Supporting information

Organocatalytic Enantioselective Friedel-Crafts Reactions of 1-Naphthols with

Aldimines

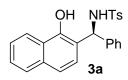
Guixia Liu,[†] Shilei Zhang,[†] Hao Li,[‡] Tangzhi Zhang,[†] and Wei Wang^{†,‡*}

[†]Department of Chemistry and Chemical Biology, University of New Mexico, Albuqueruqe, NM 87131-0001 [‡]Shanghai Institute of Materia Medica, Chinese Academy of Sciences, 555 Zuchongzhi Road, Shanghai 201203, China **General.** Commercial reagents were used as received, unless otherwise stated. Merck 60 silica gel was used for chromatography, and Whatman silica gel plates with fluorescence F_{254} were used for thin-layer chromatography (TLC) analysis. ¹H and ¹³C NMR spectra were recorded on Bruker Avance 500, and tetramethylsilane (TMS) was used as a reference. Data for ¹H are reported as follows: chemical shift (ppm), and multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). Data for ¹³C NMR are reported as ppm.

General Procedure for Asymmetric Friedel-Crafts Reaction of Naphthol with Imines

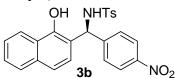
To a vial containing imine (0.2 mmol), naphthol (1.0 mmol) and 1.0 mL of anhydrous toluene was added catalyst (0.02 mmol). The reaction mixture was stirred at 0 °C. After the reaction was completed as monitored by TLC, the reaction mixture was purified by silica gel chromatography, eluting with EtOAc/hexane (1/5) to provide the desired product.

N-((1-Hydroxynaphthalen-2-yl)(phenyl)methyl)-4-methylbenzenesulfonamide (Table 2, entry 1)



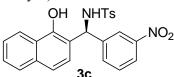
According to the general procedure, the title compound was synthesized in 80% yield. ¹H NMR (500 MHz, CDCl₃): δ 8.05-8.04 (m, 1H), 7.72-7.71 (m, 1H), 7.54-7.45 (m, 4H), 7.26-7.18 (m, 5H), 6.95-6.73 (m, 4H), 5.91 (d, *J* = 7.0 Hz, 1H), 5.46 (d, *J* = 7.5 Hz, 1H), 2.17 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 149.4, 143.6, 139.0, 136.1, 134.1, 129.2, 128.7, 127.8, 127.5, 127.1, 127.0, 126.5, 126.2, 125.5, 125.2, 121.3, 120.6, 119.5, 58.6, 21.1; HR-MS: calcd (M + Na⁺) for C₂₄H₂₁NO₃S, 426.1140; found 426.1150; elemental analysis for C₂₄H₂₁NO₃S: calcd C 71.44, H 5.25 N 3.47; found C 71.51, H 5.31, N 3.38; HPLC (Chiralpak AS-H, *i*-PrOH/hexane = 40/60, flow rate = 0.6 mL/min, λ = 235 nm): t_{minor} = 22.48 min, t_{major} = 31.29 min, ee = 94%; [α]_D²² = -38.8 (*c* = 1.0 in CH₂Cl₂).

N-((1-Hydroxynaphthalen-2-yl)(4-nitrophenyl)methyl)-4-methylbenzenesulfonamide (Table 2, entry 2)



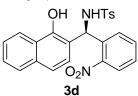
According to the general procedure, the title compound was synthesized in 88% yield. ¹H NMR (500 MHz, CDCl₃): δ 8.00 (d, *J* = 8.5 Hz, 2H), 7.93-7.92 (m, 1H), 7.75-7.73 (m, 1H), 7.51-7.48 (m, 4H), 7.37 (d, *J* = 8.5 Hz, 2H), 7.27 (d, *J* = 9.0 Hz, 1H), 6.90 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.5 Hz, 1H), 5.97 (s, 1H) 2.14 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 148.7, 147.1, 143.9, 136.2, 134.2, 129.3, 128.0, 127.8, 126.9, 126.1, 125.8, 124.6, 123.5, 121.3, 120.2, 119.3, 57.8, 21.2; HR-MS: calcd (M + Na⁺) for C₂₄H₂₀N₂O₅S, 471.0991; found 471.0003; elemental analysis for C₂₄H₂₀N₂O₅S: calcd C 64.27, H 4.49, N 6.25; found C 64.08, H 4.43, N 6.31; HPLC (Chiralpak AS-H, *i*-PrOH/hexane = 40/60, flow rate = 0.6 mL/min, λ = 254 nm): t_{minor} = 34.29 min, t_{major} = 50.04 min, ee = 95%; [α]_D²² = -73.4 (*c* = 1.0 in CH₂Cl₂).

N-((**1-Hydroxynaphthalen-2-yl**)(**3-nitrophenyl**)**methyl**)-**4-methylbenzenesulfonamide** (Table 2, entry 3)



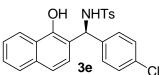
According to the general procedure, the title compound was synthesized in 91% yield. ¹H NMR (500 MHz, CDCl₃): δ 8.04 (s, 1H), 7.94 (d, *J* = 7.0 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.61-7.28 (m, 7H), 6.95 (d, *J* = 8.0 Hz, 2H), 6.89 (d, *J* = 8.0 Hz, 1H), 6.44 (s, 1H), 6.01(d, *J* = 8.5 Hz, 1H), 5.88 (d, *J* = 8.5 Hz, 1H), 2.16 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 148.8, 148.3, 143.8, 142.0, 136.3, 134.3, 133.3, 129.4, 129.3, 128.0, 127.0, 126.9, 126.1, 125.7, 124.7, 122.5, 121.9, 121.4, 120.3, 119.3, 57.6, 21.2; HR-MS: calcd (M + Na⁺) for C₂₄H₂₀N₂O₅S, 471.0991; found 471.0994; elemental analysis for C₂₄H₂₀N₂O₅S: calcd C 64.27, H 4.49, N 6.25; found C 64.38, H 4.42, N 6.19; HPLC (Chiralpak OD-H, *i*-PrOH/hexane = 15/85, flow rate = 0.6 mL/min, λ = 254 nm): t_{minor} = 25.57 min, t_{major} = 32.85 min, ee = 94\%; [α]_D²² = -44.6 (*c* = 1.0 in CH₂Cl₂).

N-((1-Hydroxynaphthalen-2-yl)(2-nitrophenyl)methyl)-4-methylbenzenesulfonamide (Table 2, entry 4)



According to the general procedure, the title compound was synthesized in 89% yield. ¹H NMR (500 MHz, CDCl₃): δ 8.15-8.14 (m, 1H), 7.75-7.73 (m, 1H), 7.82-7.68 (m, 3H), 7.58-7.36 (m, 6H), 7.26-7.19 (m, 1H), 7.04 (d, *J* = 7.5 Hz, 2H), 6.91 (s, 1H), 6.71 (d, *J* = 8.5 Hz, 1H), 6.66 (d, *J* = 7.0 Hz, 1H), 5.84 (s, 1H) 2.28 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 149.8, 148.0, 144.0, 135.8, 134.3, 133.3, 129.9, 129.7, 129.6, 128.7, 127.5, 127.2, 126.9, 126.4, 125.7, 125.1, 124.4, 121.8, 120.5, 118.0, 53.5, 21.4; HR-MS: calcd (M + Na⁺) for C₂₄H₂₀N₂O₅S, 471.0991; found 471.0982; elemental analysis for C₂₄H₂₀N₂O₅S: calcd C 64.27, H 4.49, N 6.25; found C 64.34, H 4.54, N 6.22 [α]_D²² = -57.0 (*c* = 1.0 in CH₂Cl₂);.

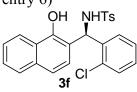
N-((4-Chlorophenyl)(1-hydroxynaphthalen-2-yl)methyl)-4-methylbenzenesulfonamide (Table 2, entry 5)



According to the general procedure, the title compound was synthesized in 66% yield. ¹H NMR (500 MHz, CDCl₃): δ 8.02-7.80 (m, 1H), 7.72-7.70 (m, 1H), 7.48-7.44 (m, 4H), 7.25 (d, J = 8.5 Hz, 1H), 7.17-7.10 (m, 4H), 6.89 (d, J = 8.0 Hz, 2H), 6.85 (d, J = 8.5 Hz, 1H), 6.71 (s, 1H), 5.89 (d, J = 8.5 Hz, 1H), 5.80-5.79 (m, 1H), 2.15 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 149.1, 143.7, 137.8, 136.2, 134.2, 133.5, 129.2, 128.6, 128.5, 127.7, 127.0, 126.6, 125.9, 125.8, 125.0, 120.9, 120.8, 119.5, 57.9, 21.2; HR-MS: calcd (M + Na⁺) for C₂₄H₂₀ClNO₃S, 460.0750; found 460.0745;

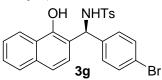
elemental analysis for C₂₄H₂₀ClNO₃S: calcd C 65.82, H 4.60, N 3.20; found C 65.94, H 4.58, N 3.31; HPLC (Chiralpak AS-H, *i*-PrOH/hexane = 40/60, flow rate = 0.6 mL/min, λ = 254 nm): t_{minor} = 16.31 min, t_{major} = 22.02 min, ee = 93%; [α]_D²² = -27.6 (*c* = 1.0 in CH₂Cl₂).

N-((2-Chlorophenyl)(1-hydroxynaphthalen-2-yl)methyl)-4-methylbenzenesulfonamide (Table 2, entry 6)

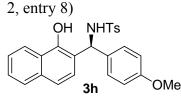


According to the general procedure, the title compound was synthesized in 79% yield. ¹H NMR (500 MHz, CDCl₃): δ 8.23-8.21 (m, 1H), 7.72-7.70 (m, 1H), 7.57 (d, *J* = 8.0 Hz, 2H), 7.49-7.47 (m, 2H), 7.30-7.15 (m, 2H), 7.02 (d, *J* = 8.0 Hz, 2H), 6.73 (d, *J* = 8.5 Hz, 1H), 6.20 (d, *J* = 7.0 Hz, 1H), 5.40 (d, *J* = 7.0 Hz, 1H), 2.26 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 150.6, 144.0, 135.5, 135.4, 134.3, 133.0, 130.1, 129.1, 127.4, 127.0, 126.8, 125.5, 125.4, 125.1, 122.1, 120.1, 117.0, 56.2, 21.4; HR-MS: calcd (M + Na⁺) for C₂₄H₂₀ClNO₃S, 460.0750; found 460.0753; elemental analysis for C₂₄H₂₀ClNO₃S: calcd C 65.82, H 4.60, N 3.20; found C 65.91, H 4.64, N 3.15; HPLC (Chiralpak AS-H, *i*-PrOH/hexane = 40/60, flow rate = 0.6 mL/min, λ = 254 nm): t_{minor} = 40.26 min, t_{major} = 26.40 min, ee = 96%; [α]_D²² = -63.0 (*c* = 1.0 in CH₂Cl₂).

N-((**4-Bromophenyl**)(**1-hydroxynaphthalen-2-yl**)**methyl**)-**4-methylbenzenesulfonamide** (Table 2, entry 7)



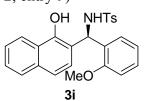
According to the general procedure, the title compound was synthesized in 81% yield. ¹H NMR (500 MHz, CDCl₃): δ 8.01-7.99 (m, 1H), 7.70-7.69 (m, 1H), 7.44 (d, *J* = 8.5 Hz, 4H), 7.27 (d, *J* = 8.5 Hz, 2H), 7.21 (d, *J* = 8.5 Hz, 1H), 7.04 (d, *J* = 8.0 Hz, 2H), 6.84 (d, *J* = 7.0 Hz, 4H), 6.02 (s, 1H), 5.86 (s, 1H), 2.12 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 149.0, 143.6, 138.3, 136.1, 134.1, 131.5, 129.1, 128.8, 127.7, 126.9, 126.5, 126.0, 125.7, 124.9, 121.5, 120.9, 120.8, 119.4, 57.9, 21.2; HR-MS: calcd (M + Na⁺) for C₂₄H₂₀BrNO₃S, 504.0245; found 504.0244; elemental analysis for C₂₄H₂₀BrNO₃S: calcd C 59.76, H 4.18, N 2.90; found C 59.94, H 4.39, N 2.84; HPLC (Chiralpak AS-H, *i*-PrOH/hexane = 40/60, flow rate = 0.6 mL/min, λ = 254 nm): t_{minor} = 17.23 min, t_{major} = 24.22 min, ee = 93%; [α]_D²² = -27.0 (*c* = 1.0 in CH₂Cl₂).



According to the general procedure, the title compound was synthesized in 62% yield. ¹H NMR (500 MHz, CDCl₃): δ 8.05-8.03 (m, 1H), 7.72-7.71 (m, 1H), 7.53-7.45 (m, 4H), 7.26-7.25 (m, 1H),

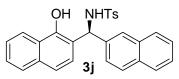
7.10 (d, J = 8.5 Hz, 2H), 6.96-6.92 (m, 3H), 6.76 (d, J = 9.0 Hz, 3H), 5.84 (d, J = 6.5 Hz, 1H), 5.34 (d, J = 6.5 Hz, 1H), 3.75 (s, 3H), 2.18 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 159.2, 149.4, 143.6, 136.1, 134.1, 130.9, 129.1, 128.4, 127.5, 127.2, 126.4, 126.2, 125.5, 125.2, 121.3, 120.5, 119.4, 114.1, 58.5, 55.3, 21.2; HR-MS: calcd (M + Na⁺) for C₂₅H₂₃NO₄S, 456.1245; found 456.1239; elemental analysis for C₂₅H₂₃NO₄S: calcd C 69.26, H 5.35, N 3.23; found C 69.01, H 5.21, N 3.11; HPLC (Chiralpak AS-H, *i*-PrOH/hexane = 40/60, flow rate = 0.6 mL/min, $\lambda = 254$ nm): t_{minor} = 34.29 min, t_{major} = 50.04 min, ee = 95%; [α]_D²² = -73.4 (*c* = 1.0 in CH₂Cl₂).

N-((1-Hydroxynaphthalen-2-yl)(2-methoxyphenyl)methyl)-4-methylbenzenesulfonamide (Table 2, entry 9)



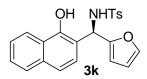
According to the general procedure, the title compound was synthesized in 76% yield. ¹H NMR (500 MHz, DMSO): δ 9.22 (s, 1H), 8.23 (d, *J* = 9.0 Hz, 1H), 8.12-8.10 (m, 1H), 7.77-7.75 (m, 1H), 7.52 (d, *J* = 8.0 Hz, 2H), 7.46 (d, *J* = 8.5 Hz, 1H), 7.42-7.40 (m, 2H), 7.30 (d, *J* = 8.5 Hz, 1H), 7.15-7.09 (m, 4H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.75 (d, *J* = 7.5 Hz, 1H), 6.46 (d, *J* = 8.5 Hz, 1H), 3.36 (s, 3H), 2.22 (s, 3H); ¹³C NMR (125 MHz, DMSO): δ 156.0, 148.5, 141.7, 138.8, 133.2, 129.4, 128.7, 128.4, 128.1, 121.4, 126.3, 126.1, 125.5, 124.8, 124.6, 123.2, 121.8, 119.7, 118.7, 110.6, 55.1, 49.6, 20.8; HR-MS: calcd (M + Na⁺) for C₂₅H₂₃NO₄S, 456.1245; found 456.1249; elemental analysis for C₂₅H₂₃NO₄S: calcd C 69.26, H 5.35, N 3.23; found C 70.02, H 5.49, N 3.04; [α]_D²² = -76.4 (*c* = 1.0 in CH₂Cl₂).

