Organocatalytic Asymmetric Synthesis of Polyfunctionalized 3-(Cyclohexenylmethyl)-indoles via a Quadruple Domino Friedel-Crafts-Type/Michael/Michael/Aldol Condensation Reaction

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General Methods

Preparative column chromatography: Merck silica gel 60, particle size 0.040-0.063 mm (230-240 mesh, flash). Analytical TLC: SIL G-25 UV_{254} from MACHEREY-NAGEL. Visualization of the developed TLC plates was performed with ultraviolet irradiation (254 nm) or by staining with anisaldehyde. 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 Thermo Fisher Scientific Orbitrap XL. IR spectra were taken on a Perkin-Elmer FT-IR Spectrum 100 using an ATR-Unit. ^{1}H- and ^{13}C- NMR spectra were recorded at ambient temperature on Gemini 300, Varian Mercury 300 or Inova 400 intruments with tetramethylsilane as an internal standard. Analytical HPLC was performed on a Hewlett-Packard 1100 Series instrument using chiral stationary phases (Chiracel OD, Chiralcel OJ, Chiralpak AD, Chiralpak AS, Chiralcel IA).

Materials

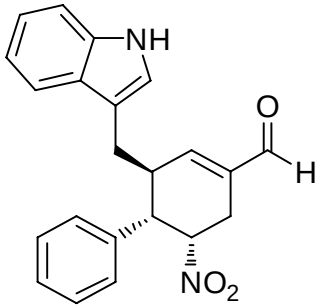
Unless otherwise noted, all commercially available compounds were used without further purification. The racemic products were prepared by mixing the induced products, which were synthesized under the catalysis of (*S*)- or (*R*)-prolinol TMS-ether.

Supplementary Material (ESI) for Chemical Communications

General Procedure

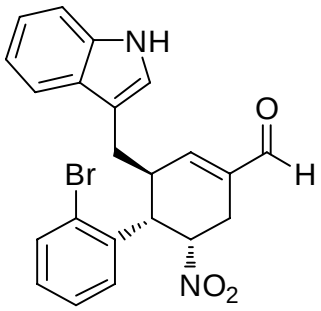
To a solution of nitroalkene (1 mmol), indole (1.5 mmol) and catalyst (10 mol %) in chloroform (1 mL) was added freshly distilled acroleine (3 mmol as a 1 M stock solution in chloroform) via a syringe pump within 12 h. The reaction mixture was stirred at room temperature for 24 h, after which the solvent was removed under reduced pressure. The crude product was directly separated by flash column chromatography on silica gel eluting with pentanes and diethyl ether.

Analytical Data



(4a)

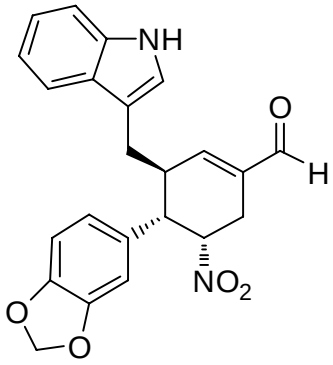
(1S, 2S, 6S)-6-((1H-indol-3-yl)methyl)-2-nitro-1,2,3,6-tetrahydro[1,1´-biphenyl]-4-carbaldehyde **(4a)** was isolated through flash chromatography (pentane:ether = 1:1) as a white solid (198 mg, 55 %). The *e.e.* (94 %) was determined by HPLC on a chiral stationary phase (Chiracel OD, *n*-heptane:*i*-propanol = 7:3, 1.0 mL/min), t_R = 9.02 min (minor), 15.57 min (major). M.p. 93 °C; $[\alpha]^{20}_D$ = +104.9 (*c* = 0.62, $CHCl_3$); IR (ATR): 3409, 3058, 2920, 2850, 2727, 2324, 2077, 1677, 1545, 1493, 1455, 1423, 1369, 1339, 1229, 1166, 1095, 1010, 982, 852, 809, 744, 701, 665 cm^{-1}; ^1H NMR (400 MHz, CD_3OD): δ = 2.54-2.63 (m, 1H), 2.67-2.75 (m, 1H), 2.88 (dd, 1H, *J* = 7.96, 14.55 Hz), 3.02 (dd, 1H, *J* = 5.91, 14.55 Hz), 3.36-3.50 (m, 2H), 4.93-4.99 (m, 1H), 6.95-7.00 (m, 1H), 7.05-7.12 (m, 6H), 7.23-7.31 (m, 3H), 7.35 (d, 1H, *J* = 7.14 Hz), 7.40 (d, 1H, *J* = 7.96 Hz), 9.40 (s, 1H) ppm; ^{13}C NMR (101 MHz, CD_3OD): δ = 23.7, 28.8, 40.7, 46.7, 83.6, 110.9, 111.0, 118.0, 118.4, 121.1, 123.1, 127.3, 127.5, 127.7, 128.4, 136.3, 136.7, 138.2, 153.4, 193.1 ppm; MS (EI, 70 eV): *m/z* (%): 361 (3) [M+1], 360 (11), 131 (11), 130 (100), 129 (3), 103 (3), 77 (4); HRMS (ESI): calcd. for $C_{22}H_{20}O_3N_2$: 360.1468 found: 360.1462.



(4b)

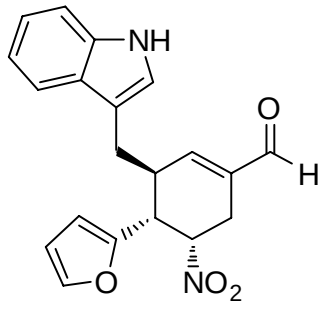
(1S, 2S, 6S)-6-((1H-indol-3-yl)methyl)-2´-bromo-2-nitro-1,2,3,6-tetrahydro [1,1´-biphenyl]-4-carbaldehyde (4b) was isolated through flash chromatography (pentane:ether = 1:1) as a white solid (211 mg, 48 %). The *e.e.* (>99 %) was determined by HPLC on a chiral stationary phase (Chiracel OD, *n*-heptane:*i*-propanol = 7:3, 0.7 mL/min), t_R = 9.36 min (minor, based on the racemic mixture), 11.98 min (major). M.p. 126 °C; $[\alpha]^{20}_D$ = +155.0 (*c* = 0.50, $CHCl_3$); IR (ATR): 3411, 3059, 2916, 2845, 2728, 2090, 1721, 1678, 1545, 1457, 1426, 1366, 1337, 1226, 1097, 1022, 922, 847, 821, 743, 675 cm^{-1}; ^1H NMR (300 MHz, CD_3COCD_3): δ = 2.73-3.04 (m, 3H), 3.10 (dd, 1H, *J* = 4.45, 14.59 Hz), 3.51-3.65 (m, 1H), 3.81-3.88 (dd, 1H, *J* = 3.46, 10.14 Hz), 5.20-5.27 (m, 1H), 6.7-7.1 (m,

1H), 7.08-7.11 (m, 1H), 7.18-7.52 (m, 5H), 7.70-7.74 (m, 1H), 9.55 (s, 3H), 10.16 (s, 1H) ppm; ^{13}C NMR (75 MHz, CD_3COCD_3): δ = 25.9, 27.7, 38.0, 45.5, 83.3, 110.6, 111.4, 118.8, 121.4, 123.6, 123.8, 125.6, 127.7, 128.2, 128.5, 129.6, 133.5, 136.3, 136.8, 137.1, 152.1, 192.6 ppm; MS (EI, 70 eV): *m/z* (%): 440 (5), 438 (4), 131 (10), 130 (100), 129 (3), 117 (2), 103 (3); HRMS (ESI): calcd. for $C_{22}H_{19}O_3N_2Br$: 438.0574, found: 438.0569.



(4c)

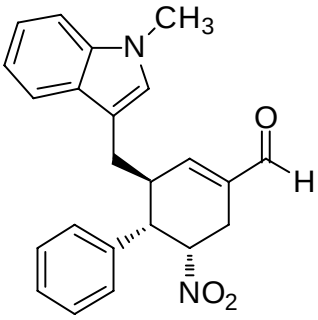
(3S, 4S, 5S)-3-((1H-indol-3-yl)methyl)-4-benzo[d][1,3]dioxol-5-yl)-5-nitrocyclohex-1-enecarbaldehyde (4c) was prepared according the general procedure (332 mg, 82 %) and obtained as a white solid after flash chromatography (pentane:ether = 2:3). The *e.e.* (>99 %) was determined by HPLC on a chiral stationary phase (Chiracel OD, heptane:*i*-propanol 7:3, 1.0 mL/min), t_R = 13.24 min (minor, based on the racemic mixture), 26.06 min (major). M.p. 92 °C; $[\alpha]_D^{20}$ = + 84.95 (*c* = 0.51 in $CHCl_3$); IR (ATR): 3412, 2916, 1721, 1677, 1545, 1503, 1487, 1443, 1370, 1337, 1285, 1234, 1165, 1123, 1096, 1036, 983, 929, 860, 812, 744, 669 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD): δ = 2.62 (dd, 1H, *J* = 6.04, 18.40 Hz), 2.70-2.80 (m, 1H), 2.93 (dd, 1H, *J* = 7.96, 14.56 Hz), 3.07 (dd, 1H, *J* = 6.04, 14.56 Hz), 3.30-3.50 (m, 2H), 4.96-5.01 (m, 1H), 5.92 (s, 2H), 6.58-6.62 (m, 2H), 6.77 (d, 1H, *J* = 8.79 Hz), 6.96-7.13 (m, 5H), 7.34 (d, 1H, *J* = 7.97 Hz), 7.43 (d, 1H, *J* = 7.97 Hz), 9.45 (s, 1H) ppm. ^{13}C NMR (101 MHz, CD_3OD): δ = 23.7, 28.8, 41.2, 46.4, 83.7, 101.1, 107.7, 107.9, 110.8, 110.9, 118.0, 118.3, 121.1, 123.1, 127.3, 127.4, 131.9, 136.3, 136.7, 147.2, 148.0, 153.3, 193.2 ppm; MS (EI, 70 eV): *m/z* (%): 404 (21) [M^+], 131 (10), 130 (100); HRMS (ESI): calcd. for $C_{23}H_{20}O_5N_2$: 404.1367, found: 404.1366.



(4d)

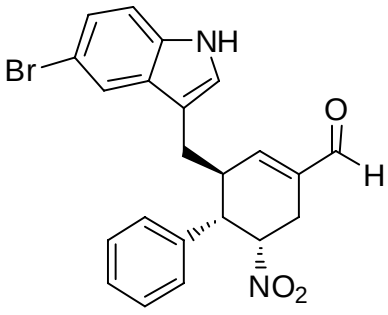
(3S, 4R, 5S)-3-((1H-indol-3-yl)methyl)-4-(furan-2-yl)-5-nitrocyclohex-1-enecarbaldehyde (4d) was prepared according the general procedure (105 mg, 30 %) and obtained as a white solid after flash chromatography (pentane:ether = 2:3). The *e.e.* (>99 %) was determined by HPLC on a chiral stationary phase (Chiracel OD, heptane:*i*-propanol 7:3, 0.7 mL/min), t_R = 13.34 min (minor, based on the racemic mixture), 20.09 min (major). M.p. 96 °C; $[\alpha]_D^{20}$ = + 87.40 (*c* = 0.5 in $CHCl_3$); IR (ATR): 3411, 2922, 2848, 1720, 1678, 1646, 1547, 1503, 1457, 1424, 1368, 1338, 1283, 1232, 1182, 1161, 1093, 1069, 1012, 983, 930, 882, 854, 815, 740, 666 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD): δ = 2.60 (dd, 1H, *J* = 7.41, 17.85 Hz), 2.76 (dd, 1H, *J* = 5.5, 18.13 Hz), 3.06 (d, 2H, *J* = 7.14 Hz), 3.37-3.44 (m, 1H), 3.75-3.77 (m, 1H), 5.00-5.06 (m, 1H), 6.13-6.16 (d, 1H, *J* = 3.30 Hz), 6.33-6.35 (dd, 1H, *J* = 1.93 Hz, *J* = 3.30 Hz), 7.00-7.06 (m, 3H), 7.11-7.18 (m, 2H), 7.37-7.41 (m, 2H), 7.49-7.53 (m, 1H), 9.43 (s, 1H) ppm; ^{13}C NMR (101 MHz, CD_3OD): δ = 23.3,

28.7, 40.3, 40.7, 81.1, 107.4, 110.0, 110.8, 111.0, 118.0, 118.5, 121.2, 123.2, 127.2, 136.2, 136.7, 142.1, 152.0, 152.3, 193.0 ppm; MS (EI, 70 eV): *m/z* (%): 350 (5) [M^+], 149 (7), 131 (11), 130 (100), 129 (8), 117 (4), 103 (7), 97 (5), 85 (6), 77 (7), 71 (8), 69 (6), 57 (17), 55 (13); HRMS (ESI): calcd. for $C_{20}H_{18}O_4N_2$: 350.1261, found: 350.1257.



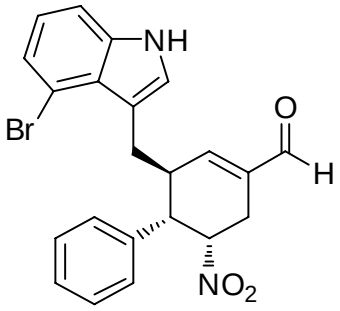
(4f)

(1S, 2S, 6S)-6-((1-methyl-1H-indol-3-yl)methyl)-2-nitro-1,2,3,6-tetrahydro[1,1´-biphenyl]-4-carbaldehyde **(4f)** was isolated through flash chromatography (pentane:ether = 1:1) as a bright yellow solid (201 mg, 54 %). The *e.e.* (97 %) was determined by HPLC on a chiral stationary phase (Chiracel OD = *n*-heptane:*i*-propanol 7:3, 1.0 mL/min), t_R = 21.57 min (major), 33.18 min (minor, based on the racemic mixture). M.p. 75 °C; $[\alpha]_D^{20}$ = +116 (*c* = 0.50 in $CHCl_3$); IR (ATR): 3057, 2923, 2822, 2725, 2090, 1726, 1681, 1646, 1545, 1474, 1371, 1330, 1249, 1212, 1165, 1121, 1066, 1010, 983, 927, 846, 741, 701, 668 cm^{-1}; ^1H NMR (400 MHz, C_6D_6): δ = 2.39 (dd, 1H, *J* = 5.50, 18.41 Hz), 2.54 (dd, 1H, *J* = 8.51, 14.56 Hz), 2.65 (dd, 1H, *J* = 6.32, 18.41 Hz), 2.77 (dd, 1H, *J* = 5.50, 14.56 Hz), 3.01 (s, 3H), 3.14-3.26 (m, 2H), 4.26-4.34 (m, 1H), 6.37 (s, 1H), 6.40-6.43 (m, 1H), 6.95-7.09 (m, 5H), 7.18-7.27 (m, 3H), 7.45 (d, 1H, *J* = 7.96 Hz), 9.17 (s, 1H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 24.2, 29.5, 31.9, 41.1, 47.4, 83.5, 109.6, 110.8, 119.0, 119.4, 122.1, 127.0, 127.9, 128.3, 128.8, 129.0, 136.6, 137.3, 138.0, 151.4, 191.3 ppm; MS (EI, 70 eV): *m/z* (%): 374 (11) [M^+], 145 (12), 144 (100), 143 (5), 77 (3); HRMS (ESI): calcd. for $C_{23}H_{22}O_3N_2$: 374.1625, found: 374.1625.



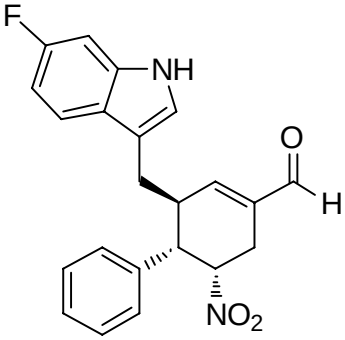
(4g)

(1S, 2S, 6S)-6-((5-bromo-1H-indol-3-yl)methyl)-2-nitro-1,2,3,6-tetrahydro [1,1´-biphenyl]-4-carbaldehyde (4g) was isolated through flash chromatography (pentane:ether = 2:3) as a white solid (220 mg, 50 %). The *e.e.* (>99 %) was determined by HPLC on a chiral stationary phase (Chiracel OD, heptane:*i*-propanol 7:3, 1.0 mL/min), t_R = 7.20 min (minor), 10.48 min (major). M.p. 104 °C; $[\alpha]_D^{20}$ = +77.2 (*c* = 0.50 in $CHCl_3$); IR (ATR): 3418, 2923, 2854, 2726, 2097, 1723, 1678, 1602, 1545, 1494, 1371, 1339, 1228, 1166, 1097, 1074, 1030, 982, 928, 880, 860, 796, 764, 701, 660 cm^{-1}; ^1H NMR (400 MHz, CD_3OD): δ = 2.64 (dd, 1H, *J* = 5.49, 18.40 Hz), 2.75 (dd, 1H, *J* = 5.77, 18.41 Hz), 3.03 (dd, 1H, *J* = 5.22, 14.83 Hz), 3.39-3.52 (m, 2H), 5.01-5.07 (m, 1H), 7.11-7.18 (m, 6H), 7.24-7.37 (m, 5H), 7.46-7.49 (m, 1H), 9.51 (s, 1H); ^{13}C NMR (101 MHz, CD_3OD): δ = 24.0, 28.3, 40.6, 46.4, 83.8, 110.7, 111.5, 112.6, 120.6, 123.8, 124.6, 127.5, 127.7, 128.5, 129.2, 135.2, 136.5, 138.1, 153.2, 193.0 ppm; HRMS (ESI): calcd. for $C_{22}H_{19}O_3N_2Br$: 438.0574, found: 438.0577.



