 34.03, 33.80, 32.80, 29.67, 27.12, 26.14, 25.48, 18.13 ppm; IR (neat): 3444 (OH), 2923, 1471, 1252, 1111, 823, 740, 702 cm^{-1} HRMS-CI m/z 503.1994 $[(MH)^+$; calcd for $C_{27}H_{40}BrO_2Si$: 503.1981].

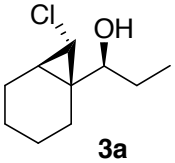
General Procedure D.



3b

1-(3-chloro-2,2-dimethylcyclopropyl)ethanol.A 10 mL Schlenk flask was charged with (–)-MIB (4.7 mg, 0.02 mmol, 4 mol %) and cooled to 0 °C. A solution of Et_2Zn (0.50 mL, 1.0 mmol, 2.0 M in DCM) was added, followed by dropwise addition of 3-methyl-2-butenal (48 μL, 0.5 mmol). The reaction was stirred at 0 °C for 8 h until alkyl addition was complete by TLC. Next, a solution of Et_2Zn (1.25 mL, 2.5 mmol, 2.0 M in DCM) and neat CF_3CH_2OH (286 μL, 2.5 mmol) were added slowly at 0 °C. After stirring at 0 °C for 5 min, dibromochloromethane (212 μL, 2.5 mmol) was added. The flask was covered with aluminum foil and the solution was stirred at

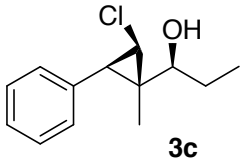
room temperature for 24 h. It was then quenched with saturated solution of NH_4Cl (15 mL). The organic and aqueous layers were separated and the aqueous layer was extracted with 3X20 mL dichloromethane. The combined organic layers were then washed with brine and dried over $MgSO_4$. The filtrate was concentrated *in vacuo* and the residue was chromatographed on deactivated silica (3% ethyl acetate in hexanes) to afford the title compound as a colorless oil in 70% yield. $[\alpha]_D^{20}$ = + 11.20 (c = 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz): δ 3.55 (m, 1H), 3.01 (d, 1H, *J* = 7.47 Hz), 1.88 (br s, 1H), 1.59 (m, 2H), 1.14 (s, 3H), 1.08 (s, 3H), 0.98 (t, 3H, *J* = 7.52 Hz), 0.89 (dd, 1H, *J* = 7.47, 9.77 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz,): δ 70.79, 43.66, 34.23, 29.93, 27.34, 21.53, 16.23, 10.22 ppm; IR (neat): 3407 (OH), 2859, 1450, 1259, 1085, 801, 749 cm^{-1}; HRMS-CI m/z 145.0779 [(M-OH)$^+$; calcd for $C_8H_{14}Cl$: 145.0784].



3a

1-(7-chlorobicyclo[4.1.0]heptan-1-yl)propan-1-ol.

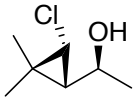
The product was prepared by General Procedure D using 1-cyclohexenecarboxaldehyde (54 μL, 0.5 mmol). The crude product was purified by column chromatography on deactivated silica (5% ethyl acetate in hexanes) to afford the title compound as a colorless oil in 65% yield. $[\alpha]_D^{20}$ = +11.20 (c = 1.00, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz); δ 3.39 (m, 1H), 2.92 (d, 1H, *J* = 4.11 Hz), 2.06 (m, 1H), 1.78 (m, 3H), 1.43 (m, 2H), 1.36 (m, 3H), 1.11 (m, 2H), 0.99 (t, 3H, *J* = 7.53 Hz), 0.88 (m, 1H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz,): δ 78.07, 43.90, 29.41, 26.92, 26.50, 23.56, 21.84, 21.83, 21.37, 11.28 ppm; IR (neat): 3407 (OH), 2930, 1450, 1085, 1043, 967, 749, 626 cm^{-1} HRMS-CI m/z 171.0932 [(M-OH)$^+$; calcd for $C_{10}H_{16}Cl$: 171.0940].



3c

1-(2-chloro-1-methyl-3-phenylcyclopropyl)propan-1-ol.

The product was prepared by General Procedure D using 2-methylcinnamaldehyde (70 μL, 0.5 mmol). The crude product was purified by column chromatography on deactivated silica (5% ethyl acetate in hexanes) to afford the title compound as a colorless oil in 70% yield. $[\alpha]_D^{20}$ = +2.30 (c = 0.45, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz); δ 7.31 (m, 5H), 3.48 (d, 1H, *J* = 7.96 Hz), 3.10 (m, 1H), 2.25 (d, 1H, *J* = 7.96 Hz), 1.97 (br s, 1H), 1.74 (m, 2H), 1.08 (s 3H), 1.07 (t, 3H, *J* = 7.62 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz,): δ 134.90, 131.30, 128.56, 127.02, 80.30, 42.64, 30.79, 28.51, 27.27, 11.19, 10.74 ppm; IR (neat): 3406 (OH), 3058, 2936, 1603, 1498, 1287, 1073, 966, 832, 743, 699 cm^{-1} HRMS-CI m/z 207.0943 $[(M\text{-}OH)^+$; calcd for $C_{13}H_{16}Cl$: 207.0940].



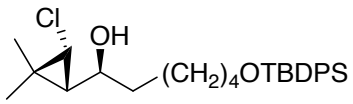
3d

1-(3-chloro-2,2-dimethylcyclopropyl)ethanol.

The product was prepared by General Procedure D using (–)-MIB (12 mg, 0.05 mmol), a solution of Me_2Zn (1.0 mL, 2.0 mmol, 2.0 M in toluene) and 3-methyl-2-butenal (48 μL, 0.5 mmol) for addition step. The addition reaction was stirred at room temperature for 20 h until addition was complete by TLC. The crude product was purified by column chromatography on deactivated silica (5% ethyl acetate in hexanes) to afford the title compound as a light yellow oil in 59% yield. $[\alpha]_D^{20}$ = - 28.10 (c = 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz); δ 3.74 (m, 1H), 3.10 (d, 1H, *J* = 7.62 Hz), 1.98 (br s, 1H), 1.41 (d, 3H, *J* = 6.26 Hz), 1.19 (s, 3H), 1.18 (s, 3H), 0.95 (m, 1H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz,): δ 68.48, 42.02, 37.12, 26.53, 22.65, 21.03, 18.77 ppm; IR (neat): 3423 (OH), 2870,

1458, 1380, 1275, 1096, 802 cm^{-1} HRMS-CI m/z 131.0635 [$(M\text{-}OH)^+$; calcd for $C_7H_{12}Cl$: 131.0627].

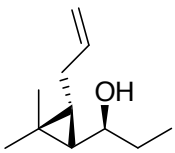
6-(tButyl-diphenyl-silanyloxy)-1-(3-chloro-2,2-dimethyl-cyclopropyl)-hexan-1-ol



3e

The product was prepared by General Procedure D using 3-methyl-2-butenal (48 μL, 0.5 mmol) and a solution of dialkylzinc (1.0 mL, 1.0 mmol, 1.0 M in hexanes). The addition reaction was stirred at room temperature for 15 h until addition was complete by TLC. The crude product was purified by column chromatography on deactivated silica (3% ethyl acetate in hexanes) to afford the title compound as a light yellow oil in 70% yield. $[\alpha]_D^{20}$ = +3.10 (c = 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz); δ 7.70 (m, 4H), 7.40 (m, 6H), 3.68 (t, 2H, *J* = 6.35 Hz), 3.62 (m, 1H), 3.03 (d, 1H, *J* = 7.43 Hz), 1.80 (br s, 1H), 1.62 (m, 4H), 1.418 (m, 4H), 1.14 (s, 3H), 1.09 (s, 3H), 1.07 (s, 9H), 0.980 (m, 1H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz,): δ 135.96, 134.54, 129.89, 127.97, 69.44, 64.29, 43.67, 37.13, 34.53, 34.23, 32.95, 29.94, 27.27. 26.29, 25.52, 16.13 ppm; IR (neat): 3444 (OH), 2923, 1471, 1252, 1111, 823, 740, 702 cm^{-1} HRMS-CI m/z 441.2330 [$(M\text{-}OH)^+$; calcd for $C_{27}H_{38}ClOSi$: 441.2380].

General Procedure E.

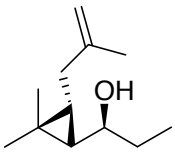


4

1-(3-allyl-2,2-dimethylcyclopropyl)propan-1-ol.

An oven-dried 25 mL round bottom flask that had been thoroughly purged with N_2 was charged with CuI (266 mg, 1.4 mmol) with dry THF (3 mL) and cooled to -50°C. A solution of *n*-BuLi (1.12 mL, 2.8 mmol, 2.5 M in decane) was slowly added and allowed to stir for 10 min at this temperature. 1-(3-iodo-2,2-

dimethylcyclopropyl)propan-1-ol (0.28 mmol) in dry THF (2 mL) was added to the resulting black solution of LiCu(*n*-Bu)$_2$ and the reaction was stirred for 30 min at -50^{o}C. Allyl bromide (121 μL, 1.4 mmol) was added and the solution was stirred at this temperature for 30 min and quenched with saturated solution of NH_4Cl (10 mL). The organic and aqueous layers were separated, and the aqueous layer was extracted with 3X10 mL dichloromethane. The combined organic layers were then washed with brine and dried over $MgSO_4$. The filtrate was concentrated *in vacuo* and the residue was chromatographed on deactivated silica (3% ethyl acetate in hexanes) to afford the title compound as a colorless oil in 75% yield. $[\alpha]_D^{20}$ = + 9.40 (c = 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 6.02 (m, 1H), 5.22 (m, 1H), 5.09 (m, 1H), 3.30 (m, 1H), 2.11 (m, 2H), 1.66 (m, 2H), 1.10 (t, 3H, *J* = 7.37 Hz), 1.02 (s, 3H), 0.91 (s, 3H), 0.75 (dt, 1H, *J* = 7.1, 8.3 Hz), 0.67 (dd, 1H, *J* = 8.3, 9.8 Hz) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz,): δ 139.78, 114.55, 70.54, 33.85, 31.56, 29.45, 29.28, 26.03, 22.15, 15.75, 10.44 ppm; IR (neat): 3459 (OH), 2929, 1619, 1376, 1114, 958, 801, 726, 660, 597 cm^{-1}; HRMS-CI m/z 151.1478 [(M-OH)$^+$; calcd for $C_{11}H_{19}$: 151.1491].



5

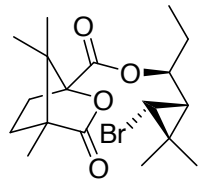
1-(2,2-dimethyl-3-(2-methylallyl)cyclopropyl)propan-1-ol.

The product was prepared by General Procedure E using 3-bromo-2-methylpropene (252 μL, 2.5 mmol). The crude product was purified by column chromatography on deactivated silica (5% ethyl acetate in hexanes) to afford the title compound as a colorless oil in 71% yield. $[\alpha]_D^{20}$ = +5.33 (c = 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 4.90 (m, 2H), 3.37 (dt, 1H, *J* = 4.6, 10.2 Hz), 2.19 (m, 2H), 1.84 (s. 3H), 1.70 (br s, 1H), 1.59 (m. 2H), 1.12 (s, 3H), 1.02 (s, 3H), 0.99 (t, 3H, *J* = 7.47 Hz), 0.85 (dt, 1H, *J* = 6.9,

8.1 Hz), 0.72 (dd, 1H, J = 8.1, 10.1 Hz) ppm; $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 75 MHz,): δ 147.99, 110.05. 71.32, 33.57, 32.93, 31.06, 29.70, 25.13, 23.67, 19.04, 16.10, 10.40 ppm; IR (neat): 3550 (OH), 2959, 2873, 1456, 1152, 1014, 958, 801, 672 cm^{-1}; HRMS-CI m/z 164.1567 [(M-$H_2O)^+$; calcd for $C_{12}H_{20}$: 164.1565].

Crystallizations

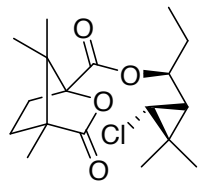
General Procedure F.



1-(3-bromo-2,2-dimethylcyclopropyl)propyl 4,7,7-trimethyl-3-oxo-2-oxa-bicyclo[2.2.1]heptane-1-carboxylate

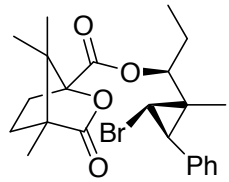
(-)-Camphanic chloride (0.9 mmol) was added to 1-(3-bromo-2,2-dimethylcyclopropyl)propan-1-ol (0.3 mmol) with 1.5 equiv DMAP and 2.0 mL CH_2Cl_2. The solution was stirred for 6 h until the reaction was complete by TLC. It was then quenched with H_2O (5 mL). The organic and aqueous layers were separated, and the aqueous layer was extracted with 3X15 mL dichloromethane. The combined organic layers were dried over $MgSO_4$. The filtrate was concentrated *in vacuo* and the residue was chromatographed on deactivated silica (5% ethyl acetate in hexanes) to afford the title compound. The compound was dissolved in minimum amount of *n*-pentane and crystals were grown by slow evaporation of the solvent at room temperature. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 4.88 (dt, 1H, J = 10.30, 6.15 Hz), 2.83 (d, 1H, J = 7.46 Hz), 2.37 (m, 1H), 2.02 (m, 1H), 1.84 (m, 1H), 1.65 (m, 2H), 1.57 (m, 1H), 1.09 (s, 3H), 1.07 (m, 1H), 1.06 (s, 3H), 1.03 (s, 3H), 1.02 (s. 3H), 0.90 (s, 3H), 0.85 (t, 3H, J = 7.47 Hz) ppm; $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz,): δ 178.67, 166.95, 91.49,

76.25, 55.23, 54.46, 34.26, 31.19, 30.34, 29.41, 28.14, 27.39, 21.21, 18.52, 17.16, 16.98, 10.03, 9.44 ppm; HRMS-CI m/z 387.1187 [$(MH)^+$; calcd for $C_{18}H_{28}BrO_4$: 387.1170].



1-(3-chloro-2,2-dimethylcyclopropyl)propyl 4,7,7-trimethyl-3-oxo-2-oxa-bicyclo[2.2.1]heptane-1-carboxylate.

The product was prepared by General Procedure F using 1-(3-chloro-2,2-dimethylcyclopropyl)propan-1-ol (0.3 mmol). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 4.89 (dt, 1H, *J* = 10.57, 6.02 Hz), 2.92 (d, 1H, *J* = 7.47 Hz), 2.35 (m, 1H), 1.99 (m, 1H), 1.85 (m, 1H), 1.67 (m, 2H), 1.61 (m, 1H), 1.12 (s, 3H), 1.08 (m, 1H), 1.06 (s, 3H), 1.05 (s, 3H), 1.03 (s. 3H), 0.93 (s, 3H), 0.88 (t, 3H, *J* = 7.47 Hz) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz,): δ 178.64, 166.80, 91.40, 74.56, 55.09, 54.34, 42.84, 30.98, 30.59, 29.28, 28.11, 27.10, 21.50, 17.00, 16.79, 16.21, 9.91, 9.31 ppm; HRMS-CI m/z 343.1688 [$(MH)^+$; calcd for $C_{18}H_{28}ClO_4$: 343.1675].



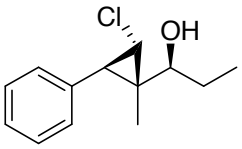
1-(2-bromo-1-methyl-3-phenylcyclopropyl)propyl 4,7,7-trimethyl-3-oxo-2-oxabicyclo[2.2.1]heptane-1-carboxylate.

The product was prepared by General Procedure F using 1-(2-bromo-1-methyl-3-phenylcyclopropyl)propan-1-ol (0.3 mmol). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.27 (m, 2H), 7.21 (m, 3H), 4.48 (dt, 1H, *J* = 8.65, 5.04 Hz), 3.55 (d, 1H, *J* = 8.92 Hz), 2.40 (m, 1H), 2.22 (d, 1H, *J* = 8.35 Hz), 2.02 (m, 1H), 1.85 (m, 3H), 1.66 (m, 1H), 1.08 (s, 3H), 1.06 (s, 3H), 1.03 (s, 3H), 0.96 (s. 3H), 0.94 (s, 3H) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz,): δ 178.3, 167.7, 133.6, 130.9, 128.5, 127.1, 91.5, 83.1, 55.1, 54.3, 42.6, 31.0, 29.3, 29.2, 29.0, 28.8,

25.2, 24.9, 17.1, 16.9, 13.3, 10.8, 10.7, 9.9 ppm; HRMS-CI m/z 449.1349 [$(MH)^+$; calcd for $C_{23}H_{30}BrO_4$: 449.1327].

Preparation of diastereomers of 3c

The diastereomers of **3c** were prepared by literature method [4-5] using (*E*)-2-methyl-1-phenylpent-1-en-3-ol and detail procedures are below.



To a stirred solution of (*E*)-2-methyl-1-phenylpent-1-en-3-ol (176 mg, 1 mmol) in $CHCl_3$ (1 mL) at 0 ^oC, was added 50 w/w% NaOH (1 mL) dropwise. The resulting solution was stirred for 4 h after which water and diethyl ether (10 mL: 10 mL) were added. After normal workup procedure, the dichlorocyclopropane was obtained.[4] (^1H NMR ($CDCl_3$, 500 MHz): δ 7.36 (m, 2H), 7.30 (m, 1H), 7.26 (m, 2H), 3.62 (dd, 1H, *J* = 3.6, 8.8 Hz), 2.58 (s, 1H), 2.15 (br s, 1H), 1.84 (m, 2H), 1.21 (s, 3H), 1.11 (t, 3H, *J* = 7.48 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz,): δ 132.75, 130.00, 128.40, 127.40, 79.07, 70.46, 40.22, 38.99, 26.93, 11.25, 10.84 ppm). To a solution of dichlorocyclopropane (225 mg, 0.87 mmol) in dry toluene (2 mL) at 60 ^oC, was added AIBN (1.8 mg, 0.01 mmol) followed by *n*-Bu_3SnH (0.29 mL, 1.1 mmol). The resulting solution was heated at 120 ^oC for 4 h and cooled to ambient temperature. The reaction mixture was diluted with hexanes (2 mL) and directly loaded on flash column packed with SiO_2. A gradual increase of eluent (from 100% hexanes to 3% ethyl acetate in hexanes) gave the fractions containing unreacted dichlorocyclopropyl alcohol and the desired chlorocyclopropyl alcohol.[5] Unfortunately, we were unable to separate the starting dichlorocyclopropyl alcohol from the

monochlorocyclopropyl alcohol.; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.30 (m, 2H), 7.25 (m, 2H), 7.13 (m, 1H), 3.58 (m, 1H), 3.39 (d, 1H, *J* = 4.60 Hz), 2.32 (d, 1H, *J* = 4.60 Hz), 2.03 (br s, 1H), 1.70 (m, 2H), 1.20 (s 3H), 1.08 (t, 3H, *J* = 7.49 Hz) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz,): δ 135.48, 131.16, 128.35, 126.77, 77.69, 43.55, 36.83, 33.75, 26.18, 11.94, 11.03 ppm. Further elution gave the major diastereomer **3c** which was identical to the chlorocyclopropyl alcohol obtained in Scheme 7.