N-((1-Hydroxynaphthalen-2-yl)(naphthalen-2-yl)methyl)-4-methylbenzenesulfonamide (Table 2, entry 10)



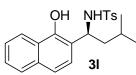
According to the general procedure, the title compound was synthesized in 77% yield. ¹H NMR (500 MHz, CD₃Cl): δ 8.09-8.07 (m, 1H), 7.76-7.72 (m, 4H), 7.71-7.43 (m, 7H), 7.27-7.22 (m, 2H), 6.90-6.80 (m, 4H), 6.09 (d, J = 7.5 Hz, 1H), 5.65 (d, J = 7.5 Hz, 1H), 2.54 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 149.6, 143.6, 136.1, 134.2, 133.0, 132.7, 129.1, 128.6, 128.0, 127.6, 127.1, 126.6, 126.4, 126.3, 126.1, 125.8, 125.6, 125.2, 125.0, 121.4, 120.6, 119.4, 58.6, 21.2; HR-MS: calcd (M + Na⁺) for C₂₈H₂₃NO₃S, 476.1296; found 476.1291; elemental analysis for C₂₈H₂₃NO₃S: calcd C 74.15, H 5.11, N 3.09; found C 74.92, H 5.03, N 3.20; HPLC (Chiralpak AS-H, *i*-PrOH/hexane = 40/60, flow rate = 0.6 mL/min, λ = 254 nm): t_{minor} = 23.81 min, t_{major} = 32.42 min, ee = 94%; [α]_D²² = -42.6 (*c* = 1.0 in CH₂Cl₂).

N-(Furan-2-yl(1-hydroxynaphthalen-2-yl)methyl)-4-methylbenzenesulfonamide (Table 2, entry 11)



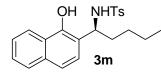
According to the general procedure, the title compound was synthesized in 92% yield. ¹H NMR (500 MHz, CDCl₃): δ 8.09 (m, 1H), 7.72 (m, 1H), 7.62 (d, J = 4.8 Hz, 2H), 7.47-7.45 (m, 2H), 7.31-7.28 (m, 2H), 6.99-6.93 (m, 4H), 6.22 (m, 1H), 6.03 (m, 1H), 5.89 (d, J = 4.0 Hz, 1H), 5.44 (d, J = 4.0 Hz, 1H), 2.20 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 143.7, 142.8, 134.5, 129.2, 127.4, 126.7, 125.7, 125.4, 121.8, 120.4, 116.9, 110.5, 108.6, 53.5, 29.7, 25.3, 21.3; HR-MS: calcd (M + Na⁺) for C₂₂H₁₉NO₄S, 416.0932; found 416.0927; elemental analysis for C₂₂H₁₉NO₄S: calcd C 67.16, H 4.87, N 3.56; found C 66.89, H 4.77, N 3.44; HPLC (Chiralpak AS-H, *i*-PrOH/hexane = 40/60, flow rate = 0.6 mL/min, $\lambda = 254$ nm): t_{minor} = 31.15 min, t_{major} = 34.96 min, ee = 93%; [α]_D²² = -41.1 (*c* = 1.0 in CH₂Cl₂).

N-(1-(1-Hydroxynaphthalen-2-yl)-3-methylbutyl)-4-methylbenzenesulfonamide (Table 2, entry 12)



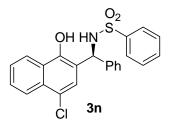
According to the general procedure, the title compound was synthesized in 63% yield. ¹H NMR (500 MHz, CDCl₃): δ 7.97 (m, 1H), 7.69 (m, 1H), 7.47-7.42 (m, 4H), 7.25 (s, 1H), 7.02 (d, *J* = 4.8 Hz, 1H), 6.85 (d, *J* = 4.8 Hz, 1H), 6.70 (m, 1H), 5.23 (d, *J* = 4.0 Hz, 1H), 4.72 (m, 1H), 2.08 (s, 3H), 1.77-1.43 (s, 3), 0.88 (d, *J* = 11.2 Hz, 3H), 0.83 (d, *J* = 11.2 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 149.0, 143.3, 136.6, 133.9, 128.9, 127.5, 126.9, 126.2, 125.3, 125.2, 121.0, 120.6, 119.9, 53.6, 44.0, 24.7, 22.4, 22.1, 21.1; HR-MS: calcd (M + Na⁺) for C₂₂H₂₅NO₃S 406.1453; found 406.1454; elemental analysis for C₂₂H₂₅NO₃S: calcd C 68.90, H 6.57, N 3.65; found C 69.16, H 6.45, N 3.61; HPLC (Chiralpak OJ-H, *i*-PrOH/hexane = 13/87, flow rate = 0.45 mL/min, λ = 254 nm): t_{majorr} = 18.07 min, t_{minor} = 26.98 min, ee = 90%; [α]_D²² = -40.0 (*c* = 1.0 in CH₂Cl₂).

N-(1-(1-Hydroxynaphthalen-2-yl)pentyl)-4-methylbenzenesulfonamide (Table 2, entry 13)



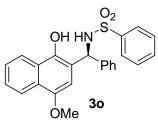
According to the general procedure, the title compound was synthesized in 87% yield. ¹H NMR (500 MHz, CDCl₃): δ 7.98 (m, 1H), 7.69 (m, 1H), 7.48 (d, J = 4.8 Hz, 2H), 7.42 (m, 2H), 7.25 (m, 1H), 7.01 (d, J = 5.0 Hz, 1H), 6.85 (d, J = 4.6 Hz, 2H), 6.80 (s, 1H), 5.44 (m, 1H), 4.60 (m, 1H), 2.07 (s, 3H), 1.82 (m, 2H), 1.25 (m, 4H), 1.08 (m, 1H), 0.75 (t, J = 4.0 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 149.0, 143.3, 136.5, 133.8, 128.9, 127.4, 126.9, 126.1, 125.4, 125.3, 125.2, 121.1, 120.5, 119.9, 55.7, 34.8, 28.3, 22.1, 21.1, 13.7; HR-MS: calcd (M + Na⁺) for C₂₂H₂₅NO₃S, 406.1453; found 406.1451; elemental analysis for C₂₂H₂₅NO₃S: calcd C 68.90, H 6.57, N 3.65; found C 69.12, H 6.63, N 3.58; HPLC (Chiralpak OJ-H, *i*-PrOH/hexane = 11/89, flow rate = 0.4 mL/min, $\lambda = 254$ nm): t_{majorr} = 28.17 min, t_{minor} = 37.55 min, ee = 92%; [α]_D²² = -38.2 (c = 1.0 in CH₂Cl₂).

N-((4-Chloro-1-hydroxynaphthalen-2-yl)(phenyl)methyl)benzenesulfonamide (Table 2, entry 14)



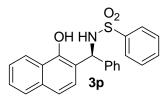
According to the general procedure, the title compound was synthesized in 100% yield. ¹H NMR (500 MHz, CDCl₃): δ 8.12 (d, J = 8.5 Hz, 1H), 8.08 (d, J = 8.0 Hz, 1H), 7.64-7.49 (m, 4H), 7.29-7.14 (m, 8H), 6.97 (s, 1H), 6.94 (s, 1H), 5.91 (d, J = 8.0 Hz, 1H), 5.85-5.77 (m, 1H); ¹³C NMR (125 MHz, CDCl₃): δ 148.7, 139.0, 138.1, 132.7, 130.9, 128.8, 128.7, 128.0, 127.6, 127.0, 126.9, 126.3, 125.7, 124.3, 123.5, 122.0, 120.1, 57.9; HR-MS: calcd (M + Na⁺) for C₂₃H₁₈ClNO₃S, 446.0594; found 446.0599; elemental analysis for C₂₃H₁₈ClNO₃S: calcd C 65.17, H 4.28, N 3.30; found C 65.49, H 4.41, N 3.19; HPLC (Chiralpak AS-H, *i*-PrOH/hexane = 40/60, flow rate = 0.6 mL/min, $\lambda = 254$ nm): t_{minor} = 19.60 min, t_{major} = 37.16 min, ee = 94%; [α]_D²² = -65.4 (c = 1.0 in CH₂Cl₂).

N-((1-Hydroxy-4-methoxynaphthalen-2-yl)(phenyl)methyl)benzenesulfonamide (Table 2, entry 15)



According to the general procedure, the title compound was synthesized in 97% yield. ¹H NMR (500 MHz, CDCl₃): δ 8.09 (s, 2H), 7.95 (s, 1H), 7.62 (d, *J* = 7.5 Hz, 2H), 7.46 (s, 2H), 7.25-7.23 (m, 6H), 7.11-7.09 (m, 2H), 6.21 (s, 1H), 5.92 (s, 2H), 5.84 (s, 1H), 3.71 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 149.8, 142.5, 139.6, 139.2, 132.4, 128.6, 128.5, 127.8, 126.9, 126.3, 125.9, 121.9, 120.9, 120.0, 103.8, 58.5, 55.5; HR-MS: calcd (M + Na⁺) for C₂₄H₂₁NO₄S, 442.1089; found 442.1094; C, H, N analysis for C₂₄H₂₁NO₄S: calcd C 68.72, H 5.05, N 3.34; found C 68.95, H 4.96, N 3.55; HPLC (Chiralpak AS-H, *i*-PrOH/hexane = 40/60, flow rate = 0.6 mL/min, λ = 254 nm): t_{minor} = 20.76 min, t_{major} = 44.58 min, ee = 95%; [α]_D²² = -45.2 (*c* = 1.0 in CH₂Cl₂).

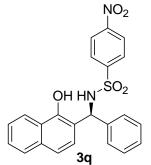
N-((1-Hydroxynaphthalen-2-yl)(phenyl)methyl)benzenesulfonamide (Table 2, entry 16)



According to the general procedure, the title compound was synthesized in 83% yield. ¹H NMR (500 MHz, DMSO): δ 9.49-9.48 (m, 1H), 8.76-8.75 (m, 1H), 8.14 (s, 1H), 7.74-7.64 (m, 3H), 7.43-7.13 (m, 12H), 6.33-6.31 (m, 1H); ¹³C NMR (125 MHz, DMSO): δ 148.2, 141.9, 141.3, 133.2, 131.7, 128.4, 127.9, 127.4, 126.8, 126.6, 126.2, 125.7, 125.2, 124.9, 123.1, 122.0, 119.5, 54.2;

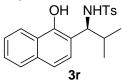
HR-MS: calcd (M + Na⁺) for C₂₃H₁₉NO₃S, 412.0983; found 412.0985; elemental analysis for C₂₃H₁₉NO₃S: calcd C 70.93, H 4.92, N 3.60; found C 70.14, H 4.99, N 3.58; HPLC (Chiralpak AS-H, *i*-PrOH/hexane = 40/60, flow rate = 0.6 mL/min, λ = 254 nm): t_{minor} = 22.87 min, t_{major} = 38.6 min, ee = 94%; [α]_D²² = -40.1 (*c* = 1.0 in CH₂Cl₂).

N-((1-Hydroxynaphthalen-2-yl)(phenyl)methyl)-4-nitrobenzenesulfonamide (Table 2, entry 17)



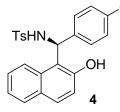
According to the general procedure, the title compound was synthesized in 94% yield. ¹H NMR (300 MHz, CDCl₃:CD₃OD = 10:1): δ 7.82-7.78 (m, 1H), 7.69-7.56 (m, 5H), 7.34-7.30 (m, 2H), 7.29-7.23 (m, 2H), 7.20-7.12 (m, 4H), 6.94-6.92 (m, 1H), 5.94 (s, 1H); ¹³C NMR (75 MHz, CDCl₃:CD₃OD = 10:1): δ 149.1, 148.7, 145.7, 139.6, 133.9, 128.2, 127.7, 127.5, 127.3, 126.9, 126.5, 126.3, 125.4, 125.0, 122.9, 120.6, 120.3, 120.1, 58.3; HR-MS: calcd (M + Na⁺) for C₂₃H₁₈N₂O₅S, 457.0834; found 457.0832; elemental analysis for C₂₃H₁₈N₂O₅S: calcd C 63.58, H 4.18, N 6.45; found C 63.78, H 4.27, N 6.33; HPLC (Chiralpak AS-H, *i*-PrOH/hexane = 30/70, flow rate = 0.6 mL/min, λ = 210 nm): t_{minor} = 26.38 min, t_{major} = 47.13 min, ee = 85%.

N-(1-(1-Hydroxynaphthalen-2-yl)-2-methylpropyl)-4-methylbenzenesulfonamide (Table 2, entry 18)



According to the general procedure, the title compound was synthesized in 55% yield. ¹H NMR (300 MHz, acetone- d_6): δ 8.20 (s, 1H), 8.13 (d, J = 8.1 Hz, 1H), 7.72 (d, J = 7.5 Hz, 1H), 7.47-7.38 (m, 4H), 7.21 (m, 2H), 6.79 (d, J = 7.8 Hz, 2H), 6.71 (d, J = 9.6 Hz, 1H), 4.67 (t, J = 9.3 Hz, 1H), 2.11 (m, 1H), 1.96 (s, 3H), 1.06 (d, J = 6.6 Hz, 3H), 0.76 (d, J = 6.9 Hz, 3H); ¹³C NMR (75 MHz, acetone- d_6): δ 149.5, 142.7, 139.4, 134.5, 129.3, 128.3, 127.3, 126.4, 126.3, 125.9, 125.7, 122.8, 122.0, 120.7, 59.7, 34.3, 20.9, 19.9, 19.8; HR-MS: calcd (M + Na⁺) for C₂₁H₂₃NO₃S, 392.1296; found 392.1291; HPLC (Chiralpak AS-H, *i*-PrOH/hexane = 40/60, flow rate = 0.6 mL/min, $\lambda = 254$ nm): t_{minor} = 14.59 min, t_{major} = 18.29 min, ee = 85%.

