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Supporting Information

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Asymmetric Brønsted Acid-Catalyzed Isoindoline Synthesis: Enhancement of Enantiomeric Ratio by Stereoablative Kinetic Resolution

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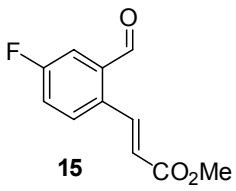
General Experimental

Unless otherwise noted, all commercially available compounds were used without further purification. 4 Å molecular sieves (MS) were activated by heating at 240°C under vacuum (0.5 mmHg) for 6 h. Toluene was freshly distilled under Ar from sodium-lead alloy. Dichloromethane was freshly distilled under Ar from calcium hydride. Chloroform was distilled from phosphorus pentoxide and stored over 4 Å MS. Chlorobenzene (PhCl) and 1,2-dichloroethane (DCE) were passed through a column of neutral alumina and stored over 4 Å MS. Preparative column chromatography: Merck silica gel 60, particle size 0.040-0.063 mm (230-240 mesh, flash). Analytical TLC: silica gel 60 F_{254} plates from Merck, Darmstadt. Visualization of the developed TLC plates was performed with ultraviolet irradiation (254 nm) or by staining with phosphomolybdic acid. Optical rotation values were measured on a Perkin-Elmer 241 polarimeter. Microanalyses were performed with a Vario EL element analyser. Mass spectra were acquired on a Finnigan SSQ7000 (EI 70 eV) spectrometer and high resolution mass spectra on a Finnigan MAT 95. IR spectra were taken on a Perkin-Elmer FT-IR 1760. ^{1}H- and ^{13}C- NMR spectra were recorded at ambient temperature on Varian Mercury 300 or Inova 400 with tetramethylsilane as an internal standard. Analytical HPLC was performed on a Hewlett-Packard 1100 Series instrument using chiral stationary phases (Chiralcel OD, Chiralcel OJ, Chiralpak AD, Chiralpak AS, Chiralcel IA). Racemic samples of isoindoline **10a-j** were prepared using *p*-toluenesulfonic acid (10 mol%) as catalyst. BINOL-derived phosphoric acids and *N*-triflylphosphoramidates **7a-f** (X = OH, NHTf) were prepared as described in the literature.[1] The yields and recorded NMR spectra of isoindolines **10a-j** are for inseparable/partially-separable diastereomeric mixtures.

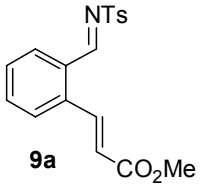
ε-Iminoacrylate Synthesis

(*E*)-methyl 3-(2-formylphenyl)acrylate and (*E*)-*t*-butyl-3-(2-formylphenyl)acrylate were prepared as described in the literature.[2] (*E*)-Methyl 3-(4-fluoro-2-formylphenyl)acrylate (**15**) was prepared in an analogous manner. Imines were synthesized using a previously described method.[3]

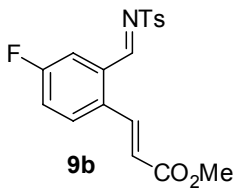
(E)-Methyl 3-(4-fluoro-2-formylphenyl)acrylate (**15**). To a solution of 2-bromo-5-fluoro-benzaldehyde (500 mg, 2.46 mmol) in toluene (5 mL) were successively added $Pd(OAc)_2$ (11 mg, 0.05 mmol), tri-*o*-tolylphosphine (30 mg, 0.1 mmol), (*E*)-methylacrylate (340 µL, 3.70 mmol) and triethylamine (1 mL, 7.2 mmol) at room temperature. The reaction mixture was heated at reflux for 2 days, cooled to rt, diluted with water (100 mL) and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried over $MgSO_4$, filtered and evaporated under reduced pressure. The crude product was purified by flash chromatography (5:1 pentane/ether) to afford aldehyde **15** as a yellow solid (475 mg, 91%). M.p. 141°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.29 (d, *J* = 1.7 Hz, 1H), 8.43 (d, *J* = 15.9 Hz, 1H), 7.64 (dd, *J* = 5.1, 8.7 Hz, 1H), 7.58 (dd, *J* = 2.8, 8.5 Hz, 1H), 7.32 (m, 1H), 6.35 (d, *J* = 15.9 Hz, 1H), 3.83 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.6, 165.3 (d, *J* = 172.8 Hz), 161.9, 139.4, 135.4 (d, *J* = 6.1 Hz), 132.6 (d, *J* = 3.4 Hz), 130.0 (d, *J* = 7.6 Hz), 122.7, 121.1 (d, *J* = 22.0 Hz), 117.5 (d, *J* = 22.3 Hz), 51.9; IR (KBr) *v* = 3065 (w), 3014 (w), 2959 (m), 2890 (w), 1728 (vs), 1684 (vs), 1640 (m), 1602 (s), 1492 (s), 1434 (s), 1374 (m), 1330 (s), 1281 (vs), 1245 (vs), 1201 (s), 1177 (s), 1150 (s), 1061 (w), 982 (m), 886 (m), 834 (s), 775 (m), 774 (s), 633 (m), 551 (m), 508 (w), 458 (m) cm^{-1}; MS (CI, CH_4) *m/z* (%) 209 (9) [M^++1], 178.1 (10), 177.0 (100), 149.0 (28). Anal. Calcd for $C_{11}H_9FO_3$: C, 63.46; H, 4.36; found: C, 63.51; H, 4.75.



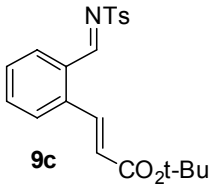
(E)-Methyl 3-(2-((tosylimino)methyl)phenyl)acrylate (**9a**). Titanium tetrachloride (5.2 mL, 26.3 mmol) in CH_2Cl_2 (50 mL) was added dropwise to a stirred ice-cooled solution of (*E*)-methyl 3-(2-formylphenyl)acrylate[2] (10.0 g, 52.6 mmol), *p*-toluenesulfonamide (9.0 g, 52.6 mmol) and triethylamine (2.2 mL, 158 mmol) in CH_2Cl_2 (100 mL). After the addition was complete, the mixture was stirred at 0°C for 1 h. The resultant titanium dioxide was removed by vacuum filtration through Celite washing with CH_2Cl_2. The filtrate was evaporated under reduced pressure to afford solid mixture of the imine **9a** and triethylamine hydrochloride which was crushed into a fine powder and heated at reflux in dry ether (125 mL). The undissolved triethylamine hydrochloride was removed by vacuum filtration and the residue was further extracted with ether (2 × 50 mL). The solvent was evaporated under reduced pressure and the solid was recrystallized twice (ethyl acetate/pentane) to afford imine **9a** as a white solid (9.7 g, 53%). M.p. 126°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.33 (s, 1H), 8.27 (d, *J* = 15.6 Hz, 1H), 8.06 (d, *J* = 8.0 Hz, 1H), 7.92 (d, *J* = 8.2 Hz, 2H), 7.64 – 7. 58 (m, 2H), 7.51 – 7.45 (m, 1H), 7.36 (d, *J* = 8.0 Hz, 2H), 6.30 (d, *J* = 15.8 Hz, 1H), 3.85 (s, 3H), 2.45 (s, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.2, 166.0, 144.6, 140.2, 138.0, 134.7, 134.3, 131.1, 130.2, 129.8, 129.7, 128.1, 128.0, 123.4, 51.9, 21.7 ppm; IR (KBr) 2956 (w), 1717 (vs), 1635 (s), 1582 (vs), 1557 (s), 1474 (w), 1434 (m), 1388 (m), 1320 (vs), 1284 (s), 1227 (w), 1155 (vs), 1087 (s), 999 (m), 969 (m), 932 (w), 865 (w), 841 (w), 811 (m), 782 (s), 721 (m), 674 (s), 616 (w), 589 (m), 549 (s), 469 (s) cm^{-1}; MS (CI, CH_4) *m/z* (%) 344.1 (32) [M^++1], 313.1 (20), 312.0 (100), 284.0 (19). Anal. Calcd for $C_{18}H_{17}NO_4S$: C, 62.96; H, 4.99; N, 4.08; found: C, 63.24; H, 5.240; N, 4.118.



(E)-Methyl 3-(4-fluoro-2-((tosylimino)methyl)phenyl)acrylate (**9b**). Titanium tetrachloride (650 µL, 3.3 mmol) in CH_2Cl_2 (6 mL) was added dropwise to a stirred ice-cooled solution of aldehyde **15** (1.37 g, 6.6 mmol), *p*-toluenesulfonamide (1.13 g, 6.6 mmol) and triethylamine (2.75 mL, 19.8 mmol) in CH_2Cl_2 (20 mL). After the addition was complete, the mixture was stirred at 0°C for 1 h. The resultant titanium dioxide was removed by vacuum filtration through Celite washing with CH_2Cl_2. The filtrate was evaporated under reduced pressure to afford solid mixture of the imine **9a** and triethylamine hydrochloride which was crushed into a fine powder and heated at reflux in dry ether (50 mL). The undissolved triethylamine hydrochloride was removed by vacuum filtration and the residue was further extracted with ether (2 × 15 mL). The solvent was evaporated under reduced pressure and the solid was recrystallized (ethyl acetate/pentane) to afford imine **9a** as a yellow solid (1.1 g, 47%). M.p. 132°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.32 (d, *J* = 1.8 Hz, 1H), 8.15 (d, *J* = 15.8 Hz, 1H), 7.91 (d, *J* = 8.3 Hz, 2H), 7.78 (dd, *J* = 2.7, 9.0 Hz, 1H), 7.60 (dd, *J* = 5.2, 8.7 Hz, 1H), 7.37 (d, *J* = 8.3 Hz, 2H), 7.31 (m, 1H), 6.28 (d, *J* = 15.8 Hz, 1H), 3.84 (s, 3H), 2.45 (s, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.6, 165.0 (d, *J* = 165.6 Hz), 161.6, 144.8, 138.5, 134.3, 134.3, 132.2 (d, *J* = 7.7 Hz), 130.1 (d, *J* = 8.0 Hz), 129.7, 128.1, 123.6, 121.7 (d, *J* = 22.2 Hz), 116.4 (d, *J* = 23.2 Hz), 52.0, 21.7 ppm ; IR (KBr) 3072 (w), 2966 (w), 1724 (s), 1636 (m), 1591 (s), 1486 (m), 1435 (m), 1386 (w), 1320 (vs), 1285 (s), 1155 (vs), 1088 (s), 991 (m), 973 (m), 928 (w), 890 (w), 841 (m), 791 (s), 752 (m), 713 (w), 676 (s), 617 (w), 578 (s), 537 (m), 472 (m), cm^{-1}; MS (CI, CH_4) *m/z* (%) 362.0 (11) [M^++1], 331.1 (19), 330.0 (100), 302.0 (17). Anal. Calcd for $C_{18}H_{16}FNO_4S$: C, 59.82; H, 4.46; N, 3.88; found: C, 59.90; H, 4.66; N, 3.85.



(E)-t-Butyl 3-(2-((tosylimino)methyl)phenyl)acrylate (**9c**). Titanium tetrachloride (1.3 mL, 6.7 mmol) in dry dichloromethane (15 mL) was added dropwise to a stirred ice-cooled solution of *(E)*-*t*-butyl 3-(2-formylphenyl)acrylate[2] (3.11 g, 13.4 mmol), *p*-toluenesulfonamide (2.30 g, 13.4 mmol) and triethylamine (5.5 mL, 40.1 mmol) in CH_2Cl_2 (30 mL). After the addition was complete, the mixture was stirred at 0°C for 1 h. The resultant titanium dioxide was removed by vacuum filtration through Celite washing with CH_2Cl_2. The filtrate was evaporated under reduced pressure to afford solid mixture of the imine **9a** and triethylamine hydrochloride which was crushed into a fine powder and heated at reflux in dry ether (50 mL). The undissolved triethylamine hydrochloride was removed by vacuum filtration and the residue was further extracted with ether (2 × 15 mL). The solvent was evaporated under reduced pressure and the solid was recrystallized (ethyl acetate/pentane) to afford imine **9a** as a white solid (2.61 g, 51%). M.p. 97°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.34 (s, 1H), 8.16 (d, *J* = 15.7 Hz, 1H), 8.06 (d, *J* = 7.8 Hz, 1H), 7.92 (d, *J* = 8.2 Hz, 2H), 7.59 (m, 2H), 7.45 (m, 1H), 7.36 (d, *J* = 8.2 Hz, 2H), 6.23 (d, *J* = 15.7 Hz, 1H), 2.44 (s, 3H), 1.56 (s, 9H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4, 164.8, 144.5, 138.8, 138.4, 134.8, 134.2, 130.9, 130.1, 129.7, 129.5, 128.0, 125.9, 111.4, 81.0, 28.1, 21.6 ppm; IR (KBr) 3060 (w), 2973 (m), 2928 (w), 1704 (s), 1635 (m), 1581 (s), 1479 (w), 1445 (m), 1368 (m), 1326 (vs), 1265 (m), 1211 (s), 1161 (vs),

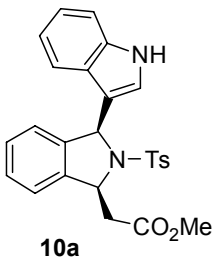


1090 (m), 990 (m), 844 (m), 807 (m), 784 (s), 768 (s), 724 (m), 668 (s), 617 (w), 587 (w), 554 (s), 476 (m) cm^{-1}; MS (CI, CH_4) *m/z* (%) 386.0 (2) [M^++1], 330.0 (100), 312.0 (98), 284.0 (31). HRMS (ESI-TOF) calcd. for $C_{21}H_{23}NO_4S$: 474.1613[M^+]; found: 474.1620.

Isoindoline Synthesis

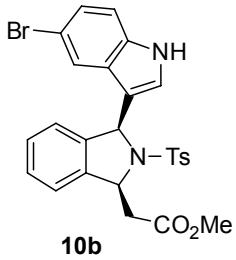
General procedure: To a solution of imine **9a-c** (0.29 mmol) and *N*-triflyl phosphoramide **7b-g** (0.029 mmol, 10 mol%) in CH_2Cl_2 (2.0 mL) were added 4 Å MS (10 beads, 0.12 – 0.14 g) and indole **8a-e** (0.873 mmol, 3.00 equiv). The reaction vessel was stoppered and stirred at rt for 10 to 90 min. DBU (22 μL, 0.15 mmol, 50 mol%) was added and the reaction mixture was stirred for an additional 15 min. The solvent was evaporated under reduced pressure and the crude product was purified by flash chromatography (2:1 pentane/ether, dry loaded) to afford isoindoline **10a-j**.

(1S,3S)-Methyl 2-(3-(1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10a**) was isolated after 25 min as a white solid (126 mg, 94%). The *e.r.* (95:5) was determined by HPLC on a chiral stationary phase [Chiralcel OD, *n*-heptane:*i*PrOH = 7:3, 1.0 mL/min), t_R = 6.82 min (major), 9.41 min (minor)]. M.p. 75°C; $[\alpha]^{20}_D$ = -63.3 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.71 (d, *J* = 8.2 Hz, 2H), 7.40 – 6.88 (m, 11H), 6.26 (s, 1H), 5.50 (dd, *J* = 4.2, 8.8 Hz, 1H), 3.77 (s, 3H), 3.34 (dd, *J* = 4.3, 16.1 Hz, 1H), 2.92 (dd, *J* = 8.8, 16.1 Hz, 1H), 2.34 (s, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.3, 143.3, 139.4, 138.6, 136.4, 134.6, 129.4, 128.2, 128.1, 127.4, 125.3, 124.5, 123.4, 122.5, 121.9, 119.6, 119.2, 116.7, 111.2, 62.7, 61.7, 51.8, 43.4, 21.4 ppm; IR (KBr) 3923 (w), 3893 (w), 3668 (w), 3396 (s), 3051 (w), 2950 (w), 2917 (w), 1732 (vs), 1598 (w), 1546 (w), 1488 (m), 1456 (s), 1436 (s), 1344 (s), 1303 (s), 1210 (w), 1161 (vs), 1094 (s), 1043 (s), 949 (w), 844 (w), 815 (m), 747 (s), 712 (m), 667 (s), 607 (m), 563 (s), 462 (m) cm^{-1}; MS (CI, CH_4) *m/z* (%) 461.2 (32) [M^++1], 344.1 (100). Anal. Calcd. for $C_{27}H_{28}N_2O_4S$: C, 68.04; H, 5.92; N, 5.88; found: C, 67.71; H, 5.63; N, 5.82.



10a

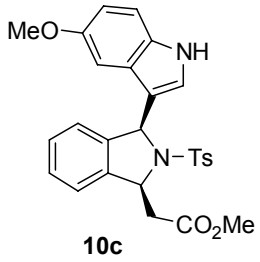
(1S,3S)-Methyl 2-(3-(5-bromo-1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10b**) was isolated after 35 min as a white solid (156 mg, 99%). The *e.r.* (94:6) was determined by HPLC on a chiral stationary phase (Chiralpak OD, *n*-heptane:*i*PrOH = 7:3, 0.5 mL/min), t_R = 13.05 min (major), 18.46 min (minor). M.p. 64°C; $[\alpha]^{20}_D$ -75.9 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.41 (s, 1H), 7.74 (d, *J* = 8.3 Hz, 2H), 7.36 – 7.10 (m, 9H), 6.98 (d, *J* = 7.6 Hz, 1H), 6.16 (s, 1H), 5.49 (dd, *J* = 4.5, 8.1 Hz, 1H), 3.79 (s, 3H), 3.37 (dd, *J* = 4.5, 16.0 Hz, 1H), 2.95 (dd, *J* = 8.2, 16.0 Hz, 1H), 2.35 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.5, 143.8, 139.3, 138.6, 135.2, 134.3, 129.8, 128.6, 128.5, 127.7, 127.1, 125.7, 124.9, 123.5, 122.7, 121.7, 116.6, 113.1, 113.0, 62.6, 62.0, 51.9, 43.6, 21.5 ppm; IR (KBr) 3397 (vs), 3039 (w), 2950 (w), 1724 (vs), 1597 (w), 1456 (s), 1354 (vs), 1306 (s), 1222 (s), 1169 (vs), 1092 (s), 1041 (s), 991 (w), 749 (m), 712 (m), 666 (s), 619 (m), 592 (m), 568 (s), 545 (s), 479 (w)



10b

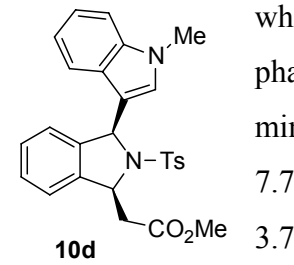
cm^{-1}; MS (EI) *m/z* (%) 538.1 (23) [M$^+$]. Anal. Calcd for $C_{26}H_{23}BrN_2O_4S$: C, 57.89; H, 4.30; N, 5.19; found: C, 57.80; H, 4.65; N, 4.94.

(1S,3S)-Methyl 2-(3-(5-methoxy-1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10c**) was isolated after 105 min as a white solid (133 mg, 93%). The *e.r.* (76:24) was determined by HPLC on a chiral stationary phase after reduction of the a sample of the ester **10c** with $LiAlH_4$ [(Chiralpak AD, *n*-heptane:*i*PrOH = 7:3, 1.0 mL/min), t_R = 11.50 min (major), 15.36 min (minor)]. M.p. 69°C; $[\alpha]^{20}_D$ = -47.2 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.72 (d, *J* = 8.1 Hz, 2H), 7.27 – 7.12 (m, 7H), 7.03 (d, *J* = 7.4 Hz, 1H), 6.77 (dd, *J* = 2.4, 8.8 Hz, 1H), 6.44 (d, *J* = 2.4 Hz, 1H), 6.26 (s, 1H), 5.49 (dd, *J* = 4.4, 8.8 Hz, 1H), 3.75 (s, 3H), 3.63 (s, 3H), 3.31 (dd, *J* = 16.0, 4.5 Hz, 1H), 2.90 (dd, *J* = 8.9, 15.9 Hz, 1H), 2.33 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.5, 153.9, 143.6, 139.6, 139.0, 135.0, 131.7, 129.6, 128.5, 128.3, 127.6, 125.9, 125.6, 123.8, 122.6, 116.2, 112.3, 112.2, 101.1, 62.9, 61.8, 55.5, 51.8, 43.5, 21.5 ppm; IR (KBr) 3399 (s), 2948 (m), 2830 (w), 1733 (vs), 1625 (m), 1587 (m), 1486 (s), 1441 (s), 1344 (s), 1305 (s), 1250 (w), 1216 (s), 1162 (vs), 1094 (s), 1035 (s), 921 (w), 807 (w), 753 (m), 705 (s), 668 (s), 630 (m), 567 (s), 459 (w) cm^{-1}; MS (EI) *m/z* 490.1 (79) [M$^+$], 491.1 (22) [M$^+$], 492.1 (8) [M$^+$], 335.1 (100) [M$^+$ – Ts]. Anal. Calcd for $C_{27}H_{26}N_2O_5S$: C, 66.10; H, 5.34; N, 5.71; found: C, 66.19; H, 5.73; N, 5.53.



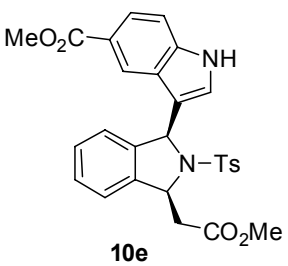
10c

(1S,3S)-Methyl 2-(3-(1-methyl-1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10d**) was isolated after 45 min as a white solid (119 mg, 86%). The *e.r.* (61:39) was determined by HPLC on a chiral stationary phase (Chiralpak IA, *n*-heptane:*i*PrOH = 8:2, 0.7 mL/min), t_R = 25.49 min (major), 27.98 min (minor). M.p. 62°C; $[\alpha]^{20}_D$ = -11.2 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.2 Hz, 2H), 7.36 – 6.87 (m, 11H), 6.25 (s, 1H), 5.50 (dd, *J* = 4.2, 8.8 Hz, 1H), 3.78 (s, 3H), 3.74 (s, 3H), 3.35 (dd, *J* = 4.2, 16.1 Hz, 1H), 2.93 (dd, *J* = 8.8, 16.1 Hz, 1H), 2.34 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.6, 143.4, 139.8, 138.8, 137.3, 135.0, 129.5, 129.3, 128.4, 128.2, 127.7, 126.0, 123.8, 123.7, 122.6, 121.6, 119.4, 115.2, 109.4, 62.7, 61.7, 51.8, 43.6, 32.8, 21.5 ppm; IR (KBr) 3926 (w), 3884 (w), 3819 (w), 3760 (w), 3710 (w), 3648 (w), 3591 (w), 3509 (m), 3418 (m), 3334 (w), 3265 (w), 3194 (w), 3053 (m), 2936 (m), 2891 (w), 2648 (w), 2430 (w), 2370 (w), 1735 (vs), 1600 (m), 1549 (m), 1470 (m), 1381 (s), 1346 (s), 1301 (m), 1248 (w), 1209 (w), 1162 (vs), 1093 (m), 1043 (s), 955 (w), 812 (m), 746 (s), 667 (s), 622 (m), 561 (s), 498 (w), 459 (w) cm^{-1}; MS (CI, CH_4) *m/z* (%) 474.2 (25) [M$^+$], 345.1 (22) [M$^+$ – *N*-Me-Ind.], 344.1 (100). HRMS (ESI-TOF) calcd. for $C_{27}H_{26}N_2O_4S$: 474.1613, found: 474.1613.



10d

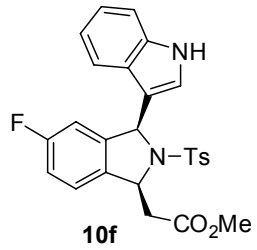
(1S,3S)-Methyl 2-(3-(5-methylcarboxylate-1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10e**) was isolated after 255 min as a white solid (107 mg, 71%). The *e.r.* (86:14) was determined by HPLC on a chiral stationary phase [(Chiralpak IA, *n*-heptane:*i*PrOH = 8:2, 0.7 mL/min), t_R = 28.10 min (major), 25.65 min (minor)]. M.p. 80°C; $[\alpha]^{20}_D$ = -101 (*c* = 1.0, $CHCl_3$); ^{1}H NMR



10e

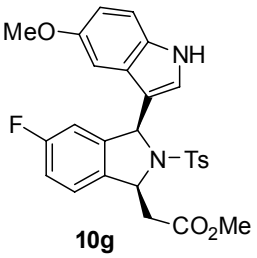
(400 MHz, $CDCl_3$) δ 8.50 (s, 1H), 8.04 (s, 1H), 7.75 (d, *J* = 8.2 Hz, 2H), 7.38 – 7.08 (m, 8H), 7.01 (d, *J* = 7.9 Hz, 1H), 6.23 (s, 1H), 5.52 (dd, *J* = 4.4, 8.3 Hz, 1H), 3.89 (s, 3H), 3.78 (s, 3H), 3.42 (dd, *J* = 4.4, 16.1 Hz, 1H), 3.02 (dd, *J* = 8.3, 16.1 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.4, 167.7, 143.6, 139.2, 138.9, 138.3, 134.1, 129.6, 128.3, 128.3, 127.8, 127.6, 125.2, 124.9, 123.2, 122.5, 122.0, 121.6, 118.6, 111.0, 62.5, 62.0, 51.8, 51.8, 43.5, 21.5. IR (KBr) 3980 (w), 3911 (w), 3862 (w), 3817 (w), 3751 (w), 3684 (w), 3600 (w), 3534 (w), 3437 (w), 3258 (w), 3193 (w), 3085 (w), 2925 (vs), 2857 (s), 2729 (w), 2560 (w), 2376 (w), 2364 (w), 2344 (m), 1724 (s), 1602 (s), 1448 (s), 1385 (m), 1323 (m), 1241 (s), 1162 (s), 1116 (m), 1054 (m), 849 (w), 757 (m), 718 (w), 669 (w), 632 (m), 547 (s), 468 (m) cm^{-1}; MS (CI, CH_4) *m/z* (%) 176.1 (100%) [MeO_2C-Indole +1], 344.2 (54%) [M+ -MeO_2C-Indole] 400.2 (11%). Anal. Calcd for $C_{27}H_{26}N_2O_4S$: C, 64.85; H, 5.05; N, 5.40; C, 64.71; H, 5.12; N, 5.20.

(1S,3S)-Methyl 2-(5-fluoro-3-(1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10f**) was isolated after 45 min as a white solid (104 mg, 75%). The *e.r.* (91:9) was determined by HPLC on a chiral stationary phase (Chiralpak OD, *n*-heptane:*i*PrOH = 7:3, 0.7 mL/min), t_R = 10.07 min (major), 14.01 min (minor). M.p. 96°C; $[\alpha]^{20}_D$ -59.1 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.23 (s, 1H), 7.73 – 7.64 (m, 2H), 7.38 – 7.09 (m, 7H), 7.05 – 6.88 (m, 2H), 6.70 (dd, *J* = 2.0, 8.5 Hz, 1H), 6.21 (s, 1H), 5.45 (dd, *J* = 4.0, 8.6 Hz, 1H), 3.76 (s, 3H), 3.33 (dd, *J* = 4.1, 16.3 Hz, 1H), 2.91 (dd, *J* = 8.9, 16.3 Hz, 1H), 2.34 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.4, 162.9 (d, *J* = 246.4 Hz), 143.6, 141.8 (d, *J* = 8.4 Hz), 136.6, 134.6, 134.3, 129.6, 127.6, 125.2, 124.8, 124.2 (d, *J* = 9.2 Hz), 122.2, 119.9, 119.1, 116.0, 115.8 (d, *J* = 23.7 Hz), 111.5, 110.6 (d, *J* = 22.9 Hz), 62.7, 61.4, 52.0, 43.5, 21.6; IR (KBr) 3398 (s), 3062 (w), 2952 (w), 2856 (w), 2369 (w), 2345 (s), 1731 (vs), 1618 (m), 1546 (w), 1493(s), 1437 (s), 1342 (s), 1306 (m), 1249 (m), 1162 (vs), 1095 (s), 1040 (m), 1014 (m), 943 (w), 876 (w), 820 (m), 746 (s), 706 (m), 673 (s), 588 (m), 552 (s), 486 (w) cm^{-1}; MS (EI) *m/z* (%) 478.1 (29) [M^+], 323.2 (89) [M^+ – Ts], 117.0 (100). Anal. calcd. for $C_{26}H_{23}FN_2O_4S$: C, 65.26; H, 4.84; N, 5.85; found: C, 64.93; H, 4.95; N, 5.76.



