Supporting Information for:

Iridium-Catalyzed Enantioselective Hydrogenation of α,β-Unsaturated Carboxylic Acids

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CONTENTS:

General. Unless otherwise noted, all reactions and manipulations were performed in an argon-filled glovebox (VAC DRI-LAB HE 493) or using standard Schlenk techniques. Melting points were measured on a RY-I apparatus and uncorrected. ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded on a Varian Mercury Plus 400 spectrometer at 400 MHz (^{1}H NMR), 100 MHz (^{13}C NMR) and 162 MHz (^{31}P NMR) or a Bruker AV 300 spectrometer at 300 MHz (^{1}H NMR), 75 MHz (^{13}C NMR) and 121.5 MHz (^{31}P NMR) in $CDCl_3$. Chemical shifts were reported in ppm down field from internal Me_4Si and external 85% H_3PO_4, respectively. Optical rotations were determined using a Perkin Elmer 341 MC polarimeter. Mass spectra were recorded on IonSpec FT-ICR mass spectrometer with ESI or MALDI resource. Enantiomeric excesses of the asymmetric hydrogenation products were determined by chiral HPLC or SFC. HPLC analyses were performed using a Hewlett Packard Model HP 1100 Series instruments. SFC analyses were performed using a Mettler-Toledo Model Analytix SFC. Anhydrous Et_2O, THF and toluene were distilled from sodium benzophenone ketyl. Anhydrous CH_2Cl_2, NEt_3, DMSO and DMF were freshly distilled from calcium hydride under nitrogen atmosphere. Anhydrous MeOH and EtOH were distilled from magnesium under nitrogen atmosphere. $Pd(OAc)_2$, 1,4-bis(diphenylphospino)butane (dppb) and 1,3-bis(diphenylphosphino)propane (dppp) were purchased from Acros or Aldrich Co. and used as received. Hydrogen gas (99.999%) was purchased from Boc Gas Inc., Tianjin. $[Ir(COD)Cl]_2$ was prepared from $IrCl_3 \cdot 3H_2O$ according to the literatures.[1] $NaBARF \cdot 3H_2O$ was prepared according to the literatures.[2] The catalysts **1a-1c** were prepared according to our previous procedure.[3]

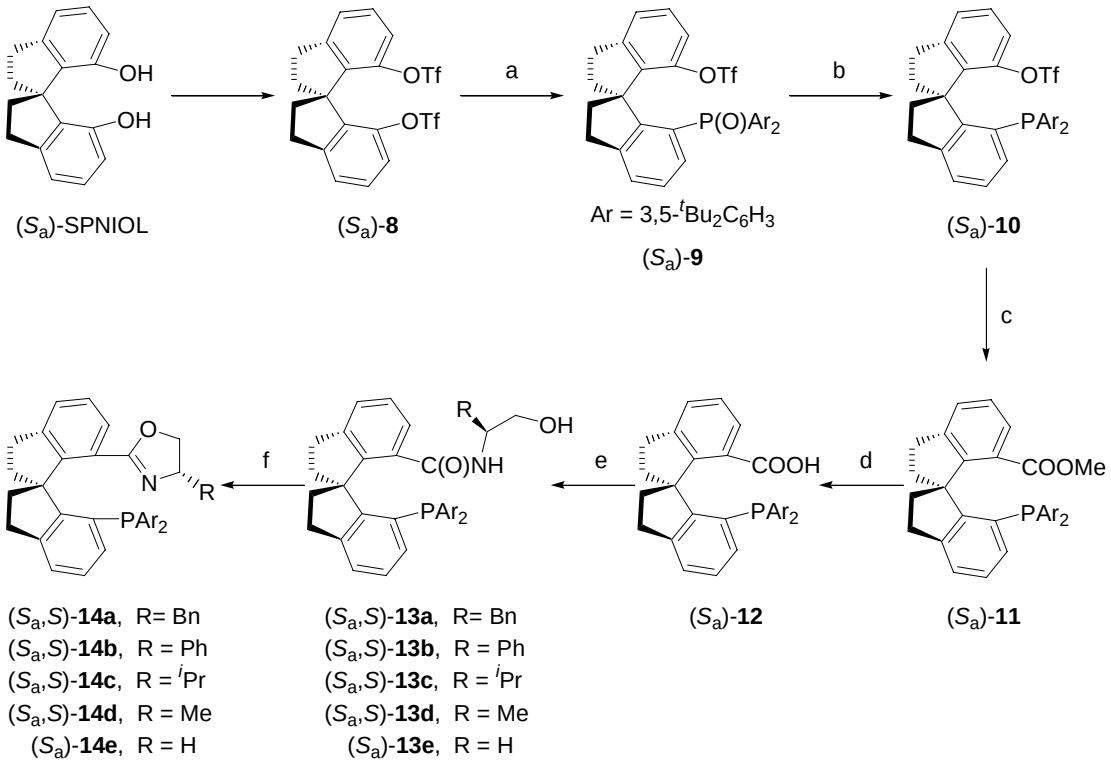
[1] Herde, J. L.; Lambert, J. C.; Senoff, C. V. *Inorg. Synth.* **1974**, *15*, 18–20.

[2] (a) Nishida, H.; Takada, N.; Yoshimura, M.; Sonoda, T.; Kobayashi, H. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 2600–2604. (b) Brookhart, M.; Grant, B.; Jr. Volpe, A. F. *Organometallics* **1992**, *11*, 3920–3922.

[3] Zhu, S.-F.; Xie J.-B.; Zhang, Y.-Z.; Li, S.; Zhou, Q.-L. *J. Am. Chem. Soc.* **2006**, *128*, 12886–12891.

(A) Preparation and Analytical Data of Chiral Spiro Phosphino-Oxazoline Ligands

The synthetic pathway of the ligands is outlined as follow:

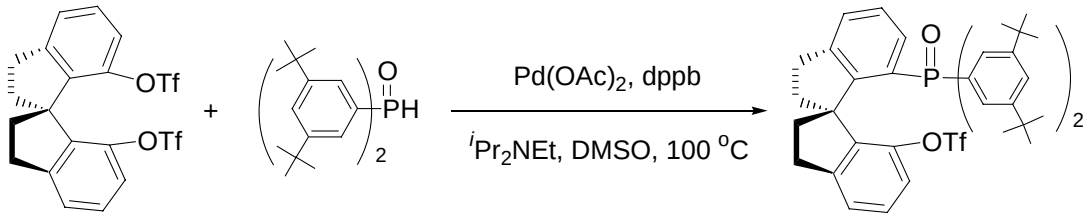


(S_a)-SPNIOL (S_a)-**8** Ar = 3,5-^{t}Bu$_2$C$_6$H$_3$ (S_a)-**9** (S_a)-**10** (S_a)-**11** (S_a)-**12**

(S_a,*S*)-**14a**, R= Bn
(S_a,*S*)-**14b**, R = Ph
(S_a,*S*)-**14c**, R = ^{i}Pr
(S_a,*S*)-**14d**, R = Me
(S_a)-**14e**, R = H

(S_a,*S*)-**13a**, R= Bn
(S_a,*S*)-**13b**, R = Ph
(S_a,*S*)-**13c**, R = ^{i}Pr
(S_a,*S*)-**13d**, R = Me
(S_a)-**13e**, R = H

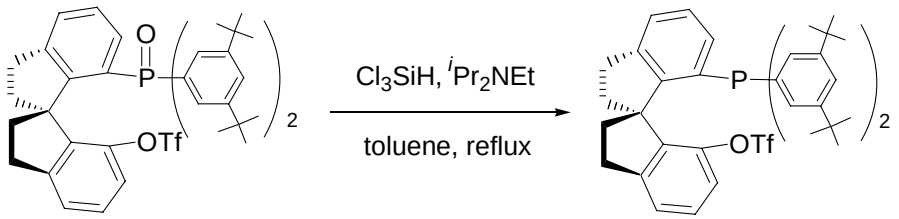
Synthesis of (S_a)-7-di(3,5-di-*tert*-butylphenyl)phosphinyl-7′-trifluoromethanesulfonyloxy-1,1′-spirobiindane ((S_a)-9)



(S_a)-**8** (S_a)-**9**

To a mixture of (S_a)-7,7′-bis(trifluoromethanesulfonyloxy)-1,1′-spirobiindane [3] ((S_a)-**8**, 10.0 g, 19.4 mmol), di(3,5-di-*tert*-butylphenyl)phosphine oxide (16.5 g, 38.7 mmol), palladium acetate (220 mg, 0.98 mmol) and dppb (415 mg, 0.98 mmol) was added 75 mL of degassed DMSO and diisopropylethylamine (10.5 g, 81.3 mmol). The resulting mixture was heated with stirring at 100 °C for 6 hours. After cooling to room temperature, the reaction mixture was diluted with EtOAc, washed with 5% aqueous HCl and saturated $NaHCO_3$. The organic phase was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was chromatographed on a silica gel column eluted with petroleum ether/EtOAc (7:1 in volume) to give (S_a)-7-di(3,5-di-*tert*-butylphenyl)phosphinyl-7′-trifluoromethanesulfonyloxy-1,1′-spirobiindane ((S_a)-**9**, 14.0 g, 91%) as a white solid, mp: 235–236 °C. $[\alpha]_D^{28}$ –172.6 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (s, 1H, Ar-H), 7.42–7.40 (m, 2H, Ar-H), 7.26–7.03 (m, 8H, Ar-H), 6.56 (d, *J* = 8.0 Hz, 1H, Ar-H), 3.27–3.22 (m, 1H, CH_2), 3.15–3.01 (m, 4H, CH_2), 2.38–2.24 (m, 3H, CH_2), 1.26 (s, 18H, CH_3), 1.17 (s, 18H, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$) δ 32.5 (s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.1, 153.0, 150.5, 150.4, 149.4, 146.2, 146.1, 145.3, 142.1, 136.5, 135.4, 133.5, 133.4, 131.8, 130.8, 128.8, 128.3, 128.0, 127.8, 126.2, 126.1, 125.9, 125.6, 125.5, 124.9, 123.9, 119.7, 117.7, 116.5, 62.2, 40.0, 39.8, 35.1, 31.9, 31.4, 31.3, 31.0. HRMS (MALDI) calcd for [M+H, $C_{46}H_{57}F_3O_4PS]^+$: 793.3662. Found 793.3667.

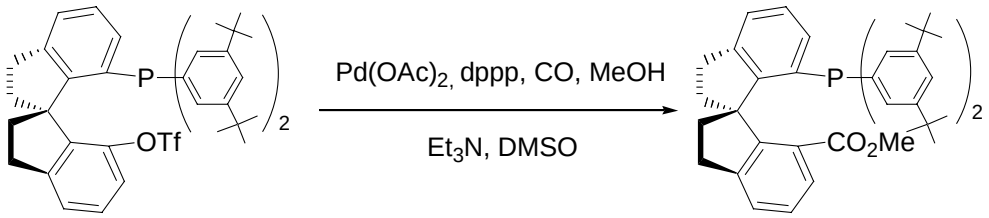
Synthesis of (S_a)-7-di(3,5-di-*tert*-butylphenyl)phosphino-7′-trifluoromethanesulfonyloxy-1,1′-spirobiindane ((S_a)-10)



(S_a)-**9** (S_a)-**10**

To a mixture of (S_a)-**9** (13.8 g, 17.4 mmol) and diisopropylethylamine (110 mL, 714 mmol) in toluene (175 mL) was added Cl_3SiH (30 mL, 280 mmol) at 0 °C. The reaction mixture was stirred at 110 °C for 3 days. After cooling to room temperature, the mixture was quenched with small amount of 12 N aqueous NaOH and diluted with EtOAc. The resulting suspension was filtered through Celite and the solid was washed with EtOAc. The combined organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel with petroleum ether/EtOAc (10:1 in volume) to give (S_a)-7-di(3,5-di-*tert*-butylphenyl)phosphino-7′-trifluoromethanesulfonyloxy-1,1′-spirobiindane ((S_a)-**3d**, 13.0 g, 96%) as a white solid, mp: 170–172 °C. $[\alpha]_D^{31}$ –108.6 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29–7.22 (m, 5H, Ar-H), 7.16 (t, *J* = 7.6 Hz, 1H, Ar-H), 7.03–6.99 (m, 2H, Ar-H), 6.89 (dd, *J* = 8.0 and 1.6 Hz, 2H, Ar-H), 6.81 (dd, *J* = 8.0 and 1.6 Hz, 2H, Ar-H), 3.07–2.95 (m, 3H, CH_2), 2.84–2.78 (m, 1H, CH_2), 2.38–2.27 (m, 2H, CH_2), 2.13–2.01 (m, 2H, CH_2), 1.20 (s, 18H, CH_3), 1.18 (s, 18H, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$) δ –16.6 (s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.2, 152.0, 150.4, 150.3, 148.4, 146.5, 143.6, 143.5, 141.4, 137.4, 137.3, 136.5, 136.3, 134.0, 133.8, 133.7, 129.0, 128.6, 128.4, 128.0, 127.8, 127.2, 125.4, 124.2, 122.2, 122.1, 118.5, 61.9, 39.3, 39.1, 35.0, 31.6, 31.5, 30.9. HRMS (MALDI) calcd for $[M+H, C_{46}H_{57}F_3O_3PS]^+$: 777.3713. Found 777.3714.

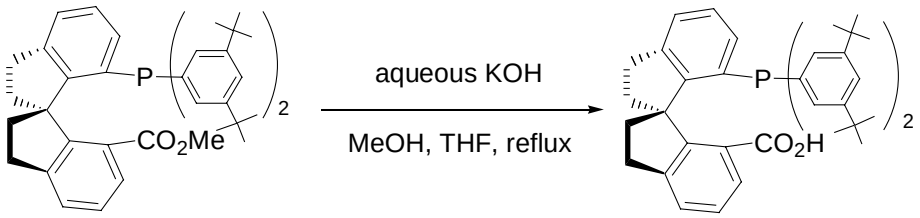
Synthesis of (S_a)-7-di(3,5-di-*tert*-butylphenyl)phosphino-7′-carbomethoxy-1,1′-spirobiindane ((S_a)-11)



(S_a)-**10** (S_a)-**11**

A mixture of (S_a)-**10** (10.0 g, 12.9 mmol), $Pd(OAc)_2$ (444 mg, 2.0 mmol), dppp (820 mg, 2.0 mmol), MeOH (72 mL), DMSO (104 mL) and NEt_3 (29 mL) was saturated with CO and heated to 70 °C with stirring at CO atmosphere. The reaction was monitored by TLC for a full conversion. After cooling to room temperature, the mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with petroleum ether/EtOAc (20:1 in volume) to afford (S_a)-7-di(3,5-di-*tert*-butylphenyl)phosphino-7′-carbomethoxy-1,1′-spirobiindane ((S_a)-**11**, 7.6 g, 86%) as a white solid, mp: 231–233 °C. $[\alpha]_D^{32}$ –120.8 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.2 Hz, 1H, Ar-H), 7.44 (d, *J* = 7.2 Hz, 1H, Ar-H), 7.33–7.26 (m, 4H, Ar-H), 7.13 (t, *J* = 7.2 Hz, 1H, Ar-H), 7.03–7.02 (m, 1H, Ar-H), 6.90 (d, *J* = 7.6 Hz, 2H, Ar-H), 6.79 (d, *J* = 7.6 Hz, 2H, Ar-H), 3.12 (s, 3H, CH_3), 3.10–2.97 (m, 3H, CH_2), 2.87–2.84 (m, 1H, CH_2), 2.64–2.56 (m, 1H, CH_2), 2.28–2.24 (m, 1H, CH_2), 2.16–2.14 (m, 2H, CH_2), 1.25 (s, 18H, CH_3), 1.19 (s, 18H, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$) δ –17.0 (s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 155.7, 155.4, 150.7, 150.2, 150.1, 150.0, 145.8, 143.4, 138.0, 137.9, 136.6, 136.5, 133.9, 132.9, 132.7, 129.6, 128.7, 128.6, 128.5, 128.4, 128.3, 128.1, 126.8, 126.2, 125.1, 122.0, 121.7, 64.0, 51.0, 40.2, 38.3, 34.0, 31.6, 31.2, 30.8. HRMS (EI) calcd for [M, $C_{47}H_{59}O_2P$]: 686.4253. Found 686.4251.

Synthesis of (S_a)-7-di(3,5-di-*tert*-butylphenyl)phosphino-7′-carboxy-1,1′-spirobiindane ((S_a)-12)

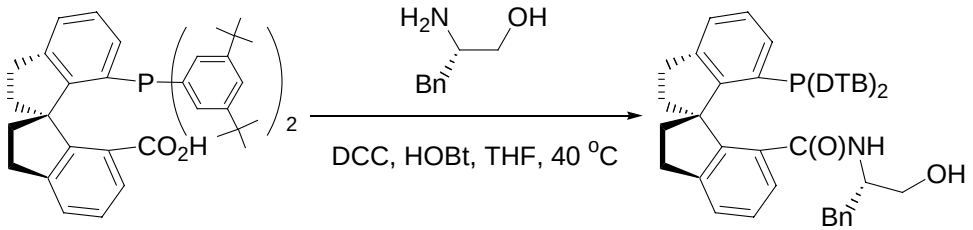


(S_a)-**11** (S_a)-**12**

A mixture of (S_a)-**11** (7.3 g, 10.6 mmol), MeOH (150 mL), THF (150 mL) and 60% aqueous KOH (30 mL) was heated to 90 °C with stirring under nitrogen atmosphere and monitored with TLC for full conversion. After cooling to room temperature, the concentrated hydrochloric acid was carefully added with vigorous stirring to pH < 2. The mixture was diluted with water (100 mL) and extracted with EtOAc (200 mL) for three times. The organic lays was combined and washed with saturate brine and dried over anhydrous Na_2SO_4. After evaporated under reduced pressure, the residue was subjected to chromatography on silica gel column with petroleum ether/EtOAc (6:1 in volume) to afford (S_a)-7-di(3,5-di-*tert*-butylphenyl)phosphino-7′-carboxy-1,1′-spirobiindane ((S_a)-**12**, 6.3 g, 88%) as a white solid, mp: 245–247 °C. $[\alpha]_D^{26}$ –105.2 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.16 (brs, 1H, COOH), 7.55 (d, *J* = 7.6 Hz, 1H, Ar-H), 7.43 (d, *J* = 7.2 Hz, 1H, Ar-H), 7.24–7.19 (m, 4H, Ar-H), 7.05 (t, *J* = 7.2 Hz, 1H, Ar-H), 6.87 (dd, *J* = 7.2 and 4.4 Hz, 1H, Ar-H), 6.77 (dd, *J* = 8.0 and 1.6 Hz, 2H, Ar-H), 6.71 (dd, *J* = 7.6 and 1.6 Hz, 2H, Ar-H), 3.12–2.90 (m, 4H, CH_2), 2.53–2.45 (m, 1H, CH_2), 2.37–2.29 (m, 1H, CH_2), 2.23–2.17 (m, 2H, CH_2), 1.14 (s, 18H, CH_3), 1.13 (s, 18H, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$) δ –17.0 (s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 155.8, 155.5, 152.4, 150.0, 146.1, 143.8, 138.3, 138.2, 136.2, 136.1, 133.8, 132.1, 131.9, 130.2, 129.1, 128.1, 127.9, 127.1, 126.7, 126.1, 124.9, 122.0, 121.6, 63.9, 41.0, 38.1, 34.9, 31.5, 31.4, 30.9. HRMS (MALDI) calcd for $[M–H, C_{46}H_{56}O_2P]^-$: 671.4023. Found 671.4012.

Synthesis of Compounds 13

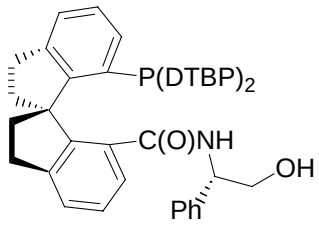
(S_a,*S*)-*N*-(1-Benzyl-2-hydroxy-ethyl)-7′-di(3,5-di-*tert*-butylphenyl)phosphino-1,1′-spirobiindane-7-carboxylamide ((S_a,*S*)-13a)



(S_a)-**12** (S_a,*S*)-**13a**

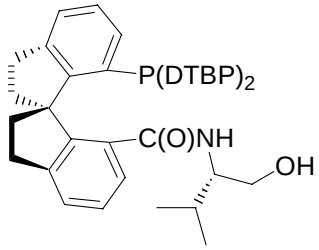
Typical procedure: To a mixture of (S_a)-**12** (1.0 g, 1.48 mmol), *L*-phenylalaninol (702 mg, 4.65 mmol), 1-hydroxybenzotriazole (HOBt, 504 mg, 3.29 mmol) and dicyclohexylcarbodiimide (DCC, 881 mg, 4.27 mmol), 80 mL THF was added with stirring at 0 °C under nitrogen atmosphere. The resulting mixture was heated at 40 °C for36 h. After concentration under reduced pressure the residue was chromatographied on silica gel column with petroleum ether/EtOAc (4:1 in volume) to afford (S_a,*S*)-*N*-(1-Hydroxymethyl-2-methylbenzyl)-7′-di(3,5-di-*tert*-butylphenyl)phosphino-1,1′-spirobiindane-7-carboxylamide ((S_a,*S*)-**13a**, 840 mg, 71%) as a white solid, mp: 211–212 °C. $[\alpha]_D^{26}$ –167.4 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (s, 1H, Ar-H), 7.33–7.16 (m, 9H, Ar-H), 7.06 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.00 (d, *J* = 7.6 Hz, 3H, Ar-H), 6.67 (d, *J* = 7.2 Hz, 2H, Ar-H), 5.26 (d, *J* = 6.0 Hz, 1H, NH), 3.17–2.75 (m, 9H, OH, CH and CH_2), 2.45–2.15 (m, 5H, CH_2), 1.20 (s, 18H, CH_3), 1.16 (s, 18H, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$) δ –16.4 (s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 155.5, 155.3, 151.1, 151.0, 150.1, 148.3, 146.0, 145.2, 145.1, 139.3, 139.2, 138.8, 137.0, 136.9, 134.1, 133.8, 133.7, 129.4, 129.3, 129.2, 128.6, 127.5, 127.3, 127.1, 127.0, 126.7, 126.6, 126.1, 123.7, 121.5, 64.4, 63.3, 56.1, 41.8, 41.7, 40.4, 35.4, 35.2, 35.0, 31.6, 31.5, 31.0, 25.2. HRMS (MALDI) calcd for $[M+H, C_{55}H_{69}NO_2P]^+$: 806.5060. Found 806.5065.

(S_a,*S*)-*N*-(2-Hydroxy-1-phenyl-ethyl)-7′-di(3,5-di-*tert*-butylphenyl)phosphino-1,1′-spirobiindane-7-carboxylamide ((S_a,*S*)-13b)



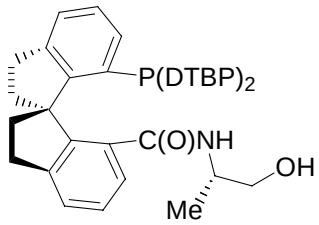
Yield: 81%, white solid, mp: 150–152 °C. $[\alpha]_D^{25}$ –150.6 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.23 (m, 5H, Ar-H), 7.16–6.98 (m, 8H, Ar-H), 6.82 (d, *J* = 7.2 Hz, 2H, Ar-H), 6.70 (d, *J* = 7.6 Hz, 2H, Ar-H), 5.80 (d, *J* = 5.6 Hz, 1H, NH), 4.34 (dd, *J* = 10.4 and 6.4 Hz, 1H, CH), 3.49–3.43 (m, 1H, CH_2), 3.31–3.26 (m, 1H, CH_2), 3.06–2.82 (m, 4H, OH and CH_2), 2.74–2.62 (m, 2H, CH_2), 2.23–2.10 (m, 3H, CH_2), 1.19 (s, 18H, CH_3), 1.15 (s, 18H, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$) δ –16.1 (s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 155.5, 155.3, 150.8, 150.7, 150.2, 150.1, 146.9, 146.6, 144.1, 144.0, 138.7, 138.3, 138.2, 136.8, 136.6, 134.1, 133.8, 133.7, 133.5, 129.1, 128.9, 128.7, 127.7, 127.5, 127.3, 126.9, 126.1, 123.3, 121.8, 66.1, 63.3, 60.6, 58.3, 41.0, 40.9, 40.8, 35.1, 35.0, 31.6, 31.5, 31.0, 30.9. HRMS (ESI) calcd for $[M+H, C_{54}H_{67}NO_2P]^+$: 792.4904. Found 792.4905.

(*S*$_a$,*S*)-*N*-(2-Hydroxy-1-isopropyl-ethyl)-7′-di(3,5-di-*tert*-butylphenyl)phosphino-1,1′-spirobiindane-7-carboxylamide ((*S*$_a$,*S*)-13c)



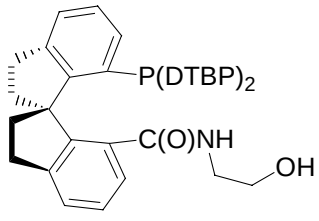
Yield: 72%, white solid, mp: 164–166 °C. $[\alpha]_D^{26}$ –169.8 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (s, 1H, Ar-H), 7.33–7.13 (m, 7H, Ar-H), 7.07 (d, *J* = 8.4 Hz, 2H, Ar-H), 6.65 (d, *J* = 7.6 Hz, 2H, Ar-H), 5.31 (d, *J* = 6.4 Hz, 1H, NH), 3.79 (brs, 1H, OH), 3.29 (dd, *J* = 12.0 and 5.6 Hz, 1H, CH), 3.16–2.76 (m, 6H, CH_2), 2.45–2.24 (m, 4H, CH_2), 1.74–1.62 (m, 1H, CH), 1.24 (s, 18H, CH_3), 1.15 (s, 18H, CH_3), 0.64 (d, *J* = 6.8 Hz, 6H, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$) δ –16.2 (s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 155.5, 155.3, 151.0, 150.9, 150.1, 148.1, 146.2, 145.0, 144.9, 139.4, 139.3, 137.0, 136.8, 134.0, 133.9, 133.8, 133.7, 129.4, 129.2, 127.4, 127.3, 127.1, 127.0, 126.6, 126.0, 123.8, 121.5, 63.3, 61.6, 41.8, 41.7, 40.3, 35.2, 34.9, 31.6, 31.5, 31.0, 27.7, 20.4, 19.2. HRMS (ESI) calcd for $[M+H, C_{51}H_{69}NO_2P]^+$: 758.5060. Found 758.5056.

(*S*$_a$,*S*)-*N*-(2-Hydroxy-1-methyl-ethyl)-7′-di(3,5-di-*tert*-butylphenyl)phosphino-1,1′-spirobiindane-7-carboxylamide ((*S*$_a$,*S*)-13d)



Yield: 70%, white solid, mp: 236–238 °C. $[\alpha]_D^{27}$ –144.5 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (s, 1H, Ar-H), 7.31–7.14 (m, 7H, Ar-H), 7.07 (d, *J* = 8.0 Hz, 2H, Ar-H), 6.75 (d, *J* = 7.6 Hz, 2H, Ar-H), 5.35 (d, *J* = 6.4 Hz, 1H, NH), 3.46 (brs, 1H, OH), 3.35–3.29 (m, 1H, CH), 3.11–2.91 (m, 5H, CH_2), 2.84–2.71 (m, 2H, CH_2), 2.39–2.24 (m, 3H, CH), 1.27 (s, 18H, CH_3), 1.20 (s, 18H, CH_3), 0.27 (d, *J* = 6.8 Hz, 3H, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$) δ –16.2 (s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 155.9, 155.6, 151.0, 150.3, 150.1, 147.2, 146.2, 144.7, 139.0, 138.9, 136.9, 136.8, 134.3, 134.1, 133.9, 133.6, 129.5, 129.3, 127.5, 127.4, 127.3, 127.2, 127.1, 126.5, 126.0, 123.7, 121.6, 67.2, 63.3, 48.7, 41.5, 41.4, 41.0, 35.2, 35.0, 31.7, 31.6, 31.1, 31.0, 15.6. HRMS (ESI) calcd for $[M+H, C_{49}H_{65}NO_2P]^+$: 730.4747, Found 730.4744.

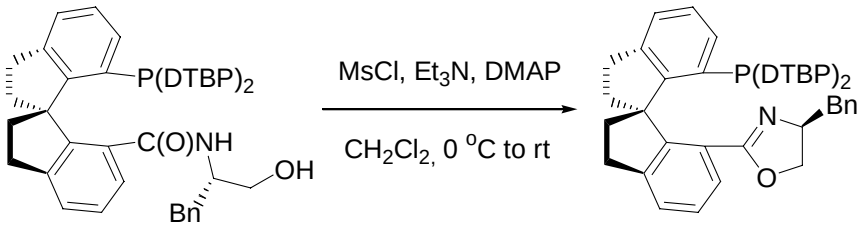
(*S*$_a$)-*N*-(2-Hydroxyethyl)-7′-di(3,5-di-*tert*-butylphenyl)phosphino-1,1′-spirobiindane-7-carboxylamide ((*S*$_a$)-13e)



Yield: 62%, white solid, mp: 170–172 °C. $[\alpha]_D^{18}$ –122.6 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (s, 1H, Ar-H), 7.34–7.15 (m, 7H, Ar-H), 7.03 (d, *J* = 8.4 Hz, 2H, Ar-H), 6.71 (d, *J* = 7.6 Hz, 2H, Ar-H), 5.45 (t, *J* = 4.8 Hz, 1H, NH), 3.15–2.76 (m, 9H, OH and CH_2), 2.69–2.62 (m, 1H, CH_2), 2.43–2.25 (m, 3H, CH_2), 1.25 (s, 18H, CH_3), 1.18 (s, 18H, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$) δ –16.6 (s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 155.9, 155.7, 151.0, 150.2, 147.5, 146.1, 144.8, 144.7, 138.7, 138.6, 136.5, 136.3, 134.0, 133.8, 133.6, 129.0, 128.7, 127.5, 127.4, 127.3, 127.2, 126.7, 126.5, 126.0, 123.7, 121.7, 63.3, 62.4, 60.6, 43.7, 41.2, 40.8, 35.2, 35.0, 31.6, 31.5, 31.2, 31.0, 21.2, 14.4. HRMS (ESI) calcd for $[M+H, C_{48}H_{63}NO_2P]^+$: 716.4591. Found 716.4590.

Synthesis of Ligands 14

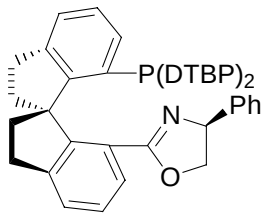
(*S*$_a$,*S*)-7-[4,5-Dihydro-4-benzyloxazol-2-yl]-7′-di(3,5-di-*tert*-butylphenyl)phosphino-1,1′-spirobiinane ((*S*$_a$,*S*)-14a)



(S_a,*S*)-**13a** (S_a,*S*)-**14a**

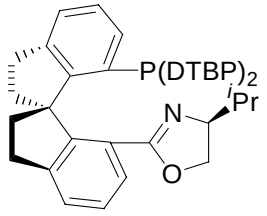
Typical procedure: To a solution of (S_a,*S*)-**13a** (840 mg, 1.04 mmol), triethylamine (0.32 mL), and 4-dimethylaminopyridine (DMAP, 5 mg, 0.04 mmol) in 65 mL dichloromethane was added methanesulfonyl chloride (120 μL, 1.55 mmol) at 0 °C. The mixture was stirred for 30 min, then another portion of triethylamine (1.35 mL) was added. The resulting mixture was warmed to room temperature. The reaction was monitored with TLC for a complete conversion. The crude product was purified by chromatography on a silica gel column with petroleum ether/ethyl acetate (8:1 in volume with 2% triethylamine) to afford (S_a,*S*)-7-[4,5-dihydro-4-benzyloxazol-2-yl]-7′-di(3,5-di-*tert*-butylphenyl)phosphino-1,1′-spirobiinane ((S_a,*S*)-**14a**, 682 mg, 83%) as a white solid, mp: 159–161 °C. $[\alpha]_D^{25}$ –185.6 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 6.8 Hz, 1H, Ar-H), 7.34–7.04 (m, 11H, Ar-H), 6.94–6.91 (m, 3H, Ar-H), 6.82 (d, *J* = 8.0 Hz, 1H, Ar-H), 4.17–4.09 (m, 1H, CH), 3.51 (t, *J* = 7.6 Hz, 1H, CH_2), 3.37 (t, *J* = 8.8 Hz, 1H, CH_2), 3.04–2.84 (m, 4H, CH_2), 2.78 (dd, *J* = 13.6 and 4.4 Hz, 1H, CH_2), 2.63 (dd, *J* = 15.6 and 8.8 Hz, 1H, CH_2), 2.20 (dd, *J* = 12.0 and 7.6 Hz, 1H, CH_2), 2.02 (dd, *J* = 13.6 and 9.6 Hz, 1H, CH_2), 1.91 (dd, *J* = 12.8 and 8.0 Hz, 1H, CH_2), 1.81–1.72 (m, 1H, CH_2), 1.20 (s, 18H, CH_3), 1.18 (s, 18H, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$) δ –15.6 (s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 154.2, 154.0, 150.2, 150.1, 149.9, 149.0, 145.4, 144.6, 144.5, 138.9, 137.6, 137.5, 137.4, 134.3, 134.0, 132.9, 129.3, 129.0, 128.8, 128.5, 128.3, 126.8, 126.7, 126.3, 126.2, 124.8, 121.9, 121.5, 71.1, 67.5, 63.5, 41.2, 39.3, 39.1, 35.0, 31.6, 31.2, 30.9. HRMS (MALDI) calcd for [M+H, $C_{55}H_{67}NOP$]$^+$: 788.4955. Found 788.4961.

(S_a,*S*)-7-[4,5-Dihydro-4-phenyloxazol-2-yl]-7′-di(3,5-di-*tert*-butylphenyl)phosphino-1,1′-spirobiinane ((S_a,*S*)-14b)



Yield: 81%. White solid, mp: 153–155 °C. $[\alpha]_D^{17}$ –180.9 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.6 Hz, 1H, Ar-H), 7.45–7.25 (m, 8H, Ar-H), 7.18 (t, *J* = 7.2 Hz, 1H, Ar-H), 7.07 (dd, *J* = 13.6 and 7.6 Hz, 5H, Ar-H), 6.92 (d, *J* = 8.0 Hz, 2H, Ar-H), 4.97–4.93 (m, 1H, CH), 3.71–3.62 (m, 2H, CH_2), 3.17–3.00 (m, 3H, CH_2), 2.90–2.76 (m, 2H, CH_2), 2.31 (dd, *J* = 12.0 and 8.0 Hz, 1H, CH_2), 2.10–1.95 (m, 2H, CH_2), 1.27 (s, 18H, CH_3), 1.24 (s, 18H, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$) δ –15.7 (s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 154.4, 154.2, 150.3, 150.2, 150.0, 149.4, 145.5, 144.4, 144.3, 143.1, 138.0, 137.9, 137.4, 137.3, 134.1, 133.9, 133.2, 129.2, 128.9, 128.7, 128.5, 127.3, 127.1, 126.9, 126.8, 126.3, 124.9, 121.9, 121.7, 74.0, 69.7, 63.7, 39.9, 38.9, 35.1, 35.0, 32.7, 31.2, 31.0. HRMS (ESI) calcd for [M+H, $C_{54}H_{65}NOP$]$^+$: 774.4798. Found 774.4800.

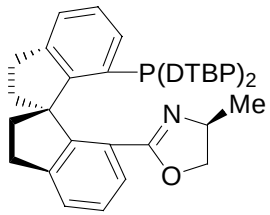
(S_a,*S*)-7-[4,5-Dihydro-4-isopropyloxazol-2-yl]-7′-di(3,5-di-*tert*-butylphenyl)phosphino-1,1′-spirobiinane ((S_a,*S*)-14c)



Yield: 72%, white solid, mp: 173–175 °C. $[\alpha]_D^{26}$ –224.0 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (d, *J* = 5.7 Hz, 1H, Ar-H), 7.20–7.08 (m, 5H, Ar-H), 6.96 (t, *J* = 7.5 Hz, 1H, Ar-H), 6.82 (d, *J* = 6.9 Hz, 3H, Ar-H), 6.73 (d, *J* = 7.2 Hz, 2H, Ar-H), 3.54–3.46 (m, 1H, CH), 3.38–3.32 (m, 2H, CH_2), 3.01–2.70 (m, 5H, CH_2), 2.57–2.49 (m, 1H, CH_2), 2.12–2.06 (m, 1H, CH_2), 1.86–1.79 (m, 1H, CH_2), 1.73–1.62 (m, 1H, CH), 1.11 (s, 18H, CH_3), 1.09 (s, 18H, CH_3), 0.77 (d, *J* = 6.6 Hz, 3H, CH_3), 0.63 (d, *J* = 6.6 Hz, 3H, CH_3); ^{31}P NMR (122 MHz, $CDCl_3$) δ –16.3 (s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.0, 154.2, 153.9, 150.0, 149.9, 149.7, 149.6, 148.6, 145.1, 144.1, 144.0, 137.6, 137.5, 137.4, 137.2, 133.9, 133.6, 132.6, 128.8, 128.6, 128.4, 128.1, 126.6, 126.4, 125.9, 124.6, 121.7, 121.3, 72.6, 69.7, 63.3, 39.0, 38.9, 34.8, 33.0, 31.4, 31.0, 30.7, 19.6, 18.4. HRMS (ESI) calcd for [M+H, $C_{51}H_{67}NOP$]$^+$: 740.4955. Found 740.4959.

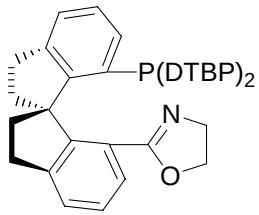
(S_a,*S*)-7-[4,5-Dihydro-4-methyloxazol-2-yl]-7′-di(3,5-di-*tert*-butylphenyl)phosphino-1,1′-spirobiinane ((S_a,*S*)-14d)

Yield: 87%, white solid, mp: 153–155 °C. $[\alpha]_D^{22}$ –186.6 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.6 Hz, 1H, Ar-H), 7.40–7.32 (m, 4H, Ar-H), 7.25 (d, *J* = 7.2 Hz, 1H, Ar-H), 7.14 (t, *J* = 7.6 Hz, 1H, Ar-H),



7.02–7.00 (m, 3H, Ar-H), 6.92–6.90 (m, 2H, Ar-H), 4.03–3.94 (m, 1H, CH), 3.68 (t, J = 8.0 Hz, 1H, CH_2), 3.37 (t, J = 7.6 Hz, 1H, CH_2), 3.14–2.93 (m, 4H, CH_2), 2.74 (dd, J = 15.6 and 8.8 Hz, 1H, CH_2), 2.29–2.25 (m, 1H, CH_2), 2.06–1.89 (m, 2H, CH_2), 1.29 (s, 18H, CH_3), 1.26 (s, 18H, CH_3), 0.89 (d, J = 6.8 Hz, 3H, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$) δ –15.8 (s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 154.7, 154.4, 150.2, 149.9, 149.2, 145.4, 144.6, 144.5, 138.0, 137.9, 137.6, 137.5, 134.0, 133.8, 133.0, 128.9, 128.7, 128.6, 128.4, 126.8, 126.7, 126.2, 124.8, 121.9, 121.6, 73.2, 63.6, 61.8, 39.8, 38.9, 35.1, 35.0, 31.7, 31.3, 31.0, 21.1. HRMS (ESI) calcd for [M+H, $C_{49}H_{63}NOP$]$^+$: 712.4642. Found 712.4639.

(S_a)-7-(4,5-Dihydrooxazol-2-yl)-7′-di(3,5-di-*tert*-butylphenyl)phosphino-1,1′-spirobiinane ((S_a)-14e)

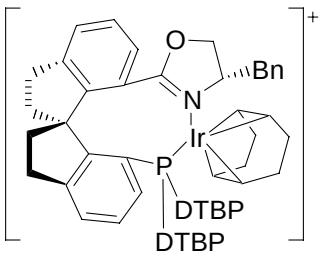


Yield: 72%, white solid, mp: 229–231 °C. $[\alpha]_D^{22}$ –184.4 (c 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 7.2 Hz, 1H, Ar-H), 7.35–7.20 (m, 5H, Ar-H), 7.06 (t, J = 7.6 Hz, 1H, Ar-H), 6.93–6.89 (m, 3H, Ar-H), 6.82 (d, J = 8.0 Hz, 2H, Ar-H), 3.75–3.69 (m, 1H, CH_2), 3.56–3.50 (m, 1H, CH_2), 3.41–3.28 (m, 2H, CH_2), 3.06–2.91 (m, 3H, CH_2), 2.78–2.69 (m, 2H, CH_2), 2.06–2.21 (m, 1H, CH_2), 1.99–1.89 (m, 2H, CH_2), 1.20 (s, 18H, CH_3), 1.17 (s, 18H, CH_3); ^{31}P NMR (162 MHz, $CDCl_3$) δ –15.8 (s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 154.0, 153.8, 150.2, 150.2, 149.9, 149.9, 149.7, 145.2, 144.7, 144.6, 138.0, 137.9, 137.5, 137.4, 133.9, 133.7, 133.0, 128.8, 128.7, 128.6, 128.4, 126.8, 126.7, 126.2, 124.5, 121.8, 121.5, 66.8, 63.5, 54.8, 40.0, 39.3, 35.1, 35.0, 31.7, 31.3, 31.0. HRMS (ESI) calcd for [M+H, $C_{48}H_{61}NOP$]$^+$: 698.4485. Found 698.4483.