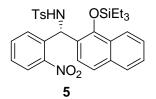
N-((4-Chlorophenyl)(2-hydroxynaphthalen-1-yl)methyl)-4-methylbenzenesulfonamide (4)



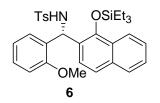
According to the general procedure, the title compound was synthesized in 92% yield. ¹H NMR (500 MHz, CDCl₃): δ 7.67-7.63 (m, 2H), 7.50 (d, J = 9.0 Hz, 1H), 7.38 (t, J = 7.5 Hz, 1H), 7.31-7.25 (m, 3H), 7.22 (d, J = 8.5 Hz, 2H), 7.14 (d, J = 8.5 Hz, 2H), 6.89-6.81 (m, 3H), 6.60 (d, J = 8.0 Hz, 2H), 6.32 (d, J = 10.5 Hz, 1H), 2.06 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 150.9, 142.9, 138.7, 136.0, 133.1, 132.2, 129.9, 128.9, 128.7, 128.4, 128.3, 128.2, 127.3, 126.5, 123.5, 121.7, 117.9, 117.2, 53.8, 21.2; HR-MS: calcd (M + Na⁺) for C₂₅H₂₄ClNO₃S, 476.1063; found 476.1066; elemental analysis for C₂₅H₂₄ClNO₃S: calcd C 66.14, H 5.53, N 3.09; found C 66.02, H 5.37, N 3.17; HPLC (Chiralpak AS-H, *i*-PrOH/hexane = 40/60, flow rate = 0.6 mL/min, $\lambda = 254$ nm): t_{minor} = 10.09 min, t_{major} = 14.75 min, ee = 62%.

General procedure for the derivation of the Friedel-Crafts products.

At 0 °C, to a vial containing the product (0.06 mmol) and 1.1 mL of anhydrous CH_2Cl_2 was added 2,6-lutidine (17.5 µL, 0.15 mmol) and TESOTF (16.4 µL, 0.072 mmol). The reaction solution was stirred at 0 °C for 0.5 h before 0.1 mL of methol and 3 mL of brine was added. The mixture was extracted with CH_2Cl_2 . The combined extracts were dried over MgSO₄, filtered and concentrated in vacuo. The resulting residue was then purified by silica gel chromatography, eluting with EtOAc/hexane (1/7) to provide the corresponding derivative.



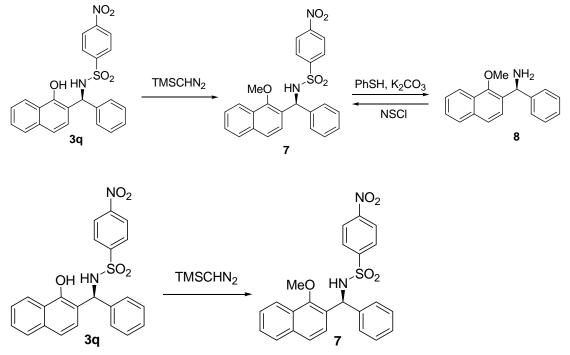
The title compound was obtained in 92% yield. ¹H NMR (500 MHz, CD₃Cl): δ 7.96-7.94 (m, 1H), 7.77-7.70 (m, 2H), 7.48-7.43 (m, 4H), 7.37-7.26 (m, 4H), 7.05 (d, *J* = 8.5 Hz, 1H), 6.94 (d, *J* = 8.0 Hz, 2H), 6.72 (d, *J* = 7.5 Hz, 1H), 5.48 (d, *J* = 7.5 Hz, 1H), 2.21 (s, 3H), 0.90 (t, *J* = 7.5 Hz, 9H), 0.81-0.79 (m, 6H); ¹³C NMR (125 MHz, CD₃Cl): δ 149.8, 149.4, 143.0, 137.5, 134.5, 134.2, 132.1, 131.1, 129.0, 128.6, 127.8, 127.7, 127.1, 126.4, 125.3, 124.7, 122.9, 122.6, 121.5, 53.4, 21.3, 6.8, 5.7; HR-MS: calcd (M + Na⁺) for C₃₀H₃₄N₂O₅SSi, 585.1855; found 585.1859; HPLC (Chiralpak OD-H, *i*-PrOH/hexane = 5/95, flow rate = 0.6 mL/min, λ = 254 nm): t_{minor} = 32.99 min, t_{major} = 20.39 min, ee = 91%; $\lceil \alpha \rceil_D^{22} = -76.4$ (*c* = 1.0 in CH₂Cl₂).



The title compound was obtained in 90% yield. ¹H NMR (500 MHz, CD₃Cl): δ 7.99-7.97 (m, 1H), 7.76-7.74 (m, 1H), 7.67 (t, *J* = 8.0 Hz, 3H), 7.43-7.39 (m, 3H), 7.15-7.14 (m, 1H), 7.05 (d, *J* = 8.0 Hz, 2H), 6.89 (d, *J* = 6.5 Hz, 1H), 6.75-6.68 (m, 2H), 6.23 (d, *J* = 6.0 Hz, 1H), 5.33 (d, *J* = 5.5 Hz, 1H), 3.67 (s, 3H), 2.30 (s, 3H), 0.97-0.89 (m, 9H), 0.73-0.72 (m, 6H); ¹³C NMR (125 MHz, CD₃Cl): δ 156.7, 148.9, 142.7, 137.4, 134.2, 129.6, 129.1,128.9, 127.9, 127.8, 127.6, 127.5, 126.4, 125.8, 124.9, 124.6, 122.9, 121.0, 120.3, 110.5, 54.9, 52.5, 21.3, 6.7, 5.5; HR-MS: calcd (M + Na⁺) for C₃₁H₃₇NO₄SSi, 570.2110; found 570.2111; HPLC (Chiralpak OD-H, *i*-PrOH/hexane = 5/95, flow

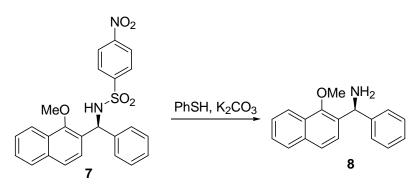
rate = 0.6 mL/min, λ = 254 nm): t_{minor} = 22.95 min, t_{major} = 15.58 min, ee = 80%; [α]_D²² = -89.6 (*c* = 1.0 in CH₂Cl₂).

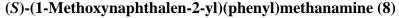
Procedures for the deprotection of sulfonamide group



(S)-N-((1-Methoxynaphthalen-2-yl)(phenyl)methyl)-4-nitrobenzenesulfonamide (7)

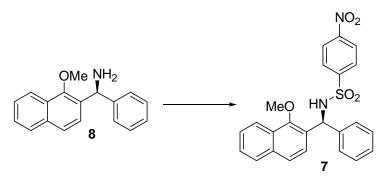
To a solution of compound **3q** (43.5 mg, 0.1 mmol) in MeOH (2 mL) and CH₂Cl₂ (2 mL), TMSCHN₂ (2N solution in hexane, 0.5 mL, 1.0 mmol) was added in 5 portions within 30 min at rt. The reaction mixture was then stirred at rt for another 30 min. The solvent was removed under reduced pressure. The residue was purified through chromatography and got the desired product 38 mg, 85% yield. ¹H NMR (300 MHz, CDCl₃:CD₃OD = 10:1): δ 7.81-7.64 (m, 6H), 7.47-7.41 (m, 3H), 7.35-7.11 (m, 5H), 7.12 (d, *J* = 8.4 Hz, 1H), 6.27 (d, *J* = 9.6 Hz, 1H), 6.04 (d, *J* = 9.6 Hz, 1H), 3.52 (s, 3H); ¹³C NMR (75 MHz, CDCl₃:CD₃OD = 10:1): δ 153.1, 148.9, 145.7, 139.9, 134.6, 128.6, 128.0, 127.9, 127.8, 127.5, 126.9, 126.8, 126.6, 126.1, 124.5, 123.2, 121.7, 62.4, 57.9;





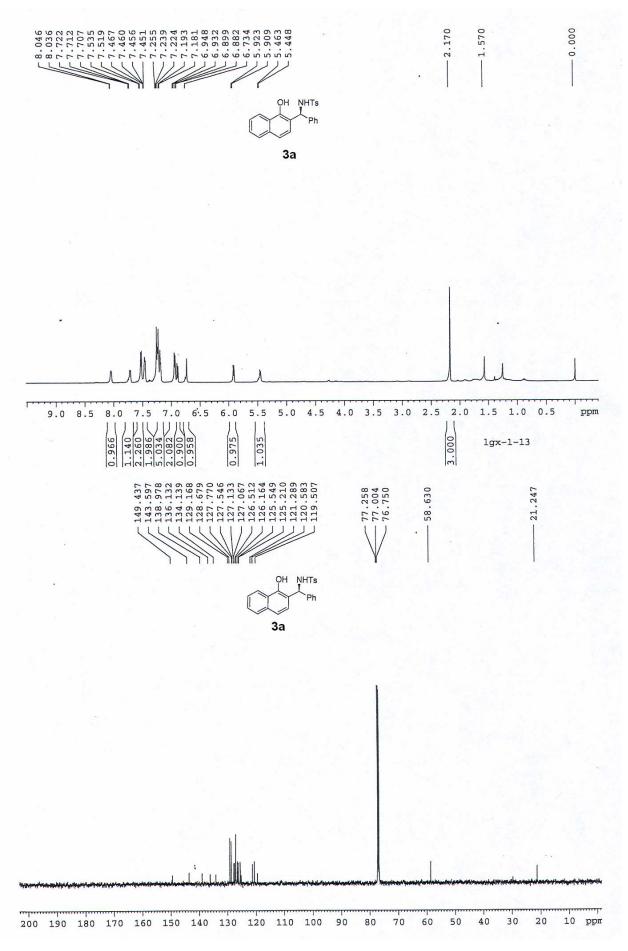
PhSH (148 mg, 1.34 mmol) was added to a solution of compound **7** (30 mg, 0.067 mmol) and K_2CO_3 (185 mg, 1.34 mmol) in DMF (0.5 mL) and CH₃CN (0.5 mL). The mixture was stirred at 50 °C for 30 min. Water (10 mL) was added and extracted with EtOAc (5 mL × 2). The combined organic layer was back extracted with 0.5 N HCl (3 mL) and then the aqueous layer was basified with NaOH

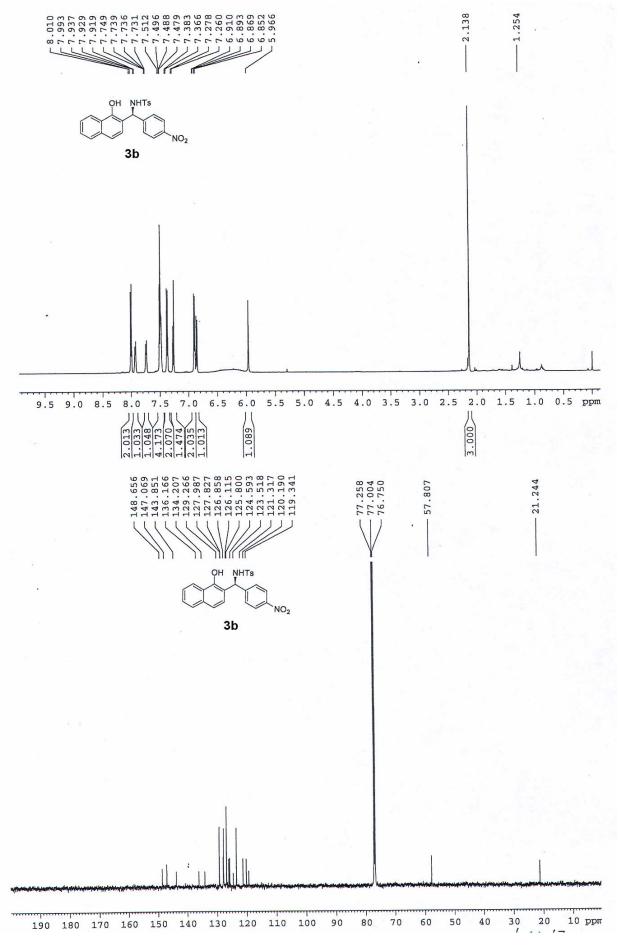
and extracted with EtOAc. The combined EtOAc layer was dried over Na₂SO₄ and the solvent was removed. The crude product (13 mg) was pure enough in 74% yield. ¹H NMR (300 MHz, CDCl₃:CD₃OD = 10:1): δ 8.00 (d, *J* = 8.1 Hz, 1H), 7.82 (d, *J* = 8.7 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.54-7.45 (m, 5H), 7.47-7.41 (m, 3H), 7.34-7.15 (m, 3H), 5.84 (s, 1H), 3.89 (s, 3H); ¹³C NMR (75 MHz, CDCl₃:CD₃OD = 10:1): δ 152.9, 134.3, 128.4, 128.1, 127.8, 126.9, 126.8, 126.0, 125.4, 124.6, 122.3, 62.6, 52.9;

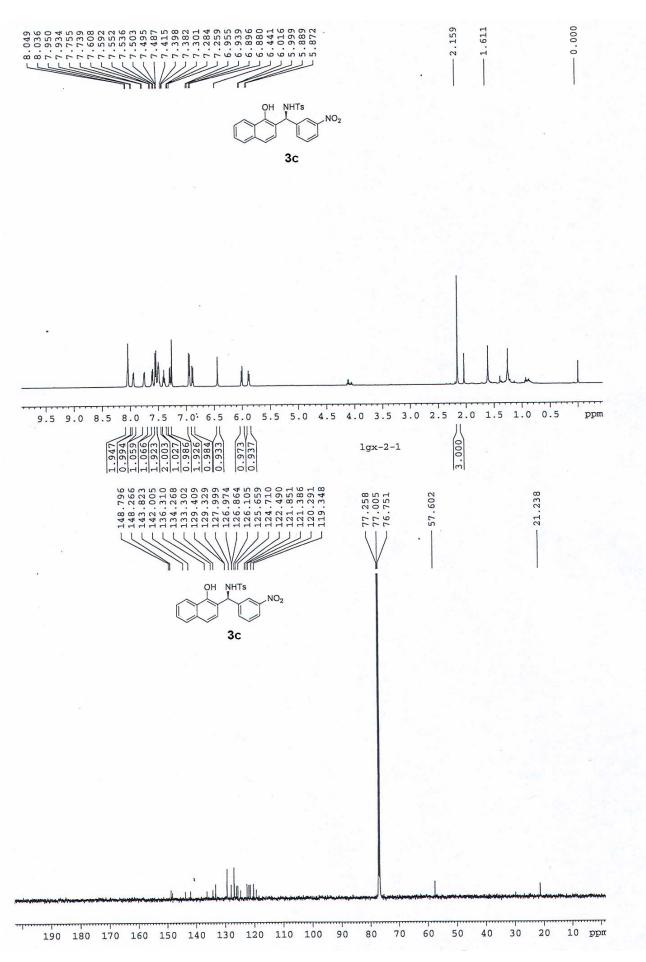


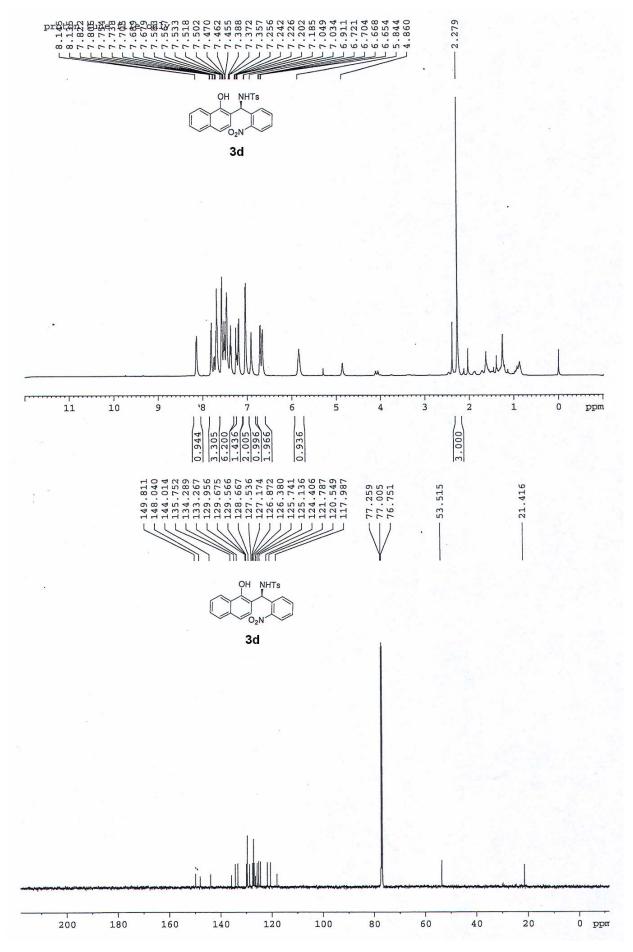
(S)-N-((1-Methoxynaphthalen-2-yl)(phenyl)methyl)-4-nitrobenzenesulfonamide (7) (Converted to 7 for chiral HPLC analysis)

