Supporting Information

Asymmetric Simmons-Smith Cyclopropanation of Allylic Amines

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Experimental Procedures and spectral data

General procedures

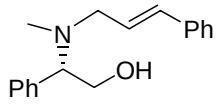
All air and water sensitive reactions were carried out in oven dried glassware under an argon atmosphere. Solvents were dried by standard methods.[1] NMR spectra were recorded on Jeol 270 MHz or Jeol 400 MHz spectrometers using tetramethylsilane as the internal standard (0.00 ppm). $CDCl_3$ was used as the internal standard for ^{13}C NMR spectra. CI mass spectra were obtained using a VG Platform mass spectrometer. IR spectra were obtained on a Perkin-Elmer Spectrum One FT-IR spectrometer. Flash chromatography was performed using silica gel (Merck Kieselgel 60). Melting points were determined with a Kofler hot stage apparatus and were not corrected. Optical rotations were determined using a Perkin-Elmer 241MC polarimeter.

(*S*)-*N*-(2-Hydroxy-1-phenyl-ethyl)-formamide[2], (*S*)-*N*-methyl-2-phenylglycinol[3] and compounds (**9**)[4] and (**10**)[5] were prepared by literature methods.

General Procedures for 3a-h, 5a-f and 7

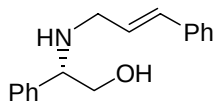
The 1,2-aminoalcohol (15.0 mmol) was mixed with $NaHCO_3$ (30.0 mmol) in DMF (15 mL) and then heated to 70 °C. The allylic bromide (15.7 mmol) in DMF (5 mL) was added to this solution over 3 hours. After the addition was complete the reactants were stirred for another 2 hours and the reaction was then quenched with water (100 mL). The mixture was extracted with petrol (2 x 30 mL). The organic solution was dried over Na_2SO_4 and concentrated under reduced pressure. The crude products were used in the next transformation without further purification.

(2*S*)-2-{Methyl[(*E*)-3-phenyl-2-propenyl]amino}-2-phenylethan-1-ol (3a)



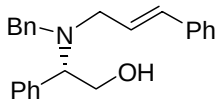
The compound was obtained as a pale yellow oil (1.430 g, 89%), $[\alpha]_D^{20}$ +91 (*c* = 0.005 g/mL, $CHCl_3$). ν_{max}/cm^{-1} (neat) 3409, 3026, 2938, 2794, 1599, 1450. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.20 (10H, m, ArH), 6.48 (1H, d, *J*=15.8 Hz, PhC*H*CH), 6.22 (1H, ddd, *J*=15.8, 7.3, 6.2 Hz, PhCHC*H*), 4.01 (1H, dd, *J*=10.6, 9.6 Hz, OC*H*HCH), 3.85 (1H, dd, *J*=9.6, 5.2 Hz, PhCHN), 3.69 (1H, dd, *J*=10.6, 5.2 Hz, OCH*H*CH), 3.26 (1H, ddd, *J*=13.7, 6.2, 1.3 Hz, NC*H*HCH), 3.06 (1H, dd, *J*=13.7, 7.3 Hz, NCH*H*CH), 2.20 (3H, s, NCH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.0, 135.7, 132.7, 129.1, 128.6, 128.4, 128.0, 127.7, 127.6, 126.4, 68.1, 61.0, 56.8, 37.2. *m/z* (CI) 268 (M+1, 8), 250 (11), 117 (100). HRMS found: 268.1689, $C_{18}H_{22}NO$ required: 268.1701.

(2*S*)-2-Phenyl-2-{[(*E*)-3-phenyl-2-propenyl]amino}ethan-1-ol (3b)



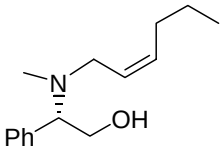
The compound was obtained as pale yellow oil (2.873 g, 84%), $[\alpha]_D^{20}$ +66 (*c* = 0.013 g/mL, $CHCl_3$). ν_{max}/cm^{-1} (neat) 3325, 3060, 3026, 2835, 1599, 1449. ^1H NMR (270 MHz, $CDCl_3$) δ 7.34-7.21 (10H, m, ArH), 6.44 (1H, d, *J*=15.9 Hz, PhC*H*CH), 6.23 (1H, dt, *J*=15.9, 6.3 Hz, NCH_2C*H*), 3.84 (1H, dd, *J*=8.6, 4.3 Hz, PhCHN), 3.72 (1H, dd, *J*=10.3, 4.3 Hz, OC*H*HCH), 3.58 (1H, dd, *J*=10.3, 8.6 Hz, OCH*H*CH), 3.35 (1H, ddd, *J*=14.2, 6.0, 1.6 Hz, NC*H*HCH), 3.22 (1H, ddd, *J*=14.2, 6.6, 1.0 Hz, NCH*H*CH). ^{13}C NMR (68 MHz, $CDCl_3$) δ 140.6, 137.1, 131.6, 128.8, 128.6, 128.2, 127.7, 127.5, 127.4, 126.4, 66.8, 64.0, 49.4. *m/z* (CI) 254 (M+1, 91), 222 (52), 117 (100). HRMS found: 254.2539, $C_{17}H_{20}NO$ required: 254.1544.

(2*S*)-2-{Methyl[(*E*)-3-phenyl-2-propenyl]amino}-2-phenylethan-1-ol (3c)



The compound was obtained as white solid (0.943 g, 93%), $[\alpha]_D^{20}$ +170 (*c* = 0.007 g/mL, $CHCl_3$). M.p.: 93-5 ^oC. ν_{max}/cm^{-1} (neat) 3348, 2926, 2778, 1456. ^1H NMR (400 MHz, $CDCl_3$) δ 7.21-7.43 (15H, m, ArH), 6.51 (1H, d, *J*=15.6 Hz, PhC*H*CH), 6.19 (1H, ddd, *J*=15.6, 8.3, 4.9 Hz, PhCHC*H*), 4.17-4.08 (2H, m, PhCHN+ OCH*H*CH), 4.04 (1H, d, *J*=13.7 Hz, PhCH*H*N), 3.52-3.78 (2H, br, OCH*H*C*H* + NC*H*HCH), 3.21 (1H, d, 13.7 Hz, PhC*H*HN), 3.00 (1H, dd, *J*=14.2, 8.3 Hz, NCH*H*CH). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.6, 136.8, 135.4, 129.4, 128.2, 128.0, 127.6, 127.4, 127.3, 126.4, 1251, 64.2, 60.7, 53.9, 52.2, 20.4, 17.3, 12.0. *m/z* (CI) 344 (M+1, 53), 326 (31), 312 (52), 117 (100). HRMS found: 344.2026, $C_{24}H_{26}NO$ required: 344.2014.

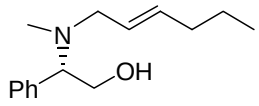
(2*S*)-2-[(*Z*)-2-Hexenyl(methyl)amino]-2-phenylethan-1-ol (3d)



The compound was obtained as a colourless oil (1.052 g, 78%), $[\alpha]_D^{20}$ +56 (*c* = 0.008 g/mL, $CHCl_3$). ν_{max}/cm^{-1} (neat) 3418, 2957, 2871, 1452. ^1H NMR (400 MHz, $CDCl_3$) δ 7.38-7.29 (3H, m, ArH), 7.21-7.15 (2H, m, ArH), 5.55 (1H, ddd, *J*=7.5, 6.2, 5.5 Hz,

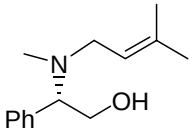
NCH_2CH), 5.47 (1H, dt, *J*=7.5, 7.0 Hz, $CHCH_2CH_2$), 3.97 (1H, dd, *J*=10.8, 10.0 Hz, $OCHHCH$), 3.82 (1H, dd, *J*= 10.0 Hz, 4.9 Hz, PhCHN), 3.65 (1H, dd, *J*=10.8, 4.9 Hz, $OCHHCH$), 3.07 (1H, dd, *J*=13.9, 5.5 Hz, $NCHHCH$), 2.96 (1H, dd, *J*=13.9, 6.2 Hz, $NCHHCH$), 2.15 (3H, s, NCH_3), 1.97 (2H, tdd, *J*=7.0, 7.3, 2.5 Hz, $CHCH_2CH_2$), 1.36 (2H, sextet, *J*=7.3 Hz, CH_3CH_2), 0.87 (3H, t, *J*=7.3 Hz, CH_2CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.8, 134.2, 129.1, 128.3, 127.9, 127.7, 67.5, 60.8, 56.6, 36.9, 34.6, 22.6, 13.8. *m/z* (CI) 234 (M+1, 74), 216 (39), 202 (100). HRMS found: 234.1849, $C_{15}H_{24}NO$ required: 234.1858.

(2*S*)-2-[(*E*)-2-Hexenyl(methyl)amino]-2-phenylethan-1-ol (3e)



The compound was obtained as a colourless oil (1.266 g, 81%), $[\alpha]_D^{20}$ +63 (*c* = 0.006 g/mL, $CHCl_3$). ν_{max}/cm^{-1} (neat) 3418, 2957, 2872, 1452. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.31 (3H, m, ArH), 7.21-7.17 (2H, m, ArH), 5.55 (1H, dt, *J*=15.4, 6.6 Hz, NCH_2CH), 5.46 (1H, dt, *J*=15.4, 7.3 Hz, $CHCH_2CH_2$), 3.97 (1H, t, *J*=10.2 Hz, $OCHHCH$), 3.82 (1H, dd, *J*=10.2, 5.1 Hz, PhCHN), 3.64 (1H, dd, *J*=10.2, 5.1 Hz, $OCHHCH$), 3.06 (1H, dd, *J*=13.2, 5.5 Hz, $NCHHCH$), 2.83 (1H, dd, *J*=13.2, 7.0 Hz, $NCHHCH$), 2.13 (3H, s, NCH_3), 2.01 (2H, q, *J*=7.3 Hz, $CHCH_2CH_2$), 1.39 (2H, sextet, *J*=7.3 Hz, CH_2CH_3), 0.90 (3H, t, *J*=7.3 Hz, CH_2CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.7, 134.1, 129.1, 128.2, 127.8, 127.6, 67.5, 60.8, 56.5, 36.8, 34.5, 22.5, 13.7. *m/z* (CI) 234 (M+1, 88), 216 (67), 202 (100). HRMS found: 234.1857, $C_{15}H_{24}NO$ required: 234.1858.

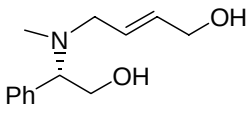
(2*S*)-2-[Methyl(3-methyl-2-butenyl)amino]-2-phenylethanol (3f)



The compound was obtained as a colourless oil (1.540 g, 97%), $[\alpha]_D^{20}$ +72 (*c* = 0.007 g/mL, $CHCl_3$). ν_{max}/cm^{-1} (neat) 3408, 3060, 3029, 2969, 2792, 1673, 1451. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.33 (3H, m, ArH), 7.21-7.15 (2H, m, ArH), 5.24 (1H, t, *J*=6.6 Hz, CH_2CH), 3.97 (1H, t, *J*=10.0 Hz, $OCHHCH$), 3.81 (1H, dd, *J*=10.0, 4.8 Hz, PhCHN), 3.62 (1H, dd, *J*=10.0, 5.1 Hz, $OCHHCH$), 3.02 (1H, dd, *J*=13.6, 6.2 Hz, $NCHHCH$), 2.88 (1H, dd,

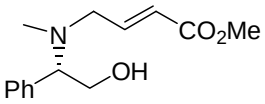
J=13.6, 7.7 Hz NCH*H*CH), 2.12 (3H, s, NCH_3), 1.71 (3H, s, CHC(C*H*$_3$)CH_3), 1.59 (3H, s, CHC(CH_3)C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.8, 135.1, 129.1, 128.2, 127.8, 122.0, 67.6, 60.8, 51.9, 36.9, 25.9, 18.2. *m/z* (CI) 220 (M+1, 19), 202 (39), 188 (47), 134 (50), 121 (54), 105 (62), 69 (100). HRMS found: 220.1694, $C_{14}H_{22}NO$ required: 220.1701.

(*E*)-4-{[(1*S*)-2-Hydroxy-1-phenylethyl](methyl)amino]-2-buten-1-ol (3g)



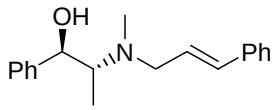
The compound was obtained as a colourless oil (0.762 g, 75%), $[\alpha]_D^{20}$ +34 (*c* = 0.008 g/mL, $CHCl_3$). ν_{max}/cm^{-1} (neat) 3332, 2850, 1452. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.31 (3H, ArH), 7.22-7.16 (2H, m, ArH), 5.81-5.72 (2H, m, C*H*C*H*), 4.14 (2H, d, *J*=5.2 Hz, OC*H*$_2$CH), 3.97 (1H, t, *J*=9.6 Hz, OC*H*HCH), 3.81 (1H, dd, *J*=9.6, 4.8 Hz, PhCHN), 3.65 (1H, dd, *J*=9.6, 4.8 Hz, OCH*H*CH), 3.12 (1H, dd, *J*=13.3, 4.8 Hz, NCH*H*CH), 2.92 (1H, dd, *J*=13.3, 6.4 Hz, NC*H*HCH), 2.16 (3H, s, NCH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.5, 132.6, 129.2, 129.1, 128.3, 128.0, 67.7, 63.1, 60.9, 55.9, 37.1. *m/z* (CI) 222 (M+1, 82), 204 (100), 190 (95). HRMS found: 222.1490, $C_{13}H_{20}NO_2$ required: 222.1494.

