Electronic Supplementary Material (ESI) for Chemical Communications


**Supporting Information for**

# Asymmetric *Anti*-Aldol Addition of Achiral Ketones via Chiral *N*-Amino Cyclic Carbamate Hydrazones

John D. Knight and Don M. Coltart*

*Department of Chemistry, University of Houston, Houston, TX, 772404-5003*
*dcoltart@uh.edu*

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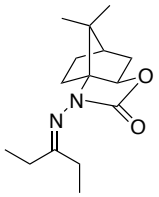
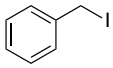
# I. Experimental

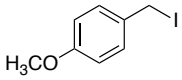
**General Considerations***:* Unless stated to the contrary, where applicable, the following conditions apply: Reactions were carried out using dried solvents (see below) and under a slight static pressure of Ar (pre-purified quality) that had been passed through a column (5 x 20 cm) of Drierite. Glassware was dried in an oven at 180 °C for at least 12 h prior to use and then either cooled in a desiccator cabinet over Drierite or assembled quickly while hot, sealed with rubber septa, and allowed to cool under a stream of Ar. Reactions were stirred magnetically using Teflon-coated magnetic stirring bars. Teflon-coated magnetic stirring bars and syringe needles were dried in an oven at 180 °C for at least 12 h prior to use. Hamilton microsyringes were dried in an oven at 60 °C for at least 12 h prior to use and cooled in the same manner. Commercially available Norm-Ject disposable syringes were used. Dry benzene, toluene, $Et_2O$, $CH_2Cl_2$, THF, MeCN and DME were obtained using an Innovative Technologies solvent purification system. All other dry solvents were of anhydrous quality purchased from Aldrich. Commercial grade solvents were used for routine purposes without further purification. $Et_3N$, pyridine, *i*-$Pr_2NEt$, 2,6-lutidine, *i*-$Pr_2NH$, TMEDA were distilled over $CaH_2$ under a $N_2$ atmosphere prior to use. Flash column chromatography was performed on silica gel 60 (230–400 mesh) or, where indicated, high-grade silica gel (5-20 mesh). The syn-anti ratios reported were computed from the $^1H$ NMR spectrum of the crude material. Reactions were visualized on TLC plates using phosphomolybdic acid (PMA) stain. All $^1H$ chemical shifts are reported in ppm (δ) relative to TMS; $^{13}C$ shifts are reported in ppm (δ) relative to $CDCl_3$ (77.23).




**ACC 3-pentanone hydrazone (5).** To a stirred solution of (*S*)-camphorsulfonic acid-derived ACC auxiliary (710 mg, 3.62 mmol, 1.0 eq.) in dichlormethane (30 mL) was added 3-pentanone (3.85 mL, 3.14 g, 36.18 mmol, 10.0 eq.) and *p*-toluenesulfonic acid (103 mg, 0.543 mmol, 0.15 eq.). After stirring for 12 hours at room temperature, the reaction mixture was treated with saturated sodium bicarbonate solution (2 mL) and then diluted with deionized water. Separation of the layers was followed by extraction of the aqueous layer with dichloromethane (2 x 50 mL), and the combined extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated *in vacuo*. Purification via flash chromatography over silica gel (10% EtOAc/90% hexanes) gave **5** as an off-white solid (870 mg, 91%). Spectral characteristics of this compound were consistent with previous characterization in the literature [1].



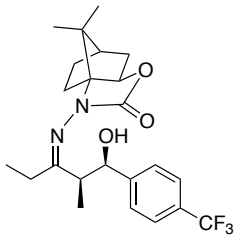
**Benzyl iodide.** A 100 mL round bottom flask was charged with of benzyl bromide (1.0 mL, 1.44 g, 4.09 mmol, 1.0 eq.), which was subsequently dissolved in 65 mL of acetone. The resulting clear solution was treated with solid sodium iodide (1.60 g, 5.32 mmol, 1.3 eq.), and the solid momentarily dissolved before a white precipitate formed. Stirring was continued in the dark for 12 hours. The mixture was then concentrated *in vacuo*, and the crude paste was taken up into 50 mL of deionized water. The aqueous mixture was extracted three times with diethyl ether (3 x 30 mL), and the combined extracts were washed with 1 M sodium thiosulfate solution to remove excess iodine. Drying over anhydrous magnesium sulfate and concentration *in vacuo* gave a light-yellow, lachrymatory oil (857 mg, 96%) that solidified upon storage in the freezer. Prior to use, the solid was allowed to melt at room temperature to allow for easy addition to the reaction flask. Purification proved unnecessary as long as the material was properly stored in the freezer in the absence of light. Spectral characteristics of this compound were consistent with previous characterization in the literature [2].



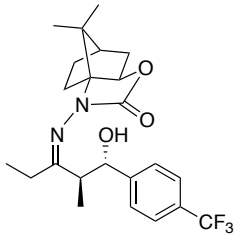
**4-Methoxybenzyl iodide.** This compound was prepared in the same manner described for benzyl iodide above using 4-methoxybenzyl chloride (346 µL, 400 mg, 2.55 mmol, 1.0 eq.), sodium iodide (1.15 g, 3.32 mmol, 1.30 eq.), and acetone (10 mL). A yellow oil with a strong, pleasant aroma (563 mg, 89%) was obtained that quickly turned brown upon exposure to light. Due to the high light sensitivity of the neat liquid, a solution in anhydrous THF (0.15M) was prepared for use in subsequent reactions. Spectral characteristics of the neat compound were consistent with previous characterization in the literature [3].

**General procedure for *anti* selective ACC-mediated aldol additions.** *n*-Butyllithium (2.5 M in hexanes, 90 µL, 0.270 mmol) was added dropwise to a stirred and cooled (-78 °C) solution of diisopropylamine (38 µL, 0.270 mmol) in THF (1.5 mL). After being stirred for 20 min, **5** (50 mg, 0.1892 mmol) was added directly into the solution of LDA. A slightly yellow solution developed that was stirred for 45 min at -78 °C. Then, the aldehyde used was added to the azaenolate solution. The reaction mixture was allowed to room temperature over a period of two hours. The reaction was then quenched with saturated ammonium chloride solution (2 mL) under vigorous stirring. The mixture was partitioned between $Et_2O$ (10 mL) and $H_2O$ (10 mL), and the layers were separated. The aqueous phase was extracted with $Et_2O$ (2 x 10 mL), and the combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated *in vacuo*. Purification of the resulting crude oil was achieved using flash chromatography over silica gel (10% EtOAc/90% Hexanes) gave the *anti* aldol diastereomer.

**General procedure for low temperature (*syn* selective) ACC-mediated aldol additions.** These reactions were conducted in a similar manner to the *anti* selective aldol reaction mentioned above except that the reaction mixture was kept at -78 °C after the addition of the aldehyde. After stirring for 30 minutes at this temperature, the reaction was quenched in the previously described manner. The crude product consisted of a mixture of unreacted 3-pentanone hydrazone, a *syn* aldol diastereomer, and an *anti* aldol diastereomer. Purification was achieved using flash chromatography over silica gel (pretreated with $Et_3N$, 7.5% EtOAc/92.5% Hexanes) to give the separate diastereomers.

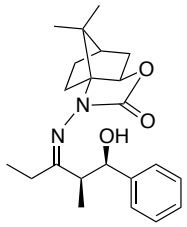



**ACC (1*R*,2*R*)-1-hydroxy-2-methyl-1-(4-(trifluoromethyl)phenyl)pentan-3-one (6a).** This *syn* diastereomer was isolated from the low temperature aldol reaction of SACC 3-pentanone hydrazone and 4-trifluoromethylbenzaldehyde. **$^1$H NMR** ($CDCl_3$,4 MHz): δ 7.58-7.52 (m, 4H), 5.27 (app. s, 1H), 4.26 (dd, 1H, *J* = 3.6 Hz, 7.6 Hz), 3.24 (m, 1H), 2.82 (bs, OH), 2.64 (dq, 1H, *J* = 7.2 Hz, 17.6 Hz), 2.34-2.31 (m, 2H), 1.96-1.78 (m 5H), 1.30-1.04 (m, 12H, containing a s at δ 1.24 (3H), a s at δ 1.17 (3H), and a t at δ 1.13 (3H, *J* = 7.2 Hz), and 0.93 (d, 3H, *J* = 7.2 Hz); **$^{13}$C NMR** ($CDCl_3$, 100 MHz): 183.81, 156.20, 147.94, 126.84, 125.19, 83.41, 73.77, 72.76, 48.08, 43.06, 41.95, 35.54, 27.00, 26.52, 25.80, 21.50, 19.31, 10.62, and 10.44; **ESI-MS** *m/Z* calculated for $C_{23}H_{29}F_3N_2O_3$ $(M+H)^+$: 438.21, found: 438.19.

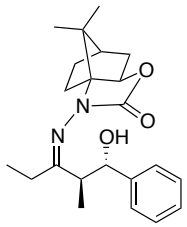



**ACC (1*S*,2*R*)-1-hydroxy-2-methyl-1-(4-(trifluoromethyl)phenyl)pentan-3-one (6b).** This *anti* diastereomer was isolated from the room temperature aldol reaction of SACC 3-pentanone hydrazone and 4-trifluoromethylbenzaldehyde. **$^1$H NMR** ($CDCl_3$, 400 MHz): δ 7.57 (d, 2H, *J* = 8 Hz), 7.43 (d, 2H, *J* = 8 Hz), , 5.66 (d, OH, *J* = 10 Hz), 4.51 (app. t, 1H, *J* = 10.4 Hz), 4.30 (dd, 1H, *J* = 4 Hz, 8 Hz), 3.18 (dq, 1H, *J* = 6.8 Hz, 10.4 Hz), 2.69 (dq, 1H, *J* = 7.2 Hz, 17.2 Hz), 2.53 (dq, 1H, *J* = 7.2 Hz, 17.2 Hz), 2.36-2.31 (m, 1H), 2.04-1.93 (m, 2H), 1.89 (dd, 1H, *J* = 8.4 Hz, 14 Hz), 1.80 (app. t, 1H, *J* = 3.6 Hz), 1.30-1.03 (m, 12H, containing a s at δ 1.26 (3H), a t at δ 1.20 (3H, *J* = 7.2 Hz), and a s at δ 1.15 (3H)), and 0.79 (d, 3H, *J* = 6.8 Hz); **$^{13}$C NMR** ($CDCl_3$, 100 MHz): 181.21 156.55, 147.92, 129.99, 129.67, 127.58, 125.70, 125.41, 125.38, 123.00, 83.78, 76.05, 73.99, 48.09,

43.98, 43.04, 35.39, 26.44, 25.66, 24.39, 21.39, 15.72, and 10.16; **ESI-MS** *m/Z* calculated for $C_{23}H_{29}F_3N_2O_3$ $(M+H)^+$: 438.21, found: 438.19.



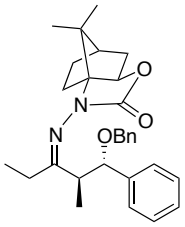
**ACC (1*R*,2*R*)-1-hydroxy-2-methyl-1-phenylpentan-3-one (7a).** This *syn* diastereomer was isolated from the low temperature aldol reaction of SACC 3-pentanone hydrazone and benzaldehyde. **$^1$H NMR** ($CDCl_3$, 400 MHz): δ 7.42 (d, 2H, *J* = 7.5 Hz), 7.33 (app. t, 2H, *J* = 7.2 Hz), 7.25 (d, 1H, *J* = 7.2 Hz), 5.17 (app. s, 1H), 4.25 (dd, 1H, *J* = 4.5 Hz, 8.5 Hz), 3.31 (dq, 1H, *J* = 2.4 Hz, 7.2 Hz), 2.61 (dq, 1H, *J* = 7.2 Hz, 17.8 Hz), 2.51 (dq, 1H, *J* = 7.2 Hz, 17.8 Hz), 2.35-2.29 (m, 2H), 1.95-1.92 (m, 2H), 1.85 (dd, 2, *J* = 8 Hz, 13.6 Hz), 1.77 (app. t, 1H, 4.4 Hz), 1.27-1.08 (m, 12H, containing a s at δ 1.23 (3H), a s at δ 1.19 (3H, and a t at δ 1.03 (3H, *J* = 7.2 Hz)), and 0.96 (d, 3H, *J* = 7.2 Hz); **$^{13}$C NMR** ($CDCl_3$, 100 MHz): 189.67, 156.20, 143.74, 128.33, 127.32, 126.47, 83.28, 73.71, 73.51, 48.03, 43.06, 42.13, 35.55, 26.97, 26.51, 25.79, 21.49, 19.33, 10.75, and 10.61; **ESI-MS** *m/Z* calculated for $C_{22}H_{30}N_2O_3$ $(M+H)^+$: 370.23, found: 370.21.



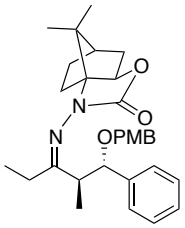
**ACC (1*S*,2*R*)-1-hydroxy-2-methyl-1-phenylpentan-3-one (7b).** This *anti* aldol diastereomer was isolated from the room temperature aldol reaction of SACC 3-pentanone hydrazone and benzaldehyde. **$^1$H NMR** ($CDCl_3$, 400 MHz): δ 7.35-7.33 (m, 4H), 7.29-7.23 (m, 1H), 5.45 (d, OH, *J* = 10.4 Hz), 4.46 (app. t, 1H, *J* = 10.4 Hz), 4.31 (dd, 1H, *J* = 4.5 Hz, 8.5 Hz), 3.25 (dq, 1H, *J* = 7.2 Hz, 14 Hz), 2.75 (dq, 1H, *J* = 7.2 Hz, 17.6 Hz), 2.57 (dq, 1H, *J* = 7.2 Hz, 17.6 Hz), 2.38-2.33 (m, 1H), 2.05-1.95 (m, 2H), 1.89 (dd, 1H, *J* = 8 Hz, 13.6 Hz), 1.81 (app. t, 1H, *J* = 4.4 Hz), 1.33-1.07 (m, 12H, containing a s at δ 1.28 (3H), a t at δ 1.22 (3H, *J* = 7.2 Hz), and a s at δ 1.18 (3H)), and 0.80 (d, 3H, *J* = 6.8 Hz); **$^{13}$C NMR** ($CDCl_3$, 100 MHz): 182.02, 156.47, 143.83, 128.49, 127.71, 127.21, 83.70, 73.94, 48.12, 44.18, 43.13, 35.49, 26.55, 25.76, 24.33, 21.47, 19.33, 15.94, and 10.24; **ESI-MS** *m/Z* calculated for $C_{22}H_{30}N_2O_3$ $(M+H)^+$: 370.23, found: 370.21.

**General procedure for *anti* selective ACC-mediated aldol additions with *in situ* *O*-benzylation.** *n*-Butyllithium (1.20 eq.) was added dropwise to a stirred and cooled (-78 °C) solution of diisopropylamine (1.20 eq.) in THF (0.5 mL). After being stirred for 20 min, hydrazone **5** (50 mg, 1.0 eq., in 1.0 mL of THF) was

added to the solution of LDA A slightly yellow solution developed that was stirred for 45 min at -78 °C. Then, the aldehyde (1.25 eq.) was directly added to the azaenolate solution, which was allowed to warm to room temperature. After stirring for two hours at room temperature, neat benzyl iodide (1.30 eq.) was added to the solution. Stirring was continued for 12 hours, and the reaction mixture was then quenched with saturated ammonium chloride solution (2 mL) and partitioned between $Et_2O$ (10 mL) and $H_2O$ (10 mL). The layers were separated, and the aqueous phase was extracted with $Et_2O$ (2 x 10 mL). The combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated *in vacuo*. Purification of the resulting crude oil was achieved using flash chromatography over silica gel (pretreated with triethylamine, 10% EtOAc/90% Hexanes, phosphomolybdic acid (PMA) TLC stain) to give the *O*-benzylated ACC *anti* aldol product.

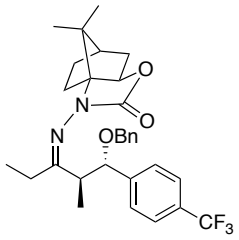



**ACC (1*S*,2*R*)-1-(benzyloxy)-2-methyl-1-phenylpentan-3-one (10a).** This compound was isolated in 91% yield as a single diastereomer from the *anti*-selective ACC aldol reaction described above using ACC 3-pentanone hydrazone, benzaldehyde, and benzyl iodide. **$^1$H NMR** ($CDCl_3$, 500 MHz): δ 7.41-7.24 (m, 10H), 4.43 (d, 1H, *J* = 12.5 Hz), 4.35 (d, 1H, *J* = 9 Hz), 4.23 (dd, 1H, *J* = 4 Hz, 8Hz), 4.17 (d, 1H, *J* = 12.5 Hz), 3.55-3.50 (m, 1H), 2.43-2.18 (m, 4H), 1.97-1.64 (m, 5H), 1.25-1.23 (multiplet containing methyl singlet at 1.23, 4H), 1.17-1.12 (multiplet containing methyl singlet at 1.17, 5H), 1.08 (t, 3H, *J* = 7 Hz), and 0.77 (d, 3H, *J* = 7 Hz); **$^{13}$C NMR** ($CDCl_3$, 125 MHz): 184.31, 155.89, 139.82, 138.36, 128.51, 128.36, 128.30, 127.92, 127.39, 83.05, 81.90, 73.59, 69.87, 47.85, 42.65, 35.55, 26.69, 19.49, 14.04, and 10.47; **ESI-MS** *m/Z* calculated for $C_{29}H_{36}N_2O_3$ $(M+H)^+$: 460.27, found: 460.26.