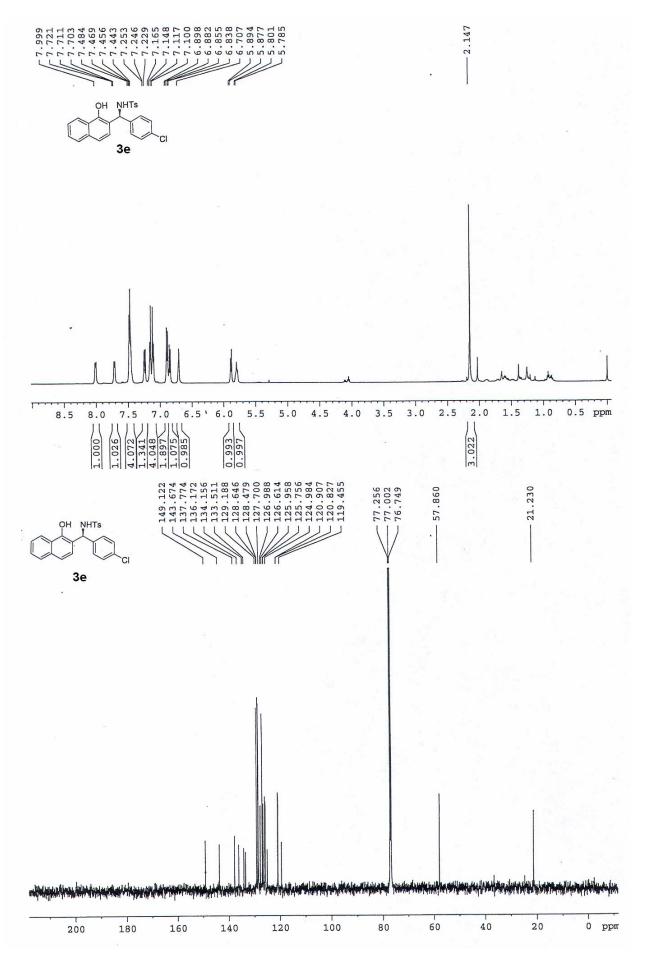
p-NO₂C₆H₄SO₂Cl (16.8 mg, 0.076 mmol) was added to a solution of compound **8** (10 mg, 0.038 mmol) and Et₃N (11.5 mg, 0.11 mmol) in CH₂Cl₂ (0.4 mL) at 0 °C. The reaction mixture was stirred at the same temperature for 3 h. Direct chromatography gave the desired product 15 mg, 88% yield. HPLC (Chiralpak AS-H, *i*-PrOH/hexane = 30/70, flow rate = 0.6 mL/min, λ = 210 nm): t_{minor} = 30.06 min, t_{major} = 39.88 min, ee = 85%.

