Supplementary Material (ESI) for Chemical Communications

Supporting Information

Selectivity Control in Enantioselective Four-component Reactions of Aryl Diazoacetates with Alcohols, Aldehydes and Amines: An Efficient Approach to Synthesizing Chiral β-Amino-α-Hydroxyesters

Xinfang Xu, Jing Zhou, Liping Yang and Wenhao Hu*

Department of Chemistry, East China Normal University, Shanghai, 200062, China

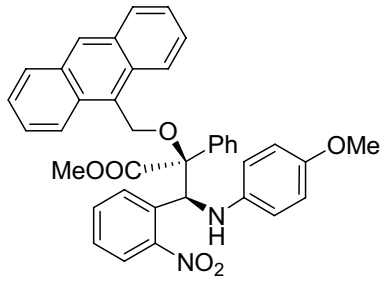
E-mail: whu@chem.ecnu.edu.cn

General: HRMS (ESI) Mass spectra were recorded on a Bio TOF ⅢQ from Bruker Daltonics Inc. at Chengdu Institute of Biology (CIB), the Chinese Academy of Sciences (CAS). NMR spectra were recorded on a Brucker-500 MHz spectrometer. HPLC analysis was performed on Waters-Breeze (2487 Dual Absorbance Detector and 1525 Binary HPLC Pump) & Shimadzu (SPD-20AV UV-VIS Detector and LC-20AT Liquid Chromatograph Pump). Chiralpak OD, AD, IA were purchased from Daicel Chemical Industries, LTD. The racemic standards used in HPLC studies were prepared according to the general procedure by using racemic BINOL derivatived phosphoric acid catalysts.

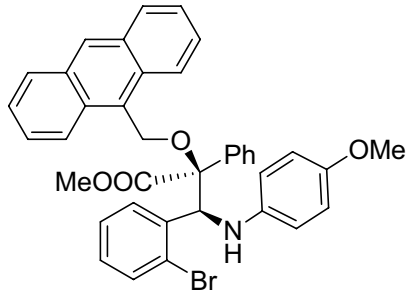
Materials: Dichloromethane was distilled over calcium hydride. Aldehydes, amines and alcohols were purified by recrystalization or distillation before using. Chiral phosphoric acid **5** were prepared according to the literature procedure.[1] Solvents for the column chromatography were distilled before using. Data of compounds **6a, 6b, 6c, 6e, 6i, 6n, 6q, 6s, 6v, 6w** are consistant with those reported previously.[2]

General Procedure for the Enantioselective Four-Component Reactions (Table 3 in the manuscript**):**

A solution of amine (0.25 mmol, 1.0 eq), aldehyde (0.30 mmol, 1.2 eq), chiral phosphoric acid **5** (0.005 mmol，2 mol%), $MgSO_4$ (0.1 g) and 4Å MS (0.1 g) in CH_2Cl_2 (1.5 mL) was stirred for 0.5 ~ 1 h in room temperature. Then $Rh_2(OAc)_4$ (0.005 mmol, 2 mol%), alcohol **2b** (0.25 mmol) were added to the reaction mixture. The reaction mixture was cooled to –20°C. Diazo compound **1** (0.275 mmol) in 1.0 mL CH_2Cl_2 was then added over 1 h period of time *via* a syringe pump. After completion of the addition, the reaction mixture was stirred for additional 1 ~ 3 h and followed by addition of saturated aqueous $NaHCO_3$ (0.1 mL) to quench the reaction. Solvents were removed to give the crude products, which were subjected to ^1H NMR spectroscopy analysis for the determination of diastereoselectivity. The crude products were purified by flash chromatography on silica gel (eluent: EtOAc/light petroleum ether = 1:50 ~ 1:20) to give the pure products.

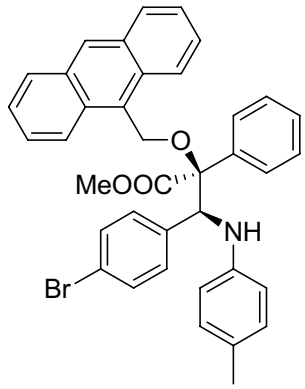


Methyl 2-(9-anthrylmethoxy)-3-(4-methoxyphenylamino)-3-(2-nitrophenyl)-2-phenylpropanoate (6d): yield 81%; $[\alpha]_D^{20}$ = +72.0° (c = 1, EtOAc); 92% ee, determined by HPLC (Daicel Chirapak IA, flow rate 1.0 mL/min, hexane / isopropanol = 80 : 20, 254nm, Retention time: t_{major} = 6.4 min, and t_{minor} = 8.0 min.); ^1H NMR ($CDCl_3$, 500 MHz) δ (ppm) 3.63 (s, 3H), 3.74 (s, 3H), 4.42 (d, *J* = 10.5 Hz, 1H), 5.20 (d, *J* = 10.5 Hz, 1H), 5.53 (d, *J* = 10.5 Hz, 1H), 6.45 (d, *J* = 10.5 Hz, 1H), 6.59 (dd, J_1 = 9.5 Hz, J_2 = 18.5 Hz, 4H), 6.97-7.128 (m, 3H), 7.41-7.63 (m, 10H) , 8.05 (m, 2H), 8. 18 (m, 2H), 8.52 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm) 29.60, 52.33, 55.47, 57.08, 60.63, 87.23, 114.59, 115.51, 123.98, 124.64, 124.91, 126.00, 127.84, 128.01, 128.15, 128.59, 128.80, 128.95, 129.88, 131.08, 131.37, 131.66, 133.31, 135.10, 139.18, 150.64, 152.49, 171.04; HRMS (ESI) calcd for $C_{38}H_{32}KN_2O_6$ $(M+K)^+$ 651.1892, found 651.1895.

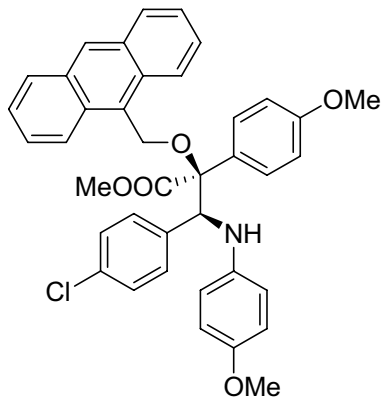


Methyl 2-(9-anthrylmethoxy)-3-(4-methoxyphenylamino)-3-(2-bromophenyl)-2-phenylpropanoate (6f): yield 96%; $[\alpha]_D^{20}$ = +9.9° (c = 1, EtOAc); 97% ee, determined by HPLC (Daicel

Chirapak IA, flow rate 0.5 mL/min, hexane / isopropanol / EtOH / TFA = 450 : 25 : 25 : 1, 254nm, Retention time: t_{major} = 11.4 min, and t_{minor} = 12.0 min.); ^{1}H NMR ($CDCl_3$, 500 MHz) δ (ppm) 3.58 (s, 3H), 3.65 (s, 3H), 4.65 (d, *J* = 9.0 Hz, 1H), 5.10 (d, *J* = 10.0 Hz, 1H), 5.71 (d, *J* = 9.0 Hz, 1H), 5.78 (d, *J* = 10.0 Hz, 1H), 6.41 (d, *J* = 9.0 Hz, 2H), 6.55 (d, *J* = 9.0 Hz, 2H), 6.92-6.96 (m, 2H), 7.32 (m, 2H), 7.45-7.51 (m, 7H), 7.92 (m, 2H), 8.00 (d, *J* = 8.0 Hz, 2H), 8.31 (d, *J* = 8.0 Hz, 2H), 8.46 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm) 51.72, 55.51, 60.39, 62.07, 87.46, 114.52, 115.43, 124.96, 125.00, 125.46, 126.04, 127.34, 128.35, 128.42, 128.81, 128.94, 129.02, 129.16, 130.40, 131.16, 131.50, 132.15, 136.77, 139.11, 139.63, 152.17, 171.53; HRMS (ESI) calcd for $C_{38}H_{32}BrKNO_4$ $(M+K)^+$ 684.1146, found 684.1139.

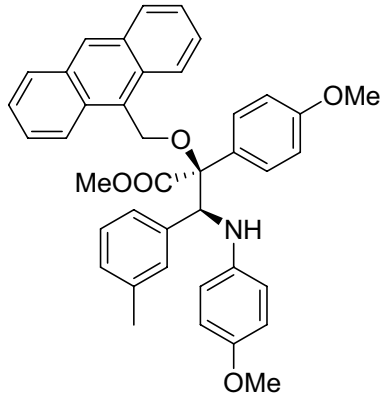


Methyl 2-(9-anthrylmethoxy)-3-(*p*-tolylamino)-3-(4-bromophenyl)-2-phenylpropanoate (6g): yield 85%; $[\alpha]_D^{20}$ = +95.5° (c = 1, EtOAc); 93% ee, determined by HPLC (Daicel Chirapak AD-H, flow rate 1.0 mL/min, hexane / isopropanol = 95 : 5, 254nm, Retention time: t_{major} = 7.0 min, and t_{minor} = 9.0 min.); ^{1}H NMR ($CDCl_3$, 500 MHz) δ (ppm) 2.18 (s, 3H), 3.79 (s, 3H), 4.72 (d, *J* = 10.0 Hz, 1H), 5.20 (d, *J* = 10.0 Hz, 1H), 5.27 (d, *J* = 10.5 Hz, 1H), 5.79 (d, *J* = 10.5 Hz, 1H), 6.38 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 7.03 (d, *J* = 8.5 Hz, 2H), 7.26 (d, *J* = 8.5 Hz, 2H), 7.52-7.61 (m, 7H), 7.87 (m, 2H), 8.11 (d, *J* = 3.5 Hz, 2H), 8.35 (d, *J* = 3.5 Hz, 2H), 8.56 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm) 20.23, 51.94, 60.50, 63.88, 87.50, 114.15, 121.50, 124.78, 124.99, 126.02, 127.08, 128.29, 128.45, 128.69, 128.88, 128.99, 129.12, 129.49, 130.56, 130.68, 130.98, 131.49, 135.85, 137.77, 143.42, 171.41; HRMS (ESI) calcd for $C_{38}H_{32}BrKNO_3$ $(M+K)^+$ 668.1197, found 668.1208.

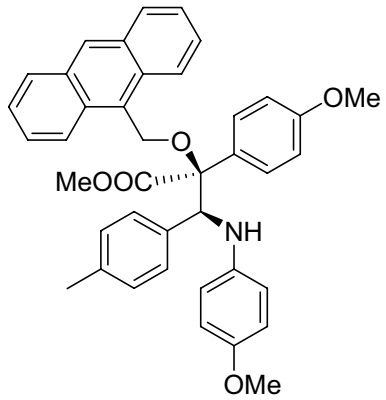


Methyl 2-(9-anthrylmethoxy)-3-(4-methoxyphenylamino)-3-(4-chlorophenyl)-2-(4-methoxyphenyl)propanoate (6h): yield 72%; $[\alpha]_D^{20}$ = +62.3° (c = 1, EtOAc); 95% ee, determined by HPLC (Daicel Chirapak IA, flow rate 1.0 mL/min, hexane / isopropanol / EtOH / TFA = 450 : 25 : 25 : 1, 254nm, Retention time: t_{major} = 8.1 min, and t_{minor} = 12.4 min.); ^{1}H NMR ($CDCl_3$, 500 MHz) δ (ppm) 3.61 (s, 3H), 3.71 (s, 3H), 3.88 (s, 3H), 4.45

(bs, 1H), 5.01 (bs, 1H), 5.17 (d, J = 10.0 Hz, 1H), 5.64 (d, J = 10.5 Hz, 1H), 6.30 (d, J = 9.0 Hz, 2H), 6.55 (d, J = 9.0 Hz, 2H), 6.99 (m, 6H), 7.50 (m, 4H), 7.70 (d, J = 8.5 Hz, 2H), 8.05 (m, 2H), 8.26 (d, J = 8.5 Hz, 2H), 8.50 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm) 51.96, 55.36, 55.60, 64.85, 87.34, 113.57, 114.63 115.50, 124.89, 125.04, 126.04, 127.64, 127.95, 128.42, 128.92, 130.38, 130.63, 131.05, 131.56, 133.18, 137.37, 140.02, 152.31, 159.94, 171.67; HRMS (ESI) calcd for $C_{39}H_{34}ClKNO_5$ $(M+K)^+$ 670.1757, found 670.1750;

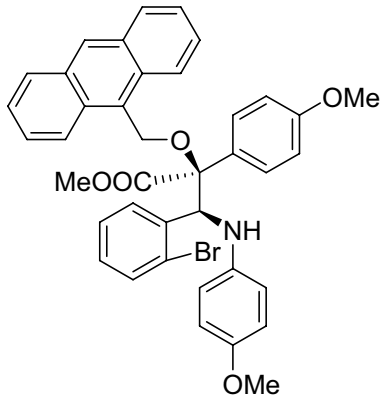


Methyl 2-(9-anthrylmethoxy)-3-(4-methoxyphenylamino)-2-(4-methoxyphenyl)-3-*m*-tolylpropanoate (6j): yield 62%; 92% ee, determined by HPLC (Daicel Chirapak IA, flow rate 1.0 mL/min, hexane / isopropanol / EtOH / TFA = 450 : 25 : 25 : 1, 254nm, Retention time: t_{major} = 6.4 min, and t_{minor} = 8.1 min.); ^{1}H NMR ($CDCl_3$, 500 MHz) δ (ppm) 2.08 (s, 3H), 3.61 (s, 3H), 3.68 (s, 3H), 3.88 (s, 3H), 4.55 (bs, 1H), 5.01 (bs, 1H), 5.18 (d, J = 10.5 Hz, 1H), 5.68 (d, J = 10.5 Hz, 1H), 6.35 (d, J = 9.0 Hz, 2H), 6.56 (d, J = 8.5 Hz, 2H), 6.84-6.97 (m, 6H), 7.49-7.51 (m, 4H), 7.74 (d, J = 8.5 Hz, 2H), 8.03 (m, 2H), 8.29 (d, J = 9.0 Hz, 2H), 8.49 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm) 21.28, 51.73, 55.30, 55.56, 60.12, 65.24, 87.46, 113.38, 114.54, 115.28, 124.94, 124.98, 125.96, 126.07, 127.14, 128.14, 128.25, 128.47, 128.79, 129.18, 129.78, 130.69, 131.05, 136.75, 138.66, 140.46, 151.98, 159.76, 171.86; HRMS (ESI) calcd for $C_{40}H_{37}KNO_5$ $(M+K)^+$ 650.2303, found 650.2297.

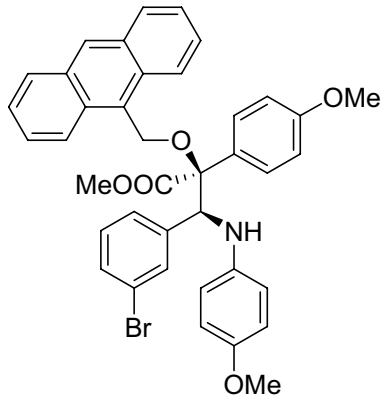


Methyl 2-(9-anthrylmethoxy)-3-(4-methoxyphenylamino)-2-(4-methoxyphenyl)-3-*p*-tolylpropanoate (6k): yield 54%; 91% ee, determined by HPLC (Daicel Chirapak IA, flow rate 1.0 mL/min, hexane / isopropanol / EtOH / TFA = 400 : 50 : 50 : 1, 254nm, Retention time: t_{minor} = 6.2 min, and t_{major} = 8.2 min.); ^{1}H NMR ($CDCl_3$, 500 MHz) δ (ppm) 2.21 (s, 3H), 3.60 (s, 3H), 3.67 (s, 3H), 3.87 (s, 3H), 4.53 (d, J = 9.5 Hz, 1H), 4.99 (d, J = 9.0 Hz, 1H), 5.15 (d, J = 10.5 Hz, 1H), 5.67 (d, J = 10.5 Hz, 1H), 6.32 (d, J = 9.0 Hz, 2H), 6.54 (d, J = 8.5 Hz, 2H), 6.85-6.96 (m, 6H), 7.47-7.52 (m, 4H), 7.74 (d, J = 8.0 Hz, 2H), 8.02 (m, 2H), 8.28 (d, J = 8.0 Hz, 2H), 8.49 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz)

δ (ppm) 21.10, 57.76, 55.31, 55.58, 60.22, 65.04, 87.55, 113.44, 114.55, 115.31, 124.98, 125.05, 125.92, 128.18, 128.25, 128.58, 128.81, 128.88, 129.21, 130.68, 131.07, 131.53, 135.73, 136.86, 140.48, 159.77, 171.91; HRMS (ESI) calcd for $C_{40}H_{37}NNaO_5$ $(M+Na)^+$ 634.2564, found 634.2547.

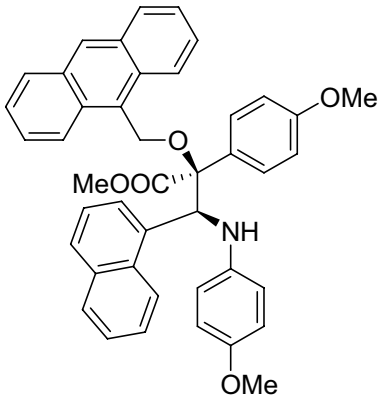


Methyl 2-(9-anthrylmethoxy)-3-(4-methoxyphenylamino)-3-(2-bromophenyl)-2-(4-methoxyphenyl)propanoate (6l): yield 79%; $[\alpha]_D^{20}$ = -15.8° (c = 1, EtOAc); 95% ee, determined by HPLC (Daicel Chirapak IA, flow rate 0.6 mL/min, hexane / isopropanol / EtOH / TFA = 450 : 25 : 25 : 1, 254nm, Retention time: t_{major} = 11.1 min, and t_{minor} = 11.9 min.); ^{1}H NMR ($CDCl_3$, 500 MHz) δ (ppm) 3.63 (s, 3H), 3.66 (s, 3H), 3.90 (s, 3H), 4.70 (bs, 1H), 5.12 (d, *J* = 10.0 Hz, 1H), 5.70 (bs, 1H), 5.78 (d, *J* = 10.0 Hz, 1H), 6.45 (d, *J* = 9.0 Hz, 2H), 6.59 (d, *J* = 9.0 Hz, 2H), 6.96-7.03 (m, 4H), 7.35 (m, 2H), 7.53 (m, 4H), 7.87 (d, *J* = 9.0 Hz, 2H), 8.05 (d, *J* = 8.0 Hz, 2H), 8.35 (d, *J* = 8.0 Hz, 2H), 8.52 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm) 51.71, 55.34, 55.58, 60.22, 62.07, 87.13, 113.68, 114.58, 115.45, 125.03, 125.05, 125.50, 126.07, 127.40, 128.38, 128.83, 128.96, 128.98, 129.01, 130.46, 130.57, 131.22, 131.56, 132.18, 139.69, 152.17, 159.97, 171.82; HRMS (ESI) calcd for $C_{39}H_{34}BrKNO_5$ $(M+K)^+$ 714.1252, found 714.1254.