Methyl (*E*)-4-{[(1*S*)-2-hydroxy-1-phenyl-ethyl](methyl)amino}-2-butenoate (3h)



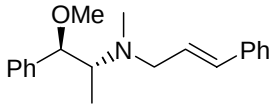
The compound was obtained as a colourless oil (1.827 g, 89%), $[\alpha]_D^{20}$ +47 (*c* = 0.015 g/mL, $CHCl_3$). ν_{max}/cm^{-1} (neat) 3425, 3029, 2950, 2797, 1721, 1658, 1436. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.31 (3H, m, ArH), 7.24-7.18 (2H, m, ArH), 6.36 (1H, dt, *J*=11.4, 6.2 Hz, NCH_2C*H*), 5.97 (1H, d, *J*=11.4 Hz, C*H*CO_2Me), 3.95 (1H, dd, *J*=8.4, 6.7 Hz, PhCHN), 3.74 (1H, dd, *J*=12.5, 8.4 Hz, OC*H*HCH), 3.73 (3H, s, CO_2CH_3), 3.68 (1H, dd, *J*=12.5, 6.7 Hz, OCH*H*CH), 3.23 (1H, dd, *J*=13.8, 6.3 Hz, NC*H*HCH), 3.06 (1H, dd, *J*=13.8, 7.3 Hz, NCH*H*CH), 2.19 (3H, s, NCH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 146.4, 136.3, 128.9, 128.4, 128.0, 122.6, 69.0, 61.6, 55.3, 51.2, 38.0. *m/z* (CI) 250 (M+1, 100), 232 (47), 218 (60), 130 (77). HRMS found: 250.1441, $C_{14}H_{20}NO_3$ required: 250.1443.

(1*R*, 2*R*)-2-{Methyl-[(*E*)-3-phenyl-2-propenyl]amino}-1-phenylpropan-1-ol (5a)



The compound was obtained as a white solid (2.548 g, 92%), $[\alpha]_D^{20}$ -130 (*c* = 0.021 g/mL, $CHCl_3$). M.p.: 60-2 °C. ν_{max}/cm^{-1} (CH_2Cl_2) 3381, 3062, 3031, 2975, 2844, 1604, 1448. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.27 (10H, m, ArH), 6.54 (1H, d, *J*=16.1 Hz, PhCH=), 6.27 (1H, dt, *J*=16.1, 6.4 Hz, NCH_2CH), 4.27 (1H, d, *J*=9.8 Hz, PhC*H*OH), 3.39 (1H, dd, *J*=13.7, 6.4 Hz, NC*H*HCH), 3.17 (1H, dd, *J*=13.7, 6.4 Hz, NCH*H*CH), 2.77-2.73 (1H, m, CH_3CHN), 2.30 (3H, s, NCH_3), 0.77 (3H, d, *J*=6.4 Hz, CH_3CHN). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.2, 137.1, 132.6, 128.7, 128.3, 127.7, 127.6, 127.5, 126.5, 75.0, 65.0, 56.5, 36.0, 7.6. *m/z* (CI) 282 (M+1, 17), 176 (56), 117 (85), 91 (100). HRMS found: 282.1859, $C_{19}H_{24}NO$ required: 282.1858.

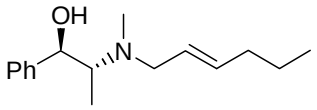
***N*-[(1*R*, 2*R*)-2-Methoxy-1-methyl-2-phenylethyl]-*N*-methyl-*N*-[(*E*)-3-phenyl-2-propenyl]amine (5b)**



2-[Methyl-(3-phenyl-allyl)-amino]-1-phenyl-propan-1-ol (562 mg, 2.0 mmol) was dissolved in anhydrous THF (15 mL). To this solution was added NaH (60% in mineral oil, 120 mg, 3.0 mmol) at 0 °C. After 1 hour, methyl iodide (0.15 mL, 2.4 mmol) was added. The reactants were stirred at room temperature for 24 hours. The reaction was quenched with sat. $NaHCO_3$ (20 mL) and extracted with petrol. The organic solution was dried over Na_2SO_4. After removing the solvent, the residue was further purified by chromatography (silica gel, 5% methanol in DCM, R_f=0.12) to yield the product as a pale yellow oil (529 mg, 90%), $[\alpha]_D^{20}$ –98 (*c* = 0.013 g/mL, $CHCl_3$). ν_{max}/cm^{-1} (neat) 3060, 3026, 2970, 2933, 2874, 1600. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.37-7.24 (10H, m, ArH), 6.54 (1H, d, *J*=15.9 Hz, CH_2CH), 6.31 (1H, ddd, *J*=15.9, 7.3, 6.0 Hz, =CHPh), 4.08 (1H, d, *J*=9.0 Hz, PhCH), 3.48 (1H, dd, *J*=14.0, 6.0 Hz, NC*H*HCH), 3.28 (1H, dd, *J*=14.0, 7.3 Hz, NCH*H*CH), 3.19 (3H, s, OCH_3), 3.11-3.07 (1H, m, $NCHCH_3$), 2.38 (3H, S, NCH_3), 0.71 (3H, d, *J*=7.0 Hz, $CHCH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.9, 137.6, 131.6, 129.3, 128.5, 127.9, 127.7, 127.2, 126.4,

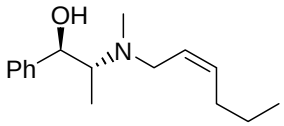
86.8, 62.4, 57.2, 56.5, 37.5, 11.7. *m/z* (CI) 296 (M+1, 47), 174 (88), 117 (100). HRMS found: 296.2017, $C_{20}H_{25}NO$ required: 296.2014.

(1*R*, 2*R*)-2-[(*E*)-2-Hexenyl(methyl)amino]-1-phenylpropan-1-ol (5c)



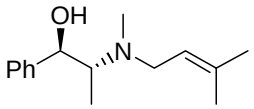
The compound was obtained as a colourless oil (1.134 g, 85%), $[\alpha]_D^{20}$- 63 (*c* = 0.007 g/mL, $CHCl_3$). ν_{max}/cm^{-1} (neat) 3348, 2959, 2928, 2872, 1453. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.24 (5H, m, ArH), 5.62-5.54 (1H, m, C*H*CH), 5.52-5.43 (1H, m, CHC*H*), 4.22 (1H, d, *J*=9.6Hz, PhC*H*OH), 3.16 (1H, dd, *J*=13.2, 5.5 Hz, NCH*H*CH), 2.93 (1H, dd, *J*=13.2, 7.1Hz, NCH*H*CH), 2.70 (1H, dq, *J*=9.6, 6.6Hz, CH_3C*H*N), 2.23 (3H, s, NCH_3), 2.03 (2H, dt, *J*=7.0, 6.6Hz, CHCH_2CH_2), 1.40 (2H, tq, *J*=7.3, 7.0Hz, CHCH_2CH_2), 0.91 (3H, t, *J*=7.3Hz, CH_2CH_3), 0.72 (3H, d, *J*=6.6 Hz, CH_3CHN). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.4, 133.9, 128.2, 127.8, 127.7, 127.4, 74.8, 64.3, 56.2, 35.7, 34.4, 22.5, 13.7, 7.3. *m/z* (CI) 248 (M+1, 39), 230 (20), 140 (100). HRMS found: 248.2017, $C_{16}H_{25}NO$ required: 248.2014.

(1*R*, 2*R*)-2-[(*Z*)-2-Hexenyl(methyl)amino]-1-phenylpropan-1-ol (5d)



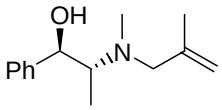
The compound was obtained as a colourless oil (1.241 g, 87%), $[\alpha]_D^{20}$ - 42 (*c*=0.010 g/mL, $CHCl_3$). ν_{max}/cm^{-1} (neat) 3362, 2960, 2871, 1453. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.24 (5H, m, ArH), 5.61-5.47 (2H, m, C*HCH*), 4.22 (1H, d, *J*=11.7Hz, PhC*H*OH), 3.17 (1H, dd, *J*=13.7, 5.8 Hz, NCH*H*CH), 3.08 (1H, dd, *J*=13.7, 6.9Hz, NCH*H*CH), 2.69 (1H, dq, *J*=11.7, 6.8Hz, CH_3C*H*N), 2.25 (3H, s, NCH_3), 2.04 (2H, dt, *J*=7.3, 6.9Hz, CHCH_2CH_2), 1.39 (2H, sextet, *J*=7.3Hz, CHCH_2CH_2), 0.90 (3H, t, *J*=7.3Hz, CH_2CH_3), 0.74 (3H, d, *J*=6.8 Hz, CH_3CHN). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.3, 133.0, 128.2, 127.7, 127.5, 127.3, 74.8, 64.3, 50.4, 35.8, 29.6, 22.8, 13.8, 7.3. *m/z* (CI) 248 (M+1, 36), 230 (20), 140 (94), 83 (100). HRMS found: 248.2014, $C_{16}H_{25}NO$ required: 248.2014.

(1*R*, 2*R*)-2-[Methyl(3-methyl-2-butenyl)amino]-1-phenylpropan-1-ol (5e)



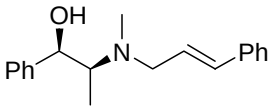
The compound was obtained as a pale yellow oil (1.036 g, 99%), $[\alpha]_D^{20}$ –76 (*c* = 0.007 g/mL, $CHCl_3$), ν_{max}/cm^{-1} (neat) 3333, 3030, 2970, 2853, 1451. ^1H NMR (400 MHz, $CDCl_3$) δ 7.42-7.24 (5H, m, ArH), 5.34-5.13 (1H, m, C*H*C$(CH_3)_2$), 4.21 (1H, d, *J*=9.7Hz, PhC*H*OH), 3.12 (1H, dd, *J*=13.2, 6.4 Hz, NCH*H*CH), 3.00 (1H, dd, *J*=13.7, 7.3Hz, NCH*H*CH), 2.68 (1H, dq, *J*=9.7, 6.4Hz, CH_3C*H*N), 2.23 (3H, s, NCH_3), 1.76 (3H, s, C(C*H*$_3$)CH_3), 1.65 (3H, s, C(CH_3)C*H*$_3$), 0.74 (3H, d, *J*=6.4 Hz, C*H*$_3$CHN). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.5, 136.3, 129.3, 128.7, 128.5, 123.2, 75.8, 65.2, 52.4, 36.7, 26.9, 19.1, 8.4. *m/z* (CI) 234 (M+1, 29), 216 (10), 178 (18), 148 (30), 126 (100). HRMS found: 234.1847, $C_{15}H_{23}NO$ required: 234.1858.

(1*R*, 2*R*)-2-[Methyl-(2-methyl-allyl)-amino]-1-phenylpropan-1-ol (5f)



The compound was obtained as a colourless oil (1.125 g, 96%), $[\alpha]_D^{20}$ 67 (*c*=0.007 g/mL, $CHCl_3$). ν_{max}/cm^{-1} (neat) 3351, 2970, 2850, 1450. ^1H NMR (400 MHz, $CDCl_3$) δ 7.37-7.25 (5H, m, ArH), 4.91-4.90 (2H, m, CC*H*$_2$), 4.26 (1H, d, *J*=9.5Hz, PhC*H*OH), 3.12 (1H, d, *J*=13.2Hz, NCH*H*C), 2.92 (1H, d, *J*=13.2, NCH*H*C), 2.67 (1H, dq, *J*=9.5, 6.6Hz, CH_3C*H*N), 2.20 (3H, s, NCH_3), 1.83 (3H, s, C*H*$_3$CCH_2), 0.73 (3H, d, *J*=6.6Hz, C*H*$_3$CHN). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.7, 142.2, 128.2, 127.7, 127.4, 113.6, 74.9, 64.7, 60.6, 35.6, 20.5, 7.1. *m/z* (CI) 220 (M+1, 43), 202 (50), 112 (100). HRMS found: 220.1700, $C_{14}H_{21}NO$ required: 220.1701.

(1*R*, 2*S*)-2-{Methyl-[(*E*)-3-phenyl-2-propenyl]amino}-1-phenylpropan-1-ol (7)



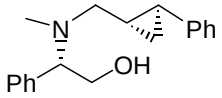
The compound was obtained as a white solid (1.356 g, 96%), $[\alpha]_D^{20}$ -108 (*c* = 0.007 g/mL, $CHCl_3$). M.p.: 80-1^oC. ν_{max}/cm^{-1} (CH_2Cl_2) 3210, 3058, 3031, 2828, 1450. ^1H NMR

(400 MHz, $CDCl_3$) δ 7.38-7.27 (10H, m, ArH), 6.50 (1H, d, *J*=16.1 Hz, PhCH=), 6.22 (1H, dt, *J*=16.1, 6.8 Hz, NCH_2CH), 4.87 (1H, d, *J*=3.9 Hz, PhC*H*OH), 3.34-3.24 (2H, m, NCH_2), 2.91 (1H, dq, *J* = 6.8, 3.9 Hz, CH_3CHN), 2.32 (3H, s, NCH_3), 0.92 (3H, d, *J*=6.8 Hz, CH_3CHN). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.5, 137.1, 132,4, 128.6, 128.0, 127.5, 127.0, 126.4, 126.2, 73.2, 63.0, 57.2, 39.2, 10.1. *m/z* (CI) 282 (M+1, 28), 264 (20), 174 (75), 117 (100). HRMS found: 282.1861, $C_{19}H_{24}NO$ required: 282.1858.

General Procedures for 4b-f and 6a-f

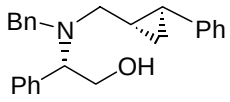
Et_2Zn (1M solution in hexane, 0.60 mL, 0.60 mmol for **4b-f**, and 0.50 mL, 0.50 mmol for **6a-f**) was diluted in anhydrous DCM (2.0 mL). Diiodomethane (182 μL, 1.20 mmol for **4b-f**, and 81 μL, 1.00 mmol for **6a-f**) was added to this solution at 0 ^{o}C. Twenty minutes after the addition, the allylic amine derivative (**4b-f** or **6a-f**, 0.46 mmol) in DCM (0.5 mL) was added. The mixture was allowed to stir for 48 hours. The reaction was quenched with 10% EDTA (5.0 mL) at room temperature and the product was extracted with DCM (2 × 30 mL). The organic solution was dried over Na_2SO_4 and concentrated to yield the crude product, which was further purified by chromatography on silica gel.