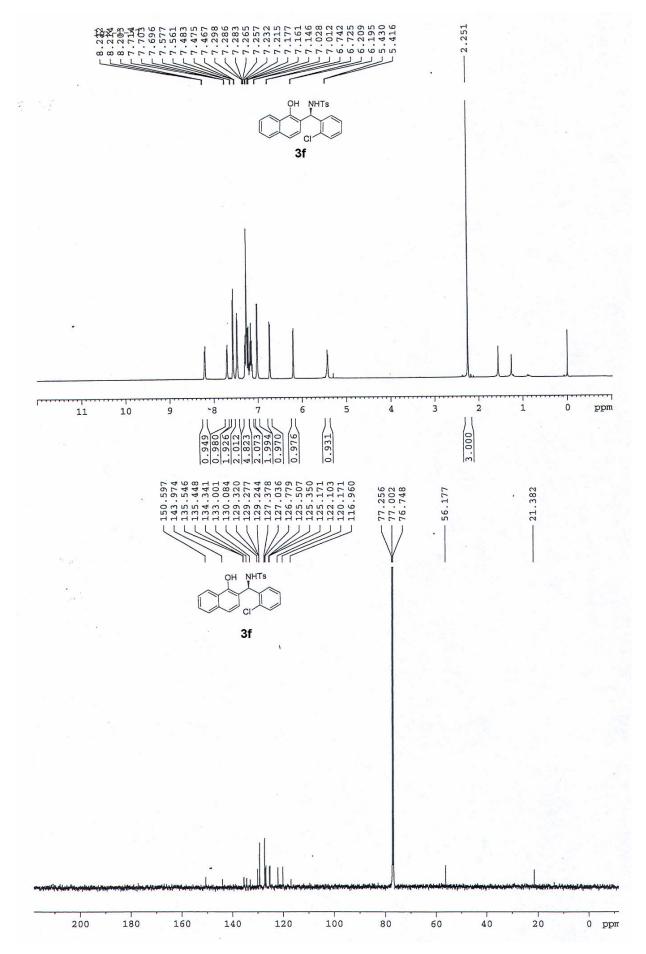


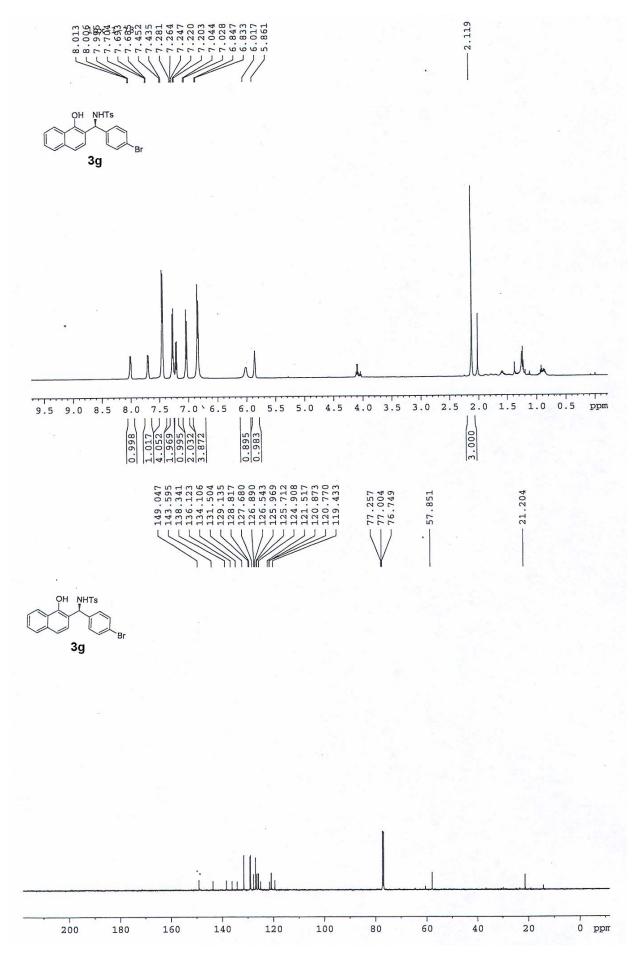


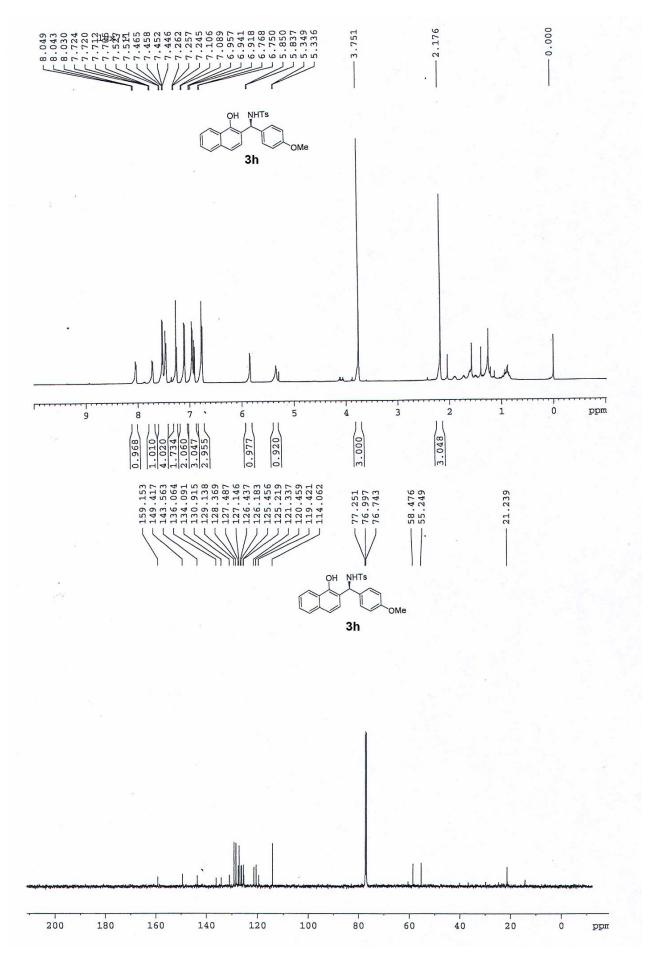


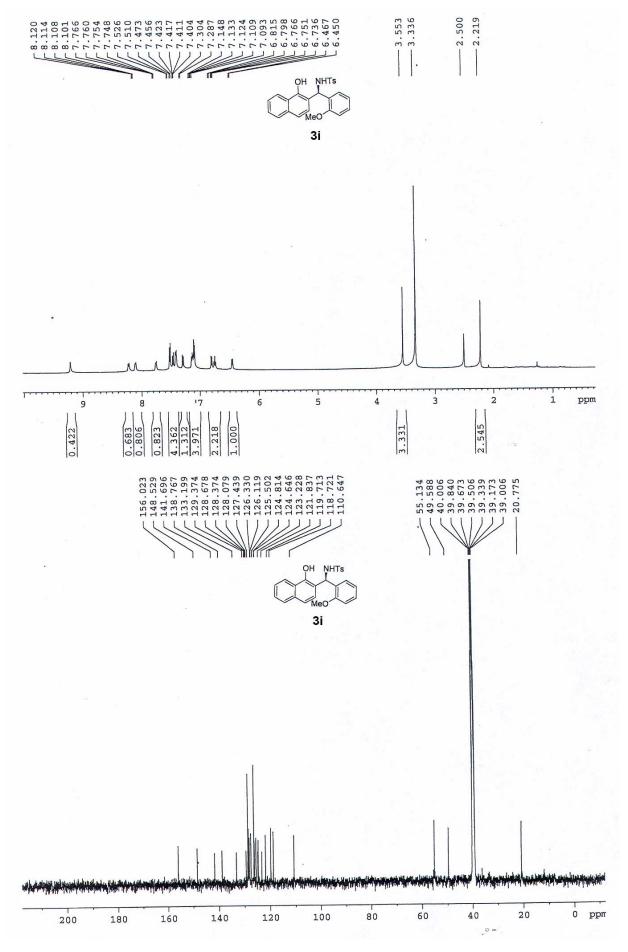


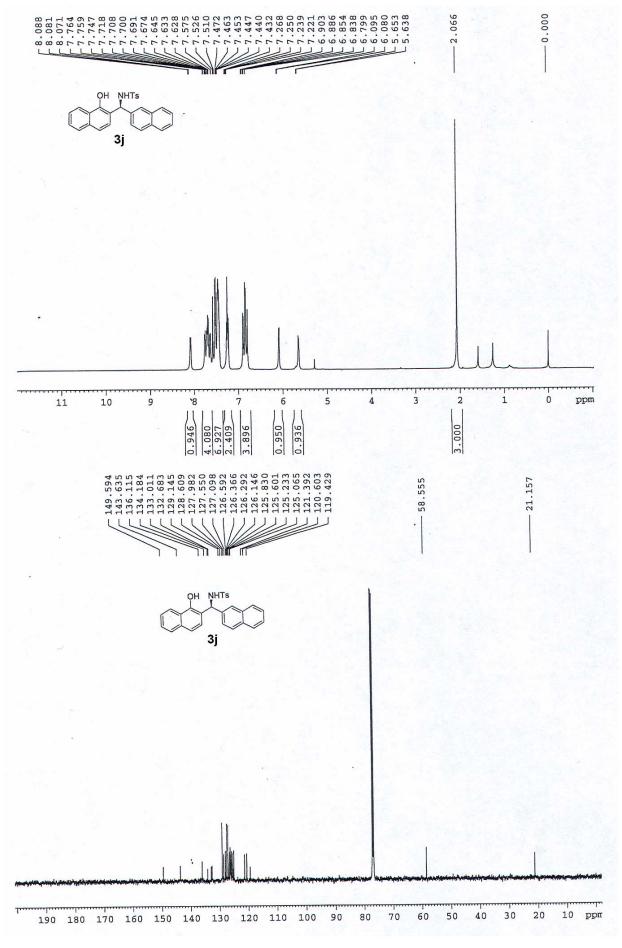


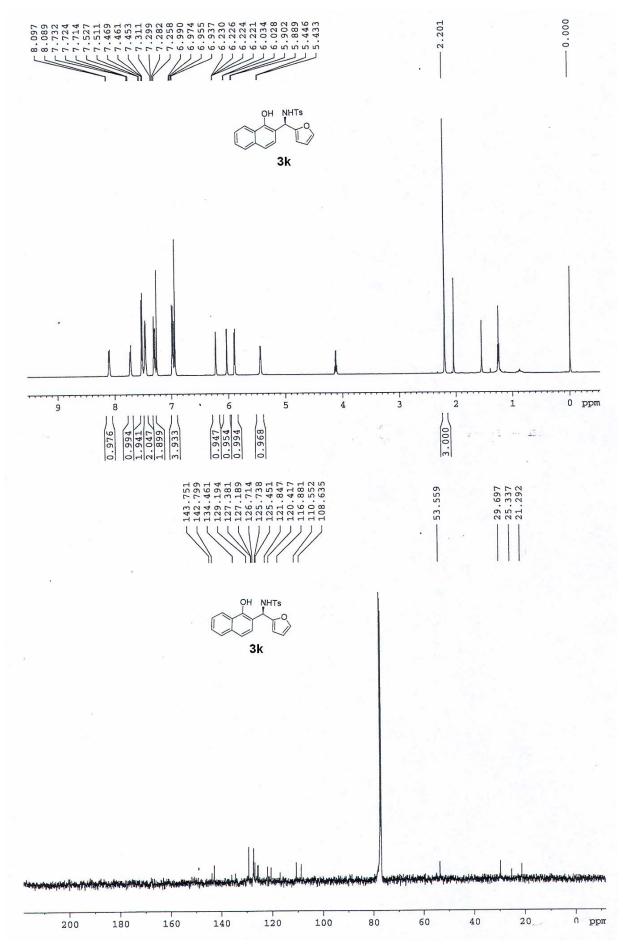


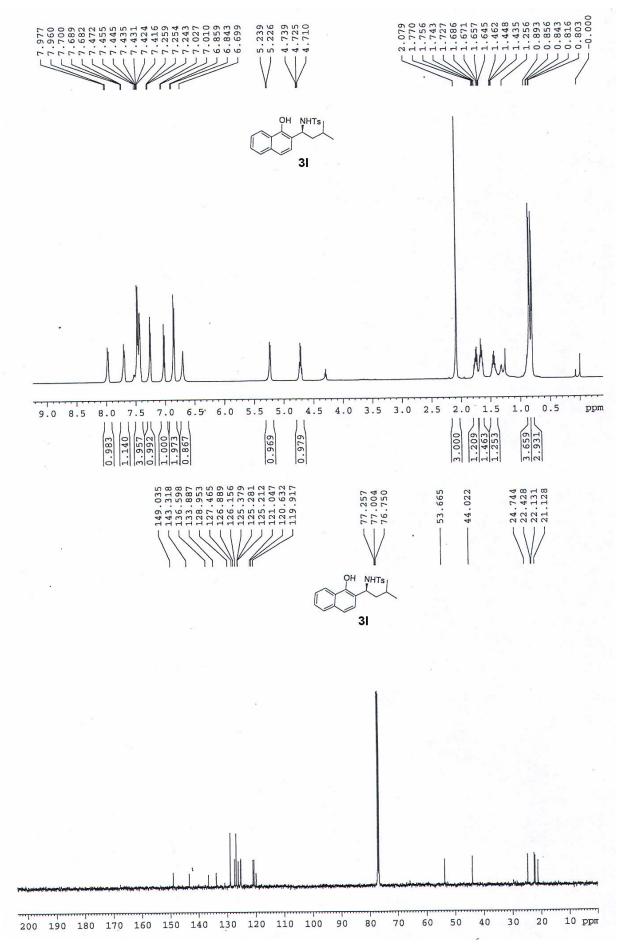


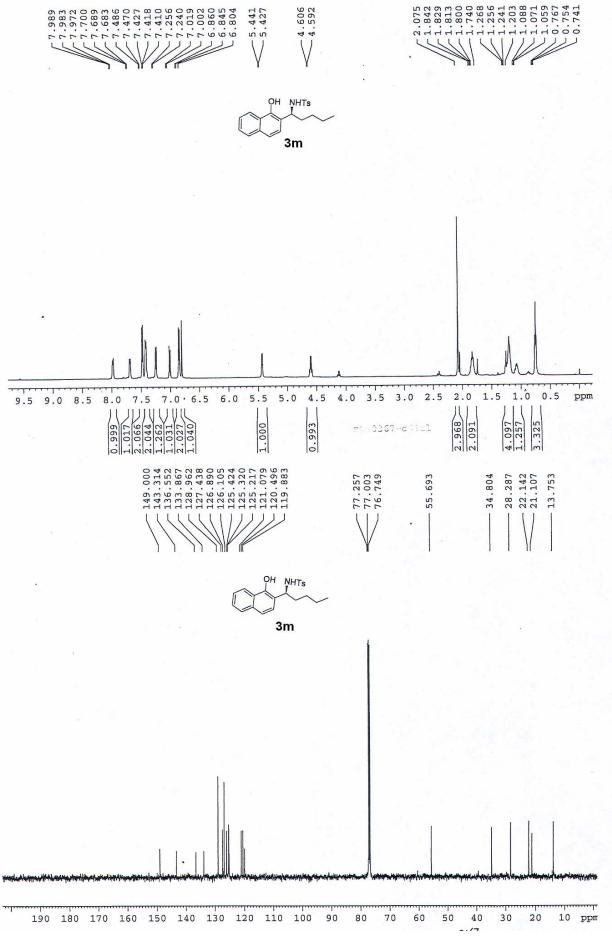


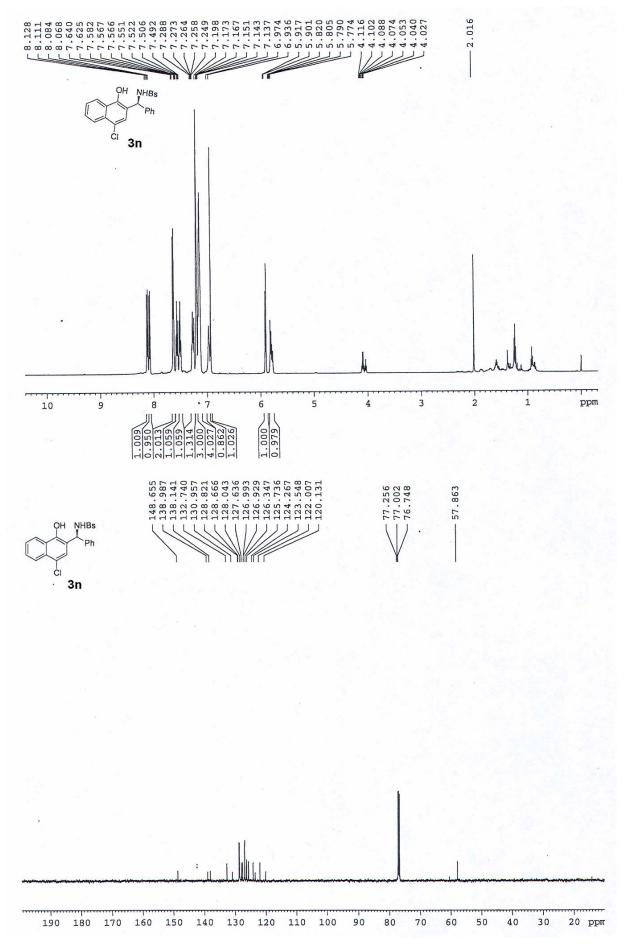


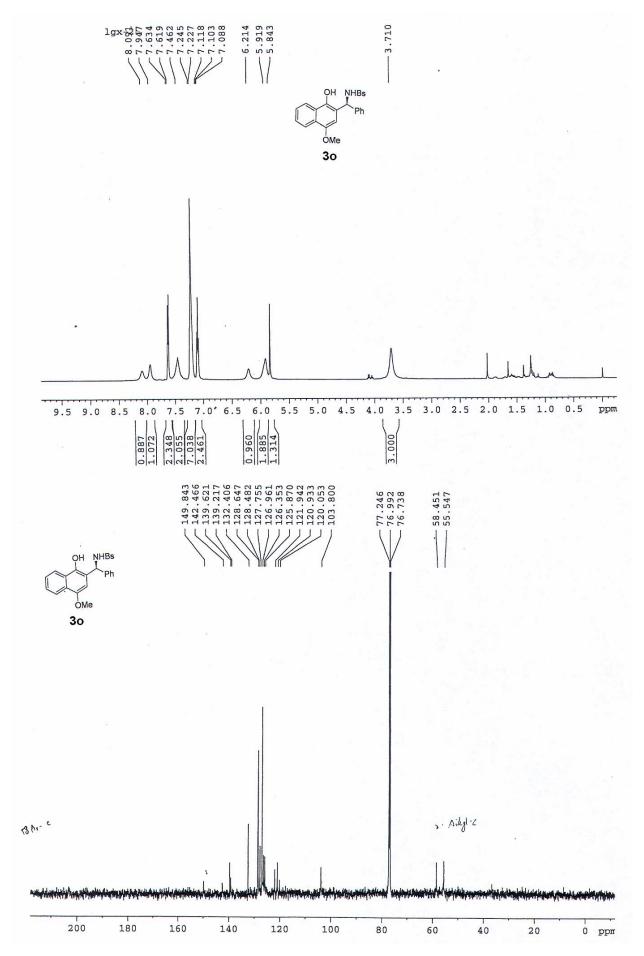