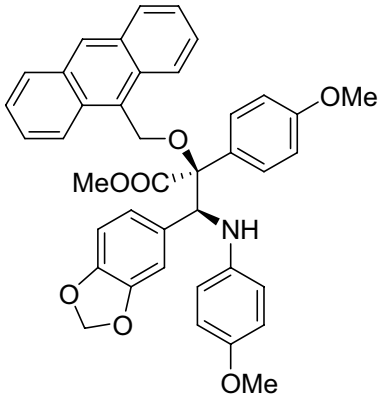


Methyl 2-(9-anthrylmethoxy)-3-(4-methoxyphenylamino)-3-(3-bromophenyl)-2-(4-methoxyphenyl)propanoate (6m): yield 61%; $[\alpha]_D^{20}$ = +13.2° (c = 1, EtOAc); 97% ee, determined by HPLC (Daicel Chirapak IA, flow rate 1.0 mL/min, hexane / isopropanol / EtOH / TFA = 400 : 50 : 50 : 1, 254nm, Retention time: t_{major} = 6.9 min, and t_{minor} = 8.0 min.); ^{1}H NMR ($CDCl_3$, 500 MHz) δ (ppm) 3.60 (s, 3H), 3.70 (s, 3H), 3.87 (s, 3H), 4.44 (d, *J* = 9.0 Hz, 1H), 4.98 (d, *J* = 9.0 Hz, 1H) 5.19 (d, *J* = 10.5 Hz, 1H), 5.66 (d, *J* = 10.5 Hz, 1H), 6.31 (d, *J* = 8.5 Hz, 2H), 6.55 (d, *J* = 8.5 Hz, 2H), 6.89-6.96 (m, 4H), 7.23 (m, 2H), 7.46-7.53 (m, 4H), 7.68 (d, *J* = 8.5 Hz, 2H), 8.02 (d, *J* = 8.0 Hz, 2H), 8.25 (d, *J* = 8.5 Hz, 2H), 8.48 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm) 51.85, 55.34, 55.59, 60.36,

65.21, 87.42, 113.57, 114.68, 115.47, 121.59, 124.81, 124.97, 126.13, 127.59, 127.94, 128.37, 128.86, 128.91, 128.97, 130.51, 130.62, 131.04, 131.55, 132.09, 140.01, 141.36, 152.39, 159.99, 171.54; HRMS (ESI) calcd for $C_{39}H_{34}BrKNO_5$ $(M+K)^+$ 714.1252, found 714.1244.

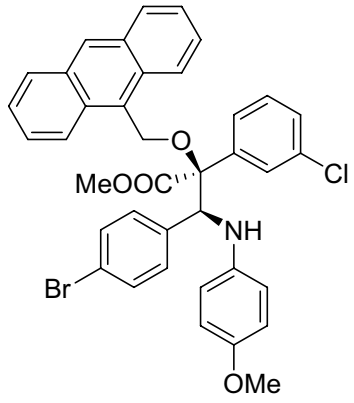


Methyl 2-(9-anthrylmethoxy)-3-(4-methoxyphenylamino)-2-(4-methoxyphenyl)-3-(1-naphthyl)propanoate (6o): yield 42%; $[\alpha]_D^{20}$ = -120.0° (c = 1, EtOAc); 96% ee, determined by HPLC (Daicel Chirapak IA, flow rate 1.0 mL/min, hexane / isopropanol / EtOH / TFA = 450 : 25 : 25 : 1, 254nm, Retention time: t_{major} = 7.4 min, and t_{minor} = 8.3 min.); ^{1}H NMR ($CDCl_3$, 500 MHz) δ (ppm) 3.36 (s, 3H), 3.55 (s, 3H), 3.89 (s, 3H), 4.60 (bs, 1H), 5.17 (d, *J* = 10.5 Hz, 1H), 5.58 (d, *J* = 10.5 Hz, 1H), 6.10 (bs, 1H), 6.34 (d, *J* = 9.0 Hz, 2H), 6.47 (d, *J* = 9.0 Hz, 2H), 6.96 (d, *J* = 9.0 Hz, 2H), 7.11-7.25 (m, 4H), 7.50 (m, 4H), 7.59 (m, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 8.5 Hz, 2H), 8.02 (m, 2H), 8.22 (d, *J* = 9.0 Hz, 1H), 8.27 (d, *J* = 9.5 Hz, 2H), 8.46 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm) 51.66, 55.35, 55.53, 60.25, 87.72, 113.40, 114.57, 115.26, 124.05, 124.75, 124.93, 124.99, 125.26, 125.93, 127.97, 128.28, 128.31, 128.82, 128.86, 130.86, 131.01, 131.47, 132.49, 133.14, 135.33, 140.25, 152.10, 159.85, 171.74; HRMS (ESI) calcd for $C_{43}H_{37}KNO_5$ $(M+K)^+$ 686.2303, found 686.2287.

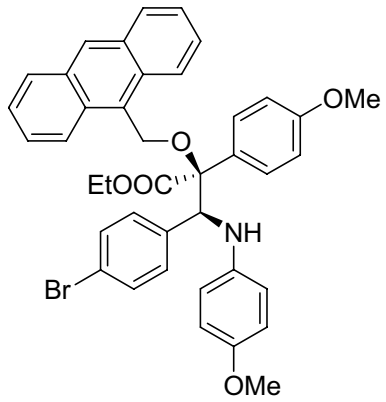


Methyl 2-(9-anthrylmethoxy)-3-(4-methoxyphenylamino)-3-(5-benzo[*d*][1,3]dioxolyl)-2-(4-methoxyphenyl)propanoate (6p): yield 68%; 92% ee, determined by HPLC (Daicel Chirapak IA, flow rate 1.0 mL/min, hexane / isopropanol / EtOH / TFA = 450 : 25 : 25 : 1, 254nm, Retention time: t_{major} = 12.0 min, and t_{minor} = 14.4 min.); ^{1}H NMR ($CDCl_3$, 500 MHz) δ (ppm) 3.61 (s, 3H), 3.71 (s, 3H), 3.88 (s, 3H), 4.49 (d, *J* = 7.5 Hz, 1H), 4.94 (d, *J* = 7.5 Hz, 1H), 5.16 (d, *J* = 10.5 Hz, 1H), 5.69 (d, *J* = 10.5 Hz, 1H), 5.81 (s, 1H), 5.86 (s, 1H), 6.32 (d, *J* = 9.0 Hz, 2H), 6.55 (m, 4H), 6.62 (s, 1H), 6.96 (d, *J* = 9.0 Hz, 2H), 7.47-7.53 (m, 4H), 7.76 (d, *J* = 8.5 Hz, 2H), 8.03 (d, *J* = 8.0 Hz, 2H), 8.28 (d, *J* = 8.5 Hz, 2H), 8.49 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm) 51.82, 55.30, 55.56, 60.25,

65.00, 87.53, 100.72, 107.09, 109.26, 113.47, 114.54, 115.32, 122.65, 124.91, 124.97, 126.00, 128.28, 128.44, 128.82, 129.06, 130.63, 131.02, 131.50, 132.79, 140.23, 146.74, 147.03, 152.06, 159.80, 171.81; HRMS (ESI) calcd for $C_{40}H_{35}KNO_7$ $(M+K)^+$ 680.2045, found 680.2041.

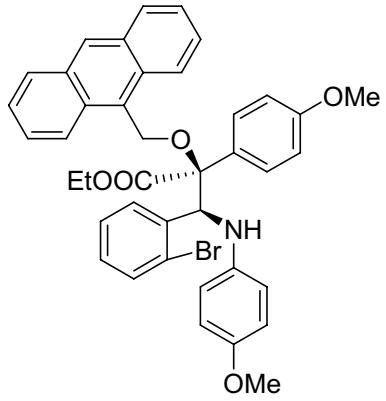


Methyl 2-(9-anthrylmethoxy)-3-(4-methoxyphenylamino)-3-(4-bromophenyl)-2-(3-chlorophenyl)propanoate (6r): yield 75%; 87% ee, determined by HPLC (Daicel Chirapak AD-H, flow rate 1.0 mL/min, hexane / isopropanol / EtOH / TFA = 490 : 10 : 10 : 1, 254nm, Retention time: t_{major} = 12.7 min, and t_{minor} = 18.2 min.); ^{1}H NMR ($CDCl_3$, 500 MHz) δ (ppm) 3.62 (s, 3H), 3.80 (s, 3H), 4.32 (bs, 1H), 4.99 (bs, 1H), 5.29 (d, *J* = 10.5 Hz, 1H), 5.71 (d, *J* = 10.5 Hz, 1H), 6.35 (d, *J* = 9.0 Hz, 2H), 6.58 (d, *J* = 8.5 Hz, 2H), 6.94 (d, *J* = 8.5 Hz, 2H), 7.23 (d, *J* = 8.5 Hz, 2H), 7.38-7.59 (m, 6H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.83 (s, 1H), 8.07 (d, *J* = 8.5 Hz, 2H), 8.30 (d, *J* = 9.0 Hz, 2H), 8.52 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm) 52.13, 55.45, 60.69, 65.53, 87.21, 114.49, 115.75, 121.63, 124.59, 125.00, 126.20, 127.28, 128.23, 128.61, 128.91, 129.03, 129.33, 129.36, 130.53, 130.61, 130.88, 131.44, 134.25, 137.24, 137.83, 139.77, 152.51, 170.76; HRMS (ESI) calcd for $C_{38}H_{31}BrClKNO_4$ $(M+K)^+$ 718.0757, found 718.0735.



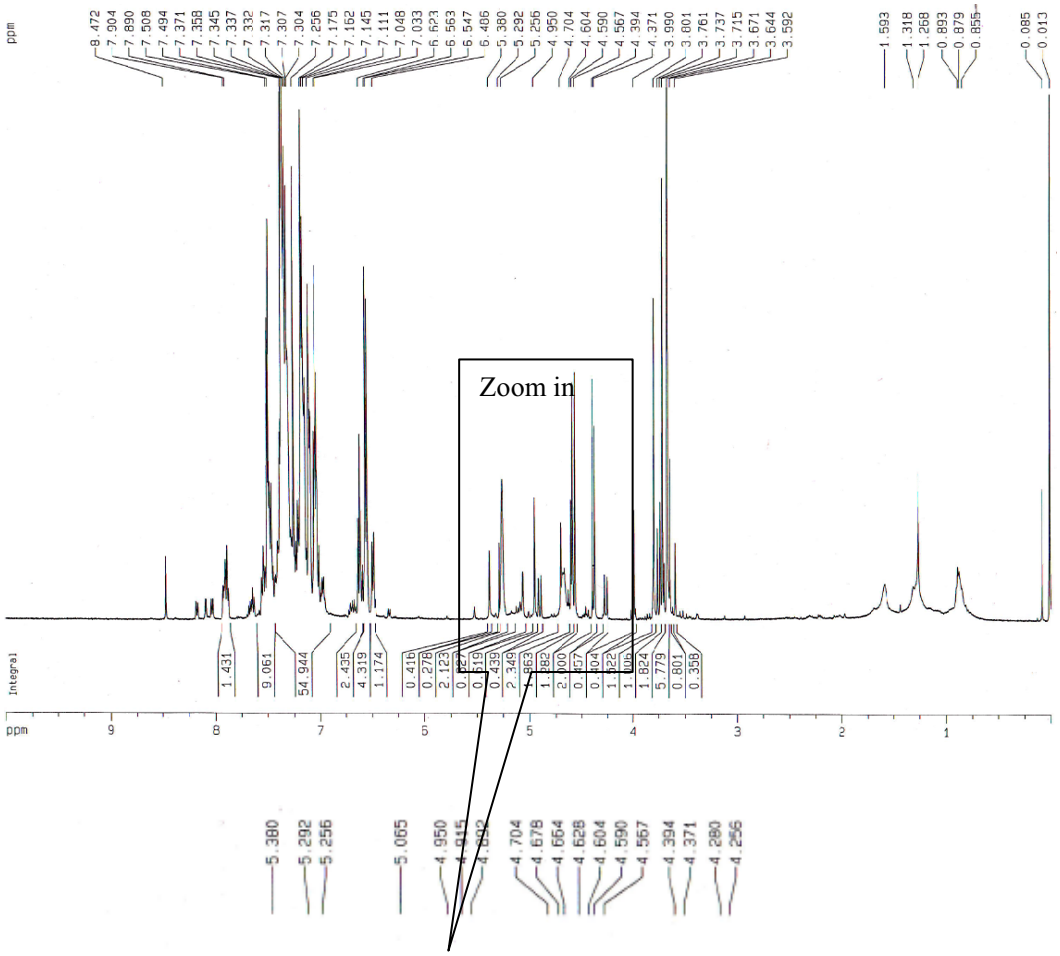
Ethyl 2-(9-anthrylmethoxy)-3-(4-methoxyphenylamino)-3-(4-bromophenyl)-2-(4-methoxyphenyl)propanoate (6t): yield 87%;91% ee, determined by HPLC (Daicel Chirapak IA, flow rate 1.0 mL/min, hexane / isopropanol / EtOH / TFA = 450 : 25 : 25 : 1, 254nm, Retention time: t_{major} = 7.3 min, and t_{minor} = 13.8 min.); ^{1}H NMR ($CDCl_3$, 500 MHz) δ (ppm) 1.26 (t, *J* = 14.0, 3H), 3.58 (s, 3H), 3.86 (s, 3H), 4.12 (m, 1H), 4.25 (m, 1H), 4.50 (d, *J* = 9.5 Hz, 1H), 5.00 (d, *J* = 9.5 Hz, 1H), 5.17 (d, *J* = 10.0 Hz, 1H), 5.61 (d, *J* = 10.5 Hz, 1H), 6.31 (d, *J* = 9.0 Hz, 2H), 6.54 (d, *J* = 9.0 Hz, 2H), 6.91 (d, *J* = 8.0 Hz, 2H), 6.95 (d, *J* = 9.0 Hz, 2H), 7.14 (d, *J* = 8.5 Hz, 2H), 7.46-7.52 (m, 4H), 7.71 (d, *J* = 8.5 Hz, 2H), 8.01 (d, *J* = 8.0 Hz, 2H), 8.29 (d, *J* = 8.5 Hz, 2H), 8.46 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm) 14.06, 55.27, 55.50, 60.23, 61.46, 64.98, 87.02, 113.42, 114.52, 115.41, 121.34, 124.88,

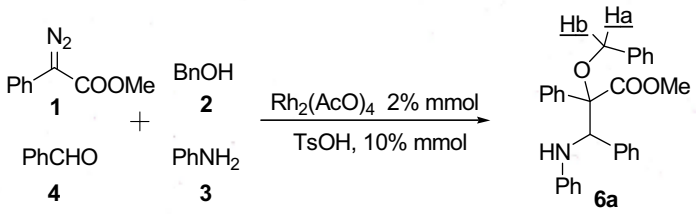
124.98, 125.93, 127.89, 128.36, 128.87, 130.44, 130.60, 130.76, 130.96, 131.46, 137.80, 139.99, 152.21, 159.78, 171.07; HRMS (ESI) calcd for $C_{40}H_{36}BrKNO_5$ $(M+K)^+$ 728.1408, found 728.1417.



Ethyl 2-(9-anthrylmethoxy)-3-(4-methoxyphenylamino)-3-(2-bromophenyl)-2-(4-methoxyphenyl)propanoate (6u): yield 90%; $[\alpha]_D^{20}$ = -14.7° (c = 1, EtOAc); 97% ee, determined by HPLC (Daicel Chirapak IA, flow rate 1.0 mL/min, hexane / isopropanol / EtOH / TFA = 450 : 25 : 25 : 1, 254nm, Retention time: t_{minor} = 5.6 min, and t_{major} = 6.4 min.); ^{1}H NMR ($CDCl_3$, 500 MHz) δ (ppm) 1.25 (t, *J* = 14.0, 3H), 3.60 (s, 3H), 3.88 (s, 3H), 4.05 (m, 1H), 4.22 (m, 1H), 4.56 (d, *J* = 10.5 Hz, 1H), 5.14 (d, *J* = 10.5 Hz, 1H), 5.67-5.70 (m, 2H), 6.41 (d, *J* = 9.0 Hz, 1H), 6.56 (d, *J* = 9.0 Hz, 2H), 6.92-6.99 (m, 4H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.48-7.51 (m, 4H), 7.83 (d, *J* = 8.5 Hz, 2H), 8.02 (d, *J* = 9.0 Hz, 2H), 8.35 (d, *J* = 9.0 Hz, 2H), 8.49 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ (ppm) 13.99, 55.30, 55.55, 60.28, 61.41, 62.42, 87.13, 113.51, 114.51, 115.64, 125.00, 125.13, 125.70, 125.94, 127.18, 128.35, 128.80, 128.89, 129.01, 130.39, 130.61, 131.15, 131.51, 132.14, 139.26, 139.78, 152.14, 159.83, 171.20; HRMS (ESI) calcd for $C_{40}H_{36}BrKNO_5$ $(M+K)^+$ 728.1408, found 728.1392.

Fig . Diastereocontrol measurement of **6a** by ^{1}H NMR spectroscopy of the crude reaction mixture





^{1}H NMR spectroscopy of the crude reaction mixture

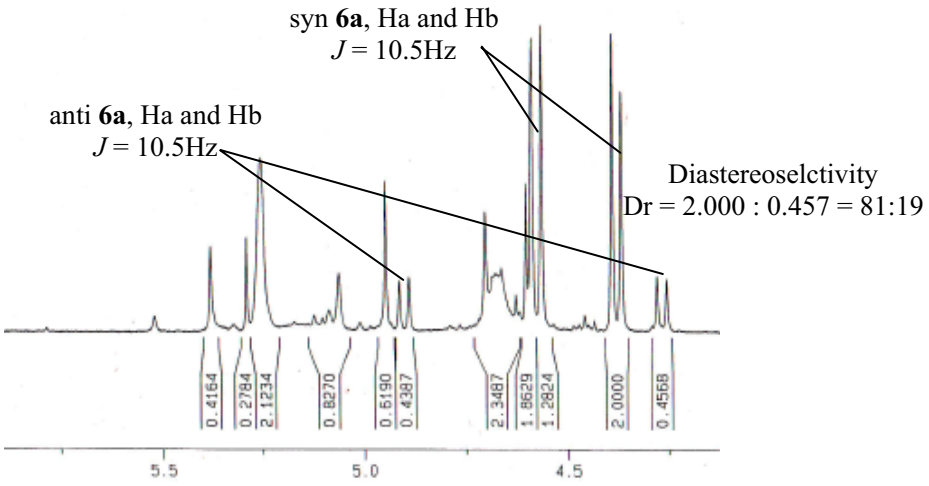
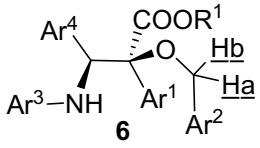


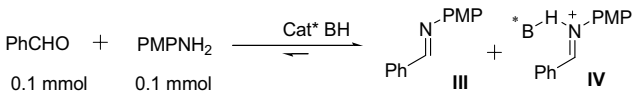
Table . Diastereocontrol measurement by ^{1}H NMR spectroscopy of the crude reaction mixture



6

Entry	**6**	Dr	δ_{syn} Ha and Hb (ppm)	J_{syn} (Hz)	δ_{anti} Ha and Hb (ppm)	J_{anti} (Hz)
1	**6a**	81:19	4.38, 4.61	10.5	4.27, 4.90	10.5
2	**6d**	82:18	5.19, 5.52	10.2	4.98, 5.85	10.2
3	**6g**	95:5	5.17, 5.69	10.5	4.97, 5.79	10.5
4	**6w**	95:5	5.34, 5.54	11.0	5.23, 5.80	11.0

Table 1. Effect of phosphoric acid **5** in promoting the equilibrium to imine formation.[a]

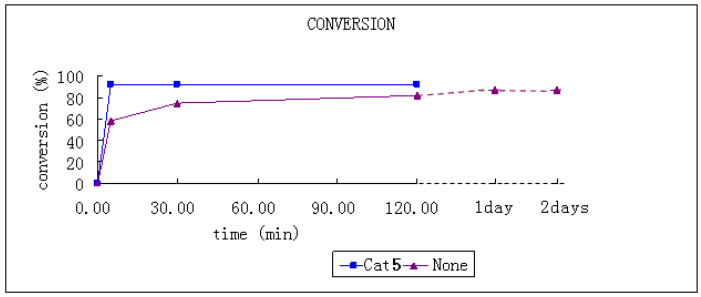


0.1 mmol 0.1 mmol

Time	Conversion (%) [b]	
	Cat = None	Cat = Cat **5** (2 mol%)
0	0	0
5 mins	58	92
30 mins	75	92
2 hrs	82	92
1 day	89	-[c]
2 days	88	-[c]

[a] The reaction was carried out in NMR tube with 0.5 ml CD2Cl2. [b] Determined by 1H NMR spectroscopy of the reaction mixture in the NMR tube. [c] Not determined.