Stereochemistry Assignment

Table S1. Stereochemistry Assignment of Compounds in Table 2

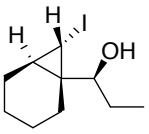
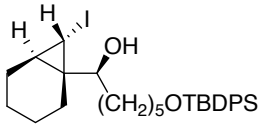
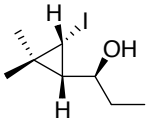
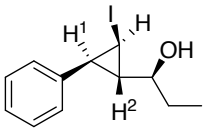
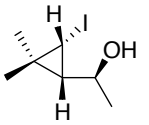
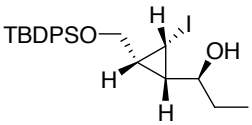
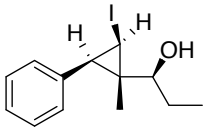
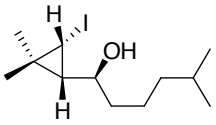
compound	coupling constant	compound	coupling constant
	*J* = 4.9 Hz		*J* = 4.9 Hz
	*J* = 7.8 Hz		*J* (H-H^1) = 8.2 Hz J (H-H^2) = 4.9 Hz
	*J* = 7.8 Hz		*J* = 7.8, 7.7 Hz
	*J* = 8.4 Hz		*J* = 7.8 Hz

Table S2. Stereochemistry Assignment of Compounds in Table 3

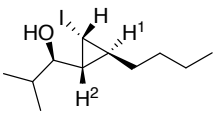
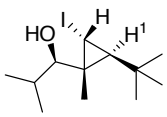
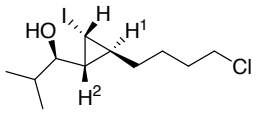
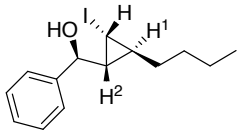
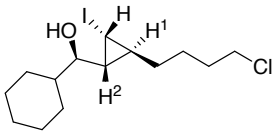
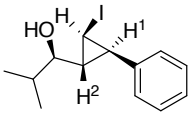
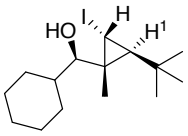
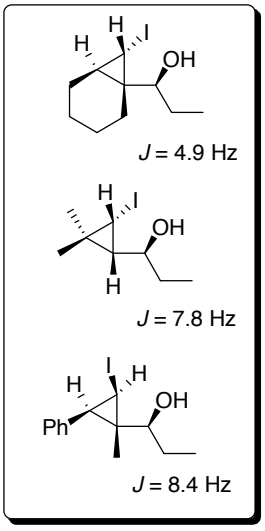
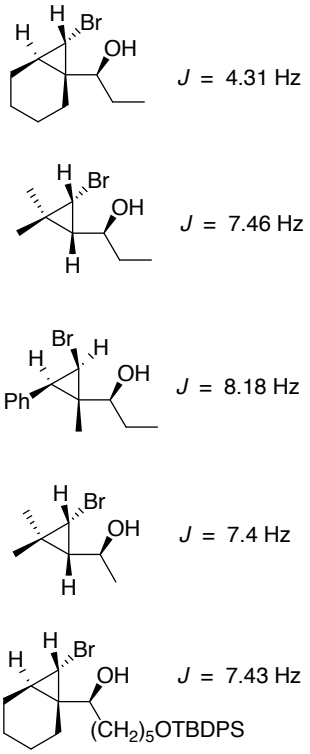
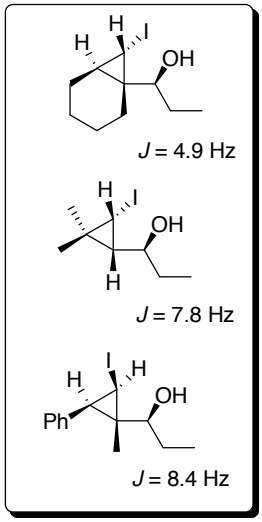
compound	coupling constant	compound	coupling constant
	J (H-H^1) =4.4 Hz J (H-H^2) = 7.8 Hz		J (H-H^1) = 6.72 Hz
	J (H-H^1) = 4.49 Hz J (H-H^2) = 7.93 Hz		J (H-H^1) = 4.49 Hz J (H-H^2) = 7.73 Hz
	J (H-H^1) =4.4 Hz J (H-H^2) = 7.6 Hz		J (H-H^1) = 8.23 Hz J (H-H^2) = 4.50 Hz
	J (H-H^1) = 6.76 Hz		

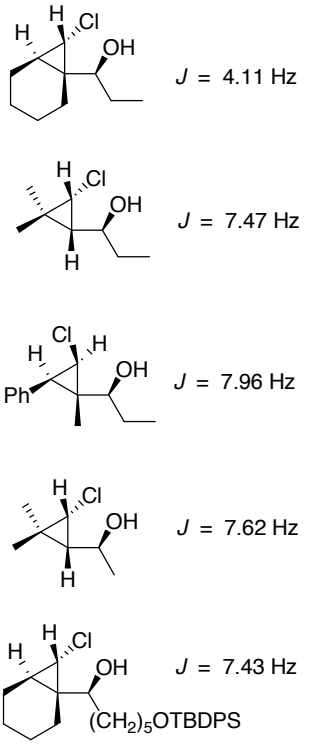
Table S3. Stereochemistry Assignment of Compounds in Table 4

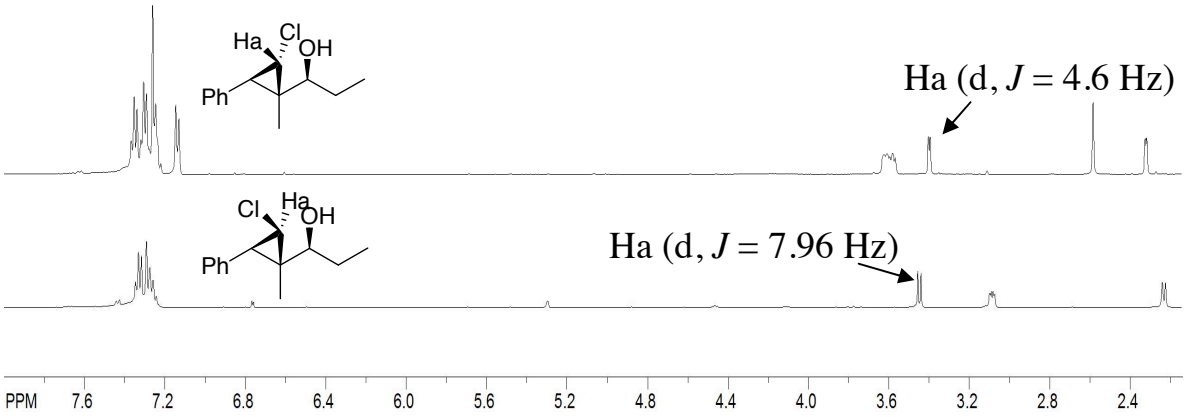
Stereochemistry of entry 2 and 7 (compounds **2b** and **3b**) were confirmed by X-ray structure determinations. The relative stereochemistry of bromide and chloride were compared to that of iodide previously reported[3] and assigned using NMR coupling constants, as shown below.

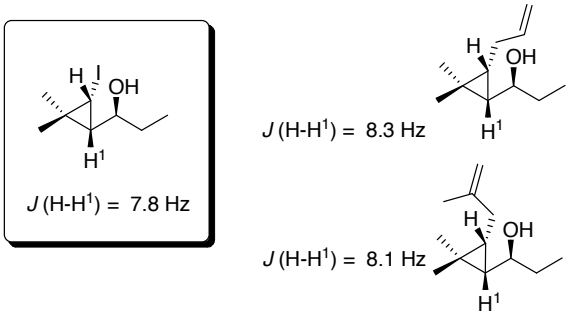

H
I
OH
J = 4.9 Hz
H
I
OH
H
J = 7.8 Hz
I
H
H
OH
Ph
J = 8.4 Hz


H
Br
H
OH
J = 4.31 Hz
H
Br
OH
H
J = 7.46 Hz
Br
H
H
OH
Ph
J = 8.18 Hz
H
Br
OH
H
J = 7.4 Hz
H
Br
H
OH
J = 7.43 Hz
(CH2)5OTBDPS


H
I
H
OH
J = 4.9 Hz
H
I
OH
H
J = 7.8 Hz
I
H
H
OH
Ph
J = 8.4 Hz


H
Cl
H
OH
J = 4.11 Hz
H
Cl
OH
H
J = 7.47 Hz
Cl
H
H
OH
Ph
J = 7.96 Hz
H
Cl
OH
H
J = 7.62 Hz
H
Cl
H
OH
J = 7.43 Hz
(CH2)5OTBDPS





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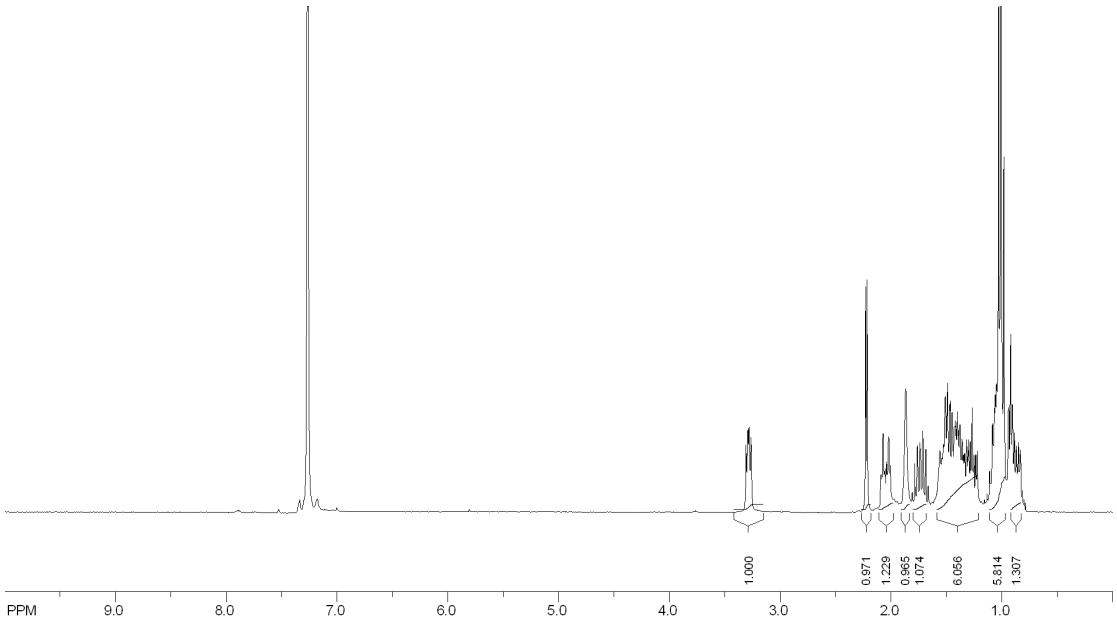
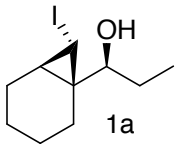
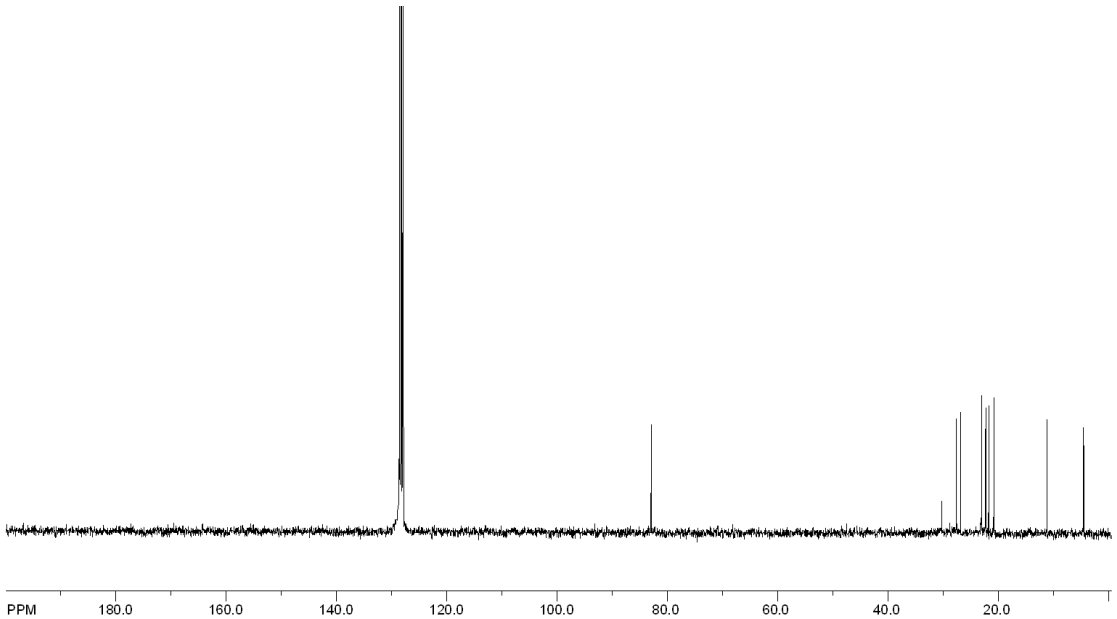
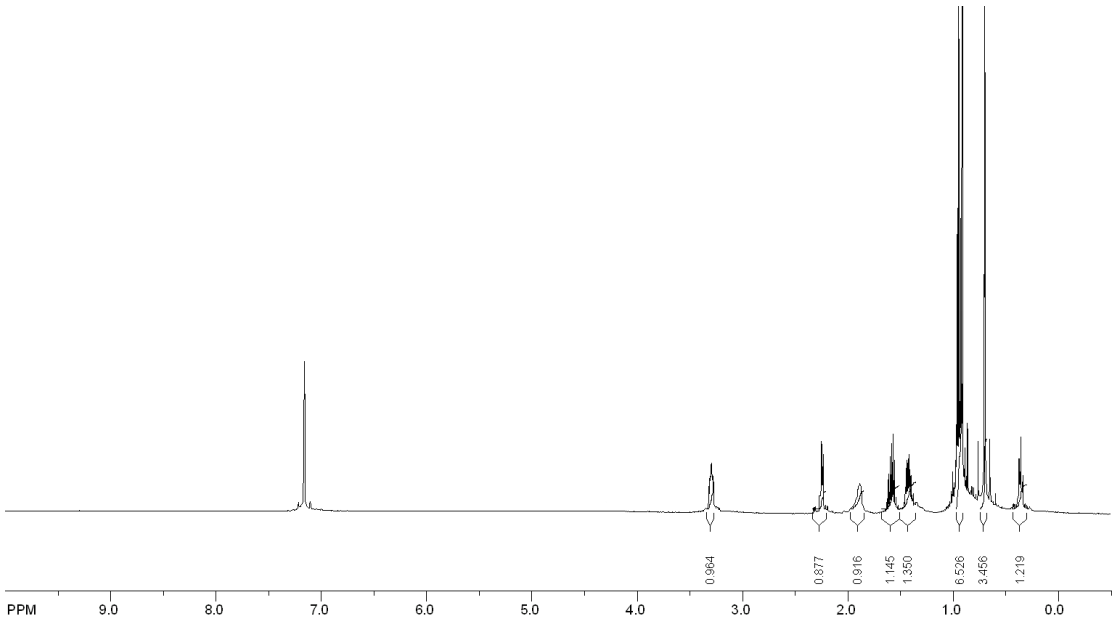


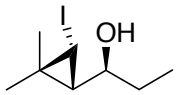


1a

1-(7-iodobicyclo[4.1.0]heptan-1-yl)propan-1-ol

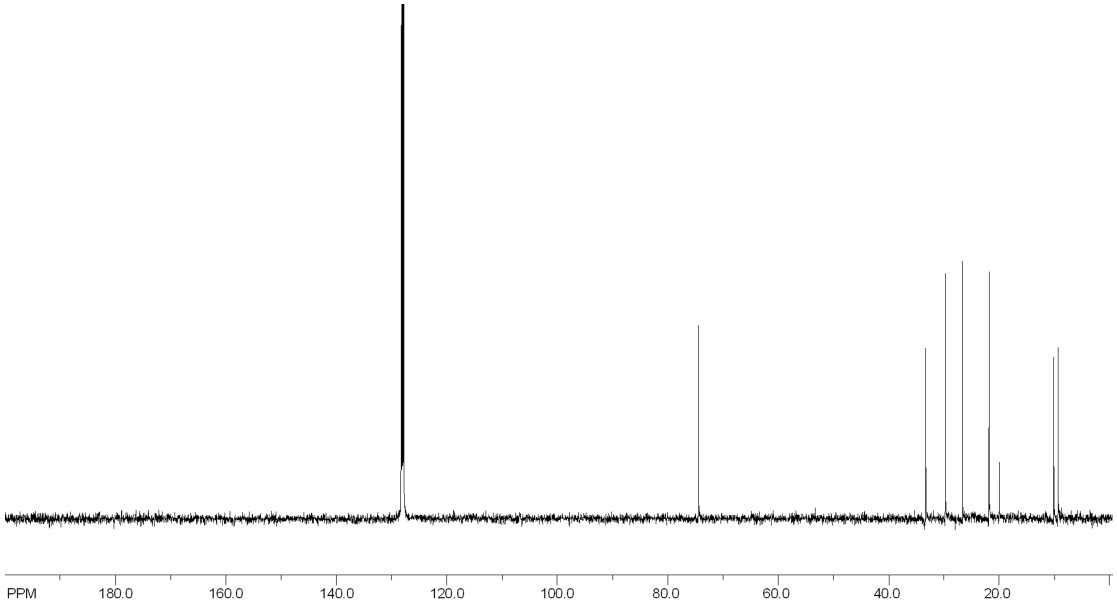


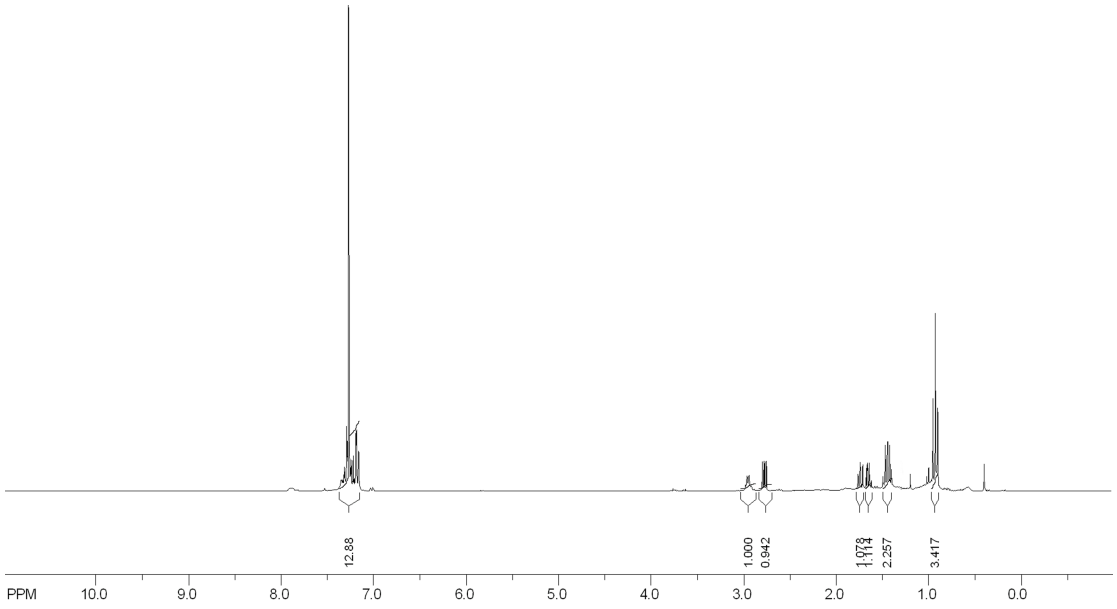


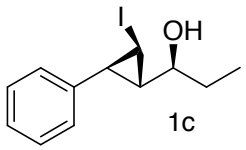


1b

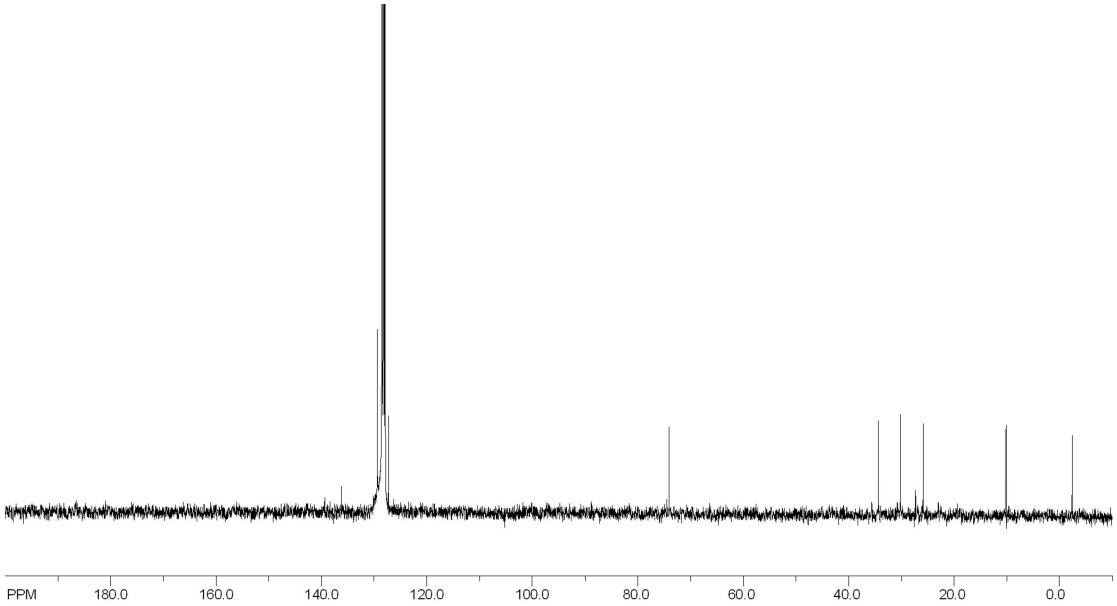
1-(3-iodo-2,2-dimethylcyclopropyl)propan-1-ol

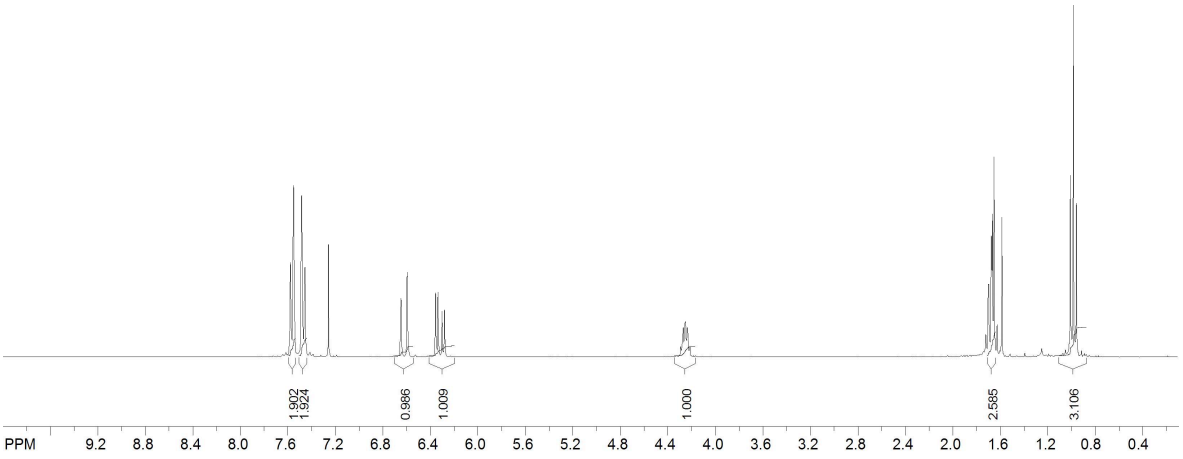


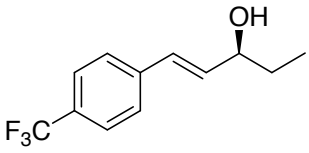




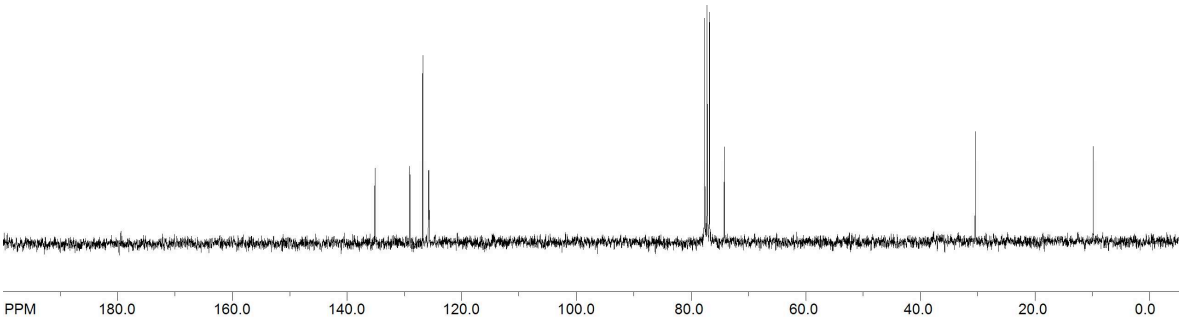
1-(2-iodo-3-phenylcyclopropyl)propan-1-ol