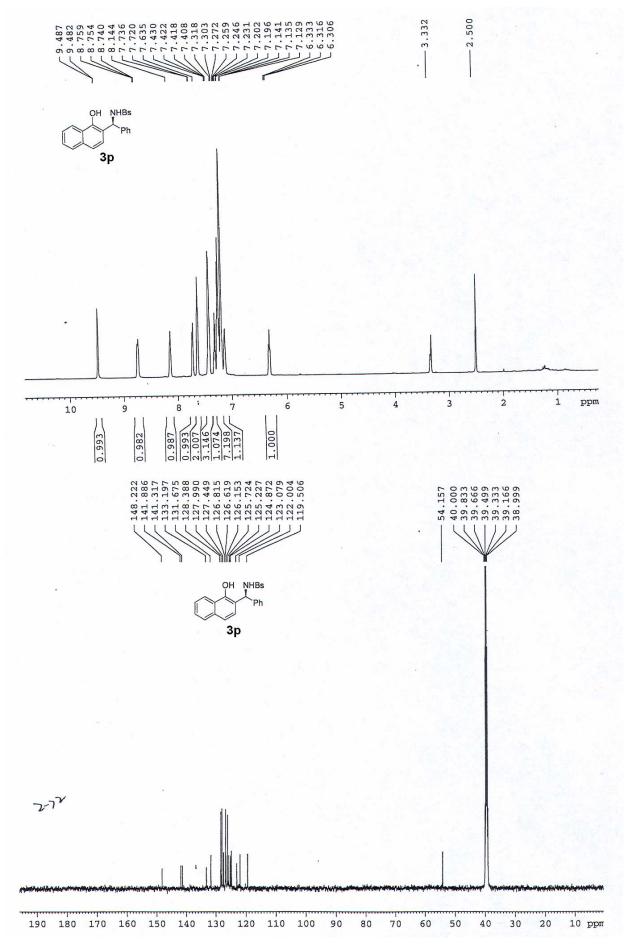




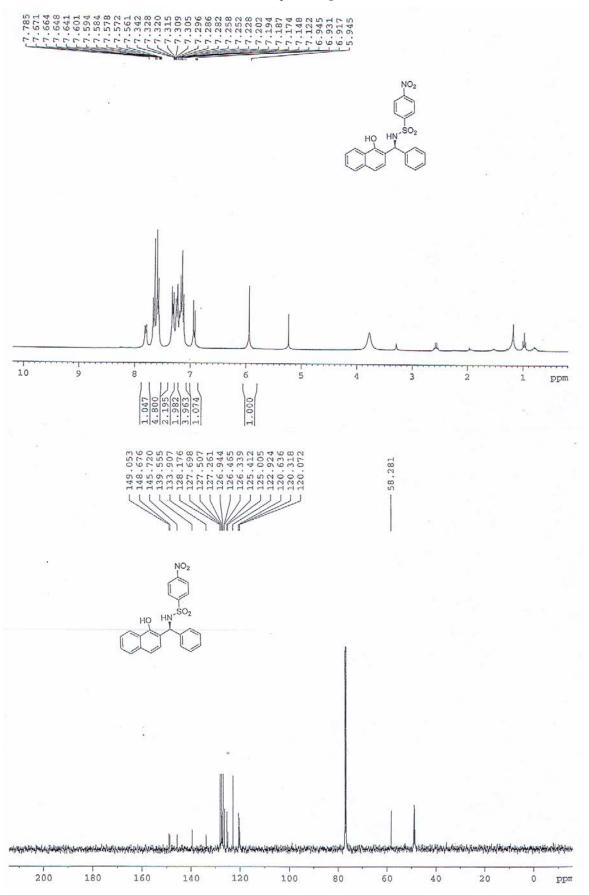


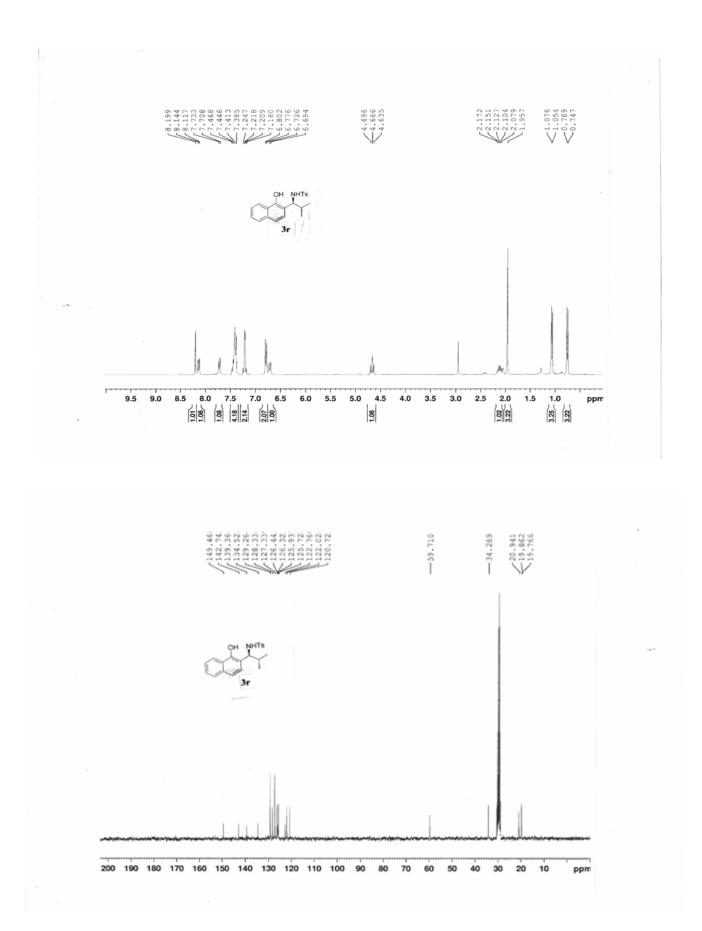




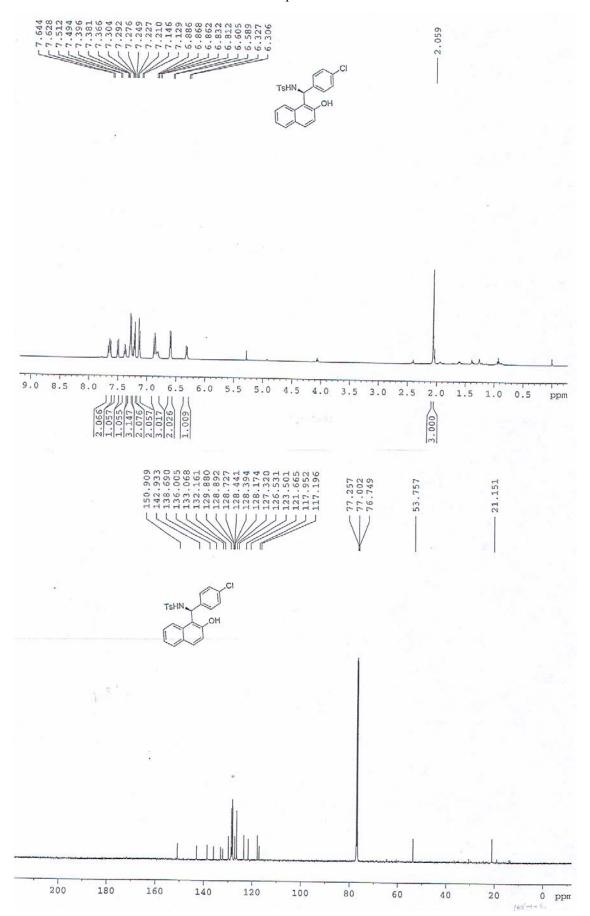


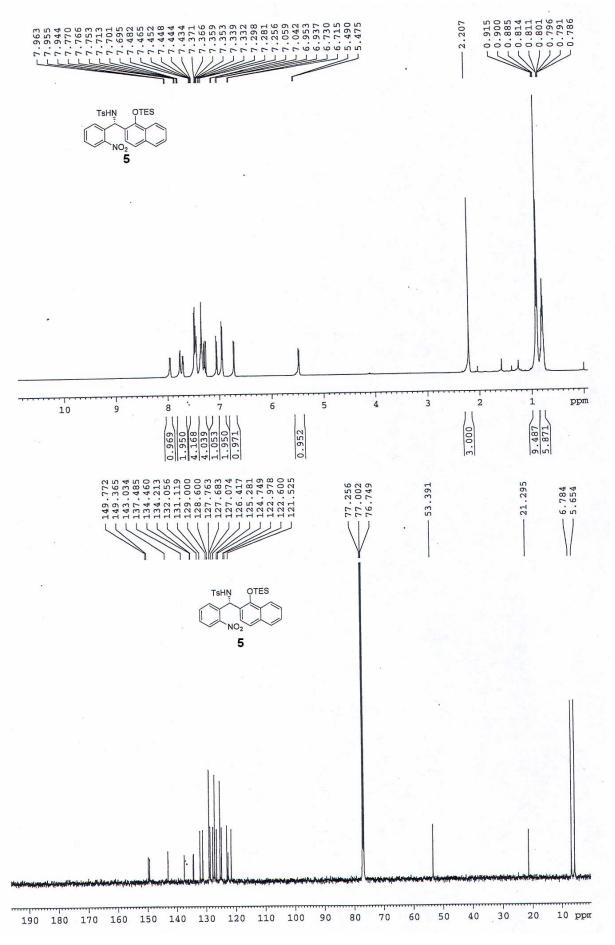


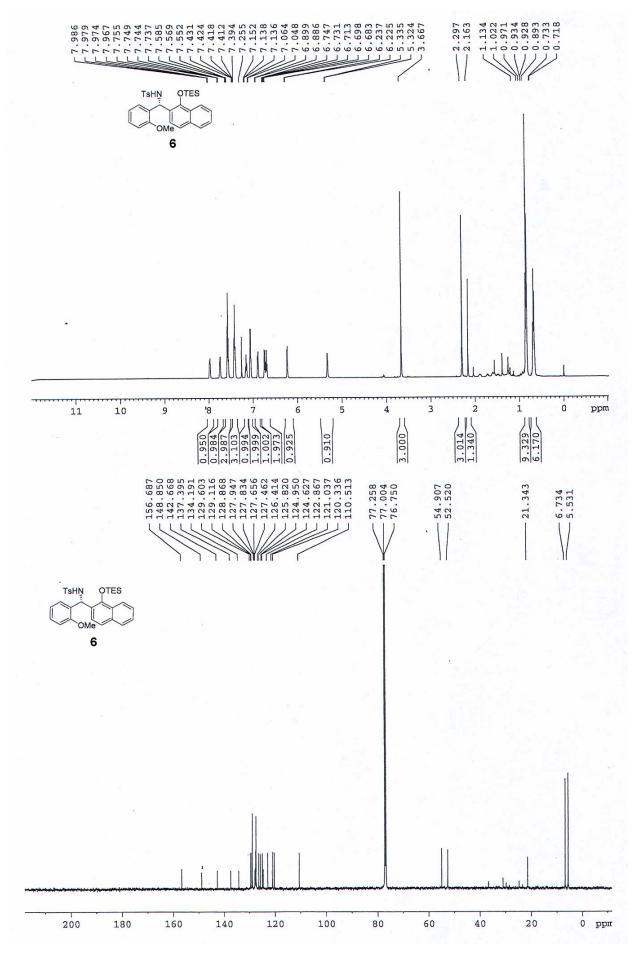


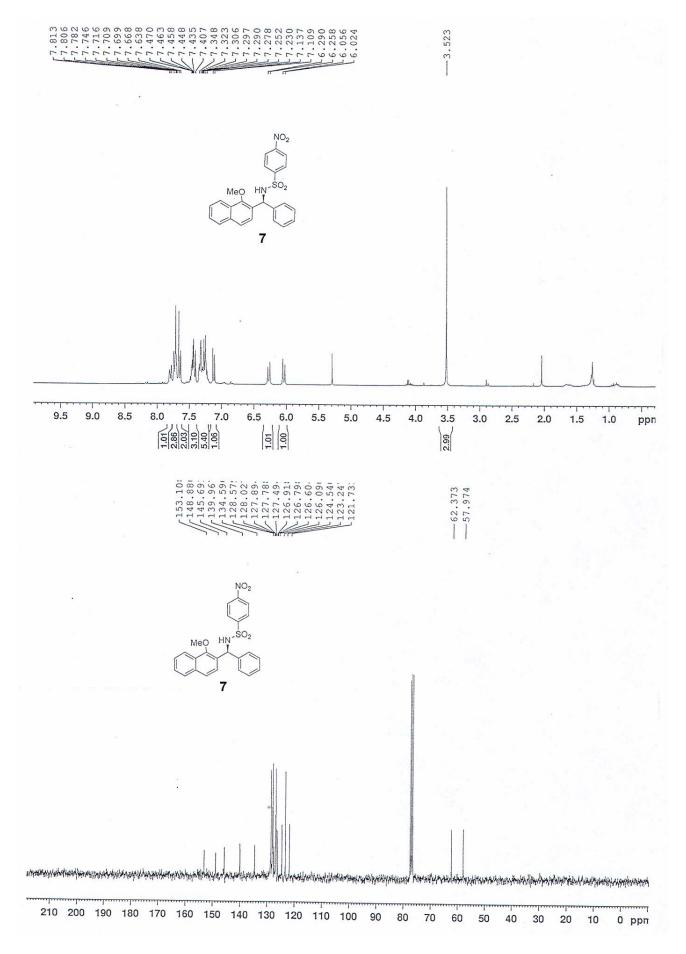


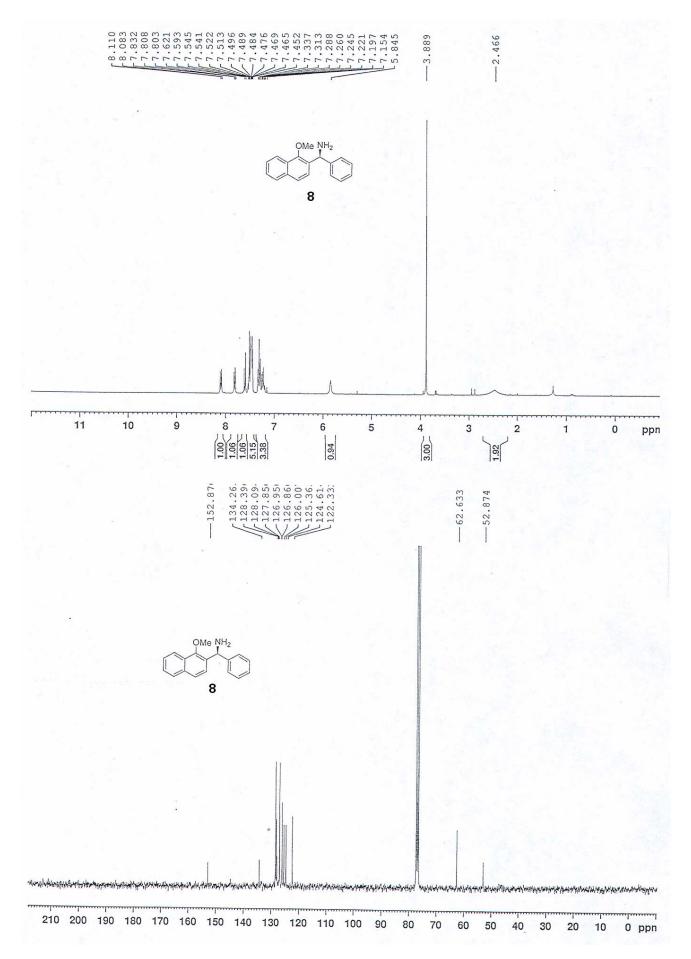
Compound 4

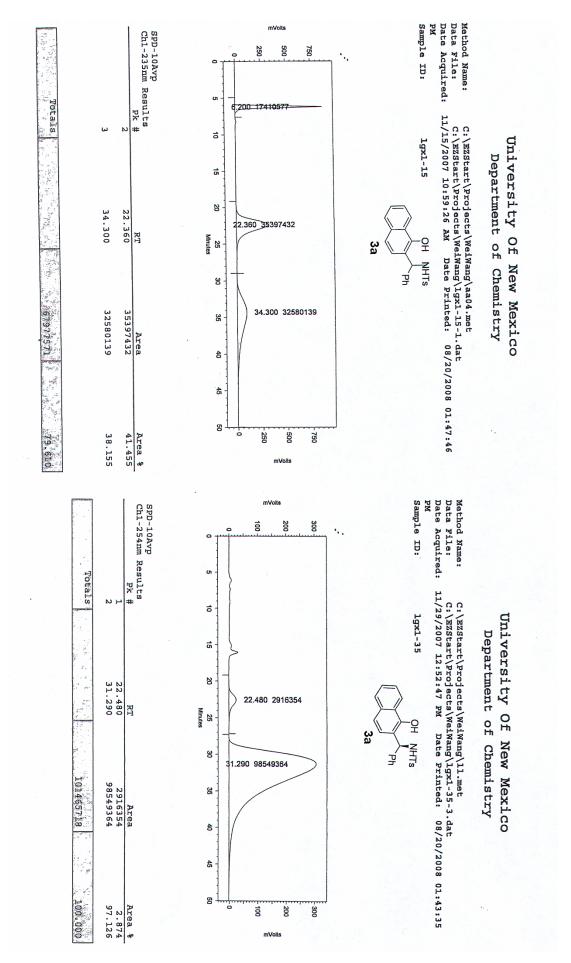


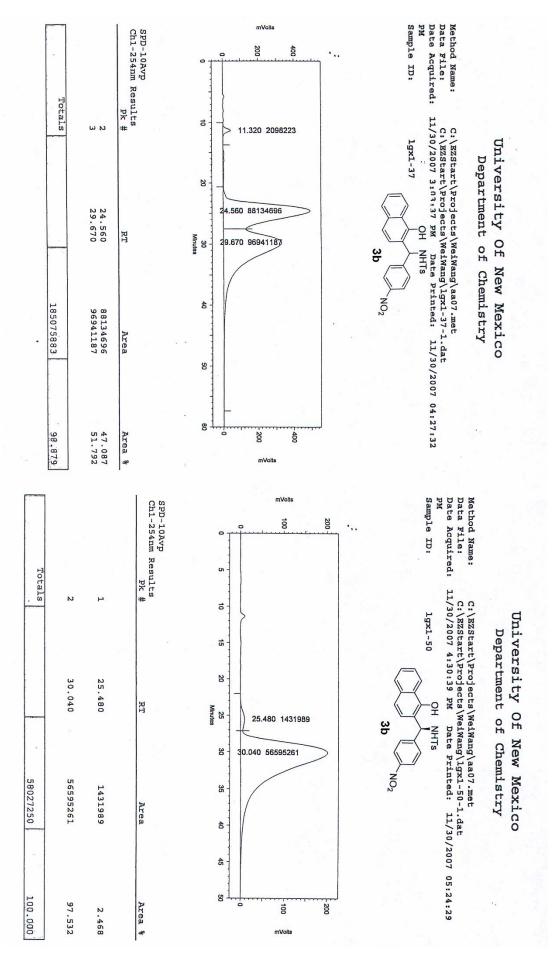