(B) Preparation and Analytical Data of Iridium Complexes

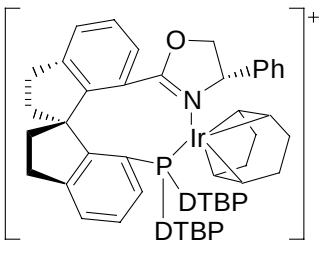
Typical procedure: Ligand (0.085 mmol), $[Ir(COD)Cl]_2$ (32 mg, 0.047 mmol) and NaBARF·$3H_2O$ (100 mg, 0.107 mmol) were added to 2 mL of CH_2Cl_2 in a Schlenk tube under argon atmosphere. The mixture was heated to reflux for 0.5 hours. The TLC analysis revealed no free ligand existed. After cooling to room temperature, the mixture was concentrated under reduced pressure and the residue was purified by a flash column chromatography on silica gel with CH_2Cl_2/petroleum ether (1:1) to offer an orange-yellow solid.

(S_a,*S*)-1d



Yield: 83%. mp: 204 °C. $[\alpha]_D^{21}$ +119.8 (c 0.5, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (d, J = 6.3 Hz, 2H, Ar-H), 7.65 (brs, 9H, Ar-H), 7.49–7.43 (m, 8H, Ar-H), 7.24–7.13 (m, 6H, Ar-H), 6.98 (d, J = 6.9 Hz, 2H, Ar-H), 6.68 (d, J = 8.1 Hz, 1H, Ar-H), 6.09 (d, J = 12.6 Hz, 1H, Ar-H), 4.81–4.68 (m, 1H, CH=CH), 4.16–4.12 (m, 1H, CH=CH), 4.01–3.92 (m, 1H, CH=CH), 3.87–3.71 (m, 2H, CH=CH and CH), 3.13–2.43 (m, 7H, CH_2), 2.18–1.94 (m, 5H, CH_2), 1.47–0.71 (m, 42H, CH_2 and CH_3), 0.32–0.13 (m, 2H, CH_2); ^{31}P NMR (122 MHz, $CDCl_3$) δ 16.2 (s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.1, 173.0, 162.1, 161.5, 160.8, 152.9, 152.1, 148.3, 148.2, 147.8, 147.7, 145.8, 144.0, 134.9, 134.1, 132.6, 132.3, 132.2, 132.0, 131.3, 130.5, 130.0, 129.6, 129.4, 129.2, 128.8, 128.3, 128.1, 128.0, 127.9, 127.5, 127.3, 127.0, 126.6, 126.4, 75.0, 73.9, 73.8, 70.7, 67.9, 67.6, 66.9, 62.9, 41.4, 40.8, 35.1, 33.7, 31.2, 31.0, 30.7, 30.6, 30.4, 30.1, 29.7, 29.0. HRMS (ESI) calcd for $C_{63}H_{78}IrNOP^+$: 1088.5445. Found 1088.5441.

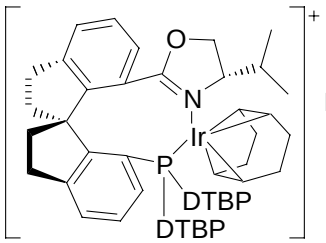
(S_a,*S*)-1e



Yield: 85%. mp: 231 °C. $[\alpha]_D^{21}$ +165.6 (c 0.5, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06–8.04 (m, 1H, Ar-H), 7.78–7.64 (m, 9H, Ar-H), 7.50–7.13 (m, 17H, Ar-H), 6.69 (brs, 1H, Ar-H), 6.17 (brs, 1H, Ar-H), 4.41 (dd, J = 9.6 and 3.9 Hz, 1H, CH=CH), 4.21 (dd, J = 9.0 and 3.9 Hz, 1H, CH=CH), 3.88–3.79 (m, 2H, CH=CH), 3.47–3.41 (m, 1H, CH), 3.16 (t, J = 9.3 H, 1H, CH_2), 2.95–2.63 (m, 4H, CH_2), 2.32–2.14 (m, 2H, CH_2), 2.06–1.93 (m, 3H, CH_2), 1.71–1.68 (m, 1H, CH_2), 1.51–0.75 (m, 40H, CH_2 and CH_3), 0.53–0.16 (m, 3H, CH_2); ^{31}P NMR (122 MHz, $CDCl_3$) δ 16.9 (s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.5, 172.4, 162.8, 162.1, 161.5, 160.8, 152.5, 150.8, 148.4, 148.2, 147.9, 147.8, 145.8, 144.0, 138.2, 134.9, 132.7, 132.3, 132.2, 132.0, 130.4,

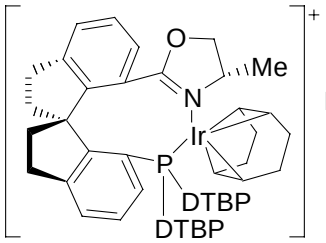
130.3, 130.0, 129.8, 129.6, 129.2, 128.7, 128.3, 128.0, 127.9, 127.7, 127.4, 127.3, 126.6, 126.4, 126.0, 124.1, 122.8, 120.8, 119.2, 117.5, 79.1, 76.4, 76.3, 70.1, 69.9, 69.8, 69.5, 68.1, 63.0, 41.6, 35.0, 33.6, 31.2, 31.1, 30.7, 30.4, 29.8, 28.7. HRMS (ESI) calcd for $C_{62}H_{76}IrNOP^+$: 1074.5288. Found 1074.5282.

(S_a,*S*)-1f



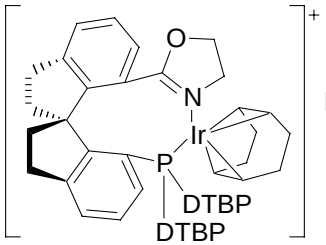
Yield: 74%. mp: 201 °C. $[\alpha]_D^{21}$ +128.8 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (d, *J* = 6.9 Hz, 1H, Ar-H), 7.66–7.59 (m, 10H, Ar-H), 7.43–7.32 (m, 8H, Ar-H), 7.17–7.00 (m, 3H, Ar-H), 6.76 (d, *J* = 9.0 Hz, 1H, Ar-H), 6.05 (d, *J* = 12.9 Hz, 1H, Ar-H), 4.55–4.54 (m, 1H, CH=CH), 4.12–4.08 (m, 1H, CH=CH), 3.78–3.77 (m, 2H, CH=CH), 3.52 (d, *J* = 8.4 Hz, 1H, CH), 3.10–3.07 (m, 1H, CH_2), 2.84–2.52 (m, 4H, CH_2), 2.15–1.92 (m, 4H, CH_2 and CH), 1.12–0.65 (m, 50H, CH_2 and CH_3), 0.24–0.07 (m, 2H, CH_2); ^{31}P NMR (122 MHz, $CDCl_3$) δ 16.1 (s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.0, 172.9, 162.9, 162.2, 161.6, 160.9, 153.0, 152.2, 152.1, 148.4, 148.3, 147.7, 147.6, 145.7, 144.0, 134.9, 132.8, 132.4, 132.3, 132.1, 131.4, 130.4, 130.1, 129.7, 129.3, 128.9, 128.5, 128.1, 127.9, 127.8, 127.5, 127.4, 126.5, 125.5, 124.1, 122.9, 120.6, 119.3, 117.5, 74.2, 71.5, 70.9, 70.7, 67.4, 66.7, 66.4, 62.9, 41.3, 35.0, 33.6, 31.2, 31.0, 30.9, 30.6, 30.5, 30.4, 30.0, 29.3, 18.8, 14.1. HRMS (ESI) calcd for $C_{59}H_{78}IrNOP^+$: 1040.5445. Found 1040.5438.

(S_a,*S*)-1g



Yield: 81%. mp: 216 °C. $[\alpha]_D^{21}$ +125.6 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (d, *J* = 5.7 Hz, 1H, Ar-H), 7.66–7.57 (m, 10H, Ar-H), 7.44–7.33 (m, 8H, Ar-H), 7.19–7.06 (m, 3H, Ar-H), 6.67 (brs, 1H, Ar-H), 6.10 (brs, 1H, Ar-H), 4.56 (brs, 1H, CH=CH), 3.83–3.76 (m, 3H, CH=CH), 3.52 (brs, 1H, CH), 3.05–2.40 (m, 6H, CH_2), 2.08–1.93 (m, 4H, CH_2), 1.43–0.66 (m, 45H, CH_2 and CH_3), 0.27–0.14 (m, 2H, CH_2); ^{31}P NMR (122 MHz, $CDCl_3$) δ 15.8 (s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.7, 162.9, 162.2, 161.5, 160.9, 152.8, 148.1, 148.0, 147.8, 147.7, 145.6, 143.9, 134.9, 132.5, 132.3, 132.2, 131.8, 130.1, 129.7, 129.3, 128.9, 128.4, 128.0, 127.9, 127.8, 127.6, 127.4, 127.1, 126.5, 126.0, 124.1, 122.9, 120.6, 119.2, 117.5, 76.5, 74.8, 70.2, 69.1, 68.8, 67.7, 63.0, 61.8, 41.4, 35.0, 33.7, 31.0, 30.6, 30.4, 30.1, 28.7, 21.2. HRMS (ESI) calcd for $C_{57}H_{74}IrNOP^+$: 1012.5132. Found 1012.5141.

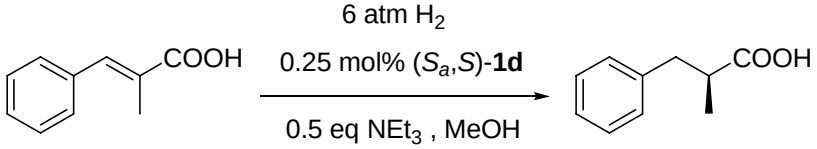
(S_a)-1h



Yield: 82%. mp: 196 °C. $[\alpha]_D^{21}$ +122.6 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (brs, 9H, Ar-H), 7.50–7.35 (m, 8H, Ar-H), 7.27–7.24 (m, 1H, Ar-H), 7.18–7.07 (m, 4H, Ar-H), 6.75 (brs, 1H, Ar-H), 6.24 (br d, *J* = 10.8 Hz, 1H, Ar-H), 4.38–4.24 (m, 2H, CH=CH), 3.90–3.63 (m, 3H, CH=CH and CH_2), 3.39–3.29 (m, 1H, CH_2), 3.16–3.07 (m, 1H, CH_2), 2.95–2.56 (m, 4H, CH_2), 2.43–2.30 (m, 1H, CH_2), 2.08–1.90 (m, 5H, CH_2), 1.48–0.80 (m, 40H, CH_2 and CH_3), 0.47–0.40 (m, 3H, CH_2); ^{31}P NMR (122 MHz, $CDCl_3$) δ 16.7 (s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 162.8, 162.1, 161.5, 160.8, 152.3, 150.9, 150.8, 148.0, 147.9, 147.7, 147.6, 145.5, 143.8, 134.9, 132.3, 132.2, 131.5, 130.9, 130.0, 129.7, 129.2, 128.8, 128.4, 128.0, 127.9, 127.8, 127.7, 127.6, 127.1, 126.9, 126.7, 126.4, 126.3, 124.3, 122.8, 121.1, 119.2, 117.5, 76.7, 71.9, 71.6, 70.7, 70.5, 69.4, 63.1, 51.6, 41.7, 35.0, 34.0, 31.6, 31.5, 31.0, 30.5, 30.2, 29.7, 29.6, 28.8. HRMS (ESI) calcd for $C_{56}H_{72}IrNOP^+$: 998.4975. Found 998.4977.

(C) General Procedure for Asymmetric Hydrogenation

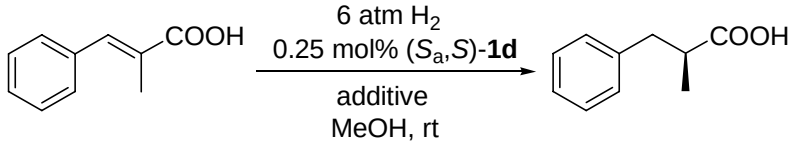
Asymmetric hydrogenation of α-methylcinnamic acid (2a)



2a **3a**

To a hydrogenation tube was charged with a stir bar, α-methylcinnamic acid (2**a**, 81 mg, 0.5 mmol), catalyst (S_a,*S*)-**1d** (2.4 mg, 0.00125 mmol), NEt_3 (25 mg, 0.25 mmol) and 2 mL MeOH at ambient atmosphere. The hydrogenation tube was then put into an autoclave. The air in the autoclave was replaced with hydrogen for three times. The autoclave was then charged with hydrogen to 6 atm, and the reaction mixture was stirred at room temperature for 30 min. After releasing hydrogen, the reaction mixture was concentrated on a rotator vapor. The conversion of substrate was determined by ^{1}H NMR analysis. The crude product was purified by a flash chromatography on silica gel column to give pure product as a colorless liquid that offered the yield. 2-Methyl-3-phenyl-propionic acid (**3a**, 82 mg, 0.5 mmol) was reacted with aniline (50 μL, 0.55 mmol) in the presences of DMAP (4 mg, 0.033 mmol) and DCC (110 mg, 0.53 mmol) in 0.5 mL THF for 30 min. The reaction mixture was filtrated through celite. The filtrate was diluted with Et_2O, washed with 3 N HCl, saturated $NaHCO_3$ and dried with Na_2SO_4. After a flash chromatography on silica gel column with Et_2O, the desired amide was obtained. The ee value of product was determined by HPLC with Chiralpak AS column.

Effect of amount of triethylamine in asymmetric hydrogenation of *α*-methylcinnamic acid

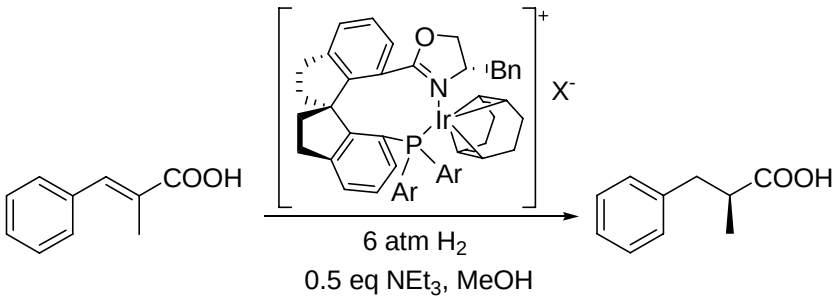


Additive	Reaction time (h)	Conversion (%)	Ee (%)
none	2	60	99
0.1 eq NEt3	2	65	>99
0.2 eq NEt3	2	75	>99
0.5 eq NEt3	0.5	100	>99
1.0 eq NEt3	0.5	100	>99

Reaction conditions: 0.5 mmol α-methylcinnamic acid, 0.25 mol% (*S*a,*S*)-**1d**, 2 mL MeOH, *P*H2 = 6 atm, room temperature.

Comparison of anions of catalysts in asymmetric hydrogenation of *α*-methylcinnamic acid

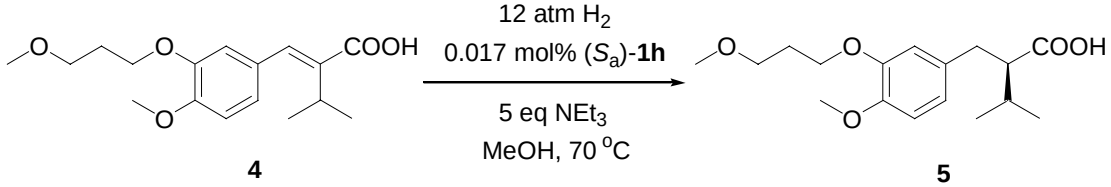
The catalysts with different anions were prepared in situ and evaluated in asymmetric hydrogenation of *α*-methylcinnamic acid. All tested catalysts can catalyze the reaction, providing desired hydrogenated product with >99% ee. The catalysts with anions OTf, ClO_4 and BARF gave full conversions. Among these catalysts, only the catalyst with anion BARF is stable in air, it can be purified by a column chromatography on silica gel and can be handled in air. So we used this catalyst for all following experiments.



Anions	Reaction time (h)	Conversion (%)	Ee (%)
BARF	0.5	100	>99
OTf	1	100	>99
ClO4	0.5	100	>99
BF4	18	45	>99
PF6	18	80	>99

Reaction conditions: 0.5 mmol α-methylcinnamic acid, 0.25 mol% catalysts (Ar = 3,5-^{t}Bu$_2$C$_6$H$_3$), 2 mL MeOH, *P*H2 = 6 atm, room temperature.

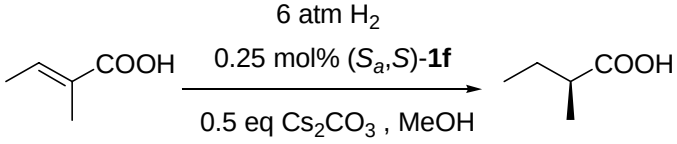
Asymmetric hydrogenation of (*E*)-2-[3-(3-methoxypropoxy)-4-methoxybenzylidene]-3-methylbutanoic acid (4)



4 **5**

To a 20 mL hydrogenation tube was charged with a stir bar, (*E*)-2-[3-(3-methoxypropoxy)-4-methoxybenzylidene]-3-methylbutanoic acid (**4**, 771 mg, 2.5 mmol), catalyst (S_a)-**1h** (0.8 mg, 0.000417 mmol), NEt_3 (1.26 g, 12.5 mmol) and 3.5 mL MeOH at ambient atmosphere. The hydrogenation tube was put into an autoclave. The air in the autoclave was replaced with hydrogen for three times. The autoclave was then charged with hydrogen to 12 atm, and the reaction mixture was stirred at 70 ^{o}C for 7 h. After releasing hydrogen, the reaction mixture was concentrated on a rotator vapor. The crude product was acidified with 3N aqueous HCl and extracted with Et_2O. The conversion of substrate was determined by ^{1}H NMR analysis. A flash chromatography on silica gel column gave pure product **5** as a white solid that offered the yield. The product **5** (155 mg, 0.5 mmol) was reacted with aniline (50 μL, 0.55 mmol) in the presences of DMAP (4 mg, 0.033 mmol) and DCC (110 mg, 0.53 mmol) in 0.5 mL THF for 30 min. The reaction mixture was filtrated through celite. The filtrate was diluted with Et_2O, washed with 3 N HCl, saturated $NaHCO_3$ and dried with Na_2SO_4. After a flash chromatography on silica gel column with Et_2O, the desired amide was obtained and analyzed on SFC with a Chiralpak AD-H column to determined ee value.

Asymmetric hydrogenation of tiglic acid (6a)

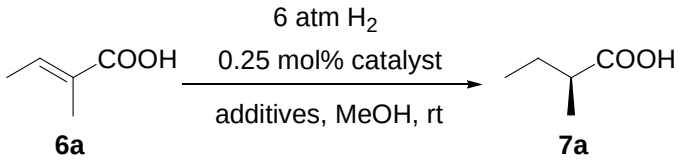


6a **7a**

To a hydrogenation tube was added a stir bar, tiglic acid (**6a**, 50 mg, 0.5 mmol), catalyst (S_a,*S*)-**1f** (2.4 mg, 0.00125 mmol), Cs_2CO_3 (82 mg, 0.25 mmol) and 2 mL MeOH at ambient atmosphere. The hydrogenation tube was put into an autoclave. The air in the autoclave was replaced with hydrogen for three times. The autoclave was then charged with hydrogen to 6 atm, and the reaction mixture was stirred at room temperature for 30 min. After releasing hydrogen, the reaction mixture was acidified with 3N aqueous HCl and extracted with Et_2O. The extract was concentrated on a rotator vapor. The conversion of substrate was determined by ^{1}H NMR analysis. The crude product was purified by a flash chromatography on silica gel column to give pure product **7a** as a colorless liquid that offered the yield. The product **7a** (51 mg, 0.5 mmol) was reacted with aniline (50 μL, 0.55 mmol) in the prensences of DMAP (4 mg, 0.033 mmol) and DCC (110 mg, 0.53 mmol) in 0.5 mL THF for 30 min. The reaction mixture was filtrated through celite. The filtrate was diluted with Et_2O, washed with 3 N HCl, saturated $NaHCO_3$ and dried with Na_2SO_4. After a flash chromatography on silica gel column with Et_2O, the desired amide was obtained and analyzed on HPLC with a Chiralpak AD-H column to determined ee value.

Comparison of catalysts and additives in asymmetric hydrogenation of tiglic acid

A number of organic and inorganic bases gave full conversions and high enantioselectivities, with Cs_2CO_3 being the best choice in the asymmetric hydrogenation of tiglic acids.

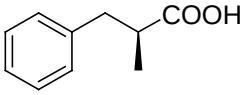


Catalyst	Additive	Time (h)	Conversion (%)	Ee (%)
(*Sa*,*S*)-**1d**	0.5 eq NEt_3	2	95	97
(*Sa*,*S*)-**1e**	0.5 eq NEt_3	1	100	94
(*Sa*,*S*)-**1f**	0.5 eq NEt_3	1	95	98
(*Sa*,*S*)-**1g**	0.5 eq NEt_3	1	90	97
(*Sa*)-**1h**	0.5 eq NEt_3	3	100	96
(*Sa*,*S*)-**1f**	0.5 eq pyridine	24	0	
(*Sa*,*S*)-**1f**	0.5 eq iPr_2NEt	1	95	99
(*Sa*,*S*)-**1f**	0.5 eq KOH	4	95	98
(*Sa*,*S*)-**1f**	0.5 eq $NaHCO_3$	18	85	98
(*Sa*,*S*)-**1f**	0.5 eq Na_2CO_3	1	100	98
(*Sa*,*S*)-**1f**	0.5 eq Cs_2CO_3	0.5	100	>99

Reaction conditions: 0.5 mmol tiglic acid, 0.25 mol% catalyst, 2 mL MeOH, *P*H2 = 6 atm, room temperature.

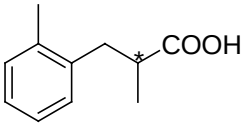
(D) Analytical Data of Hydrogenation Products

(*S*)-2-Methyl-3-phenylpropionic acid (3a)[4]



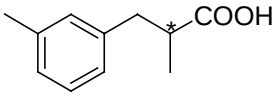
Colorless oil, 99% yield, 99.2% ee (*S*), $[\alpha]_D^{20}$ +30.2 (*c* 0.82, $CHCl_3$), HPLC condition for corresponding amide: Chiralpak AS column (25 cm × 0.46 cm ID), *n*-hexane/2-propanol = 95:5, 1.0 mL/min, 254 nm UV detector, t_R = 18.14 min for (*S*)-enantiomer and t_R = 22.03 min for (*R*)-enantiomer. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.95 (brs, 1H, COOH), 7.31–7.18 (m, 5H, Ar-H), 3.08 (dd, *J* = 13.2 and 6.4 Hz, 1H, CH_2), 2.77 (sextet, *J* = 6.8 Hz, 1H, CH), 2.67 (dd, *J* = 13.2 and 8.0 Hz, 1H, CH_2), 1.18 (d, *J* = 6.8 Hz, 3H, CH_3).

(+)-2-Methyl-3-*o*-tolylpropionic acid (3b)[5]



Colorless oil, 97% yield, 99% ee, $[\alpha]_D^{26}$ +37.3 (*c* 0.55, acetone), HPLC condition for corresponding amide: Chiralcel OD-H column (25 cm × 0.46 cm ID), *n*-hexane/2-propanol = 90:10, 1.0 mL/min, 254 nm UV detector, t_R = 12.61 min (major) and t_R = 16.39 min (minor). ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.65 (brs, 1H, COOH), 7.17–7.12 (m, 4H, Ar-H), 3.11 (dd, *J* = 13.2 and 6.0 Hz, 1H, CH_2), 2.76 (sextet, *J* = 6.9 Hz, 1H, CH), 2.65 (dd, *J* = 13.5 and 8.4 Hz, 1H, CH_2), 2.33 (s, 3H, CH_3), 1.20 (d, *J* = 6.9 Hz, 3H, CH_3).

(+)-2-Methyl-3-*m*-tolylpropionic acid (3c)[5]

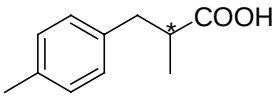


Colorless oil, 98% yield, 99% ee, $[\alpha]_D^{26}$ +35.1 (*c* 0.52, acetone), HPLC condition for corresponding amide: Chiralpak AS column (25 cm × 0.46 cm ID), *n*-hexane/2-propanol = 98:2, 1.0 mL/min, 254 nm UV detector, t_R = 26.54 min (major)

[4] Davies, S. G.; Dixon, D. J.; Doisneau, G. J.-M.; Prodger, J. C.; Sanganee, H. J. *Tetrahedron: Asymmetry* **2002**, *13*, 647–658.
[5] Cheng, X.; Zhang, Q.; Xie, J.-H.; Wang, L.-X.; Zhou, Q.-L. *Angew. Chem. Int. Ed.* **2005**, *44*, 1118–1121.

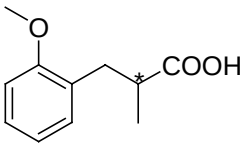
and t_R = 32.74 min (minor). ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.60 (brs, 1H, COOH), 7.18 (t, J = 7.5 Hz, 1H, Ar-H), 7.04–6.96 (m, 3H, Ar-H), 3.05 (dd, J = 13.2 and 6.3 Hz, 1H, CH_2), 2.76 (sextet, J = 6.9 Hz, 1H, CH), 2.62 (dd, J = 13.2 and 8.1 Hz, 1H, CH_2), 2.32 (s, 3H, CH_3), 1.17 (d, J = 6.9 Hz, 3H, CH_3).

(+)-2-Methyl-3-*p*-tolyl-propionic acid (3d)[5]



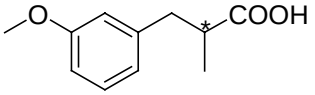
Colorless oil, 98% yield, 99% ee, $[\alpha]_D^{26}$ +32.2 (*c* 0.58, acetone), HPLC condition for corresponding amide: Chiralpak AD-H column (25 cm × 0.46 cm ID), *n*-hexane/2-propanol = 94:6, 1.0 mL/min, 254 nm UV detector, t_R = 16.33 min (minor) and t_R = 18.49 min (major). ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.50 (brs, 1H, COOH), 7.11–7.05 (m, 4H, Ar-H), 3.03 (dd, J = 13.2 and 6.3 Hz, 1H, CH_2), 2.74 (sextet, J = 7.5 Hz, 1H, CH), 2.63 (dd, J = 13.2 and 7.8 Hz, 1H, CH_2), 2.32 (s, 3H, CH_3), 1.17 (d, J = 6.9 Hz, 3H, CH_3).

(+)-3-(2-Methoxyphenyl)-2-methylpropionic acid (3e)[5]



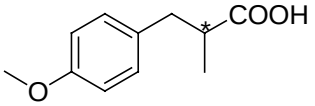
Colorless oil, 98% yield, 99% ee, $[\alpha]_D^{25}$ +33.6 (*c* 0.54, acetone), HPLC condition for corresponding amide: Chiralpak AS column (25 cm × 0.46 cm ID), *n*-hexane/2-propanol = 98:2, 1.0 mL/min, 254 nm UV detector, t_R = 34.58 min (major) and t_R = 40.72 min (minor). ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.53 (brs, 1H, COOH), 7.23–7.11 (m, 2H, Ar-H), 6.89–6.83 (m, 2H, Ar-H), 3.80 (s, 3H, CH_3), 3.05 (dd, J = 13.2 and 6.6 Hz, 1H, CH_2), 2.86 (sextet, J = 7.2 Hz, 1H, CH), 2.70 (dd, J = 13.2 and 7.8 Hz, 1H, CH_2), 1.16 (d, J = 6.9 Hz, 3H, CH_3).

(+)-3-(3-Methoxyphenyl)-2-methylpropionic acid (3f)[5]



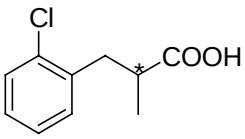
Colorless oil, 99% yield, 98% ee, $[\alpha]_D^{25}$ +24.8 (*c* 0.62, acetone), HPLC condition for corresponding amide: Chiralpak AS column (25 cm × 0.46 cm ID), *n*-hexane/2-propanol = 97:3, 1.0 mL/min, 254 nm UV detector, t_R = 32.28 min (major) and t_R = 37.52 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.98 (brs, 1H, COOH), 7.20 (t, J = 8.0 Hz, 1H, Ar-H), 6.78–6.73 (m, 3H, Ar-H), 3.79 (s, 3H, CH_3), 3.06 (dd, J = 13.6 and 6.4 Hz, 1H, CH_2), 2.77 (sextet, J = 7.2 Hz, 1H, CH), 2.64 (dd, J = 13.6 and 8.0 Hz, 1H, CH_2), 1.18 (d, J = 6.8 Hz, 3H, CH_3).

(+)-3-(4-Methoxyphenyl)-2-methylpropionic acid (3g)[5]



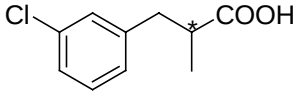
Colorless oil, 97% yield, 99% ee, $[\alpha]_D^{25}$ +31.0 (*c* 0.51, acetone), HPLC condition for corresponding amide: Chiralcel OD-H column (25 cm × 0.46 cm ID), *n*-hexane/2-propanol = 90:10, 1.0 mL/min, 254 nm UV detector, t_R = 16.91 min (minor) and t_R = 20.12 min (major). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.94 (brs, 1H, COOH), 7.10 (d, J = 8.4 Hz, 2H, Ar-H), 6.83 (d, J = 8.4 Hz, 2H, Ar-H), 3.79 (s, 3H, CH_3), 3.01 (dd, J = 13.6 and 6.4 Hz, 1H, CH_2), 2.72 (sextet, J = 7.2 Hz, 1H, CH), 2.62 (dd, J = 13.6 and 8.0 Hz, 1H, CH_2), 1.16 (d, J = 6.8 Hz, 3H, CH_3).

(+)-3-(2-Chlorophenyl)-2-methylpropionic acid (3h)[5]



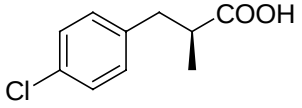
Colorless oil, 97% yield, 96% ee, $[\alpha]_D^{29}$ +36.8 (*c* 0.66, acetone), HPLC condition for corresponding amide: Chiralpak AD-H column (25 cm × 0.46 cm ID), *n*-hexane/2-propanol = 94:6, 1.0 mL/min, 254 nm UV detector, t_R = 14.65 min (major) and t_R = 16.37 min (minor). ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.56 (brs, 1H, COOH), 7.37–7.34 (m, 1H, Ar-H), 7.25–7.16 (m, 3H, Ar-H), 3.18 (dd, J = 12.9 and 6.3 Hz, 1H, CH_2), 2.97–2.79 (m, 2H, CH and CH_2), 1.22 (d, J = 6.6 Hz, 3H, CH_3).

(+)-3-(3-Chlorophenyl)-2-methylpropionic acid (3i)[5]



Colorless oil, 98% yield, 99% ee, $[\alpha]_D^{29}$ +36.3 (*c* 0.74, acetone), HPLC condition for corresponding amide: Chiralcel OD-H column (25 cm × 0.46 cm ID), *n*-hexane/2-propanol = 97:3, 1.0 mL/min, 254 nm UV detector, t_R = 52.69 min (minor) and t_R = 57.72 min (major). ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.53 (brs, 1H, COOH), 7.22–7.18 (m, 3H, Ar-H), 7.08–7.05 (m, 1H, Ar-H), 3.05 (dd, J = 13.2 and 6.3 Hz, 1H, CH_2), 2.76 (sextet, J = 6.9 Hz, 1H, CH), 2.65 (dd, J = 13.2 and 7.8 Hz, 1H, CH_2), 1.19 (d, J = 6.9 Hz, 3H, CH_3).

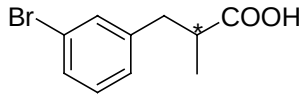
(*S*)-3-(4-Chlorophenyl)-2-methylpropionic acid (3j)[5]



Colorless oil, 97% yield, 98% ee, $[\alpha]_D^{27}$ +30.2 (*c* 0.60, acetone), HPLC condition for

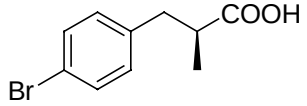
corresponding amide: Chiralpak AS column (25 cm × 0.46 cm ID), *n*-hexane/2-propanol = 95:5, 1.0 mL/min, 254 nm UV detector, t_R = 19.61 min for (*S*)-enantiomer and t_R = 25.02 min for (*R*)-enantiomer. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.73 (brs, 1H, COOH), 7.26 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.12 (d, *J* = 8.1 Hz, 2H, Ar-H), 3.02 (dd, *J* = 12.9 and 6.3 Hz, 1H, CH_2), 2.78–2.62 (m, 2H, CH and CH_2), 1.19 (d, *J* = 6.6 Hz, 3H, CH_3).

(+)-3-(3-Bromophenyl)-2-methylpropionic acid (3k)[5]



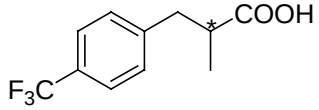
Colorless oil, 97% yield, 99% ee, $[\alpha]_D^{26}$ +25.4 (c 0.52, acetone), HPLC condition for corresponding amide: Chiralpak AS column (25 cm × 0.46 cm ID), *n*-hexane/2-propanol = 98:2, 1.0 mL/min, 254 nm UV detector, t_R = 44.55 min (major) and t_R = 54.12 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.49 (brs, 1H, COOH), 7.36–7.34 (m, 2H, Ar-H), 7.18–7.10 (m, 2H, Ar-H), 3.04 (dd, *J* = 13.2 and 7.2 Hz, 1H, CH_2), 2.75 (sextet, *J* = 7.2 Hz, 1H, CH), 2.65 (dd, *J* = 13.2 and 7.6 Hz, 1H, CH_2), 1.19 (d, *J* = 6.9 Hz, 3H, CH_3).

(*S*)-3-(4-Bromophenyl)-2-methylpropionic acid (3l)[6]



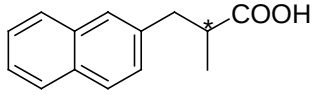
Colorless oil, 97% yield, 98% ee, $[\alpha]_D^{26}$ +28.8 (*c* 0.56, $CHCl_3$), HPLC condition for corresponding amide: Chiralpak AS column (25 cm × 0.46 cm ID), *n*-hexane/2-propanol = 95:5, 1.0 mL/min, 254 nm UV detector, t_R = 23.67 min for (*S*)-enantiomer and t_R = 29.95 min for (*R*)-enantiomer. ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.95 (brs, 1H, COOH), 7.40 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.06 (d, *J* = 8.4 Hz, 2H, Ar-H), 3.01 (dd, *J* = 13.2 and 6.8 Hz, 1H, CH_2), 2.74 (sextet, *J* = 7.2 Hz, 1H, CH), 2.64 (dd, *J* = 13.6 and 7.6 Hz, 1H, CH_2), 1.18 (d, *J* = 6.8 Hz, 3H, CH_3).

(+)-2-Methyl-3-(4-trifluoromethylphenyl)propionic acid (3m)[5]



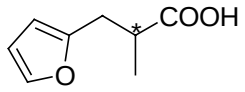
White solid, mp 58–60 °C, 98% yield, 97% ee, $[\alpha]_D^{25}$ +25.8 (*c* 0.62, acetone), HPLC condition for corresponding amide: Chiralpak AD-H column (25 cm × 0.46 cm ID), *n*-hexane/2-propanol = 95:5, 1.0 mL/min, 254 nm UV detector, t_R = 21.20 min (minor) and t_R = 24.23 min (major). ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.15 (brs, 1H, COOH), 7.55 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.30 (d, *J* = 8.0 Hz, 2H, Ar-H), 3.11 (dd, *J* = 12.8 and 6.0 Hz, 1H, CH_2), 2.84–2.72 (m, 2H, CH and CH_2), 1.21 (d, *J* = 6.4 Hz, 3H, CH_3).

(+)-2-Methyl-3-(naphthalen-2-yl)propionic acid (3n)[5]



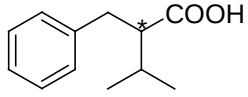
White solid, mp 74–76 °C, 96% yield, 99% ee, $[\alpha]_D^{25}$ +32.4 (*c* 0.70, acetone), HPLC condition for corresponding amide: Chiralpak AD-H column (25 cm × 0.46 cm ID), *n*-hexane/2-propanol = 97:3, 1.0 mL/min, 254 nm UV detector, t_R = 65.29 min (minor) and t_R = 67.22 min (major). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.97 (brs, 1H, COOH), 7.82–7.77 (m, 3H, Ar-H), 7.64 (s, 1H, Ar-H), 7.48–7.42 (m, 2H, Ar-H), 7.34–7.31 (m, 1H, Ar-H), 3.25 (dd, *J* = 12.8 and 5.6 Hz, 1H, CH_2), 2.93–2.81 (m, 2H, CH and CH_2), 1.22 (d, *J* = 6.8 Hz, 3H, CH_3).

(-)-3-Furan-2-yl-2-methylpropionic acid (3o)[7]



Yellow solid, mp 112–113 °C, 98% yield, 98% ee, $[\alpha]_D^{26}$ –5.33 (*c* 0.60, acetone), HPLC condition for corresponding amide: Chiralcel OD-H column (25 cm × 0.46 cm ID), *n*-hexane/2-propanol = 90:10, 1.0 mL/min, 254 nm UV detector, t_R = 12.37 min (minor) and t_R = 15.54 min (major). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.98 (brs, 1H, COOH), 7.31–7.30 (m, 1H, CH), 6.28–6.27 (m, 1H, CH), 6.06 (d, *J* = 3.2 Hz, 1H, CH), 3.06 (dd, *J* = 14.8 and 6.4 Hz, 1H, CH_2), 2.86 (sextet, *J* = 6.8 Hz, 1H, CH), 2.75 (dd, *J* = 14.8 and 7.2 Hz, 1H, CH_2), 1.22 (d, *J* = 6.8 Hz, 3H, CH_3).

(+)-2-Benzyl-3-methylbutanoic acid (3p)[8]

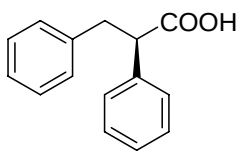


Colorless oil, 97% yield, 99% ee, $[\alpha]_D^{26}$ +50.4 (*c* 0.56, acetone), HPLC condition for corresponding amide: Chiralcel OD-H column (25 cm × 0.46 cm ID), *n*-hexane/2-propanol = 94:6, 1.0 mL/min, 254 nm UV detector, t_R = 14.91 min (major) and t_R = 18.82 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.81 (brs, 1H, COOH),

[6] Kotake, T.; Hayashi, Y.; Rajesh, S.; Mukai, Y.; Takiguchi, Y.; Kimura, T.; Kiso, Y. *Tetrahedron* **2005**, *61*, 3819–3833.
[7] Harmata, M.; Gamlath, C. B.; Barnes, C. L.; Jones, D. E. *J. Org. Chem.* **1995**, *60*, 5077–5092.
[8] Hoen, R.; Boogers, J. A. F.; Bernsmann, H.; Minnaard, A. J.; Meetsma, A.; de Vries, A. H. M.; de Vries, J. G.; Feringa, B. L. *Angew. Chem. Int. Ed.* **2005**, *44*, 4209–4212.

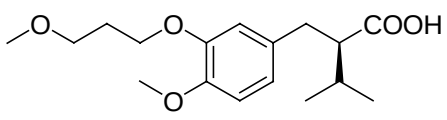
7.26–7.15 (m, 5H, Ar-H), 2.89–2.80 (m, 2H, CH_2 and CH), 2.50–2.45 (m, 1H, CH_2), 2.01–1.89 (m, 1H, CH), 1.02 (dd, J = 11.6 and 6.8 Hz, 6H, CH_3).

(*R*)-2,3-diphenylpropionic acid (3q)[9]



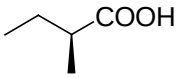
White solid, mp 79–81 °C, 95% yield, 94% ee, $[\alpha]_D^{25}$ –120 (*c* 0.53, acetone), SFC condition for corresponding amide: Chiralpak OJ-H column (25 cm × 0.46 cm ID), CO_2/2-propanol = 70:30, 2.0 mL/min, 100 bar, 254 nm UV detector, t_R = 3.98 min for (*R*)-enantiomer and t_R = 4.40 min for (*S*)-enantiomer. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.41 (brs, 1H, COOH), 7.31–7.08 (m, 10H, Ar-H), 3.84 (t, J = 7.8 Hz, 1H, CH), 3.40 (dd, J = 13.8 and 8.4 Hz, 1H, CH_2), 3.02 (dd, J = 13.8 and 6.9 Hz, 1H, CH_2).