(4h)

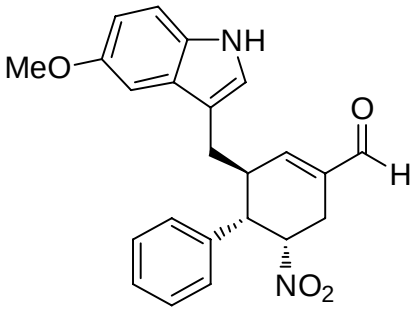
(1S, 2S, 6S)-6-((4-bromo-1H-indol-3-yl)methyl)-2-nitro- 1,2,3,6- tetrahydro [1,1´-biphenyl]-4-carbaldehyde (4h) was isolated through flash chromatography (pentane:ether = 1:1) as a white solid (101 mg, 23 %). The *e.e.* (>99 %) was determined by HPLC on a chiral stationary phase (Chiracel OD, *n*-heptane:*i*-propanol = 7:3, 1.0 mL/min), t_R = 11.09 min (minor, based on the racemic mixture), 15.39 min (major). M.p. 117 °C; $[\alpha]_D^{20}$ = +20.0 (*c* = 0.52 in $CHCl_3$); IR (ATR): 3415, 3061, 3032, 2971, 2924, 2852, 2730, 2324, 2074, 1723, 1678, 1643, 1614, 1545, 1493, 1424, 1371, 1337, 1284, 1248, 1196, 1173, 1098, 1072, 1043, 981, 912, 856, 800, 771, 742, 701, 666 cm^{-1}; ^1H NMR (400 MHz, CD_3OD): δ = 2.52 (dd, 1H, *J* = 8.52, 17.86 Hz), 2.85 (dd, 1H, *J* = 5.22, 17.86 Hz), 3.12 (dd, 1H, *J* = 7.69, 14.29 Hz), 3.34-3.50 (m, 1H), 3.69-3.73 (m, 1H), 4.98-5.04 (m, 1H), 6.89-7.01 (m, 4H), 7.06-7.24 (m, 7H), 7.34 (d, 1H, *J* = 8.24 Hz), 9.45 (s, 1H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 22.5, 30.4, 43.7, 46.5, 82.4, 110.8, 111,8, 113.1, 122.0, 123.0, 124.8, 125.6, 127.4, 127.7, 128.2, 136.7, 138.0, 138.3, 153.0, 192.9 ppm; MS (EI, 70 eV): *m/z* (%): 440 (7) [M+1], 438 (8), 211 (11), 210 (99), 208 (100), 129 (12); HRMS (ESI): calcd. for $C_{22}H_{19}O_3N_2Br$: 438.0574, found: 438.0569.



(4i)

(1S, 2S, 6S)-6-((6-fluoro-1H-indol-3-yl)methyl)-2-nitro-1,2,3,6-tetrahydro[1,1´-biphenyl]-4-carbaldehyde **(4i)** was isolated after flash chromatography (pentane:ether = 1:1) as a white solid (204 mg, 54 %). The *e.e.* (97 %) was determined by HPLC on a chiral stationary phase (Chiracel OD, *n*-heptane:*i*-propanol = 7:3, 0.7 mL/min), t_R = 12.14 min (minor), 21.97 min (major). M.p. 89 °C; $[\alpha]_D^{20}$ = +116 (*c* = 0.50 in $CHCl_3$);

IR (ATR): 3421, 2920, 2829, 2324, 2113, 1725, 1678, 1627, 1545, 1495, 1453, 1371, 1341, 1252, 1225, 1165, 1138, 1090, 1068, 1029, 982, 950, 837, 803, 764, 701, 664 cm^{-1}; ^1H NMR (300 MHz, CD_3OD): 2.56-2.68 (m, 1H), 2.72-2.83 (m, 1H), 2.93 (dd, 1H, *J* = 7.91, 14.59 Hz), 3.05 (dd, 1H, *J* = 5.93, 14.59 Hz), 3.39-3.56 (m, 2H), 4.99-5.08 (m, 1H), 6.72-6.81 (m, 1H), 7.01-7.17 (m, 5H), 7.25-7.42 (m, 5H), 9.51 (s, 1H) ppm; ^{13}C NMR (75 MHz, CD_3OD): δ = 23.7, 28.6, 40.7, 46.8, 83.6, 96.9 (d, J_{C-F} = 25.7 Hz), 106.9 (d, J_{C-F} = 24.5 Hz), 111.2, 118.8, 119.0, 123.6, 124.1, 127.6, 127.7, 128.3, 128.5, 136.5, 138.2, 151.8, 153.2, 159.8 (d, J_{C-F} = 253 Hz), 193.2 ppm; MS (EI, 70 eV): *m/z* (%): 378 (11) [M^+], 149 (10), 148 (100), 101 (3); HRMS (ESI): calcd. for $C_{22}H_{19}O_3N_2F$: 378.1374, found: 378.1373.



(4j)

(1S, 2S, 6S)-6-((5-methoxy-1H-indol-3-yl)methyl)-2-nitro-1,2,3,6-tetrahydro[1,1´-biphenyl]-4-carbaldehyde (4j) was isolated through flash chromatography (pentane:ether = 1:1) as a bright yellow solid (125 mg, 32%). The *e.e.* (99 %) was determined by HPLC on a chiral stationary phase (Chiracel OD, *n*-heptane:*i*-propanol = 7:3, 0.7 mL/min), t_R = 13.75 min (minor), 24.55 min (major). M.p. 78 °C; $[\alpha]_D^{20}$ = + 96.54 (*c* = 0.52 in $CHCl_3$); IR (ATR): 3411, 2937, 2830, 2726, 2101, 1721, 1678, 1624, 1583, 1583, 1545, 1484, 1453, 1440, 1371, 1339, 1292, 1214, 1170, 1096, 1059, 1027, 981, 924, 834, 798, 765, 702, 666 cm^{-1}; ^1H NMR (300 MHz, CD_3OD): δ = 2.78-2.82 (m, 2H), 2.96 (dd, 1H, *J* = 7.83, 14.56 Hz), 3.10 (dd, 1H, *J* = 5.77, 14.56 Hz), 3.45-3.58 (m, 2H), 3.89 (s, 3H), 5.04-5.10 (m, 1H), 6.92 (dd, 1H, *J* = 2.47, 8.79 Hz), 7.01 (d, 1H, *J* = 2.47 Hz), 7.19-7.27 (m, 4H), 7.35 (m, 5H), 9.56 (s, 1H) ppm; ^{13}C NMR (75 MHz, CD_3OD): δ = 23.9, 29.6, 40.7, 46.6, 55.0, 83.7, 99.8, 110.7, 111.1, 111.4, 123.9, 127.5, 127.5, 127.7, 128.5, 131.8, 136.2, 138.3, 153.3, 153.6, 193.1 ppm; MS (EI, 70 eV): *m/z* (%): 390 (12) [M^+], 161 (12), 160 (100), 145 (8), 129 (5), 117 (4); HRMS (ESI): calcd. for $C_{23}H_{22}O_4N_2$: 390.1574, found: 390.1569.

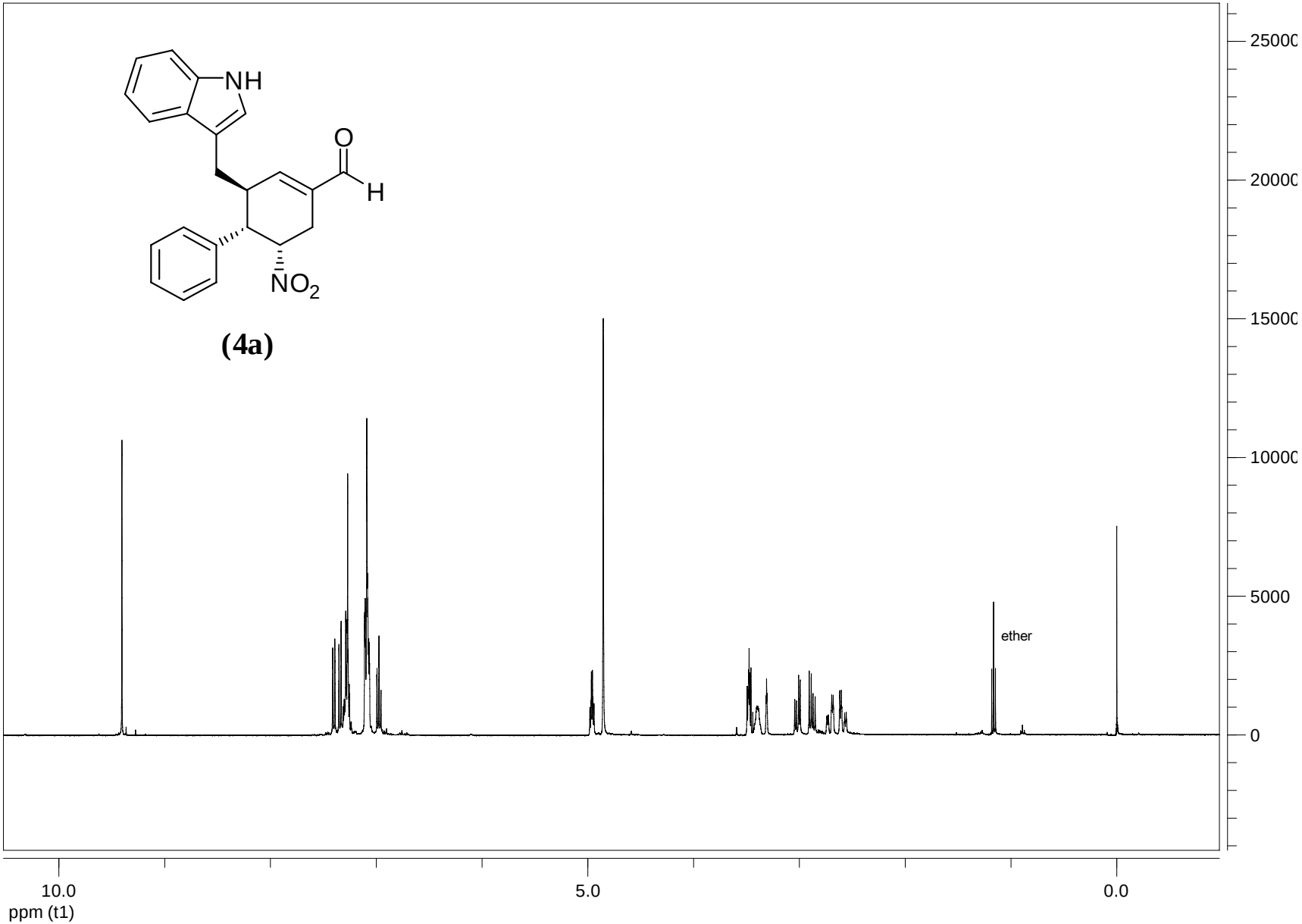


Figure S1. ^{1}H NMR (400 MHz, CD_3OD) spectrum of (1*S*, 2*S*, 6*S)*-6-((1*H*-indol-3-yl)methyl)-2-nitro-1,2,3,6-tetrahydro[1,1´-biphenyl]-4-carbaldehyde (**4a**).

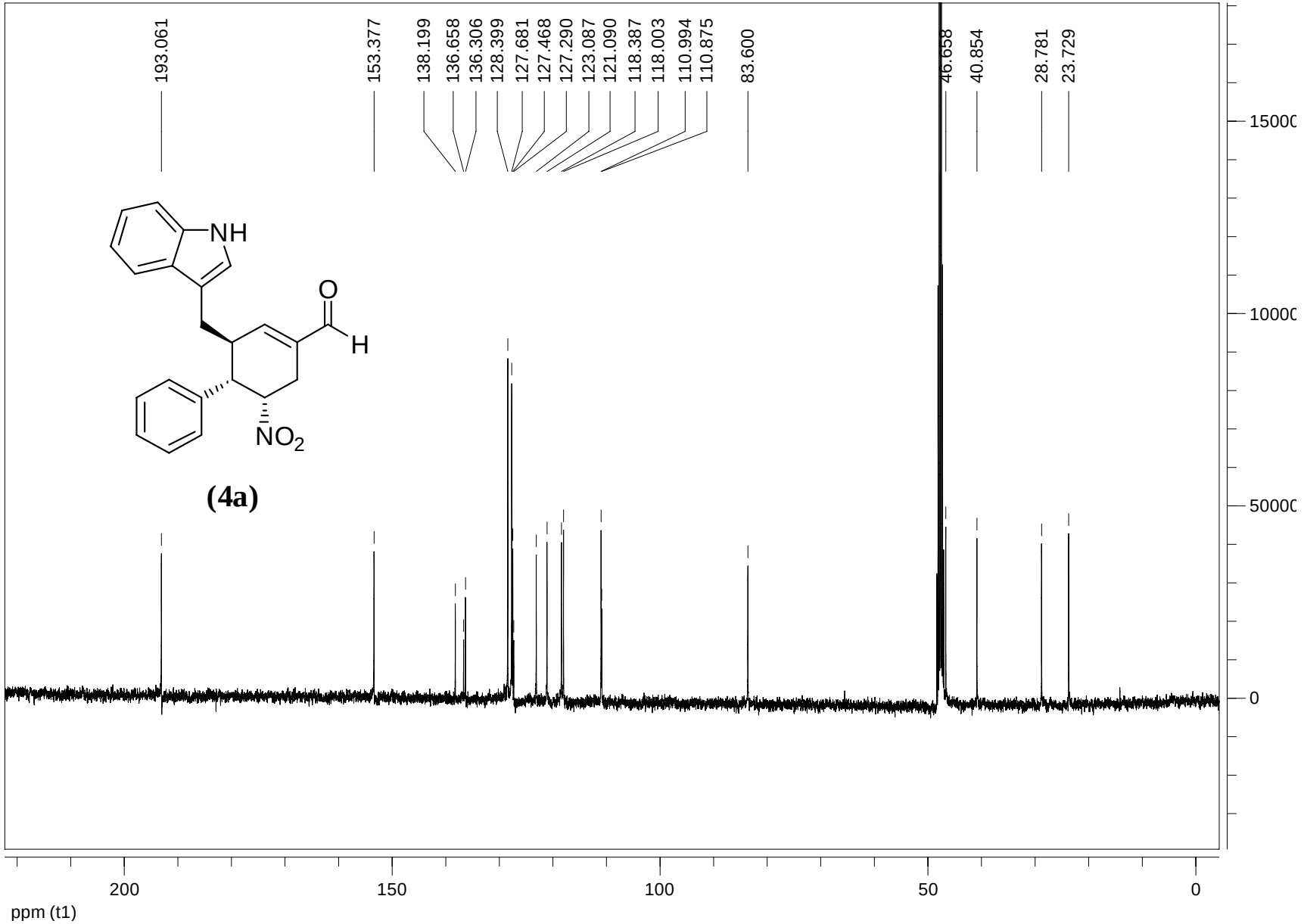
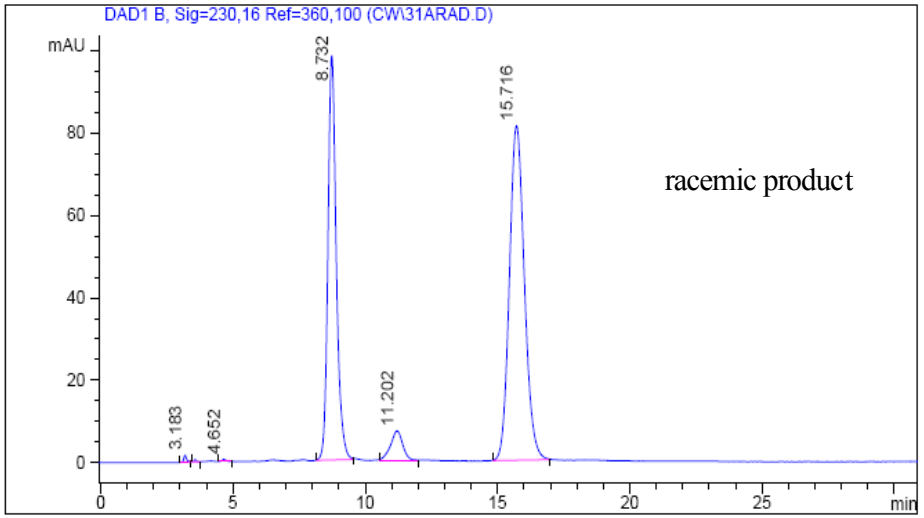
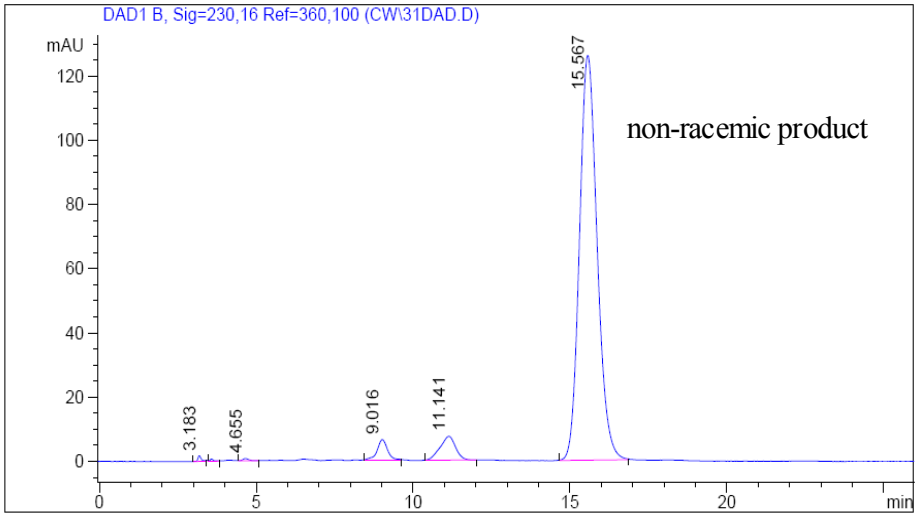


Figure S2. ^{13}C NMR spectrum (CD_3OD, 101 MHz) of (1*S*, 2*S*, 6*S)*-6-((1*H*-indol-3-yl)methyl)-2-nitro-1,2,3,6-tetrahydro[1,1´-biphenyl]-4-carbaldehyde (**4a**)



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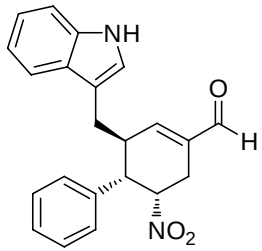
Sample Name:          CW 31 d
Data file:            D:\GONZO\CW\31DAD.D
Sample Info:          Laufmittel: n-Heptan/IP 7:3
                      Probe ist in DCM/LM gelöst

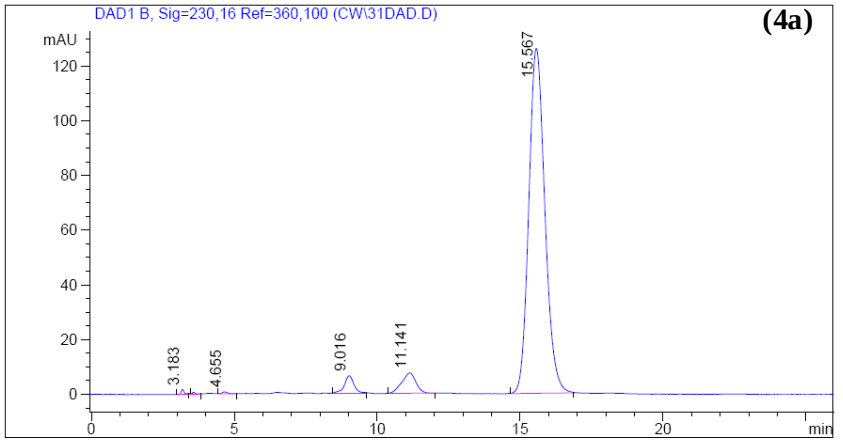
Säule:                DAICELAD.M
Säuleninfo:           (250x4,6)mm
Operator:             Analytik Labor AKEN