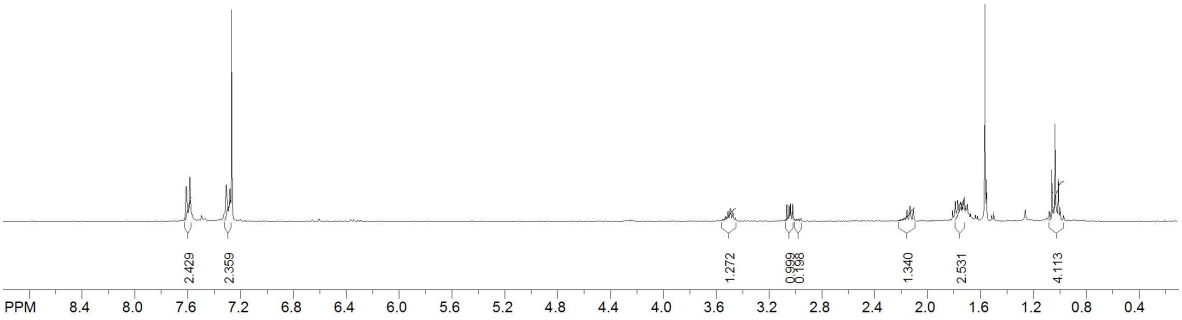


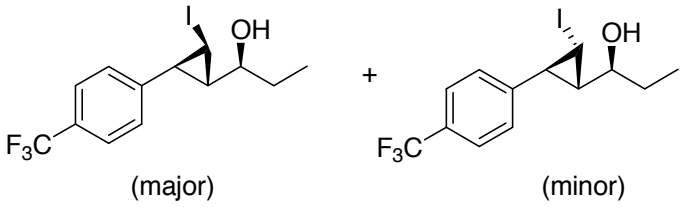




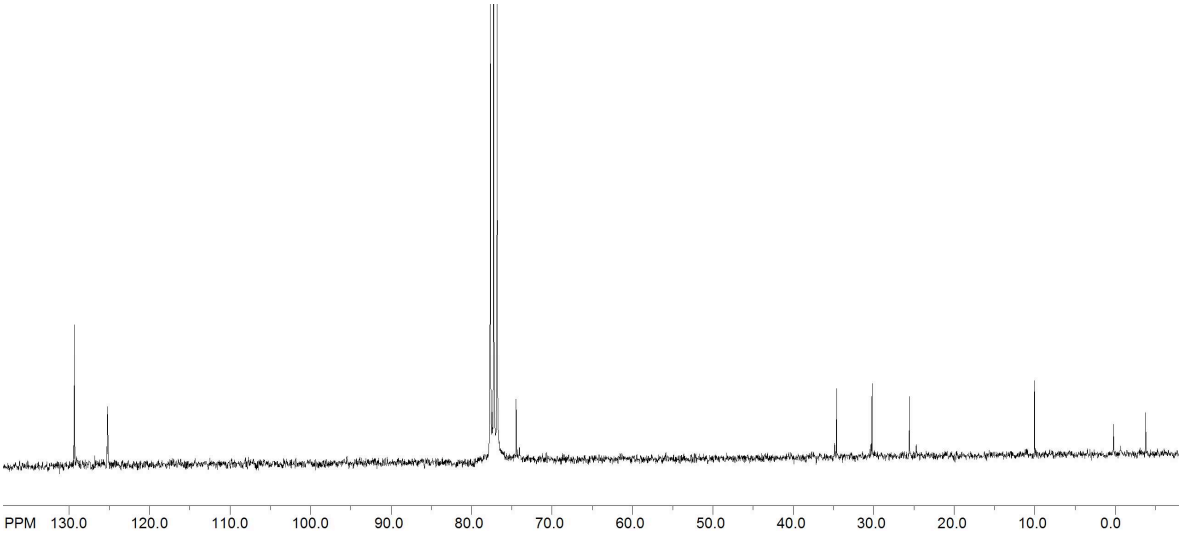
(*E*)-1-(4-(trifluoromethyl)phenyl)pent-1-en-3-ol

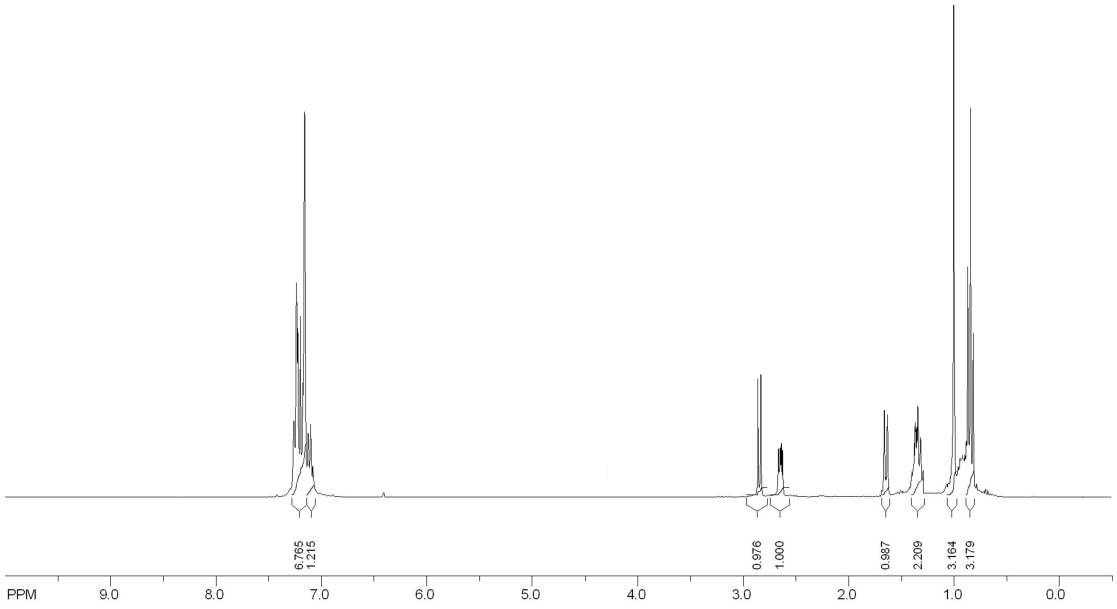


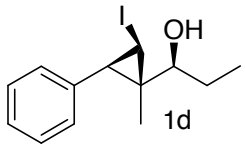




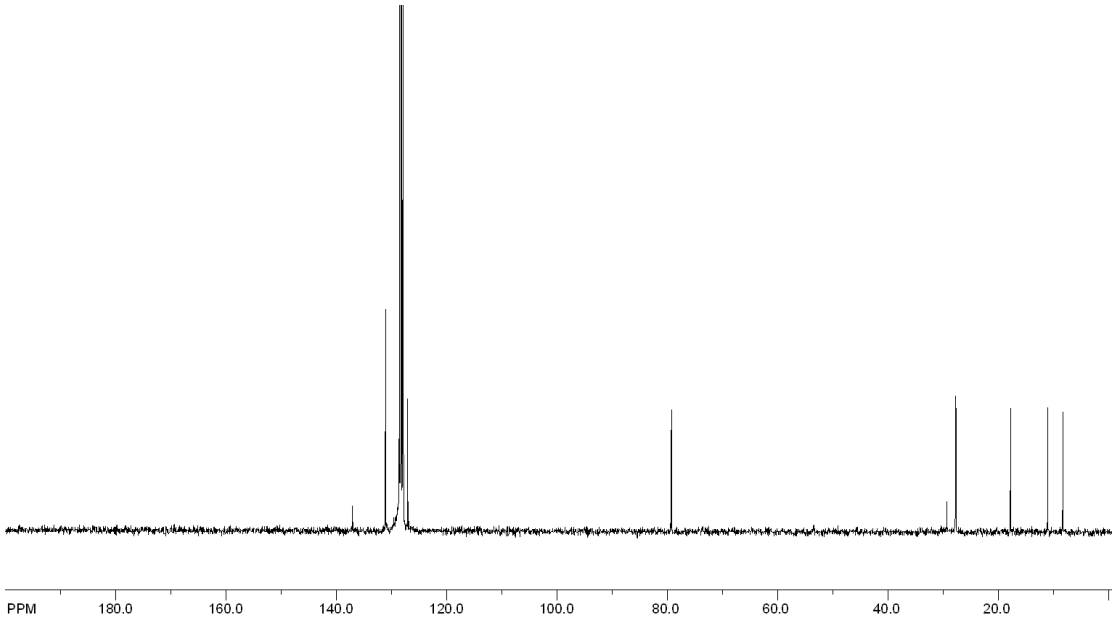
1-(2-(4-(trifluoromethyl)phenyl)-3-iodocyclopropyl)propan-1-ol

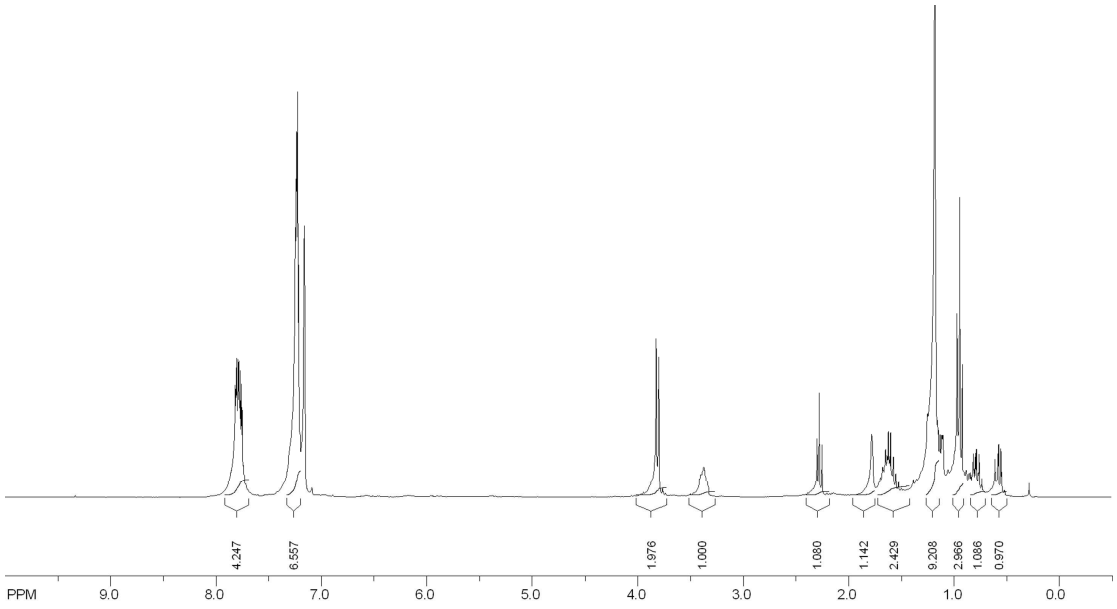


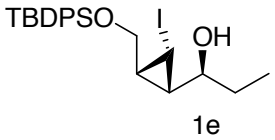




1-(2-iodo-1-methyl-3-phenylcyclopropyl)propan-1-ol

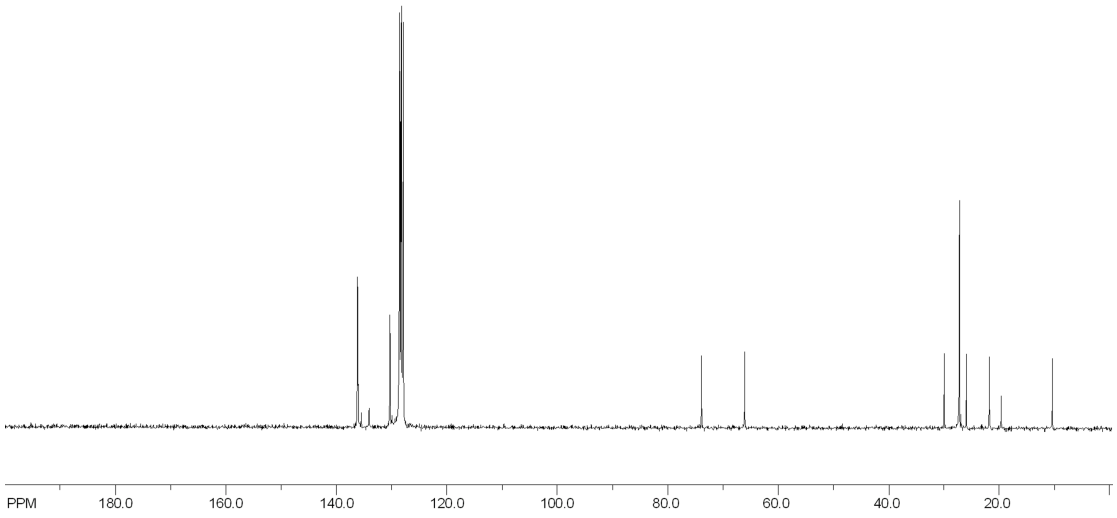


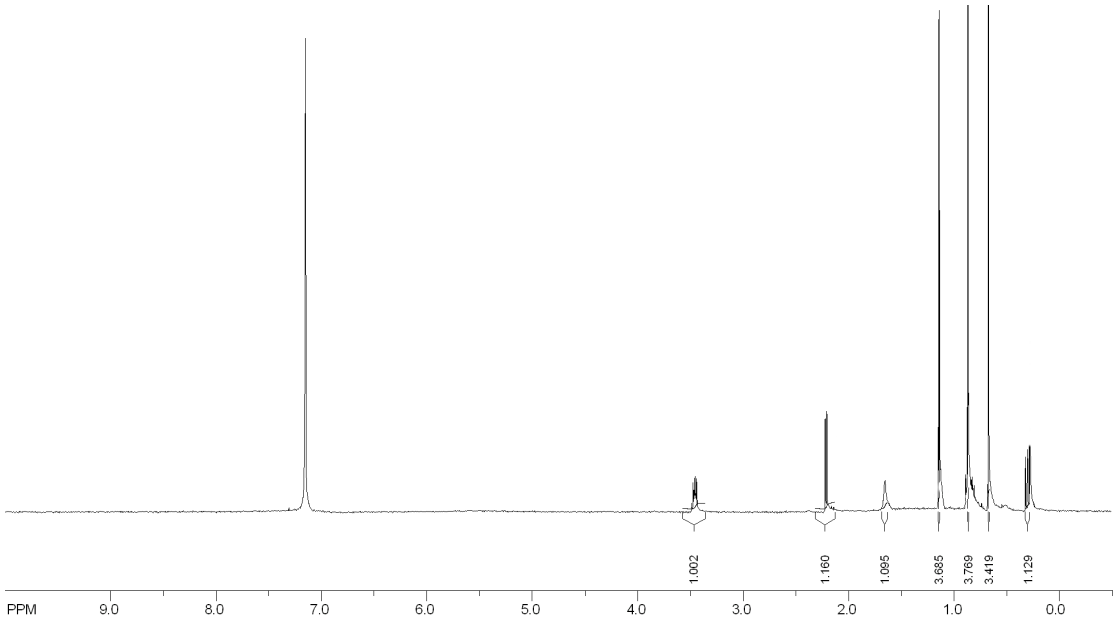


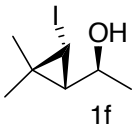


1e

1-[2-(tert-Butyl-diphenyl-silanyloxymethyl)-3-iodo-cyclopropyl]-propan-1-ol

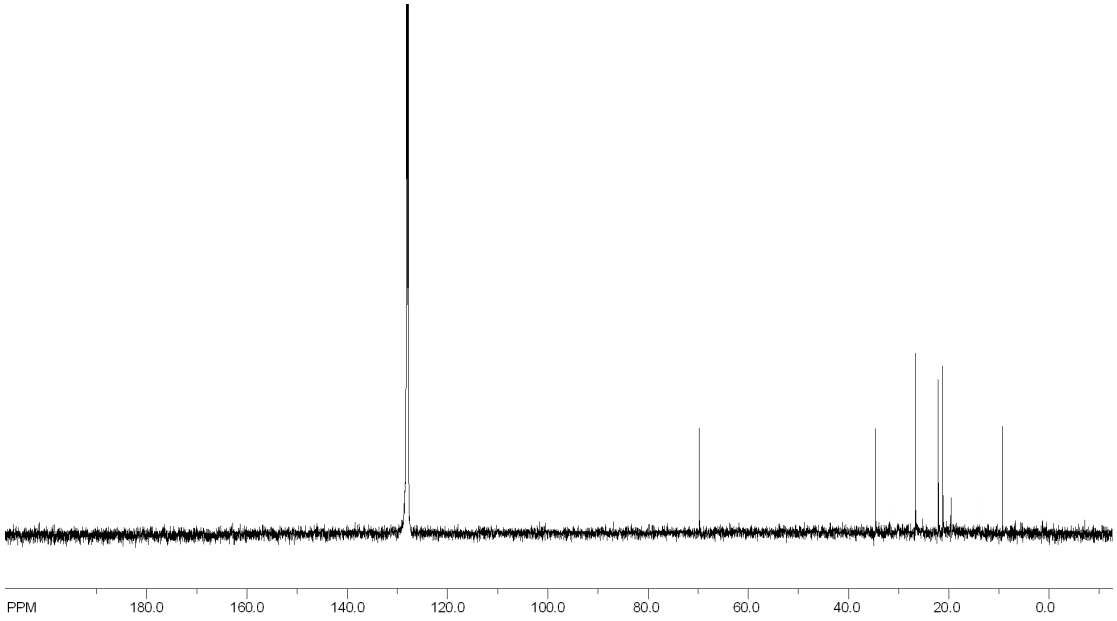


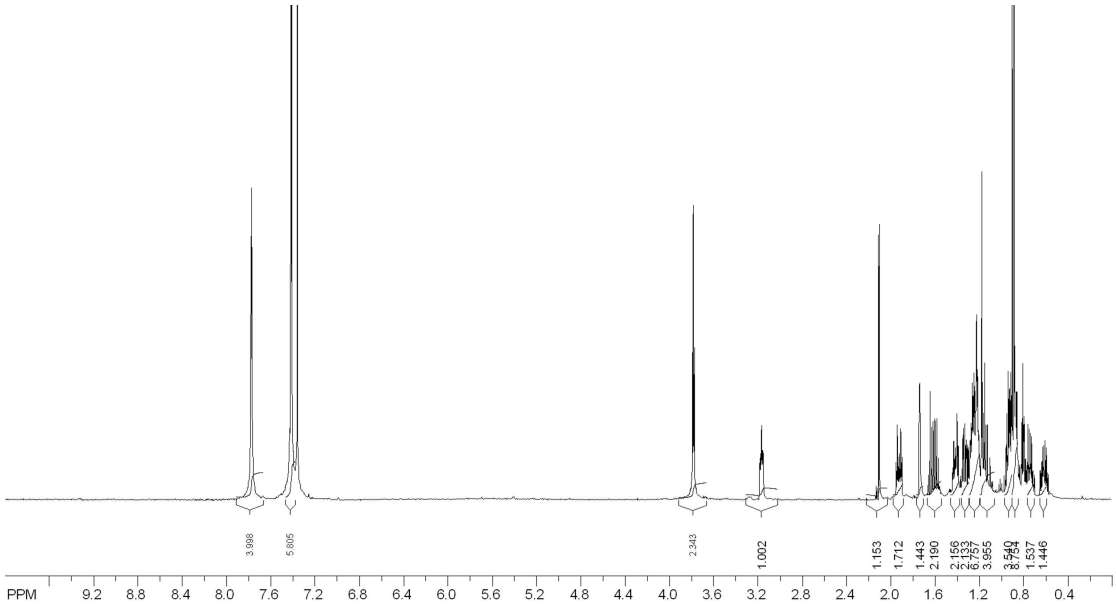


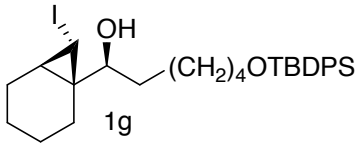


1f

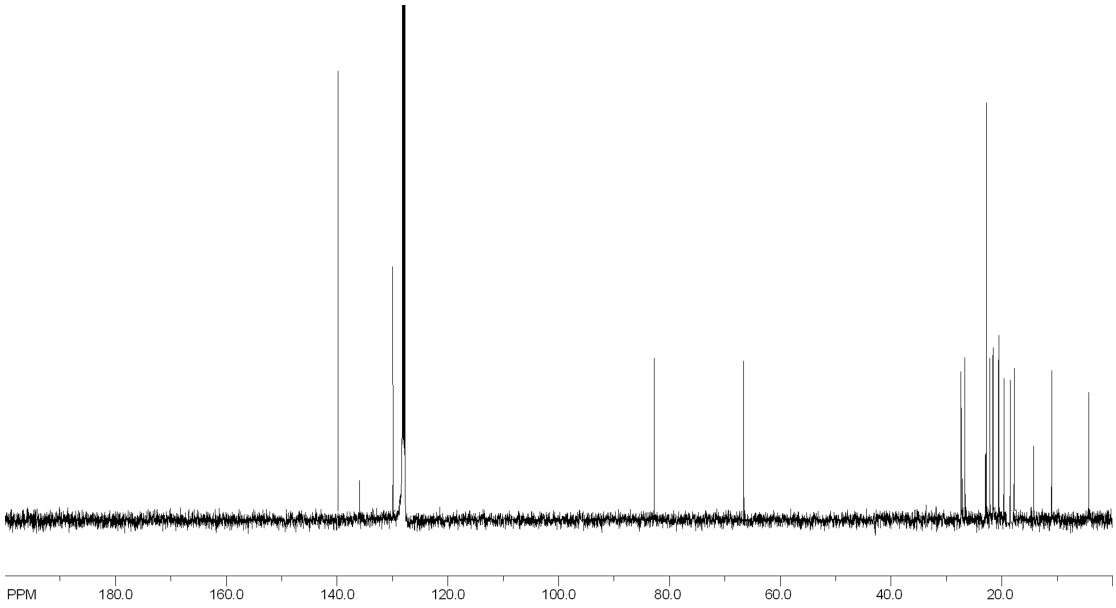
1-(3-iodo-2,2-dimethylcyclopropyl)ethanol