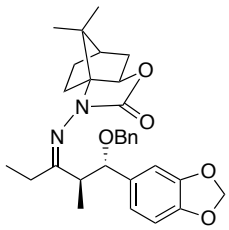



**ACC (1S,2R)-1-((4-methoxybenzyl)oxy)-2-methyl-1-phenylpentan-3-one (10b).** This compound was isolated in 87% yield as a single diastereomer from the *anti*-selective ACC aldol reaction described above using ACC 3-pentanone hydrazone, benzaldehyde, and *para*-methoxybenzyl iodide. **$^1$H NMR** ($CDCl_3$, 500 MHz): δ 7.39-7.30 (m, 5H), 7.21 (d, 2H, *J* = 8.5 Hz), 6.85 (d, 2H, *J* = 8.5 Hz), 4.39 (d, 1H, *J* = 12 Hz), 4.31 (d, 1H, *J* = 9 Hz), 4.22 (dd, 1H, *J* = 4 Hz, 8 Hz), 4.07 (d, 1H, *J* = 12 Hz) 3.88 (s, 3H), 3.49 (dq, 1H, *J* = 7 Hz, 9 Hz), 2.32-2.30 (m, 1H),

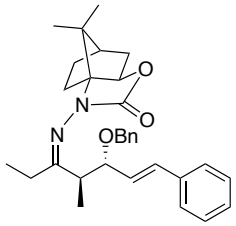
2.20-2.14 (m, 2H), 1.90-1.88 (m, 2H), 1.82 (dd, 1H, *J* = 9 Hz, 14 Hz), 1.73 (app. s, 1H), 1.26-1.06 (m, 12H, containing a s at δ 1..22, a s at δ 1.16, and a t at δ 1.08 with *J* = 7 Hz), and 0.75 (d, 3H, *J* = 7.5 Hz); **$^{13}$C NMR** ($CDCl_3$, 125 MHz): 184.40, 159.06, 155.90, 139.92, 128.49, 128.18, 113.70, 83.04, 81.34, 73.58, 69.37, 55.41, 42.66, 35.55, 26.68, 25.81, 25.44, 21.37, 19.49, 14.07, and 10.47; **ESI-MS** *m/Z* calculated for $C_{30}H_{38}N_2O_4$ $(M+H)^+$: 490.28, found: 490.26.



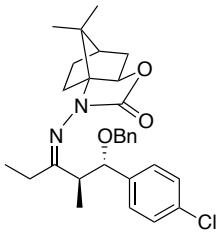

**ACC (1*S*,2*R*)-1-(benzyloxy)-2-methyl-1-(4-(trifluoromethyl)phenyl)pentan-3-one (10c).** This compound was isolated in 83% yield as a single diastereomer from the *anti*-selective ACC aldol reaction described above using ACC 3-pentanone hydrazone, 4-trifluoromethylbenzaldehyde, and benzyl iodide. **$^{1}$H NMR** ($CDCl_3$, 500 MHz): δ 7.62 (d, 2H, *J* = 8 Hz), 7.54 (d, 2H, *J* = 8 Hz), 7.33-7.25 (m, 5H), 4.45-4.42 (m, 2H), 4.22 (dd, 1H, *J* = 4 Hz, 8 Hz), 4.19 (d, 1H, *J* = 12 Hz), 3.53 (dq, 1H, *J* = 7.5 Hz, 10 Hz), 2.33-2.30 (m, 1H), 2.19 (m, 2H), 1.92-1.81 (m, 3H), 1.75 (app. t, 1H, *J* = 4 Hz), 1.27-1.07 (m, 12H, containing a s at δ 1.22, a s at δ 1.18, and a t at 1.09 with *J* = 7 Hz), and 0.79 (d, 3H, *J* = 7.5 Hz); **$^{13}$C NMR** ($CDCl_3$, 125 MHz): 183.47, 155.91, 144.18, 137.83, 128.40, 127.62, 125.51 125.48, 125.45, 123.19, 83.09, 81.26, 73.62, 70.27, 47.84, 42.52, 35.53, 25.57, 19.28, 13.75, and 10.39; **ESI-MS** *m/Z* calculated for $C_{30}H_{35}F_3N_2O_3$ $(M+H)^+$: 528.26, found: 528.25.



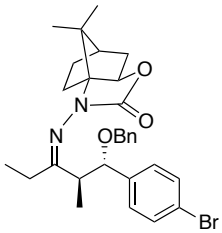

**ACC (1*S*,2*R*)-1-(benzo[d][1,3]dioxol-5-yl)-1-(benzyloxy)-2-methylpentan-3-one (10d).** This compound was isolated in 85% yield as a single diastereomer from the *anti*-selective ACC aldol reaction described above using ACC 3-pentanone hydrazone, piperonal, and benzyl iodide. **$^{1}$H NMR** ($CDCl_3$, 500 MHz): δ 7.32-7.24 (m, 5H), 6.94 (s, 1H), 6.82-6.76 (m, 2H), 5.96 (s, 2H), 4.44 (d, 1H, *J* = 12.5 Hz), 4.27-4.23 (m, 2H), 4.16 (d, 1H, *J* = 12.5 Hz), 3.51-3.46 (m, 1H), 2.32-2.17 (m, 3H), 1.86-1.81 (m, 3H), 1.74-1.72 (m, 1H), 1.27-1.06 (multiplet containing methyl singlets at 1.20 and 1.16 and a triplet at 1.08 (*J* = 7 Hz), 15H), and 0.78 (d, 3H, *J* = 7 Hz); **$^{13}$C NMR** ($CDCl_3$, 125 MHz): 184.20, 155.88, 147.57, 133.76, 127.92, 122.13, 108.05, 107.98, 101.21, 83.04, 73.58, 69.70, 47.84, 43.02, 42.63, 35.56, 26.70, 25.82, 25.46, 21.38, 19.48, 14.10, and 10.46; **ESI-MS** *m/Z* calculated for $C_{30}H_{36}N_2O_5$ $(M+H)^+$: 504.26, found: 504.24.



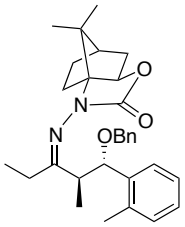
**ACC (4*R*,5*R*,*E*)-5-(benzyloxy)-4-methyl-7-phenylhept-6-en-3-one (10e).** This compound was isolated in 87% yield as a single diastereomer from the *anti*-selective ACC aldol reaction described above using ACC 3-pentanone hydrazone, *trans*-cinnamaldehyde, and benzyl iodide. **$^{1}$H NMR** ($CDCl_3$, 500 MHz): δ 7.43-7.24 (m, 9H), 6.60 (d, 1H, *J* = 16 Hz), 6.13 (dd, 1H, *J* = 8 Hz, 16 Hz), 4.65 (d, 1H, *J* = 12.5 Hz), 4.39 (d, 1H, *J* = 12.5 Hz), 4.25 (dd, 1H, *J* = 4 Hz, 8 Hz), 4.04 (app. t, 1H, *J* = 8 Hz), 4.38 (dq, 1H, *J* = 7.5 Hz, 8 Hz), 2.38-2.27 (m, 3H), 1.94-1.92 (m, 2H), 1.84 (dd, 2H, *J* = 8 Hz, 13.5 Hz), 1.74 (app. t, 1H, *J* = 3.5 Hz), 1.28-1.08 (m, 12H, containing a s at δ 1.21, a s at δ 1.17, and a t at 1.10 with *J* = 7.5 Hz), and 1.01 (d, 3H, *J* = 7 Hz); **$^{13}$C NMR** ($CDCl_3$, 125 MHz): 184.29, 156.01, 138.65, 136.48, 134.68, 128.38, 127.96, 127.88, 127.41, 126.82, 83.05, 81.17, 73.64, 70.10, 47.88, 40.60, 35.57, 25.82, 19.45, 14.30, and 10.54; **ESI-MS** *m/Z* calculated for $C_{31}H_{38}N_2O_3$ $(M+H)^+$: 486.29, found: 486.27.



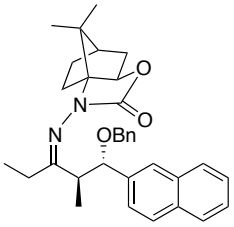
**ACC (1*S*,2*R*)-1-(benzyloxy)-1-(4-chlorophenyl)-2-methylpentan-3-one (10f).** This compound was isolated in 80% yield as a single diastereomer from the *anti*-selective ACC aldol reaction described above using ACC 3-pentanone hydrazone, 4-chlorobenzaldehyde, and benzyl iodide. **$^{1}$H NMR** ($CDCl_3$, 500 MHz): δ 7.34-7.26 (m, 9H), 4.42 (d, 1H, *J* = 12 Hz), 4.35 (d, 1H, *J* = 9 Hz), 4.22 (dd, 1H, *J* = 4 Hz, 8 Hz), 4.16 (d, 1H, *J* = 12 Hz), 4.39 (dq, 1H, *J* = 7.5 Hz, 9 Hz), 2.42-2.30 (m, 1H), 2.19-2.17 (m, 2H), 1.90-1.84 (m, 1H), 1.82 (dd, 2H, *J* = 8.5 Hz, 13.5 Hz), 1.74 (app. s, 1H), 1.44-1.06 (m, 12H, containing a s at δ 1.17, a s at δ 1.14, and a t at 1.07 with *J* = 7 Hz), and 0.77 (d, 3H, *J* = 7 Hz); **$^{13}$C NMR** ($CDCl_3$, 125 MHz): 183.86, 155.95, 138.42, 138.06, 133.98, 129.72, 128.76, 128.39, 128.35, 127.95, 127.56, 83.11, 81.09, 73.64, 70.04, 47.87, 42.58, 35.58, 26.69, 19.49, 13.78, and 10.45; **ESI-MS** *m/Z* calculated for $C_{29}H_{35}ClN_2O_3$ $(M+H)^+$: 494.23, found: 494.20.



**ACC (1*S*,2*R*)-1-(benzyloxy)-1-(4-bromophenyl)-2-methylpentan-3-one (10g).** This compound was isolated in 89% yield as a single diastereomer from the *anti*-selective ACC aldol reaction described above using ACC 3-pentanone hydrazone, 4-bromobenzaldehyde, and benzyl iodide. **$^1$H NMR** ($CDCl_3$, 500 MHz): δ 7.49 (d, 2H, *J* = 8.5 Hz), 7.34-7.26 (m, 7H), 4.43 (d, 1H, *J* = 12 Hz), 4.33 (d, 1H, *J* = 9 Hz), 4.23 (dd, 1H, *J* = 4 Hz, 8 Hz), 4.16 (d. 1H, *J* = 12 Hz), 3.49 (dq, 1H, *J* = 7 Hz, 9 Hz), 2.33-2.30 (m, 1H), 2.22-2.16 (m, 2H), 1.92-1.81 (m, 3H), 1.75 (app. t., 1H, *J* = 3.5 Hz), 1.26-1.06 (m, 12H, containing a s at δ 1.22, a s at δ 1.17, and a t at 1.08 with *J* = 7 Hz), and 0.77 (d, 3H, *J* = 7 Hz); **$^{13}$C NMR** ($CDCl_3$, 125 MHz): 183.81, 155.93, 138.96, 138.02, 131.69, 127.56, 127.55, 122.16, 83.08, 81.14, 73.63, 70.05, 70.03, 47.87, 43.03, 42.53, 35.57, 25.59, 19.48, 13.78, 13.77, and 10.44; **ESI-MS** *m/Z* calculated for $C_{29}H_{35}BrN_2O_3$ $(M+H)^+$: 539.50, found: 539.48.

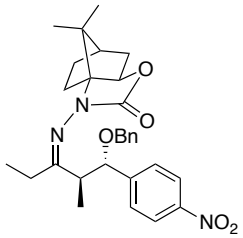



**ACC (1*S*,2*R*)-1-(benzyloxy)-2-methyl-1-(o-tolyl)pentan-3-one (10h).** This compound was isolated in 85% yield as a single diastereomer from the *anti*-selective ACC aldol reaction described above using ACC 3-pentanone hydrazone, *ortho*-tolualdehyde, and benzyl iodide. **$^1$H NMR** ($CDCl_3$, 500 MHz): δ 7.48 (d, 1H, *J* = 7 Hz), 7.30-7.18 (m, 7H), 7.13 (d, 1H, *J* = 7.5 Hz), 4.64 (d, 1H, *J* = 9.5 Hz), 4.21 (d, 1H, *J* = 12 Hz), 4.24 (dd, 1H, *J* = 4 Hz, 8 Hz), 4.11 (d, 1H, *J* = 12 Hz), 3.60 (dq, 1H, *J* = 7.5 Hz, 9.5 Hz), 2.45-2.25 (m, 8H, containing a s at δ 2.32), 1.91-1.81 (m, 4H), 1.74 (app. t, 1H, *J* = 4 Hz), 1.26-1.12 (m, 12H, containing a s at δ 1.23, a s at δ 1.18, and a t at 1.14 with *J* = 7 Hz), and 0.74 (d, 3H, *J* = 7 Hz); **$^{13}$C NMR** ($CDCl_3$, 125 MHz): 184.16, 155.64, 138.45, 137.02, 130.48, 128.31, 127.95, 127.80, 127.38, 126.62, 82.99, 69.59, 47.90, 43.03, 35.58, 25.34, 19.51, 14.30, and 10.57.; **ESI-MS** *m/Z* calculated for $C_{30}H_{38}N_2O_3$ $(M+H)^+$: 474.29, found: 474.27.



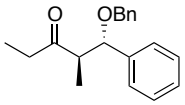

**ACC (1*S*,2*R*)-1-(benzyloxy)-2-methyl-1-(naphthalen-2-yl)pentan-3-one (10i).** This compound was isolated in 91% yield as a single diastereomer from the *anti*-selective ACC aldol reaction described above using ACC 3-pentanone hydrazone, 2-napthaldehyde, and benzyl iodide. **$^1$H NMR** ($CDCl_3$, 500 MHz): δ 7.88-7.85 (m, 3H), 7.80 (s, 1H), 7.60 (d, 1H, *J* = 8.5 Hz), 7.50 (m, 2H), 4.52 (d, 1H, *J* = 9 Hz), 4.87 (d, 1H, *J* = 12 Hz), 4.25 (dd, 1H, *J* = 4 Hz, 8 Hz), 4.21 (d, 1H,

*J* = 12 Hz), 3.65 (dq, 1H, *J* = 7.5 Hz, 9 Hz), 2.34-2.22 (m, 4H), 1.93-1.90 (m, 2H), 1..84 (dd, 1H, *J* = 8 Hz, 13.5 Hz), 1.75 (app. t, 1H, *J* = 4 Hz), 1.30-1.21 (m, 6H, containing a s at δ 1.23), 1.19 (s, 3H), 1.15-1.09 (m, 5H, containing a t at δ 1.11 with *J* = 7.5 Hz), and 0.80 (d, 1H, *J* = 7.5 Hz); **$^{13}$C NMR** ($CDCl_3$, 125 MHz): 184.22, 155.90, 137.36, 128.35, 127.98, 127.81, 126.33, 125.73, 83.07, 82.12, 73.63, 69.99, 47.89, 43.06, 42.51, 35.60, 26.74, 25.85, 25.53, 21.43, 19.54, 14.31, and 10.52; **ESI-MS** *m/Z* calculated for $C_{33}H_{38}N_2O_3$ $(M+H)^+$: 510.29, found: 510.28.



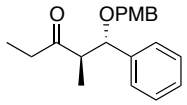

**ACC (1*S*,2*R*)-1-(benzyloxy)-1-(4-nitrophenyl)-2-methylpentan-3-one (10j).** This compound was isolated in 87% yield as a single diastereomer from the *anti*-selective ACC aldol reaction described above using ACC 3-pentanone hydrazone, 4-nitrobenzaldehyde, and benzyl iodide. **$^1$H NMR** ($CDCl_3$, 500 MHz): δ 8.23 (d, 2H, *J* = 8.5 Hz), 7.62 (d, 2H, *J* = 8.5 Hz), 7.56-7.29 (m, 5H), 4.55 (d, 1H, *J* = 8.5 Hz), 4.46 (d, 1H, *J* = 12 Hz), 4.26-4.22 (m, 2H), 3.57 (dq, 1H, *J* = 7 Hz, 8.5 Hz), 2.36-2.32 (m, 1H), 2.24-2.21 (m, 2H), 1.94-1.85 (m, 3H), 1.78 (app. t, 1H, *J* = 4 Hz), 1.28 (d, 1H, *J* = 7.5 Hz), 1.23 (s, 3H), 1.19 (s, 3H), 1.09 (t, 3H, *J* = 7 Hz), and 0.84 (d, 3H, 7 Hz).; **$^{13}$C NMR** ($CDCl_3$, 125 MHz): 183.06, 156.06, 147.65, 137.53, 128.50, 127.96, 127.83, 123.77, 83.19, 80.89, 73.70, 70.68, 47.88, 43.03, 42.42, 35.43, 25.81, 19.45, 13.49, and 10.41; **ESI-MS** *m/Z* calculated for $C_{29}H_{35}N_3O_5$ $(M+H)^+$: 505.26, found: 505.23.

