

Rhodium-Catalyzed Asymmetric 1,4-Additions, in Water at Room Temperature, with In-Flask Catalyst Recycling

Bruce H. Lipshutz,* Nicholas A. Isley, Ralph Moser, Subir Ghorai,
Helena Leuser, and Benjamin R. Taft
*Department of Chemistry & Biochemistry,
University of California, Santa Barbara, CA 93106 USA*

Phone: 805-893-2521

Fax: 805-893-8265

Email: lipshutz@chem.ucsb.edu

Website: <http://www.chem.ucsb.edu/~lipshutzgroup/>

Supporting Information

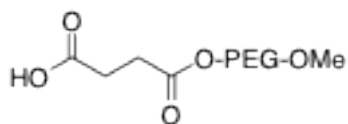
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Experimental

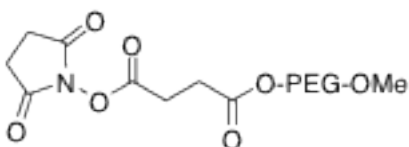
I. General Information

Herein polyethyleneglycol ubiquinol sebacate will be abbreviated as PQS. When the modified chiral ligand BINAP is covalently bound to PQS it will be abbreviated as PQS-BINAP. When the BINAP is coordinated to rhodium it will be abbreviated as PQS-BINAP-Rh. Unless otherwise noted, all reactions were performed in oven-dried glassware under an atmosphere of Argon. The water for this study was HPLC grade and was degassed prior to use by standard freeze-pump-thaw technique. Poly(ethylene glycol) methyl ether (M-PEG-2000) was obtained from Aldrich (catalog # 202509). All commercially available reagents were used without further purification (e.g. cyclic/acyclic enones, arylboronic acids). Analytical thin layer chromatography (TLC) was performed using Silica Gel 60 F₂₅₄ plates (Merck, 0.25 mm thick). The developed chromatogram was analyzed by UV lamp (254 nm) or aqueous potassium permanganate (KMnO₄) or vanillin stain. Flash chromatography was performed in glass columns using Silica Flash[®] P60 (SiliCycle, 40-63 μm). ¹H, ¹³C, ³¹P spectra were recorded at 22 °C on a Varian UNITY INOVA Advance 400 MHz or a Varian UNITY INOVA Advance 500 MHz. Chemical shifts in ¹H NMR spectra are reported in parts per million (ppm) on the δ scale from an internal standard of residual chloroform (7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant in hertz (Hz), and integration. Chemical shifts of ¹³C NMR spectra are reported in ppm from the central peak of CDCl₃ (77.23 ppm) on the δ scale. Chemical shifts of ³¹P NMR spectra are reported in ppm and were unreferenced. Chiral HPLC data were collected using a Shimadzu SPD-m20a Prominence diode array detector. IR measurements were performed on a Jasco FT/IR-430 instrument. High resolution mass analyses were obtained using a VG70 double-focusing magnetic sector instrument (VG Analytical) for EI and a PE Sciex QStar Pulsar quadrupole/TOF instrument (API) for ESI. ICP analysis was performed by Sean Duncan at Scripps Institute of Oceanography on a Thermo Finnigan Element 2 plasma mass spectrometer.

II. Synthetic route to PQS

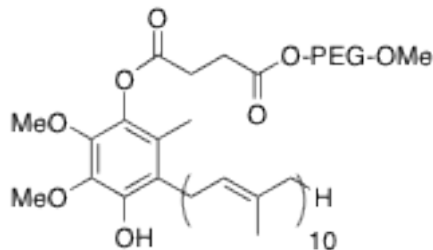


Synthesis of mono-PEGylated succinic acid. – To a solution of poly(ethylene glycol) monomethyl ether-2000 (15.00 g, 7.50 mmol) and succinic anhydride (1.50 g, 15.00 mmol) in toluene (7.5 mL), Et₃N (0.53 mL, 3.75 mmol) was added at *rt* with stirring, and the stirring was continued at 60 °C for 8 h. Water was added to the reaction mixture and extracted with CH₂Cl₂. The combined organic layers were washed with 1 N HCl (3 x 50 mL), brine (2 x 30 mL), dried over anhydrous Na₂SO₄ and concentrated *in vacuo* to afford the poly(ethylene glycol) monomethyl ether-2000 succinate **12** (15.6 g, 99%) as a white solid. IR (thin-film): 3512, 2874, 1734, 1647, 1468, 1349, 1284, 1250, 1109, 949, 844 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 4.28-4.25 (m, 2H), 3.83-3.46 (m, PEG), 3.38 (s, 3H), 2.69-2.61 (m, 4H); ¹³C NMR (100 MHz, CDCl₃): δ 173.1, 171.7, 71.4-68.5 (m, PEG), 63.2, 58.5, 28.6, 28.2; MS (ESI): *m/z* ~ 551 (M + 4Na)⁺⁴.



Synthesis of activated PEGylated succinic acid. Poly(ethylene glycol) monomethyl ether-2000 succinate **12** (2.10 g, 1.00 mmol) was dissolved in CH₂Cl₂ (10 mL) and cooled to 0 °C. *N*-Hydroxysuccinimide (0.14 g, 1.20 mmol) and 1-(3-dimethylaminopropyl)-3-ethyl carbodiimide (EDCI, 0.25 g, 1.30 mmol) were then directly added in succession to the mixture as solids. The resulting mixture was stirred at *rt* for 12 h. Water was added to the reaction mixture and extracted with CH₂Cl₂. The combined organic layers were washed with water, brine, dried, and concentrated *in vacuo* to afford **13** (2.17 g, 99%) as a white waxy solid. IR (thin-film): 2883, 1814, 1784, 1739, 1645, 1468, 1360, 1280, 1234, 1205, 1147, 1116, 1062, 947, 843 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 4.29-4.27 (m, 2H),

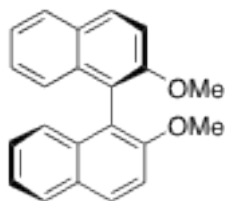
3.83-3.46 (m, PEG), 3.38 (s, 3H), 2.97 (t, $J = 7.2$ Hz, 2H), 2.84 (br s, 4H), 2.79 (t, $J = 7.2$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3): δ 170.9, 168.9, 167.6, 71.8-68.8 (m, PEG), 64.1, 59.0, 28.6, 26.2, 25.5; MS (ESI): $m/z \sim 576$ ($\text{M} + 4\text{Na}$) $^{+4}$.



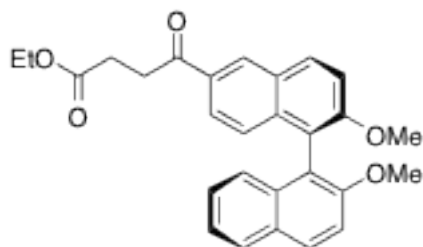
Synthesis of PQS (2). NaH (0.026 g, 0.65 mmol, 60% suspension in mineral oil) was added to a stirred solution of ubiquinol (0.52 g, 0.60 mmol) in THF (5.0 mL) at 0 °C. After addition, the reaction mixture was stirred at 22 °C for 1 h. A solution of **13** (1.10 g, 0.50 mmol) in THF (5.0 mL) was added to the mixture at 0 °C, and the stirring was continued for 30 min. The mixture was then stirred for another 8 h at *rt*. It was then cooled to 0 °C and saturated aqueous NH_4Cl was added and then extracted with CH_2Cl_2 . The combined organic layers were washed with water, brine, dried, and concentrated *in vacuo* affording a yellowish liquid, which was purified by flash column chromatography on silica gel eluting with a CH_2Cl_2 to 1:19 MeOH/ CH_2Cl_2 gradient to afford PQS-3 (0.95 g, 65%, mixture of two regioisomers) as a white waxy solid. IR (thin-film): 3518, 2885, 2740, 1761, 1738, 1663, 1467, 1360, 1343, 1280, 1242, 1147, 1114, 1062, 964, 843 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 5.78 (s, 0.3H), 5.74 (s, 0.7H), 5.12-5.06 (m, 9H), 4.98-4.93 (m, 1H), 4.27-4.24 (m, 2H), 3.89 (s, 3H), 3.78 (s, 3H), 3.70-3.44 (m, PEG), 3.37 (s, 3H), 3.31 (d, $J = 6.4$ Hz, 1.4H), 3.16 (d, $J = 6.4$ Hz, 0.6H), 2.94-2.89 (m, 2H), 2.80-2.75 (m, 2H), 2.11-1.96 (m, 39H), 1.74 (s, 2.1H), 1.72 (s, 0.9H), 1.66 (s, 3H), 1.58-1.56 (m, 27H); ^{13}C NMR (100 MHz, CDCl_3): δ 172.04, 171.96, 170.9, 170.7, 145.4, 145.0, 142.1, 141.9, 137.8, 137.6, 135.3, 135.1, 135.0, 134.9, 134.8, 131.1, 128.4, 124.9, 124.4, 124.2, 124.1, 124.0, 121.9, 121.6, 117.9, 71.9-69.0 (m, PEG), 63.9, 60.9, 60.8, 60.6, 60.5, 59.0, 39.7, 29.0, 28.8, 28.7, 26.7, 26.6, 26.0, 25.7, 25.3, 17.7, 16.3, 16.2, 16.0, 12.0, 11.3; MS (ESI): $m/z \sim 763$ ($\text{M} + 4\text{Na}$) $^{+4}$.

III. Synthesis of (*R*)-BINAP acid

The procedure was followed from previously published work¹ with slight modifications. See text below for details.

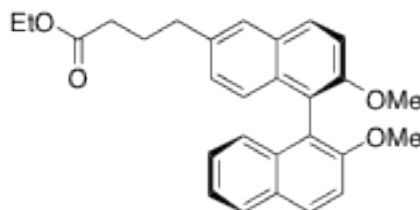


(*R*)-2,2'-Dimethoxy-1,1'-binaphthalene (5). To a well-stirred solution of (*R*)-binaphthol (2.50 g, 8.73 mmol) in anhydrous acetone (80 mL) were added anhydrous K_2CO_3 (3.62 g, 26.2 mmol) and methyl iodide (1.65 mL, 26.2 mmol). The mixture was heated at reflux for 18 h. After cooling, the volatiles were removed *in vacuo* and the residual solids dissolved in CH_2Cl_2 and H_2O . The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layers were dried over anhydrous Na_2SO_4 , and the solvent was removed *in vacuo* to leave a pale yellow solid which was purified by washing with MeOH (3 x 10 mL) and concentrated *in vacuo* to afford the title compound **5** (2.74 g, 99%) as a white solid. 1H NMR (400 MHz, $CDCl_3$): δ 7.99 (d, $J = 9.2$ Hz, 2H), 7.87 (d, $J = 8.4$ Hz, 2H), 7.47 (d, $J = 9.2$ Hz, 2H), 7.32 (ddd, $J = 8.0, 6.8, 1.2$ Hz, 2H), 7.22 (ddd, $J = 8.4, 6.8, 1.2$ Hz, 2H), 7.11 (d, $J = 8.4$ Hz, 2H), 3.78 (s, 6H).¹



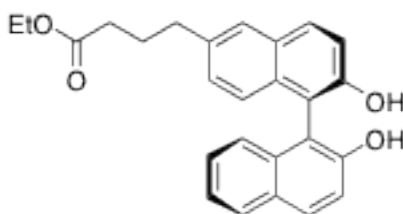
(*R*)-Ethyl 4-(2,2'-Dimethoxy-1,1'-binaphth-6-yl)-4-oxobutanoate (6). To a cooled (0 °C) solution of **5** (2.67 g, 8.49 mmol) in CH_2Cl_2 (65 mL) under argon was added solid $AlCl_3$ (1.36 g, 10.19 mmol). The red solution was stirred for 10 min, and to this was added dropwise ethyl succinyl chloride (1.33 mL,

9.34 mmol). The resulting brown solution was warmed to rt, stirred for 18 h, and poured carefully onto H₂O (60 mL). The layers were separated, and the aqueous phase was extracted with CH₂Cl₂ (2 x 30 mL). The combined organic layers were washed with H₂O (2 x 30 mL), dried over anhydrous Na₂SO₄ and concentrated *in vacuo* to afford the crude product which was subsequently purified by flash chromatography on silica gel (eluting with 30% EtOAc/hexanes) to afford the product **6** as a white solid (2.63 g, 70%). ¹H NMR (400 MHz, CDCl₃): δ 8.57 (d, *J* = 1.6 Hz, 1H), 8.12 (d, *J* = 8.8 Hz, 1H), 8.01 (d, *J* = 8.8 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.78 (dd, *J* = 8.8, 1.6 Hz, 1H), 7.53 (d, *J* = 9.2 Hz, 1H), 7.47 (d, *J* = 9.2 Hz, 1H), 7.33 (ddd, *J* = 8.0, 6.8, 1.2 Hz, 1H), 7.23 (ddd, *J* = 8.4, 6.8, 1.2 Hz, 1H), 7.16 (d, *J* = 8.8 Hz, 1H), 7.07 (d, *J* = 8.4 Hz, 1H), 4.18 (q, *J* = 7.2 Hz, 2H), 3.82 (s, 3H), 3.77 (s, 3H), 3.42 (t, *J* = 6.8 Hz, 2H), 2.80 (t, *J* = 6.8 Hz, 2H), 1.28 (t, *J* = 7.2 Hz, 3H).¹

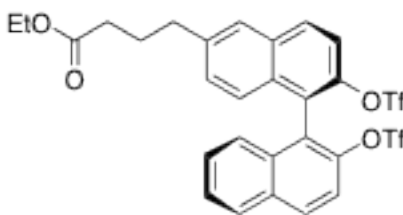


(R)-Ethyl 4-(2,2'-Dimethoxy-1,1'-binaphth-6-yl)butanoate (7). To a solution of compound **6** (3.80 g, 8.60 mmol) in CH₂Cl₂ (5.3 mL) under an argon atmosphere, trifluoroacetic acid (10.6 mL) and triethylsilane (3.5 mL) were added dropwise at 0 °C. The mixture was stirred at rt for 7 h. The reaction was quenched with water (5 mL) in an ice bath and then neutralized with saturated aqueous Na₂CO₃ (10 mL), and the aqueous phase was extracted with CH₂Cl₂ (2 x 30 mL). The combined organic layers were washed with brine (2 x 30 mL), dried over anhydrous Na₂SO₄ and concentrated *in vacuo* to afford the crude product which was subsequently purified by flash chromatography on silica gel (eluting with 15% EtOAc/hexanes) to afford the product **7** as a colorless oil (3.50 g, 95%). ¹H NMR (400 MHz, CDCl₃): δ 7.98 (d, *J* = 8.8 Hz, 1H), 7.91 (d, *J* = 8.8 Hz, 1H), 7.87 (d, *J* = 8.4 Hz, 1H), 7.64 (s, 1H), 7.45 (t, *J* = 8.8 Hz, 2H), 7.32 (ddd, *J* = 8.0, 6.8, 1.2 Hz, 1H), 7.29-7.25 (m, 1H), 7.21 (ddd, *J* = 8.4, 6.8, 1.2 Hz, 1H),

7.01-7.11 (m, 2H), 4.11 (q, $J = 7.2$ Hz, 2H), 3.78 (s, 3H), 3.76 (s, 3H), 2.75 (t, $J = 7.6$ Hz, 2H), 2.34 (t, $J = 7.6$ Hz, 2H), 2.00 (quint, $J = 7.6$ Hz, 2H), 1.24 (t, $J = 7.2$ Hz, 3H).¹

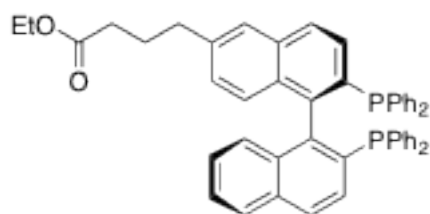


(R)-Ethyl 4-(2,2'-Dihydroxy-1,1'-binaphth-6-yl)butanoate (8). To a cooled (-78 °C) solution of **7** (3.35 g, 7.82 mmol) in anhydrous CH₂Cl₂ (54 mL) was added dropwise a 1.0 M CH₂Cl₂ solution of BBr₃ (17.3 mL, 17.3 mmol). The mixture was warmed over 7 h to 0 °C and then poured carefully onto saturated aqueous NaHCO₃ (50 mL). The layers were separated, and the aqueous phase was extracted with CH₂Cl₂ (3 x 20 mL). The combined organic layers were washed with H₂O (2 x 30 mL), dried over anhydrous Na₂SO₄ and concentrated *in vacuo* to afford the crude product which was subsequently purified by flash chromatography on silica gel (eluting with 20% EtOAc/hexanes) to afford the product **7** as a white solid (3.10 g, 99%). ¹H NMR (400 MHz, CDCl₃): δ 7.99 (d, $J = 8.8$ Hz, 1H), 7.93-7.90 (m, 2H), 7.68 (s, 1H), 7.41-7.36 (m, 3H), 7.32 (ddd, $J = 8.4, 6.8, 1.6$ Hz, 1H), 7.17 (d, $J = 8.8$ Hz, 2H), 7.09 (d, $J = 8.4$ Hz, 1H), 5.08 (s, 1H), 5.02 (s, 1H), 4.12 (q, $J = 7.2$ Hz, 2H), 2.78 (t, $J = 7.6$ Hz, 2H), 2.35 (t, $J = 7.6$ Hz, 2H), 2.02 (quint, $J = 7.6$ Hz, 2H), 1.25 (t, $J = 7.2$ Hz, 3H).¹