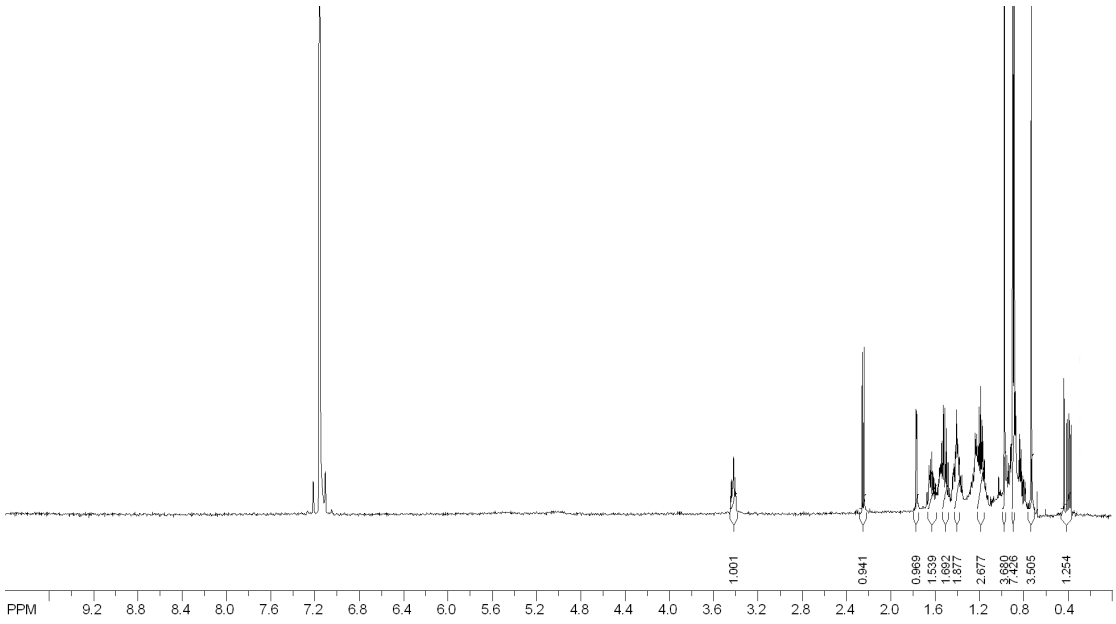


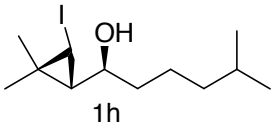




6-(tert-Butyl-diphenyl-silanyloxy)-1-(7-iodo-bicyclo[4,1,0]hept-1-yl)-hexan-1-ol

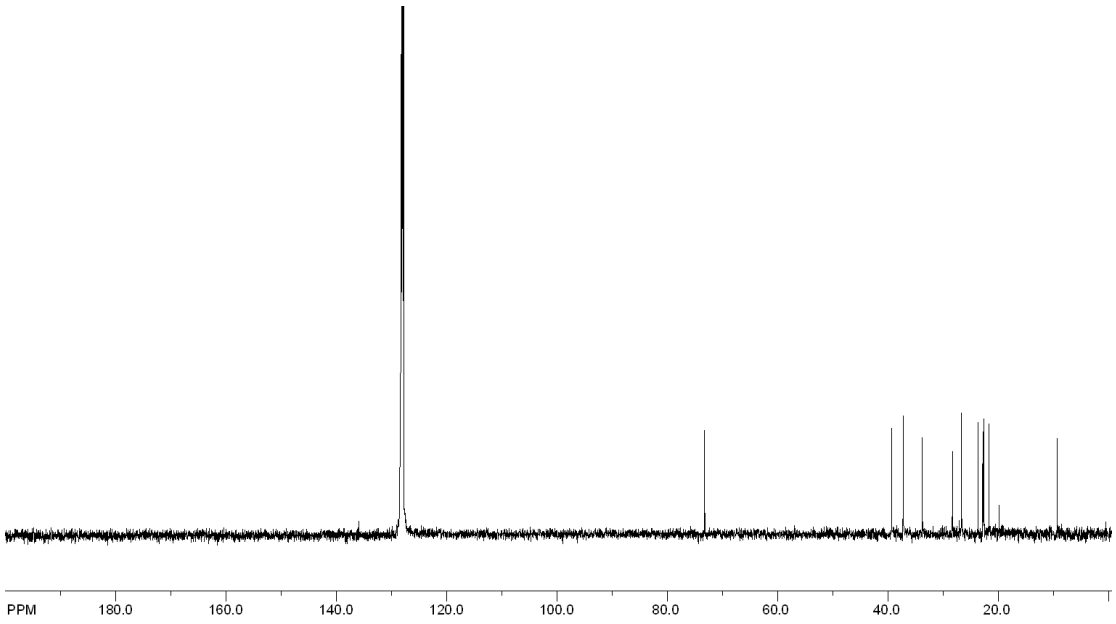


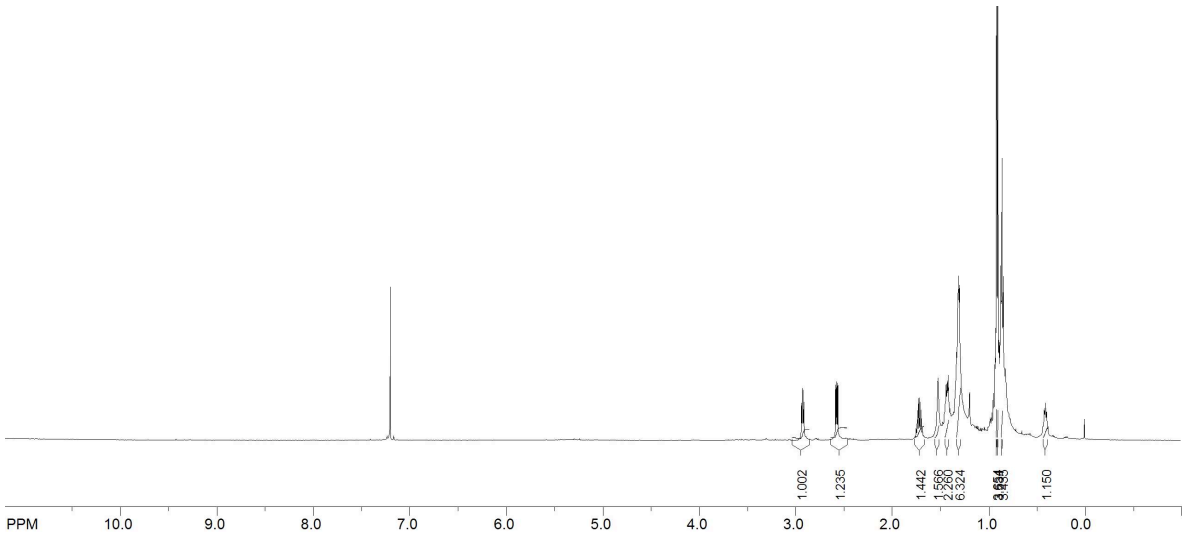


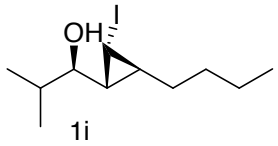


1h

1-(3-iodo-2,2-dimethylcyclopropyl)-5-methylhexan-1-ol

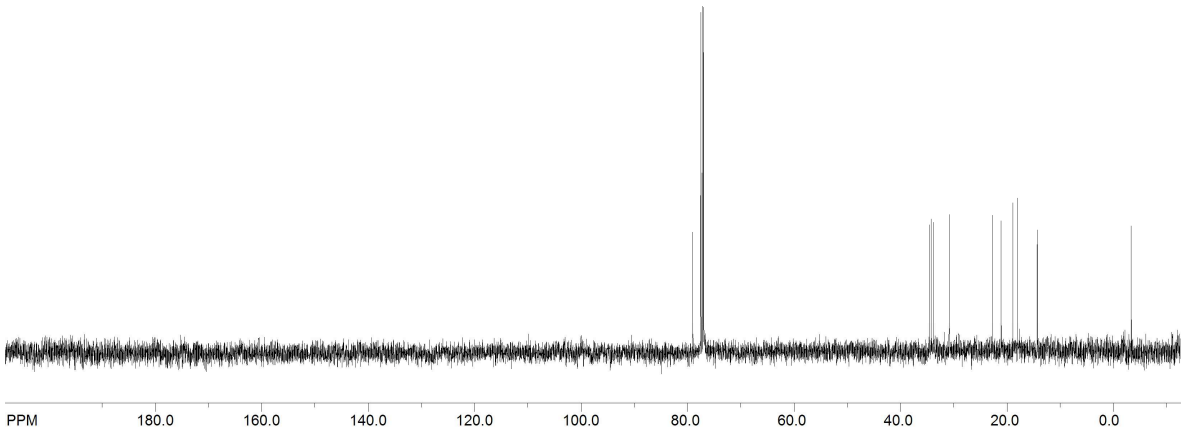


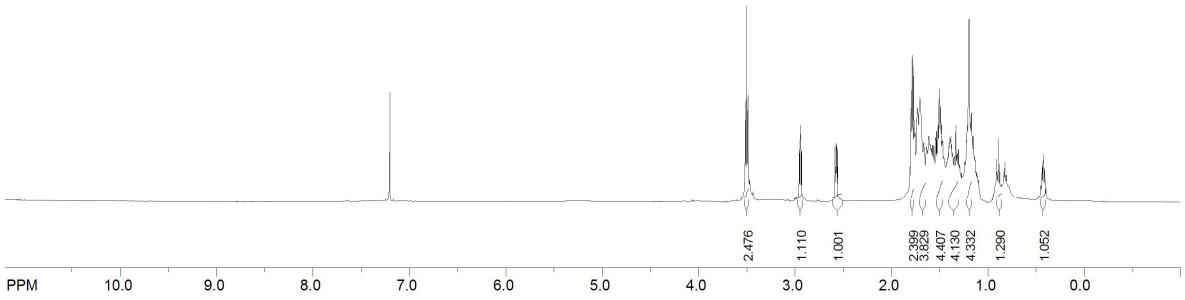


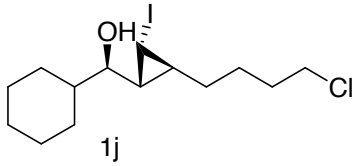


1i

1-(2-butyl-3-iodocyclopropyl)-2-methylpropan-1-ol

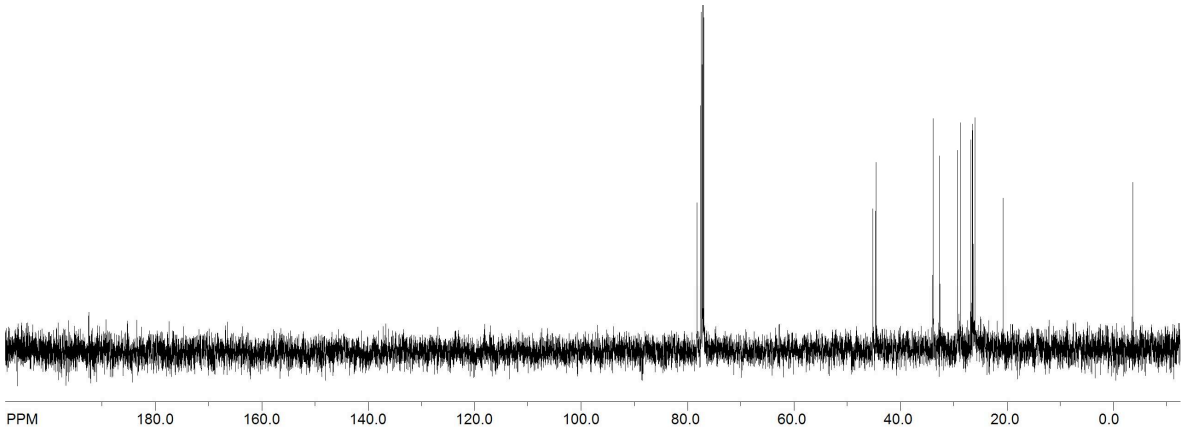


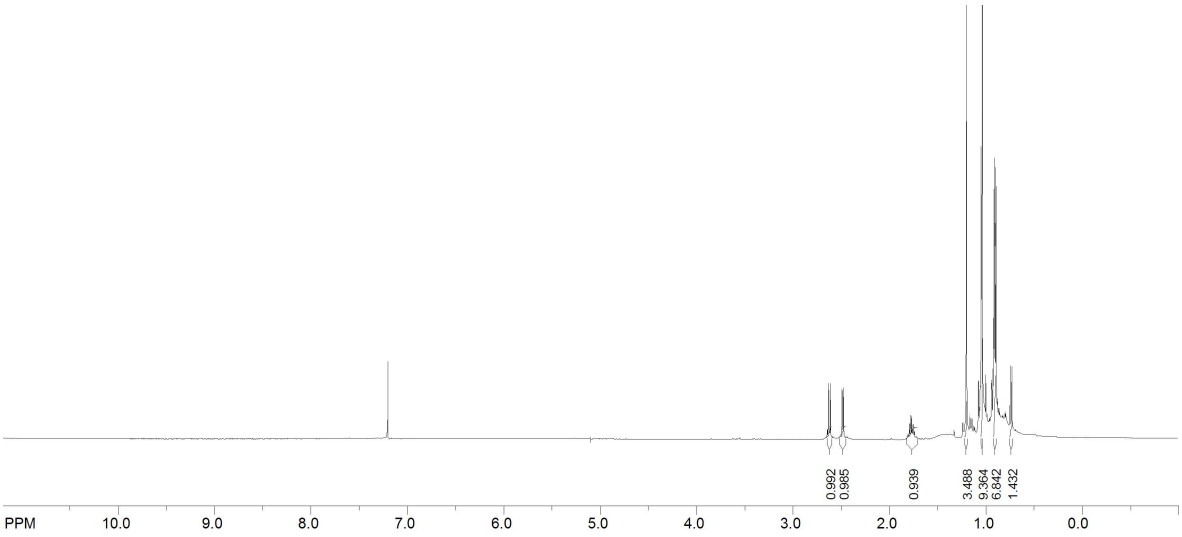


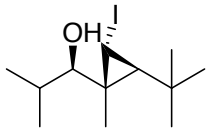


1j

(2-(4-chlorobutyl)-3-iodocyclopropyl)(cyclohexyl)methanol

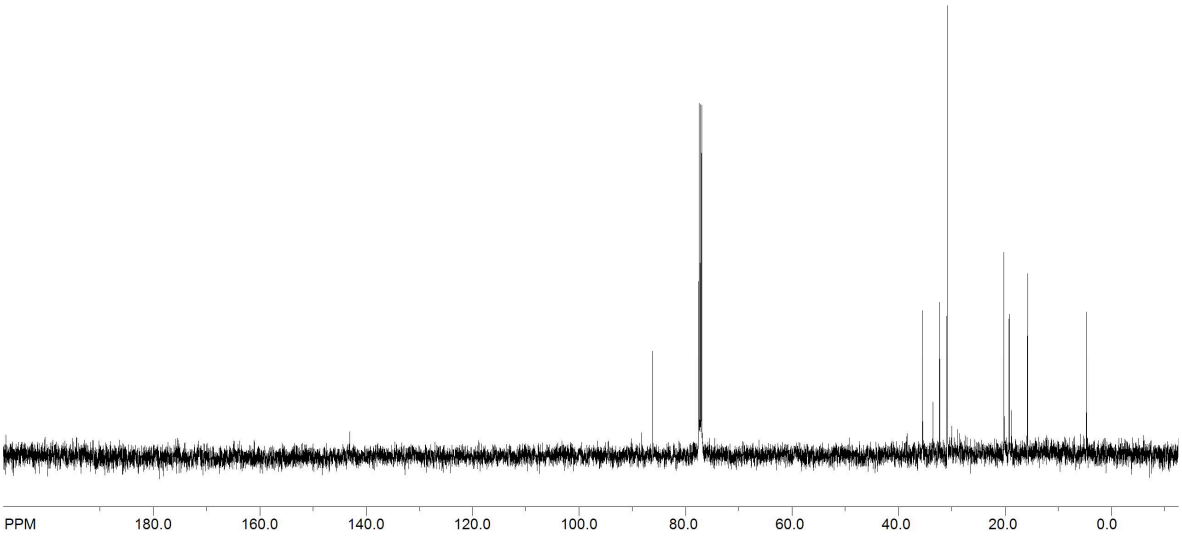


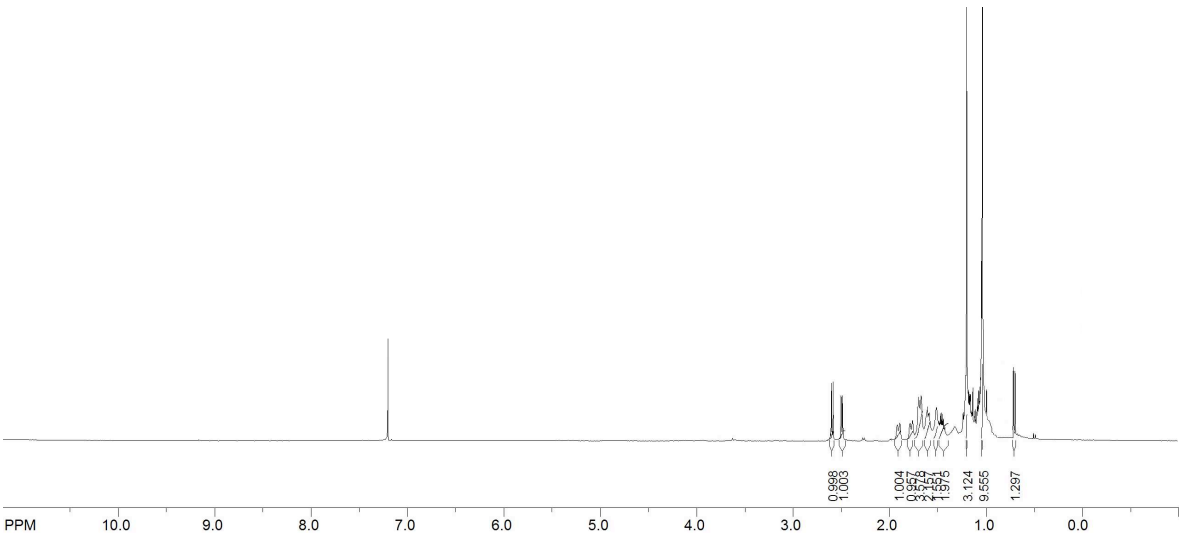


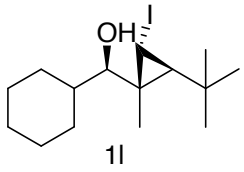


1k

1-(2-*tert*-butyl-3-iodo-1-methylcyclopropyl)-2-methylpropan-1-ol

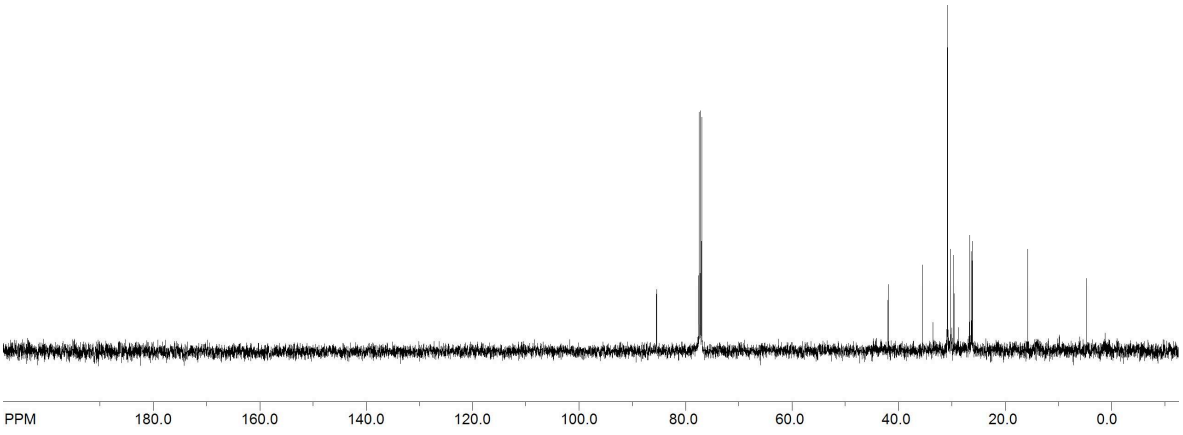


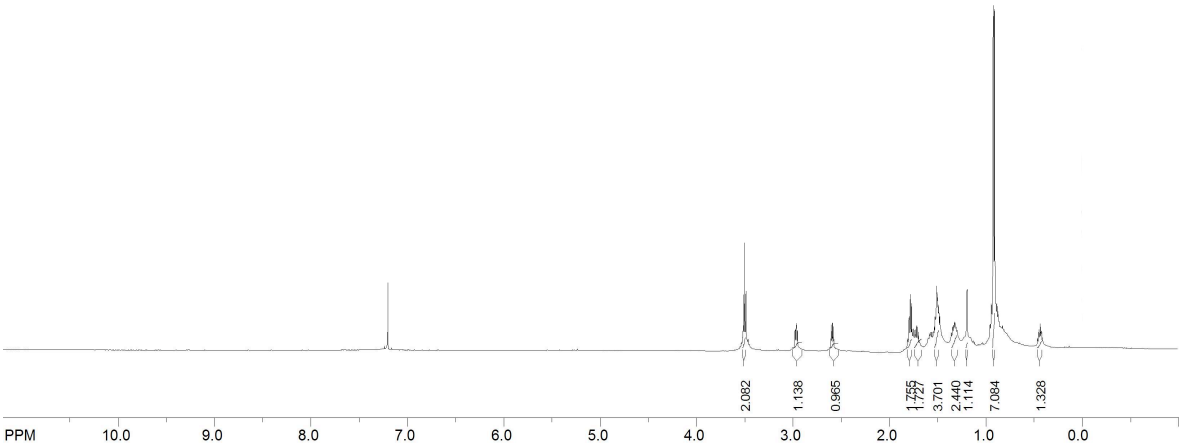


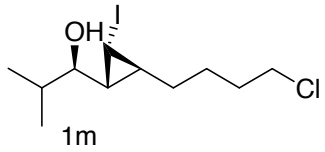


1l

((3*R*)-2-*tert*-butyl-3-iodo-1-methylcyclopropyl)(cyclohexyl)methanol

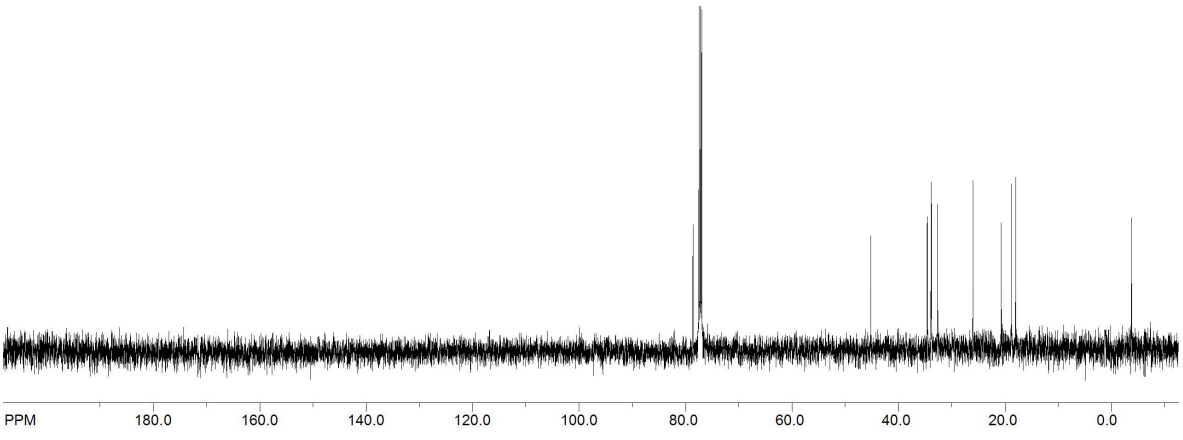


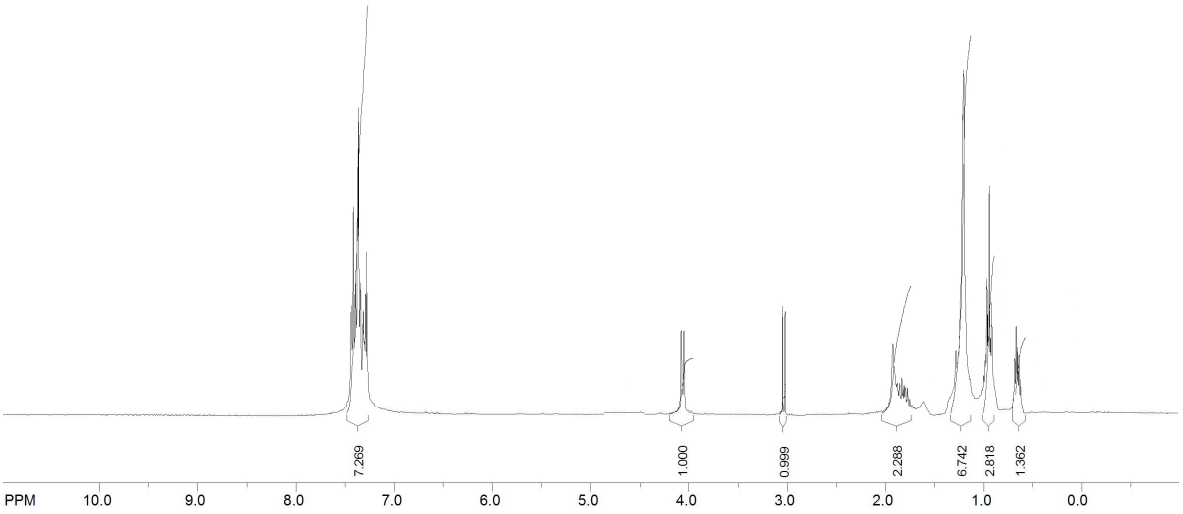


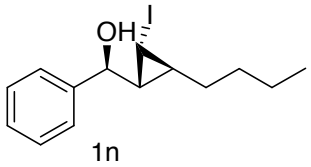


1m

1-(2-(4-chlorobutyl)-3-iodocyclopropyl)-2-methylpropan-1-ol