(2*S*)-2-(Methyl-{[(1*S*, 2*S*)-*2*-phenyl-cyclopropyl](methyl)}amino)-2-phenylethan-1-ol (4a)



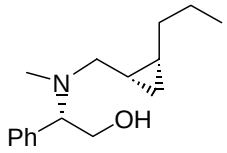
The compound was obtained as a white solid (0.122 g, 95%) and a 21:1 mixture of diastereoisomers. ^{1}H NMR (400 MHz, $CDCl_3$) δ (major isomer) 7.38-7.03 (10H, m, ArH), 3.96 (1H, t, *J*=10.2 Hz, OC*H*HCH), 3.81 (1H, dd, *J*=10.2, 5.0 Hz, PhCHN), 3.65 (1H, dd, *J*=10.2, 5.0 Hz, OCH*H*CH), 2.51 (1H, dd, *J*=12.8, 6.2 Hz, NC*H*HCH), 2.32 (1H, dd, *J*=12.8, 6.8 Hz, NCH*H*CH), 2.30 (3H, s, NCH_3), 1.66 (1H, dt, *J*=9.3, 4.5Hz, PhC*H*CH), 1.21 (1H, m, NCH_2CH), 0.97 (1H, dt, *J*=8.4, 4.5 Hz, PhCHC*H*H), 0.79 (1H, dt, *J*=8.4, 5.4 Hz, PhCHCH*H*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.8, 128.9, 128.4, 128.3, 127.9, 125.8, 125.6, 69.0, 60.8, 58.1, 37.8, 23.1, 22.1, 14.8. *m/z* (CI) 282 (M+1, 33), 250 (58), 131 (100). HRMS found: 282.1858 $C_{19}H_{24}NO$ required: 282.1858.

(2*S*)-2-(Benzyl-{[(1*S*, 2*S*)-2-phenylcyclopropyl](methyl)amino}-2-phenylethan-1-ol (4c)



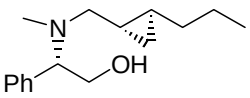
The compound was obtained as a white solid (0.142 g, 87%) and a 12:1 mixture of diastereoisomers. ^{1}H NMR (400 MHz, $CDCl_3$) δ (major isomer) 7.40-6.96 (15H, m, ArH), 4.08-4.02 (2H, m, OCHHCH + PhCHN), 3.68-3.57 (3H, m, $PhCH_2N$ + OCH*H*CH), 2.61 (1H, dd, *J*=13.7, 6.5 Hz, NC*H*HCH), 2.38 (1H, dd, *J*=13.7, 6.3 Hz, NCH*H*CH), 1.63 (1H, dt, *J*=4.5, 9.3 Hz, PhC*H*CH), 1.27-1.22 (1H, m, NCH_2CH), 0.89 (1H, dt, *J*=8.4, 4.5 Hz, PhCHC*H*H), 0.71 (1H, dt, *J*=8.4, 5.4 Hz, PhCHCH*H*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.3, 138.0, 137.2, 135.7, 134.1, 132.5, 129.4, 128.3, 127.5, 127.2, 125.4, 64.1, 60.3, *m/z* (CI) 358 (M+1, 33), 340 (23), 326 (57), 131 (100). HRMS found: 358.2176, $C_{25}H_{27}NO$ required: 358.2171).

(2*S*)-2-(Methyl-{[(1*S*, 2*R*)-2-propylcyclopropyl](methyl)amino)-2-phenylethan-1-ol (4d)



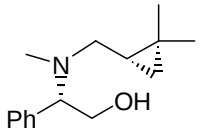
The compound was obtained as a colourless oil (0.104 g, 92%) and a 20:1 mixture of diastereoisomers. ν_{max}/cm^{-1} (neat) 3422, 3060, 2927, 2871, 1453, 1025. ^{1}H NMR (400 MHz $CDCl_3$) δ (major isomer) 7.35 (3H, m, ArH), 7.20 (2H, m, ArH), 3.98 (1H, t, *J*=10.2 Hz, OC*H*HCH), 3.82 (1H, dd, *J*=10.2, 5.0 Hz, OCH*H*CH), 3.64 (1H, dd, *J*=10.2, 5.0 Hz, PhCHN), 2.51 (1H, dd, *J*=12.8, 6.2 Hz, NC*H*HCH), 2.32 (1H, dd, *J*=12.8, 7.7 Hz, NCH*H*CH), 2.24 (3H, s, NCH_3), 1.40 (4H, m, CH_2CH_2), 1.06 (1H, m, NCH_2CH), 0.92 (3H, t, *J*=7.2 Hz, CH_2CH_3), 0.80 (1H, m, $CHCH_2CH_2$), 0.72 (1H, dt, *J*=8.6, 4.4 Hz, CHCH*H*CH), -0.14 (1H, dd, *J*=9.9, 5.5 Hz, CHC*H*HCH). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.80, 129.1, 128.2, 127.8, 69.0, 60.6, 54.1, 36.5, 31.1, 23.3, 15.8, 14.3, 14.1, 10.9. *m/z* (CI) 248 (M+1, 88), 230 (57), 216 (100). HRMS found: 248.2011, $C_{16}H_{26}NO$ required: 248.2014.

(2*S*)-2-(Methyl-{[(1*S*, 2*S*)-2-propylcyclopropyl](methyl)amino)-2-phenylethan-1-ol (4e)



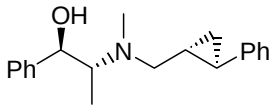
The compound was obtained as a colourless oil (0.108 g, 96%) and as a single diasteroisomer, $[\alpha]_D^{20}$ +69 (*c* = 0.0059 g/mL, $CHCl_3$). ν_{max}/cm^{-1} (neat) 3418, 2955, 2872, 1453, 1026. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (3H, m, ArH), 7.17 (2H, m, ArH), 3.95 (1H, t, *J*=10.5 Hz, C*H*HCH), 3.82 (1H, dd, *J*=10.5, 4.8 Hz, OCH*H*CH), 3.63 (1H, dd, *J*=10.5, 4.8 Hz, PhCHN), 2.34 (1H, dd, *J*=12.4, 6.8 Hz, NC*H*HCH), 2.25 (3H, m, NCH_3), 2.16 (1H, dd, *J*=12.4, 6.8 Hz, NCH*H*CH), 1.41 (2H, m, $CHCH_2CH_2$), 1.20 (2H, m, $CHCH_2CH_2$), 0.90 (3H, t, *J*=7.2 Hz, CH_2CH_3), 0.62 (1H, m, NCH_2CH), 0.48 (1H, m, $CHCH_2CH_2$), 0.24 (2H, m, $CHCH_2CH$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.6, 129.0, 128.3, 127.9, 68.8, 60.6, 58.6, 37.4, 36.1, 22.6, 18.4, 17.1, 14.1, 11.0. *m/z* (CI) 248 (M+1, 40), 230 (52), 216 (68), 105 (100). HRMS found: 248.2009, $C_{16}H_{26}NO$ required: 248.2014).

(2*S*)-2-{[(1*S*)-2,2-Dimethylcyclopropyl](methyl)amino}-2-phenylethan-1-ol (4f)



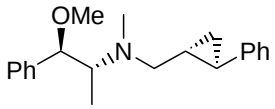
The compound was obtained as a colourless oil (0.100 g, 94%) and as a 12:1 mixture of diastereoisomers. ν_{max}/cm^{-1} (neat) 3411, 3029, 2941, 2866, 1452, 1024. ^{1}H NMR (400 MHz, $CDCl_3$) δ (major isomer) 7.35 (3H, m, ArH), 7.20 (2H, m, ArH), 3.98 (1H, t, *J*=10.2 Hz, OC*H*HCH), 3.82 (1H, dd, *J*=10.2, 5.1 Hz, OCH*H*CH), 3.64 (1H, dd, *J*=10.2, 5.0 Hz, PhCHN), 2.51 (1H, dd, *J*=12.8, 6.2 Hz, NC*H*HCH), 2.32 (1H, dd, *J*=12.8, 6.8 Hz, NCH*H*CH), 2.23 (3H, s, NCH_3), 1.05 (3H, s, $C(CH_3)CH_3$), 1.02 (3H, s, $C(CH_3)CH_3$), 0.69 (1H, tt, *J*= 8.8, 6.2 Hz, NCH_2CH), 0.48 (2H, dd, *J*=8.8, 4.4 Hz, CCH*H*CH), 0.00 (1H, m, CC*H*HCH). ^{13}C NMR (101 MHz, $CDCl_3$) δ 129.0, 128.3, 127.9, 69.1, 60.5, 54.3, 36.7, 27.3, 23.2, 20.3, 19.1, 15. *m/z* (CI) 234 (M+1, 15), 216 (23), 202 (50), 134 (72), 105 (100). HRMS found: 234.1852, $C_{15}H_{24}NO$ required: 234.1858.

(1*R*, 2*R*)-2-(Methyl{[(1*R*, 2*R*)-2-phenylcycloproyl](methyl)}amino)-1-phenylpropan-1-ol (6a)



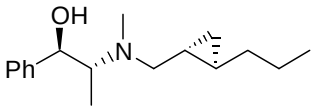
The compound was obtained as a white solid (0.128 g, 95%) and as a single diastereoisomer, $[\alpha]_D^{20}$-141 (*c* = 0.0123 g/mL, $CHCl_3$). Mp: 60-2 ^oC. ν_{max}/cm^{-1} (neat) 3331, 3060, 3028, 2969, 2797, 1604, 1452, 1036, 1026. ^1H NMR (400 MHz, $CDCl_3$) δ 7.19 (10H, m, ArH), 4.20 (1H, d, *J*=9.3 Hz, PhC*H*OH), 2.80 (1H, dq, *J*=9.3, 6.8 Hz, C*H*NCHH), 2.70 (1H, dd, *J*=12.7, 5.9 Hz, NCH*H*), 2.35 (1H, dd, *J*=12.7, 7.3 Hz, NC*H*H), 2.32 (3H, s, NCH_3), 1.68 (1H, dt, *J*=8.8, 4.9 Hz, PhC*H*CH_2), 1.23 (1H, m, NCH_2C*H*), 1.02 (1H, dt, *J*=8.3, 4.9 Hz, CHC*H*HCH), 0.85 (1H, *J*=8.8, 5.3 Hz, CHCH*H*CH) 0.71(3H, d, J=6.8 Hz, NCHCH_3) ^{13}C NMR (400 MHz, $CDCl_3$) δ 142.7, 142.3, 128.5, 127.7, 127.5, 125.9, 125.7, 74.8, 64.6, 58.2, 36.4, 23.5, 22.6, 14.2, 7.4. *m/z* (CI) 296 (M+1, 15), 188 (31), 148 (50), 131 (100). HRMS found: 296.2016, $C_{20}H_{25}NO$ required: 296.2014.

_N_-[(1_R_, 2_R_)-2-Methoxy-1-methyl-2-phenylethyl]-_N_-methyl-_N_-{[(1_R_, 2_R_)-2-phenylcyclopropyl](methyl)}amine (6b)



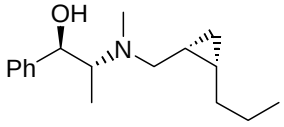
The compound was obtained as a white solid (0.131 g, 93%) and as a 3:2 mixture of diastereoisomers. ν_{max}/cm^{-1} (neat) 3062, 3027, 2976, 2817, 1604, 1452, 1091. ^1H NMR (400 MHz, $CDCl_3$) δ (major isomer) 7.20 (10H, m, ArH), 4.01 (1H, d, *J*=8.9 Hz, MeOCH), 3.15 (4H, m, OCH_3 + NC*H*CH_3), 2.76 (1H, dd, *J*=12.6, 5.6 Hz, NC*H*HCH), 2.53 (1H, dd, *J*=12.6, 5.2 Hz, NCH*H*CH), 2.42 (3H, s, NCH_3), 1.67 (1H, dt, *J*=8.6, 5.0 Hz, PhC*H*CH_2), 1.26 (1H, m, NCH_2C*H*), 0.97 (1H, dt, *J*=8.7, 4.5 Hz, CHC*H*HCH), 0.87 (1H, dt, *J*=8.7, 4.0 Hz, CHCH*H*CH). ^{13}C NMR (101 MHz, $CDCl_3$) δ (two diastereomers)143.4, 141.0, 128.4, 128.2, 127.9, 127.6, 125.9, 125.4, 86.7, 62.7, 62.4, 58.8, 56.5, 37.9, 37.8, 23.3, 22.9, 22.7, 22.4, 15.6, 14.6, 12.0, 11.5. *m/z* (CI) 310 (M+1, 37), 188 (75), 148 (69), 131 (100). HRMS found: 310.2167, $C_{21}H_{27}NO$ required: 310.2171).

(1_R_, 2_R_)-2-(Methyl-{[(1_R_, 2_R_)-2-propylcyclopropyl](methyl)}amino)-1-phenyl-propan-1-ol (6c)



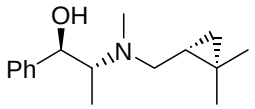
The compound was obtained as a colourless oil (0.114 g, 96%) and as a single diastereoisomer, $[\alpha]_D^{20}$ -85 (*c* = 0.0179 g/mL, $CHCl_3$). ν_{max}/cm^{-1} (neat) 3345, 2958, 2924, 2878, 1453, 1027, 1037. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.25 (5H, m, ArH), 4.21 (1H, d, *J*=9.8 Hz, PhC*H*OH), 2.73 (1H, dq, *J*=9.8, 6.8Hz, NC*H*CH_3), 2.49 (1H, dd, *J*=12.7, 6.3 Hz, NC*H*H), 2.32 (3H, s, NCH_3), 2.22 (1H, dd, *J*=12.7, 9.1Hz, NCH*H*), 1.42 (2H, sextet, *J*=7.1 Hz, C*H*$_2$$CH_3$), 1.34-1.28 (1H, m, CHCH*H*CH_2), 1.24-1.19 (1H, m, CHC*H*HCH_2), 0.92 (3H, t, *J*=7.1Hz, CH_2C*H*$_3$), 0.71 (3H, d, *J*=6.8 Hz, NCHC*H*$_3$), 0.69-0.64 (1H, m, NCH_2C*H*), 0.56-0.52 (1H, m, C*H*CH_2CH_2), 0.32 (2H, dd, *J*=6.3, 3.9 Hz, CHC*H*$_2$CH). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.4, 128.2, 127.7, 127.4, 74.7, 64.8, 58.4, 36.1, 22.7, 18.6, 17.6, 14.0, 10.7, 7.3. *m/z* (CI) 262 (M+1, 30), 244 (15), 154 (100). HRMS found:262.2176, $C_{17}H_{27}NO$ required: 262.2171.

