Supplementary Material (ESI) for Chemical Communications

Organocatalytic Asymmetric Allylic Alkylation of Oxindoles with Morita-Baylis-Hillman Carbonates

Kun Jiang,[a] Jing Peng,[a] Hai-Lei Cui,[a] and Ying-Chun Chen*[a,b]

[a] *Key Laboratory of Drug-Targeting and Drug Delivery System of Education Ministry, Department of Medicinal Chemistry, West China School of Pharmacy, Sichuan University, Chengdu 610041, China; Fax: 86 28 85502609; E-mail: ycchenhuaxi@yahoo.com.cn.*

[b] *State Key Laboratory of Biotherapy, West China Hospital, Sichuan University, Chengdu, China.*

Supplementary Information

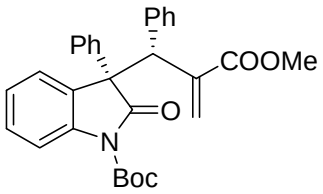
Table of Contents

1. General Methods

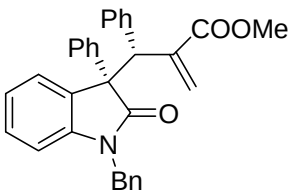
NMR spectra were recorded with tetramethylsilane as the internal standard. Column chromatography was performed using silica gel (200-300 mesh) eluting with ethyl acetate and petroleum ether. TLC was performed on glass-backed silica plates. Optical rotations were measured at 589 nm at 20 °C. Enantiomeric excess was determined by HPLC analysis on Chiralpak AD, IC and Chiralcel OD columns. DCE was distilled from CaH_2. All other chemicals were used without purification as commercially available. Cinchona alkaloids catalysts **1a–1d** were purchased from Aldrich Chemical Company. The substrates 3-substituted oxindoles[1] **2** and Morita-Baylis-Hillman carbonates[2] **3** were prepared according to the procedures previously reported.

2. General procedure for the asymmetric allylic alkylation of oxindoles with Morita-Baylis-Hillman carbonates:

N-Boc-3-substituted oxindole **2** (0.1 mmol), Morita-Baylis-Hillman carbonate **3** (0.2 mmol) and catalyst $(DHQD)_2AQN$ **1a** (8.6 mg, 10 mol %) were stirred in dry DCE (1 mL) at 35 °C for a specified reaction time. When the reaction was complete, the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 50:1) to give compound **4**. The analytic data were related to the major diastereomer.

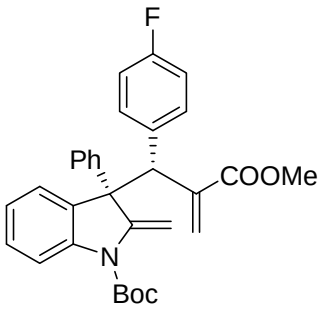


4a 98% yield; $[\alpha]_D^{20}$ = -134.0 (*c* = 1.45 in EtOAc); 85:15 dr, determined by ^{1}H NMR; 93% ee, determined by HPLC analysis [Daicel chiralcel OD, *n*-hexane/*i*-PrOH = 95/5, 1.0 mL/min, λ = 254 nm, t_{major} = 10.06 min, t_{minor} = 17.21 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72-7.61 (m, 2H), 7.50-7.47 (m, 2H), 7.35-7.22 (m, 6H), 7.07-7.03 (m, 2H), 6.94-6.90 (m, 2H), 6.22 (s, 1H), 5.52 (d, *J* = 1.2 Hz, 1H), 5.42 (s, 1H), 3.43 (s, 3H), 1.52 (s, 9H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 175.4, 166.1, 146.8, 140.2, 140.1, 137.4, 137.2, 129.8, 128.8, 128.3, 127.9, 127.2, 127.0, 123.7, 115.0, 84.1, 60.4, 53.9, 51.9, 28.0 ppm; ESI-HRMS: calcd. for $C_{30}H_{29}NO_5$+Na 506.1943, found 506.1951.

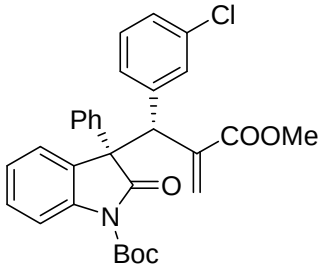


4b 91% yield; $[\alpha]_D^{20}$ = -15.23 (*c* = 0.35 in EtOAc); 79:21 dr, determined by ^{1}H NMR; 94% ee, determined by HPLC analysis [Daicel chiralpak IC, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL/min, λ = 254 nm, t_{major} = 32.78 min,

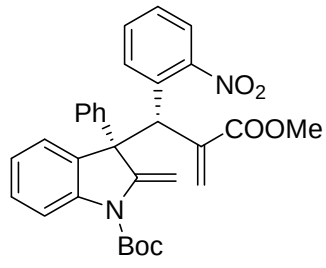
t_{minor} = 10.98 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70 (d, *J* = 7.6 Hz, 1H), 7.62-7.59 (m, 2H), 7.32-7.22 (m, 4H), 7.14-6.93 (m, 9H), 6.70 (d, *J* = 6.4 Hz, 2H), 6.53 (d, *J* = 8.0 Hz, 1H), 6.21 (s, 1H), 5.57 (d, *J* = 1.2 Hz, 1H), 5.51 (s, 1H), 4.81 (d, *J* = 16.0 Hz, 1H), 4.48 (d, *J* = 16.0 Hz, 1H), 3.41 (s, 3H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 176.9, 168.3, 143.4, 140.6, 138.3, 138.0, 137.9, 136.3, 135.3, 130.1, 128.5, 128.3, 128.1, 127.9, 127.7, 127.5, 127.4, 127.2, 126.9, 121.9, 109.6, 60.1, 53.1, 51.8, 43.9, 29.7 ppm; ESI-HRMS: calcd.for$C_{32}H_{27}NO_3$+Na 496.1889, found 496.1883.



4c 94% yield; $[\alpha]_D^{20}$ = -85.8 (*c* = 0.61 in EtOAc); 81:19 dr, determined by ^{1}H NMR; 96% ee, determined by HPLC analysis [Daicel chiralcel OD, *n*-hexane/*i*-PrOH = 98/2, 1.0 mL/min, λ = 254 nm, t_{major} = 6.97 min, t_{minor} = 27.35 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71 (d, *J* = 7.6 Hz, 1H), 7.62 (dd, *J* = 1.2, 7.6 Hz, 1H), 7.47-7.42 (m, 2H), 7.31-7.23 (m, 4H), 6.92-6.87 (m, 2H), 6.77-6.71 (m, 3H), 6.22 (s, 1H), 5.52 (d, *J* = 1.6 Hz, 1H), 5.40 (s, 1H), 3.45 (s, 3H), 1.54 (s, 9H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 175.3, 167.9, 164.2, 159.4, 146.7, 140.1, 139.9, 137.2, 133.0, 131.5, 131.4, 128.9, 128.4, 128.1, 127.7, 127.6, 127.1, 123.8, 115.1, 114.7, 114.3, 84.3, 60.4, 53.1, 51.9, 28.0 ppm; ESI-HRMS: calcd. for $C_{30}H_{28}FNO_5$+Na 524.1849, found 524.1844.

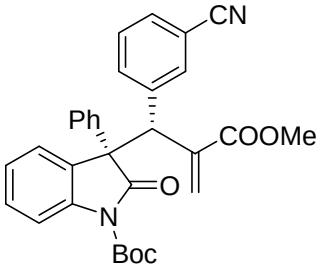


4d 90% yield; $[\alpha]_D^{20}$ = -155.2 (*c* = 0.46 in EtOAc); 81:19 dr, determined by ^{1}H NMR; 94% ee, determined by HPLC analysis [Daicel chiralcel OD, *n*-hexane/*i*-PrOH = 95/5, 1.0 mL/min, λ = 254 nm, t_{major} = 5.24 min, t_{minor} = 17.94 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.73 (d, *J* = 7.6 Hz, 1H), 7.60 (dd, *J* = 1.2, 7.6 Hz, 1H), 7.45-7.42 (m, 2H), 7.30-7.21 (m, 5H), 7.07-6.80 (m, 3H), 6.78-6.77 (m, 1H), 6.26 (s, 1H), 5.54 (d, *J* = 1.2 Hz, 1H), 5.39 (s, 1H), 3.47 (s, 3H), 1.55 (s, 9H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 171.2, 163.7, 163.0, 144.7, 136.0, 135.4, 135.1, 134.5, 134.0, 133.9, 133.1, 129.5, 125.9, 125.0, 124.8, 124.6, 124.4, 124.1, 123.8, 123.7, 123.2, 123.0, 119.8, 111.1, 80.4, 56.5, 49.4, 48.0, 23.9 ppm; ESI-HRMS: calcd. for $C_{30}H_{28}ClNO_5$+Na 540.1554, found 540.1551.

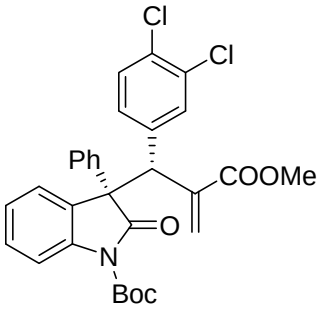


4e 50% yield; $[\alpha]_D^{20}$ = +69.8 (*c* = 0.40 in EtOAc); 92:8 dr, determined by ^{1}H NMR; 92% ee, determined by HPLC analysis [Daicel chiralcel OD, *n*-hexane/*i*-PrOH = 90/10, 1.0 mL/min, λ = 254 nm, t_{major} = 10.50 min, t_{minor} = 8.79 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ =7.77 (d, *J* =

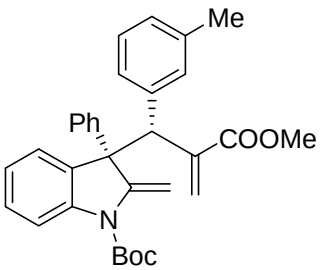
8.4 Hz, 1H), 7.70-7.53 (m, 3H), 7.39-7.18 (m, 9H), 6.25 (s, 1H), 6.11 (s, 1H), 5.44 (s, 1H), 3.35 (s, 3H), 1.57 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.1, 167.0, 150.5, 148.8, 139.5, 139.0, 136.8, 132.4, 132.1, 131.5, 129.0, 128.9, 128.4, 128.1, 127.9, 127.7, 126.5, 124.4, 124.2, 115.0, 84.6, 59.8, 51.9, 47.1, 28.0 ppm; ESI-HRMS: calcd. for $C_{30}H_{28}N_2O_7$+Na 551.1794, found 551.1798.



4f 85% yield; $[\alpha]_D^{20}$ = -192.9 (*c* = 0.81 in EtOAc); 83:17 dr, determined by ^{1}H NMR; 92% ee, determined by HPLC analysis [Daicel chiralpak AD, *n*-hexane/*i*-PrOH = 90/10, 1.0 mL/min, λ = 254 nm, t_{major} = 8.33 min, t_{minor} = 9.97 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66 (d, *J* = 8.0 Hz, 1H), 7.45-7.41 (m, 3H), 7.36-7.28 (m, 4H), 7.17-7.10 (m, 3H), 7.02-6.94 (m, 2H), 6.48 (s, 1H), 5.97 (s, 1H), 5.32 (s, 1H), 3.65 (s, 3H), 1.59 (s, 9H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 175.4, 166.8, 139.0, 138.2, 137.8, 137.3, 134.3, 133.3, 131.0, 130.5, 129.3, 129.0, 128.8, 128.3, 127.8, 127.6, 125.4, 125.0, 124.3, 116.6, 115.0, 111.7, 84.7, 60.4, 53.1, 52.3, 28.0 ppm; ESI-HRMS: calcd. for $C_{31}H_{28}N_2O_5$+Na 531.1896, found 531.1896.

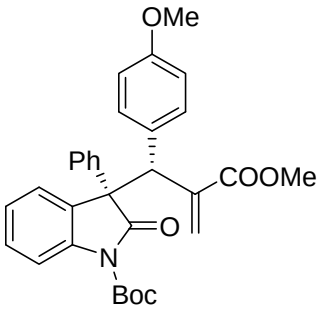


4g 84% yield; $[\alpha]_D^{20}$ = -117.26 (*c* = 0.45 in EtOAc); 85:15 dr, determined by ^{1}H NMR; 95% ee, determined by HPLC analysis [Daicel chiralpak AD, *n*-hexane/*i*-PrOH = 98/2, 1.0 mL/min, λ = 254 nm, t_{major} = 13.41 min, t_{minor} = 20.24 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.73 (d, *J* = 8.0 Hz, 1H), 7.59 (dd, *J* = 0.8, 7.6 Hz, 1H), 7.44-7.23 (m, 8H), 7.18-7.06 (m, 2H), 6.79 (dd, *J* = 2.0, 8.4 Hz, 1H), 6.27 (s, 1H), 5.54 (d, *J* = 1.6 Hz, 1H), 5.36 (s, 1H), 3.48 (s, 3H), 1.56 (s, 9H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 175.3, 167.6, 146.7, 140.1, 139.2, 137.7, 137.1, 132.0, 131.3, 130.5, 130.1, 129.6, 129.3, 128.6, 128.1, 128.0, 127.0, 124.1, 115.3, 84.7, 60.3, 52.9, 52.2, 26.1 ppm; ESI-HRMS: calcd. for $C_{30}H_{27}Cl_2NO_5$+Na 574.1164, found 574.1158.

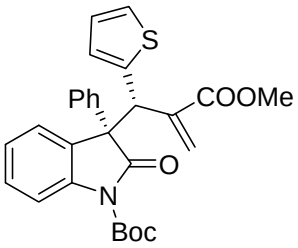


4h 96% yield; $[\alpha]_D^{20}$ = -71.2 (*c* = 0.87 in EtOAc); 86:14 dr, determined by ^{1}H NMR; 95% ee, determined by HPLC analysis [Daicel chiralpak AD, *n*-hexane/*i*-PrOH = 98/2, 1.0 mL/min, λ = 254 nm, t_{major} = 8.61 min, t_{minor} = 13.04 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71 (dd, *J* = 1.2, 8.4 Hz, 1H), 7.62 (dd, *J* = 1.2, 8.0 Hz, 1H), 7.51-7.46 (m, 2H),

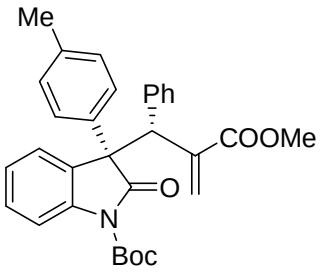
7.35-7.22 (m, 5H), 6.95-6.87 (m, 2H), 6.71-6.66 (m, 2H), 6.21 (s, 1H), 5.51 (d, *J* = 1.2 Hz, 1H), 5.38 (s, 1H), 3.43(s, 3H), 2.13 (s, 3H), 1.52 (s, 9H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 175.4, 166.2, 146.8, 140.3, 140.1, 137.3, 137.2, 137.0, 130.6, 128.7, 128.3, 127.7, 127.6, 127.5, 127.3, 126.7, 126.1, 123.6, 115.0, 84.0, 60.4, 53.9, 51.9, 28.0, 21.2 ppm; ESI-HRMS: calcd. for $C_{31}H_{31}NO_5$+Na 520.2100, found 520.2108.



4i 71% yield; $[\alpha]_D^{20}$ = -135.4(*c* = 0.86 in EtOAc); 90:10 dr, determined by ^{1}H NMR; 97% ee, determined by HPLC analysis [Daicel chiralpak IC, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL/min, λ = 254 nm, t_{major} = 8.55 min, t_{minor} = 9.96 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (d, *J* = 7.2 Hz, 1H), 7.62 (dd, *J* = 0.8, 7.6 Hz, 1H), 7.49-7.46 (m, 2H), 7.30-7.21 (m, 5H), 6.83-6.80 (m, 2H), 6.60-6.55 (m, 2H), 6.17 (s, 1H), 5.49 (d, *J* = 1.2 Hz, 1H), 5.36 (s, 1H), 3.69 (s, 3H), 3.43 (s, 3H), 1.52 (s, 9H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 175.4, 166.2, 158.4, 146.8, 140.4, 140.2, 137.3, 130.9, 129.1, 128.7, 128.2, 127.6, 127.2, 123.6, 115.0, 113.0, 84.0, 60.4, 55.0, 53.2, 51.8, 27.9; ESI-HRMS: calcd. for $C_{31}H_{31}NO_6$+Na 536.2049, found 536.2058.

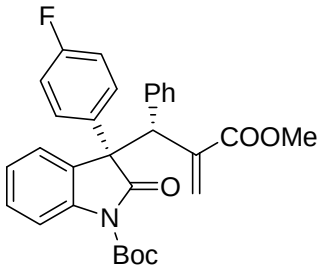


4j 94% yield; $[\alpha]_D^{20}$ = +14.33 (*c* = 0.33 in EtOAc); 79:21 dr, determined by ^{1}H NMR; 90% ee, determined by HPLC analysis [Daicel chiralcel OD, *n*-hexane/*i*-PrOH = 95/5, 1.0 mL/min, λ = 254 nm, t_{major} = 27.17 min, t_{minor} = 10.41 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (t, *J* = 8.4 Hz, 1H), 7.64-7.55 (m, 2H), 7.44-7.34 (m, 5H), 7.08-7.02 (m, 1H), 6.80-6.78 (m, 1H), 6.620-6.61 (m, 1H), 6.39-6.38 (m, 1H), 6.24 (s, 1H), 5.74 (s, 1H), 5.62 (s, 1H), 3.41 (s, 3H), 1.58 (s, 9H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 175.0, 166.8, 149.0, 140.6, 140.2, 138.1, 129.0, 128.4, 128.3, 128.2, 127.9, 127.6, 126.7, 126.6, 126.2, 125.2, 123.9, 115.1, 84.4, 72.1, 60.5, 52.4, 47.6, 28.0 ppm; ESI-HRMS: calcd. for $C_{28}H_{27}NO_5S$+Na 512.1508, found 512.1517.

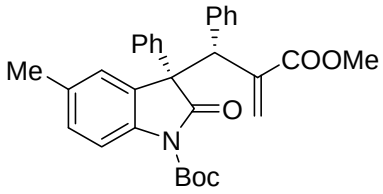


4k 75% yield; $[\alpha]_D^{20}$ = -96.31 (*c* = 0.39 in EtOAc); 82:18 dr, determined by ^{1}H NMR; 88% ee, determined by HPLC analysis [Daicel chiralpak AD, *n*-hexane/*i*-PrOH = 95/5, 1.0 mL/min, λ = 254 nm, t_{major} = 6.74 min, t_{minor} = 17.23 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70 (d, *J* = 8.4 Hz, 1H), 7.61 (dd, *J* = 0.8, 7.6 Hz, 2H), 7.36-7.19 (m, 4H), 7.14-6.94 (m, 5H), 6.92-6.90 (m, 2H), 6.22 (s, 1H), 5.54 (d, *J* = 1.2 Hz, 1H), 5.38 (s, 1H), 3.44 (s, 3H), 2.30 (s, 3H), 1.52 (s, 9H) ppm; ^{13}C NMR (50 MHz,

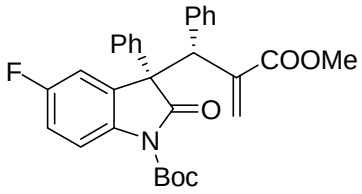
$CDCl_3$): δ = 175.5, 166.1, 140.1, 137.3, 134.4, 129.8, 129.0, 128.7, 128.3, 128.1, 127.7, 127.4, 127.2, 127.0, 126.8, 123.7, 115.0, 84.0, 60.2, 53.8, 51.9, 28.0, 20.9 ppm; ESI-HRMS: calcd. for $C_{31}H_{31}NO_5$+Na 520.2100, found 520.2100.



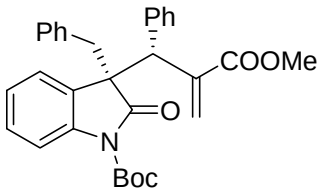
4l 90% yield; $[\alpha]_D^{20}$ = -166.0 (*c* = 0.75 in EtOAc); 81:19 dr, determined by ^{1}H NMR; 93% ee, determined by HPLC analysis [Daicel chiralpak AD, *n*-hexane/*i*-PrOH = 95/5, 1.0 mL/min, λ = 254 nm, t_{major} = 6.53 min, t_{minor} = 9.86 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71 (d, *J* = 7.6 Hz, 1H), 7.60 (dd, *J* = 0.8, 7.6 Hz, 1H), 7.50-7.44 (m, 2H), 7.37-7.33 (m, 1H), 7.27-7.25 (m, 1H), 7.10-6.93 (m, 7H), 6.23 (s, 1H), 5.52 (d, *J* = 1.6 Hz, 1H), 5.35 (s, 1H), 3.46 (s, 3H), 1.52 (s, 9H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 175.4, 166.0, 164.8, 146.7, 140.2, 140.0, 137.0, 133.0, 130.2, 130.0,129.8, 129.0, 128.7, 127.8, 127.2, 127.1, 126.1, 123.6, 115.3, 115.2, 114.7, 84.3, 59.8, 54.1, 52.0, 28.0 ppm; ESI-HRMS: calcd. for $C_{30}H_{28}FNO_5$+Na 524.1849, found 524.1836.



4m 82% yield; $[\alpha]_D^{20}$ = -117.45 (*c* = 0.47 in EtOAc); 89:11 dr, determined by ^{1}H NMR; 94% ee, determined by HPLC analysis [Daicel chiralpak AD, *n*-hexane/*i*-PrOH = 95/5, 1.0 mL/min, λ = 254 nm, t_{major} = 5.58 min, t_{minor} = 8.28 min]; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.60-7.41 (m, 4H), 7.30-6.91 (m, 9H), 6.22 (s, 1H), 5.53 (s, 1H), 5.40 (s, 1H), 3.44 (s, 3H), 2.43 (s, 3H), 1.52 (s, 9H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.5, 168.1, 148.8, 140.2, 137.8, 137.5, 137.4, 133.2, 129.8, 129.3, 128.5, 128.2, 127.8, 127.7, 127.6, 127.5, 127.0, 114.8, 83.9, 60.5, 53.8, 51.9, 28.1, 21.4 ppm; ESI-HRMS: calcd. for $C_{31}H_{31}NO_5$+Na 520.2100, found 520.2106.

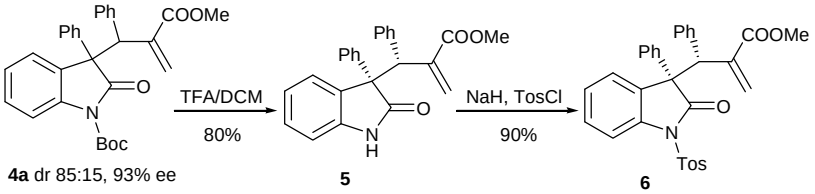


4n 80% yield; $[\alpha]_D^{20}$ = -117.8 (*c* = 0.54 in EtOAc); 87:13 dr, determined by ^{1}H NMR; 95% ee, determined by HPLC analysis [Daicel chiralcel OD, *n*-hexane/*i*-PrOH = 95/5, 1.0 mL/min, λ = 254 nm, t_{major} = 7.58 min, t_{minor} = 11.63 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71 (q, *J* = 4.8 Hz, 1H), 7.47-7.44 (m, 2H), 7.37-7.24 (m, 4H), 7.09-7.01 (m, 4H), 6.94-6.91 (m, 2H), 6.23 (s, 1H), 5.48 (d, *J* = 1.2 Hz, 1H), 5.41 (s, 1H), 3.44 (s, 3H), 1.52 (s, 9H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 175.0, 167.9, 161.7, 156.9, 146.7, 139.7, 136.9, 136.2, 129.7, 128.5, 128.0, 127.9, 127.6, 127.4, 127.2, 116.4, 116.2, 115.6, 115.2, 114.9, 114.4, 84.3, 60.7, 53.8, 51.9, 28.0 ppm; ESI-HRMS: calcd. for $C_{30}H_{28}FNO_5$+Na 524.1849, found 524.1844.



4o 79% yield; $[\alpha]_D^{20}$ = +6.4 (*c* = 0.75 in EtOAc); 63:37 dr, determined by the isolated yields of two isomers; 86% ee, determined by HPLC analysis [Daicel chiralpak AD, *n*-hexane/*i*-PrOH = 90/10, 1.0 mL/min, λ = 254 nm, t_{major} = 9.34 min, t_{minor} = 11.52 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50-7.43 (m, 2H), 7.27-7.17 (m, 7H), 7.01-6.92 (m, 3H), 6.69 (d, *J* = 7.2 Hz, 2H), 6.36 (s, 1H), 5.75 (s, 1H), 4.97 (s, 1H), 3.70 (s, 3H), 3.35 (d, *J* = 12.8 Hz, 1H), 2.94 (d, *J* = 12.8 Hz, 1H), 1.46 (s, 9H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 176.2, 167.9, 148.5, 140.1, 139.8, 138.1, 134.8, 130.2, 129.9, 128.9, 128.4, 128.2, 128.1, 127.5, 127.3, 126.5, 124.0, 123.7, 114.7, 83.7, 57.7, 52.3, 51.9, 44.4, 27.9 ppm; ESI-HRMS: calcd. for $C_{31}H_{31}NO_5$+Na 520.2100, found 520.2105.

Synthesis of *N*-Tos derivative 6

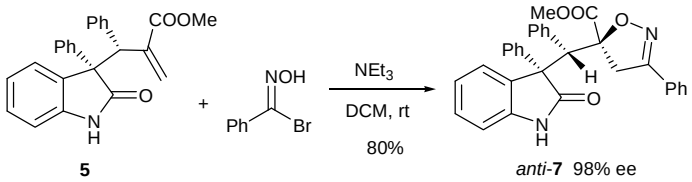


4a dr 85:15, 93% ee **5** **6**

Compound **4a** (100 mg, 0.21 mmol) was dissolved in DCM (5 mL) and TFA (46 uL, 0.63 mmol) was added at room temperature. After 5 h, the reaction was diluted with DCM (5 mL), washed successively with saturated Na_2CO_3 and brine. The organic layer was dried over Na_2SO_4, concentrated. Then the product was purified by chromatography to yield the pure **5** as a white solid (64 mg, 80%).