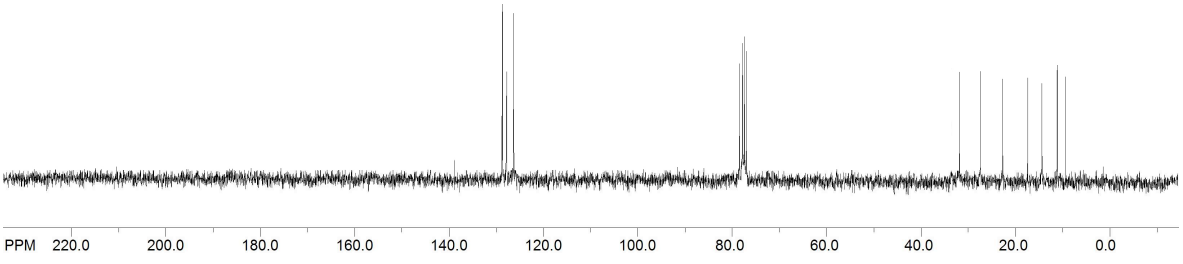


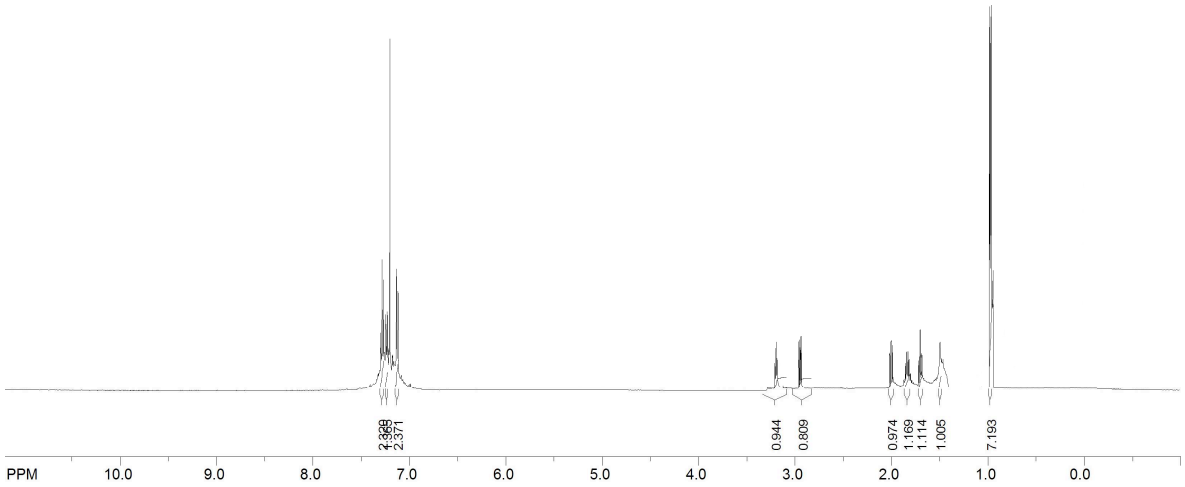


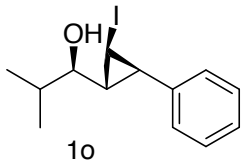


1n

(2-butyl-3-iodocyclopropyl)(phenyl)methanol

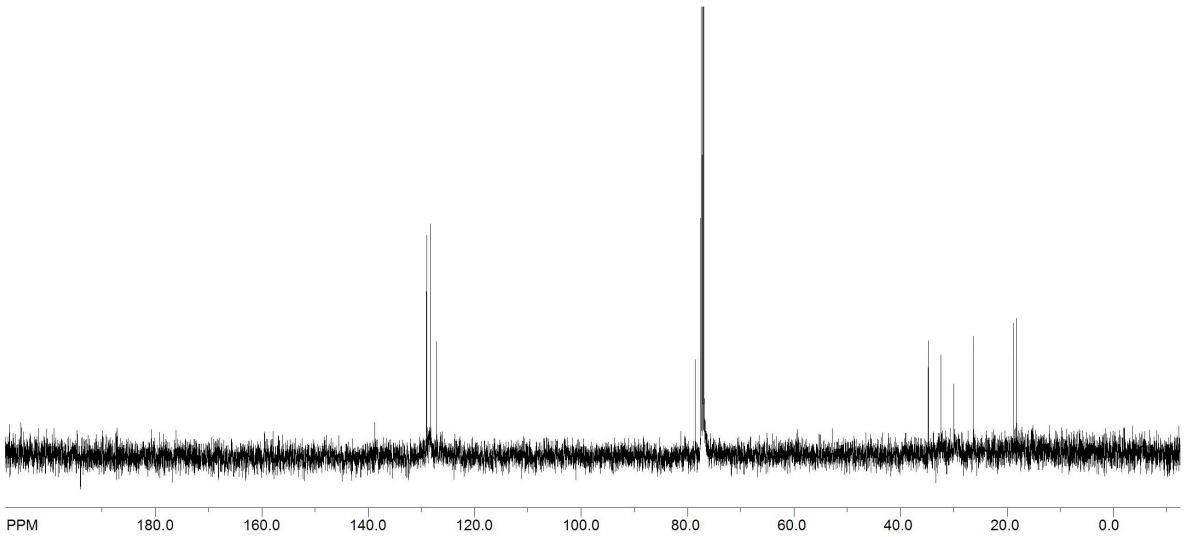


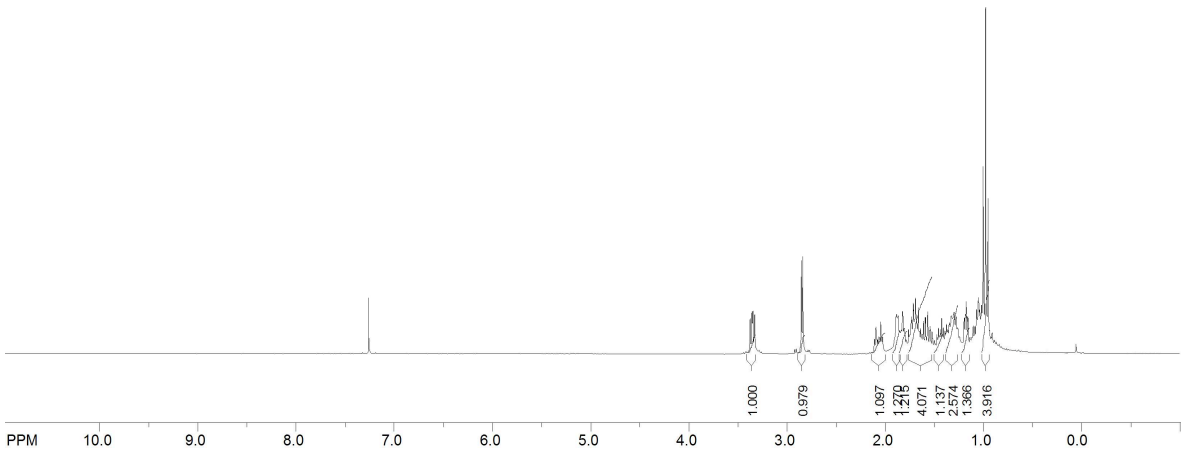


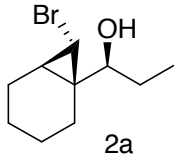


1o

1-(2-iodo-3-phenylcyclopropyl)-2-methylpropan-1-ol

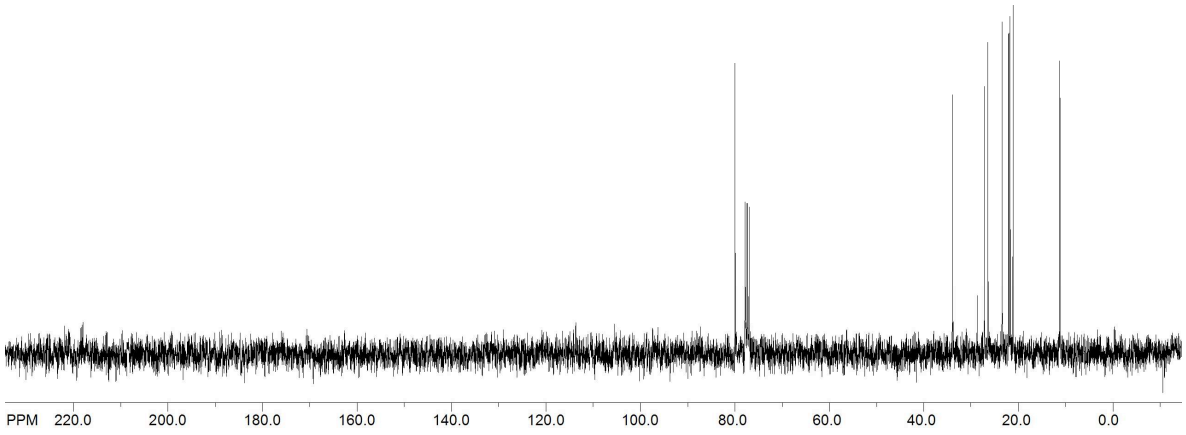


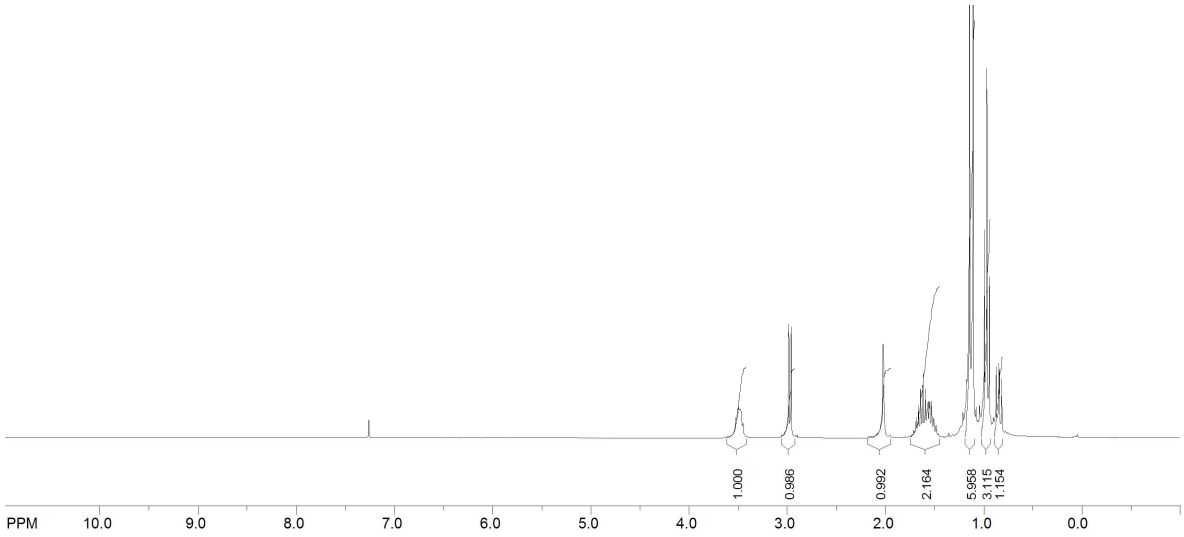


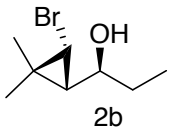


2a

1-(7-bromobicyclo[4.1.0]heptan-1-yl)propan-1-ol

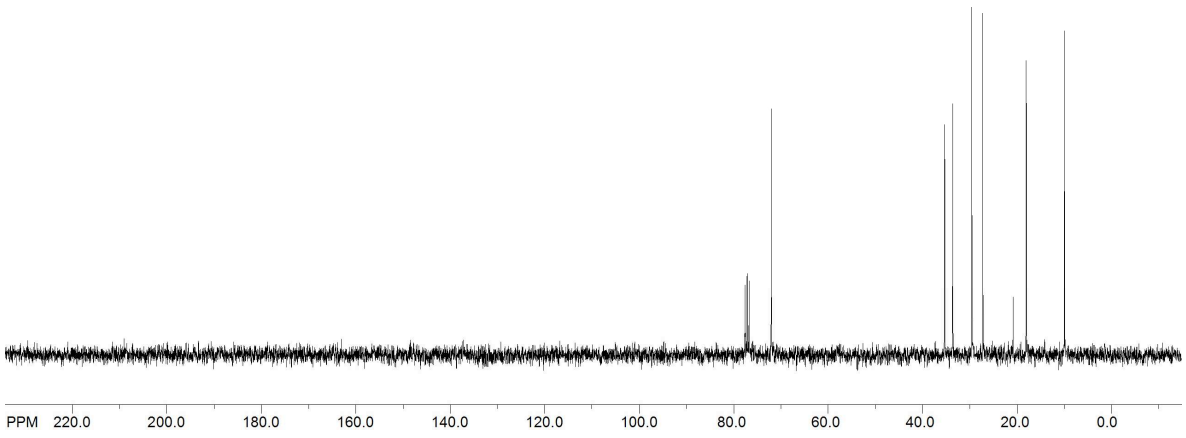


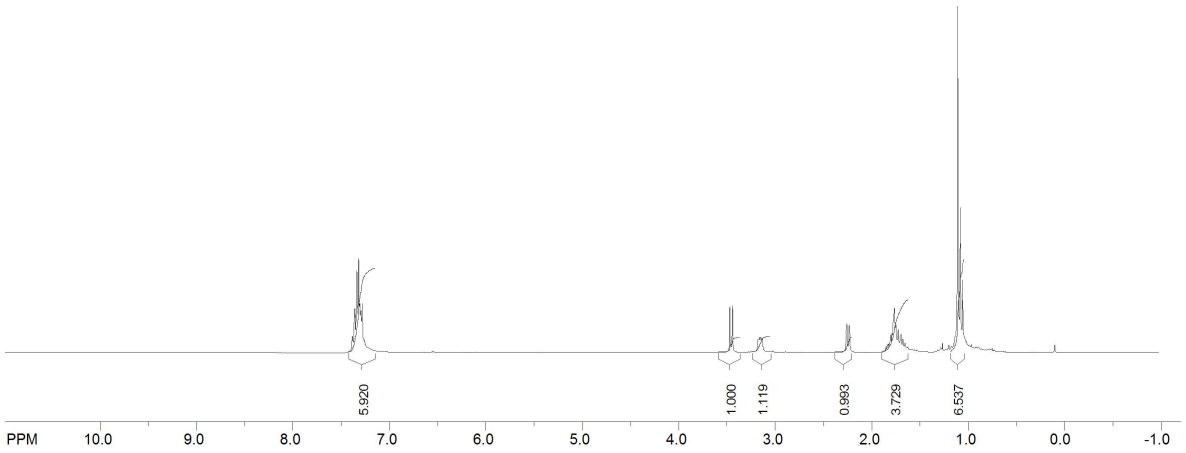


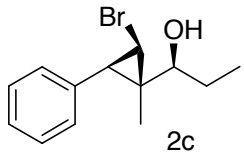


2b

1-(3-bromo-2,2-dimethylcyclopropyl)propan-1-ol

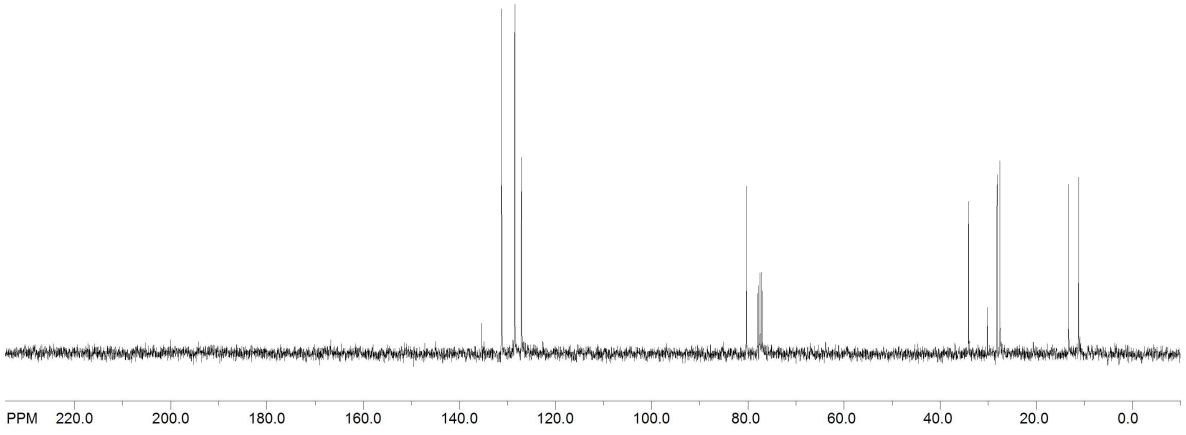


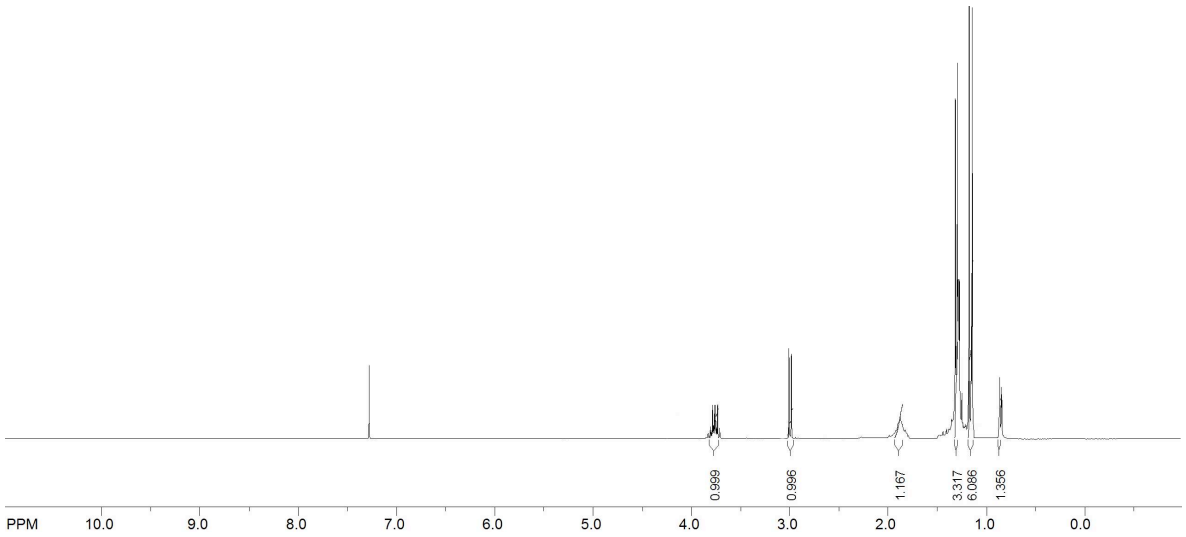


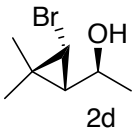


2c

1-(2-bromo-1-methyl-3-phenylcyclopropyl)propan-1-ol

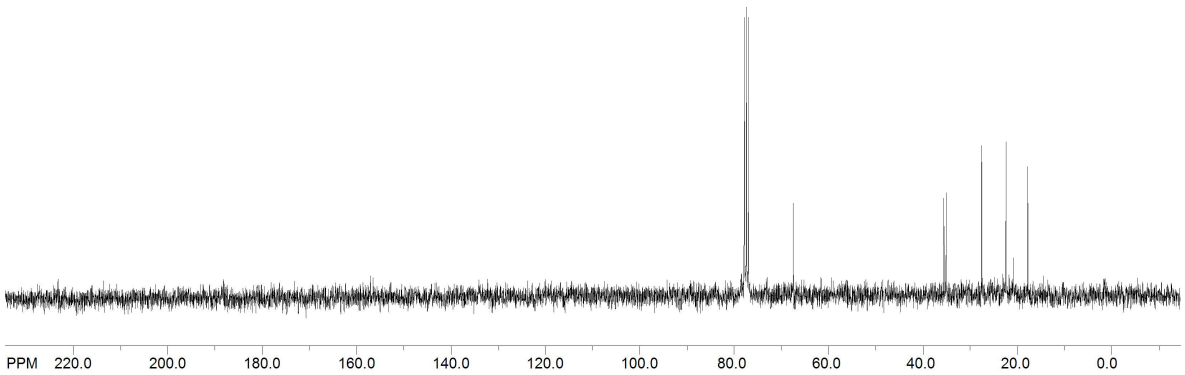


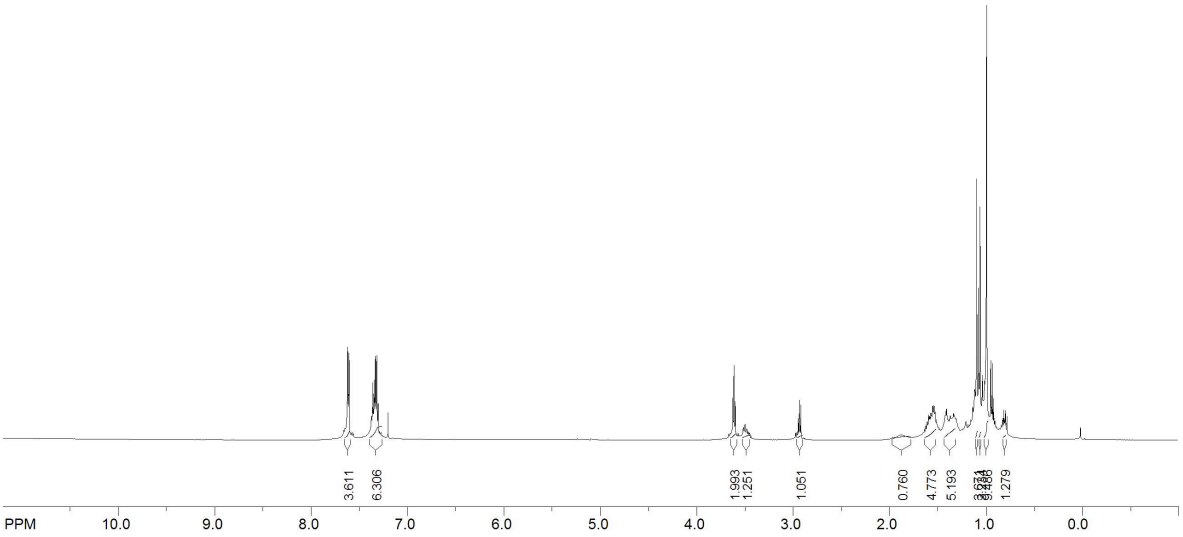


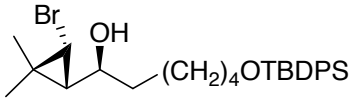


2d

1-(3-bromo-2,2-dimethylcyclopropyl)ethanol

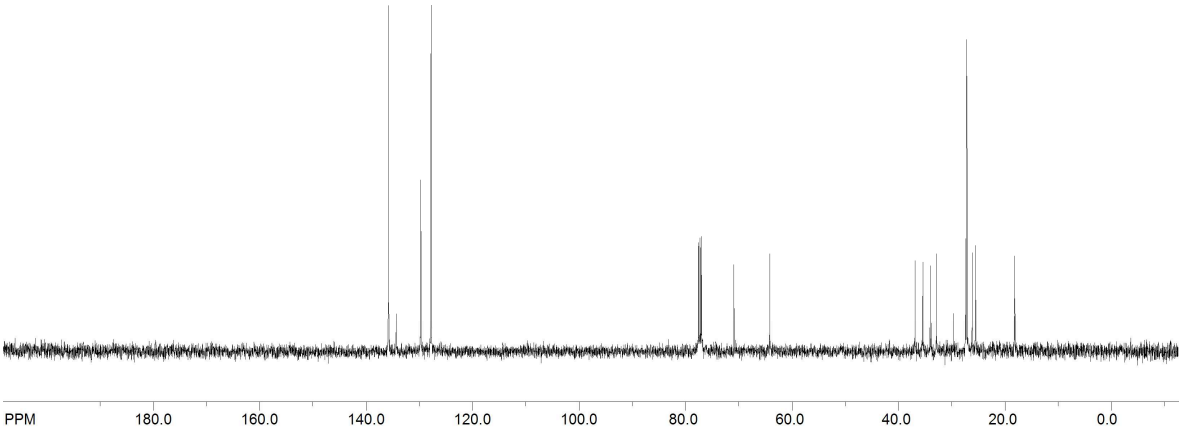


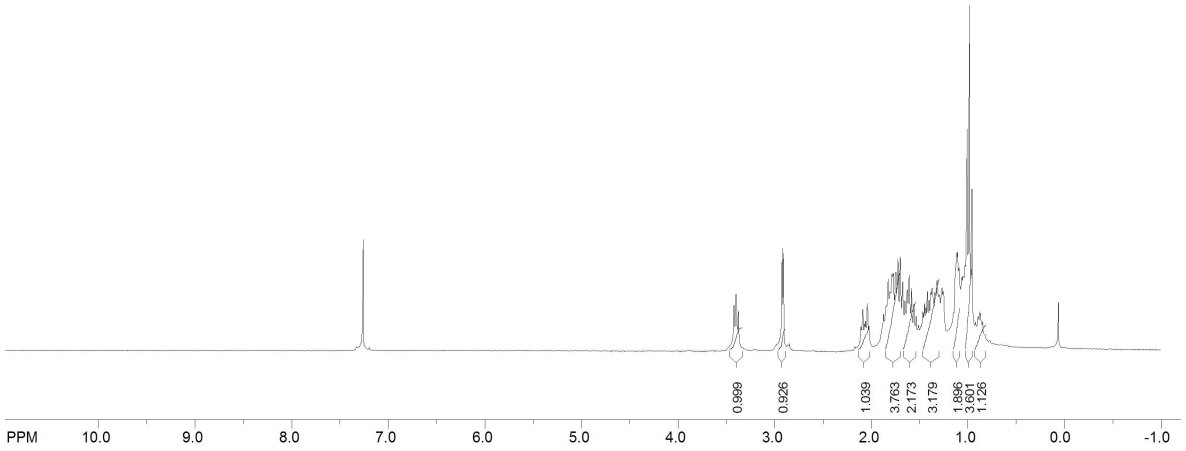


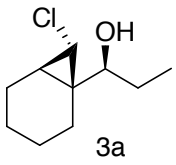


2e

1-(3-Bromo-2,2-dimethyl-cyclopropyl)-6-(tert-butyl-diphenyl-silanyloxy)-hexan-1-ol