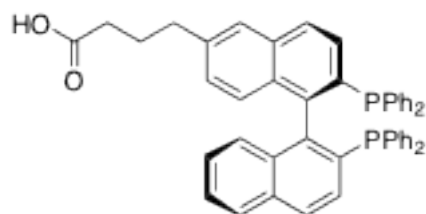
(R)-Ethyl 4-[2,2'-bis(trifluoromethanesulfoxy)-1,1'-binaphth-6-yl]butanoate (9). To a cooled (0 °C) mixture of **8** (2.59 g, 6.47 mmol), 2,6-lutidine (2.26 mL, 19.4 mmol), and DMAP (0.16 g, 1.31 mmol) was added dropwise trifluoromethanesulfonyl anhydride (2.8 mL, 16.9 mmol). The resulting orange solution was warmed to rt, stirred for 20 h, and then poured onto saturated aqueous NaHCO₃ (20

mL). The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (3 x 15 mL). The combined organic layers were washed with 0.5 M aqueous HCl (20 mL), H_2O (2 x 30 mL), dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to afford the crude product which was subsequently purified by flash chromatography on silica gel (eluting with 10% EtOAc/hexanes) to afford the product **9** as a colorless oil (4.17 g, 97%). ^1H NMR (400 MHz, CDCl_3): δ 8.15 (d, $J = 8.8$ Hz, 1H), 8.07 (d, $J = 9.2$ Hz, 1H), 8.02 (d, $J = 8.4$ Hz, 1H), 7.79 (s, 1H), 7.63-7.58 (m, 3H), 7.43 (t, $J = 8.4$ Hz, 1H), 7.28-7.25 (m, 2H), 7.18 (d, $J = 8.8$ Hz, 1H), 4.14 (q, $J = 7.2$ Hz, 2H), 2.84 (t, $J = 7.6$ Hz, 2H), 2.37 (t, $J = 7.6$ Hz, 2H), 2.06 (quint, $J = 7.6$ Hz, 2H), 1.26 (t, $J = 7.2$ Hz, 3H).¹



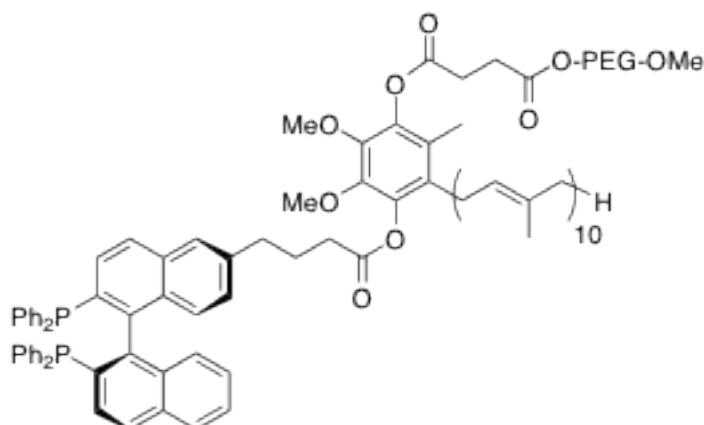
(R)-Ethyl 4-[2,2'-(Diphenylphosphino)-1,1'-binaphth-6-yl]butanoate (10). To a solution of NiCl_2dppe (0.122 g, 0.23 mmol) in anhydrous DMF (3 mL) was added diphenylphosphine (0.16 mL, 0.92 mmol). The dark brown solution was then heated to 110 °C for 1 h. A solution of chiral ditriflate **9** (1.02 g, 1.53 mmol) and DABCO (0.69 g, 6.15 mmol) in anhydrous DMF (4.5 mL) was added in one portion to the reaction flask and the resulting dark green solution is kept at 110 °C. Three additional portions of diphenylphosphine (3 x 0.16 mL) are added by syringe after 1 h, 3 h, and 7 h. Heating and stirring was continued for 72 h. The reaction was allowed to cool to rt and the DMF distilled from the reaction mixture. The resulting brown solid was stirred for 30 min in MeOH (20 mL) and filtered. The crude product was washed with methanol and dried *in vacuo* which was subsequently purified by flash chromatography on silica gel (eluting with 10% EtOAc/hexanes) to afford the product **10** as a white solid (0.84 g, 75%). ^1H NMR (400 MHz, CDCl_3): δ 7.90 (d, $J = 8.4$ Hz, 1H), 7.85 (d, $J = 8.0$ Hz, 1H), 7.83 (d, $J = 8.8$ Hz, 1H), 7.61 (s, 1H), 7.44 (dt, $J = 8.4, 2.4$ Hz, 2H), 7.36 (t, $J = 8.0$ Hz, 1H), 7.22-7.05

(m, 20H), 6.94 (t, $J = 8.4$ Hz, 1H), 6.87 (d, $J = 8.4$ Hz, 1H), 6.72 (s, 2H), 4.15 (q, $J = 7.2$ Hz, 2H), 2.71 (t, $J = 7.2$ Hz, 2H), 2.31 (t, $J = 7.2$ Hz, 2H), 1.96 (quint, $J = 7.2$ Hz, 2H), 1.27 (t, $J = 7.2$ Hz, 3H).¹

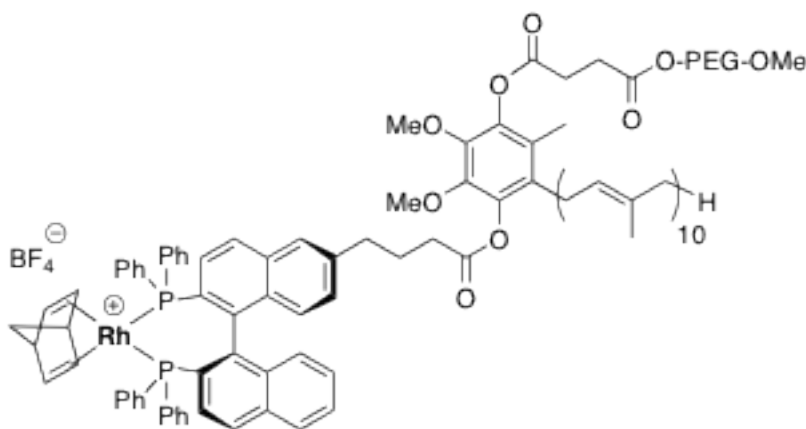


(*R*)-4-[2,2'-(Diphenylphosphino)-1,1'-binaphth-6-yl]butanoic acid (3). To a solution of ester **10** (0.71 g, 0.96 mmol) in THF (8 mL) was added 8 mL of aqueous LiOH·H₂O (2.02 g, 48.00 mmol) and the mixture heated at reflux for 20 h. After being cooled to rt, the solution was acidified to pH 3 with 2.0 M aqueous HCl and extracted with EtOAc (3 x 20 mL). The combined organic extracts were dried over anhydrous Na₂SO₄, and the solvent was removed *in vacuo*. Recrystallization from methanol afforded the title compound **3** as a white solid (0.67 g, 99%). ¹H NMR (400 MHz, CDCl₃): δ 7.89 (d, $J = 8.4$ Hz, 1H), 7.85-7.82 (m, 2H), 7.60 (s, 1H), 7.44 (dd, $J = 8.0, 1.6$ Hz, 2H), 7.36 (t, $J = 8.0$ Hz, 1H), 7.21-7.06 (m, 20H), 6.94 (t, $J = 8.4$ Hz, 1H), 6.86 (d, $J = 8.4$ Hz, 1H), 6.71 (s, 2H), 2.73 (t, $J = 7.2$ Hz, 2H), 2.35 (t, $J = 7.2$ Hz, 2H), 1.97 (quint, $J = 7.2$ Hz, 2H).¹

IV. Synthesis of PQS-BINAP-Rh



PQS-BINAP (4). PQS-3 (1.00 g, 0.34 mmol) and BINAP acid **22** (0.31 g, 0.44 mmol) were dissolved in CH_2Cl_2 (5 mL) and cooled to $0\text{ }^\circ\text{C}$. 1-(3-Dimethylaminopropyl)-3-ethyl carbodiimide (EDCI) (0.10 g, 0.52 mmol), and DMAP (0.02 g, 0.16 mmol) were then directly added in succession to the mixture as solids. Et_3N (0.08 mL, 0.57 mmol) was added through a syringe. The resulting mixture was stirred at $22\text{ }^\circ\text{C}$ for 20 h. Water was added to the reaction mixture and extracted with CH_2Cl_2 . The combined organic layers were washed with saturated NaHCO_3 , water, brine, dried and concentrated *in vacuo* affording a colorless liquid, which was purified by flash column chromatography on silica gel, eluting with Et_2O , followed by 10% $\text{MeOH}/\text{CH}_2\text{Cl}_2$ afforded PQS-BINAP (1.20 g, 98%) as a white foam. IR (thin-film): 3051, 2872, 1764, 1738, 1647, 1457, 1350, 1301, 1250, 1116, 951, 846 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 7.89 (d, $J = 8.8$ Hz, 1H), 7.85-7.82 (m, 2H), 7.64 (s, 1H), 7.43 (d, $J = 8.4$ Hz, 2H), 7.35 (t, $J = 8.0$ Hz, 1H), 7.21-7.05 (m, 20H), 6.93 (t, $J = 8.0$ Hz, 1H), 6.86 (d, $J = 8.4$ Hz, 1H), 6.73 (s, 2H), 5.13-4.97 (m, 10H), 4.29-4.26 (m, 2H), 3.81-3.80 (m, 6H), 3.72-3.46 (m, PEG), 3.39 (s, 3H), 3.21-3.19 (m, 2H), 2.97-2.92 (m, 2H), 2.84-2.77 (m, 4H), 2.63-2.56 (m, 2H), 2.10-1.92 (m, 41H), 1.73-1.55 (m, 33H); ^{13}C NMR (100 MHz, CDCl_3): δ 171.9, 171.8, 171.3, 171.2, 170.3, 170.2, 145.1, 144.8, 143.3, 143.1, 140.6, 140.5, 140.3, 140.2, 139.3, 137.9, 137.8, 137.7, 137.5, 137.4, 137.1, 137.0, 135.7, 135.5, 135.4, 134.9, 134.7, 134.5, 134.3, 134.1, 133.9, 133.3, 133.1, 132.8, 132.7, 132.6, 131.9, 131.0, 130.6, 130.3, 128.3, 128.0, 127.9, 127.6, 127.5, 127.3, 126.9, 126.4, 125.7, 124.9, 124.7, 124.3, 124.1, 123.8, 121.1, 71.8-68.9 (PEG), 63.8, 60.6, 60.5, 58.9, 39.6, 34.8, 33.0, 28.9, 28.6, 26.6, 26.5, 26.3, 26.1, 25.6, 17.6, 16.2, 15.9, 12.1, 12.0; ^{31}P NMR (160 MHz, CDCl_3 , UNREFERENCED) δ 2.2; MS (ESI): $m/z \sim 936$ ($\text{M} + 4\text{Na}$) $^{+4}$. *Note:* The extra peak near 45 ppm on the ^{31}P NMR spectrum is thought to be from trace amounts of the oxidized complex present.

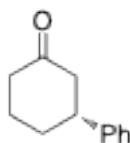


PQS-BINAP-Rh(nbd)BF₄ (1). To a 10 mL round bottom flask purged with argon and equipped with a stir bar was added PQS-BINAP (600 mg, 0.164 mmol) and Rh(nbd)₂BF₄ (48 mg, 0.131 mmol). Degassed CH₂Cl₂ (8.0 mL) was added via syringe and the mixture was stirred at rt. ³¹P NMR analysis confirmed instantaneous complexation. The solvent was removed *in vacuo* to yield PQS-BINAP-Rh(nbd)BF₄ as a dark-red, viscous oil (622 mg, 96%). ³¹P NMR (160 MHz, CDCl₃, UNREFERENCED) δ 43.3, 42.6. *Note:* The extra peak near 45 ppm on the ³¹P NMR spectrum is thought to be from trace amounts of the oxidized version of complex 4 present. The presence of PQS-BINAP (peak at 2.2 ppm) unbound to rhodium is important for high enantioselectivity, as the catalyst is active without a chiral ligand bound, thus degrading selectivity.

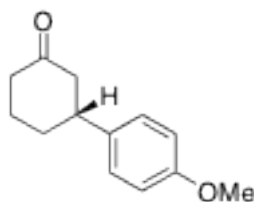
V. Rh-catalyzed asymmetric conjugate addition reactions

General procedure for the 1,4-addition of boronic acids to enones (GP1). Under an atmosphere of argon a 1 mL screwcap vial was charged with PQS-BINAP-Rh precatalyst (30 mg, 0.006 mmol), boronic acid (0.24 mmol), and removed from the glovebox. Water (0.4 mL) and Et₃N (84 μL, 0.6 mmol) were added to the vial and stirred for 15 min. When the solution became homogeneous, enone (0.2 mmol) was added via syringe and the mixture was stirred at rt for 12 h. The homogeneous reaction mixture was then diluted with EtOAc (0.5 mL), filtered through a bed of silica gel, and the bed further washed (3 x 2 mL) with EtOAc to collect all of the coupled material. The volatiles were removed *in*

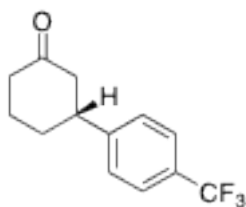
vacuo to afford the crude product which was subsequently purified by flash chromatography on silica gel.



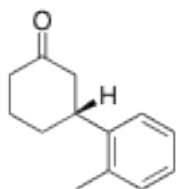
(R)-3-Phenylcyclohexanone. Following the general procedure **GP1** using 2-cyclohexenone (20 μ L, 0.20 mmol), and phenylboronic acid (30 mg, 0.24 mmol), column chromatography on silica gel (eluting with 10% Et₂O/hexanes) afforded the title product as a pale yellow oil (33 mg, 95%); ¹H NMR (400 MHz, CDCl₃): δ 7.34-7.41 (m, 2H), 7.24-7.31 (m, 3H), 3.00-3.12 (m, 1H), 2.37-2.68 (m, 4H), 2.10-2.24 (m, 2H), 1.76-1.96 (m, 2H); HPLC separation conditions: CHIRALCEL OD-H, 210 nm, 2% IPA/hexanes, 1.0 mL/min, t_R = 12.1 and 13.4 min, 99% *ee*.²



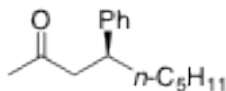
(R)-3-(4-Methoxyphenyl)cyclohexanone. Following the general procedure **GP1** using 2-cyclohexenone (20 μ L, 0.20 mmol), and 4-methoxyphenylboronic acid (37 mg, 0.24 mmol), column chromatography on silica gel (eluting with 10% Et₂O/hexanes) afforded the title product as a pale yellow oil (40 mg, 99%); ¹H NMR (400 MHz, CDCl₃): δ 7.15 (d, J = 11.8 Hz, 2H), 6.86 (d, J = 11.8 Hz, 2H), 3.79 (s, 3H), 2.91-3.02 (m, 1H), 2.30-2.62 (m, 4H), 2.00-2.19 (m, 2H), 1.67-1.88 (m, 2H); HPLC separation conditions: CHIRALCEL OD-H, 210 nm, 5% IPA/hexanes, 1.0 mL/min, t_R = 10.7 and 11.2 min, >99% *ee*.³



(R)-3-(4-Trifluoromethylphenyl)cyclohexanone. Following the general procedure **GP1** using 2-cyclohexenone (20 μ L, 0.20 mmol), and 4-trifluoromethylphenylboronic acid (46 mg, 0.24 mmol), column chromatography on silica gel (eluting with 10% Et₂O/hexanes) afforded the title product as a colorless oil (42 mg, 87%). ¹H NMR (400 MHz, CDCl₃): δ 7.59 (d, J = 8.2 Hz, 2H), 7.34 (d, J = 8.2 Hz, 2H), 3.02-3.17 (m, 1H), 2.33-2.65 (m, 4H), 2.06-2.13 (m, 2H), 1.76-1.94 (m, 2H); HPLC separation conditions: CHIRALCEL OD-H, 210 nm, 1% IPA/hexanes, 0.5 mL/min, t_R = 30.4 and 32.0 min, >99% *ee*.⁴

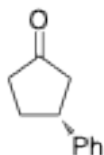


(R)-3-(2-Methylphenyl)cyclohexanone. Following the general procedure **GP1** using 2-cyclohexenone (20 μ L, 0.20 mmol), and 2-methylphenylboronic acid (33 mg, 0.24 mmol), column chromatography on silica gel (eluting with 10% Et₂O/hexanes) afforded the title product as a colorless oil (30 mg, 80%). ¹H NMR (400 MHz, CDCl₃): δ 7.05-7.21 (m, 4H), 3.11-3.24 (m, 1H), 2.30-2.48 (m, 4H), 2.24 (s, 3H), 2.08-2.18 (m, 1H), 1.93-1.98 (m, 1H), 1.75-1.88 (m, 2H); HPLC separation conditions: CHIRALCEL AD-H, 210 nm, 1% IPA/hexanes, 0.5 mL/min, t_R = 21.9 and 26.3 min, 98% *ee*.³