NaH (8 mg, 0.324 mmol) was suspended in THF (3 mL), and the above compound **5** (64 mg, 0.16 mmol) in THF (2 mL) was added at 0 °C. Then TosCl (37 mg, 0.194 mmol) was added. After 6 h, the reaction was quenched with water (0.5 mL). The mixture was diluted with EtOAc (5 mL), washed with brine. The organic layer was dried (Na_2SO_4), and concentrate. The crude product was purified by flash chromatography PE/EA (10:1) to afford **6** as a white solid (80 mg, 90%). $[\alpha]_D^{20}$ = -79.2 (*c* = 0.63 in EtOAc); 99% ee, determined by HPLC analysis [Daicel chiralcel OD, *n*-hexane/*i*-PrOH = 80/20, 1.0 mL/min, λ = 254 nm, t_{major} = 17.55 min, t_{minor} = 11.61 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89 (d, *J* = 8.4Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 2H), 7.64 (d, *J* = 7.6 Hz, 1H), 7.41-7.17 (m, 10H), 6.96-6.72 (m, 5H), 6.02 (s, 1H), 5.31 (s, 1H), 5.25 (s, 1H), 3.35 (s, 3H), 2.42 (s, 3H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 175.2, 167.9, 145.2, 140.2, 139.2, 137.3, 136.5, 134.8, 129.6, 129.2, 128.6, 128.3, 128.1, 127.9, 127.8, 127.4, 126.7, 124.1, 113.7, 59.9, 53.3, 52.6, 51.9, 21.7 ppm; ESI-HRMS: calcd. for $C_{32}H_{27}NO_5S$+Na 560.1508, found 560.1526.

Synthesis of compound 7

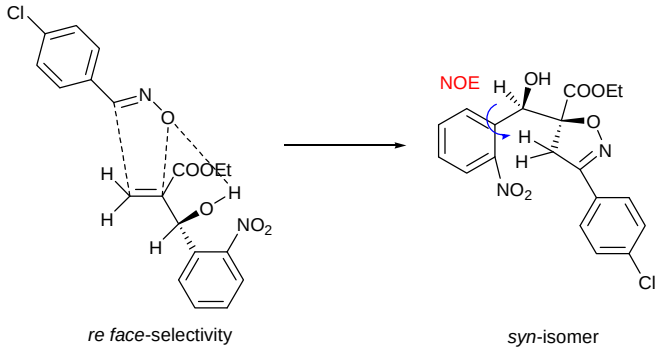


Compound **5** (40 mg, 0.11 mmol) and benzaldoxime bromide (32.2 mg, 0.16 mmol) were dissolved in DCM (2 mL), then Et_3N (22.6 uL, 0.16 mmol) was added at room temperature. After 60 h, the mixture was concentrated and purified by flash column chromatography on silica gel (PE/EA = 15:1) to afford diastereomerically pure product **7** as a white solid (45.6 mg, 80%). $[\alpha]_D^{20}$ = -7.8 (*c* = 0.812 in EtOAc); 98% ee, determined by HPLC analysis [Daicel chiralcel OD, *n*-hexane/*i*-PrOH = 70/30, 1.0 mL/min, λ = 254 nm, t_{major} = 6.18 min, t_{minor} = 7.60 min]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.30-8.28 (m, 1H), 7.88-7.71 (m, 3H), 7.37-6.98 (m, 14H), 6.68-6.65 (m, 1H), 4.81 (s, 1H), 3.36 (d, *J* = 17.6 Hz, 1H), 3.15 (d, *J* = 18.0 Hz,1H), 3.14 (s, 3H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): δ = 178.2, 172.7, 157.3, 140.8, 136.6, 135.5, 130.5, 130.2, 128.6, 128.5, 128.4, 127.8, 127.4, 127.3, 126.6, 122.1, 109.8, 91.9, 60.6, 56.6, 53.4, 52.4, 43.1, 29.7 ppm; ESI-HRMS: calcd. for $C_{32}H_{26}N_2O_4$+K : 541.1530, found 541.1546.

Assignment of the absolute configuration of the newly generated chiral centre of 7

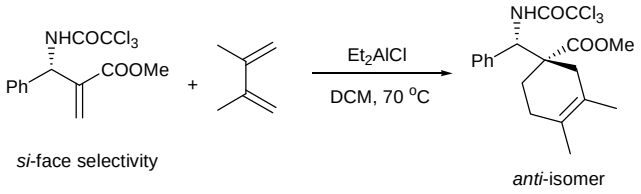
In order to assign the absolute configuration of the newly generated quaternary carbon centre, we investigated the NOE spectrum of compound **7** and also took advantage of the information on the diastereoselectivity in the cycloaddition by the previous literatures.

In an *Eur. J. Org. Chem.* paper (2008, 5446–5460), Batra et al. investigated the dipolar cycloaddition of Morita-Baylis-Hillman product with in situ generated nitrile *N*-oxide. As outlined in **Scheme A**, the *syn*-isomer was afforded from *re*-face attack owing to the hydrogen bonding between the nitrile oxide and the hydroxyl group of MBH product. Moreover, NOE effect was noted between the CH_2 signal of the five member ring and the benzylic proton.



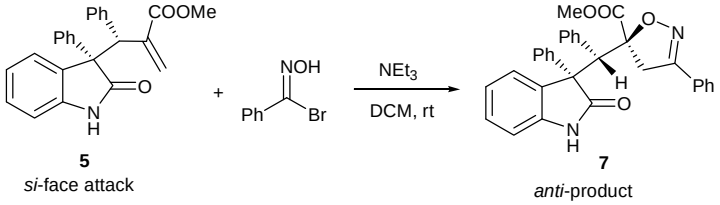
Scheme A

In addition, in a *Chem. Eur. J.* paper (2008, **14**, 1464–1471), Jorgensen et al. reported the Diels-Alder reaction of aza-MBH product with a buta-1,3-diene. As outlined in **Scheme B**, the *anti*-isomer was obtained from the *si*-face attack. In this case, steric hindrance may account for the face selectivity.

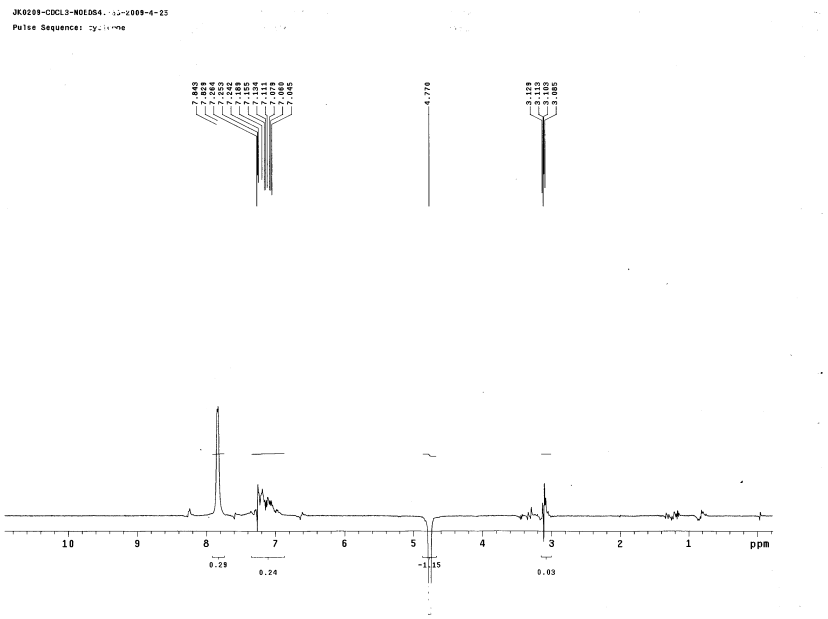


Scheme B

In the dipolar cycloaddition reported in this paper, there is no hydrogen bonding between compound **5** and in situ generated nitrile *N*-oxide. Therefore, the *si*-face attack of the C=C bond might be favored, from which the *anti*-product **7** would be formed.

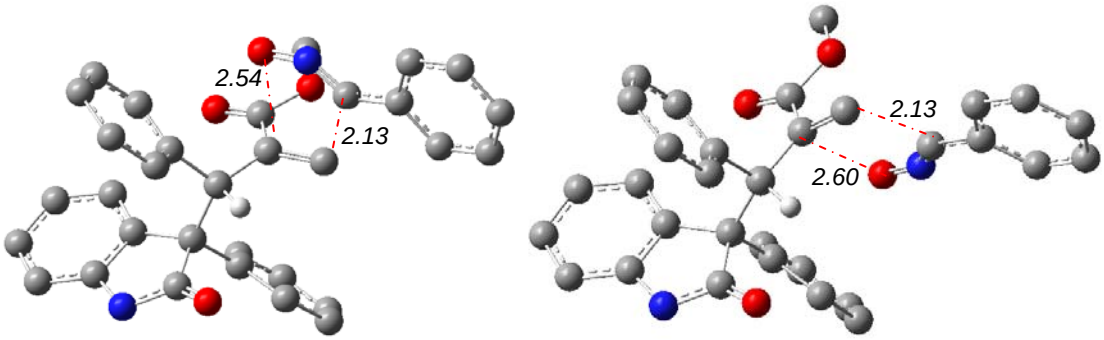


Moreover, in the NOE study of compound **7**, there is no NOE effects observed between the CH_2 signal of the five member ring and the benzylic proton. Taking advantage of the information reported by Batra et al, in which NOE effect has been noted in the *syn*-isomer, we proposed that compound **7** might have an *anti*-structure.



NOE spectrum of compound **7**

Furthermore, we also conducted DFT computational calculations to supply some support for the face selectivity. As noted in **Scheme C**, we compared the transitional states for *si*-face and *re*-face attack in the dipolar cycloaddition. Indeed, the energy is lower in *si*-face attack in comparison with that of *re*-face attack. This study is in fine accordance with the above elucidations.[3]



si-face attack -1650.0066951 a.u. *re*-face attack -1650.0001550 a.u.

0 KJ/mol *favored* 17.2 KJ/mol *disfavored*

Scheme C

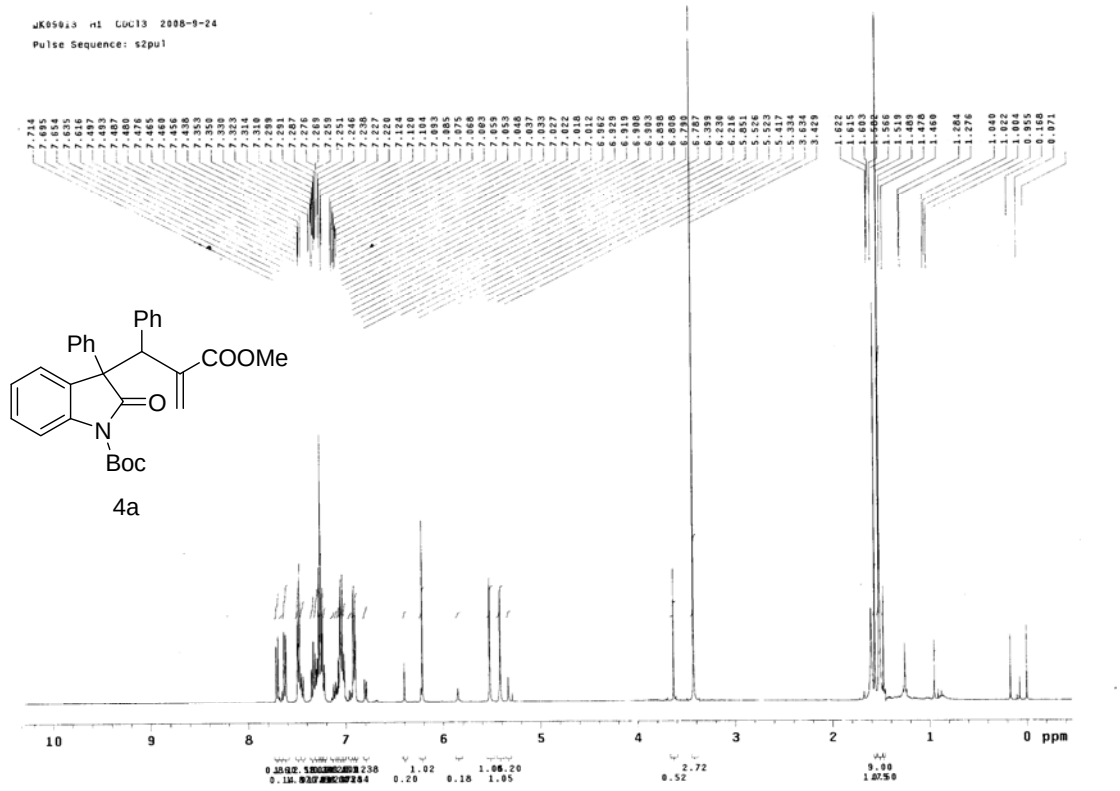
Therefore, compound **7** might have the structure outlined above.

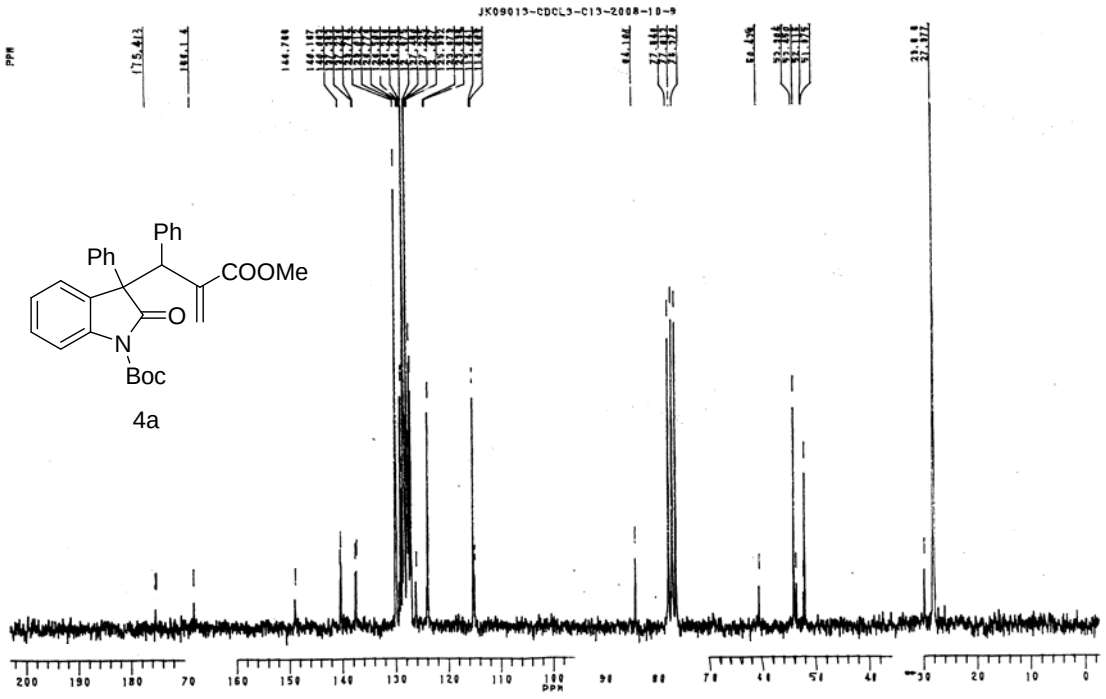
(1) (*a*) H. Yamashima, T. Suzuki, H. Takano, Y. Simura and M. Sodeoka, *J. Am. Chem. Soc.*, 2005, **127**, 10164; (*b*) T. Ishimaru, N. Shibata, J. Nagai, S. Nakamura, T. Toru and S. Kanemasa, *J. Am. Chem. Soc.*, 2006, **128**, 16488.

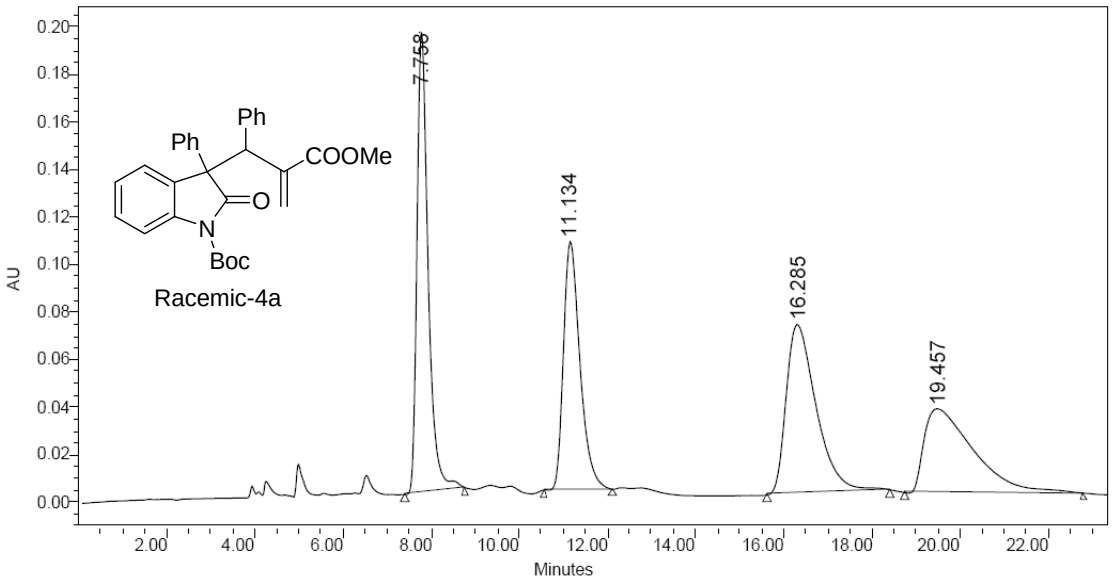
(2) J. Feng, X. Lu, A. Kong and X. Han, *Tetrahedron*, 2007, **63**, 6035.

(3) All the calculations were carried out using the Gaussian 03 program. Geometries of the related ions and transition-state species were optimized at the B3LYP/6-31G(d) level, and there structures were verified by frequency calculations at the same level. Single-point energies on the optimized structures were computed with B3P86 and 6-311+G(d, p) basis set, which had been reported to be promising in energetic calculations. Zero-point energy was considered and scaled by 0.9806. Crucial bond lengths are shown in Å.

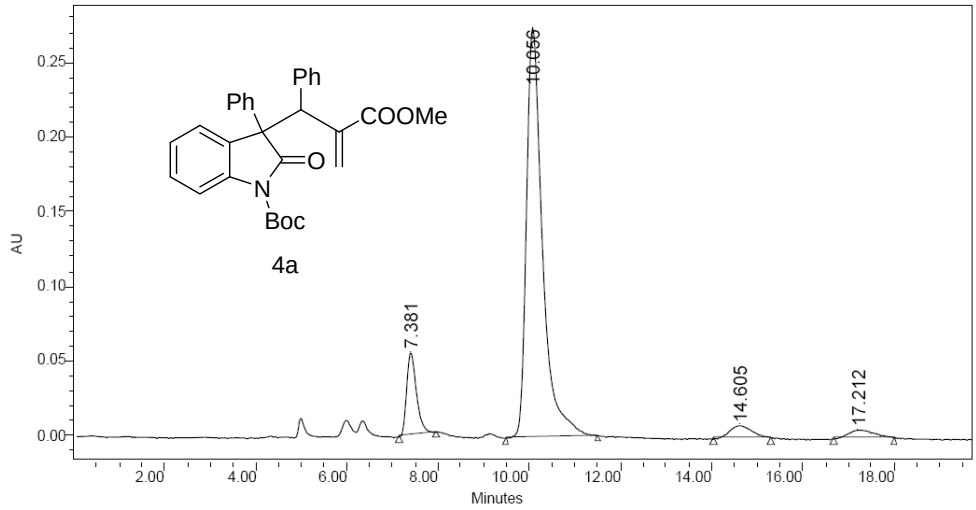
3. NMR and HPLC spectra



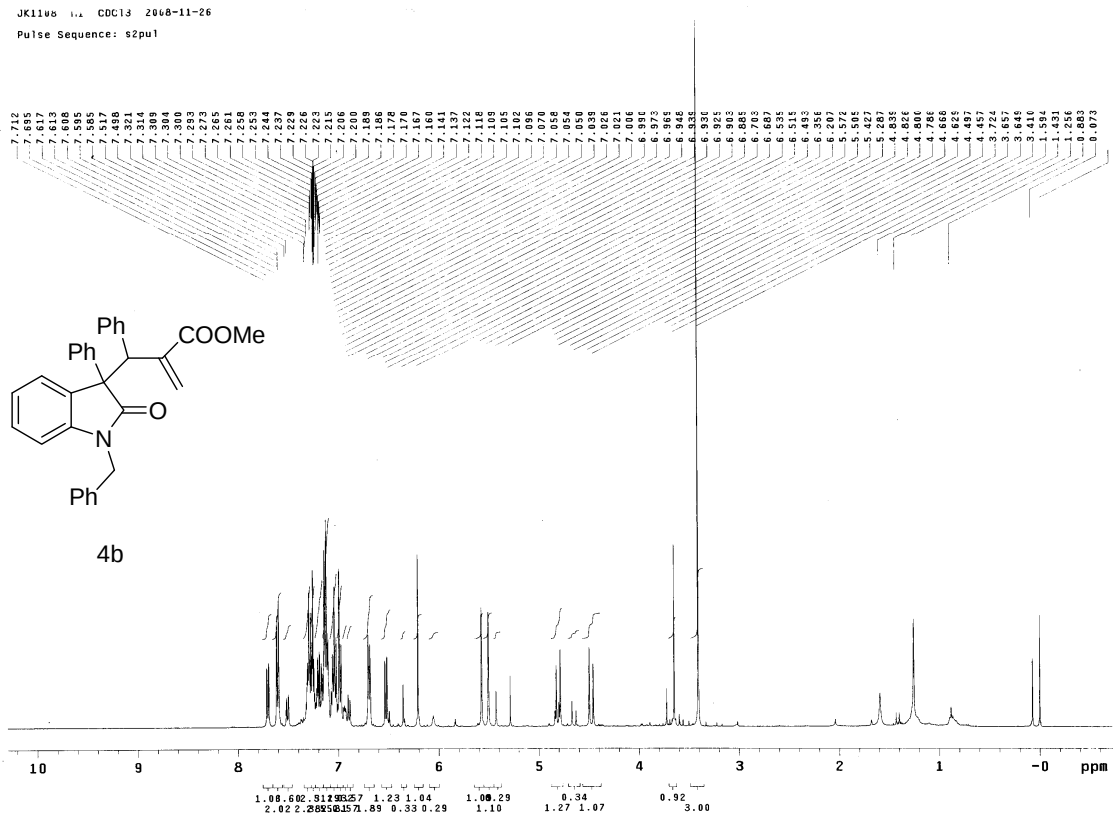


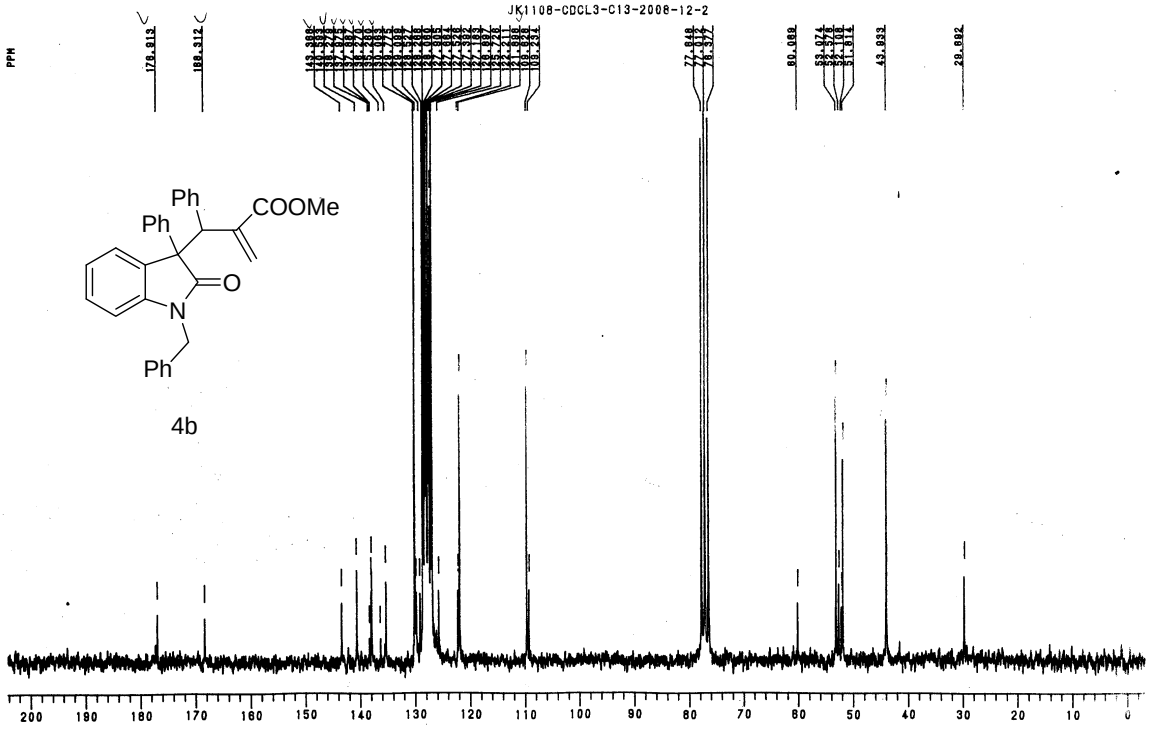


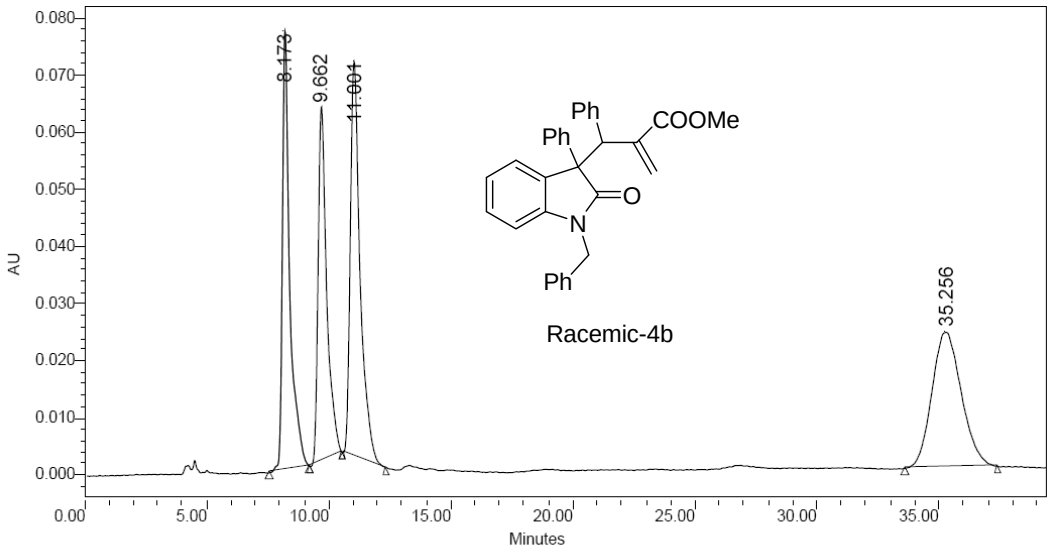
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	7.758	3428073	27.89	194244	47.97
2	11.134	2719724	22.13	104247	25.74
3	16.285	3378559	27.49	71065	17.55
4	19.457	2764350	22.49	35412	8.74