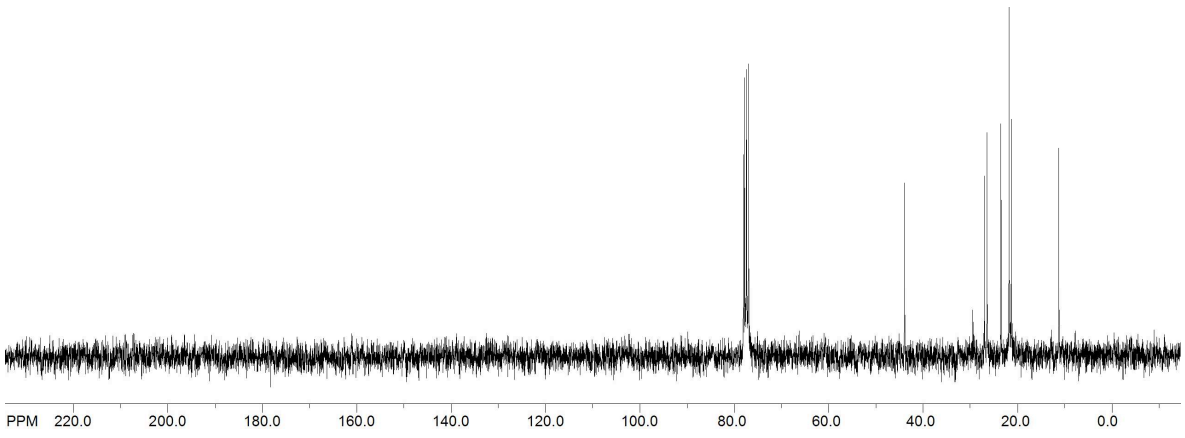


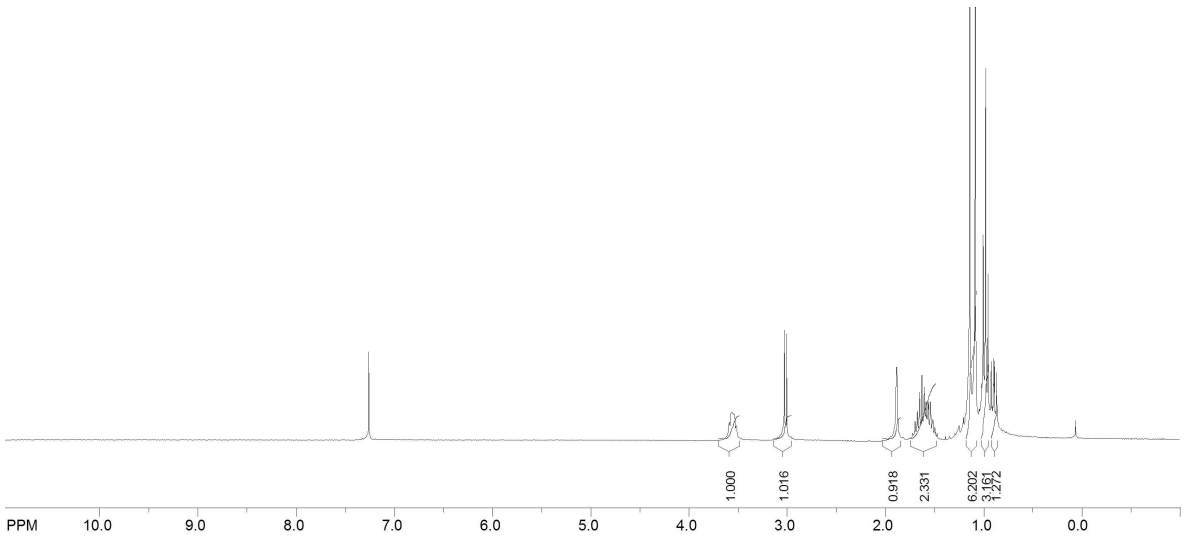


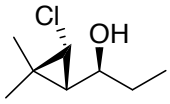


3a

1-(7-chlorobicyclo[4.1.0]heptan-1-yl)propan-1-ol

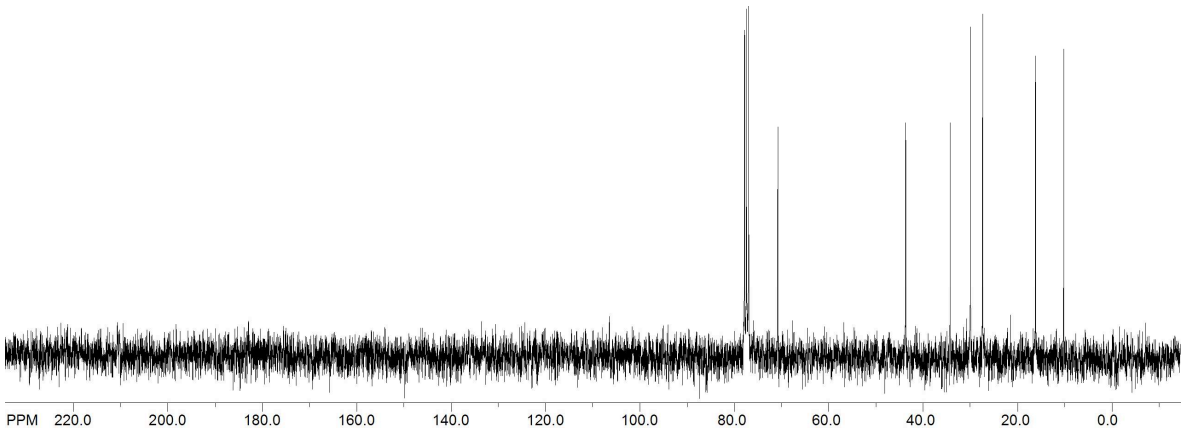


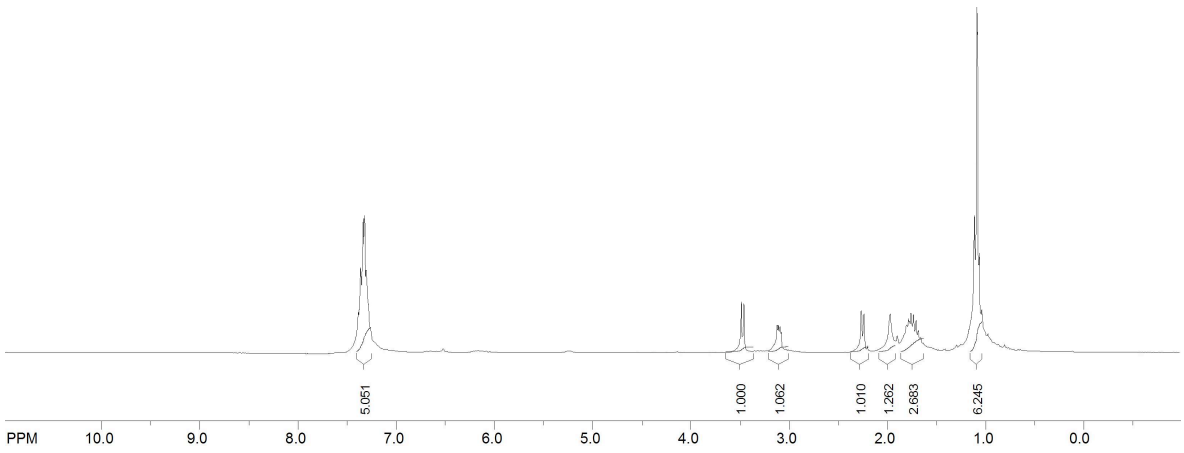


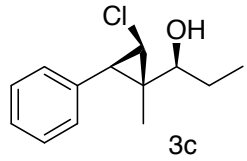


3b

1-(3-chloro-2,2-dimethylcyclopropyl)propan-1-ol

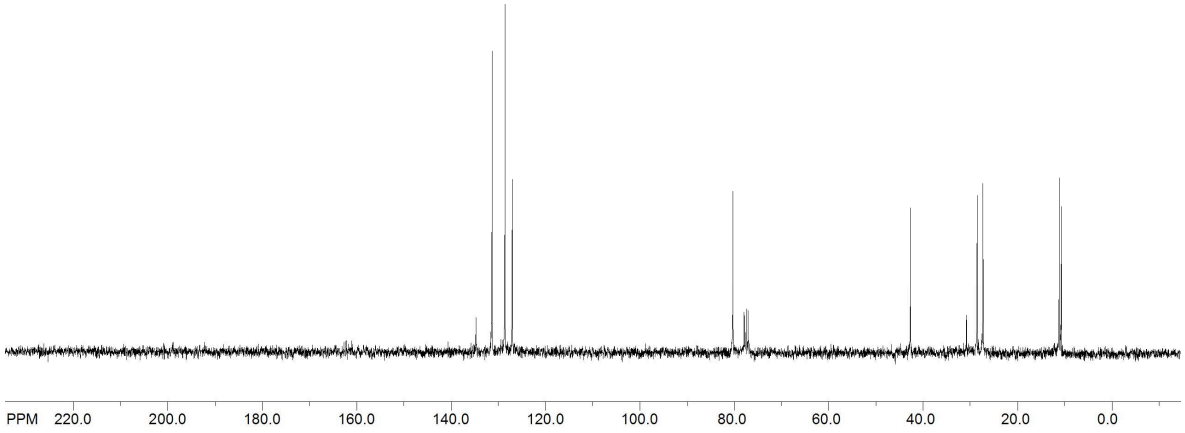


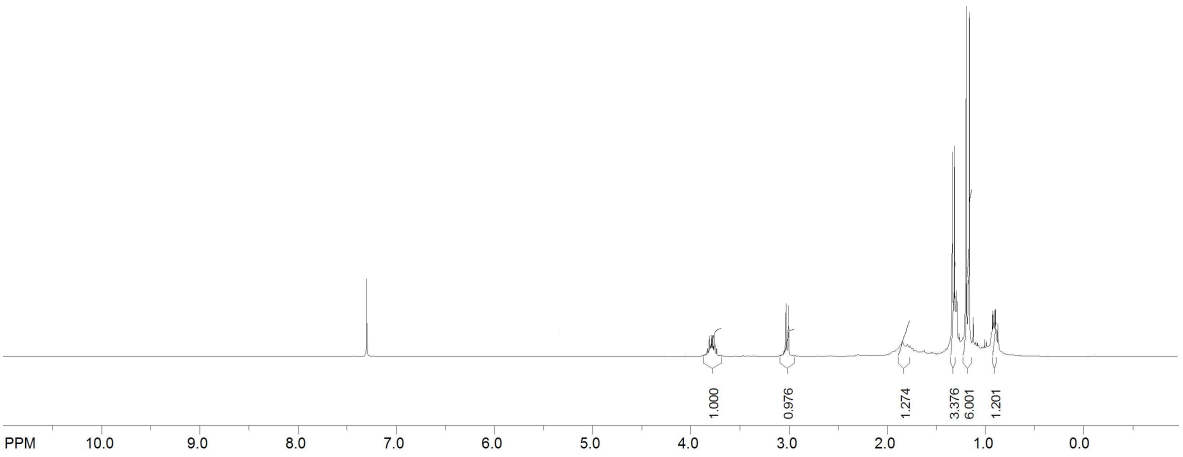


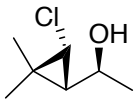


3c

1-(2-chloro-1-methyl-3-phenylcyclopropyl)propan-1-ol

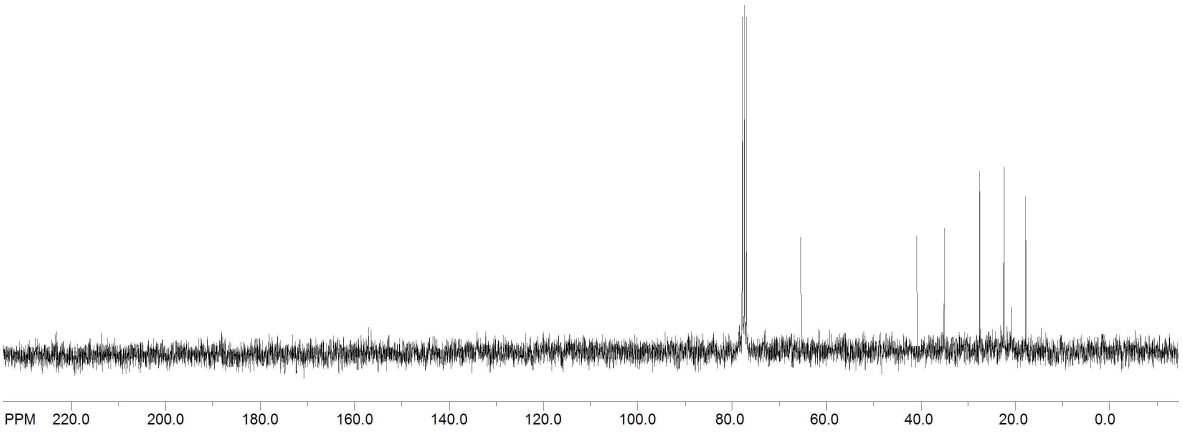


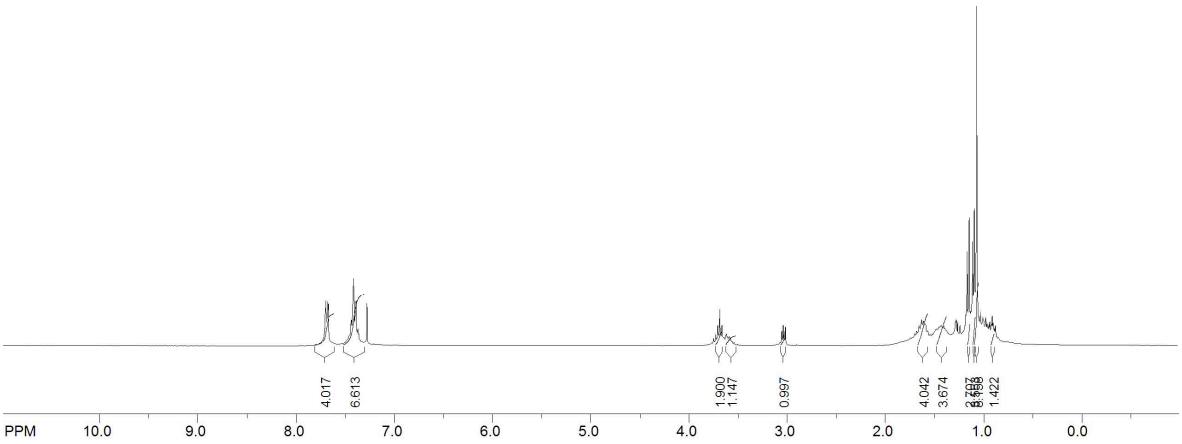


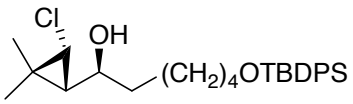


3d

1-(3-chloro-2,2-dimethylcyclopropyl)ethanol

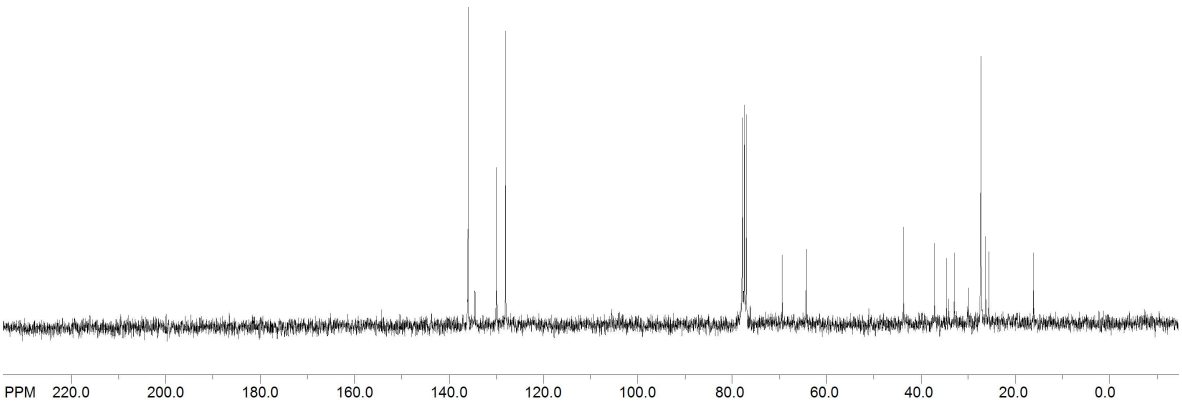


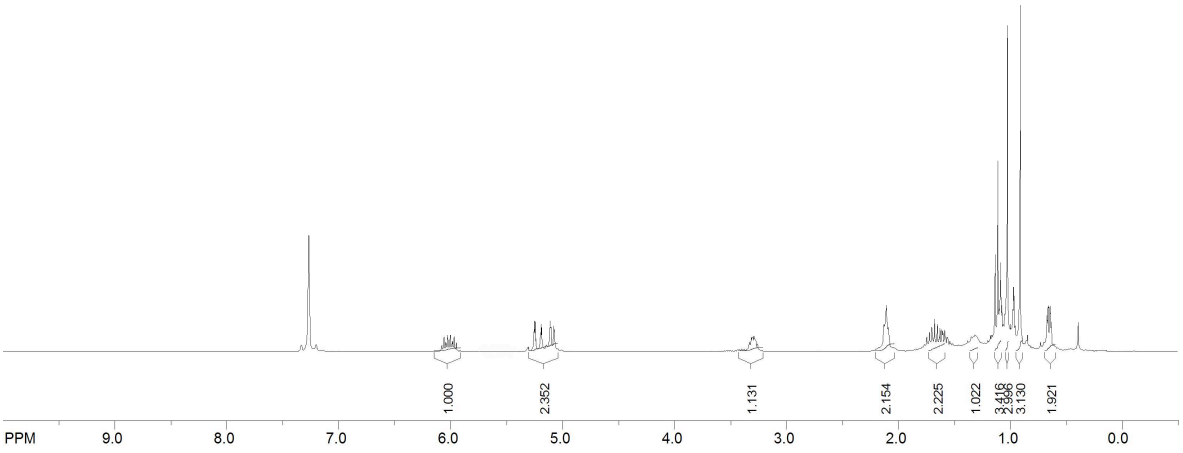


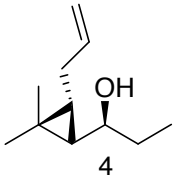


3e

6-(tert-Butyl-diphenyl-silanyloxy)-1-(3-chloro-2,2-dimethyl-cyclopropyl)-hexan-1-ol