**General procedure for hydrolysis of ACC hydrazones to ketones.** To a 10 mL round bottom flask was added a solution of hydrazone aldol product (1.0 eq) dissolved in 4 mL of acetone. This solution was then treated with solid *para*-toluenesulfonic acid monohydrate (2.5 eq). The clear solution was allowed to stir at room temperature for 6 hours, after which it was quenched with the addition of saturated sodium bicarbonate solution and water. The mixture was extracted with diethyl ether (3 x 10 mL) followed by drying of the organic extracts over anhydrous magnesium sulfate. Concentration *in vacuo* gave a crude oil that consisted of ACC acetone hydrazone and the β-benzyloxy ketone. The ketone could be isolated via flash chromatography over silica gel (7.5% EtOAc, 92.5% Hexanes).

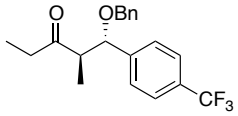



**(1*S*,2*R*)-1-(benzyloxy)-2-methyl-1-phenylpentan-3-one (11a).** This compound was isolated in 91% yield as a viscous oil. **$^1$H NMR** ($CDCl_3$, 500 MHz): δ 7.38-

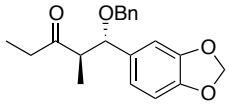
7.24 (m, 8H), 7.17 (d, 2H, *J* = 8 Hz), 4.44 (d, 1H, *J* = 10 Hz), 4.30 (d, 1H, *J* = 11.5 Hz), 4.19 (d, 1H, *J* = 11.5 Hz), 2.97 (dq, 1H, *J* = 7 Hz, 10 Hz), 2.66 (dq, 1H, *J* = 7 Hz, 14.5 Hz), 2.54 (dq, 1H, *J* = 7 Hz, 14.5 Hz), 1.09 (t, 3H, *J* = 7 Hz), and 0.75 (d, 3H, *J* = 7 Hz); **$^{13}$C NMR** ($CDCl_3$, 125 MHz): 214.68, 139.82, 138.38, 128.42, 128.39, 127.90, 127.86, 127.68, 84.82, 70.87, 52.43, 37.19, 14.03, and 7.75; **ESI-MS** *m/Z* calculated for $C_{19s}H_{22}O_2$ $(M+Na)^+$: 305.16, found: 305.14.




**(1S,2R)-1-((4-methoxybenzyl)oxy)-2-methyl-1-phenylpentan-3-one (11b).** This compound was isolated in 93% yield as a viscous oil. **$^1$H NMR** ($CDCl_3$, 500 MHz): δ 7.39-7.32 (m, 5H), 7.08 (d, 2H, *J* = 8.5 Hz), 6.83 (d, 2H, *J* = 8.5 Hz), 4.40 (d, 1H, *J* = 9.5 Hz), 4.23 (d, 1H, *J* = 11.5 Hz), 4.10 (d, 1H, *J* = 11.5 Hz), 3.78 (s, 3H), 2.94 (dq, 1H, *J* = 9.5 Hz, 7 Hz), 2.64 (dq, 1H, *J* = 7 Hz, 14 Hz), 2.501 (dq, 1H, *J* = 7 Hz, 14 Hz), 1.08 (t, 3H, *J* = 7 Hz), and 0.73 (d, 3H, *J* = 7 Hz); **$^{13}$C NMR** ($CDCl_3$, 125 MHz): 184.40, 159.06, 155.90, 139.92, 128.49, 128.18, 113.70, 83.04, 81.34, 73.58, 69.37, 55.41, 42.66, 35.55, 26.68, 25.81, 25.44, 21.37, 19.49, 14.07, and 10.47; **ESI-MS** *m/Z* calculated for $C_{20}H_{24}O_3$ $(M+Na)^+$: 355.17, found: 335.14.

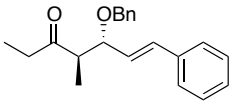



**(1*S*,2*R*)-1-(benzyloxy)-2-methyl-1-(4-(trifluoromethyl)phenyl)pentan-3-one (11c).** This compound was isolated in 91% yield as a viscous oil. **$^1$H NMR** ($CDCl_3$, 500 MHz): δ 7.65 (d, 2H, *J* = 8 Hz), 7.48 (d, 2H, *J* = 8 Hz), 7.30-7.24 (m, 3H), 7.16 (d, 2H, *J* = 8 Hz), 4.52 (d, 1H, *J* = 10 Hz), 4.28 (d, 1H, *J* = 11.5 Hz), 4.20 (d, 1H, *J* = 11.5Hz), 2.91 (dq, 1H, *J* = 7 Hz, 10 Hz), 2.65 (dq, 1H, *J* = 7 Hz, 14.5 Hz), 2.54 (dq, 1H, *J* = 7 Hz, 14.5 Hz), 1.09 (t, 3H, *J* = 7 Hz), and 0.75 (d, 3H, *J* = 7 Hz); **$^{13}$C NMR** ($CDCl_3$, 125 MHz): 213.91, 144.11, 144.09, 137.85, 128.77, 127.89, 125.74, 123.19, 84.05, 70.29, 52.20, 37.18, 13.87, 7.70; **ESI-MS** *m/Z* calculated for $C_{20}H_{21}F_3O_2$ $(M+Na)^+$: 373.15, found: 373.17.

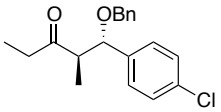



**(1*S*,2*R*)-1-(benzo[d][1,3]dioxol-5-yl)-1-(benzyloxy)-2-methylpentan-3-one (11d).** This compound was isolated in 94% yield as a viscous oil. **$^1$H NMR** ($CDCl_3$, 500 MHz): δ 7.29.7.24 (m, 3H), 7.17 (d, 2H, *J* = 7 Hz), 6.87 (s, 1H), 6.80-6.76 (m, 2H), 5.98 (s, 2H), 4.34 (d, 1H, *J* = 10 Hz), 4.30 (d, 1H, *J* = 11.5 Hz), 4.16 (d, 1H, *J* = 11.5 Hz), 2.91 (dq, 1H, *J* = 7 Hz, 10 Hz), 2.63 (dq, 1H, *J* = 7 Hz, 14.5 Hz), 2.51 (dq, 1H, *J* = 7 Hz, 14.5 Hz), 1.07 (t, 3H, *J* = 7 Hz), and 0.75 (d, 3H, *J* = 7 Hz); **$^{13}$C NMR** ($CDCl_3$, 125 MHz): 214.57, 148.28, 147.68, 128.41, 127.65,

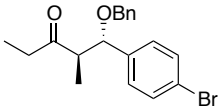
121.83, 108.14, 107.39, 101.30, 1.22, 84.55, 70.66, 52.40, 37.16, 14.03, 7.72; **ESI-MS** *m/Z* calculated for $C_{20}H_{22}O_4$ $(M+Na)^+$: 349.15, found: 349.07.



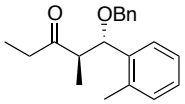

**(4*R*,5*R*,*E*)-5-(benzyloxy)-4-methyl-7-phenylhept-6-en-3-one (11e).** This compound was isolated in 92% yield as colorless oil that solidified upon standing. **$^1$H NMR** ($CDCl_3$, 500 MHz): δ 7.41 (d, 2H, *J* = 7 Hz), 7.36-7.22 (m, 8H), 6.60 (d, 1H, *J* = 15.5 Hz), 6.04 (dd, 1H, *J* = 16, 8.5 Hz), 4.54 (d, 1H, *J* = 11.5 Hz), 4.32 (d, 1H, *J* = 11.5 Hz), 4.08 (app. t, 1H, *J* = 9 Hz), 2.90-2.83 (dq, 1H, *J* = 7 Hz, 9 Hz), 2.64-2.56 (dq, 1H, *J* = 7.5 Hz, 14.5 Hz), 2.54-2.46 (dq, 1H, *J* = 7.5 Hz, 14.5 Hz), 1.06 (t, 3H, *J* = 7 Hz), 0.98 (d, 3H, *J* = 7 Hz); **$^{13}$C NMR** ($CDCl_3$, 125 MHz): 214.27, 138.41, 136.37 134.84, 134.83, 128.86, 127.89, 127.88, 127.69, 126.80, 83.71, 70.84, 50.47, 37.16, 13.87, 7.70; **ESI-MS** *m/Z* calculated for $C_{21}H_{24}O_2$ $(M+Na)^+$: 331.18, found: 331.11.



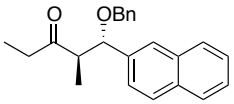

**(1S,2R)-1-(benzyloxy)-1-(4-chlorophenyl)-2-methylpentan-3-one (11f).** This compound was isolated in 92% yield as thick film. **$^1$H NMR** ($CDCl_3$, 500 MHz): δ 7.35 (d, 2H, *J* = 8.5 Hz), 7.31-7.25 (m, 5H), 7.15 (d, 2H , *J* = 8 Hz), 4.42 (d, 1H, *J* = 10Hz), 4.27 (d, 1H, *J* = 11.5 Hz), 4.16 (d, 1H, *J* = 11.5 Hz), 2.91 (dq, 1H, *J* = 7 Hz, 10 Hz), 2.63 (dq, 1H, *J* = 7 Hz, 14.5 Hz), 2.52 (dq, 1H, *J* = 7 Hz, 14.5 Hz), 1.08 (t, 3H, *J* = 7 Hz), and 0.74 (d, 3H, *J* = 7 Hz); **$^{13}$C NMR** ($CDCl_3$, 125 MHz): 214.18, 138.41, 138.03, 134.10, 129.19, 128.93, 127.86, 127.79, 83.99, 71.00, 52.26, 37.21, 13.91, 7.70; **ESI-MS** *m/Z* calculated for $C_{19}H_{21}ClO_2$ $(M+Na)^+$: 339.12, found: 339.06.



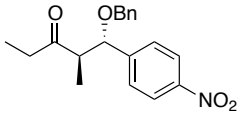

**(1*S*,2*R*)-1-(benzyloxy)-1-(4-bromophenyl)-2-methylpentan-3-one (11g).** This compound was isolated in 93% yield as a viscous oil. **$^1$H NMR** ($CDCl_3$, 500 MHz): δ 7.51 (d, 2H, *J* = 8.5 Hz), 7.31-7.22 (m, 5H) 7.25 (app. d, 2H, *J* = 7 Hz), 4.40 (d, 1H, *J* = 10 Hz), 4.27 (d, 1H, *J* = 11.5 Hz), 4.17 (d, 1H, *J* = 11.5 Hz), 2.91 (dq, 1H, *J* = 7 Hz, 10 Hz), 2.64 (dq, 1H, *J* = 7 Hz, 14.5 Hz), 2.52 (dq, 1H, *J* = 7 Hz, 14.5 Hz), 1.08 (t, 3H, *J* = 5 Hz), and 0.74 (d, 3H, *J* = 5 Hz); **$^{13}$C NMR** ($CDCl_3$, 125 MHz): 214.11, 138.89, 137.96, 127.71, 122.21, 84.00, 70.98, 52.19, 37.16, 13.86, and 7.65; **ESI-MS** *m/Z* calculated for $C_{19}H_{21}BrO_2$ $(M+Na)^+$: 383.07, found: 383.04.




**(1*S*,2*R*)-1-(benzyloxy)-2-methyl-1-(o-tolyl)pentan-3-one (11h).** This compound was isolated in 95% yield as clear film. **$^{1}$H NMR** ($CDCl_3$, 500 MHz): δ 7.42 (d, 1H, *J* = 7 Hz), 7.30-7.14 (m, 8H), 4.79 (d, 1H, *J* = 10 Hz), 4.26 (d, 1H, *J* = 11.5 Hz), 4.14 (d, 1H, *J* = 11.5 Hz), 3.05 (dq, 1H, *J* = 7 Hz, 10 Hz), 2.68 (dq, 1H, *J* = 7 Hz, 14.5 Hz), 2.54 (dq, 1H, *J* = 7 Hz, 14.5 Hz), 2.35 (s, 3H), 1.09 (t, 3H, *J* = 7 Hz), 0.76 (d, 3H, 7 Hz); **$^{13}$C NMR** ($CDCl_3$, 125 MHz): 214.71, 138.46, 137.07, 128.38, 127.80, 127.62, 127.51, 126.60, 70.56, 37.33, 19.82, 13.47, 7.75; **ESI-MS** *m/Z* calculated for $C_{20}H_{24}O_2$ $(M+H)^+$: 296.18, found: 296.16.

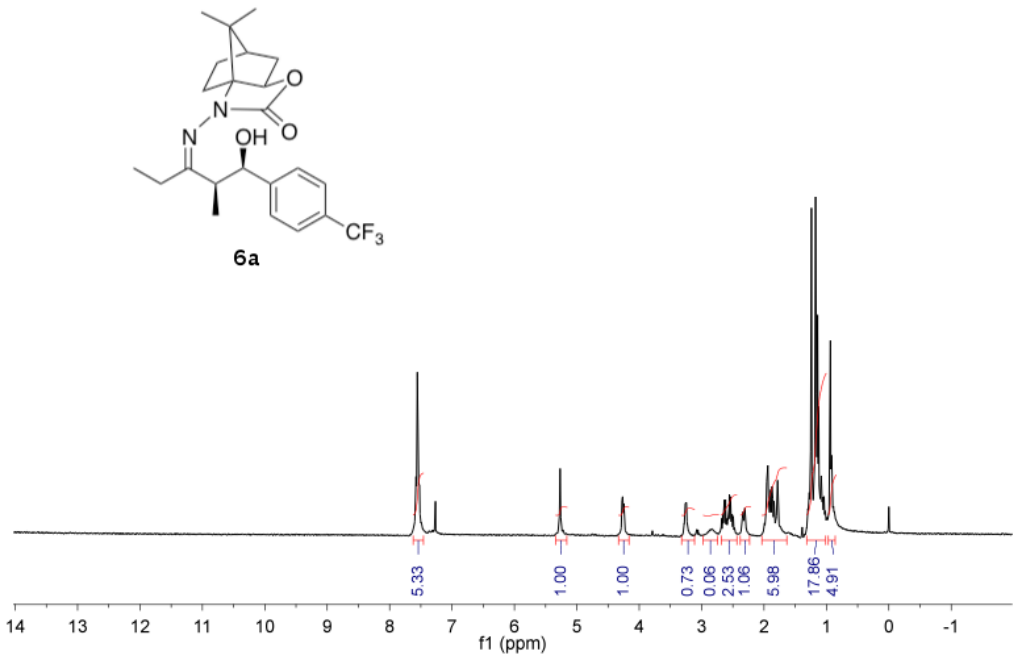


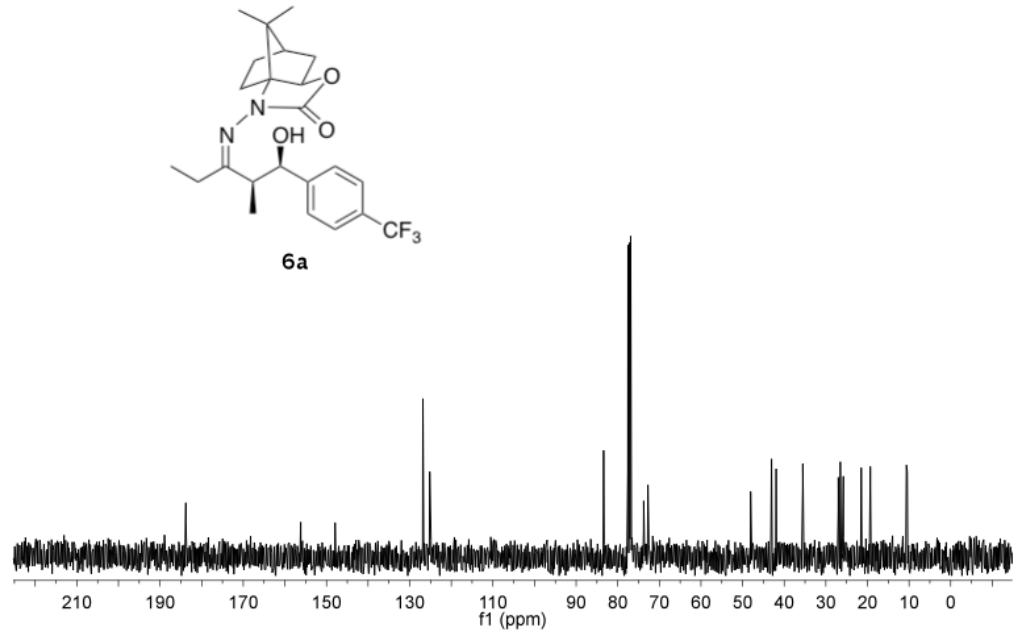

**(1S,2R)-1-(benzyloxy)-2-methyl-1-(naphthalen-2-yl)pentan-3-one (11i).** This compound was isolated in 91% yield as a viscous oil. **$^{1}$H NMR** ($CDCl_3$, 500 MHz): δ 7.90-7.85 (m, 3H), 7.77 (s, 1H), 7.54-7.30 (m, 3H), 7.27-7.23 (m, 3H), 7.17 (d, 2H, *J* = 7.5 Hz), 4.60 (d, 1H, *J* = 10 Hz), 4.31 (d, 1H, *J* = 11.5 Hz), 4.21 (d, 1H, *J* = 11.5 Hz), 3.09 (dq, 1H, *J* = 7 Hz, 10 Hz), 2.70 (dq, 1H, *J* = 7 Hz, 14 Hz), 2.58 (dq, 1H, *J* = 7 Hz, 14 Hz), 1.11 (t, 3H, *J* = 7 Hz), 0.77 (d, 3H, *J* = 7 Hz); **$^{13}$C NMR** ($CDCl_3$, 125 MHz): 214.52, 128.77, 128.44, 128.36, 128.05, 127.86, 127.80, 127.77, 127.60, 127.50, 126.41, 126.28, 124.84, 124.80, 84.93, 70.88, 52.10, 37.17, 14.03, and 7.71; **ESI-MS** *m/Z* calculated for $C_{23}H_{24}O_2$ $(M+Na)^+$: 355.18, found: 355.16.