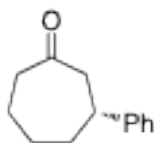


(S)-4-Phenylnonan-2-one. Following the general procedure **GP1** using (*E*)-non-3-en-2-one (28 mg, 0.20 mmol), and phenylboronic acid (30 mg, 0.24 mmol), column chromatography on silica gel (eluting with 5% Et₂O/hexanes) afforded the title product as a colorless oil (43 mg, 98%). ¹H NMR (400 MHz,

CDCl₃): δ 7.29-7.24 (m, 2H), 7.20-7.15 (m, 3H), 3.12-3.05 (m, 1H), 2.71 (dd, $J = 16.0, 7.2$ Hz, 1H), 2.69 (dd, $J = 16.0, 6.8$ Hz, 1H), 2.00 (s, 3H), 1.59-1.50 (m, 2H), 1.21-1.08 (m, 6H), 0.83-0.79 (m, 3H); HPLC separation conditions: CHIRALCEL OD-H, 210 nm, 2% IPA/hexanes, 0.5 mL/min, $t_R = 12.2$ and 12.8 min, 79% *ee*.⁵



(R)-3-Phenylcyclopentanone. Following the general procedure **GP1** using 2-cyclopentenone (17 μ L, 0.20 mmol), and phenylboronic acid (30 mg, 0.24 mmol), column chromatography on silica gel (eluting with 10% Et₂O/hexanes) afforded the title product as a colorless oil (31 mg, 96%); ¹H NMR (400 MHz, CDCl₃): δ 7.36-7.33 (m, 2H), 7.27-7.23 (m, 3H), 3.47-3.38 (m, 1H), 2.67 (dd, $J = 18.0, 7.6$ Hz, 1H), 2.51-2.41 (m, 2H), 2.38-2.26 (m, 2H), 2.04-1.94 (m, 1H); HPLC separation conditions: CHIRALCEL OB-H, 210 nm, 0.5% IPA/hexanes, 1.0 mL/min, $t_R = 32.7$ and 35.5 min, 97% *ee*.⁴



(R)-3-Phenylcycloheptanone. Following the general procedure **GP1** using 2-cycloheptenone (28 μ L, 0.20 mmol), and phenylboronic acid (30 mg, 0.24 mmol), column chromatography on silica gel (eluting with 10% Et₂O/hexanes) afforded the title product as a colorless oil (31 mg, 83%); ¹H NMR (400 MHz, CDCl₃): δ 7.32-7.25 (m, 2H), 7.22-7.16 (m, 3H), 2.97-2.86 (m, 2H), 2.66-2.56 (m, 3H), 2.11-1.97 (m, 3H), 1.79-1.66 (m, 2H), 1.56-1.44 (m, 1H); HPLC separation conditions: CHIRALCEL OD-H, 210 nm, 2.0% IPA/hexanes, 1.0 mL/min, $t_R = 10.9$ and 12.0 min, 96% *ee*.⁴

VI. Catalyst recycling

General procedure for catalyst recycling. Inside a glovebox, a 3 mL vial was charged with PQS-BINAP-Rh (75 mg, 0.015 mmol), phenylboronic acid (75 mg, 0.60 mmol), and removed from the glovebox. Water (1 mL) and Et₃N (0.21 mL, 1.5 mmol) were added to the vial and stirred for 15 min. When the solution became homogeneous 2-cyclopentenone (43 μ L, 0.50 mmol) was added via syringe and the mixture was stirred at rt for 12 h. The homogeneous reaction mixture was then diluted with toluene-Et₂O mixture (1:1; 1 mL) and stirred for 10 s. The reaction mixture was then allowed to separate and the upper (toluene-Et₂O) layer was removed by pipette. The aqueous layer was successively washed with toluene-Et₂O mixture (1:1; 3 x 1 mL). The combined toluene-Et₂O extracts layers were evaporated to afford the crude product, which was purified by flash column chromatography on silica gel, eluting with 10% Et₂O/hexanes afforded the desired compound (0.083 g, 95%) as a colorless liquid. For the second run, 2-cyclohexenone (49 μ L, 0.50 mmol), phenylboronic acid (75 mg, 0.60 mmol), and Et₃N (0.21 mL, 1.5 mmol) were added again to the same reaction vessel and stirred at rt for another 12 h. The work up was conducted in exactly the same way as described for the first cycle. This reaction was repeated again using 2-cyclohexenone (49 μ L, 0.50 mmol).

VII. ICP-MS analysis

Each sample corresponds to the cycle number analyzed (e.g. NI#2-1 is extract from cycle 1). The deviation in concentration is expected with the extraction method (with a syringe and needle). If a drop more or less of PQS-BINAP-Rh solution was extracted due to the inaccuracy of the human eye, such a deviation would occur. Contact Sean Duncan for details and associated spectra from analysis.

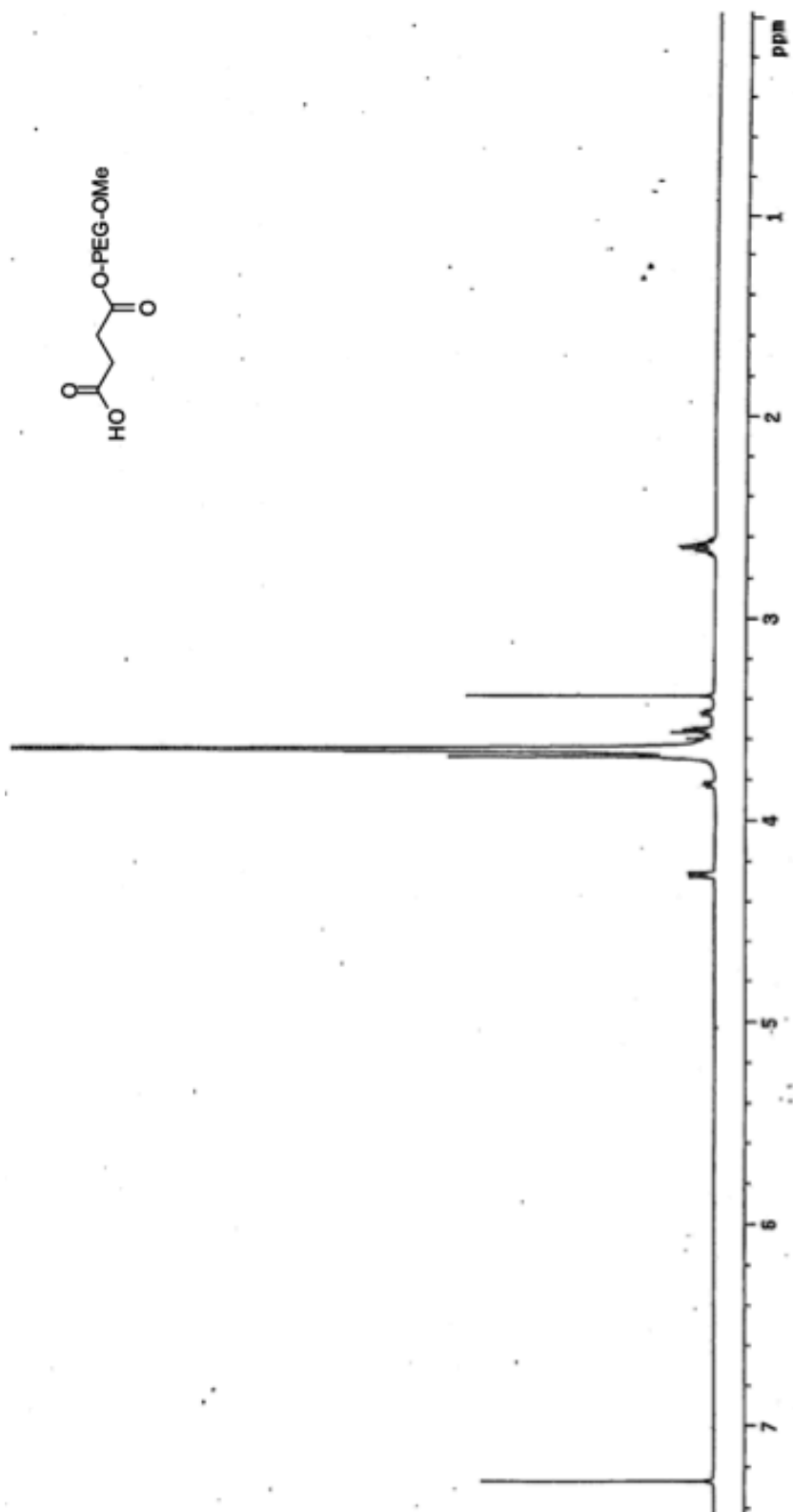
Sample	Element	Concentration
NI#2-1	Rh	41.2843 ppb
NI#2-2	Rh	5.7856 ppb
NI#2-3	Rh	20.7885 ppb
NI#2-4	Rh	1.0437 ppb

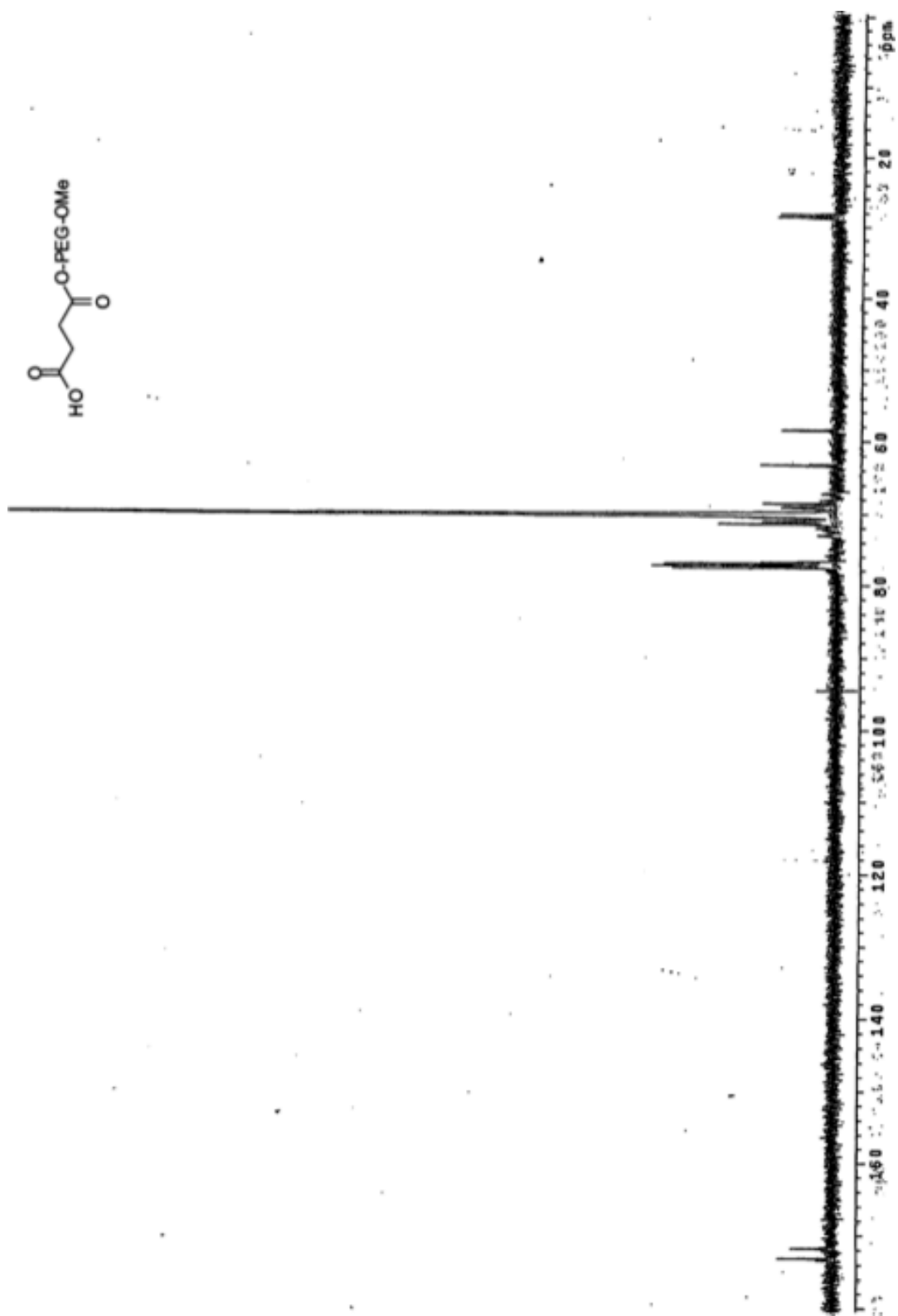
Sean Duncan
Research Associate III
Scripps Institute of Oceanography,
University of California San Diego
tsduncan@ucsd.edu