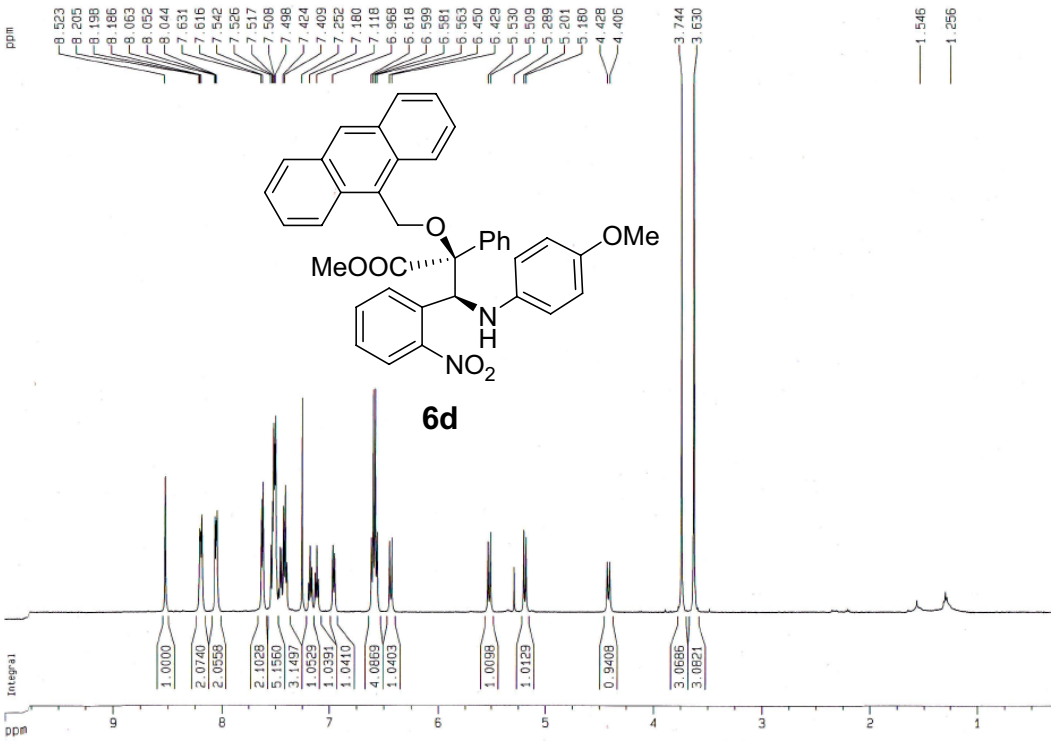
Fig 1. Effect of phosphoric acid **5** in promoting the equilibrium to imine formation.



Reference and notes:

1 (a) D. Uraguchi and M. Terada, *J. Am. Chem. Soc.*, 2004, **126**, 5356; (b) T. Akiyama, H. Morita, J. Itoh and K. Fuchibe, *Org. Lett.*, 2005, **7**, 2583; (c) R. I. Storer, D. E. Carrera, Y. Ni and D. W. C. MacMillan, *J. Am. Chem. Soc.*, 2006, **128**, 84; (d) D. Uraguchi, K. Sorimachi and M. Terada, *Angew. Chem. Int. Ed.*, 2006, **45**, 2254; (e) M. Yamanaka, I. Junji, K. Fuchibe and T. Akiyama, *J. Am Chem. Soc.*, 2007, **129**, 6756; (f) Q.-X. Guo, H. Liu, C. Guo, S.-W. Luo, Y. Gu and L.-Z. Gong, *J. Am. Chem. Soc.*, 2007, **129**, 3790; (g) J. Jiang, J. Yu, X.-X. Sun, Q.-Q. Rao and L.-Z. Gong, *Angew. Chem. Int. Ed.*, 2008, **47**, 2458; (h) T. Masahiro, U. Daisuke, S. Keiichi and S. Hideo, *PCT Int. Appl.,* 2005, WO2005070875.

2 (a) C.-D. Lu, H. Liu, Z.-Y. Chen, W.-H. Hu and A.-Q. Mi, *Org. Lett.*, 2005, **7**, 83; (b) W.-H. Hu, X.-F. Xu, J. Zhou, W.-J. Liu, H.-X. Huang, J. Hu, L.-P. Yang and L.-Z. Gong, *J. Am. Chem. Soc.*, 2008, **130**, 7782; (c) H.-X. Huang, X. Guo and W.-H. Hu, *Angew. Chem. Int. Ed.*, 2007, **46**, 1337.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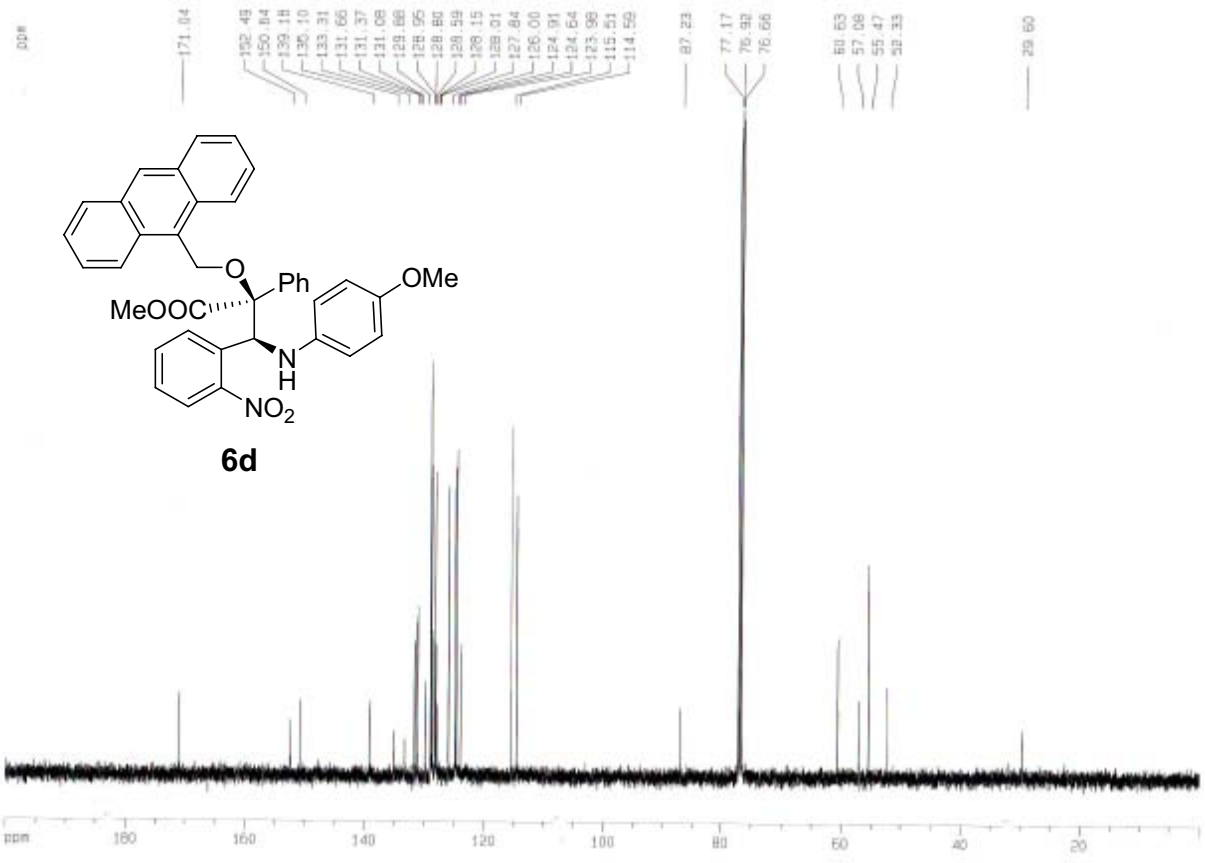
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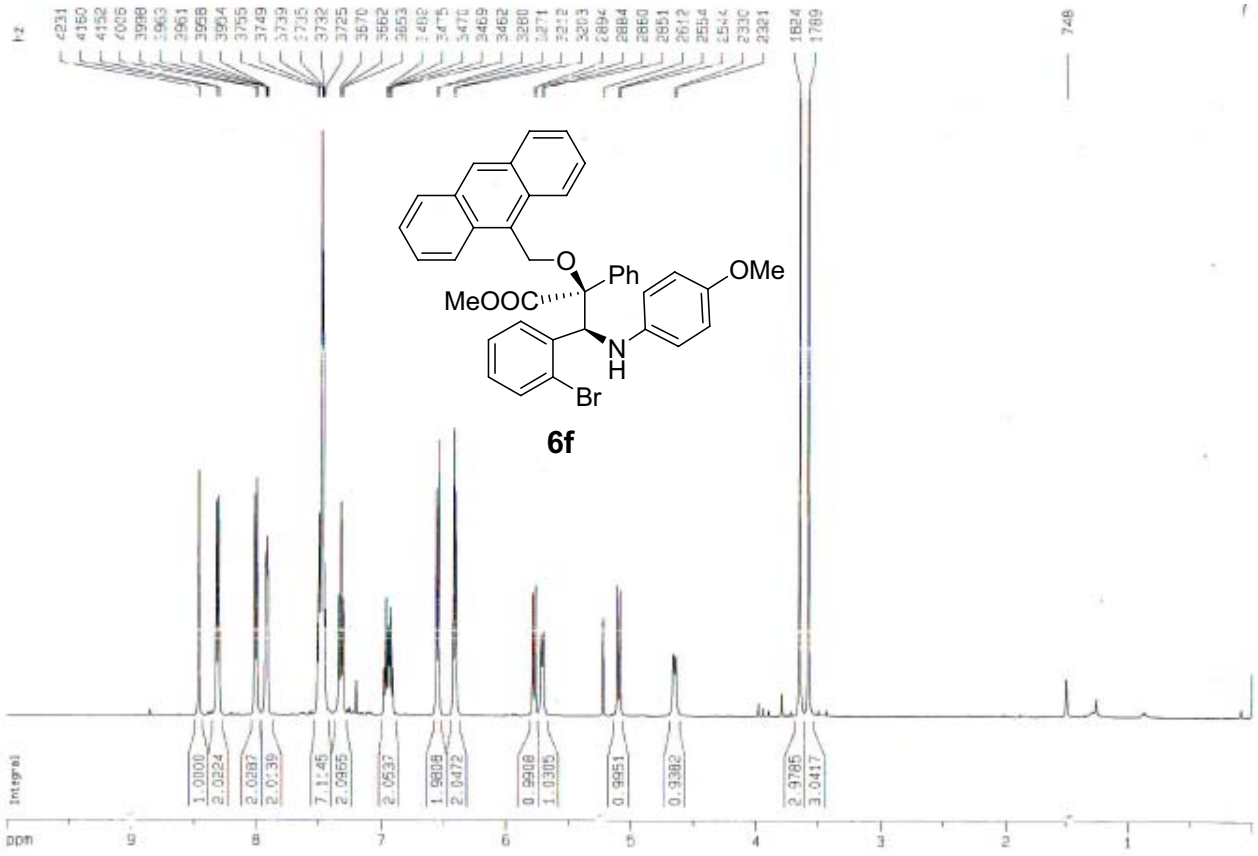

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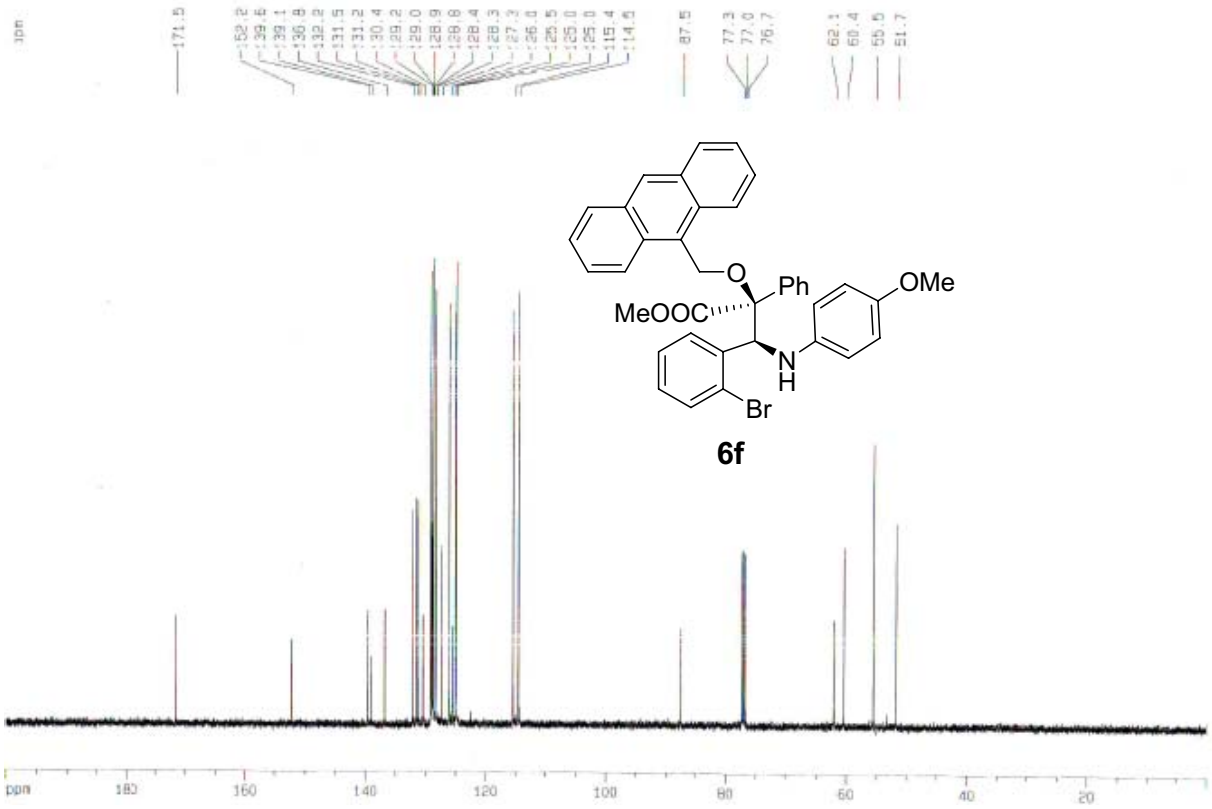