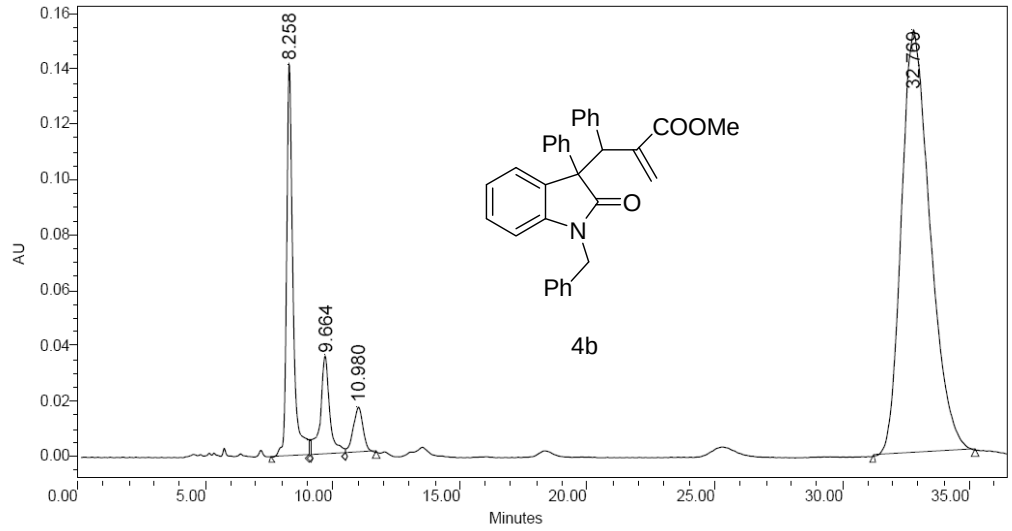
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	7.381	828048	10.29	55082	16.04
2	10.056	6696079	83.20	274391	79.88
3	14.605	294597	3.66	8462	2.46
4	17.212	229318	2.85	5560	1.62


Pulse Sequence: s2pul
Ph
Ph
COOMe
O
N
Ph
4b
ppm

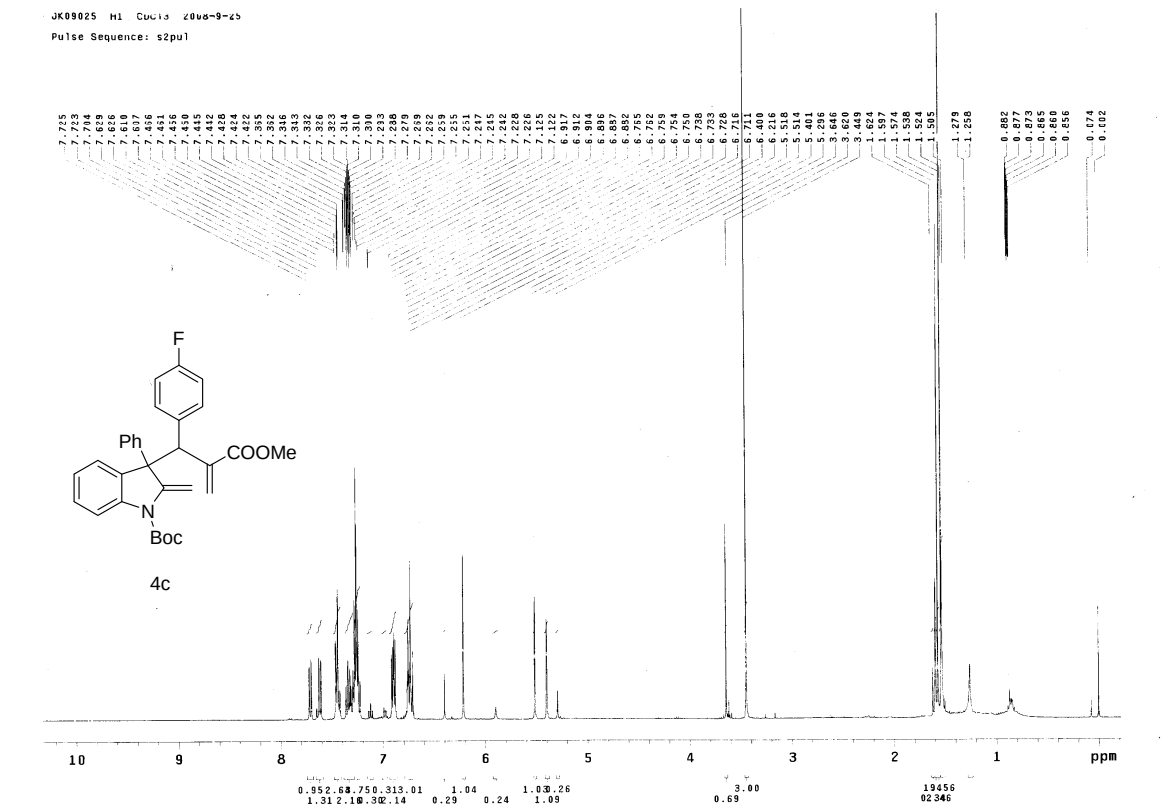

JK1108-CDCL3-C13-2008-12-2
PPM
Ph
Ph
COOMe
O
N
Ph
4b

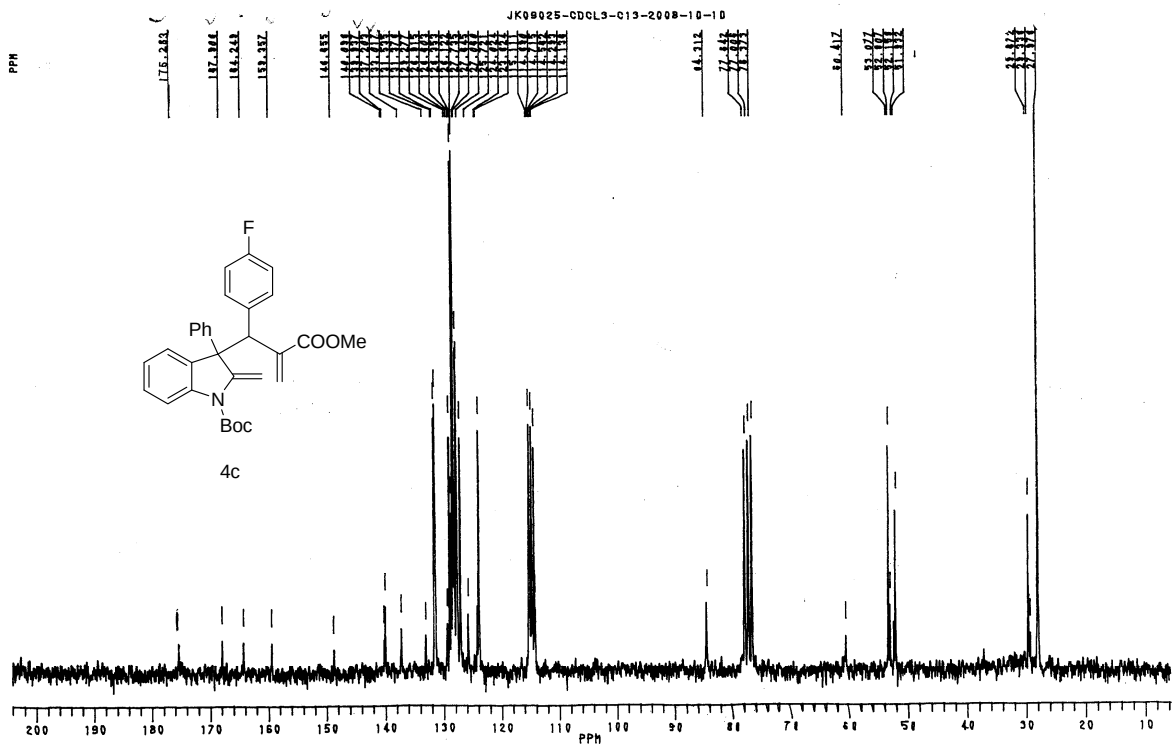


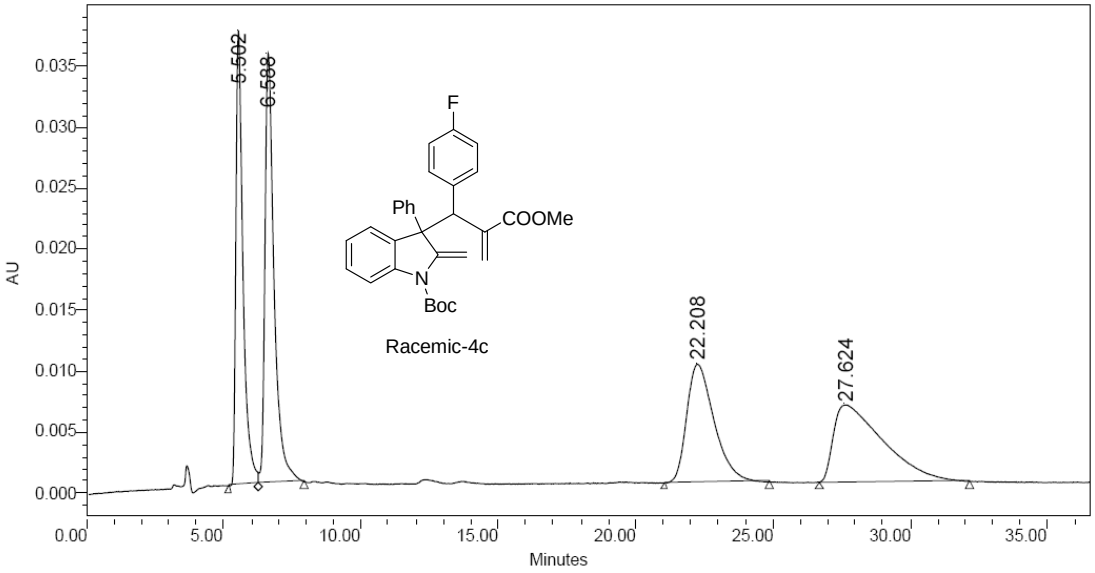
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	8.173	1621594	22.87	77042	33.21
2	9.662	1536416	21.67	62237	26.83
3	11.001	1934894	27.29	69084	29.78
4	35.256	1996228	28.16	23646	10.19



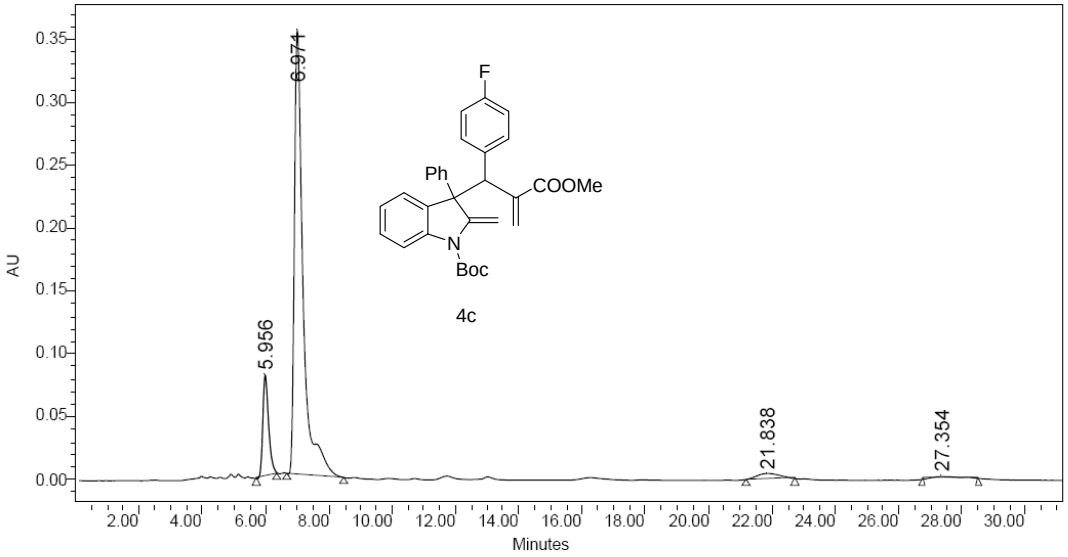
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	8.258	2079353	13.66	137360	40.82
2	9.664	533931	3.51	30238	8.99
3	10.980	379371	2.49	15361	4.56
4	32.769	12224840	80.33	153563	45.63


JK09025 H1 CDCl3 2008-9-25
Pulse Sequence: s2pul
F
Ph
COOMe
N
Boc
4c
ppm

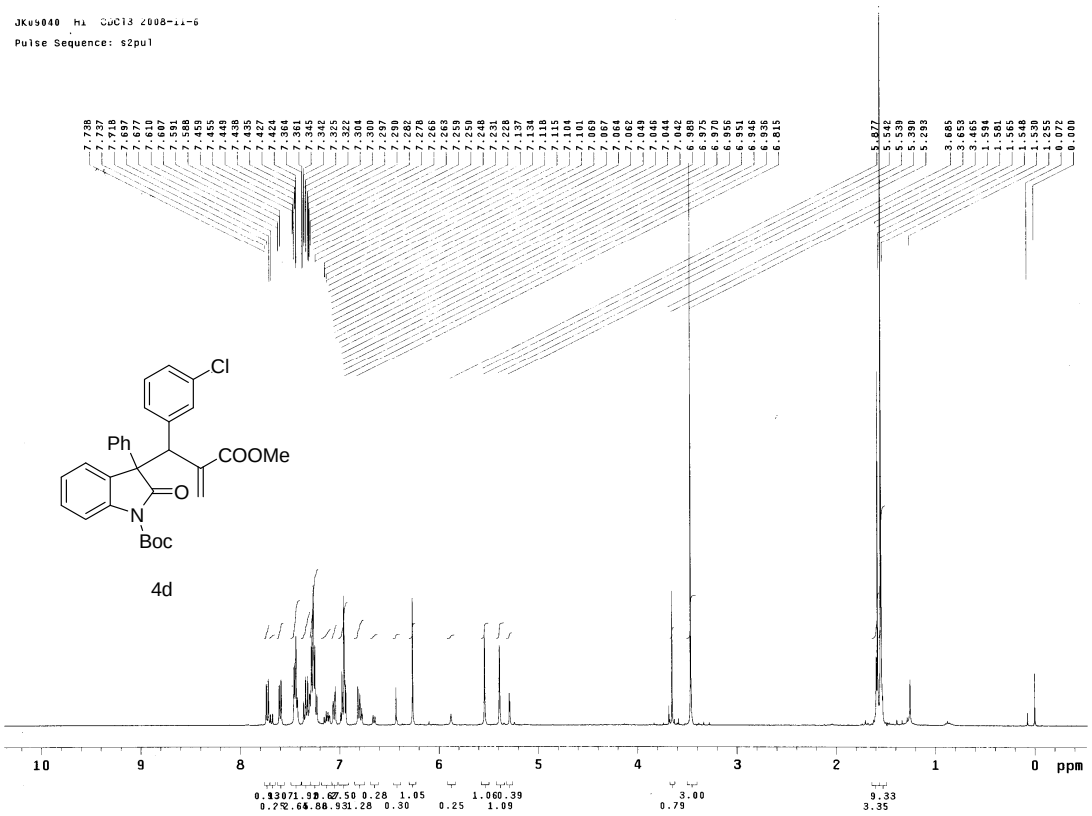

JK09025-CDCL3-C13-2008-10-10
PPM
F
Ph
COOMe
N
Boc
4c

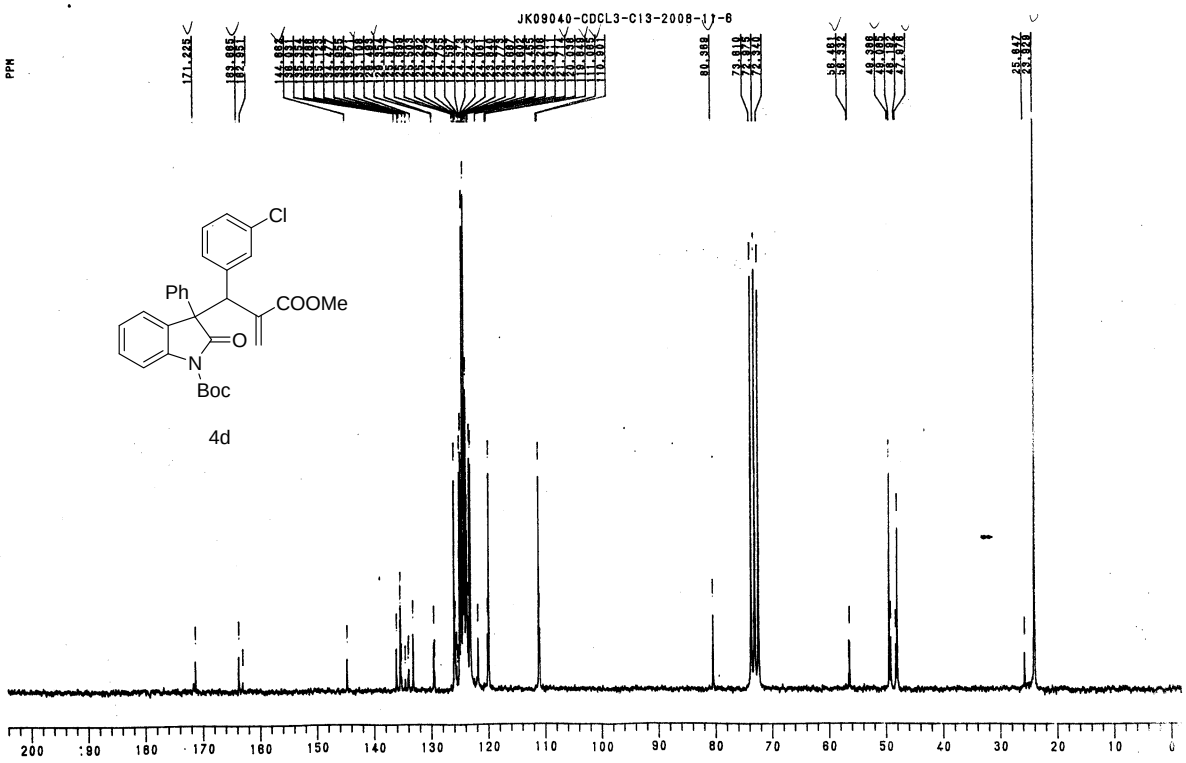


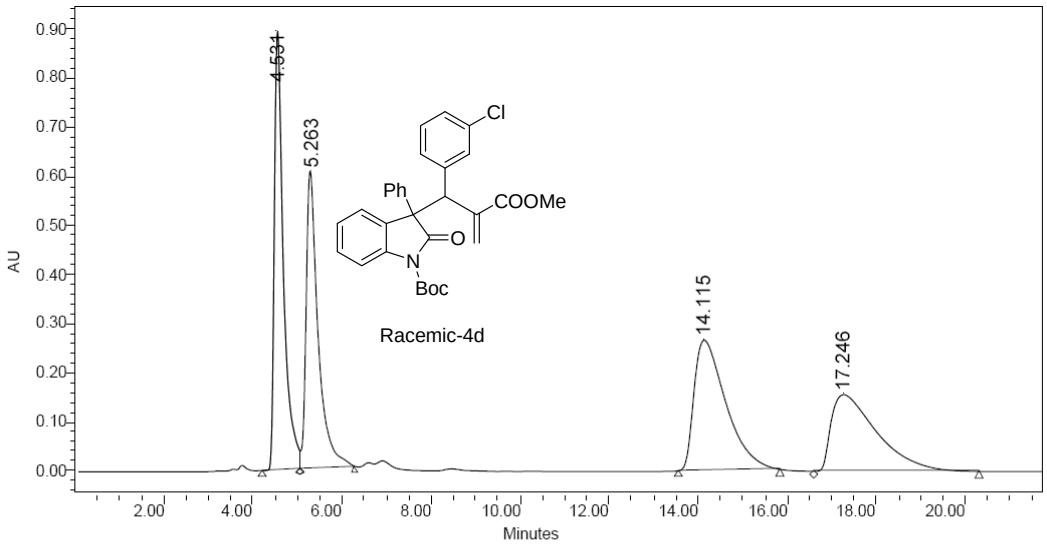
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	5.502	676269	22.76	37291	42.09
2	6.588	819791	27.59	35280	39.82
3	22.208	675687	22.74	9704	10.95
4	27.624	799634	26.91	6330	7.14



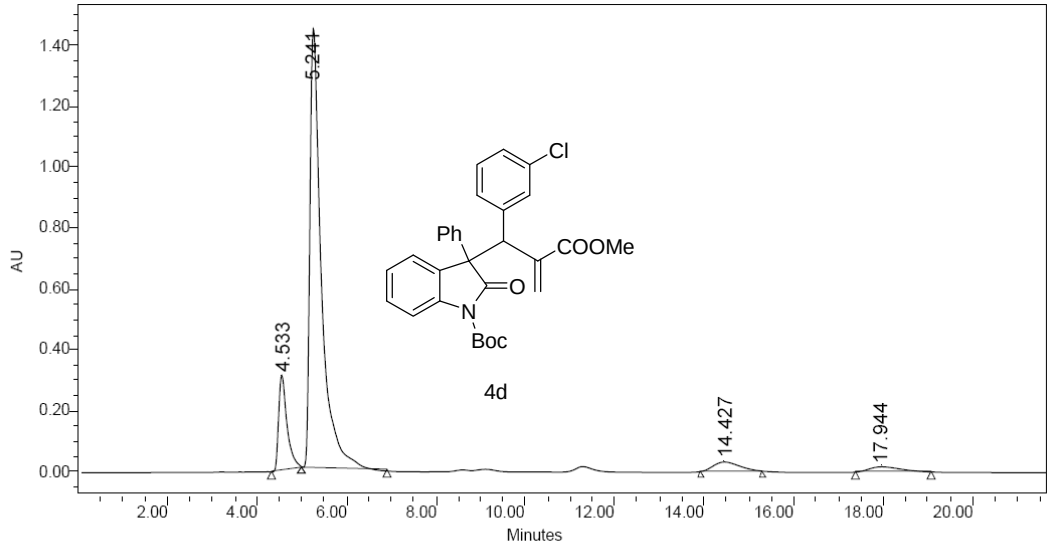
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	5.956	1035762	12.66	81038	18.36
2	6.971	6797406	83.11	353992	80.20
3	21.838	224309	2.74	4462	1.01
4	27.354	121584	1.49	1914	0.43