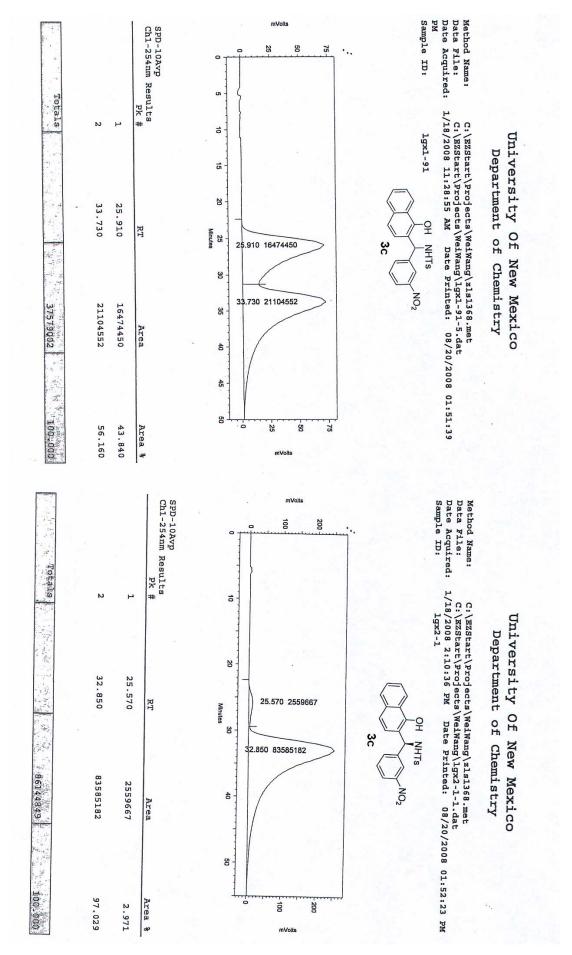


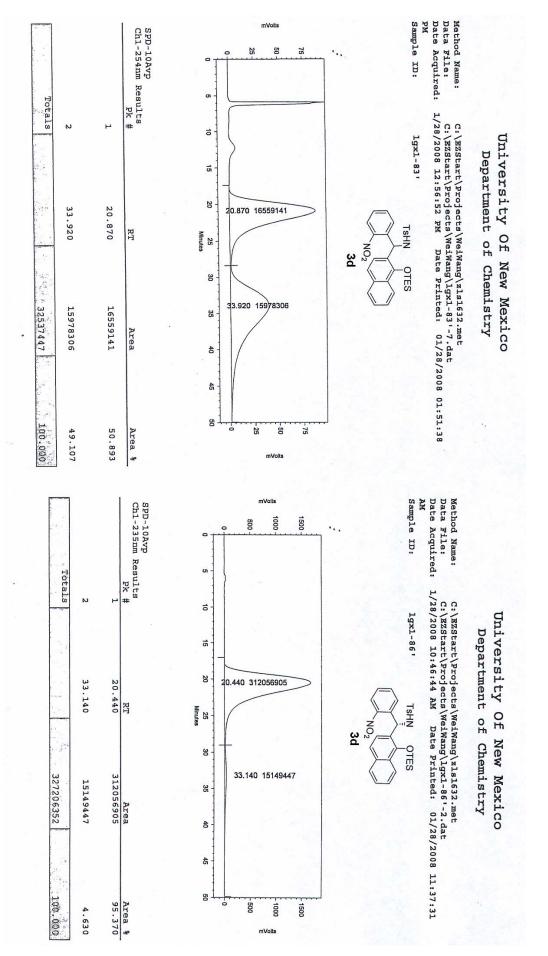


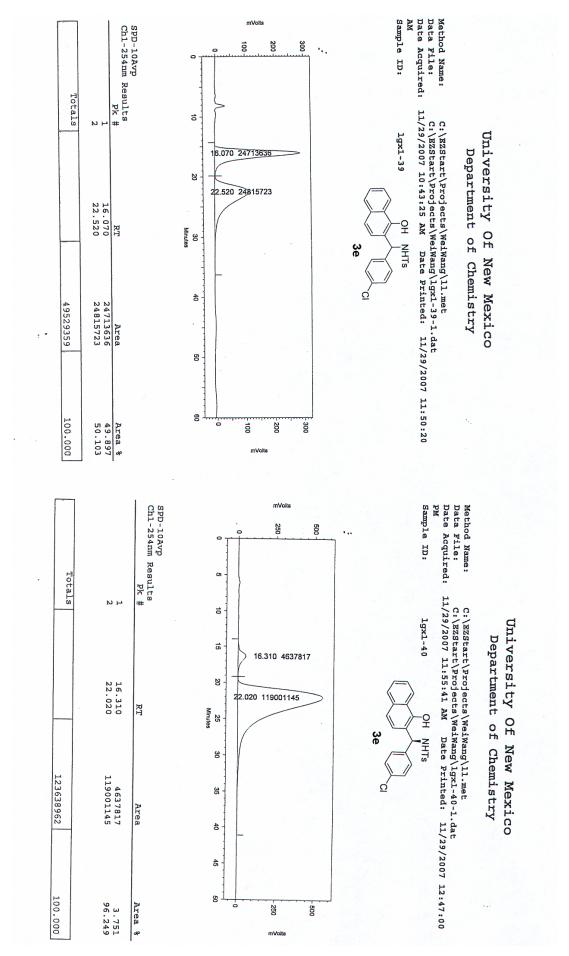


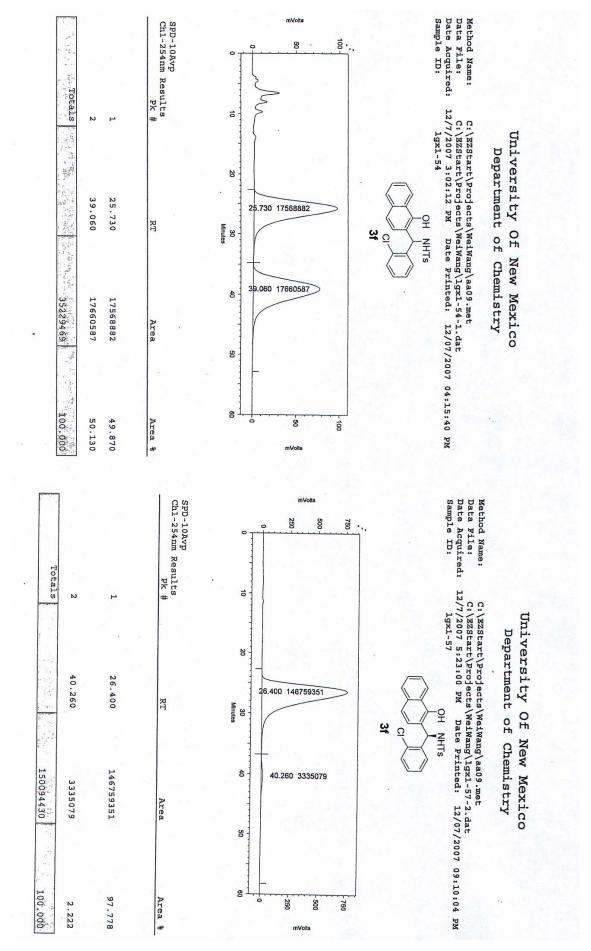


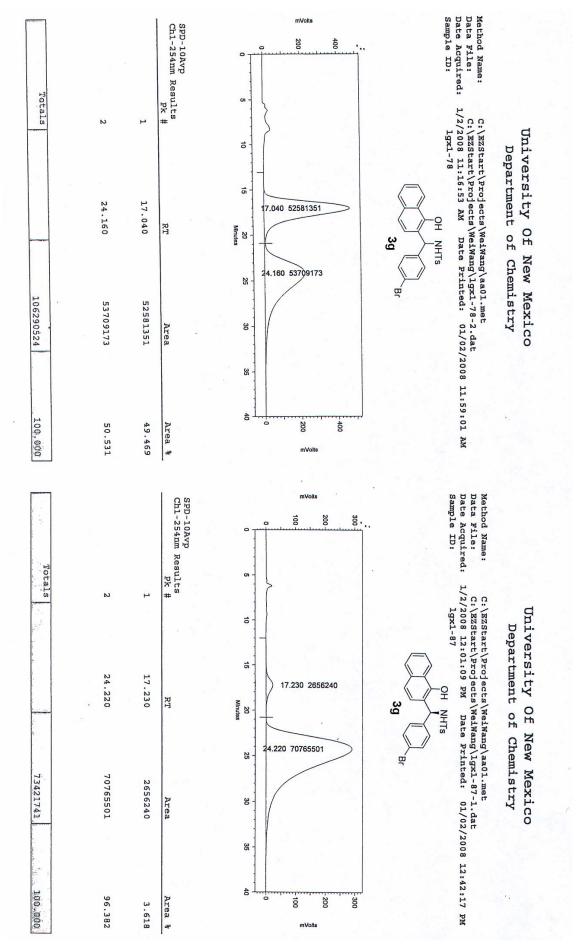


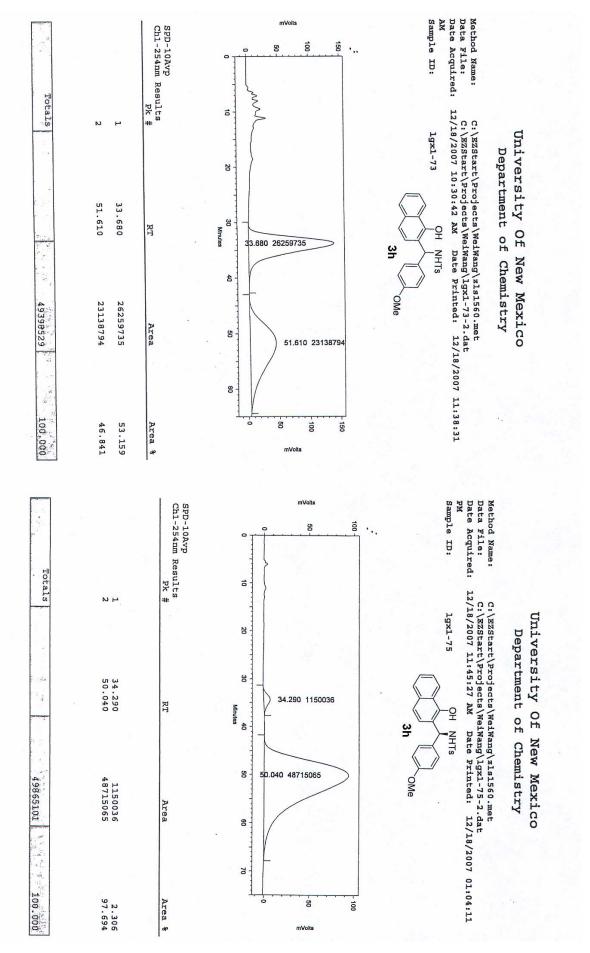


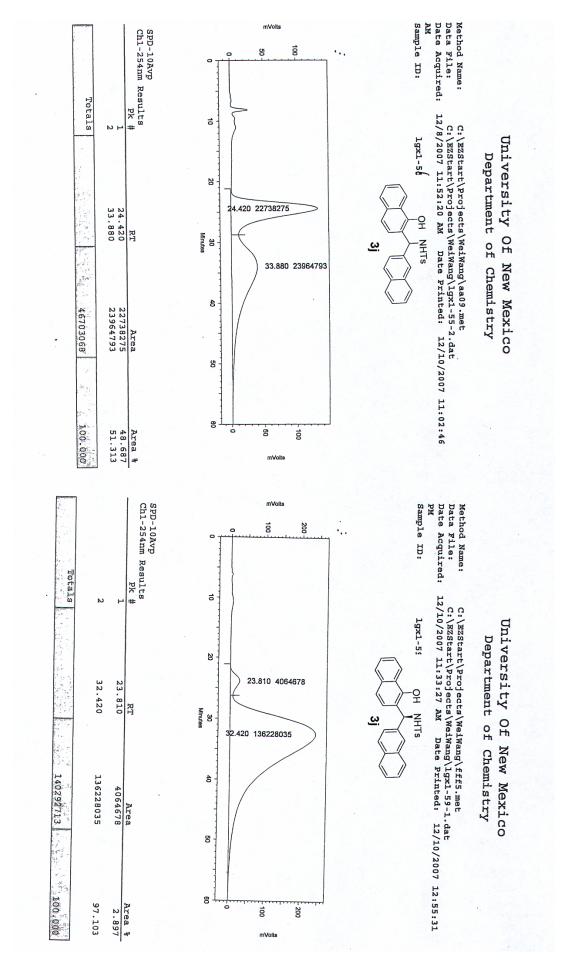


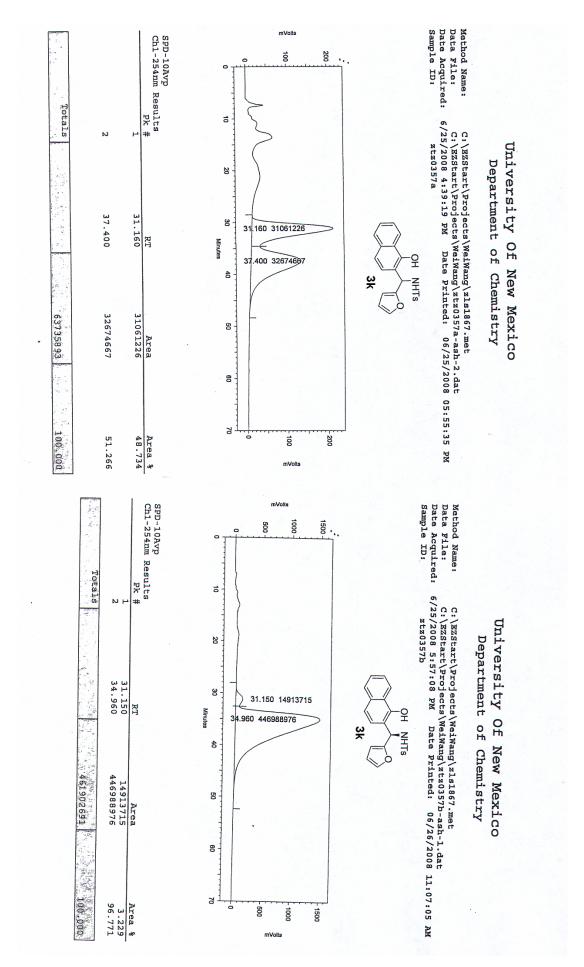


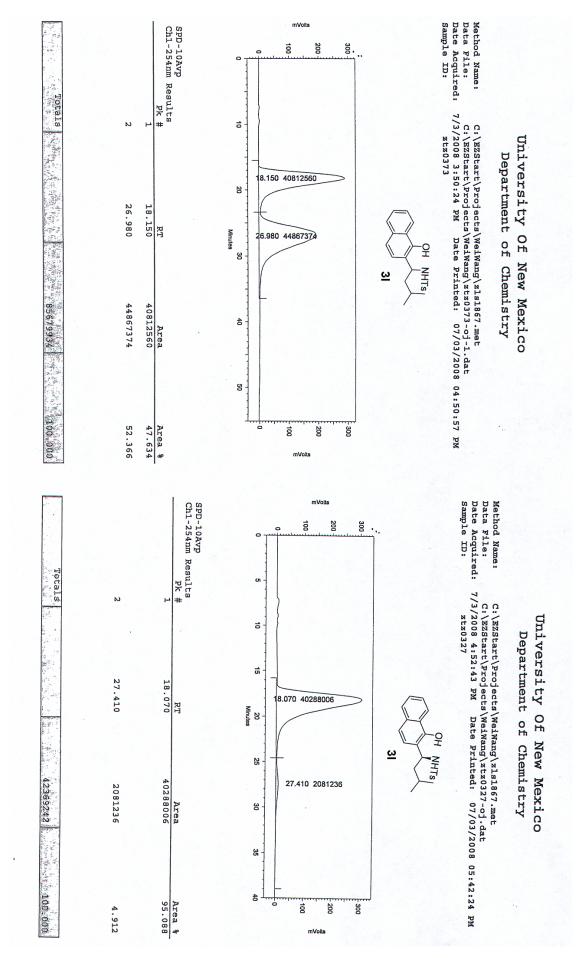


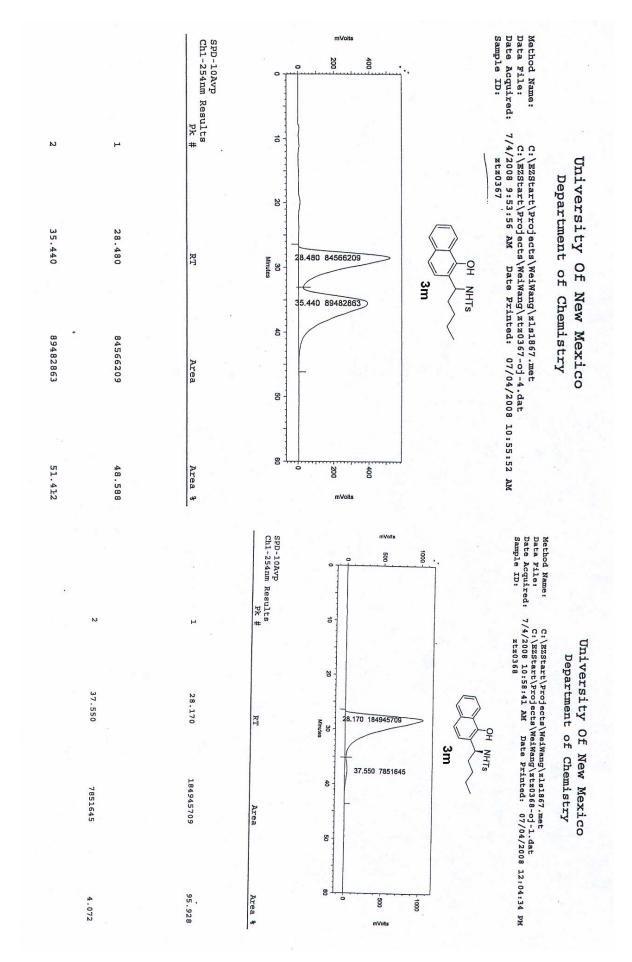


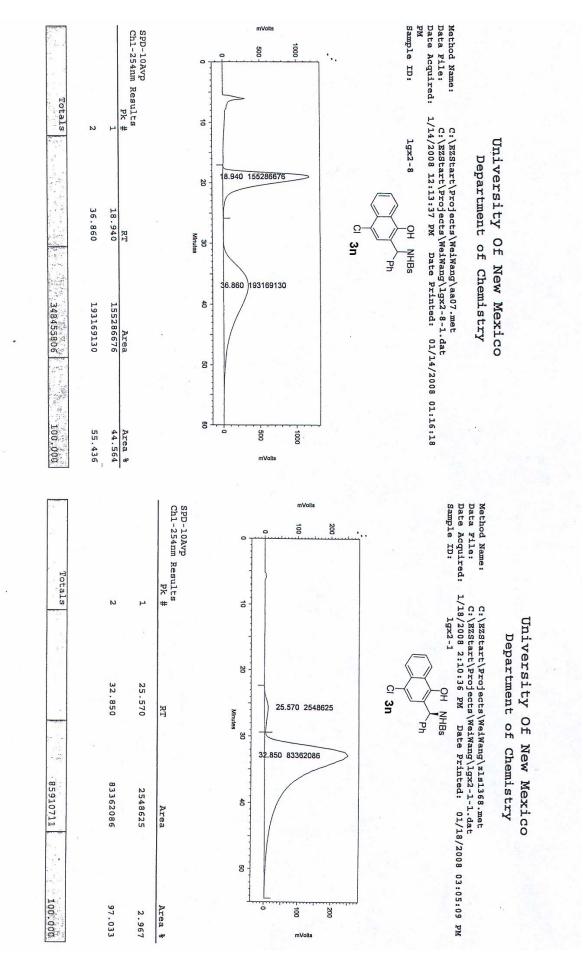