 Injektion Time:       12:05:37
 Injektion Date:       30.09.2009

 Instrument Conditions:   At Start          At Stop
 Temperature in°C:          30.0°C           30.0°C
 Pressure in bar:           41.2             42.4
 Flow in ml/min:            1.0              1.0
```

HEWLETT PACKARD





#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	3.18	0.12	1.80	14.06	0.26
2	3.58	0.12	0.71	6.26	0.12
3	4.65	0.19	0.75	10.18	0.19
4	9.02	0.34	6.42	150.68	2.81
5	11.14	0.49	7.43	256.96	4.79
6	15.57	0.60	126.05	4930.69	91.84
Total				5368.85	100.00

Figure S3. HPLC traces of 4**a**; overlay of racemic and non-racemic (left), non-racemic (right)

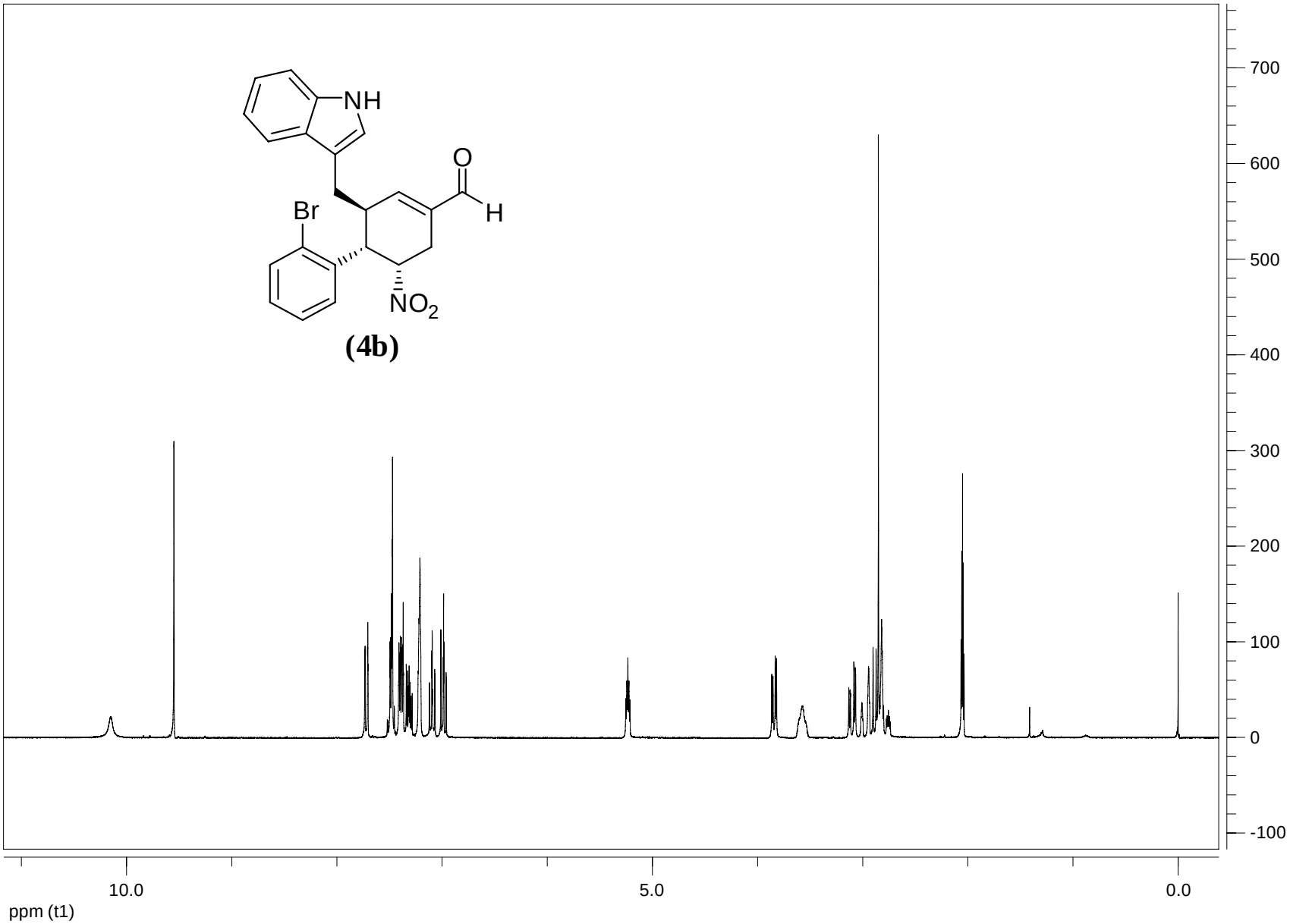


Figure S4. ^{1}H NMR (300 MHz, CD_3COCD_3) spectrum of (1*S*, 2*S*, 6*S*)-6-((1*H*-indol-3-yl)methyl)-2´-bromo-2-nitro-1,2,3,6-tetrahydro [1,1´-biphenyl]-4-carbaldehyde (**4b**)

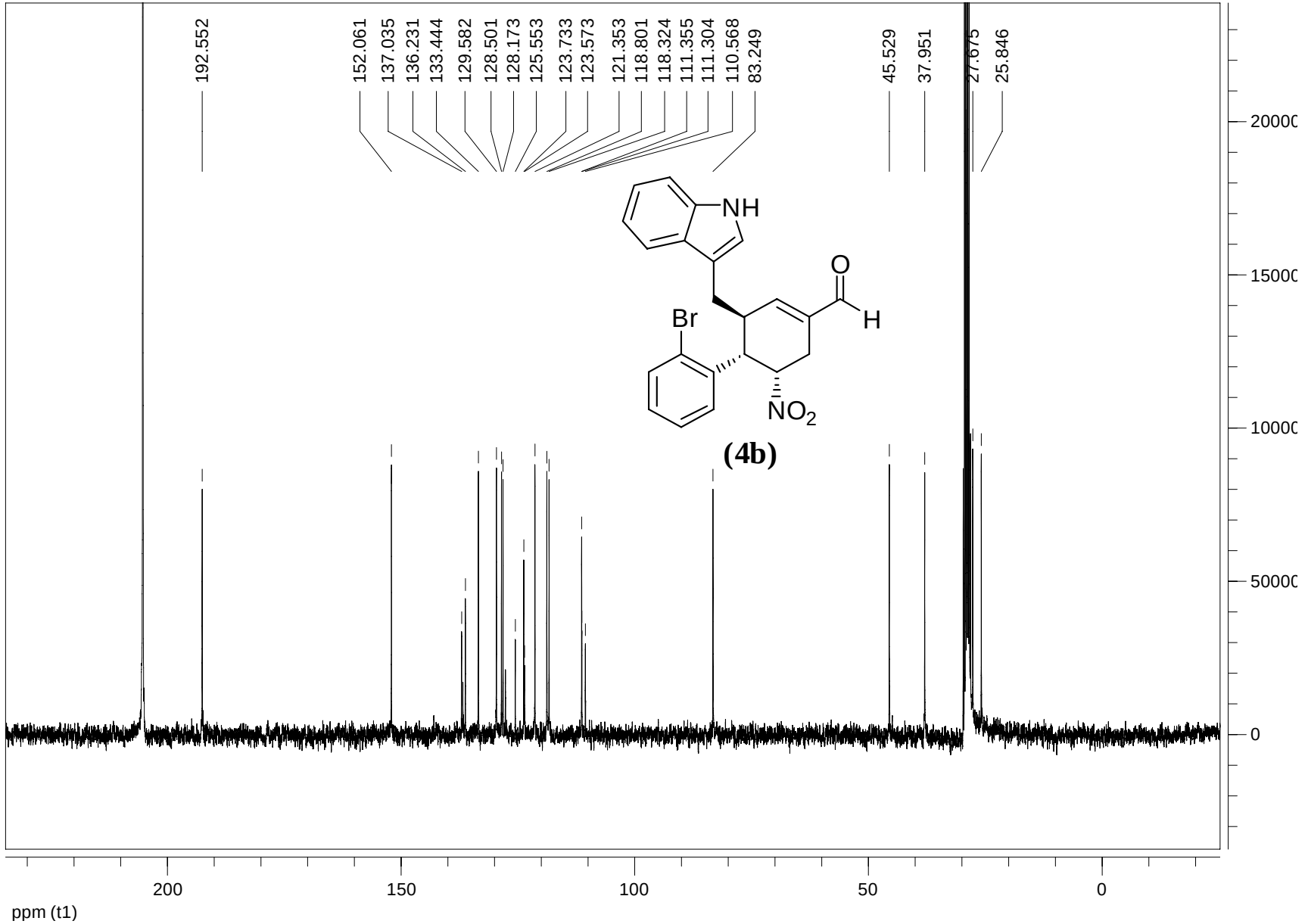
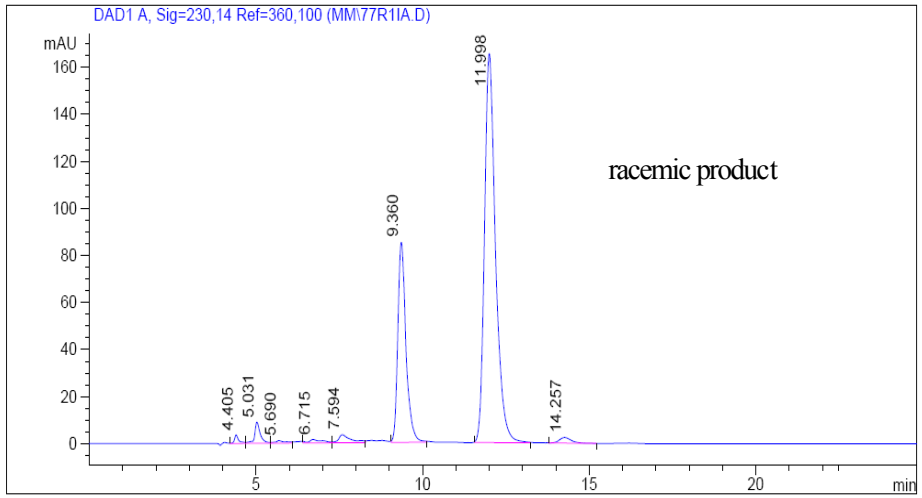
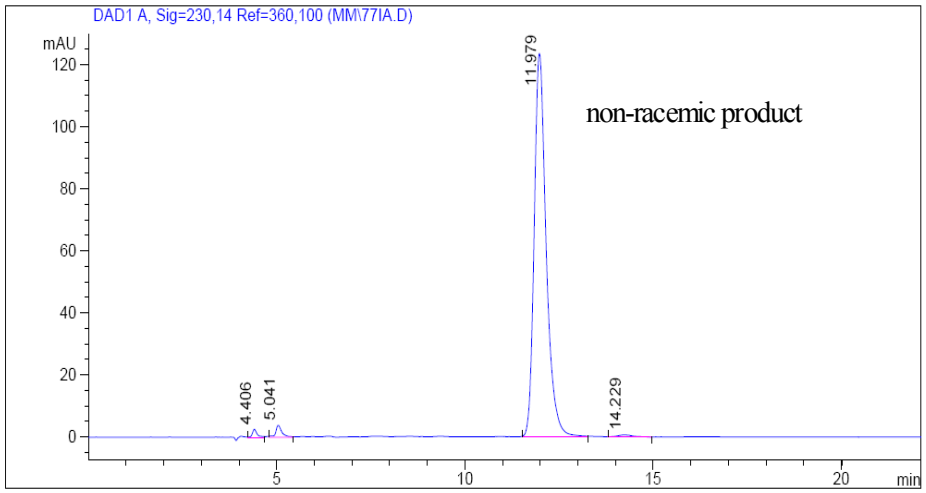


Figure S5. ^{13}C NMR (101 MHz, CD_3COCD_3) spectrum of (1*S*, 2*S*, 6*S*)-6-((1*H*-indol-3-yl)methyl)-2´-bromo-2-nitro-1,2,3,6-tetrahydro [1,1´-biphenyl]-4-carbaldehyde (**4b**)






```
Sample Name:      MM 77
Data file:        D:\BERT\MM\77IA.D
Sample Info:      Laufmittel: n-Heptan/IP 7:3;
                  Die Probe ist in DCM/LM gelöst