(*R*)-2-(3-(3-Methoxypropoxy)-4-methoxybenzyl)-3-methylbutanoic acid (5)[10]



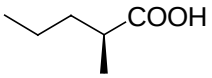
White solid, mp 44–45 °C, 96% yield, 98% ee, $[\alpha]_D^{21}$ +42.2 (*c* 1.0, CH_2Cl_2), SFC condition for corresponding amide: Chiralpak AD-H column (25 cm × 0.46 cm ID), CO_2/2-propanol = 80:20, 2.0 mL/min, 100 bar, 254 nm UV detector, t_R = 5.40 min for (*S*)-enantiomer and t_R = 5.93 min for (*R*)-enantiomer. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.71 (brs, 1H, COOH), 6.73–6.68 (m, 3H, Ar-H), 4.06 (t, J = 6.4 Hz, 2H, CH_2), 3.79 (s, 3H, CH_3), 3.53 (t, J = 6.4 Hz, 2H, CH_2), 3.32 (s, 3H, CH_3), 2.81–2.71 (m, 2H, CH_2 and CH), 2.43–2.38 (m, 1H, CH_2), 2.08–2.01 (m, 2H, CH_2), 1.90 (sextet, J = 6.4 Hz, 1H, CH), 1.00 (dd, J = 13.2 and 6.8 Hz, 6H, CH_3).

(*S*)-2-Methylbutanoic acid (7a)[11]



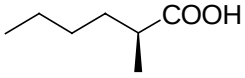
Colorless oil, 92% yield, 99.1% ee, $[\alpha]_D^{16}$ +19.8 (*c* 0.76, ethanol), HPLC condition for corresponding amide: Chiralpak AD-H column (25 cm × 0.46 cm ID), *n*-hexane/2-propanol = 99:1, 1.0 mL/min, 254 nm UV detector, t_R = 35.91 min for (*S*)-enantiomer and t_R = 39.43 min for (*R*)-enantiomer. ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.69 (brs, 1H, COOH), 2.44–2.36 (m, 1H, CH), 1.76–1.65 (m, 1H, CH_2), 1.55–1.44 (m, 1H, CH_2), 1.17 (d, J = 7.2 Hz, 3H, CH_3), 0.94 (t, J = 7.2 Hz, 3H, CH_3).

(*S*)-2-Methylpentanoic acid (7b)[12]



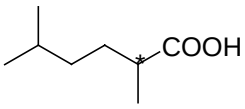
Colorless oil, 93% yield, 98% ee (*S*), $[\alpha]_D^{18}$ +14.9 (*c* 0.94, $CHCl_3$), HPLC condition for corresponding amide: Chiralpak AD-H column (25 cm × 0.46 cm ID), *n*-hexane/2-propanol = 90:10, 1.0 mL/min, 254 nm UV detector, t_R = 6.99 min for (*S*)-enantiomer and t_R = 7.81 min for (*R*)-enantiomer. ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.57 (brs, 1H, COOH), 2.52–2.43 (m, 1H, CH), 1.71–1.63 (m, 1H, CH_2), 1.46–1.31 (m, 3H, CH_2), 1.17 (d, J = 6.8 Hz, 3H, CH_3), 0.91 (t, J = 7.2 Hz, 3H, CH_3).

(*S*)-2-Methylhexanoic acid (7c)[13]



Colorless oil, 89% yield, 99% ee, $[\alpha]_D^{18}$ +19.6 (c 1.30, ether), HPLC condition for corresponding amide: Chiralpak AD-H column (25 cm × 0.46 cm ID), *n*-hexane/2-propanol = 97:3, 1.0 mL/min, 254 nm UV detector, t_R = 25.35 min for (*S*)-enantiomer and t_R = 29.83 min for (*R*)-enantiomer. ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.64 (brs, 1H, COOH), 2.50–2.41 (m, 1H, CH), 1.73–1.64 (m, 1H, CH_2), 1.48–1.39 (m, 1H, CH_2), 1.34–1.29 (m, 4H, CH_2), 1.17 (d, J = 7.2 Hz, 3H, CH_3), 0.89 (t, J = 6.8 Hz, 3H, CH_3).

(+)-2,5-Dimethylhexanoic acid (7d)[14]



Colorless oil, 97% yield, 90% ee, $[\alpha]_D^{18}$ +14.5 (*c* 1.1, ethanol), HPLC condition for corresponding amide: Chiralpak AD-H column (25 cm × 0.46 cm ID), *n*-hexane/2-propanol = 97:3, 1.0 mL/min, 254 nm UV detector, t_R = 9.21 min (major) and t_R = 10.12 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.33 (brs, 1H, COOH), 2.47–2.38 (m, 1H, CH), 1.72–1.63 (m, 1H, CH_2), 1.58–1.48 (m, 1H, CH), 1.46–1.39 (m, 1H, CH_2), 1.25–1.17 (m,

[9] Fox, M. E.; Jackson, M.; Lennon, I. C.; Klosin, J.; Abboud, K. A. *J. Org. Chem.* **2008**, *73*, 775–784

[10] Göschke, R.; Stutz, S.; Heinzelmann, W.; Maibaum, J. *Helv. Chim. Acta.* **2003**, *86*, 2848–2870.

[11] Jansen, R.; Sheldrick, W. S.; Höfle, G. *Liebigs. Ann. Chem.* **1984**, 78–84.

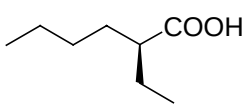
[12] Riley, R. G.; Silverstein, R. M. *Tetrahedron* **1974**, *30*, 1171–1174.

[13] Levene, P. A.; Bass, L. W. *J. Biol. Chem.* **1926**, *70*, 211–217.

[14] Boogaard, P. J.; Van Elburg, P. A.; De Kloe, K. P.; Watson, W. P.; Van Sittert, N. J. *Xenobiotica* **1999**, *29*, 987–1006.

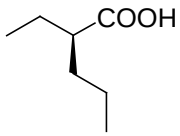
5H, CH_2 and CH_3), 0.88 (d, J = 7.2 Hz, 6H, CH_3).

(*S*)-2-Ethylhexanoic acid (7e)[15]



Colorless oil, 89% yield, 99.4% ee, $[\alpha]_D^{18}$ +10.5 (*c* 0.88, $CHCl_3$), HPLC condition for corresponding amide: Chiralpak AD-H column (25 cm × 0.46 cm ID), *n*-hexane/2-propanol = 99:1, 1.0 mL/min, 254 nm UV detector, t_R = 26.31 min for (*S*)-enantiomer and t_R = 29.88 min for (*R*)-enantiomer. ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.17 (brs, 1H, COOH), 2.32–2.25 (m, 1H, CH), 1.70–1.44 (m, 4H, CH_2), 1.37–1.25 (m, 4H, CH_2), 0.96–0.87 (m, 6H, CH_3).

(*R*)-2-Ethylpentanoic acid (7f)[16]

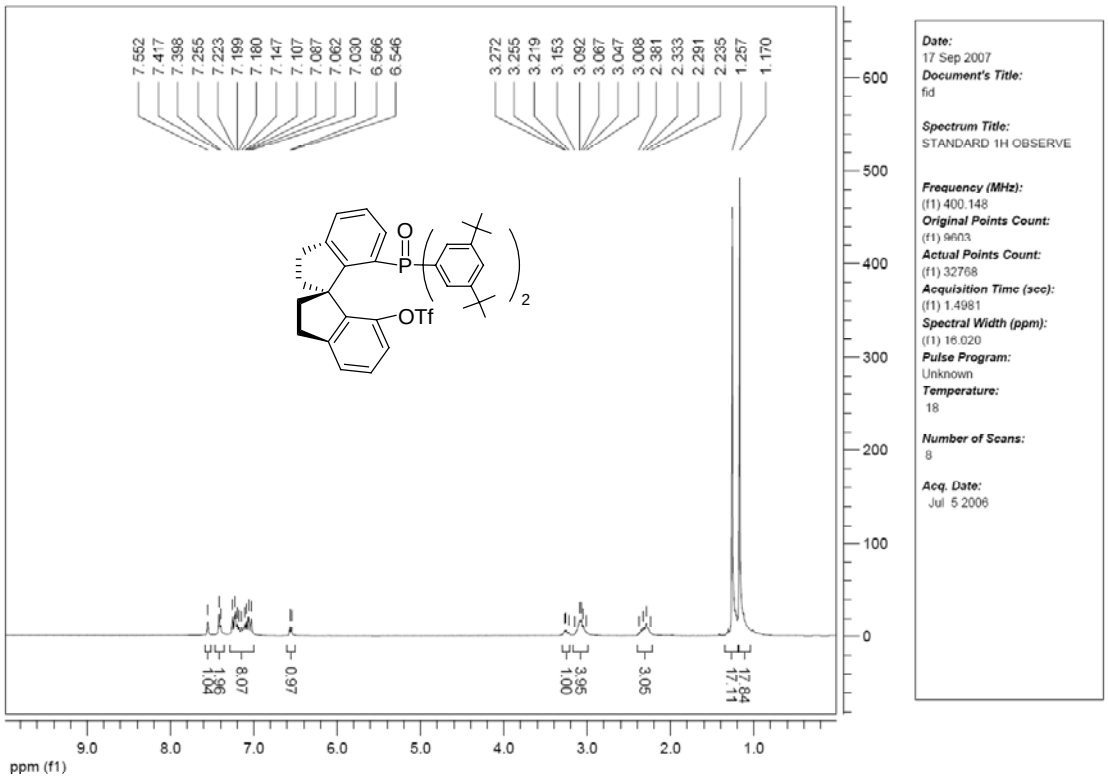


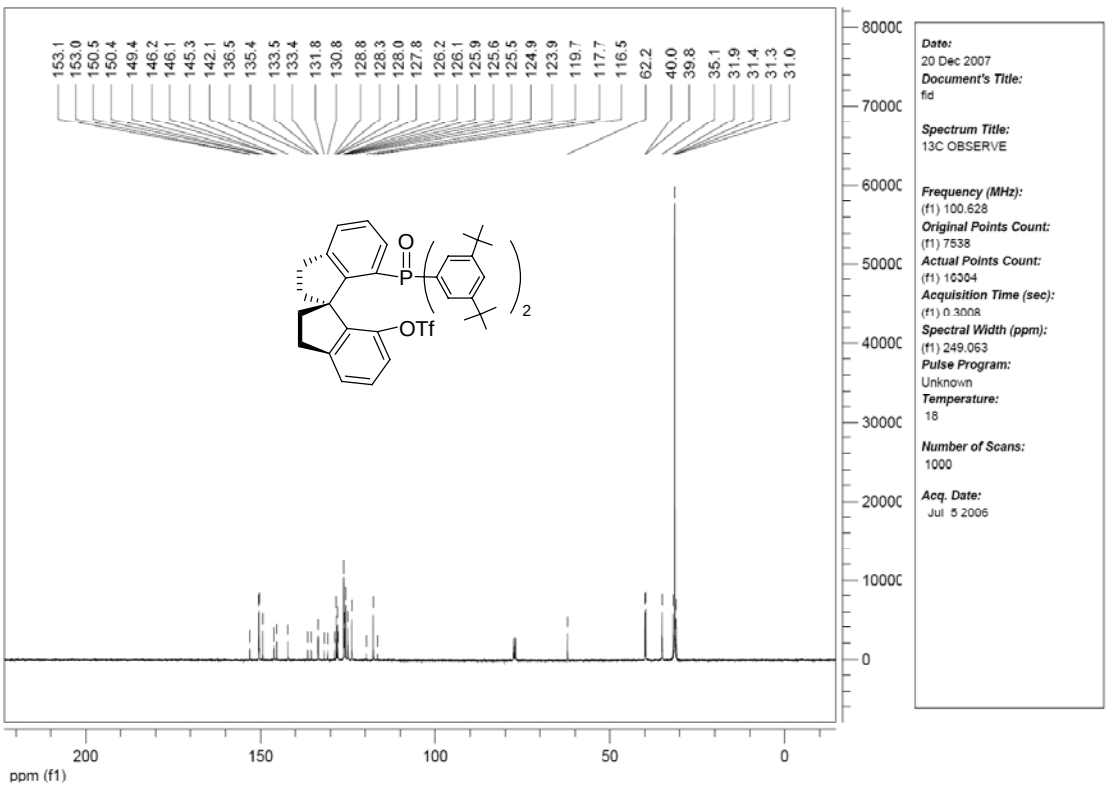
Colorless oil, 92% yield, 98% ee, $[\alpha]_D^{17}$ –4.1 (*c* 1.0, $CHCl_3$), HPLC condition for corresponding amide: Chiralpak AD-H column (25 cm × 0.46 cm ID), *n*-hexane/2-propanol = 95:5, 1.0 mL/min, 254 nm UV detector, t_R = 8.64 min for (*S*)-enantiomer and t_R = 9.84 min for (*R*)-enantiomer. ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.28 (brs, 1H, COOH), 2.34–2.27 (m, 1H, CH), 1.70–1.28 (m, 6H, CH_2), 0.95–0.89 (m, 6H, CH_3).

[15] Larcheveque, M.; Ignatova, E.; Cuvigny, T. *J. Organomet. Chem.* **1979**, *177*, 5–15.
[16] Cassani, F.; Celentano, G.; Erba, E.; Pocar, D. *Synthesis* **2004**, 1041–1046.

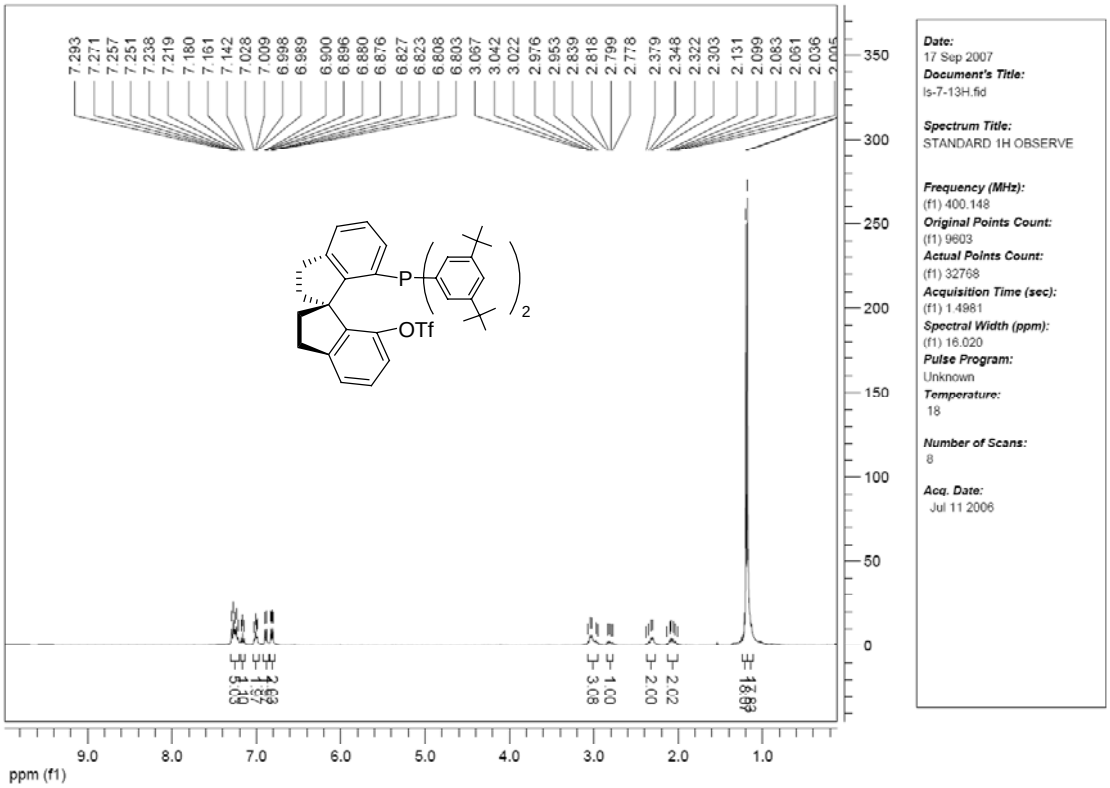
(E) NMR Spectra of New Ligands

(S_a)-9





(S_a)-10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6.827
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Actual Points Count:
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Jul 11 2006
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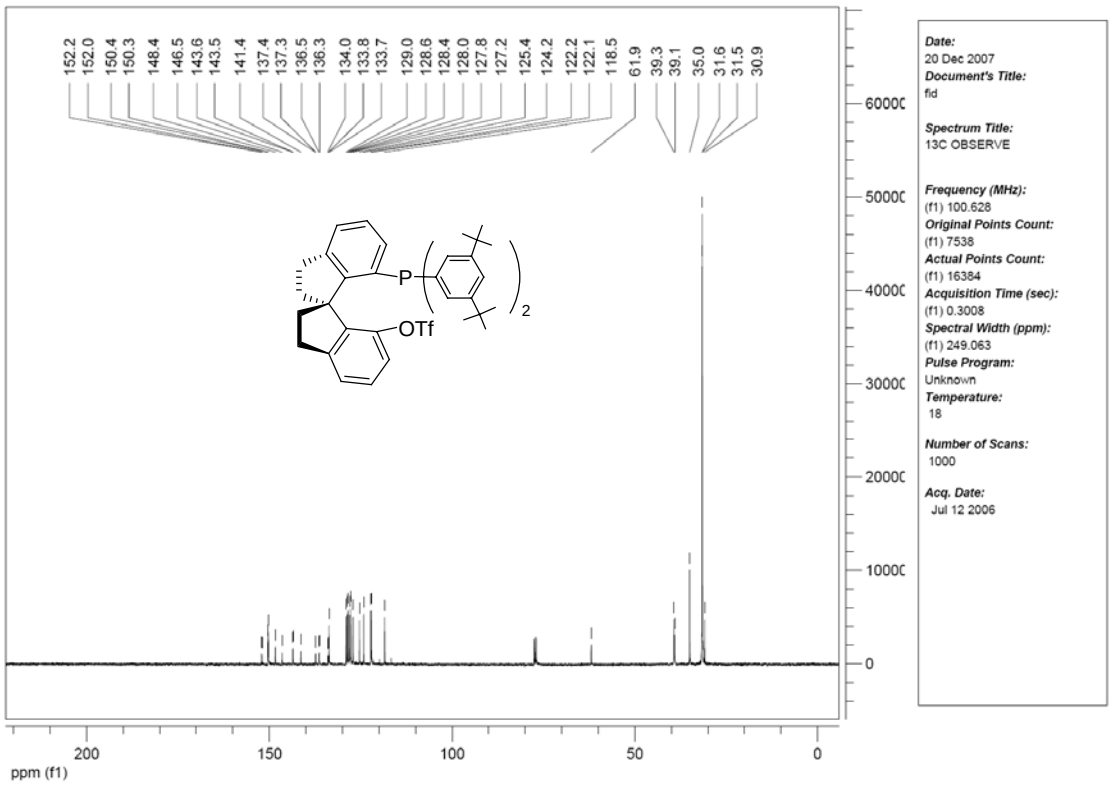
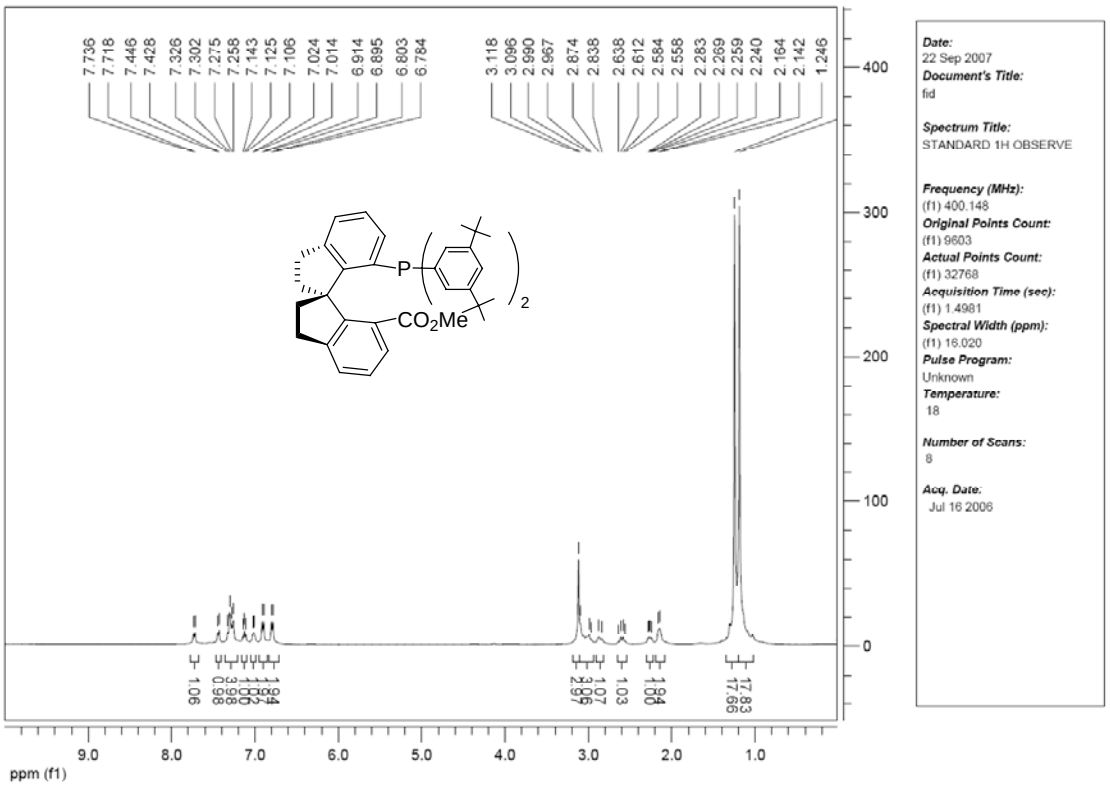
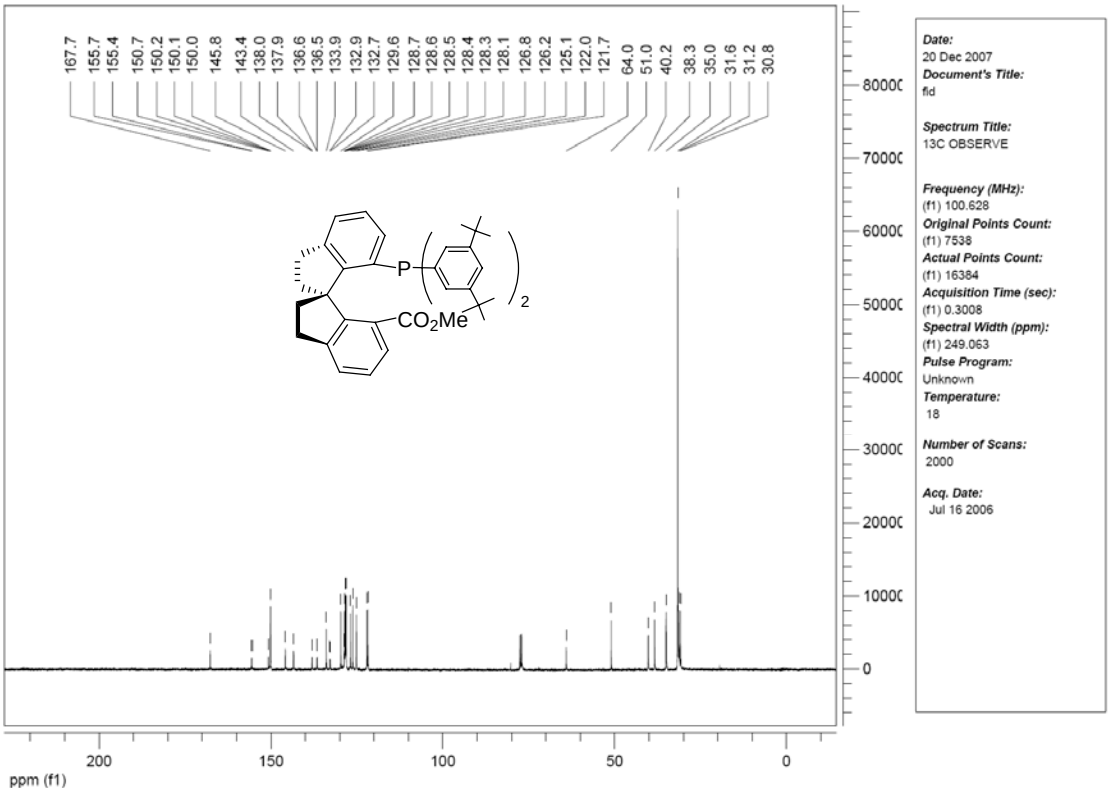
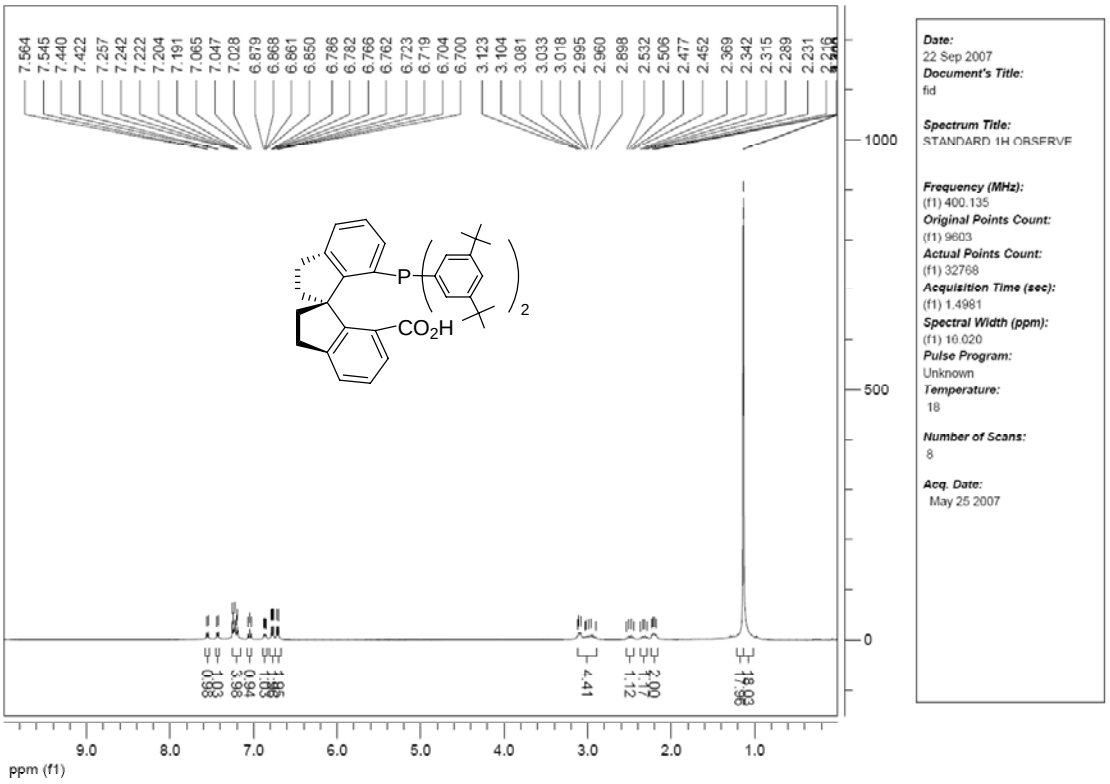

152.2
152.0
150.4
150.3
148.4
146.5
143.6
143.5
141.4
137.4
137.3
136.5
136.3
134.0
133.8
133.7
129.0
128.6
128.4
128.0
127.8
127.2
125.4
124.2
122.2
122.1
118.5
61.9
39.3
39.1
35.0
31.6
31.5
30.9
P
OTf
2
Date:
20 Dec 2007
Document's Title:
fid
Spectrum Title:
13C OBSERVE
Frequency (MHz):
(f1) 100.628
Original Points Count:
(f1) 7538
Actual Points Count:
(f1) 16384
Acquisition Time (sec):
(f1) 0.3008
Spectral Width (ppm):
(f1) 249.063
Pulse Program:
Unknown
Temperature:
18
Number of Scans:
1000
Acq. Date:
Jul 12 2006
ppm (f1)

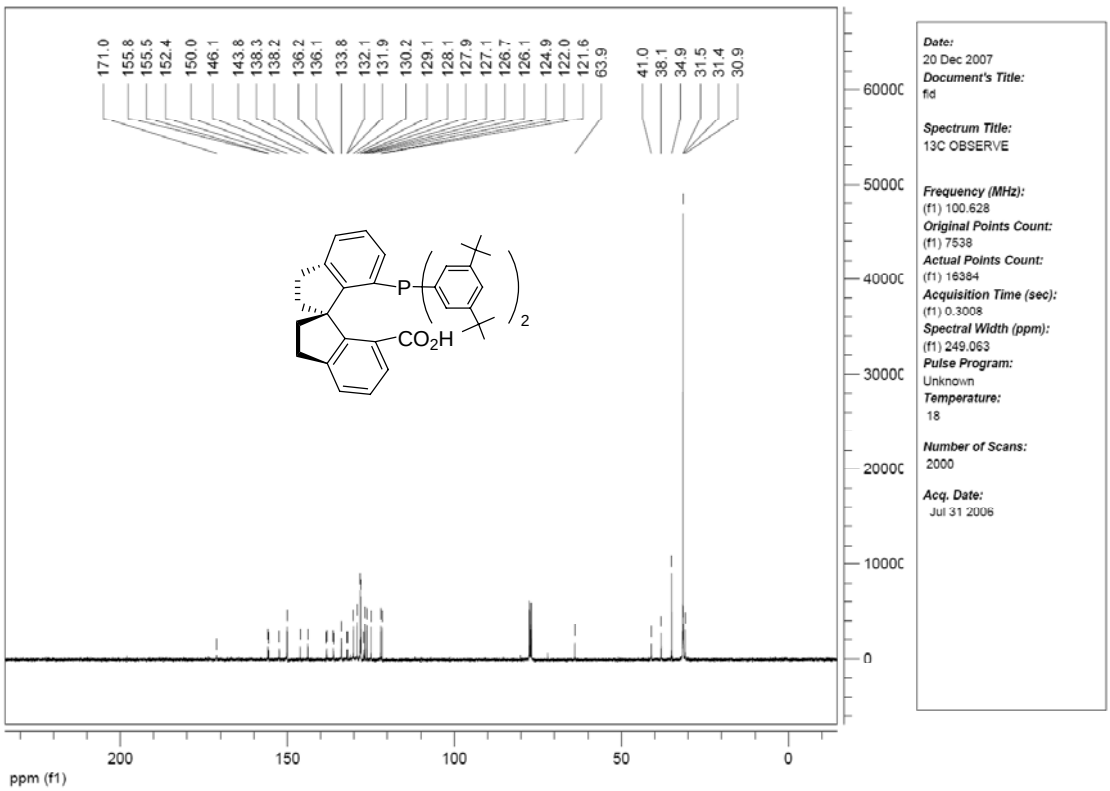
(S_a)-11


7.736
7.718
7.446
7.428
7.326
7.302
7.275
7.258
7.143
7.125
7.106
7.024
7.014
6.914
6.895
6.803
6.784
3.118
3.096
2.990
2.967
2.874
2.838
2.638
2.612
2.584
2.558
2.283
2.269
2.259
2.240
2.164
2.142
1.246
P
CO2Me
2
1.06
0.98
3.89
2.97
1.07
1.03
1.84
17.88
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (f1)
400
300
200
100
0
Date:
22 Sep 2007
Document's Title:
fid
Spectrum Title:
STANDARD 1H OBSERVE
Frequency (MHz):
(f1) 400.148
Original Points Count:
(f1) 9603
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 1.4981
Spectral Width (ppm):
(f1) 16.020
Pulse Program:
Unknown
Temperature:
18
Number of Scans:
8
Acq. Date:
Jul 16 2006

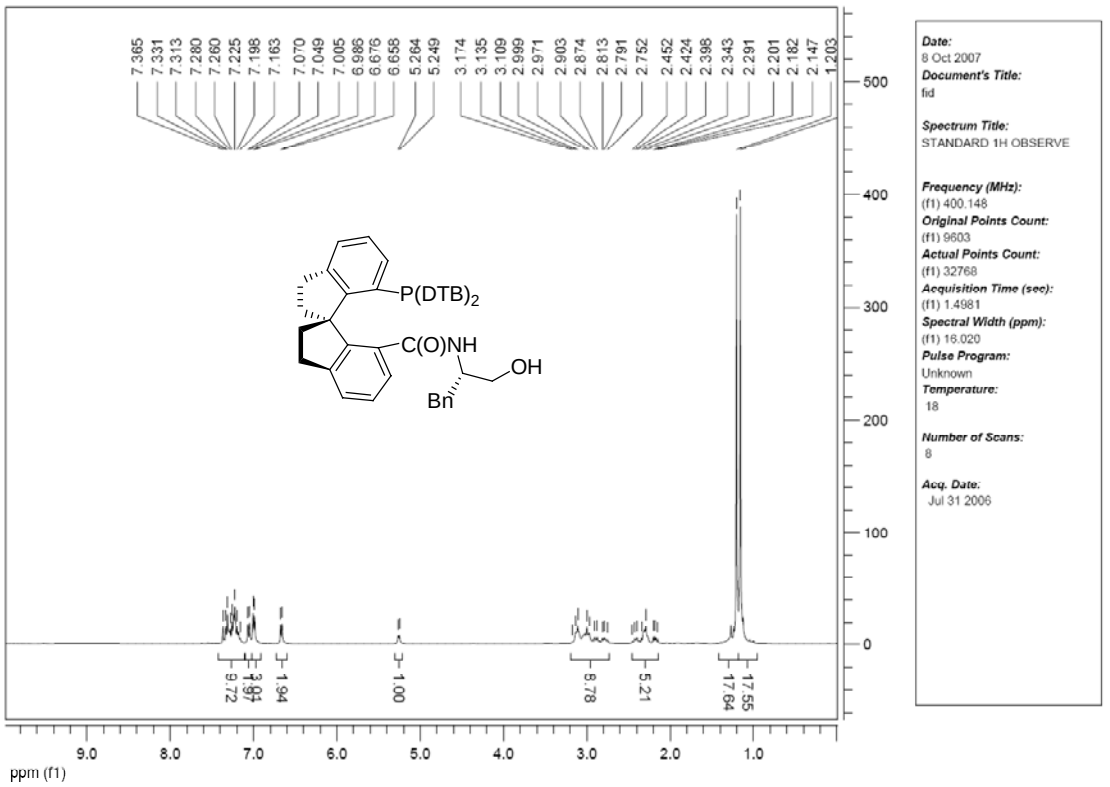

167.7
155.7
155.4
150.7
150.2
150.1
150.0
145.8
143.4
138.0
137.9
136.6
136.5
133.9
132.9
132.7
129.6
128.7
128.6
128.5
128.4
128.3
128.1
126.8
126.2
125.1
122.0
121.7
64.0
51.0
40.2
38.3
35.0
31.6
31.2
30.8
P
CO2Me
2
200
150
100
50
0
ppm (f1)
80000
70000
60000
50000
40000
30000
20000
10000
0
Date:
20 Dec 2007
Document's Title:
fid
Spectrum Title:
13C OBSERVE
Frequency (MHz):
(f1) 100.628
Original Points Count:
(f1) 7538
Actual Points Count:
(f1) 16384
Acquisition Time (sec):
(f1) 0.3008
Spectral Width (ppm):
(f1) 249.063
Pulse Program:
Unknown
Temperature:
18
Number of Scans:
2000
Acq. Date:
Jul 16 2006

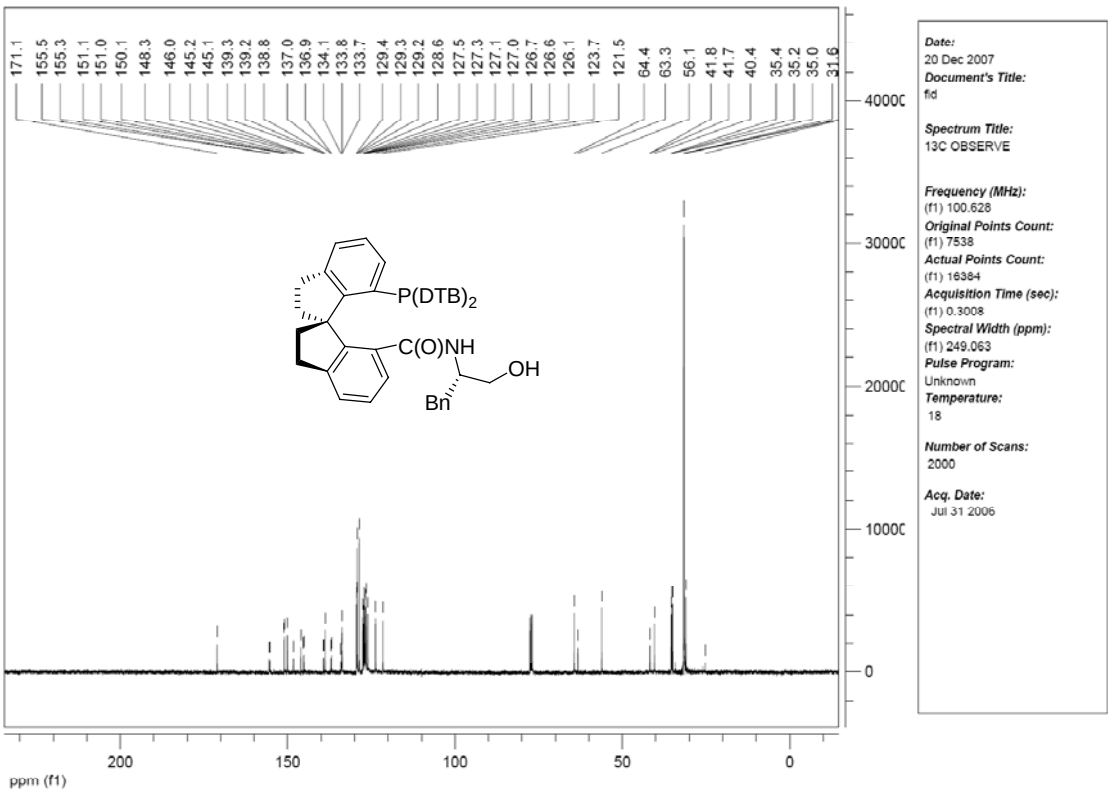
(S_a)-12


7.564
7.545
7.440
7.422
7.257
7.242
7.222
7.204
7.191
7.065
7.047
7.028
6.879
6.868
6.861
6.850
6.786
6.782
6.766
6.762
6.723
6.719
6.704
6.700
3.123
3.104
3.081
3.033
3.018
2.995
2.960
2.898
2.532
2.506
2.477
2.452
2.369
2.342
2.315
2.289
2.231
P
CO2H
2
1000
500
0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (f1)
Date:
22 Sep 2007
Document's Title:
fid
Spectrum Title:
STANDARD 1H OBSERVE
Frequency (MHz):
(f1) 400.135
Original Points Count:
(f1) 9603
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 1.4981
Spectral Width (ppm):
(f1) 16.020
Pulse Program:
Unknown
Temperature:
18
Number of Scans:
8
Acq. Date:
May 25 2007

