Supporting Information

for

Highly enantioselective access to cannabinoid-type tricyles by organocatalytic Diels–Alder reactions

Stefan Bräse*[1,2], Nicole Volz[1], Franziska Gläser[1] and Martin Nieger[3]

Address: [1]Karlsruhe Institute of Technology (KIT), Institute of Organic Chemistry, Fritz-Haber-Weg 6, D-76131 Karlsruhe; Tel: (+49) 721 608-48581, [2]Institute of Toxicology and Genetics, Hermann-von-Helmholtz-Platz 1, D-76344 Eggenstein-Leopoldshafen, Germany and [3]Laboratory of Inorganic Chemistry, Department of Chemistry, University of Helsinki, P.O. Box 55, FIN-00014 Helsinki, Finland

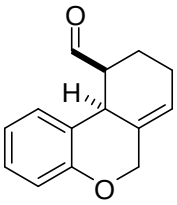
Email: Stefan Bräse* - braese@kit.edu

* Corresponding author

Experimental data for all new compounds

General: All reactions were carried out in flame-dried glassware under argon. The solvents were purified by distillation over the drying solvents indicated and were transferred under argon. THF (Na/K), CH_2Cl_2 ($CaCl_2$). IR: Bruker IFS 88 spectrometer, wavenumbers in cm^{-1}. MS (EI): Finnigan MAT 95. NMR: Spectra were recorded on a Bruker Avance 400 or Avance DRX 500 spectrometer in the solvents indicated; ^1H and ^{13}C chemical shifts (δ) are given in ppm relative to TMS, coupling constants (*J*) in Hz. The solvent signals were used as references and the chemical shifts were converted to the TMS scale. Melting points: Laboratory Devices Inc., model Mel-Temp II; elemental analyses: elementar (model vario MICRO CUBE). Unless stated otherwise, all commercially available compounds (Acros, Fluka, Aldrich) were used as received.

***cis*-8,9,10,10a-Tetrahydro-6*H*-benzo[*c*]chromene-10-carbaldehyde (*cis*-5):**



Acrolein (**11**, 235 µL, 197 mg, 3.16 mmol, 5.00 equiv) was added to a solution of 1,3-bis(3,5-bis(trifluoromethyl)phenyl)thiourea (31.6 mg, 63.2 µmol, 0.10 equiv) in methanol/water (4.3 mL/0.4 mL). The mixture was stirred for 2 min at rt, before 3-vinyl-2*H*-chromene (100 mg, 632 µmol, 1.00 equiv), dissolved in methanol (2 mL), was added at 0 °C over a period of 20 min. The resulting mixture was stirred for 2 d at 40 °C. For workup, the reaction mixture was diluted with Et_2O (5 mL), and the organic phase was washed with brine (10 mL) and dried over sodium sulfate. The solvent was removed under reduced pressure and the product was purified by flash column chromatography (*n*-Hex/EtOAc 80:1).

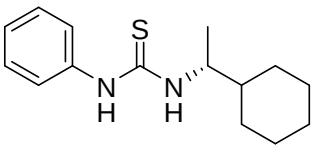
75.8 mg (56%). – R_f (*n*-Hex/EtOAc 1:1) = 0.40. – ^1H NMR (500 MHz, $CDCl_3$): δ/ppm = 1.88 (ddt, ^2J = 11.4 Hz, ^3J = 3.5 Hz, ^3J = 1.1 Hz, 1 H, 9-*H*), 2.15–2.19 (m, 2 H, 8-*H*), 2.36 (ddt, ^2J = 11.4 Hz, ^3J = 6.2 Hz, ^3J = 3.5 Hz, 1 H, 9-*H*), 3.11 (dtd, ^3J = 6.8 Hz, ^3J = 3.5 Hz, ^3J = 1.6 Hz, 1 H, 10-*H*), 3.95 (d, ^3J = 6.8 Hz, ^4J = 3.5 Hz, 1 H, 10a-*H*), 4.50 (s, 2 H, 6-*H*), 5.87 (q, ^3J = 3.7 Hz, 1 H, 7-*H*), 6.88 (dd, ^3J = 8.1 Hz, ^4J = 0.7 Hz, 1 H, 4-H_{ar}), 6.95 (dd, ^3J = 8.1 Hz, ^3J = 7.6 Hz, 1 H, 2-H_{ar}), 7.13 (dd, ^3J = 8.1 Hz, ^3J = 7.6 Hz, 1 H, 3-H_{ar}), 7.19 (d, ^3J = 7.6 Hz, 1 H, 1-H_{ar}), 9.30 (dd, ^3J = ^3J = 1.6 Hz, 1 H, C*H*O). – ^{13}C NMR (125 MHz, $CDCl_3$): δ/ppm = 21.5 (s, *C*-8), 23.6 (s, *C*-9), 35.6 (t, *C*-10a), 48.6 (t, *C*-10), 70.2 (s, *C*-6), 117.6 (t, C_{ar}-4), 121.6 (t, C_{ar}-2), 123.0 (q, C_{ar}-10b), 126.1 (t, *C*-7), 127.7 (t, C_{ar}-3), 127.9 (t, C_{ar}-1), 131.1 (q, *C*-6a), 155.9 (q, C_{ar}-4a), 204.7 (t, *C*HO). – IR (KBr): ṽ/cm^{-1} = 2926 (w), 2841 (w),

1718 (s), 1606 (w), 1580 (w), 1487 (s), 1458 (m), 1376 (w), 1306 (m), 1278 (w), 1240 (m), 1220 (m), 1182 (w), 1118 (w), 1039 (m), 998 (m), 940 (w), 757 (m), 723 (w). – EI-MS (70 eV) *m/z* (%): 214 (100) [M^+], 185 (30) [M^+-CO], 158 (78) [$M^+-C_3H_4O$], 131 (30) [$M^+-C_5H_7O$]. – EI-HRMS ($C_{14}H_{14}O_2$): calcd. 214.0992, found 214.0994.

General procedure for the preparation of thiourea-catalysts 9

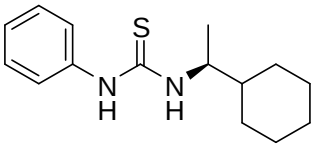
Substituted amine **8** (1.00 equiv) was added to a solution of isothiocyanate **7** (1.00 equiv) in CH_2Cl_2 (2 mL/mmol amine). The resulting mixture was stirred for 3 h at rt. The solvent was removed under reduced pressure and the product was purified by flash column chromatography.

(*R*)-1-(1-Cyclohexylethyl)-3-phenylthiourea ((*R*)-9a) [1]:



377 mg, 99% (scale: 1.45 mmol). – R_f (*n*-Hex/EtOAc 10:1) = 0.20. – mp: 119–121 °C. – $[\alpha]_D^{20}$ = −68.0 (*c* = 1.05, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 0.86–1.27 (m, 5 H, C*H*$_2$), 1.10 (d, ^3J = 6.7 Hz, 3 H, C*H*$_3$), 1.37–1.46 (m, 1 H, C*H*), 1.57–1.74 (m, 5 H, C*H*$_2$), 4.40 (dd, ^3J = 8.3 Hz, ^3J = 6.7 Hz, 1 H, NHC*H*), 5.87 (d, ^3J = 8.3 Hz, 1 H, N*H*), 7.18–7.31 (m, 2 H, 2 × H_{ar}), 7.27–7.31 (m, 1 H, H_{ar}), 7.41–7.45 (m, 2 H, 2 × H_{ar}), 8.03 (s, 1 H, Ar-N*H*). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 17.2 (p, *C*H$_3$), 26.0 (s, *C*H$_2$), 26.1 (s, *C*H$_2$), 26.3 (s, *C*H$_2$), 28.9 (s, *C*H$_2$), 29.2 (s, *C*H$_2$), 42.8 (t, *C*H), 55.7 (t, NH*C*H), 125.1 (t, C_{ar}H), 127.1 (t, 2 × C_{ar}H), 130.2 (t, 2 × C_{ar}H), 136.1 (q, C_{ar}), 179.6 (q, *C*=S). – IR (DRIFT): $\tilde{\nu}$/cm^{-1} = 3236 (m), 3064 (m), 2922 (m), 2852 (m), 1599 (m), 1551 (s), 1497 (m), 1449 (m), 1352 (m), 1314 (m), 1260 (m), 1207 (m), 1155 (m), 1074 (w), 1028 (w), 998 (w), 962 (w), 903 (w), 892 (w), 759 (m), 700 (m), 606 (m), 493 (w). – EI-MS *m/z* (%): 262 (100) [M^+], 153 (54), 94 (28). – EI-HRMS ($C_{15}H_{22}N_2S$): calcd. 262.1504, found 262.1507. – $C_{15}H_{22}N_2S$ (262.2): calcd. C 68.66, H 8.45, N 10.68, S 12.22, found C 68.71, H 8.02, N 10.80, S 12.39.