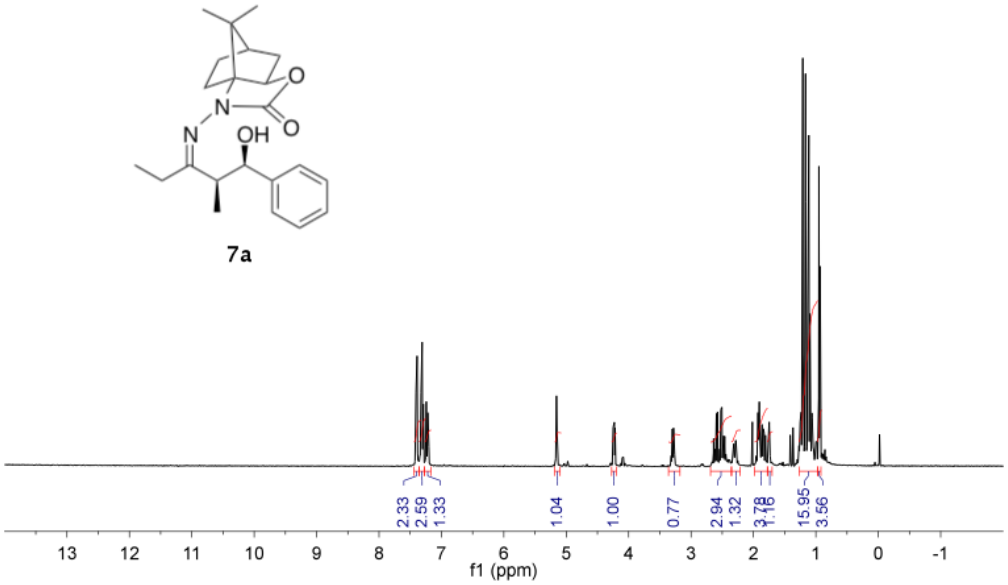



**(1*S*,2*R*)-1-(benzyloxy)-2-methyl-1-(4-nitrophenyl)pentan-3-one (11j).** This compound was isolated in 93% yield as a viscous oil. **$^{1}$H NMR** ($CDCl_3$, 500 MHz): δ 8.27 (d, 2H, *J* = 8.5 Hz), 7.55 (d, 2H, *J* = 8.5 Hz), 7.32-7.28 (m, 3H), 7.16 (m, 2H), 4.60 (d, 1H, *J* = 9.5 Hz), 4.29 (d, 1H, *J* = 11.5 Hz), 4.24 (d, 1H, *J* = 11.5 Hz), 2.93 (dq, 1H, *J* = 7 Hz, 9.5 Hz), 2.69-2.54 (m, 2H), 1.10 (t, 3H, *J* = 7 Hz), and 0.77 (d, 3H, *J* = 7 Hz); **$^{13}$C NMR** ($CDCl_3$, 125 MHz): 213.45, 147.62, 137.52, 128.66, 128.55, 128.05, 127.94, 123.98, 83.62, 71.65, 37.30, 13.82, and 7.70; **ESI-MS** *m/Z* calculated for $C_{19}H_{21}NO_4$ $(M+Na)^+$: 350.15, found: 350.12.

## II. Spectral Images

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OH
O
2.33
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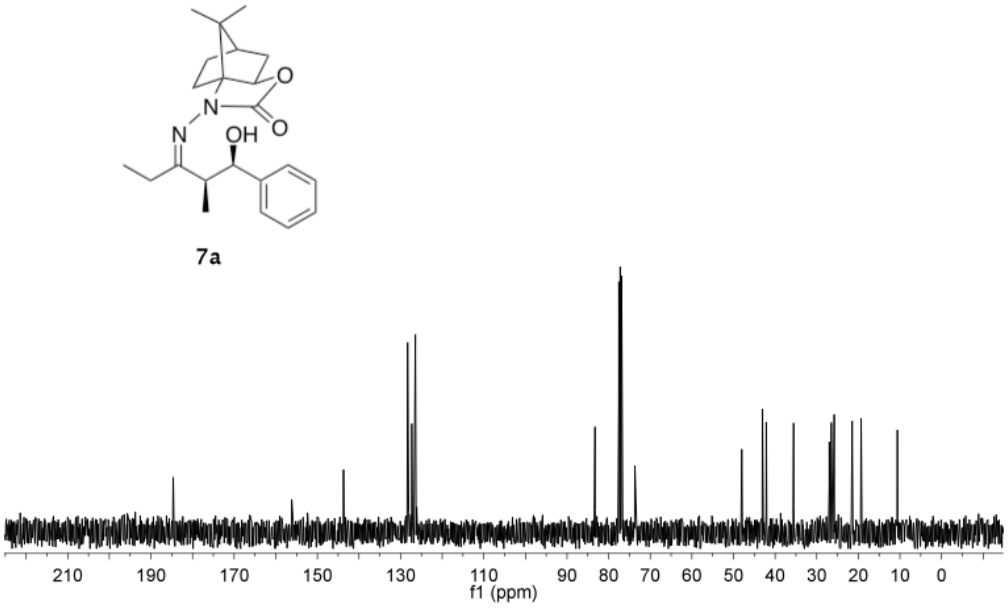
1.33
1.04
1.00
0.77
2.94
1.32
3.78
1.18
15.95
3.56
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)

**7a**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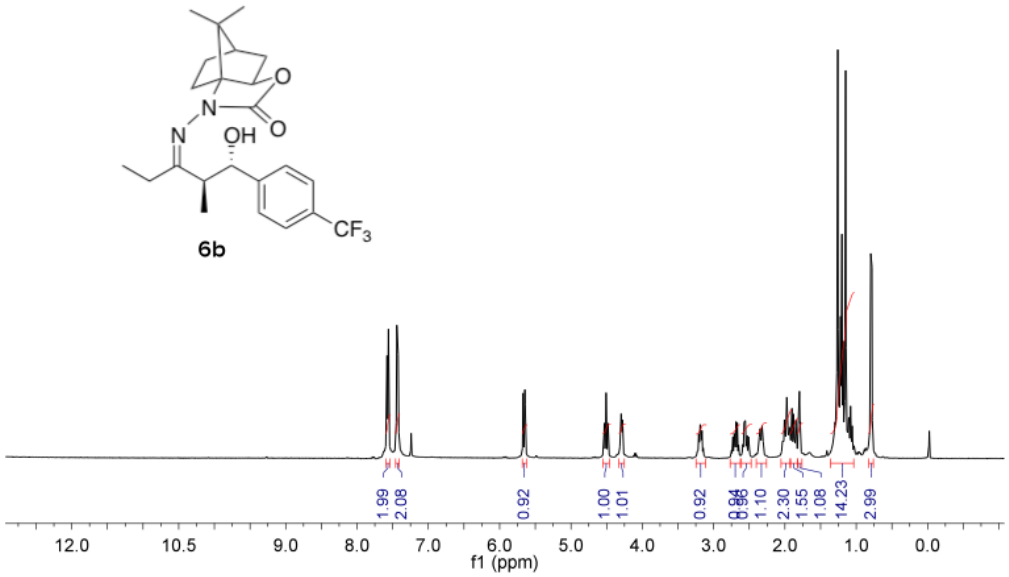
N
OH
O
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

**7a**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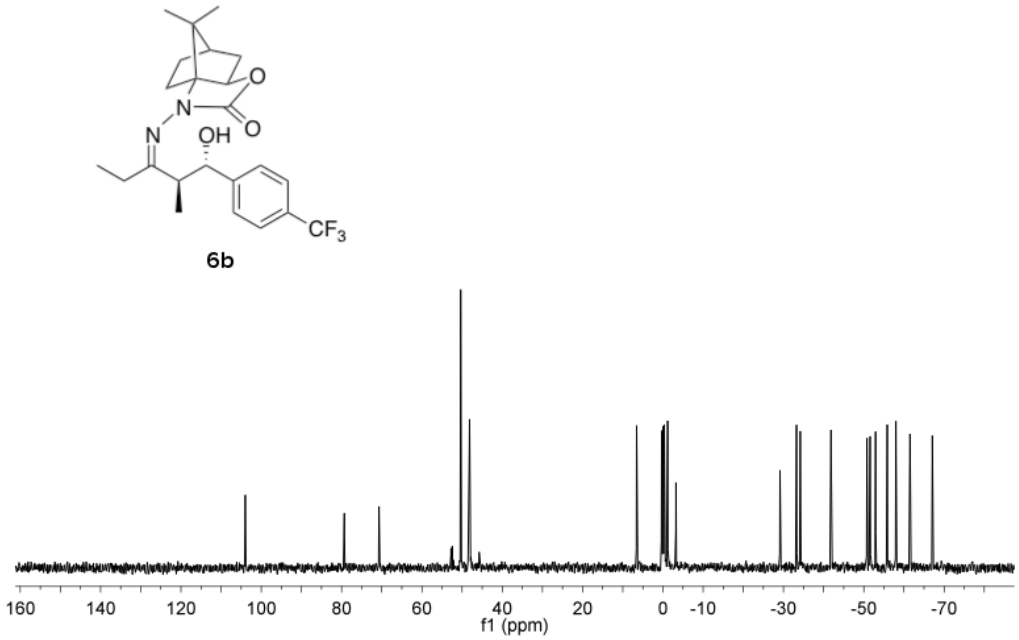
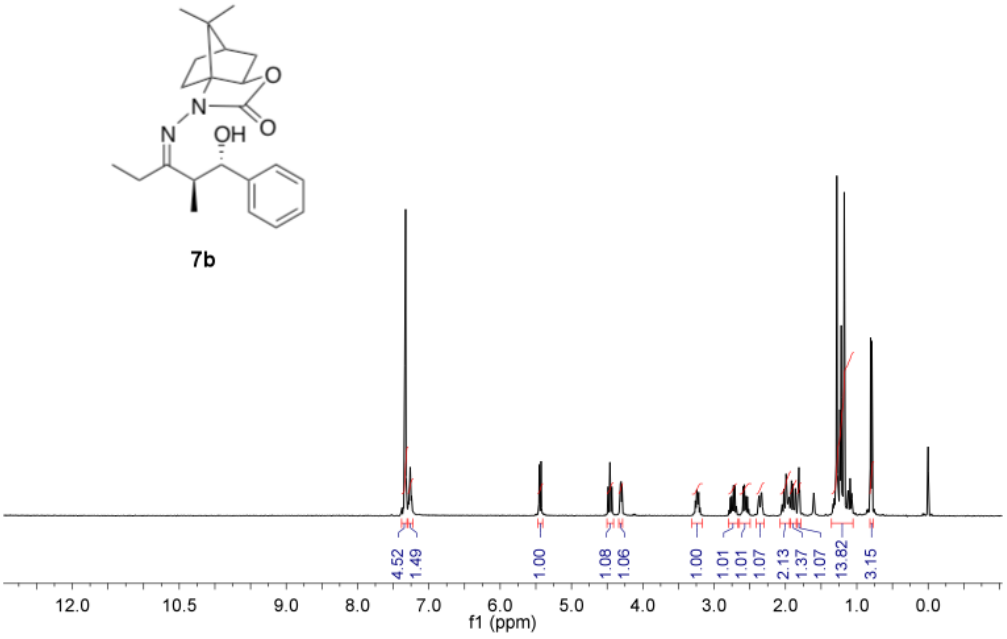
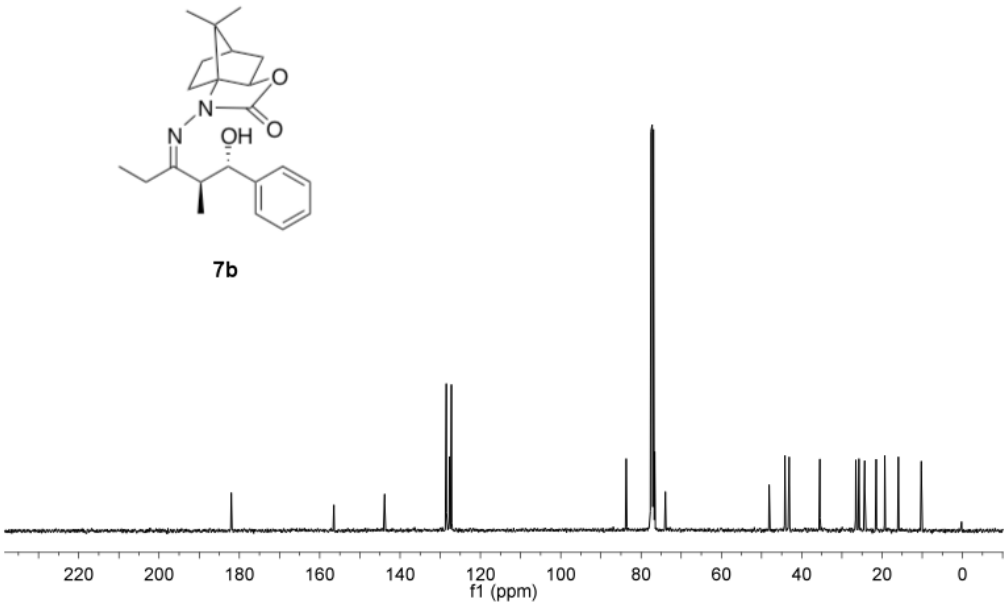
N
O
N
OH
CF3
6b
1.99
2.08
0.92
1.00
1.01
0.92
1.10
2.30
1.55
1.08
14.23
2.99
12.0
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

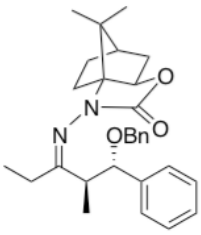

O
N
O
N
OH
CF3
6b
160
140
120
100
80
60
40
20
0
-10
-30
-50
-70
f1 (ppm)



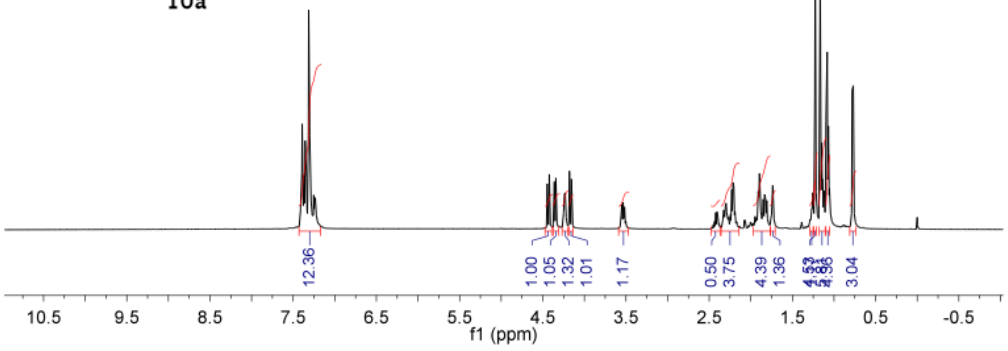

**7b**

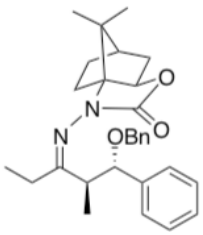



**7b**

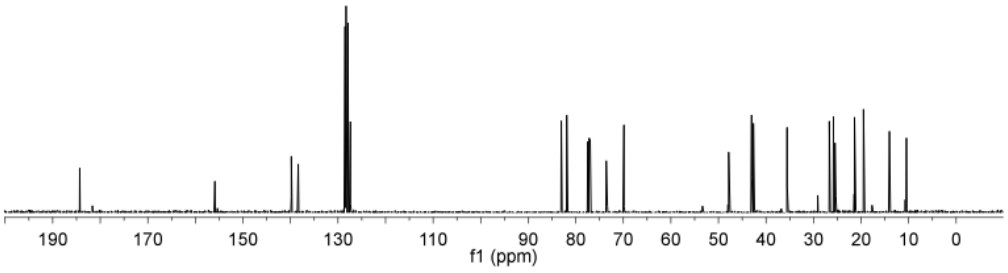

O
N
N
OBn
O

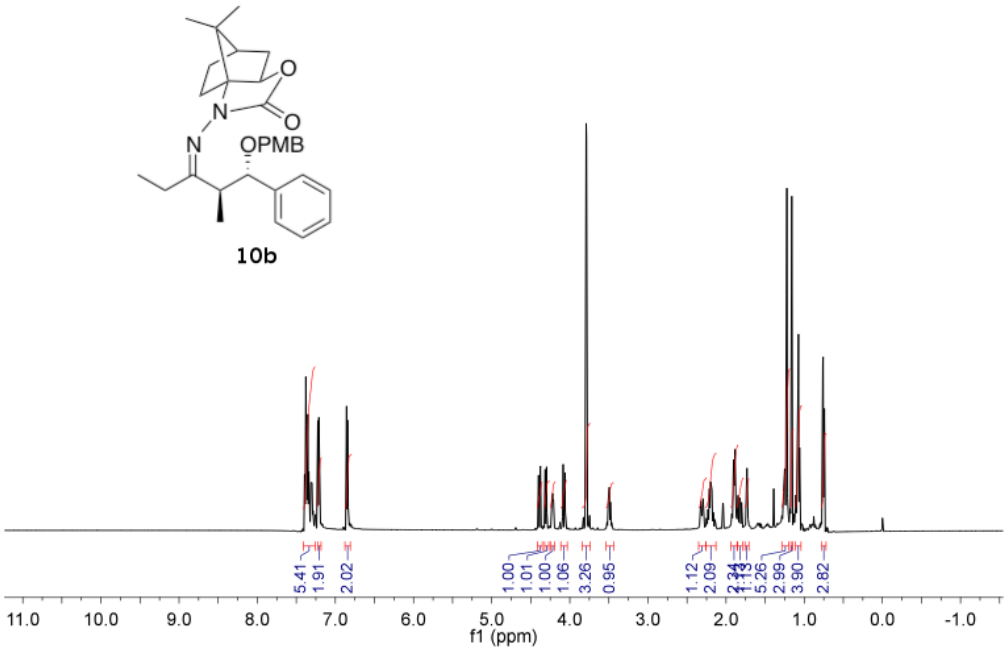
**10a**


12.36
1.00
1.05
1.32
1.01
1.17
0.50
3.75
4.39
1.36
3.04
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)