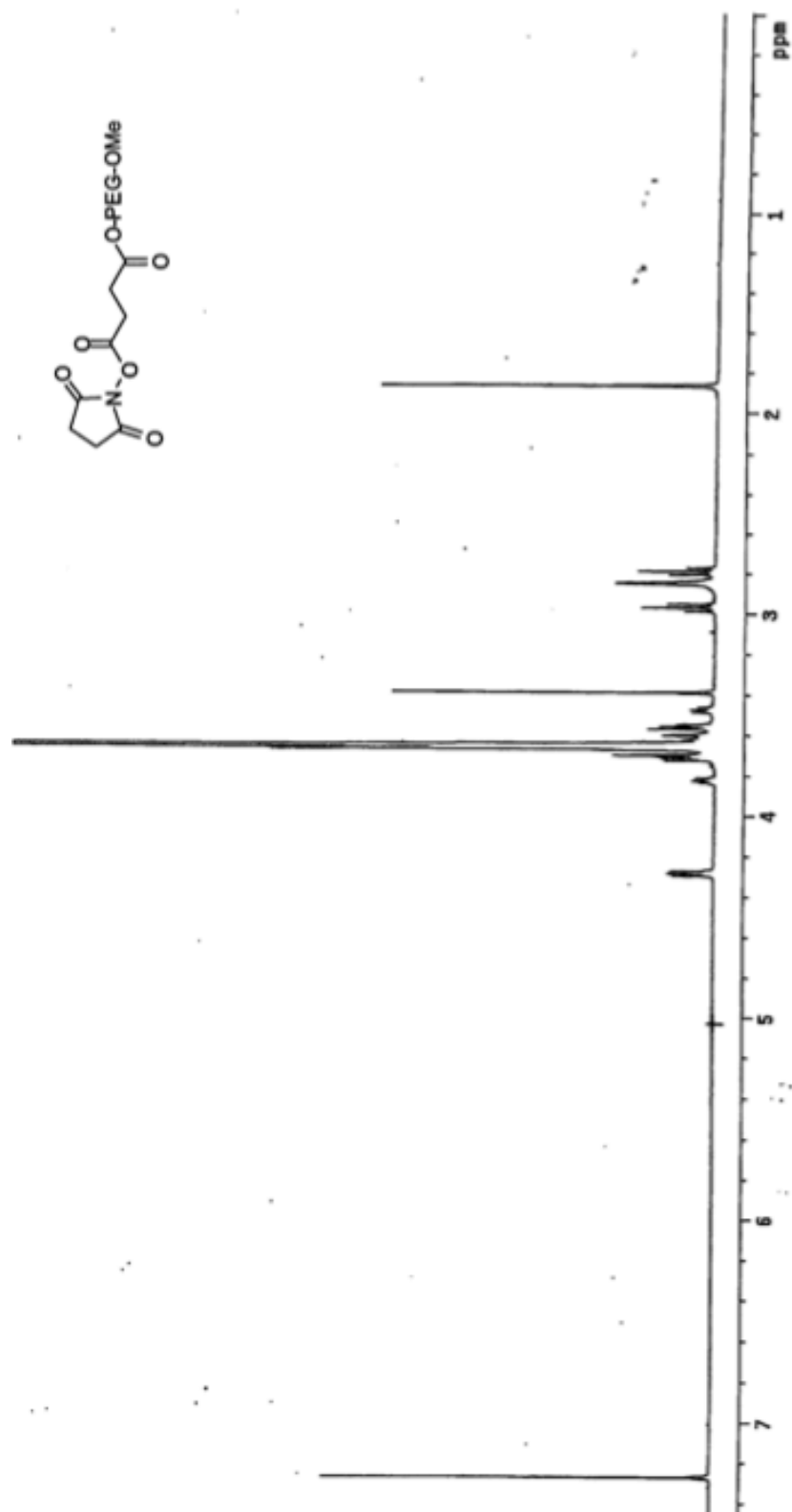
VIII. References

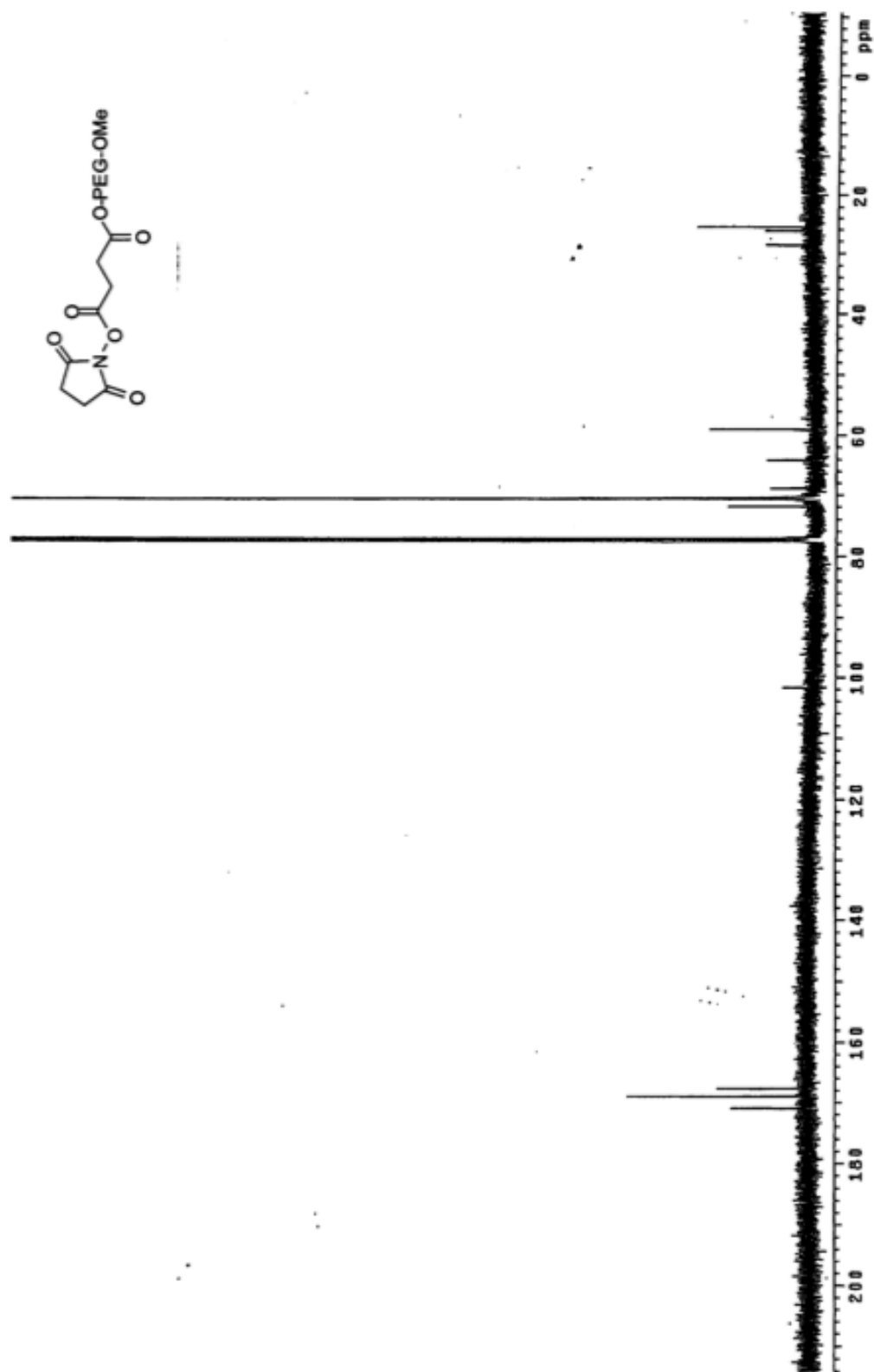
1. Bayston, D. J.; Fraser, J. L.; Ashton, M. R.; Baxter, A. D.; Polywka, M. E. C.; Moses, E. *J. Org. Chem.* **1998**, *63*, 3137-3140.
2. Hayashi, T.; Ogasawara, M.; Takaya, Y. *J. Am. Chem. Soc.* **1998**, *120*, 5579-5580.
3. Mariz, R.; Briceno, A.; Dorta, R.; Dorta, R. *Organometallics* **2008**, *27*, 6605-6613.
4. Yuan, W.-C.; Cun, L.-F.; Mi, A.-Q.; Jiang, Y.-Z.; Gong, L.-Z. *Tetrahedron* **2009**, *65*, 4130-4141.
5. Suzuma, Y.; Hayashi, S.; Yamamoto, T.; Oe, Y.; Ohta, T.; Ito, Y. *Tetrahedron: Asymmetry* **2009**, *20*, 2751-2758.

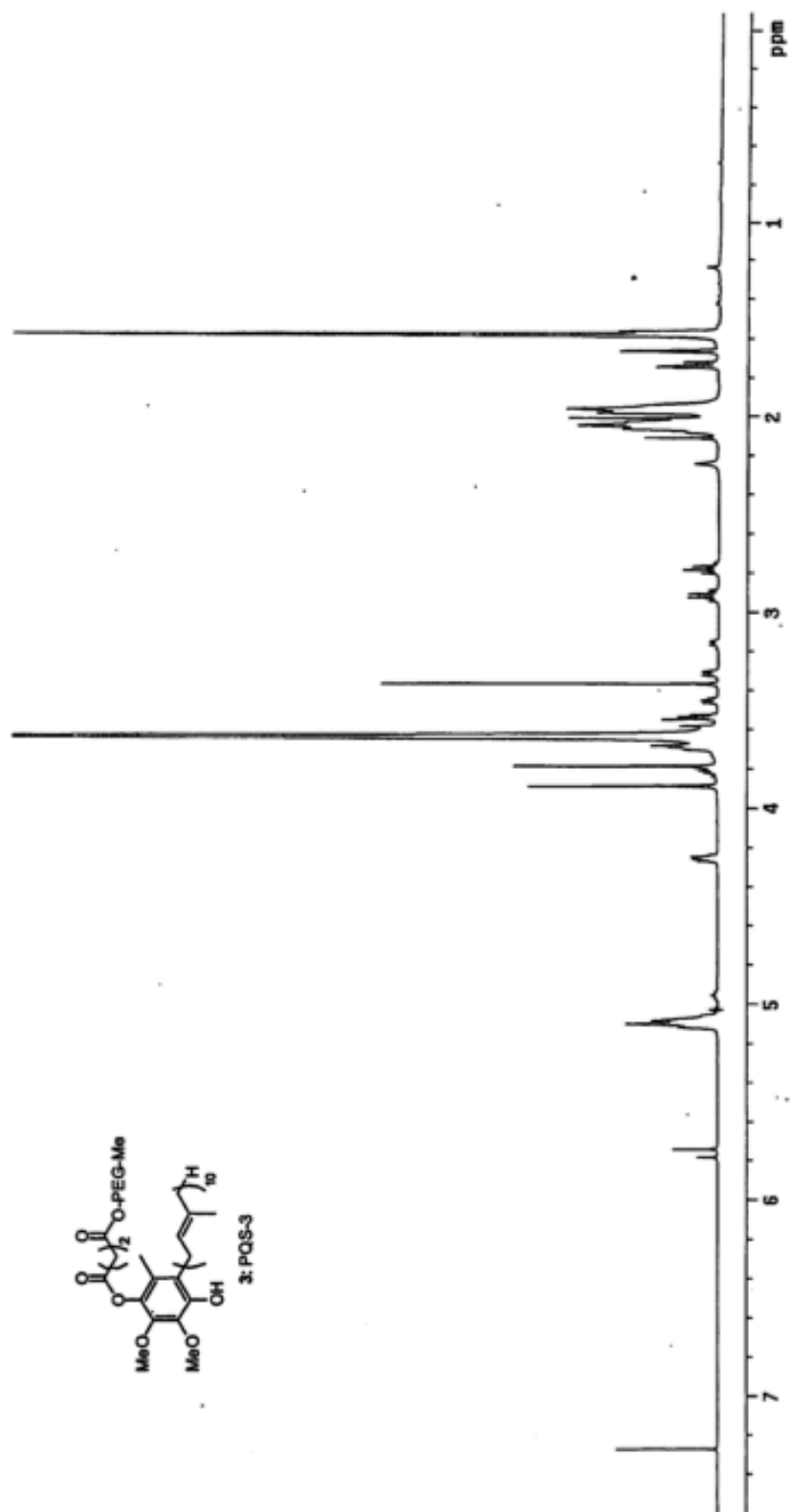
IX. ^1H and ^{13}C NMR Spectra, HPLC data, and DLS data