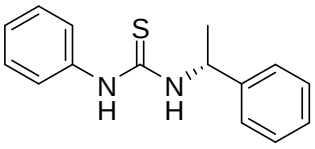
(*S*)-1-(1-Cyclohexylethyl)-3-phenylthiourea ((*S*)-9a) [1]:



360 mg, 95% (scale: 1.45 mmol). – R_f (*n*-Hex/EtOAc 5:1) = 0.30. – mp: 118–121 °C. – $[\alpha]_D^{20}$ = −77.6 (*c* = 0.99, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 0.86–1.24 (m, 5 H, C*H*$_2$), 1.10 (d, ^3J = 6.7 Hz, 3 H, C*H*$_3$), 1.37–1.46 (m, 1 H, C*H*), 1.57–1.74 (m, 5 H, C*H*$_2$), 4.39–4.41 (m, 1 H, NHC*H*), 5.87 (d, ^3J = 8.2 Hz, 1 H, N*H*), 7.18–7.20 (m,

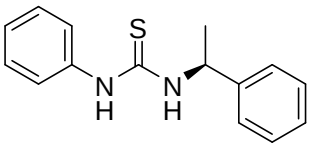
2 H, 2 × H_{ar}), 7.27–7.30 (m, 1 H, H_{ar}), 7.40–7.44 (m, 2 H, 2 × H_{ar}), 8.05 (s, 1 H, Ar-N*H*). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 17.2 (p, *C*H_3), 26.0 (s, *C*H_2), 26.1 (s, *C*H_2), 26.3 (s, *C*H_2), 28.9 (s, *C*H_2), 29.2 (s, *C*H_2), 42.8 (t, *C*H), 55.6 (t, NH*C*H), 125.1 (t, C_{ar}H), 127.1 (t, 2 × C_{ar}H), 130.2 (t, 2 × C_{ar}H), 136.1 (q, C_{ar}), 179.6 (q, *C*=S). – IR (DRIFT): $\tilde{\nu}$/cm^{-1} = 3234 (s), 3067 (s), 2930 (s), 2854 (s), 2671 (w), 1967 (w), 1947 (w), 1864 (w), 1795 (w), 1736 (w), 1602 (m), 1552 (s), 1497 (m), 1450 (m), 1352 (s), 1314 (s), 1260 (m), 1208 (m), 1155 (m), 1134 (m), 1111 (m), 1074 (m), 1046 (m), 1028 (m), 998 (m), 962 (m), 903 (m), 892 (m), 849 (w), 836 (m), 794 (w), 759 (m), 701 (s), 606 (m), 530 (w), 496 (m), 453 (w). – EI-MS *m/z* (%): 262 (100) [M^+], 153 (83) [$C_7H_9N_2S^+$], 151 (45) [$C_7H_7N_2S^+$], 136 (42) [$C_7H_6NS^+$], 93 (58) [$C_6H_7N^+$], 77 (53) [$C_6H_5^+$], 55 (85), 41 (57). – EI-HRMS ($C_{15}H_{22}N_2S$): calcd. 262.1504, found 262.1502. – $C_{15}H_{22}N_2S$ (262.2): calcd. C 68.66, H 8.45, N 10.68, S 12.22, found C 68.61, H 7.79, N 10.89, S 12.81.

(*R*)-1-Phenyl-3-(1-phenylethyl)thiourea ((*R*)-9b) [2]:



365 mg, 99% (scale: 1.45 mmol). – R_f (*n*-Hex/EtOAc 4:1) = 0.30. – mp: 62–66 °C. – $[\alpha]_D^{20}$ = −94.4 (*c* = 0.98, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.46 (d, ^3J = 6.9 Hz, 3 H, CH_3), 5.60 (bs, 1 H, NHC*H*), 6.19 (bs, 1 H, N*H*), 7.09–7.19 (m, 2 H, 2 × H_{ar}), 7.17–7.28 (m, 6 H, 6 × H_{ar}), 7.30–7.34 (m, 2 H, 2 × H_{ar}), 7.93 (bs, 1 H, Ar-N*H*). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 21.5 (p, *C*H_3), 54.3 (t, *C*H), 125.0 (t, 2 × C_{ar}H), 126.1 (t, 2 × C_{ar}H), 127.2 (t, C_{ar}H), 127.5 (t, C_{ar}H), 128.7 (t, 2 × C_{ar}H), 130.1 (t, 2 × C_{ar}H), 136.1 (q, C_{ar}), 142.1 (q, C_{ar}), 179.7 (q, *C*=S). – IR (DRIFT): $\tilde{\nu}$/cm^{-1} = 3338 (s), 3084 (m), 3058 (m), 3027 (m), 2980 (m), 2924 (m), 2866 (m), 2336 (w), 1953 (w), 1881 (w), 1809 (w), 1758 (w), 1591 (s), 1535 (s), 1496 (s), 1455 (s), 1385 (s), 1357 (m), 1312 (s), 1238 (s), 1200 (s), 1141 (m), 1085 (m), 1024 (m), 959 (m), 942 (m), 913 (m), 845 (m), 808 (w), 761 (s), 745 (m), 698 (s), 643 (m), 603 (m), 521 (s), 409 (w). – EI-MS *m/z* (%): 256 (59) [M^+], 118 (29), 105 (100) [$C_8H_9^+$], 77 (50) [$C_6H_5^+$], 57 (22) [CNS^+]. – EI-HRMS ($C_{15}H_{16}N_2S$): calcd. 256.1034, found 256.1034.

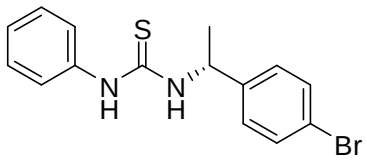
(*S*)-1-Phenyl-3-(1-phenylethyl)thiourea ((*S*)-9b) [3]:



378 mg, 99% (scale: 1.45 mmol). – R_f (*n*-Hex/EtOAc 5:1) = 0.20. – mp: 59–64 °C. – $[\alpha]_D^{20}$ = −90.0 (*c* = 1.08,