O
N
N
OBn
O

**10a**


190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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N
O
N
OPMB
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1.91
2.02
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1.01
1.00
1.06
3.26
0.95
1.12
2.09
5.26
2.99
3.90
2.82
11.0
10.0
9.0
8.0
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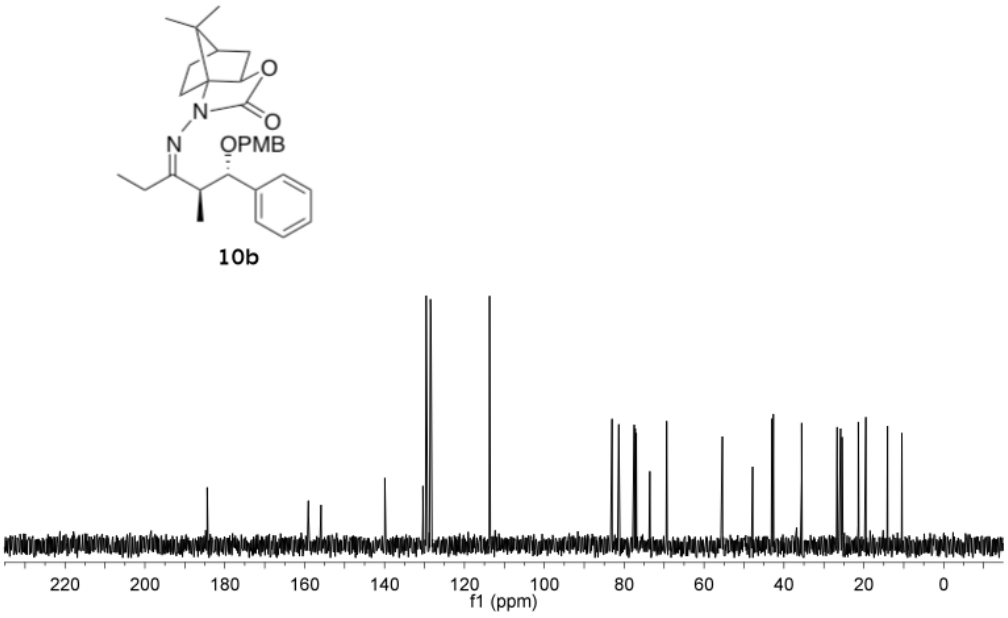
0.0
-1.0
f1 (ppm)

**10b**


O
N
O
N
OPMB
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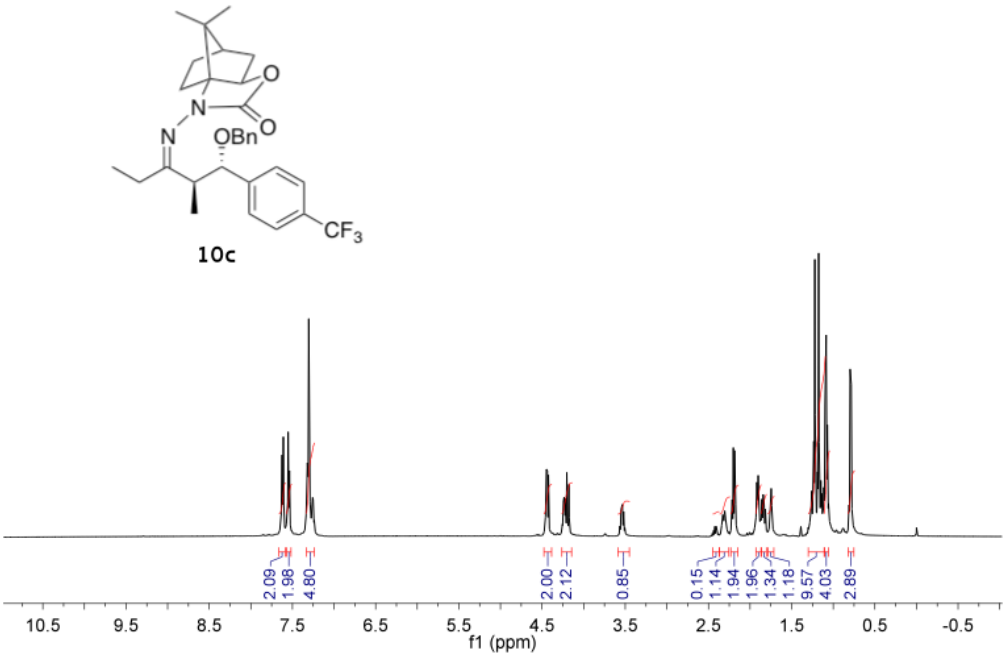
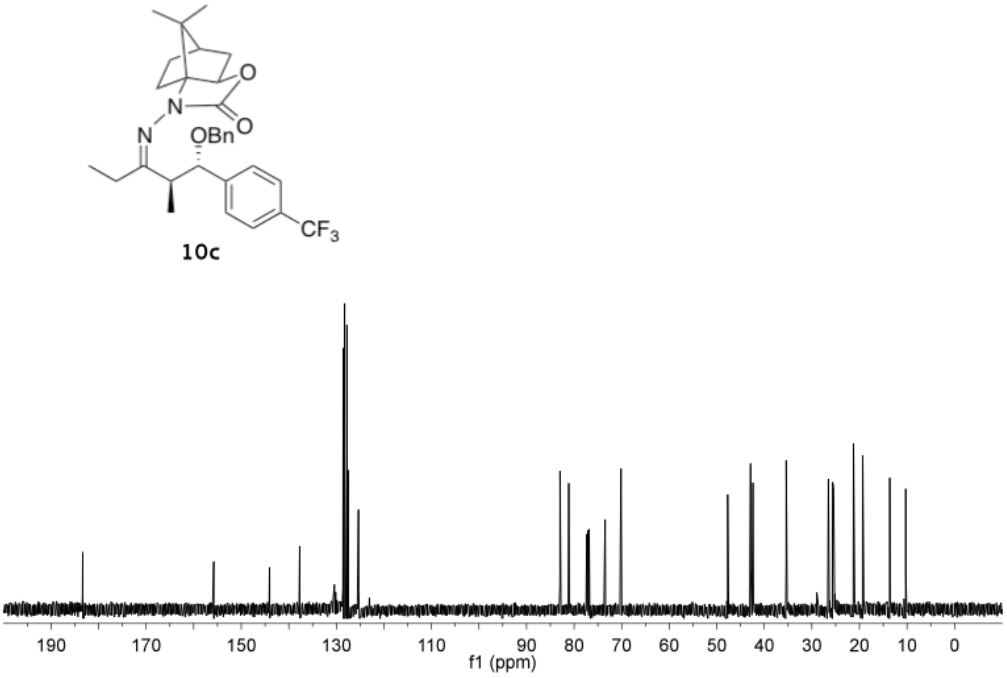
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

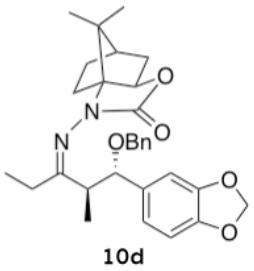
**10b**




10c




10c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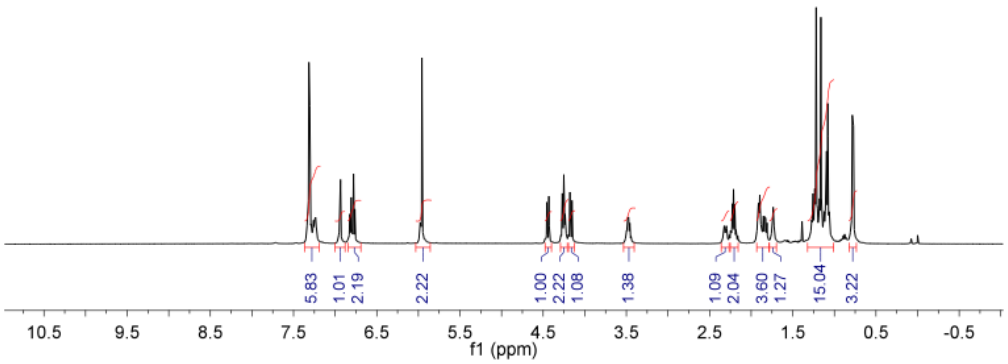
N
N
OBn
O
O
O

**10d**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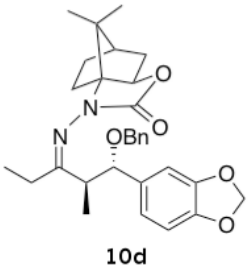
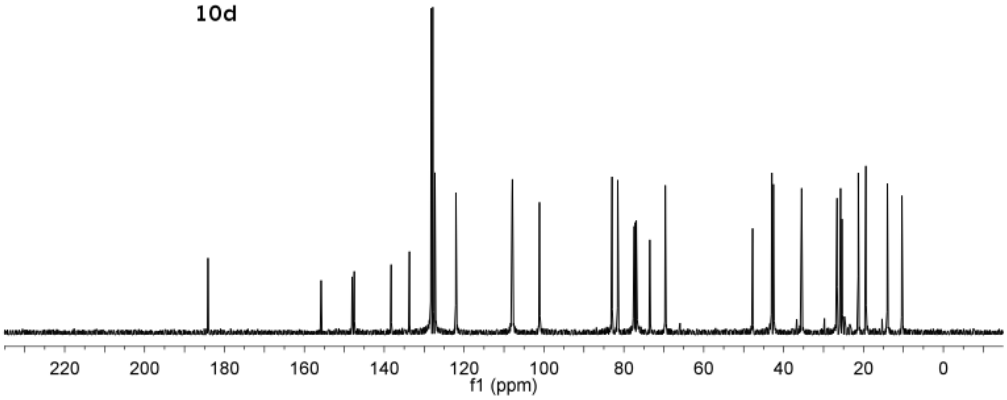
2.19
2.22
1.00
2.22
1.08
1.38
1.09
2.04
3.60
1.27
15.04
3.22
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)


O
N
N
OBn
O
O
O

**10d**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140
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100
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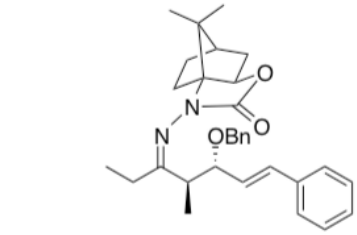
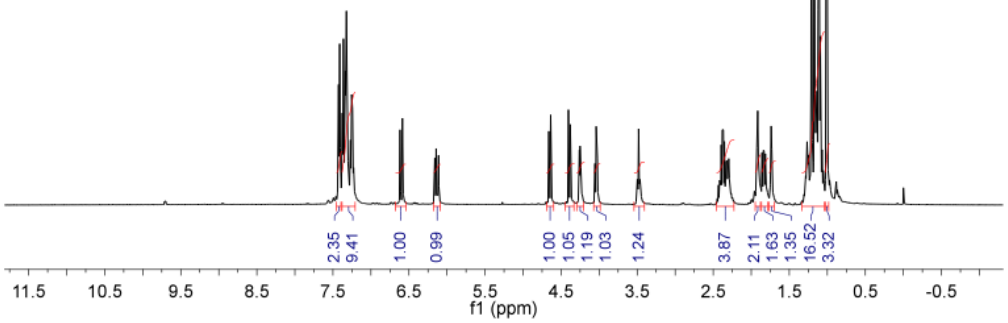
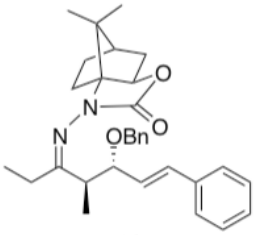
60
40
20
0
f1 (ppm)

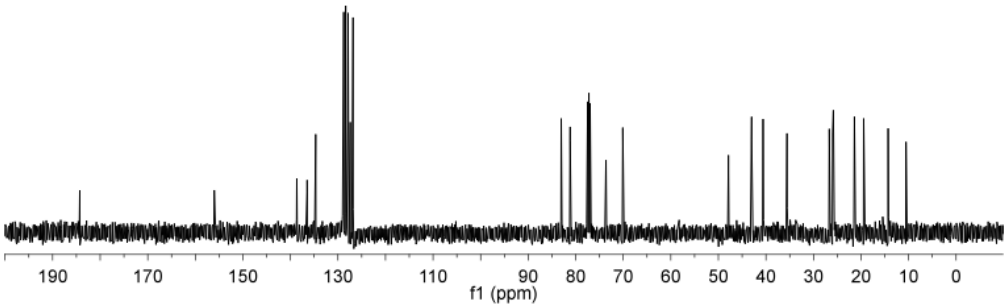


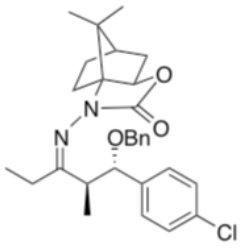

**10e**



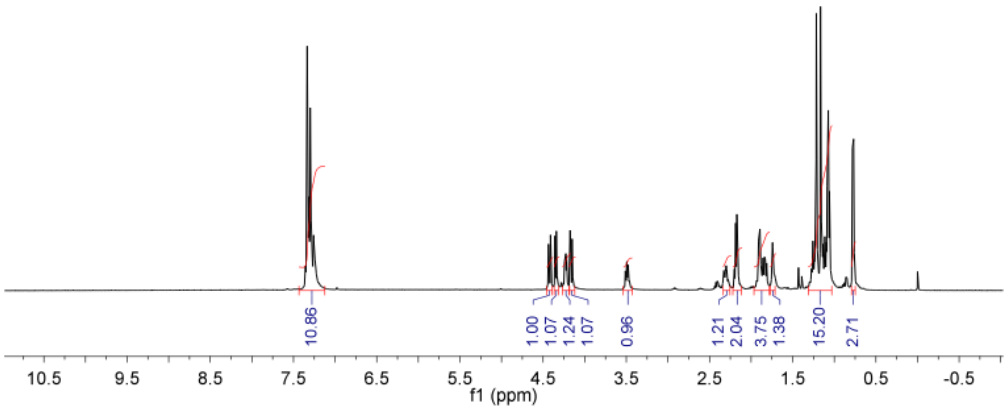




**10e**




O
N
N
OBn
O
Cl

**10f**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2.04
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15.20
2.71
10.5
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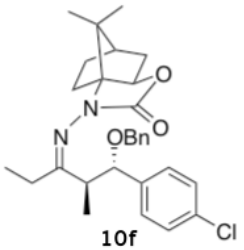
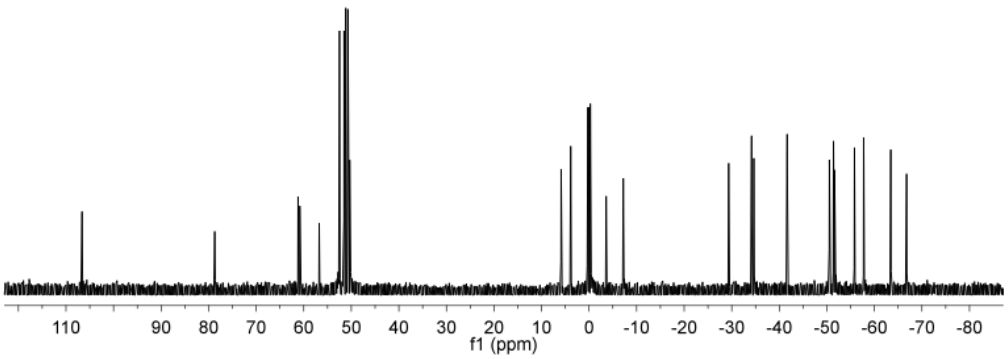
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)