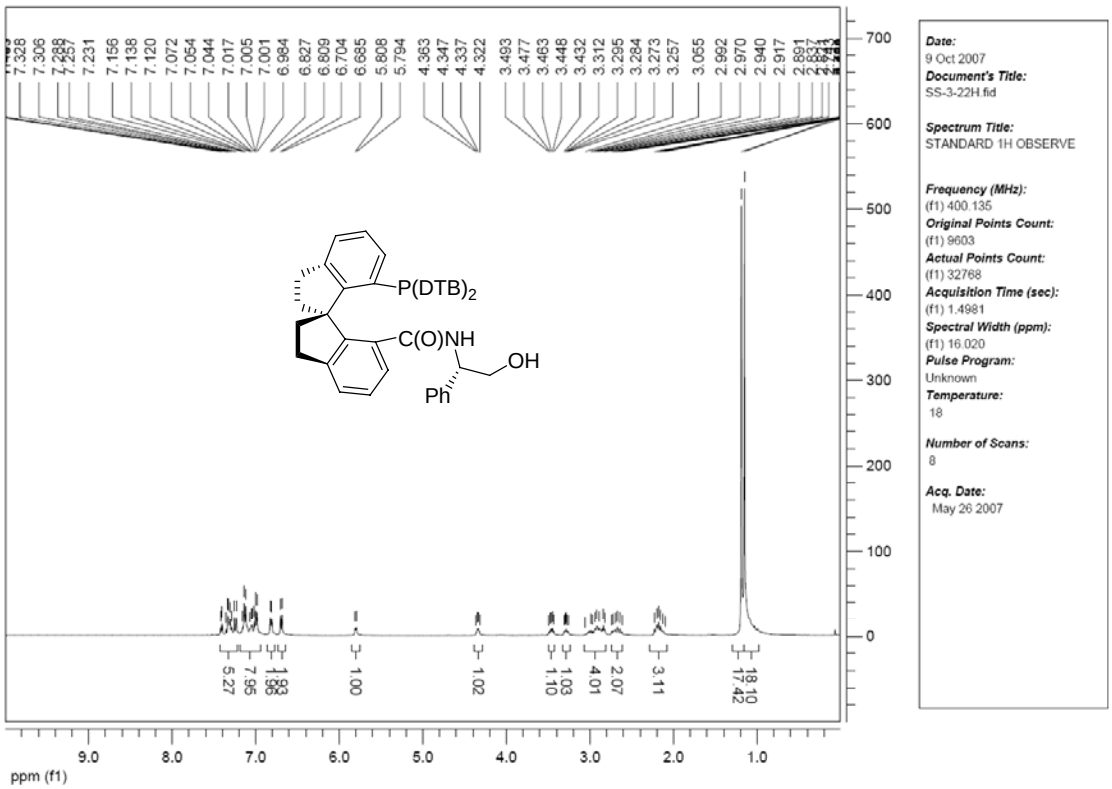

171.0
155.8
155.5
152.4
150.0
146.1
143.8
138.3
138.2
136.2
136.1
133.8
132.1
131.9
130.2
129.1
128.1
127.9
127.1
126.7
126.1
124.9
122.0
121.6
63.9
41.0
38.1
34.9
31.5
31.4
30.9
P
CO2H
2
60000
50000
40000
30000
20000
10000
0
200
150
100
50
0
ppm (f1)
Date:
20 Dec 2007
Document's Title:
fid
Spectrum Title:
13C OBSERVE
Frequency (MHz):
(f1) 100.628
Original Points Count:
(f1) 7538
Actual Points Count:
(f1) 16384
Acquisition Time (sec):
(f1) 0.3008
Spectral Width (ppm):
(f1) 249.063
Pulse Program:
Unknown
Temperature:
18
Number of Scans:
2000
Acq. Date:
Jul 31 2008

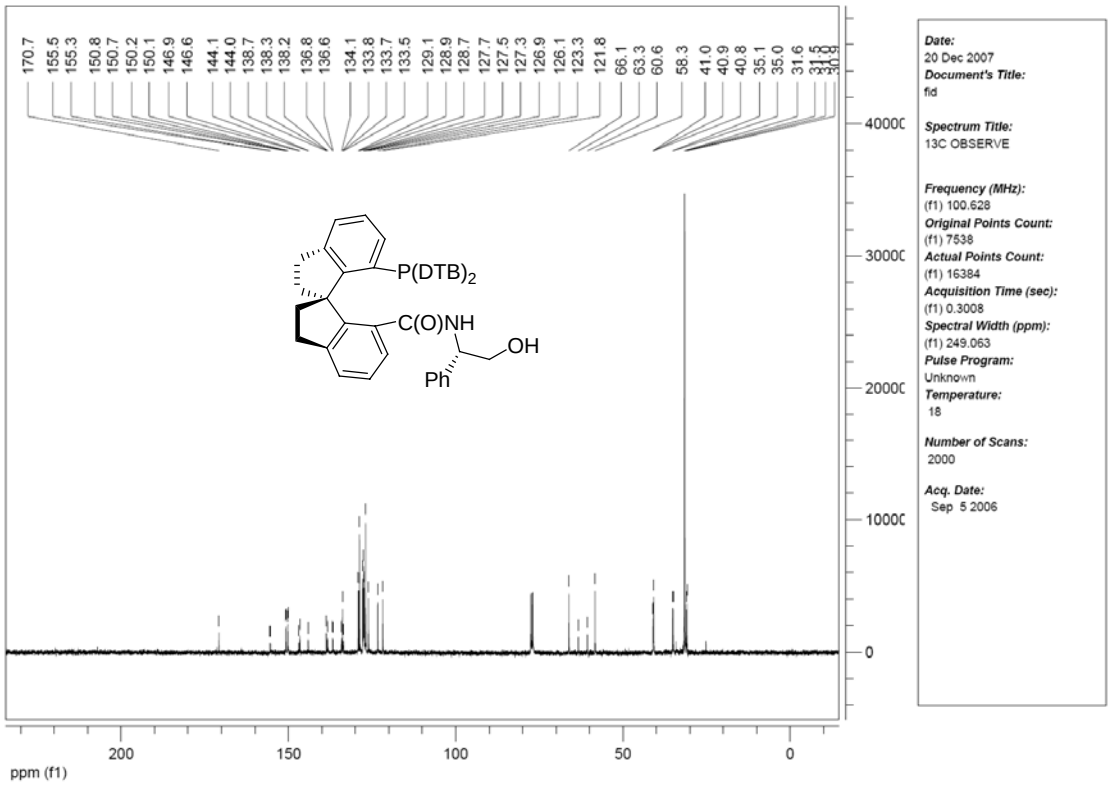
(S_a,*S*)-13a


7.365
7.331
7.313
7.280
7.260
7.225
7.198
7.163
7.070
7.049
7.005
6.986
6.676
6.658
5.264
5.249
3.174
3.135
3.109
2.999
2.971
2.903
2.874
2.813
2.791
2.752
2.452
2.424
2.398
2.343
2.291
2.201
2.182
2.147
1.203
P(DTB)2
C(O)NH
OH
Bn
9.72
3.91
3.87
1.64
1.00
8.78
5.21
17.64
17.55
ppm (f1)
Date:
8 Oct 2007
Document's Title:
fid
Spectrum Title:
STANDARD 1H OBSERVE
Frequency (MHz):
(f1) 400.148
Original Points Count:
(f1) 9603
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 1.4981
Spectral Width (ppm):
(f1) 16.020
Pulse Program:
Unknown
Temperature:
18
Number of Scans:
8
Acq. Date:
Jul 31 2006

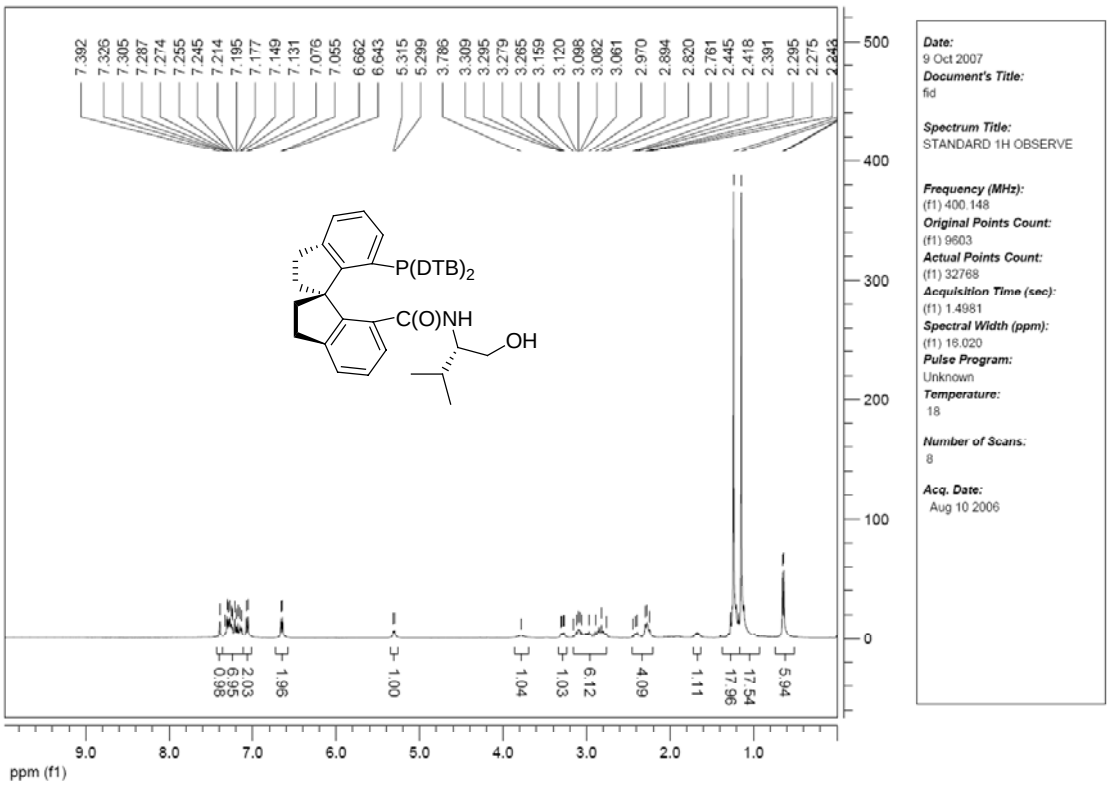

171.1
155.5
155.3
151.1
151.0
150.1
148.3
146.0
145.2
145.1
139.3
139.2
138.8
137.0
136.9
134.1
133.8
133.7
129.4
129.3
129.2
128.6
127.5
127.3
127.1
127.0
126.7
126.6
126.1
123.7
121.5
64.4
63.3
56.1
41.8
41.7
40.4
35.4
35.2
35.0
31.6
P(DTB)2
C(O)NH
OH
Bn
ppm (f1)
Date:
20 Dec 2007
Document's Title:
fid
Spectrum Title:
13C OBSERVE
Frequency (MHz):
(f1) 100.628
Original Points Count:
(f1) 7538
Actual Points Count:
(f1) 16384
Acquisition Time (sec):
(f1) 0.3008
Spectral Width (ppm):
(f1) 249.063
Pulse Program:
Unknown
Temperature:
18
Number of Scans:
2000
Acq. Date:
Jul 31 2006

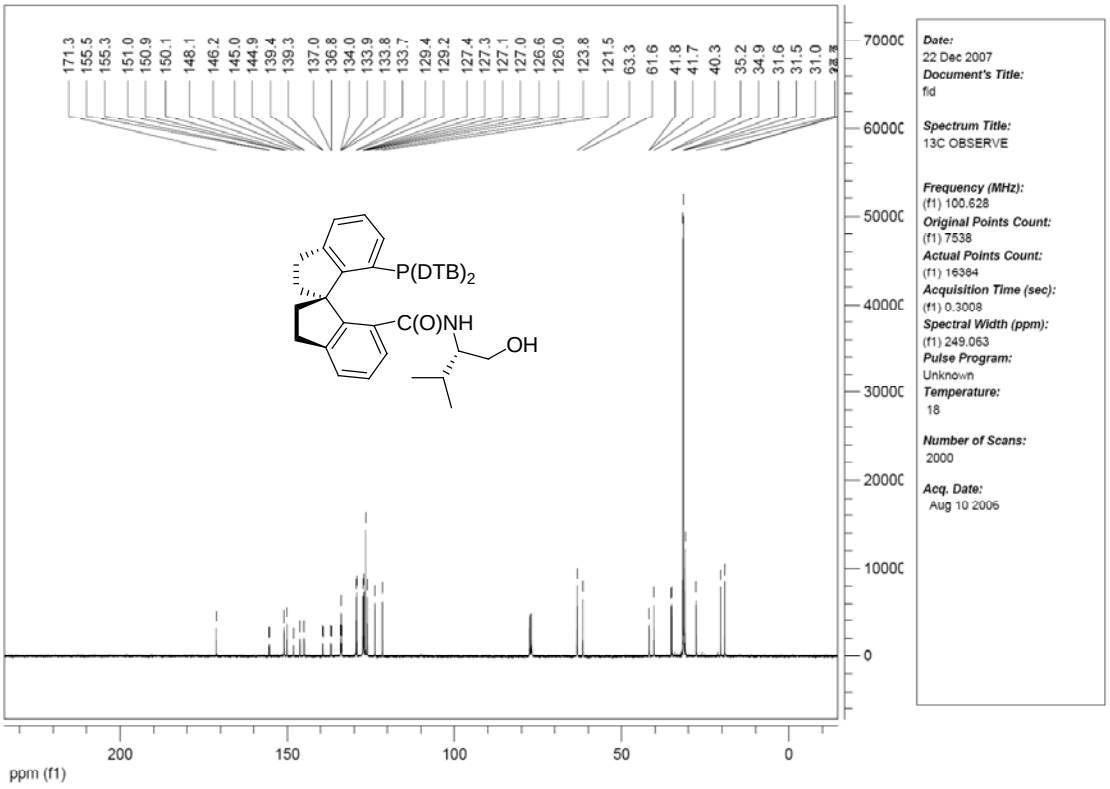
(S_a,*S*)-13b


P(DTB)2
C(O)NH
OH
Ph
ppm (f1)
Date:
9 Oct 2007
Document's Title:
SS-3-22H.fid
Spectrum Title:
STANDARD 1H OBSERVE
Frequency (MHz):
(f1) 400.135
Original Points Count:
(f1) 9603
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 1.4981
Spectral Width (ppm):
(f1) 16.020
Pulse Program:
Unknown
Temperature:
18
Number of Scans:
8
Acq. Date:
May 26 2007

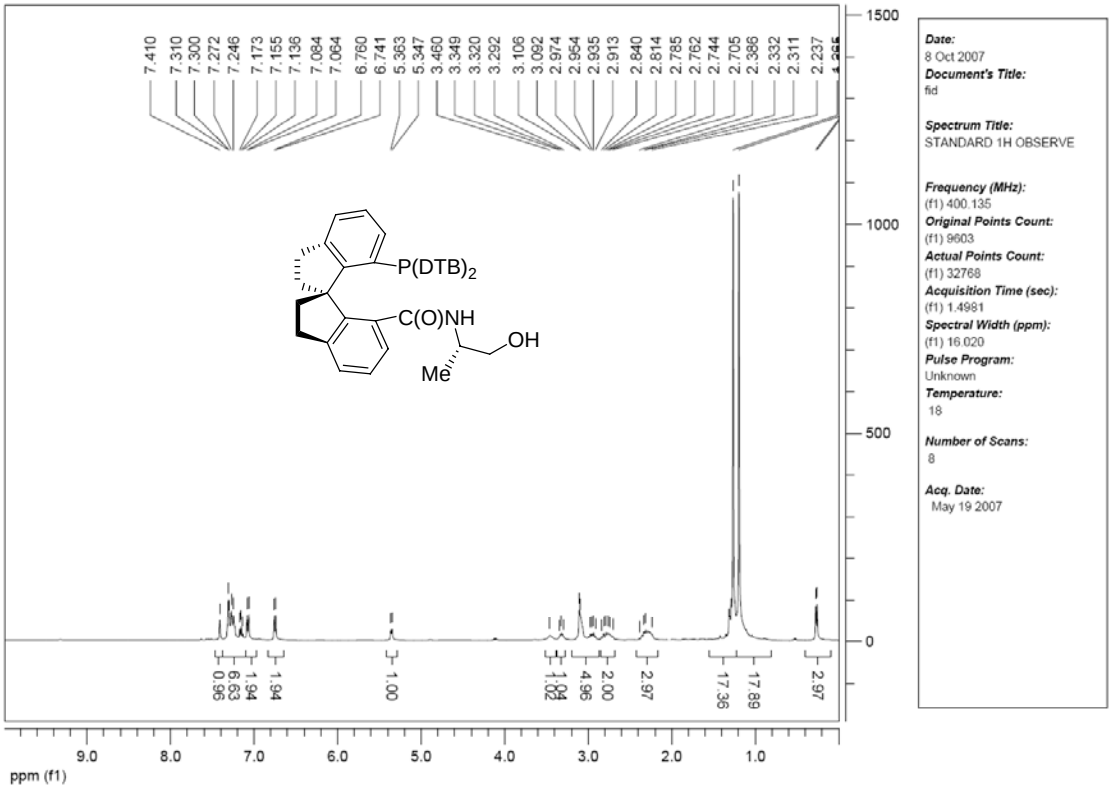

P(DTB)2
C(O)NH
OH
Ph
ppm (f1)
Date:
20 Dec 2007
Document's Title:
fid
Spectrum Title:
13C OBSERVE
Frequency (MHz):
(f1) 100.628
Original Points Count:
(f1) 7538
Actual Points Count:
(f1) 16384
Acquisition Time (sec):
(f1) 0.3008
Spectral Width (ppm):
(f1) 249.063
Pulse Program:
Unknown
Temperature:
18
Number of Scans:
2000
Acq. Date:
Sep 5 2006

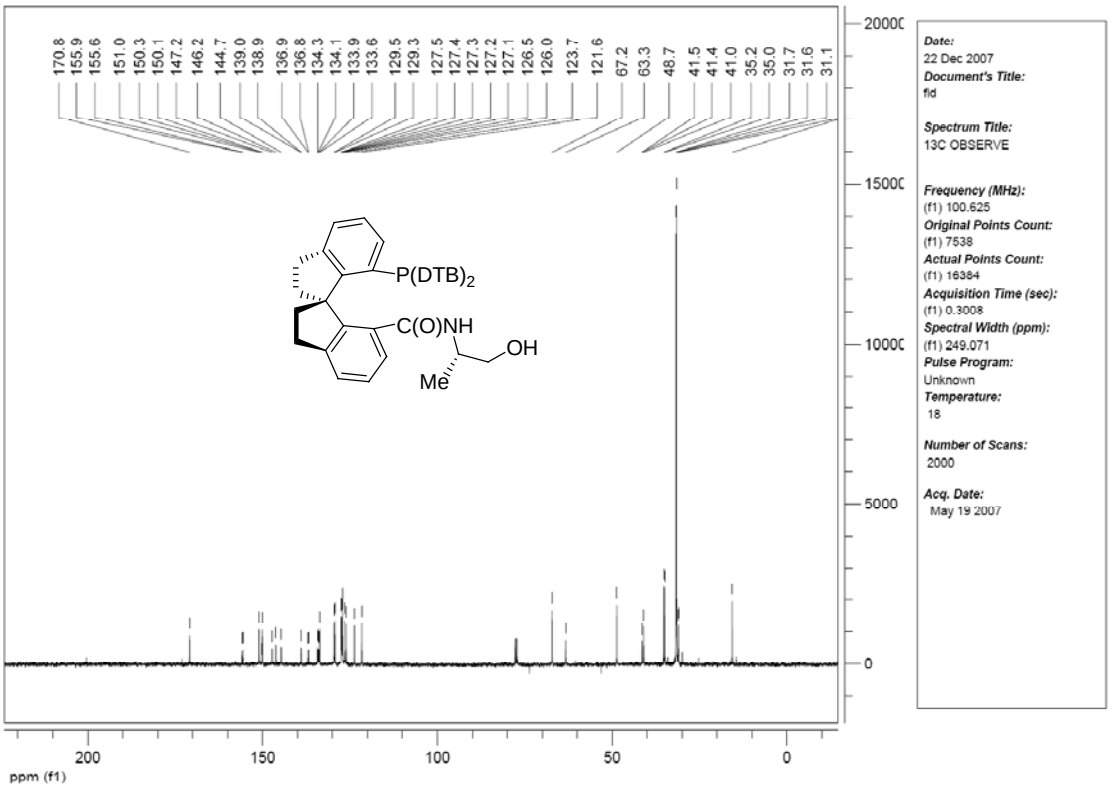
(S_a,*S*)-13c


7.392
7.326
7.305
7.287
7.274
7.255
7.245
7.214
7.195
7.177
7.149
7.131
7.076
7.055
6.662
6.643
5.315
5.299
3.786
3.309
3.295
3.279
3.265
3.159
3.120
3.098
3.082
3.061
2.970
2.894
2.820
2.761
2.445
2.418
2.391
2.295
2.275
P(DTB)2
C(O)NH
OH
0.98
0.95
2.03
1.96
1.00
1.04
1.03
6.12
4.09
1.11
17.96
17.54
5.94
ppm (f1)
Date:
9 Oct 2007
Document's Title:
fid
Spectrum Title:
STANDARD 1H OBSERVE
Frequency (MHz):
(f1) 400.148
Original Points Count:
(f1) 9603
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 1.4981
Spectral Width (ppm):
(f1) 16.020
Pulse Program:
Unknown
Temperature:
18
Number of Scans:
8
Acq. Date:
Aug 10 2006

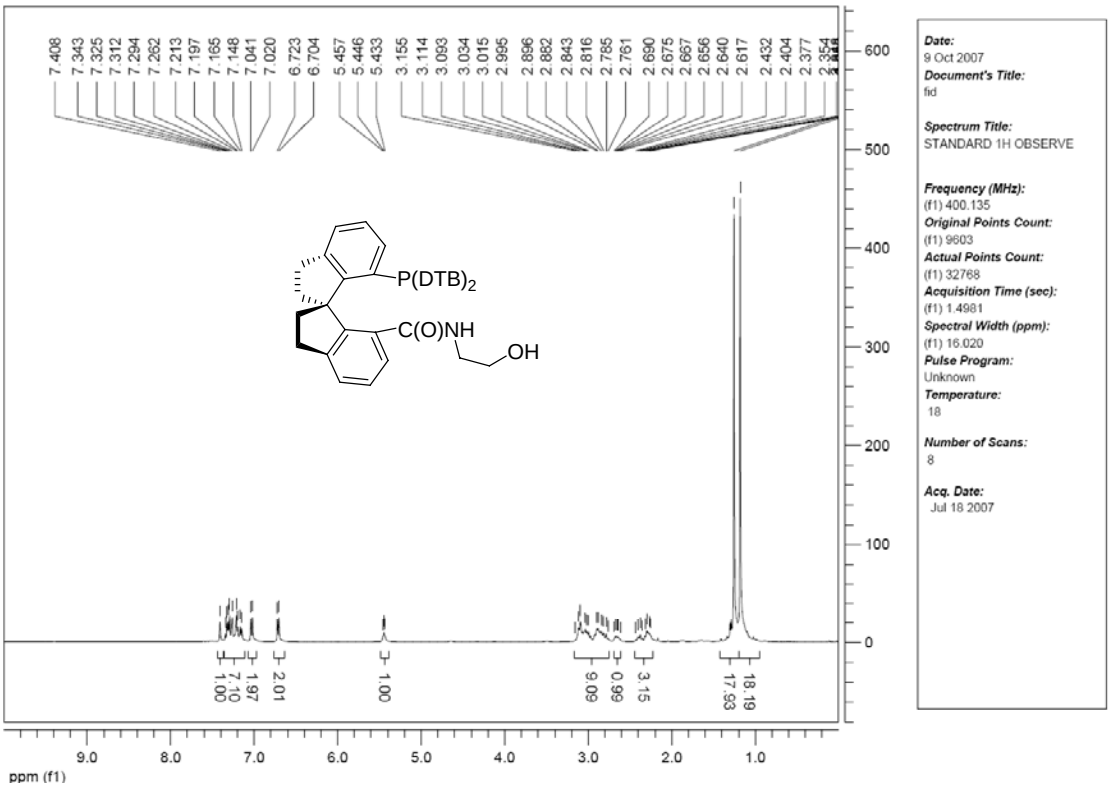

171.3
155.5
155.3
151.0
150.9
150.1
148.1
146.2
145.0
144.9
139.4
139.3
137.0
136.8
134.0
133.9
133.8
133.7
129.4
129.2
127.4
127.3
127.1
127.0
126.6
126.0
123.8
121.5
63.3
61.6
41.8
41.7
40.3
35.2
34.9
31.6
31.5
31.0
P(DTB)2
C(O)NH
OH
ppm (f1)
Date:
22 Dec 2007
Document's Title:
fid
Spectrum Title:
13C OBSERVE
Frequency (MHz):
(f1) 100.628
Original Points Count:
(f1) 7538
Actual Points Count:
(f1) 16384
Acquisition Time (sec):
(f1) 0.3008
Spectral Width (ppm):
(f1) 249.063
Pulse Program:
Unknown
Temperature:
18
Number of Scans:
2000
Acq. Date:
Aug 10 2006

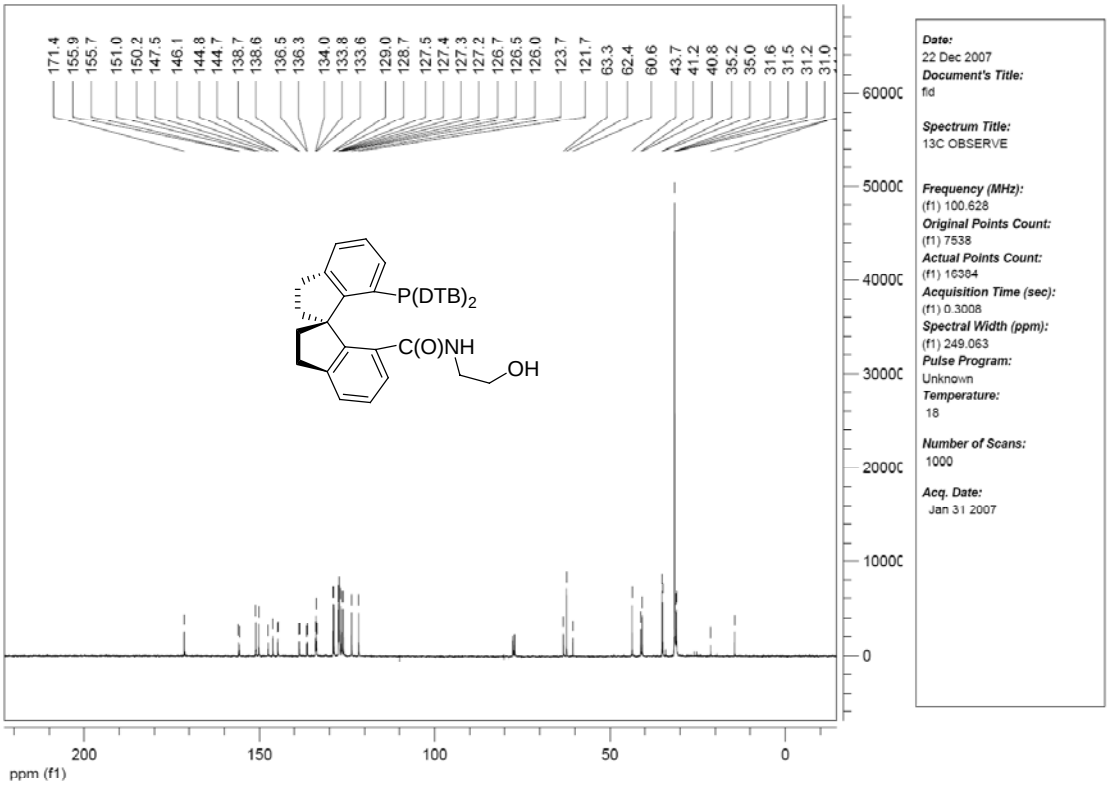
(S_a,*S*)-13d


7.410
7.310
7.300
7.272
7.246
7.173
7.155
7.136
7.084
7.064
6.760
6.741
5.363
5.347
3.460
3.349
3.320
3.292
3.106
3.092
2.974
2.964
2.935
2.913
2.840
2.814
2.785
2.762
2.744
2.705
2.386
2.332
2.311
2.237
P(DTB)2
C(O)NH
OH
Me
0.96
6.63
1.94
1.94
1.00
2.00
4.96
2.00
2.97
17.36
17.89
2.97
ppm (f1)
Date:
8 Oct 2007
Document's Title:
fid
Spectrum Title:
STANDARD 1H OBSERVE
Frequency (MHz):
(f1) 400.135
Original Points Count:
(f1) 9603
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 1.4981
Spectral Width (ppm):
(f1) 16.020
Pulse Program:
Unknown
Temperature:
18
Number of Scans:
8
Acq. Date:
May 19 2007

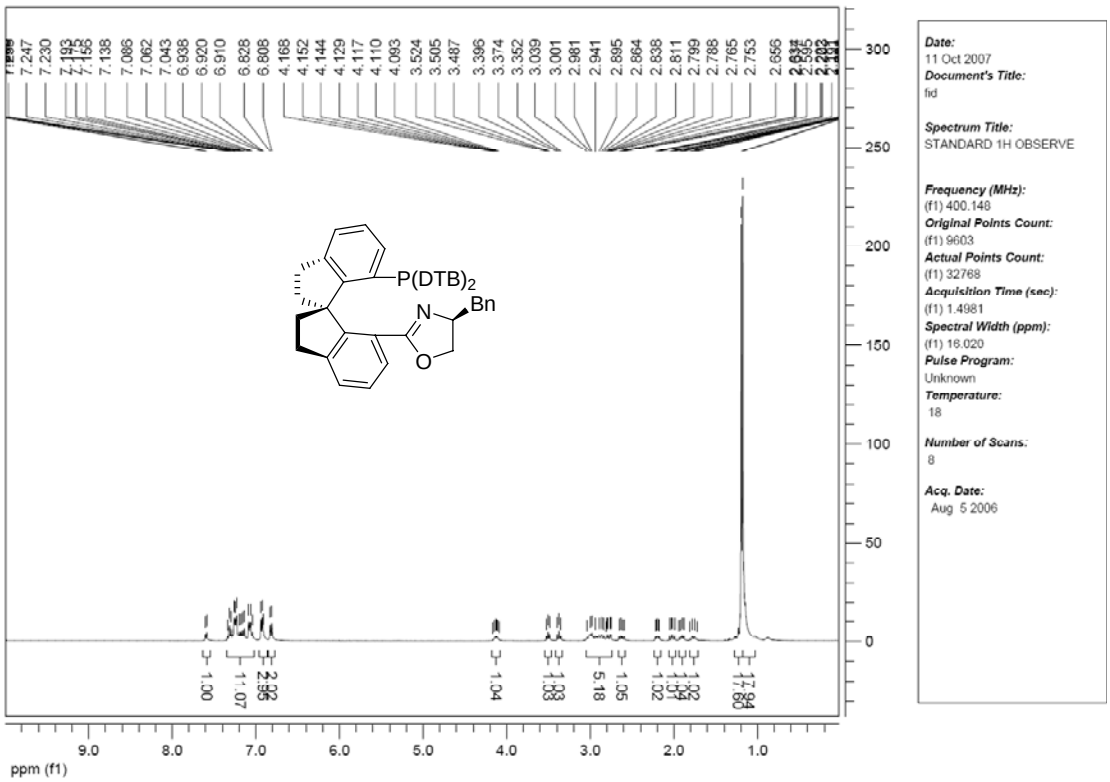

170.8
155.9
155.6
151.0
150.3
147.2
146.2
144.7
139.0
138.9
136.9
136.8
134.3
133.9
133.6
129.5
129.3
127.5
127.4
127.3
127.2
126.5
126.0
123.7
121.6
67.2
63.3
48.7
41.5
41.4
41.0
35.2
35.0
31.7
31.6
31.1
P(DTB)2
C(O)NH
OH
Me
ppm (f1)
Date:
22 Dec 2007
Document's Title:
fid
Spectrum Title:
13C OBSERVE
Frequency (MHz):
(f1) 100.625
Original Points Count:
(f1) 7538
Actual Points Count:
(f1) 16384
Acquisition Time (sec):
(f1) 0.3008
Spectral Width (ppm):
(f1) 249.071
Pulse Program:
Unknown
Temperature:
18
Number of Scans:
2000
Acq. Date:
May 19 2007

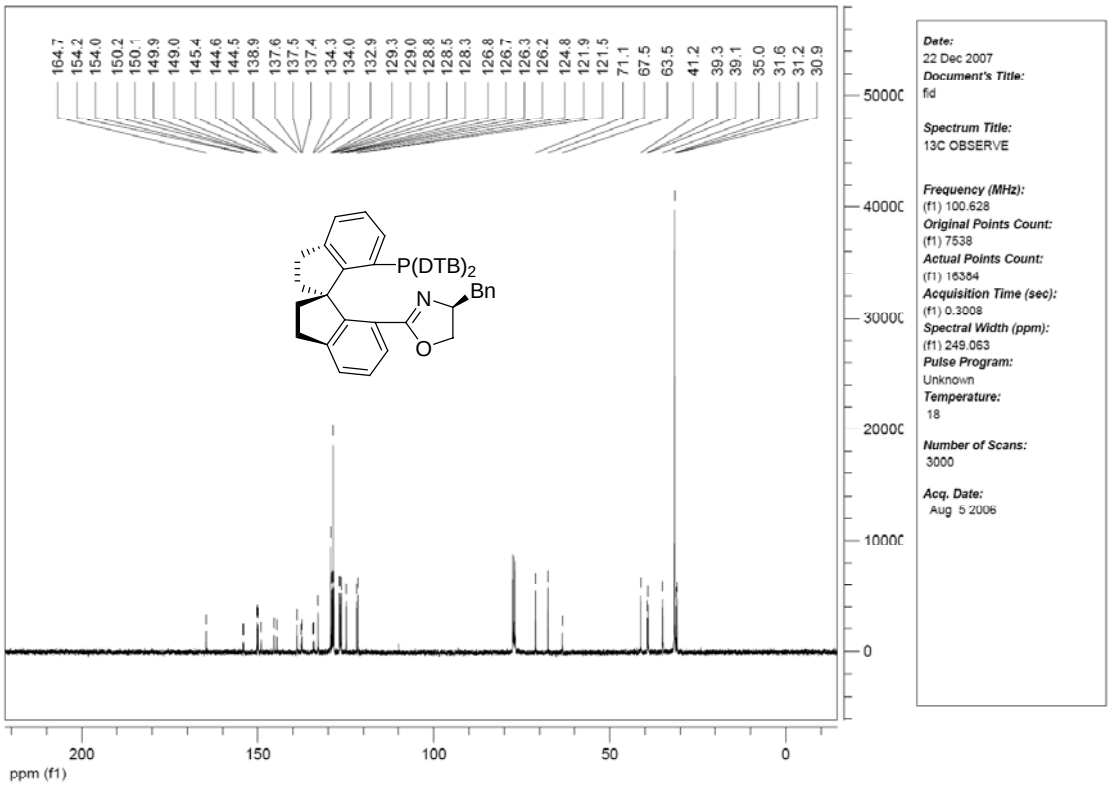
(S_a)-13e


7.408
7.343
7.325
7.312
7.294
7.262
7.213
7.197
7.165
7.148
7.041
7.020
6.723
6.704
5.457
5.446
5.433
3.155
3.114
3.093
3.034
3.015
2.995
2.896
2.882
2.843
2.816
2.785
2.761
2.690
2.675
2.667
2.656
2.640
2.617
2.432
2.404
2.377
P(DTB)2
C(O)NH
OH
1.00
1.10
1.97
2.01
1.00
9.09
0.99
3.15
17.93
18.19
ppm (f1)
Date:
9 Oct 2007
Document's Title:
fid
Spectrum Title:
STANDARD 1H OBSERVE
Frequency (MHz):
(f1) 400.135
Original Points Count:
(f1) 9603
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 1.4981
Spectral Width (ppm):
(f1) 16.020
Pulse Program:
Unknown
Temperature:
18
Number of Scans:
8
Acq. Date:
Jul 18 2007

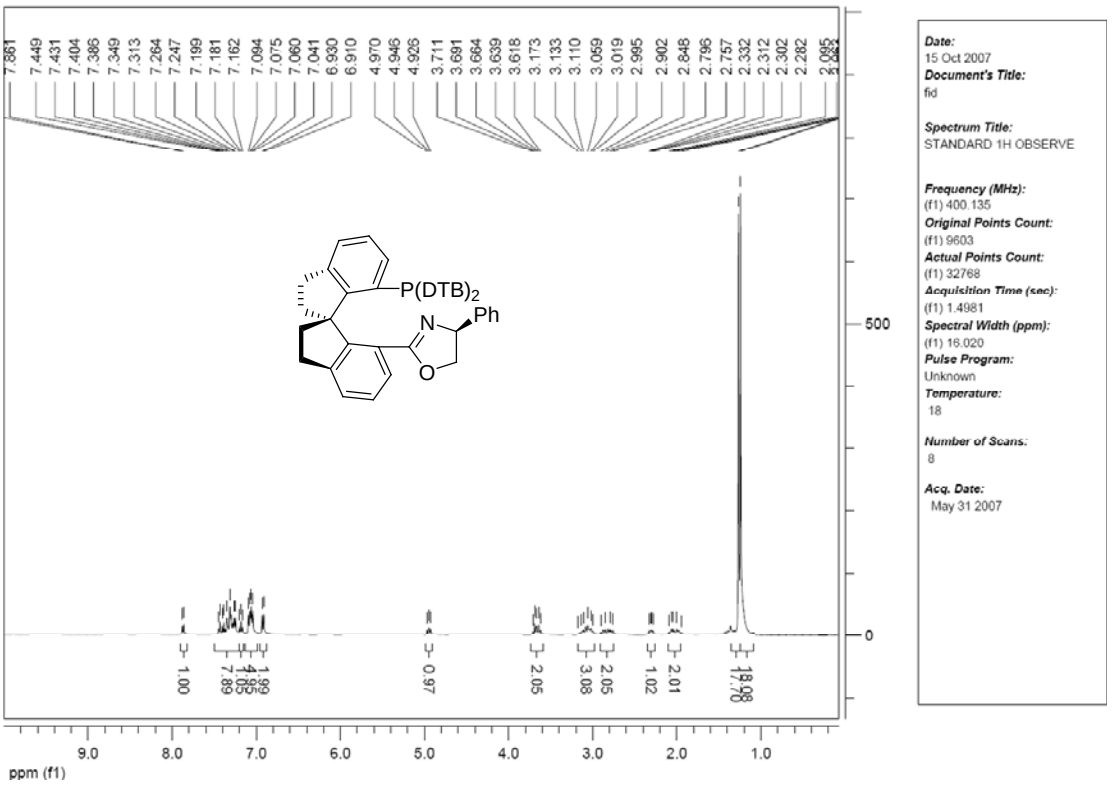

171.4
155.9
155.7
151.0
150.2
147.5
146.1
144.8
144.7
138.7
138.6
136.5
136.3
134.0
133.8
133.6
129.0
128.7
127.5
127.4
127.3
127.2
126.7
126.5
126.0
123.7
121.7
63.3
62.4
60.6
43.7
41.2
40.8
35.2
35.0
31.6
31.5
31.2
P(DTB)2
C(O)NH
OH
ppm (f1)
Date:
22 Dec 2007
Document's Title:
fid
Spectrum Title:
13C OBSERVE
Frequency (MHz):
(f1) 100.628
Original Points Count:
(f1) 7538
Actual Points Count:
(f1) 16384
Acquisition Time (sec):
(f1) 0.3008
Spectral Width (ppm):
(f1) 249.063
Pulse Program:
Unknown
Temperature:
18
Number of Scans:
1000
Acq. Date:
Jan 31 2007

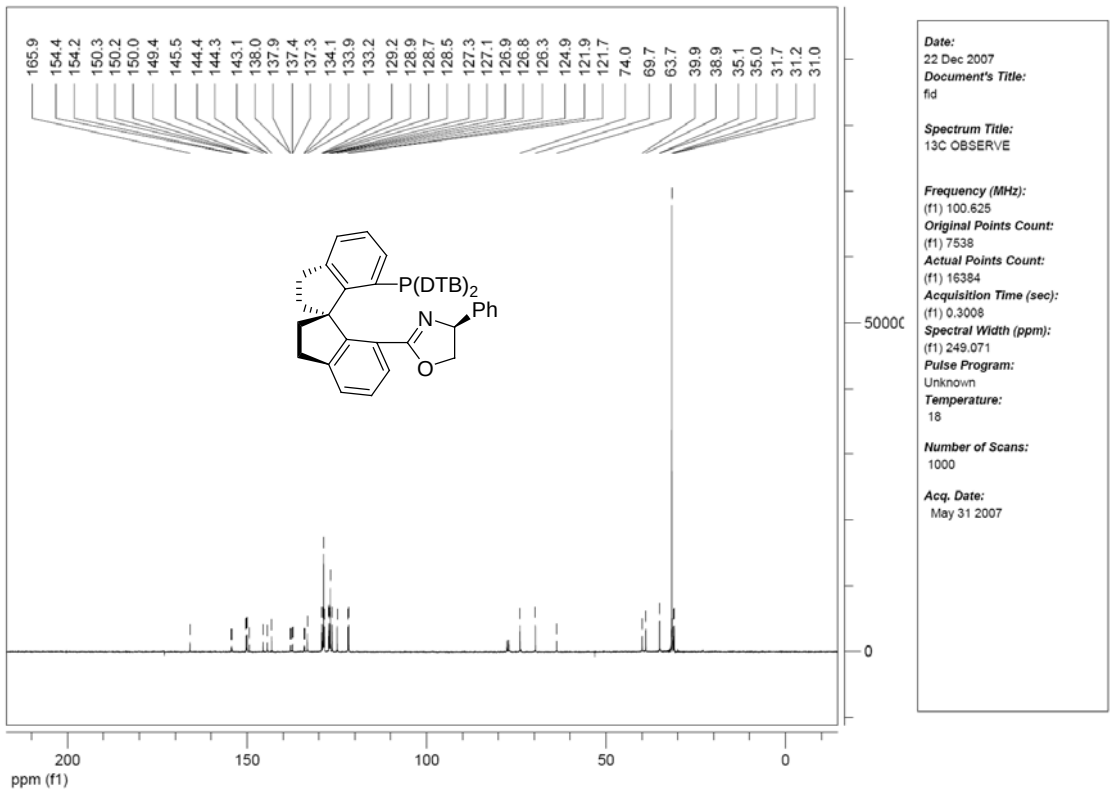
(S_a,*S*)-14a


P(DTB)2
N
Bn
O
Date:
11 Oct 2007
Document's Title:
fid
Spectrum Title:
STANDARD 1H OBSERVE
Frequency (MHz):
(f1) 400.148
Original Points Count:
(f1) 9603
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 1.4981
Spectral Width (ppm):
(f1) 16.020
Pulse Program:
Unknown
Temperature:
18
Number of Scans:
8
Acq. Date:
Aug 5 2006
ppm (f1)