10f

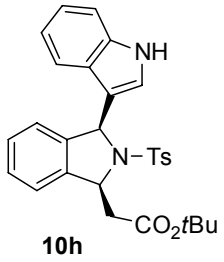
(1S,3S)-Methyl 2-(5-fluoro-3-(5-methoxy-1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10g**) was isolated after 75 min as a white solid (141 mg, 95%). The *e.r.* (88:12) was determined by HPLC on a chiral stationary phase after reduction of the ester with $LiAlH_4$ (Chiralpak AD, *n*-heptane:*i*PrOH = 7:3, 1.0 mL/min), t_R = 12.41 min (major), 18.89 min (minor). M.p. 72°C; $[\alpha]^{20}_D$ = -60.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.32 (s, 1H), 7.70 (d, *J* = 8.0 Hz, 2H), 7.24 – 7.14 (m, 4H), 7.11 (d, *J* = 2.6 Hz, 1H), 6.93 (td, *J* = 1.9, 8.3 Hz, 1H), 6.78 (dd, *J* = 2.4, 8.9 Hz, 1H), 6.70 (dd, *J* = 2.2, 8.4 Hz, 1H), 6.55 (d, *J* = 2.1 Hz, 1H), 6.21 (s, 1H), 5.44 (dd, *J* = 4.1, 8.9 Hz, 1H), 3.74 (s, 3H), 3.67 (s, 3H), 3.30 (dd, *J* = 4.2, 16.1 Hz, 1H), 2.89 (dd, *J* = 9.0, 16.1 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.5, 163.1 (d, *J* = 246.5 Hz), 154.0, 143.8, 142.0 (d, *J* =



10g

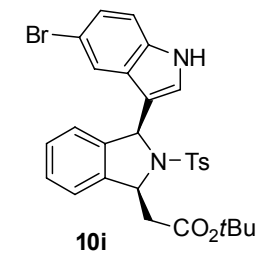
8.3 Hz), 134.7, 134.5, 131.7, 129.7, 127.6, 125.7, 125.6, 124.2 (d, J = 8.9 Hz), 115.7 (d, J = 23.4 Hz), 115.4, 112.3, 112.3, 110.8 (d, J = 23.4 Hz), 101.0, 62.7, 61.3, 55.6, 51.9, 43.4, 21.5; IR (KBr) 3402 (s), 2947 (s), 2344 (w), 1733 (vs), 1612 (s), 1545 (w), 1489 (vs), 1442 (s), 1345 (s), 1307 (m), 1250 (m), 1217 (s), 1163 (vs), 1095 (s), 1041 (s), 938 (s), 813 (s), 706 (w), 671 (s), 555 (m), 466 (m); MS (CI, CH_4) *m/z* (%) 508.2 (26) [M^+], 363.2 (20), 362.1(100) [M^+ – MeO-Ind], 148.2 (46), 147.2 (35) [MeO-Ind]. HRMS (ESI-TOF) calcd. for $C_{27}H_{25}FN_2O_5S$: 508.1468; found 508.1466.

(1S,3S)-t-Butyl 2-(3-(1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10h**) was isolated after 45 min as a white solid (109 mg, 75%). The *e.r.* (88:12) was determined by HPLC on a chiral stationary phase (Chiralcel OD, *n*-heptane:*i*PrOH = 7:3, 0.5 mL/min), t_R = 11.26 min (major), 13.73 min (minor). M.p. 64°C; $[\alpha]^{20}_D$ -27.7 (c = 0.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.73 (d, J = 8.3 Hz, 2H), 7.38 – 6.82 (m, 11H), 6.23 (s, 1H), 5.47 (dd, J = 3.7, 9.5 Hz, 1H), 3.33 (dd, J = 3.7, 16.2 Hz, 1H), 2.80 (dd, J = 9.5, 16.2 Hz, 1H), 2.33 (s, 3H), 1.52 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 143.2, 139.4, 139.0, 136.4, 134.5, 129.4, 128.0, 127.5, 126.3, 125.8, 125.3, 124.5, 123.3, 122.5, 121.8, 119.2, 116.8, 111.2, 81.1, 62.7, 61.8, 44.8, 28.1, 21.4; IR (KBr) 3963 (m), 3906 (m),3860 (m), 3823 (m), 3763 (m), 3713 (w), 3654 (m), 3626 (w), 3586 (w), 3430 (s), 3298 (m), 3187 (m), 3087 (w), 3050 (w), 2924 (vs), 2853 (s), 2755 (w), 2720 (m), 2592 (w), 2459 (w), 2372 (m), 2345 (m), 2331 (w), 2313 (w), 2280 (m), 2120 (w), 2724 (s), 1601 (s), 1503 (w), 1460 (m), 1385 (s), 1330 (m), 1239 (m), 1162 (vs), 1116 (m), 1050 (m), 958 (w), 894 (w), 856 (w), 825 (w), 763 (s), 722 (s), 634 (s), 550 (s), 484 (vs) cm^{-1}; MS (CI, CH_4) *m/z* (%) 502.1 (4) [M^+], 285.1 (21), 117 (100) [Ind]. HRMS (ESI-TOF) calcd. for $C_{29}H_{30}N_2O_4S$: 502.1926; found 502.1926.



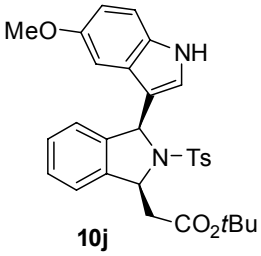
10h

(1S,3S)-t-Butyl-2-(3-(5-bromo-1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10i**) was isolated after 25 min as a white solid (144 mg, 85%). The *e.r.* (91:9) was determined by HPLC on a chiral stationary phase [(Chiralpak AD, *n*-heptane:*i*PrOH = 7:3, 0.7 mL/min), t_R = 8.08 min (major), 8.98 min (minor)]. M.p. 72°C; $[\alpha]^{20}_D$ = -70.3 (c = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.43 (s, 1H), 7.74 (d, J = 8.3 Hz, 2H), 7.35 – 7.12 (m, 9H), 6.98 (d, J = 7.7 Hz, 1H), 6.15 (s, 1H), 5.45 (dd, J = 3.9, 9.3 Hz, 1H), 3.35 (dd, J = 3.9, 16.1 Hz, 1H), 2.81 (dd, J = 9.2, 16.1 Hz, 1H), 2.35 (s, 3H), 1.52 (s, 9H); ^{13}C NMR (75 MHz, CDCl3) δ 170.4, 143.7, 139.3, 139.1, 135.1, 134.5, 129.7, 128.4, 127.7, 127.2, 125.8, 125.6, 124.9, 123.4, 122.8, 121.8, 117.0, 113.1, 112.8, 81.3, 62.4, 62.0, 44.8, 28.2, 21.5; IR (KBr) 3377 (m), 2976 (m), 2925 (m), 2858 (w), 1723 (s), 1647 (w), 1598 (w), 1458 (s), 1345 (s), 1304 (m), 1253 (w), 1223 (w), 1159 (vs), 1095 (s), 1046 (s), 958 (w), 884 (m), 802 (m), 752 (m), 666 (s), 623 (w), 565 (s), 486 (w) cm^{-1}; MS (EI) *m/z* (%) 580.1 (4) [M^+], 523.0 (14) [M^+ – *t*-Bu], 465.0 (25) [M^+ – CH_2CO_2t-Bu], 425.0 (27) [M^+ – Ts], 369.1 (100). Anal. Calcd for $C_{29}H_{29}BrN_2O_4S$: C, 59.90; H, 5.03; N, 4.82; found: C, 60.29; H, 5.43; N, 4.65.



10i

(1S,3S)-t-Butyl-2-(3-(5-methoxy-1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10j**) was isolated after 85 min as a white solid (150 mg, 97%). The *e.r.* (90:10) was determined by HPLC on a chiral stationary phase [(Chiralpak IA, *n*-heptane:*i*PrOH = 8:2, 1.0 mL/min), t_R = 17.64 min (major), 20.99 min (minor)]. M.p. 70°C; $[\alpha]^{20}_D$ = -48.2 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.76 (d, *J* = 8.2 Hz, 2H), 7.31 – 7.12 (m, 7H), 7.03 (d, *J* = 7.6 Hz, 1H), 6.78 (dd, *J* = 2.4, 8.8 Hz, 1H), 6.47 (s, 1H), 6.24 (s, 1H), 5.46 (dd, *J* = 3.8, 9.7 Hz, 1H), 3.64 (s, 3H), 3.28 (dd, *J* = 4.0, 16.2 Hz, 1H), 2.80 (dd, *J* = 9.7, 16.1 Hz, 1H), 2.33 (s, 3H), 1.50 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 153.6, 143.2, 139.3, 139.2, 134.7, 131.5, 129.4, 128.1, 128.0, 127.4, 125.3, 123.5, 122.5, 116.2, 112.2, 111.9, 100.9, 81.1, 62.7, 61.8, 55.4, 44.7, 28.1, 21.4; IR (KBr) 3397 (s), 3042 (w), 2975 (m), 2932 (m), 2831 (w) 1722(s), 1625 (w), 1588 (m), 1546 (w), 1485 (s), 1459 (s), 1345 (s), 1305 (s), 1252 (w) 1219 (s), 1158 (vs), 1095 (s), 1038 (s), 959 (w), 925 (w), 808 (m), 753 (w), 706 (w), 668 (s), 630 (w), 563 (s), 469 (w) cm^{-1}; MS (CI, CH_4) m/z (%) 532.2 (2) [M+], 385.1 (25) [M^+ – MeO-Ind], 330.1 (52), 286.2 (64), 148.2 (100), 147.2 (76) [MeO-Ind + 1]. HRMS (ESI-TOF) calcd. for for $C_{29}H_{30}N_2O_4S$: 532.2032, found: 532.2032.

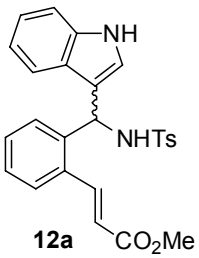


10j

Stereoablative Kinetic Resolution

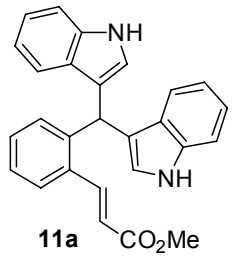
General procedure: To a solution of imine **9a-c** (0.29 mmol) and *N*-triflyl phosphoramide **7b-g** (0.029 mmol, 10 mol%) in PhCl (2.0 mL) were added 4 Å MS (10 beads, 0.12 – 0.14 g) and indole **8a-e** (0.437 mmol, 1.50 equiv). The reaction vessel was stoppered and stirred at rt for 16 h to 10 d. The resulting suspension was dissolved in CH_2Cl_2:MeOH (2:1) and concentrated onto silica gel (~10 g). The bis-indole byproduct **11** was then removed by flash chromatography (1:1 EtOAc/pentane, dry loaded). The 1,2-adduct **12** was suspended in CH_2Cl_2 (5 mL) and DBU (22 μL, 0.15 mmol) was added. After 15 min, the resultant solution was evaporated under reduced pressure and the crude product was purified by flash chromatography (2:1 pentane/ether, dry loaded) to afford isoindoline **10a-j**.

(S,E)-methyl 3-(2-((1H-indol-3-yl)(p-tosylamido)methyl)phenyl)acrylate (**12a**). White solid. M.p. 154°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (br s, 1H), 7.90 (d, *J* = 15.8 Hz, 1H), 7.55 (d, *J* = 8.3 Hz, 2H), 7.49 – 7.36 (m, 2H), 7.31 – 7.07 (m, 7H), 7.05 – 6.97 (m, 1H), 6.55 (dd, *J* = 2.6, 0.7 Hz, 1H), 6.16 (d, *J* = 5.8 Hz, 1H), 6.14 (d, *J* = 15.8 Hz, 1H), 5.15 (d, *J* = 6.2 Hz, 1H), 3.70 (s, 3H), 2.36 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.8, 143.2, 141.5, 139.1, 137.2, 136.5, 132.8, 129.8, 129.3, 127.9, 127.7, 127.2, 127.0, 125.2, 124.2, 122.7, 120.5, 120.2, 119.1, 115.6, 111.3, 51.9, 51.7, 21.5 ppm; IR (KBr) 3352 (vs), 3233 (s), 3048 (w), 2947 (w), 2864 (w), 1706 (vs), 1634 (s), 1485 (m), 1438 (s), 1316 (vs), 1198 (s), 1157 (vs), 1093 (s), 1064 (m), 1036 (m), 975 (w), 930 (m), 871 (w), 812 (m), 767 (m), 738 (s), 672 (s), 606 (m), 563 (s) cm^{-1}; MS (EI) *m/z* (%) 460.1 (2) [M^+], 91.1 (100). Anal. Calcd for $C_{26}H_{24}N_2O_4S$: C, 67.81; H, 5.25; N, 6.08; found: C, 67.78; H, 5.11; N, 6.03.



12a

(E)-methyl 3-(2-(di(1H-indol-3-yl)methyl)phenyl)acrylate (**11a**). White solid. M.p. 137°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.24 (d, J = 15.8 Hz, 1H), 7.94 (br s, 2H), 7.61 – 7.56 (m, 1H), 7.38 – 7.30 (m, 4H), 7.25 – 7.22 (m, 3H), 7.20 – 7.13 (m, 2H), 7.03 – 7.96 (m, 2H), 6.64 (dd, J = 0.9, 2.3 Hz, 2H), 6.32 (d, J = 15.8 Hz, 1H), 6.20 (br s, 1H), 3.69 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.3, 143.0, 142.9, 136.7, 133.4, 129.9, 129.4, 126.9, 126.7, 124.1, 122.0, 119.9, 119.5, 119.3, 118.7, 111.0, 51.6, 36.7 ppm; IR (KBr) 3965 (w), 3912 (m), 3884 (m), 3822 (m), 3773 (w), 3749 (w), 3696 (w), 3656 (w), 3600 (w), 3574 (w), 3410 (s), 3241 (w), 3050 (w), 2962 (m), 2909 (w), 2848 (w), 2769 (w), 2711 (w), 2346 (w), 2330 (w), 1703 (s), 1627 (m), 1455 (s), 1432 (m), 1385 (s), 1321 (m), 1263 (s), 1201 (m), 1171 (m), 1094 (vs), 1025 (s), 929 (w), 866 (m), 802 (vs), 743 (s), 609 (w), 562 (w), 502 (w), 466 (s) cm^{-1}; MS (CI, Isobutane) *m/z* (%) 407.2 (2) [M^++1], 344.1 (79.2), 172.0 (100). HRMS (ESI-TOF) calcd. for $C_{26}H_{24}N_2O_4S$: 406.1681, found: 406.1682.



11a

Single-Crystal X-ray Structure Determination

Crystals of isoindoline **10i** were obtained by evaporation of ether/*n*-hexane at room temperature. Bruker Smart APEX CCD detector (Mo-K_α radiation, λ= 0.71073 Å, graphite monochromator), D8 goniometer. Integration with SAINT,[4] structure solution by direct methods,[5] refinement on F^2.[6] Non-hydrogen atoms were refined anisotropically. Hydrogen atoms were found on the electron density map and freely refined. Absolute configuration was confirmed by evaluation of the Flack[7] parameter.

Crystal data for **10i**: Monoclinic space group $P2_1$, a = 11.7438(9), b= 18.1747(13), c = 12.7115(9), β= 93.0170(10), V = 2709.4(3), Z = 2, T = 100 K. 841 parameters, 13510 independent out of 55615 reflections, $R1$ = 0.0286, $wR2$ = 0.0637, GOF = 0.994, Flack parameter 0.001(3). Crystallographic data for the structure has been deposited at the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 682470. Copies of the data can be obtained free of charge on application to The Director, CCDC, 12 Union Road, Cambridge, CB21EZ, UK (fax: int. code + (1223) 336-033; e-mail: deposit@ccdc.cam.ac.uk; web, www: http://www.ccdc.cam.ac.uk).

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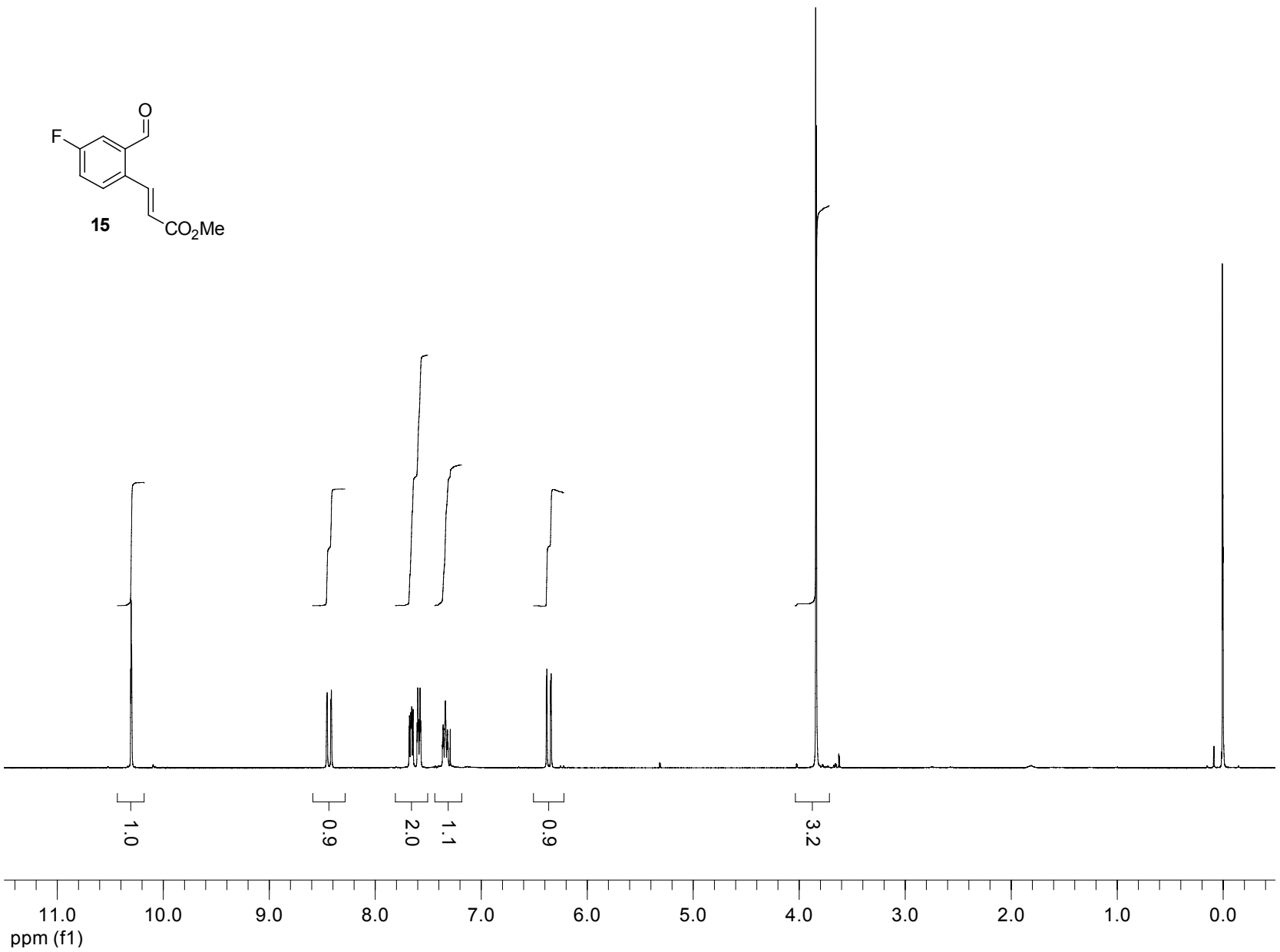


Figure S1. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of (*E*)-methyl 3-(4-fluoro-2-formylphenyl)acrylate (**15**).

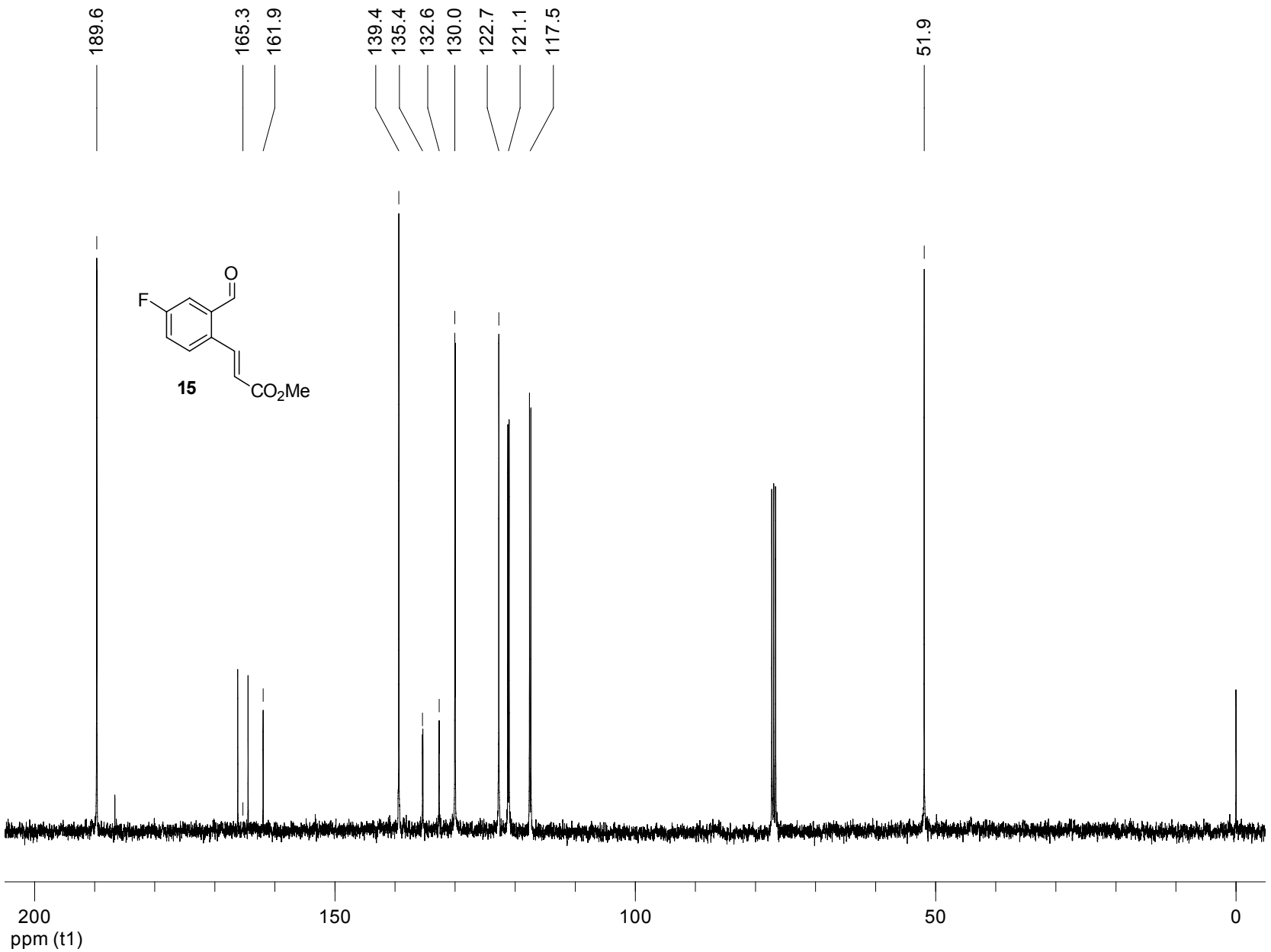


Figure S2. ^{13}C NMR spectrum ($CDCl_3$, 101 MHz) of (*E*)-methyl 3-(4-fluoro-2-formylphenyl)acrylate (**15**).

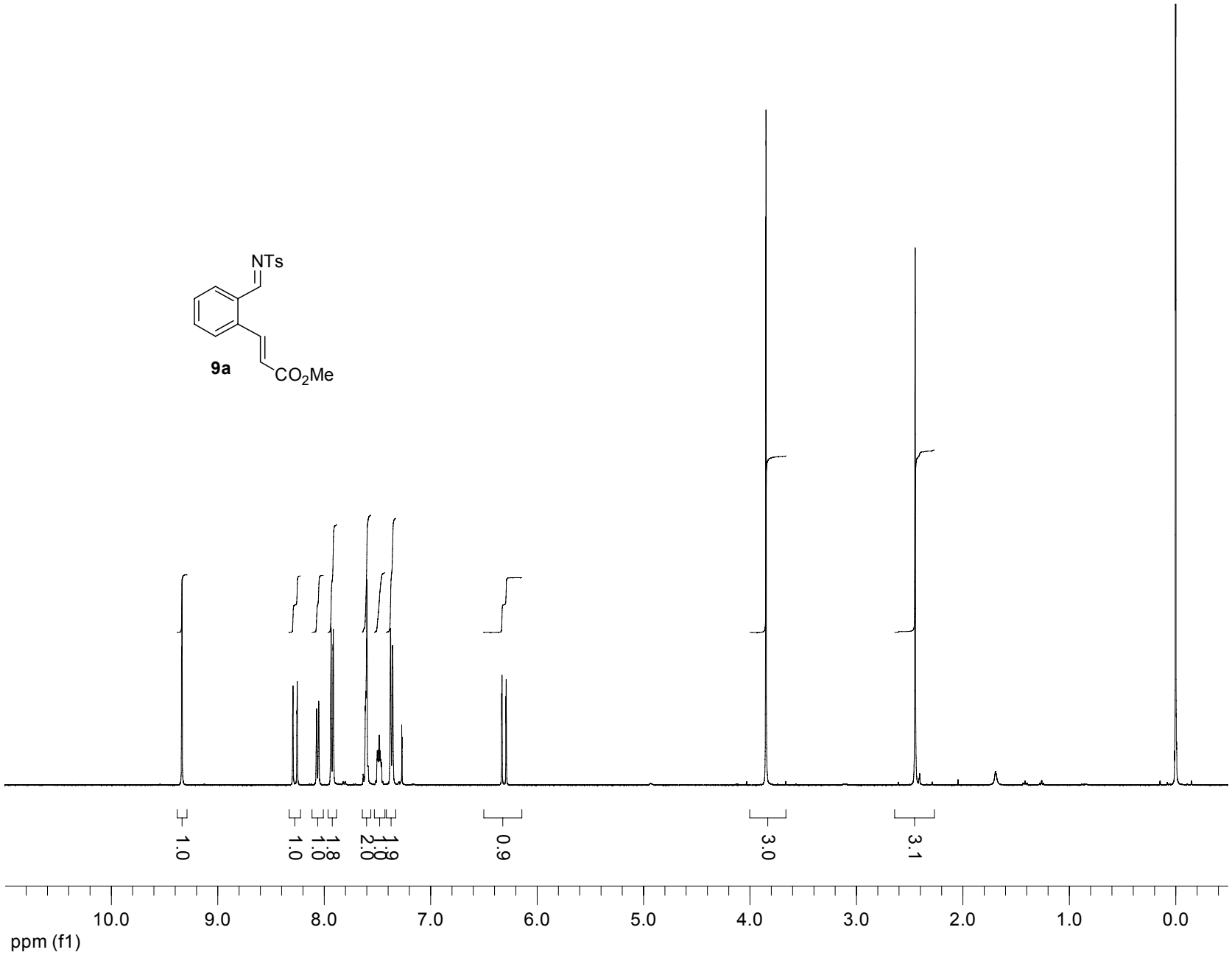


Figure S3. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of (*E*)-methyl 3-(2-((tosylimino)methyl)phenyl)acrylate (**9a**).

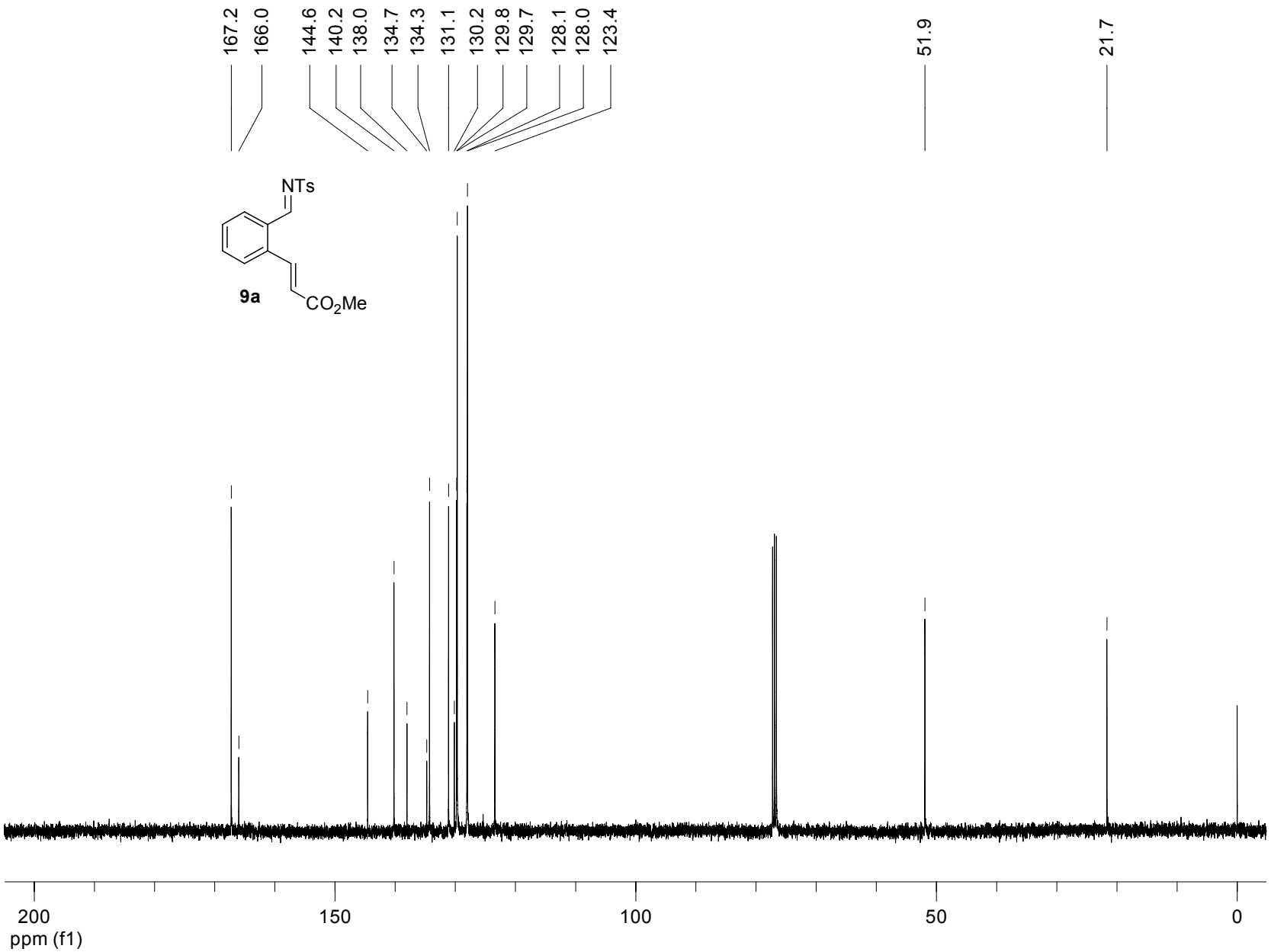


Figure S4. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum of (*E*)-methyl 3-(2-((tosylimino)methyl)phenyl)acrylate (**9a**).