O
N
N
OBn
O
Cl

**10f**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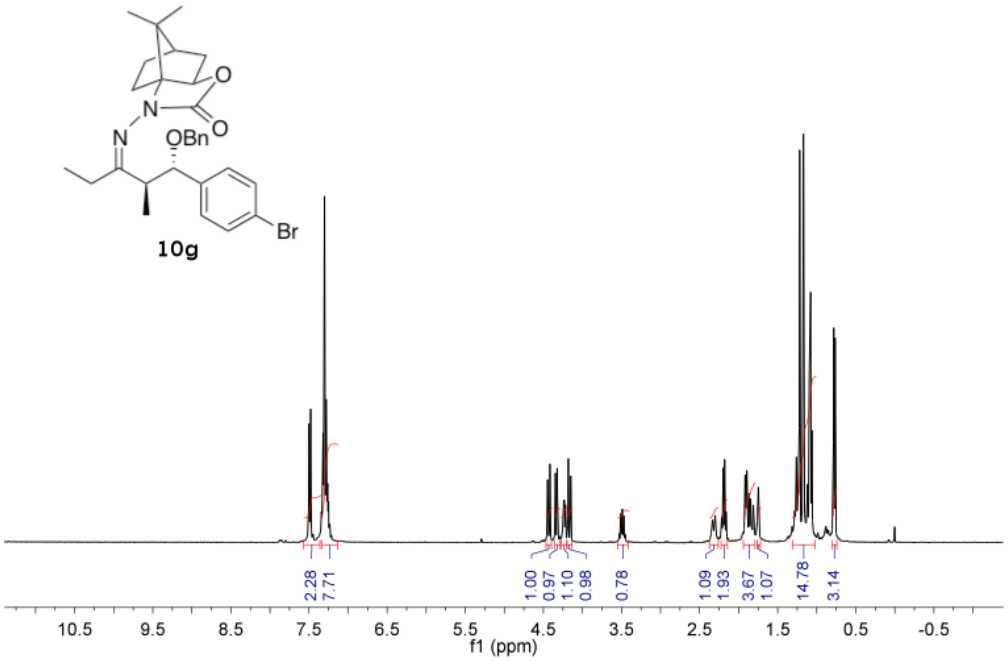
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
f1 (ppm)


O
N
N
OBn
O
Br
10g
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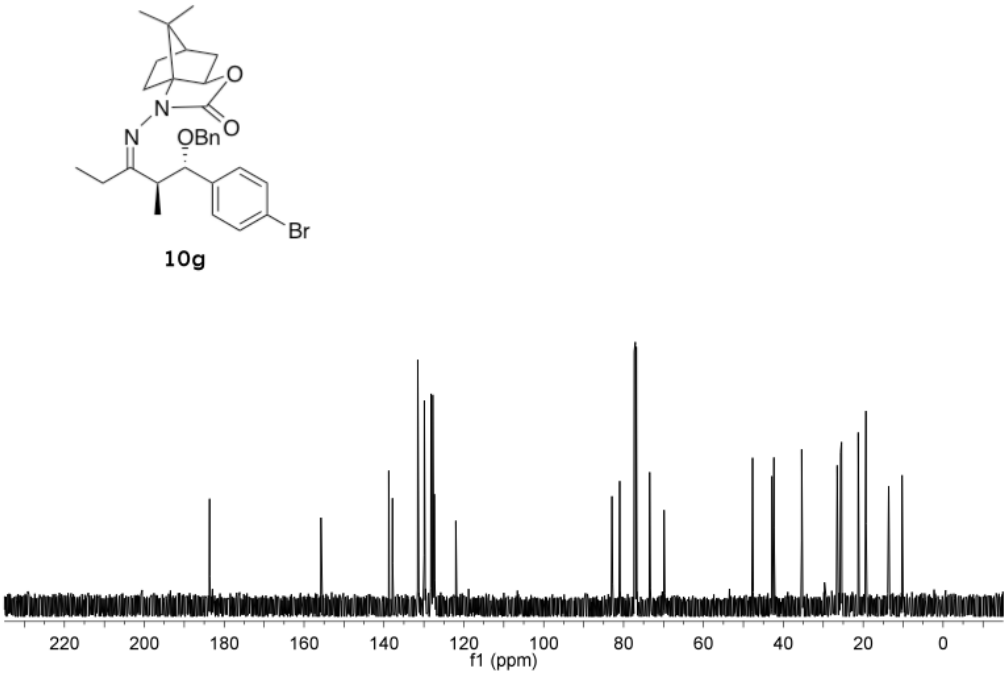
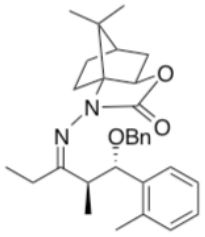
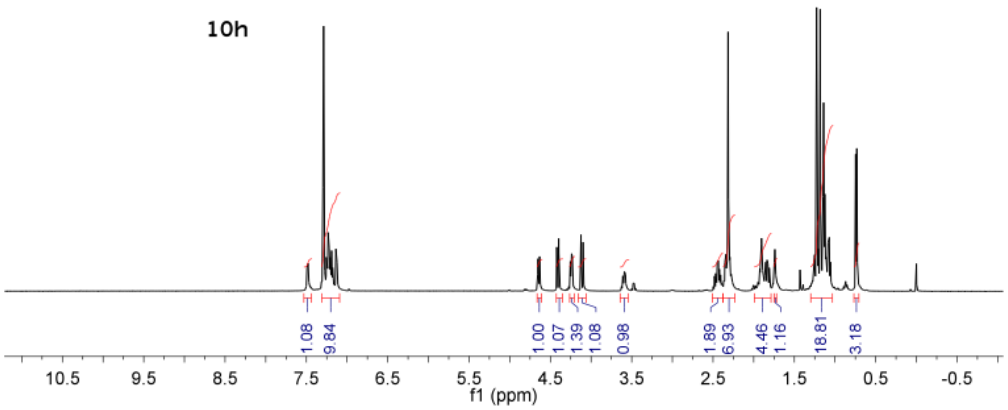
7.71
1.00
0.97
1.10
0.98
0.78
1.09
1.93
3.67
1.07
14.78
3.14
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)


O
N
N
OBn
O
Br
10g
220
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


O
N
O
N
OBn

**10h**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1.08
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1.89
6.93
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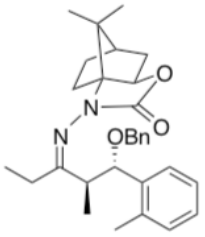
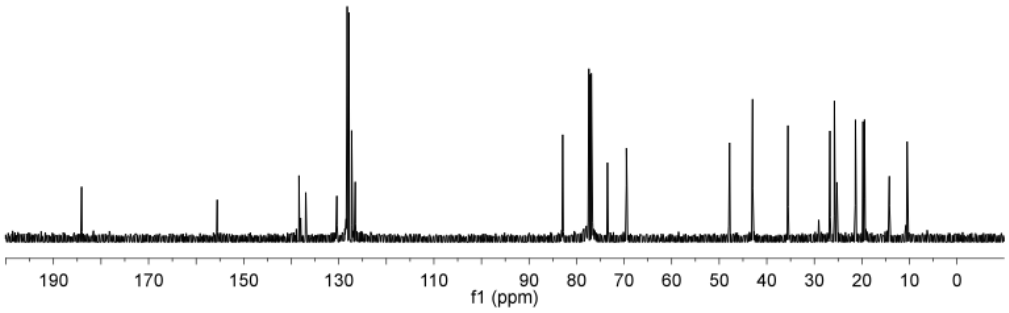
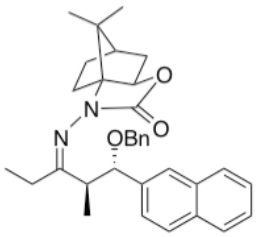
1.16
18.81
3.18
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)

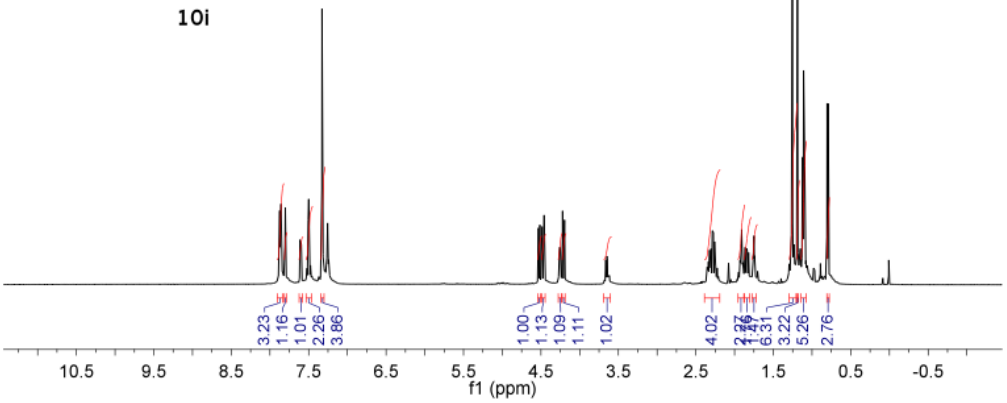

O
N
O
N
OBn

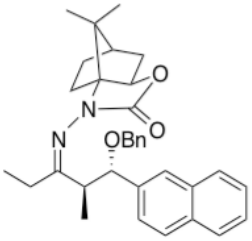
**10h**


190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

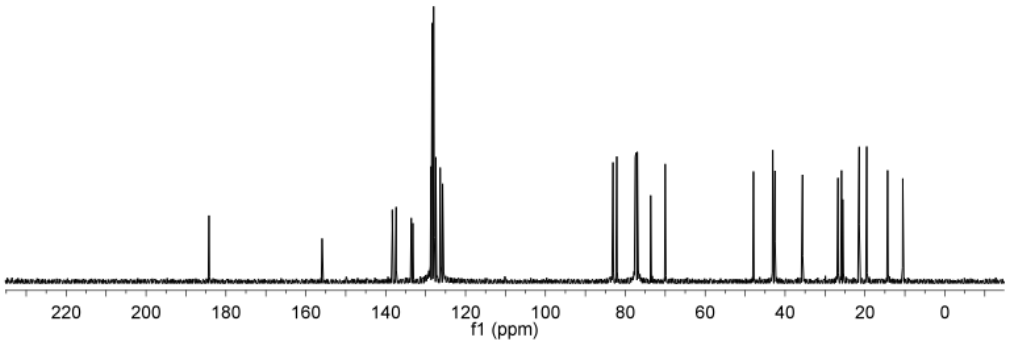

O
N
N
OBn
O

**10i**


3.23
1.16
1.01
2.26
3.86
1.00
1.13
1.09
1.11
1.02
4.02
2.27
2.26
1.49
6.31
3.22
5.26
2.76
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)


O
N
N
OBn
O

**10i**


220
200
180
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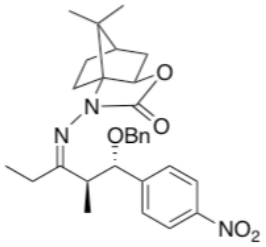
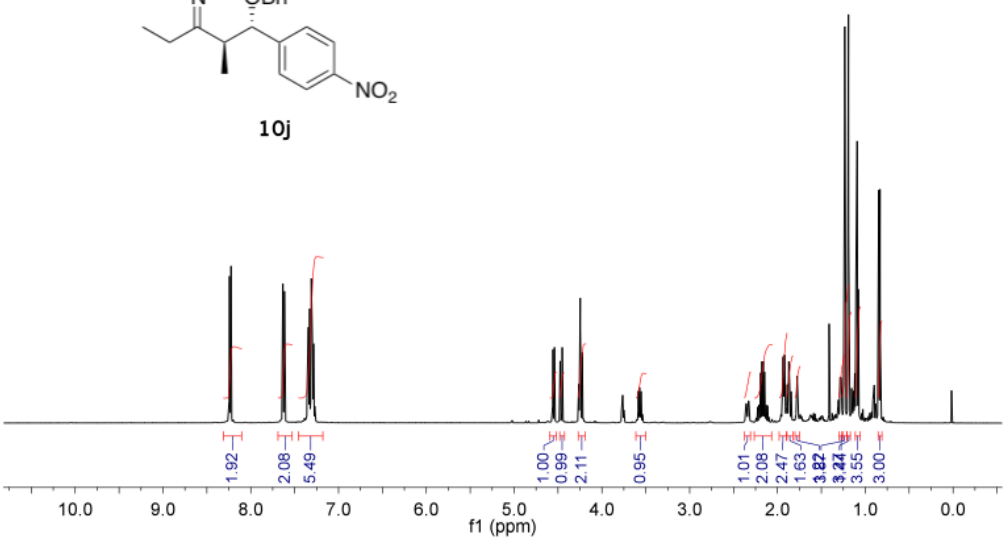
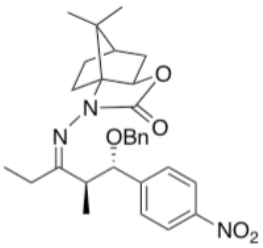
140
120
100
80
60
40
20
0
f1 (ppm)