(1*R*, 2*R*)-2-(Methyl-{[(1*R*, 2*S*)-2-propylcyclopropyl](methyl)}amino)-1-phenyl-propan-1-ol (6d)



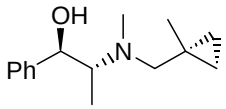
The compound was obtained as a colourless oil (0.113 g, 95%) and as an 8:1 mixture of diastereoisomers. ν_{max}/cm^{-1} (neat) 3331, 3060, 3028, 2969, 2797, 1604, 1452, 1036, 1026. ^{1}H NMR (400 MHz, $CDCl_3$) δ (major isomer) 7.43-7.29 (5H, m, ArH), 4.56 (1H, d, *J*=9.9 Hz, PhC*H*OH), 3.67-3.59 (1H, m, CH_3C*H*N), 3.16 (1H, dd, *J*=12.5, 5.5 Hz, NC*H*H), 2.99 (1H, dd, *J*=12.5, 9.1Hz, NCH*H*), 2.82 (3H, s, NCH_3), 1.49-1.39 (3H, m, C*H*$_2$C*H*HCH_3), 1.38-1.10 (2H, m, CH*H*CH_3 + NCH_2C*H*), 1.08-0.90 (8H, m, NCHC*H*$_3$ + CH_2C*H*$_3$ + C*H*CH_2CH_2 + CHC*H*HCH), 0.34 (1H, dt, *J*=5.5, 5.1 Hz, CHC*H*HCH). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.7, 128.7, 128.4, 127.4, 74.1, 65.0, 53.9, 36.1, 30.8, 23.0, 16.7, 13.9, 11.8, 11.2, 9.5. *m/z* (CI) 262 (M+1, 42), 244 (15), 154 (100). HRMS found: 262.2166, $C_{17}H_{27}NO$ required: 262.2171.

(1*R*, 2*R*)-2-{[(1*R*)-2,2-Dimethylcyclopropyl]methyl(methyl)amino}-1-phenylpropan-1-ol (6e)



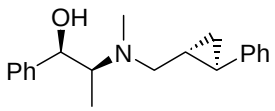
The compound was obtained as a colourless oil (0.106 g, 94%) and as a 13:1 mixture of diastereoisomers. ν_{max}/cm^{-1} (neat) 3331, 3060, 3028, 2969, 2797, 1604, 1452, 1036, 1026. ^{1}H NMR (400 MHz, $CDCl_3$) δ (major isomer) 7.45-7.23 (5H, m, ArH), 4.21 (1H, d, *J*=9.8 Hz, PhC*H*OH), 2.75-2.66 (1H, m, CH_3C*H*N), 2.63 (1H, dd, *J*=12.7, 5.9 Hz, NC*H*H), 2.38 (1H, dd, *J*=12.7, 7.8Hz, NCH*H*), 2.31 (3H, s, NCH_3), 1.10 (3H, s, C(CH_3)CH_3), 1.05 (3H, s, C(CH_3)CH_3), 0.73 (3H, d, *J*=6.3 Hz, NCHCH_3), 0.54-0.49 (1H, m, NCH_2C*H*), 0.05-0.02 (2H, m, CHCH_2C(CH_3)$_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.5, 128.2, 127.6, 127.4, 74.7, 64.4, 54.2, 35.6, 27.3, 23.8, 20.3, 18.6, 16.2, 7.5. *m/z* (CI) 248 (M+1, 25), 178 (18), 140 (100). HRMS found: 248.2010, $C_{16}H_{27}NO$ required: 248.2014.

(1*R*, 2*R*)-2-{Methyl[(1-methylcyclopropyl)methyl]amino}-1-phenylpropan-1-ol (6f)



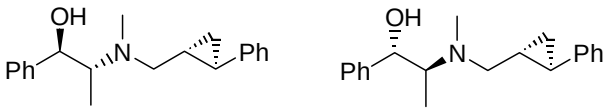
The compound was obtained as a colourless oil (99 mg, 93%) and as a single diastereoisomer, $[\alpha]_D^{20}$-63 (*c* = 0.0082 g/mL, $CHCl_3$). ν_{max}/cm^{-1} (neat) 3353, 2963, 2872, 1452, 1037, 1027. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.25 (5H, m, ArH), 4.27 (1H, d, *J*=9.8 Hz, PhC*H*OH), 2.96-2.76 (1H, m, NC*H*CH_3), 2.47 (1H, d, *J*=12.2, NC*H*H), 2.29 (3H, s, NCH_3), 2.16 (1H, d, *J*=12.2Hz, NCH*H*), 1.17 (3H, s, CH_3C), 0.69 (3H, d, *J*=6.8Hz, NCHCH_3), 0.39-0.31 (2H, m, C$H_2$$CH_2$), 0.31-0.25 (2H, m, CH_2CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.4, 128.2, 127.7, 127.4, 74.9, 65.5, 62.4, 36.1, 21.5, 13.8, 12.4, 11.8, 7.1. *m/z* (CI) 234 (M+1, 42), 216 (14), 148 (21), 126 (100). HRMS found: 234.1859, $C_{15}H_{24}NO$ required: 234.1858.

(1*R*, 2*S*)-2-(Methyl{[(1*R*, 2*R*)-2-phenylcycloproyl](methyl)}amino)-1-phenylpropan-1-ol (8)



The compound was obtained as a white solid (0.126 g, 95%) and as a single diastereoisomer, $[\alpha]_D^{20}$-123 (*c* = 0.009 g/mL, $CHCl_3$). M.p: 69-70 ^oC, ν_{max}/cm^{-1} (neat) 3330, 3060, 2977, 1603, 1494, 1046, 1029. ^1H NMR (400 MHz, $CDCl_3$) δ 7.32-7.04 (10H, m, ArH), 4.90 (1H, d, *J*=4.0 Hz, PhC*H*OH), 2.90 (1H, dq, *J*=7.0, 4.0 Hz, NC*H*CH_3), 2.71 (1H, dd, *J*=13.2, 5.8 Hz, NCH*H*), 2.53 (1H, dd, *J*=13.2, 6.8 Hz, NC*H*H), 2.36 (3H, s, NCH_3), 1.73 (1H, m, PhC*H*CH_2), 1.23-1.15 (1H, m, NCH_2C*H*), 0.97 (1H, dt, *J*=8.8, 5.1 Hz, CHC*H*HCH), 0.87 (3H, d, *J* = 7.0 Hz, NCH_3), 0.82 (1H, dt, *J*=8.8, 5.1 Hz, CHCH*H*CH). ^{13}C NMR (400 MHz, $CDCl_3$) δ 142.8, 142.4, 128.5, 128.1, 127.0, 126.2, 125.8, 125.7, 72.9, 63.5, 59.3, 39.0, 23.0, 21.5, 15.0, 9.8. *m/z* (CI) 296 (M+1, 26), 278 (87), 131 (100). HRMS found: 296.2022, $C_{20}H_{25}NO$ required: 296.2014.

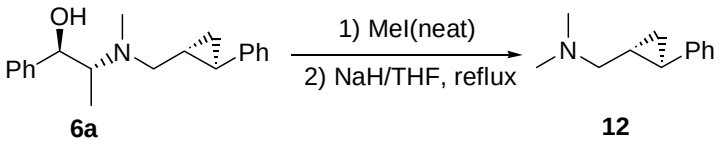
Confirmation of 6a stereochemistry by chemical correlation



11a(6a) **11b**

(*R*, *R*)-*Pseudo*-ephedrine (83 mg, 0.5 mmol) and sodium cyanoborohydride (20 mg, 0.3 mmol) were mixed in methanol (1.5 mL). Acetic acid (71 μL, 1.3 mmol) and compound **10** (80 mg, 0.6 mmol) in methanol (0.5 mL) were sequentially added. After addition, the reactants were stirred at room temperature for 24 hours and extracted with DCM. The DCM solution was dried over Na_2SO_4 and concentrated to furnish the crude product, which was further purified by chromatography (silica gel, 5% methanol in dichloromethane) to obtain **11a** (0.144 g, 97%) [or **11b** (0.140 g, 95%) in the case of (*S*, *S*)-*pseudo*-ephedrine]. **11a** is virtually compound **6a**. Spectrum data for compound **11b**: ν_{max}/cm^{-1} (neat) 3321, 3062, 3027, 1604, 1452, 1035, 1026. ^1H NMR (400 MHz, $CDCl_3$) δ 7.35-7.07 (10H, m, ArH), 4.24 (1H, d, *J*=9.5 Hz, PhC*H*OH), 2.76 (1H, dq, *J*=9.5, 6.6 Hz, NC*H*CH_3), 2.55 (2H, d, *J*=6.6 Hz, NCH_2), 2.36 (3H, s, NCH_3), 1.78 (1H, dt, *J*=8.4, 5.2 Hz, PhC*H*CH_2), 1.33-1.24 (1H, m, NCH_2C*H*), 1.07 (1H, dt, *J*=8.4, 5.1 Hz, CHC*H*HCH), 0.89 (1H, *J*=8.8, 5.1 Hz, CHCH*H*CH), 0.75 (3H, d, *J*=6.6Hz, C*H*$_3$CHN). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.8, 142.3, 128.4, 128.3, 127.7, 127.5, 125.9, 125.7, 74.8, 65.2, 58.5, 36.1, 22.6, 22.5, 15.2, 7.4. *m/z* (CI) 296 (M+1, 84), 188 (100). HRMS found: 296.2024, $C_{20}H_{25}NO$ required: 296.2014.

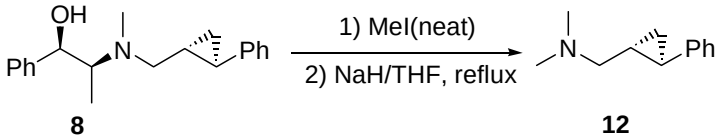
Removal of auxiliary:



6a **12**

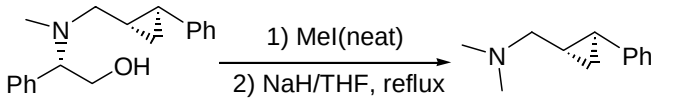
Compound **6a** (147 mg, 0.5 mmol) was dissolved in methyl iodide (5 mL), the mixture was stirred in the dark for 6 days and the excess methyl iodide was removed under reduced pressure. The residue was re-dissolved in anhydrous THF (10 mL). To this mixture was added sodium hydride (60% w/w, Aldrich, 24 mg, 0.6 mmol) and the solution was heated at reflux for 3.5 hours and then cooled to room temperature. The reactants were diluted in petrol (40 mL). The solution was extracted with 1N HCl (2 x 10 mL). The acidic solution was neutralized with 2N NaOH (30 mL) and extracted with petrol (2 × 40 mL). The petrol solution was dried over Na_2SO_4 and concentrated in vacuo to give compound **12** as a colourless oil (80 mg, 92%), $[\alpha]_D^{20}$-110 (*c* = 0.018 g/mL, $CHCl_3$). ν_{max}/cm^{-1} (neat) 3026, 2762, 1604, 1455, 1032. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.04 (5H, m, ArH), 2.39 (1H, dd, *J*=12.4, 6.2 Hz, NC*H*H), 2.30-2.25 (7H, m, N(C*H*$_3$)$_2$+NCH*H*), 1.68 (1H, dt, *J*=8.4, 5.1 Hz, CHC*H*HCH), 1.26-1.18 (1H, m, NCH_2C*H*), 0.97 (1H, dt, *J*=8.4, 5.1 Hz, CHCH*H*CH), 0.83 (1H, dt, *J*=8.4, 5.5 Hz, PhCH). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.0, 128.3, 125.8, 125.5, 64.1, 45.5, 22.7, 21.5, 15.0. *m/z* (CI) 176 (M+1, 55), 132 (100). HRMS found: 176.1439, $C_{12}H_{18}N$ required: 176.1439.

The same procedure was applied to compounds **4a** and **8**.