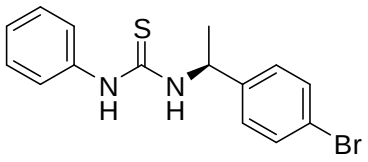
$CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.54 (d, ^3J = 6.9 Hz, 3 H, CH_3), 5.68 (s, 1 H, C*H*), 6.28 (s, 1 H, N*H*), 7.17–7.19 (m, 2 H, 2 × H_{ar}), 7.24–7.35 (m, 6 H, 6 × H_{ar}), 7.38–7.41 (m, 2 H, 2 × H_{ar}), 8.07 (s, 1 H, Ar-N*H*). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 21.5 (p, CH_3), 54.3 (t, *C*H), 125.0 (t, C_{ar}H), 126.1 (t, C_{ar}H), 127.1 (t, 2 × C_{ar}H), 127.5 (t, 2 × C_{ar}H), 128.7 (t, 2 × C_{ar}H), 130.1 (t, 2 × C_{ar}H), 136.1 (q, C_{ar}), 142.1 (q, C_{ar}), 179.7 (q, *C*=S). – IR (DRIFT): $\tilde{\nu}$/cm^{-1} = 3338 (s), 3028 (m), 2981 (m), 2924 (m), 2867 (m), 2336 (m), 1954 (w), 1881 (w), 1181 (w), 1758 (w), 1596 (s), 1536 (s), 1496 (s), 1455 (s), 1386 (m), 1357 (m), 1312 (s), 1238 (s), 1200 (s), 1141 (m), 1085 (m), 1024 (m), 959 (m), 942 (m), 913 (m), 845 (w), 809 (m), 761 (s), 699 (s), 643 (m), 604 (m), 521 (m), 409 (w). – EI-MS *m/z* (%): 256 (12) [M$^+$], 151 (24) [$C_7H_7N_2S^+$], 120 (27) [$C_8H_{10}N^+$], 105 (100) [$C_8H_9^+$], 93 (52) [$C_6H_7N^+$], 77 (67) [$C_6H_5^+$]. – EI-HRMS ($C_{15}H_{16}N_2S$): calcd. 256.1034, found 256.1031. – $C_{15}H_{16}N_2S$ (256.1): calcd. C 70.27, H 6.29, N 10.93, S 12.51, found C 70.03, H 5.82, N 11.00, S 13.27.

(*R*)-1-(1-(4-Bromophenyl)ethyl)-3-phenylthiourea ((*R*)-9c):



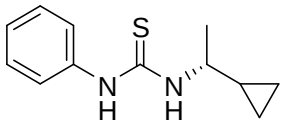
489 mg, 99% (scale: 1.45 mmol). – R_f (*n*-Hex/EtOAc 5:1) = 0.20. – mp: 128–131 °C. – $[\alpha]_D^{20}$ = −128 (*c* = 1.02, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.49 (d, ^3J = 6.9 Hz, 3 H, CH_3), 5.62–5.66 (m, 1 H, C*H*), 6.18 (d, ^3J = 4.7 Hz, 1 H, N*H*), 7.16–7.18 (m, 4 H, 4 × H_{ar}), 7.28–7.31 (m, 1 H, H_{ar}), 7.40–7.45 (m, 4 H, 4 × H_{ar}), 8.07 (s, 1 H, Ar-N*H*). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 21.4 (p, CH_3), 53.7 (t, *C*H), 121.3 (q, C_{ar}-Br), 125.1 (t, C_{ar}H), 127.4 (t, 2 × C_{ar}H), 127.9 (t, 2 × C_{ar}H), 130.3 (t, 2 × C_{ar}H), 131.8 (t, 2 × C_{ar}H), 135.9 (q, C_{ar}), 141.4 (q, C_{ar}), 179.8 (q, *C*=S). – IR (DRIFT): $\tilde{\nu}$/cm^{-1} = 3391 (m), 3204 (m), 2972 (m), 2924 (w), 2869 (w), 1956 (w), 1896 (w), 1754 (w), 1590 (m), 1541 (m), 1503 (m), 1448 (m), 1406 (m), 1379 (m), 1313 (m), 1244 (m), 1200 (m), 1176 (m), 1145 (m), 1101 (m), 1073 (m), 1028 (m), 1008 (m), 946 (w), 914 (w), 835 (w), 917 (m), 785 (w), 748 (m), 714 (m), 695 (m), 645 (m), 611 (m), 513 (m), 490 (m), 458 (w). – EI-MS *m/z* (%): 336/334 (100/98) [M$^+$], 200/198 (25/25) [$C_8H_{10}BrN^+$], 185/183 (51/50) [$C_8H_9Br^+$], 151 (30) [$C_7H_7N_2S^+$], 105 (38) [$C_8H_9^+$], 93 (75) [$C_6H_7N^+$], 77 (44) [$C_6H_5^+$]. – EI-HRMS ($C_{15}H_{15}BrN_2S$): calcd. 334.0139, found 334.0136. – $C_{15}H_{15}BrN_2S$ (334.0): calcd. C 53.74, H 4.51, N 8.36, S 9.56, found C 53.68, H 4.33, N 8.39, S 9.54.

(*S*)-1-(1-(4-Bromophenyl)ethyl)-3-phenylthiourea ((*S*)-9c):



481 mg, 99% (scale: 1.45 mmol). – R_f (*n*-Hex/EtOAc 5:1) = 0.20. – mp: 126–129 °C. – $[\alpha]_D^{20}$ = −125 (*c* = 0.98, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.49 (d, ^3J = 6.9 Hz, 3 H, CH_3), 5.62–5.66 (m, 1 H, C*H*), 6.19 (d, ^3J = 3.7 Hz, 1 H, N*H*), 7.16–7.18 (m, 4 H, 4 × H_{ar}), 7.27–7.31 (m, 1 H, H_{ar}), 7.39–7.45 (m, 4 H, 4 × H_{ar}), 8.18 (s, 1 H, Ar-N*H*). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 21.4 (p, *C*H_3), 53.7 (t, *C*H), 121.3 (q, C_{ar}-Br), 125.1 (t, C_{ar}H), 127.3 (t, 2 × C_{ar}H), 127.9 (t, 2 × C_{ar}H), 130.2 (t, 2 × C_{ar}H), 131.7 (t, 2 × C_{ar}H), 135.9 (q, C_{ar}), 141.4 (q, C_{ar}), 179.8 (q, *C*=S). – IR (DRIFT): ṽ/cm^{-1} = 3390 (s), 3205 (s), 2972 (s), 2923 (m), 2868 (m), 1956 (w), 2795 (w), 1753 (w), 1590 (s), 1542 (s), 1504 (s), 1448 (s), 1406 (m), 1381 (s), 1313 (s), 1244 (s), 1200 (s), 1175 (m), 1145 (s), 1101 (s), 1073 (s), 1028 (m), 1008 (s), 946 (m), 914 (m), 835 (m), 817 (s), 785 (m), 748 (s), 714 (s), 695 (s), 645 (s), 611 (s), 513 (s), 490 (s), 459 (s), 409 (w). – EI-MS *m/z* (%): 336/334 (94/100) [M^+], 185/183 (39/38) [$C_8H_8Br^+$], 135 (34) [$C_7H_5NS^+$], 104 (73) [$C_8H_8^+$], 93 (75) [$C_6H_7N^+$], 77 (44) [$C_6H_5^+$]. – EI-HRMS ($C_{15}H_{15}BrN_2S$): calcd. 334.0139, found 334.0143. – $C_{15}H_{15}BrN_2S$ (334): C 53.74, H 4.51, N 8.36, S 9.56, found C 53.61, H 4.21, N 8.41, S 9.74.