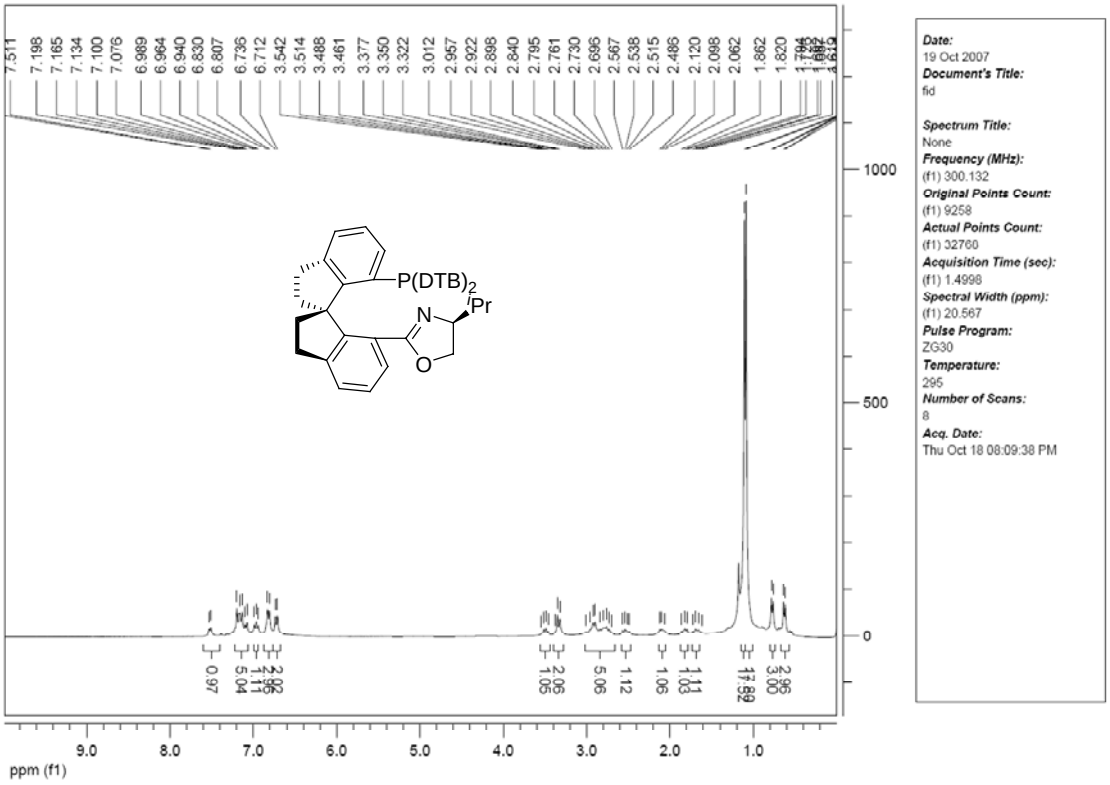

P(DTB)2
N
Bn
O
Date:
22 Dec 2007
Document's Title:
fid
Spectrum Title:
13C OBSERVE
Frequency (MHz):
(f1) 100.628
Original Points Count:
(f1) 7538
Actual Points Count:
(f1) 16384
Acquisition Time (sec):
(f1) 0.3008
Spectral Width (ppm):
(f1) 249.063
Pulse Program:
Unknown
Temperature:
18
Number of Scans:
3000
Acq. Date:
Aug 5 2006
ppm (f1)

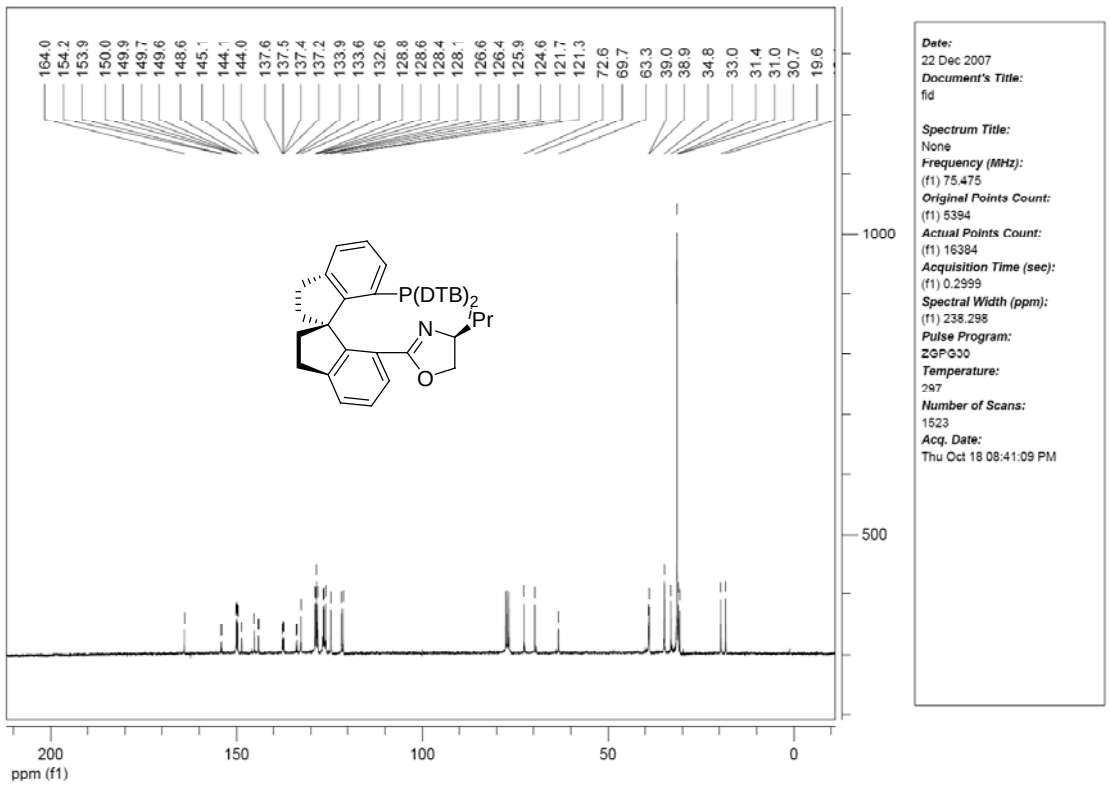
(S_a,*S*)-14b


7.861
7.449
7.431
7.404
7.386
7.349
7.313
7.264
7.247
7.199
7.181
7.162
7.094
7.075
7.060
7.041
6.930
6.910
4.970
4.946
4.926
3.711
3.691
3.664
3.639
3.618
3.173
3.133
3.110
3.069
3.019
2.995
2.902
2.848
2.796
2.757
2.332
2.312
2.302
2.282
P(DTB)2
Ph
N
O
500
0
1.00
7.89
4.45
3.85
1.99
0.97
2.05
3.08
2.05
1.02
2.01
19.08
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (f1)
Date:
15 Oct 2007
Document's Title:
fid
Spectrum Title:
STANDARD 1H OBSERVE
Frequency (MHz):
(f1) 400.135
Original Points Count:
(f1) 9603
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 1.4981
Spectral Width (ppm):
(f1) 16.020
Pulse Program:
Unknown
Temperature:
18
Number of Scans:
8
Acq. Date:
May 31 2007

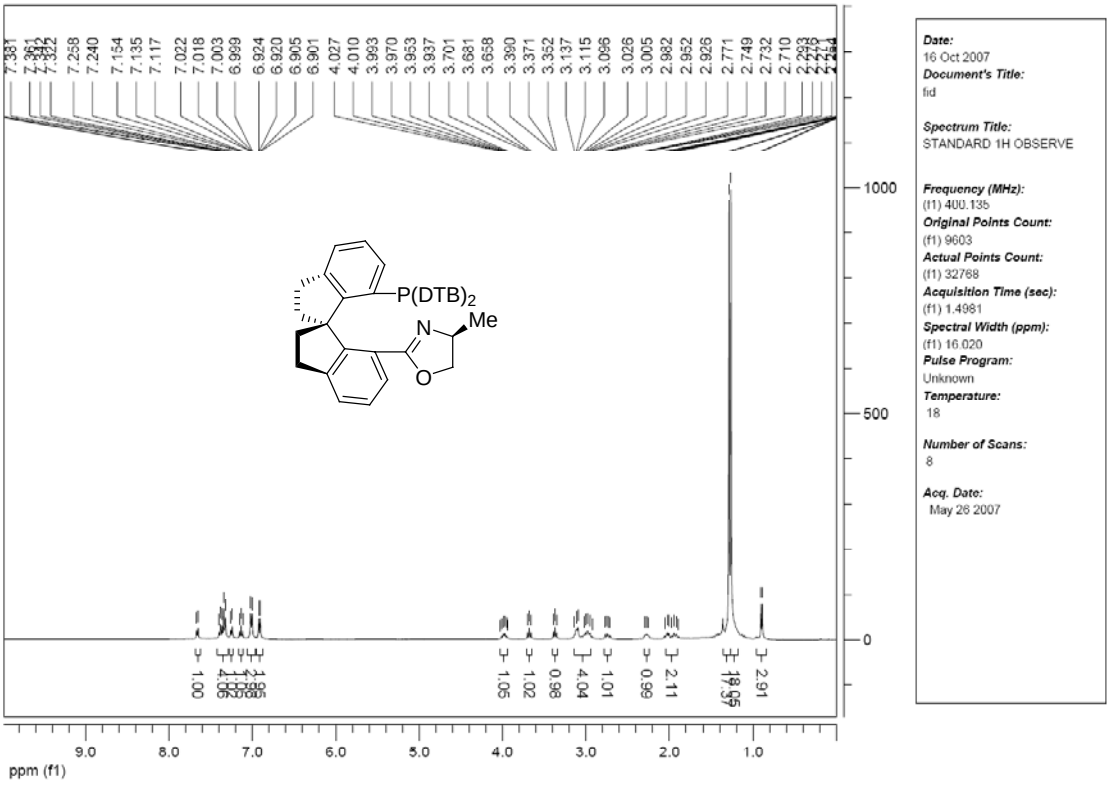

165.9
154.4
154.2
150.3
150.2
150.0
149.4
145.5
144.4
144.3
143.1
138.0
137.9
137.4
137.3
134.1
133.9
133.2
129.2
128.9
128.7
128.5
127.3
127.1
126.9
126.8
126.3
124.9
121.9
121.7
74.0
69.7
63.7
39.9
38.9
35.1
35.0
31.7
31.2
31.0
P(DTB)2
Ph
N
O
50000
0
200
150
100
50
0
ppm (f1)
Date:
22 Dec 2007
Document's Title:
fid
Spectrum Title:
13C OBSERVE
Frequency (MHz):
(f1) 100.625
Original Points Count:
(f1) 7538
Actual Points Count:
(f1) 16384
Acquisition Time (sec):
(f1) 0.3008
Spectral Width (ppm):
(f1) 249.071
Pulse Program:
Unknown
Temperature:
18
Number of Scans:
1000
Acq. Date:
May 31 2007

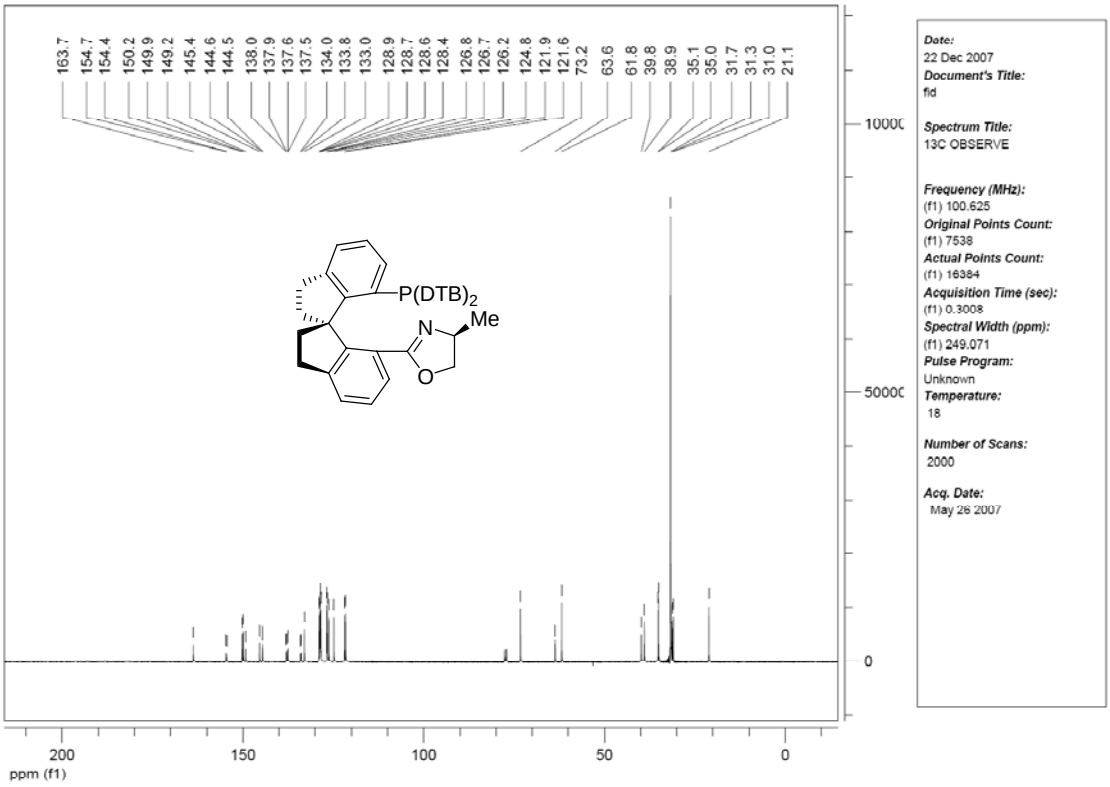
(S_a,*S*)-14c


7.511
7.198
7.165
7.134
7.100
7.076
6.989
6.964
6.940
6.830
6.807
6.736
6.712
3.542
3.514
3.488
3.461
3.377
3.350
3.322
3.012
2.957
2.922
2.896
2.840
2.795
2.761
2.730
2.696
2.567
2.538
2.515
2.486
2.120
2.098
2.062
1.862
1.820
P(DTB)2
iPr
N
O
1000
500
0
0.97
1.04
1.11
1.26
2.28
1.05
2.06
0.96
1.12
1.06
1.03
1.11
17.52
3.00
2.86
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (f1)
Date:
19 Oct 2007
Document's Title:
fid
Spectrum Title:
None
Frequency (MHz):
(f1) 300.132
Original Points Count:
(f1) 9258
Actual Points Count:
(f1) 32760
Acquisition Time (sec):
(f1) 1.4998
Spectral Width (ppm):
(f1) 20.567
Pulse Program:
ZG30
Temperature:
295
Number of Scans:
8
Acq. Date:
Thu Oct 18 08:09:38 PM

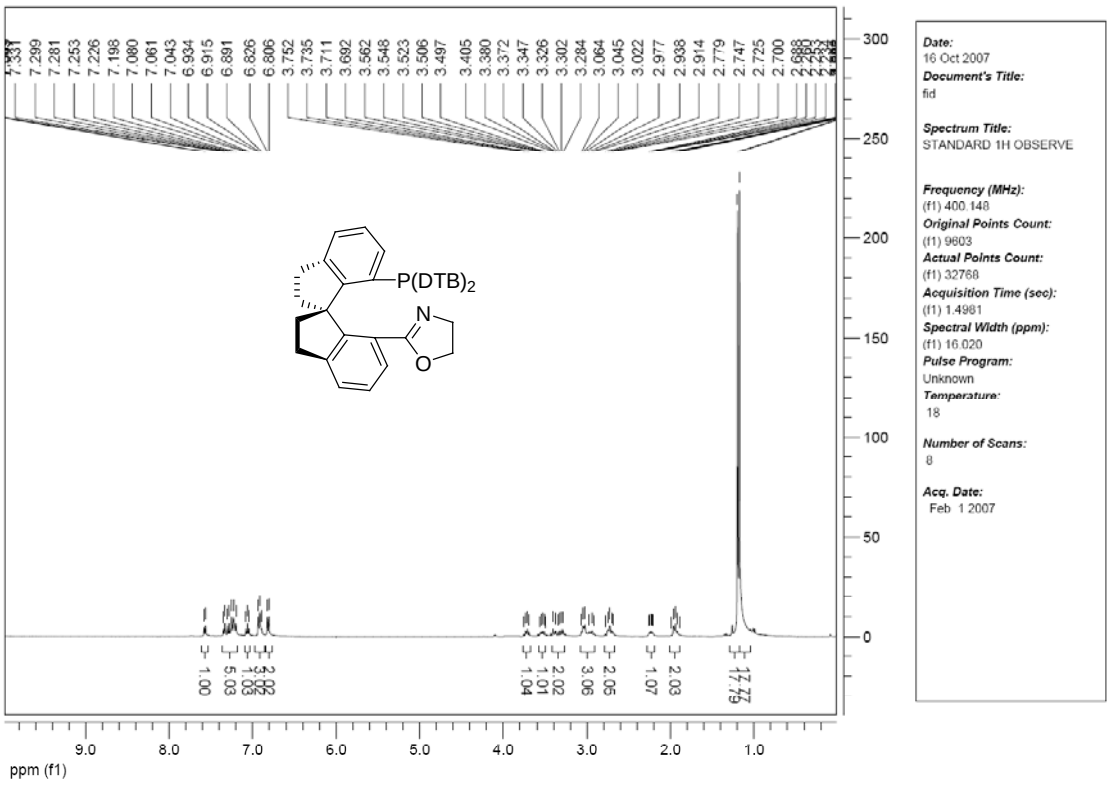

164.0
154.2
153.9
150.0
149.9
149.7
149.6
148.6
145.1
144.1
144.0
137.6
137.5
137.4
137.2
133.9
133.6
132.6
128.8
128.6
128.4
128.1
126.6
126.4
125.9
124.6
121.7
121.3
72.6
69.7
63.3
39.0
38.9
34.8
33.0
31.4
31.0
30.7
19.6
P(DTB)2
iPr
N
O
1000
500
200
150
100
50
0
ppm (f1)
Date:
22 Dec 2007
Document's Title:
fid
Spectrum Title:
None
Frequency (MHz):
(f1) 75.475
Original Points Count:
(f1) 5394
Actual Points Count:
(f1) 16384
Acquisition Time (sec):
(f1) 0.2999
Spectral Width (ppm):
(f1) 238.298
Pulse Program:
ZGPG30
Temperature:
297
Number of Scans:
1523
Acq. Date:
Thu Oct 18 08:41:09 PM

(S_a,*S*)-14d


P(DTB)2
N
Me
O
Date:
16 Oct 2007
Document's Title:
fid
Spectrum Title:
STANDARD 1H OBSERVE
Frequency (MHz):
(f1) 400.135
Original Points Count:
(f1) 9603
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 1.4981
Spectral Width (ppm):
(f1) 16.020
Pulse Program:
Unknown
Temperature:
18
Number of Scans:
8
Acq. Date:
May 26 2007
ppm (f1)


P(DTB)2
N
Me
O
Date:
22 Dec 2007
Document's Title:
fid
Spectrum Title:
13C OBSERVE
Frequency (MHz):
(f1) 100.625
Original Points Count:
(f1) 7538
Actual Points Count:
(f1) 16384
Acquisition Time (sec):
(f1) 0.3008
Spectral Width (ppm):
(f1) 249.071
Pulse Program:
Unknown
Temperature:
18
Number of Scans:
2000
Acq. Date:
May 26 2007
ppm (f1)

(S_a)-14e


P(DTB)2
N
O
Date:
16 Oct 2007
Document's Title:
fid
Spectrum Title:
STANDARD 1H OBSERVE
Frequency (MHz):
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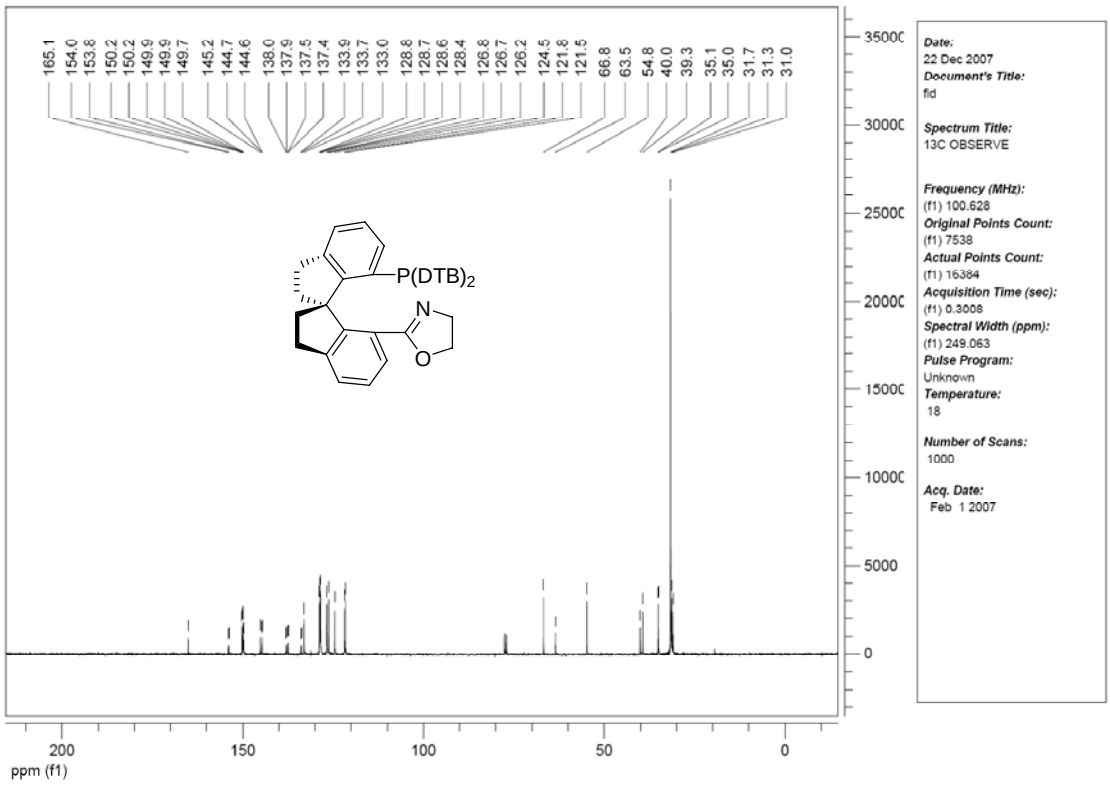
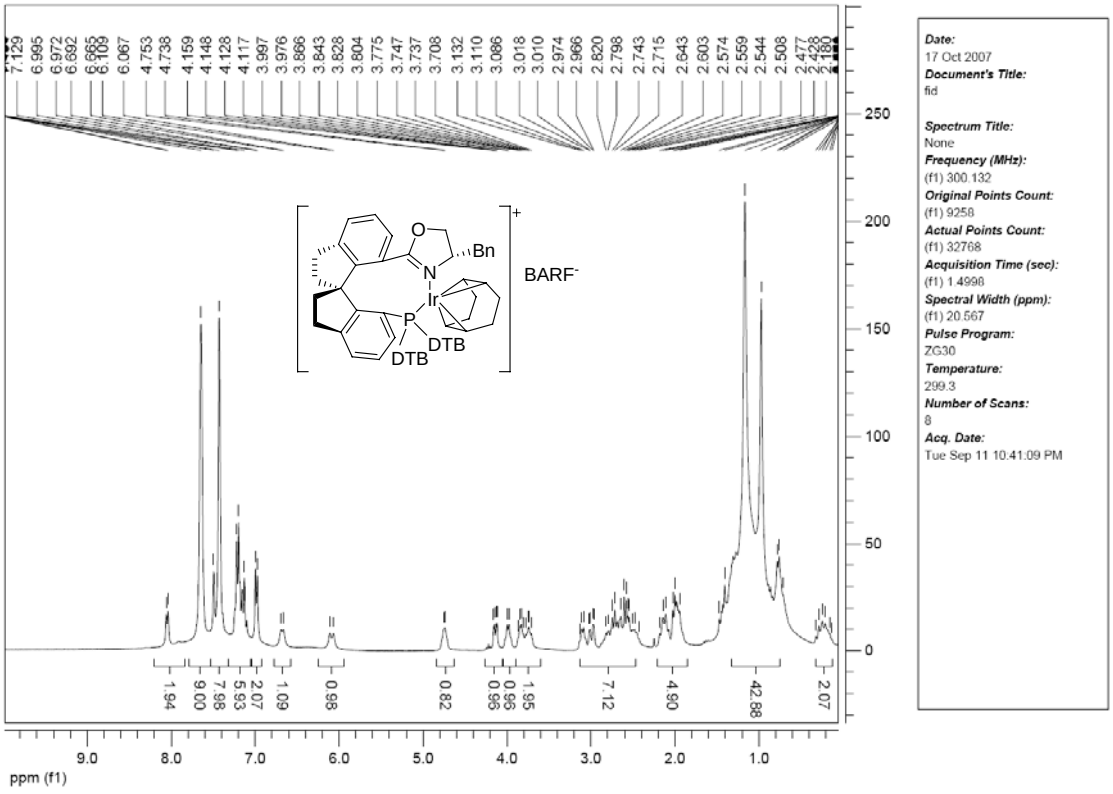
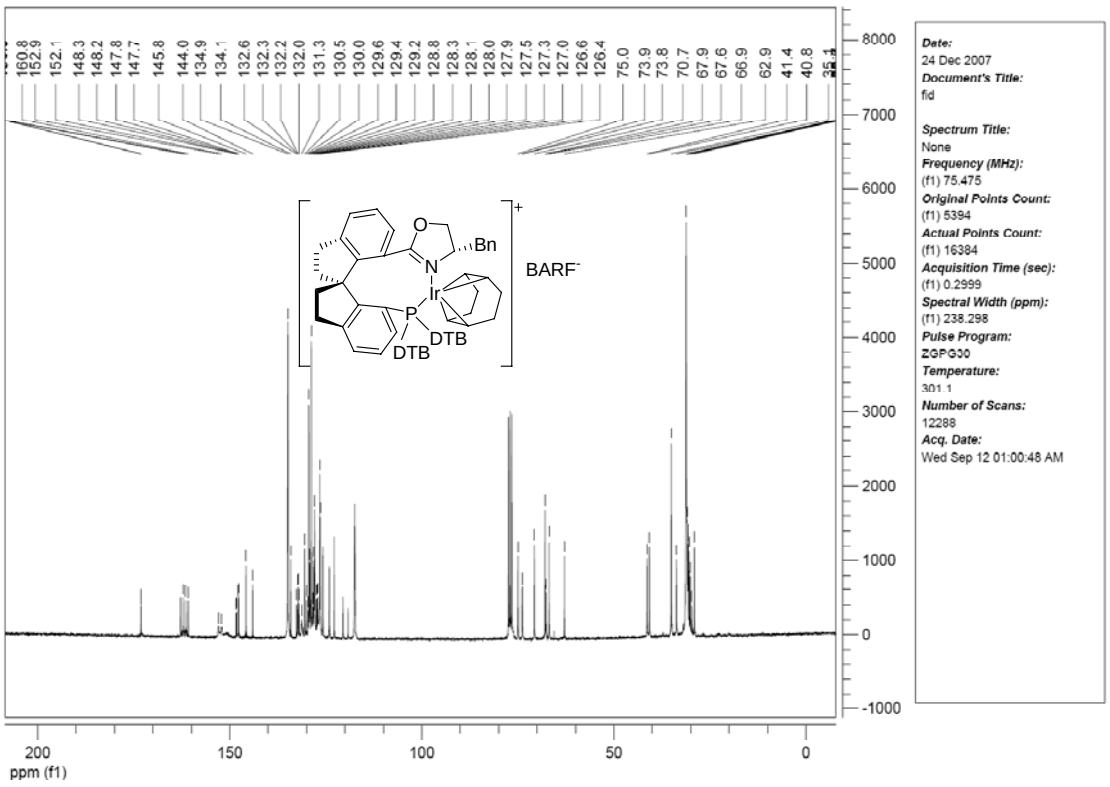
Original Points Count:
(f1) 9603
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 1.4981
Spectral Width (ppm):
(f1) 16.020
Pulse Program:
Unknown
Temperature:
18
Number of Scans:
8
Acq. Date:
Feb 1 2007
ppm (f1)


P(DTB)2
N
O
Date:
22 Dec 2007
Document's Title:
fid
Spectrum Title:
13C OBSERVE
Frequency (MHz):
(f1) 100.628
Original Points Count:
(f1) 7538
Actual Points Count:
(f1) 16384
Acquisition Time (sec):
(f1) 0.3008
Spectral Width (ppm):
(f1) 249.063
Pulse Program:
Unknown
Temperature:
18
Number of Scans:
1000
Acq. Date:
Feb 1 2007
ppm (f1)

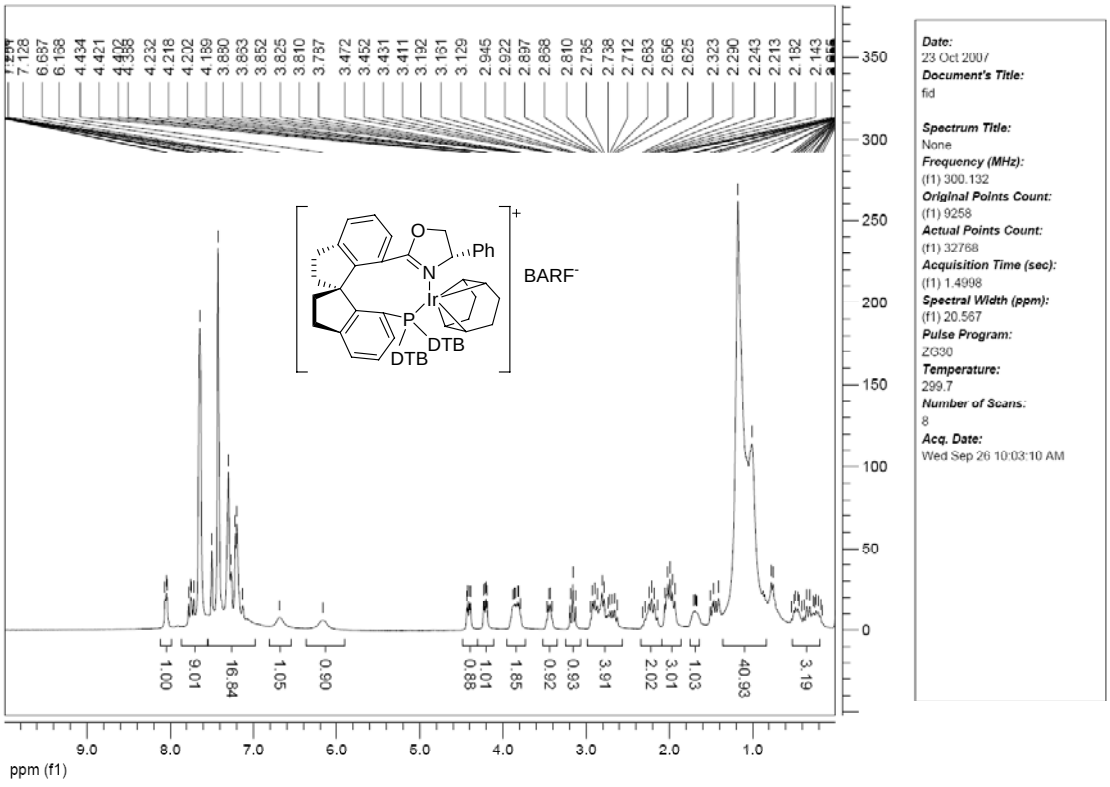
(F) NMR Spectra of Iridium Complexes

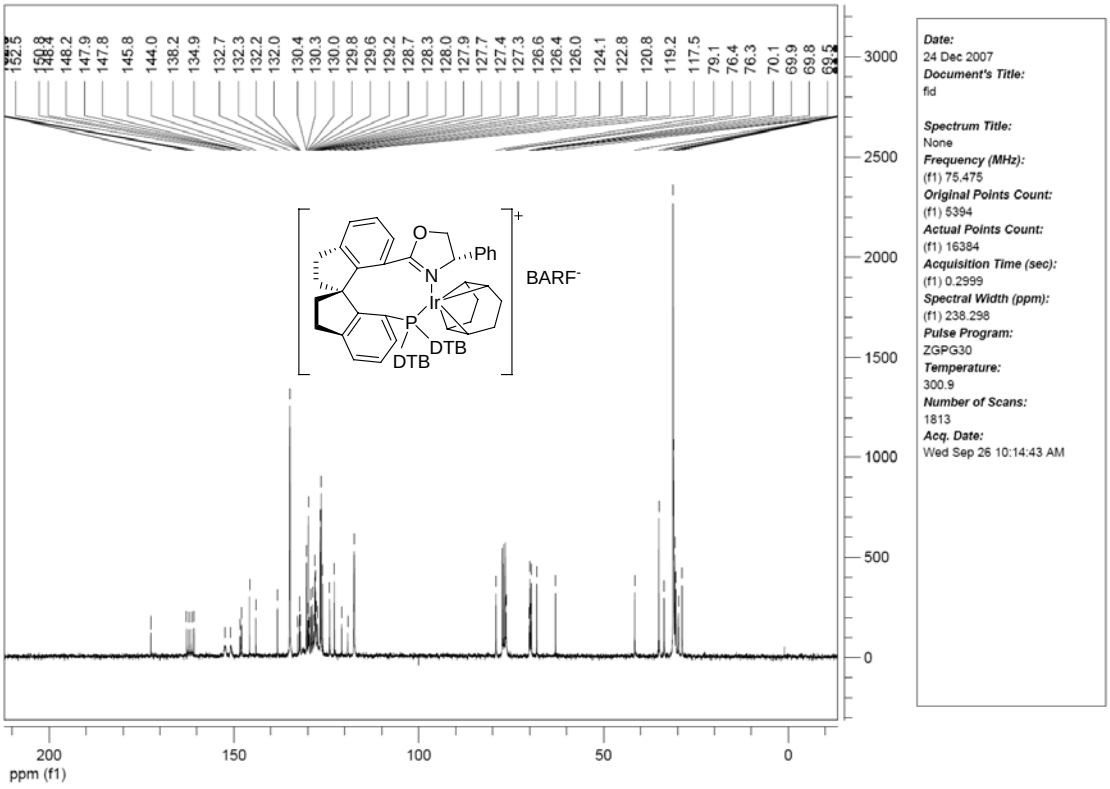
(S_a,S)-1d



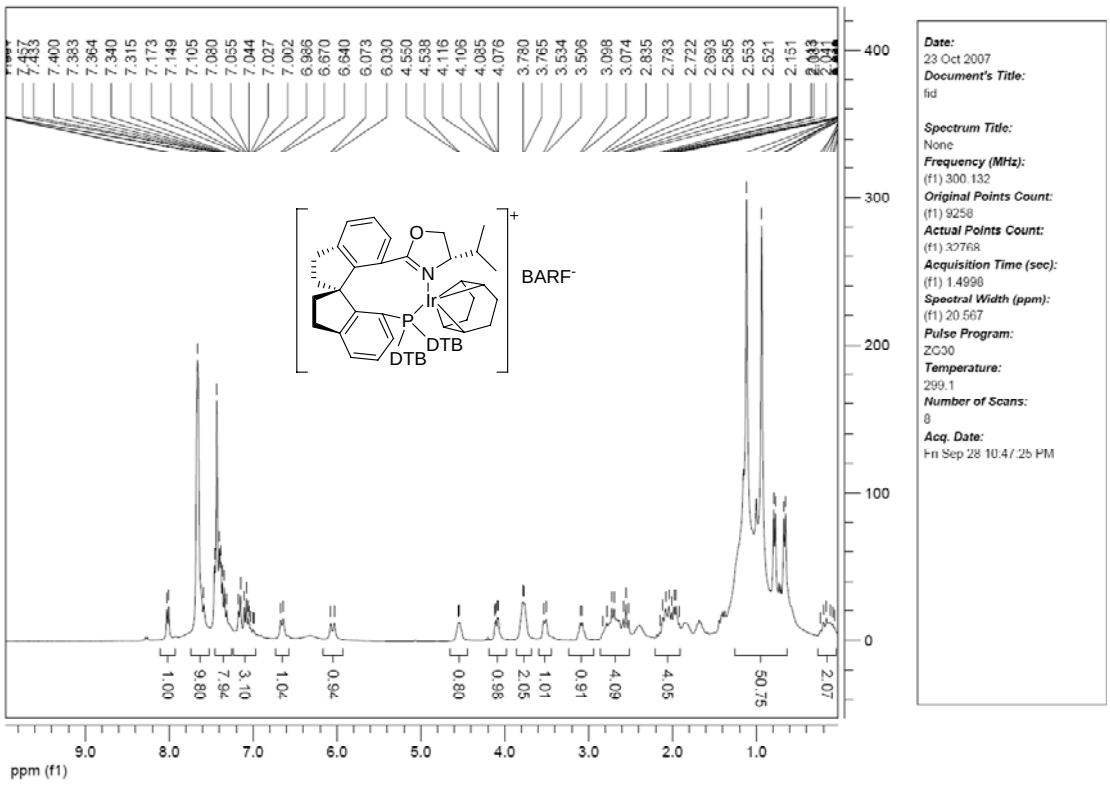


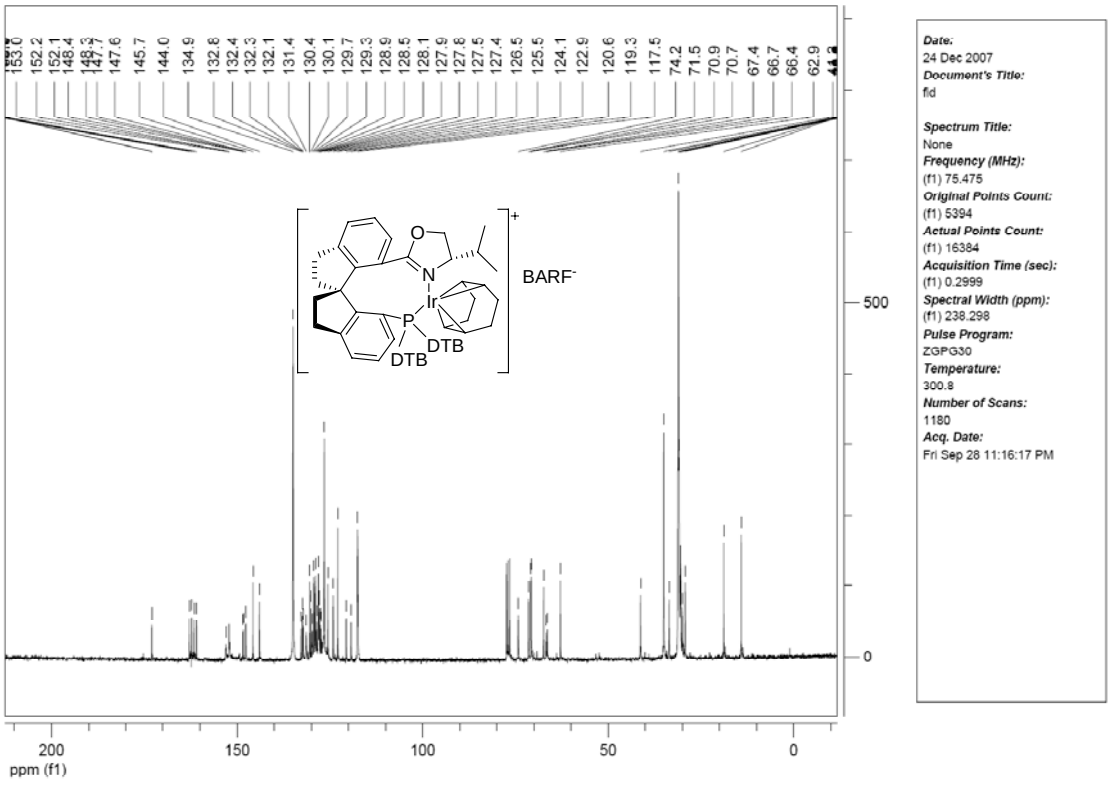
(S_a,*S*)-1e


Ph
N
O
Ir
P
DTB
DTB
BARF-
Date:
23 Oct 2007
Document's Title:
fid
Spectrum Title:
None
Frequency (MHz):
(f1) 300.132
Original Points Count:
(f1) 9258
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 1.4998
Spectral Width (ppm):
(f1) 20.567
Pulse Program:
ZG30
Temperature:
299.7
Number of Scans:
8
Acq. Date:
Wed Sep 26 10:03:10 AM
ppm (f1)