Pulse Sequence: s2pul
Cl
Ph
COOMe
O
N
Boc
4d
ppm

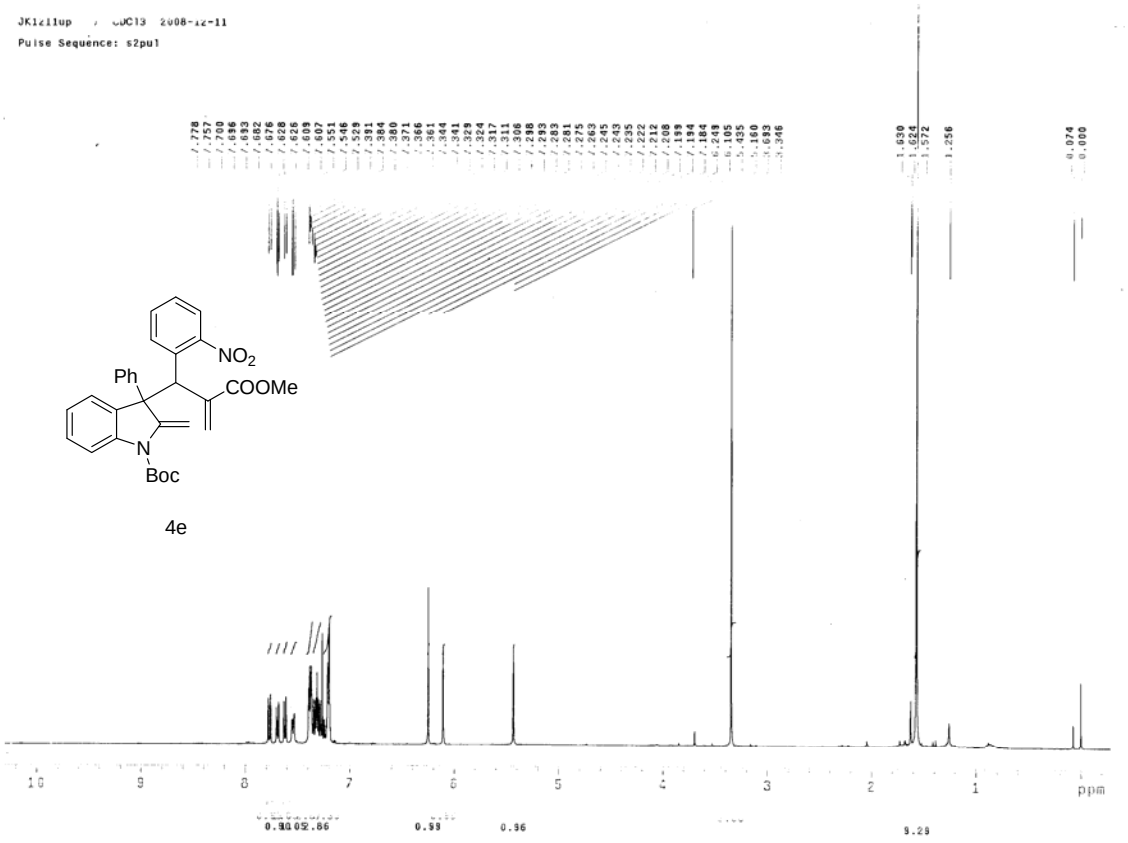

PPM
Cl
Ph
COOMe
O
N
Boc
4d

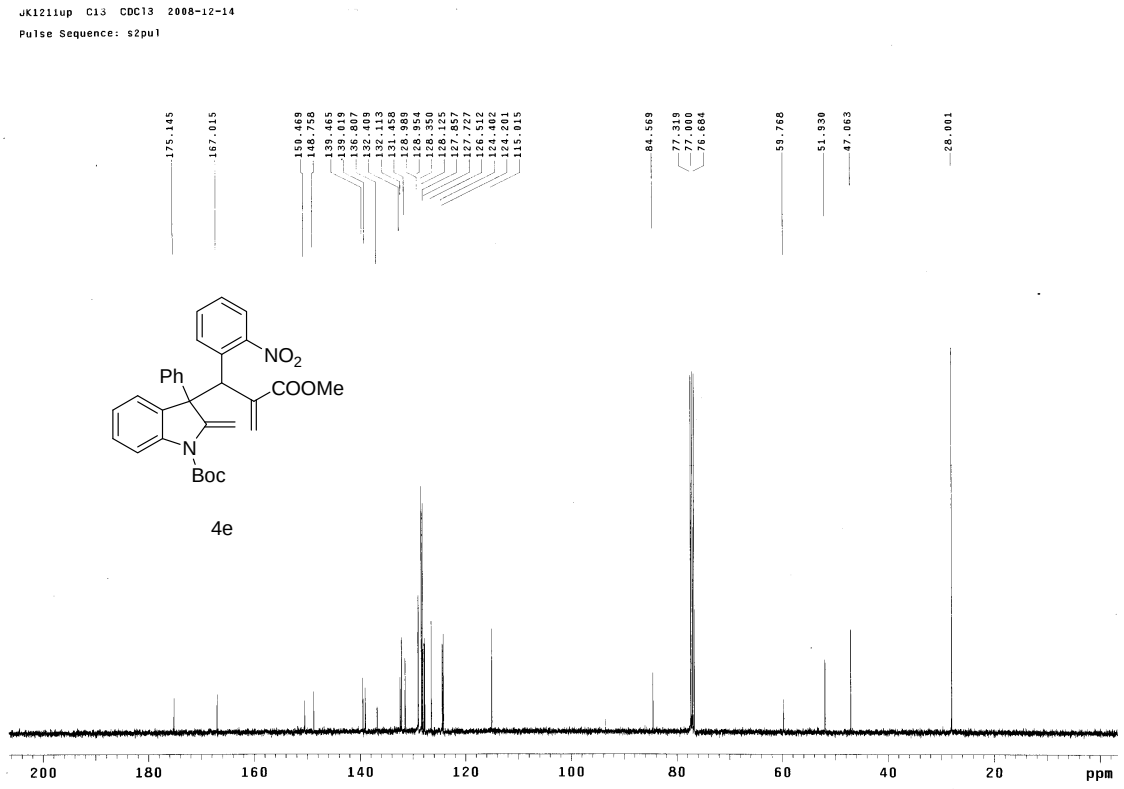


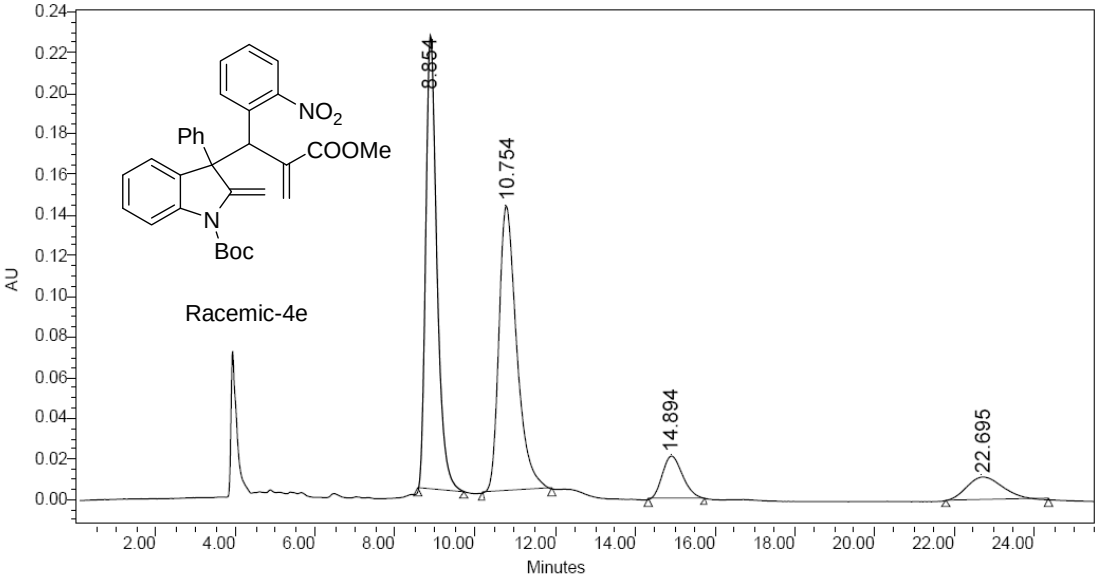
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	4.531	12815833	26.38	895596	46.52
2	5.263	11345677	23.35	607041	31.53
3	14.115	13233877	27.24	265774	13.81
4	17.246	11184190	23.02	156595	8.13



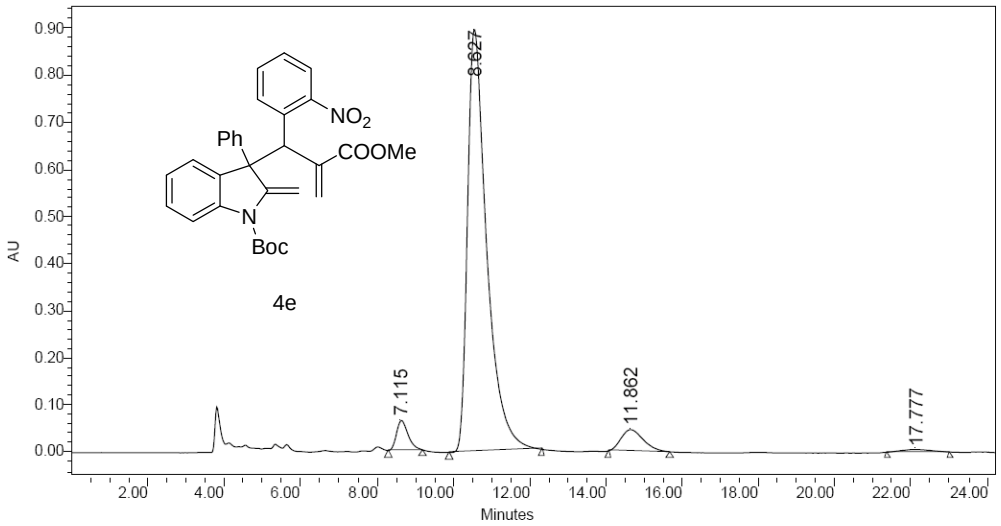
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	4.533	4087484	12.73	312016	17.28
2	5.241	25933073	80.78	1446363	80.08
3	14.427	1241661	3.87	30560	1.69
4	17.944	840065	2.62	17196	0.95


Pulse Sequence: s2pul
NO2
Ph
COOMe
N
Boc
4e
ppm

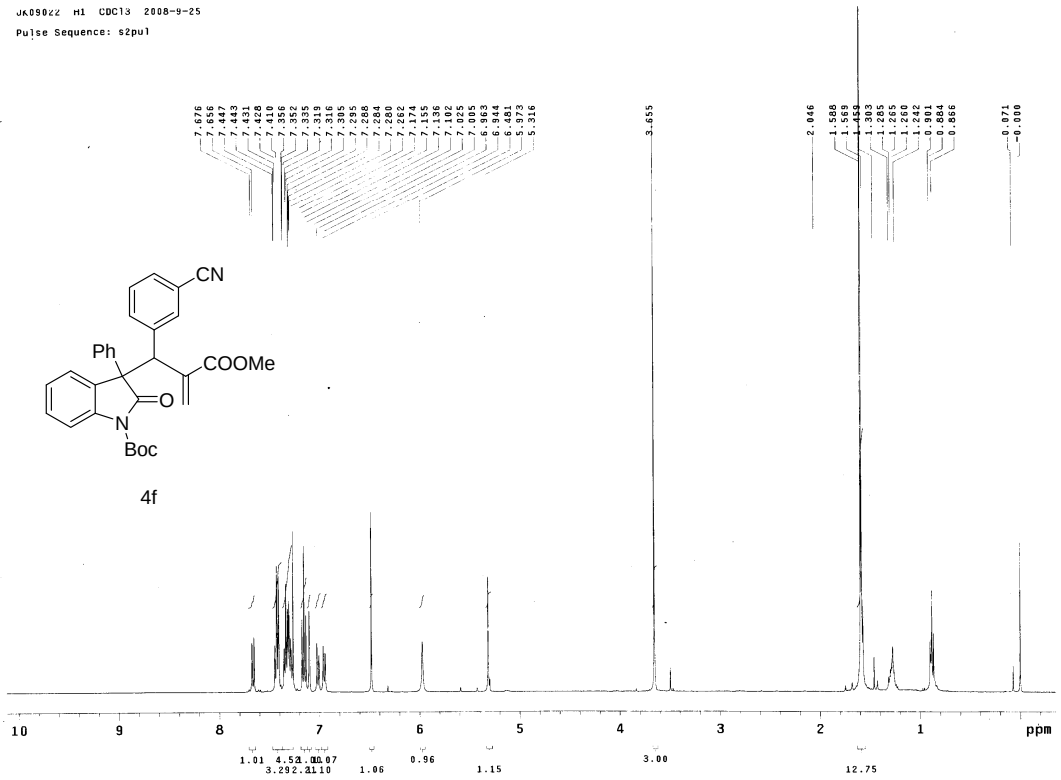

Pulse Sequence: s2pul
NO2
Ph
COOMe
N
Boc
4e
ppm

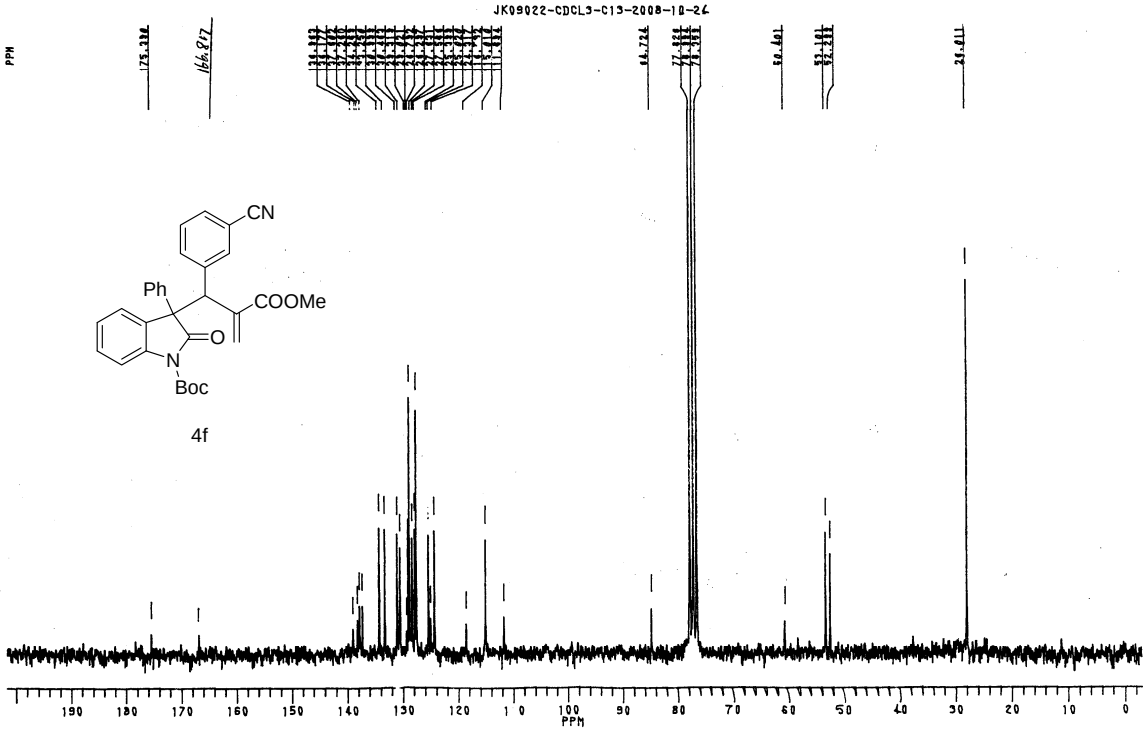


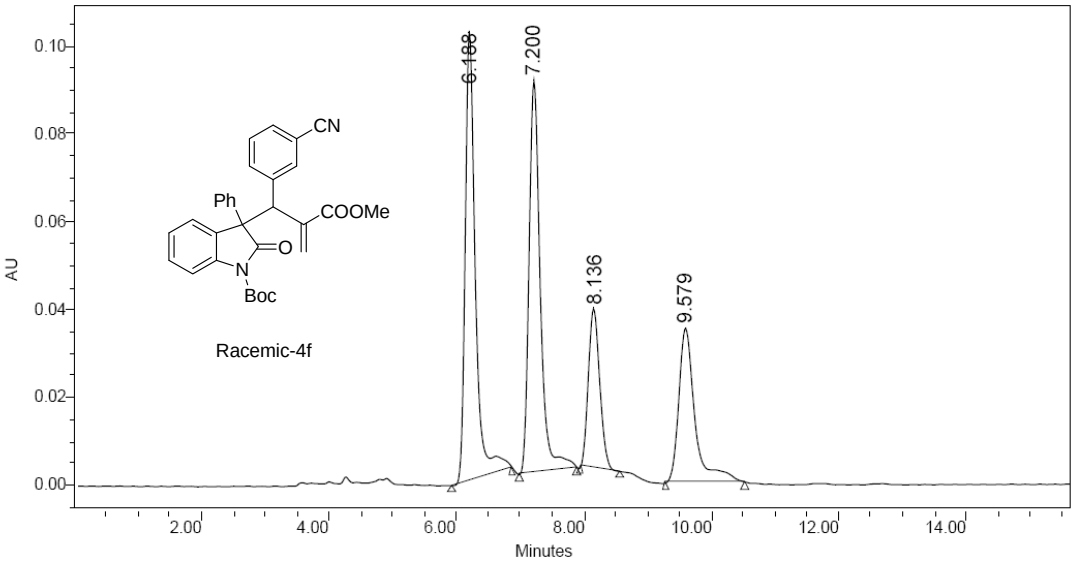
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	8.854	4365998	42.65	223967	56.40
2	10.754	4382973	42.81	140588	35.40
3	14.894	747066	7.30	21085	5.31
4	22.695	741281	7.24	11474	2.89



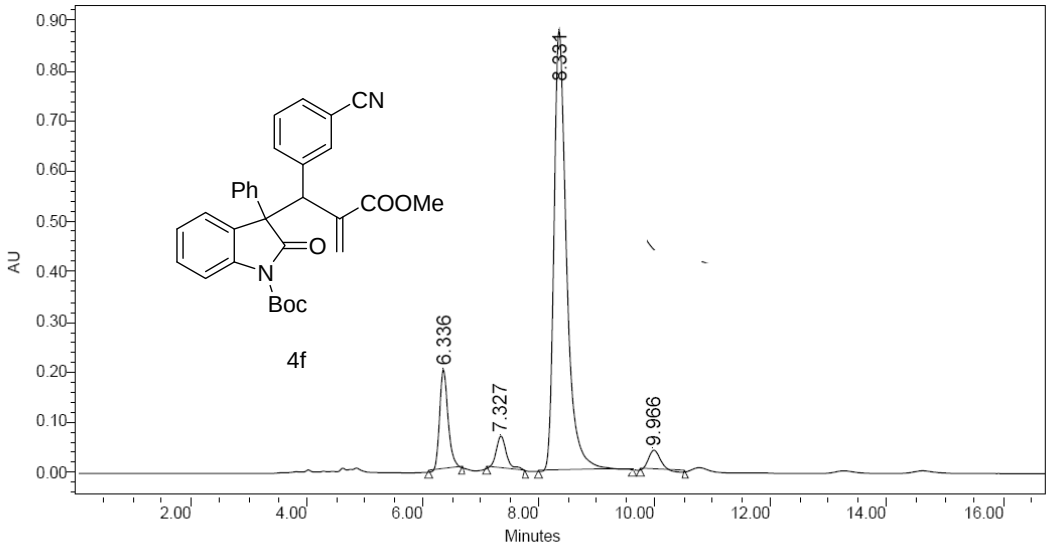
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	8.788	1060650	3.84	63423	6.26
2	10.498	24859637	89.97	897898	88.69
3	14.621	1474276	5.34	45606	4.50
4	22.228	236708	0.86	5454	0.54


JK09022 H1 CDCl3 2008-9-25
Pulse Sequence: s2pul
CN
Ph
COOMe
O
N
Boc
4f
ppm

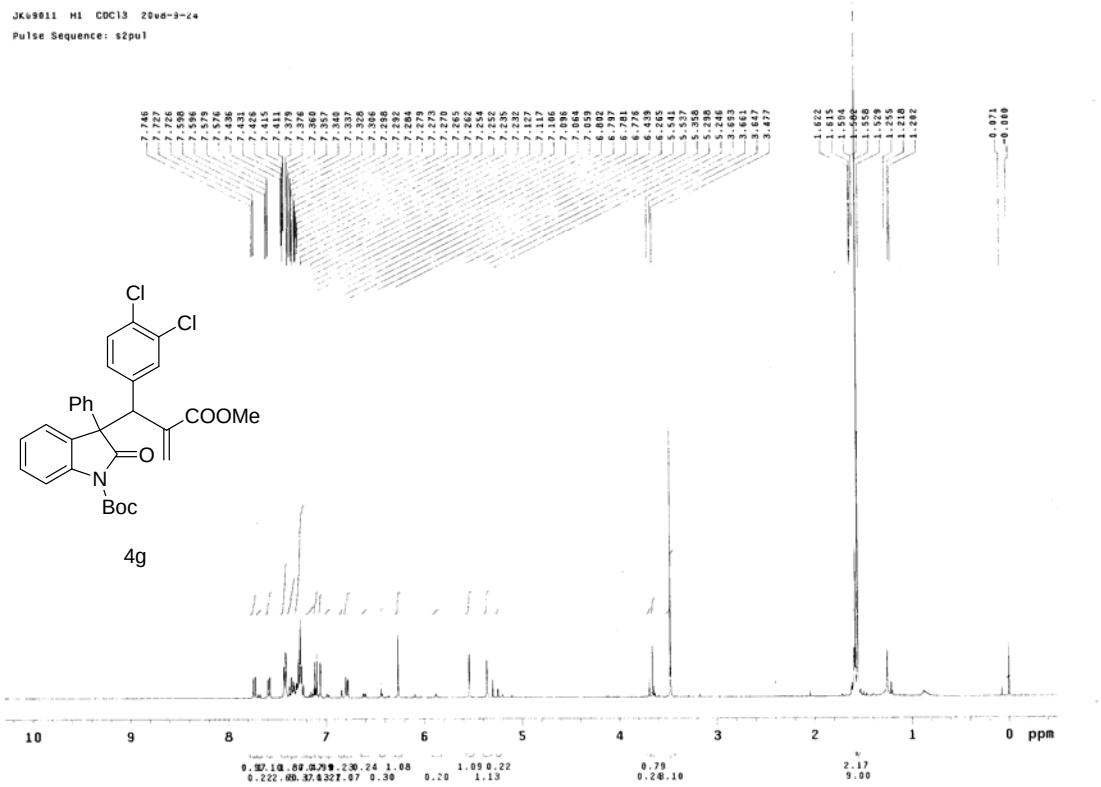

JK09022-CDCL3-C13-2008-10-24
PPM
CN
Ph
COOMe
O
N
Boc
4f

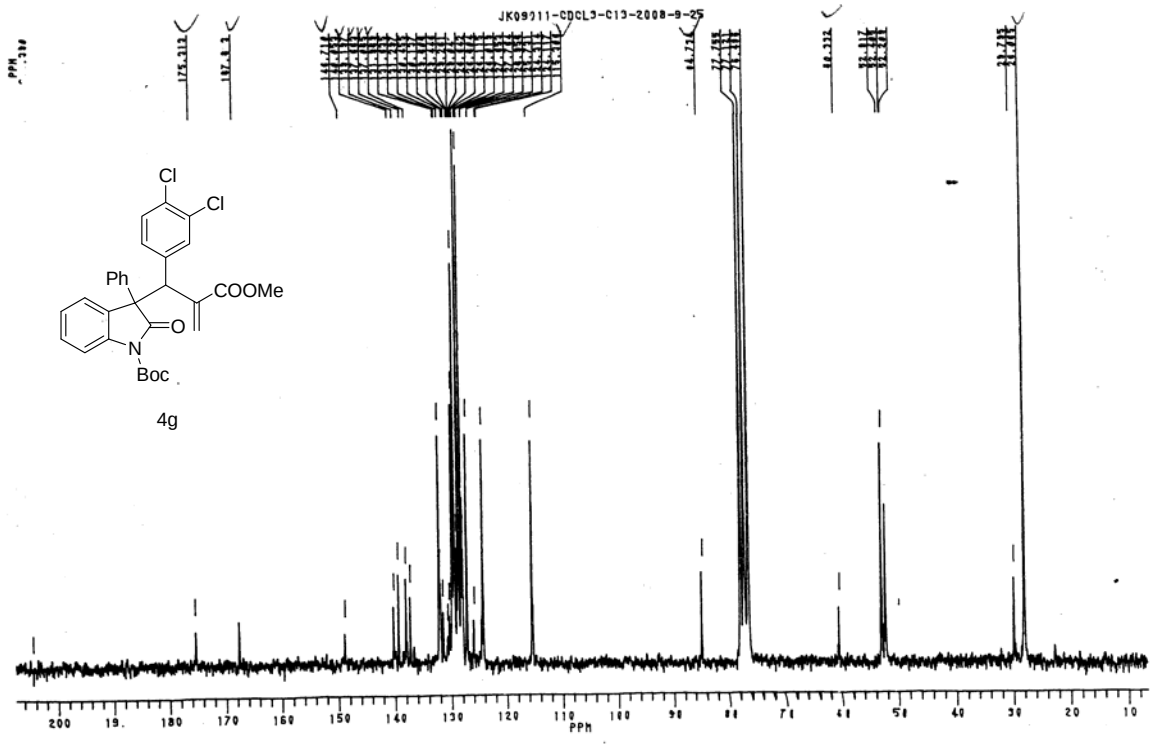


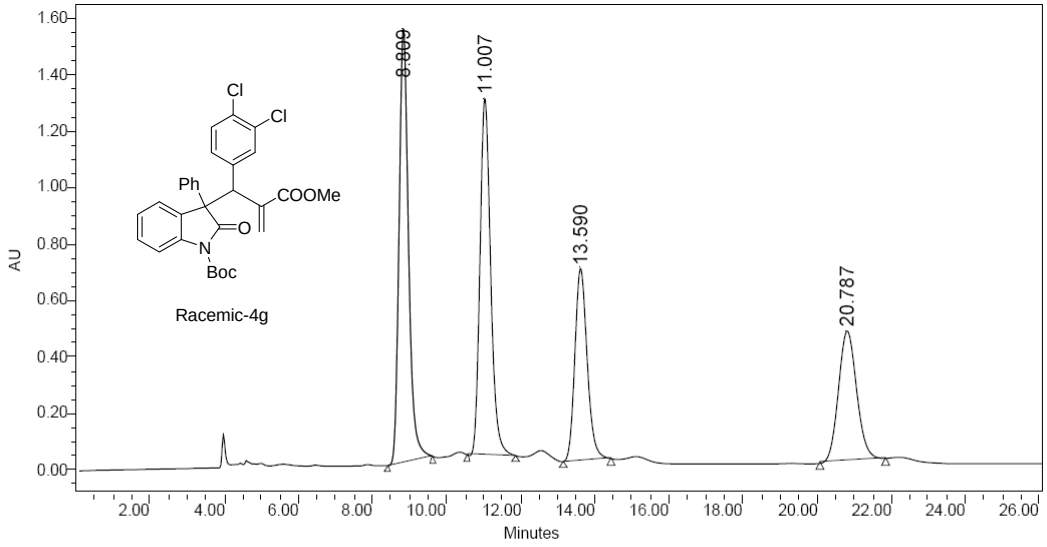
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	6.188	1133035	34.26	102590	38.96
2	7.200	1096070	33.14	89238	33.89
3	8.136	453577	13.71	36417	13.83
4	9.579	624760	18.89	35086	13.32