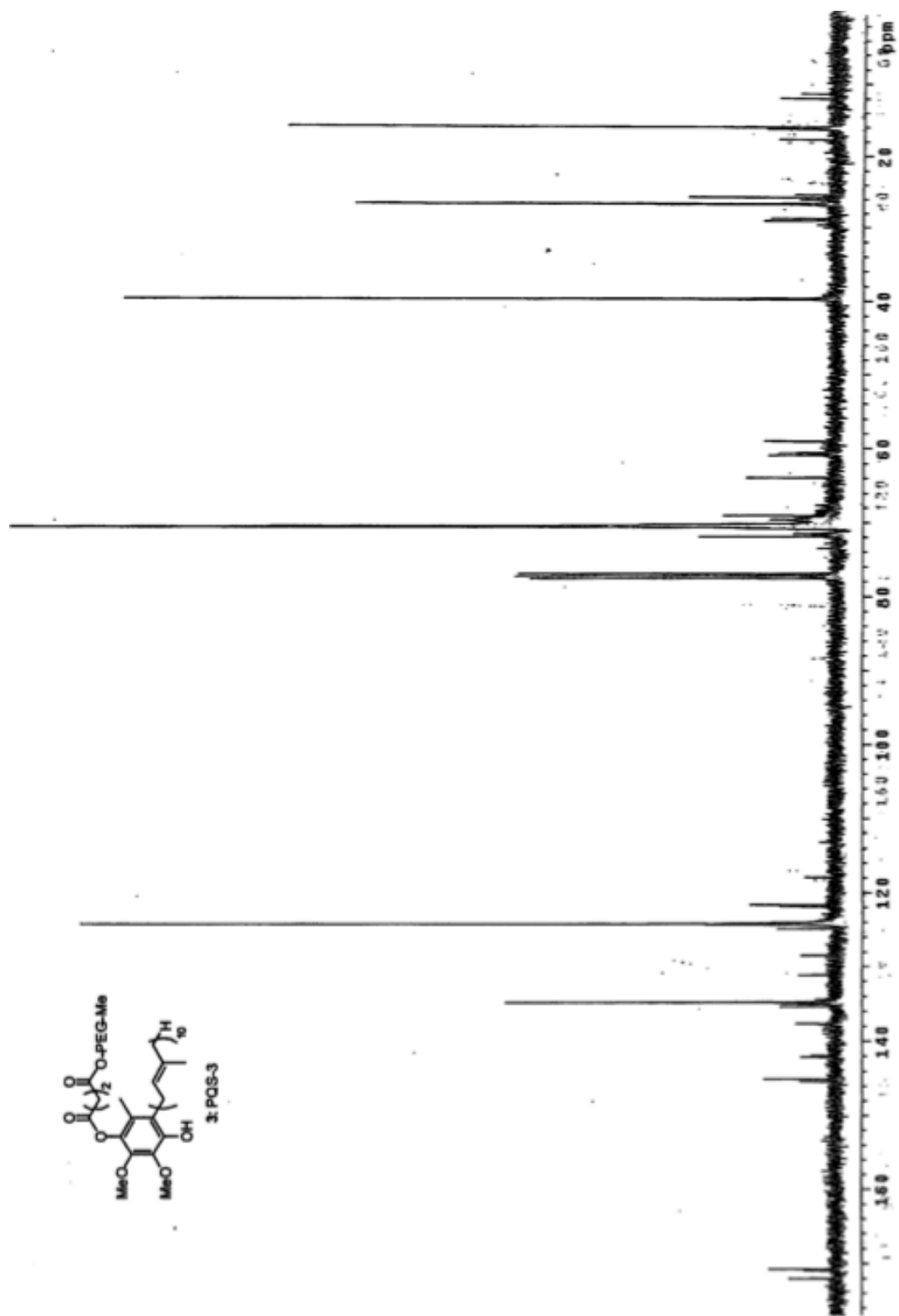


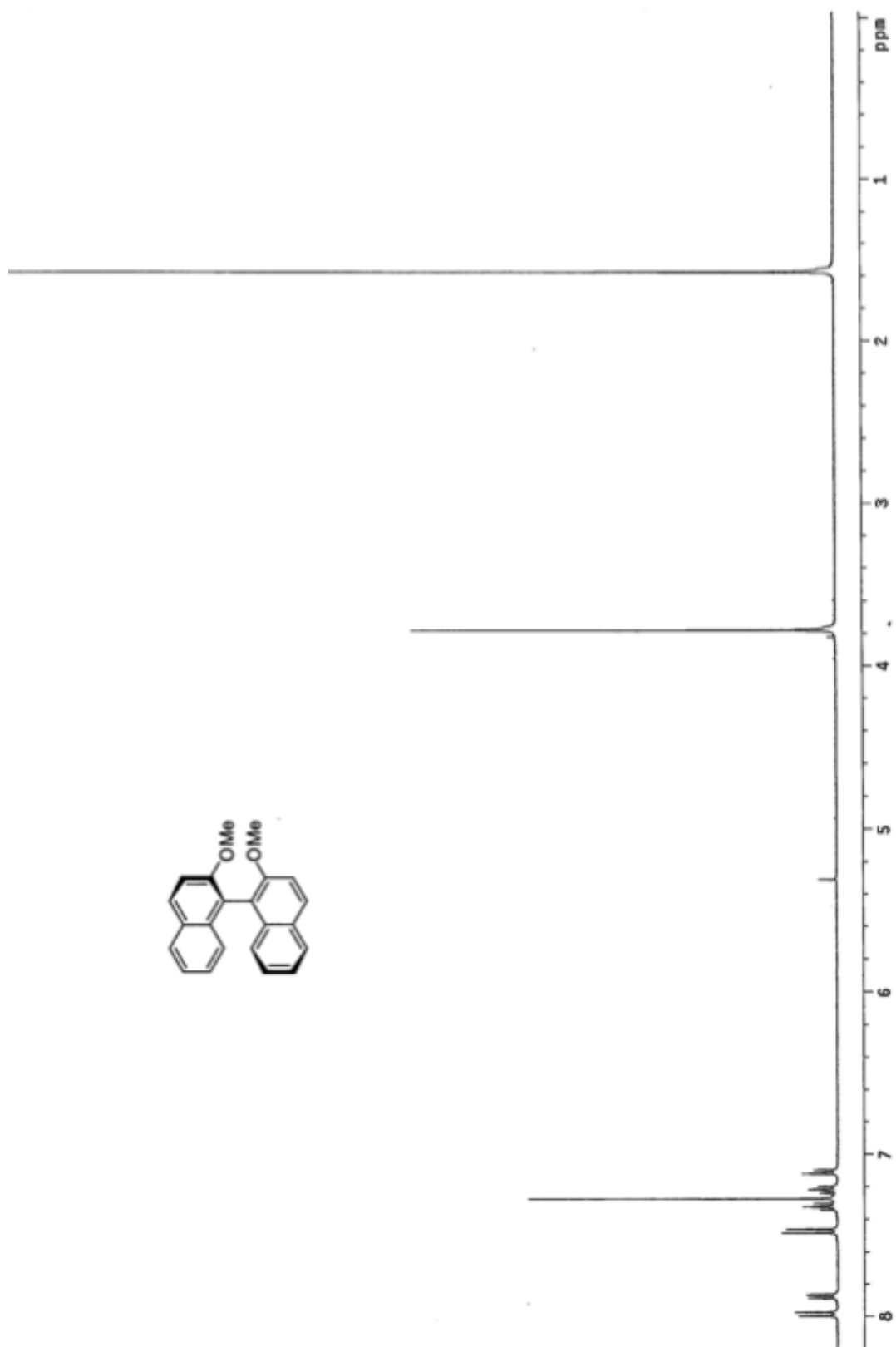


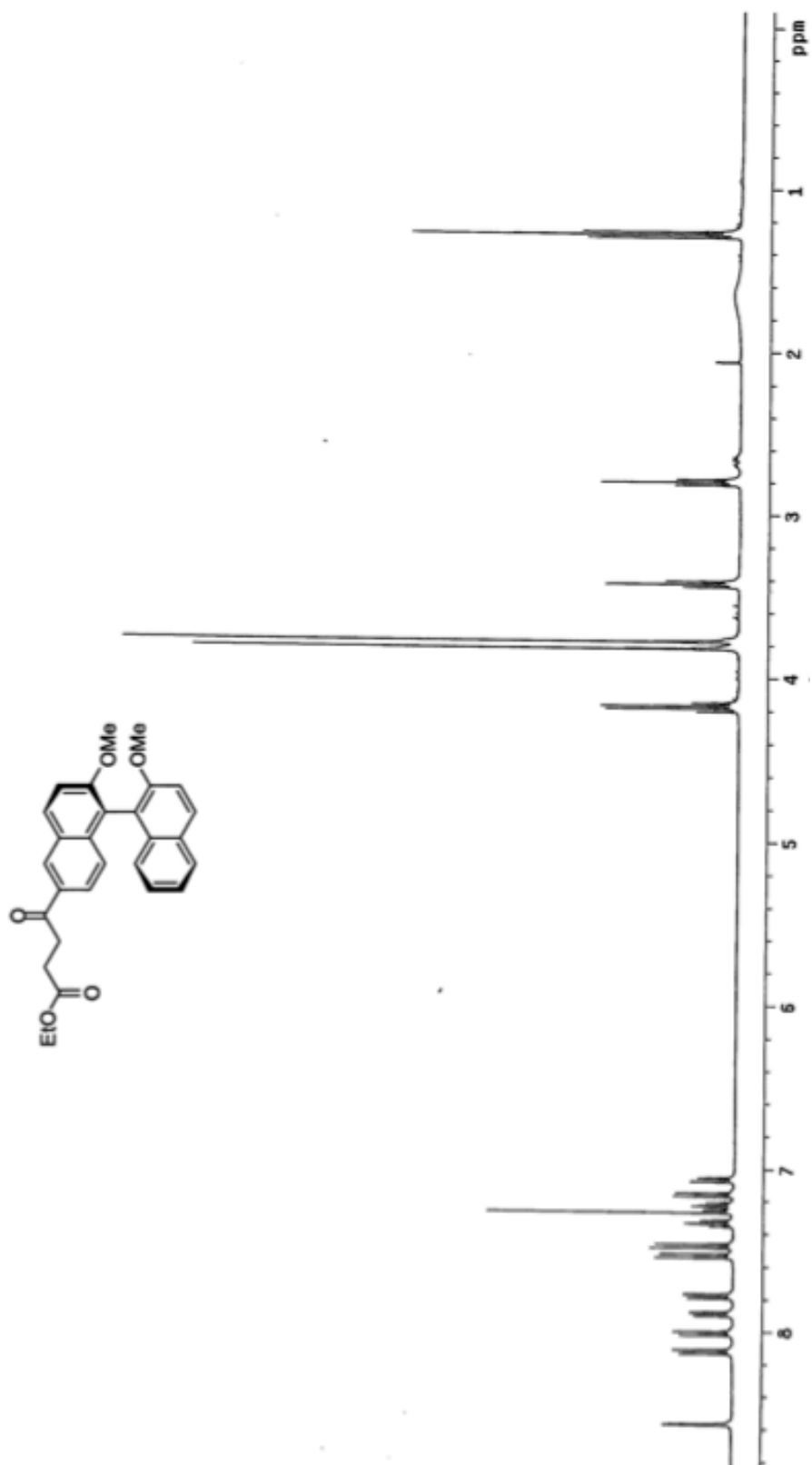


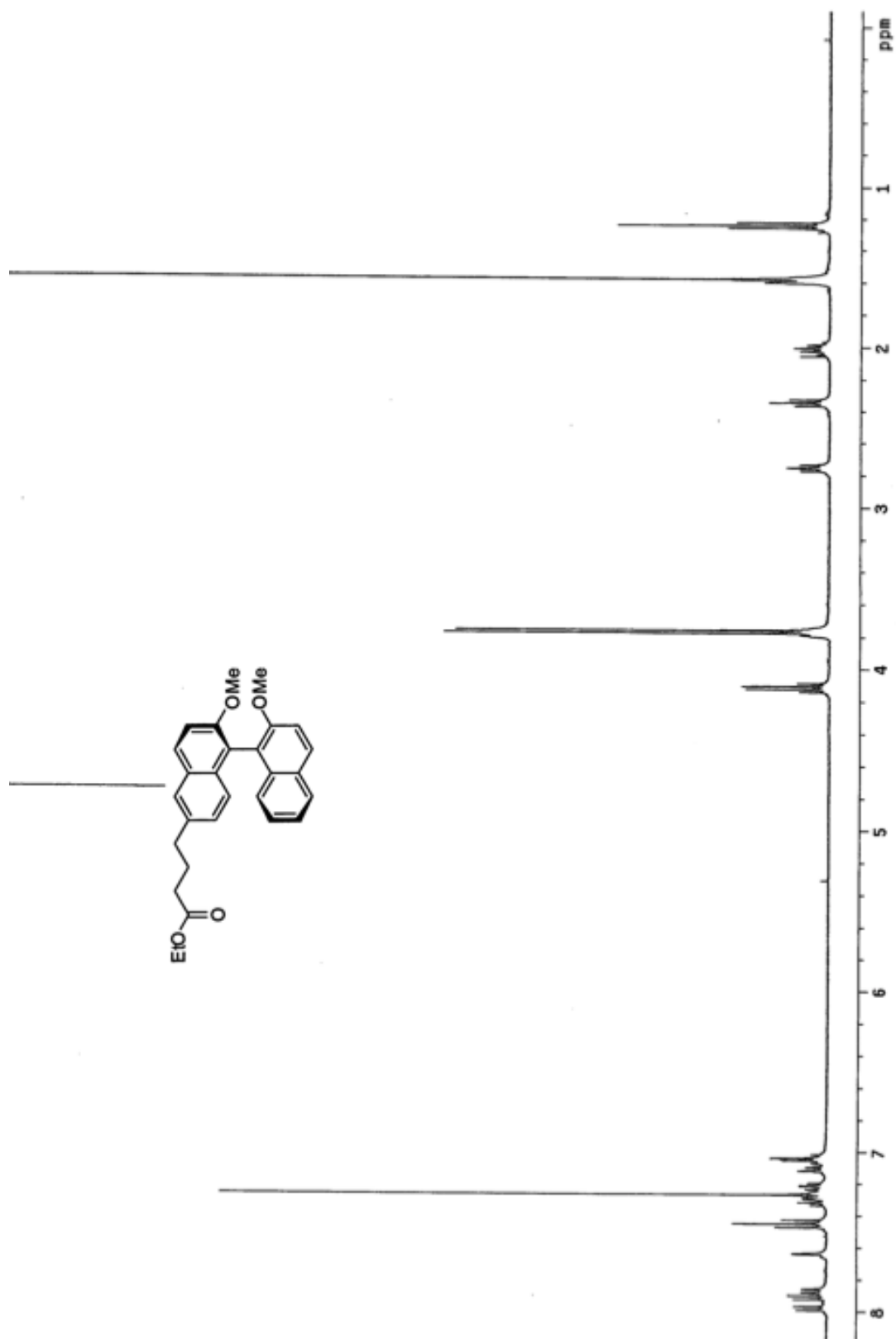


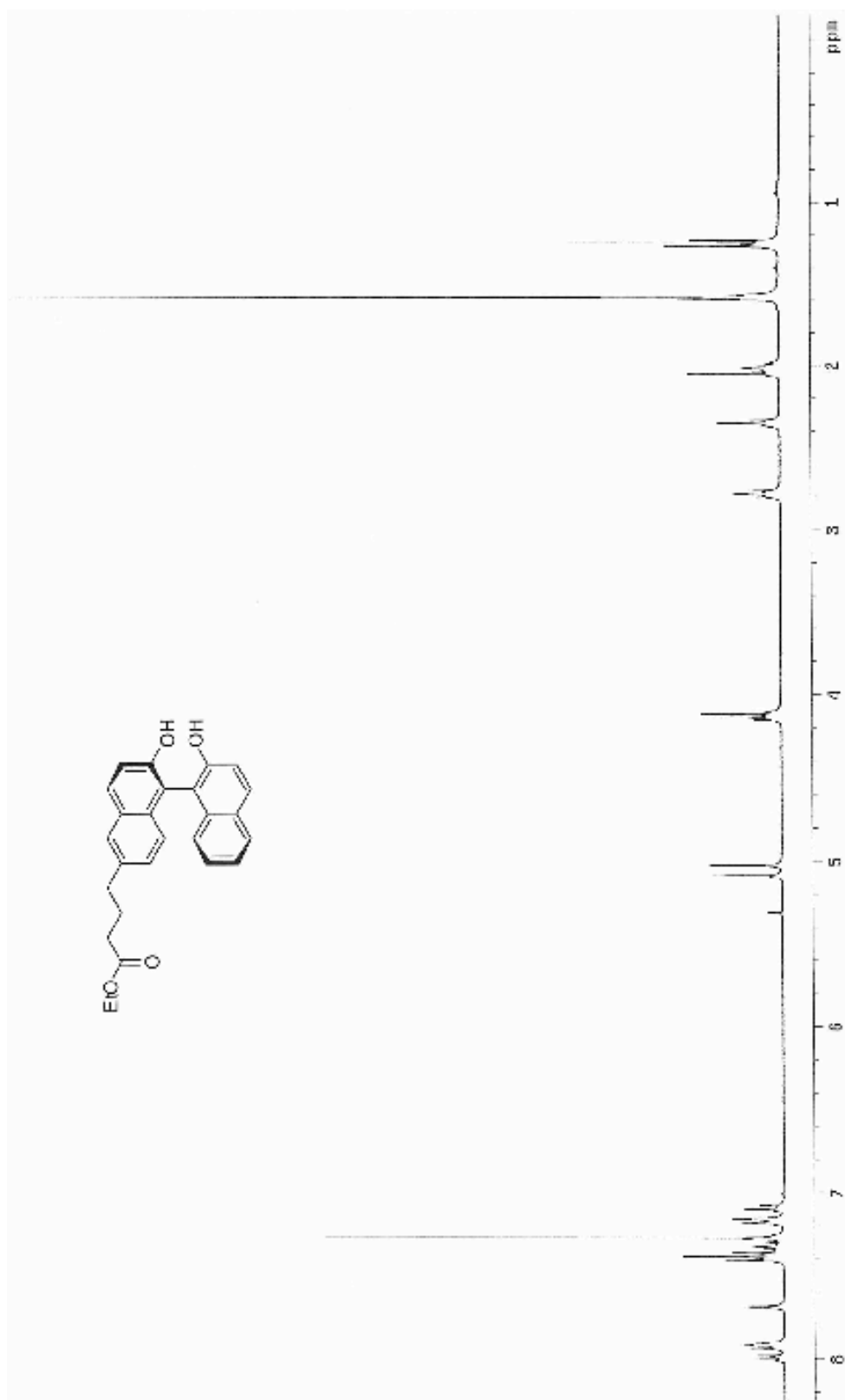


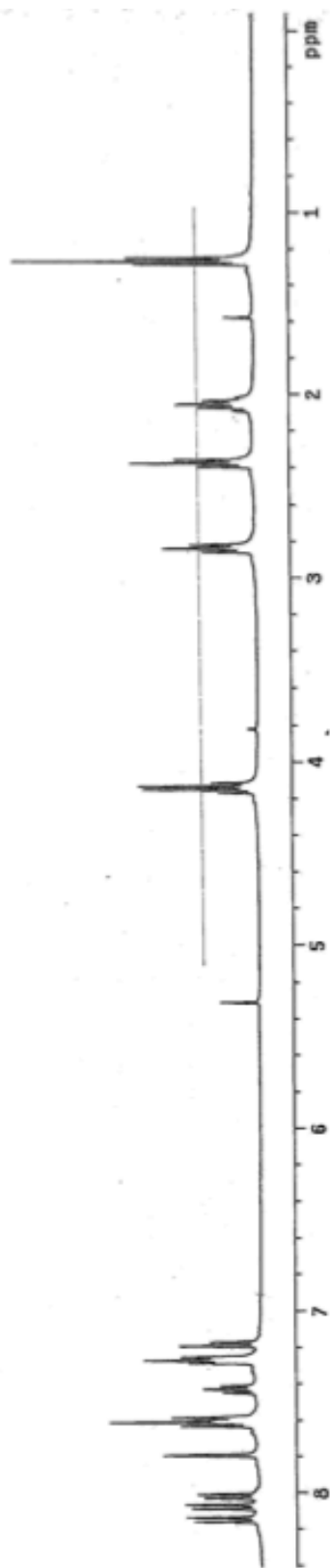
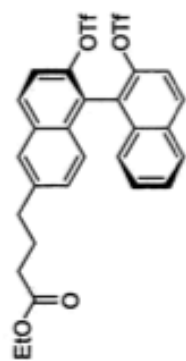


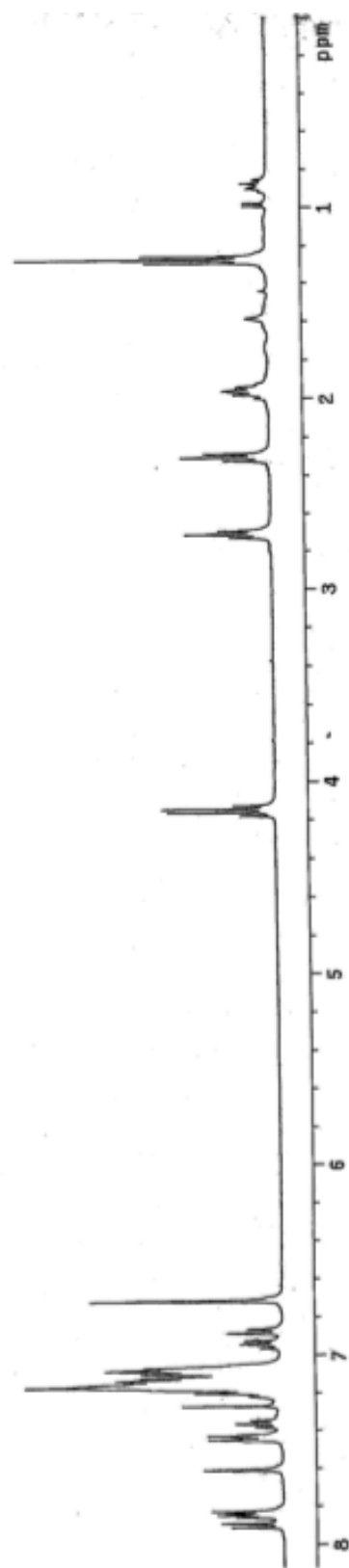
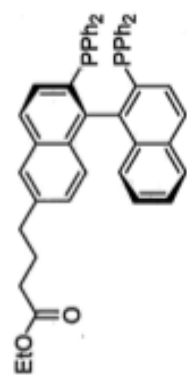


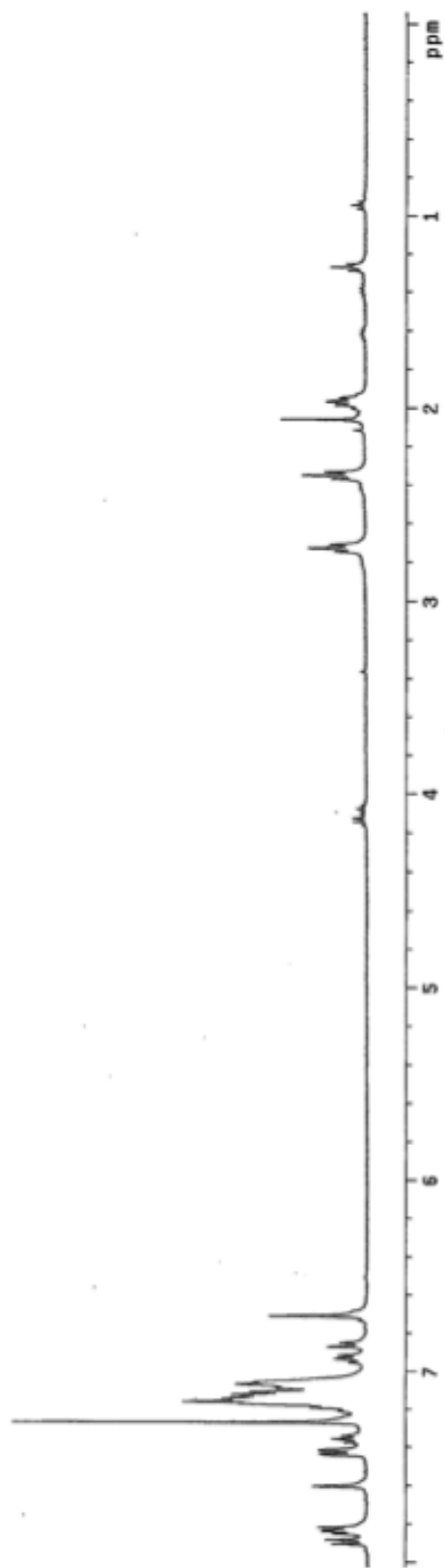
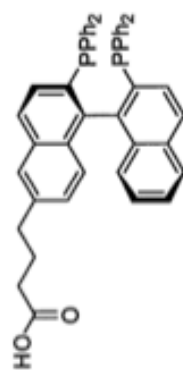