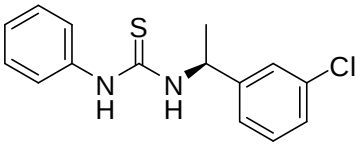
(*R*)-1-(1-Cyclopropylethyl)-3-phenylthiourea ((*R*)-9d):



316 mg, 99% (scale: 1.45 mmol). – R_f (*c*-Hex/EtOAc 5:1) = 0.18. – mp: 54–59 °C. – $[\alpha]_D^{20}$ = −29.5 (*c* = 1.01, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 0.26–0.31 (m, 1 H, CH_2), 0.40–0.45 (m, 2 H, CH_2), 0.47–0.53 (m, 1 H, CH_2), 0.77–0.86 (m, 1 H, C*H*), 1.24 (d, ^3J = 6.6 Hz, 3 H, CH_3), 3.94–4.03 (m, 1 H, NHC*H*), 6.03 (d, ^3J = 7.2 Hz, 1 H, N*H*), 7.21 (d, ^3J = 7.8 Hz, 2 H, 2 × H_{ar}), 7.26–7.31 (m, 1 H, H_{ar}), 7.41–7.45 (m, 2 H, 2 × H_{ar}), 7.96 (s, 1 H, Ar-N*H*). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 3.1 (s, 2 × *C*H_2), 16.9 (t, *C*H), 19.8 (p, *C*H_3), 55.5 (t, NH*C*H), 124.9 (t, C_{ar}H), 127.0 (t, 2 × C_{ar}H), 130.2 (t, 2 × C_{ar}H), 136.2 (q, C_{ar}), 179.3 (q, *C*=S). – IR (DRIFT): ṽ/cm^{-1} = 3379 (w), 3267 (w), 3079 (w), 3001 (w), 2928 (w), 1597 (w), 1524 (w), 1450 (w), 1351 (w), 1247 (w), 1176 (w), 1136 (w), 1021 (w), 1003 (w), 919 (w), 827 (w), 745 (w), 696 (w). – EI-MS *m/z* (%): 220 (37) [M^+], 191 (100) [$C_{10}H_{11}N_2S^+$], 177 (27), 93 (18) [$C_6H_7N^+$], 77 (11) [$C_6H_5^+$]. – EI-HRMS ($C_{12}H_{16}N_2S$): calcd. 220.1034, found

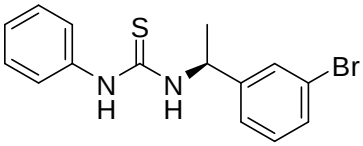
220.1032. – $C_{12}H_{16}N_2S$ (220.1): calcd. C 65.41, H 7.32, N 12.71, S 14.55, found C 65.23, H 6.92, N 12.83, S 14.31.

(*S*)-1-(1-(3-Chlorophenyl)ethyl)-3-phenylthiourea ((*S*)-9e):



417 mg, 99% (scale: 1.45 mmol). – R_f (*c*-Hex/EtOAc 5:1) = 0.22. – $[\alpha]_D^{20}$ = 101 (*c* = 0.98, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.50 (d, ^3J = 6.9 Hz, 3 H, C*H*$_3$), 5.66–5.68 (m, 1 H, C*H*), 6.19 (d, ^3J = 5.8 Hz, 1 H, N*H*), 7.17–7.22 (m, 3 H, 3 × H_{ar}), 7.23–7.26 (m, 3 H, 3 × H_{ar}), 7.28–7.32 (m, 1 H, H_{ar}), 7.41–7.45 (m, 2 H, 2 × H_{ar}), 8.08 (s, 1 H, Ar-N*H*). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 21.4 (p, CH_3), 53.8 (t, *C*H), 124.4 (t, C_{ar}H), 125.2 (t, 2 × C_{ar}H), 126.3 (t, C_{ar}H), 127.4 (t, C_{ar}H), 127.6 (t, C_{ar}H), 130.0 (t, C_{ar}H), 130.3 (t, 2 × C_{ar}H), 134.5 (q, C_{ar}-Cl), 135.9 (q, C_{ar}), 144.4 (q, C_{ar}), 179.9 (q, *C*=S). – IR (KBr): ṽ/cm^{-1} = 3376 (m), 3263 (m), 3256 (m), 2977 (m), 2929 (m), 1781 (m), 1596 (m), 1540 (m), 1450 (m), 1315 (m), 1259 (m), 1081 (w), 1028 (w), 1000 (w), 954 (w), 880 (w), 837 (w), 785 (w), 746 (w), 695 (w), 605 (w), 445 (w). – EI-MS *m/z* (%): 292/290 (37/100) [M^+], 156/154 (8/27) [$C_8H_9ClN^+$], 141/139 (11/32) [$C_8H_8Cl^+$], 93 (44) [$C_6H_7N^+$]. – EI-HRMS ($C_{15}H_{15}ClN_2S$): calcd. 290.0644, found 290.0642.

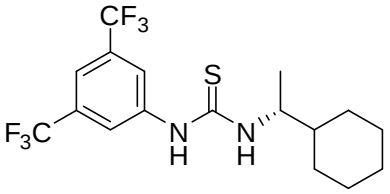
(*S*)-1-(1-(3-Bromophenyl)ethyl)-3-phenylthiourea ((*S*)-9f):



476 mg, 98% (scale: 1.45 mmol). – R_f (*c*-Hex/EtOAc 5:1) = 0.16. – $[\alpha]_D^{20}$ = 77.1 (*c* = 1.10, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.49 (d, ^3J = 6.9 Hz, 3 H, C*H*$_3$), 5.65–5.67 (m, 1 H, C*H*), 6.18 (d, ^3J = 5.8 Hz, 1 H, N*H*), 7.17–7.25 (m, 4 H, 4 × H_{ar}), 7.29–7.34 (m, 1 H, H_{ar}), 7.36–7.45 (m, 4 H, 4 × H_{ar}), 8.08 (s, 1 H, Ar-N*H*). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 21.4 (p, CH_3), 53.8 (t, *C*H), 122.7 (q, C_{ar}-Br), 124.9 (t, C_{ar}H), 125.2 (t, 2 × C_{ar}H), 127.4 (t, C_{ar}H), 129.2 (t, 2 × C_{ar}H), 130.3 (t, C_{ar}H), 130.5 (t, 2 × C_{ar}H), 135.9 (q, C_{ar}), 144.7 (q, C_{ar}), 179.9 (q, *C*=S). – IR (KBr): ṽ/cm^{-1} = 3374 (m), 3241 (m), 3040 (m), 2976 (m), 1594 (m), 1569 (m), 1530 (s), 1496 (s), 1476 (m), 1499 (m), 1427 (m), 1375 (m), 1314 (s), 1244 (m), 1200 (m), 1137 (w), 1073 (m), 1028 (w), 997 (w), 953 (w), 909 (w), 880 (w), 823 (w), 783 (m), 695 (s), 672 (m), 605 (w), 502 (w), 438 (w). – EI-MS *m/z* (%): 336/334 (19/18) [M^+], 186/184 (40/49) [$C_7H_7BrN^+$], 185/183 (36/33) [$C_8H_8Br^+$], 118 (41), 105/103 (32/44) [C_2HBr^+],

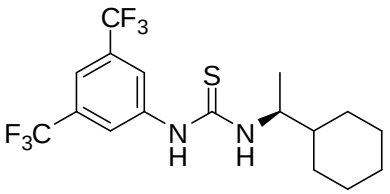
93 (35) [$C_6H_7N^+$], 86/84 (57/87), 78/76 (43/23) [Br^+], 77 (98) [$C_6H_5^+$], 65 (32) [$C_5H_5^+$], 49 (36). – EI-HRMS ($C_{15}H_{15}BrN_2S$): calcd. 334.0139, found 334.0136.