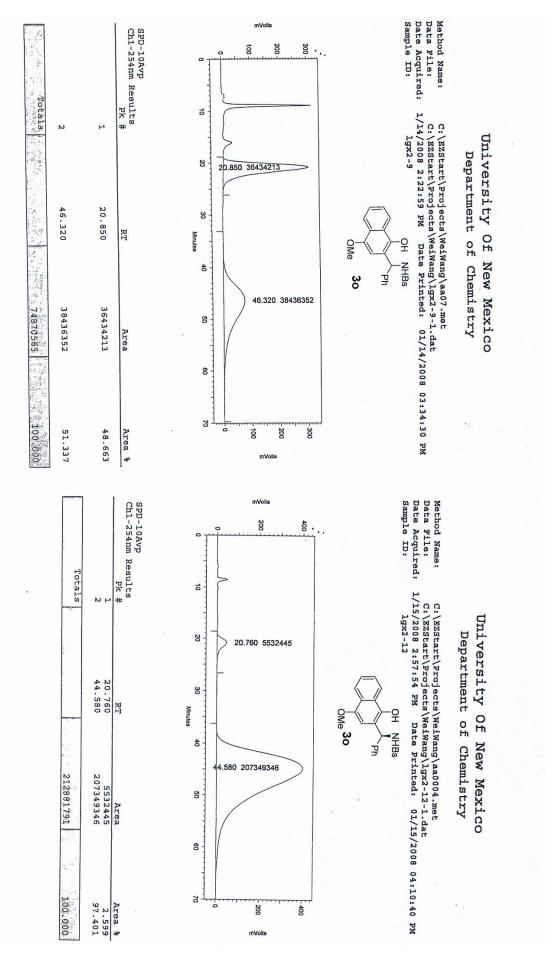


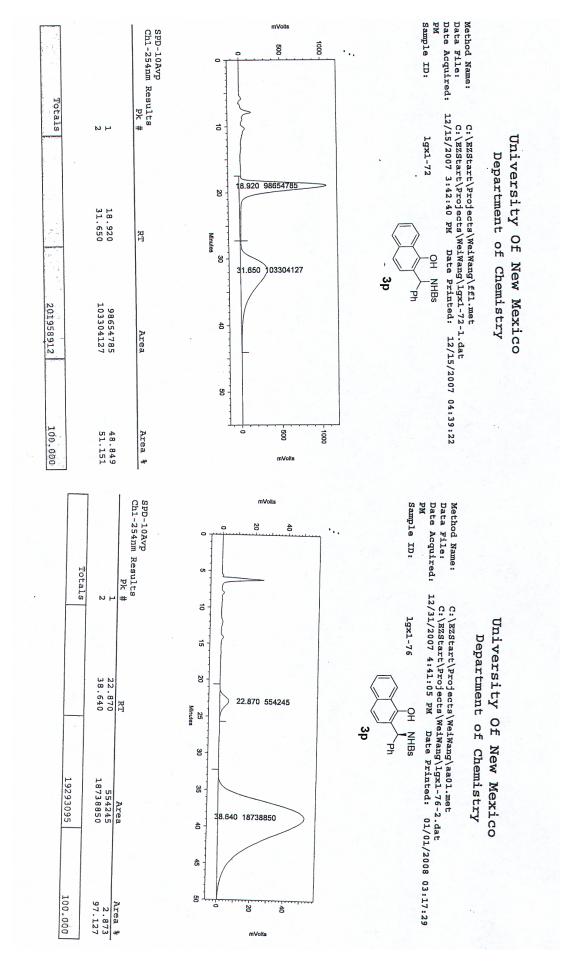




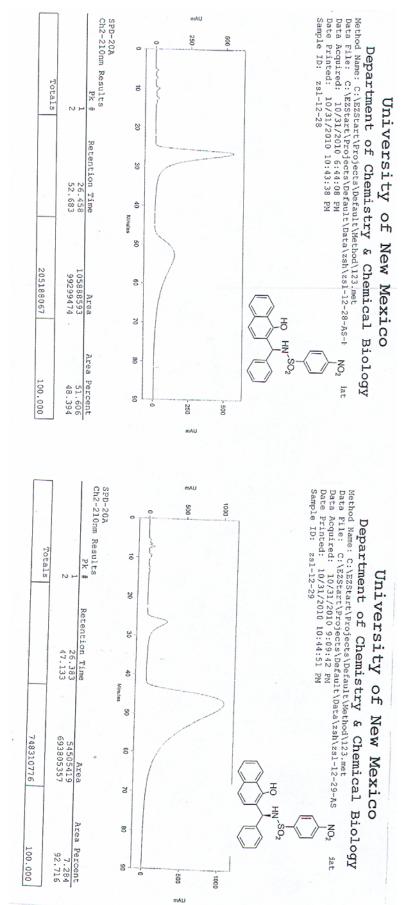


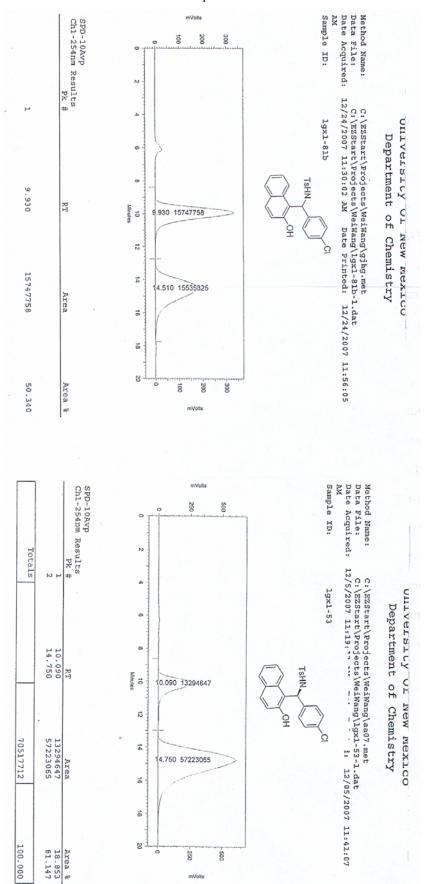






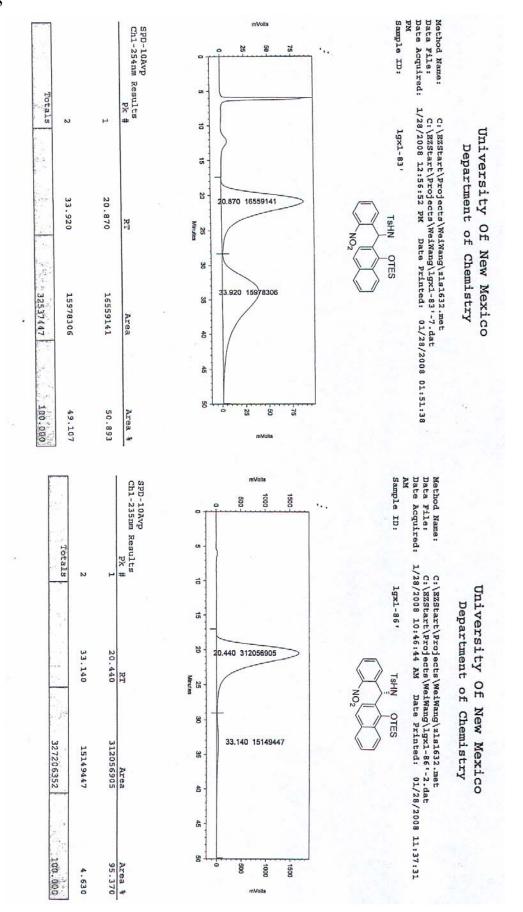


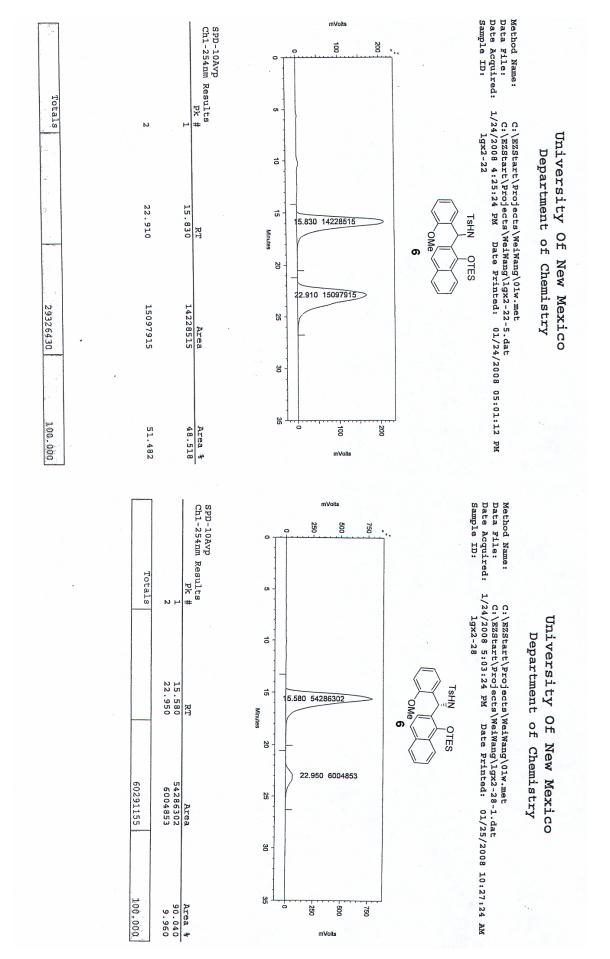


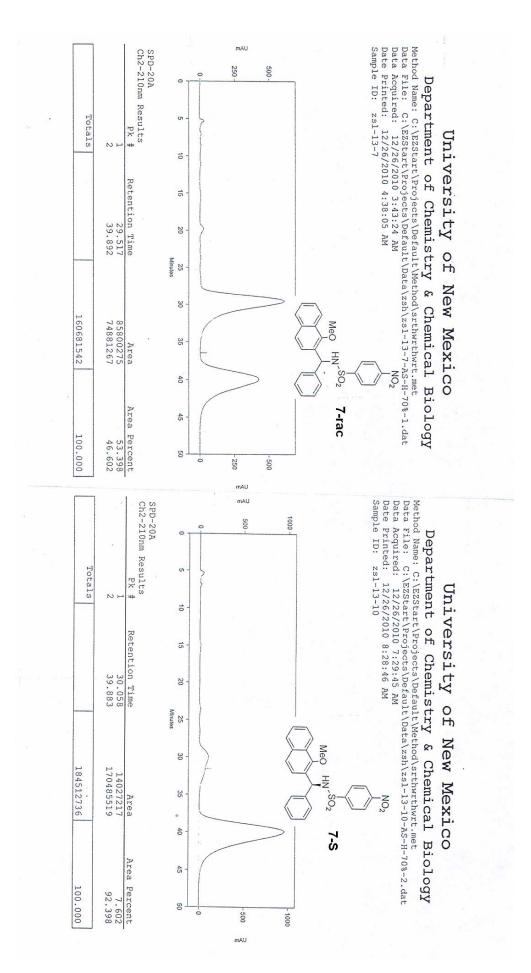


Compound 4

Compound 5

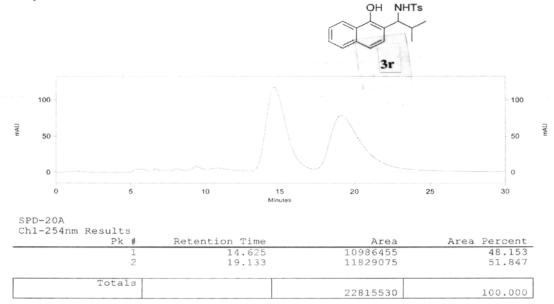






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