Säule:            DAICELIA.M
Säuleninfo:       (250x4,6)mm

Operator:         Analytik Labor AKEN

Injektion Time:       10:40:53
Injektion Date:       02.12.2009

Instrument Conditions:   At Start          At Stop

Temperature in°C:        30.0              30.0
Pressure in bar:         46.5              46.5
Flow in ml/min:          0.7               0.7
```

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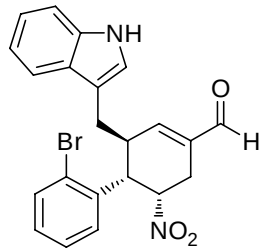
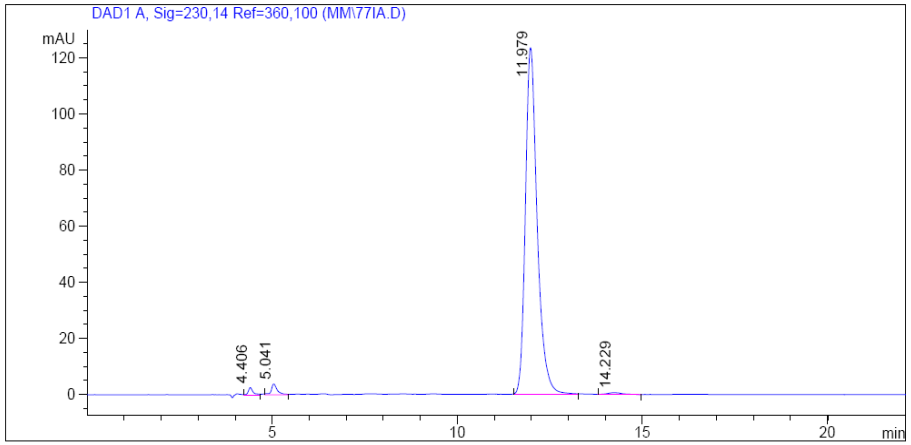


(4b)



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	4.41	0.14	2.60	23.15	0.82
2	5.04	0.17	3.86	44.68	1.58
3	11.98	0.33	123.58	2737.36	96.94
4	14.23	0.39	0.64	18.43	0.65
Total				2823.63	100.00

Figure S6. HPLC traces of **4b**; overlay of racemic and non-racemic (left), non-racemic (right)

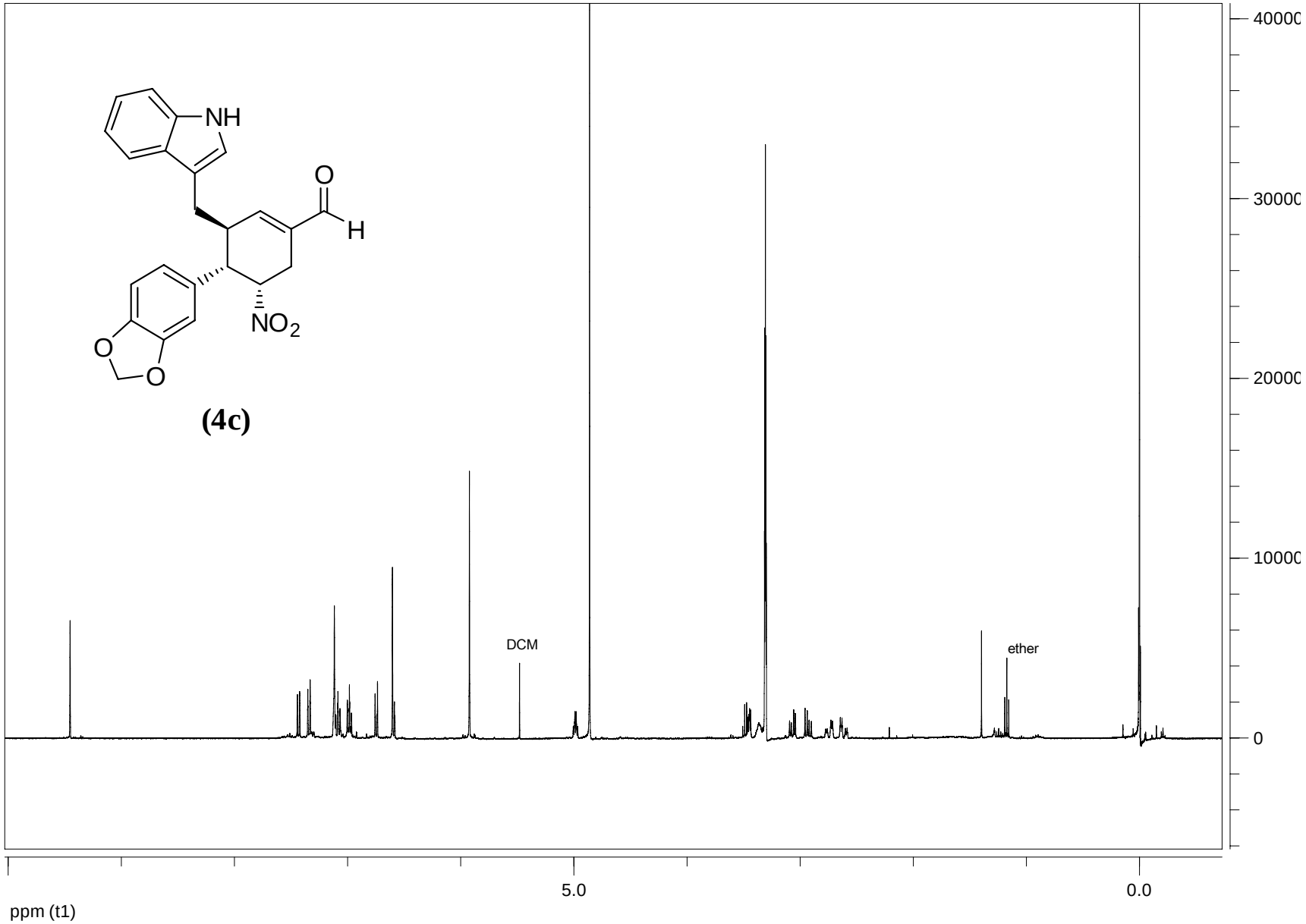


Figure S7. ^{1}H NMR spectrum (400 MHz, CD_3OD) of (3*S*, 4*S*, 5*S*)-3-((1*H*-indol-3-yl)methyl)-4-benzo[d][1,3]dioxol-5-yl)-5-nitrocyclohex-1-enecarbaldehyde (**4c**)

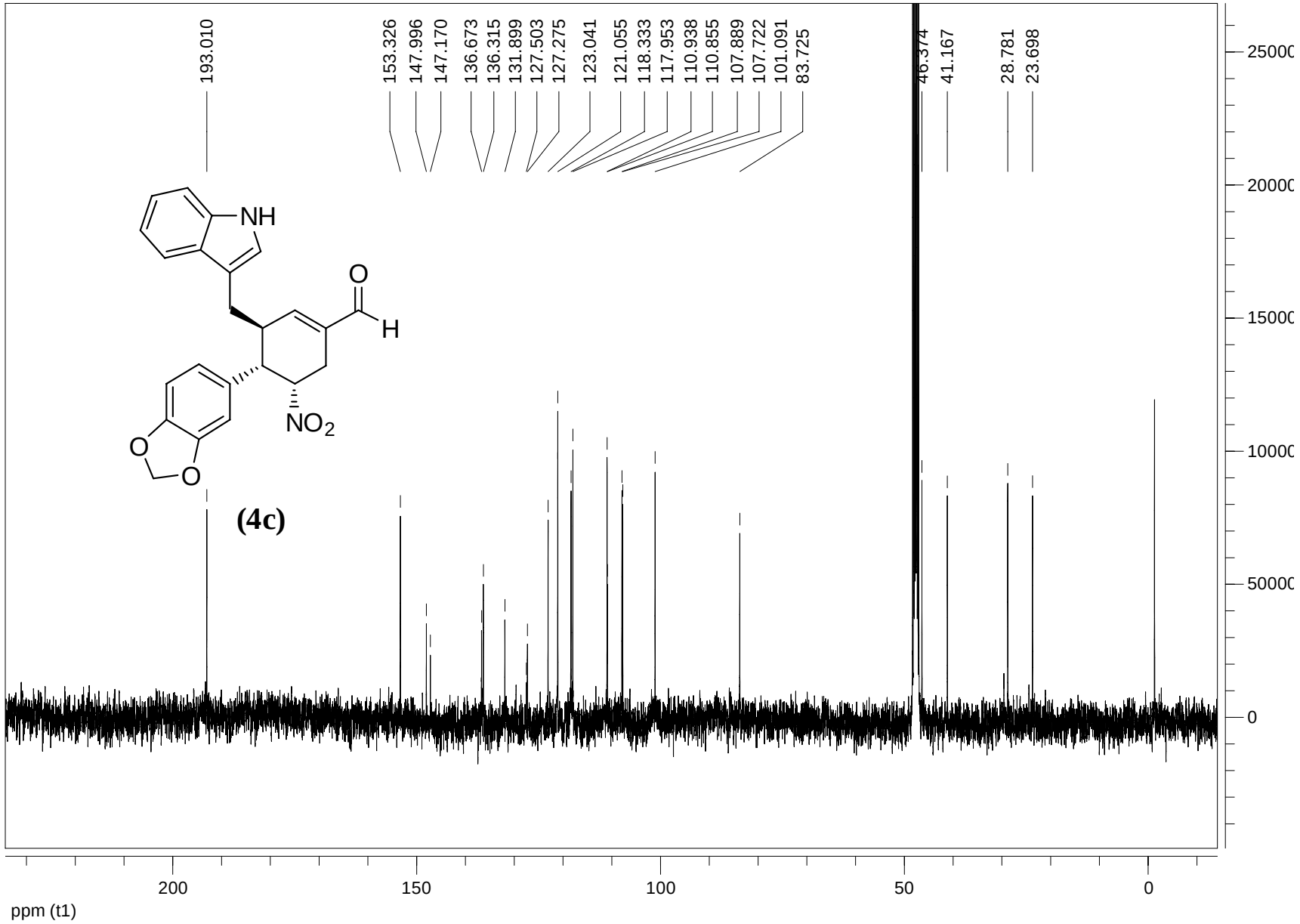
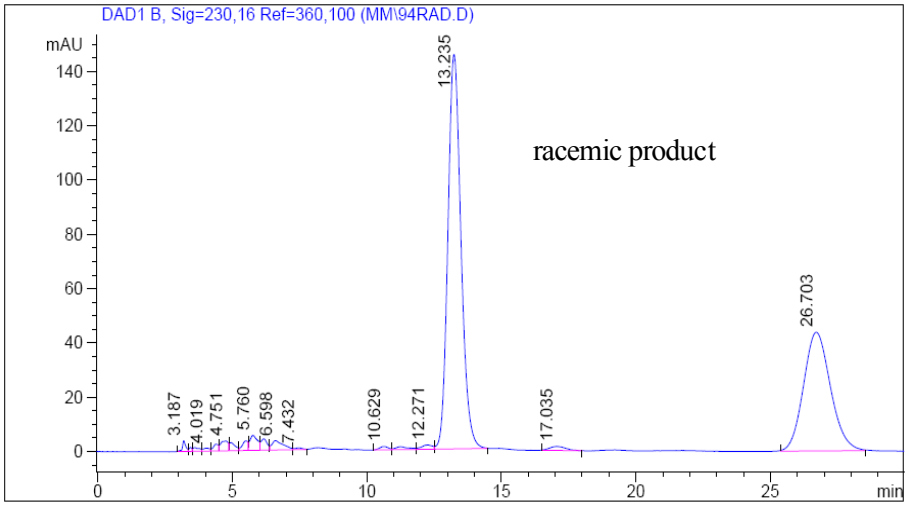
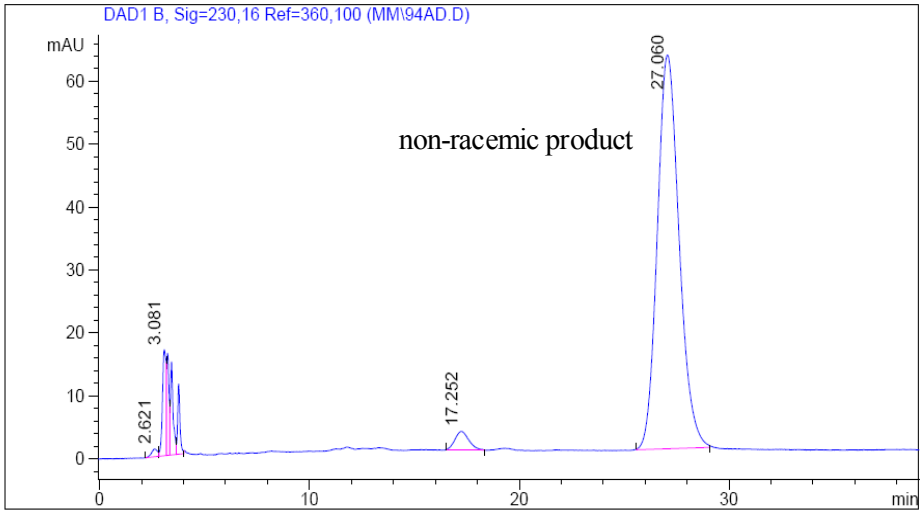


Figure S8. ^{13}C NMR spectrum (101 MHz, CD_3OD) of (3*S*, 4*S*, 5*S*)-3-((1*H*-indol-3-yl)methyl)-4-benzo[d][1,3]dioxol-5-yl)-5-nitrocyclohex-1-enecarbaldehyde (**4c**)



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Sample Name:          MM 94
Data file:            D:\GONZO\MM\94AD.D
Sample Info:          Laufmittel: n-Heptan/IP 7:3;
                      Die Probe ist im LM gelöst

Säule:                DAICELAD.M
Säuleninfo:           (250x4,6)mm
Operator:             Analytik Labor AKEN

 Injektion Time:       14:01:17
 Injektion Date:       15.01.2010

 Instrument Conditions:   At Start          At Stop
 Temperature in°C:          30.0°C           30.0°C
 Pressure in bar:           31.2             31.8
 Flow in ml/min:            1.0              1.0
```
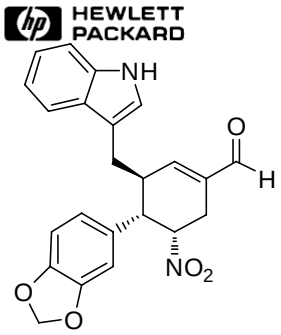
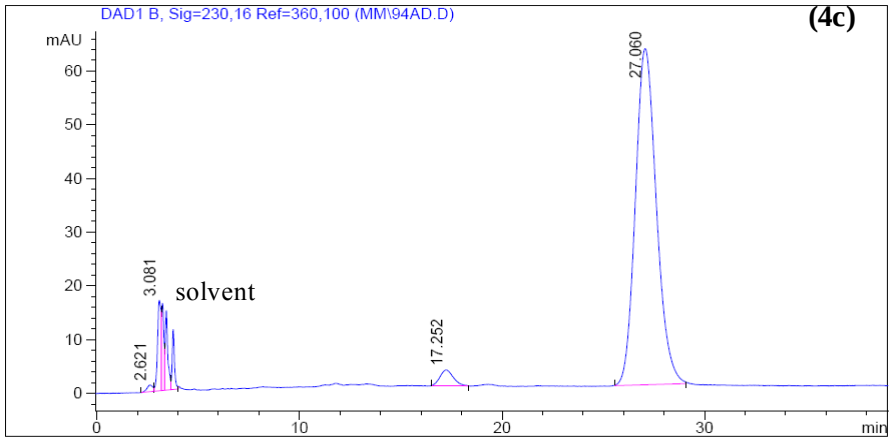





#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	2.62	0.28	1.23	24.43	0.47
2	3.08	0.17	16.86	203.83	3.89
3	3.24	0.11	16.24	125.78	2.40
4	3.43	0.13	14.80	132.95	2.54
5	3.76	0.12	11.18	88.36	1.69
6	17.25	0.56	2.94	135.41	2.59
7	27.06	1.05	62.58	4526.36	86.43
Total				5237.13	100.00

Figure S9. HPLC traces of **4c** overlay of racemic and non-racemic (left), non-racemic (right)

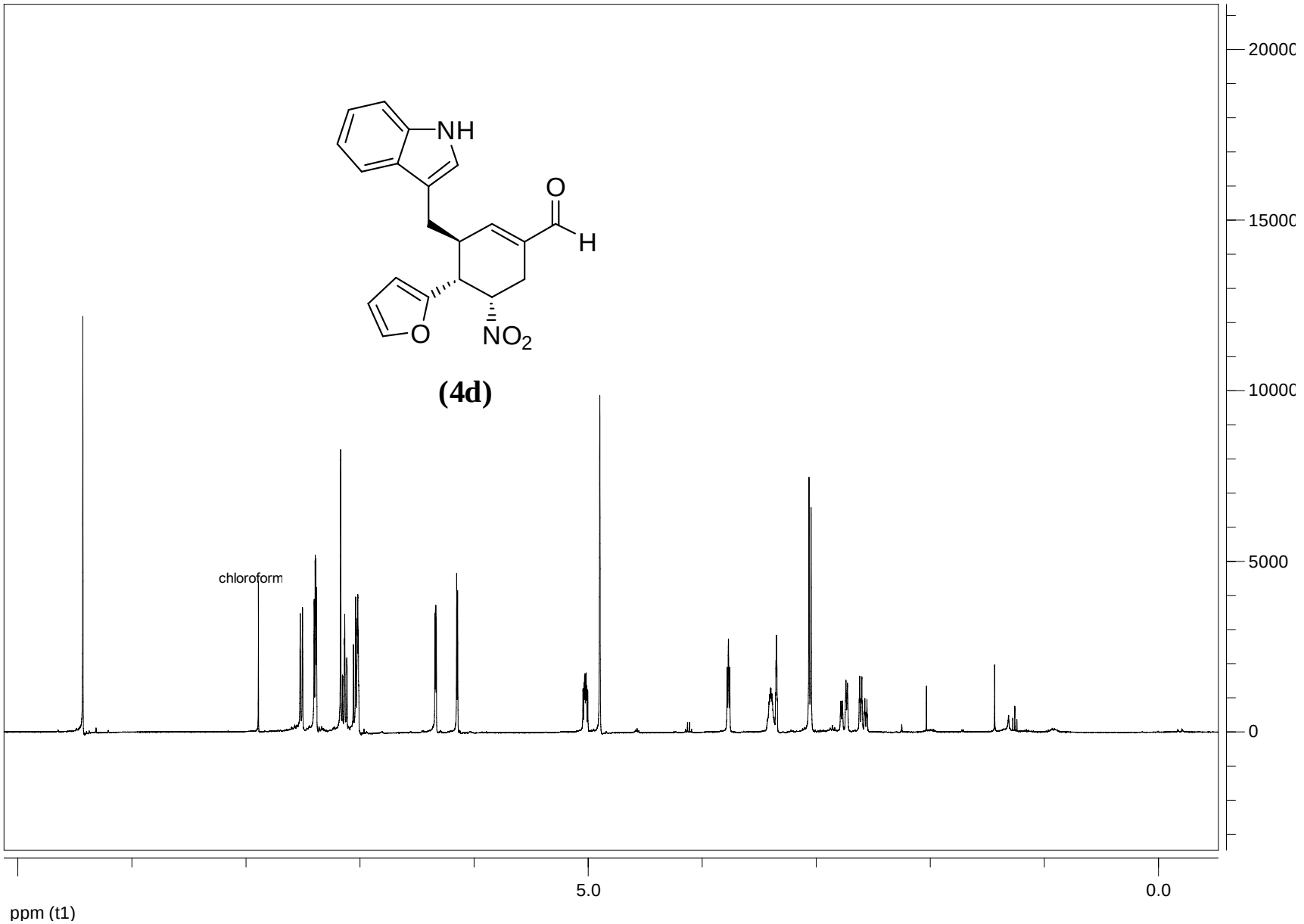


Figure S10. ^{1}H NMR spectrum (400 MHz, CD_3OD) of (3*S*, 4*R*, 5*S*)-3-((1*H*-indol-3-yl)methyl)-4-(furan-2-yl)-5-nitrocyclohex-1-enecarbaldehyde (**4d**).

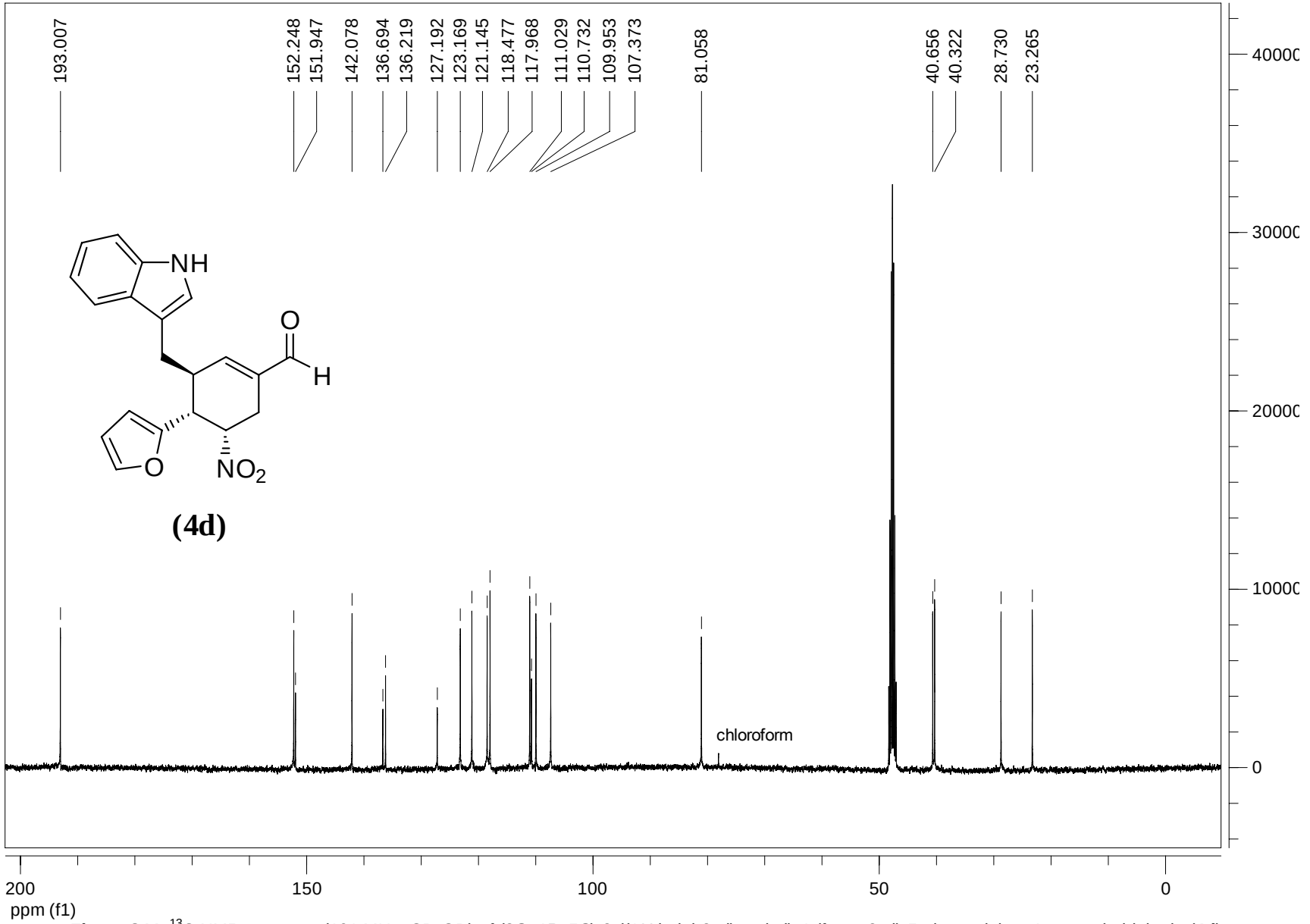
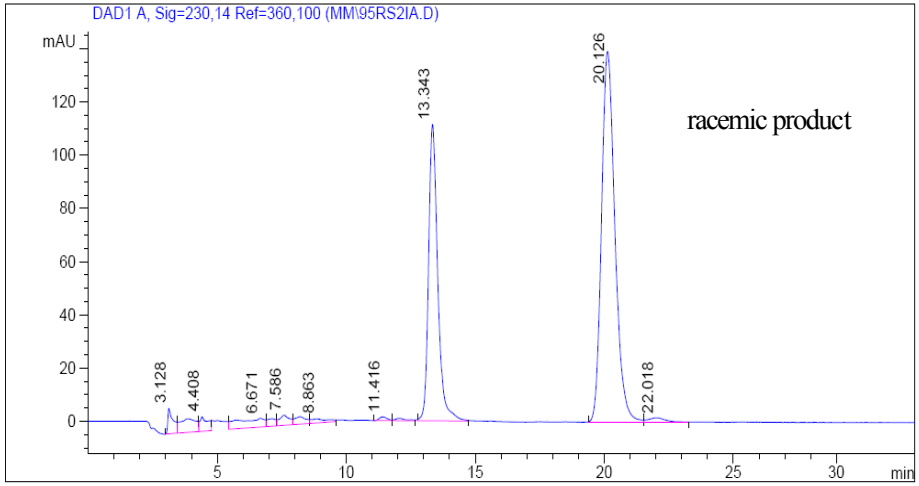
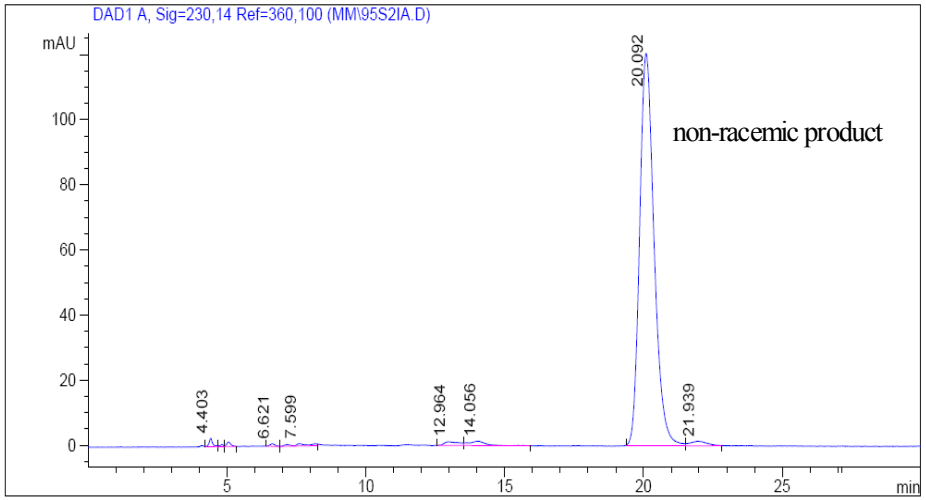