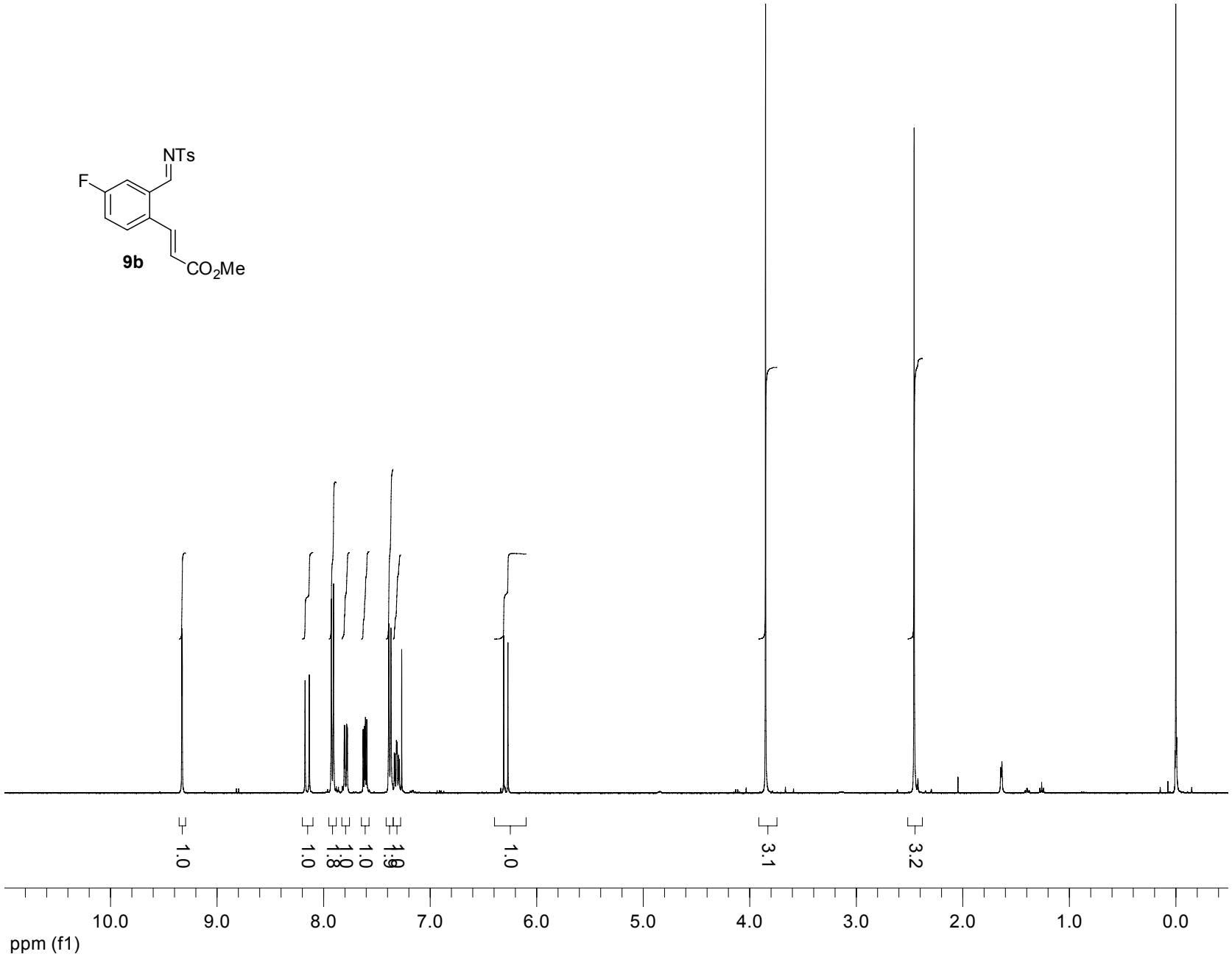


Figure S5. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of (*E*)-methyl 3-(4-fluoro-2-((tosylimino)methyl)phenyl)acrylate (**9b**).

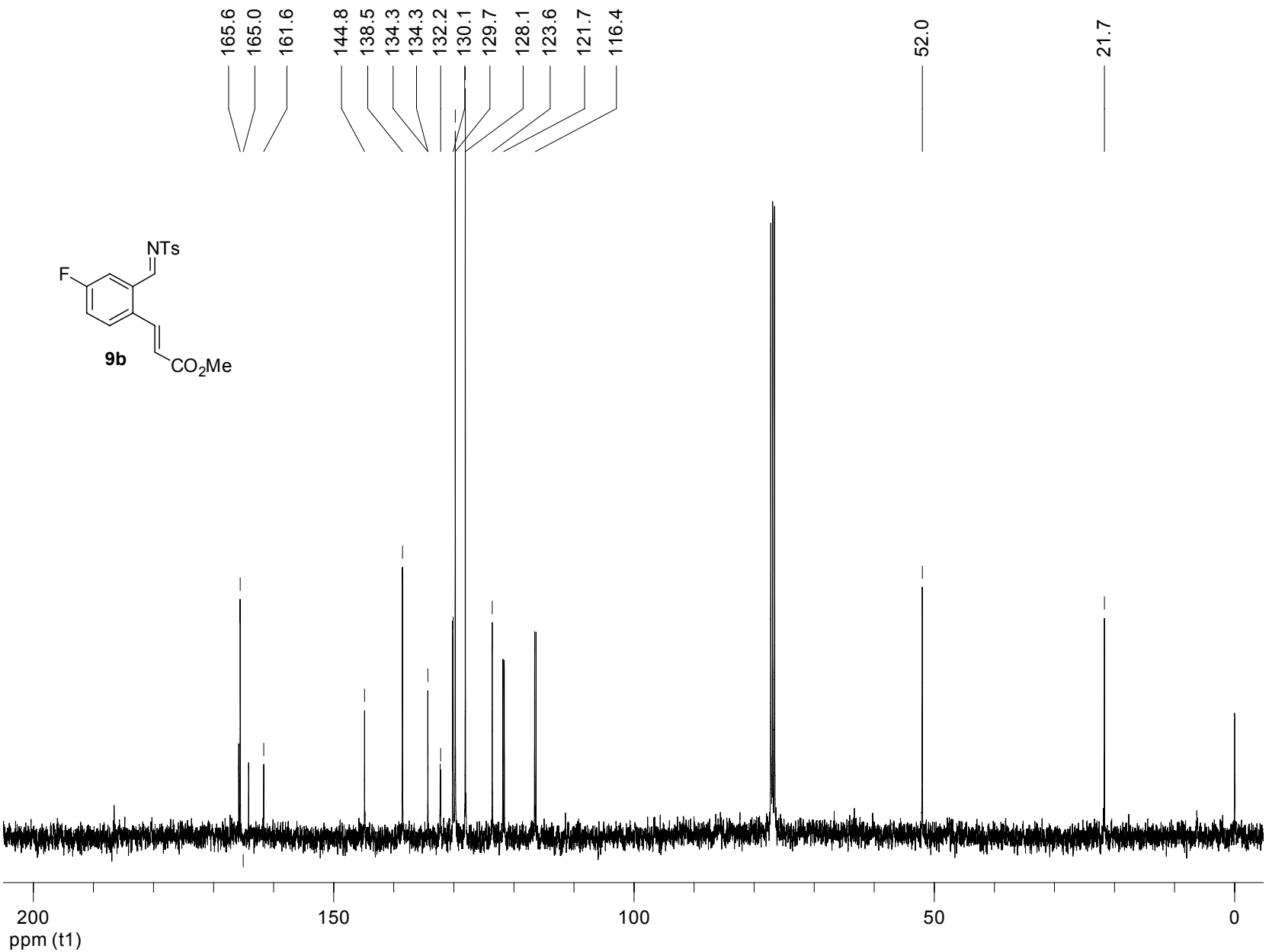


Figure S6. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum of (*E*)-methyl 3-(4-fluoro-2-((tosylimino)methyl)phenyl)acrylate (**9b**).

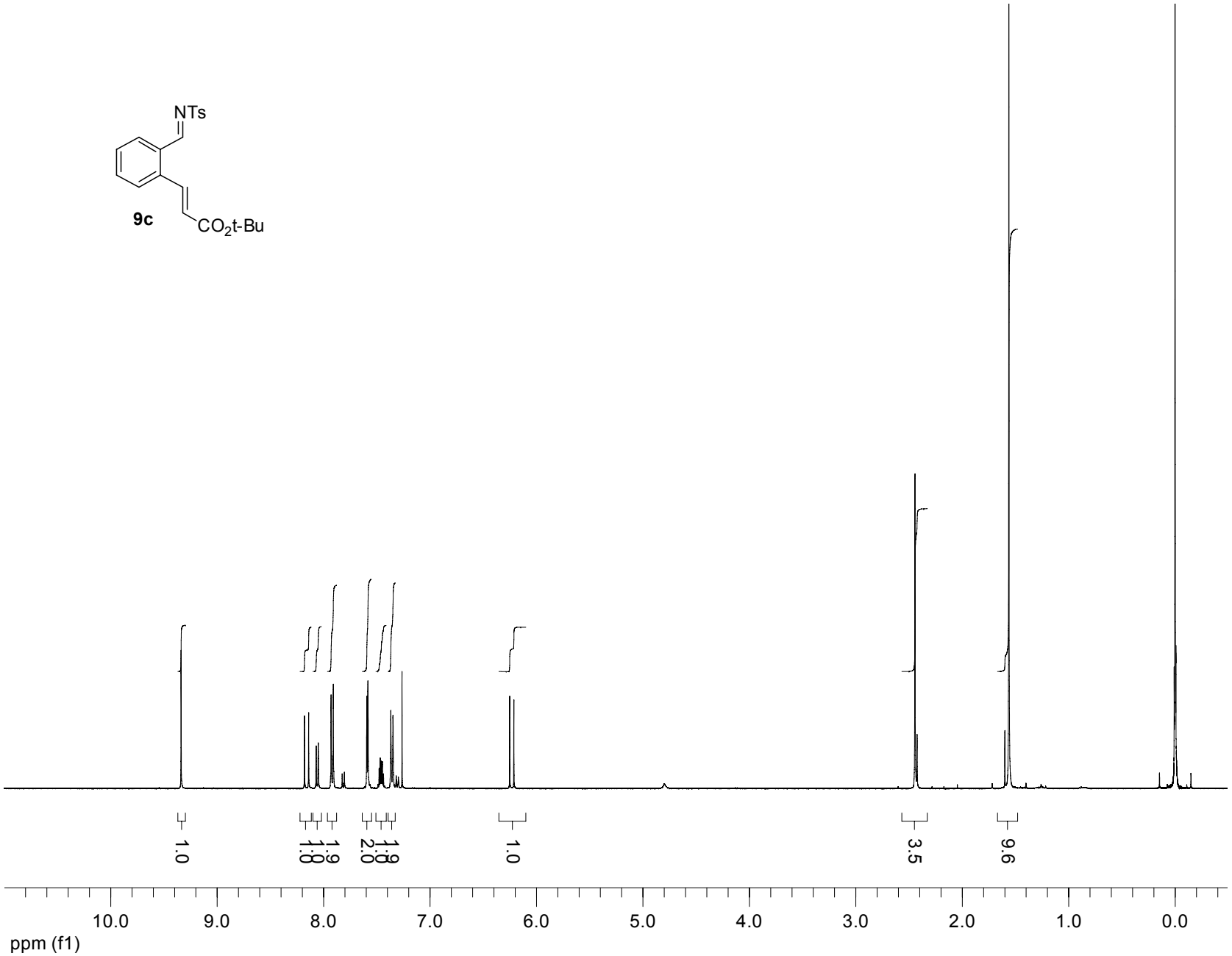


Figure S7. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of (*E*)-*t*-butyl 3-(2-((tosylimino)methyl)phenyl)acrylate (**9c**).

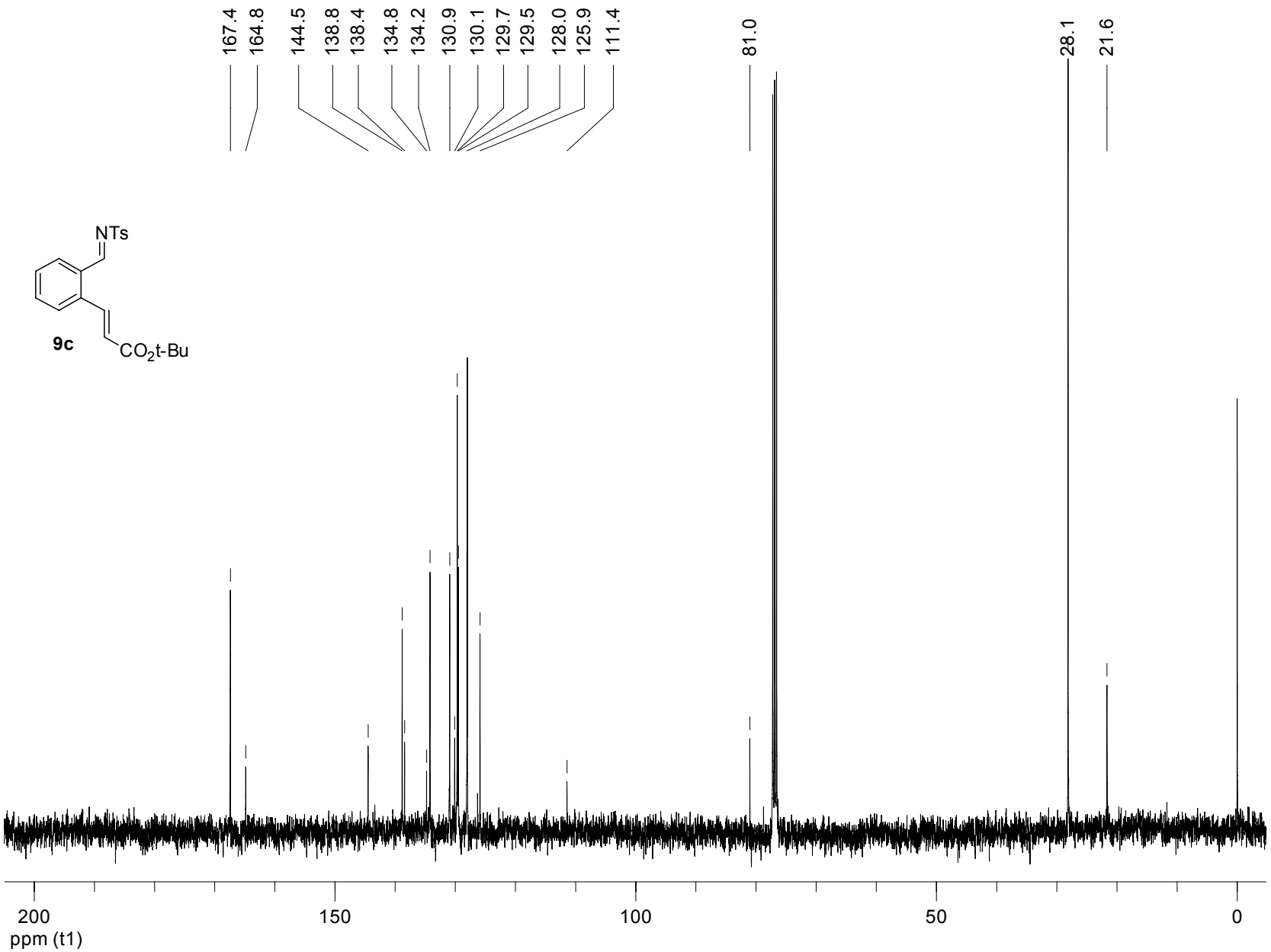


Figure S8. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum of (*E*)-*t*-butyl 3-(2-((tosylimino)methyl)phenyl)acrylate (**9c**).

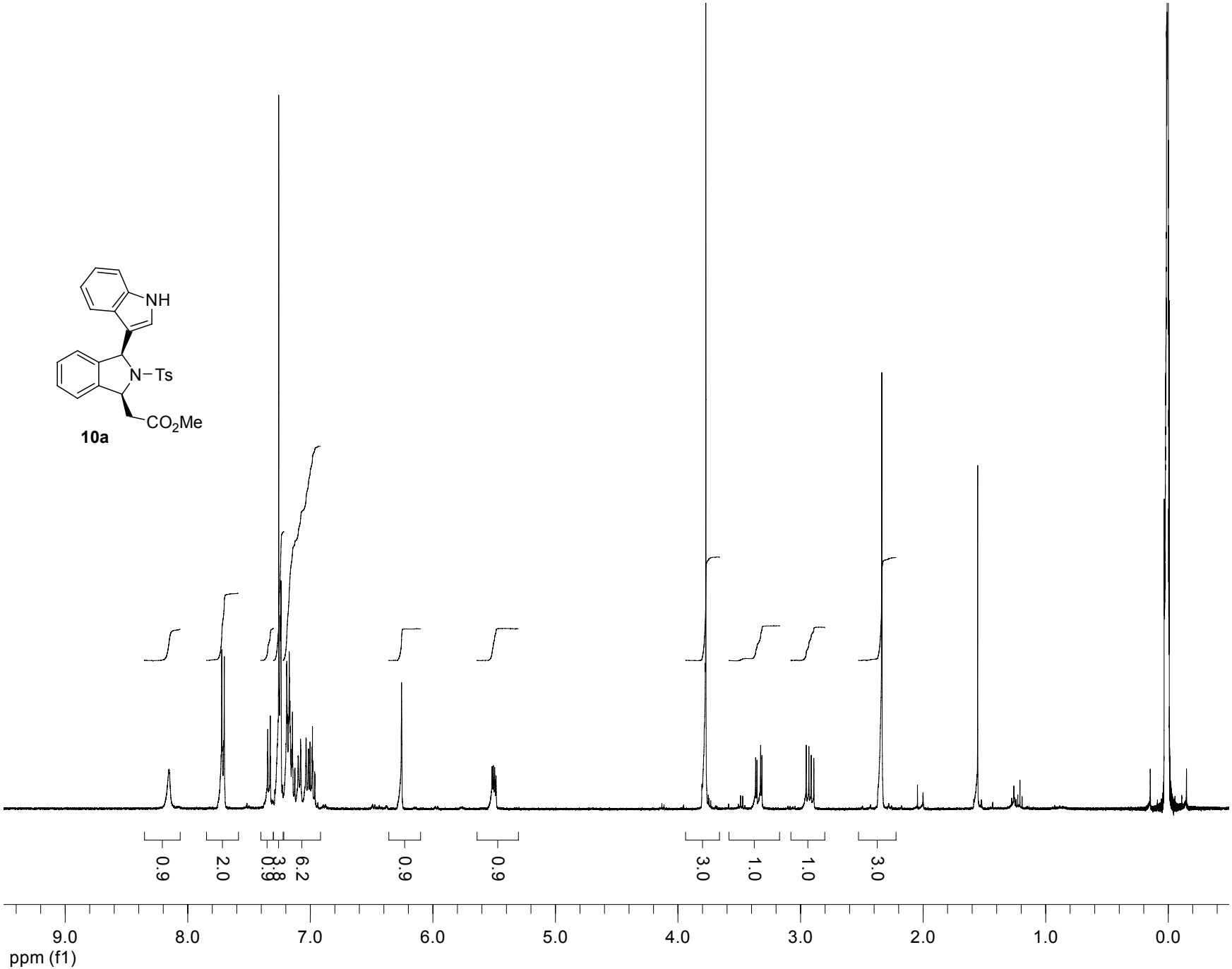


Figure S9. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of (1*S*,3*S*)-methyl 2-(3-(1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10a**).

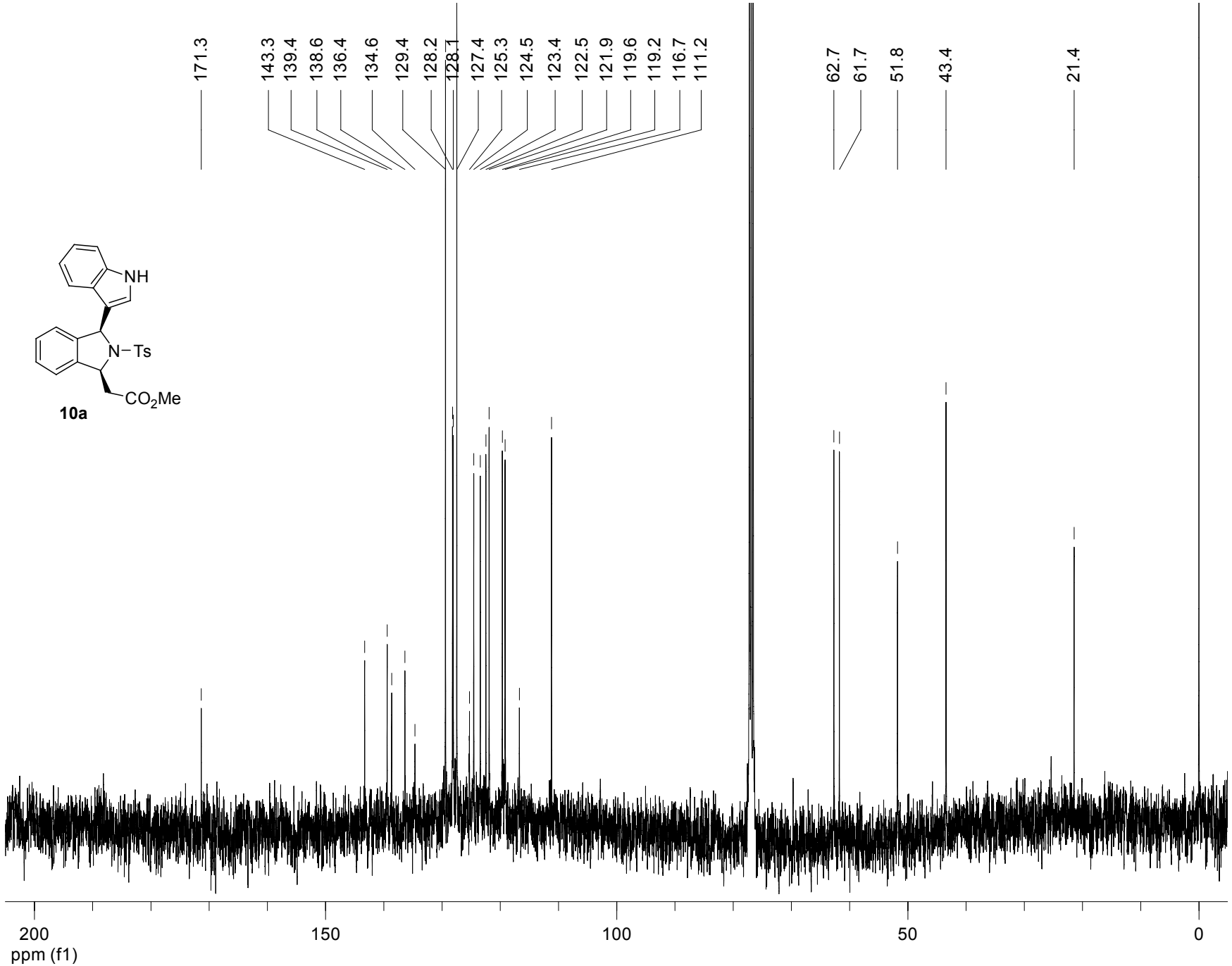
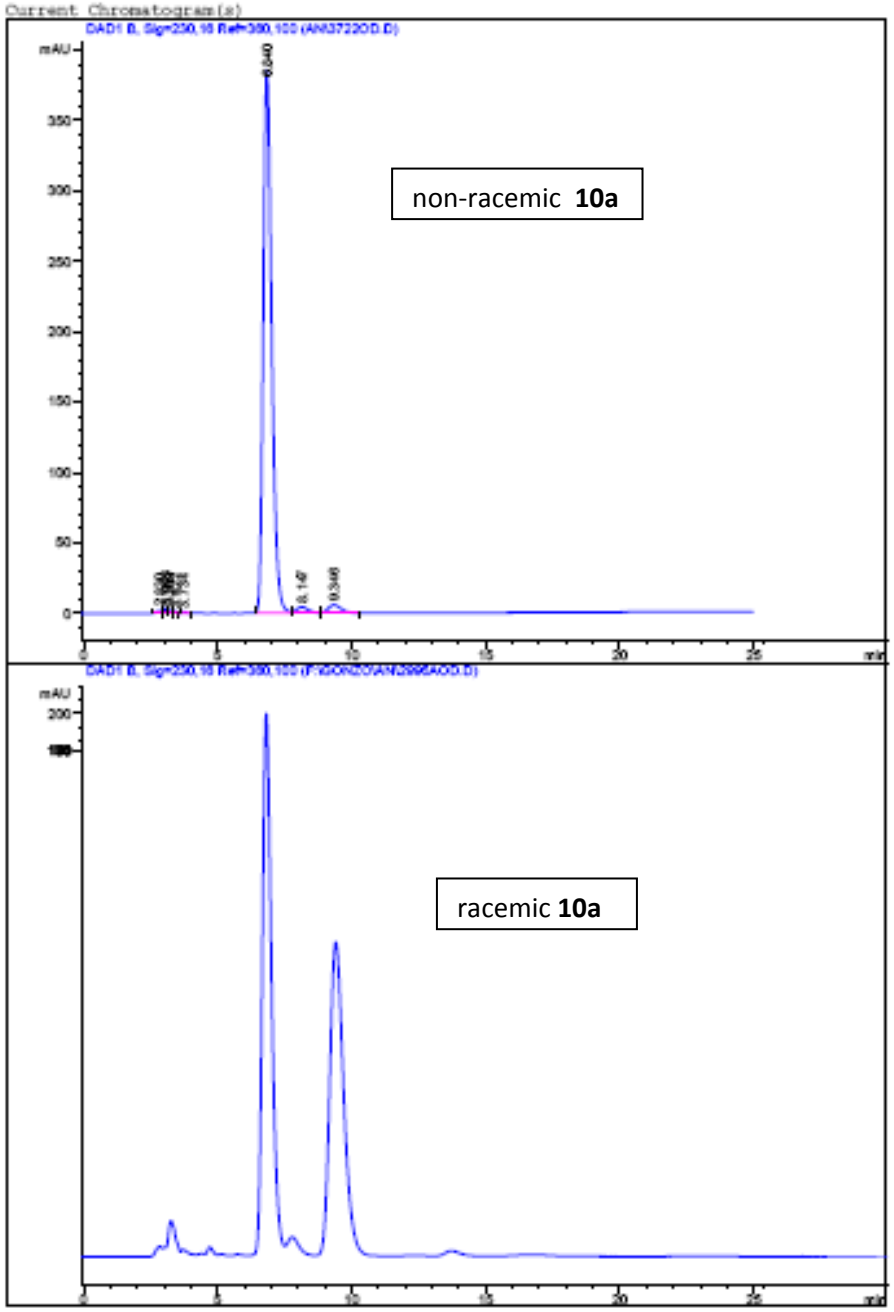


Figure S10. ^{13}C NMR spectrum (101 MHz, $CDCl_3$) of (1*S*,3*S*)-methyl 2-(3-(1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10a**).