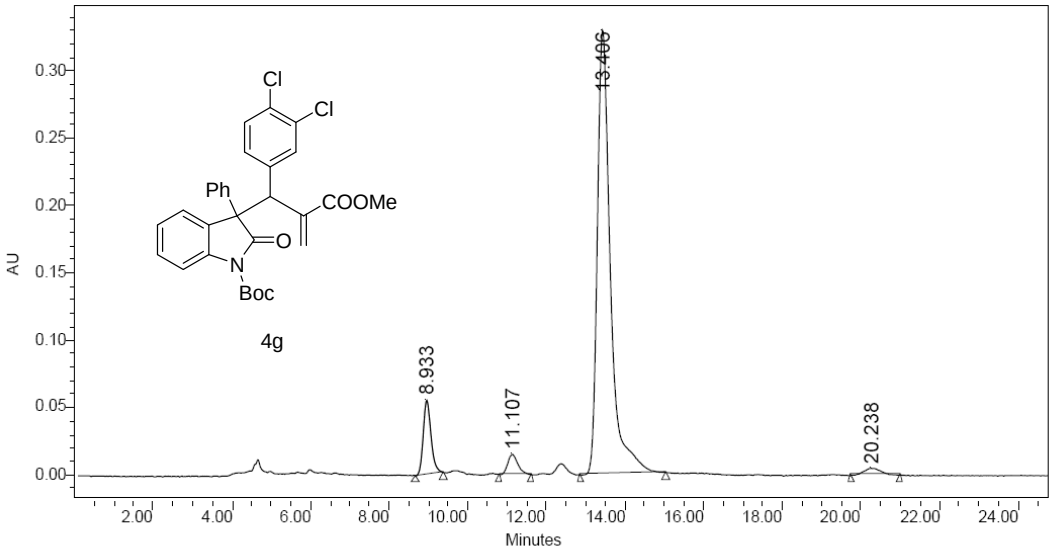
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	6.336	2068286	11.79	201008	16.96
2	7.327	833704	4.75	65588	5.53
3	8.331	14059340	80.16	879024	74.15
4	9.966	577082	3.29	39850	3.36


JK09011 H1 CDCl3 20ud-9-24
Pulse Sequence: s2pul
Cl
Cl
Ph
COOMe
O
N
Boc
4g
10
9
8
7
6
5
4
3
2
1
0 ppm

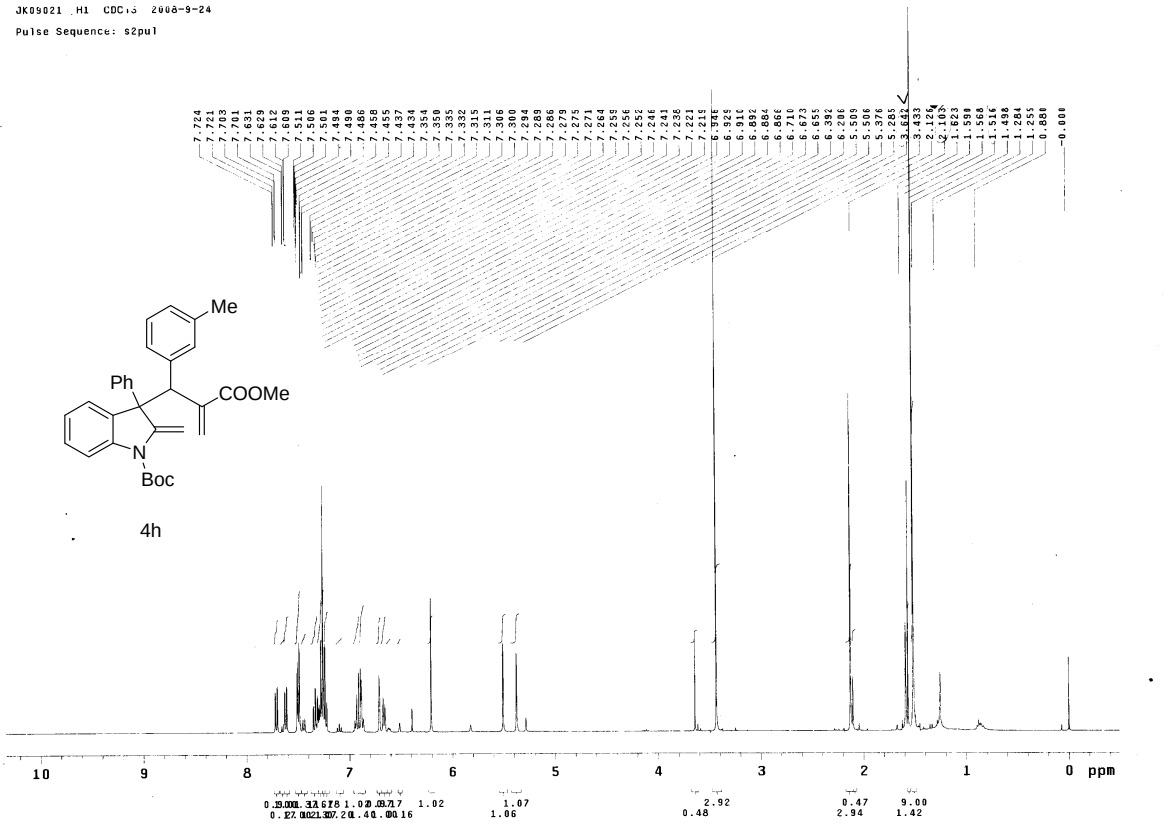

JK09011-CDCL3-C13-2008-9-25
Cl
Cl
Ph
COOMe
O
N
Boc
4g
PPM

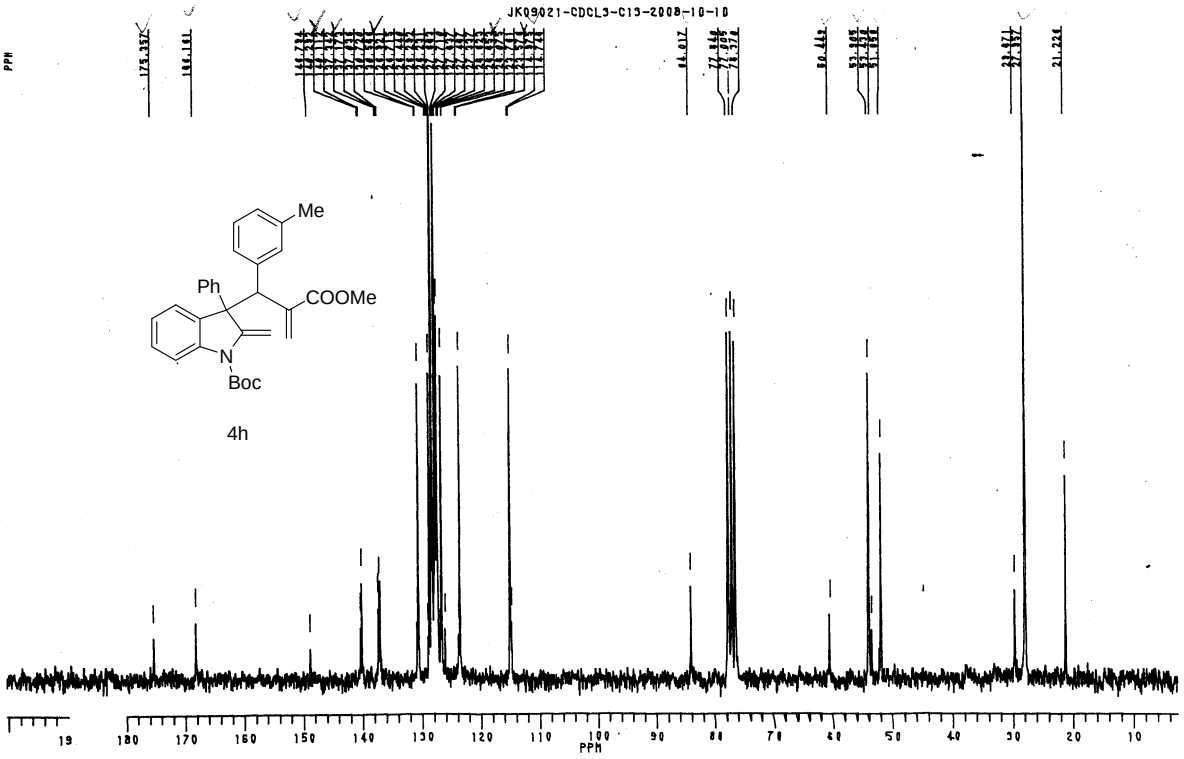


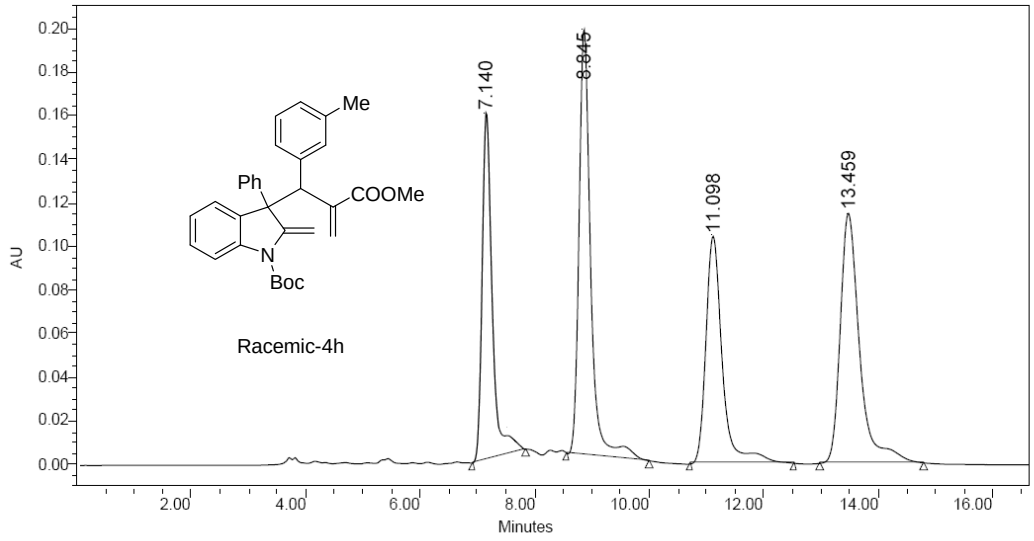
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	8.809	27361247	32.44	1542086	39.02
2	11.007	25416995	30.14	1266781	32.06
3	13.590	15766312	18.69	681235	17.24
4	20.787	15793406	18.73	461706	11.68



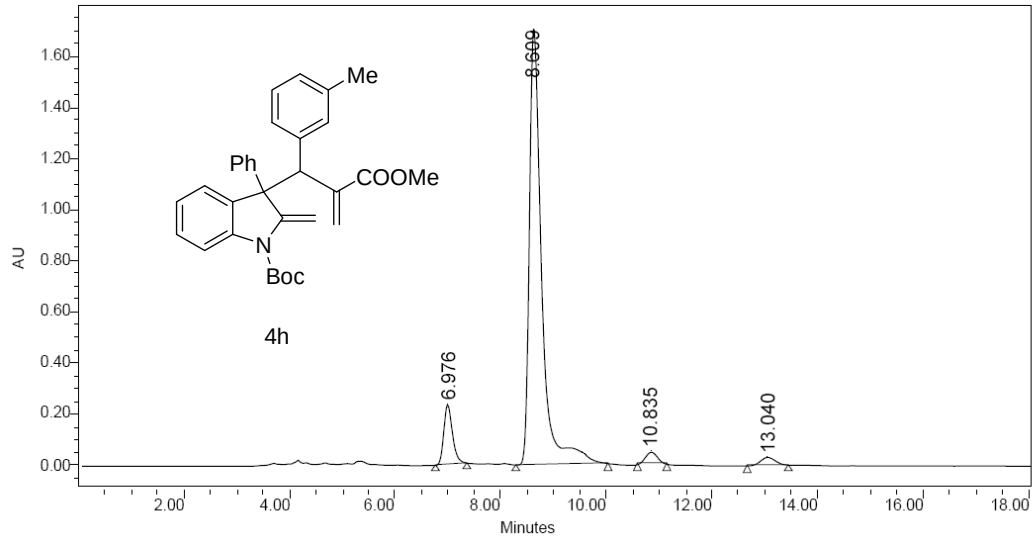
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	8.933	758894	8.63	55050	13.58
2	11.107	266913	3.04	15068	3.72
3	13.406	7616938	86.63	330377	81.48
4	20.238	149808	1.70	4973	1.23


Pulse Sequence: s2pul
Me
Ph
COOMe
N
Boc
4h
ppm

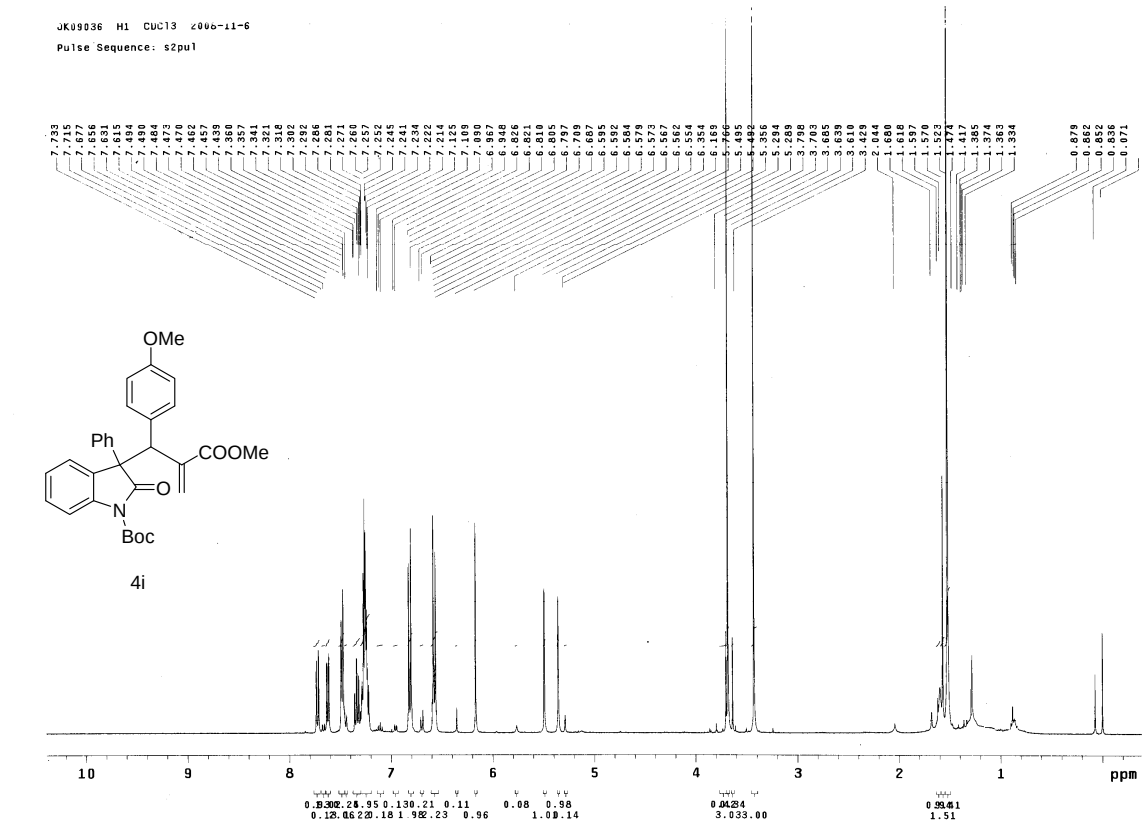

Me
Ph
COOMe
N
Boc
4h
PPM

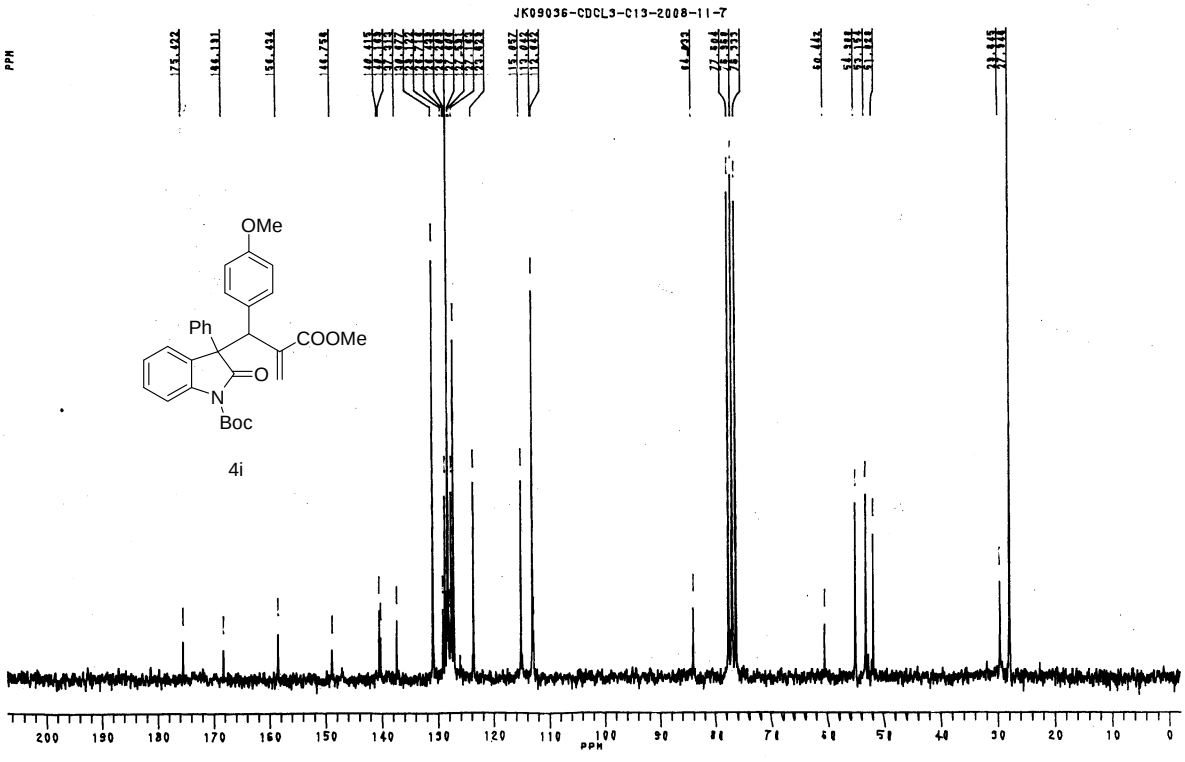


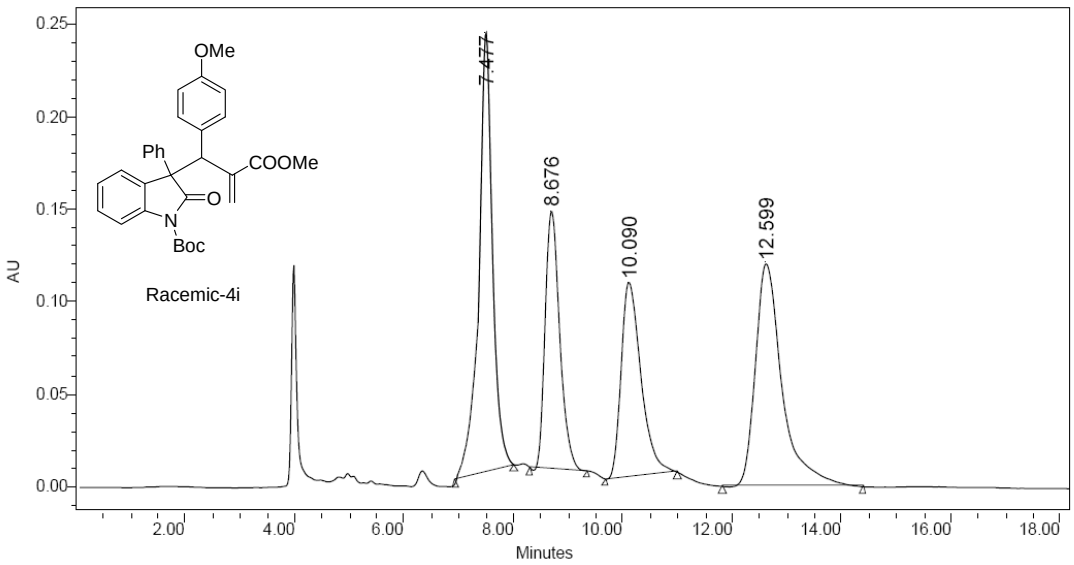
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	7.140	2022912	21.10	159547	27.79
2	8.845	2757639	28.77	195462	34.04
3	11.098	2102591	21.93	104425	18.19
4	13.459	2702768	28.20	114749	19.98



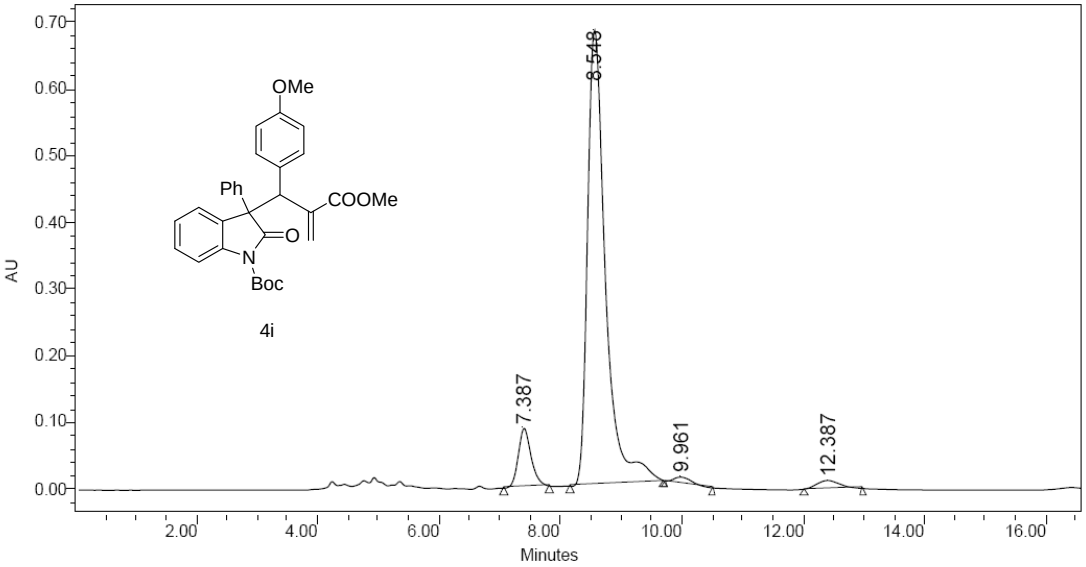
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	6.976	2691932	8.45	233513	11.53
2	8.609	27791694	87.20	1711712	84.53
3	10.835	768471	2.41	47846	2.36
4	13.040	619537	1.94	31939	1.58