Figure S11. ^{13}C NMR spectrum (101 MHz, CD_3OD) of (3*S*, 4*R*, 5*S*)-3-((1*H*-indol-3-yl)methyl)-4-(furan-2-yl)-5-nitrocyclohex-1-enecarbaldehyde (**4d**)

d



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Sample Name:      MM 95 S2
Data file:        D:\BERT\MM\95S2IA.D
Sample Info:      Laufmittel: n-Heptan/IP 7:3;
                  Die Probe ist in LM gelöst


Säule:            DAICELIA.M
Säuleninfo:       (250x4,6)mm

Operator:         Analytik Labor AKEN

Injektion Time:       13:49:48
Injektion Date:       13.01.2010

Instrument Conditions:    At Start              At Stop

Temperature in°C:         30.0                  30.0
Pressure in bar:          44.2                  44.2
Flow in ml/min:           0.7                   0.7
```

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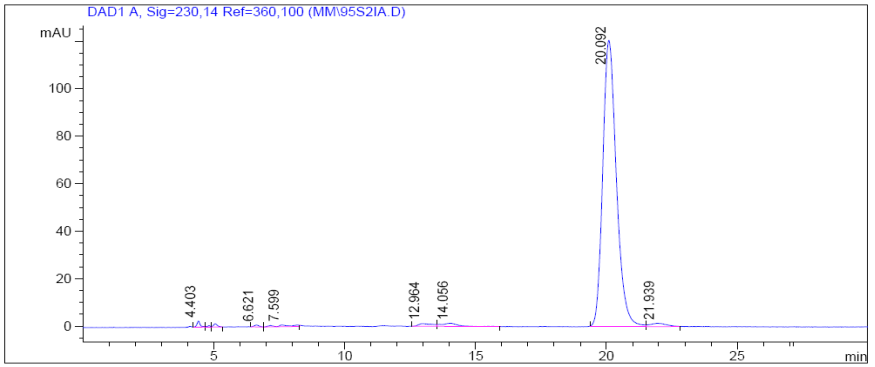


#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	4.40	0.14	2.57	22.94	0.50
2	4.80	0.14	0.63	5.82	0.13
3	5.05	0.16	1.38	14.55	0.32
4	6.62	0.19	0.83	10.56	0.23
5	7.60	0.55	0.75	31.53	0.68
6	12.96	0.63	1.11	42.30	0.92
7	14.06	0.74	1.31	58.19	1.26
8	20.09	0.56	120.58	4365.02	94.67
9	21.94	0.52	1.41	60.10	1.30
Total				4611.00	100.00

Figure S12. HPLC traces of 4**d** overlay of racemic and non-racemic (left), non-racemic (right)

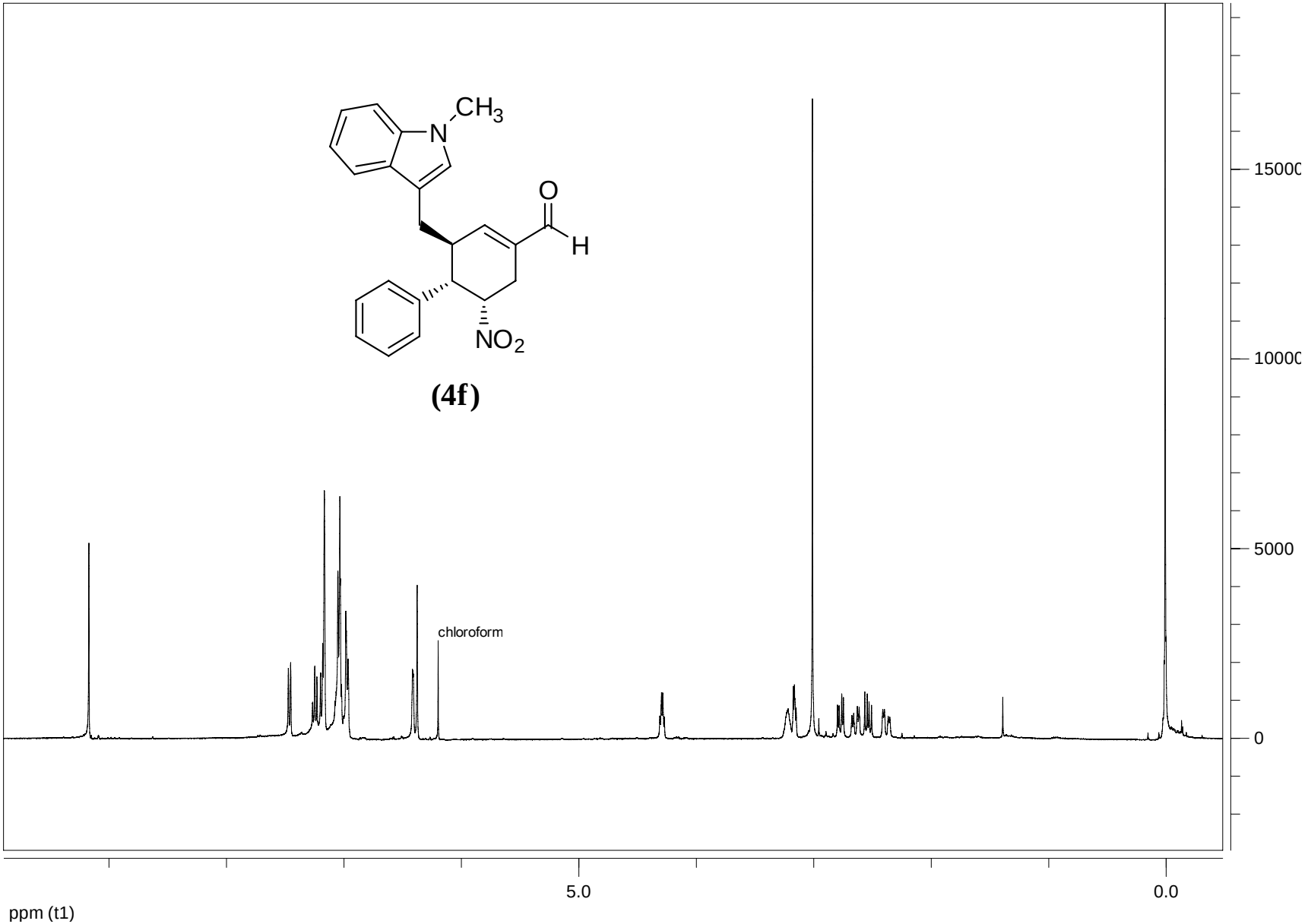


Figure S13. ^{1}H NMR spectrum (400 MHz, C_6D_6) of (1*S*, 2*S*, 6*S*)-6-((1-methyl-1*H*-indol-3-yl)methyl)-2-nitro-1,2,3,6- tetrahydro[1,1´-biphenyl]-4-carbaldehyde (**4f**).

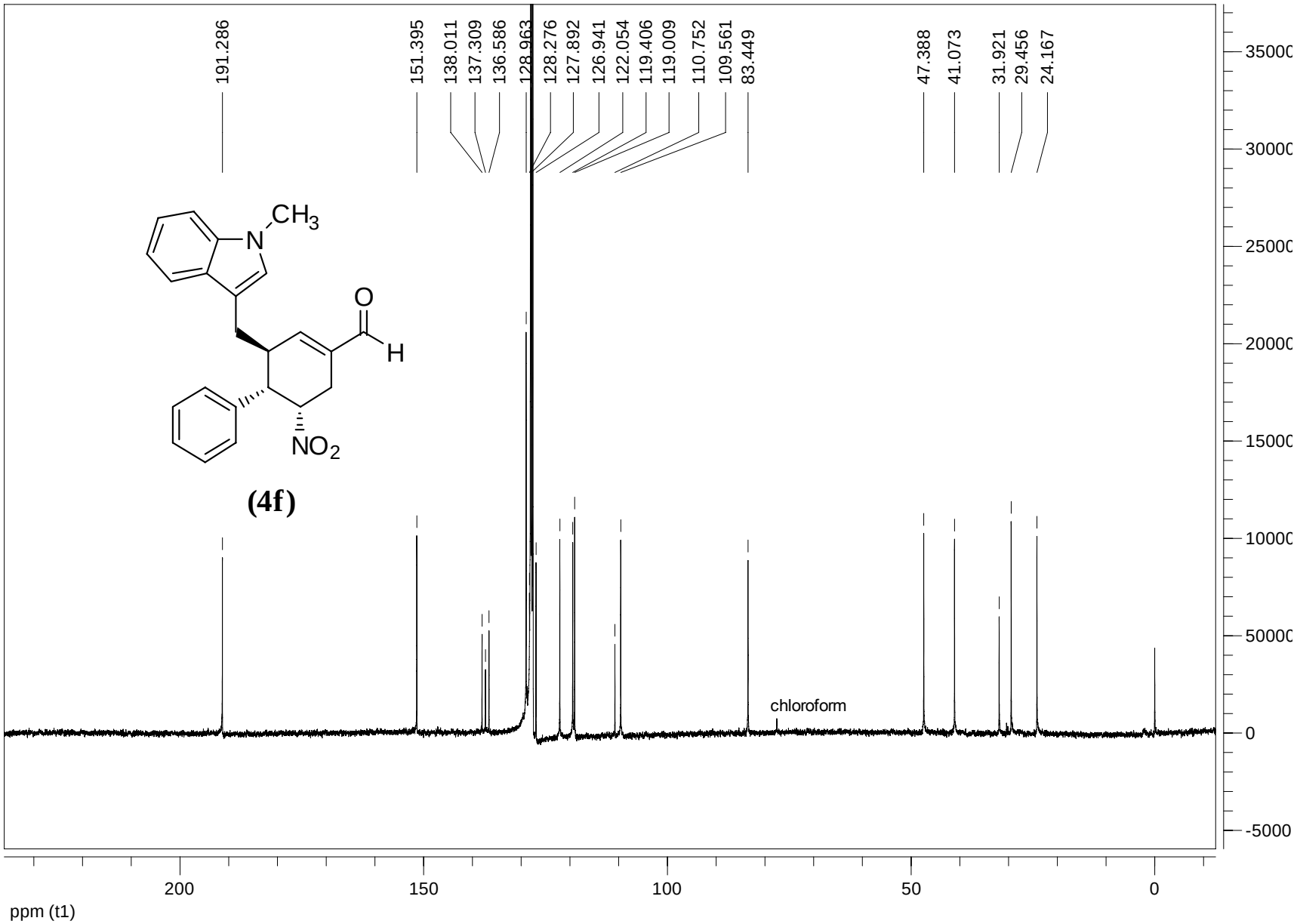
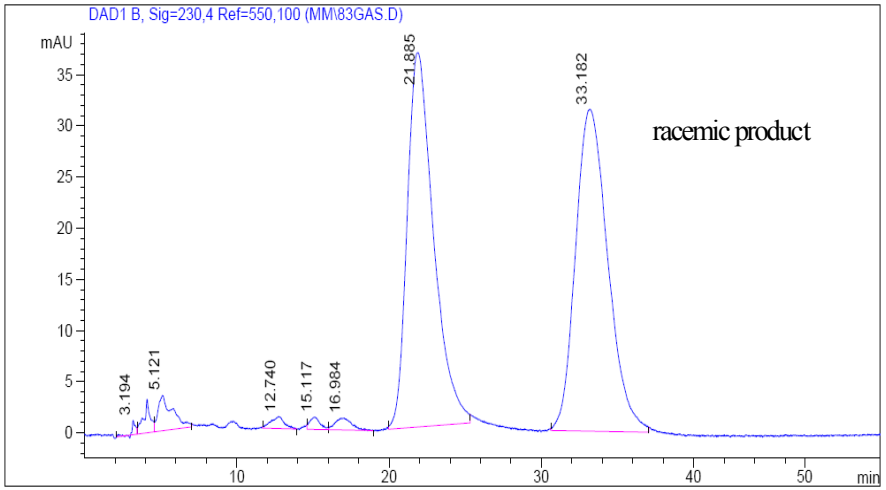
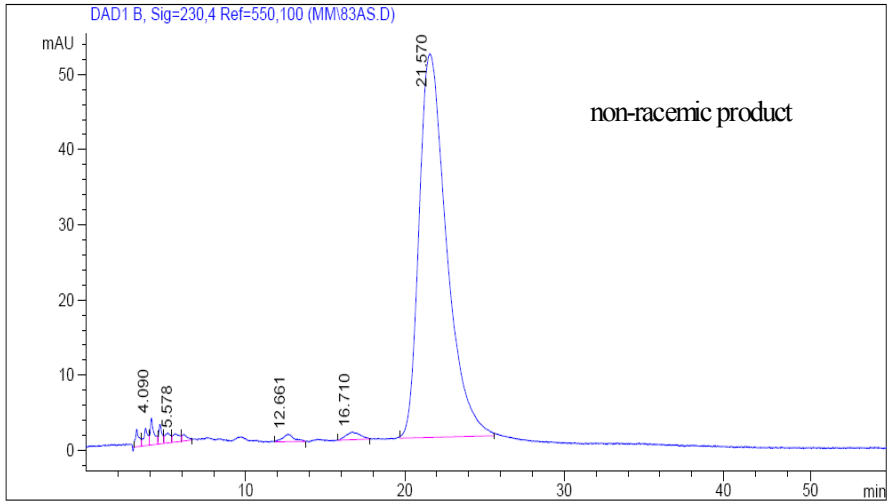


Figure S14. ^{13}C NMR spectrum (101 MHz, C_6D_6) of (1*S*, 2*S*, 6*S*)-6-((1-methyl-1*H*-indol-3-yl)methyl)-2-nitro-1,2,3,6- tetrahydro[1,1´-biphenyl]-4-carbaldehyde (**4f**)





Sample Name: MM 83
Data file: D:\BERT\MM\83AS.D
Sample Info: Laufmittel: n-Heptan/IP 7:3;
Die Probe ist in DCM/LM gelöst

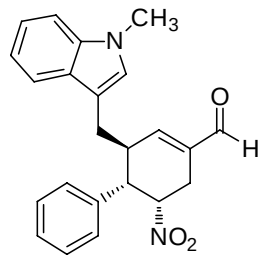
Agilent Technologies

Säule: DAICELAS.M
Säuleninfo: (250x4,6)mm

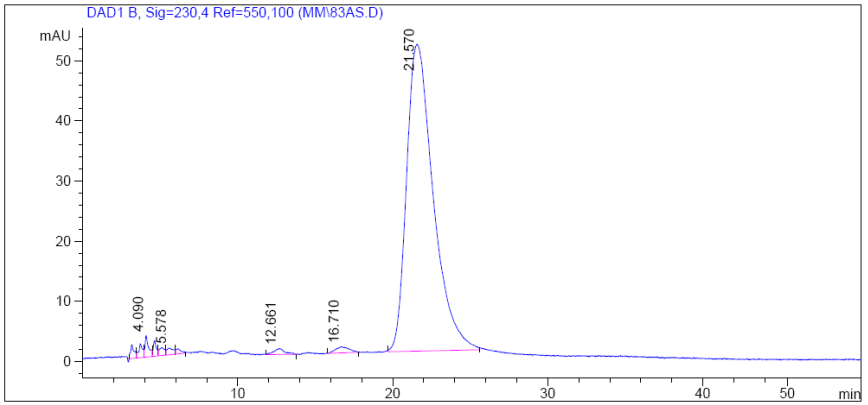
Operator: Analytik Labor AKEN