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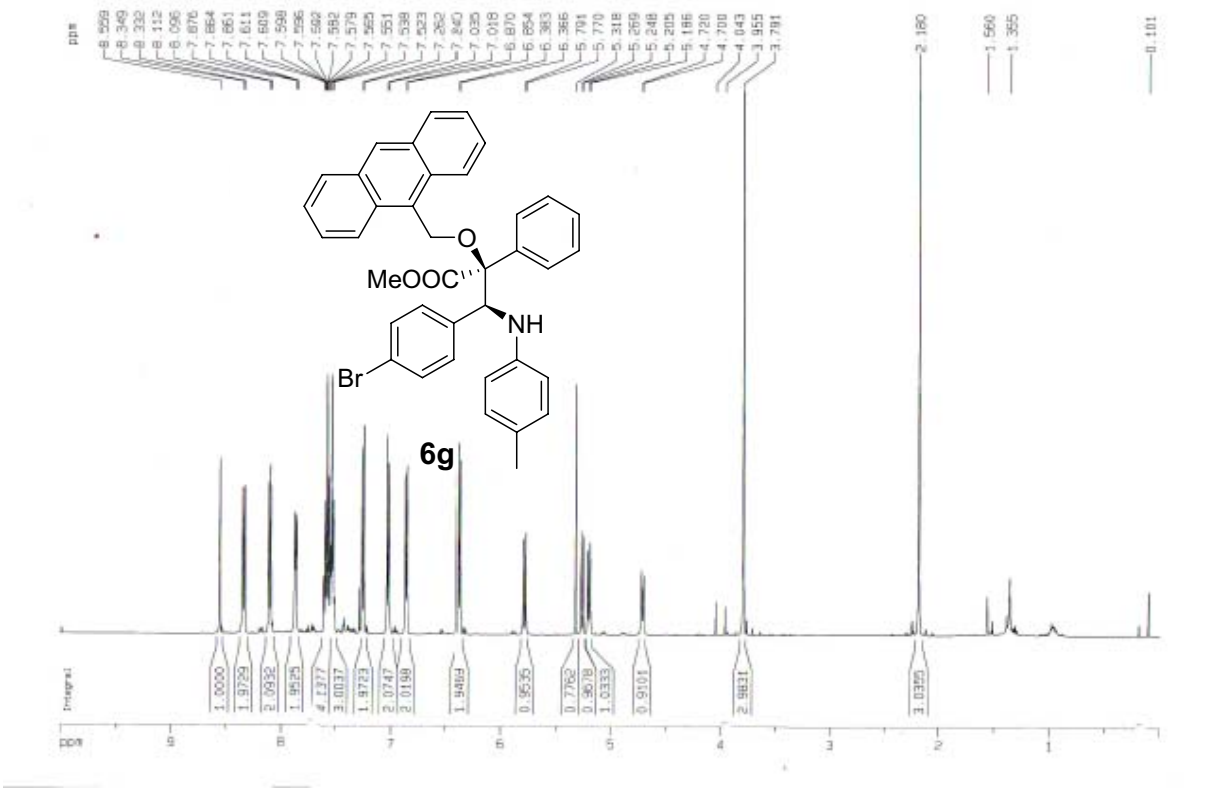
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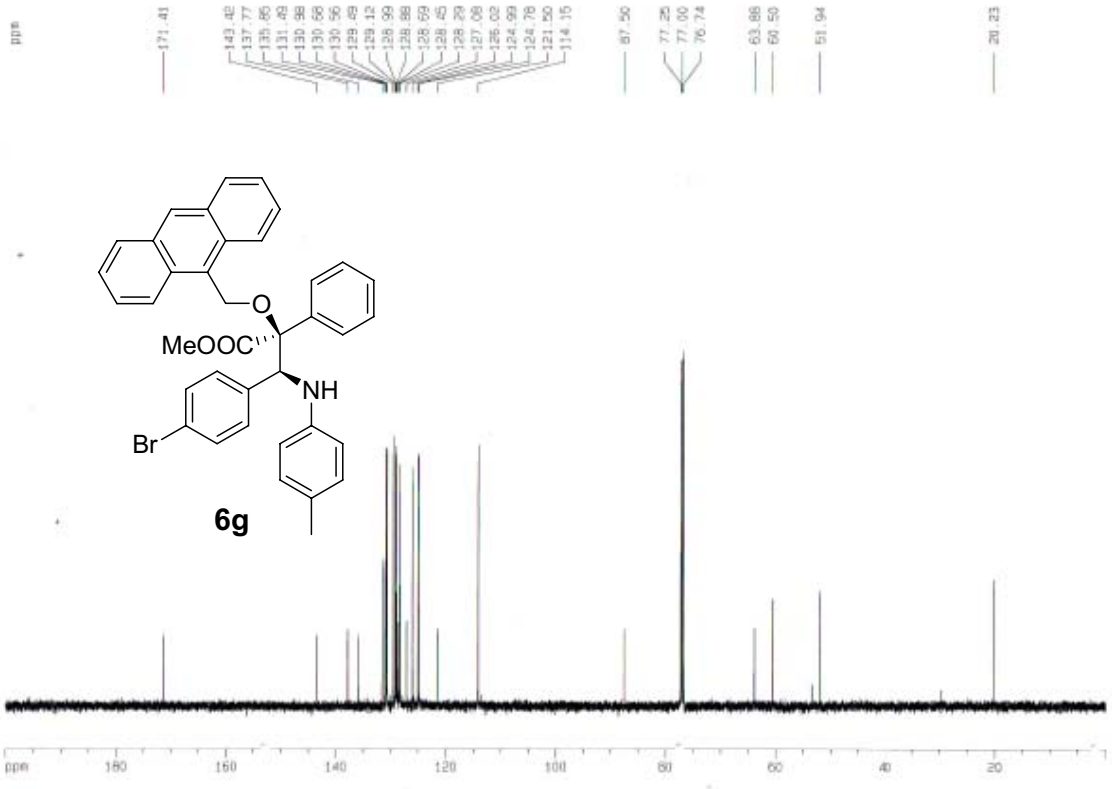
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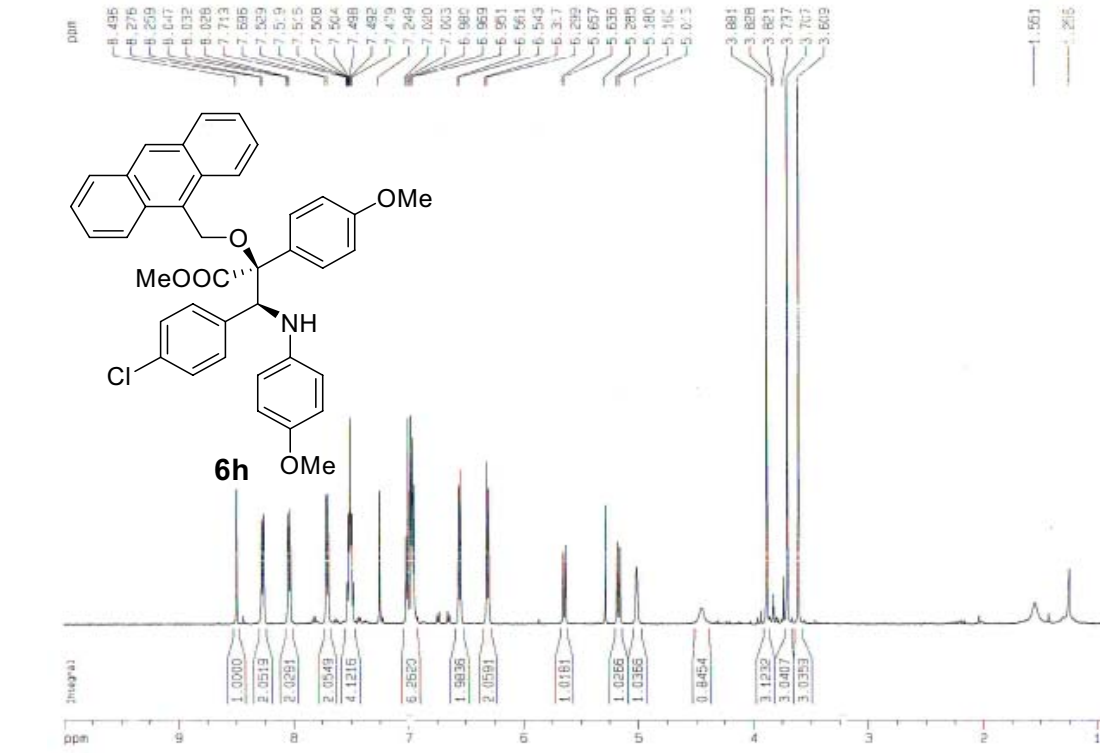
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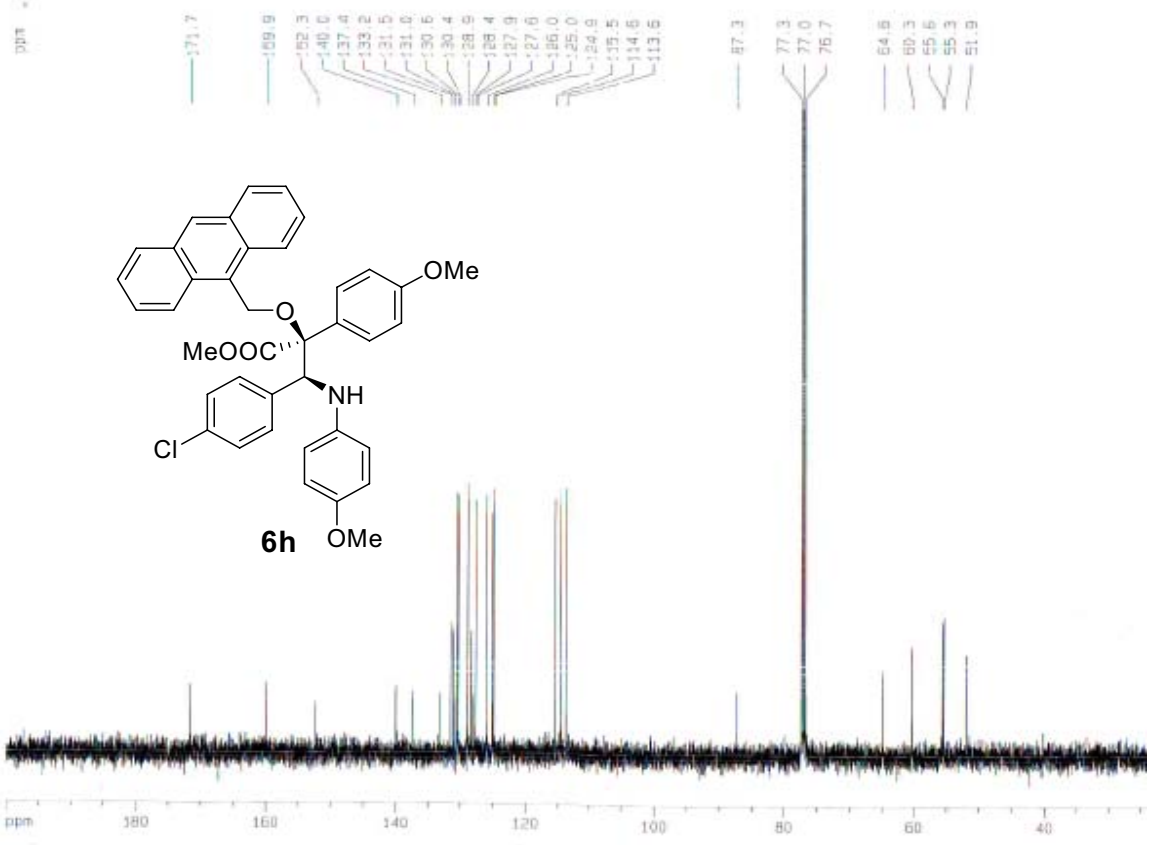
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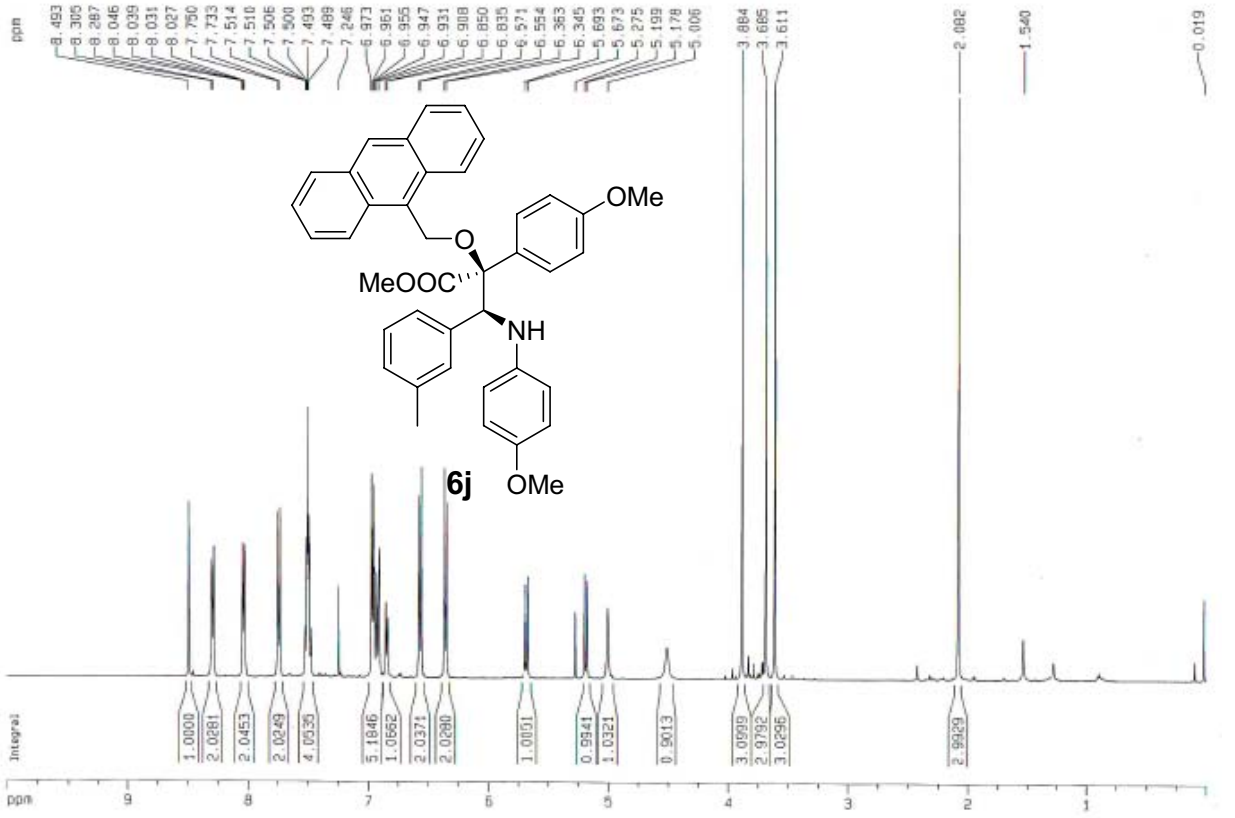
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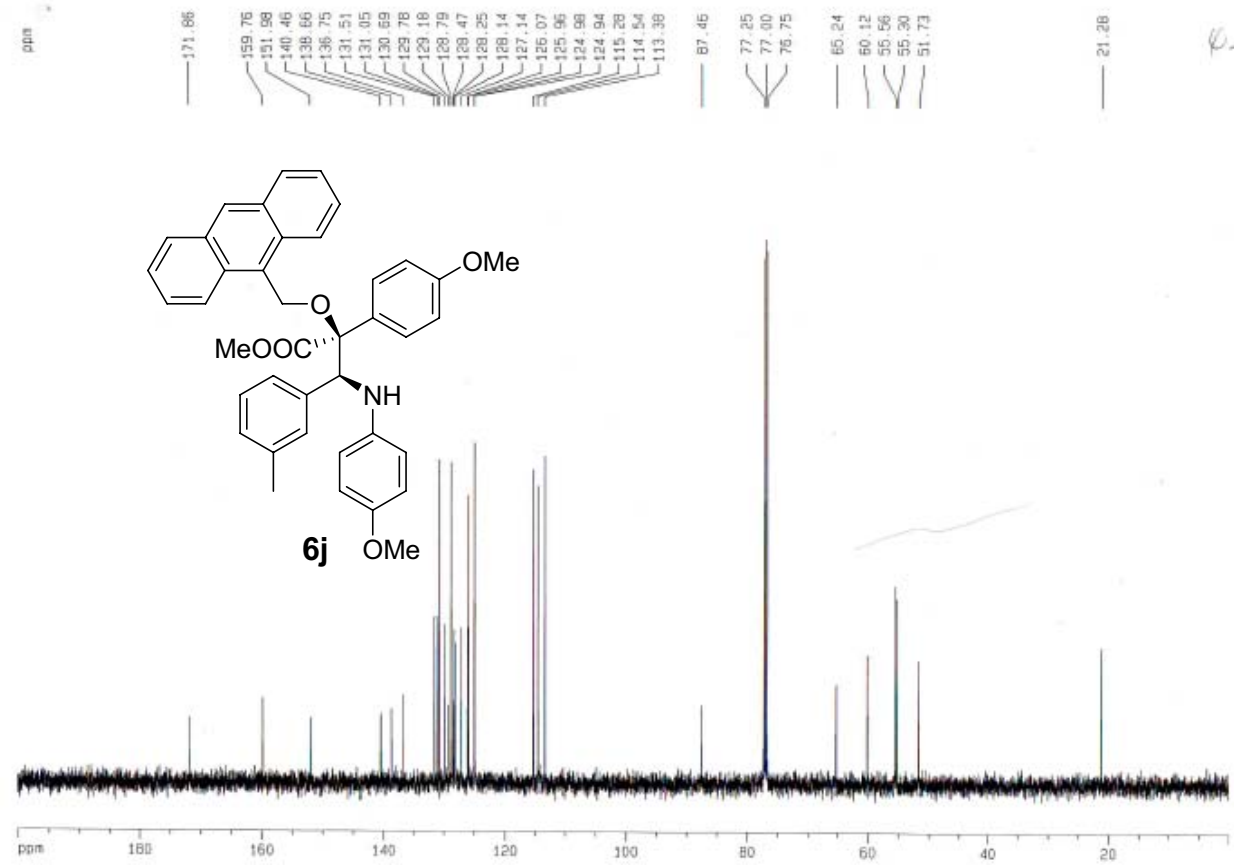
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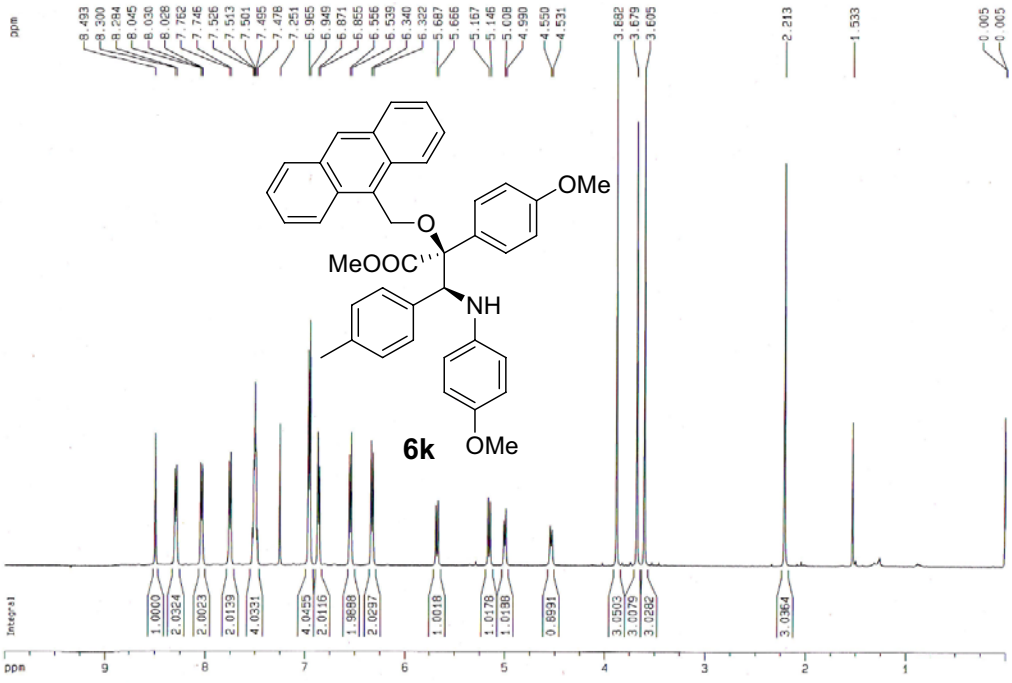
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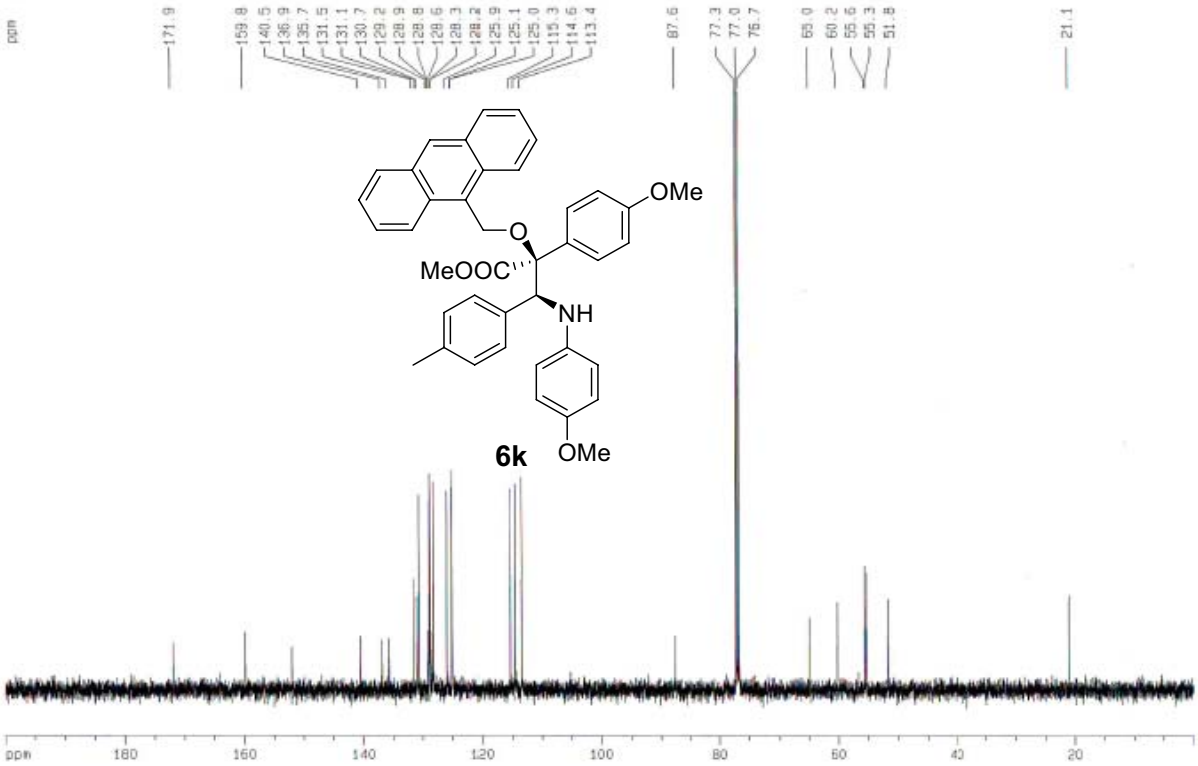
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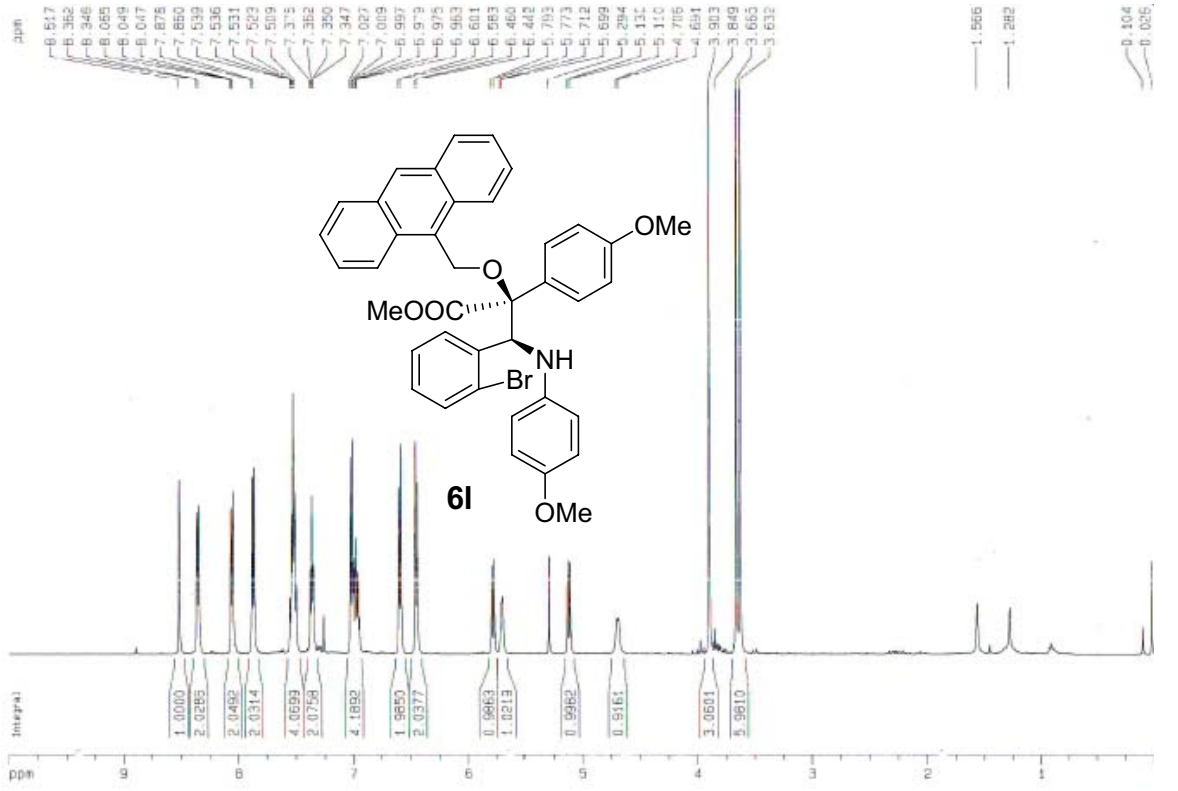
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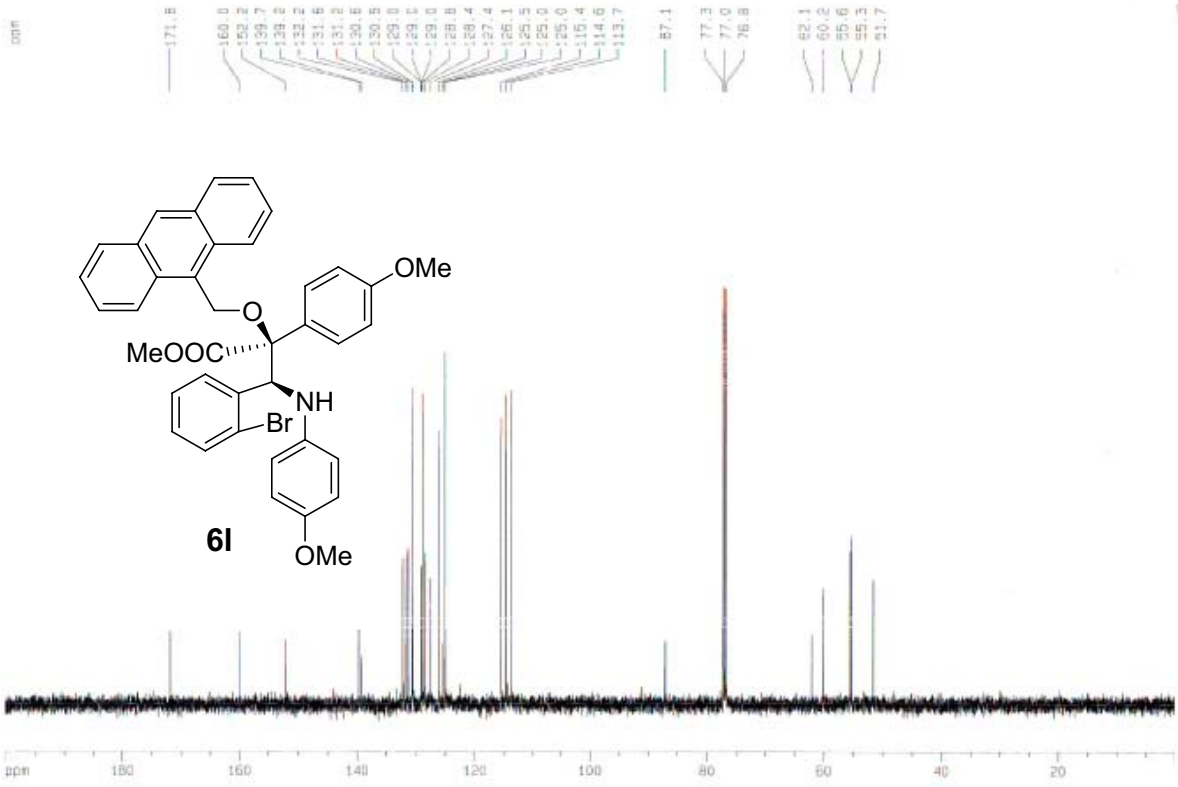
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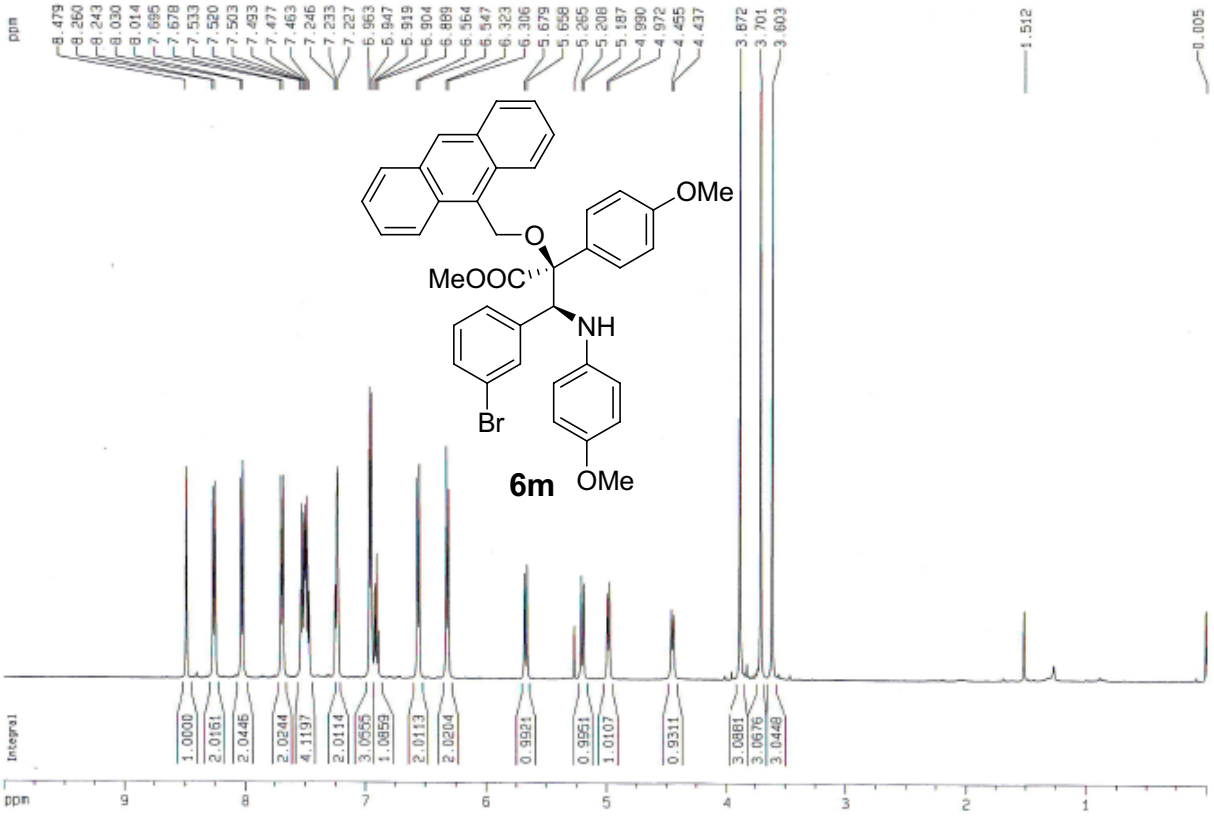
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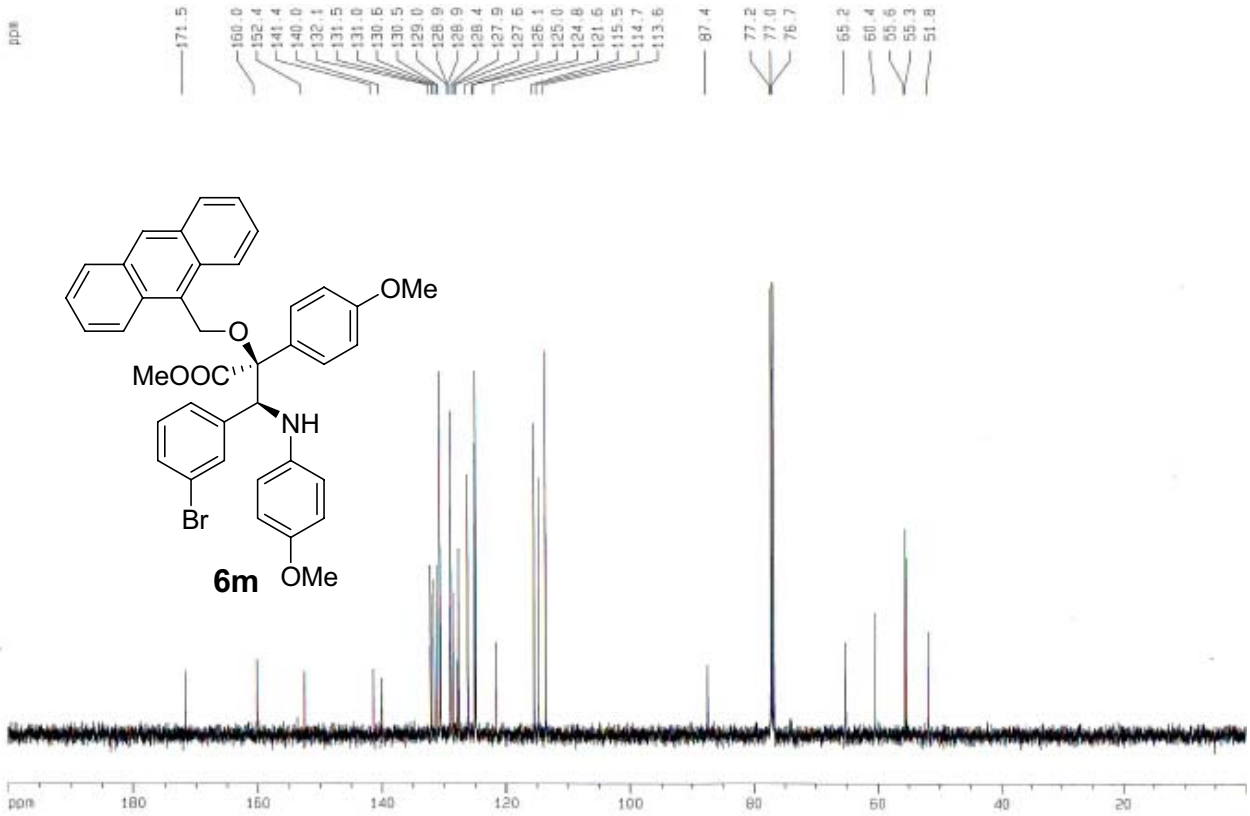