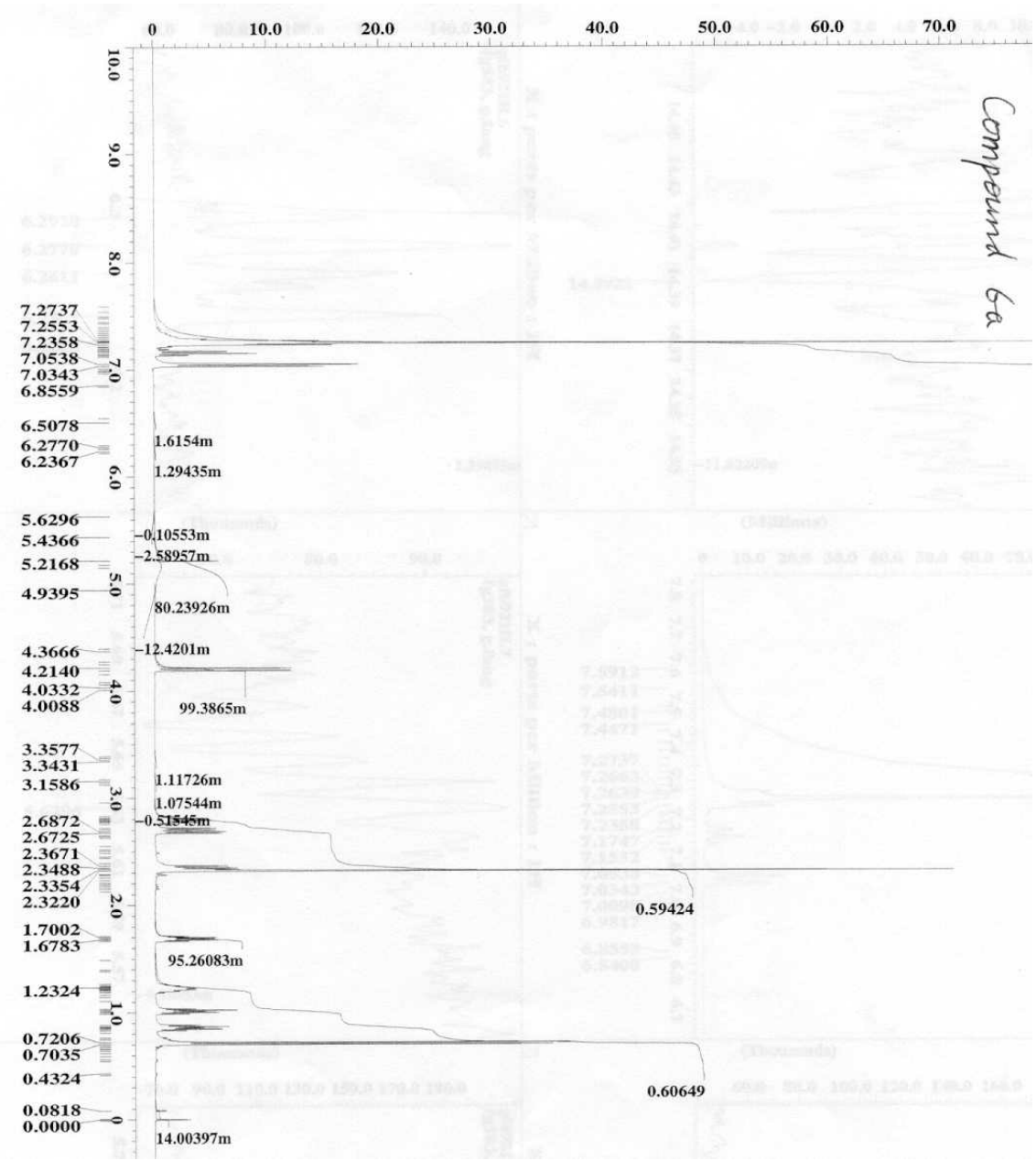
8 **12**

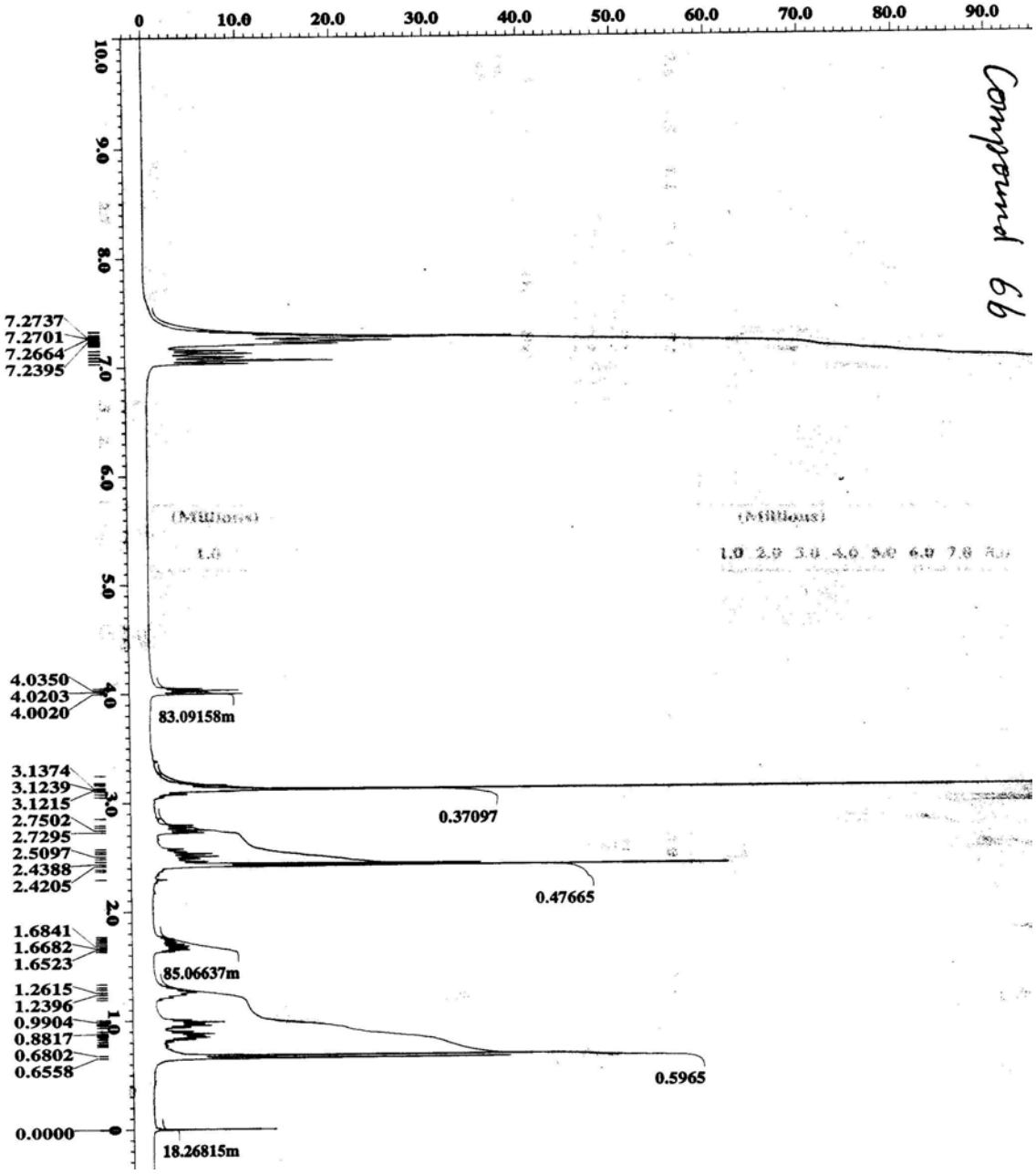
93% yield, $[\alpha]_D^{20}$: -105



4a

89% yield, $[\alpha]_D^{20}$: +98


Compound 6a
7.2737
7.2553
7.2358
7.0538
7.0343
6.8559
6.5078
6.2770
6.2367
5.6296
5.4366
5.2168
4.9395
4.3666
4.2140
4.0332
4.0088
3.3577
3.3431
3.1586
2.6872
2.6725
2.3671
2.3488
2.3354
2.3220
1.7002
1.6783
1.2324
0.7206
0.7035
0.4324
0.0818
0.0000
1.6154m
1.29435m
0.10553m
2.58957m
80.23926m
12.4201m
99.3865m
1.11726m
1.07544m
0.51545m
0.59424
95.26083m
0.60649
14.00397m


Compound 66
7.2737
7.2701
7.2664
7.2395
4.0350
4.0203
4.0020
3.1374
3.1239
3.1215
2.7502
2.7295
2.5097
2.4388
2.4205
1.6841
1.6682
1.6523
1.2615
1.2396
0.9904
0.8817
0.6802
0.6558
0.0000
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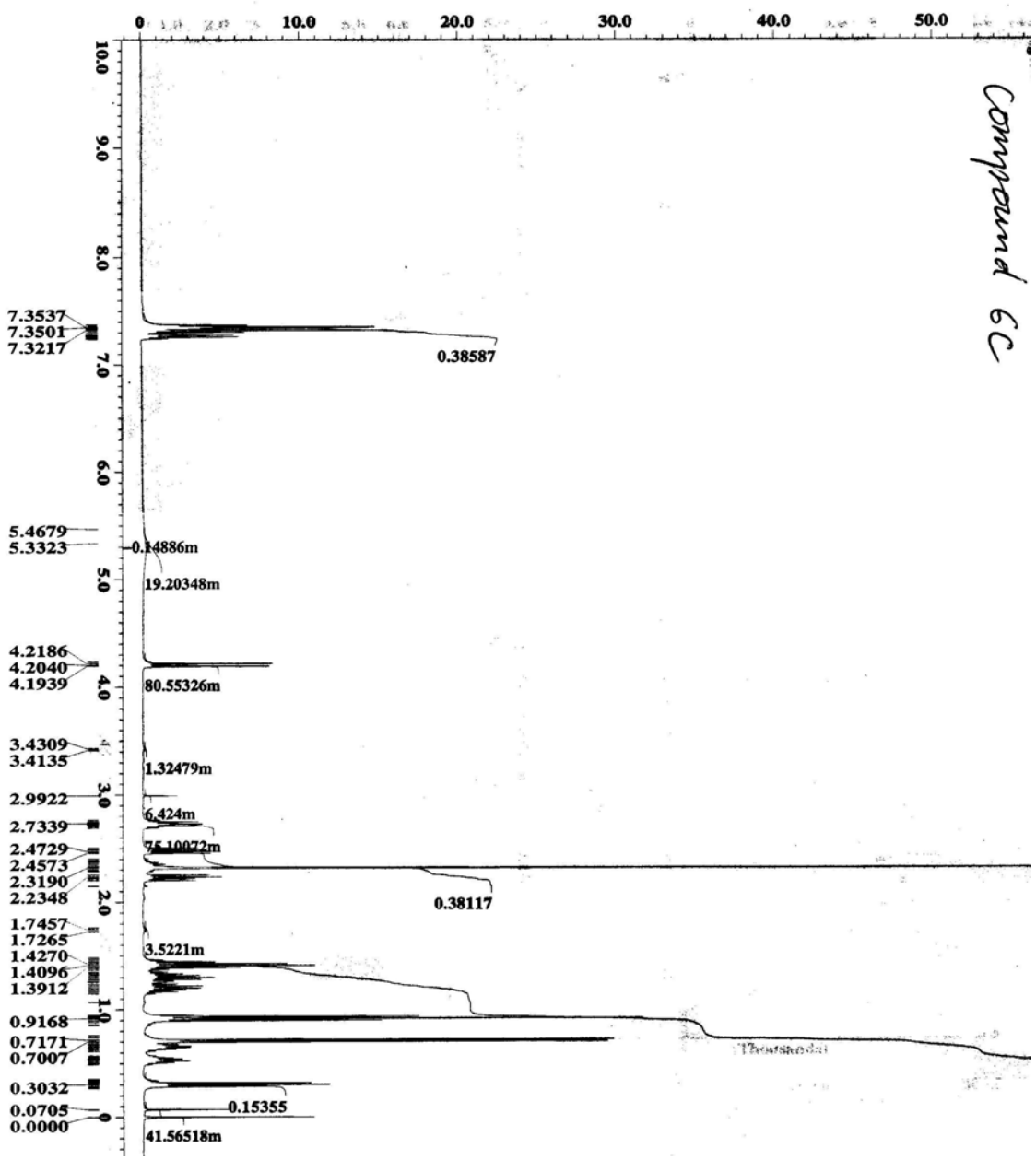
0.37097
0.47665
85.06637m
0.5965
18.26815m


Compound 6C
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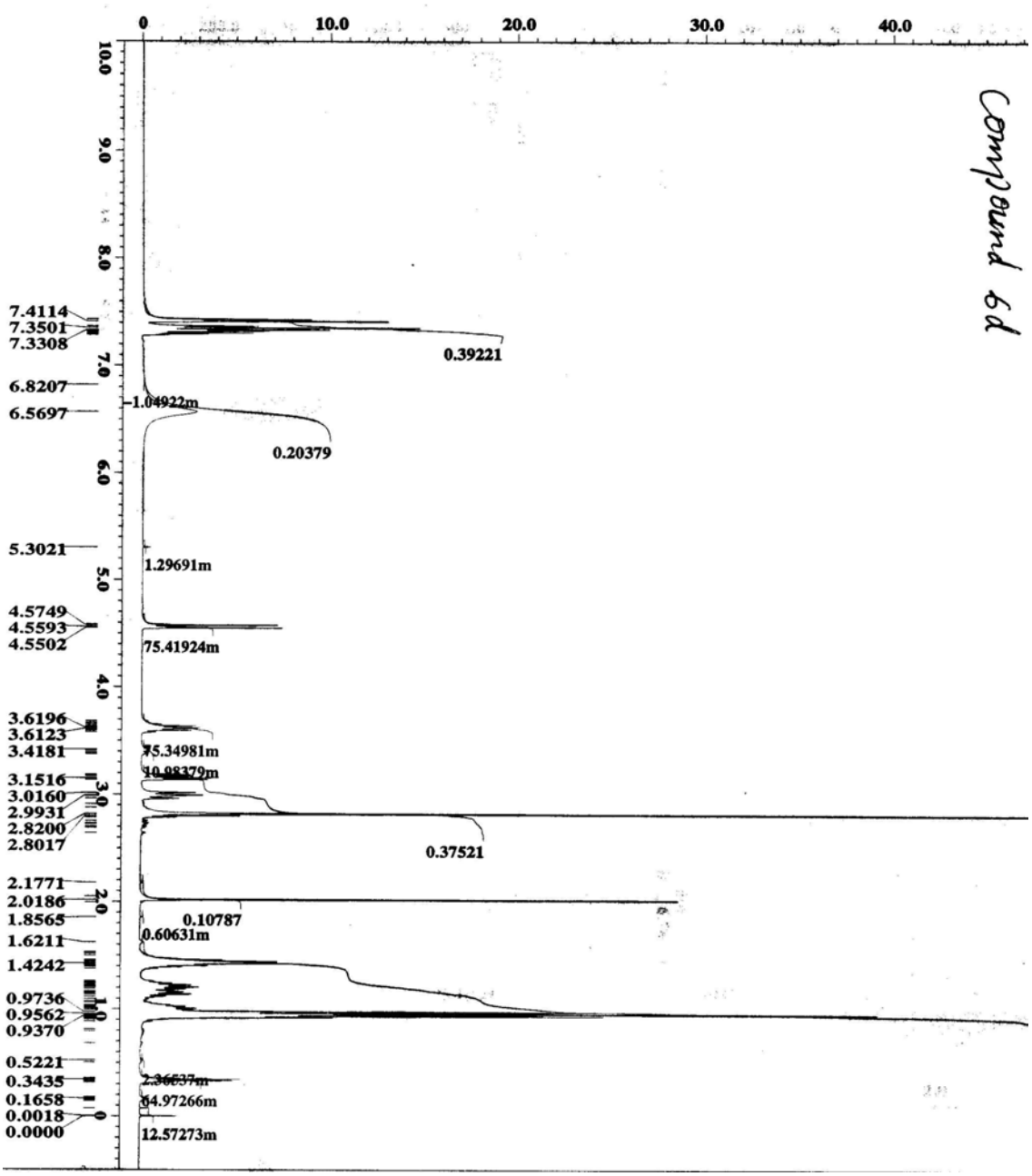
7.3501
7.3217
0.38587
5.4679
5.3323
0.14886m
19.20348m
4.2186
4.2040
4.1939
80.55326m
3.4309
3.4135
1.32479m
2.9922
6.424m
2.7339
2.4729
2.4573
2.3190
2.2348
0.38117
1.7457
1.7265
1.4270
1.4096
1.3912
3.5221m
0.9168
0.7171
0.7007
0.3032
0.0705
0.0000
0.15355
41.56518m