Injektion Time: 10:48:00
Injektion Date: 14.12.2009

Instrument Conditions:	At Start	At Stop
Temperature in°C:	30.0	30.0
Pressure in bar:	42.6	41.9
Flow in ml/min:	1.0	1.0



(4f)



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	3.17	0.22	2.32	37.65	0.58
2	3.72	0.24	2.30	41.11	0.63
3	4.09	0.22	3.62	59.04	0.91
4	4.63	0.21	2.59	37.03	0.57
5	5.11	0.34	1.31	33.47	0.52
6	5.58	0.38	1.12	33.02	0.51
7	6.12	0.29	0.88	19.59	0.30
8	12.66	0.61	0.98	49.31	0.76
9	16.71	0.77	1.01	62.07	0.96
10	21.57	1.56	51.05	6105.09	94.25
Total				6477.36	100.00

Figure S15. HPLC traces of 4**f** overlay of racemic and non-racemic (left), non-racemic (right)

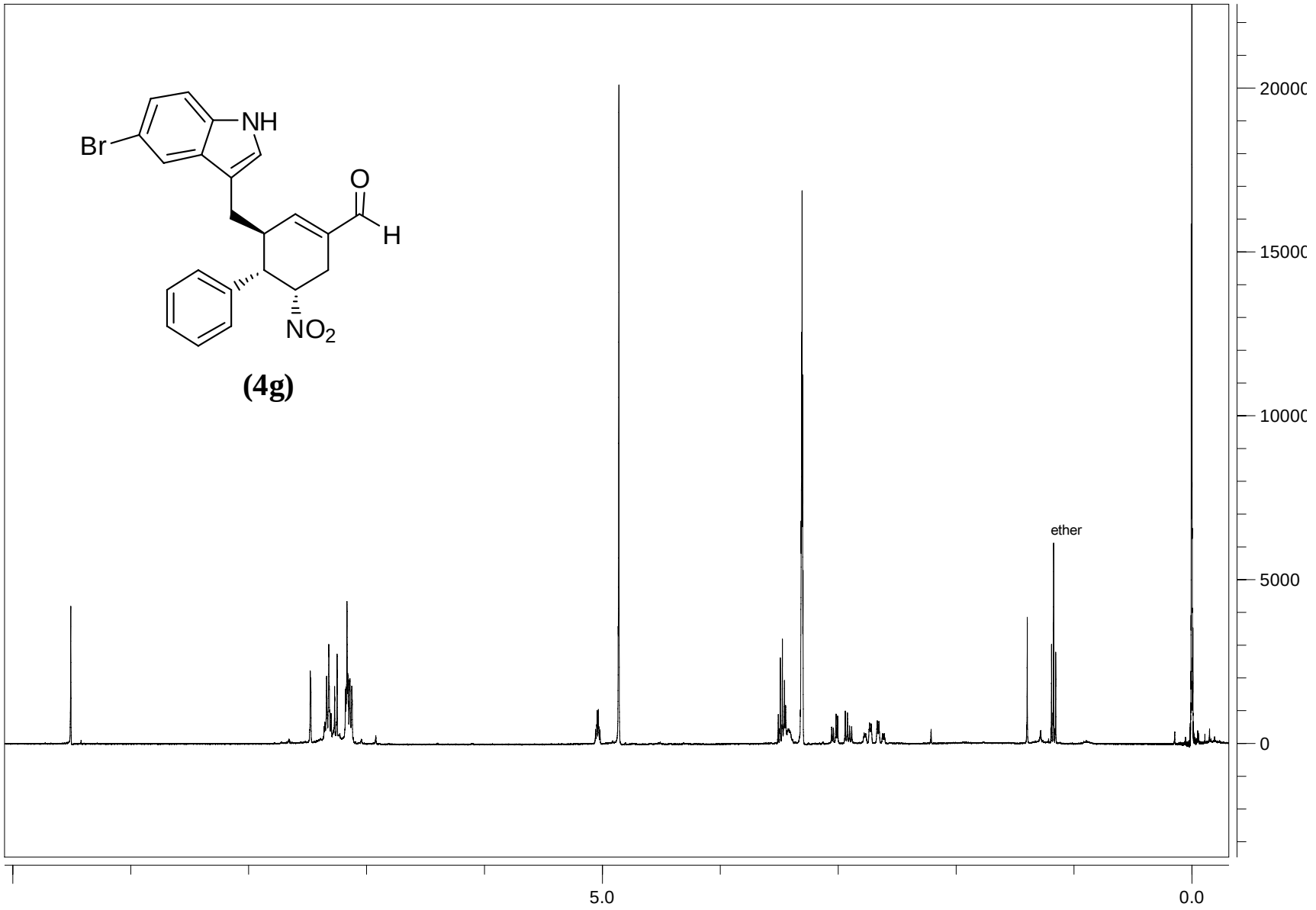


Figure S16. ^{1}H NMR spectrum (400 MHz, CD_3OD) of (1*S*, 2*S*, 6*S*)-6-((5-bromo-1*H*-indol-3-yl)methyl)-2-nitro-1,2,3,6-tetrahydro [1,1´-biphenyl]-4-carbaldehyde (**4g**).

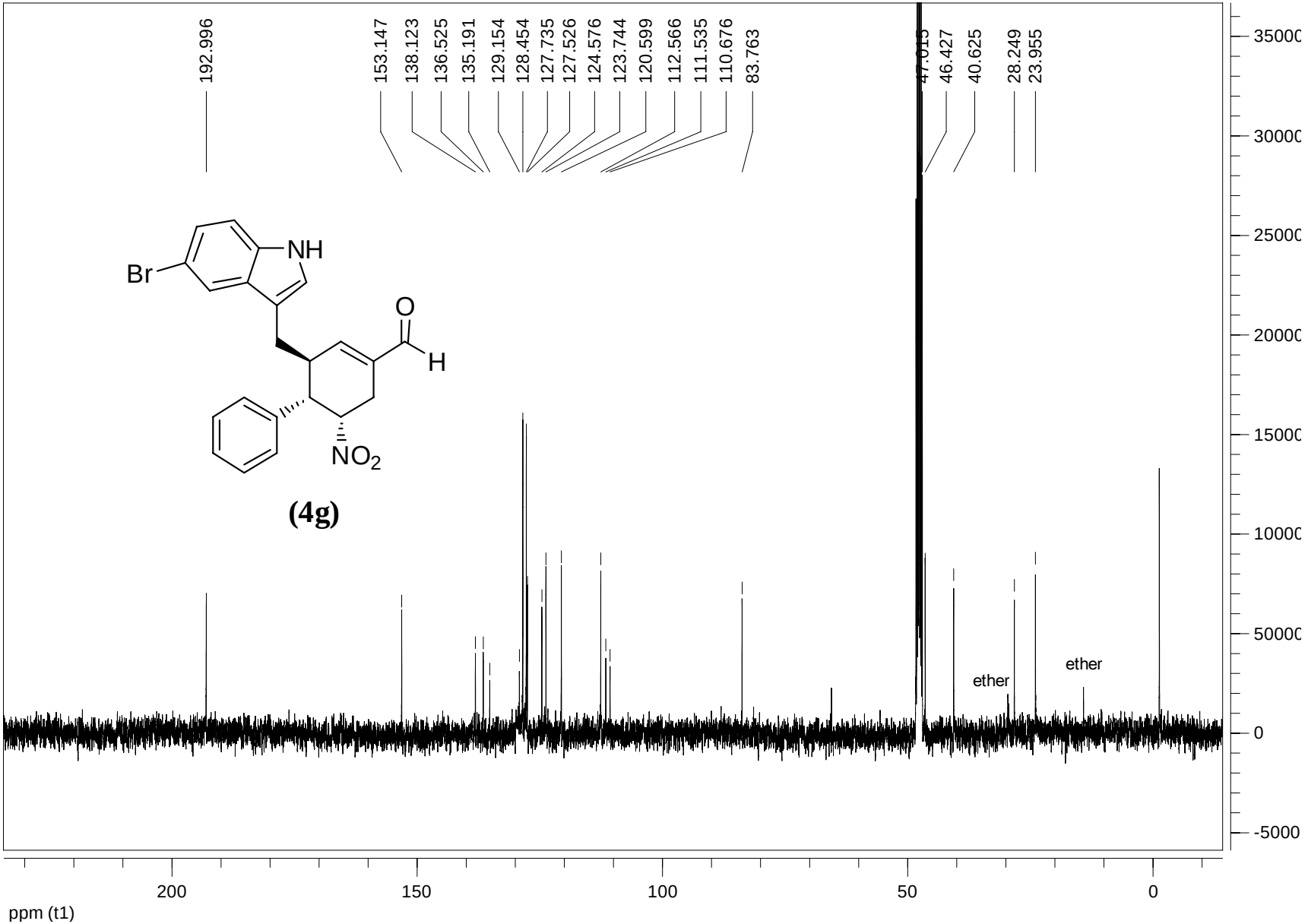
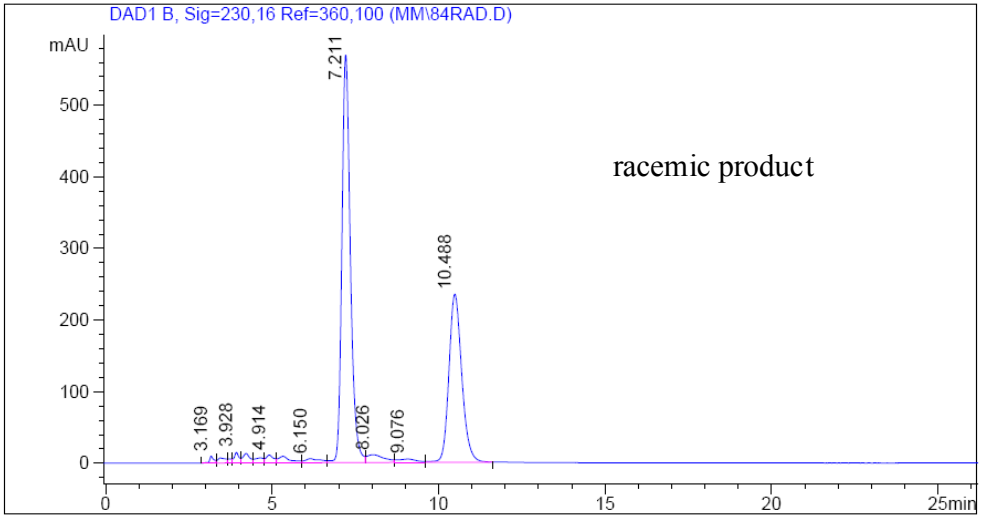
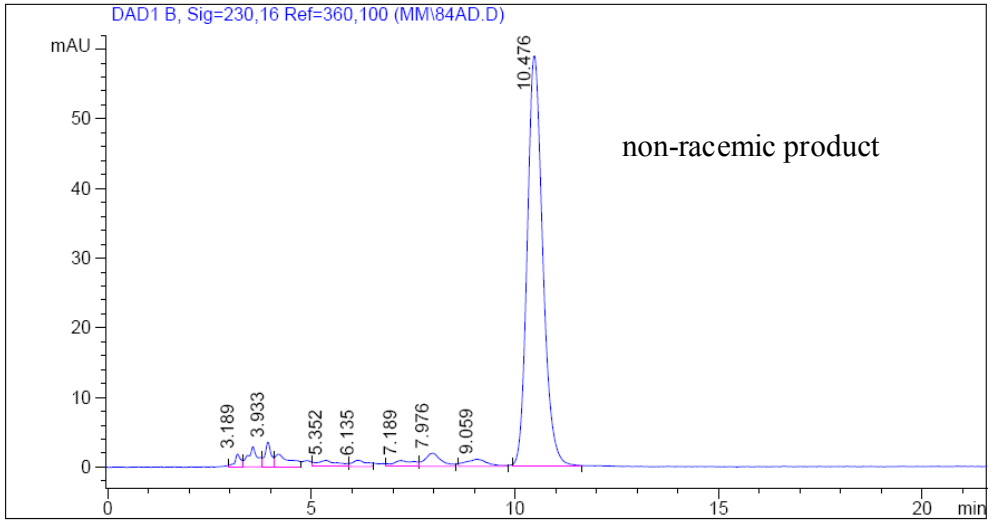


Figure S17. ^{13}C NMR spectrum (101 MHz, CD_3OD) of (1*S*, 2*S*, 6*S*)-6-((5-bromo-1*H*-indol-3-yl)methyl)-2-nitro-1,2,3,6-tetrahydro [1,1´-biphenyl]-4-carbaldehyde (**4g**)



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Sample Name:          MM 84
Data file:            D:\GONZO\MM\84AD.D
Sample Info:          Laufmittel: n-Heptan/IP 7:3;
                      Die Probe ist im LM/DCM gelöst

Säule:                DAICELAD.M
Säuleninfo:           (250x4,6)mm
Operator:             Analytik Labor AKEN

 Injektion Time:       10:51:40
 Injektion Date:       21.12.2009

 Instrument Conditions:   At Start          At Stop
 Temperature in°C:          30.0°C           30.0°C
 Pressure in bar:           46.8             47.3
 Flow in ml/min:            1.0              1.0
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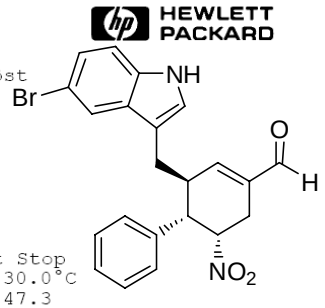
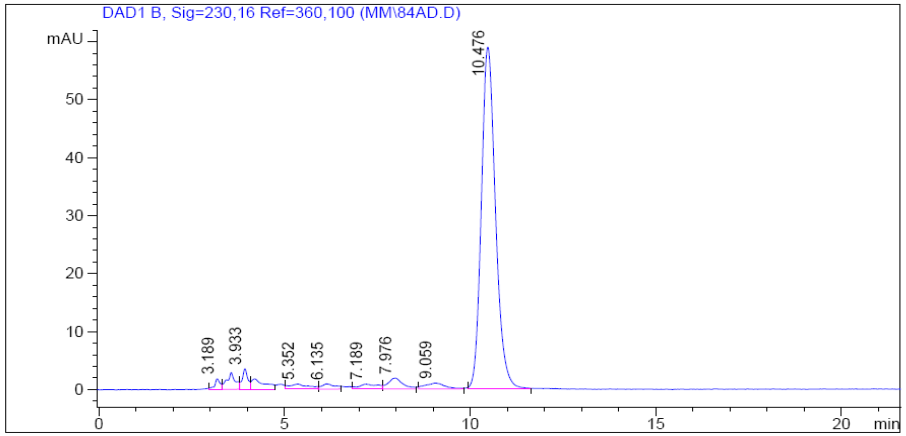


(4g)



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	3.19	0.15	1.82	18.59	0.98
2	3.57	0.21	2.89	46.82	2.48
3	3.93	0.15	3.53	36.39	1.92
4	4.19	0.34	1.80	45.63	2.41
5	5.35	0.49	0.89	32.38	1.71