JK09036 H1 CDCl3 2008-11-6
Pulse Sequence: s2pul
OMe
Ph
COOMe
O
N
Boc
4i
ppm

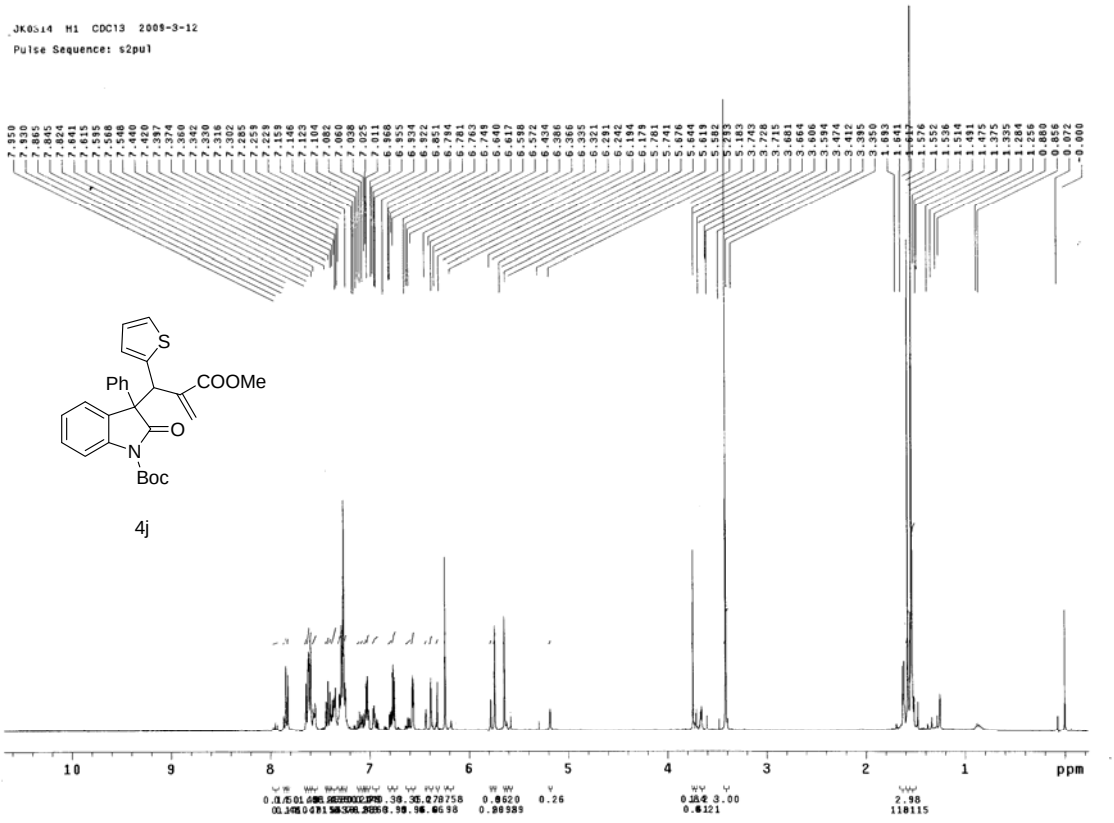

JK09036-CDCL3-C13-2008-11-7
PPM
OMe
Ph
COOMe
O
N
Boc
4i

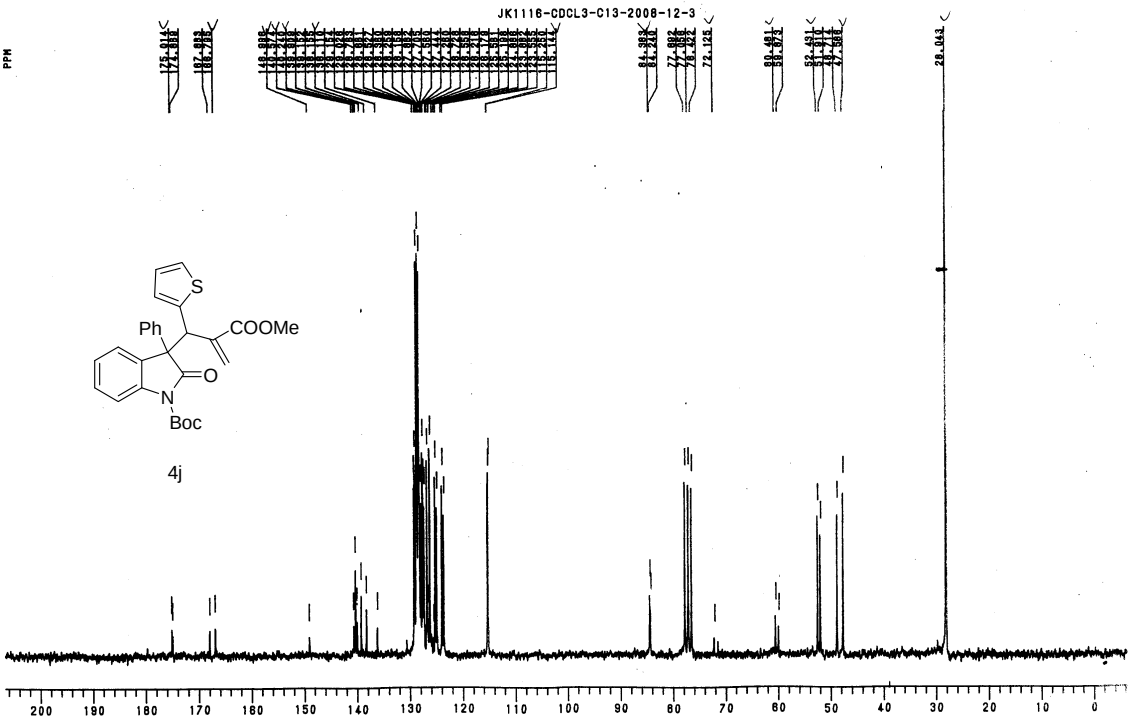


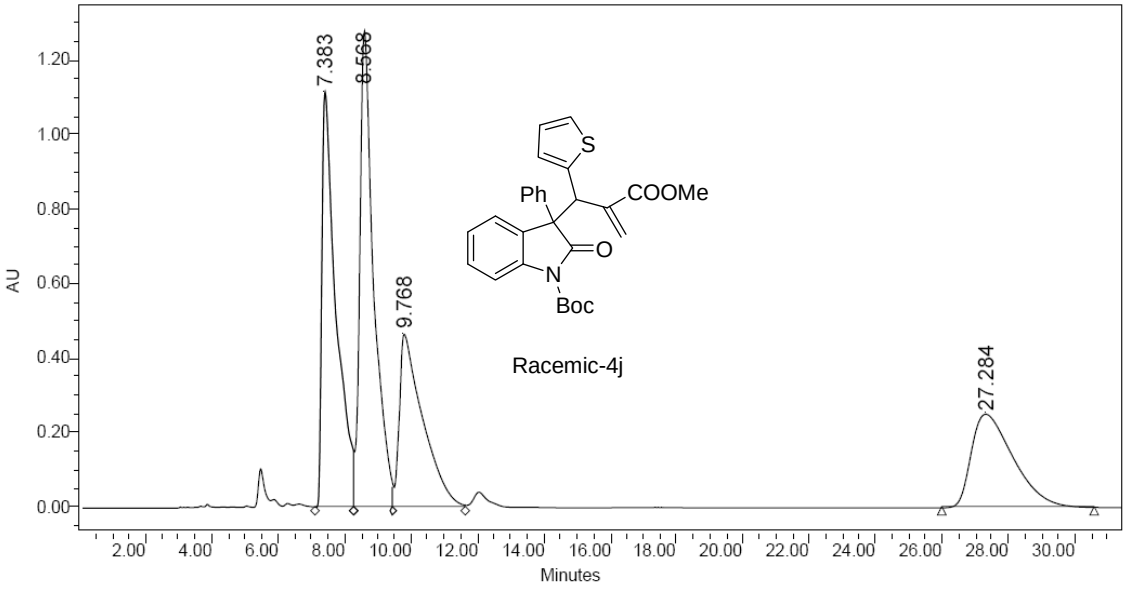
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	7.477	4401772	31.89	238270	39.46
2	8.676	2599302	18.83	139507	23.10
3	10.090	2678833	19.41	105476	17.47
4	12.599	4122177	29.87	120566	19.97



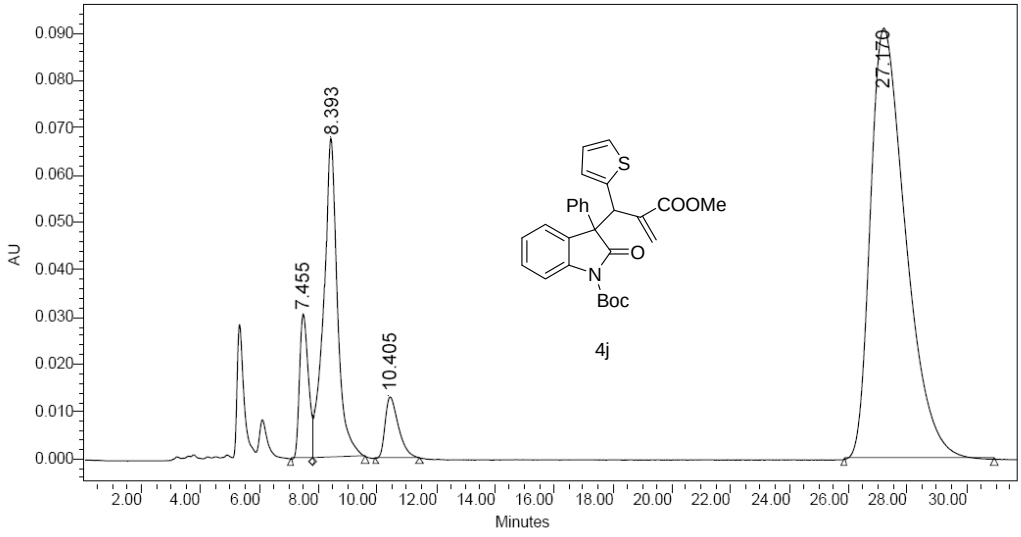
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	7.387	1317825	8.30	88570	11.17
2	8.548	14051655	88.48	682498	86.10
3	9.961	178678	1.13	9009	1.14
4	12.387	332925	2.10	12577	1.59


JK0514 H1 CDCl3 2009-3-12
Pulse Sequence: s2pul
S
Ph
COOMe
O
N
Boc
4j
ppm

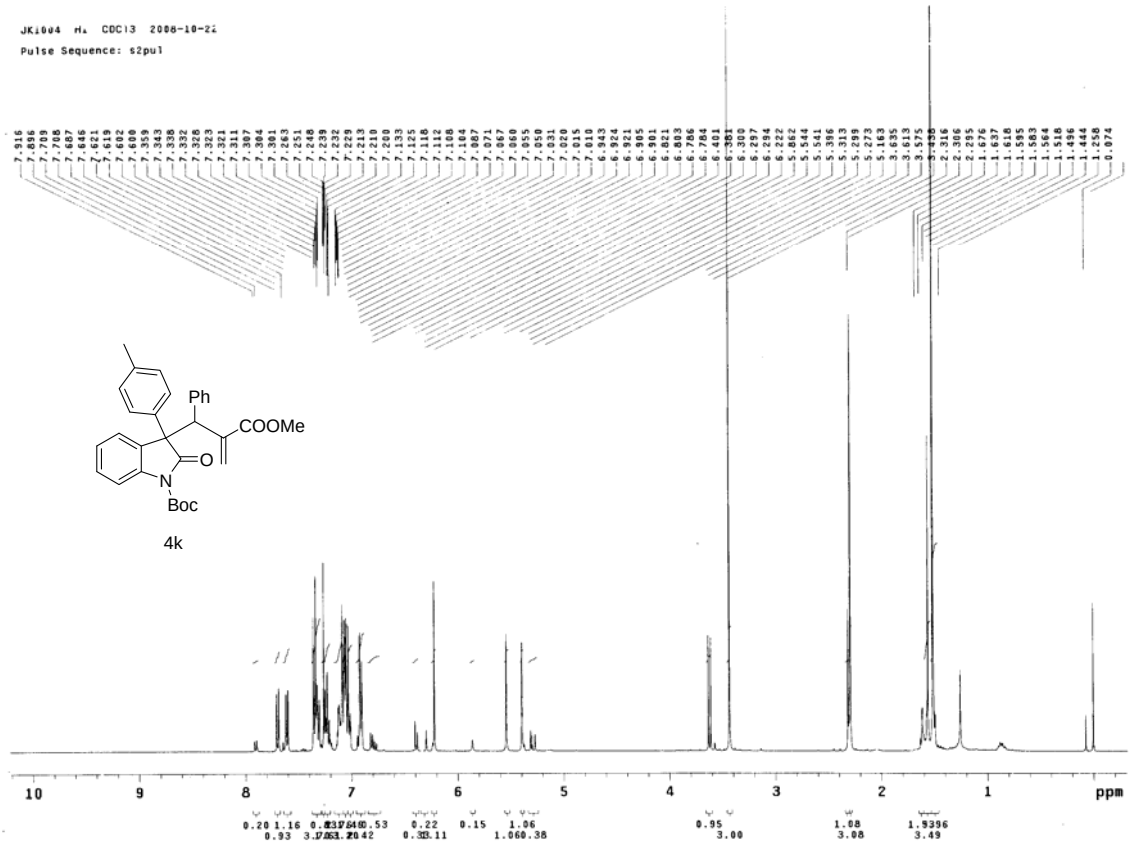

JK1116-CDCL3-C13-2008-12-3
PPM
S
Ph
COOMe
O
N
Boc
4j

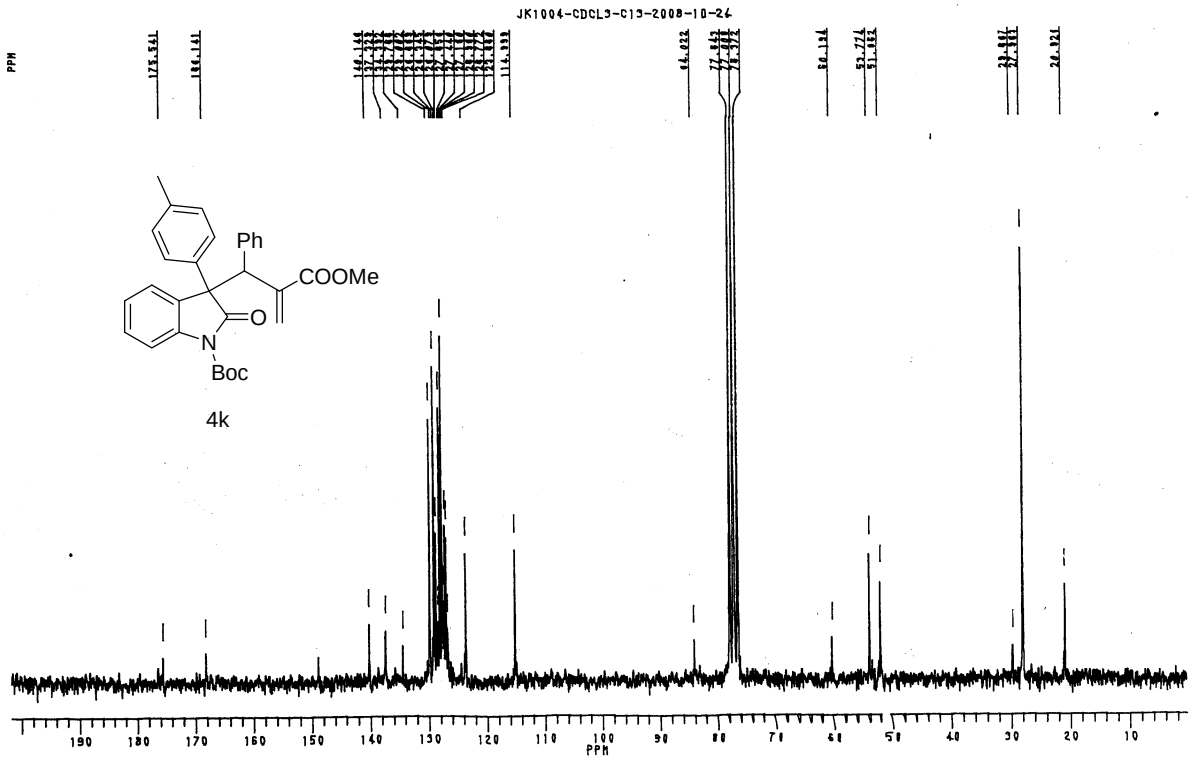


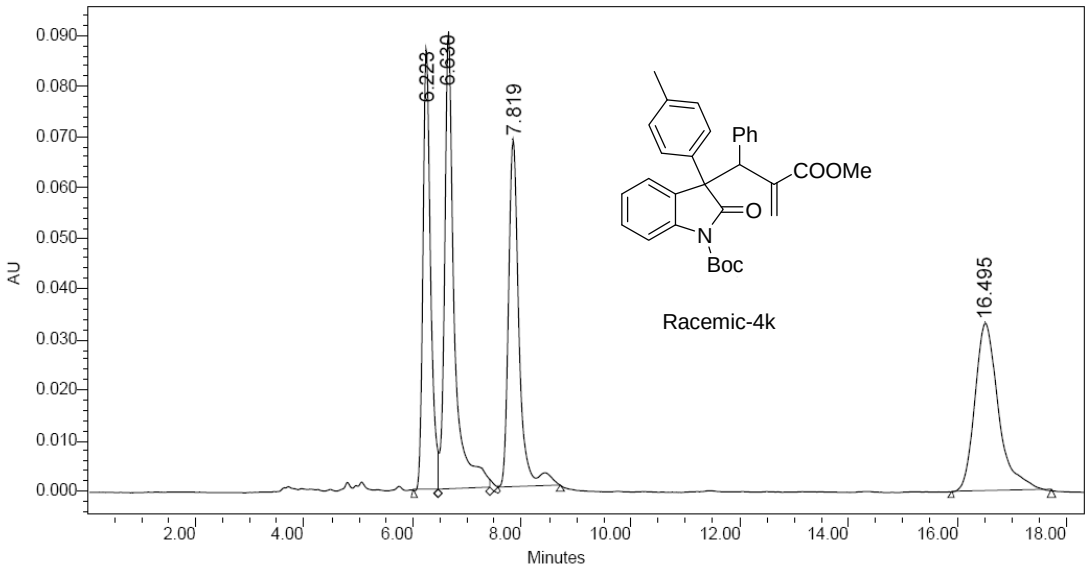
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	7.383	33504055	28.90	1117305	35.87
2	8.568	37425470	32.29	1280206	41.11
3	9.768	22868965	19.73	465767	14.96
4	27.284	22123481	19.08	251163	8.06



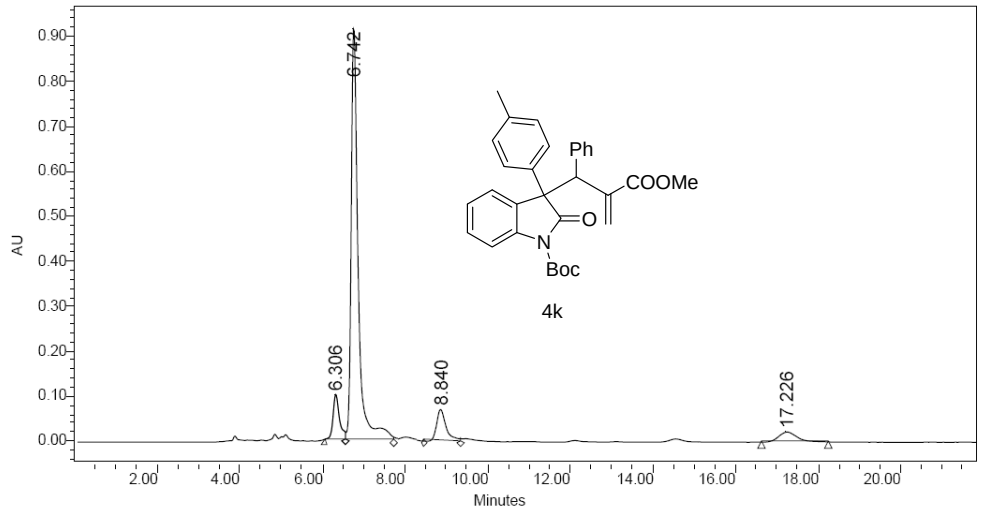
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	7.455	645072	5.84	30624	15.13
2	8.393	2384254	21.57	67648	33.43
3	10.405	408589	3.70	12943	6.40
4	27.170	7613567	68.89	91172	45.05


Pulse Sequence: s2pul
Ph
COOMe
O
N
Boc
4k
ppm

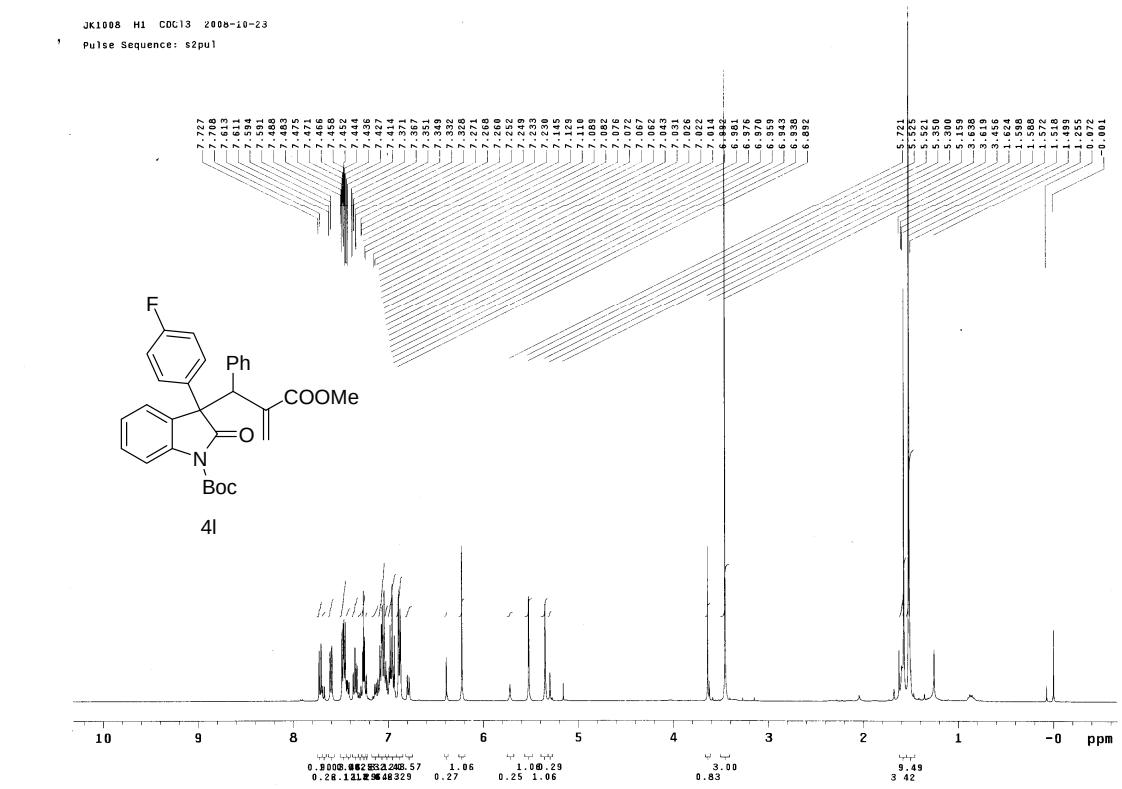

JK1004-CDCL3-C13-2008-10-24
PPM
Ph
COOMe
O
N
Boc
4k

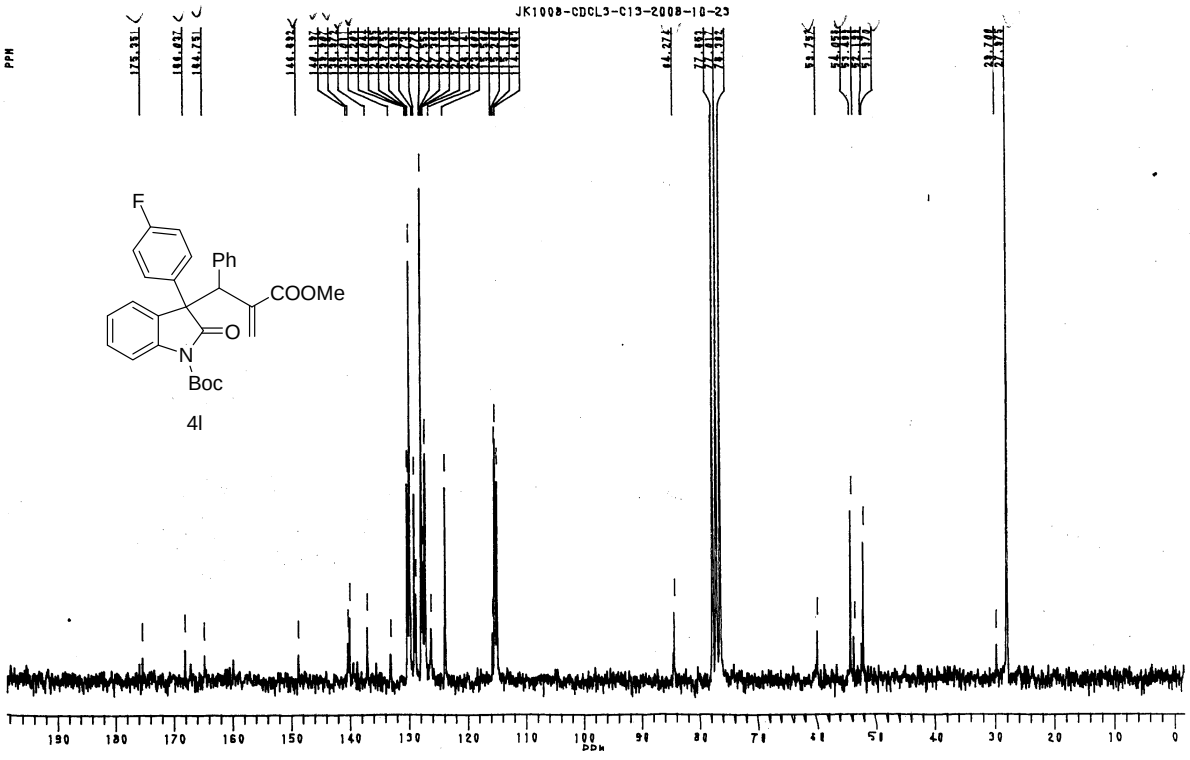


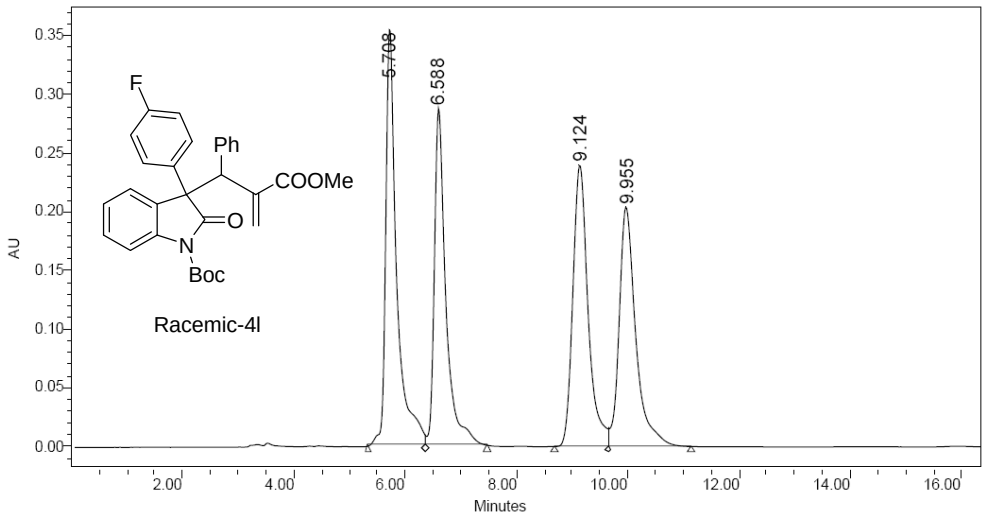
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	6.223	855197	22.40	87602	31.24
2	6.630	1051409	27.54	90502	32.28
3	7.819	904519	23.70	69078	24.64
4	16.495	1006196	26.36	33204	11.84