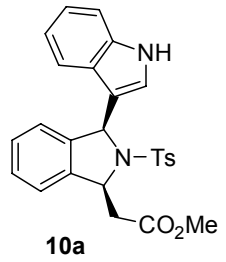
AK Enders - Analytische HPLC

Sample Name: AN 3722
Data file: D:\GONZO\AN\3722OD.D
Sample Info: Laufmittel: n-Heptan/IP 9:1;
Probe in LM gelöst

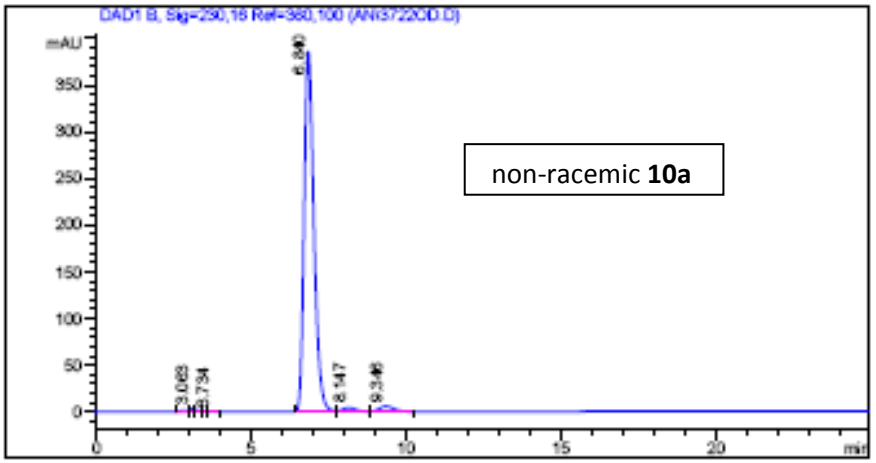
Säule: DAICELOD.M
Säuleninfo: (250x4)mm
Operator: Analytik Labor AKEN

Injektion Time: 09:34:20
Injektion Date: 14.02.2008

Instrument Conditions:	At Start	At Stop
Temperature in°C:	30.0°C	30.0°C
Pressure in bar:	42.4	43.1
Flow in ml/min:	1.0	1.0



10a



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	2.83	0.20	1.63	23.91	0.27
2	3.06	0.09	3.32	21.23	0.24
3	3.21	0.13	2.12	20.55	0.23
4	3.42	0.10	1.35	9.23	0.10
5	3.73	0.16	0.92	9.67	0.11
6	6.84	0.34	385.76	8453.29	95.34
7	8.15	0.47	4.33	131.13	1.48
8	9.35	0.51	5.84	197.21	2.22
Total				8866.21	100.00

Figure S11. HPLC traces of **10a**; overlay of racemic and non-racemic (left), non-racemic (right, Table 4, entry 1).

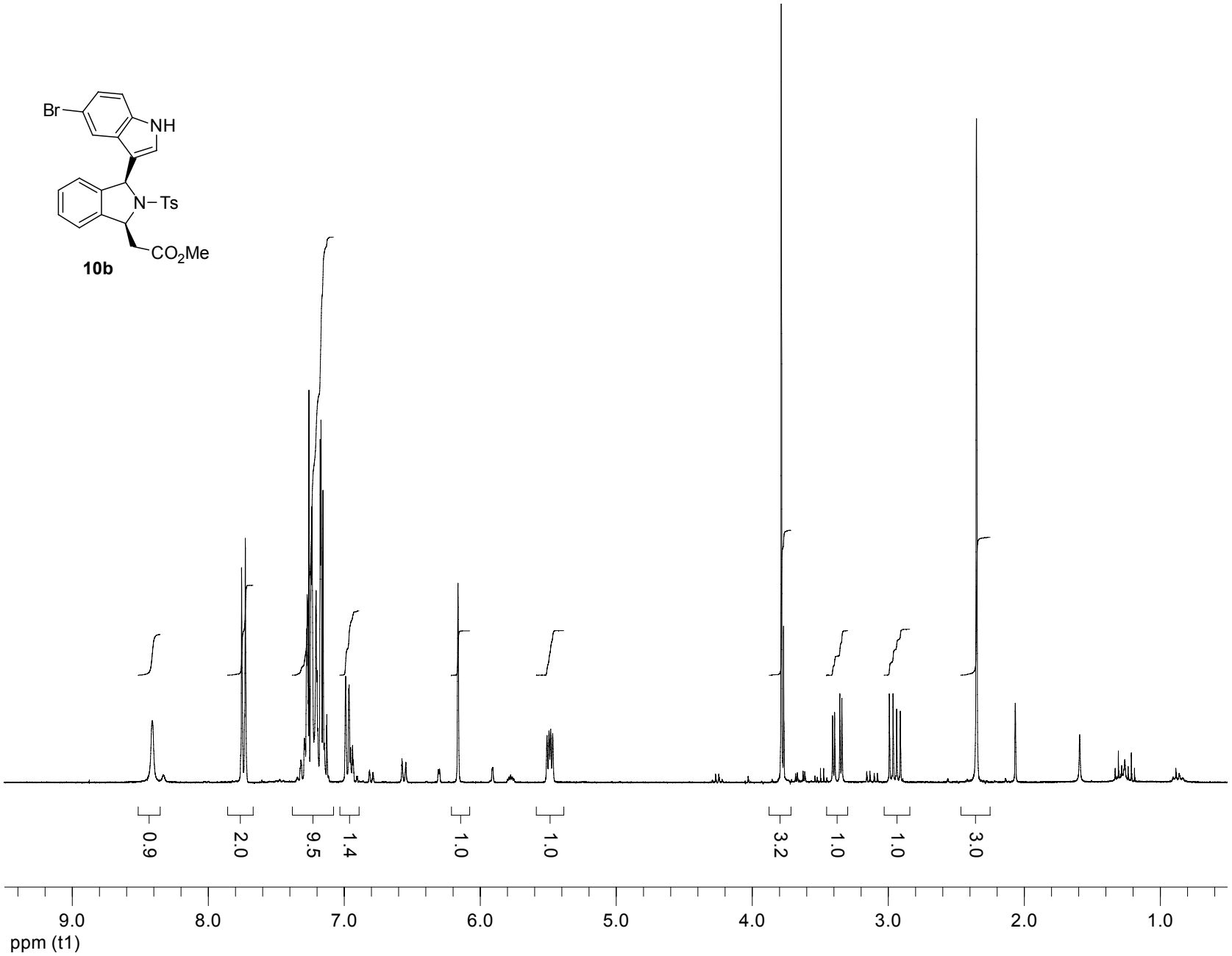


Figure S12. ^{1}H NMR spectrum of (1*S*,3*S*)-methyl 2-(3-(5-bromo-1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10b**).

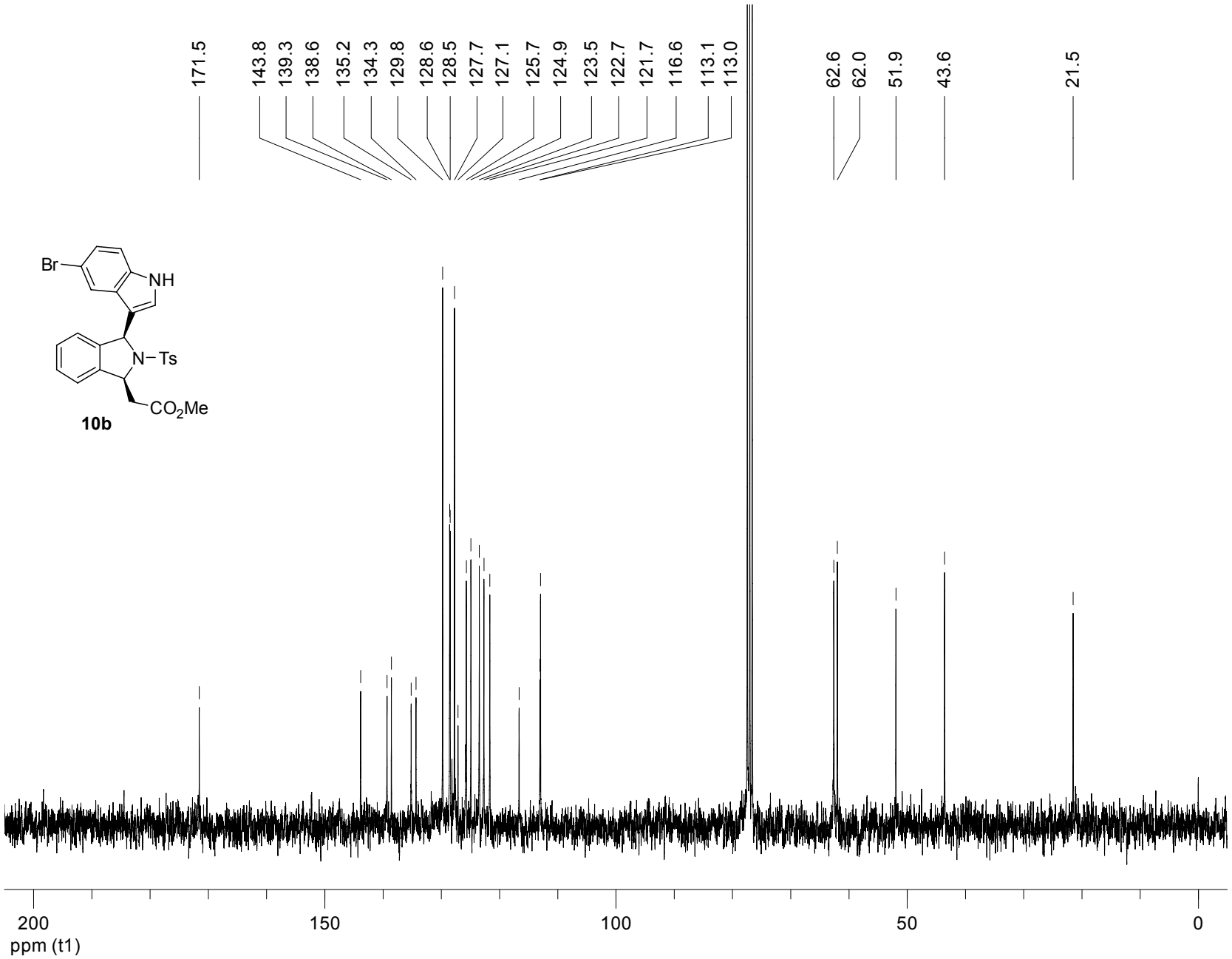
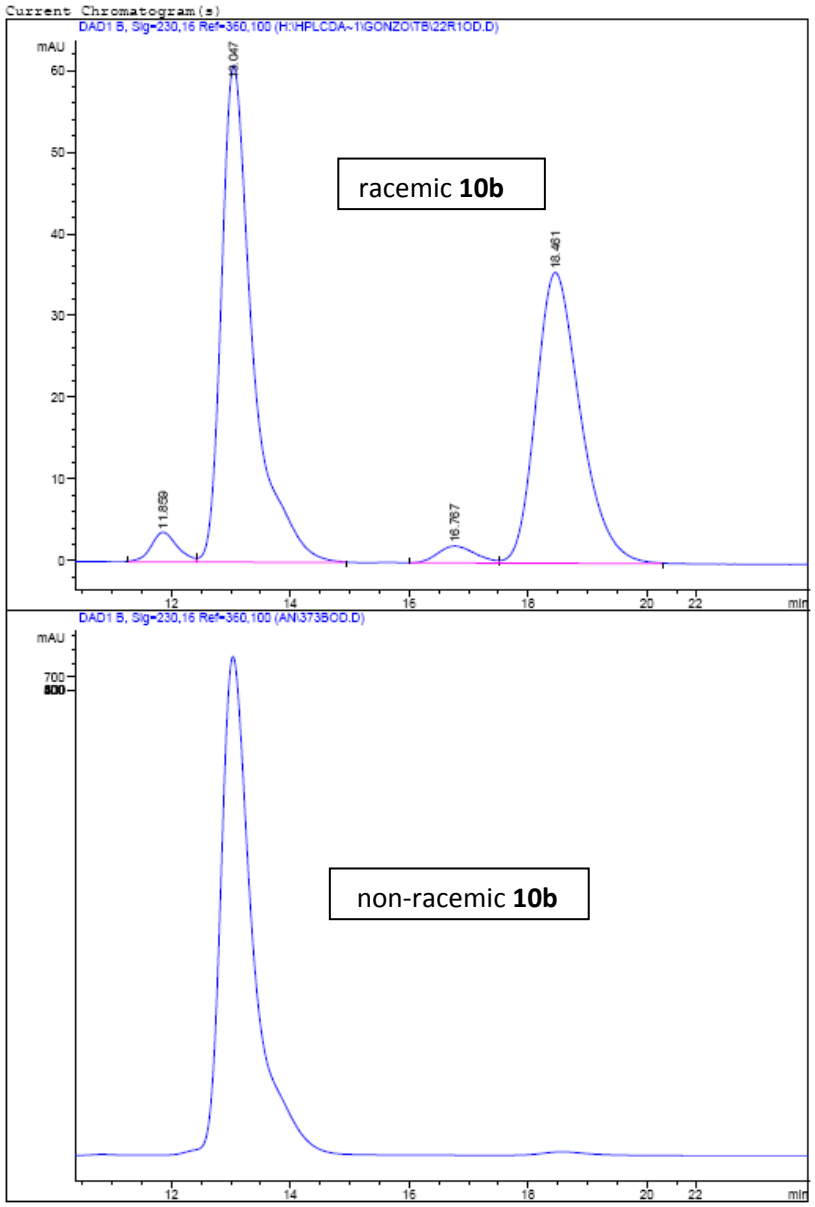


Figure S13. ^{13}C NMR spectrum of (1*S*,3*S*)-methyl 2-(3-(5-bromo-1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10b**).



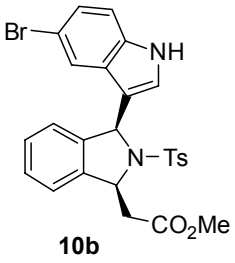
AK Enders - Analytische HPLC

Sample Name: AN 373 B
Data file: D:\GONZO\AN\373BOD.D
Sample Info: Laufmittel: n-Heptan/IP 7:3;
Probe im LM gelöst

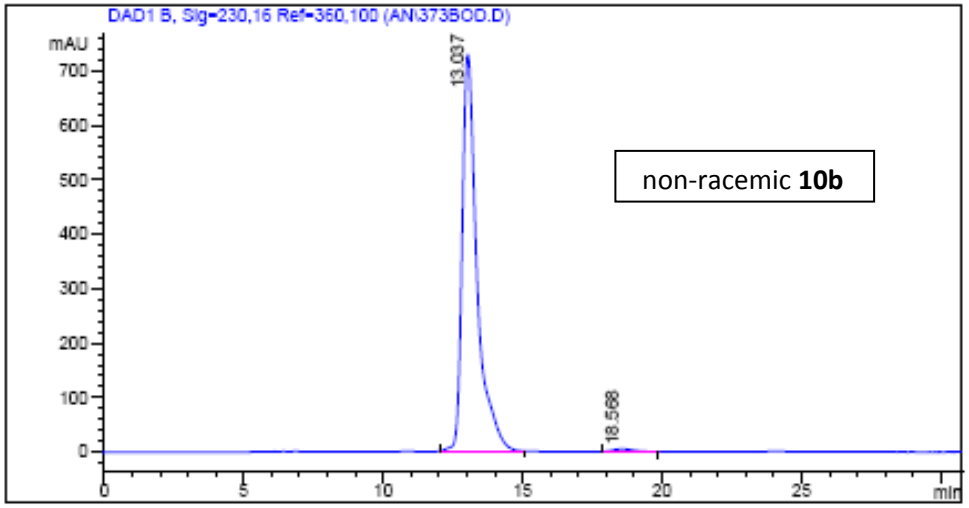
Säule: DAICELOD.M
Säuleninfo: (250x4)mm
Operator: Analytik Labor AKEN

Injektion Time: 14:33:46
Injektion Date: 07.03.2008

Instrument Conditions:	At Start	At Stop
Temperature in°C:	30.0°C	30.0°C
Pressure in bar:	17.5	17.8
Flow in ml/min:	0.5	0.5



10b



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	13.04	0.55	728.86	27104.89	99.04
2	18.57	0.80	5.07	262.61	0.96
Total				27367.51	100.00

Figure S14. HPLC traces of **10b**; overlay of racemic and non-racemic (left), non-racemic (right, Table 4, entry 2).

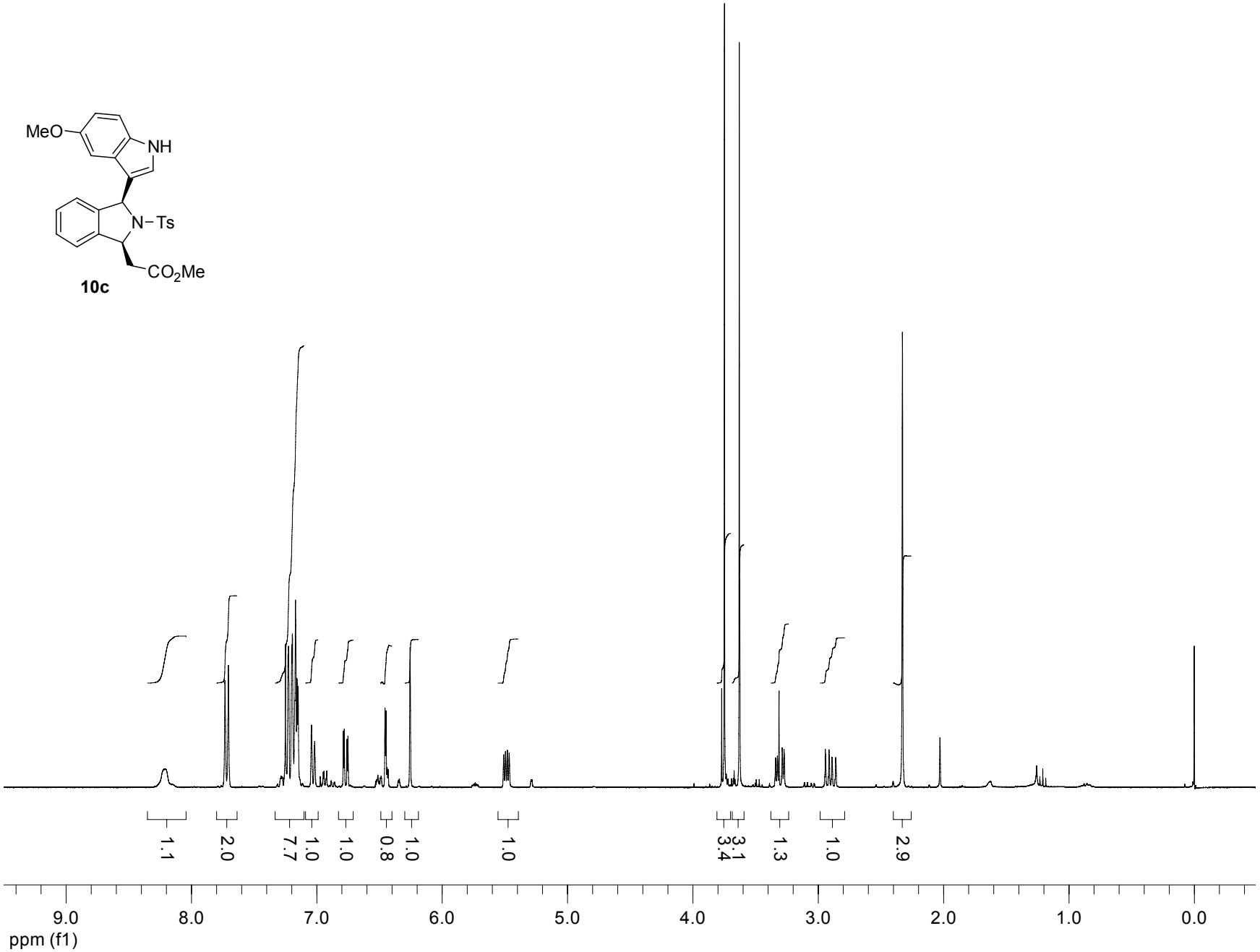


Figure S15. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of (1*S*,3*S*)-methyl 2-(3-(5-methoxy-1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10c**).

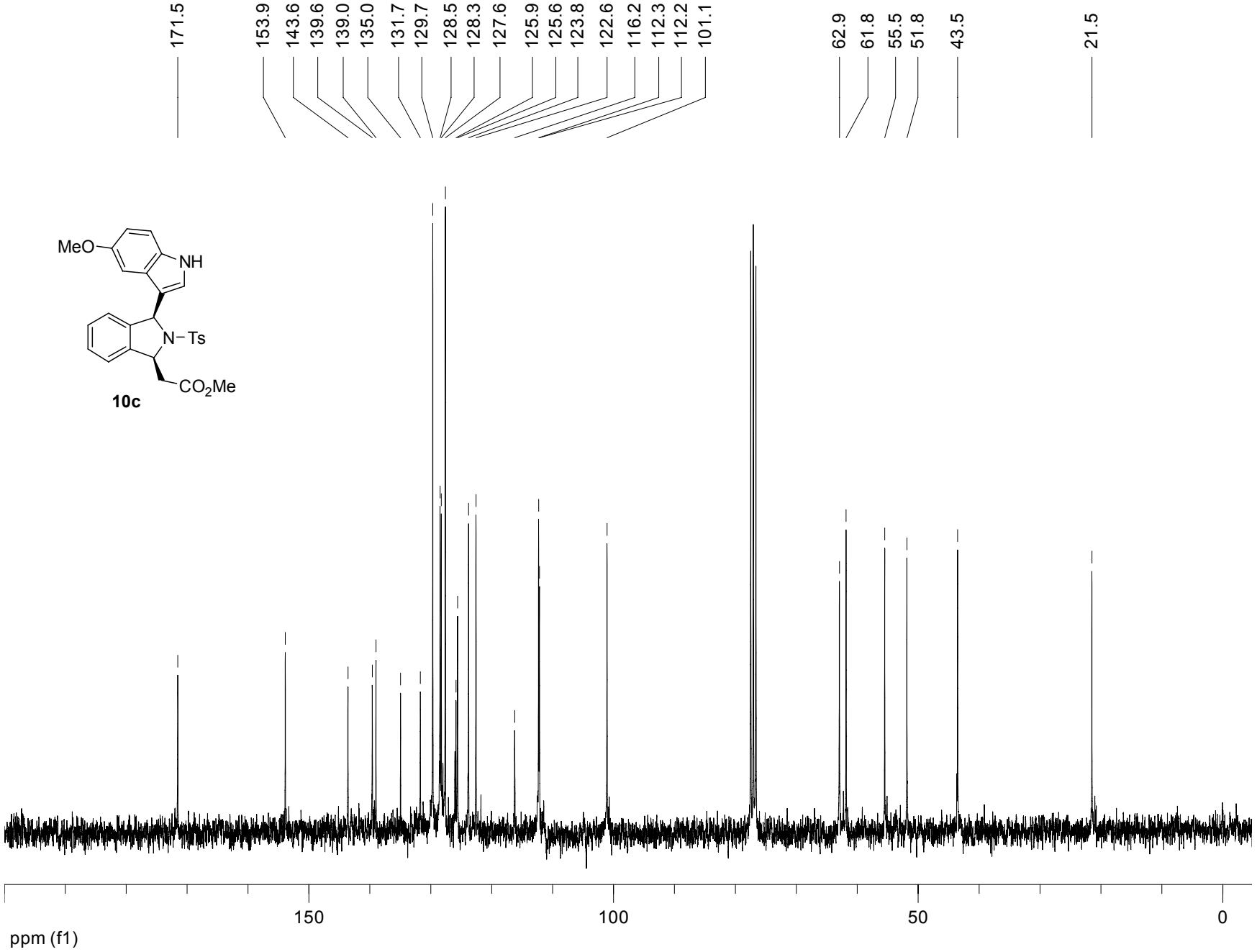
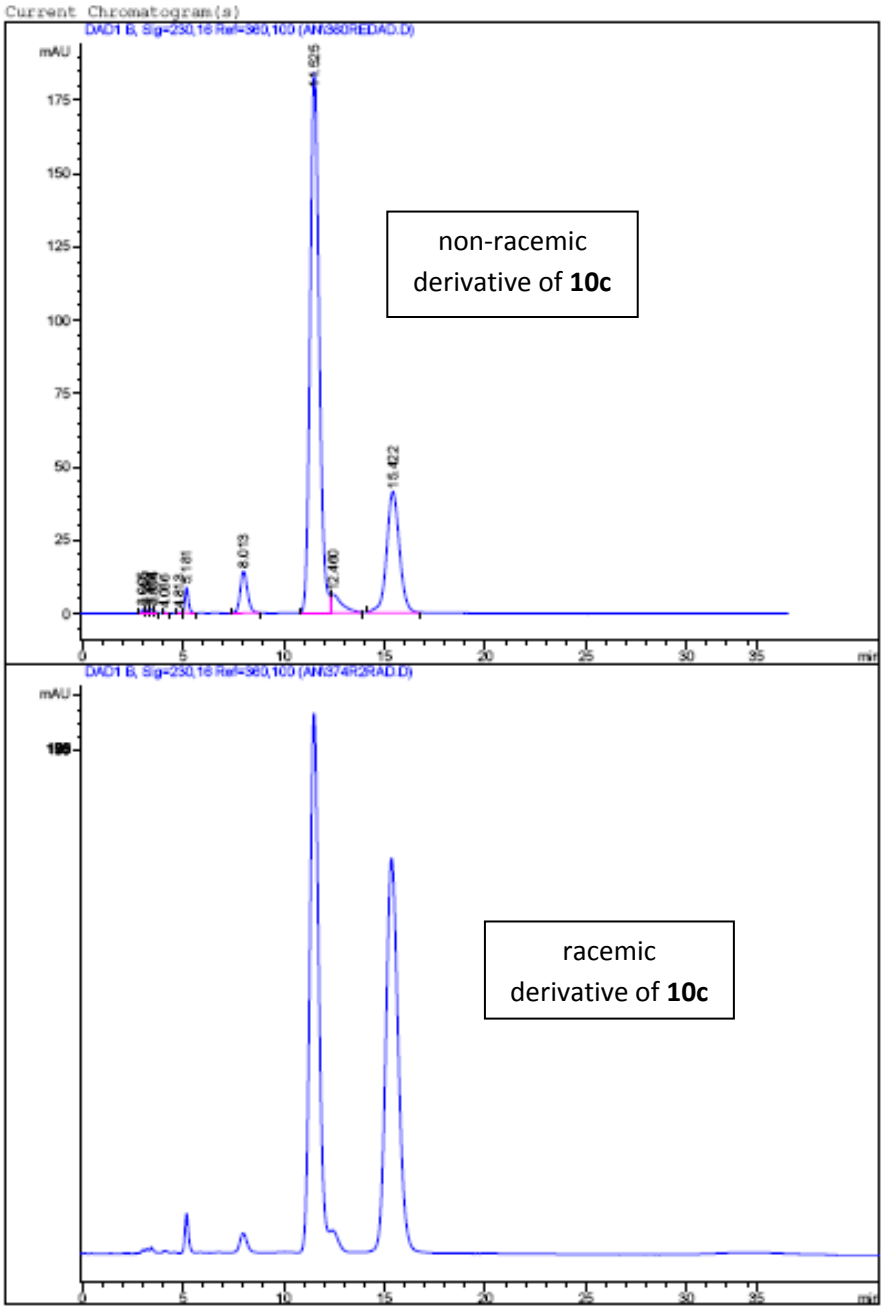


Figure S16. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of (1*S*,3*S*)-methyl 2-(3-(5-methoxy-1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10c**).



AK Enders - Analytische HPLC

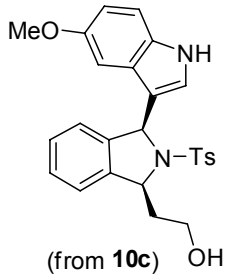
Sample Name: AN 360 RED
Data file: D:\GONZO\AN\360REDAD.D
Sample Info: Laufmittel: n-Heptan/IP 7:3;
Probe im LM/DCM gelöst

Säule: DAICELAD.M
Säuleninfo: (250x4)mm
Operator: Analytik Labor AKEN

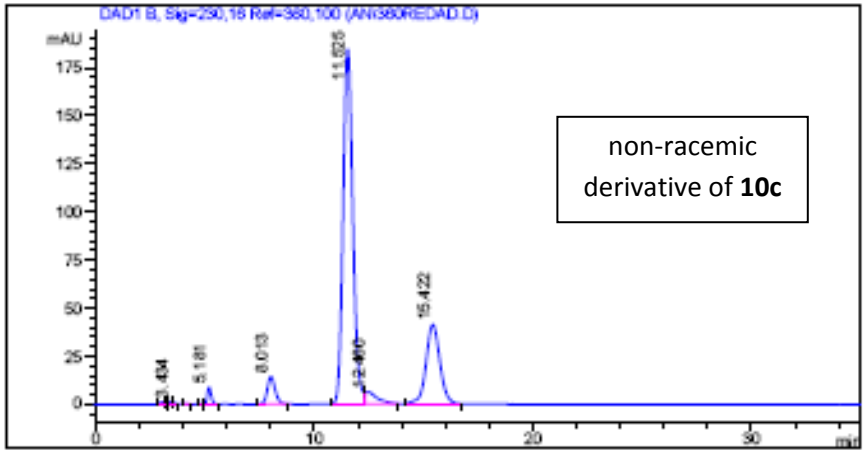
Injektion Time: 15:53:15
Injektion Date: 26.02.2008

Instrument Conditions:	At Start	At Stop
Temperature in°C:	30.0°C	30.0°C
Pressure in bar:	33.3	34.0
Flow in ml/min:	1.0	1.0

HEWLETT PACKARD



(from **10c**)



#	Ret. Time [min]	Width	Height [mAU]	Area [mAU*s]	Area %
1	3.01	0.13	1.38	12.50	0.15
2	3.20	0.12	1.17	10.09	0.12
3	3.43	0.11	1.41	11.11	0.13
4	3.55	0.11	1.15	8.47	0.10
5	4.09	0.14	0.31	2.86	0.03
6	4.81	0.13	0.22	1.95	0.02
7	5.18	0.19	8.75	109.10	1.31
8	8.01	0.39	14.27	362.08	4.35
9	11.52	0.48	184.55	5740.27	68.93
10	12.46	0.53	6.25	246.32	2.96
11	15.42	0.68	41.32	1822.85	21.89
Total				8327.60	100.00

Figure S17. HPLC traces of **10c**; overlay of racemic and non-racemic (left), non-racemic (right, Table 3, entry 3).