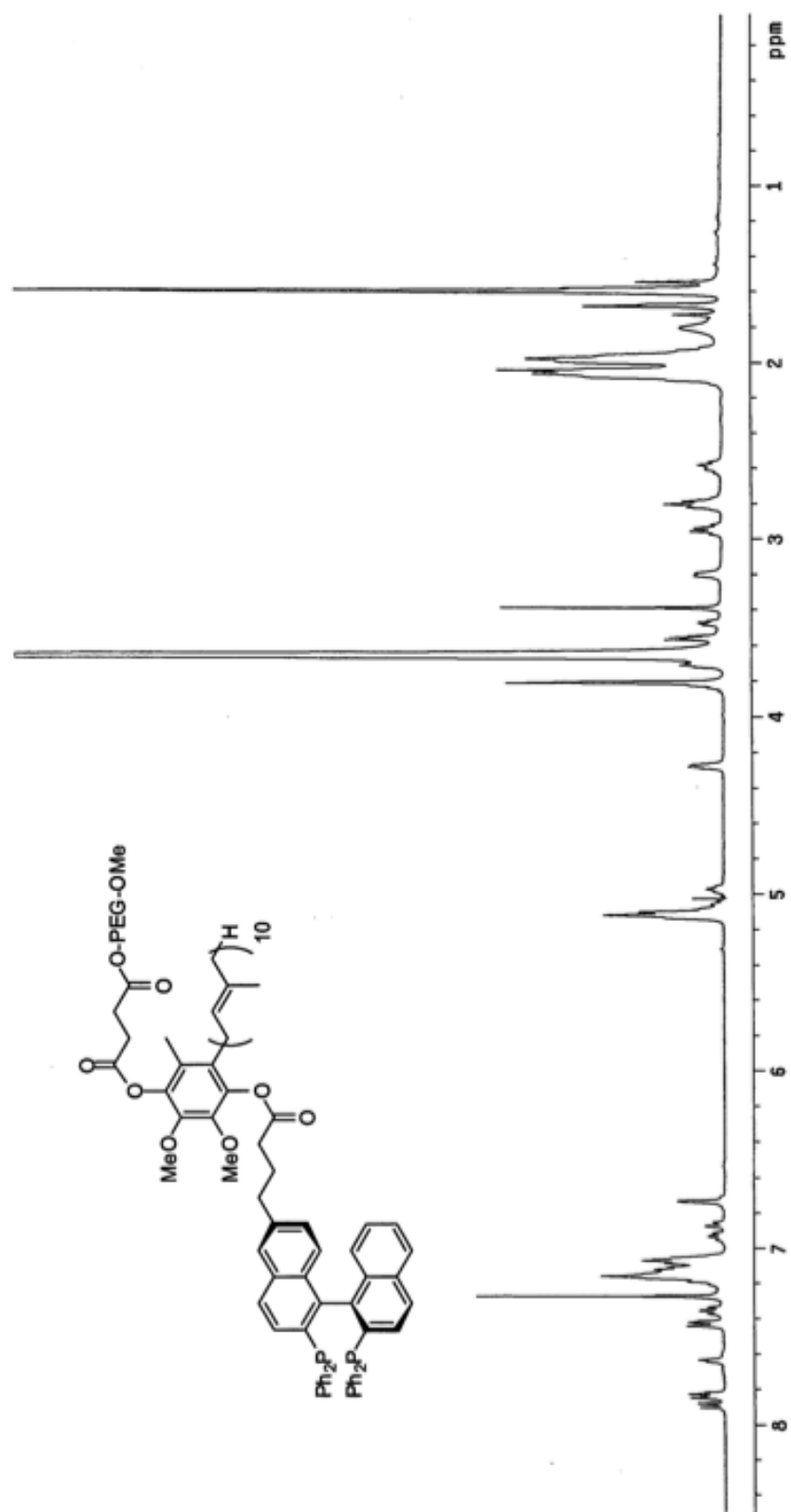


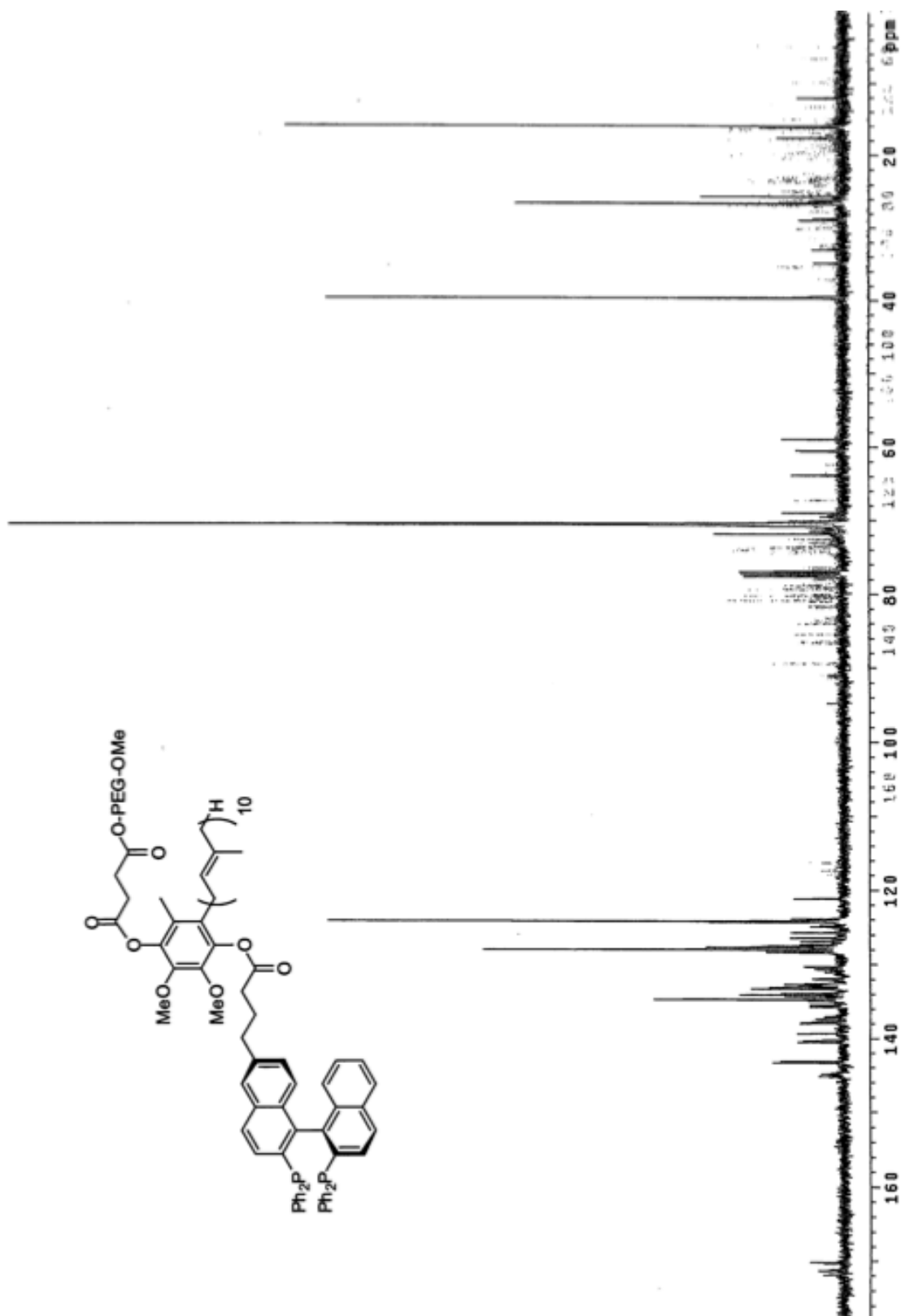


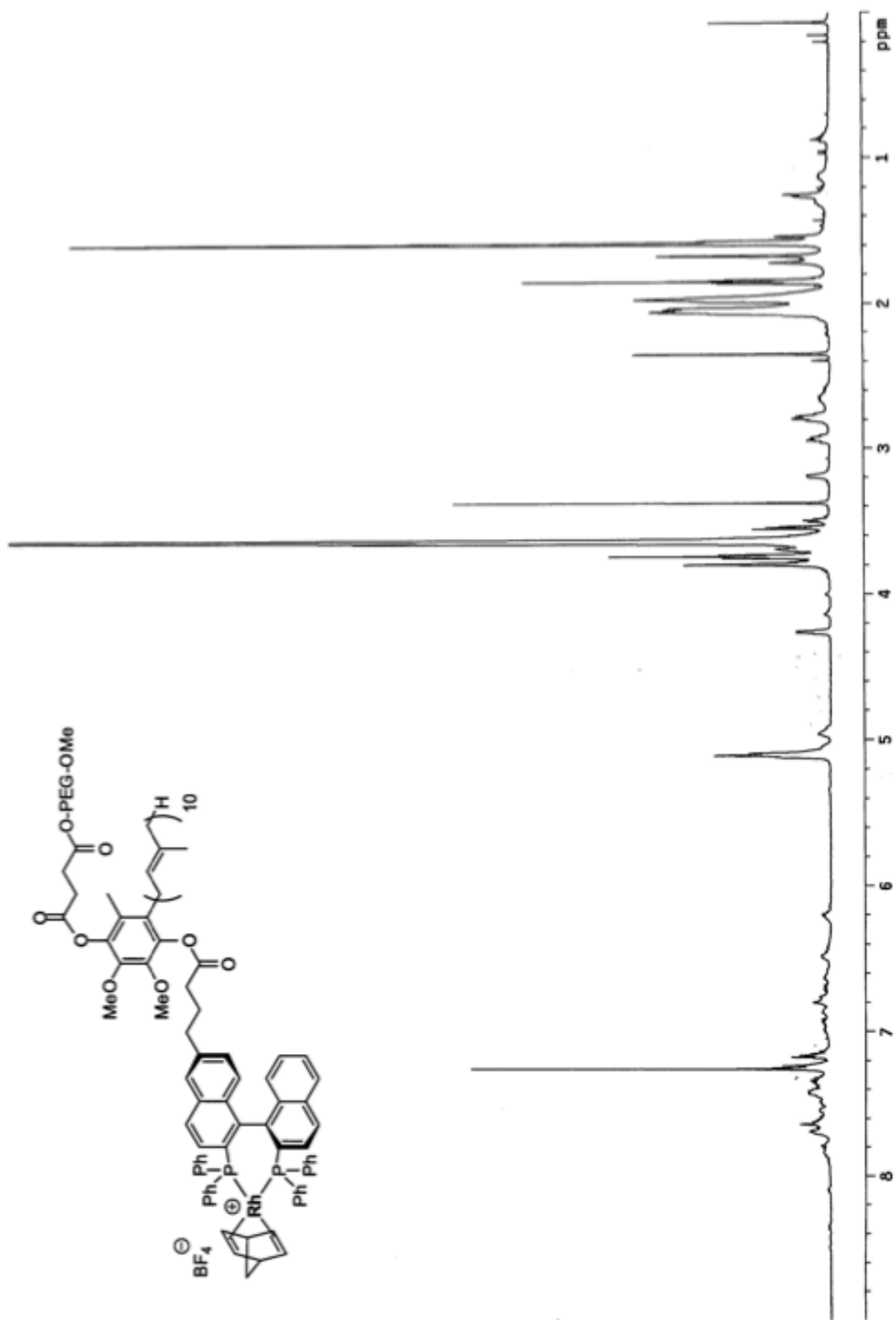


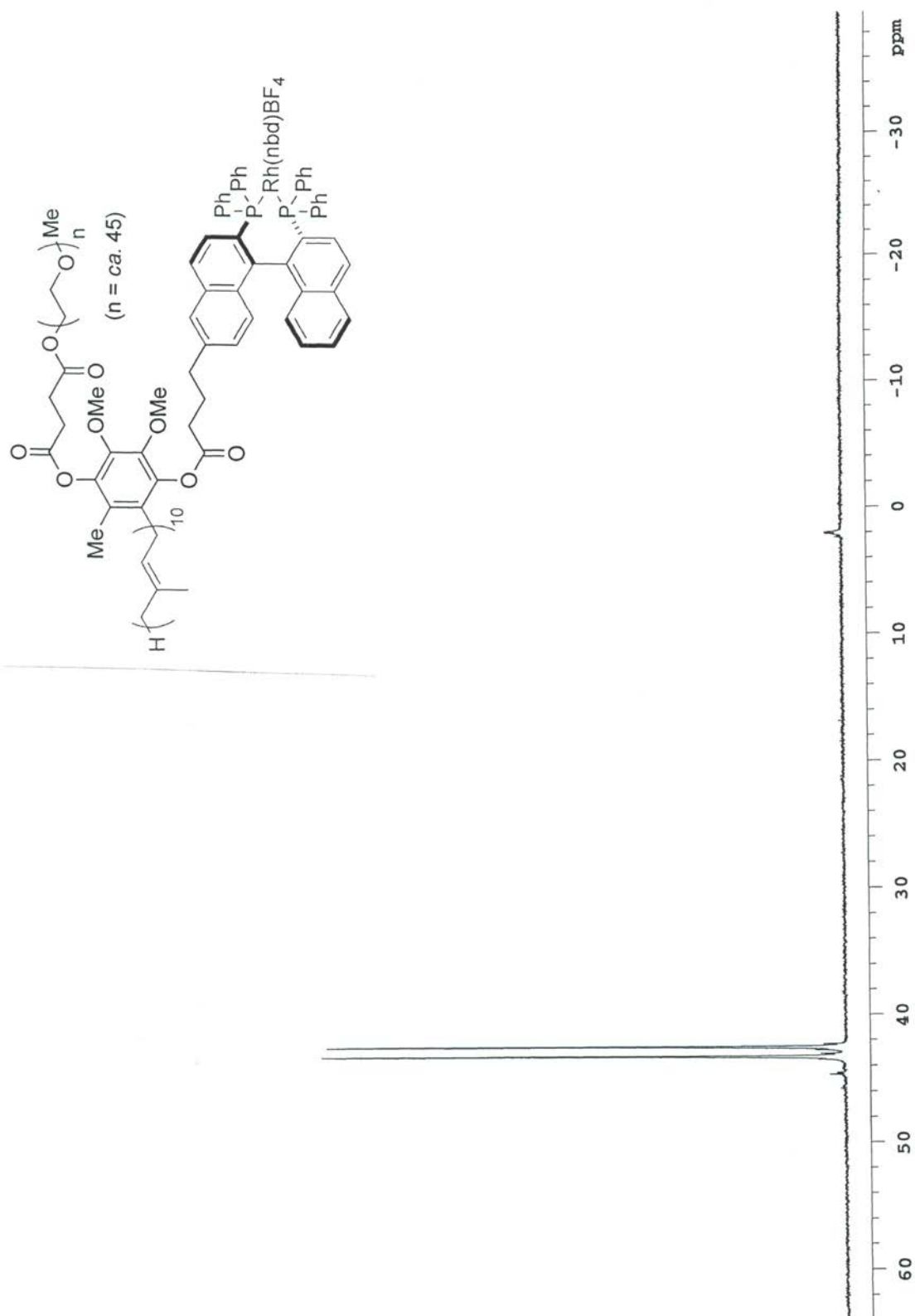


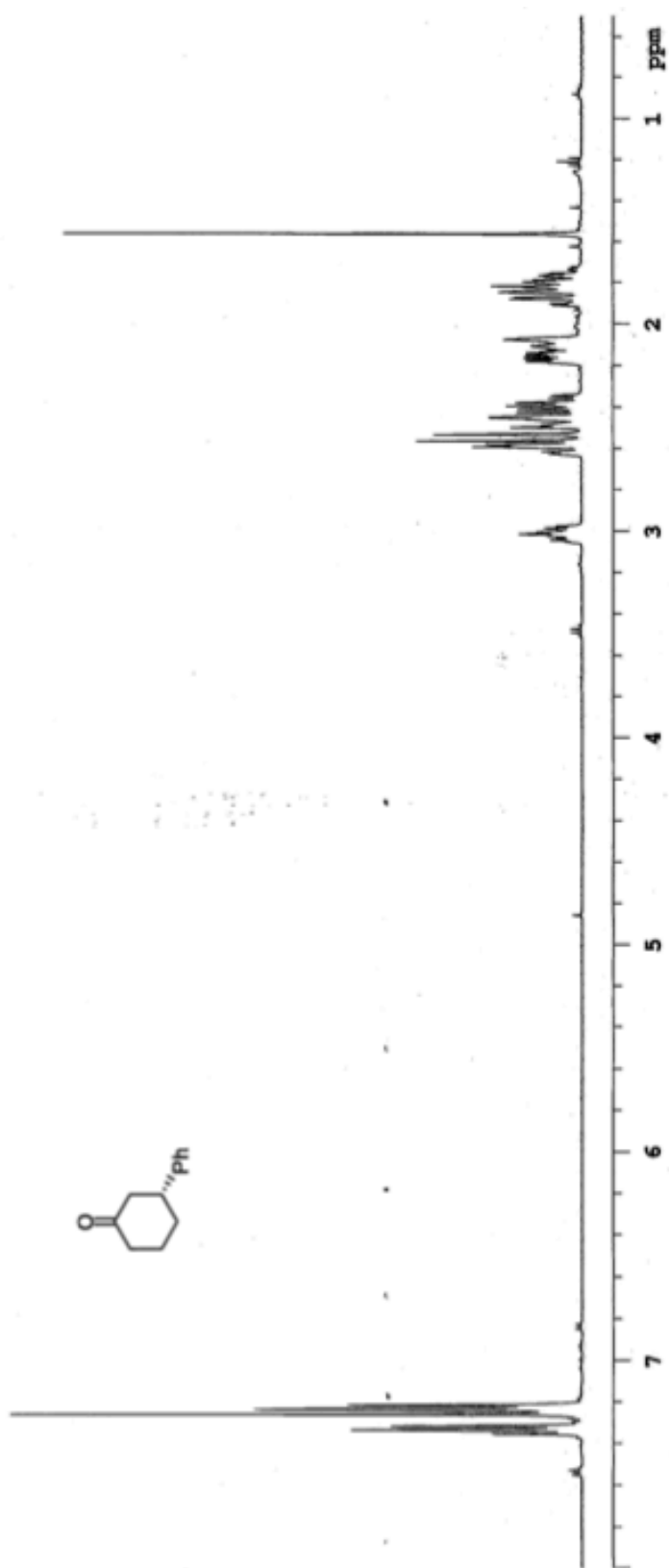










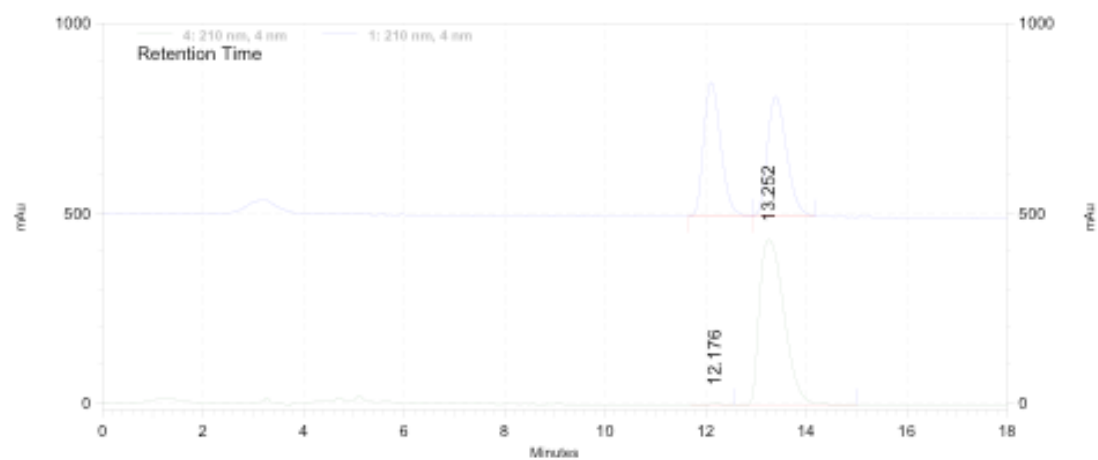


Sample: RMx147_CA_001

99.0%*ee*

Column: Daicel CHIRALCEL OD-H (0.46 cm x 25 cm; Serial: ODH0CE-DG073)

Conditions: 2% IPA/hexanes; 1.00 ml/min



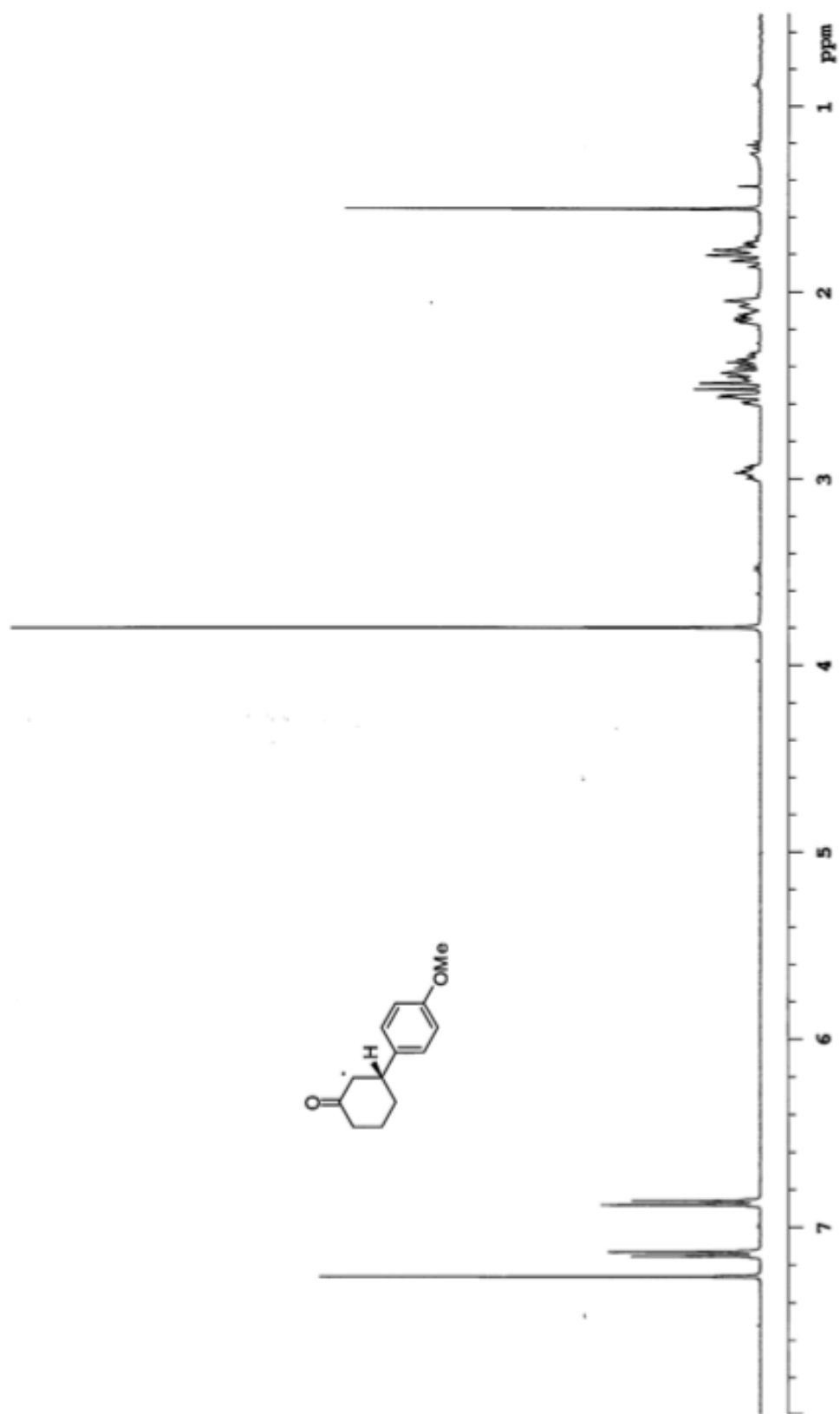
racemic sample

1: 210 nm, 4 nm Results

Retention Time	Area	Area %
12.112	8355321	49.90
13.396	8390338	50.10
Totals	16745659	100.00

4: 210 nm, 4 nm Results

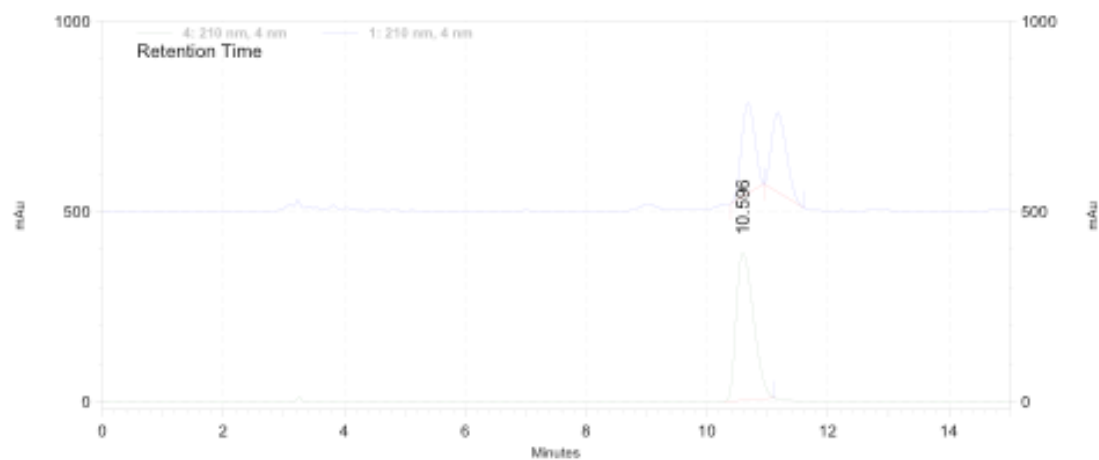
Retention Time	Area	Area %