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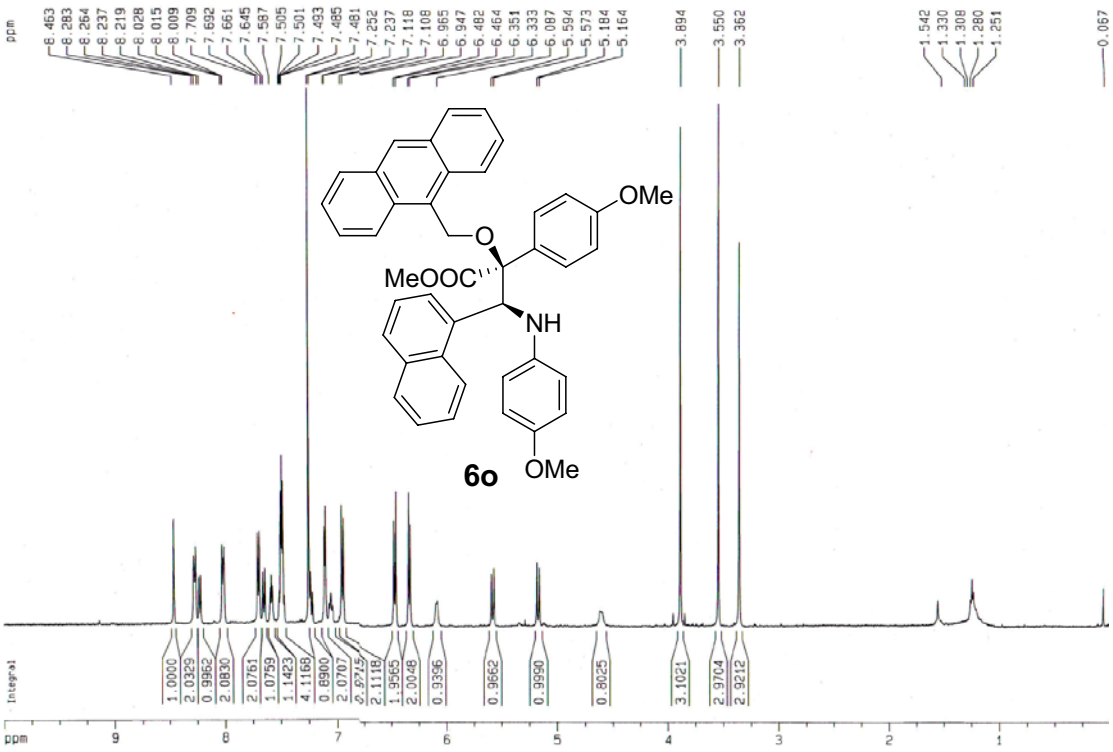
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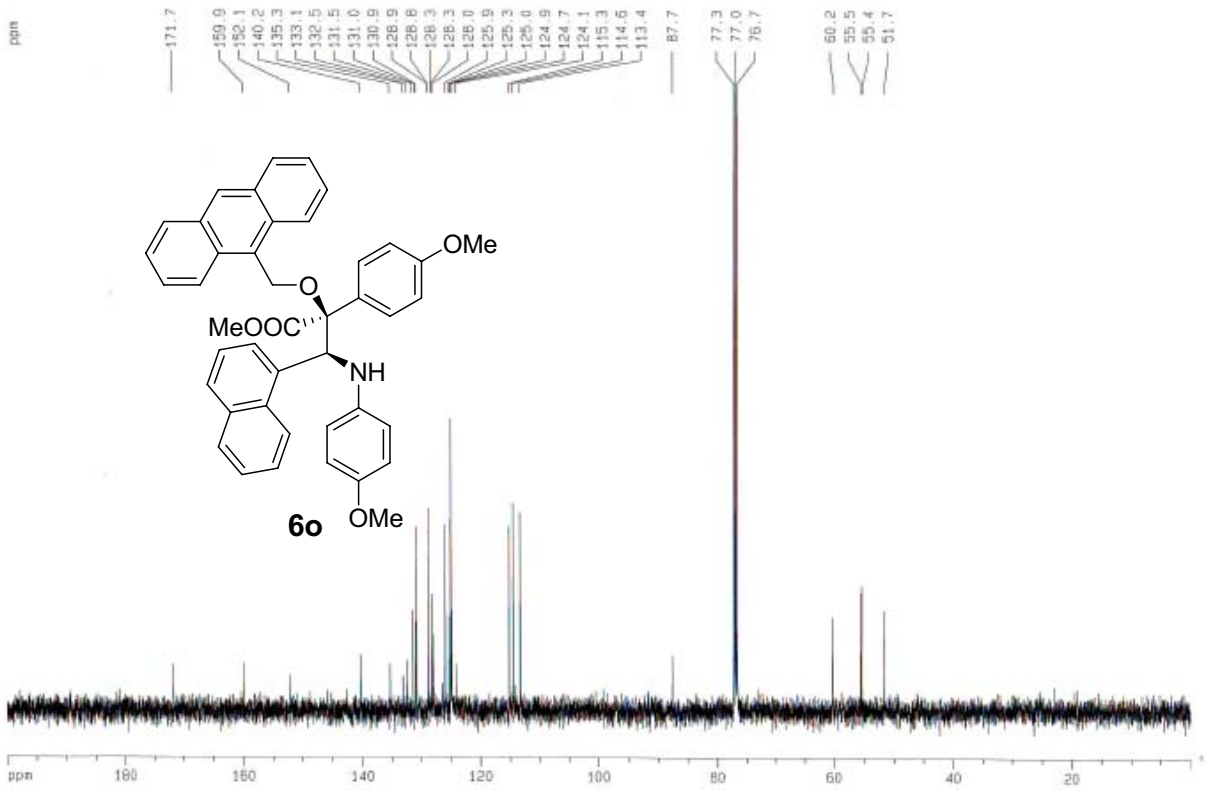
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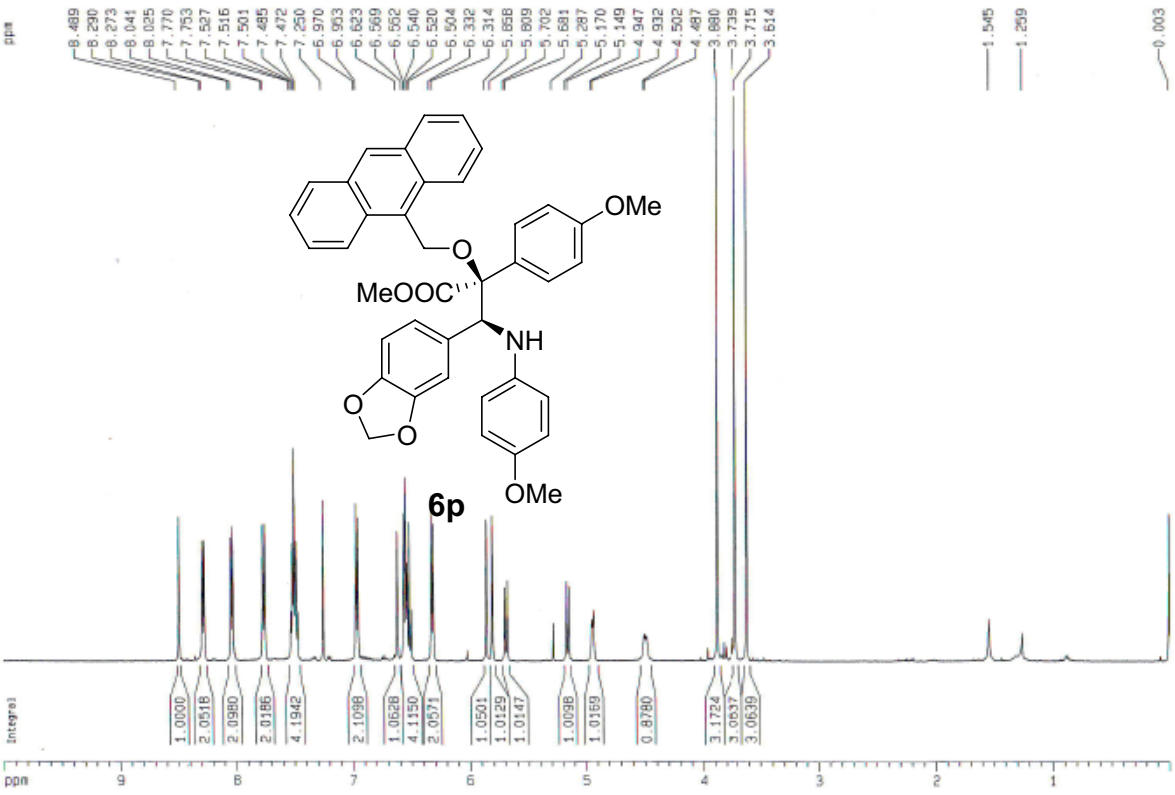
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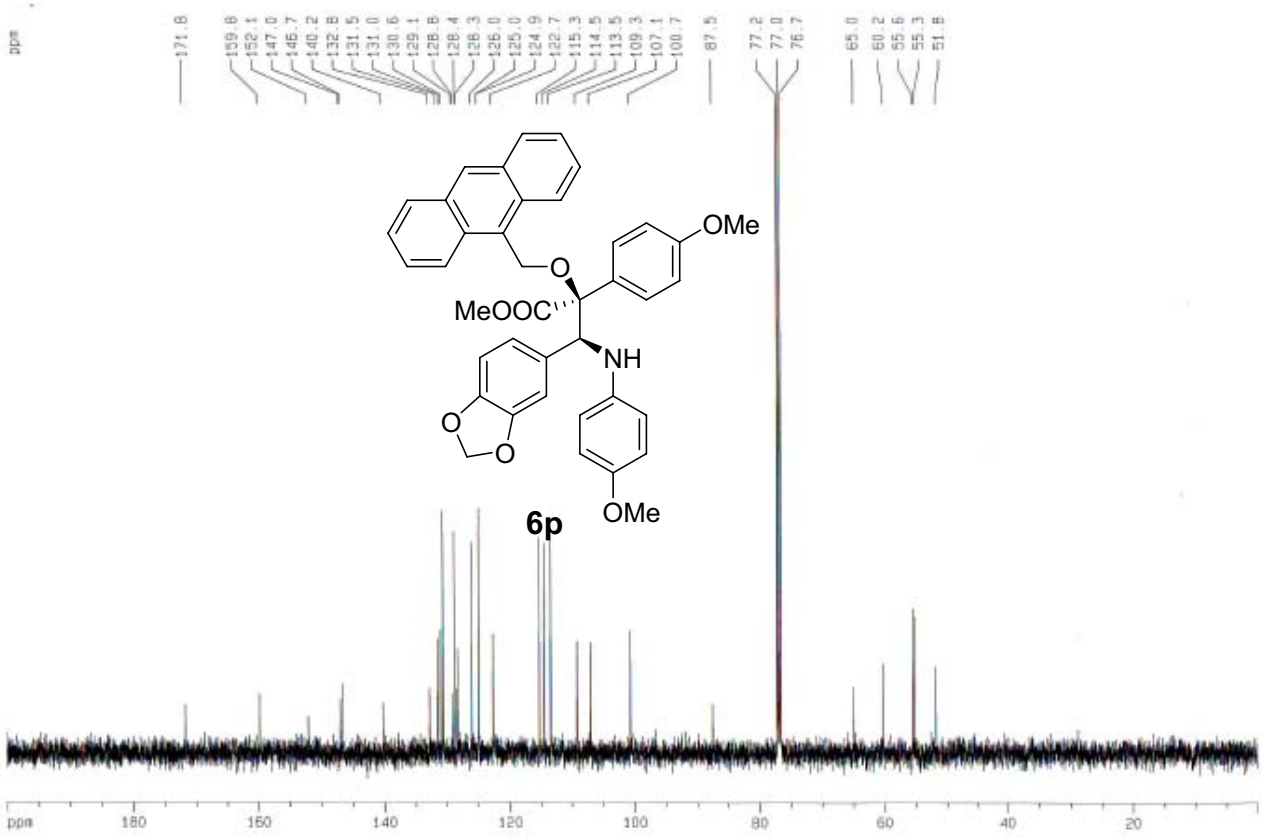
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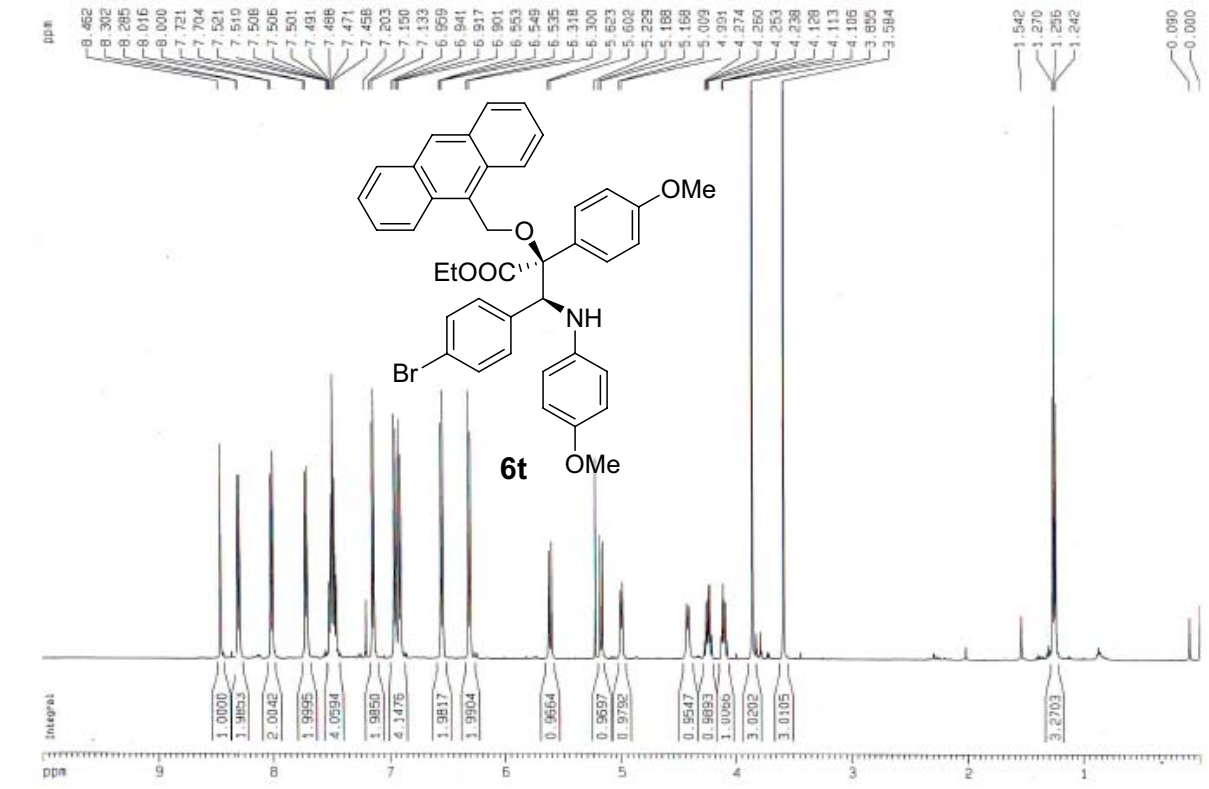
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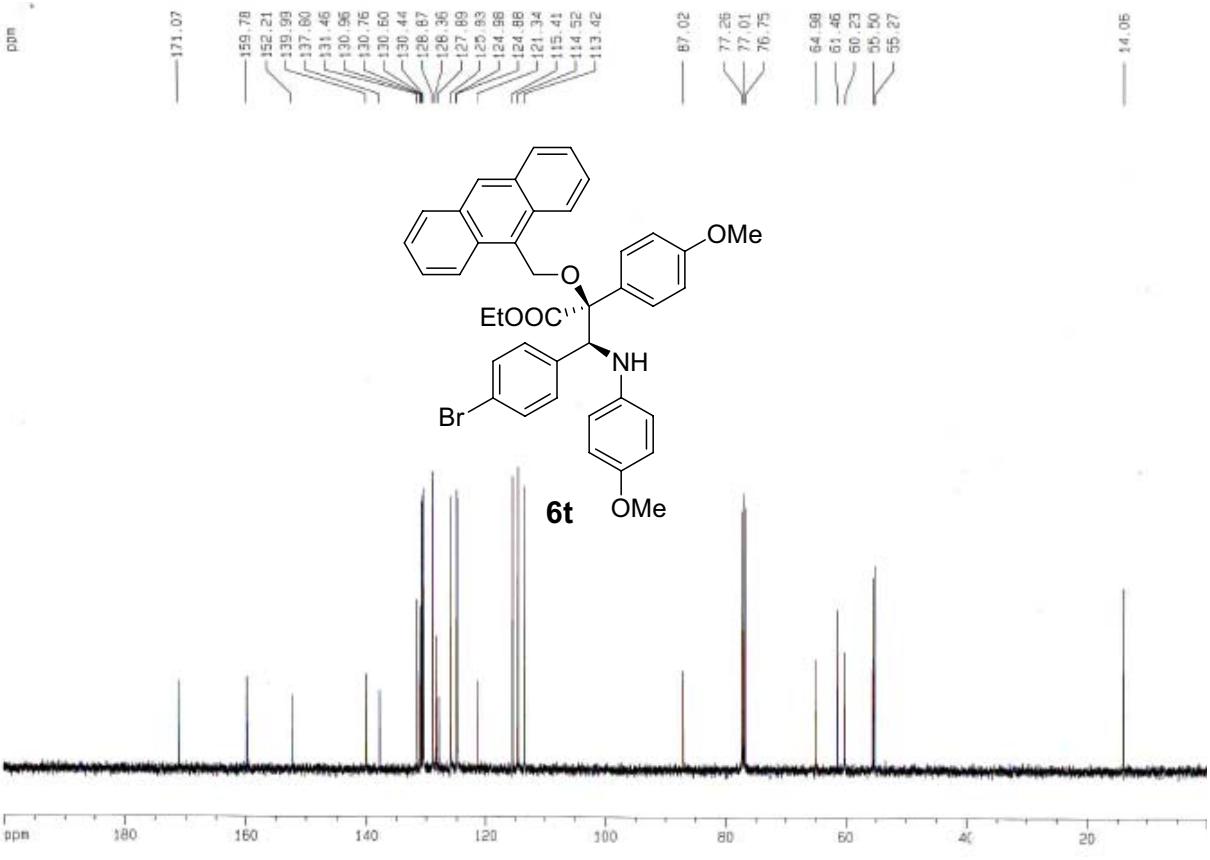
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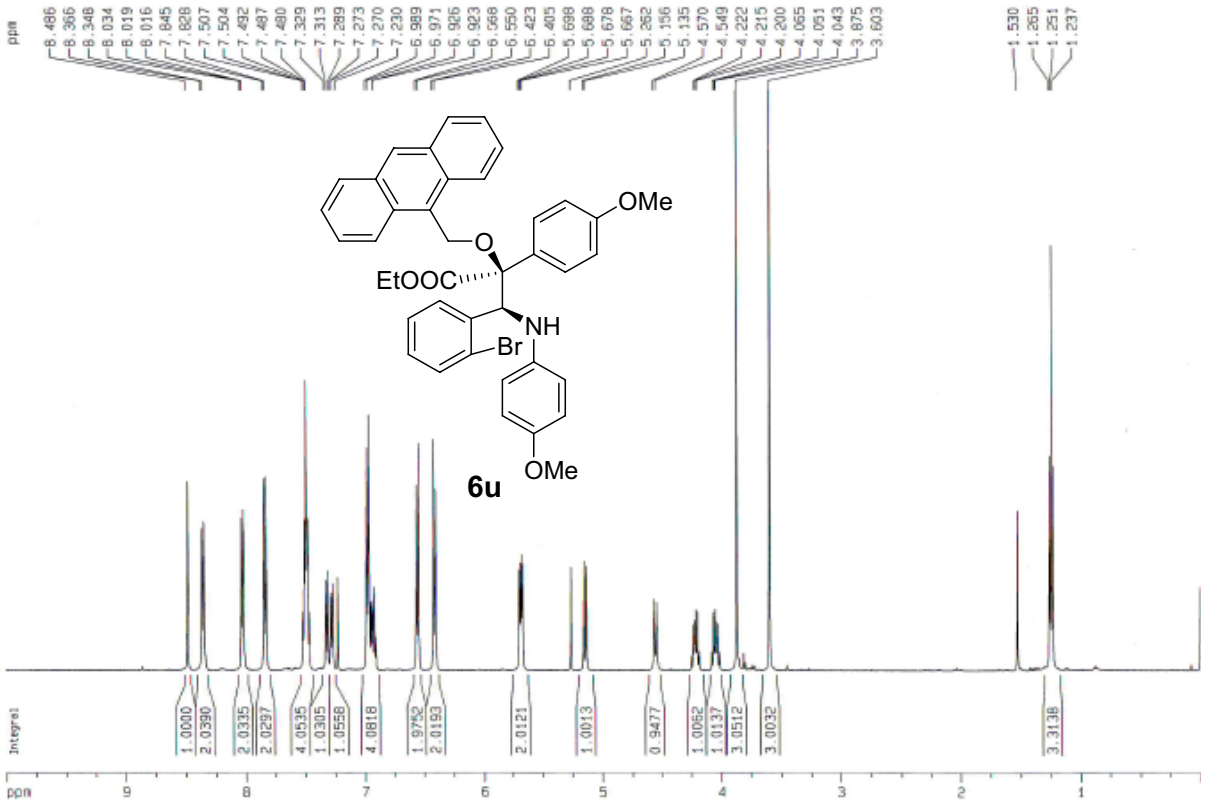
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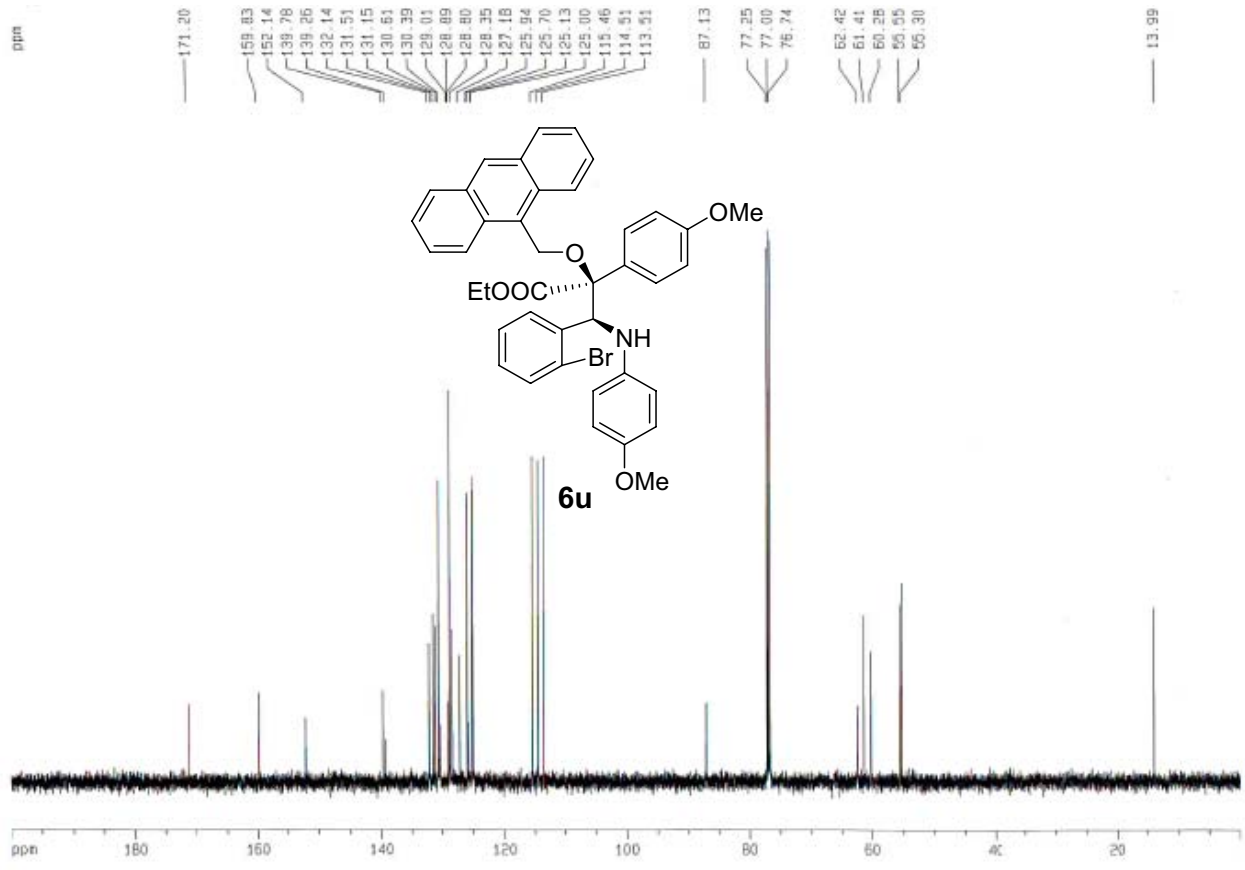
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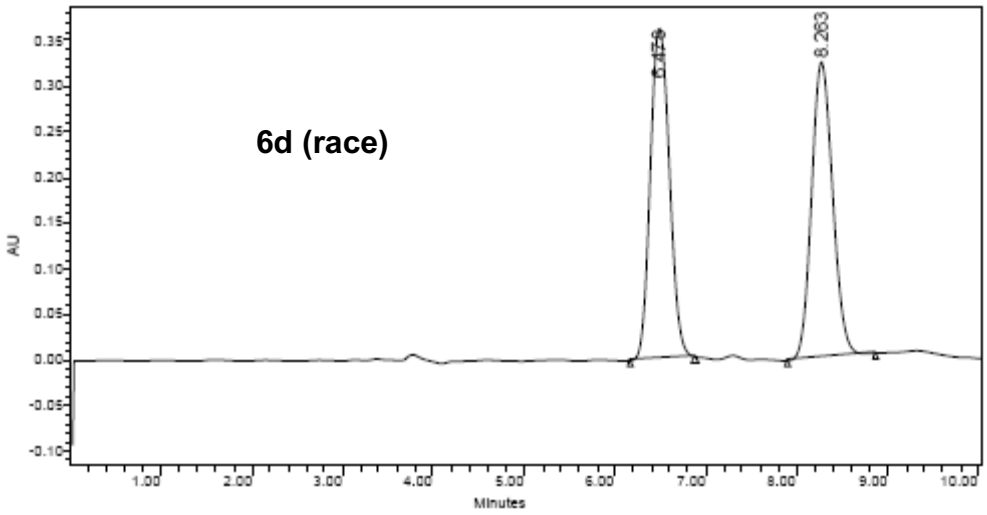
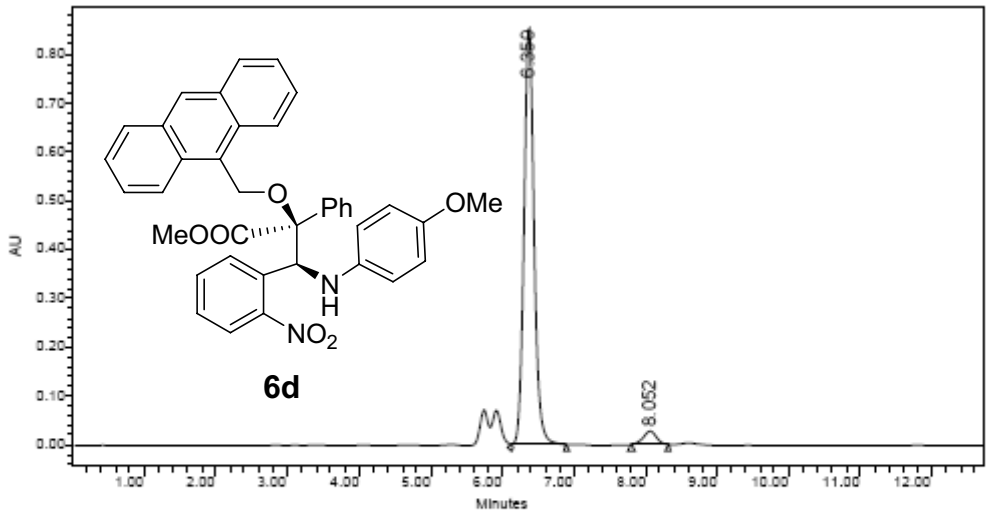
Vial:	1	Acq. Method:	XXF20%
Injection #:	1	Date Processed:	11/19/2007 10:09:11 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	60.00 Minutes	Sample Set Name:	