(*R*)-1-(3,5-Bis(trifluoromethyl)phenyl)-3-(1-cyclohexylethyl)thiourea ((*R*)-9g) [1]:



100 mg, 69% (scale: 361 µmol). – R_f (*c*-Hex/EtOAc 5:1) = 0.26. – mp: 166–170 °C. – $[\alpha]_D^{20}$ = −35.9 (*c* = 1.11, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 0.91–1.29 (m, 5 H, CH_2), 1.17 (d, ^3J = 6.6 Hz, 3 H, CH_3), 1.43–1.51 (m, 1 H, C*H*), 1.64–1.70 (m, 2 H, CH_2), 1.75–1.78 (m, 3 H, CH_2), 4.37–4.39 (m, 1 H, NHC*H*), 6.02–6.03 (m, 1 H, N*H*), 7.71 (s, 1 H, H_{ar}), 7.74 (s, 2 H, 2 × H_{ar}), 8.53 (s, 1 H, Ar-N*H*). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 17.1 (p, *C*H_3), 25.9 (s, *C*H_2), 26.0 (s, *C*H_2), 26.2 (s, *C*H_2), 29.1 (s, *C*H_2), 29.2 (s, *C*H_2), 43.0 (t, *C*H), 55.9 (t, NH*C*H), 119.4 (t, sept, ^3J = 3.7 Hz, C_{ar}-4), 122.7 (q, quart, ^1J = 273.2 Hz, 2 × *C*F_3), 123.8 (t, quart, ^3J = 3.4 Hz, C_{ar}-2, C_{ar}-6), 133.2 (q, quart, ^2J = 36.3 Hz, C_{ar}-3, C_{ar}-5), 138.7 (q, C_{ar}-1), 179.6 (q, *C*=S). – ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm = −63.1 (s, 2 × C*F*$_3$). – IR (DRIFT): $\tilde{\nu}$/cm^{-1} = 3227 (m), 3062 (m), 2935 (s), 2856 (m), 1797 (w), 1623 (m), 1552 (s), 1468 (m), 1381 (s), 1348 (s), 1279 (s), 1187 (s), 1133 (s), 1107 (m), 1067 (w), 1044 (w), 1002 (m), 977 (m), 935 (m), 891 (s), 848 (m), 748 (m), 714 (m), 682 (m), 586 (m). – EI-MS *m/z* (%): 398 (62) [M^+], 289 (100) [$C_9H_7F_6N_2S^+$]. – EI-HRMS ($C_{17}H_{20}F_6N_2S$): calcd. 398.1251, found 398.1253.

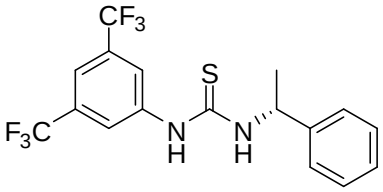
(*S*)-1-(3,5-Bis-(trifluoromethyl)phenyl)-3-(1-cyclohexylethyl)thiourea ((*S*)-9g) [1]:



89.5 mg, 62% (scale: 361 µmol). – R_f (*c*-Hex/EtOAc 5:1) = 0.19. – mp: 169–173 °C. – $[\alpha]_D^{20}$ = 31.2 (*c* = 1.05, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 0.91–1.29 (m, 5 H, CH_2), 1.18 (d, ^3J = 6.6 Hz, 3 H, CH_3), 1.43–1.52 (m, 1 H, C*H*), 1.60–1.69 (m, 2 H, CH_2), 1.72–1.83 (m, 3 H, CH_2), 4.16–4.67 (m, 1 H, NHC*H*), 5.84–6.24 (m, 1 H, N*H*CH), 7.71–7.74 (m, 3 H, 3 × H_{ar}), 8.39 (s, 1 H, Ar-N*H*). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 17.1 (p, *C*H_3), 25.9 (s, *C*H_2), 26.0 (s, *C*H_2), 26.2 (s, *C*H_2), 29.1 (s, *C*H_2), 29.2 (s, *C*H_2), 43.0 (t, *C*H), 56.0 (t, NH*C*H), 119.4 (t, sept, ^3J = 3.8 Hz, C_{ar}-4), 122.7 (q, quart, ^1J = 273.2 Hz, 2 × *C*F_3), 123.8 (t, C_{ar}-2, C_{ar}-6), 133.2 (t, quart, ^2J = 31.6 Hz, C_{ar}-3, C_{ar}-5), 138.7 (q, C_{ar}-1), 179.7 (q, *C*=S). – ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm = −63.1 (s, 2 × C*F*$_3$). –

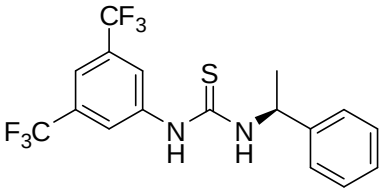
IR (DRIFT): ṽ/cm^{-1} = 3226 (m), 3060 (m), 2934 (m), 2855 (m), 1622 (w), 1552 (m), 1430 (m), 1386 (m), 1348 (m), 1280 (s), 1187 (m), 1133 (s), 1107 (m), 1102 (m), 977 (m), 935 (w), 891 (m), 848 (w), 748 (w), 713 (m), 682 (m), 586 (w). – EI-MS *m/z* (%): 398 (19) [M$^+$], 289 (65) [$C_9H_7F_6N_2S^+$], 55 (22), 43 (100) [$C_2H_5N^+$]. – EI-HRMS ($C_{17}H_{20}F_6N_2S$): calcd. 398.1251, found 398.1253.

(*R*)-1-(3,5-Bis(trifluoromethyl)phenyl)-3-(1-phenylethyl)thiourea ((*R*)-9h):



126 mg, 89% (scale: 361 µmol). – R_f (*c*-Hex/EtOAc 5:1) = 0.23. – mp: 139–143 °C. – $[\alpha]_D^{20}$ = 3.50 (*c* = 1.00, $CHCl_3$) – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.60 (d, ^3J = 6.8 Hz, 3 H, CH_3), 5.36–5.44 (m, 1 H, C*H*), 6.57–6.65 (m, 1 H, N*H*), 7.34–7.42 (m, 5 H, 5 × H_{ar}), 7.65–7.68 (m, 3 H, 3 × H_{ar}), 8.08 (s, 1 H, Ar-N*H*). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 22.1 (p, CH_3), 54.8 (t, *C*H), 119.4 (t, sept, ^3J = 3.7 Hz, C_{ar}-4), 122.8 (q, quart, ^1J = 272.9 Hz, 2 × CF_3), 123.9 (t, quart, ^3J = 3.4 Hz, C_{ar}-2, C_{ar}-6), 126.1 (t, 2 × C_{ar}H), 128.4 (t, C_{ar}H), 129.3 (t, 2 × C_{ar}H), 132.6 (q, quart, ^2J = 34.3 Hz, C_{ar}-3, C_{ar}-5), 139.0 (q, C_{ar}-1), 141.3 (q, C_{ar}), 179.9 (q, *C*=S). – ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm = −63.1 (s, 2 × CF_3). – IR (DRIFT): ṽ/cm^{-1} = 3229 (m), 3042 (m), 2808 (w), 2656 (w), 2555 (w), 2234 (w), 2041 (m), 1992 (m), 1883 (w), 1806 (w), 1624 (m), 1544 (s), 1495 (m), 1469 (m), 1379 (m), 1341 (m), 1280 (s), 1227 (m), 1176 (m), 1134 (s), 1109 (m), 1063 (m), 1023 (m), 1002 (m), 976 (m), 893 (m), 848 (m), 791 (m), 767 (m), 743 (m), 704 (m), 682 (m), 620 (m), 587 (m), 232 (m), 456 (m), 405 (w). – EI-MS *m/z* (%): 392 (74) [M$^+$], 229 (18) [$C_8H_5F_6N^+$], 120 (25) [$C_8H_{10}N^+$], 77 (18) [$C_6H_5^+$]. – EI-HRMS ($C_{17}H_{14}F_6N_2S$): calcd. 392.0782, found 392.0780. – $C_{17}H_{14}F_6N_2S$ (392.1): calcd. C 52.04, H 3.60, N 7.14, S 8.17, found C 51.23, H 3.39, N 7.06, S 8.46.