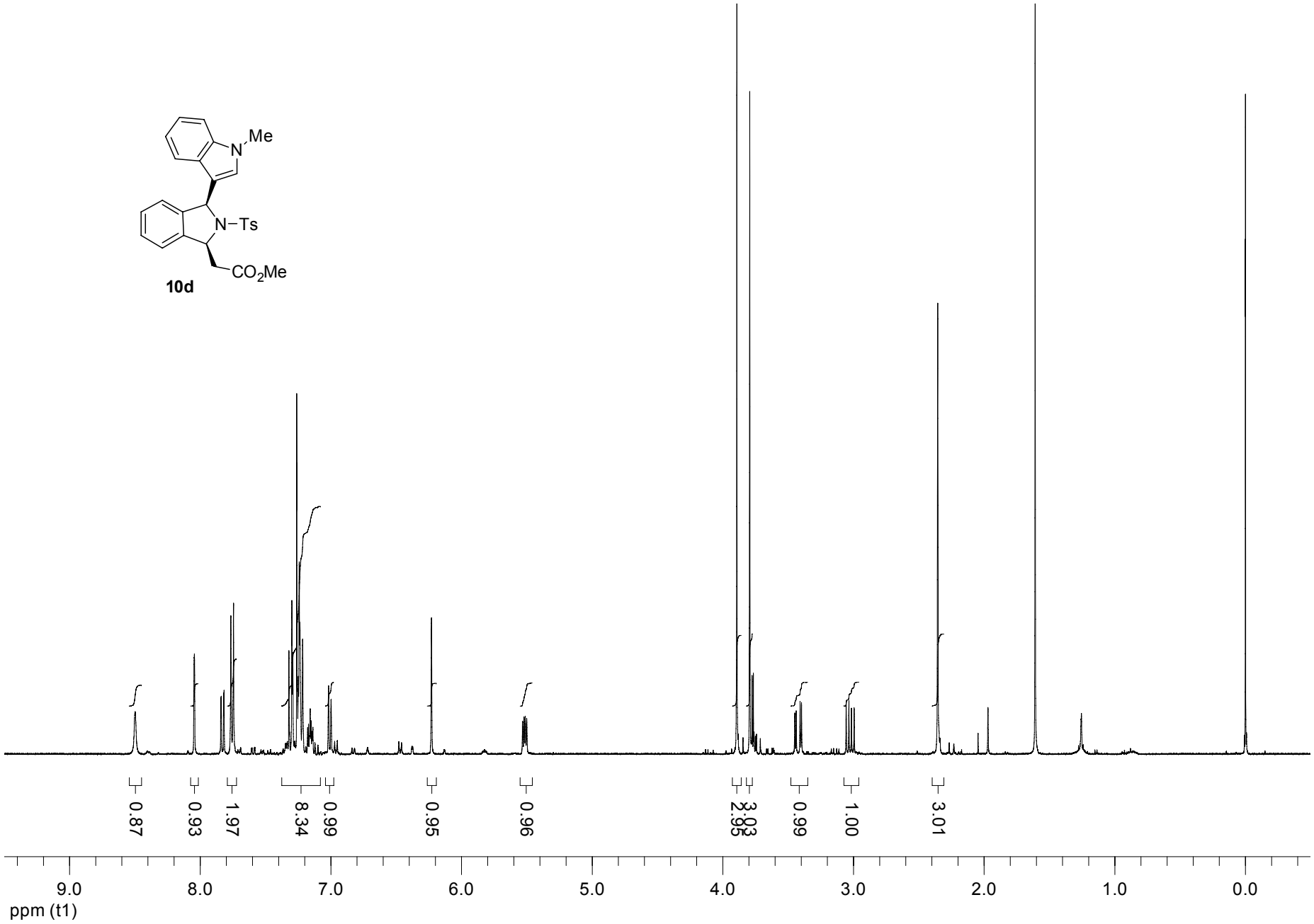


Figure S18. ^{1}H NMR spectrum of (1*S*,3*S*)-methyl 2-(3-(1-methyl-1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10d**).

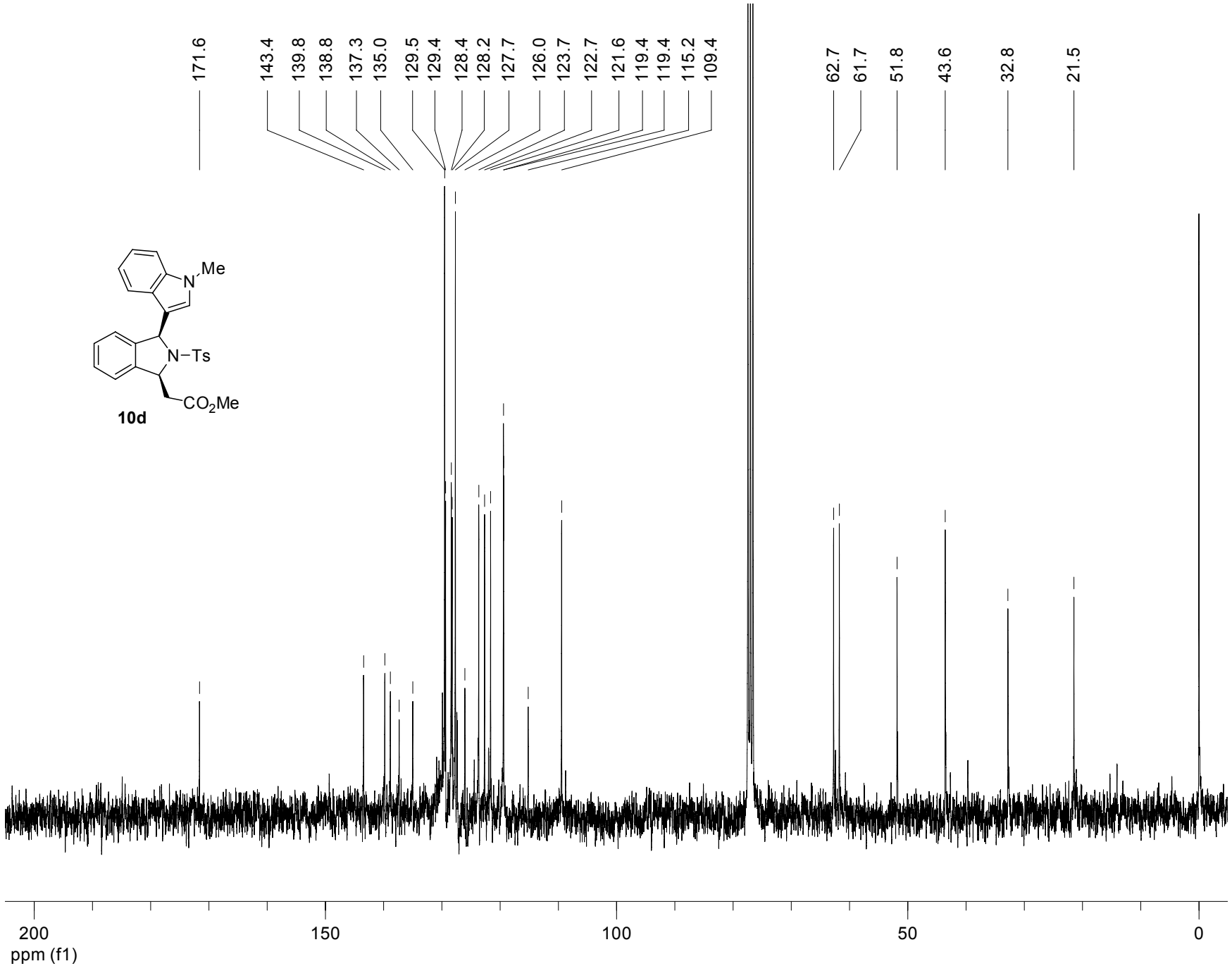
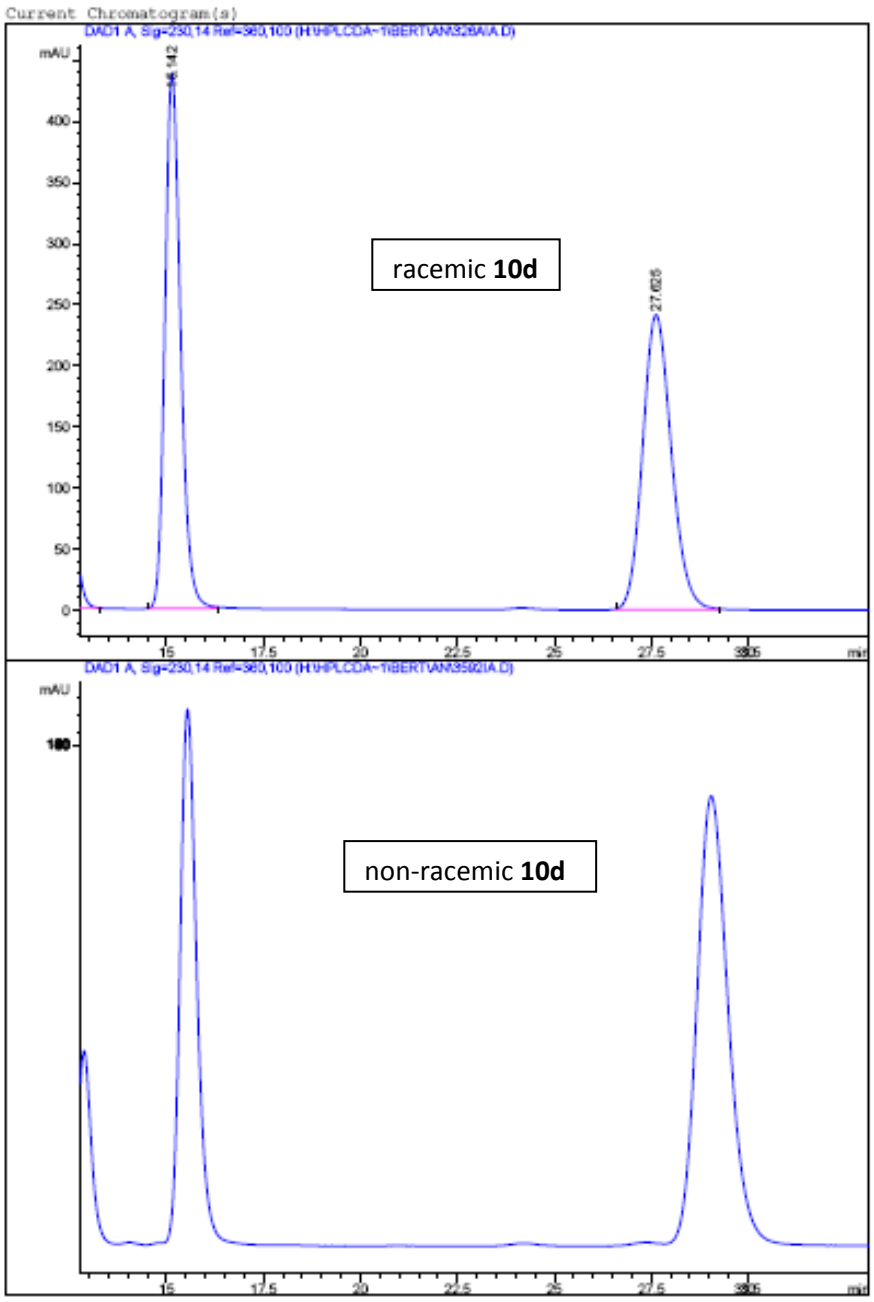


Figure S19. ^{13}C NMR spectrum of methyl (1*S*,3*S*)-methyl 2-(3-(1-methyl-1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10d**).



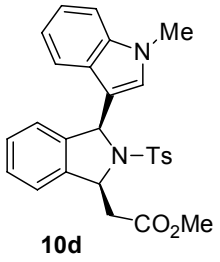
AK Endera - Analytische HPLC

Sample Name: AN 3592
Data file: H:\HPLCDA-1\BERT\AN\3592IA.D
Sample Info: Laufmittel:n-Heptan/IP 8:2;
Probe im LM gelöst

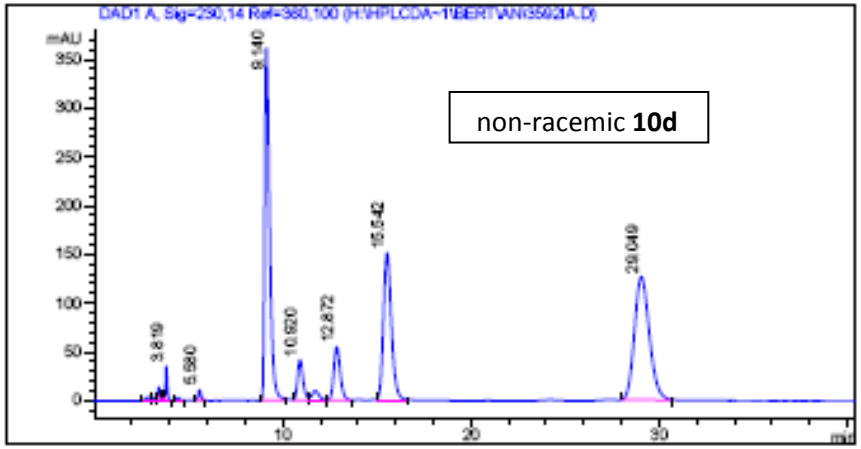
Säule: DAICELIA.M
Säuleninfo: (250x4)mm
Operator: Analytik Labor AKEN

Injektion Time: 13:59:42
Injektion Date: 23.01.2008

Instrument Conditions:	At Start	At Stop
Temperature in °C:	0.0°C	0.0°C
Pressure in bar:	57.9	54.6
Flow in ml/min:	1.0	1.0



10d



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	2.88	0.20	3.80	59.11	0.28
2	3.06	0.14	4.41	45.55	0.22
3	3.42	0.09	14.24	81.27	0.38
4	3.58	0.16	9.60	96.48	0.46
5	3.82	0.09	35.17	212.80	1.01
6	4.42	0.17	2.88	32.85	0.16
7	5.58	0.16	10.69	113.05	0.54
8	9.14	0.27	361.18	6624.96	31.38
9	10.92	0.32	41.41	852.79	4.04
10	11.73	0.40	9.52	255.57	1.21
11	12.87	0.37	54.64	1298.80	6.15
12	15.54	0.45	150.93	4458.59	21.12
13	29.05	0.86	126.40	6977.43	33.05
Total				21109.26	100.00

Figure S20. HPLC traces of **10d**; overlay of racemic and non-racemic (left), non-racemic (right, Table 3, entry 4).

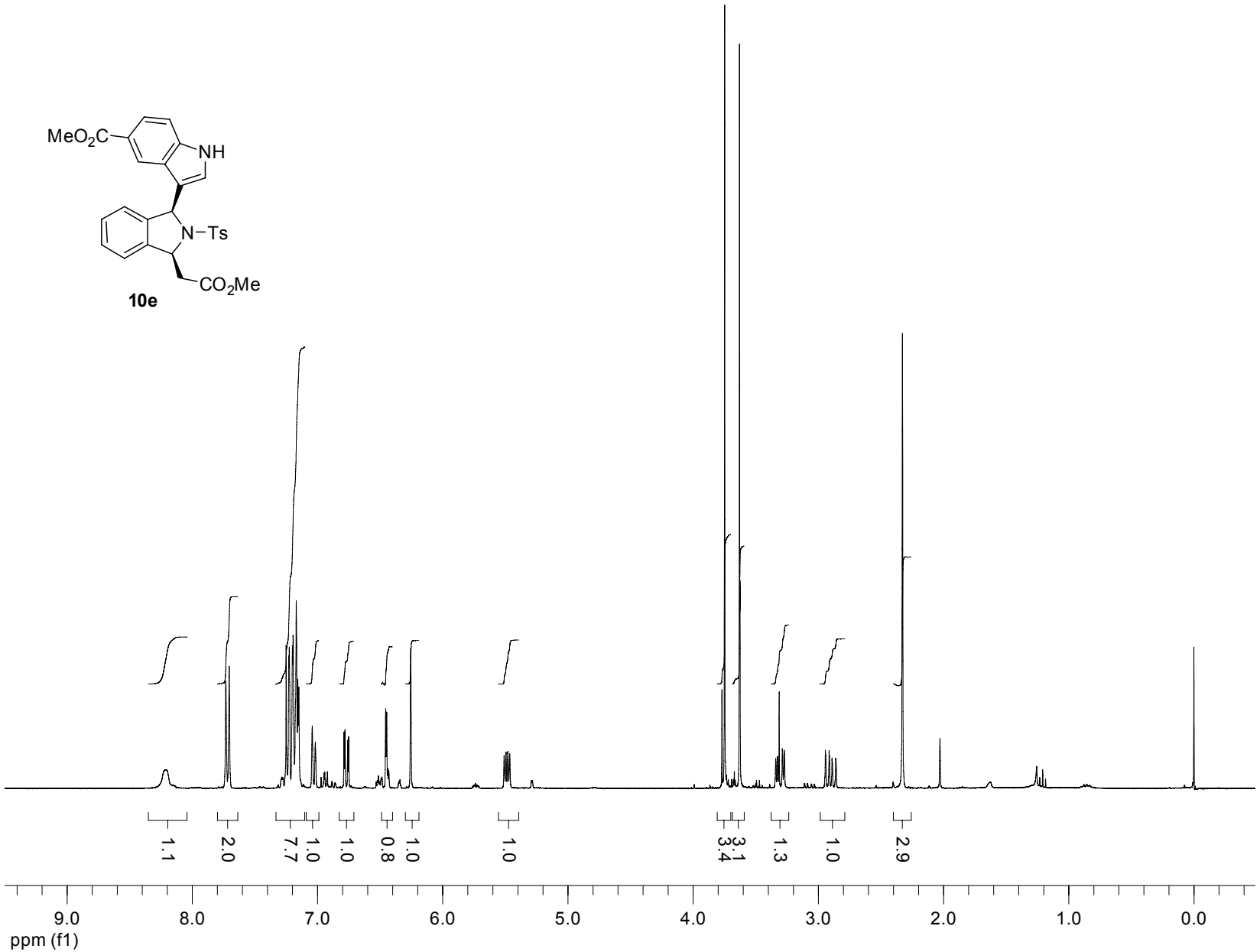


Figure S21. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of (1*S*,3*S*)-methyl 2-(3-(5-methylcarboxylate-1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10e**).

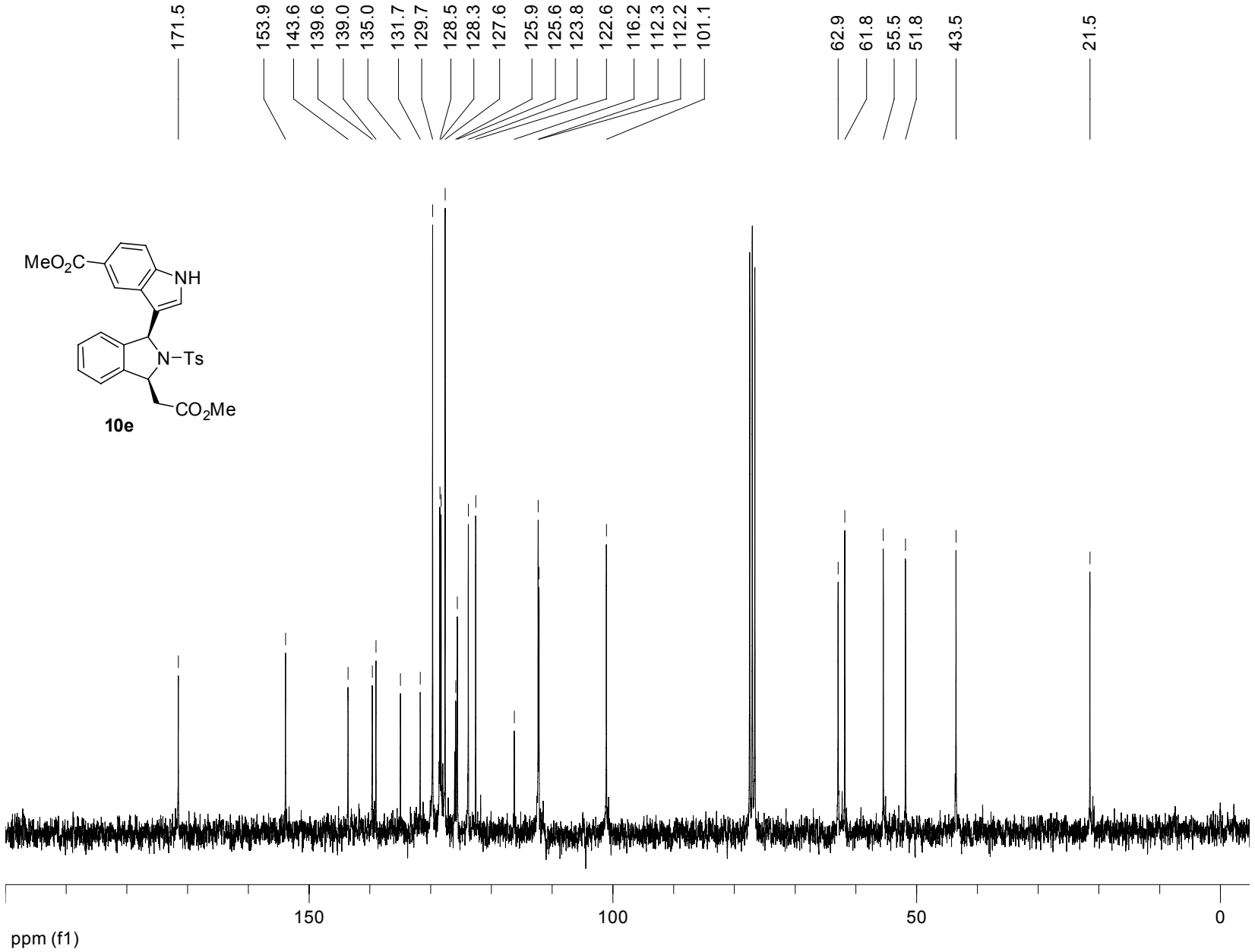
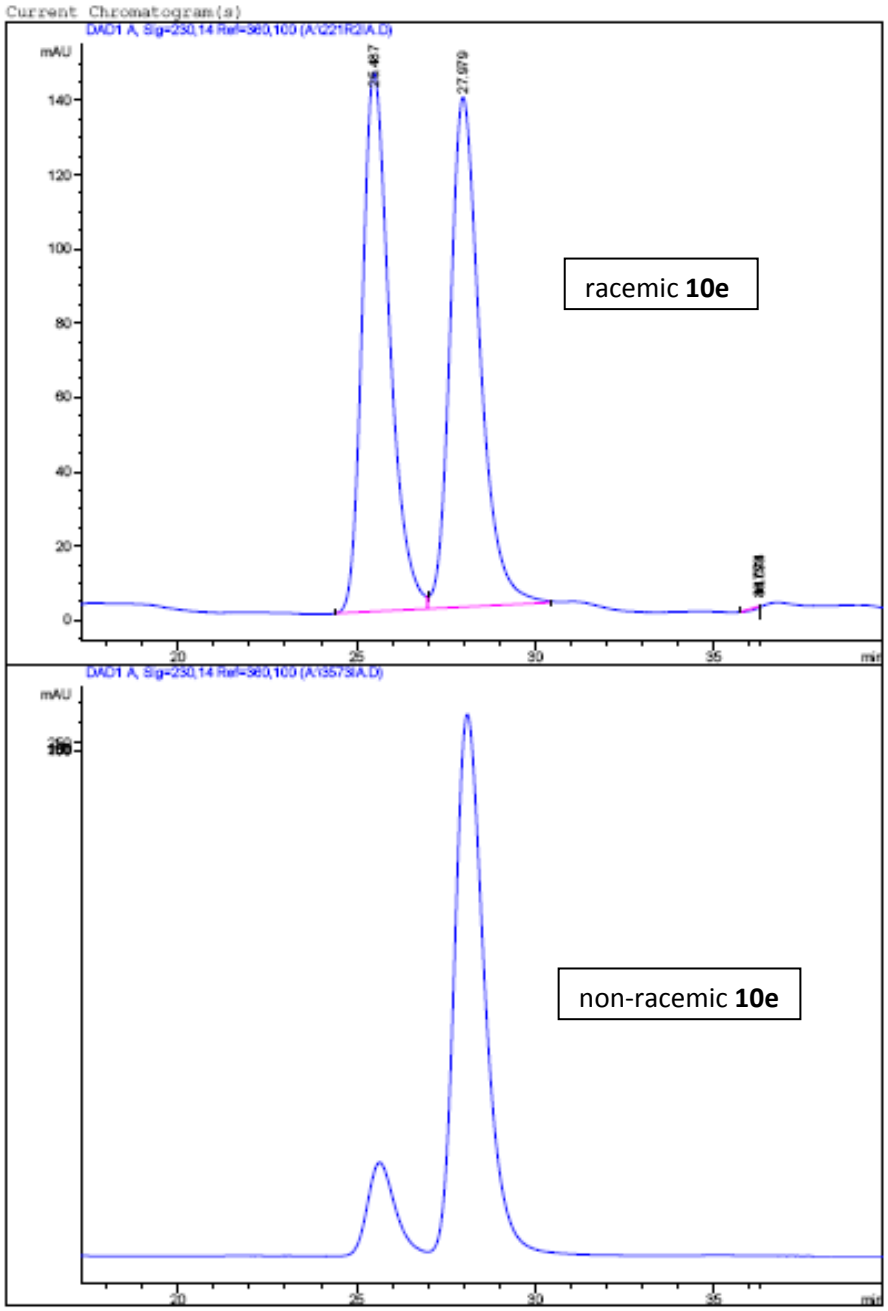


Figure S22. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of (1*S*,3*S*)-methyl 2-(3-(5-methoxycarbonyl-1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10e**).



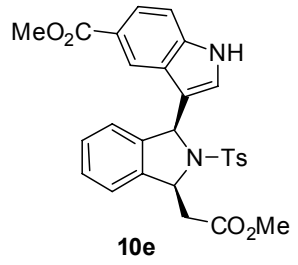
AK Enders - Analytische HPLC

Sample Name: AN 3573
Data file: A:\3573IA.D
Sample Info: Laufmittel:n-Heptan/IP 8:2;
Probe im LM/DCM gelöst

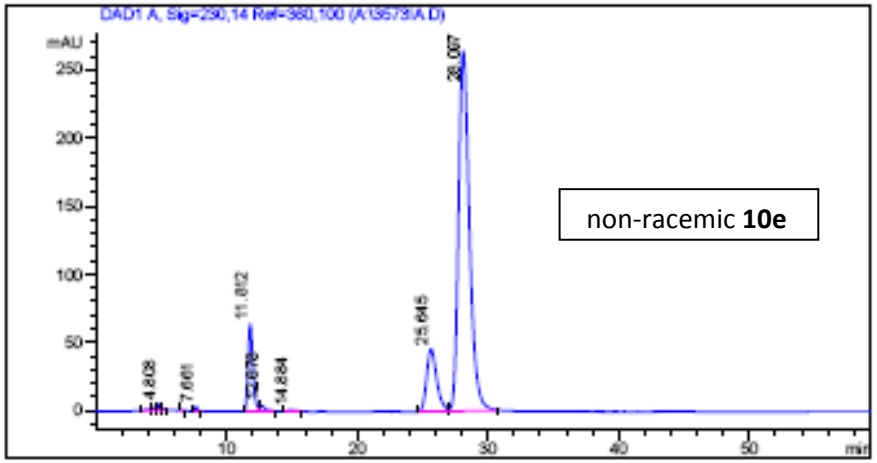
Säule: DAICELIA.M
Säuleninfo: (250x4)mm
Operator: Analytik Labor AKEN

Injektion Time: 08:16:36
Injektion Date: 29.02.2008

Instrument Conditions:	At Start	At Stop
Temperature in°C:	0.0°C	0.0°C
Pressure in bar:	38.9	37.7
Flow in ml/min:	0.7	0.7



10e



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	4.05	0.33	1.08	29.34	0.15
2	4.37	0.20	2.10	31.28	0.16
3	4.81	0.13	4.60	42.38	0.21
4	5.13	0.17	1.32	15.70	0.08
5	6.54	0.15	0.67	6.63	0.03
6	7.66	0.17	3.55	40.74	0.21
7	11.81	0.39	64.25	1658.08	8.36
8	12.68	0.46	4.45	147.17	0.74
9	14.88	0.54	1.01	46.13	0.23
10	25.64	0.77	45.63	2471.29	12.46
11	28.10	0.89	264.39	15348.37	77.37
Total				19837.12	100.00

Figure S23. HPLC traces of **10e**; overlay of racemic and non-racemic (left), non-racemic (right, Table 3, entry 5).