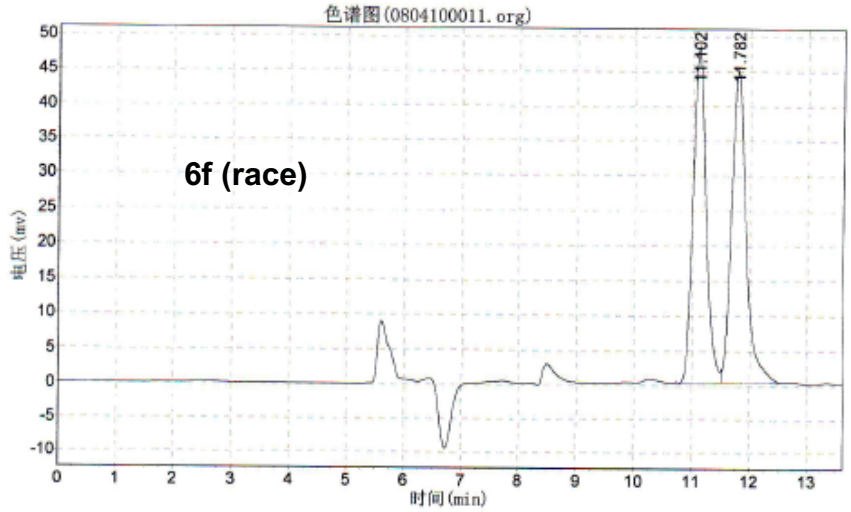
	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	6.478	5318018	50.35	362888	52.81
2	8.263	5243786	49.65	324285	47.19