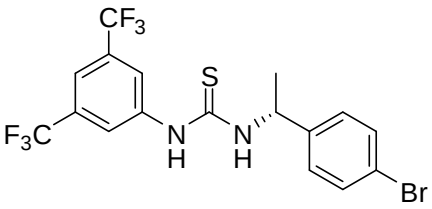
(*S*)-1-(3,5-Bis(trifluoromethyl)phenyl)-3-(1-phenylethyl)thiourea ((*S*)-9h) [4]:



140 mg, 99% (scale: 361 µmol). – R_f (*c*-Hex/EtOAc 5:1) = 0.28. – mp: 137–140 °C. – $[\alpha]_D^{20}$ = −2.7 (*c* = 1.01, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.60 (d, ^3J = 6.8 Hz, 3 H, CH_3), 4.77–5.94 (m, 1 H, C*H*), 6.14–7.00 (m, 1 H, N*H*), 7.32–7.42 (m, 5 H, 5 × H_{ar}), 7.63–7.68 (m, 3 H, 3 × H_{ar}), 7.99 (s, 1 H, Ar-N*H*). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 22.2 (p, CH_3), 54. 8 (t, *C*H), 119.4 (t, sept, ^3J = 3.6 Hz, C_{ar}-4), 122.7 (q, quart, ^1J = 273.2 Hz,

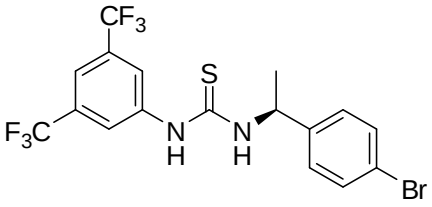
2 × CF_3), 123.9 (t, C_{ar}-2, C_{ar}-6), 126.0 (t, 2 × $C_{ar}H$), 128.3 (t, $C_{ar}H$), 129.3 (t, 2 × $C_{ar}H$), 132.7 (q, quart, ^2J = 33.7 Hz, C_{ar}-3, C_{ar}-5), 139.0 (q, C_{ar}-1), 141.2 (q, C_{ar}), 179.8 (q, *C*=S). – ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm = −63.1 (s, 2 × CF_3). – IR (DRIFT): ṽ/cm^{-1} = 3230 (m), 3042 (m), 2047 (w), 1805 (w), 1625 (m), 1544 (s), 1469 (m), 1381 (s), 1341 (m), 1283 (s), 1177 (s), 1135 (s), 1023 (m), 1002 (w), 976 (m), 893 (m), 848 (m), 791 (w), 767 (m), 743 (m), 704 (m), 682 (m), 532 (m). – EI-MS *m/z* (%): 392 (59) [M^+], 271 (44) [$C_9H_4F_6NS^+$], 213 (22) [$C_8H_3F_6^+$], 120 (23) [$C_8H_{10}N^+$], 105 (100) [$C_8H_9^+$], 77 (27) [$C_6H_5^+$]. – EI-HRMS ($C_{17}H_{14}F_6N_2S$): calcd. 392.0781, found 392.0784.

(*R*)-1-(3,5-Bis(trifluoromethyl)phenyl)-3-(1-(4-bromophenyl)ethyl)thiourea ((*R*)-9i):



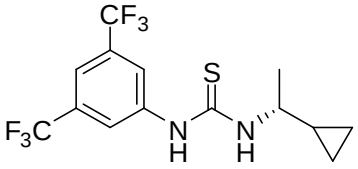
156 mg, 91% (scale: 361 µmol). – R_f (*c*-Hex/EtOAc 5:1) = 0.16. – mp: 127–131 °C. – $[\alpha]_D^{20}$ = −2.2 (*c* = 1.01, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.56 (d, ^3J = 6.9 Hz, 3 H, CH_3), 5.41–5.52 (m, 1 H, C*H*), 6.35–6.51 (m, 1 H, N*H*), 7.21–7.23 (m, 2 H, 2 × H_{ar}), 7.49–7.51 (m, 2 H, 2 × H_{ar}), 7.65–7.72 (m, 3 H, 3 × H_{ar}), 8.07 (s, 1 H, Ar-N*H*). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 21.7 (p, CH_3), 54.1 (t, *C*H), 119.6 (t, sept, ^3J = 3.6 Hz, C_{ar}-4), 122.0 (q, C_{ar}-Br), 122.0 (t, C_{ar}-2, C_{ar}-6), 122.7 (q, quart, ^1J = 273.0 Hz, 2 × CF_3), 127.8 (t, 2 × $C_{ar}H$), 132.2 (t, 2 × $C_{ar}H$), 133.0 (q, quart, ^2J = 33.7 Hz, C_{ar}-3, C_{ar}-5), 138.7 (q, C_{ar}-1), 140.5 (q, C_{ar}), 179.9 (q, *C*=S). – ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm = −63.0 (s, 2 × CF_3). – IR (DRIFT): ṽ/cm^{-1} = 3232 (m), 3032 (s), 1799 (w), 1623 (m), 1541 (s), 1491 (s), 1468 (m), 1410 (m), 1380 (s), 1338 (s), 1278 (s), 1224 (m), 1174 (s), 1137 (s), 1108 (m), 1076 (m), 1032 (m), 1011 (m), 977 (m), 893 (s), 847 (m), 827 (m), 784 (m), 750 (m), 704 (s), 682 (s), 619 (w), 587 (w), 531 (m). – EI-MS *m/z* (%): 472/470 (100/97) [M^+], 271 (54) [$C_9H_4F_6NS^+$], 229 (26) [$C_8H_5F_6N^+$], 200/198 (20/19) [$C_8H_9BrN^+$], 185/183 (69/68) [$C_8H_8Br^+$], 104 (38) [$CH_4N_2S^+$]. – EI-HRMS ($C_{17}H_{13}BrF_6N_2S$): calcd. 469.9887, found 469.9886. – $C_{17}H_{13}BrF_6N_2S$ (470.0): calcd. C 43.33, H 2.78, N 5.94, S 6.80, found C 43.34, H 2.61, N 5.97, S 7.23.

(*S*)-1-(3,5-Bis(trifluoromethyl)phenyl)-3-(1-(4-bromophenyl)ethyl)thiourea ((*S*)-9i):



169 mg, 99% (scale: 361 µmol). – R_f (*c*-Hex/EtOAc 5:1) = 0.28. – mp: 130–133 °C. – $[\alpha]_D^{20}$ = −18.7 (*c* = 1.02, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.56 (d, ^3J = 6.9 Hz, 3 H, CH_3), 5.36–5.53 (m, 1 H, C*H*), 6.32–6.55 (m, 1 H, N*H*), 7.21–7.23 (m, 2 H, 2 × H_{ar}), 7.49–7.51 (m, 2 H, 2 × H_{ar}), 7.65–7.70 (m, 3 H, 3 × H_{ar}), 8.04 (s, 1 H, Ar-N*H*). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 21.7 (p, CH_3), 54.1 (t, *C*H), 119.6 (t, sept, ^3J = 3.6 Hz, C_{ar}-4), 122.0 (q, C_{ar}-Br), 124.0 (t, C_{ar}-2, C_{ar}-6), 122.6 (q, quart, ^1J = 273.1 Hz, 2 × CF_3), 127.8 (t, 2 × C_{ar}H), 132.2 (t, 2 × C_{ar}H), 133.0 (q, quart, ^2J = 34.8 Hz, C_{ar}-3, C_{ar}-5), 138.7 (q, C_{ar}-1), 140.5 (q, C_{ar}), 179.9 (q, *C*=S). – ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm = −63.0 (s, 2 × CF_3). – IR (DRIFT): ṽ/cm^{-1} = 3238 (m), 3032 (m), 1623 (w), 1541 (s), 1491 (m), 1469 (m), 1680 (m), 1338 (m), 1279 (s), 1175 (m), 1137 (s), 1108 (m), 1076 (m), 1011 (m), 977 (m), 893 (m), 827 (m), 784 (w), 751 (w), 705 (m), 682 (m), 587 (w), 531 (m). – EI-MS *m/z* (%): 472/470 (23/23) [M^+], 271 (31) [$C_9H_4F_6NS^+$], 213 (35) [$C_8H_3F_6^+$], 185/183 (45/49) [$C_8H_9Br^+$], 184/182 (35/31) [$C_8H_8Br^+$], 104/102 (100/15) [C_2HBr^+], 78/76 (23/11) [Br^+]. – EI-HRMS ($C_{17}H_{13}BrF_6N_2S$): calcd. 469.9887, found 469.9884.