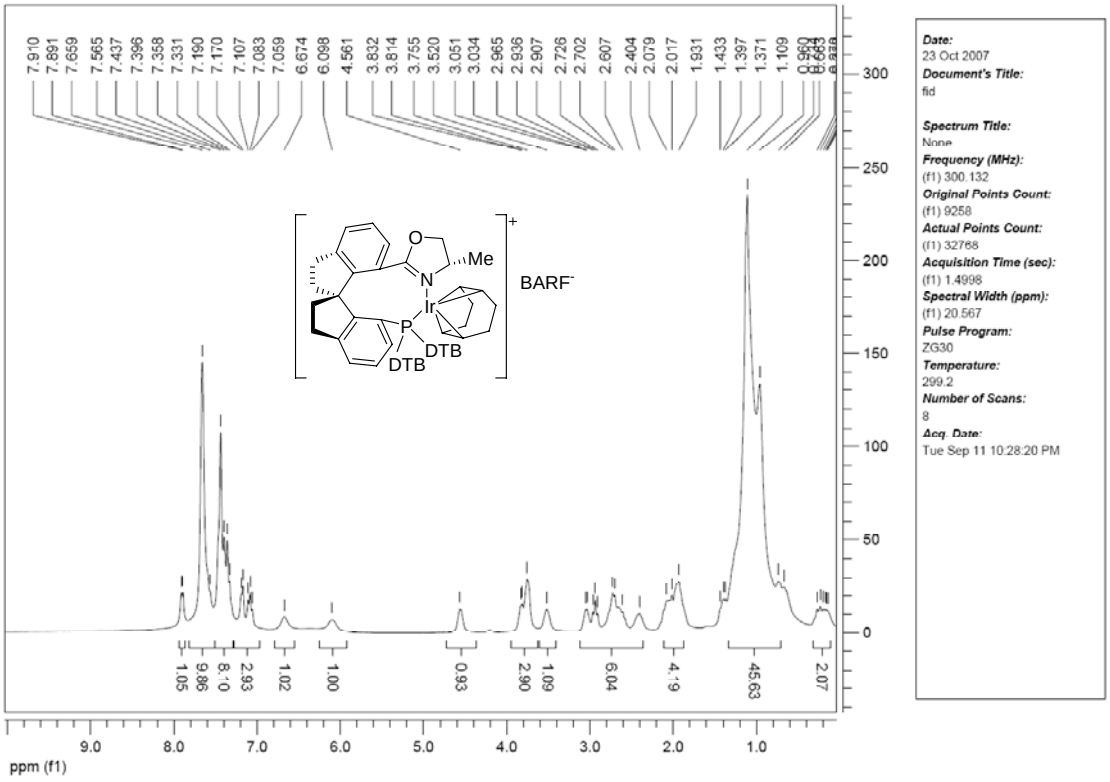

Ph
N
O
Ir
P
DTB
DTB
BARF-
Date:
24 Dec 2007
Document's Title:
fid
Spectrum Title:
None
Frequency (MHz):
(f1) 75.475
Original Points Count:
(f1) 5394
Actual Points Count:
(f1) 16384
Acquisition Time (sec):
(f1) 0.2999
Spectral Width (ppm):
(f1) 238.298
Pulse Program:
ZGPG30
Temperature:
300.9
Number of Scans:
1813
Acq. Date:
Wed Sep 26 10:14:43 AM
ppm (f1)

(S_a,*S*)-1f


BARF-
DTB
DTB
ppm (f1)
Date:
23 Oct 2007
Document's Title:
fid
Spectrum Title:
None
Frequency (MHz):
(f1) 300.132
Original Points Count:
(f1) 9258
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 1.4998
Spectral Width (ppm):
(f1) 20.567
Pulse Program:
ZG30
Temperature:
299.1
Number of Scans:
8
Acq. Date:
Fri Sep 28 10:47:25 PM


BARF-
DTB
DTB
ppm (f1)
Date:
24 Dec 2007
Document's Title:
fid
Spectrum Title:
None
Frequency (MHz):
(f1) 75.475
Original Points Count:
(f1) 5394
Actual Points Count:
(f1) 16384
Acquisition Time (sec):
(f1) 0.2999
Spectral Width (ppm):
(f1) 238.298
Pulse Program:
ZGPG30
Temperature:
300.8
Number of Scans:
1180
Acq. Date:
Fri Sep 28 11:16:17 PM

(S_a,*S*)-1g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7.659
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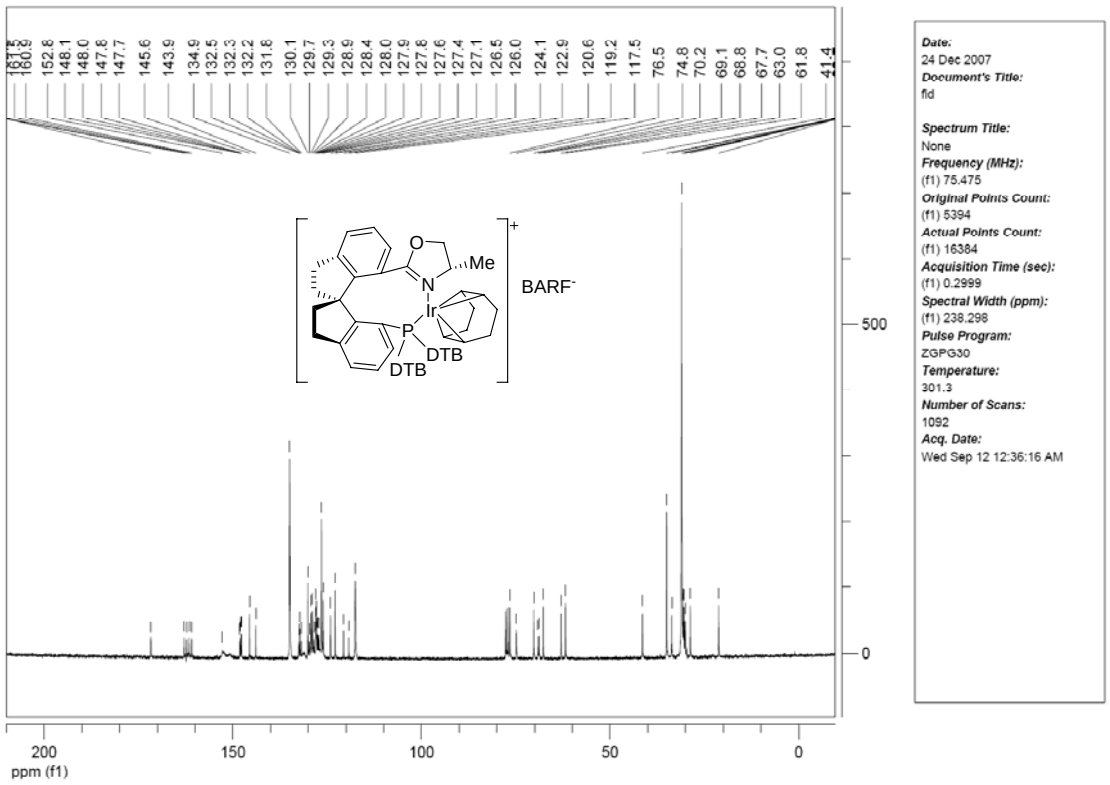
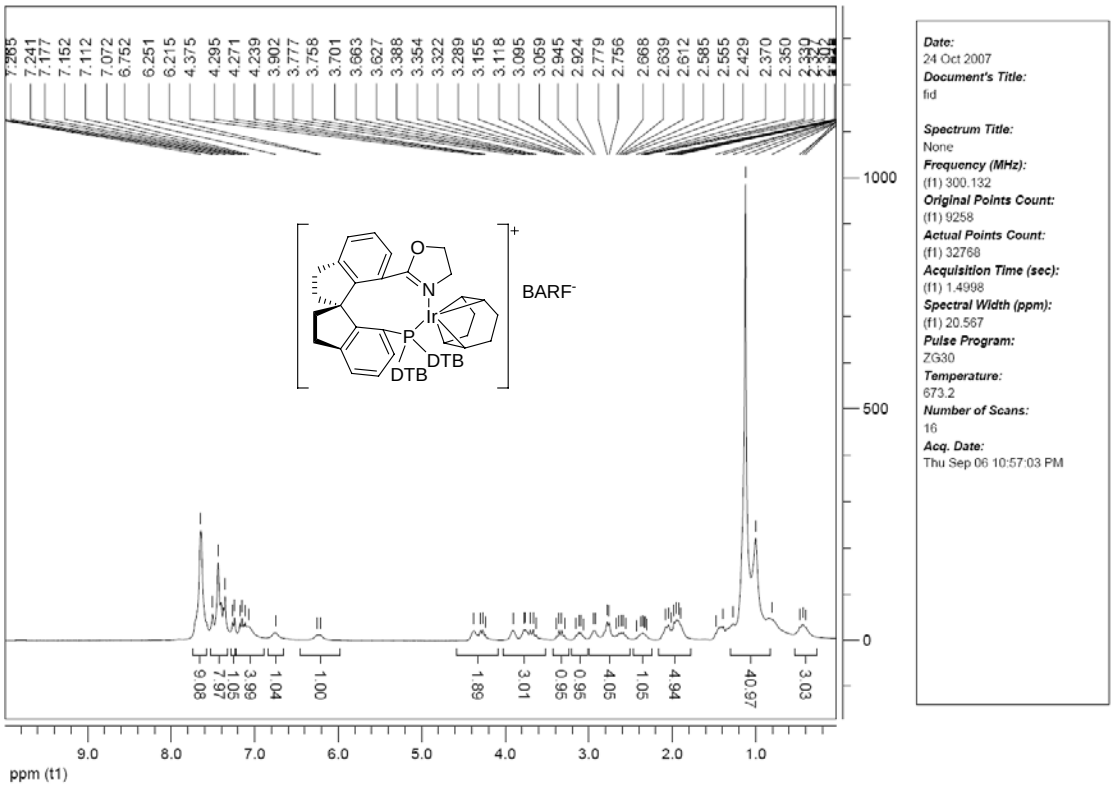
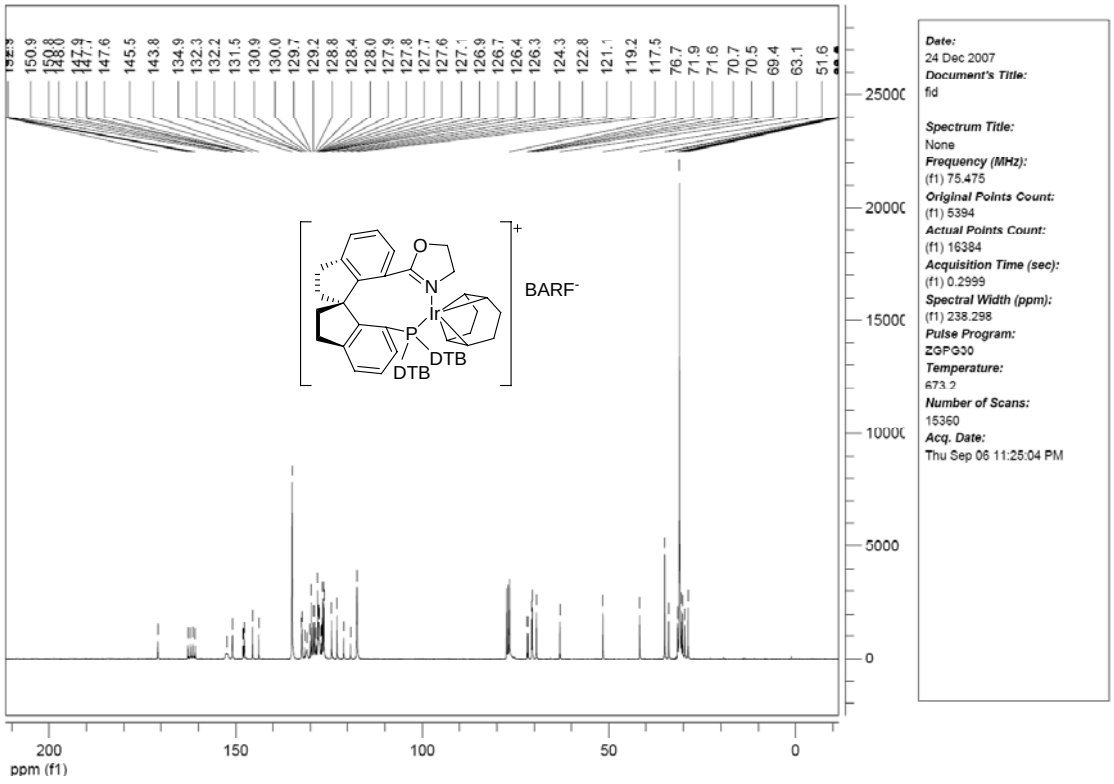
7.437
7.396
7.358
7.331
7.190
7.170
7.107
7.083
7.059
6.674
6.098
4.561
3.832
3.814
3.755
3.520
3.051
3.034
2.965
2.936
2.907
2.726
2.702
2.607
2.404
2.079
2.017
1.931
1.433
1.397
1.371
1.109
Me
N
Ir
P
DTB
DTB
BARF-
1.05
9.96
8.10
2.93
1.02
1.00
0.93
2.00
1.09
6.04
4.19
4.63
2.07
ppm (f1)
Date:
23 Oct 2007
Document's Title:
fid
Spectrum Title:
None
Frequency (MHz):
(f1) 300.132
Original Points Count:
(f1) 9258
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 1.4998
Spectral Width (ppm):
(f1) 20.567
Pulse Program:
ZG30
Temperature:
299.2
Number of Scans:
8
Acq. Date:
Tue Sep 11 10:28:20 PM


Me
N
Ir
P
DTB
DTB
BARF-
ppm (f1)
Date:
24 Dec 2007
Document's Title:
fid
Spectrum Title:
None
Frequency (MHz):
(f1) 75.475
Original Points Count:
(f1) 5394
Actual Points Count:
(f1) 16384
Acquisition Time (sec):
(f1) 0.2999
Spectral Width (ppm):
(f1) 238.298
Pulse Program:
ZGPG30
Temperature:
301.3
Number of Scans:
1092
Acq. Date:
Wed Sep 12 12:36:16 AM

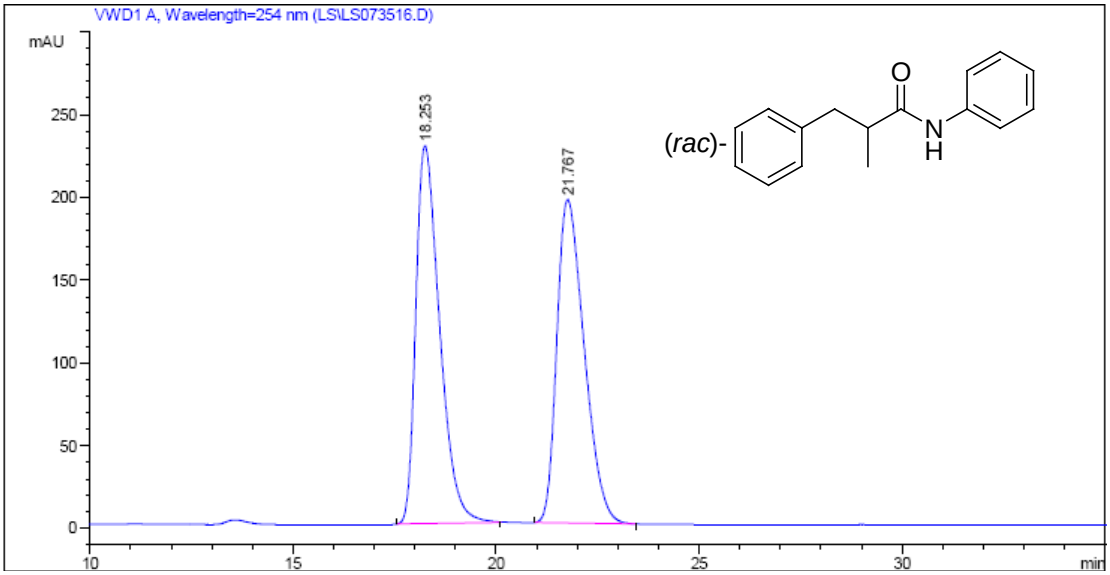
(S_a)-1h

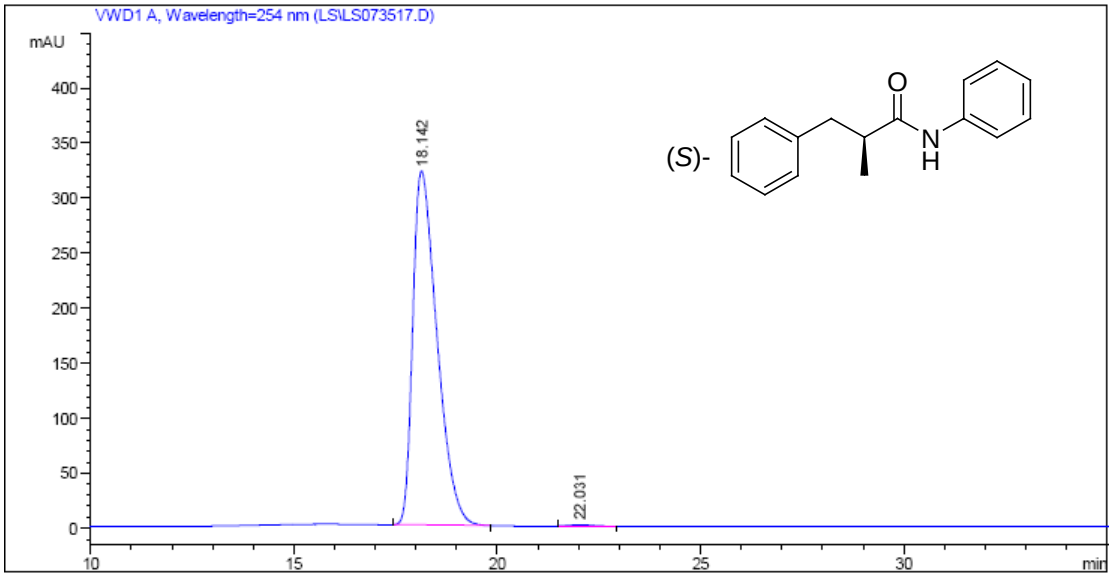

BARF-
Date:
24 Oct 2007
Document's Title:
fid
Spectrum Title:
None
Frequency (MHz):
(f1) 300.132
Original Points Count:
(f1) 9258
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 1.4998
Spectral Width (ppm):
(f1) 20.567
Pulse Program:
ZG30
Temperature:
673.2
Number of Scans:
16
Acq. Date:
Thu Sep 06 10:57:03 PM
ppm (t1)


BARF-
Date:
24 Dec 2007
Document's Title:
fid
Spectrum Title:
None
Frequency (MHz):
(f1) 75.475
Original Points Count:
(f1) 5394
Actual Points Count:
(f1) 16384
Acquisition Time (sec):
(f1) 0.2999
Spectral Width (ppm):
(f1) 238.298
Pulse Program:
ZGPG30
Temperature:
673.2
Number of Scans:
15360
Acq. Date:
Thu Sep 06 11:25:04 PM
ppm (f1)

(G) HPLC and SFC Charts of Hydrogenation Product Derivatives

2-Methyl-3,*N*-diphenyl-propionamide

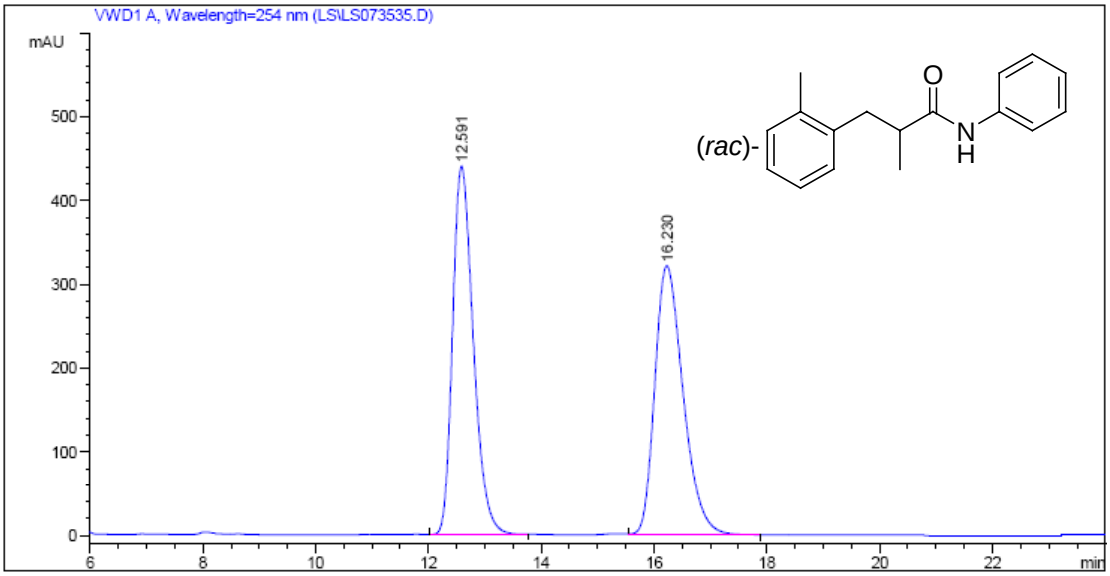


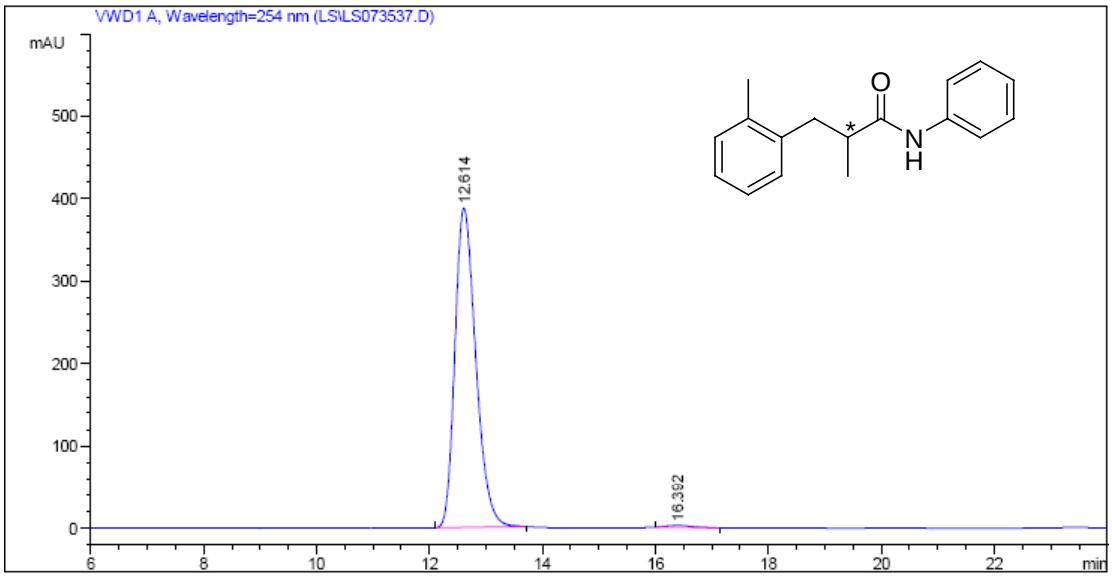


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	18.142	BB	0.6324	1.33113e4	321.88812	99.6147
2	22.031	BB	0.5067	51.48203	1.27706	0.3853
Totals :				1.33628e4	323.16518	

2-Methyl-*N*-phenyl-3-*o*-tolyl-propionamide

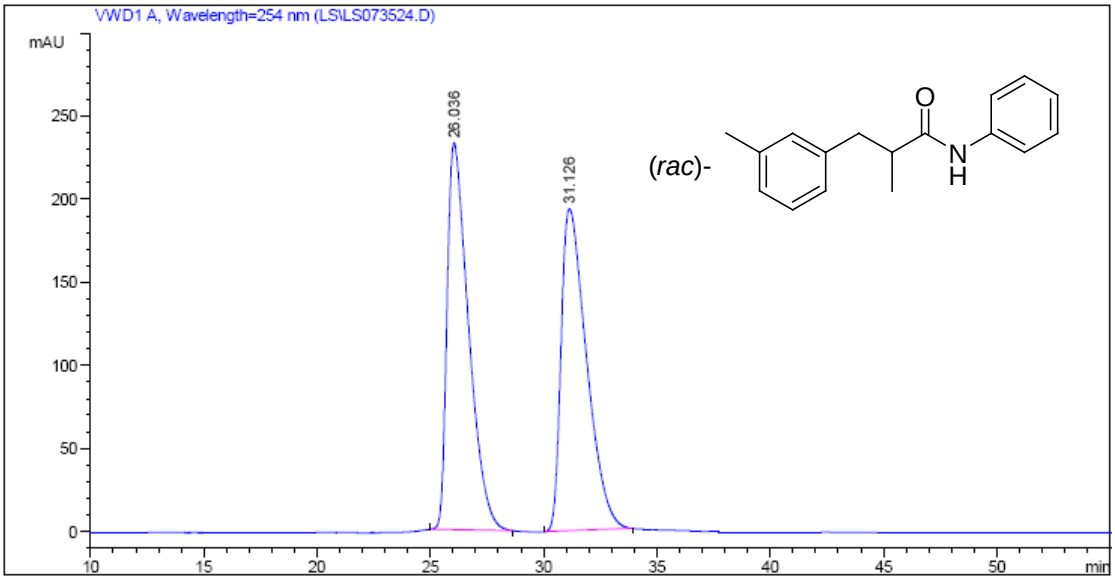


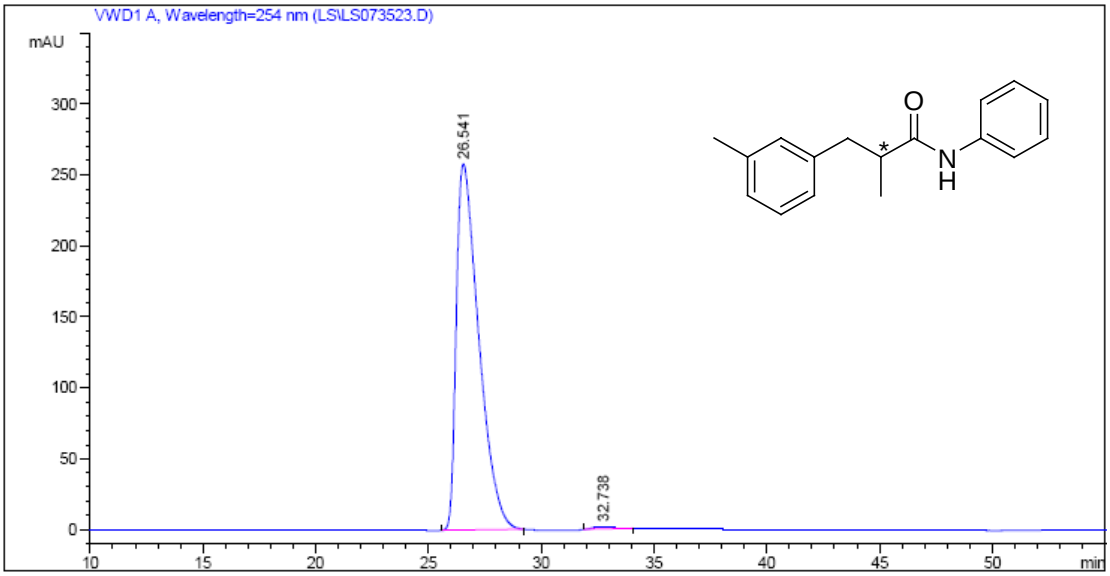


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	12.614	BB	0.3993	9978.80371	387.73157	99.2831
2	16.392	BB	0.4676	72.05061	2.35528	0.7169
Totals :				1.00509e4	390.08685	

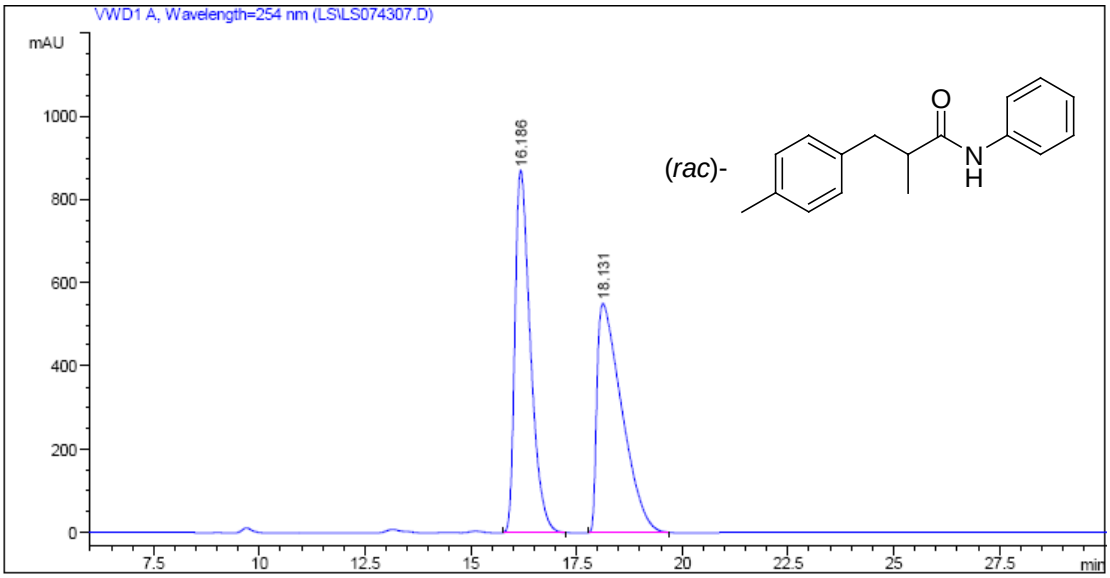
2-Methyl-*N*-phenyl-3-*m*-tolyl-propionamide

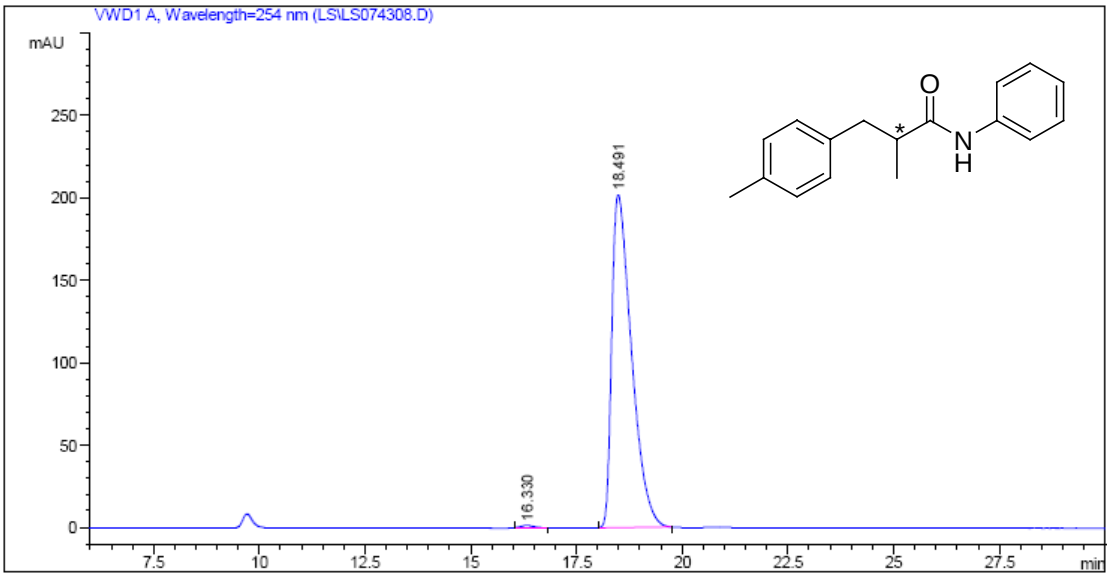




Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	26.541	BB	1.0271	1.78215e4	258.03470	99.3321
2	32.738	BB	0.7642	119.83053	1.89059	0.6679
Totals :				1.79413e4	259.92529	

2-Methyl-*N*-phenyl-3-*p*-tolyl-propionamide

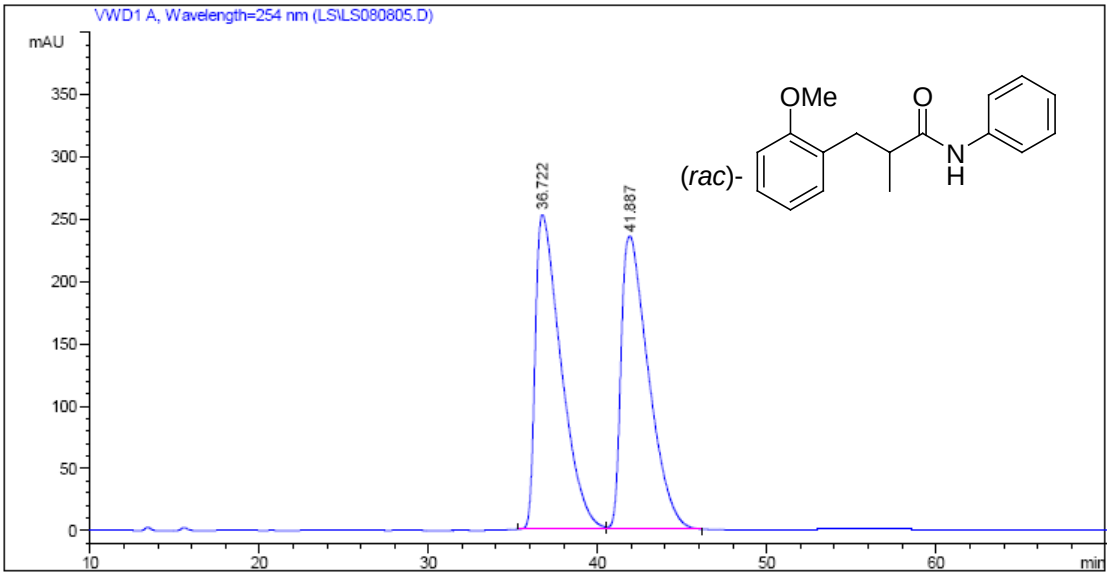


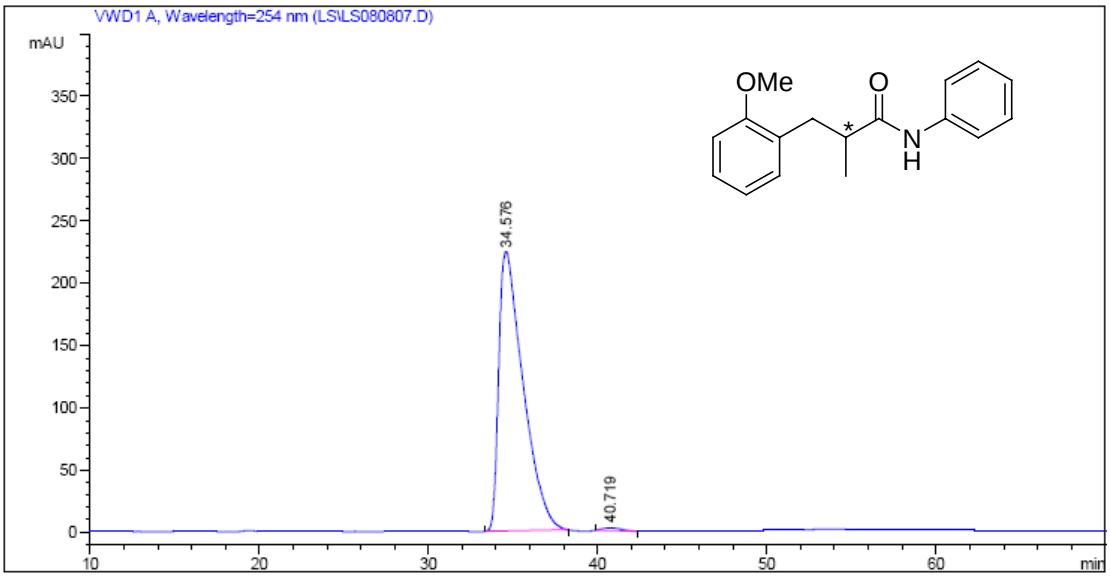


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	16.330	BB	0.3260	31.82479	1.48319	0.4826
2	18.491	BB	0.4938	6562.82666	202.13493	99.5174
Totals :				6594.65145	203.61812	

3-(2-Methoxyphenyl)-2-methyl-*N*-phenyl-propionamide

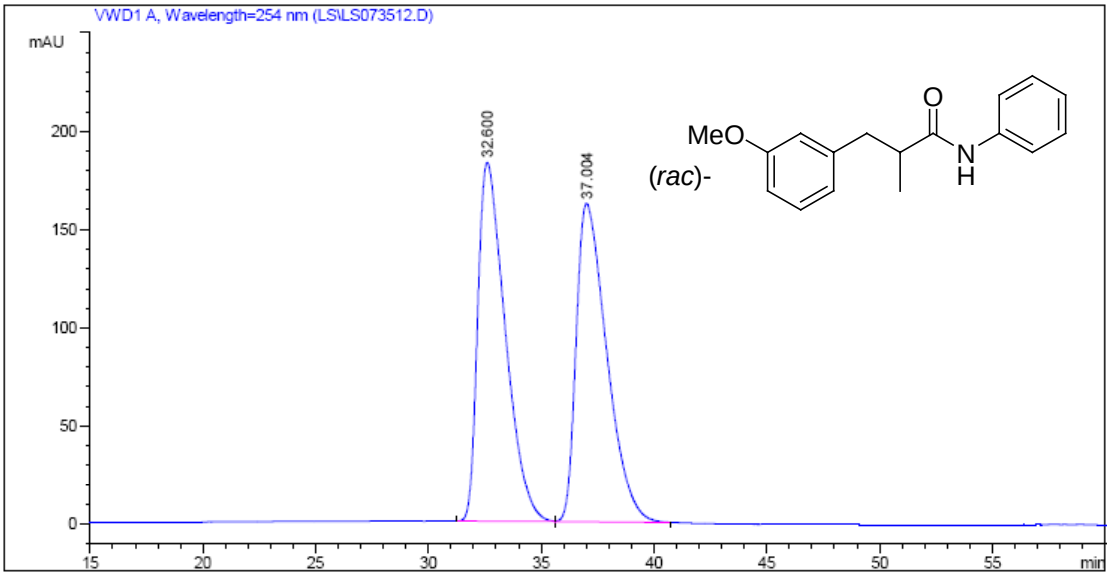


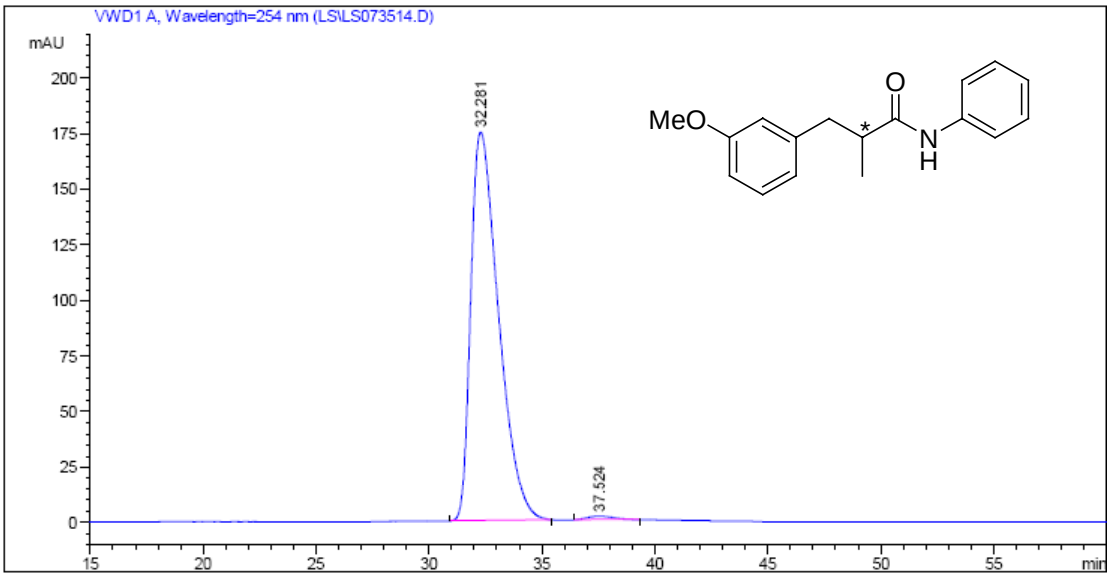


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	34.576	BB	1.4209	2.24725e4	224.27034	99.2370
2	40.719	BB	0.8694	172.79388	2.34236	0.7630
Totals :				2.26453e4	226.61269	