6d

	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	6.359	8345051	96.03	856570	96.92
2	8.052	345138	3.97	27218	3.08

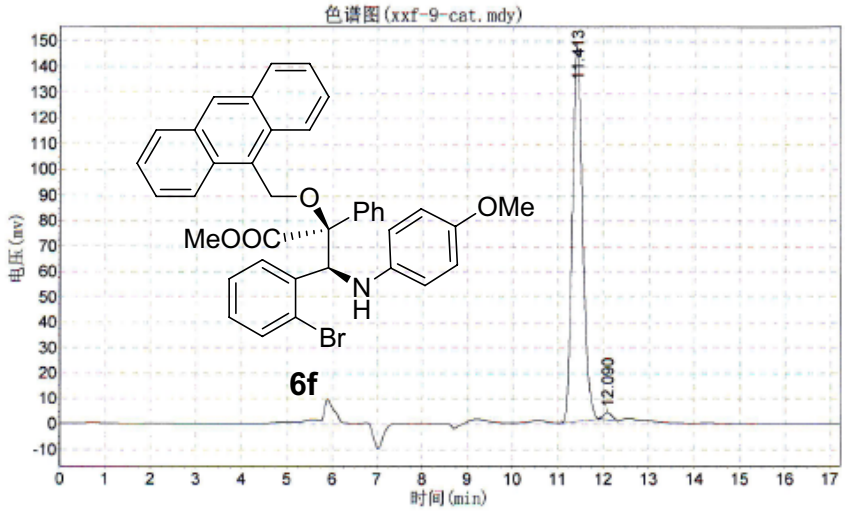
实验内容简介:
column:IA
M.P:n-Hex/i-prOH/EtOH/TEA=450:25:25:1
UV:254
0.5ml/min



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		11.102	47905.484	748084.063	49.0728
2		11.782	44571.855	776353.625	50.9272
总计			92477.340	1524437.688	100.0000

实验内容简介:
column:IA
M.P:n-Hex/i-prOH/EtOH/TEA=450:25:25:1
UV:254
0.5ml/min

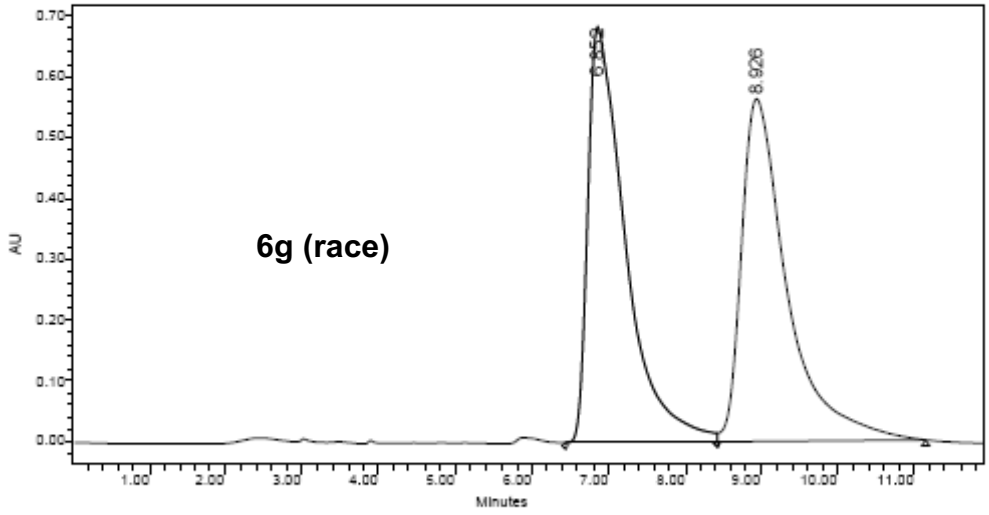


分析结果表

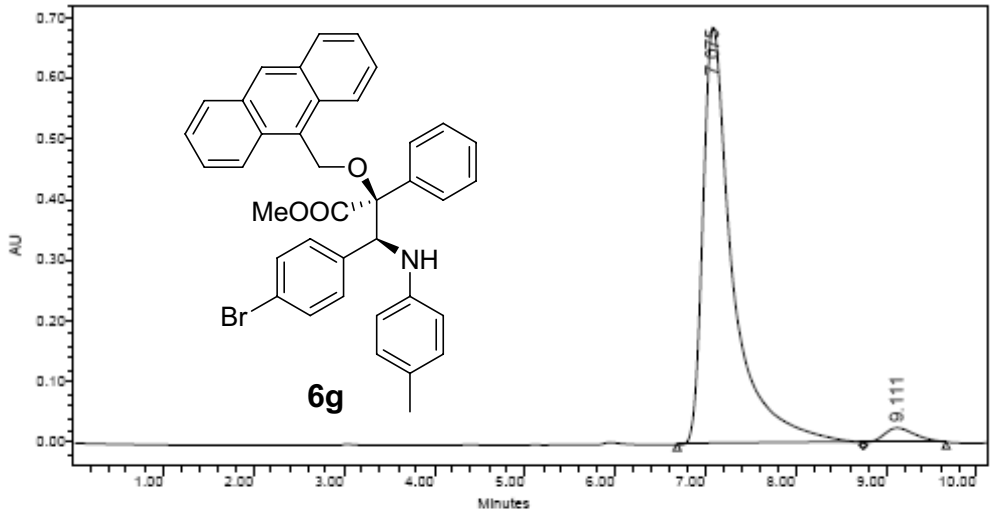
峰号	峰名	保留时间	峰高	峰面积	含量
1		11.413	146661.516	2317815.750	98.6669
2		12.090	2578.980	31316.902	1.3331
总计			149240.496	2349132.652	100.0000

SAMPLE INFORMATION

Sample Name:	xxf-33-meso-1127	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	11/27/2007 2:49:10 PM
Vial:	1	Acq. Method:	xxf5%
Injection #:	5	Date Processed:	11/27/2007 3:02:23 PM
Injection Volume:	20.00 ul	Channel Name:	2487Channel 1
Run Time:	60.00 Minutes	Sample Set Name:	

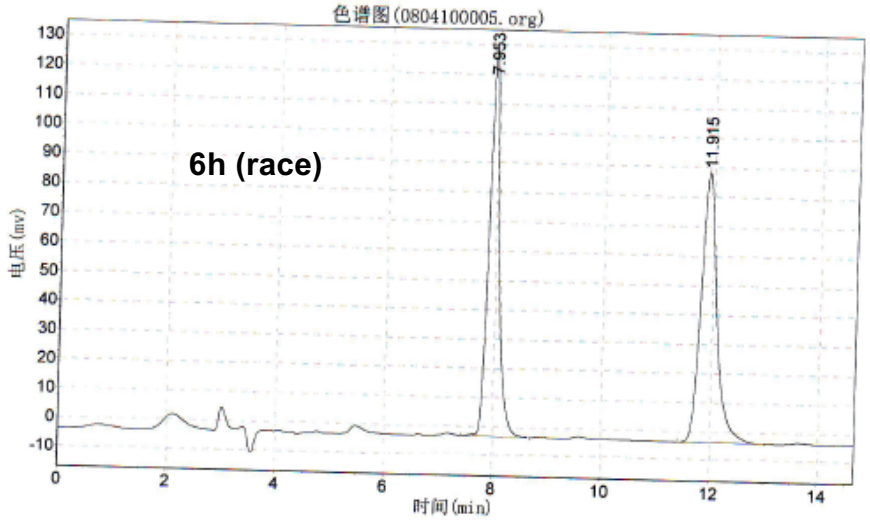


	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	6.852	23305413	49.98	683603	54.82
2	8.926	23325563	50.02	563389	45.18



	RT (min)	Area (V*sec)	% Area	Height (V)	% Height
1	7.075	15876582	96.40	689212	96.58
2	9.111	592678	3.60	24397	3.42

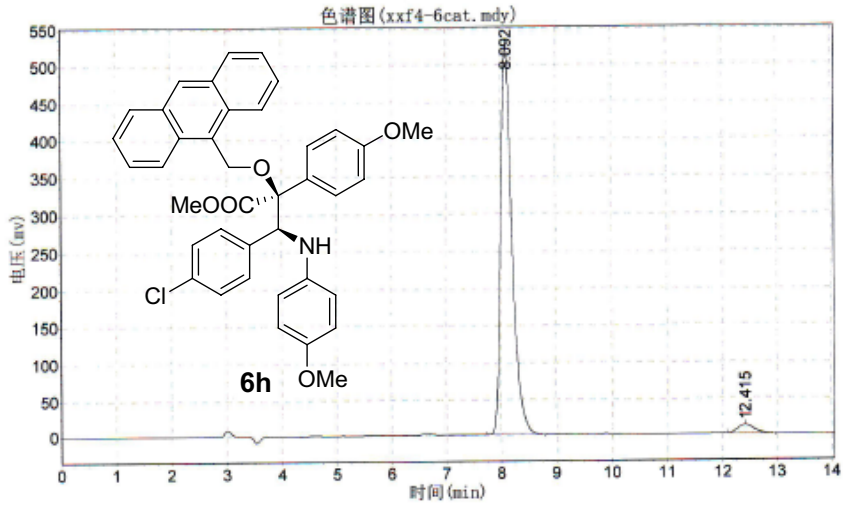
实验内容简介：
column:IA
M.P:n-Hex/i-prOH/EtOH/TEA=450:25:25:1
UV:254
1ml/min



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		7.953	131161.609	1796131.500	49.2086
2		11.915	91639.070	1853902.625	50.7914
总计			222800.680	3650034.125	100.0000

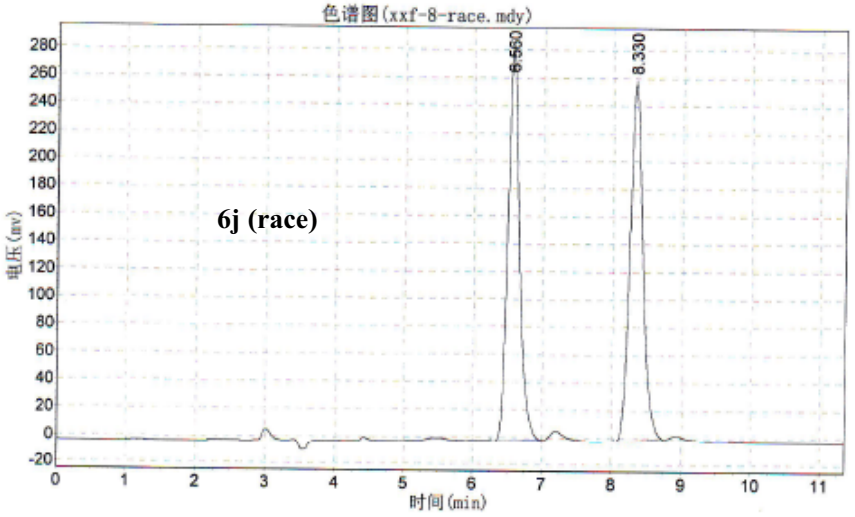
实验内容简介：
column:IA
M.P:n-Hex/i-prOH/EtOH/TEA=450:25:25:1
UV:254
1.0ml/min



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		8.092	524085.344	7581592.000	97.2072
2		12.415	11119.521	217818.250	2.7928
总计			535204.865	7799410.250	100.0000

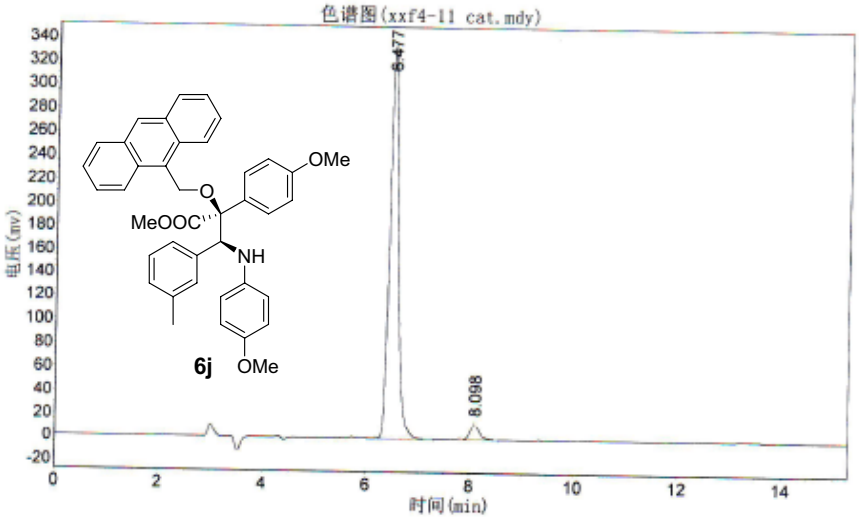
实验内容简介：
column:IA
M.P:n-Hex/i-prOH/EtOH/TEA=450:25:25:1
UV:254
1ml/min



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		6.560	283605.188	3316152.750	49.8629
2		8.330	257473.547	3334386.000	50.1371
总计			541078.734	6650538.750	100.0000

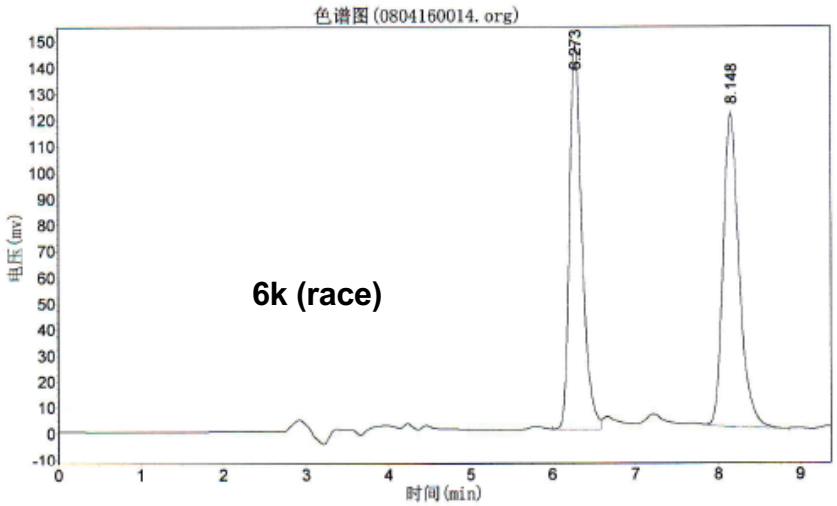
实验内容简介：
column:IA
n-Hex/i-prOH/EtOH/TFA=450:25:25:1
254nm
1.0ml/min



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		6.477	334069.781	3945600.750	96.0712
2		8.098	12323.353	161353.297	3.9288
总计			346393.134	4106954.047	100.0000

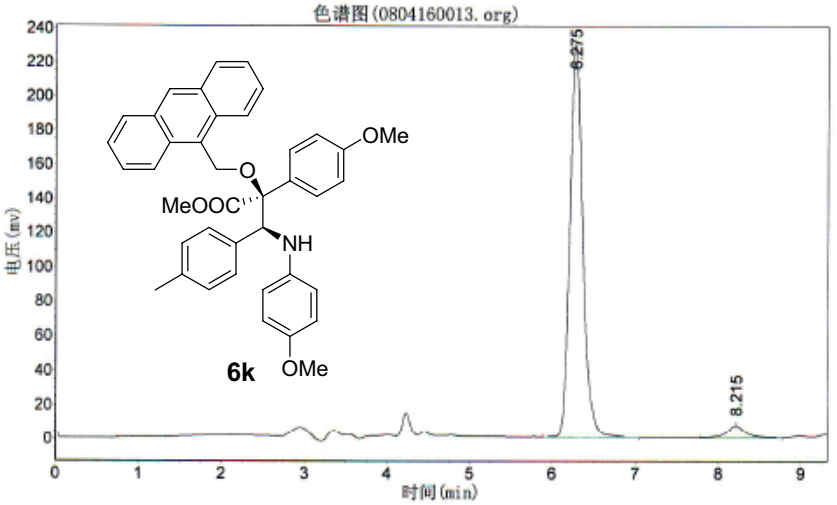
实验内容简介：
column:IA
M.P:n-Hex/i-prOH//EtOH/TFA=400:50:50:1
UV:254nm
1ml/min



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		6.273	146492.656	1555263.000	48.7102
2		8.148	119585.359	1637628.125	51.2898
总计			266078.016	3192891.125	100.0000

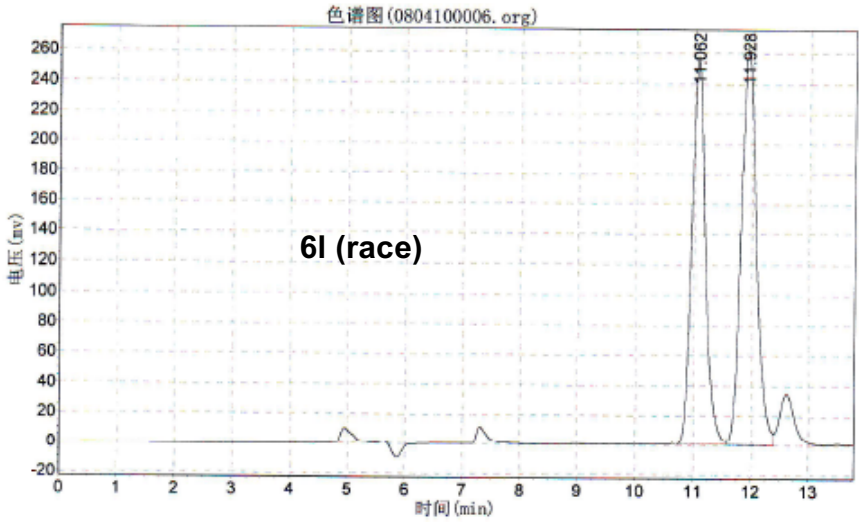
实验内容简介：
column:IA
M.P:n-Hex/i-prOH//EtOH/TFA=400:50:50:1
UV:254nm
1ml/min



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		6.275	228893.125	2469776.250	95.6150
2		8.215	7301.919	113265.297	4.3850
总计			236195.044	2583041.547	100.0000

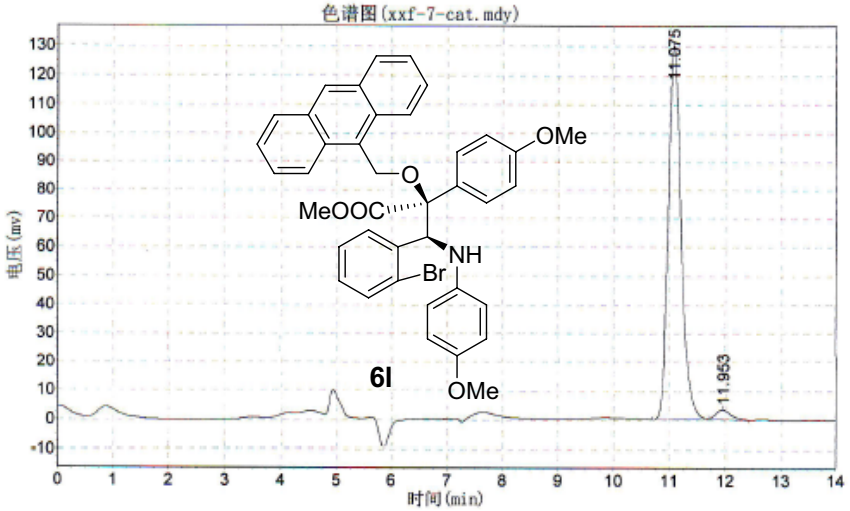
实验内容简介:
column:IA
M.P:n-Hex/i-prOH/EtOH/TEA=450:25:25:1
UV:254
0.6ml/min



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		11.062	254578.906	4150646.250	46.0598
2		11.928	261639.125	4860777.500	53.9402
总计			516218.031	9011423.750	100.0000