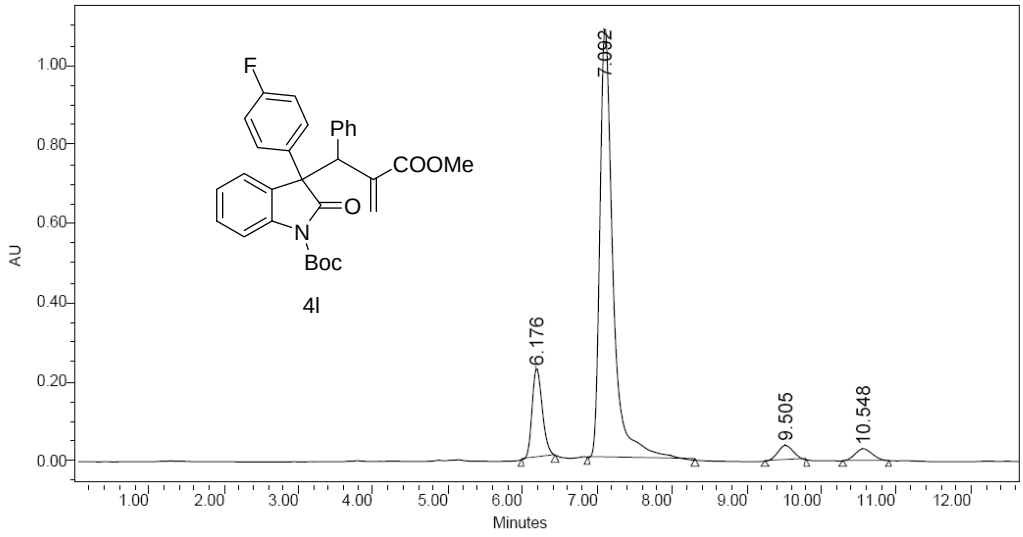
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	6.306	1081504	7.95	99463	8.95
2	6.742	10724055	78.81	919577	82.78
3	8.840	1115675	8.20	69618	6.27
4	17.226	686147	5.04	22276	2.01


JK1008 H1 CDCl3 2008-10-23
Pulse Sequence: s2pul
F
Ph
COOMe
O
N
Boc
4l
ppm

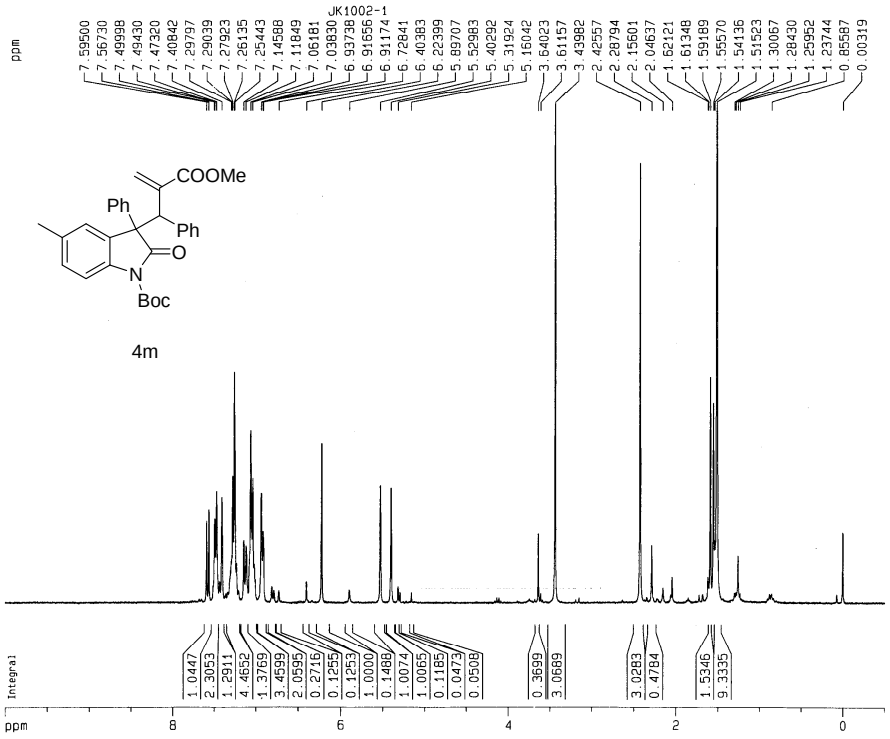

JK1008-CDCL3-C13-2008-10-23
PPM
F
Ph
COOMe
O
N
Boc
4l
ppm



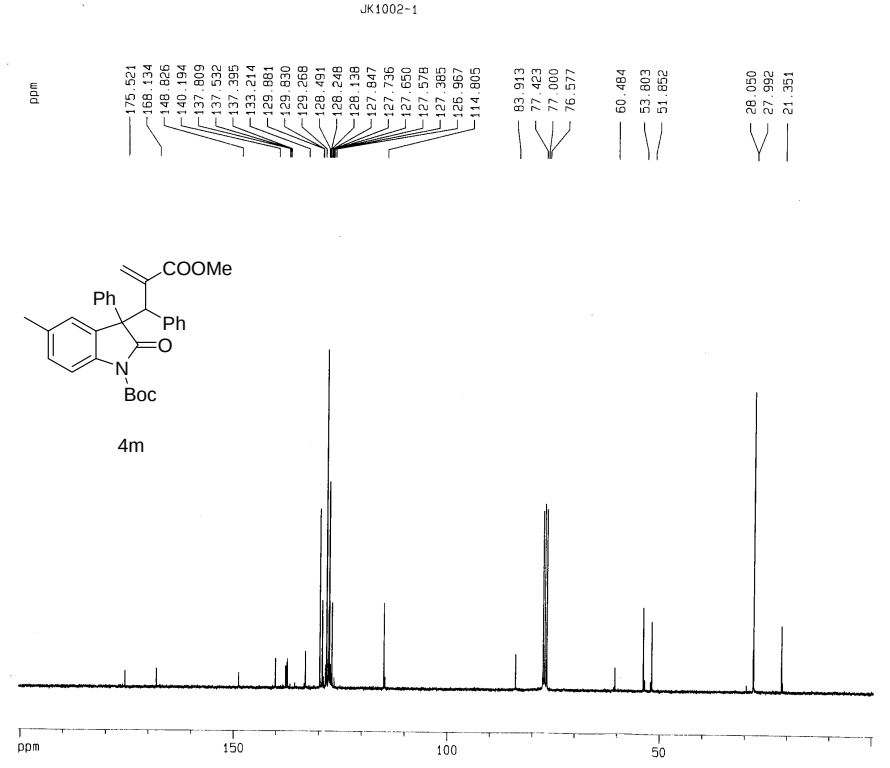
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	5.708	4868481	27.38	356284	32.75
2	6.588	4120186	23.17	287799	26.45
3	9.124	4574974	25.73	239784	22.04
4	9.955	4218528	23.72	204059	18.76



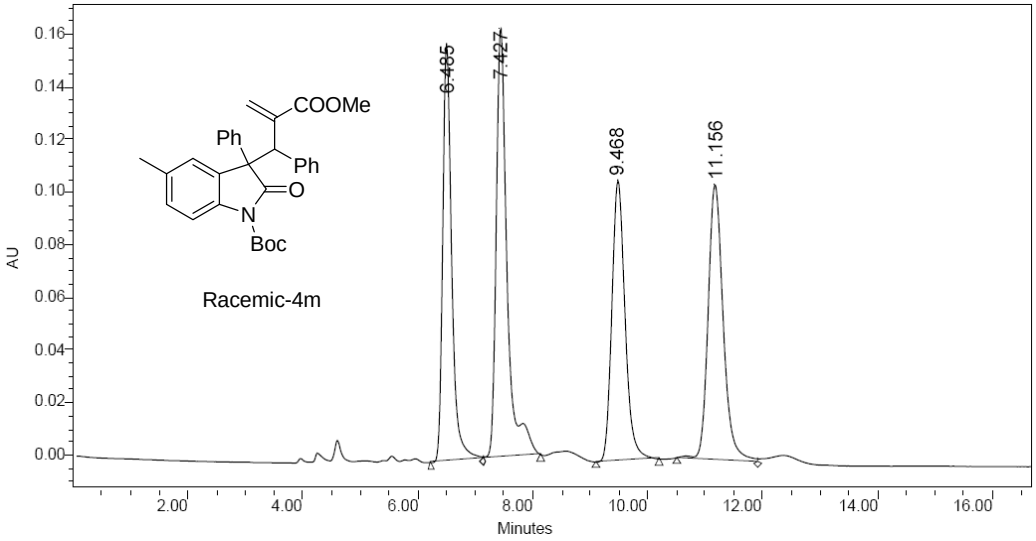
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	6.176	2161822	12.76	227638	16.40
2	7.092	13726289	81.04	1091676	78.65
3	9.505	566622	3.35	38390	2.77
4	10.548	482133	2.85	30345	2.19



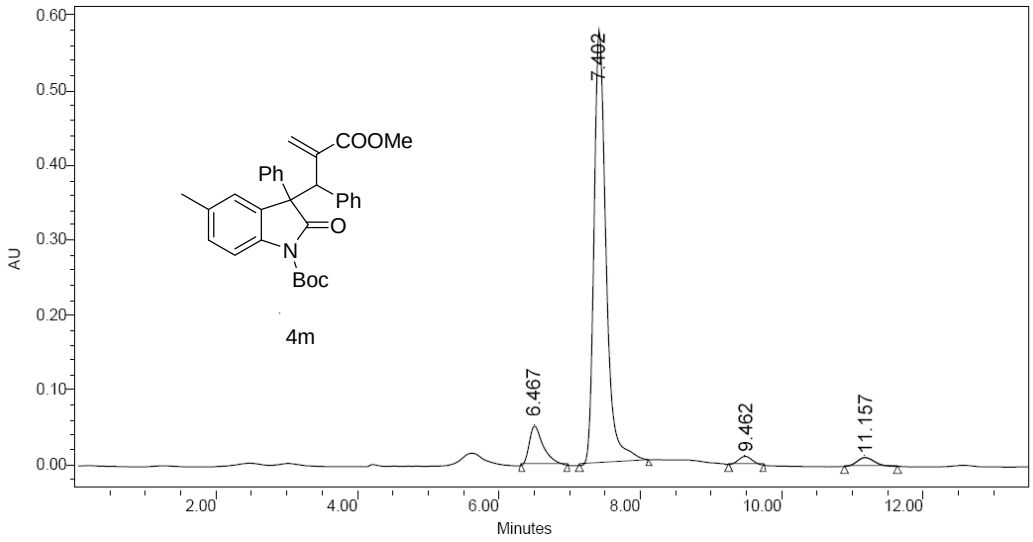

```
Current Data Parameters
NAME            cyc-2008-202
EXPNO                      1
PROCNO                     1

F2 - Acquisition Parameters
Date_           20081021
Time                 18.03
INSTRUM              av300
PROBHD    5 mm QNP 1H/13
PULPROG              zg30
TD                  32760
SOLVENT              CDCl3
NS                      16
DS                       0
SWH             5995.204 Hz
FIDRES          0.182959 Hz
AQ              2.7329011 sec
RG                     256
DW                83.400 usec
DE                 6.00 usec
TE                 300.0 K
D1              1.00000000 sec

======== CHANNEL f1 ========
NUC1                   1H
P1                  3.00 usec
PL1                -2.00 dB
SFO1         300.1320882 MHz

F2 - Processing parameters
SI                     32768
SF              300.1300121 MHz
WDW                    EM
SSB                     0
LB                   0.10 Hz
GB                      0
PC                   1.00

1D NMR plot parameters
CX                  20.00 cm
CY                  35.00 cm
F1P                10.000 ppm
F1               3001.30 Hz
F2P                -0.500 ppm
F2               -150.06 Hz
PPMCM            0.52500 ppm/cm
HZCM             157.56825 Hz/cm
```



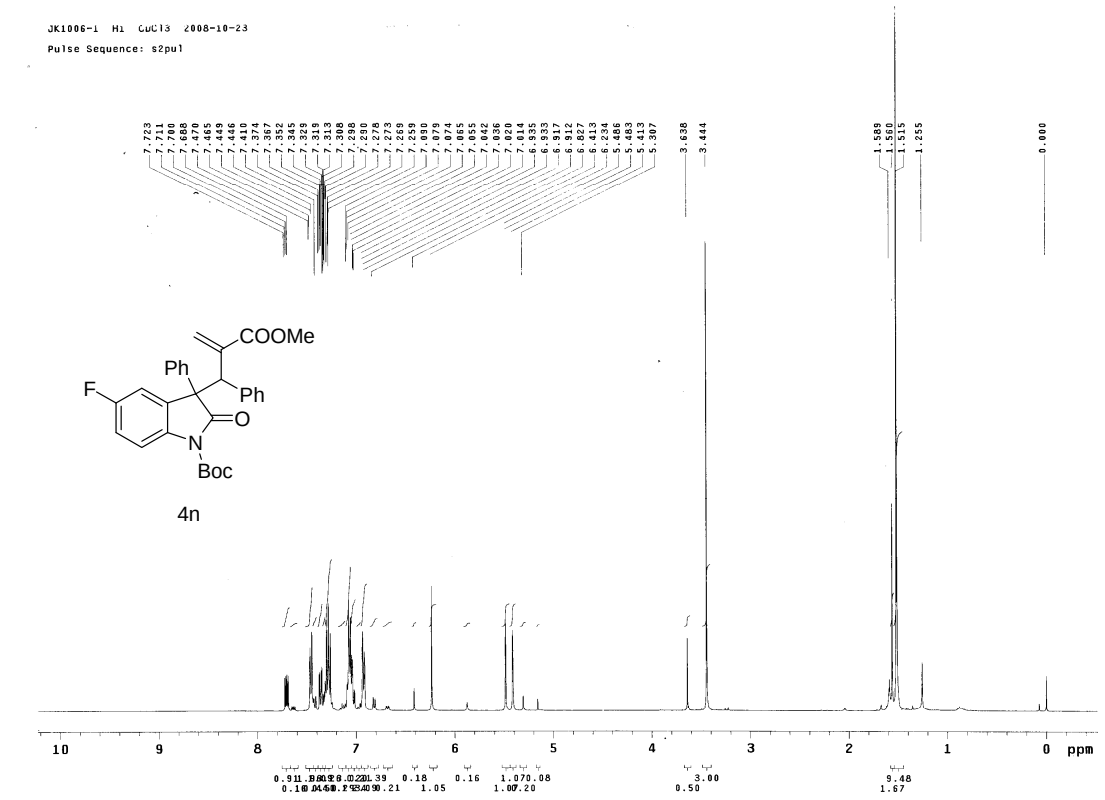

```
Current Data Parameters
NAME            cyc-2008-202
EXPNO                      2
PROCNO                     1

F2 - Acquisition Parameters
Date_           20081022
Time                 12.07
INSTRUM              av300
PROBHD    5 mm QNP 1H/13
PULPROG              zgpg
TD                  65536
SOLVENT              CDCl3
NS                    2664
DS                       4
SWH            22675.736 Hz
FIDRES          0.346004 Hz
AQ              1.4451188 sec
RG                    8192
DW                22.050 usec
DE                 6.00 usec
TE                 300.0 K
D1              2.00000000 sec
d11             0.03000000 sec
d12             0.00002000 sec

======== CHANNEL f1 ========
NUC1                   13C
P1                  5.50 usec
PL1                -6.00 dB
SFO1         75.4775598 MHz

======== CHANNEL f2 ========
CPDPRG2            waltz16
NUC2                   1H
PCPD2              80.00 usec
PL2                -2.00 dB
PL12               17.70 dB
PL13               17.71 dB
SFO2         300.1312005 MHz

F2 - Processing parameters
SI                     65536
SF              75.4677511 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40

1D NMR plot parameters
CX                  20.00 cm
CY                   8.00 cm
F1P               200.500 ppm
F1              15131.28 Hz
F2P                -0.500 ppm
F2                -37.73 Hz
PPMCM           10.05000 ppm/cm
HZCM            758.45087 Hz/cm
```

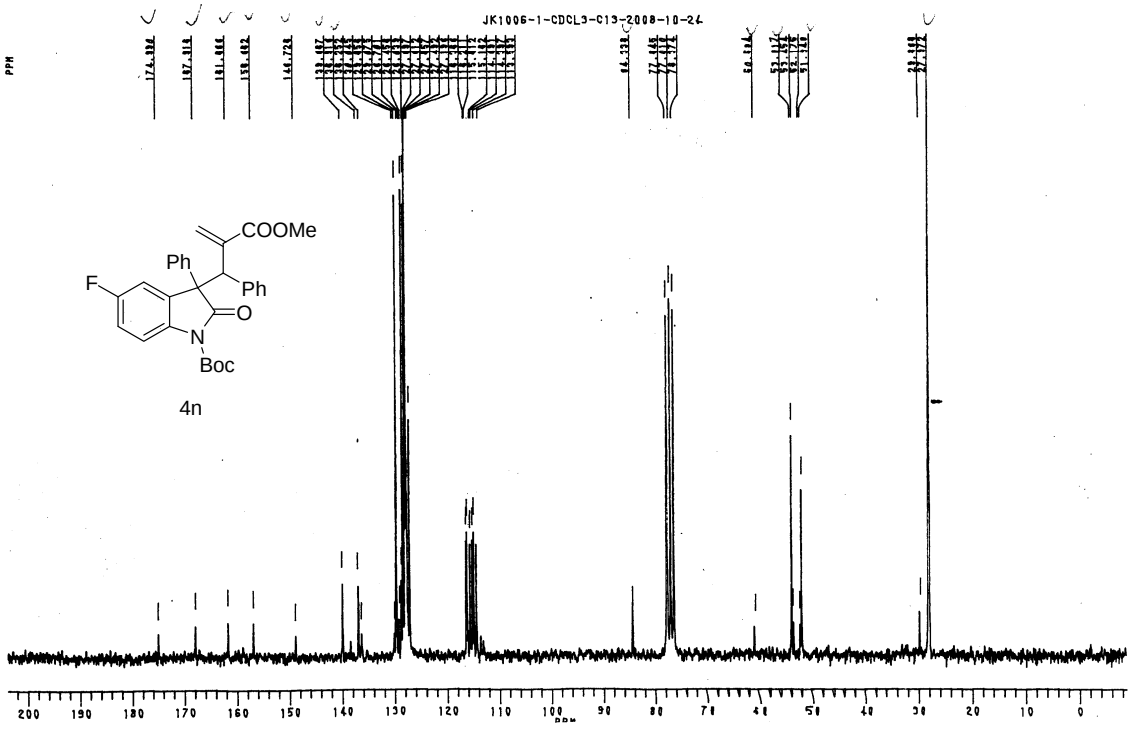


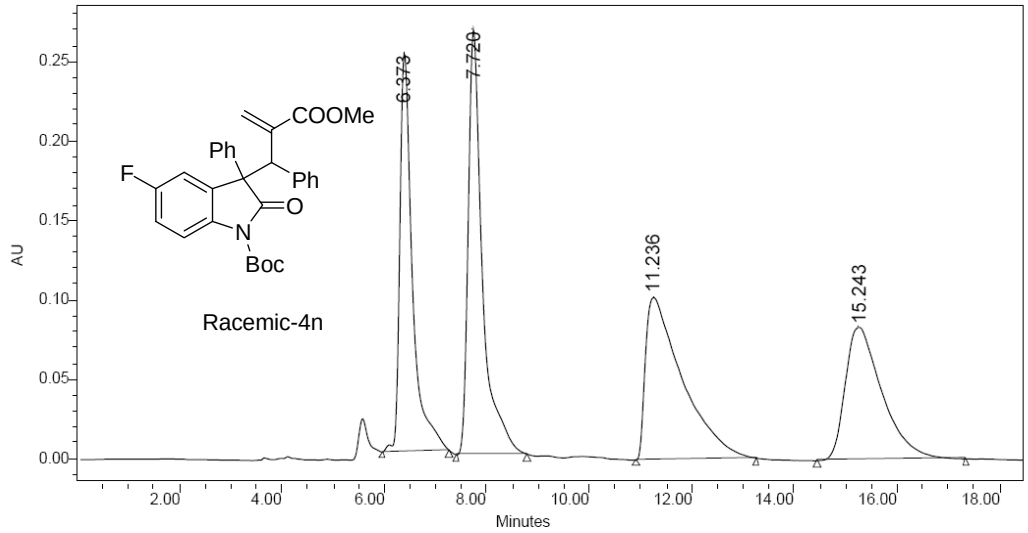
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	6.485	1735143	23.13	158967	29.79
2	7.427	2155611	28.74	163527	30.65
3	9.468	1707625	22.77	106585	19.97
4	11.156	1902464	25.36	104524	19.59



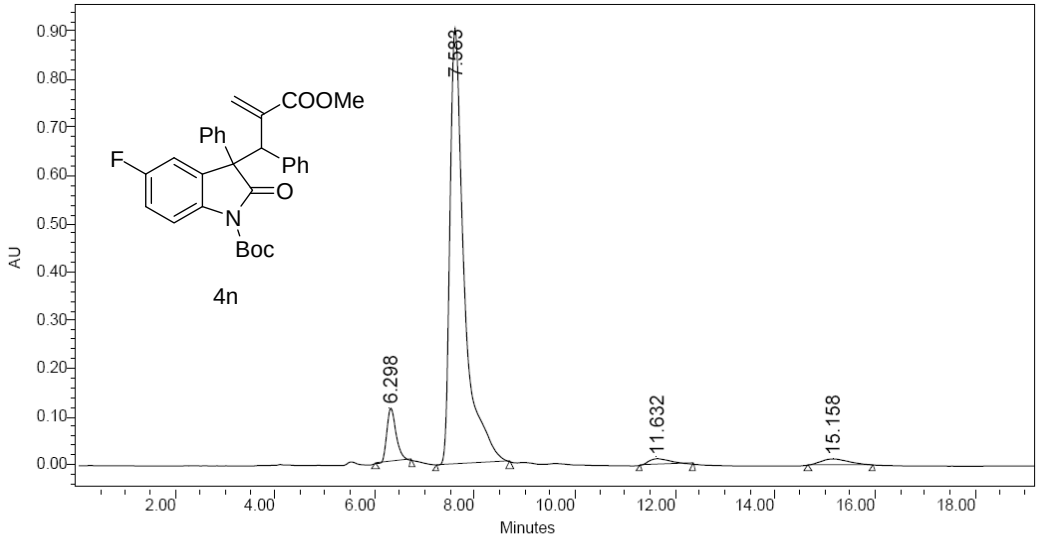
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	6.467	464221	6.06	50238	7.71
2	7.402	6841086	89.30	578742	88.77
3	9.462	151190	1.97	11168	1.71
4	11.157	204417	2.67	11788	1.81