Compound 6d
7.4114
7.3501
7.3308
6.8207
6.5697
5.3021
4.5749
4.5593
4.5502
3.6196
3.6123
3.4181
3.1516
3.0160
2.9931
2.8200
2.8017
2.1771
2.0186
1.8565
1.6211
1.4242
0.9736
0.9562
0.9370
0.5221
0.3435
0.1658
0.0018
0.0000
0.39221
1.04922m
0.20379
1.29691m
75.41924m
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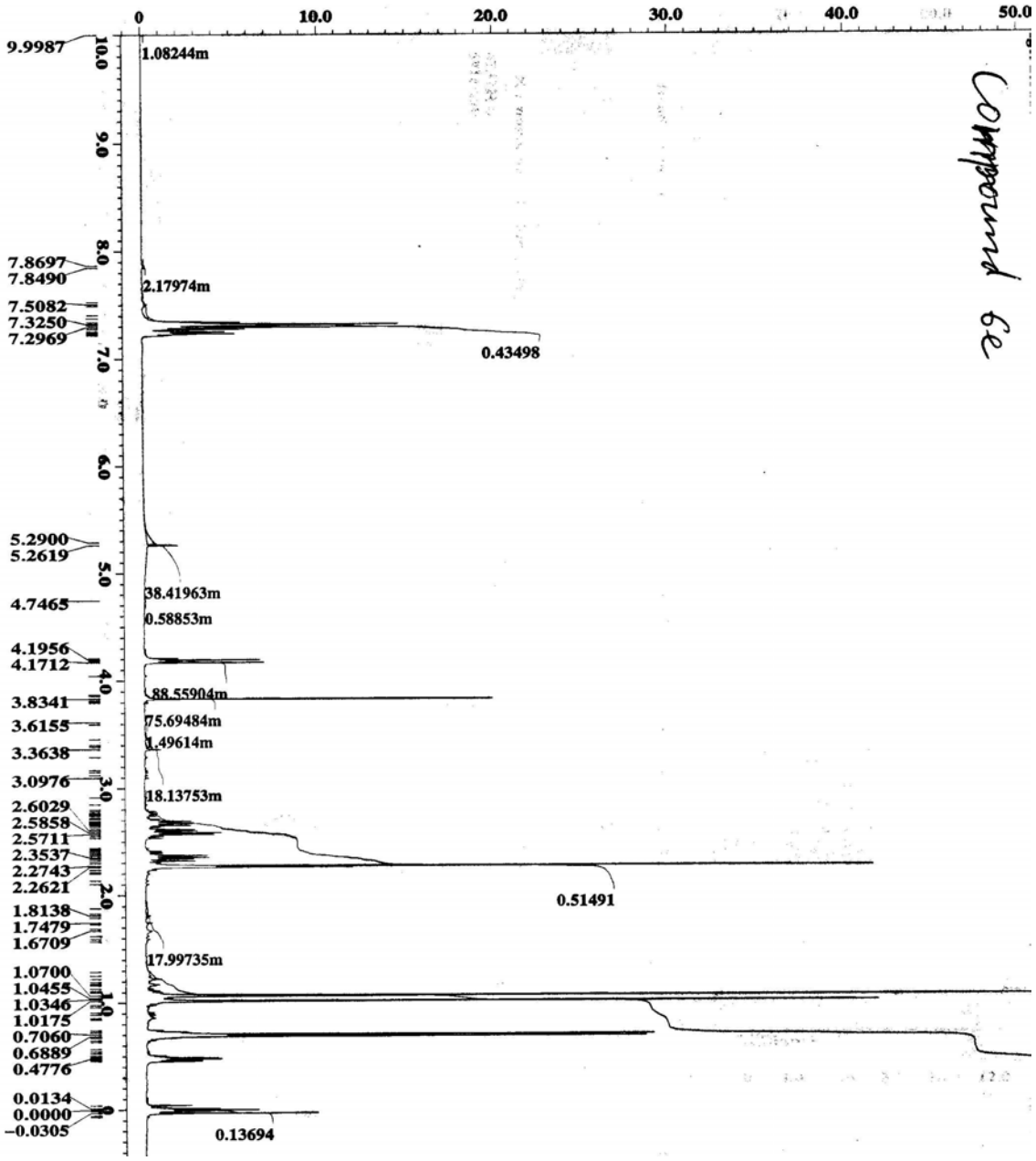
10.98379m
0.37521
0.10787
0.60631m
2.36637m
64.97266m
12.57273m


Compound 6e
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7.8697
7.8490
7.5082
7.3250
7.2969
5.2900
5.2619
4.7465
4.1956
4.1712
3.8341
3.6155
3.3638
3.0976
2.6029
2.5858
2.5711
2.3537
2.2743
2.2621
1.8138
1.7479
1.6709
1.0700
1.0455
1.0346
1.0175
0.7060
0.6889
0.4776
0.0134
0.0000
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1.08244m
2.17974m
0.43498
38.41963m
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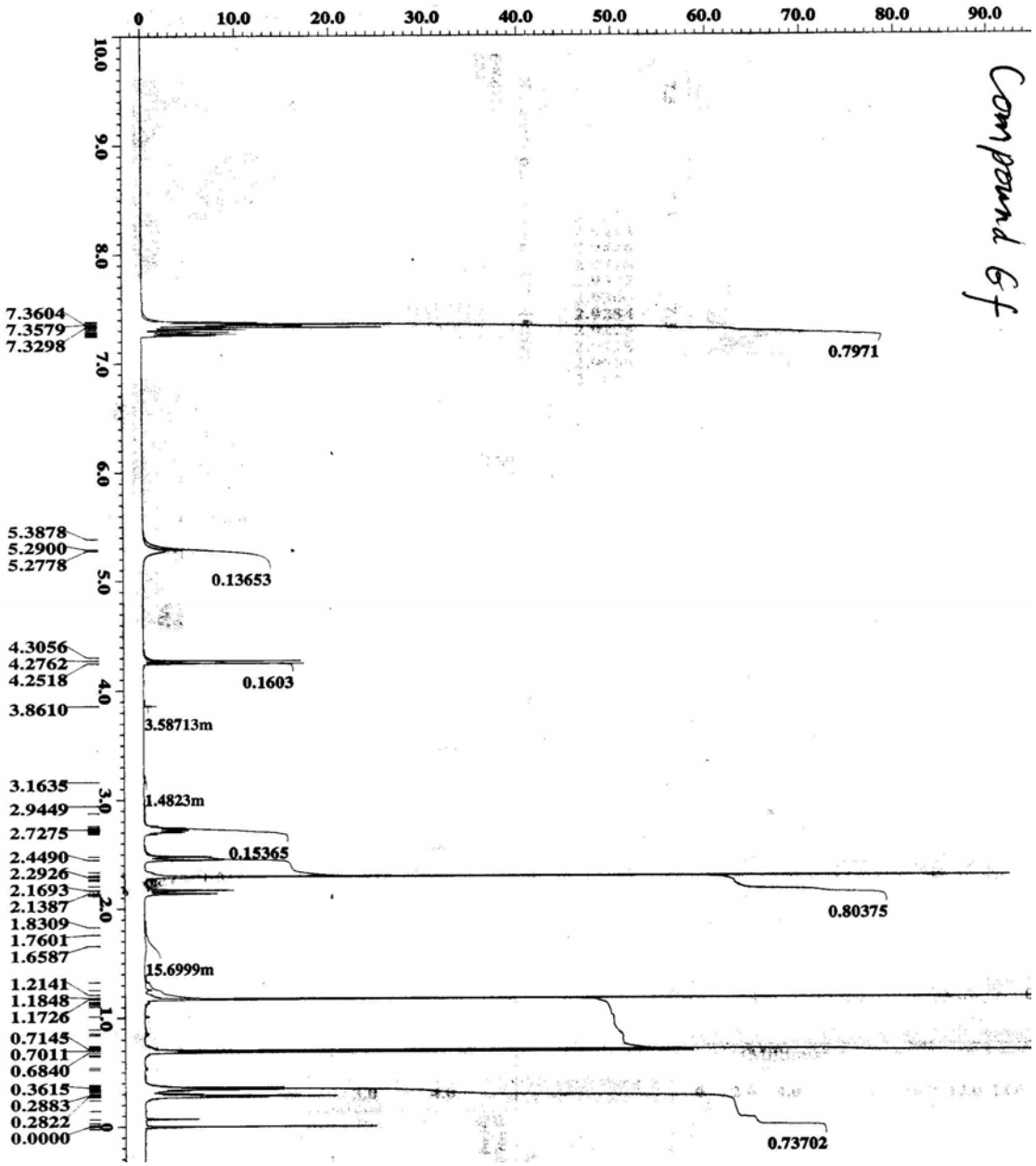
88.55904m
75.69484m
1.49614m
18.13753m
0.51491
17.99735m
0.13694


Compound 6f
7.3604
7.3579
7.3298
0.7971
5.3878
5.2900
5.2778
0.13653
4.3056
4.2762
4.2518
0.1603
3.8610
3.58713m
3.1635
2.9449
1.4823m
2.7275
0.15365
2.4490
2.2926
2.1693
2.1387
0.80375
1.8309
1.7601
1.6587
15.6999m
1.2141
1.1848
1.1726
0.7145
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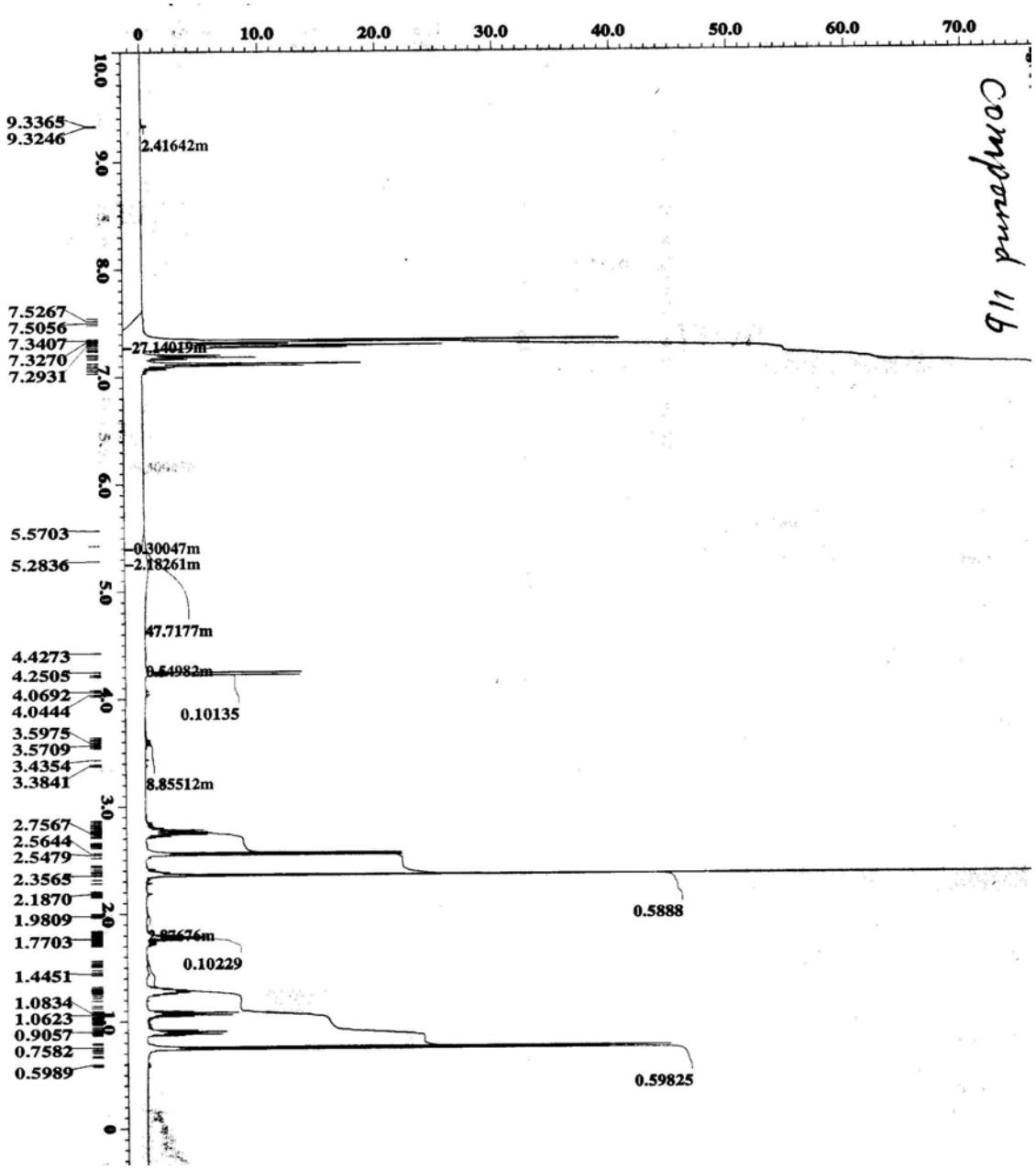
0.73702