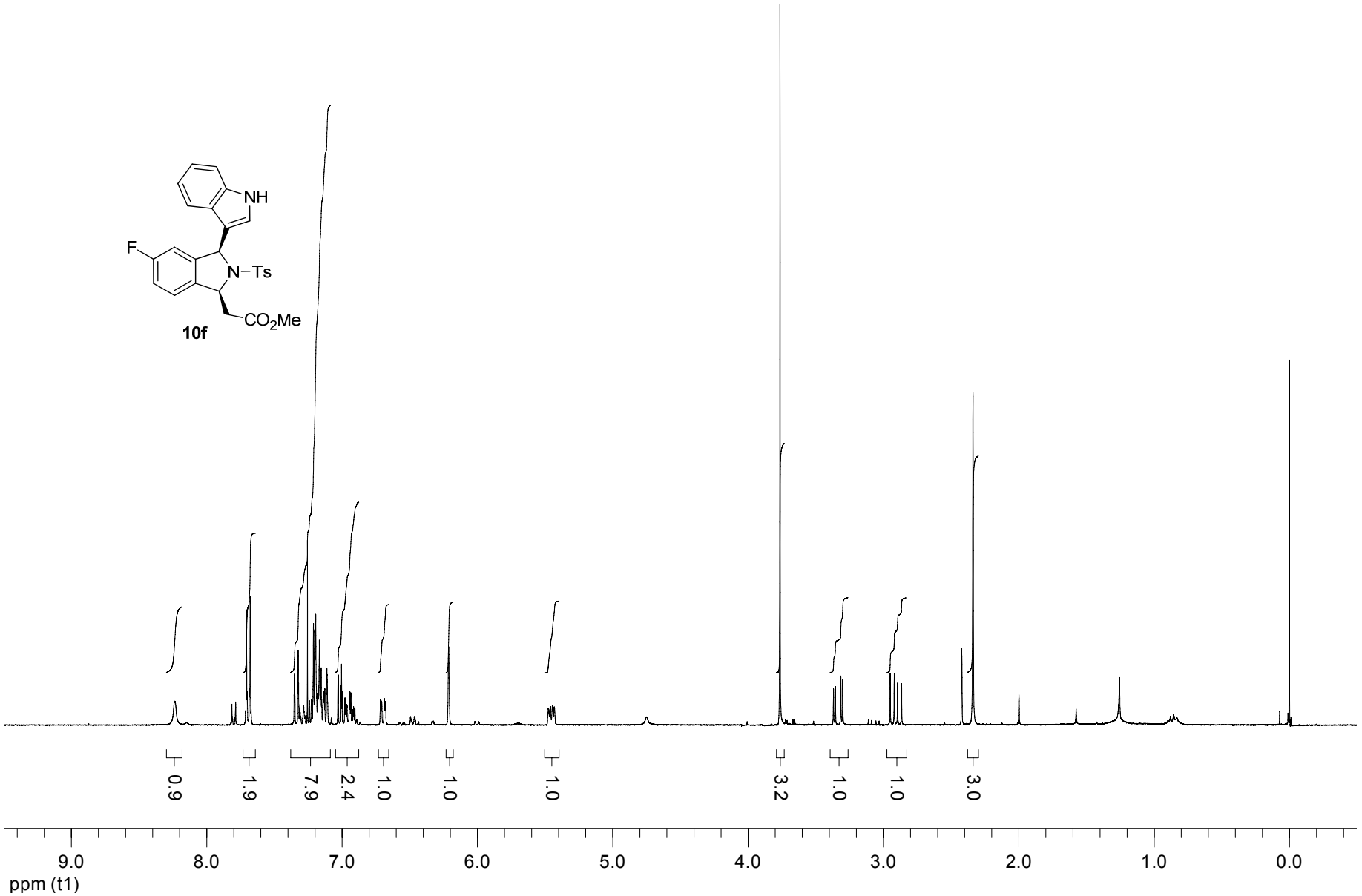


Figure S24. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of (1*S*,3*S*)-methyl 2-(5-fluoro-3-(1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10f**).

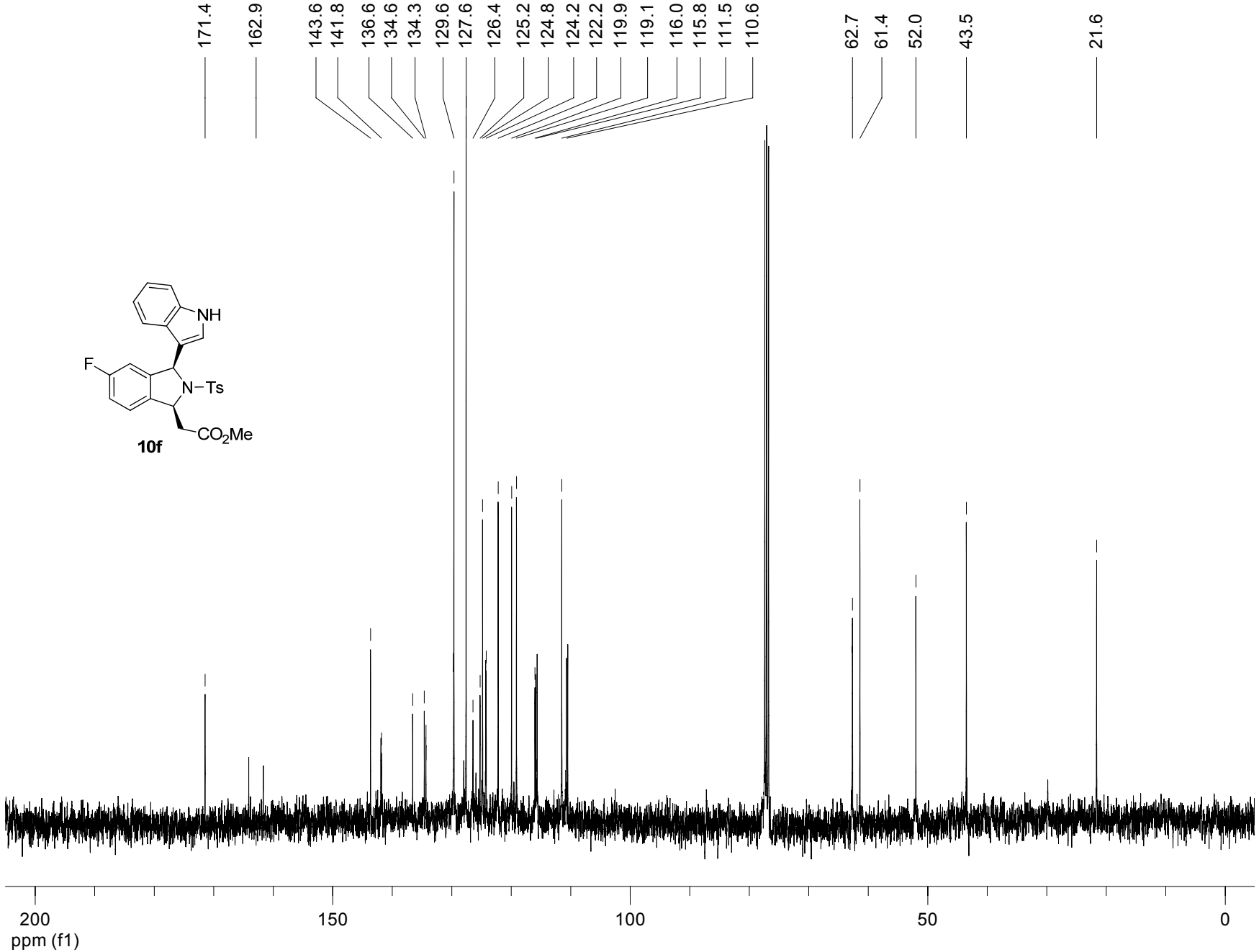
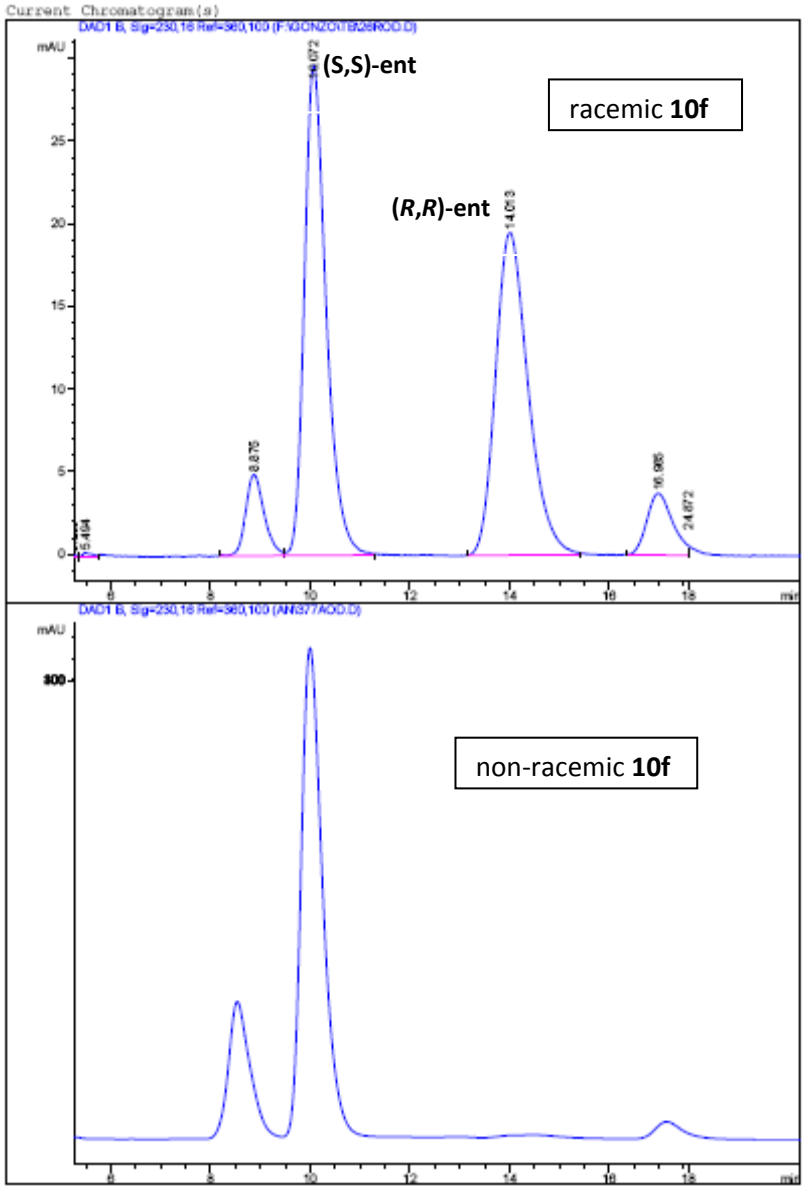


Figure S25. ^{13}C NMR spectrum (101 MHz, $CDCl_3$) of (1*S*,3*S*)-methyl 2-(5-fluoro-3-(1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10f**).



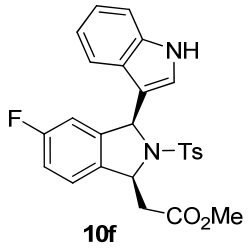
AK Enders - Analytische HPLC

Sample Name: AN 377 A
Data file: D:\GONZO\AN\377AOD.D
Sample Info: Laufmittel: n-Heptan/IP 7:3; Probe im LM gelöst

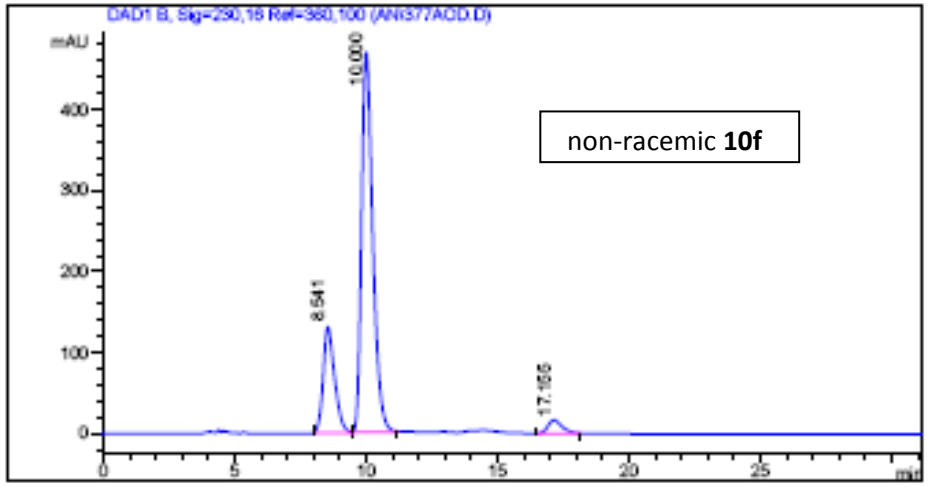
Säule: DAICELOD.M
Säuleninfo: (250x4)mm
Operator: Analytik Labor AKEN

Injektion Time: 13:58:18
Injektion Date: 07.03.2008

Instrument Conditions:	At Start	At Stop
Temperature in°C:	30.0°C	30.0°C
Pressure in bar:	25.5	25.8
Flow in ml/min:	0.7	0.7



10f



#	Ret. Time [min]	Width	Height [mAU]	Area [mAU*s]	Area %
1	8.54	0.44	130.81	3943.03	21.29
2	10.00	0.46	468.69	13940.08	75.29
3	17.15	0.58	16.53	633.19	3.42
Total				18516.30	100.00

Figure S26. HPLC traces of **10f**; overlay of racemic and non-racemic (left), non-racemic (right, Table 4, entry 3).

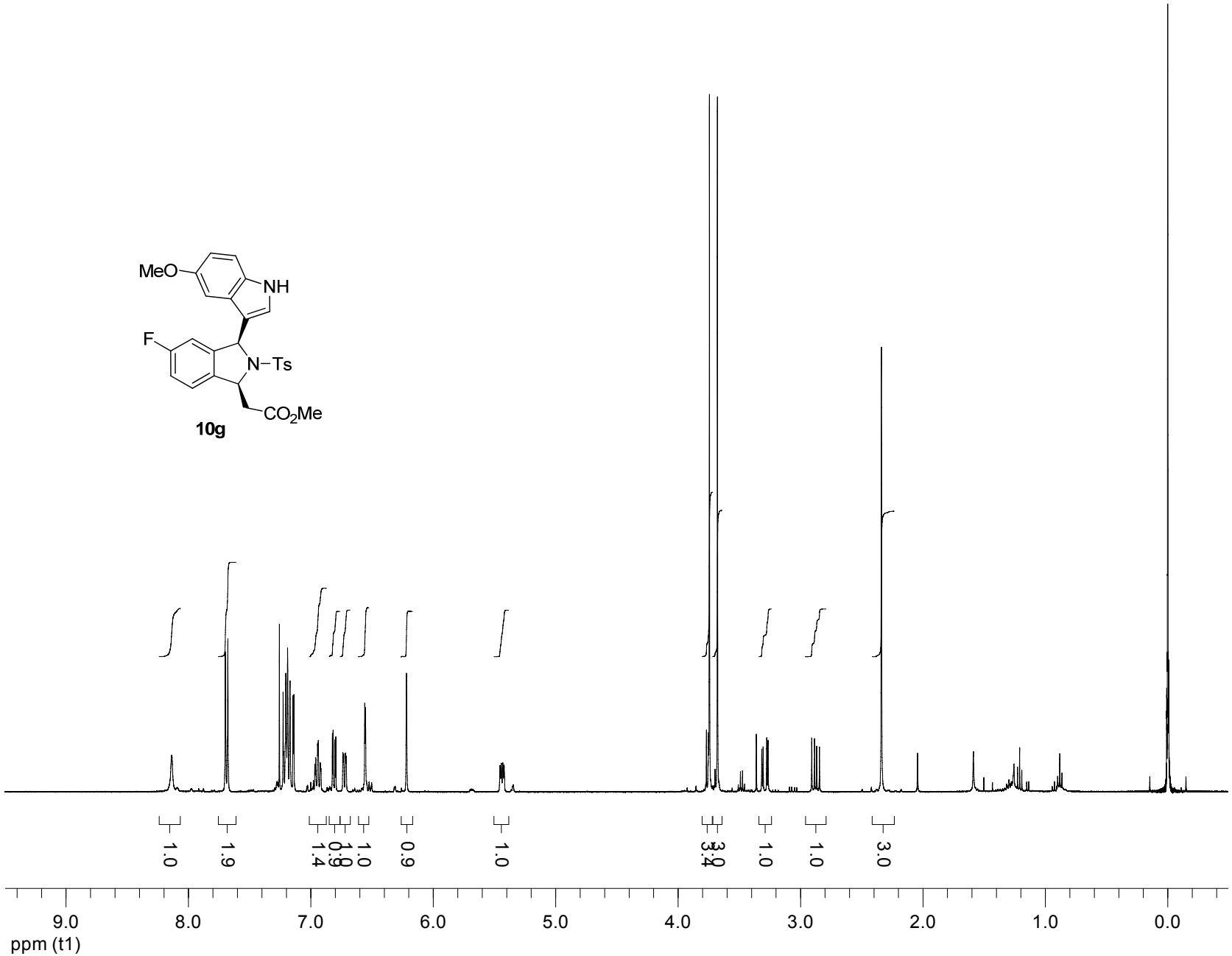


Figure S27. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of (1*S*,3*S*)-methyl 2-(5-fluoro-3-(5-methoxy-1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10g**).

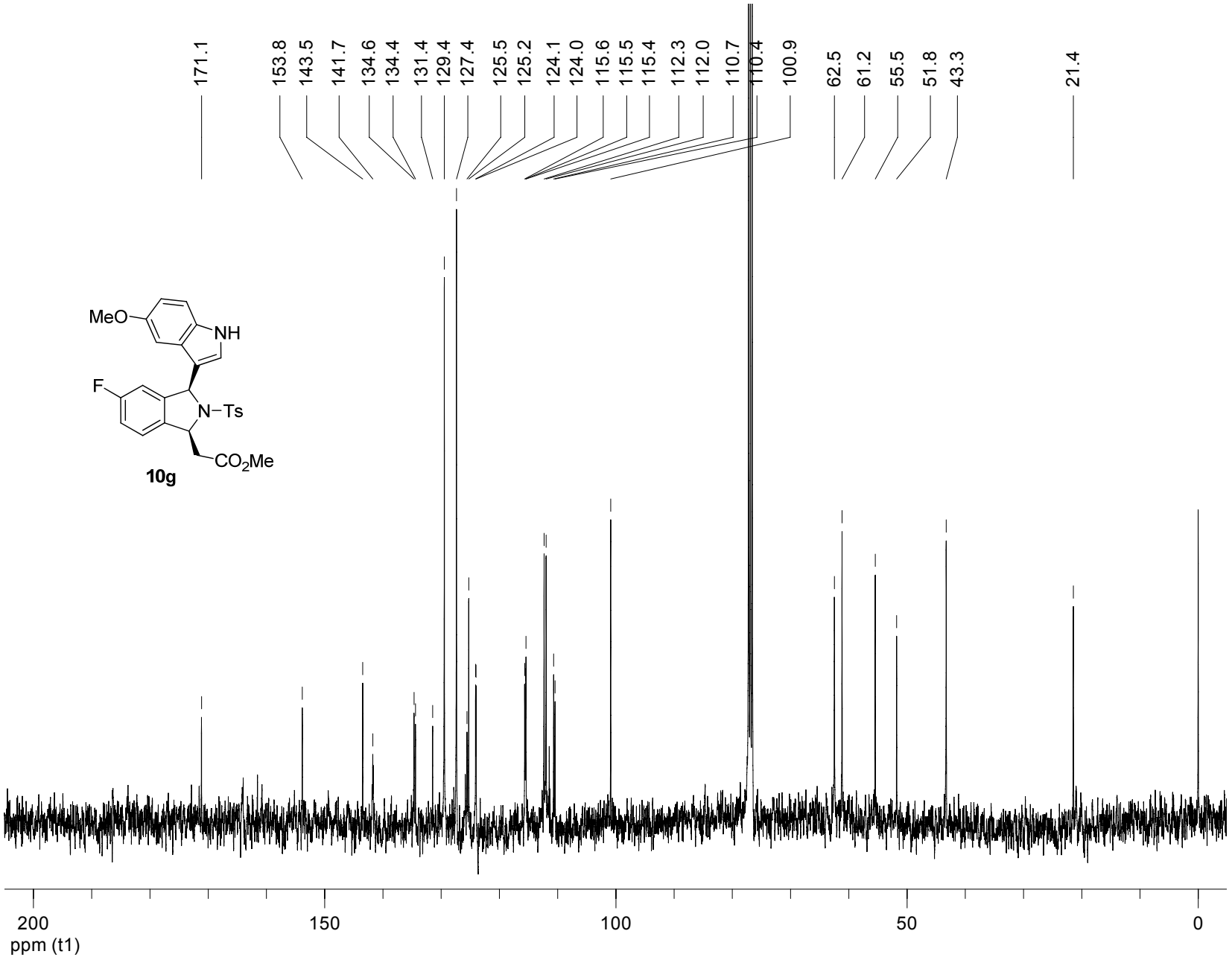
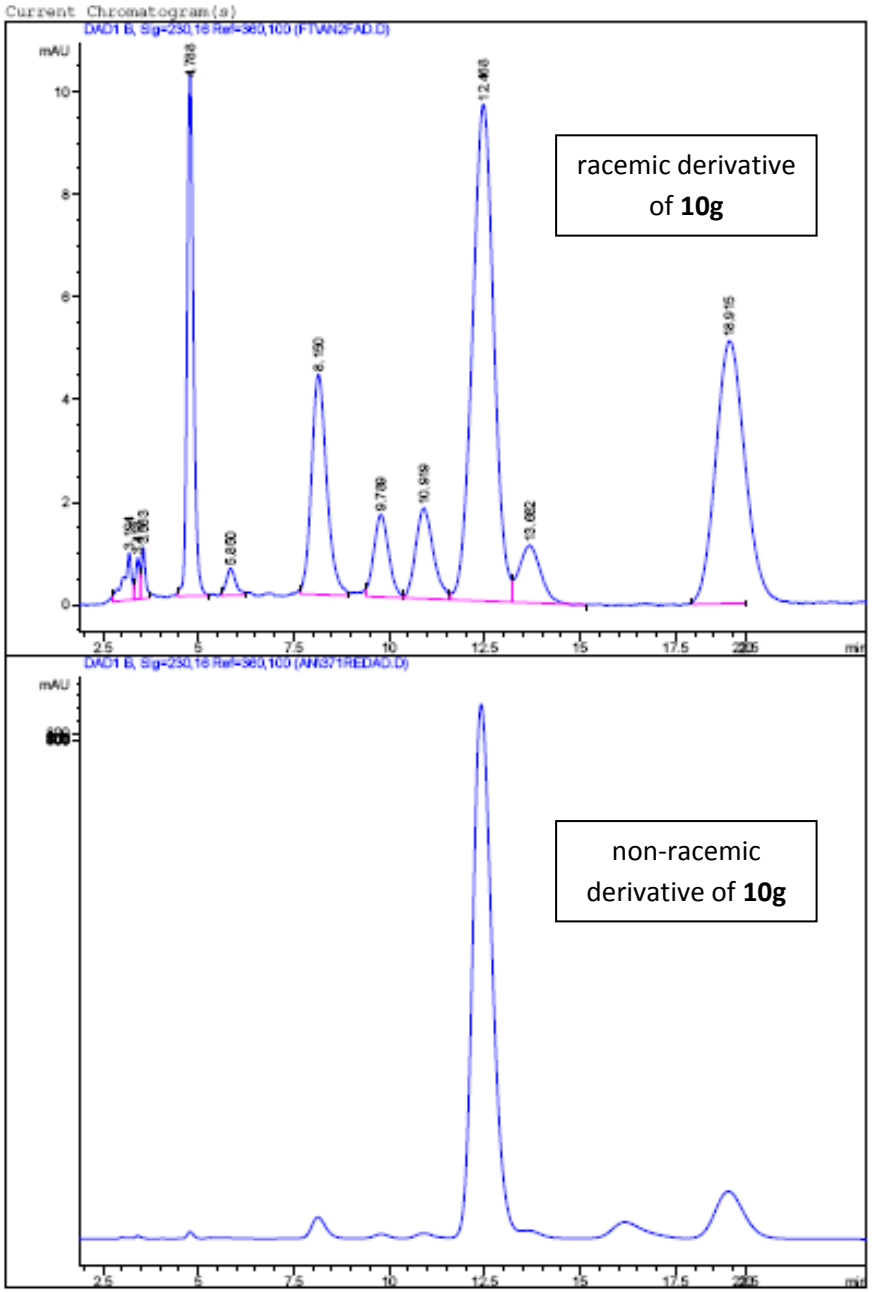


Figure S28. ^{13}C NMR (101 MHz, $CDCl_3$) spectrum of (1*S*,3*S*)-methyl 2-(5-fluoro-3-(5-methoxy-1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10g**).



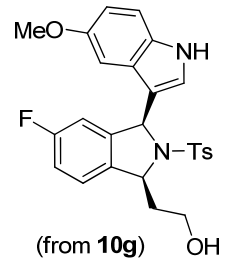
AK Endera - Analytische HPLC

Sample Name: AN 371 RED
Data file: D:\GONZO\AN\371REDAD.D
Sample Info: Laufmittel: n-Heptan/IP 7:3; Probe in LM/DCM gelöst

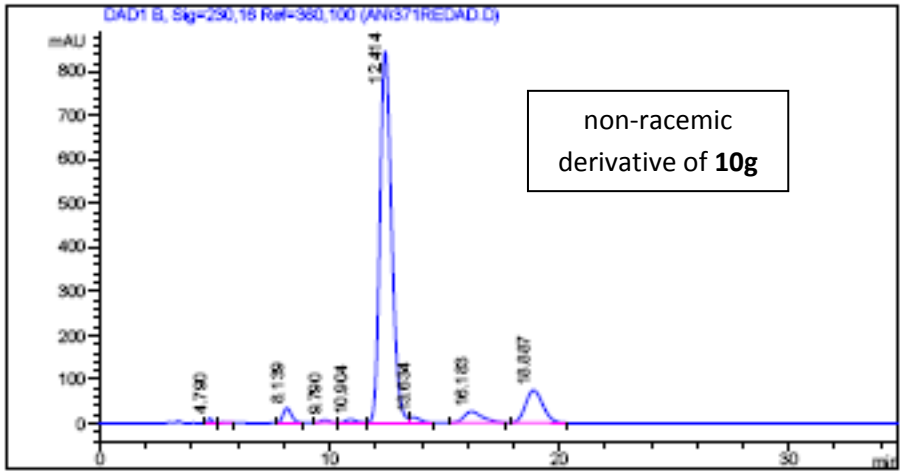
Säule: DAICELAD.M
Säuleninfo: (250x4)mm
Operator: Analytik Labor AKEN

Injektion Time: 10:08:38
Injektion Date: 26.02.2008

Instrument Conditions:	At Start	At Stop
Temperature in°C:	30.0°C	30.0°C
Pressure in bar:	33.4	34.3
Flow in ml/min:	1.0	1.0



(from **10g**)



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	4.79	0.18	11.16	129.40	0.35
2	5.31	0.35	1.56	40.40	0.11
3	8.14	0.40	33.48	867.74	2.33
4	9.79	0.40	6.73	173.35	0.46
5	10.90	0.49	8.35	270.36	0.72
6	12.41	0.54	845.34	29884.23	80.13
7	13.63	0.51	12.73	425.36	1.14
8	16.18	0.87	25.89	1520.57	4.08
9	18.89	0.83	74.79	3984.32	10.68
Total				37295.74	100.00

Figure S29. HPLC traces of **10g** derivative; overlay of racemic and non-racemic (left), non-racemic (right, Table 3, entry 7).