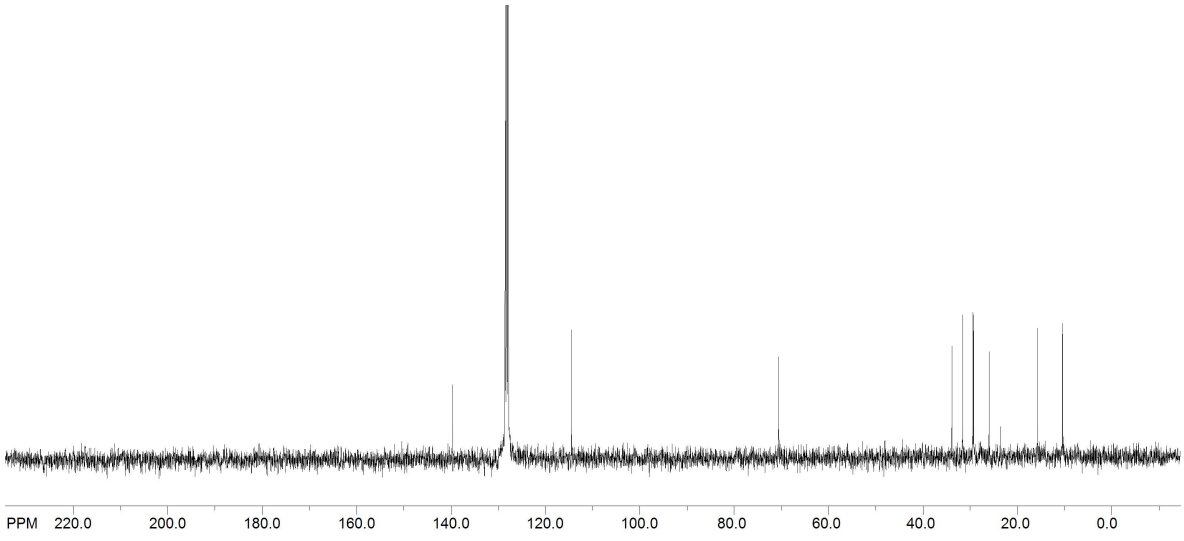


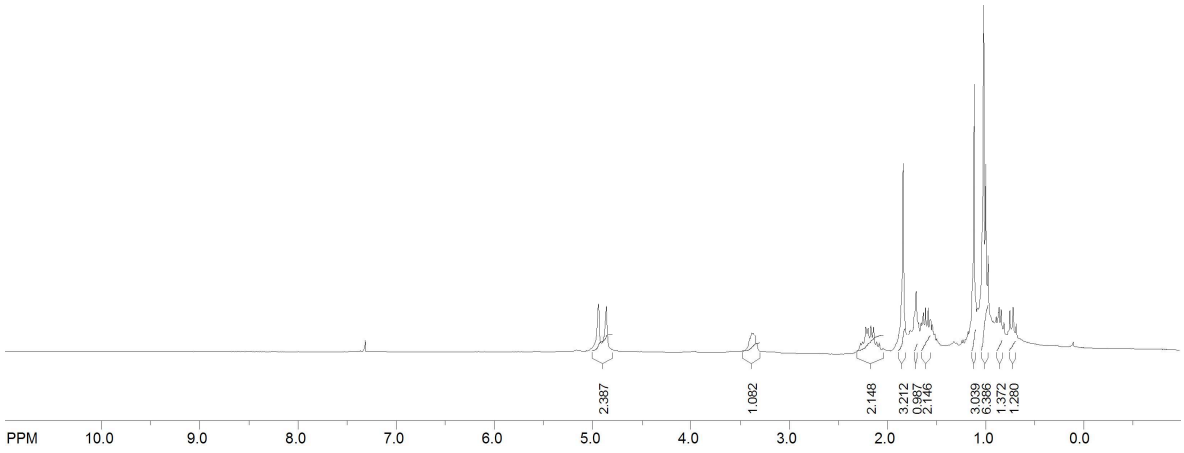


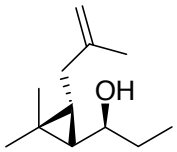


4

1-(3-allyl-2,2-dimethylcyclopropyl)propan-1-ol

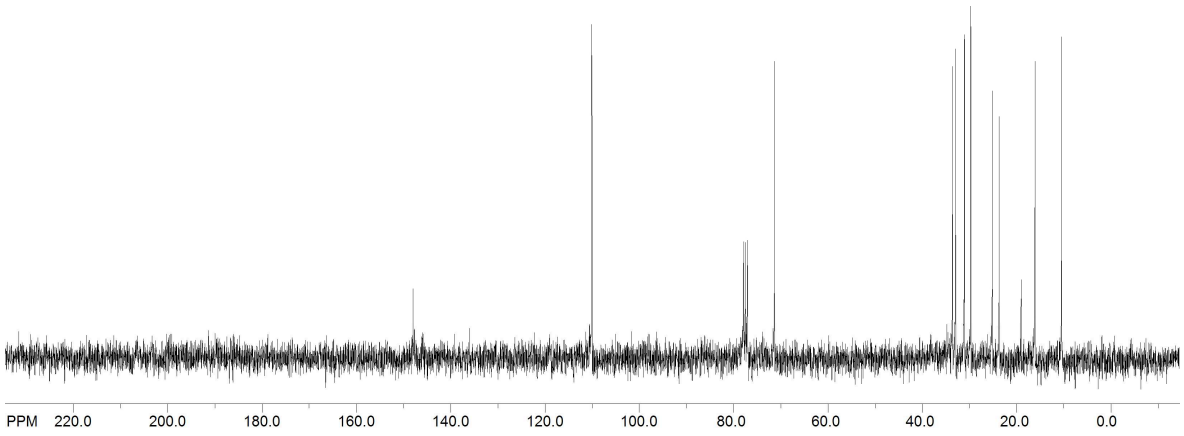


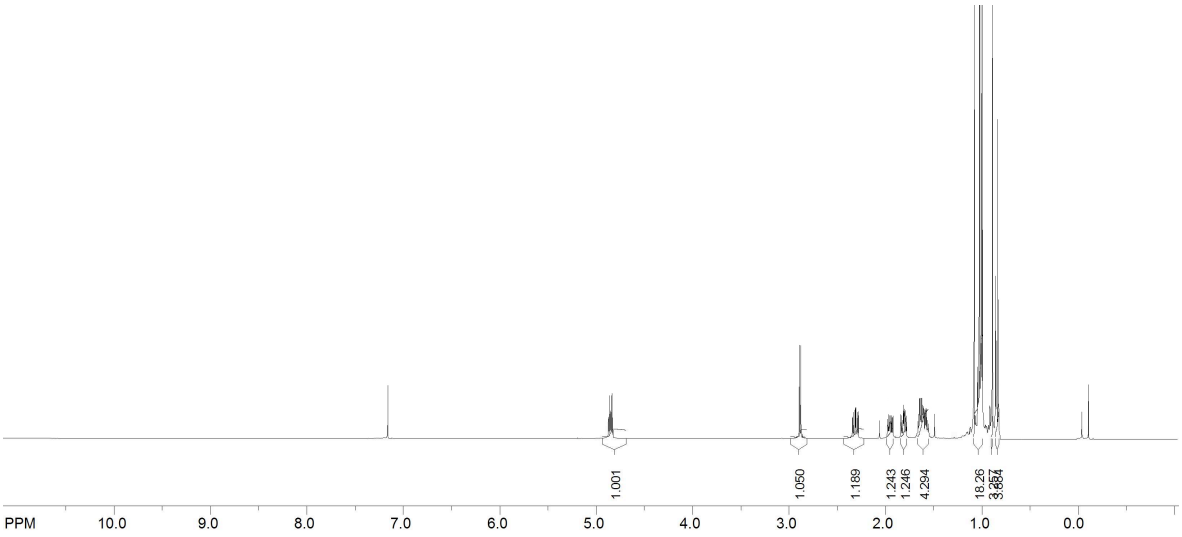


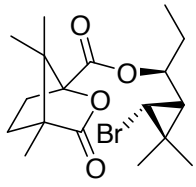


5

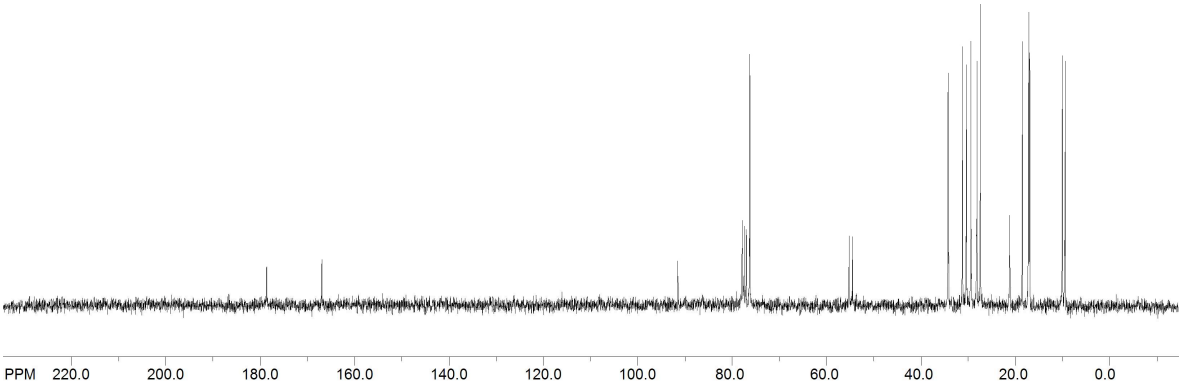
1-(2,2-dimethyl-3-(2-methylallyl)cyclopropyl)propan-1-ol

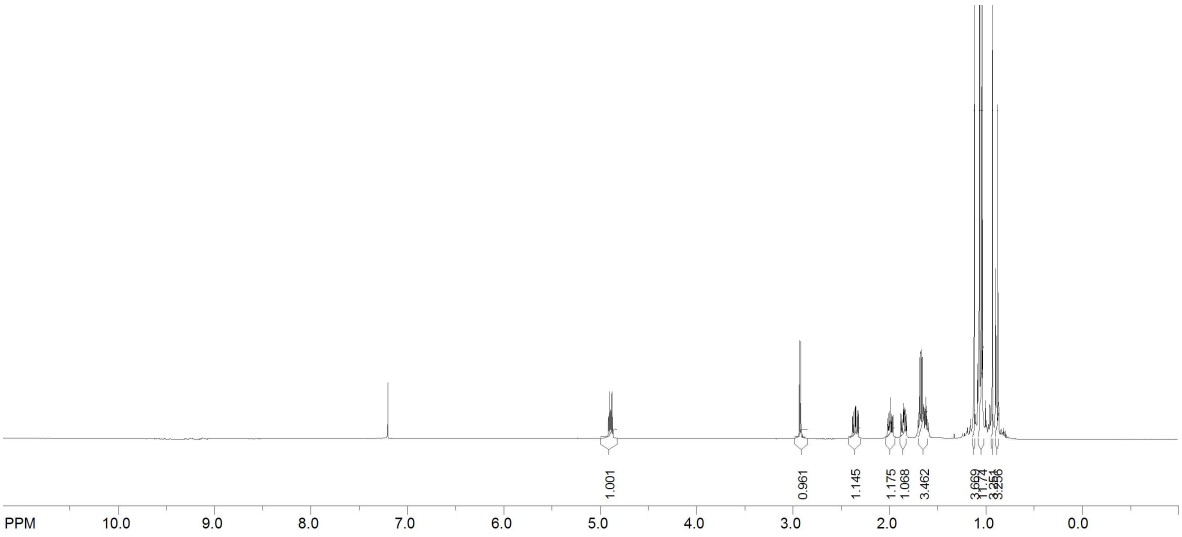


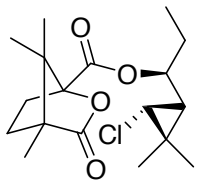




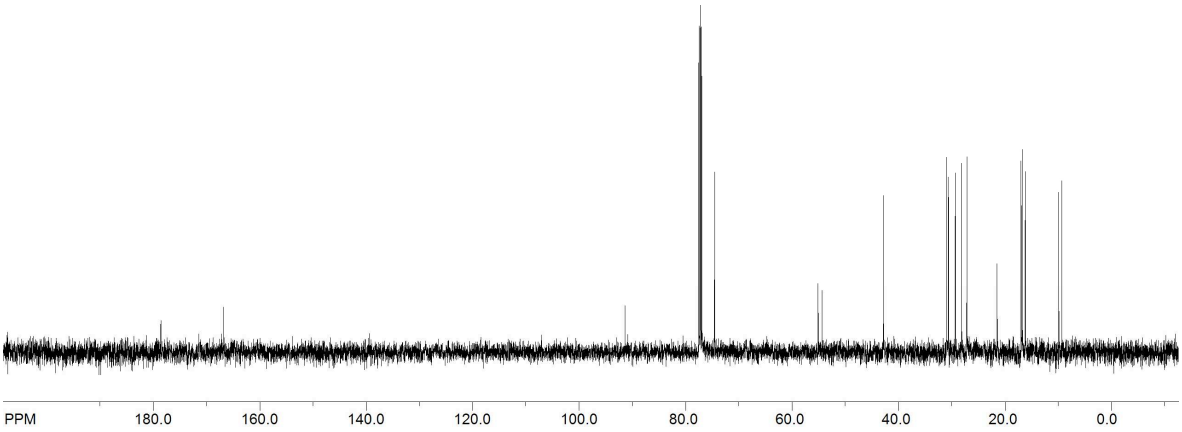
1-(3-bromo-2,2-dimethylcyclopropyl)propyl 4,7,7-trimethyl-3-oxo-2-oxa-bicyclo[2.2.1]heptane-1-carboxylate

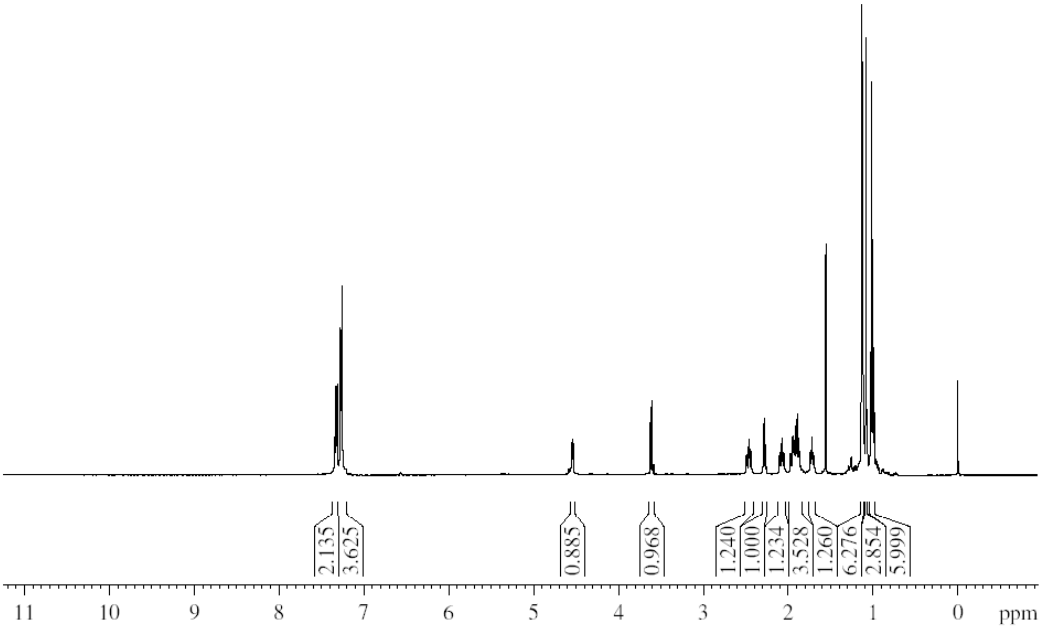


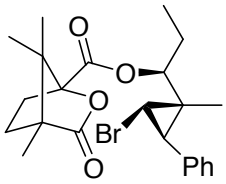




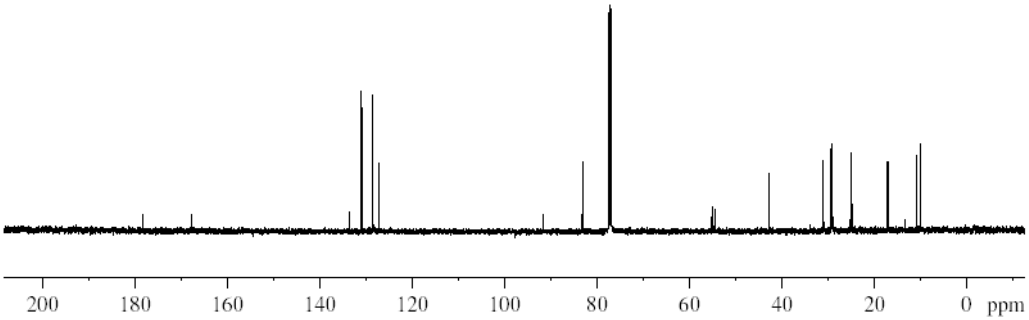
1-(3-chloro-2,2-dimethylcyclopropyl)propyl 4,7,7-trimethyl-3-oxo-2-oxa-bicyclo[2.2.1]heptane-1-carboxylate