3-(3-Methoxyphenyl)-2-methyl-*N*-phenyl-propionamide

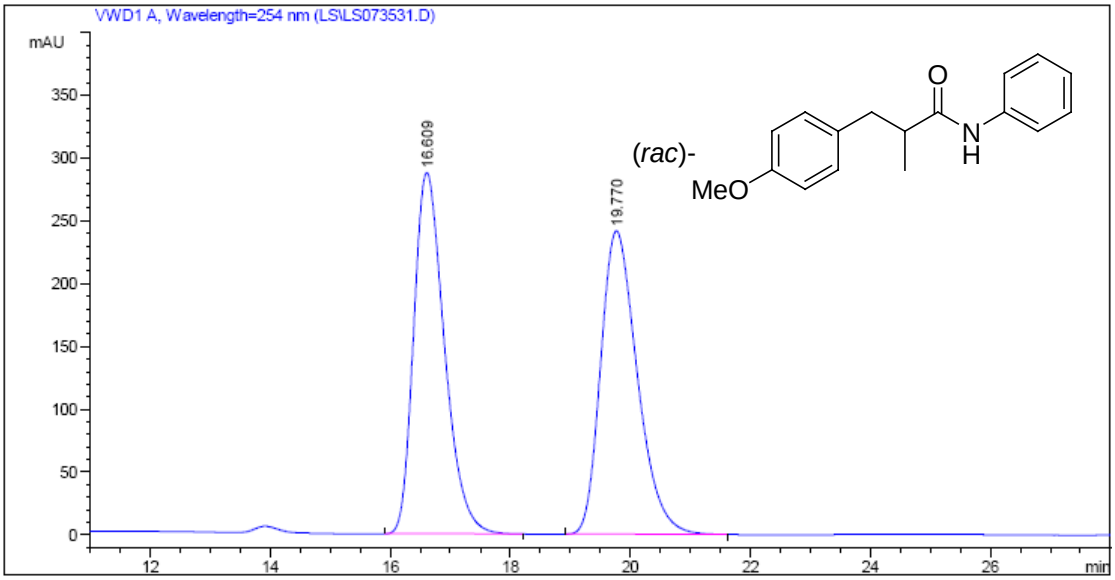


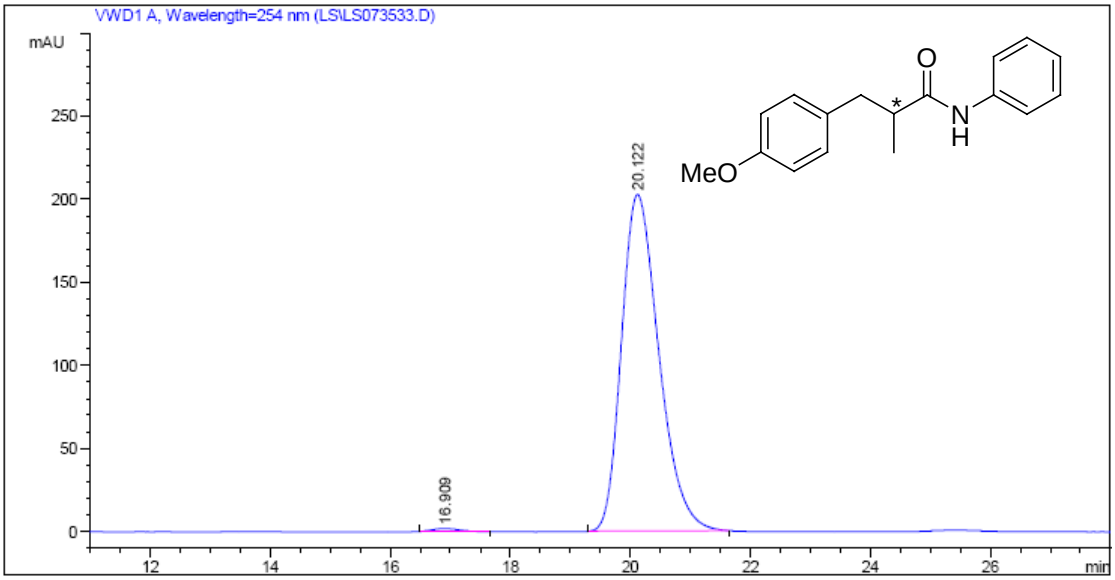


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	32.281	BB	1.2736	1.49591e4	175.05823	99.1485
2	37.524	BB	0.9447	128.47194	1.60136	0.8515
Totals :				1.50876e4	176.65958	

3-(4-Methoxyphenyl)-2-methyl-*N*-phenyl-propionamide

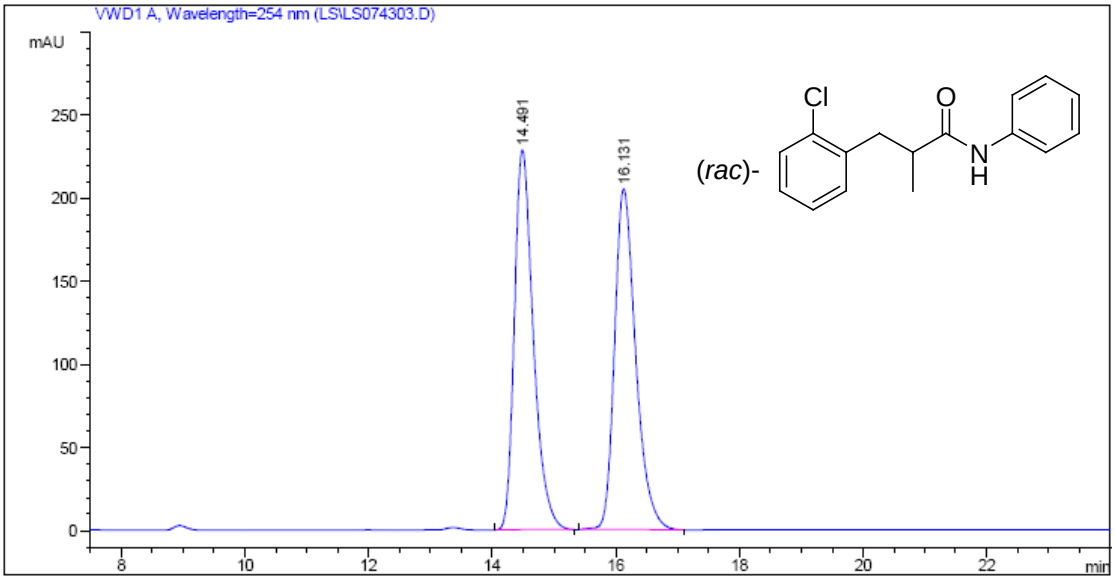


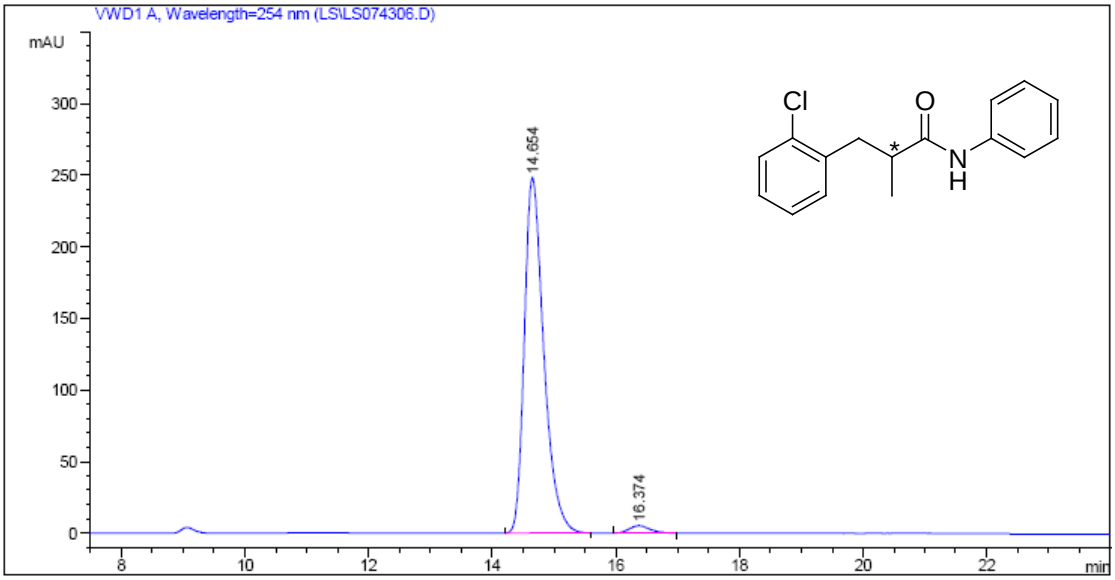


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	16.909	BB	0.4739	53.18158	1.71478	0.6023
2	20.122	BB	0.6669	8776.03027	202.64864	99.3977
Totals :				8829.21186	204.36342	

3-(2-Chlorophenyl)-2-methyl-*N*-phenyl-propionamide

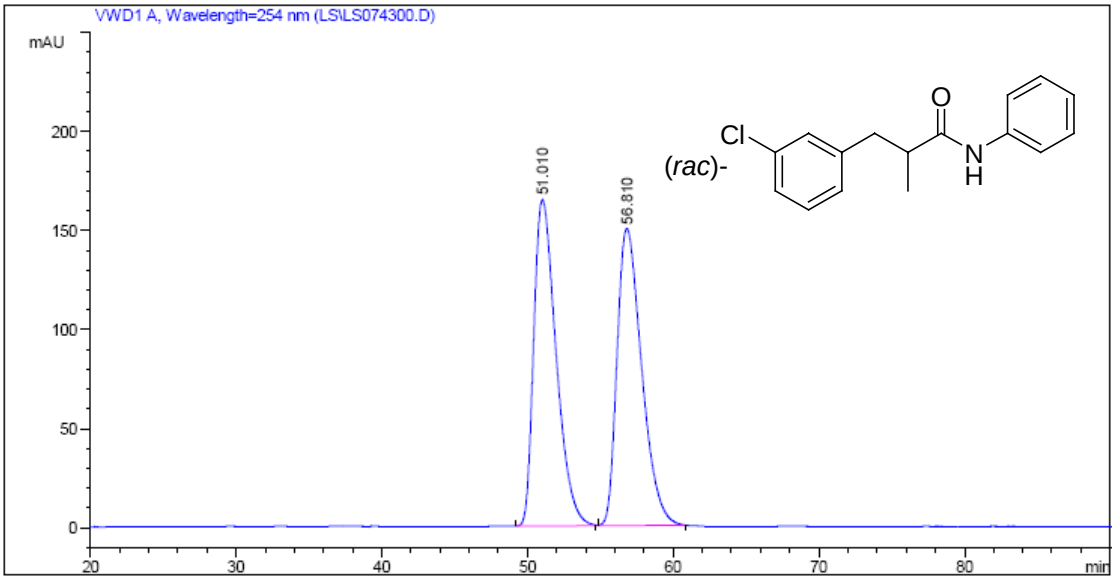


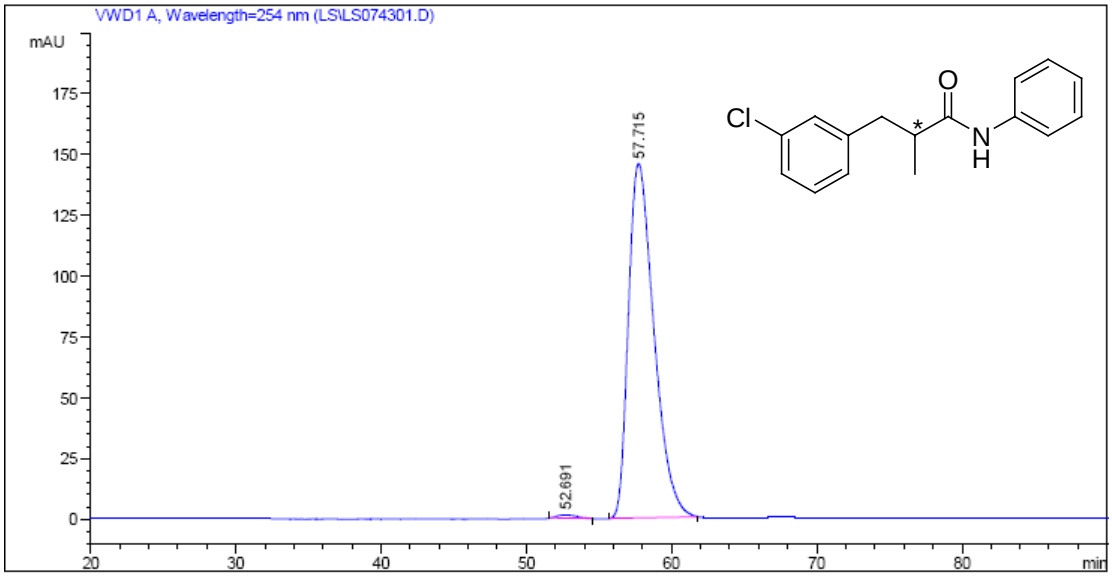


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	14.654	BB	0.3345	5447.28906	248.32088	97.8001
2	16.374	BB	0.3580	122.52940	5.25276	2.1999
Totals :				5569.81847	253.57363	

3-(3-Chlorophenyl)-2-methyl-*N*-phenyl-propionamide

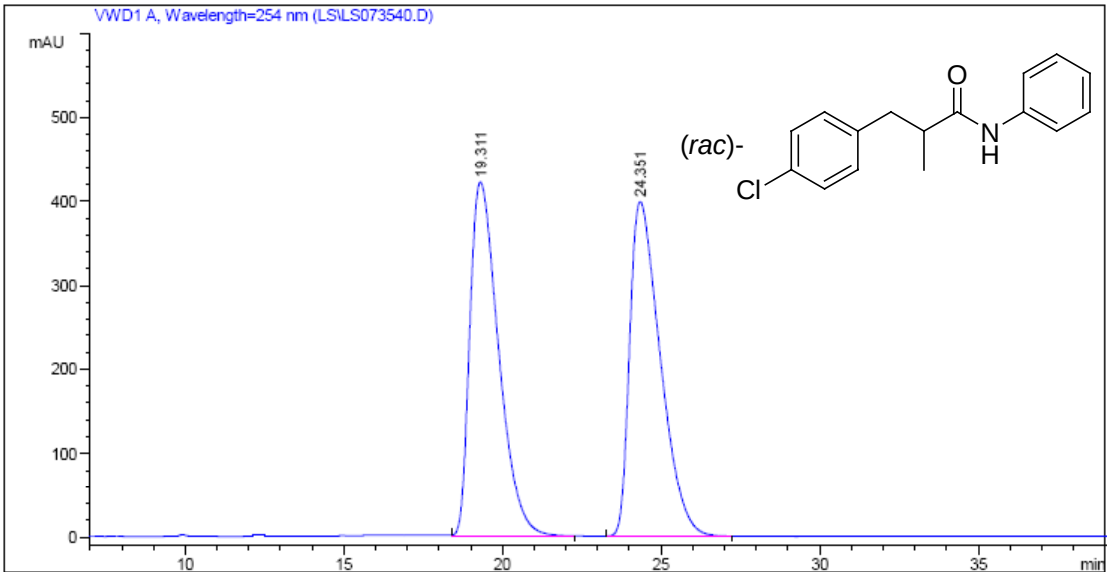


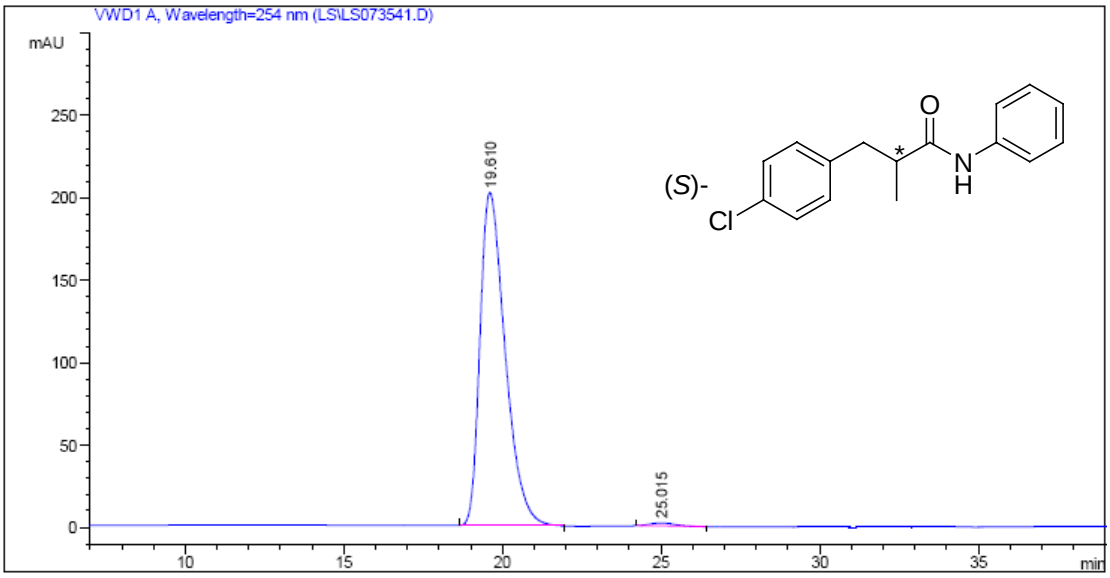


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	52.691	BB	1.0528	125.56611	1.40112	0.7016
2	57.715	BB	1.8240	1.77728e4	145.80066	99.2984
Totals :				1.78984e4	147.20178	

3-(4-Chlorophenyl)-2-methyl-*N*-phenyl-propionamide

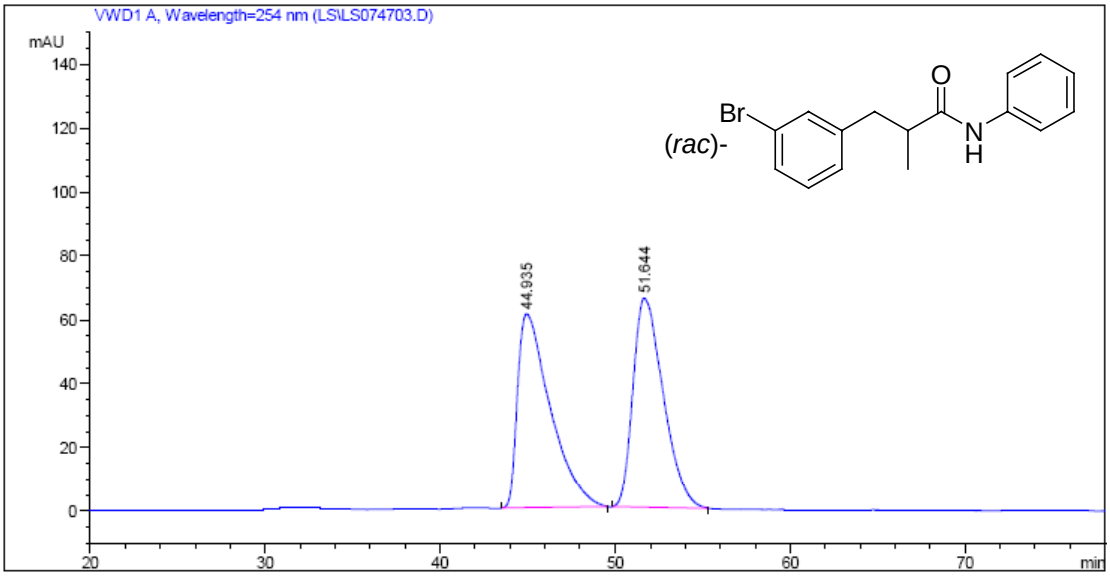


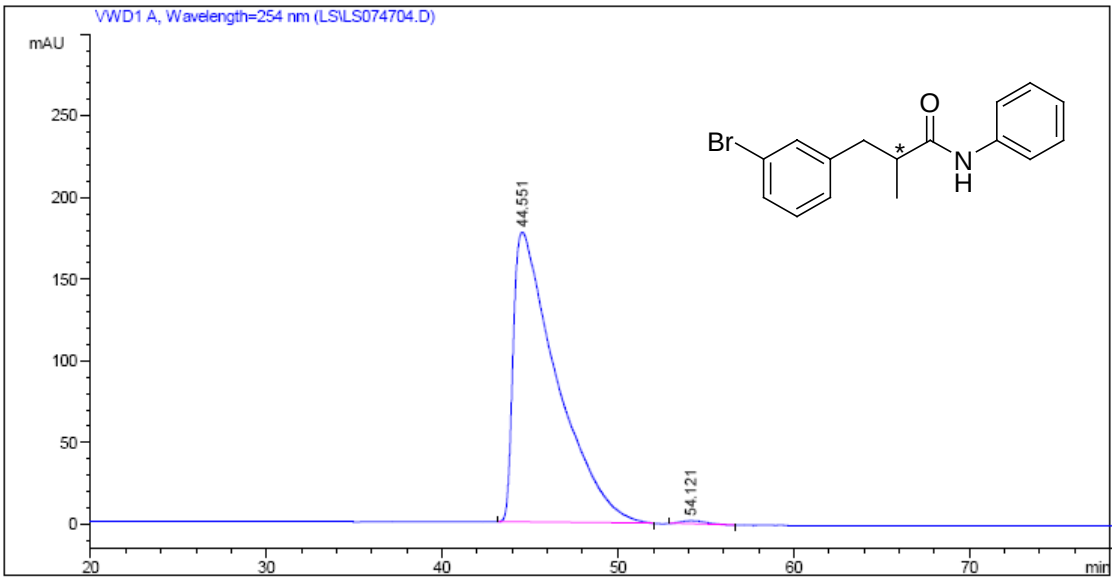


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	19.610	BB	0.8462	1.11564e4	202.17201	99.1202
2	25.015	BP	0.6772	99.02988	1.79879	0.8798
Totals :				1.12555e4	203.97081	

(3-Bromophenyl)-2-methyl-*N*-phenyl-propionamide

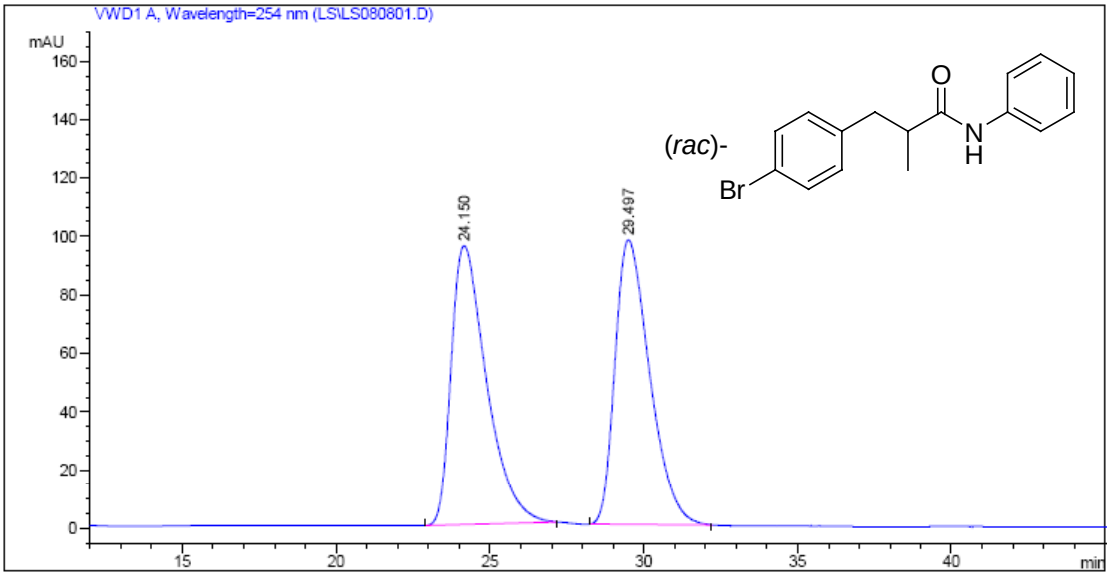


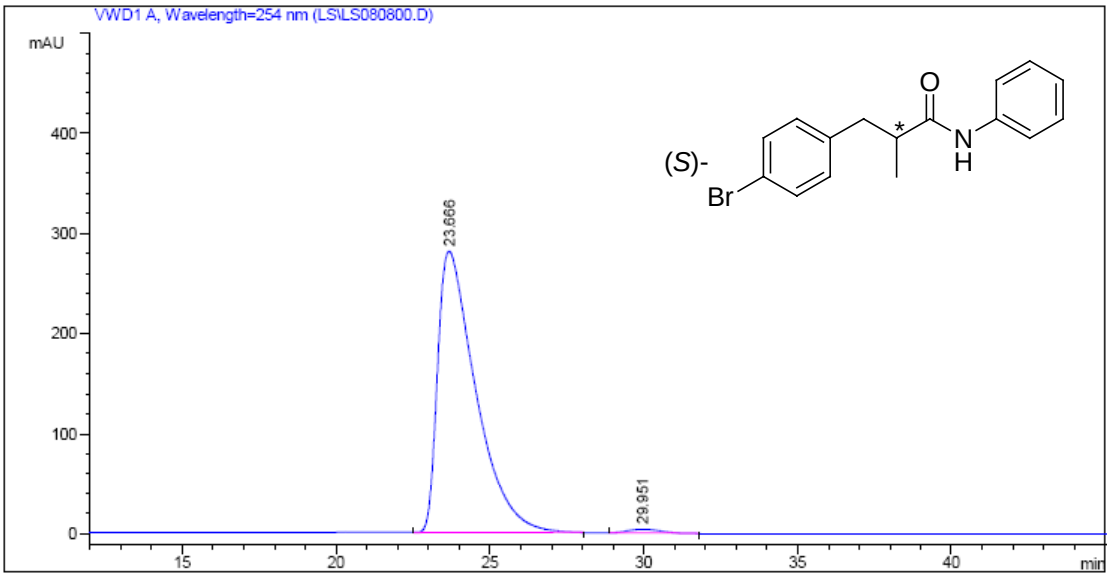


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	44.551	BB	2.2850	3.04103e4	177.42438	99.3633
2	54.121	BP	1.2071	194.85197	1.90389	0.6367
Totals :				3.06051e4	179.32826	

3-(4-Bromophenyl)-2-methyl-*N*-phenyl-propionamide

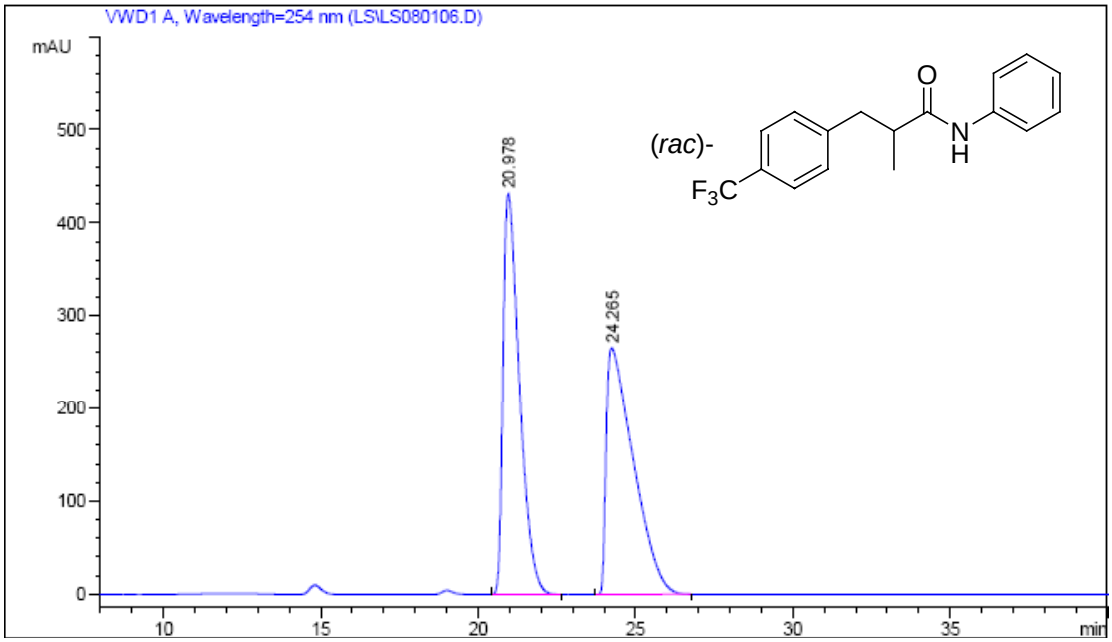


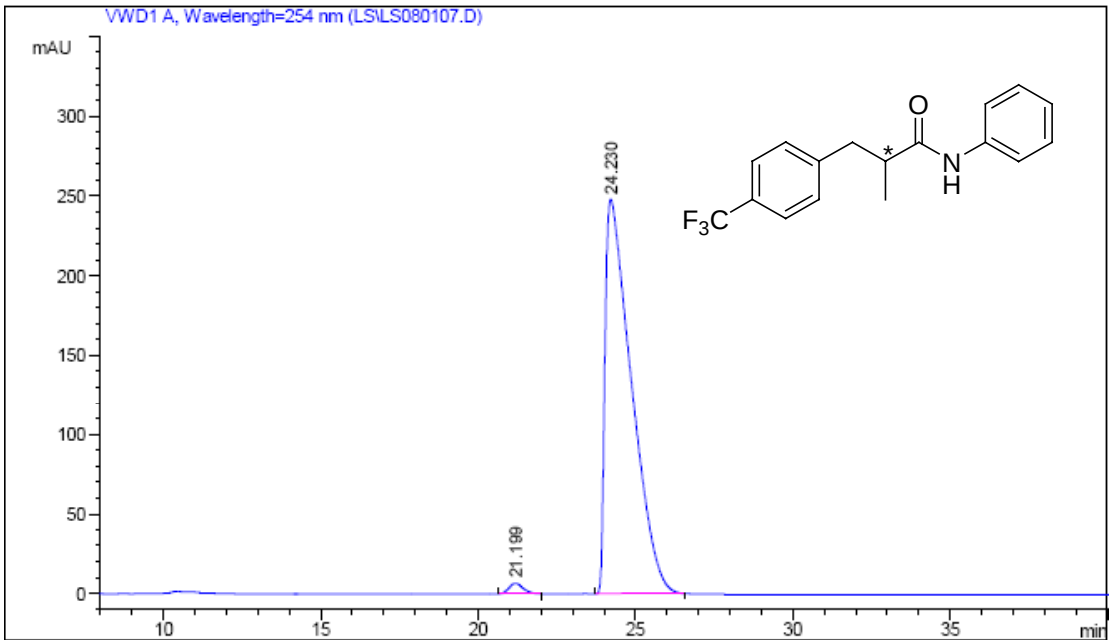


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	23.666	VB	1.2517	2.42859e4	281.34882	98.8706
2	29.951	BP	0.8547	277.42755	3.84576	1.1294
Totals :				2.45633e4	285.19458	

2-Methyl-3-(4-(trifluoromethyl)phenyl)-*N*-phenyl-propionamide

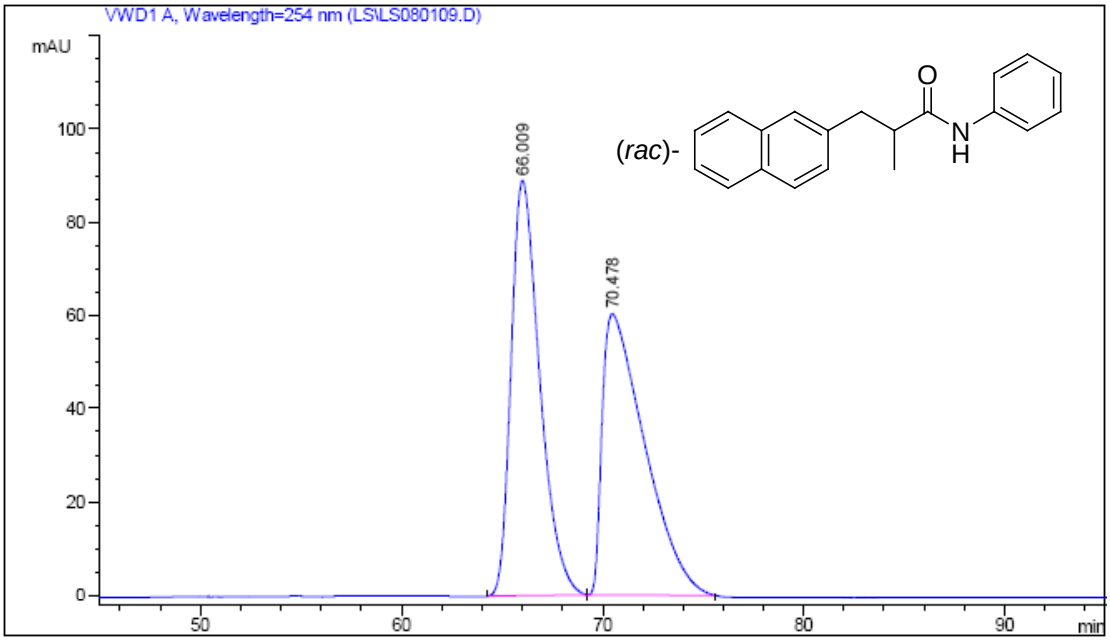


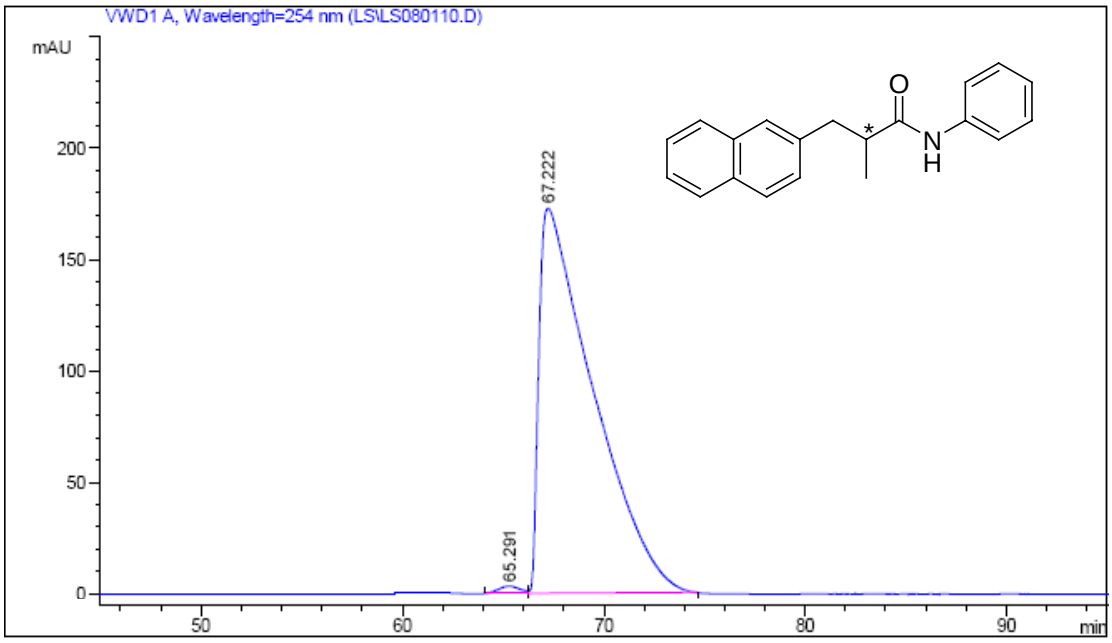


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	21.199	BB	0.4661	205.98788	6.70626	1.4097
2	24.230	BB	0.8519	1.44060e4	248.19722	98.5903
Totals :				1.46120e4	254.90348	

2-Methyl-3-(naphthalen-2-yl)-*N*-phenyl-propionamide

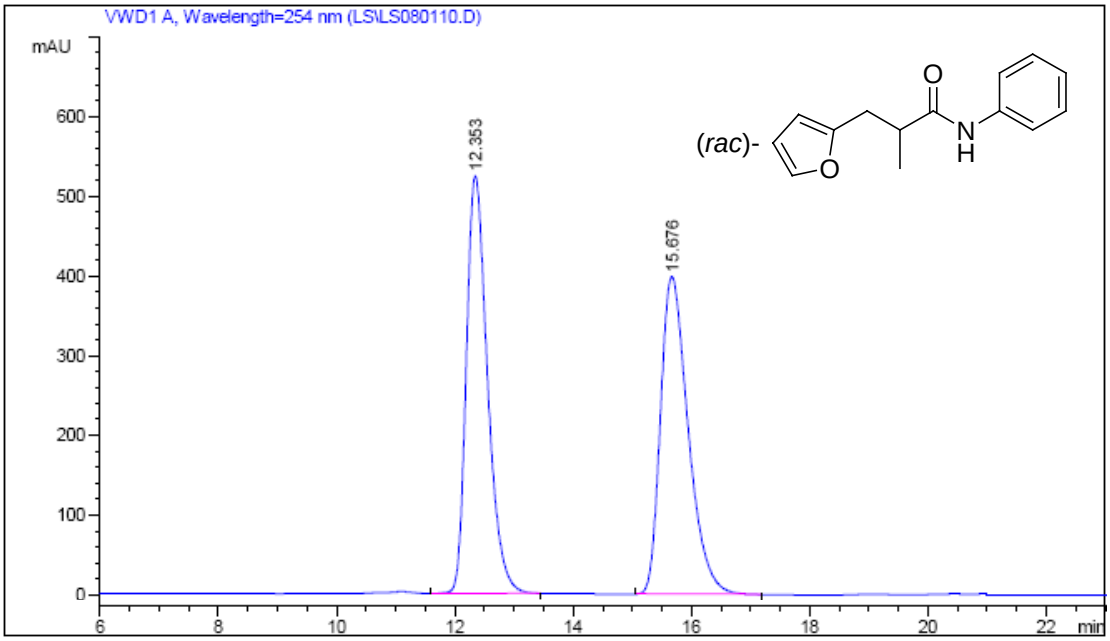


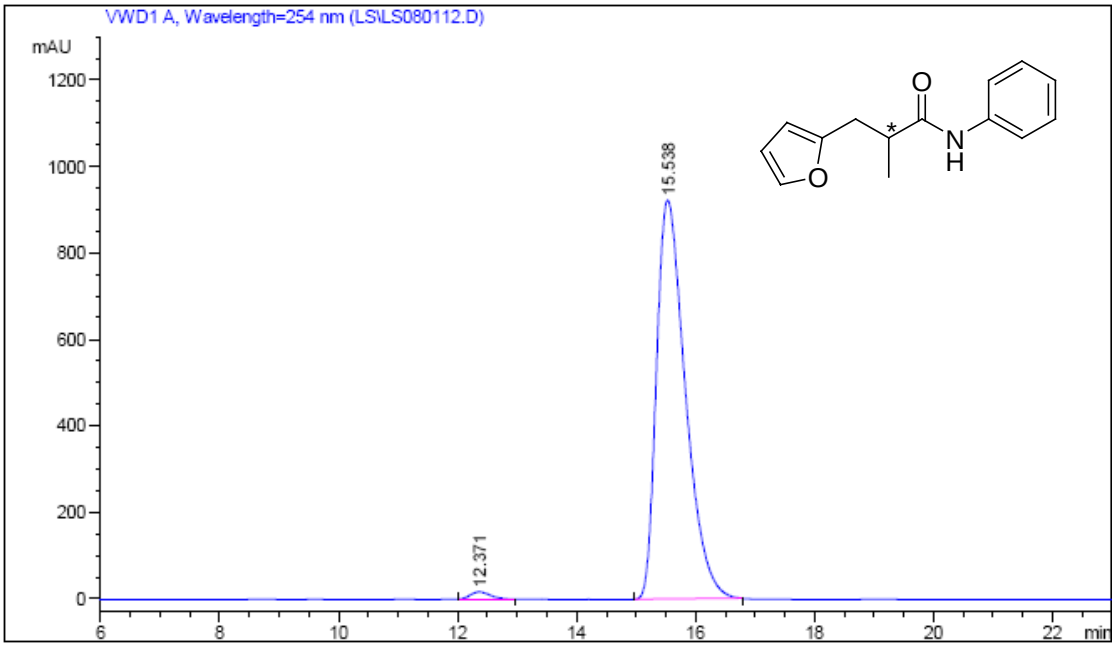


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	65.291	BV	0.8830	234.89011	3.14495	0.7202
2	67.222	VB	2.4546	3.23816e4	172.65367	99.2798
Totals :				3.26165e4	175.79862	