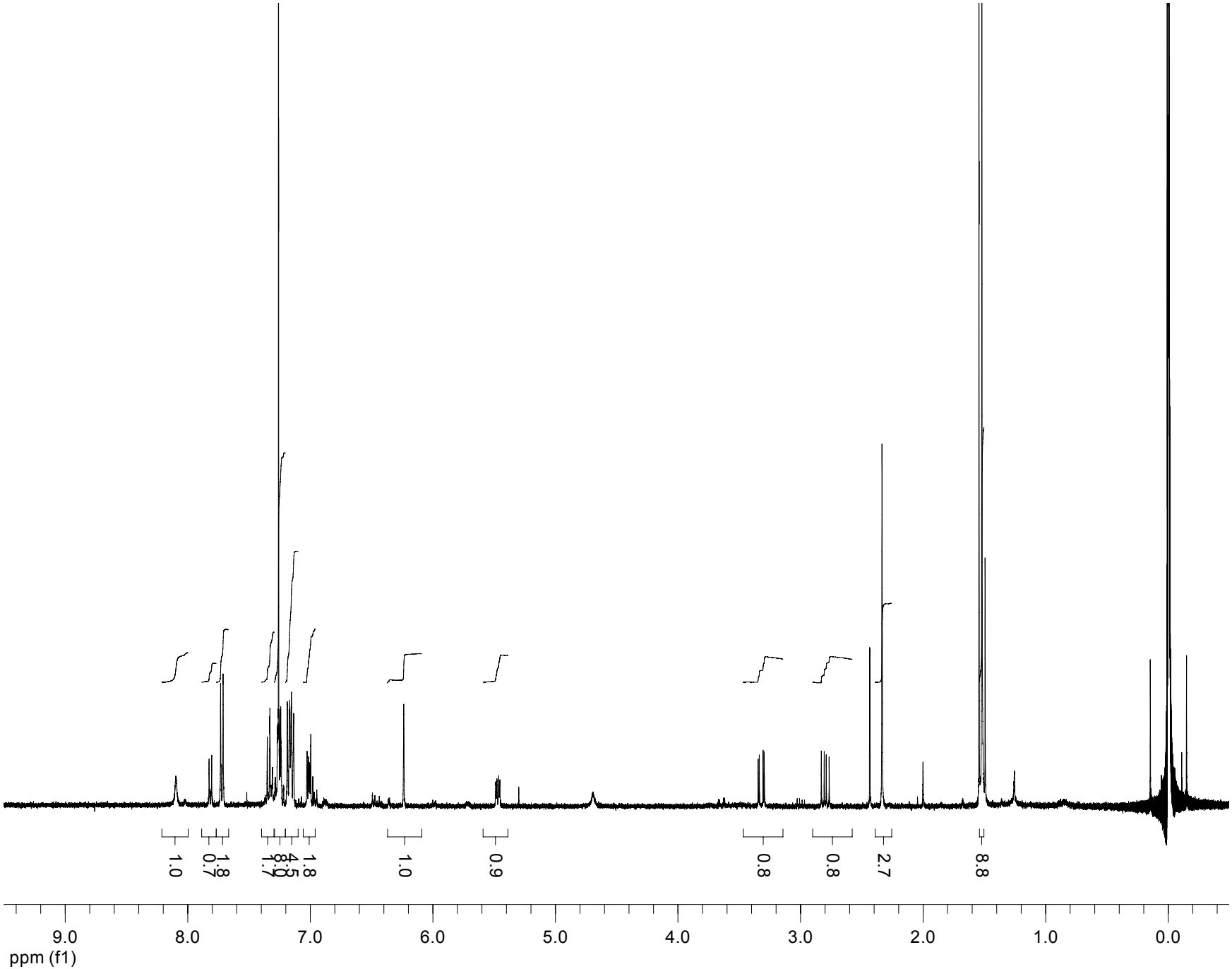


Figure S30. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of (1*S*,3*S*)-*t*-butyl 2-(3-(1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10h**).

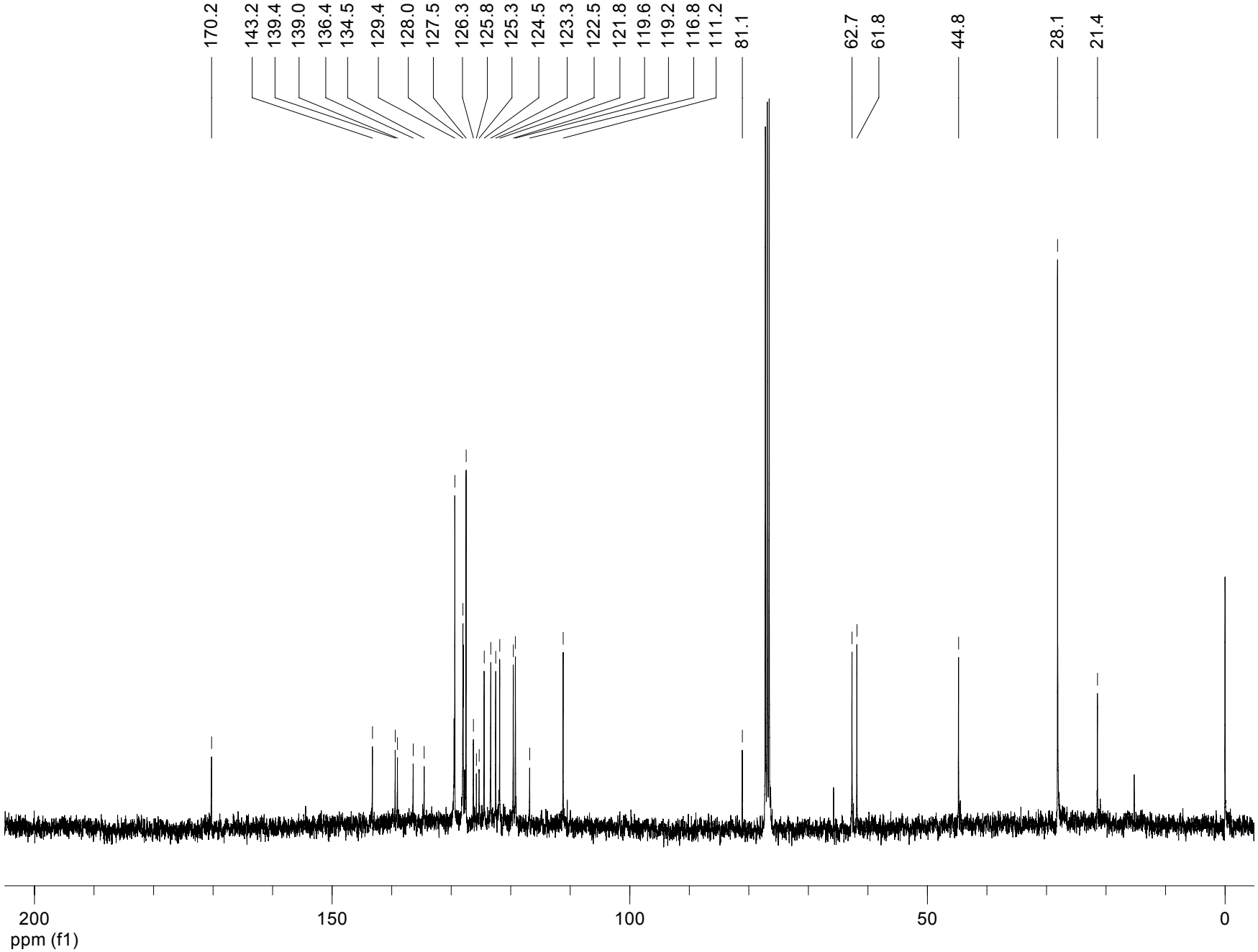
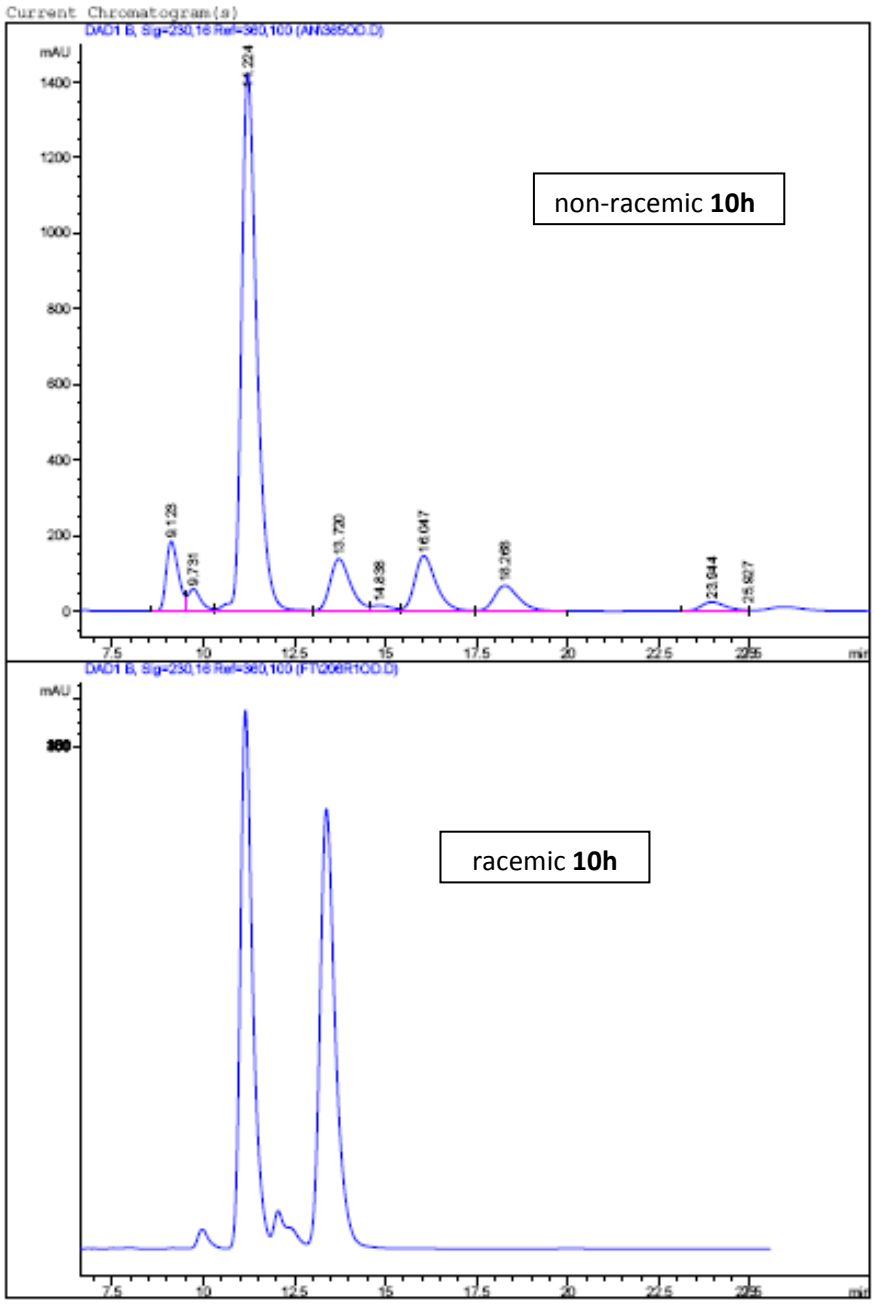


Figure S31. ^{13}C NMR spectrum (101 MHz, $CDCl_3$) of (1*S*,3*S*)-*t*-butyl 2-(3-(1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10h**).



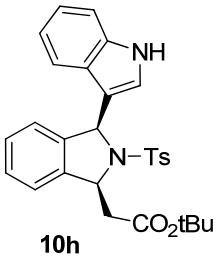
AK Enders - Analytische HPLC

Sample Name: AN 365
Data file: D:\GONZO\AN\365OD.D
Sample Info: Laufmittel: n-Heptan/IP 7:3; Probe im LM gelöst

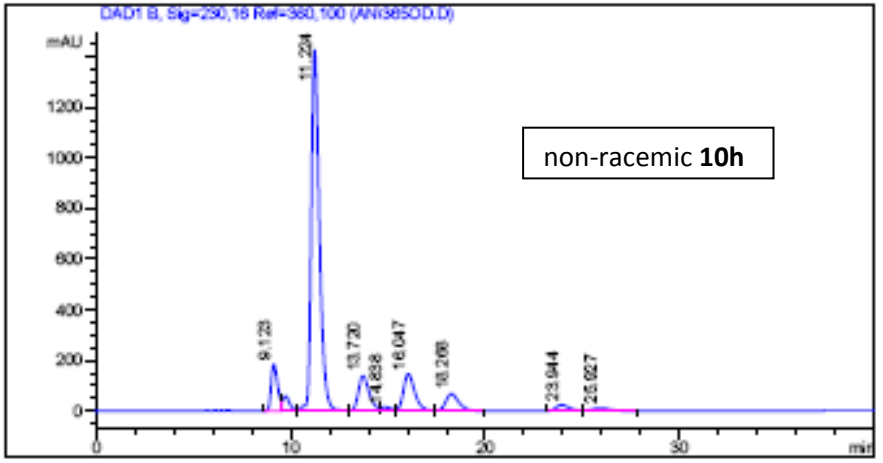
Säule: DAICELOD.M
Säuleninfo: (250x4)mm
Operator: Analytik Labor AKEN

Injektion Time: 14:15:47
Injektion Date: 30.01.2008

Instrument Conditions:	At Start	At Stop
Temperature in°C:	30.0°C	30.0°C
Pressure in bar:	17.9	18.1
Flow in ml/min:	0.5	0.5



10h



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	9.12	0.36	185.04	4332.26	6.71
2	9.73	0.36	59.36	1463.53	2.27
3	11.22	0.44	1424.92	41594.85	64.47
4	13.72	0.60	138.58	5451.50	8.45
5	14.84	0.55	15.13	563.90	0.87
6	16.05	0.62	146.38	6010.62	9.32
7	18.27	0.71	67.74	3173.46	4.92
8	23.94	0.73	24.15	1170.03	1.81
9	25.93	0.96	11.54	760.21	1.18
Total				64520.36	100.00

Figure S32. HPLC traces of **10h**; overlay of racemic and non-racemic (left), non-racemic (right, Table 3, entry 8).

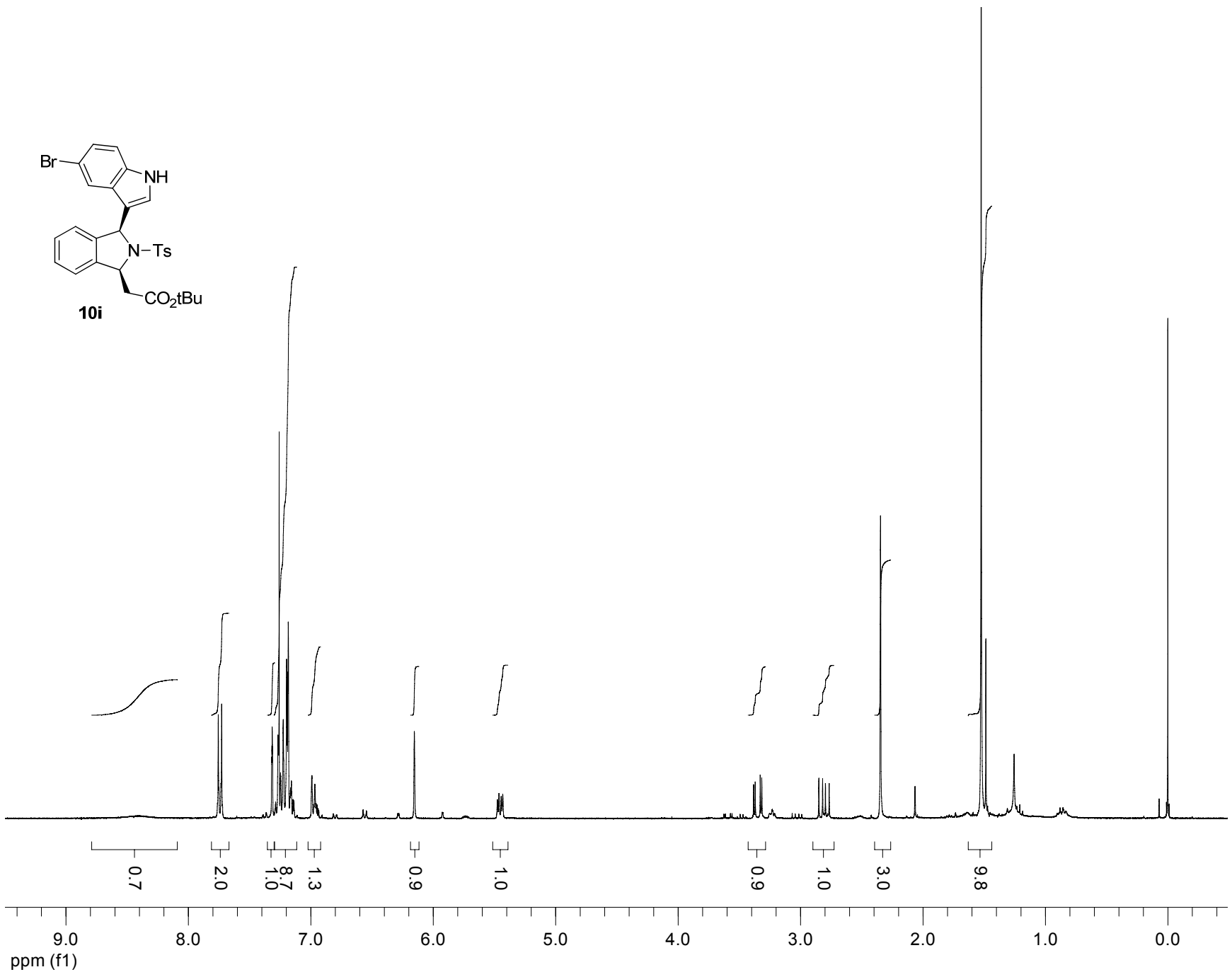


Figure S33. ^{1}H NMR spectrum (300MHz, $CDCl_3$) of (1*S*,3*S*)-*t*-butyl 2-(3-(5-bromo-1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10i**).

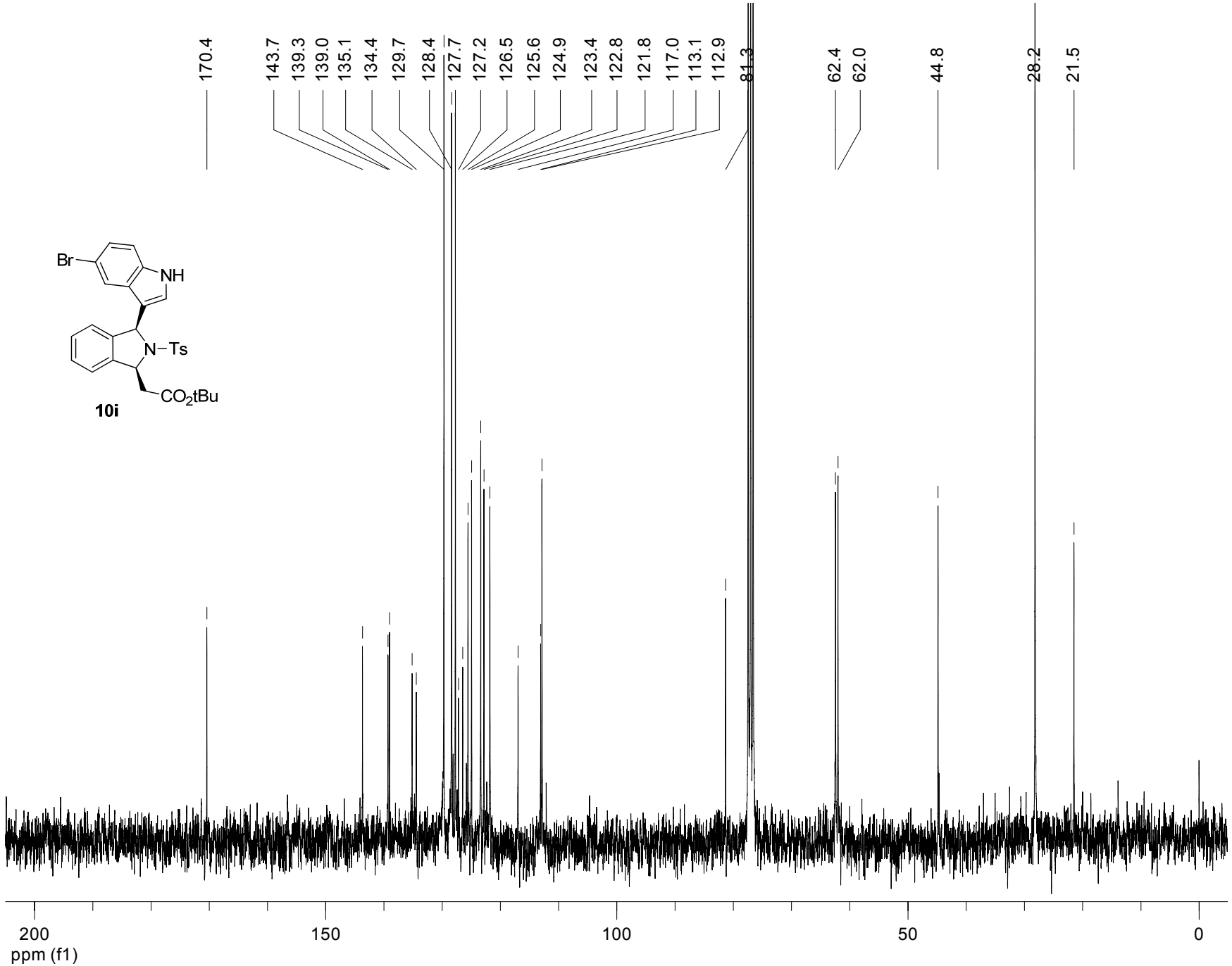
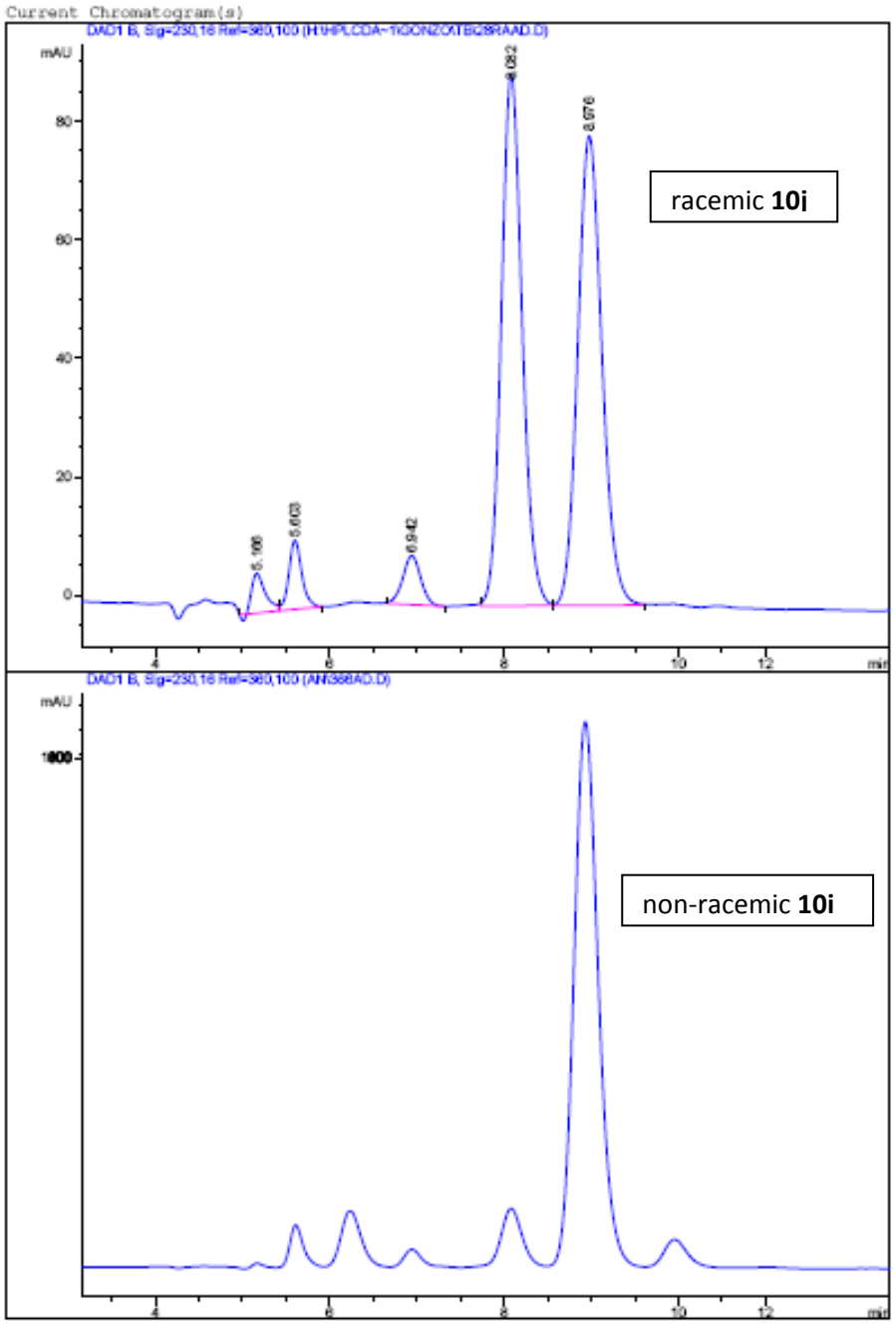


Figure S34. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of (1*S*,3*S*)-*t*-butyl 2-(3-(5-bromo-1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10i**).



AK Enders - Analytische HPLC

Sample Name: AN 366
Data file: D:\GONZO\AN\366AD.D
Sample Info: Laufmittel: n-Heptan/EtOH 7:3; Probe in LM gelöst

Säule: DAICELAD.M
Säuleninfo: (250x4)mm
Operator: Analytik Labor AKEN

Injektion Time: 10:15:05
Injektion Date: 06.02.2008

Instrument Conditions:	At Start	At Stop
Temperature in°C:	30.0°C	30.0°C
Pressure in bar:	25.4	26.1
Flow in ml/min:	0.7	0.7

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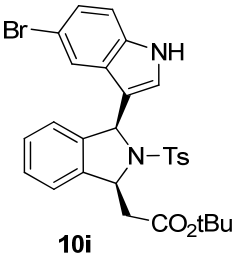
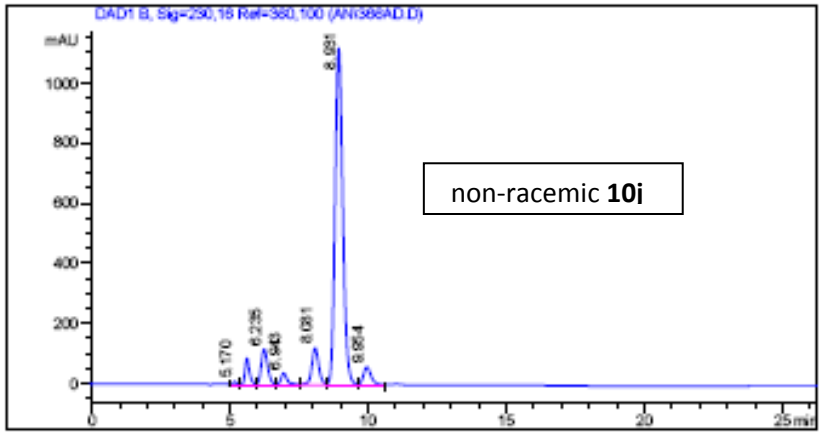


10i



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	5.17	0.15	11.68	123.14	0.42
2	5.61	0.17	90.04	1051.86	3.61
3	6.24	0.26	119.61	2012.06	6.91
4	6.94	0.25	39.87	685.46	2.35
5	8.08	0.27	123.83	2231.16	7.66
6	8.93	0.30	1120.76	21806.05	74.87
7	9.95	0.30	59.88	1215.69	4.17
Total				29125.42	100.00

Figure S35. HPLC traces of **10i**; overlay of racemic and non-racemic (left), non-racemic (right, Table 1, entry 9).