Compound 116
9.3365
9.3246
7.5267
7.5056
7.3407
7.3270
7.2931
5.5703
5.2836
4.4273
4.2505
4.0692
4.0444
3.5975
3.5709
3.4354
3.3841
2.7567
2.5644
2.5479
2.3565
2.1870
1.9809
1.7703
1.4451
1.0834
1.0623
0.9057
0.7582
0.5989
2.41642m
27.14019m
0.30047m
2.18261m
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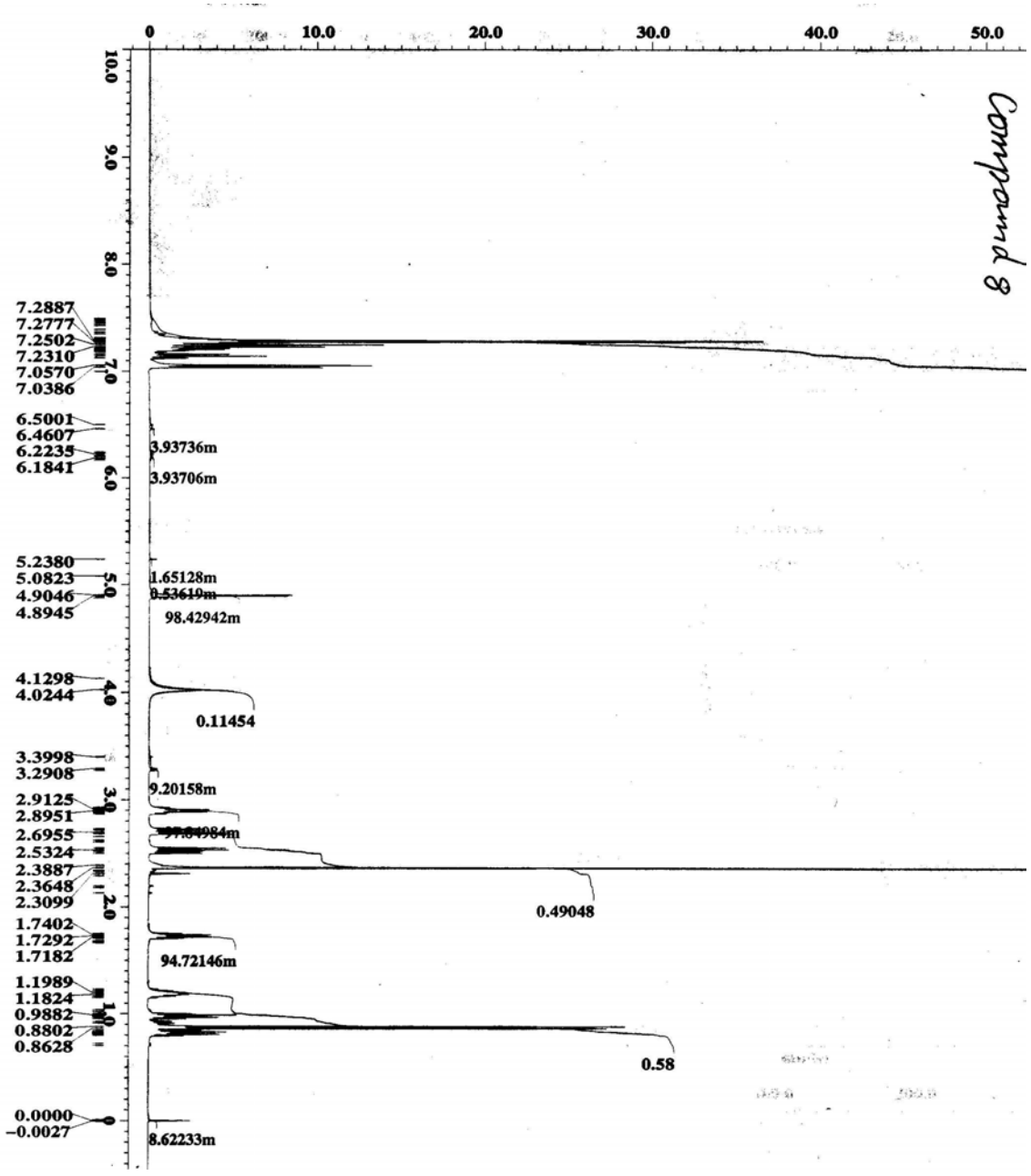
0.54982m
0.10135
8.85512m
0.5888
0.10229
0.59825


Compound 8
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7.2777
7.2502
7.2310
7.0570
7.0386
6.5001
6.4607
6.2235
6.1841
5.2380
5.0823
4.9046
4.8945
4.1298
4.0244
3.3998
3.2908
2.9125
2.8951
2.6955
2.5324
2.3887
2.3648
2.3099
1.7402
1.7292
1.7182
1.1989
1.1824
0.9882
0.8802
0.8628
0.0000
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98.42942m
0.11454
9.20158m
0.49048
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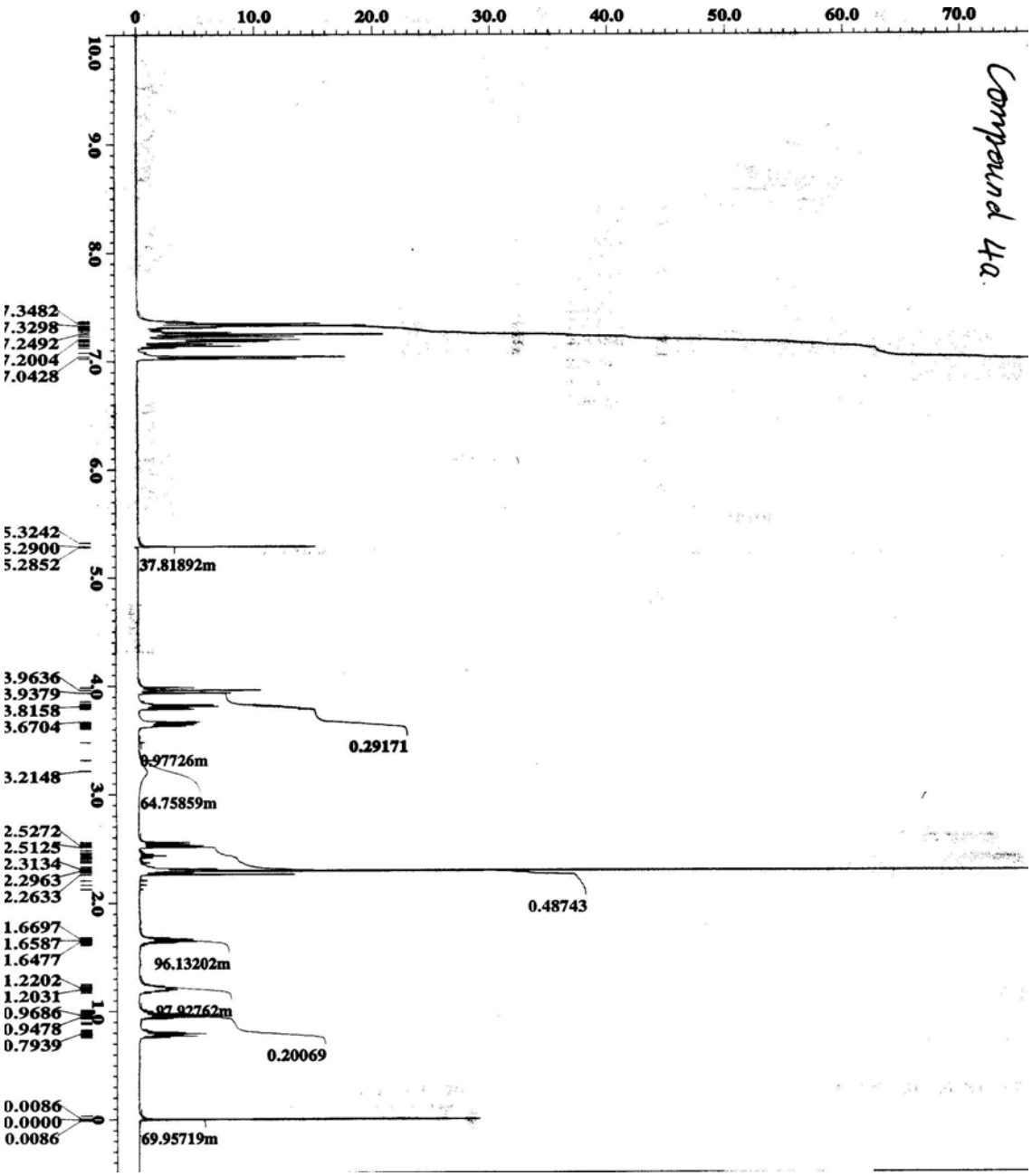
0.58
8.62233m


Compound 40.
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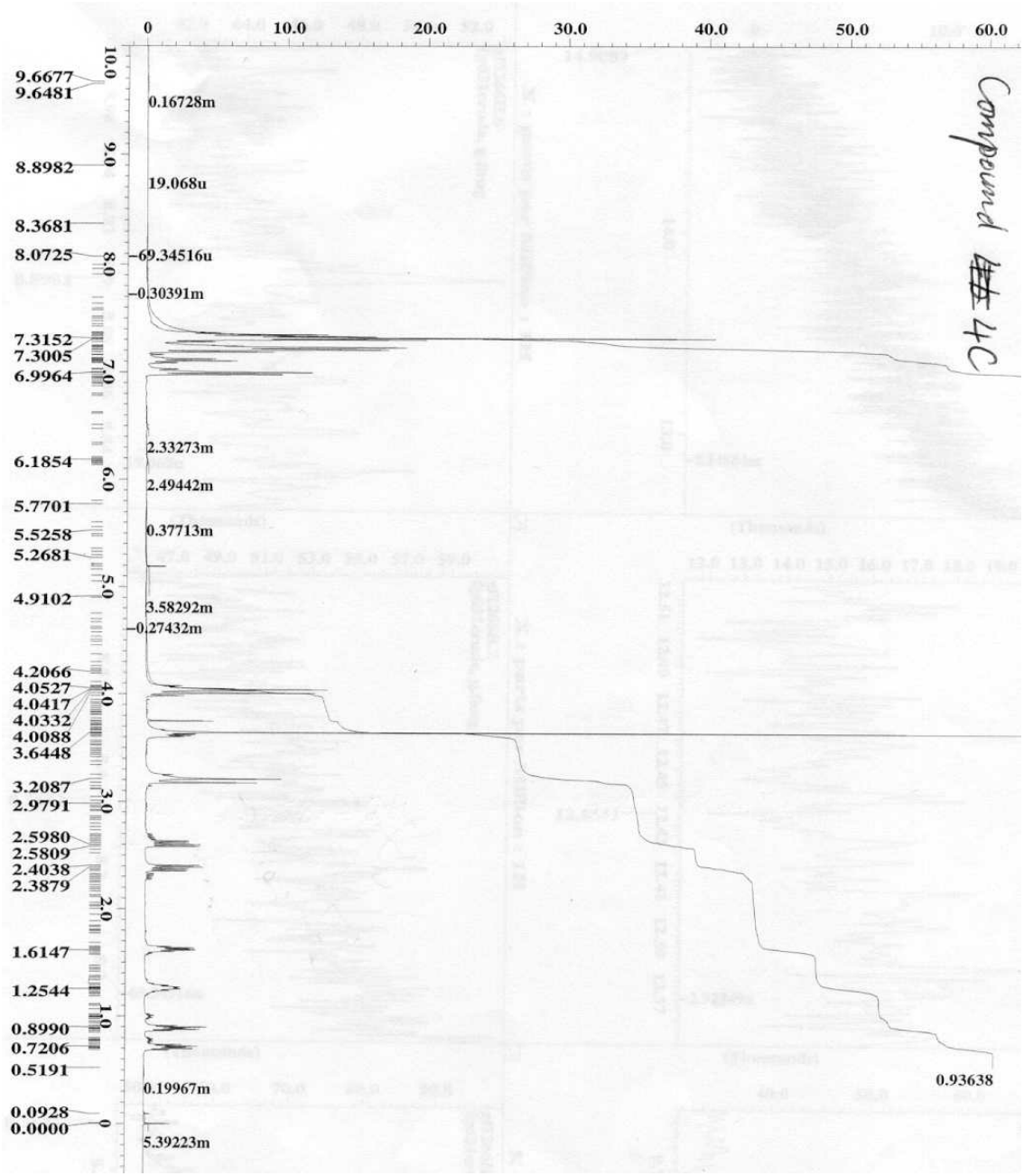
7.3298
7.2492
7.2004
7.0428
5.3242
5.2900
5.2852
37.81892m
3.9636
3.9379
3.8158
3.6704
0.29171
3.2148
64.75859m
2.5272
2.5125
2.3134
2.2963
2.2633
0.48743
1.6697
1.6587
1.6477
96.13202m
1.2202
1.2031
0.9686
0.9478
0.7939
0.20069
0.0086
0.0000
0.0086
69.95719m