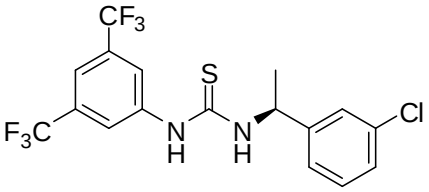
(*R*)-1-(3,5-Bis(trifluoromethyl)phenyl)-3-(1-cyclopropylethyl)thiourea ((*R*)-9j):



117 mg, 91% (scale: 361 µmol). – R_f (*c*-Hex/EtOAc 5:1) = 0.20. – mp: 160–164 °C. – $[\alpha]_D^{20}$ = −38.5 (*c* = 1.01, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 0.30–0.36 (m, 1 H, CH_2), 0.41–0.47 (m, 1 H, CH_2), 0.50–0.62 (m, 2 H, CH_2), 0.85–0.94 (m, 1 H, C*H*), 1.30 (d, ^3J = 6.6 Hz, 3 H, CH_3), 3.77–4.02 (m, 1 H, NHC*H*), 6.09–6.32 (m, 1 H, N*H*), 7.68–7.73 (m, 1 H, H_{ar}), 7.74–7.77 (m, 2 H, 2 × H_{ar}), 8.44 (s, 1 H, Ar-N*H*). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 3.2 (s, CH_2), 3.3 (s, CH_2), 16.8 (t, *C*H), 19.5 (p, CH_3), 55.8 (t, NH*C*H), 119.2 (t, sept, ^3J = 3.7 Hz, C_{ar}-4), 122.7 (q, quart, ^1J = 273.0 Hz, 2 × CF_3), 132.6 (t, C_{ar}-2, C_{ar}-6), 133.2 (q, quart, ^2J = 33.7 Hz, C_{ar}-3, C_{ar}-5), 138.9 (q, C_{ar}-1), 179.4 (q, *C*=S). – ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm = −63.1 (s, 2 × CF_3). – IR (DRIFT): ṽ/cm^{-1} = 3242 (m), 3048 (m), 1797 (w), 1624 (m), 1553 (s), 1468 (m), 1382 (m), 1348 (m), 1280 (s), 1227 (m), 1192 (s), 1133 (s), 1108 (m), 1053 (m), 1026 (m), 1013 (m), 976 (m), 939 (m), 890 (m), 848 (m), 834 (w), 748 (w), 715 (m), 704 (m), 682 (m), 620 (w), 591 (w).

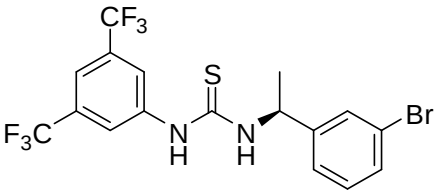
– EI-MS *m/z* (%): 356 (28) [M^+], 327 (100) [$C_{12}H_9F_6N_2S^+$], 313 (39) [$C_{11}H_7F_6N_2S^+$], 41 (18) [$C_3H_5^+$]. – EI-HRMS ($C_{14}H_{14}F_6N_2S$): calcd. 356.0779, found 356.0782.

(*S*)-1-(3,5-Bis(trifluoromethyl)phenyl)-3-(1-(3-chlorophenyl)ethyl)thiourea ((*S*)-9k):



153 mg, 99% (scale: 361 µmol). – R_f (*c*-Hex/EtOAc 5:1) = 0.20. – mp: 129–131 °C. – $[\alpha]_D^{20}$ = 48.7 (*c* = 1.01, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.57 (d, ^3J = 6.9 Hz, 3 H, CH_3), 5.32–5.62 (m, 1 H, C*H*), 6.21–6.59 (m, 1 H, N*H*), 7.22–7.24 (m, 1 H, H_{ar}), 7.27–7.33 (m, 3 H, 3 × H_{ar}), 7.69–7.71 (m, 3 H, 3 × H_{ar}), 8.03 (s, 1 H, Ar-N*H*). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 21.7 (p, CH_3), 54.2 (t, *C*H), 119.7 (t, sept, ^3J = 3.4 Hz, C_{ar}-4), 122.7 (q, quart, ^1J = 273.0 Hz, 2 × CF_3), 124.0 (t, C_{ar}-2, C_{ar}-6), 124.4 (t, C_{ar}H), 126.3 (t, C_{ar}H), 128.3 (t, C_{ar}H), 130.4 (t, C_{ar}H), 133.0 (q, quart, ^2J = 34.8 Hz, C_{ar}-3, C_{ar}-5), 135.0 (q, C_{ar}-Cl), 138.9 (q, C_{ar}-1), 143.5 (q, C_{ar}), 179.9 (q, *C*=S). – ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm = −63.1 (s, 2 × CF_3). – IR (DRIFT): $\tilde{\nu}$/cm^{-1} = 3226 (m), 3054 (m), 1807 (w), 1623 (w), 1549 (m), 1471 (m), 1431 (m), 1381 (m), 1341 (m), 1278 (m), 1231 (m), 1186 (m), 1130 (m), 1080 (m), 1032 (w), 1000 (w), 977 (m), 914 (w), 891 (m), 866 (w), 848 (w), 785 (m), 752 (w), 712 (m), 683 (m), 594 (w), 459 (w), 444 (w). – EI-MS *m/z* (%): 428/426 (17/43) [M^+], 287 (30) [$C_9H_5F_6N_2S^+$], 272 (22) [$C_9H_4F_6NS^+$], 229 (41) [$C_8H_5F_6N^+$], 228 (25) [$C_8H_4F_6N^+$], 213 (37) [$C_8H_3F^+$], 156/154 (14/44) [$C_8H_9ClN^+$], 141/139 (27/97) [$C_8H_8Cl^+$], 140/138 (19/29) [$C_8H_7Cl^+$], 103 (100) [$C_3H_7N_2S^+$], 77 (53) [$C_6H_5^+$], 43 (98) [$C_2H_5N^+$]. – EI-HRMS ($C_{17}H_{13}ClF_6N_2S$): calcd. 426.0392, found 426.0395.

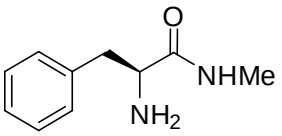
(*S*)-1-(3,5-Bis(trifluoromethyl)phenyl)-3-(1-(3-bromophenyl)ethyl)thiourea ((*S*)-9l):



130 mg, 76% (scale: 361 µmol). – R_f (*c*-Hex/EtOAc 5:1) = 0.20. – mp: 143–149 °C. – $[\alpha]_D^{20}$ = 36.5 (*c* = 0.97, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.57 (d, ^3J = 6.9 Hz, 3 H, CH_3), 5.34–5.60 (m, 1 H, C*H*), 6.30–6.56 (m, 1 H, N*H*), 7.23–7.29 (m, 2 H, 2 × H_{ar}), 7.43–7.47 (m, 2 H, 2 × H_{ar}), 7.69–7.74 (m, 3 H, 3 × H_{ar}), 8.03 (s, 1 H, Ar-N*H*). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 21.7 (p, CH_3), 54.1 (t, *C*H), 119.7 (t, sept, ^3J = 3.7 Hz, C_{ar}-4), 122.6 (q, quart,

^{1}J = 273.1 Hz, 2 × CF$_3$), 123.2 (q, C_{ar}-Br), 124.0 (t, C_{ar}-2), 124.9 (t, C_{ar}-6), 129.2 (t, C_{ar}H), 130.7 (t, 2 × C_{ar}H), 131.3 (t, 2 × C_{ar}H), 133.0 (q, quart, ^{2}J = 34.8 Hz, C_{ar}-3, C_{ar}-5), 138.7 (q, C_{ar}-1), 143.8 (q, C_{ar}), 179.9 (q, C=S). – ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm = −63.0 (s, 2 × CF_3). – IR (DRIFT): ṽ/cm^{-1} = 3326 (m), 3053 (m), 1947 (w), 1807 (w), 1623 (m), 1549 (s), 1471 (m), 1425 (m), 1381 (m), 1341 (m), 1294 (m), 1277 (m), 1232 (m), 1185 (s), 1129 (s), 1078 (m), 1030 (m), 998 (m), 976 (m), 914 (m), 890 (m), 867 (w), 849 (m), 822 (w), 784 (m), 752 (m). 708 (m), 682 (m), 593 (w), 458 (w), 437 (w). – EI-MS *m/z* (%): 473/471 (47/45) [M$^+$], 472/470 (100/99) [M$^+$−H], 316 (26) [$C_{11}H_{10}F_6N_2S^+$], 315 (22) [$C_{11}H_9F_6N_2S^+$], 287 (72) [$C_9H_5F_6N_2S^+$], 271 (52) [$C_9H_4F_6NS^+$]. – EI-HRMS ($C_{17}H_{13}BrF_6N_2S$): calcd. 469.9887, found 469.9890.