6	6.14	0.36	0.90	23.37	1.24
7	7.19	0.50	0.84	30.39	1.61
8	7.98	0.40	1.88	52.78	2.79
9	9.06	0.53	1.00	37.92	2.01
10	10.48	0.41	58.90	1566.75	82.85
Total				1891.03	100.00

Figure S18. HPLC traces of the corresponding **4g** overlay of racemic and non-racemic (left), non-racemic (right)

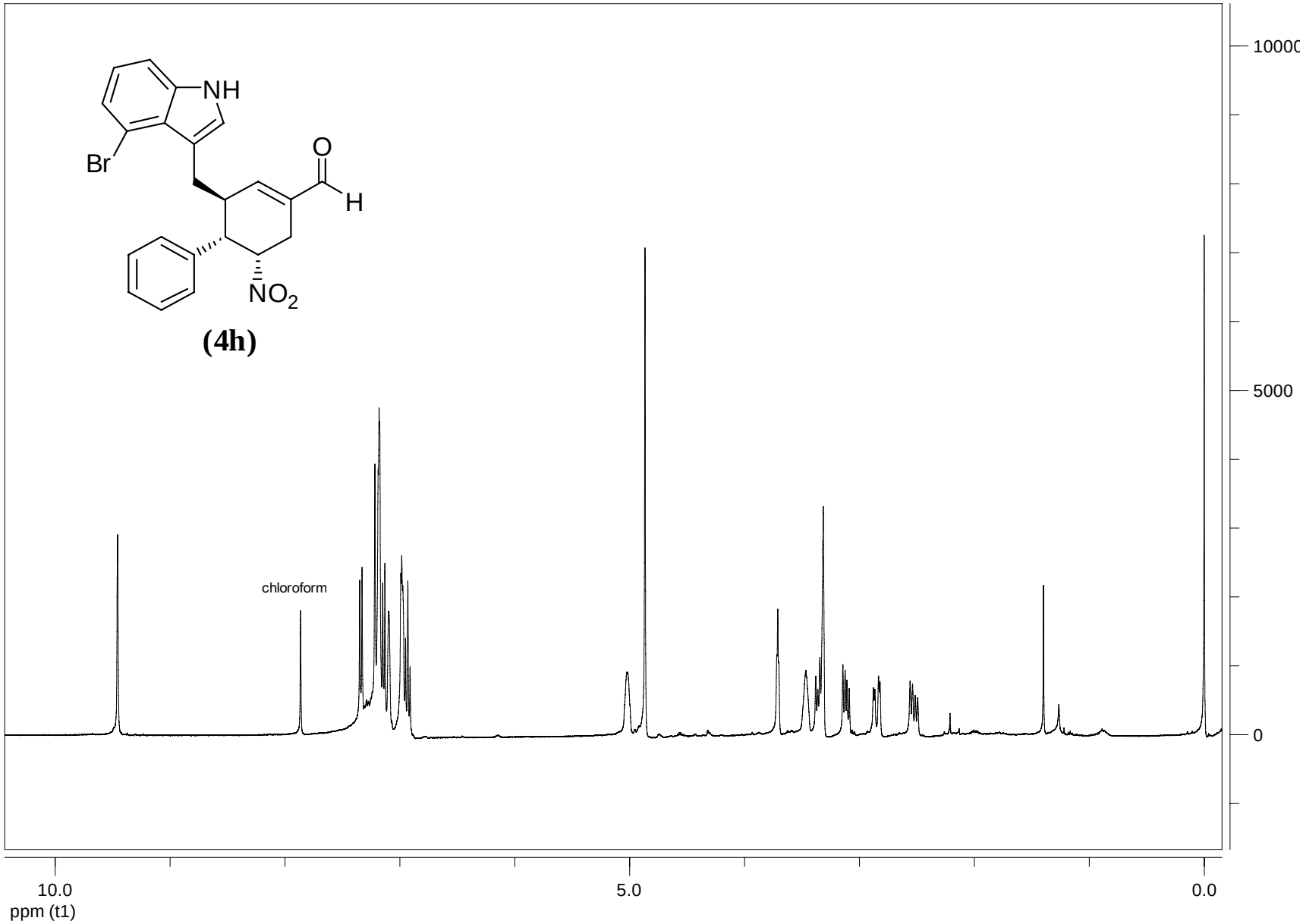


Figure S19. ^{1}H NMR spectrum (400 MHz, CD_3OD) of (1*S*, 2*S*, 6*S*)-6-((4-bromo-1*H*-indol-3-yl)methyl)-2-nitro- 1,2,3,6- tetrahydro [1,1´-biphenyl]-4-carbaldehyde (**4h**).

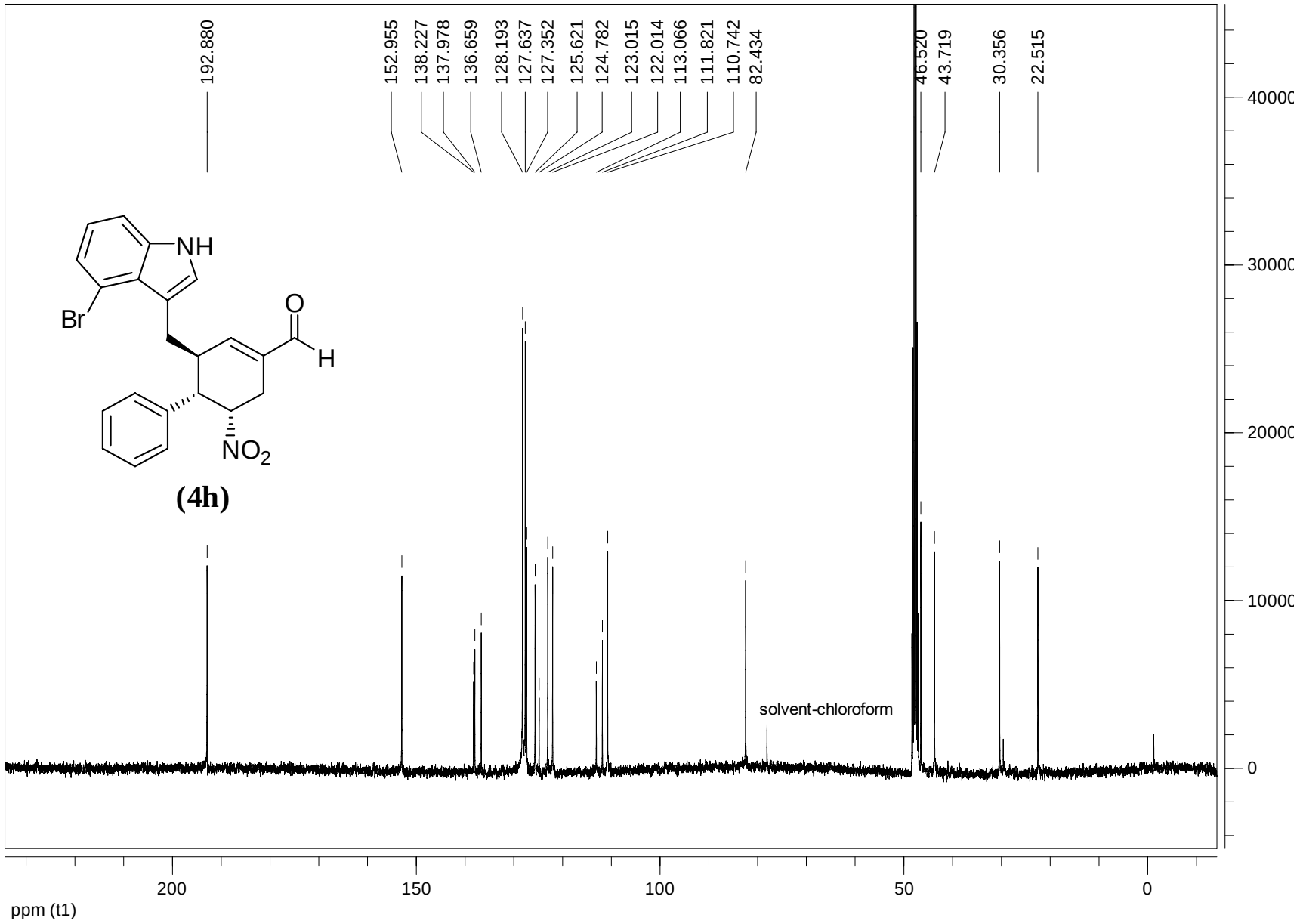
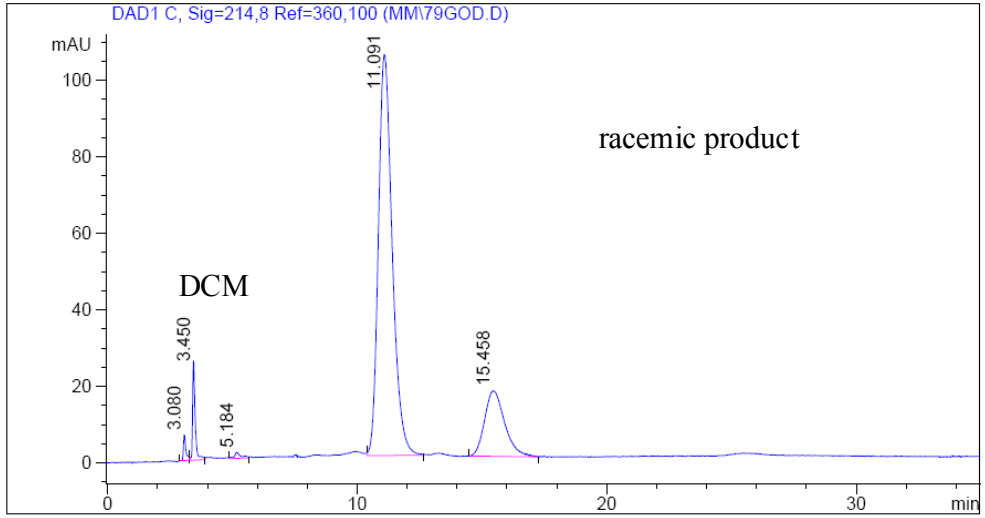
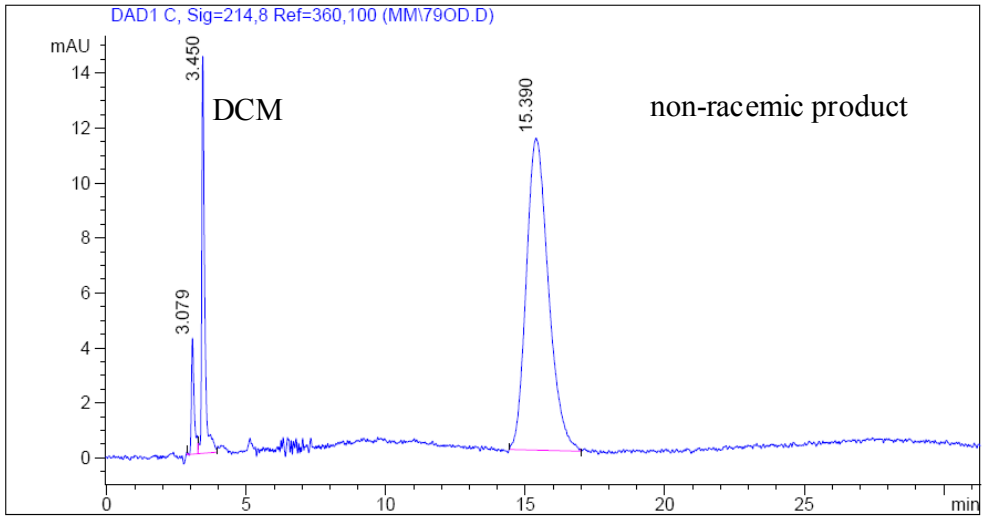


Figure S20. ^{13}C NMR spectrum (101 MHz, CD_3OD) of (1*S*, 2*S*, 6*S*)-6-((4-bromo-1*H*-indol-3-yl)methyl)-2-nitro- 1,2,3,6- tetrahydro [1,1´-biphenyl]-4-carbaldehyde (**4h**).





Sample Name: MM 79
Data file: D:\GONZO\MM\79OD.D
Sample Info: Laufmittel: n-Heptan/IP 7:3;
Die Probe ist im LM/DCM gelöst

Säule: DAICELOD.M
Säuleninfo: (250x4,6)mm
Operator: Analytik Labor AKEN

Injektion Time: 15:19:02
Injektion Date: 08.12.2009

Instrument Conditions:	At Start	At Stop
Temperature in°C:	30.0°C	30.0°C
Pressure in bar:	46.9	47.3
Flow in ml/min:	1.0	1.0

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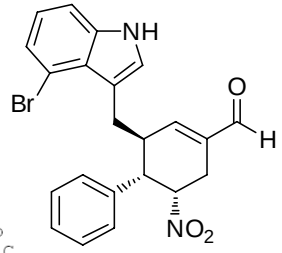
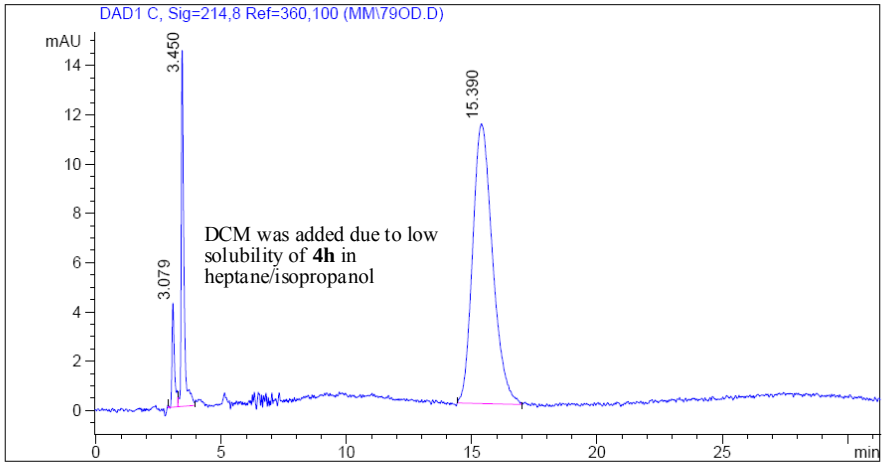


(4h)



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	3.08	0.12	4.16	29.53	3.88
2	3.45	0.13	14.09	105.23	13.81
3	15.39	0.84	11.35	627.11	82.31
Total				761.88	100.00

3g

Figure S21. HPLC traces of **4h** overlay of racemic and non-racemic (left), non-racemic (right)

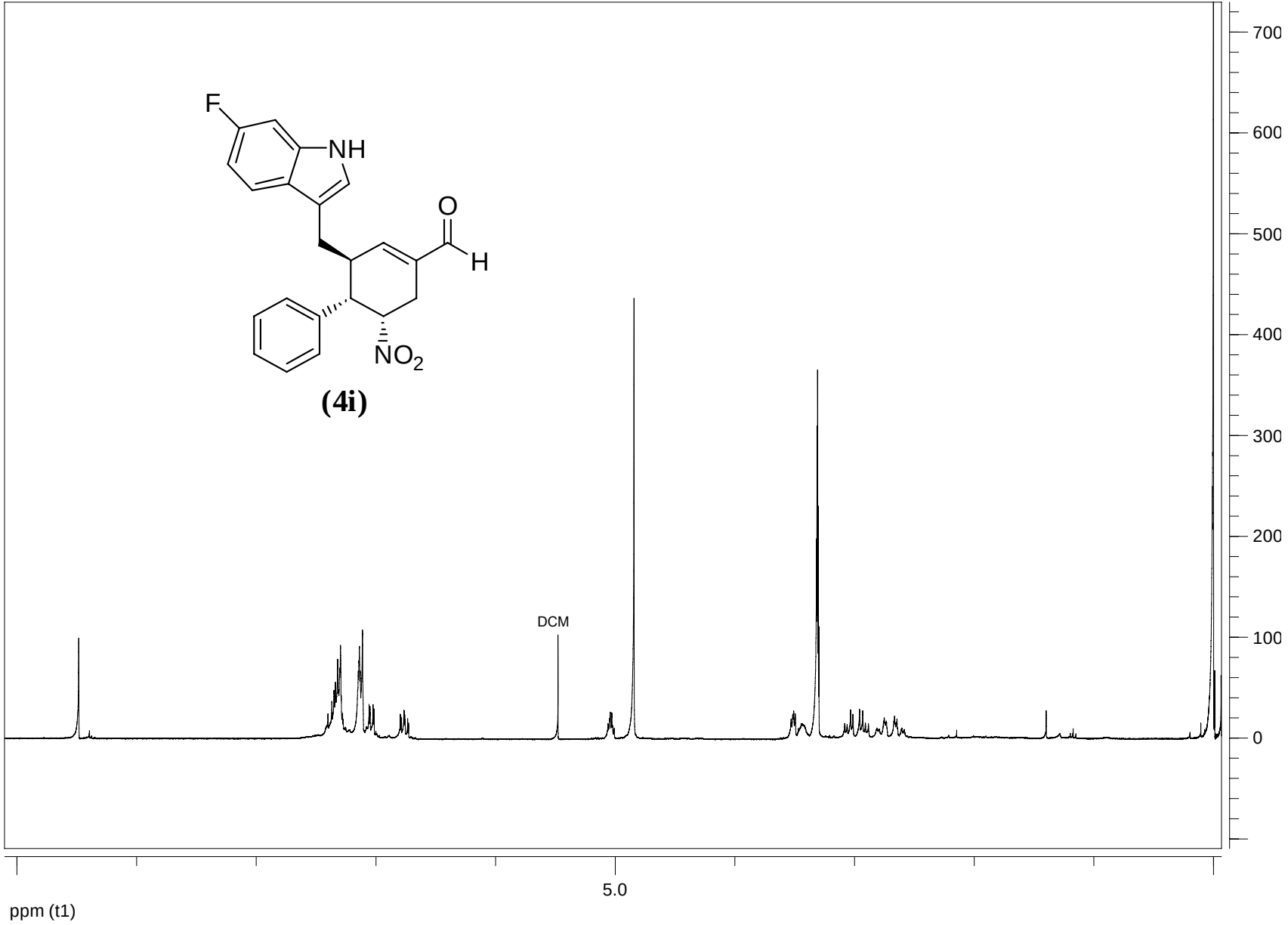


Figure S22. ^{1}H NMR spectrum (300 MHz, CD_3OD) of (1*S*, 2*S*, 6*S*)-6-((6-fluoro-1*H*-indol-3-yl)methyl)-2-nitro-1,2,3,6- tetrahydro[1,1´-biphenyl]-4-carbaldehyde (**4i**).

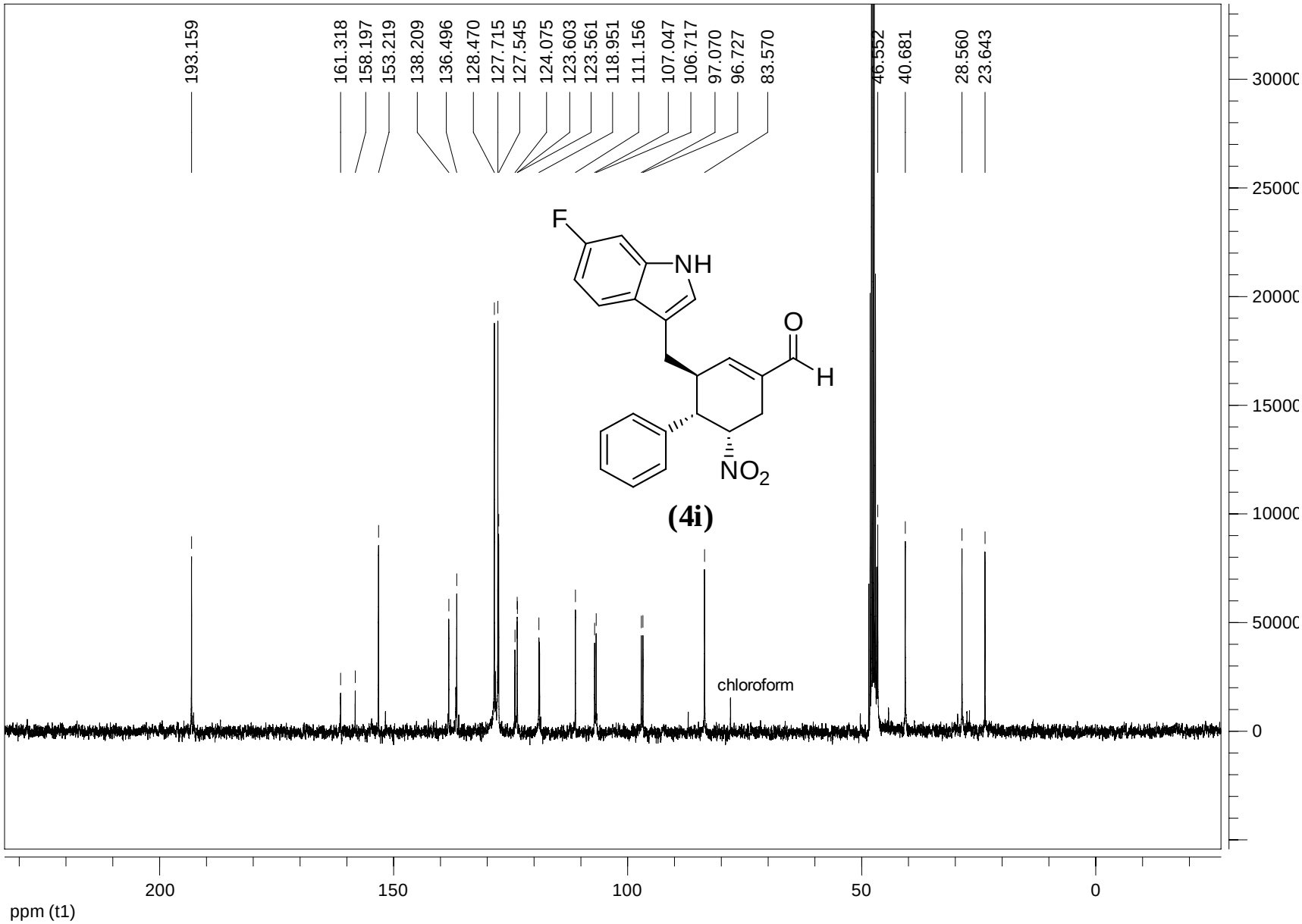
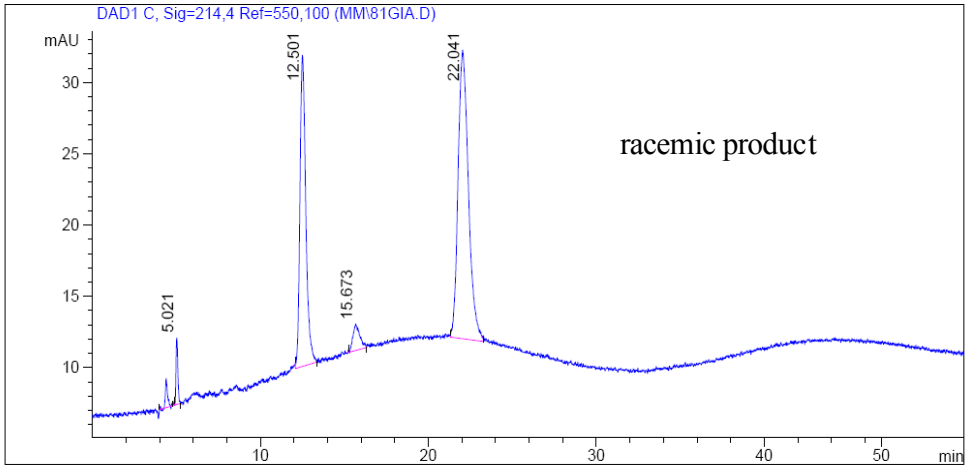
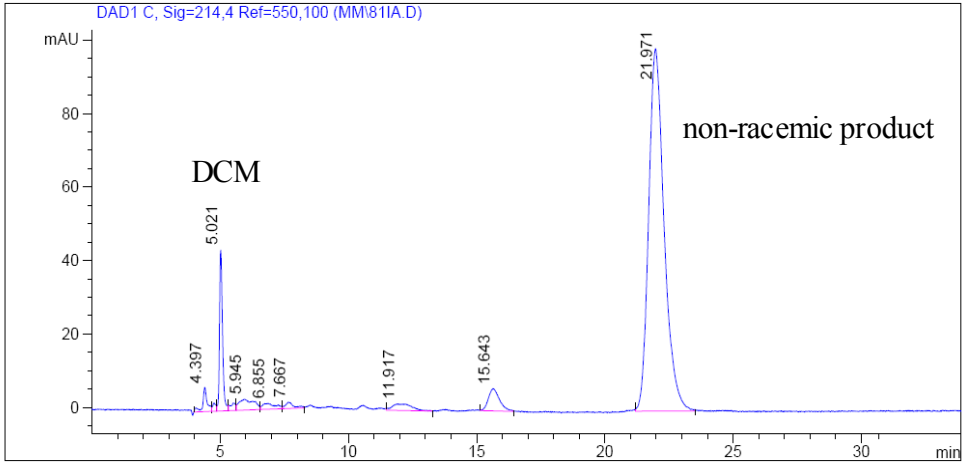


Figure S23. ^{13}C NMR spectrum (75 MHz, CD_3OD) of (1*S*, 2*S*, 6*S*)-6-((6-fluoro-1*H*-indol-3-yl)methyl)-2-nitro-1,2,3,6- tetrahydro[1,1´-biphenyl]-4-carbaldehyde (**4i**).

3g