12.176	152020	0.51
13.252	29599807	99.49
Totals	29751827	100.00



Sample: RMx152_CA_fast001

>99 %*ee*

Column: Daicel CHIRALCEL OD-H (0.46 cm x 25 cm; Serial: ODH0CE-FJ109)
 Conditions: 5% IPA/hexanes; 1.0 ml/min



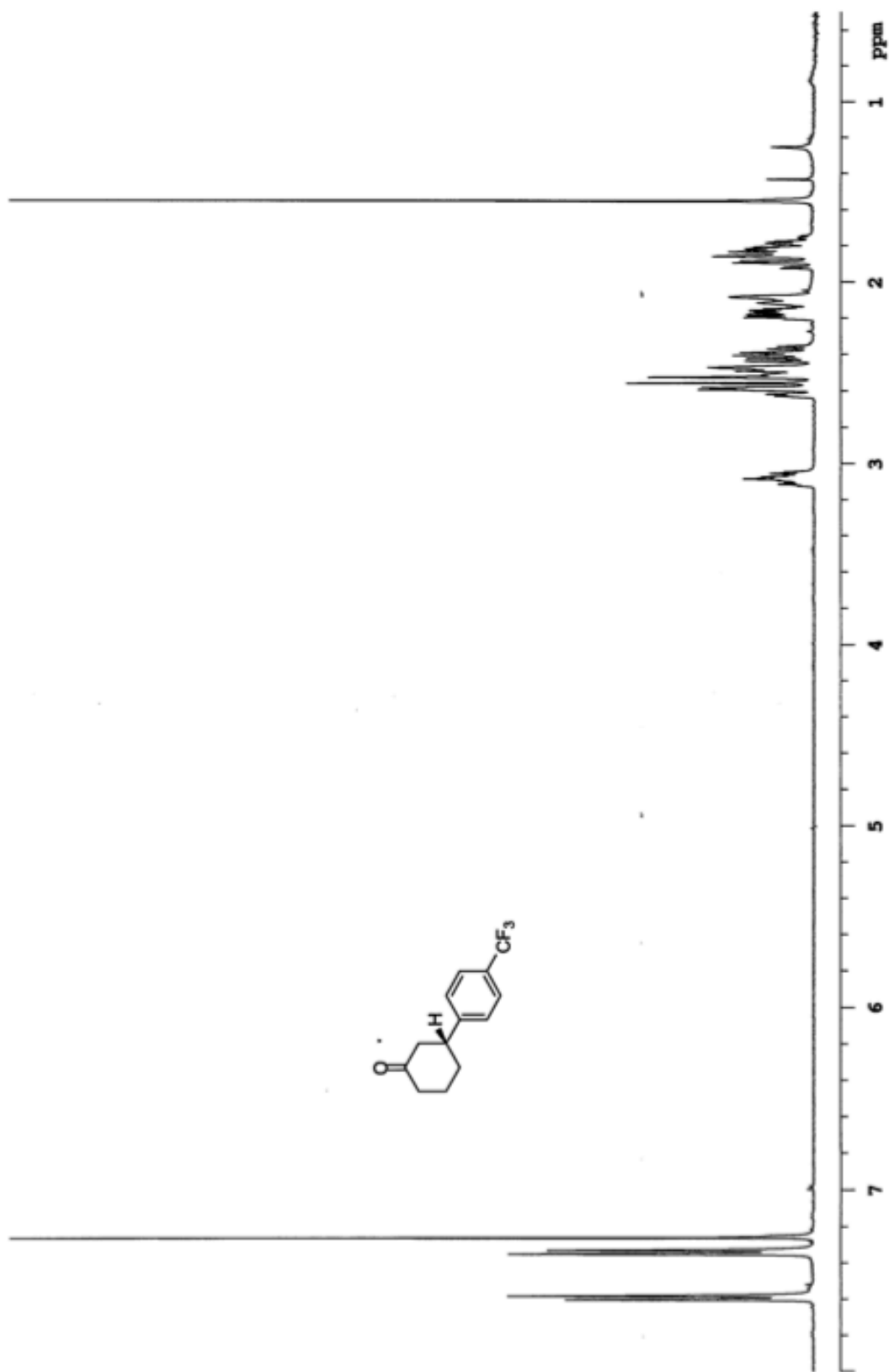
racemic sample

1: 210 nm, 4 nm Results

Retention Time	Area	Area %
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Totals	14203355	100.00

4: 210 nm, 4 nm Results

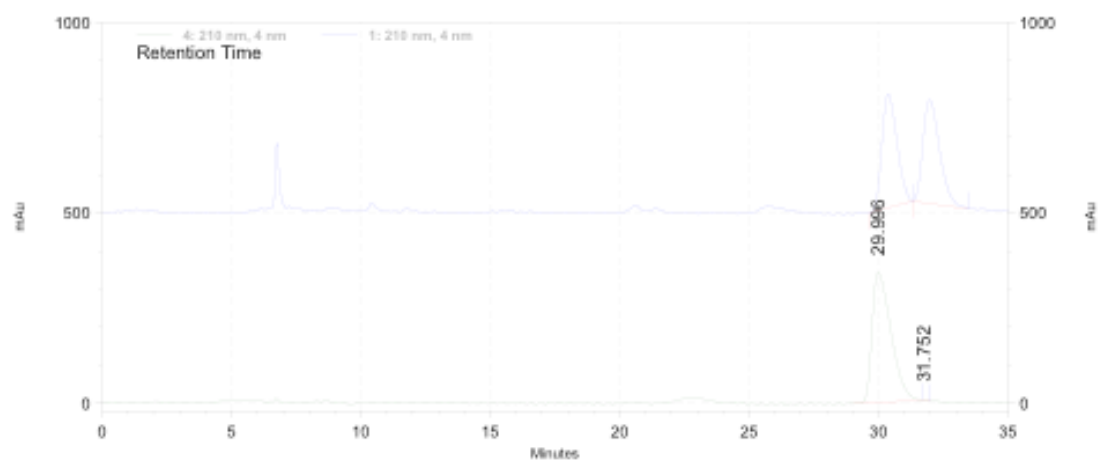
Retention Time	Area	Area %
10.596	30849896	100.00
Totals	30849896	100.00



Sample: RMx153_CA_003

99.9 %*ee*

Column: Daicel CHIRALCEL OD-H (0.46 cm x 25 cm; Serial: ODH0CE-LI108)
 Conditions: 1% IPA/hexanes; 0.50 ml/min