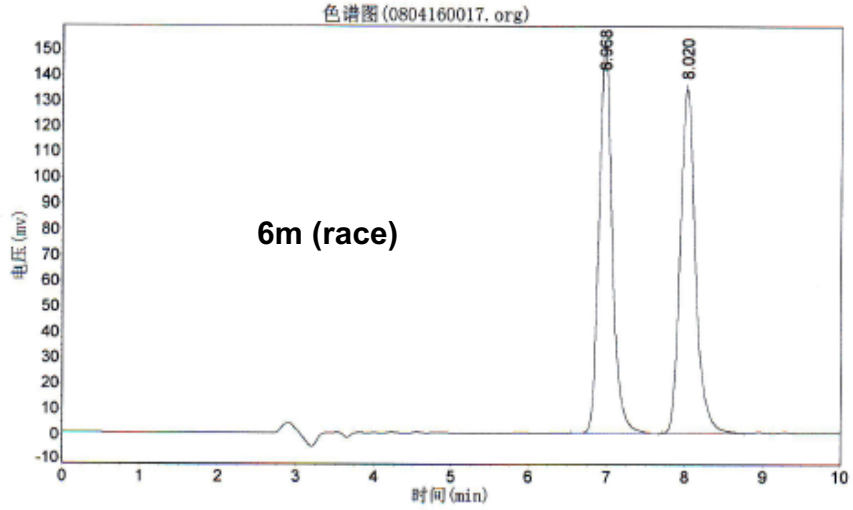
实验内容简介:
column:IA
M.P:n-Hex/i-prOH/EtOH/TEA=450:25:25:1
UV:254
0.6ml/min



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		11.075	129546.633	2069907.500	97.4219
2		11.953	3110.589	54776.203	2.5781
总计			132657.222	2124683.703	100.0000

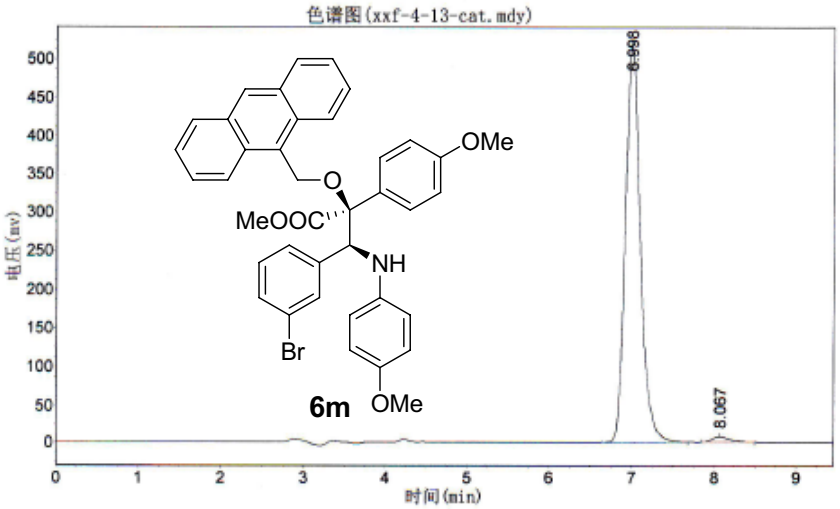
实验内容简介:
column:IA
M.P:n-Hex/i-prOH//EtOH/TFA=400:50:50:1
UV:254nm
1ml/min



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		6.968	150467.859	1794534.125	49.6129
2		8.020	133874.547	1822541.250	50.3871
总计			284342.406	3617075.375	100.0000

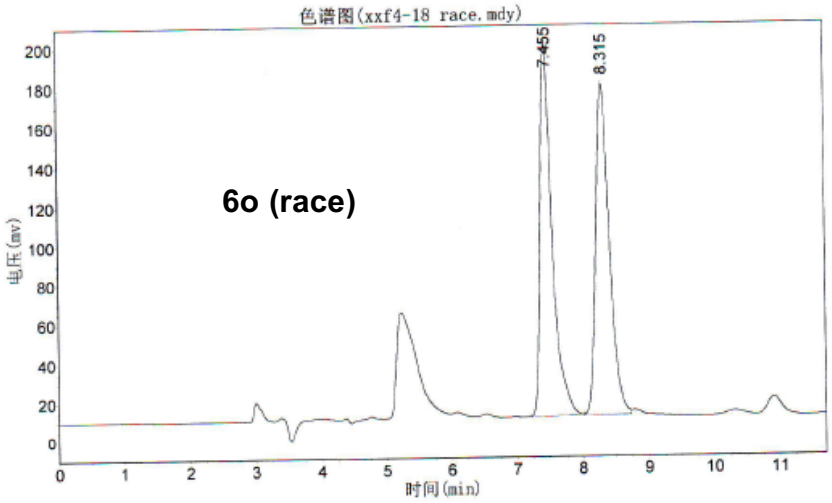
实验内容简介:
column:IA
M.P:n-Hex/i-prOH//EtOH/TFA=400:50:50:1
UV:254nm
1ml/min



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		6.998	515022.625	6595802.000	98.4052
2		8.067	7187.397	106893.156	1.5948
总计			522210.022	6702695.156	100.0000

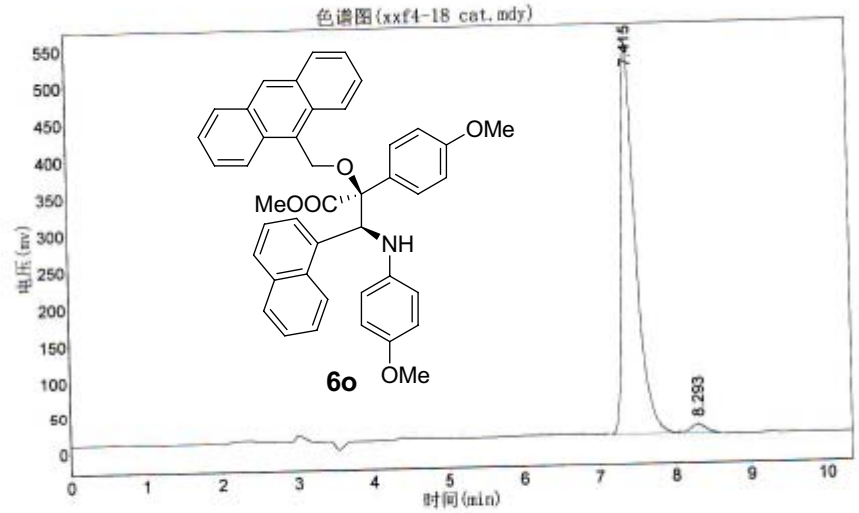
实验内容简介：
column: IA
M.P: n-Hex/EtOH/TFA=450:25：25：1
UV:254nm
1.0ml/min



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		7.455	188812.859	2386515.250	49.6150
2		8.315	167674.922	2423548.250	50.3850
总计			356487.781	4810063.500	100.0000

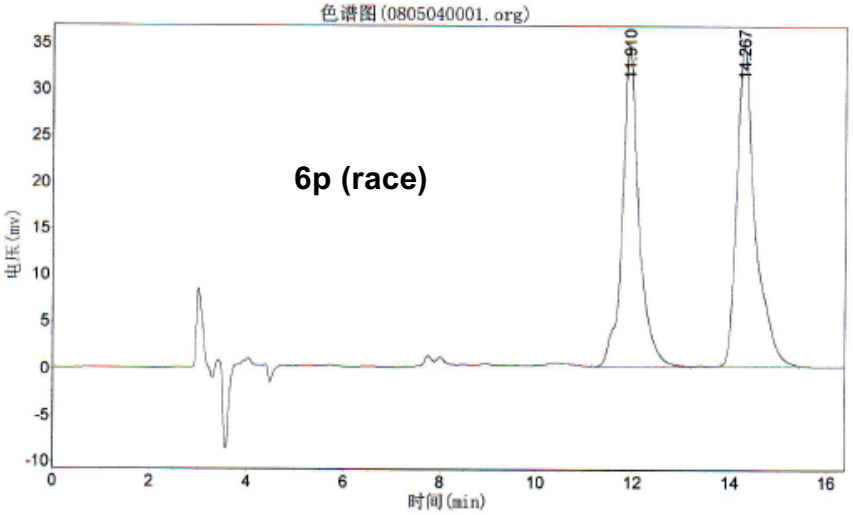
实验内容简介：
column: IA
M.P: n-Hex/EtOH/TFA=450:25：25：1
UV:254nm
1.0ml/min



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		7.415	533952.313	7048783.000	97.8634
2		8.293	11462.154	153895.109	2.1366
总计			545414.467	7202678.109	100.0000

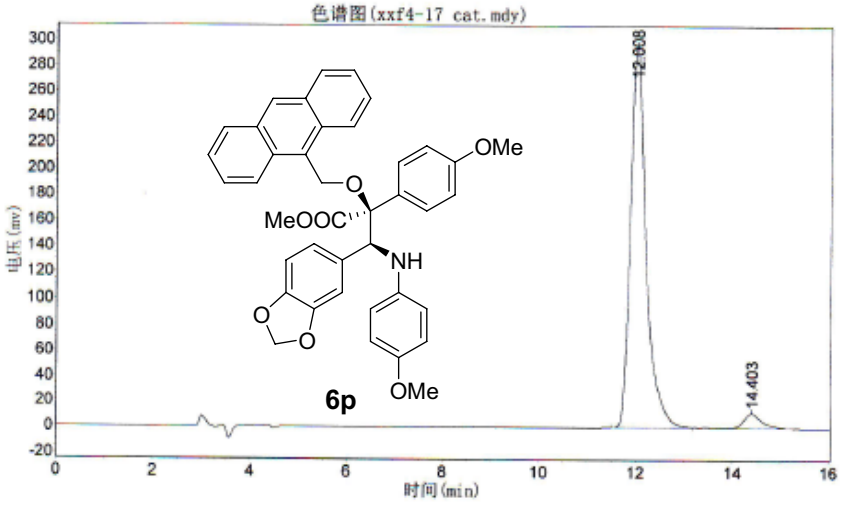
实验内容简介：
column: IA
M.P: n-Hex/EtOH/TFA=450:25: 25: 1
UV:254nm
1.0ml/min



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		11.910	34369.715	813995.875	47.4046
2		14.267	34100.934	903129.000	52.5954
总计			68470.648	1717124.875	100.0000

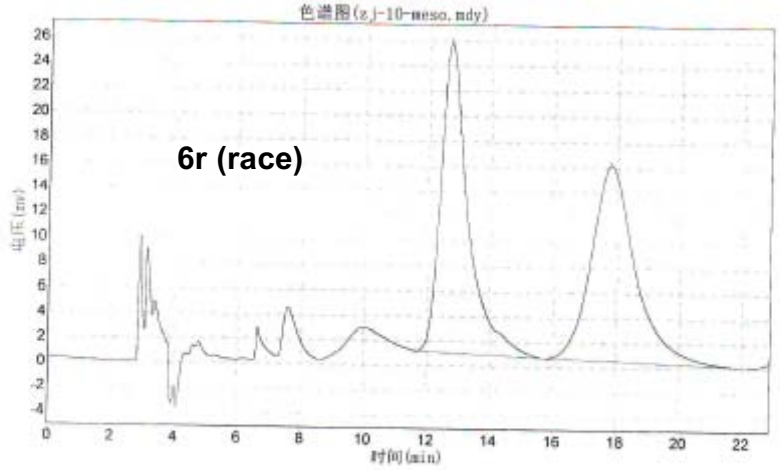
实验内容简介：
column: IA
M.P: n-Hex/EtOH/TFA=450:25: 25: 1
UV:254nm
1.0ml/min



分析结果表

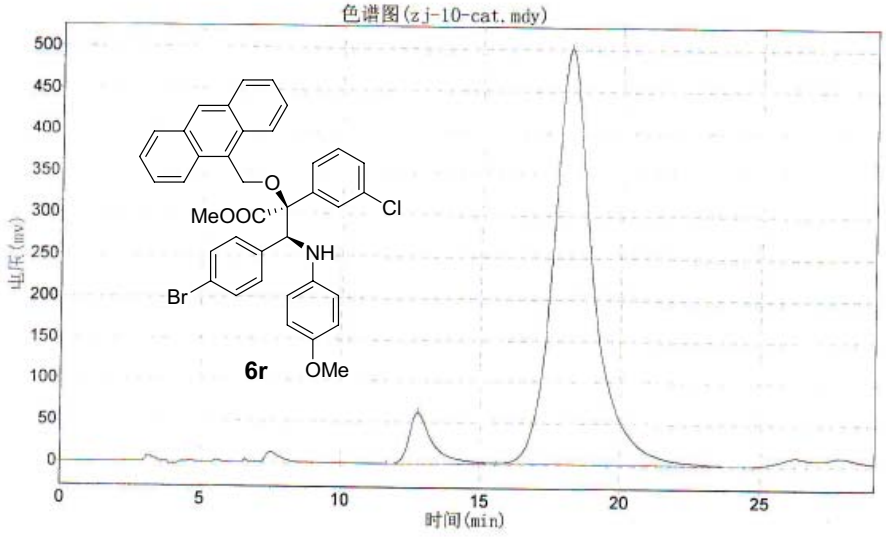
峰号	峰名	保留时间	峰高	峰面积	含量
1		12.008	296362.500	6635768.500	96.0853
2		14.403	11041.163	270356.469	3.9147
总计			307403.663	6906124.969	100.0000

实验内容简介：
AD-H
254nm
n-Hex/i-PrOH/EtOH/TFA=490:10:10:1
1ml/min



分析结果表

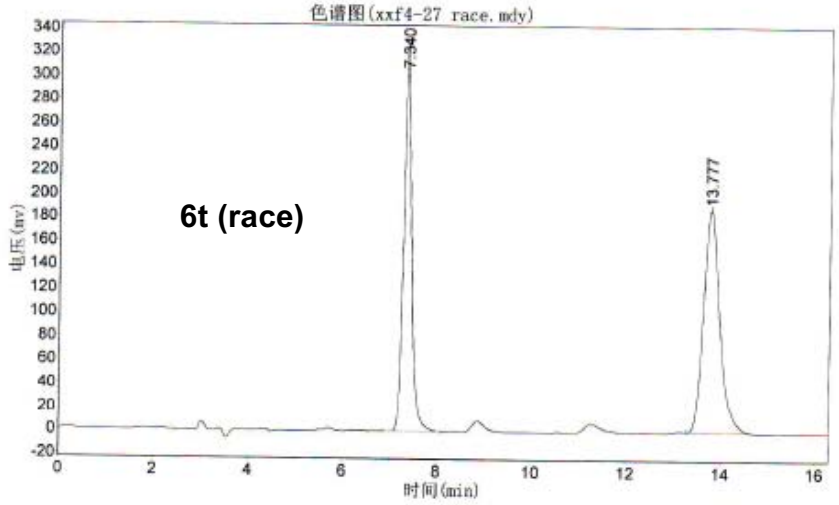
峰号	峰名	保留时间	峰高	峰面积	含量
1		12.707	24755.799	1500380.250	49.8026
2		17.785	15672.987	1512276.375	50.1974
总计			40428.786	3012656.625	100.0000



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		12.767	61042.973	3457883.000	6.6384
2		18.177	498774.625	48631408.000	93.3616
总计			559817.598	52089291.000	100.0000

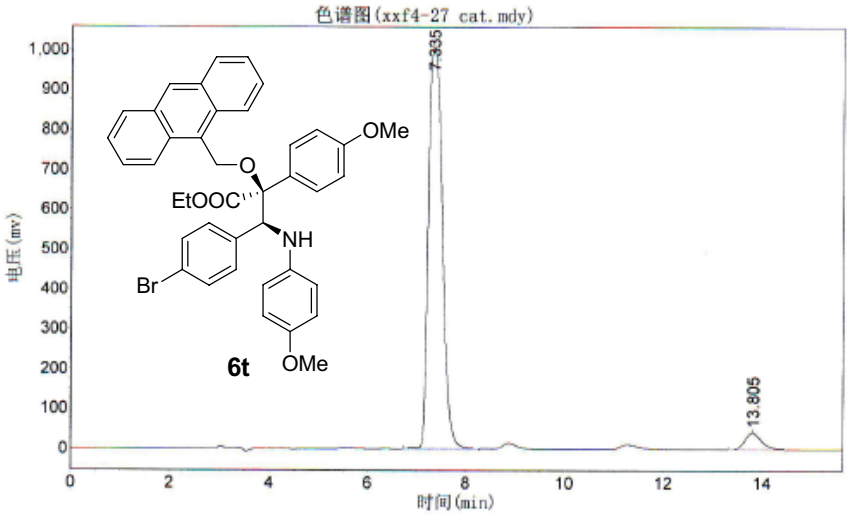
实验内容简介：
column:IA
M.P:n-Hex/i-prOH/EtOH=450:25:25:1
245nm
1ml/min



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		7.340	327324.031	3890035.750	46.1571
2		13.777	188489.328	4537775.000	53.8429
总计			515813.359	8427810.750	100.0000

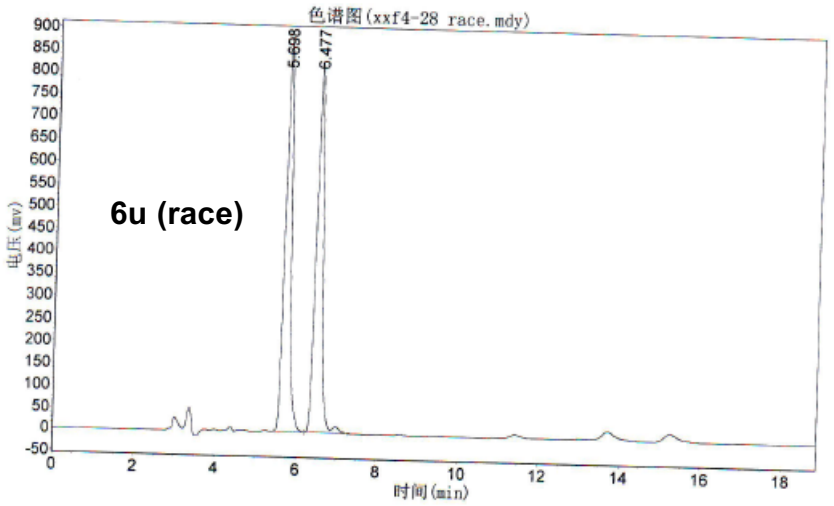
实验内容简介：
column:IA
M.P:n-Hex/i-prOH/EtOH=450:25:25:1
245nm
1ml/min



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		7.335	1007502.500	19803858.000	95.2934
2		13.805	41450.559	978115.813	4.7066
总计			1048953.059	20781973.813	100.0000

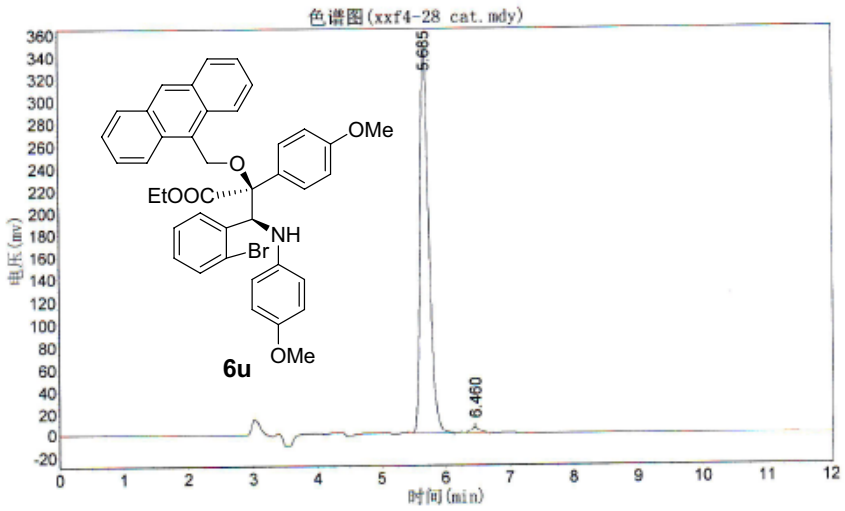
实验内容简介：
column:IA
M.P:n-Hex/i-prOH/EtOH=450:25:25:1
245nm
1ml/min



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		5.698	867827.500	9489385.000	49.2560
2		6.477	825033.438	9776044.000	50.7440
总计			1692860.938	19265429.000	100.0000

实验内容简介：
column:IA
M.P:n-Hex/i-prOH/EtOH=450:25:25:1
245nm
1ml/min



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		5.685	346551.156	3288743.750	98.2460
2		6.460	6084.989	58715.801	1.7540
总计			352636.145	3347459.551	100.0000