3-(Furan-2-yl)-2-methyl-*N*-phenyl-propionamide

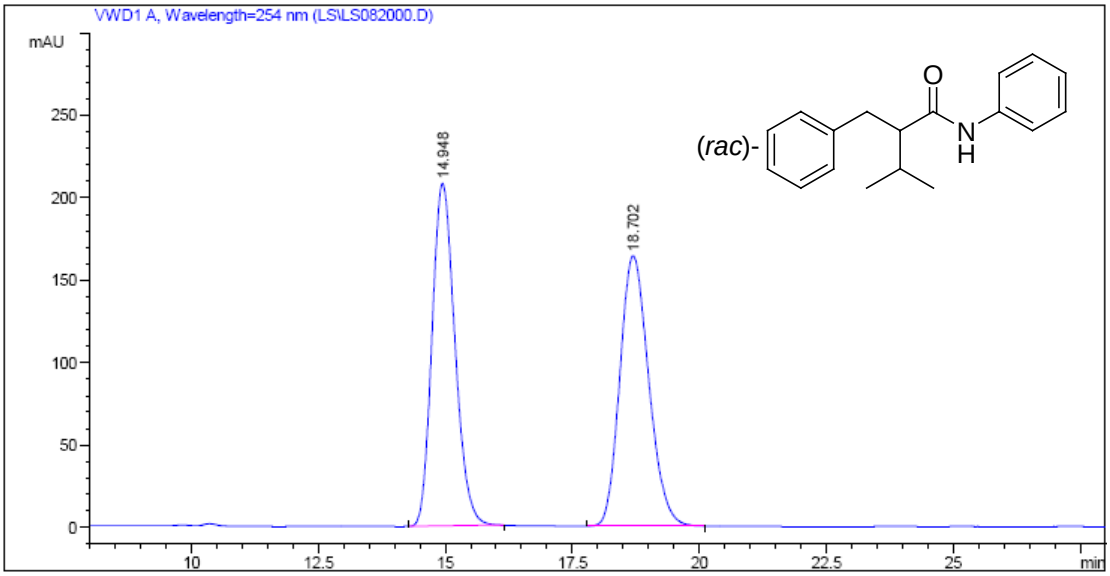


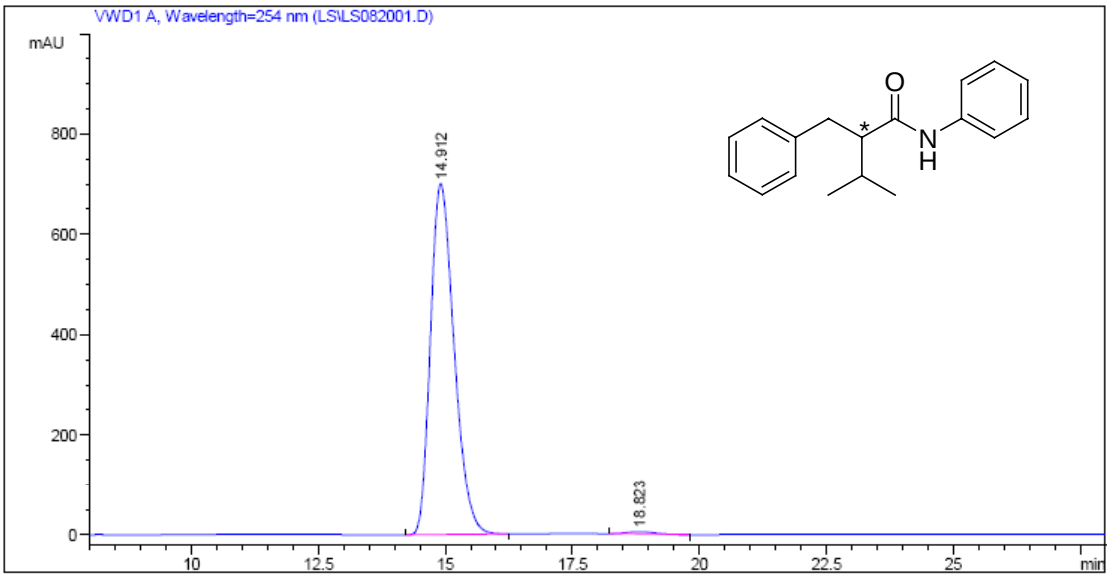


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	12.371	BB	0.3634	399.16293	16.95899	1.2666
2	15.538	BB	0.5200	3.11144e4	922.87964	98.7334
Totals :				3.15136e4	939.83863	

2-Benzyl-3-methyl-*N*-phenyl-butyramide

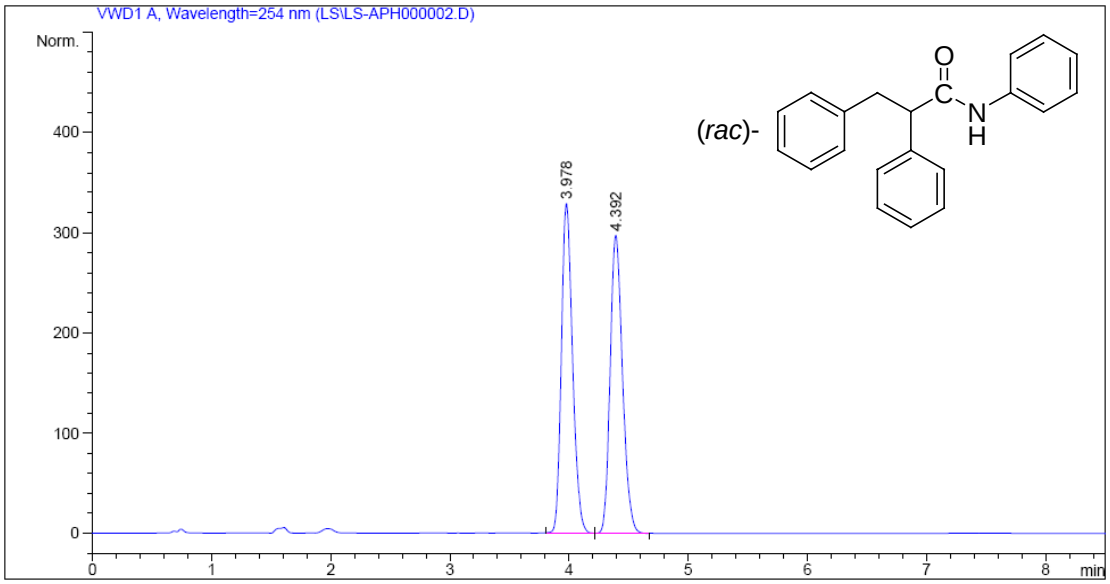


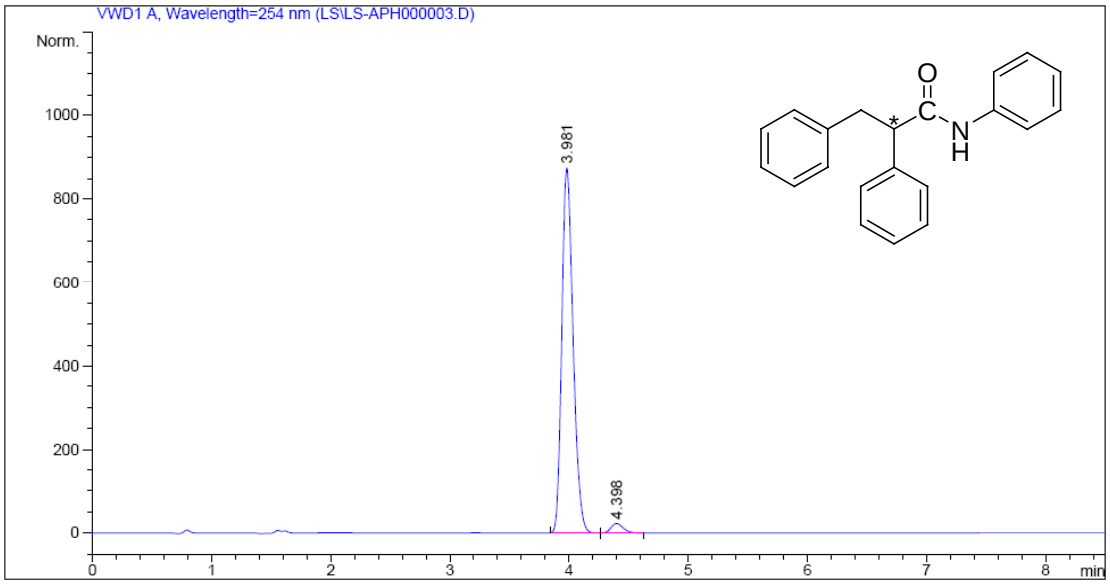


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	14.912	PB	0.5009	2.26457e4	700.53143	99.2689
2	18.823	BP	0.5790	166.78842	4.48952	0.7311
Totals :				2.28125e4	705.02096	

2,3-diphenyl- *N*-phenyl-propionamide

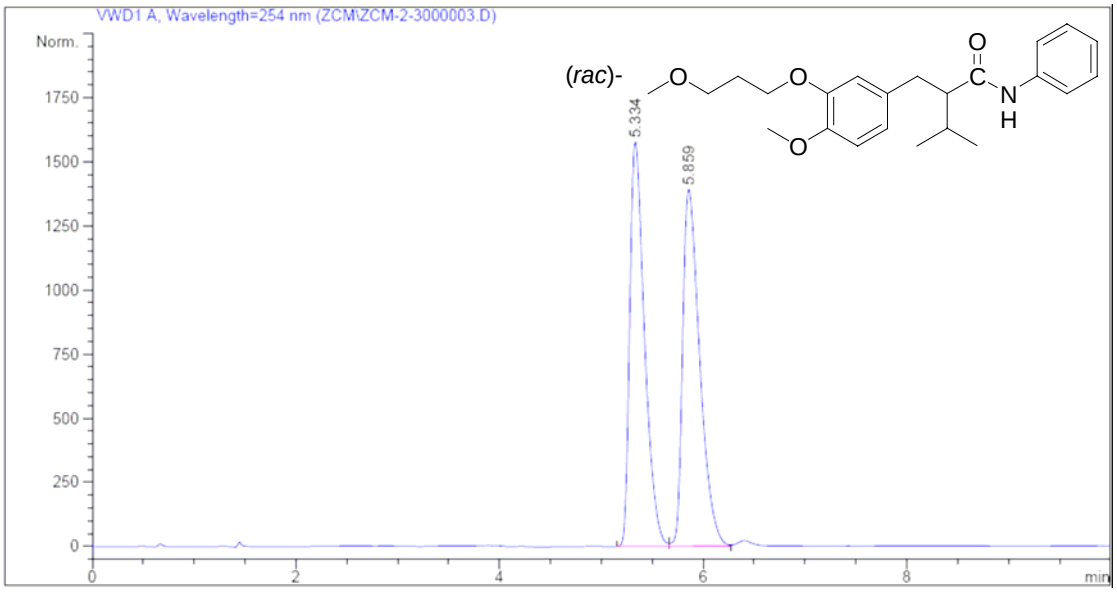


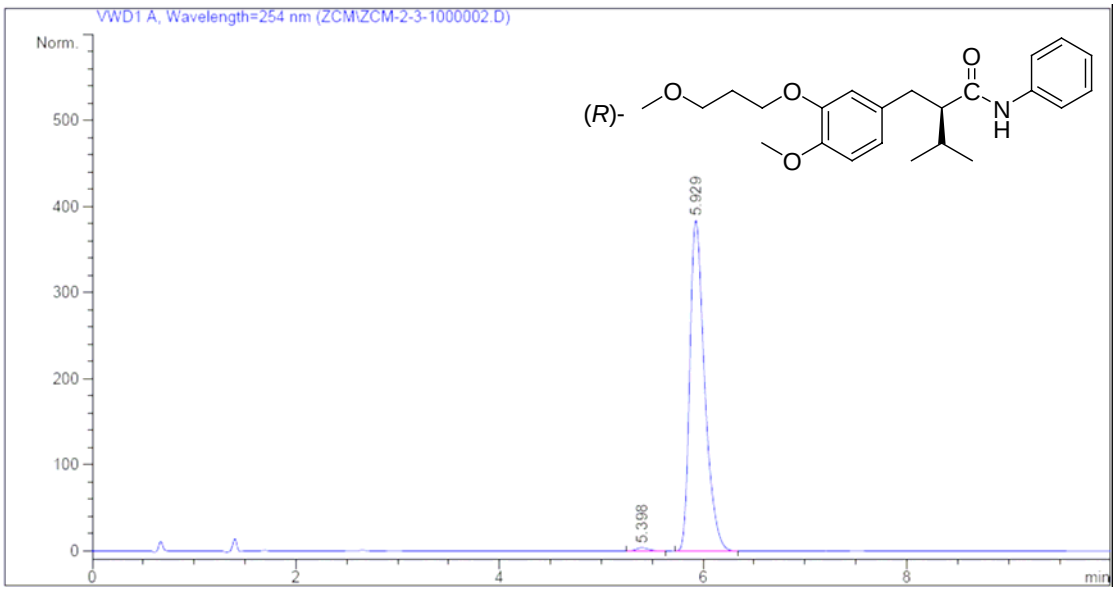


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Area %	Name
1	3.981	BB	0.1013	5748.02979	97.2362	?
2	4.398	BB	0.1118	163.37653	2.7638	?
Totals :				5911.40631		

2-(3-(3-Methoxypropoxy)-4-methoxybenzyl)-3-methyl-*N*-phenyl-butyramide

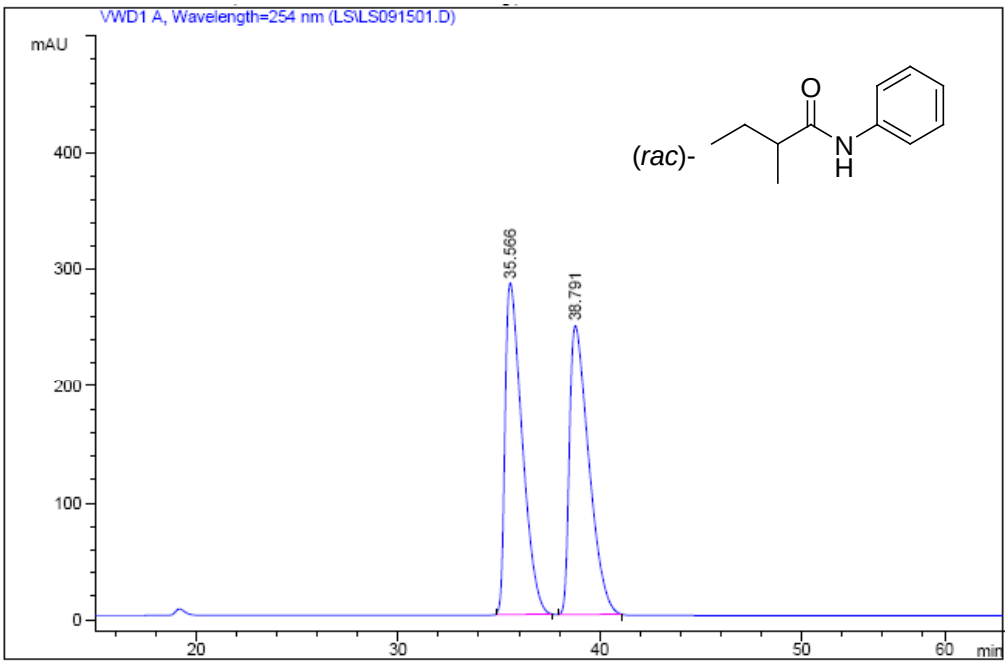


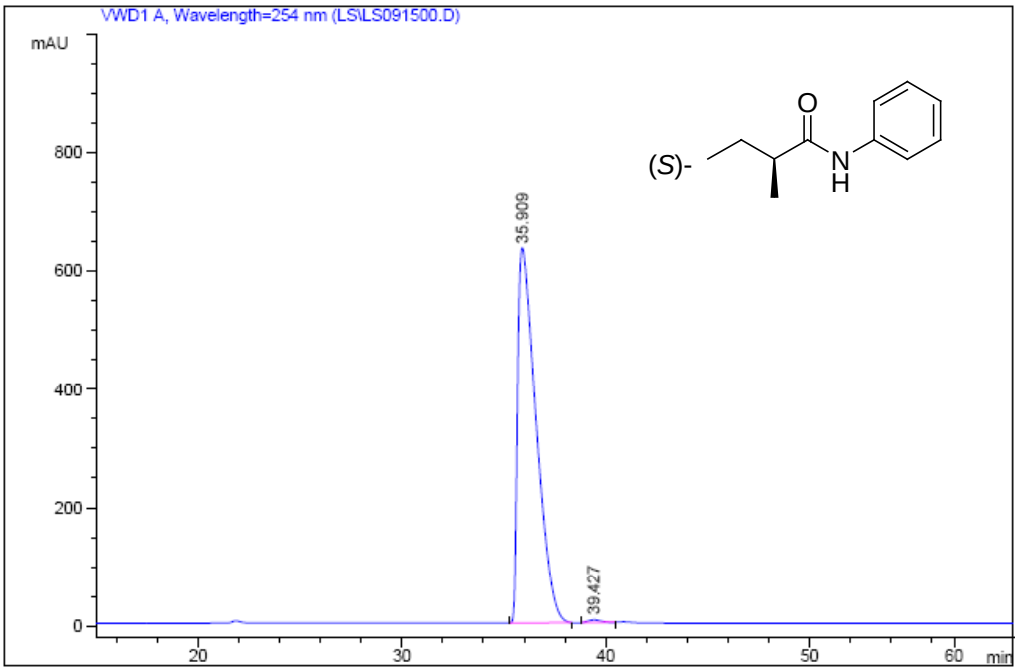


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Area %	Name
1	5.398	BB	0.1339	34.51949	0.8807	?
2	5.929	BB	0.1528	3885.20801	99.1193	?
Totals :				3919.72750		

2-Methyl-*N*-phenyl-butyramide

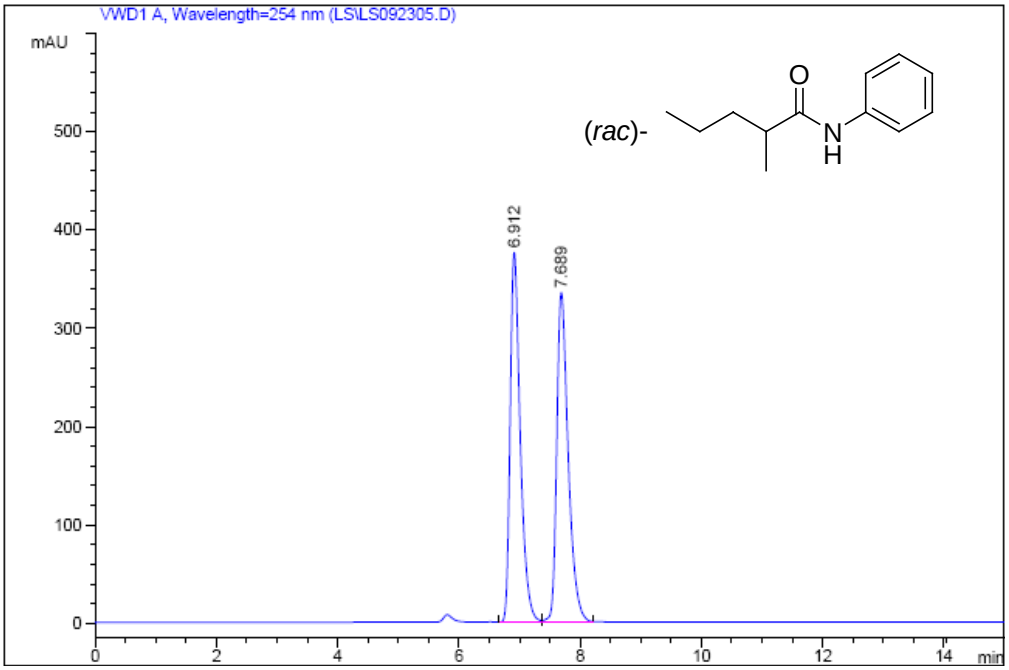


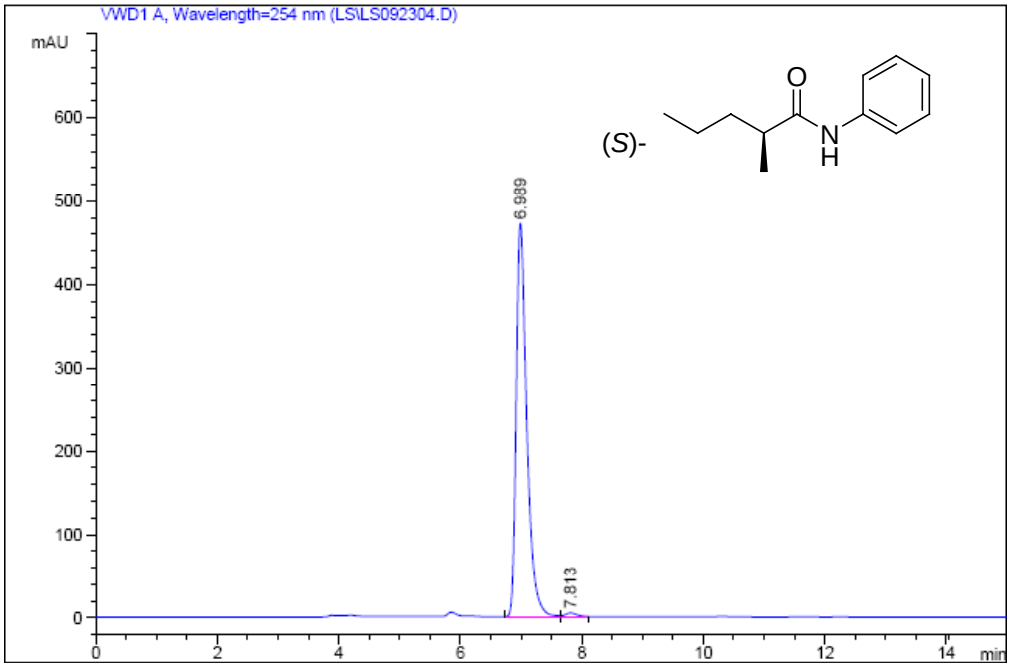


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	35.909	BB	0.9391	3.98649e4	635.04413	99.5385
2	39.427	BP	0.6066	184.81322	4.36041	0.4615
Totals :				4.00497e4	639.40454	

2-Methyl-*N*-phenyl-pentanamide

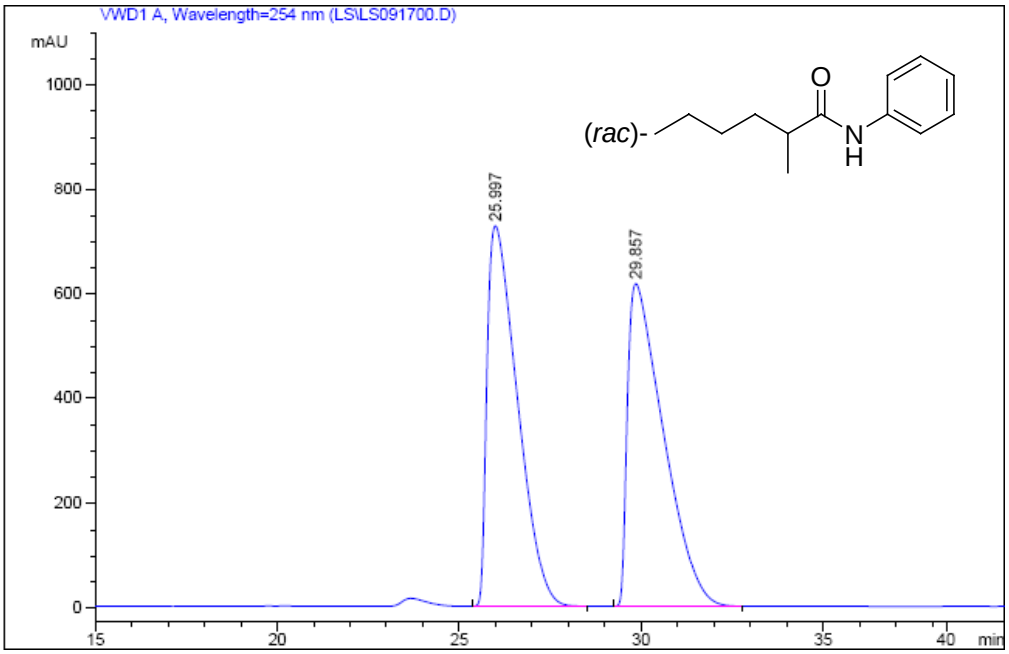


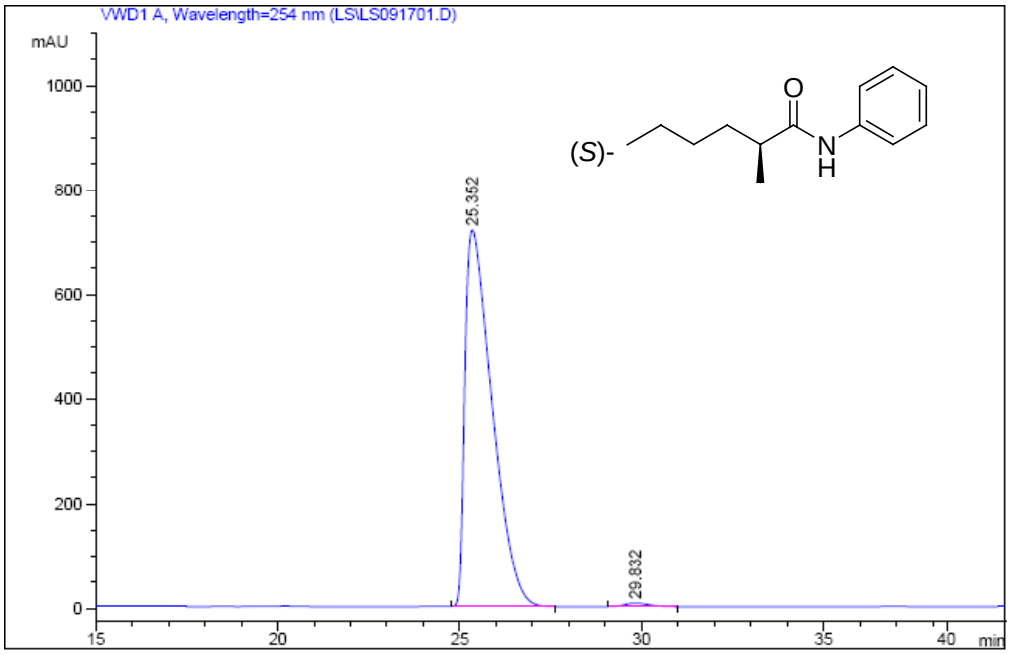


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.989	BB	0.1801	5692.83594	471.90387	98.9427
2	7.813	BB	0.2006	60.83417	4.48093	1.0573
Totals :				5753.67010	476.38480	

2-Methyl-*N*-phenyl-hexanamide

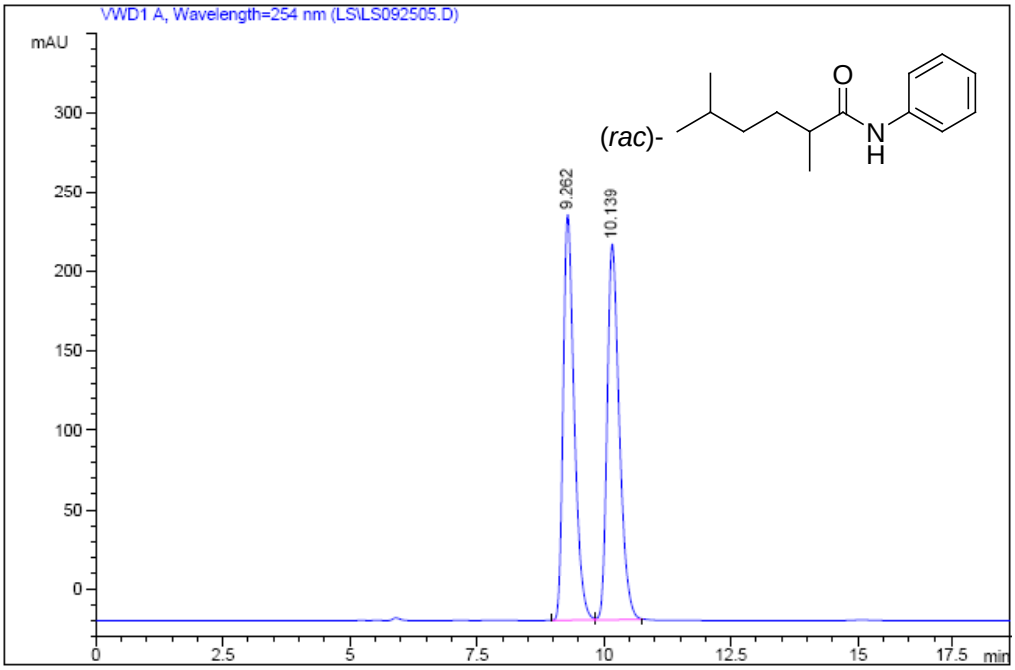


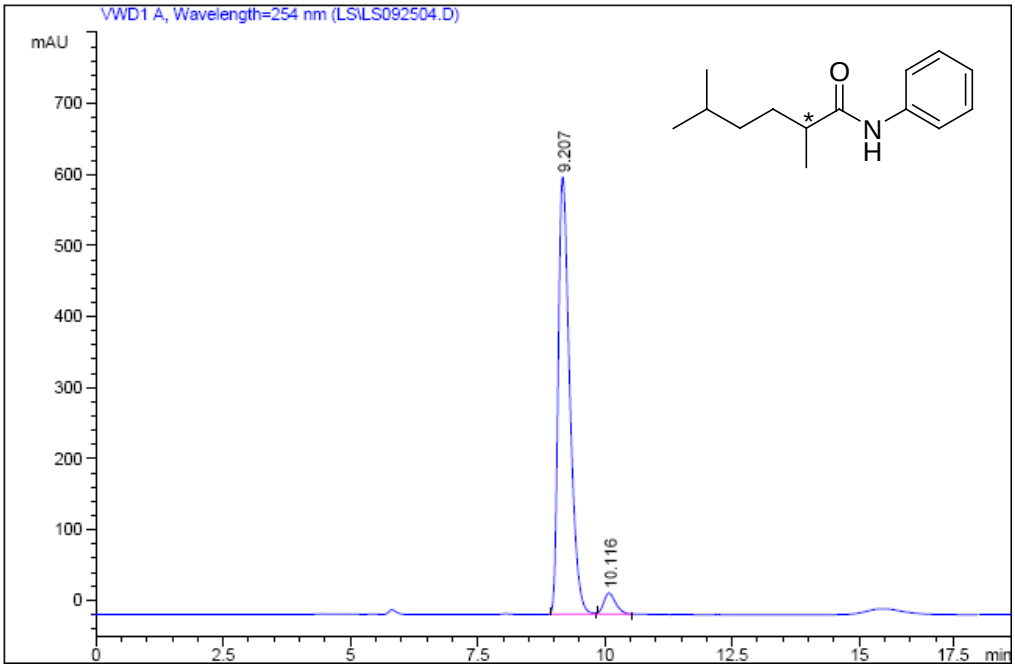


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	25.352	BB	0.7856	3.72986e4	719.19763	99.2308
2	29.832	BB	0.6289	289.11151	6.52679	0.7692
Totals :				3.75877e4	725.72442	

2,5-Dimethyl-*N*-phenyl-hexanamide

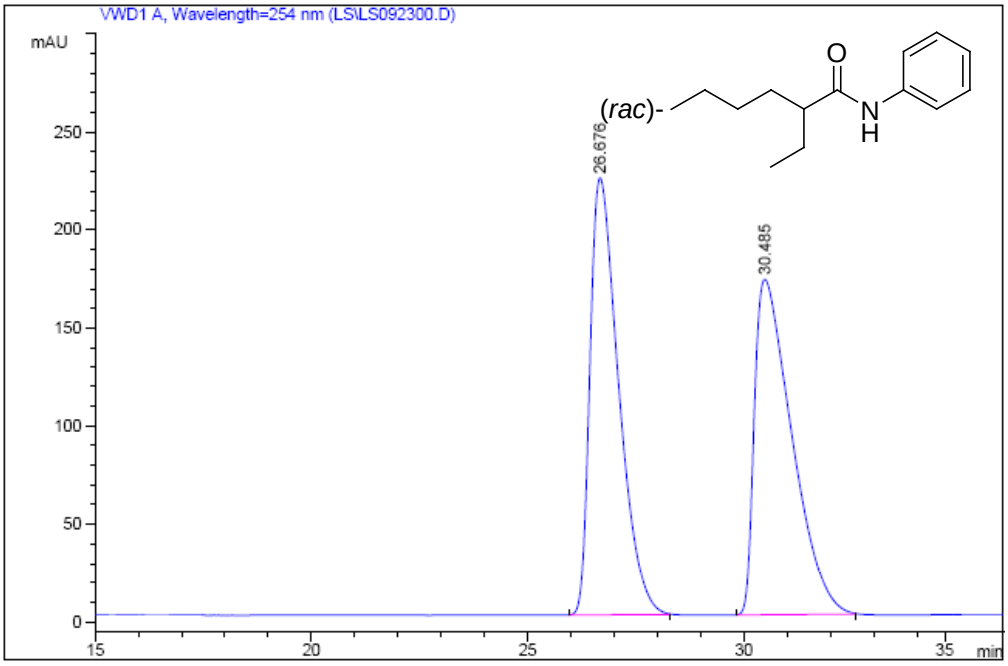


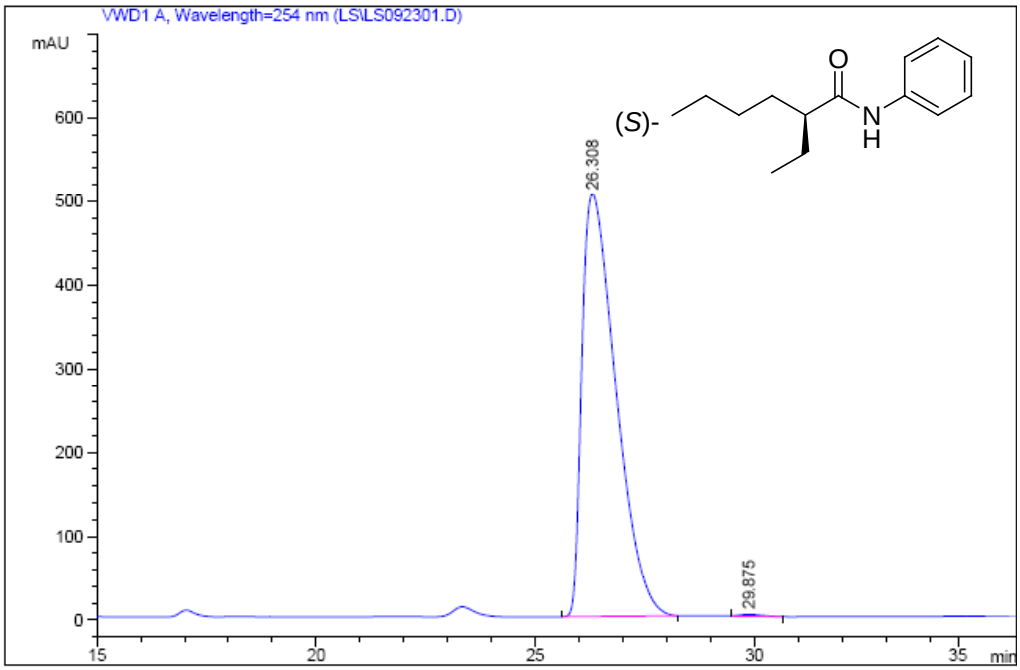


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.207	BB	0.2399	9687.69922	617.10199	95.1844
2	10.116	BB	0.2510	490.11908	29.65799	4.8156
Totals :				1.01778e4	646.75998	

2-Ethyl-*N*-phenyl-hexanamide

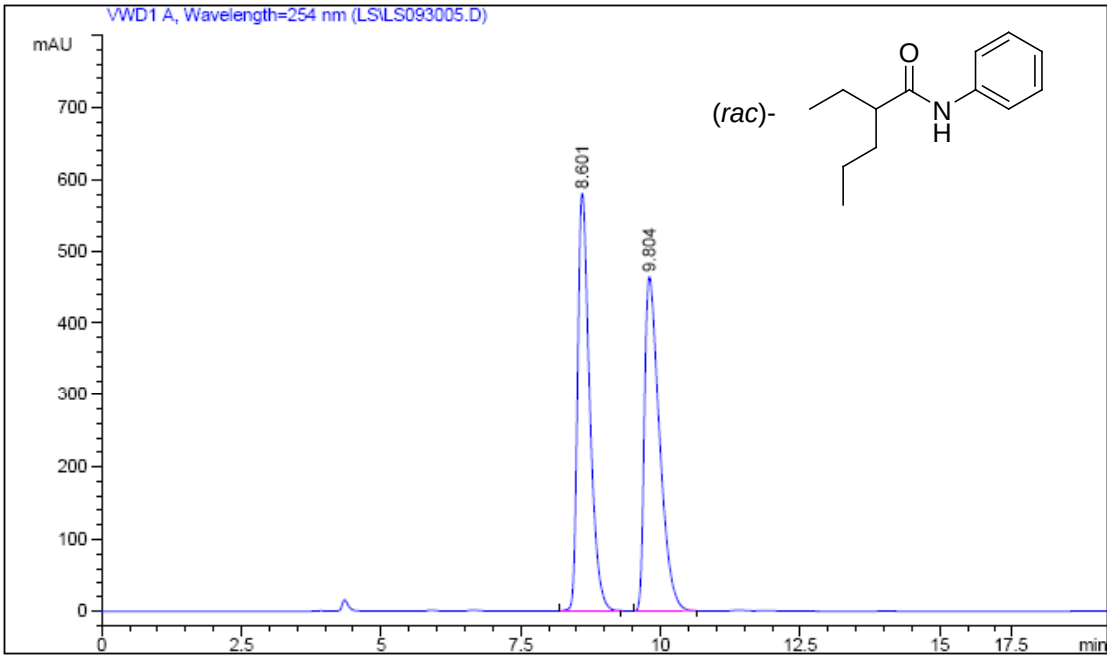


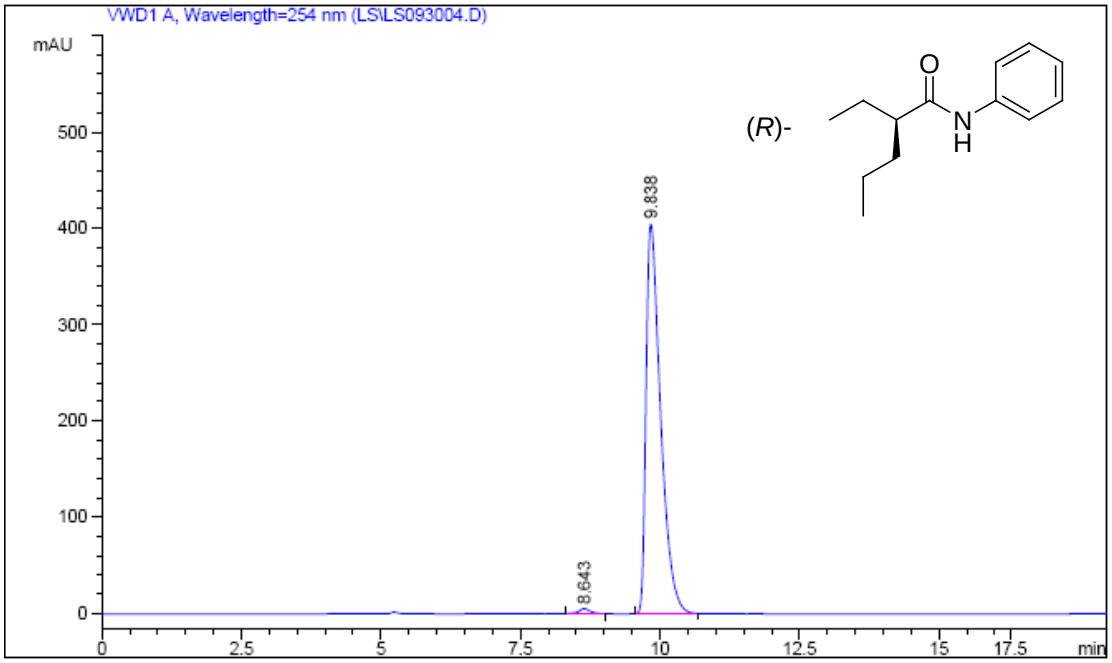


Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	26.308	PB	0.8318	2.71436e4	504.27313	99.7281
2	29.875	BB	0.4940	73.99520	2.12312	0.2719
Totals :				2.72176e4	506.39625	

2-Ethyl-*N*-phenyl-pentanamide





Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.643	BB	0.2203	78.31574	5.21740	1.0577
2	9.838	BB	0.2725	7325.79150	404.33823	98.9423
Totals :				7404.10725	409.55563	