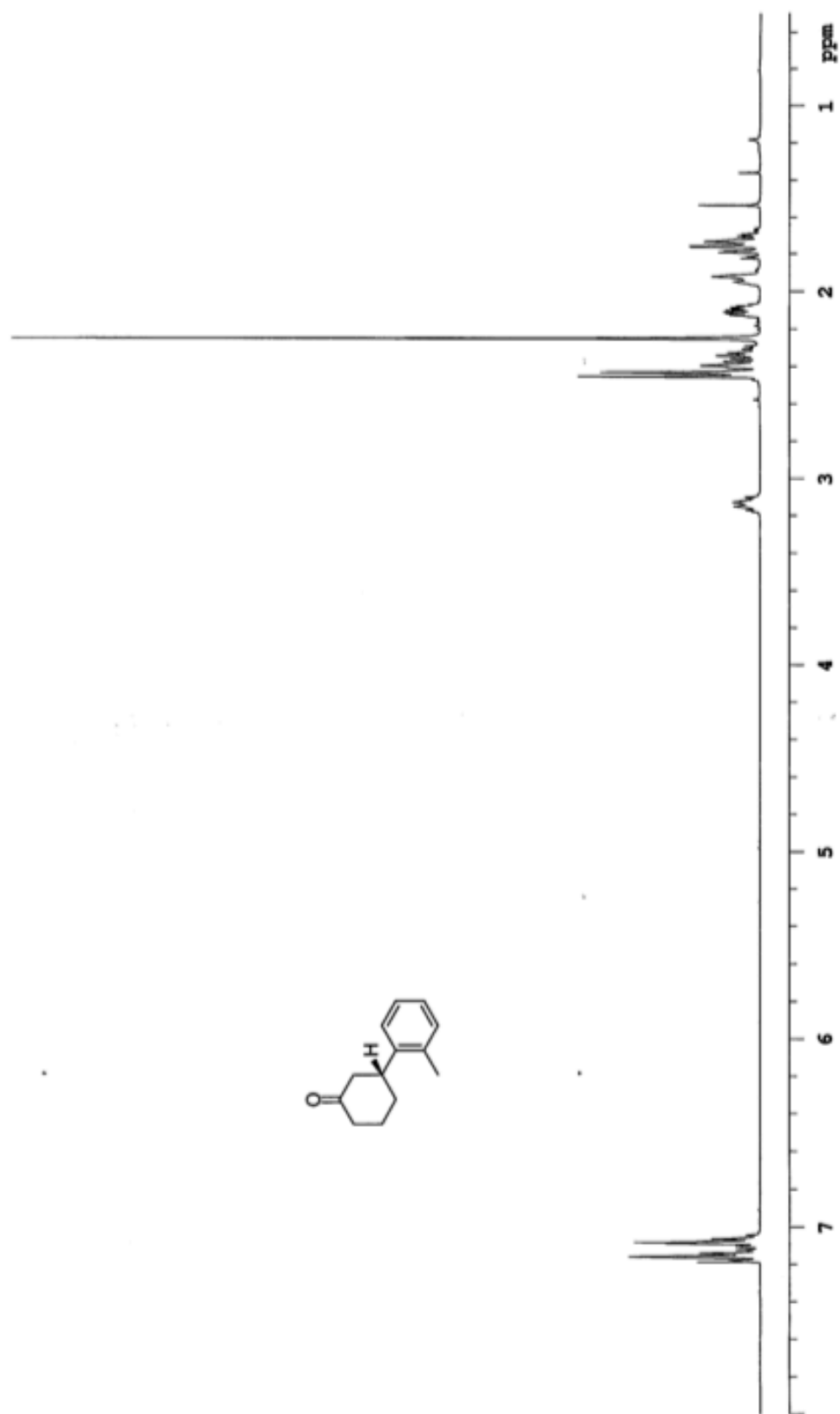
racemic sample

1: 210 nm, 4 nm Results

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Totals	24358761	100.00

4: 210 nm, 4 nm Results

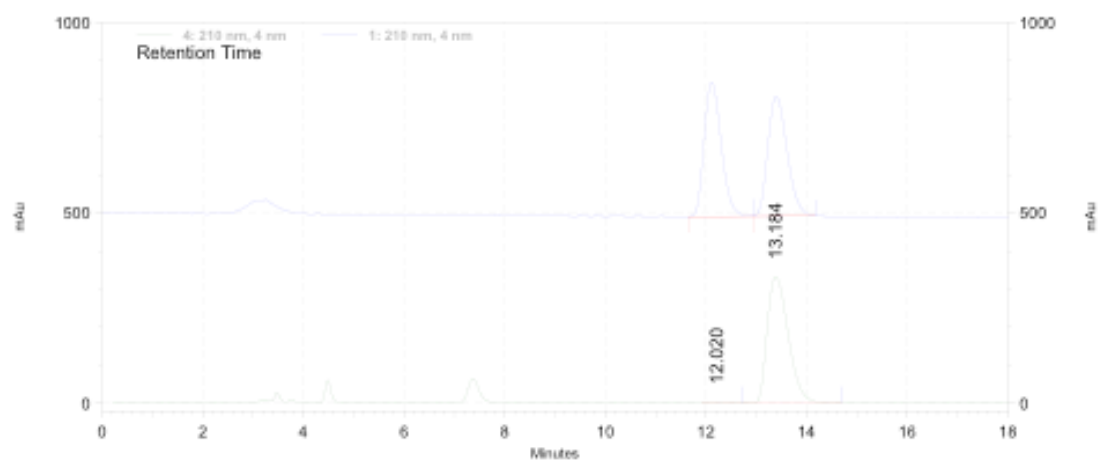
Retention Time	Area	Area %
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31.752	20628	0.05
Totals	43282466	100.00



Sample: NI_1_53_001

98.0%*ee*

Column: Daicel CHIRALCEL OD-H (0.46 cm x 25 cm; Serial: ODH0CE-DG073)
 Conditions: 2% IPA/hexanes; 1.00 ml/min



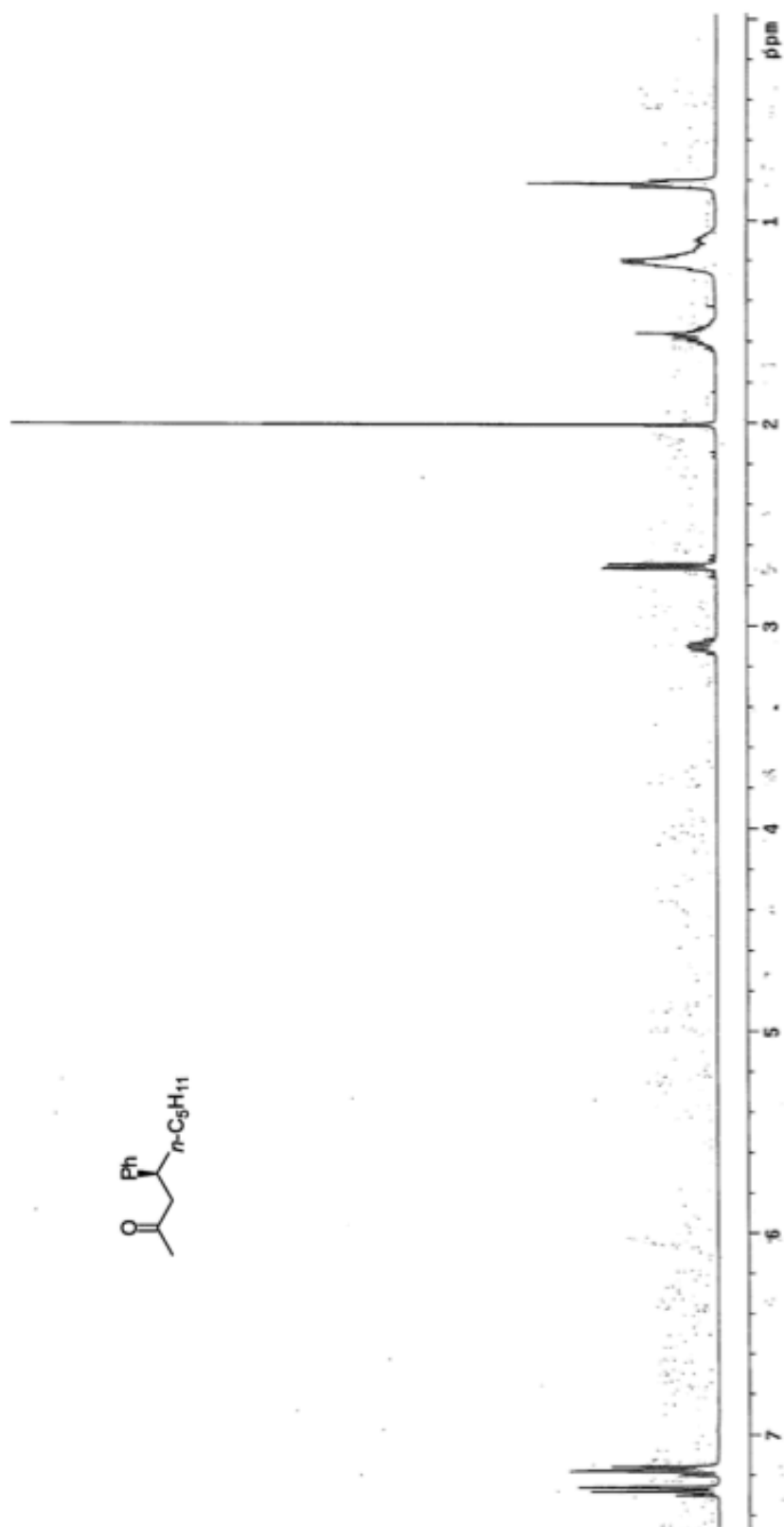
racemic sample

1: 210 nm, 4 nm Results

Retention Time	Area	Area %
12.112	8355321	49.90
13.396	8390338	50.10
Totals	16745659	100.00

4: 210 nm, 4 nm Results

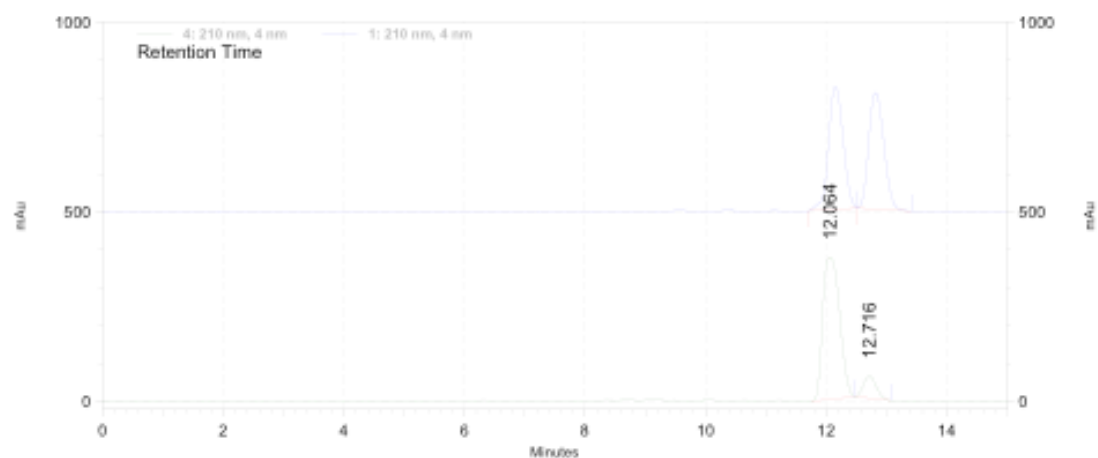
Retention Time	Area	Area %
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13.184	19289636	99.01
Totals	19482388	100.00



Sample: SG-2-177B_001

78.9 %*ee*

Column: Daicel CHIRALCEL OD-H (0.46 cm x 25 cm; Serial: ODH0CE-FJ019)
 Conditions: 2% IPA/hexanes; 0.5 ml/min



racemic sample

1: 210 nm, 4 nm Results

Retention Time	Area	Area %
12.152	10889389	50.49
12.820	10675932	49.51
Totals	21565321	100.00

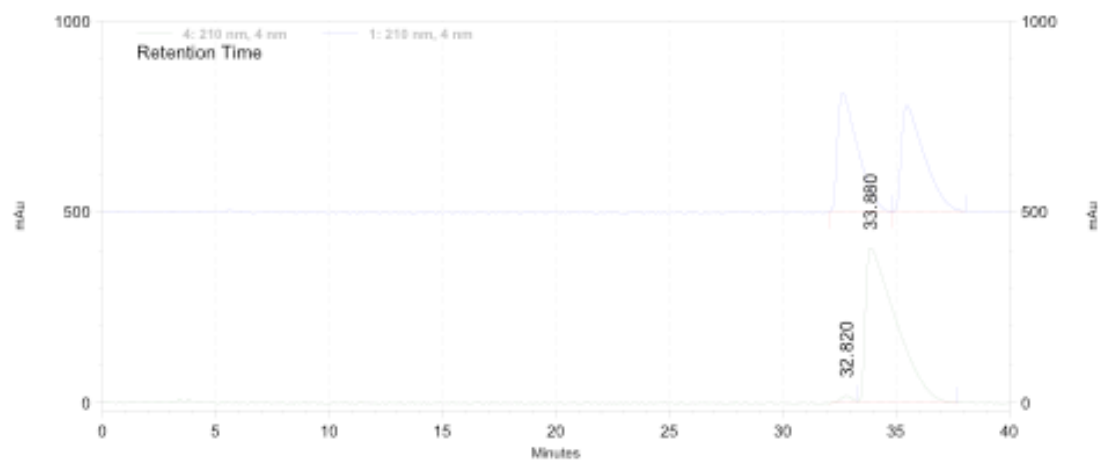
4: 210 nm, 4 nm Results

Retention Time	Area	Area %
12.064	18156129	89.45
12.716	2141959	10.55
Totals	20298088	100.00

Sample: SG-2-179B_001

97.2 %*ee*

Column: Daicel CHIRALCEL OB-H (0.46 cm x 25 cm; Serial: OBH0CE-CE001)
 Conditions: 0.5% IPA/hexanes; 1.0 ml/min



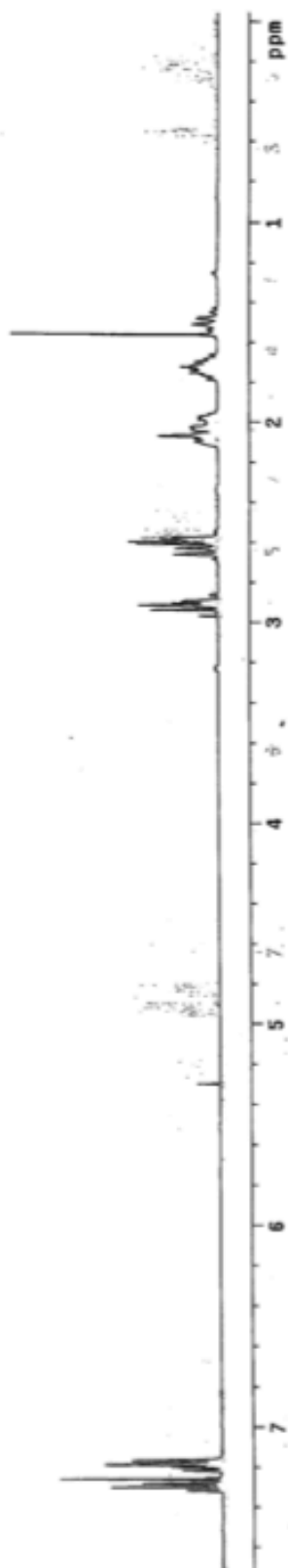
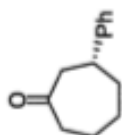
racemic sample

1: 210 nm, 4 nm Results

Retention Time	Area	Area %
32.656	19477625	49.92
35.488	19537866	50.08
Totals	39015491	100.00

4: 210 nm, 4 nm Results

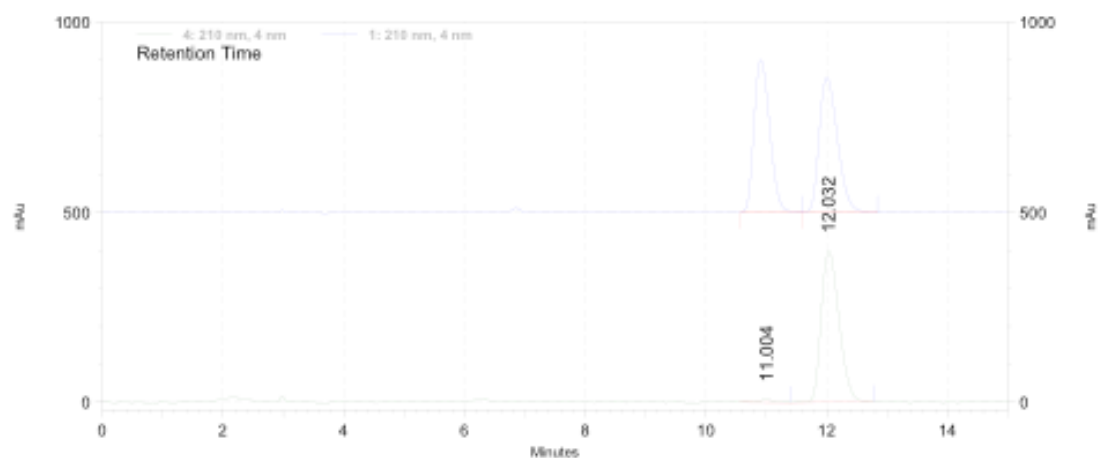
Retention Time	Area	Area %
32.820	830450	1.42
33.880	57705799	98.58
Totals	58536249	100.00



Sample: SG-2-178B_001

96.3 %*ee*

Column: Daicel CHIRALCEL OD-H (0.46 cm x 25 cm; Serial: ODH0CE-FJ019)
 Conditions: 2% IPA/hexanes; 1.0 ml/min



racemic sample

1: 210 nm, 4 nm Results

Retention Time	Area	Area %
10.908	12091715	49.21
12.000	12478870	50.79
Totals	24570585	100.00

4: 210 nm, 4 nm Results

Retention Time	Area	Area %
11.004	191182	1.83
12.032	10251153	98.17
Totals	10442335	100.00

Size Distribution Report by Intensity

v2.0



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Sample Details

Sample Name: NI_PQS3-BINAP-Rh_0.3conv(wt%)(001) 1

SOP Name: mansettings.nano

General Notes:

File Name: Micelles.dts	Dispersant Name: Water
Record Number: 39	Dispersant RI: 1.330
Material RI: 1.33	Viscosity (cP): 0.8872
Material Absorbtion: 0.00	Measurement Date and Time: Wednesday, February 01, 20...

System

Temperature (°C): 25.0	Duration Used (s): 70
Count Rate (kcps): 222.8	Measurement Position (mm): 4.65
Cell Description: Low volume disposable sizing ...	Attenuator: 9

Results

	Diam. (nm)	% Intensity	Width (nm)
Z-Average (d.nm): 42.54	Peak 1: 77.53	98.0	76.78
Pdi: 0.380	Peak 2: 4167	2.0	1022
Intercept: 0.925	Peak 3: 0.000	0.0	0.000

Result quality : **Good**