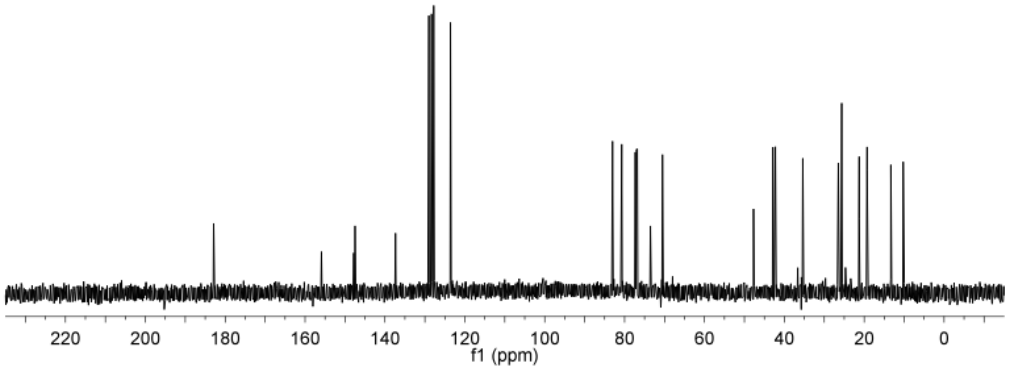


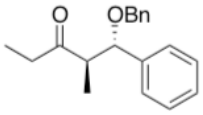

**10j**



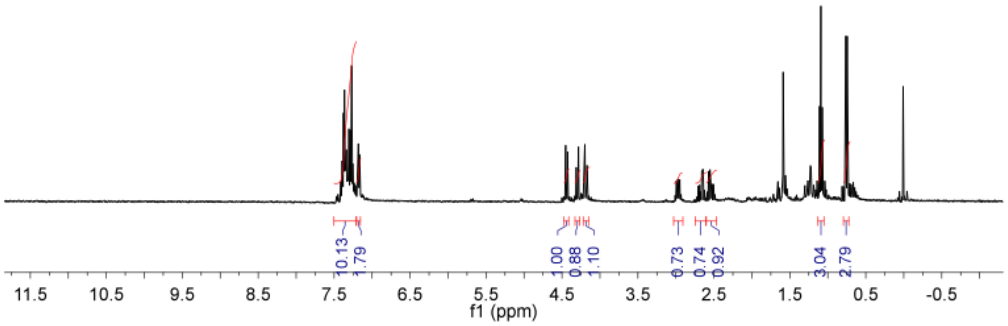



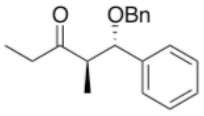

**10j**



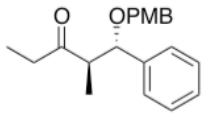



**11a**



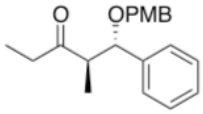




**11a**

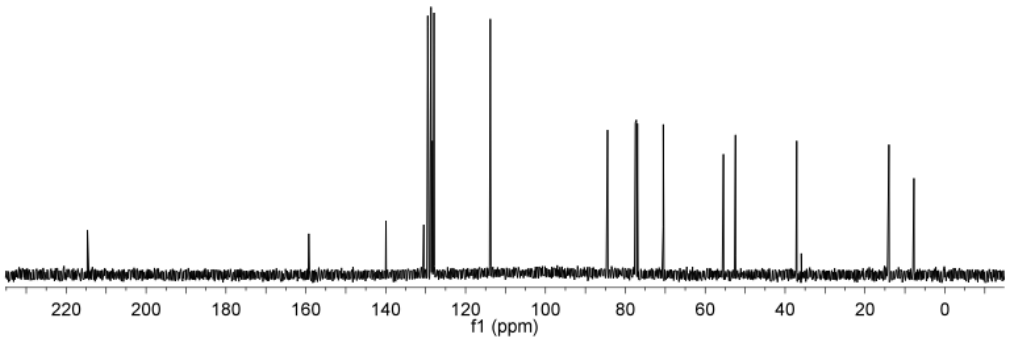

O
OPMB

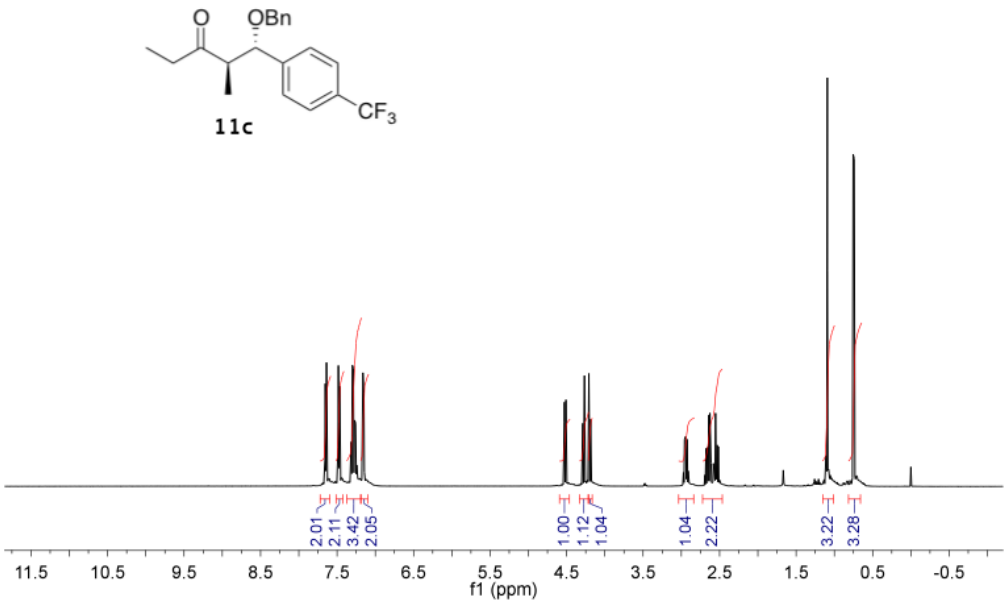
**11b**

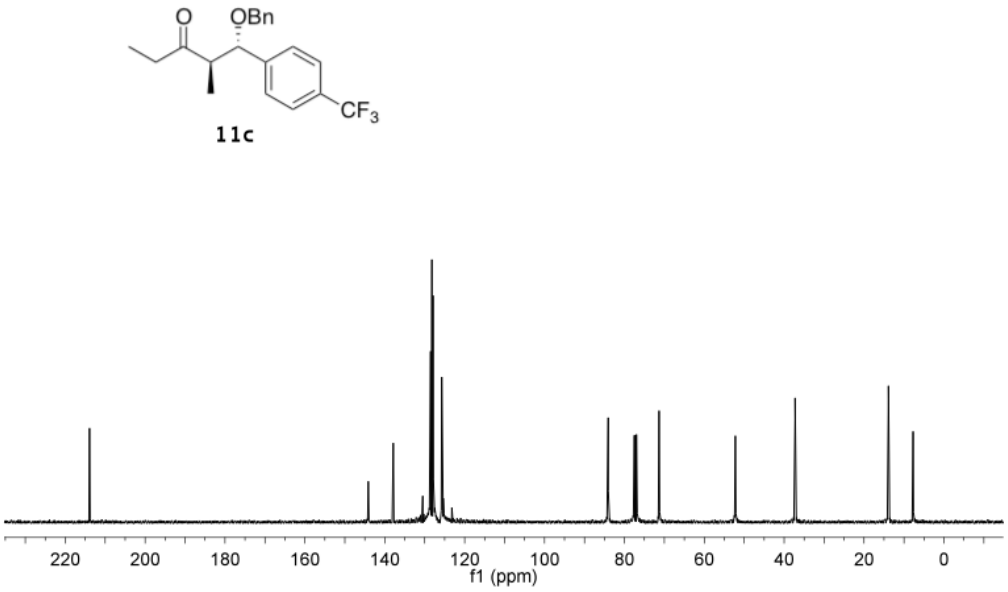

5.23
1.94
1.95
1.00
1.03
1.01
3.03
0.95
0.98
1.00
3.00
3.01
11.5
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

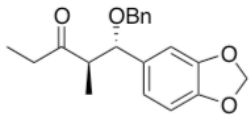

O
OPMB

**11b**

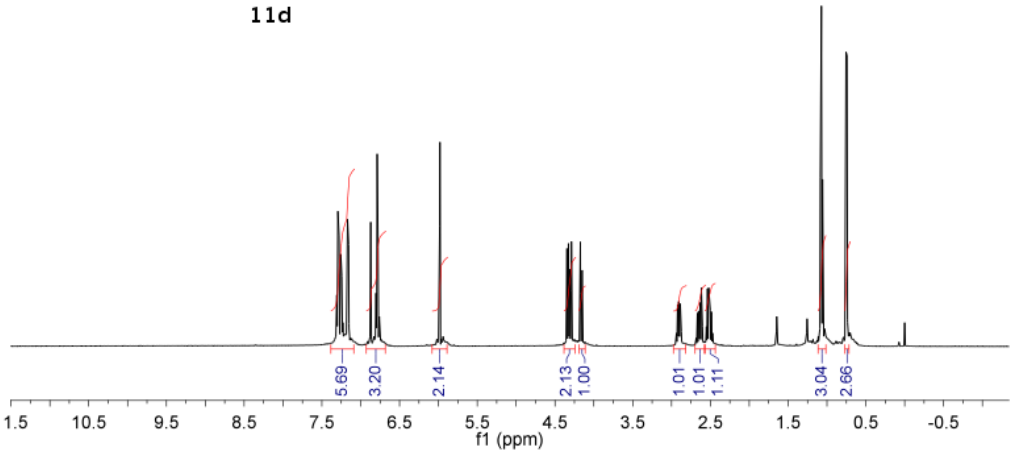

220
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

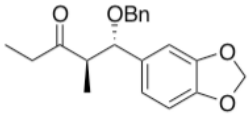

O
OBn
CF3
11c
2.01
2.11
3.42
2.05
1.00
1.12
1.04
1.04
2.22
3.22
3.28
11.5
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)


O
OBn
CF3
11c
220
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

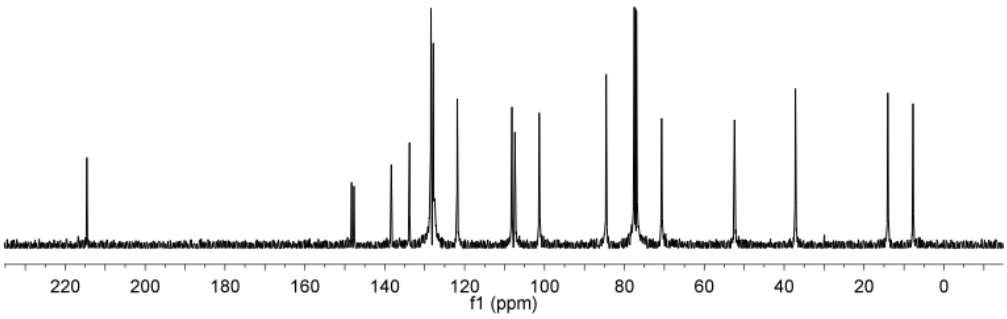


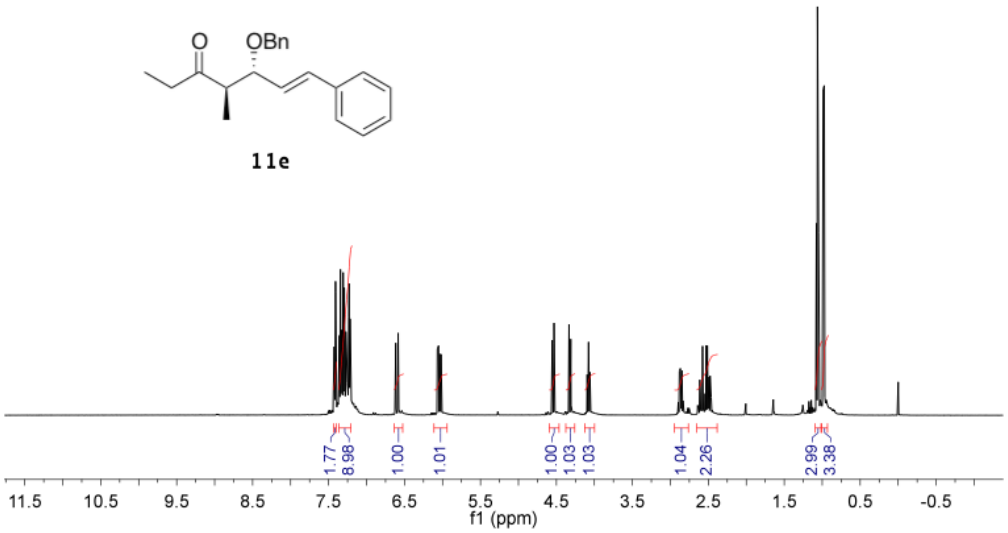

**11d**



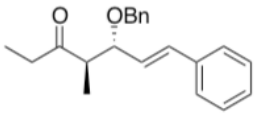




**11d**

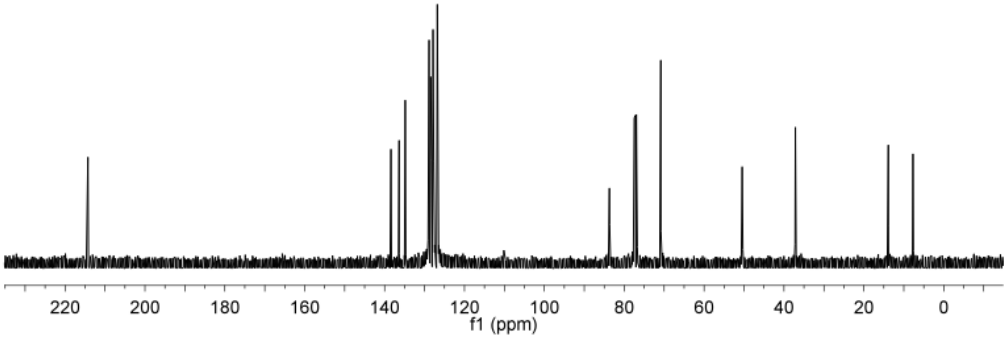


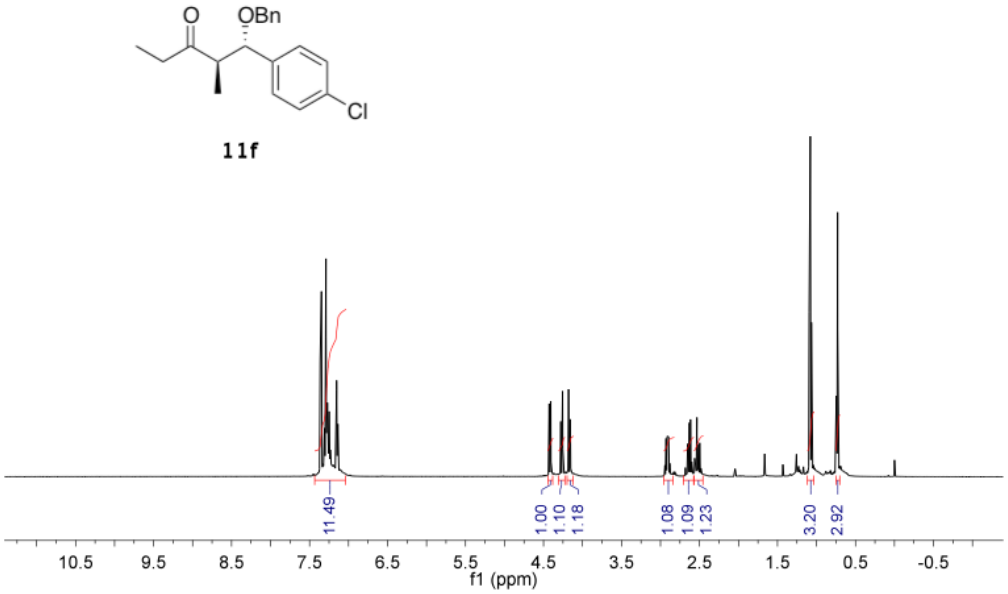


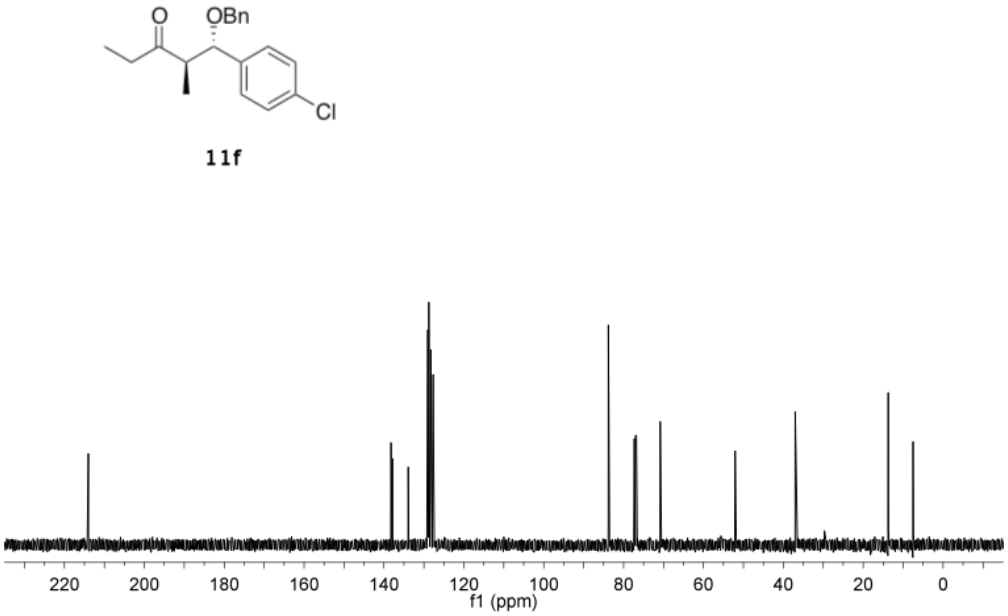

**11e**

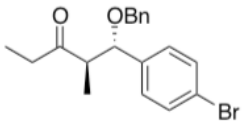



**11e**

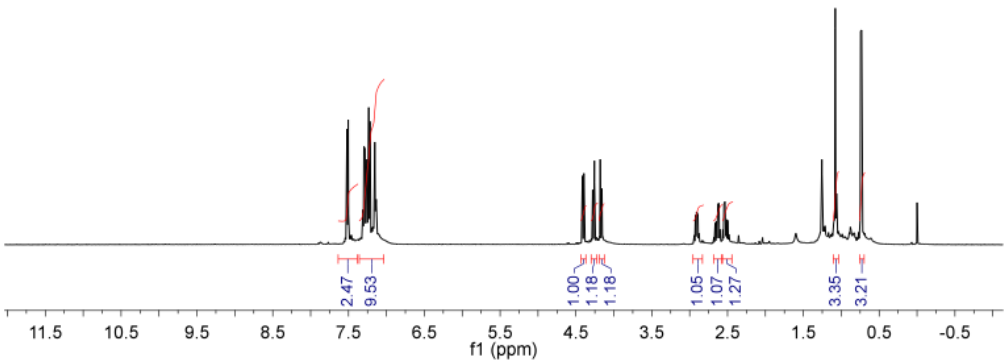


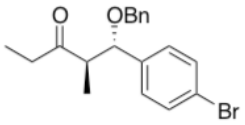

O
OBn
Cl
11f
11.49
1.00
1.10
1.18
1.08
1.09
1.23
3.20
2.92
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)