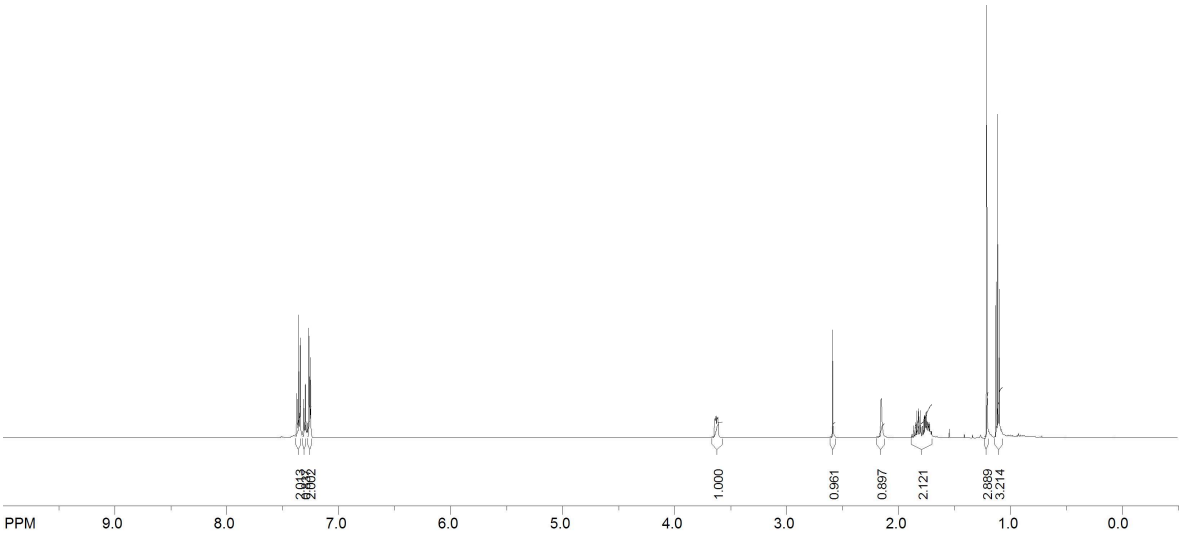


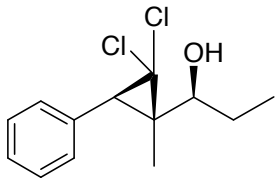




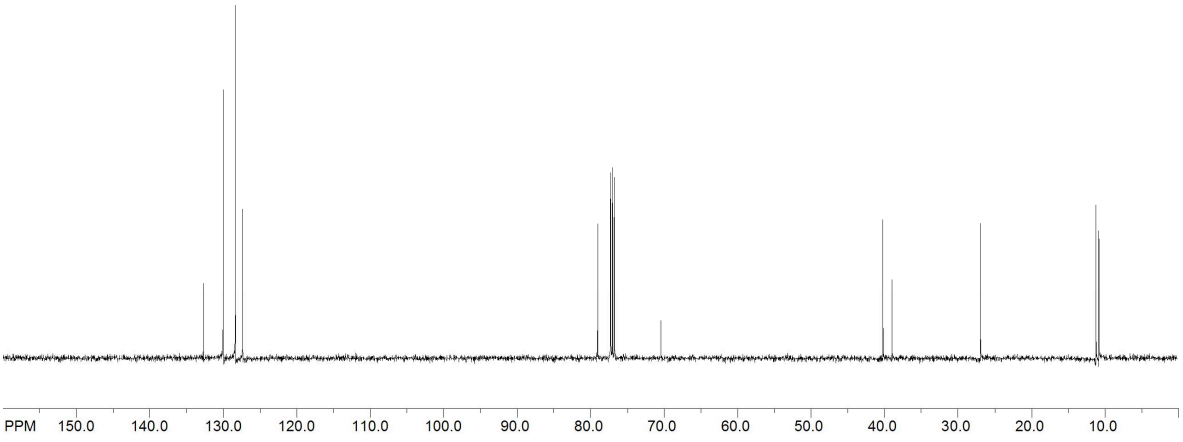
1-(2-bromo-1-methyl-3-phenylcyclopropyl)propyl 4,7,7-trimethyl-3-oxo-2-oxa-bicyclo[2.2.1]heptane-1-carboxylate

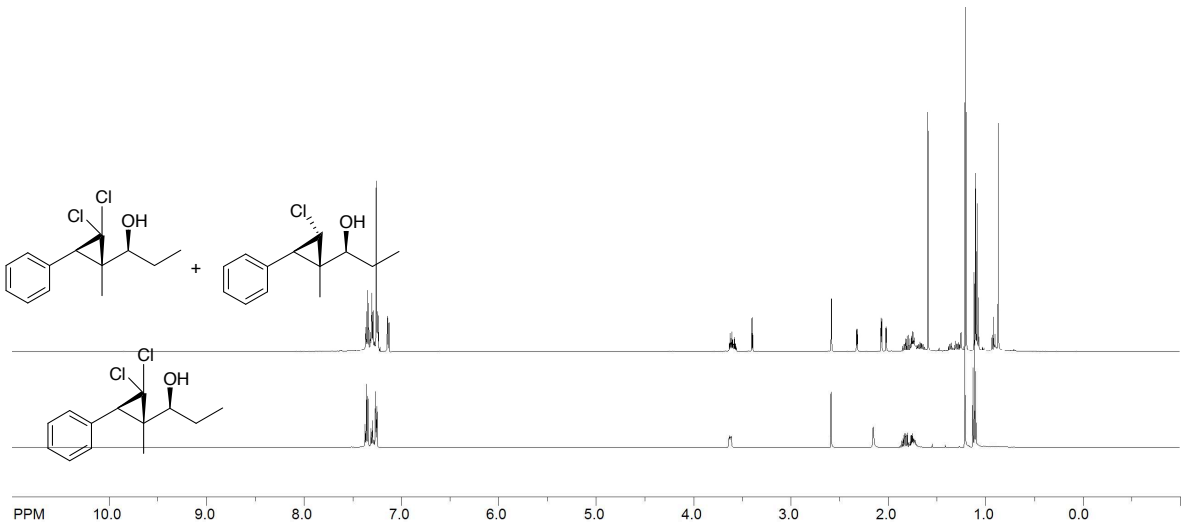


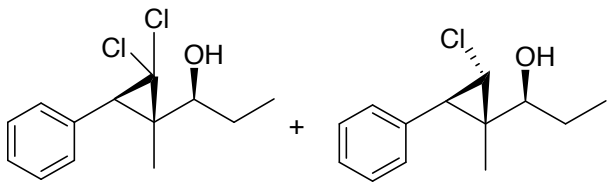




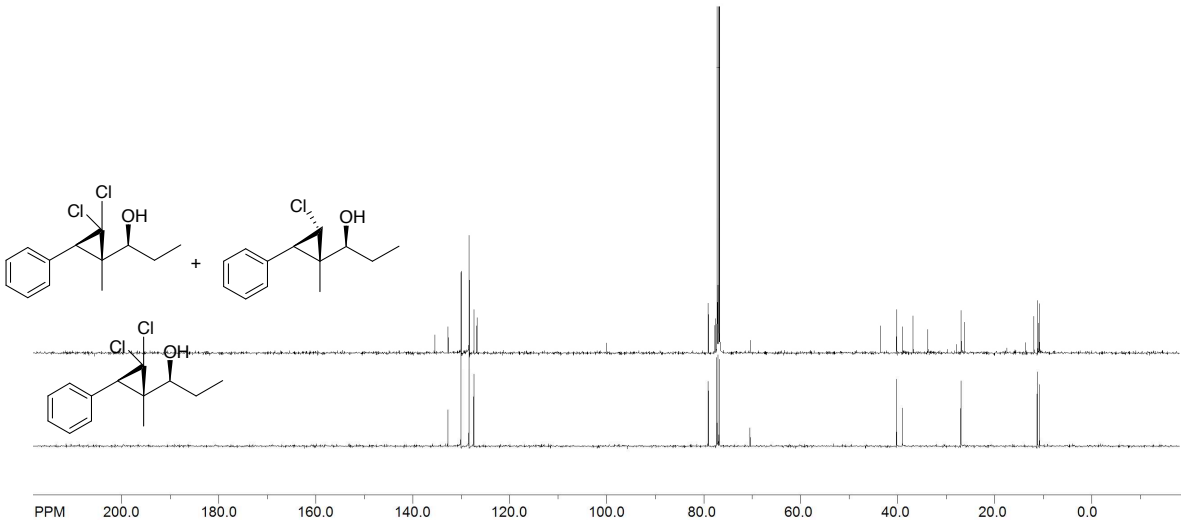
1-(2,2-dichloro-1-methyl-3-phenylcyclopropyl)propan-1-ol

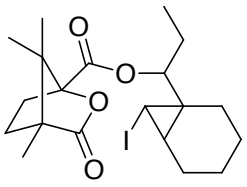




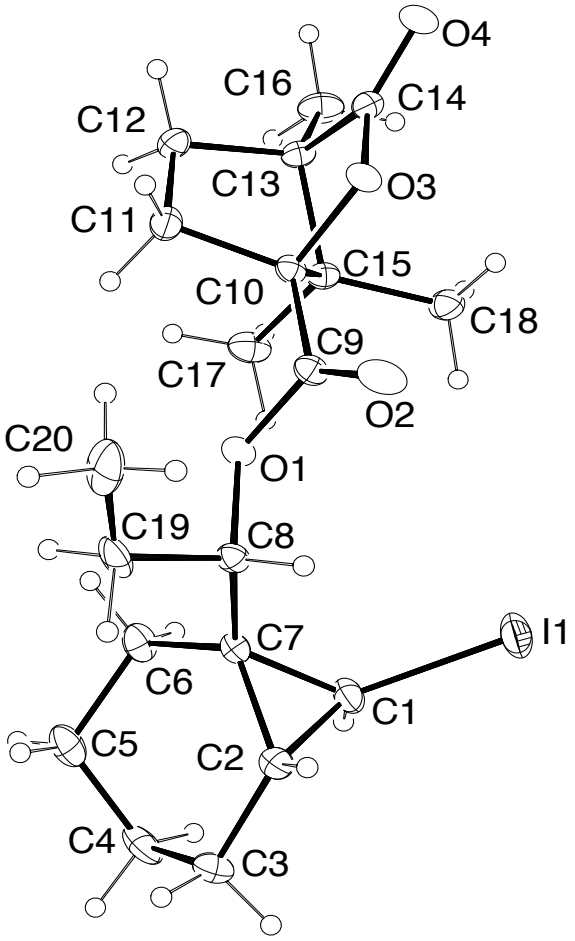


SpinWorks 2.5: ? ↕

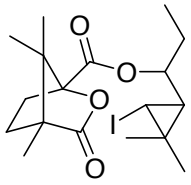




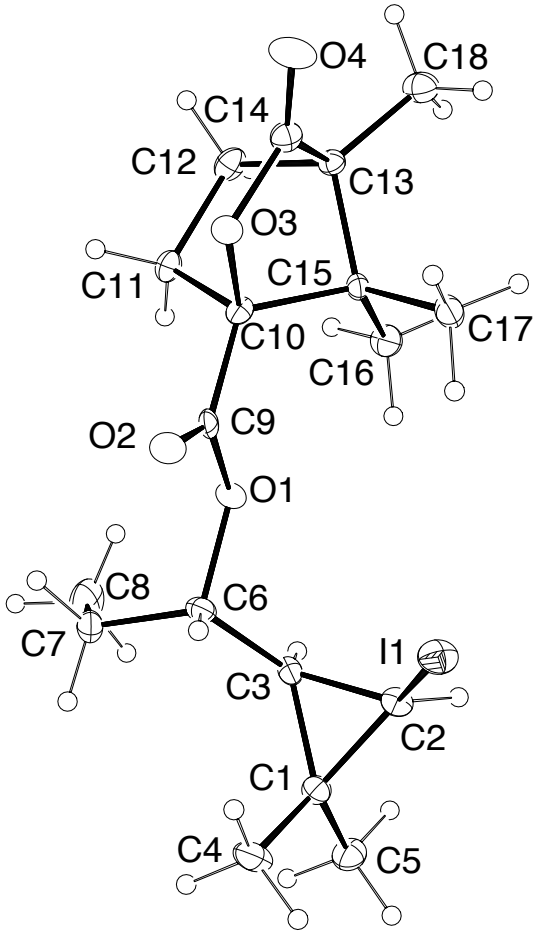
1-(7-iodobicyclo[4.1.0]heptan-1-yl)propyl 4,7,7-trimethyl-3-oxo-2-oxa-bicyclo[2.2.1]heptane-1-carboxylate



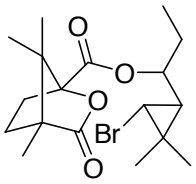
ORTEP plot with 30% probability thermal ellipsoids (entry 1 in Table 2)



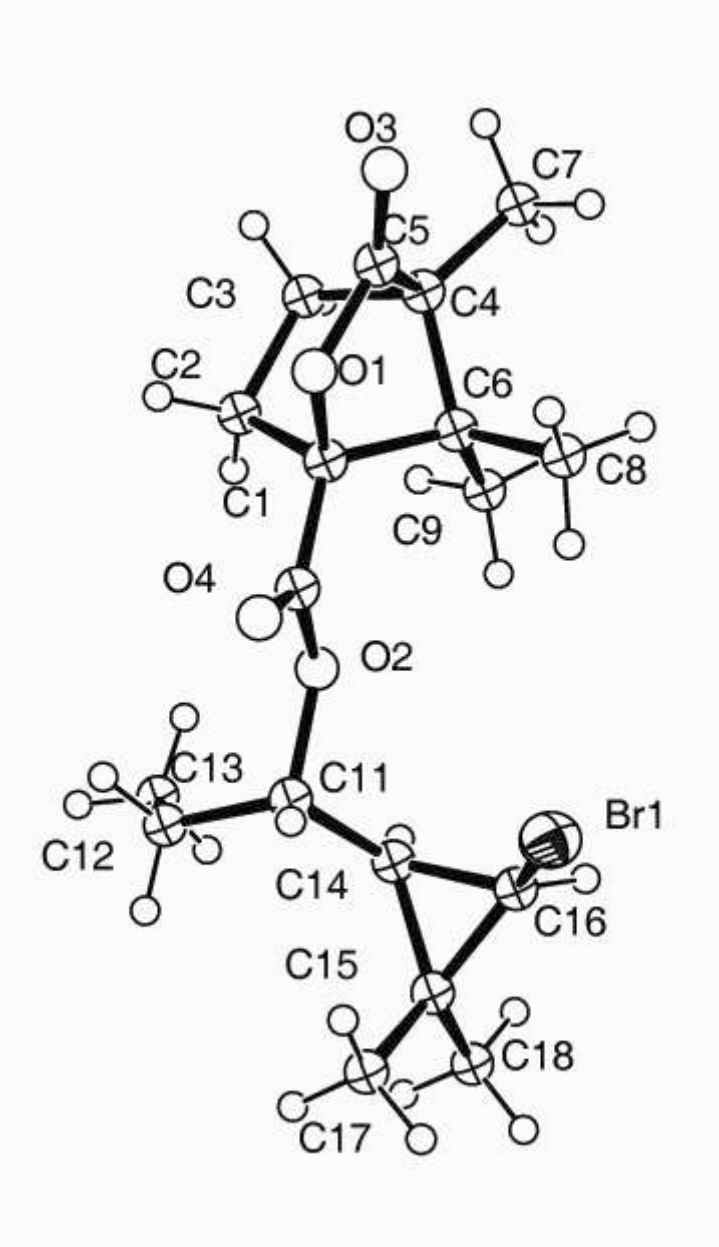
1-(3-iodo-2,2-dimethylcyclopropyl)propyl 4,7,7-trimethyl-3-oxo-2-oxa-bicyclo[2.2.1]heptane-1-carboxylate



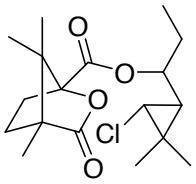
ORTEP plot with 30% probability thermal ellipsoids (entry 2 in Table 2)



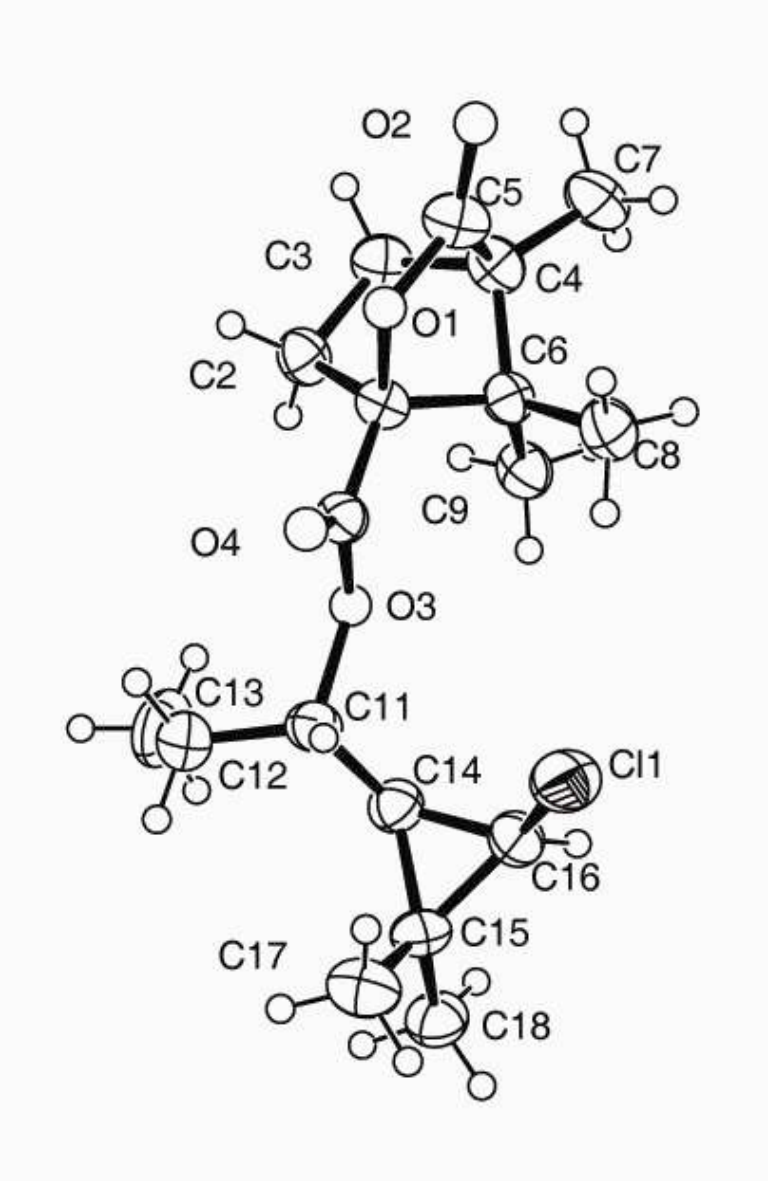
1-(3-bromo-2,2-dimethylcyclopropyl)propyl 4,7,7-trimethyl-3-oxo-2-oxa-bicyclo[2.2.1]heptane-1-carboxylate



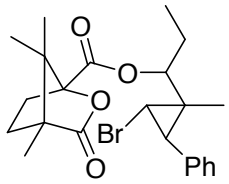
ORTEP plot with 30% probability thermal ellipsoids (entry 2 in Table 4)



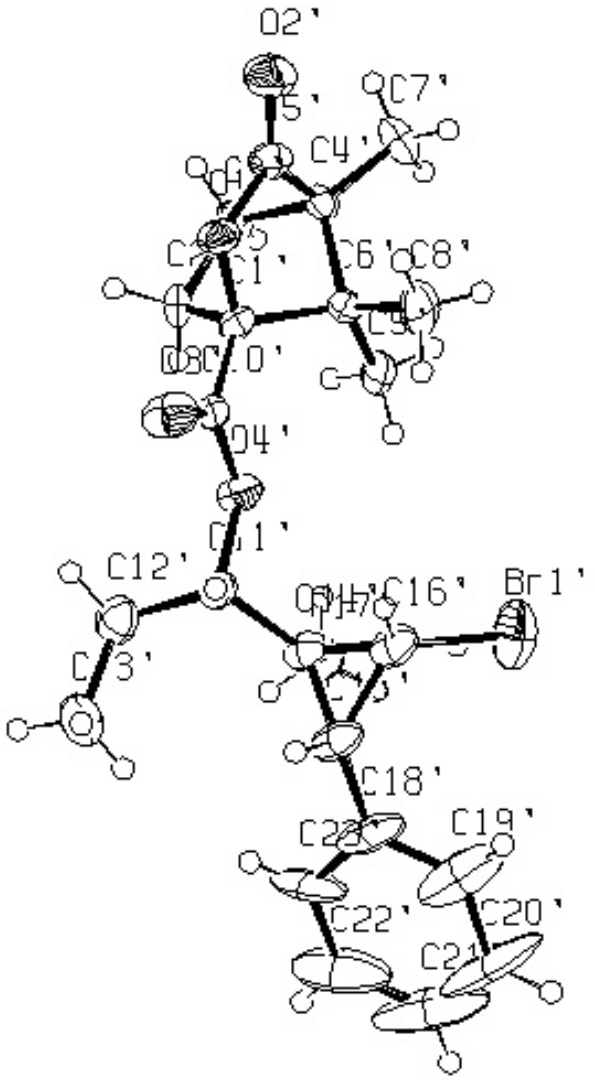
1-(3-chloro-2,2-dimethylcyclopropyl)propyl 4,7,7-trimethyl-3-oxo-2-oxa-bicyclo[2.2.1]heptane-1-carboxylate



ORTEP plot with 30% probability thermal ellipsoids (entry 7 in Table 4)



1-(2-bromo-1-methyl-3-phenylcyclopropyl)propyl 4,7,7-trimethyl-3-oxo-2-oxa-bicyclo[2.2.1]heptane-1-carboxylate



ORTEP plot with 30% probability thermal ellipsoids (entry 3 in Table 4)