JK1006-1 H1 CDCl3 2008-10-23
Pulse Sequence: s2pul
COOMe
Ph
Ph
F
O
N
Boc
4n
ppm

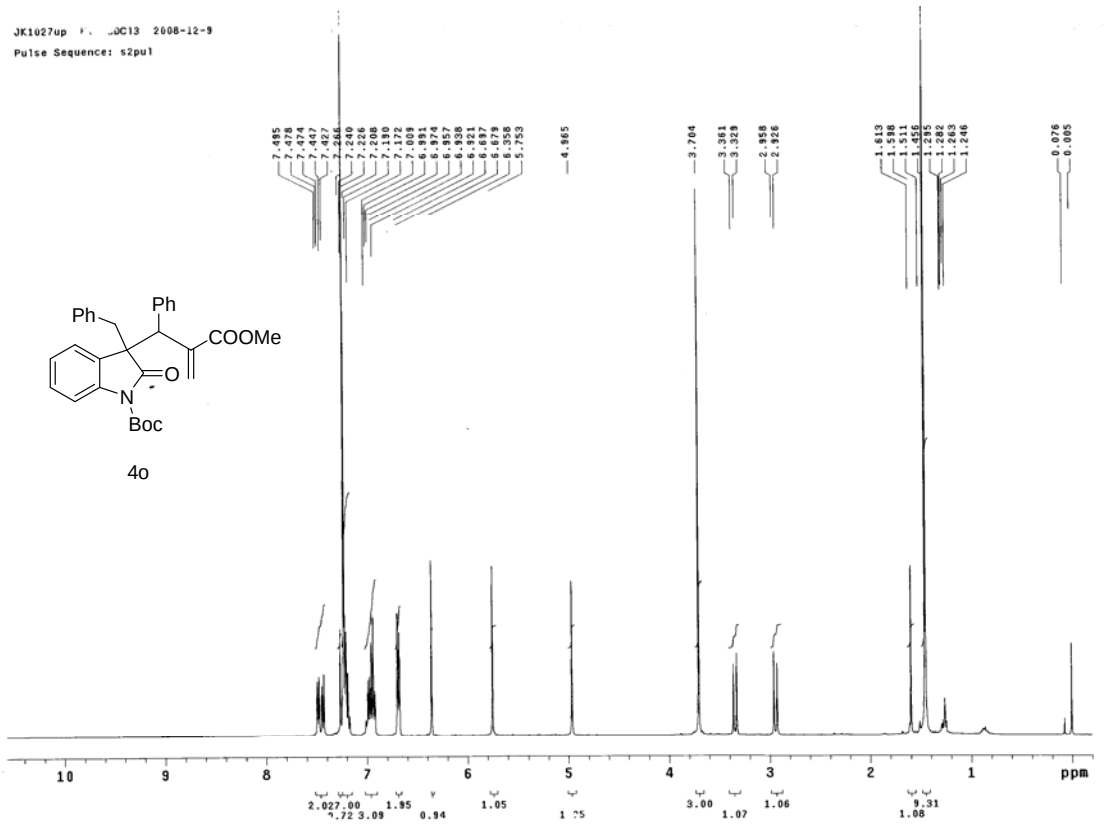

JK1006-1-CDCL3-C13-2008-10-24
PPM
COOMe
Ph
Ph
F
O
N
Boc
4n

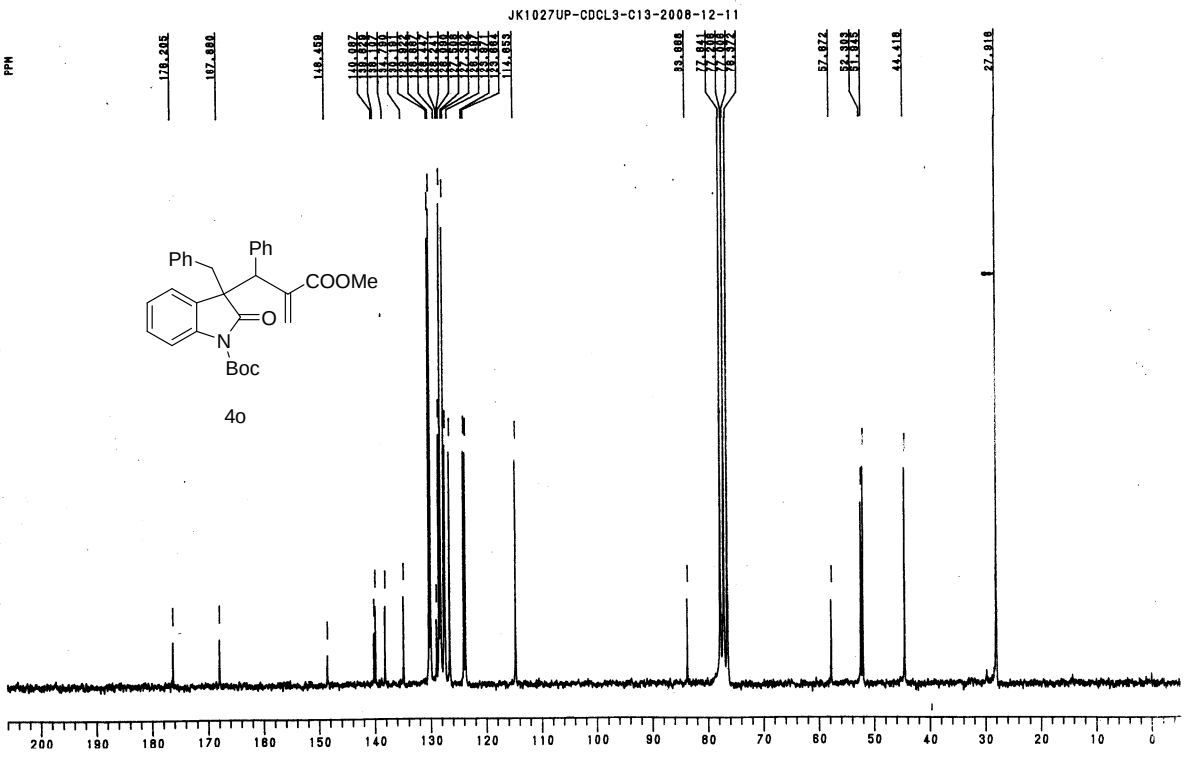


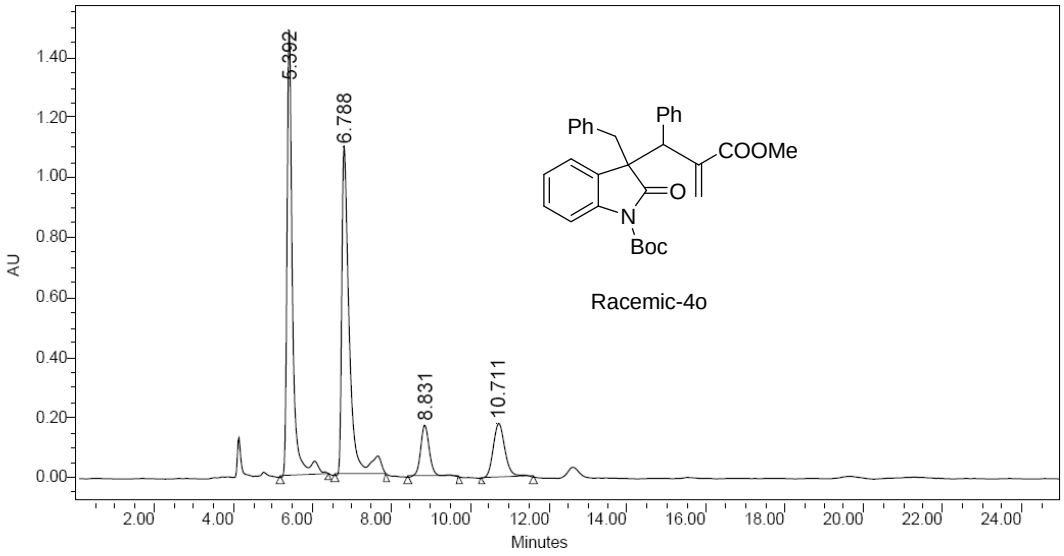
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	6.373	4312336	23.00	251118	35.67
2	7.720	5151268	27.47	267580	38.01
3	11.236	5084888	27.12	101749	14.45
4	15.243	4203843	22.42	83592	11.87



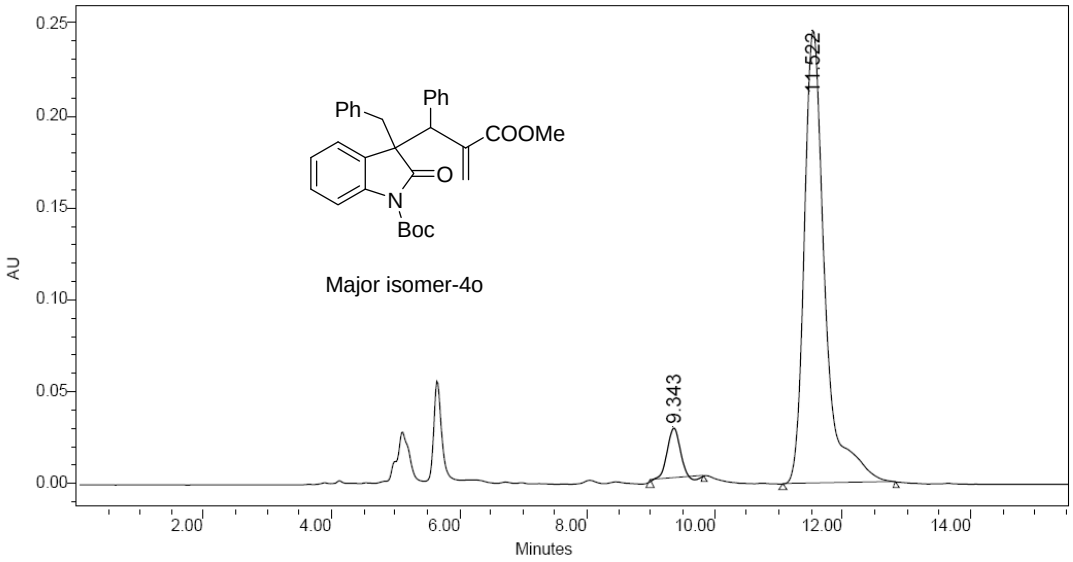
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	6.298	1478207	7.22	112007	10.75
2	7.583	18083860	88.37	904492	86.80
3	11.632	418705	2.05	13129	1.26
4	15.158	484015	2.37	12364	1.19


Ph
Ph
COOMe
O
N
Boc
4o

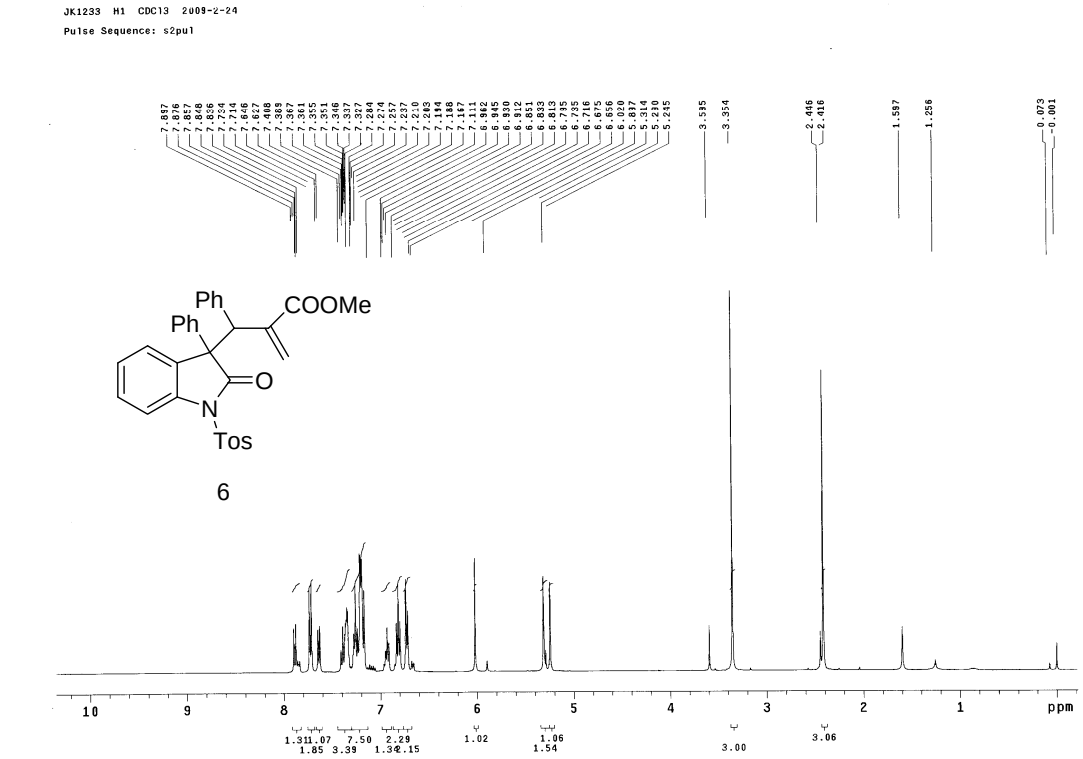

JK1027UP-CDCL3-C13-2008-12-11
Ph
Ph
COOMe
O
N
Boc
4o

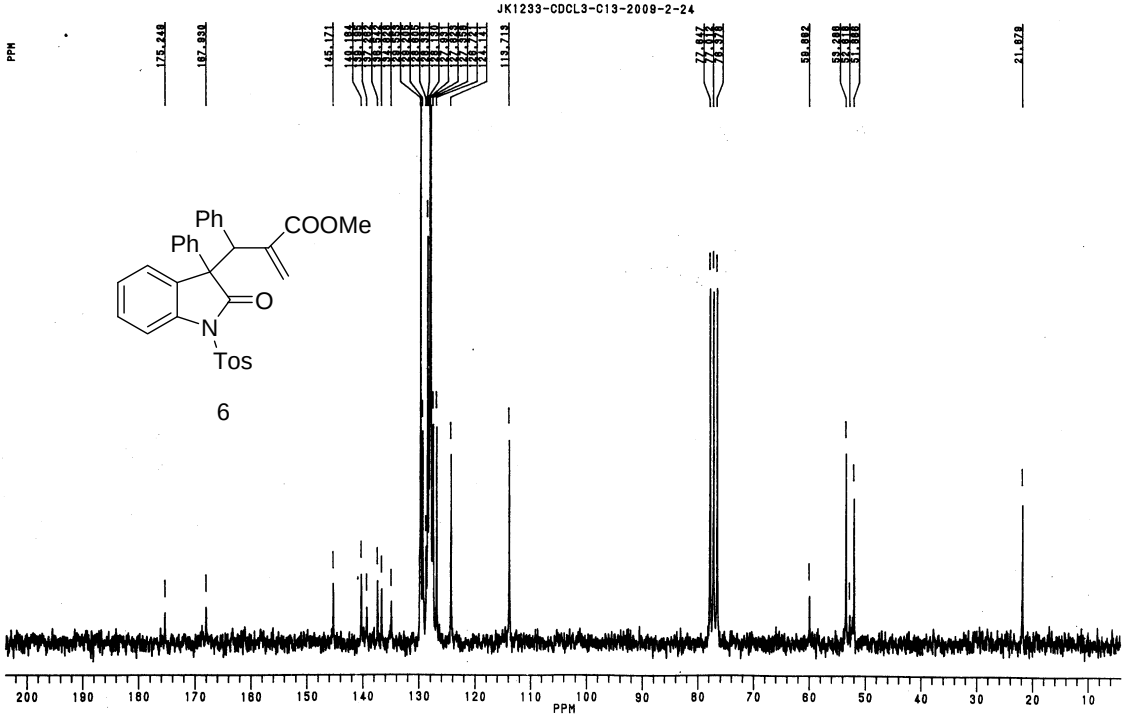


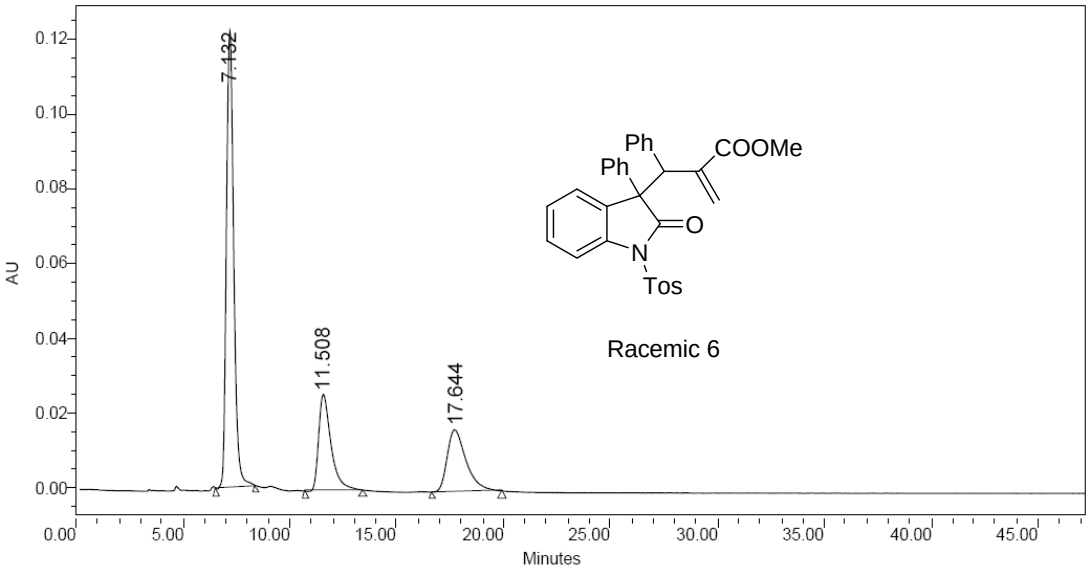
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	5.392	14612746	40.14	1503278	50.81
2	6.788	15026202	41.27	1100944	37.21
3	8.831	2882133	7.92	172776	5.84
4	10.711	3884285	10.67	181415	6.13



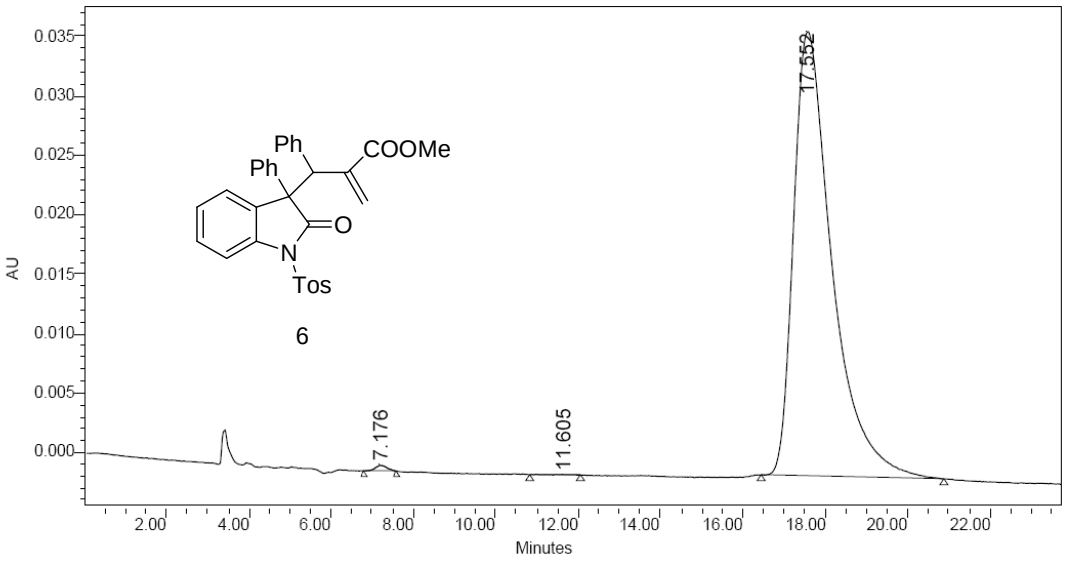
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	9.343	410891	6.92	27584	10.08
2	11.522	5527096	93.08	245985	89.92


JK1233 H1 CDCl3 2009-2-24
Pulse Sequence: s2pul
Ph
Ph
COOMe
O
N
Tos
6
ppm

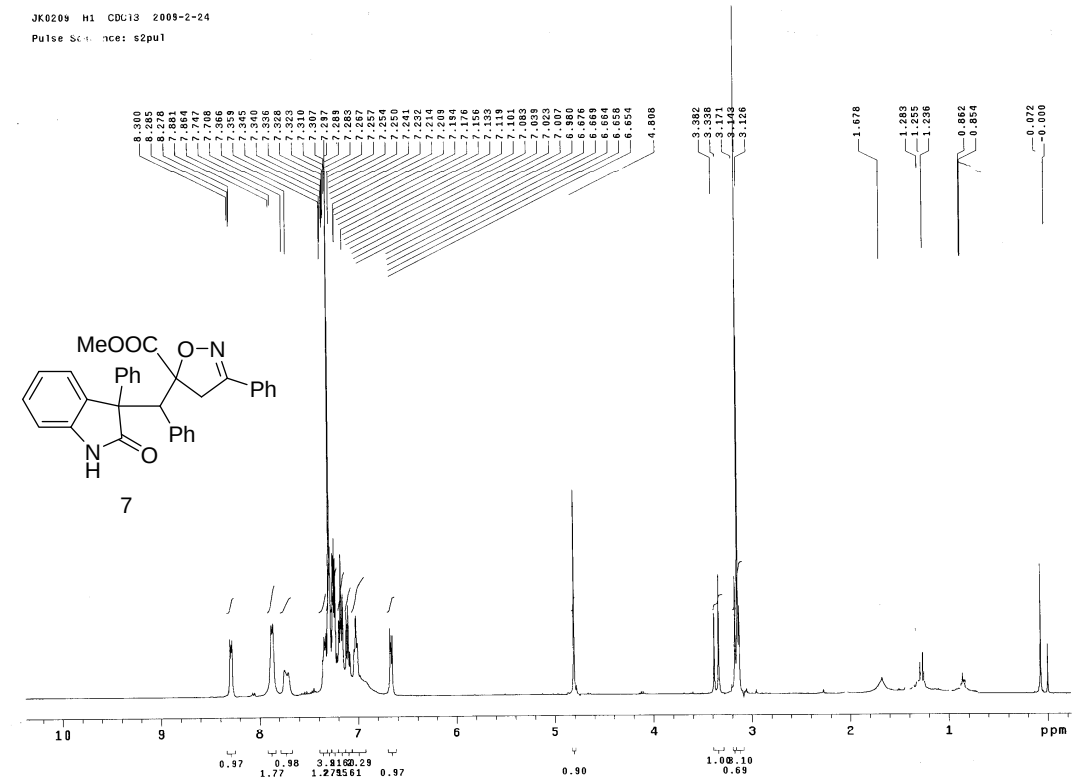

JK1233-CDCL3-C13-2009-2-24
PPM
Ph
Ph
COOMe
O
N
Tos
6

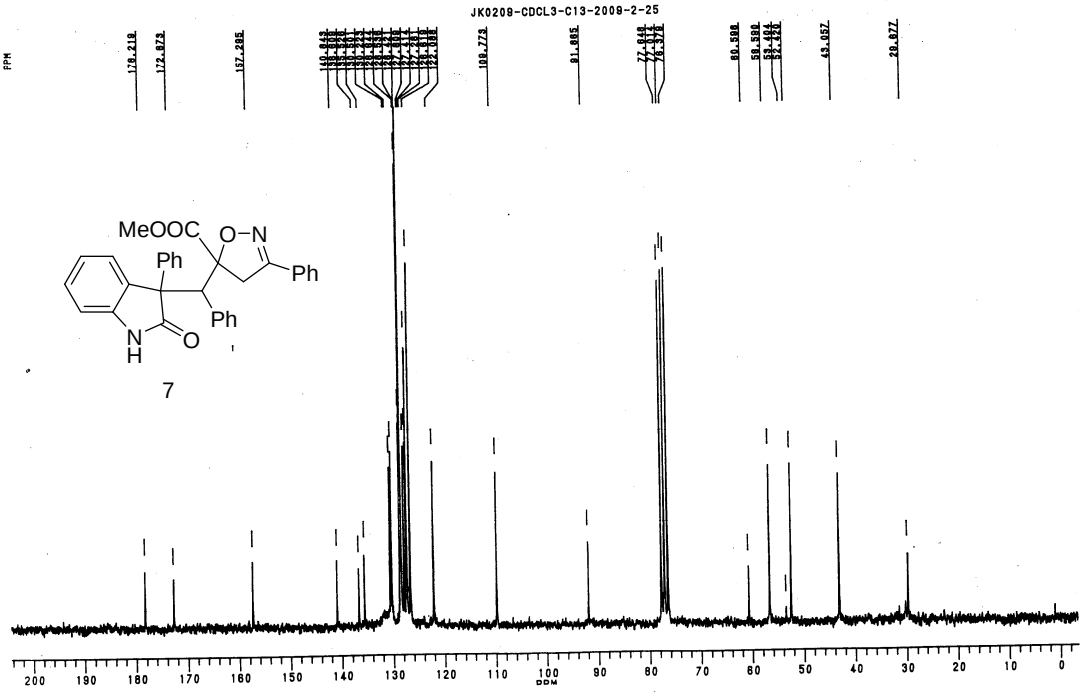


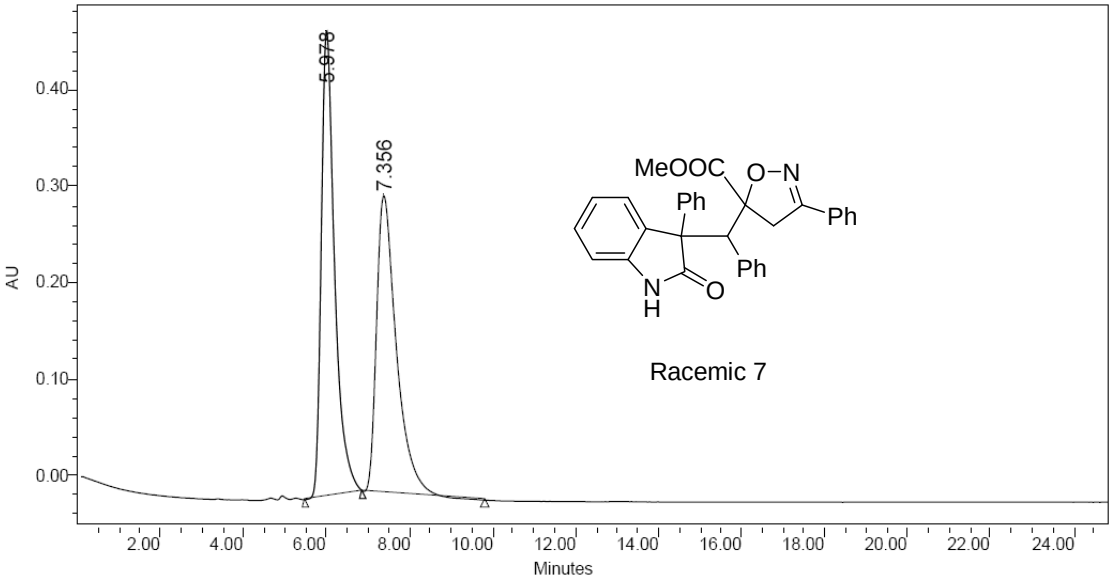
	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	7.132	2909298	58.41	122016	74.22
2	11.508	1050462	21.09	25826	15.71
3	17.644	1021372	20.50	16550	10.07



	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	7.176	9490	0.39	478	1.26
2	11.605	1349	0.06	38	0.10
3	17.552	2424324	99.55	37379	98.64

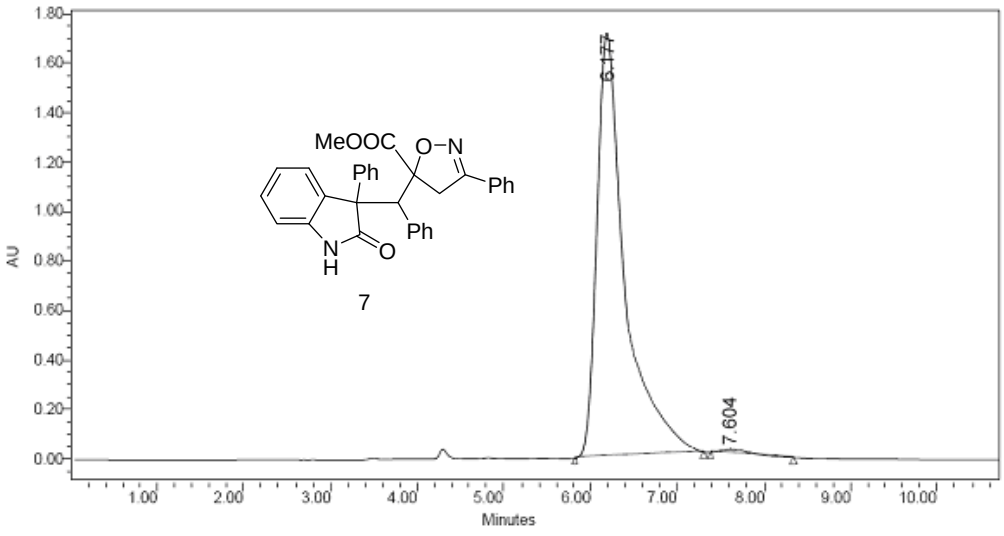

JK0209 H1 CDCl3 2009-2-24
MeOOC
O–N
Ph
Ph
Ph
N
H
O
7
ppm


JK0209-CDCL3-C13-2009-2-25
PPM
MeOOC
O–N
Ph
Ph
Ph
N
H
O
7



Racemic 7

	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	5.978	10834267	51.37	483157	61.06
2	7.356	10257457	48.63	308183	38.94



7

	RT (min)	Area (V *sec)	% Area	Height (V)	% Height
1	6.177	37332253	98.96	1713260	99.00
2	7.604	392004	1.04	17339	1.00