```
Sample Name:      MM 81
Data file:        D:\BERT\MM\81IA.D
Sample Info:      Laufmittel: n-Heptan/IP 7:3;
                  Die Probe ist in DCM/LM gelöst

Säule:            DAICELIA.M
Säuleninfo:       (250x4,6)mm

Operator:         Analytik Labor AKEN

Injektion Time:       15:17:26
Injektion Date:       08.12.2009

Instrument Conditions:   At Start          At Stop

Temperature in°C:        30.0              30.0
Pressure in bar:         47.0              47.1
Flow in ml/min:          0.7               0.7
```

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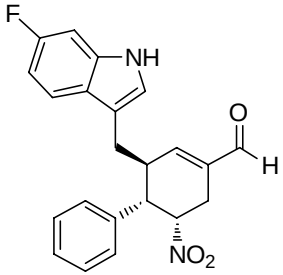
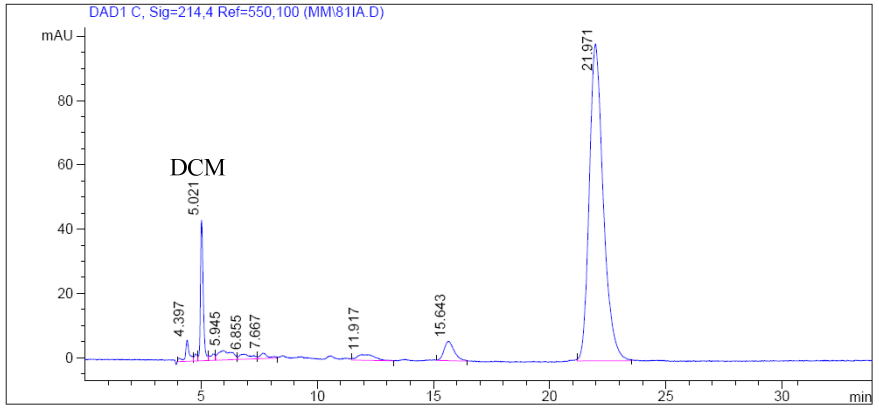


(4i)



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	4.40	0.17	6.58	80.34	1.57
2	4.76	0.13	2.22	20.48	0.40
3	5.02	0.12	43.81	357.44	6.99
4	5.53	0.21	1.96	29.88	0.58
5	5.95	0.51	2.99	121.74	2.38
6	6.86	0.43	1.64	57.13	1.12
7	7.67	0.34	1.71	40.02	0.78
8	11.92	0.69	1.77	97.45	1.90
9	15.64	0.47	5.98	183.72	3.59
10	21.97	0.64	98.65	4128.22	80.69
Total				5116.43	100.00

Figure S24. HPLC traces of **4i** overlay of racemic and non-racemic (left), non-racemic (right)

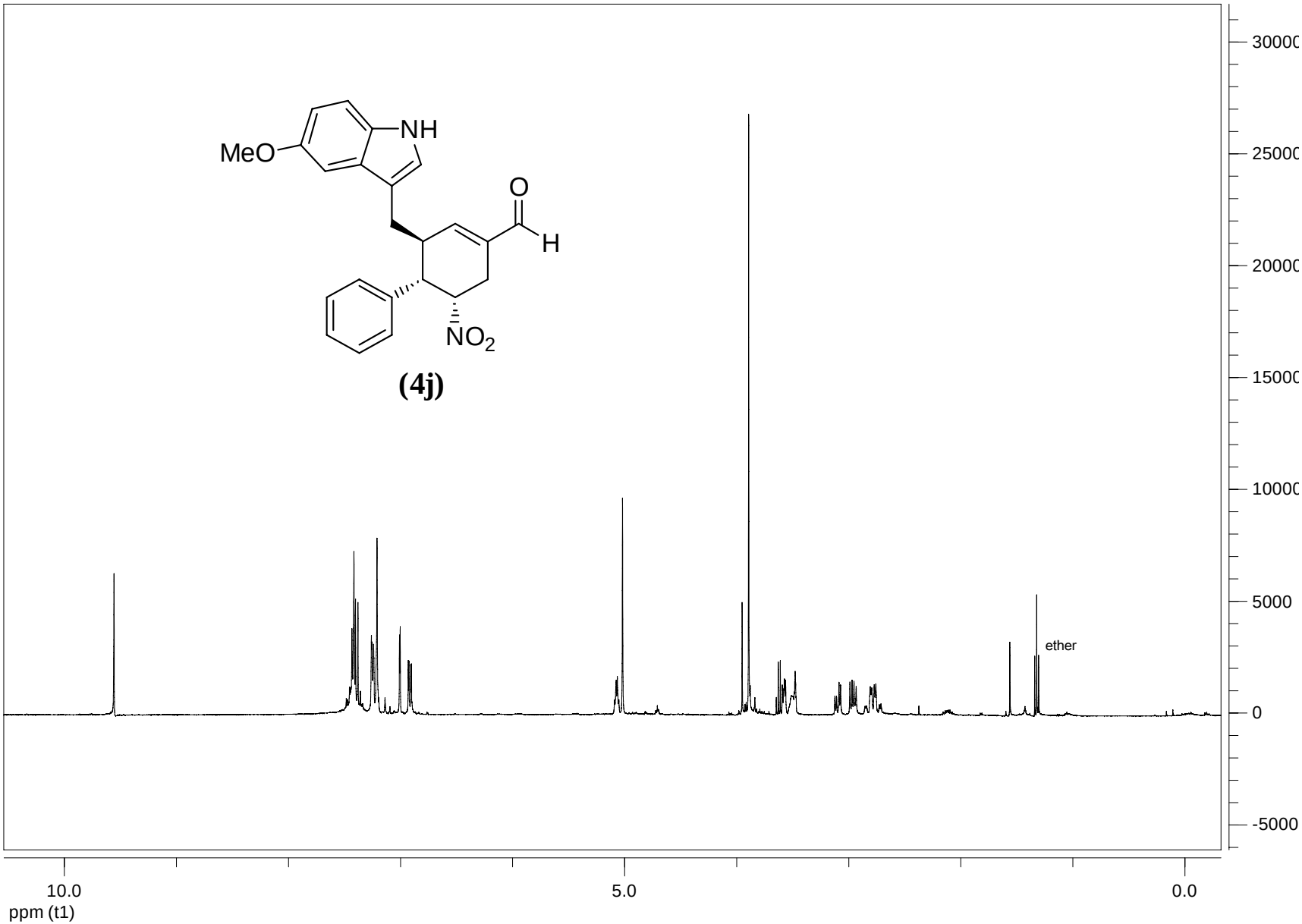


Figure S25. ^{1}H NMR spectrum (300 MHz, CD_3OD) of (1*S*, 2*S*, 6*S*)-6-((5-methoxy-1*H*-indol-3-yl)methyl)-2-nitro-1,2,3,6- tetrahydro[1,1´-biphenyl]-4-carbaldehyde (**4j**).

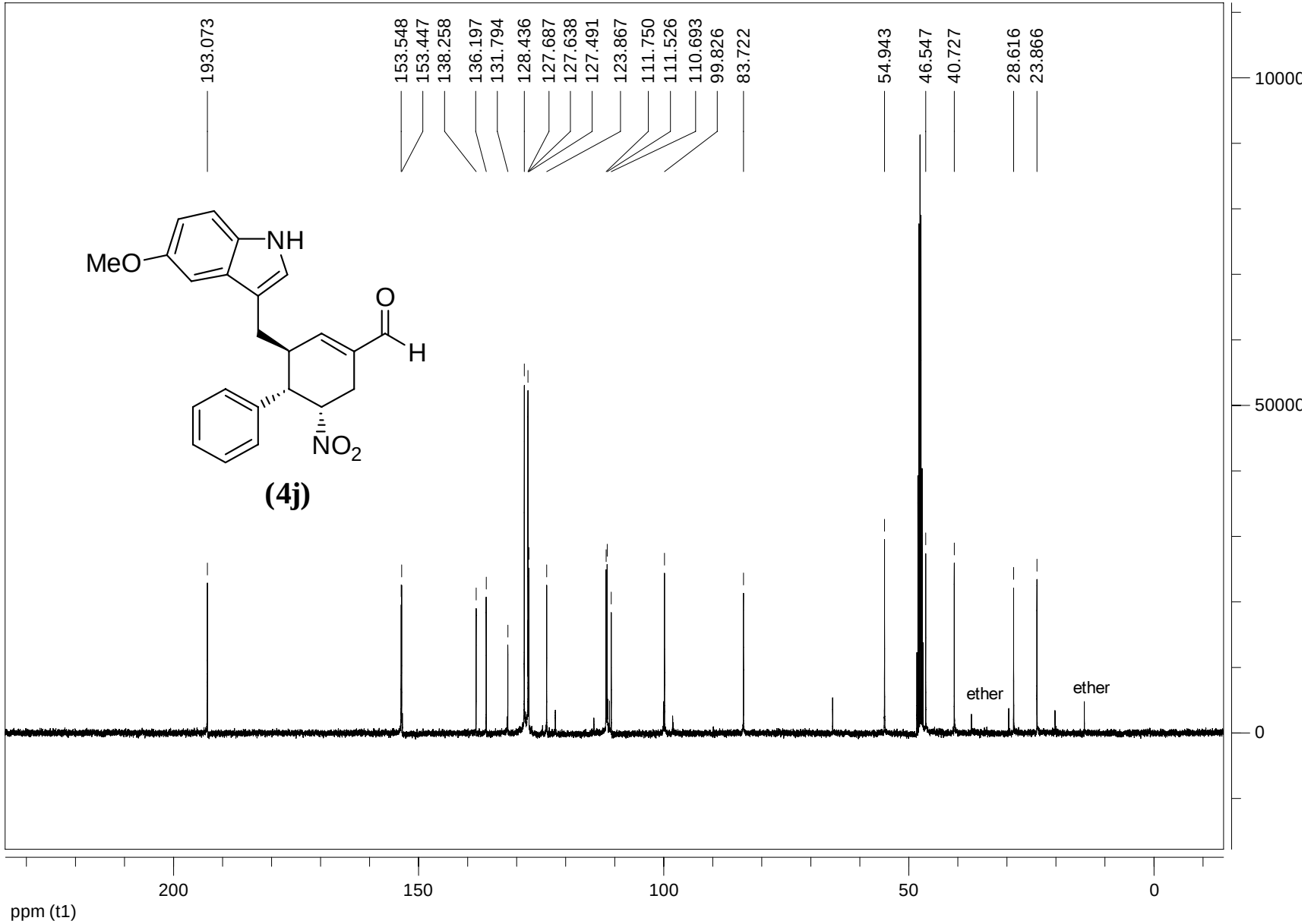
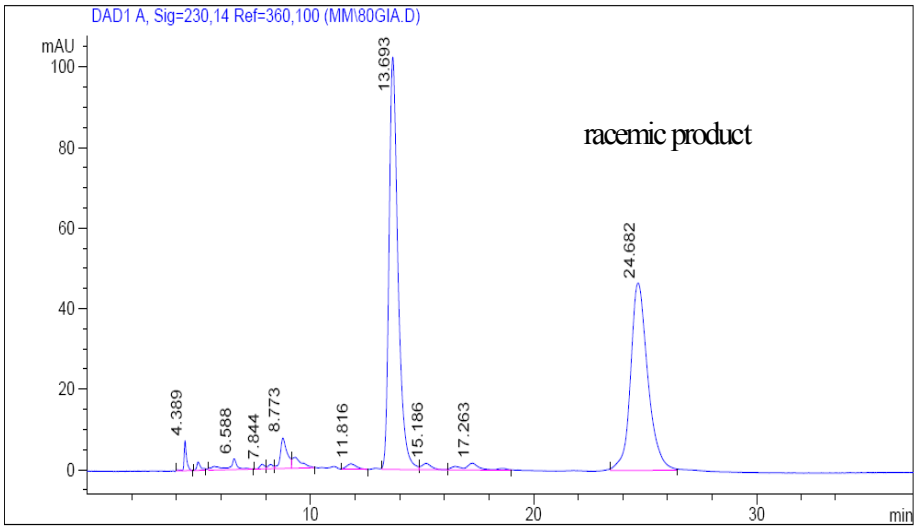
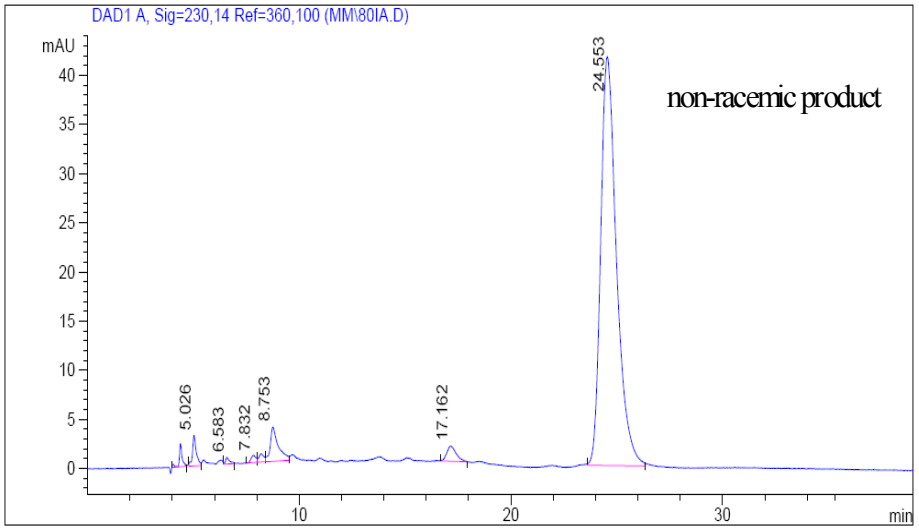


Figure S26. ^{13}C NMR spectrum (75 MHz, CD_3OD) of (1*S*, 2*S*, 6*S*)-6-((5-methoxy-1*H*-indol-3-yl)methyl)-2-nitro-1,2,3,6- tetrahydro[1,1´-biphenyl]-4-carbaldehyde (**4j**).

3g






```
Sample Name:      MM 80
Data file:        D:\BERT\MM\80IA.D
Sample Info:      Laufmittel: n-Heptan/IP 7:3;
                  Die Probe ist in DCM/LM gelöst


Säule:            DAICELIA.M
Säuleninfo:       (250x4,6)mm

Operator:         Analytik Labor AKEN

Injektion Time:       08:55:50
Injektion Date:       10.12.2009

Instrument Conditions:   At Start              At Stop

Temperature in°C:        30.0                  30.0
Pressure in bar:         47.3                  47.4
Flow in ml/min:          0.7                   0.7
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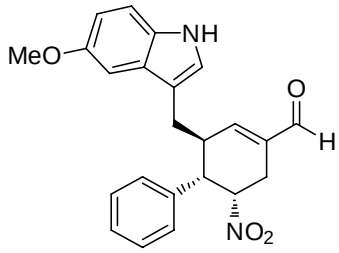
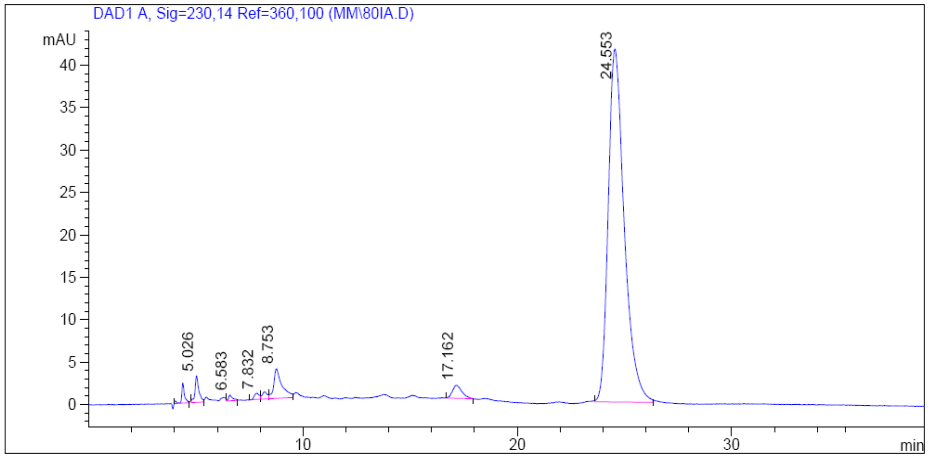


(4j)



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	4.39	0.14	2.35	22.10	0.92
2	5.03	0.19	3.12	40.02	1.67
3	6.58	0.19	0.68	9.07	0.38
4	7.83	0.25	0.72	11.62	0.48
5	8.20	0.24	0.84	13.71	0.57
6	8.75	0.37	3.49	93.91	3.91
7	17.16	0.44	1.55	47.63	1.98
8	24.55	0.78	41.62	2163.95	90.09
Total				2402.01	100.00

Figure S27. HPLC traces of **4j** overlay of racemic and non-racemic (left), non-racemic (right)