Compound 4C
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9.6481
8.8982
8.3681
8.0725
7.3152
7.3005
6.9964
6.1854
5.7701
5.5258
5.2681
4.9102
4.2066
4.0527
4.0417
4.0332
4.0088
3.6448
3.2087
2.9791
2.5980
2.5809
2.4038
2.3879
1.6147
1.2544
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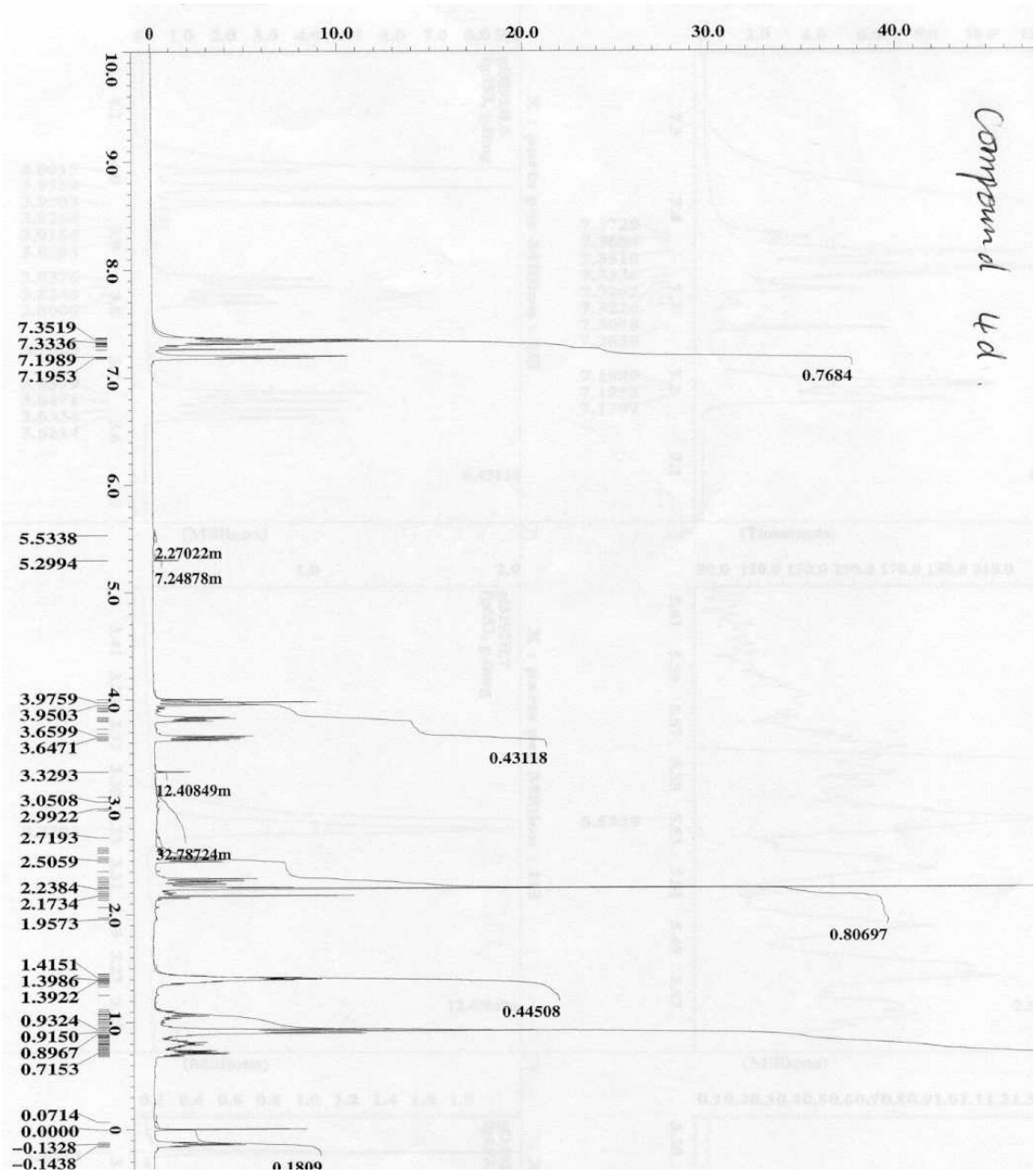
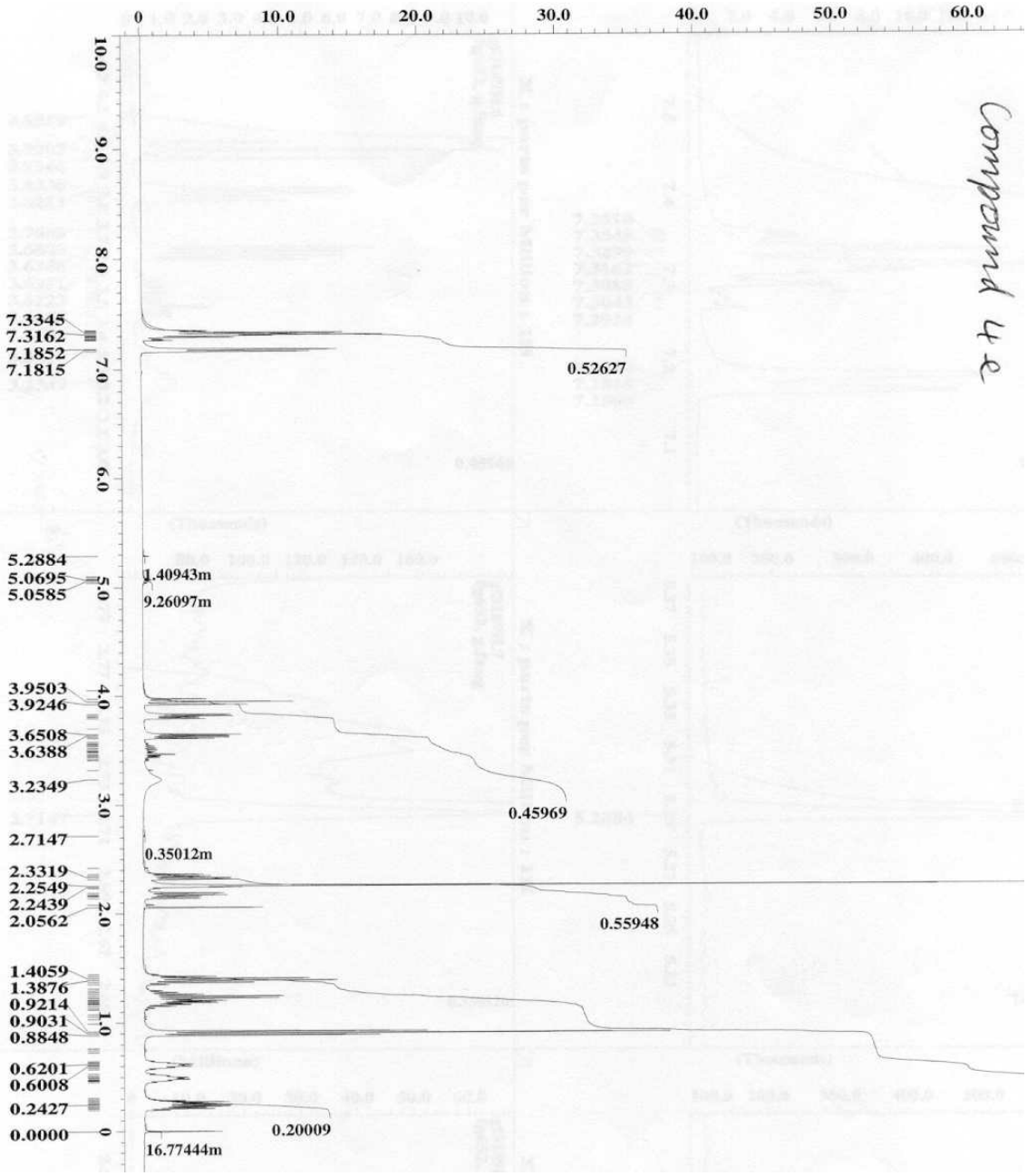
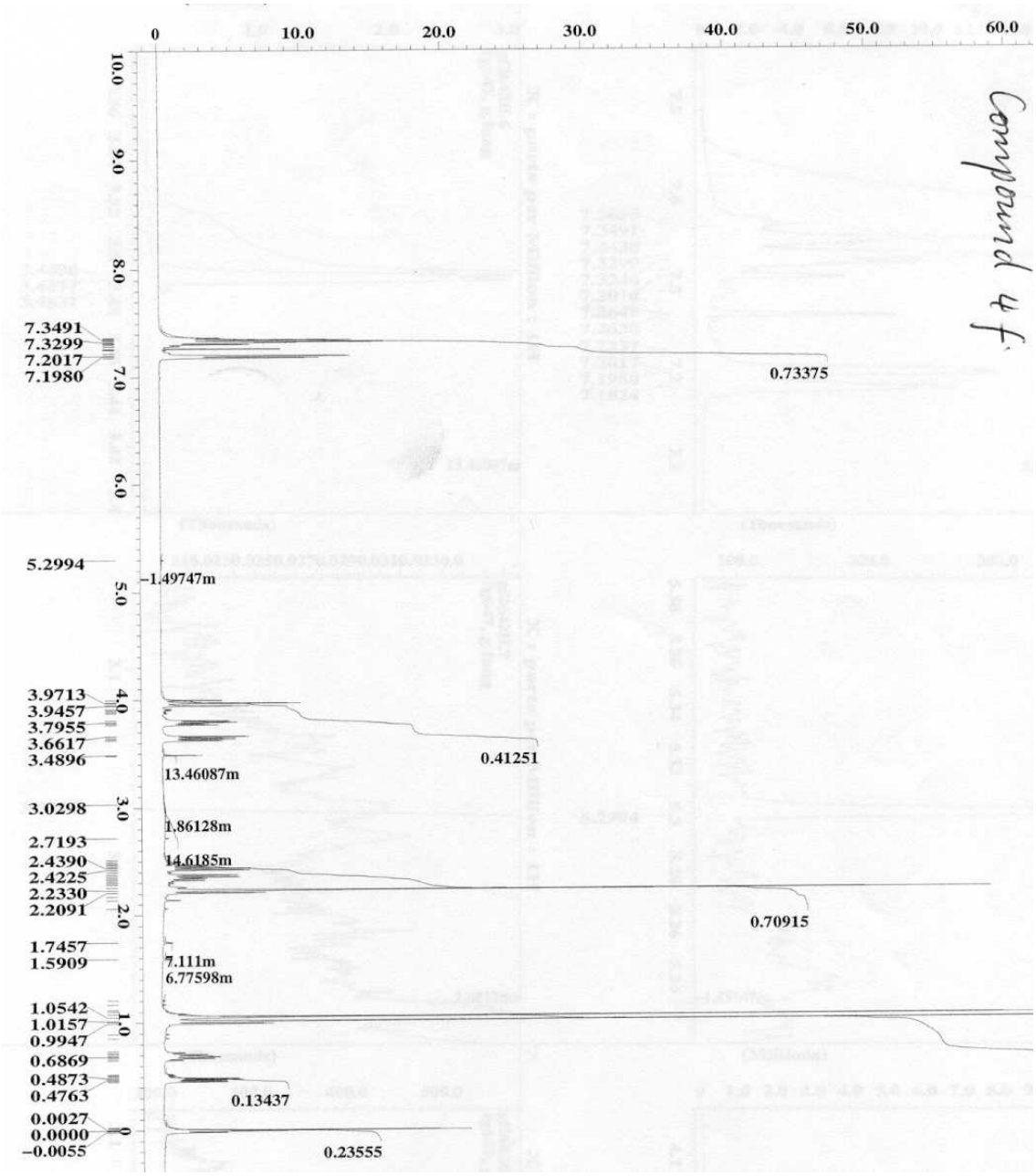
19.068u
69.34516u
0.30391m
2.33273m
2.49442m
0.37713m
3.58292m
0.27432m
0.19967m
5.39223m
0.93638


Compound 4d
0
10.0
20.0
30.0
40.0
7.3519
7.3336
7.1989
7.1953
0.7684
5.5338
5.2994
2.27022m
7.24878m
3.9759
3.9503
3.6599
3.6471
0.43118
3.3293
12.40849m
3.0508
2.9922
2.7193
2.5059
32.78724m
2.2384
2.1734
1.9573
0.80697
1.4151
1.3986
1.3922
0.44508
0.9324
0.9150
0.8967
0.7153
0.0714
0.0000
−0.1328
−0.1438
0.1809


Compound 42
0
10.0
20.0
30.0
40.0
50.0
60.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.3345
7.3162
7.1852
7.1815
0.52627
5.2884
5.0695
5.0585
1.40943m
9.26097m
3.9503
3.9246
3.6508
3.6388
3.2349
0.45969
2.7147
0.35012m
2.3319
2.2549
2.2439
2.0562
0.55948
1.4059
1.3876
0.9214
0.9031
0.8848
0.6201
0.6008
0.2427
0.0000
0.20009
16.77444m



[1] Pangborn, A. B.; Giardello, M. A.; Grubbs, R. M.; Rosen, R. K.; Timmers, F. T.

Organometallics, **1996**, *15*, 1518.

[2] Kamer, P. C. J.; Cleij, M. C.; Roeland, J. M.; Harada, T.; Hezemans, H. M. F.; Drenth, W. *J. Am. Chem. Soc*. **1988**, *110*, 1581.

[3] Huszthy, P.; et al. *J. Org. Chem*. **1992**, *57*, 5383.

[4] Denmark, S. E.; O'Connor, S. P.; Wilson, S. R. *Angew. Chem. Int. Ed*. **1998,** *37*, 1149.

[5] Reynolds, K. A.; Finn, M. G. *J. Org. Chem*. **1997**, *62*, 2574.