O
OBn
Cl
11f
220
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

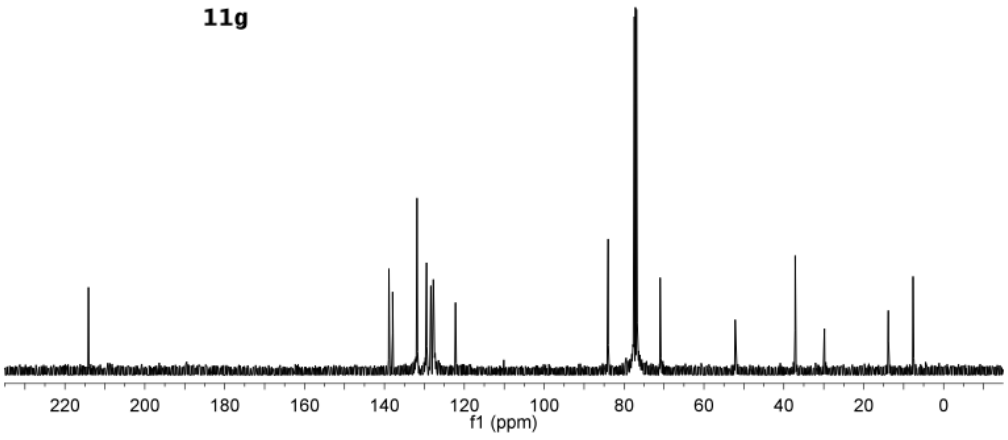


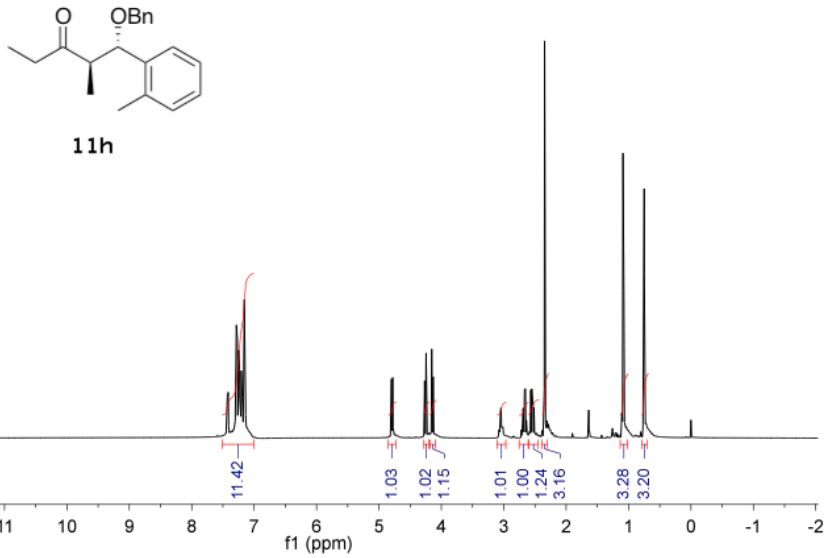

**11g**

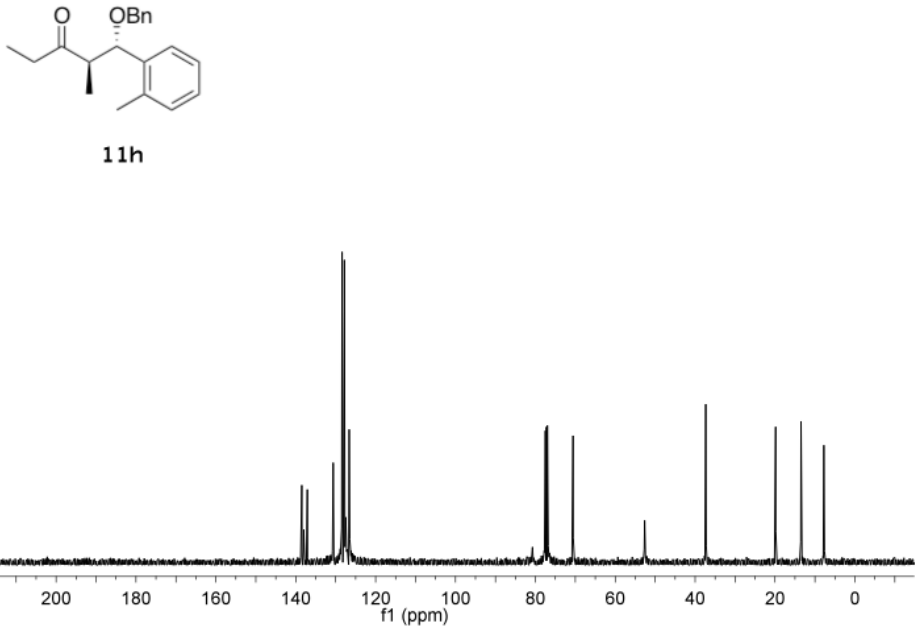


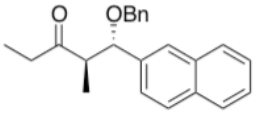




**11g**

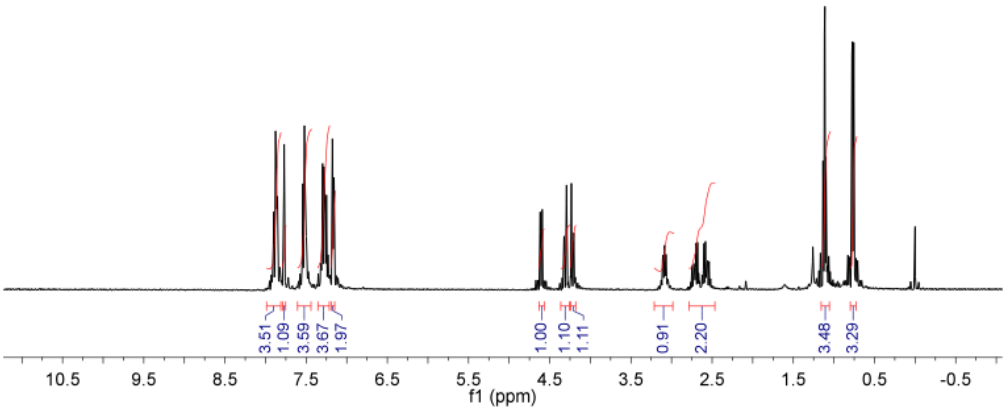


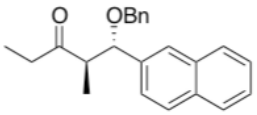

O
OBn
11h
11.42
1.03
1.02
1.15
1.01
1.00
1.24
3.16
3.28
3.20
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2
f1 (ppm)


O
OBn
11h
220 200 180 160 140 120 100 80 60 40 20 0
f1 (ppm)

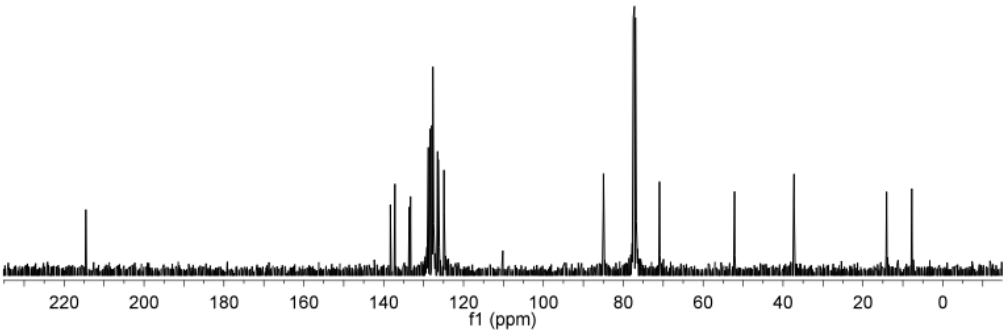


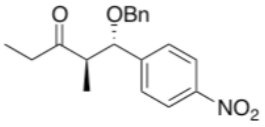

**11i**



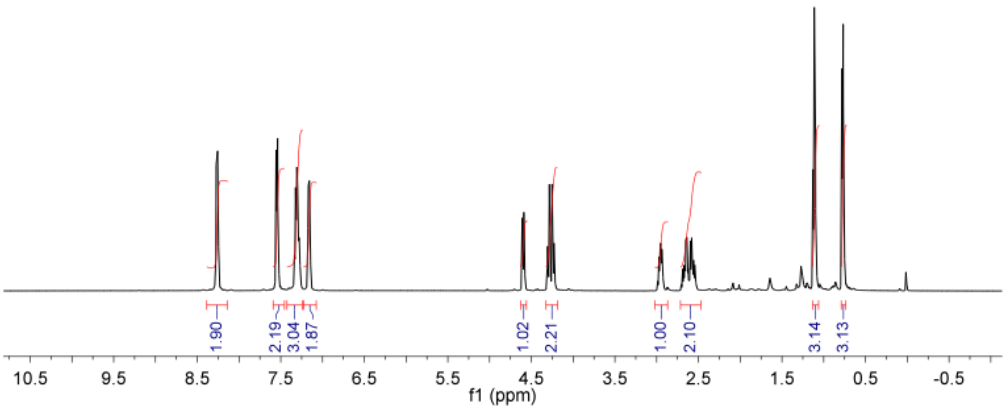



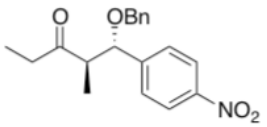

**11i**



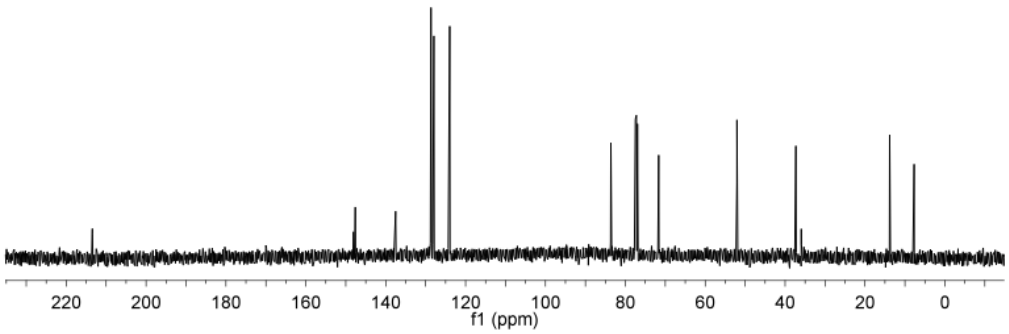

O
OBn
NO2

**11j**


1.90
2.19
3.04
1.87
1.02
2.21
1.00
2.10
3.14
3.13
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)

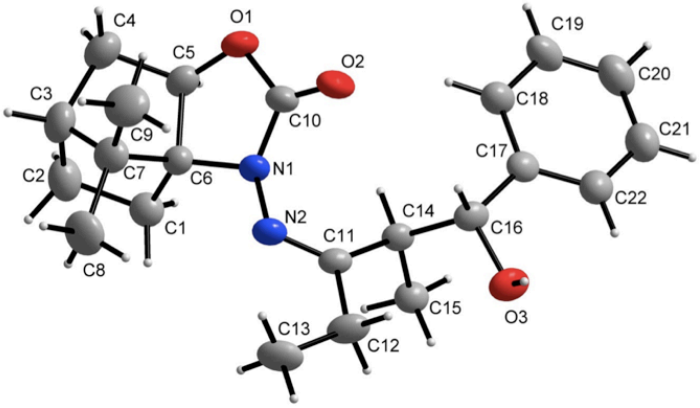

O
OBn
NO2

**11j**


220
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

## III. X-Ray Crystallographic Information

*Crystal Structure for **7a***

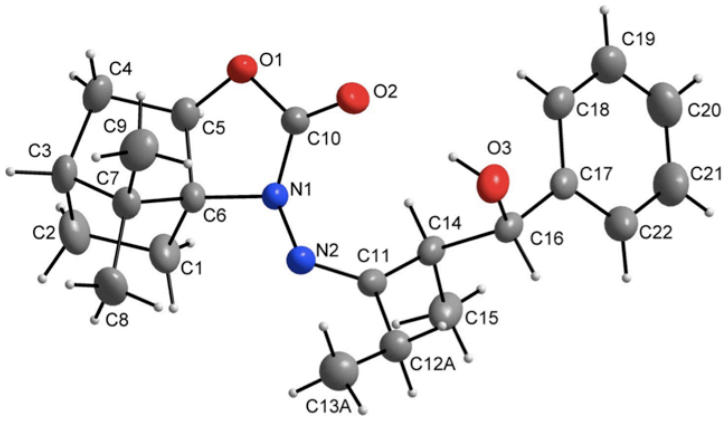



| | |
|---|---|
| empirical formula | $C_{22}H_{30}N_2O_3$ |
| fw | 370.49 |
| *T* (K) | 296(2) |
| λ (Å) | 0.71073 |
| crystal system | orthorhombic |
| space group | P $2_1$ |
| unit cell dimensions | a = 7.5478(11) Å α = 90.00ϒ<br>b = 9.9201(14 Å β = 100.024(1)ϒ<br>c = 13.996(2) Å γ = 90.00ϒ |
| *V* (Å$^3$) | 1031.95 |
| *Z* | 2 |
| $D_{calc}$ (Mg/m$^3$) | 1.192 |
| abs coeff (mm$^{-1}$) | 0.079 |
| total no. of reflns | 15398 |
| no. of unique reflns | 1945 |
| no. params refined/ restrained | 245/1 |
| $R_{int}$ | 0.0833 |
| crystal size (mm$^3$) | 0.260 ↔ 0.240 ↔ 0.050 |
| color and habit | colorless plate |
| Goodness-of-fit on $F^2$ | 1.027 |
| Final R indices [I>2σ(I)] | *R*1 = 0.0443 *wR*2 = 0.0983 |
| R indices (all data) | *R*1 = 0.0759, *wR*2 = 0.1127 |
| max, min Δρ (e$^-$/Å$^3$) | 0.163, -0.143 |

A specimen of $C_{22}H_{30}N_2O_3$, approximate dimensions 0.050 mm x 0.240 mm x 0.260 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured. The integration of the data using a monoclinic unit cell

yielded a total of 15398 reflections to a maximum θ angle of 25.15° (0.84 Å resolution), of which 1945 were independent (average redundancy 7.917, completeness = 99.0%, $R_{int}$ = 8.33%, $R_{sig}$ = 4.89%) and 1336 (68.69%) were greater than $2\sigma(F^2)$. The final cell constants of a = 7.5478(11) Å, b = 9.9201(14) Å, c = 13.996(2) Å, β = 100.024(10)°, volume = 1032.0(3) $Å^3$, are based upon the refinement of the XYZ-centroids of 2025 reflections above 20 σ(I) with 5.755° < 2θ < 35.57°. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.9797 and 0.9961. The structure was solved and refined using the Bruker SHELXTL Software Package [5], using the space group P 1 21 1, with Z = 2 for the formula unit, $C_{22}H_{30}N_2O_3$. The final anisotropic full-matrix least-squares refinement on $F^2$ with 245 variables converged at R1 = 4.43%, for the observed data and wR2 = 11.27% for all data. The goodness-of-fit was 1.027. The largest peak in the final difference electron density synthesis was 0.163 $e^-/Å^3$ and the largest hole was -0.143 $e^-/Å^3$ with an RMS deviation of 0.043 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.192 $g/cm^3$ and F(000), 400 $e^-$.

## *Crystal Structure for **7b***




| | |
|---|---|
| empirical formula | $C_{22}H_{30}N_2O_3$ |
| fw | 370.49 |
| *T* (K) | 296(2) |
| λ (Å) | 0.71073 |
| crystal system | orthorhombic |
| space group | P $2_12_12_1$ |
| unit cell dimensions | a = 6.9150(4) Å α = 90.00Υ<br>b = 12.5529(8) Å β = 90.00Υ<br>c = 24.5201(14) Å γ = 90.00Υ |
| *V* (Å$^3$) | 2128.4(2) |
| *Z* | 4 |
| $D_{calc}$ (Mg/m$^3$) | 1.156 |
| abs coeff (mm$^{-1}$) | 0.077 |
| total no. of reflns | 35155 |
| no. of unique reflns | 2371 |
| no. params refined/ restrained | 242/0 |
| $R_{int}$ | 0.0518 |
| crystal size (mm$^3$) | 0.160 ↔ 0.410 ↔ 0.460 |
| color and habit | colorless plate |
| Goodness-of-fit on $F^2$ | 1.054 |
| Final R indices [I>2σ(I)] | *R*1 = 0.0391 *wR*2 = 0.0990 |
| R indices (all data) | *R*1 = 0.0518, *wR*2 = 0.1087 |
| max, min Δρ (e$^-$/Å$^3$) | 0.224, -0.196 |

A specimen of $C_{22}H_{30}N_2O_3$, approximate dimensions 0.160 mm x 0.410 mm x 0.460 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured. The integration of the data using an orthorhombic unit cell yielded a total of 35155 reflections to a maximum θ angle of 25.89° (0.81 Å resolution), of which 2371 were independent (average redundancy 14.827,

completeness = 99.2%, $R_{int}$ = 3.80%, $R_{sig}$ = 1.45%) and 1953 (82.37%) were greater than $2\sigma(F^2)$. The final cell constants of a = 6.9150(4) Å, b = 12.5529(8) Å, c = 24.5201(14) Å, volume = 2128.4(2) $Å^3$, are based upon the refinement of the XYZ-centroids of 1547 reflections above 20 σ(I) with 4.782° < 2θ < 44.52°. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.9655 and 0.9878. The structure was solved and refined using the Bruker SHELXTL Software Package [5], using the space group P 21 21 21, with Z = 4 for the formula unit, $C_{22}H_{30}N_2O_3$. The final anisotropic full-matrix least-squares refinement on $F^2$ with 242 variables converged at R1 = 3.91%, for the observed data and wR2 = 10.87% for all data. The goodness-of-fit was 1.054. The largest peak in the final difference electron density synthesis was 0.224 $e^-/Å^3$ and the largest hole was -0.196 $e^-/Å^3$ with an RMS deviation of 0.030 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.156 $g/cm^3$ and F(000), 800 $e^-$.

## IV. References

1. D. Lim and D. M. Coltart, *Angew. Chem. Int. Ed.* 2008 **47**, *5207.*
2. R. Ding, Y. He, X. Wang, J. Xu, Y. Chen, M. Feng, and C. Qi, *Molecules*, 2011, **16**, 5665.
3. A. Mirjafari, I. Mohammadpoor-Baltork, M. Moghadam, S. Tangestaninejad, V. Mirkhani, and A. R. Khosropour, *Tet. Lett.* 2010, **16**, 5665.
4. G. M. Sheldrick, *SHELXTL*, 6.12, Bruker AXS, Inc., Madison, Wisconsin, 2001.