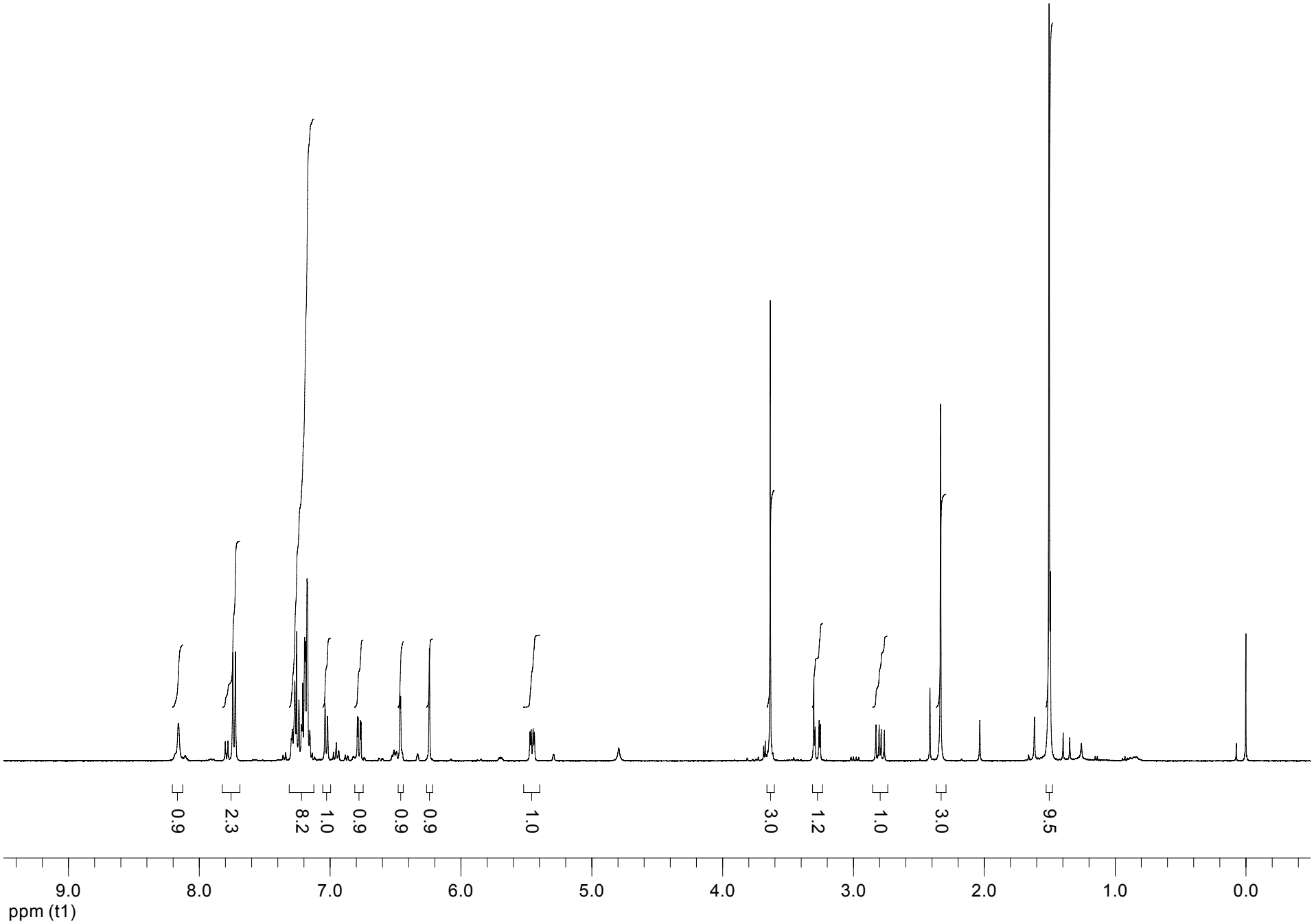


Figure S36. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of (1*S*,3*S*)-*t*-butyl 2-(3-(5-methoxy-1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10j**).

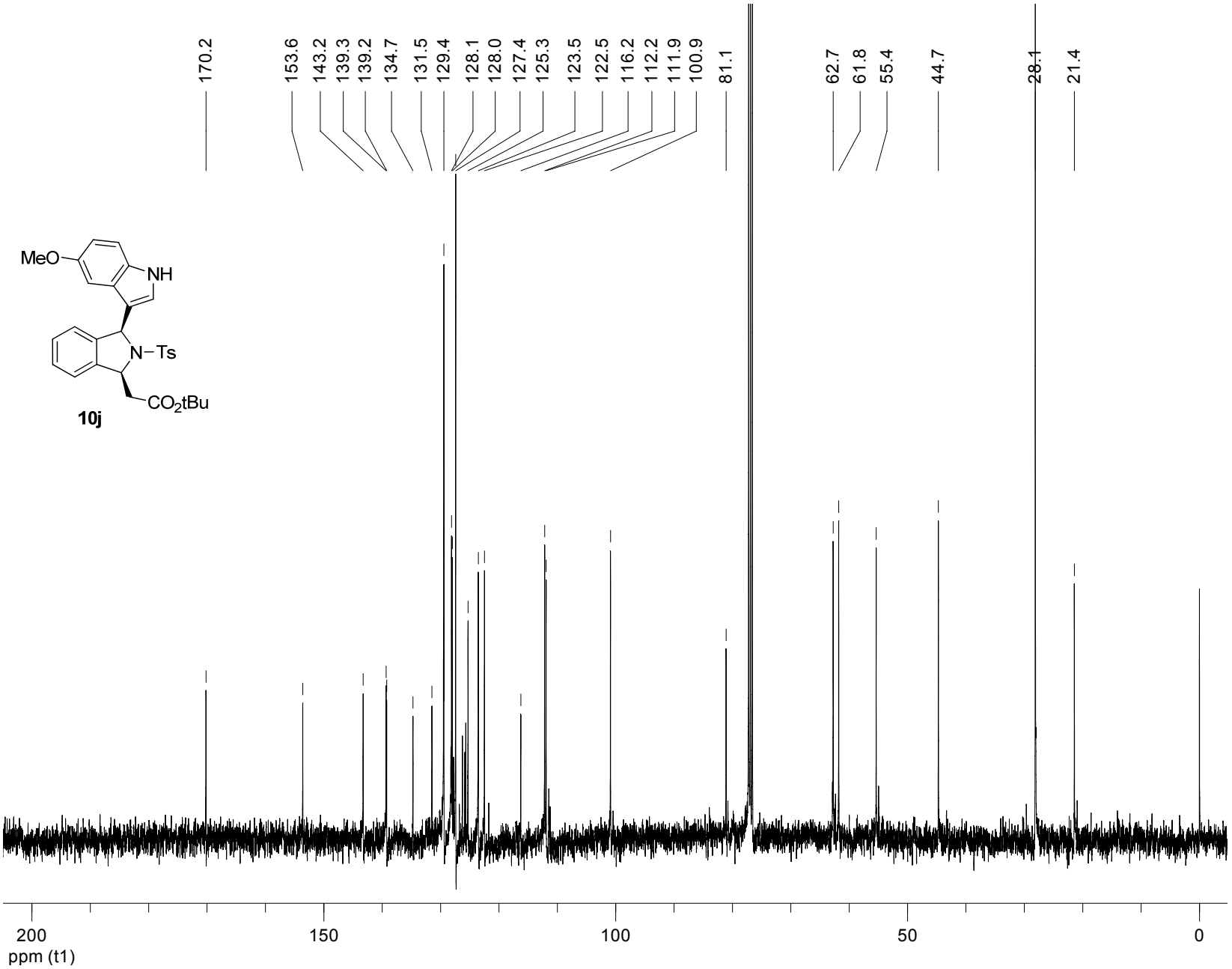
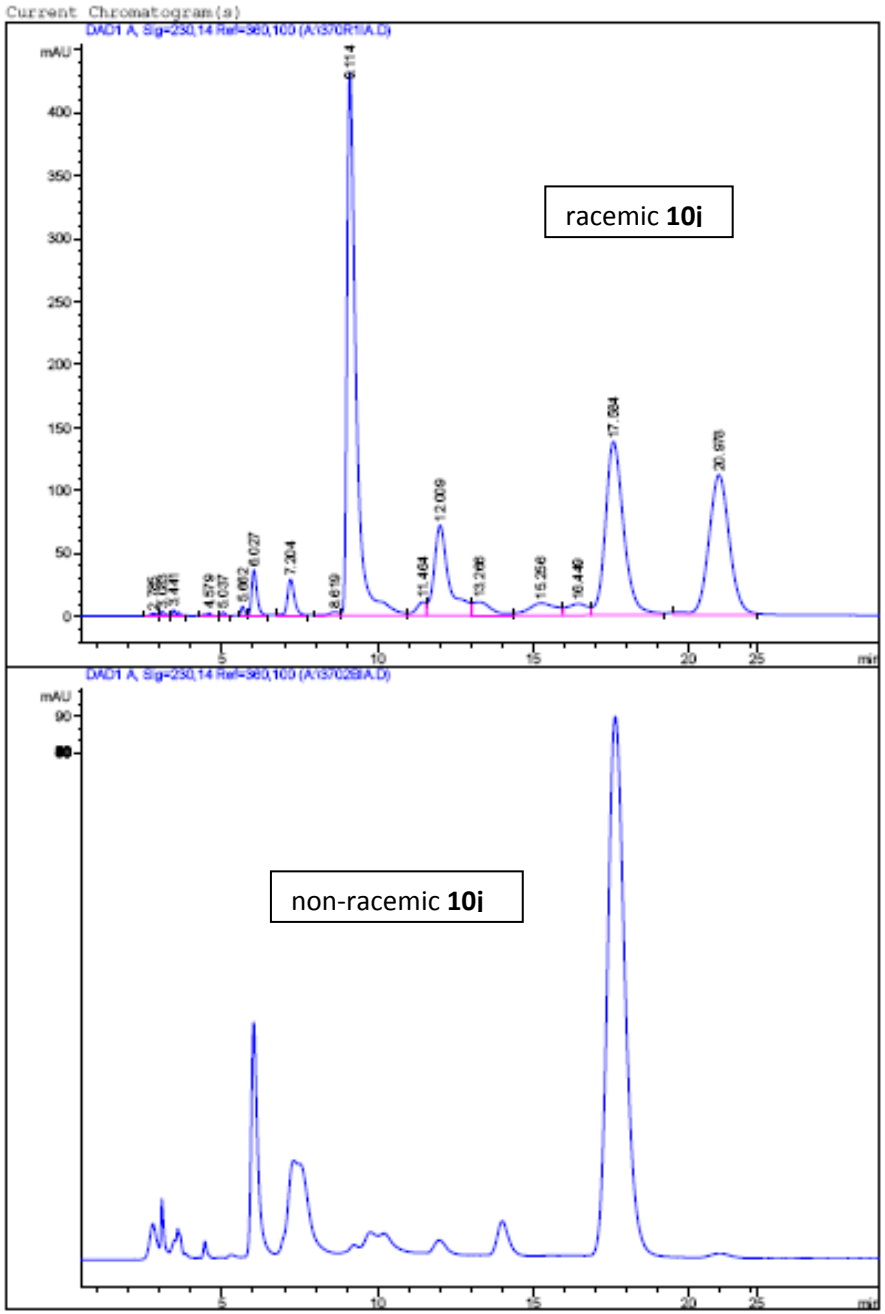


Figure S37. ^{13}C NMR spectrum (101 MHz, $CDCl_3$) of (1*S*,3*S*)-*t*-butyl 2-(3-(5-methoxy-1H-indol-3-yl)-2-tosylisoindolin-1-yl)acetate (**10j**).



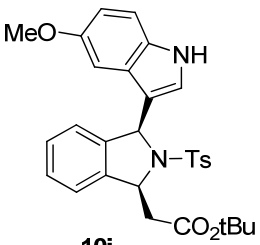
AK Enders - Analytische HPLC

Sample Name: AN 3702b
Data file: A:\3702BIA.D
Sample Info: Laufmittel:n-Heptan/IP 8:2;
Probe im LM/DCM gelöst

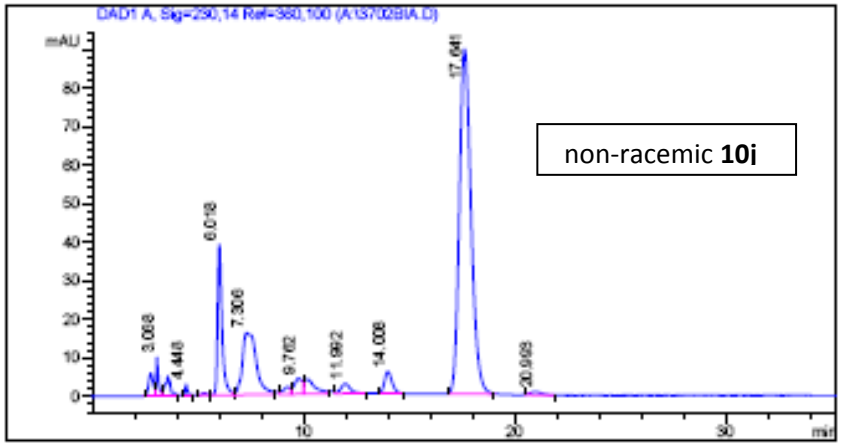
Säule: DAICELIA.M
Säuleninfo: (250x4)mm
Operator: Analytik Labor AKEN

Injektion Time: 14:57:36
Injektion Date: 18.02.2008

Instrument Conditions:	At Start	At Stop
Temperature in°C:	0.0°C	0.0°C
Pressure in bar:	53.3	53.1
Flow in ml/min:	1.0	1.0



10j



#	Ret. Time [min]	Width	Height [mAU]	Area [mAU*s]	Area %
1	2.78	0.23	5.91	90.50	1.62
2	3.07	0.10	10.05	72.87	1.30
3	3.58	0.22	5.04	88.69	1.58
4	4.45	0.12	2.87	22.71	0.41
5	5.29	0.26	0.60	10.75	0.19
6	6.02	0.22	39.06	575.21	10.28
7	7.31	0.60	16.07	742.34	13.27
8	9.25	0.34	1.96	47.51	0.85
9	9.76	0.39	4.05	109.93	1.96
10	10.21	0.48	3.81	138.40	2.47
11	11.99	0.43	2.56	80.35	1.44
12	14.01	0.37	5.68	142.42	2.55
13	17.64	0.59	89.33	3443.61	61.54
14	20.99	0.55	0.73	30.23	0.54
Total				5595.52	100.00

Figure S38. HPLC traces of **10j**; overlay of racemic and non-racemic (left), non-racemic (right, Table 4, entry 4).

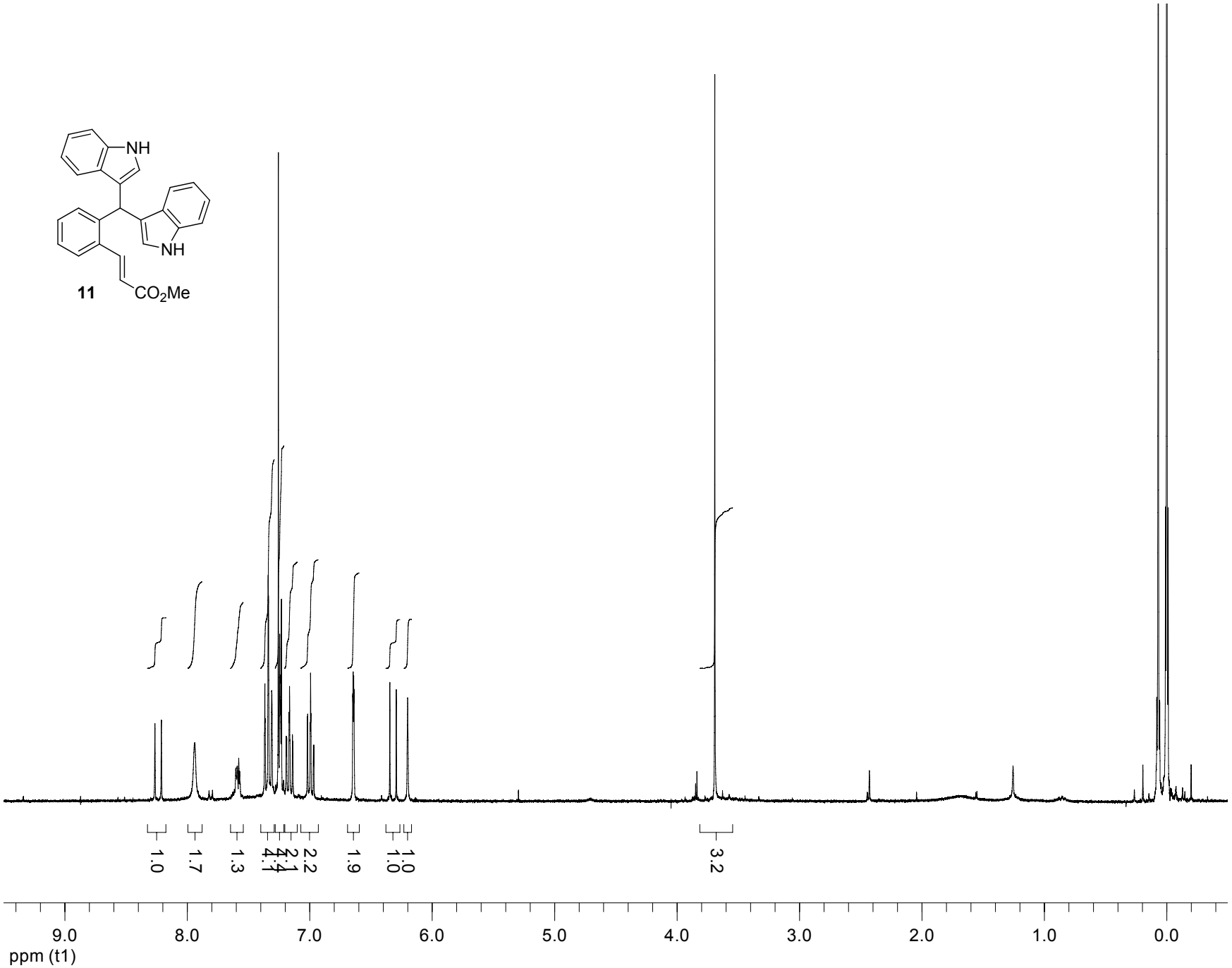


Figure S39. ^{1}H NMR (300MHz, $CDCl_3$) spectrum of ((*E*)-methyl 3-(2-((tosylimino)methyl)phenyl)acrylate (**11**).

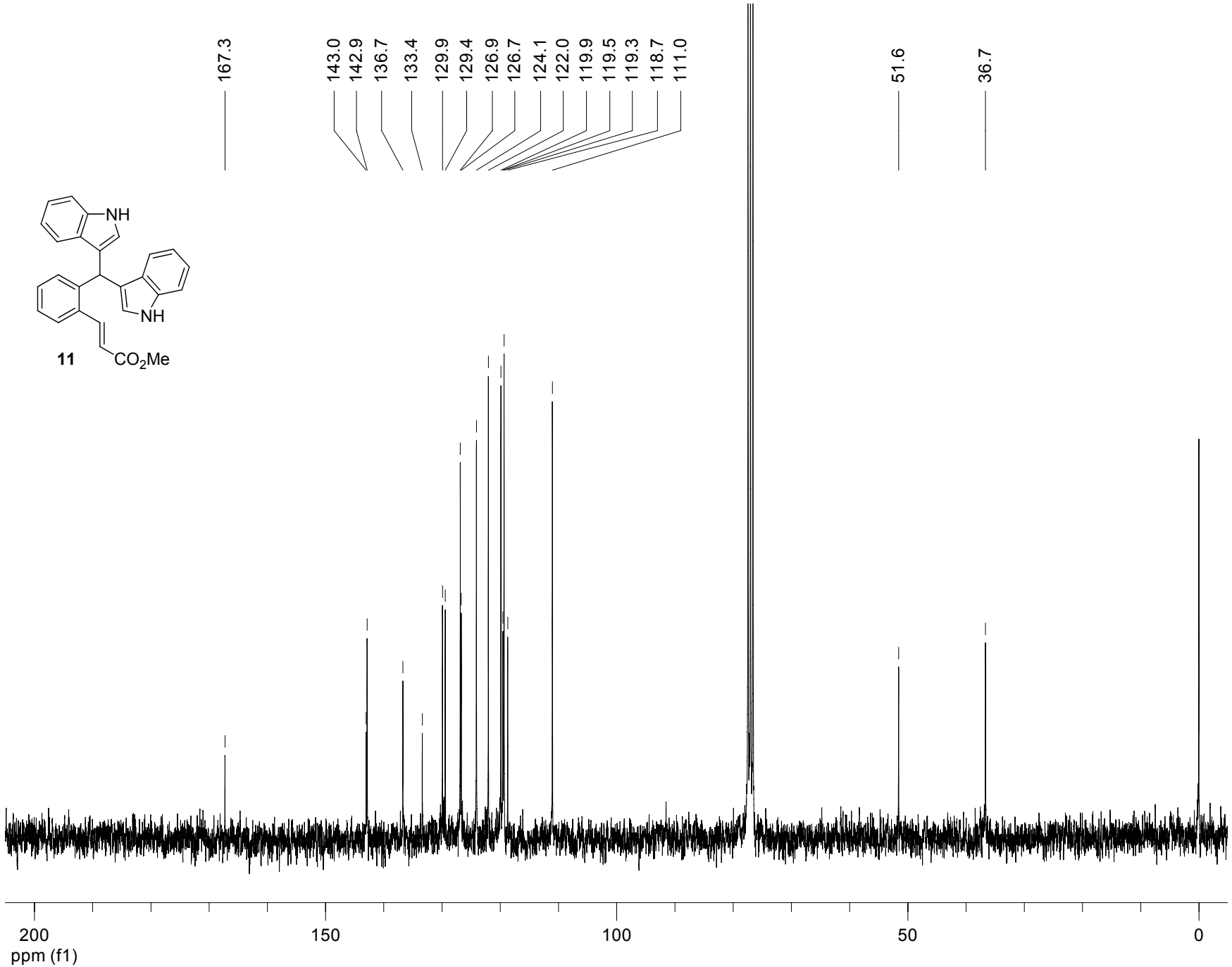


Figure S40. ^{13}C NMR (75 MHz, $CDCl_3$) spectrum of (*E*)-methyl 3-(2-((tosylimino)methyl)phenyl)acrylate (**11**).

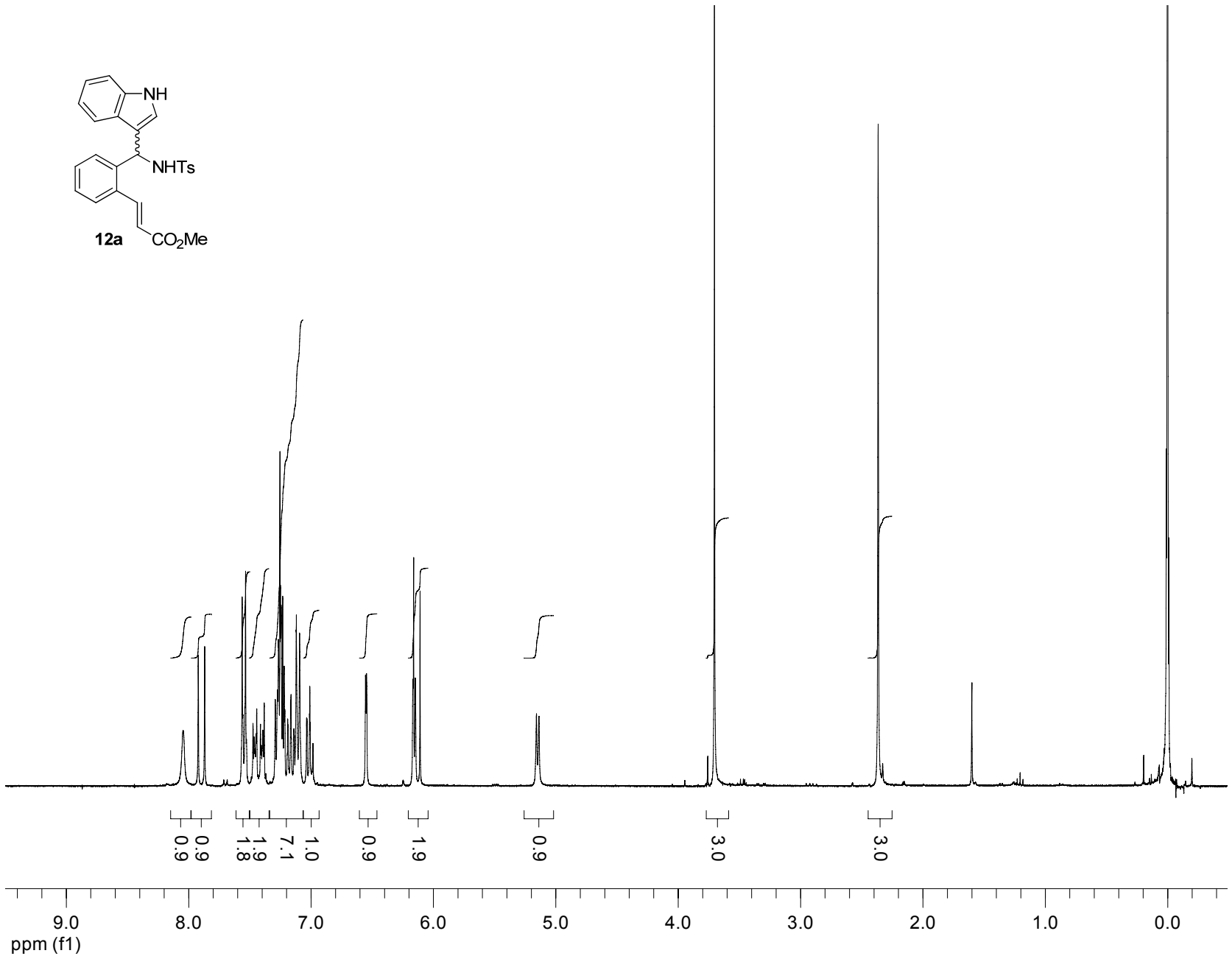


Figure S41. ^{1}H NMR (300 MHz, $CDCl_3$) spectrum of (*E*)-methyl 3-(2-((1H-indol-3-yl)(*p*-tosylamido)methyl)phenyl)acrylate (**12a**).

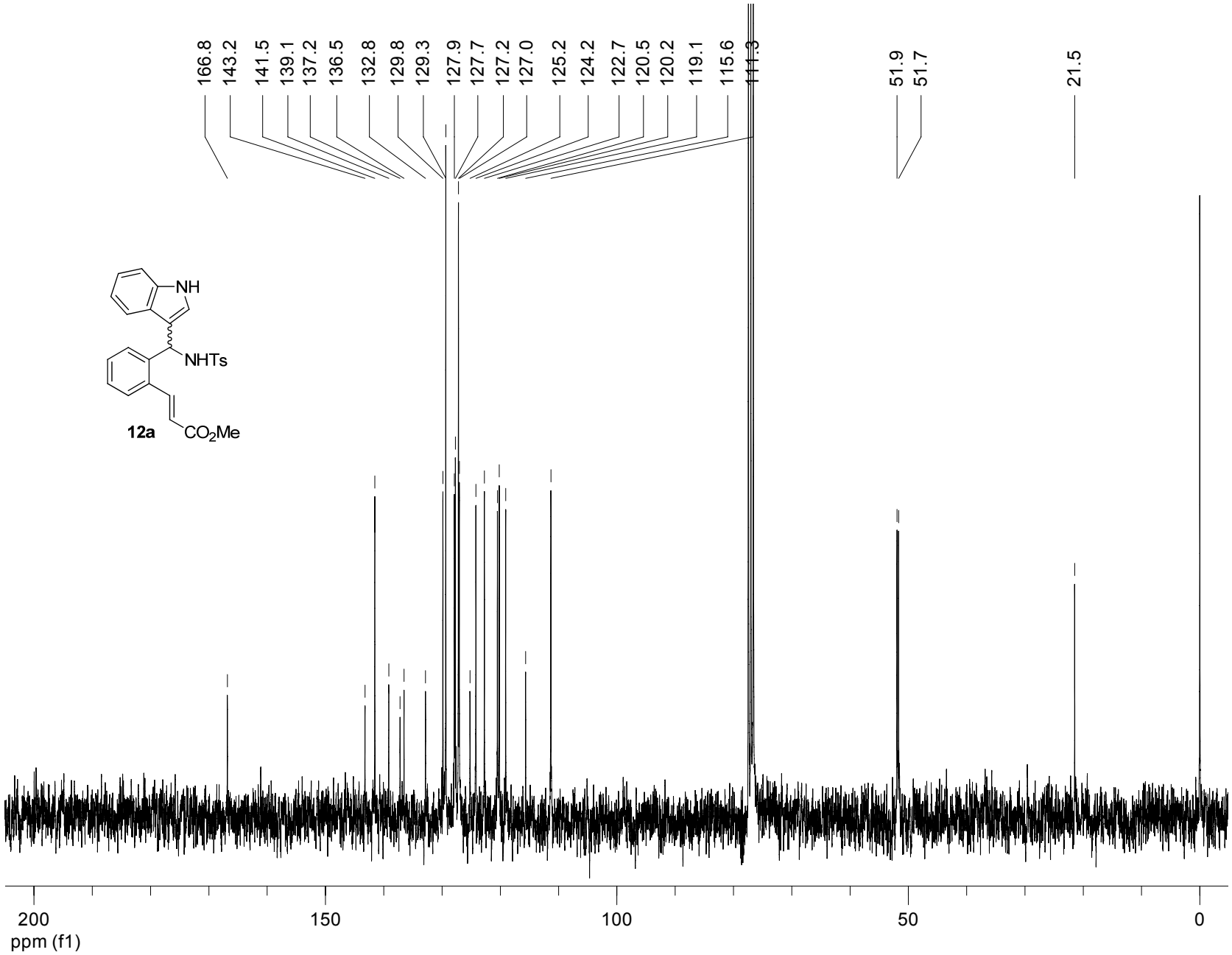


Figure S42. ^{13}C NMR (75 MHz, $CDCl_3$) spectrum of (*S*,*E*)-methyl 3-(2-((1H-indol-3-yl)(p-tosylamido)methyl)phenyl)acrylate (**12a**).