(*S*)-Phenylalanin-*N*-methylamide (13):

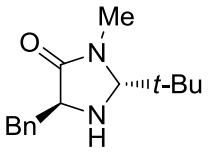


To a solution of methylamine (13.5 mL, 33% in EtOH, 45.9 mmol, 4.00 equiv) (*S*)-phenylalanine methyl ester hydrochloride (**12**, 2.50 g, 11.5 mmol, 1.00 equiv) was added, and the mixture was stirred for 2 d at room temperature. After removal of the solvent saturated $NaHCO_3$ (20 mL) was added and the free amine was extracted with dichloromethane (5 × 15 mL) and dried over Na_2SO_4, and the solvent evaporated. 2.02 g, 99%. R_f = 0.14 (EtOAc). – mp: 52–57 °C. – $[\alpha]_D^{20}$ = −48.14 (c = 1.08, $CHCl_3$). – ^{1}H NMR (400 MHz, methanol-d_4): δ/ppm = 2.66 (s, 3 H, CH_3), 2.79 (dd, ^{2}J = 13.4 Hz, ^{3}J = 7.2 Hz, 1 H, CH_2), 2.97 (dd, ^{2}J = 13.4 Hz, ^{3}J = 6.7 Hz, 1 H, CH_2), 3.49 (dd, ^{3}J = 7.2 Hz, ^{3}J = 6.7 Hz, 1 H, CH), 7.19–7.23 (m, 3 H, 2-H_{ar}, 4-H_{ar}, 6-H_{ar}), 7.27–7.30 (m, 2 H, 3-H_{ar}, 5-H_{ar}). – ^{13}C NMR (100 MHz, methanol-d_4): δ/ppm = 26.1 (p, CH$_3$), 42.6 (s, CH$_2$), 57.9 (t, CH), 127.8 (t, C_{ar}-2, C_{ar}-6), 129.6 (t, C_{ar}-4), 130.4 (t, C_{ar}-3, C_{ar}-5), 139.0 (q, C_{ar}-1), 177.3 (q, C=O). – IR (DRIFT): ṽ/cm^{-1} = 3372 (m), 3293 (m), 3086 (w), 3063 (w), 3033 (w), 2940 (m), 2915 (m), 2877 (m), 2791 (w), 1959 (w), 1773 (m), 1646 (m), 1528 (m), 1455 (m), 1401 (m), 1343 (w), 1269 (w), 1230 (m), 1160 (m), 1109 (w), 1082 (w), 1067 (w), 1031 (w), 1003 (w), 978 (w), 927 (m), 877 (m), 858 (m), 747 (m), 702 (m), 660 (w), 567 (w), 534 (w), 483 (m). – EI-MS (70 eV) *m/z* (%): 178 (2) [M$^+$], 120 (100) [M$^+$−C_2H_4NO], 91 (12) [$C_7H_7^+$], 87 (22) [M$^+$−C_7H_7]. – EI-HRMS ($C_{10}H_{14}N_2O$): calcd. 178.1110, found 178.1106.

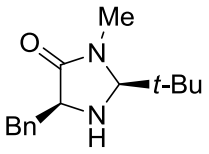
General procedure for the preparation of Imidazolidinone-catalysts 15

1.00 equiv of (*S*)-phenylalanin-*N*-methylamide (**13**), 1.00 equiv aldehyde **14**, 0.30 equiv $FeCl_3$, and 3 Å MS were solved/suspended in THF (2 mL/mmol aldehyde). The resulting mixture was heated under reflux for 24 h, filtered off and the solvent was removed under reduced pressure. The product was purified by flash column chromatography.

(2*R*,5*S*)-5-Benzyl-2-*tert*-butyl-3-methylimidazolidin-4-one ((2*R*,5*S*)-15a) and (2*S*,5*S*)-5-benzyl-2-*tert*-butyl-3-methylimidazolidin-4-one ((2*S*,5*S*)-15a) [5]:



(2*R*,5*S*)-**15a**

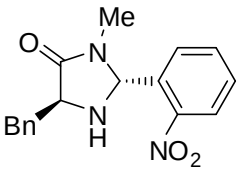


(2*S*,5*S*)-**15a**

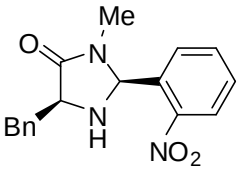
Scale: 5.00 mmol. (2*R*,5*S*)-**15a:** 428 mg, 35%. – R_f (*c*-Hex/EtOAc 4:1) = 0.10. – mp: 92–94 °C. – $[\alpha]_D^{20}$ = −80.3 (*c* = 1.08, $CHCl_3$). – ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm = 0.90 (s, 9 H, C(C*H*$_3$)$_3$), 1.88 (s, 1 H, N*H*), 2.89 (s, 3 H, NC*H*$_3$), 2.89 (dd, ^2J = 14.1 Hz, ^3J = 4.2 Hz, 1 H, C*H*$_2$), 3.11 (dd, ^2J = 14.1 Hz, ^3J = 7.2 Hz, 1 H, C*H*$_2$), 3.80 (d, ^4J = 1.7 Hz, 1 H, NC*H*N), 3.85 (ddd, ^3J = 7.2 Hz, ^3J = 4.2 Hz, ^4J = 1.7 Hz, 1 H, CH$_2$C*H*), 7.22–7.25 (m, 3 H, 3 × *H*$_{ar}$), 7.28–7.31 (m, 2 H, 2 × *H*$_{ar}$). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 25.6 (p, 3 × C(*C*H$_3$)$_3$), 31.3 (p, NC*H*$_3$), 37.7 (q, *C*(CH$_3$)$_3$), 38.5 (s, *C*H$_2$), 59.5 (t, CH$_2$*C*H), 83.4 (t, NC*H*N), 126.6 (t, *C*$_{ar}$H), 128.5 (t, 2 × *C*$_{ar}$H), 129.5 (t, 2 × *C*$_{ar}$H), 137.4 (q, *C*$_{ar}$), 175.3 (q, *C*=O). – IR (DRIFT): ṽ/cm^{-1} = 3059 (w), 3030 (w), 1897 (w), 1682 (s), 1584 (w), 1457 (m), 1433 (m), 1397 (m), 1346 (m), 1330 (m), 1307 (m), 1283 (m), 1262 (m), 1204 (m), 1160 (m), 1104 (m), 1025 (w), 902 (m), 801 (w), 756 (m), 736 (m), 704 (m), 637 (w), 541 (m), 489 (m). – EI-MS *m/z* (%): 247 (3) [M$^+$+H], 189 (100) [M$^+$−*t*-Bu]. – EI-HRMS ($C_{15}H_{22}N_2O$+H$^+$): calcd. 247.1810, found 247.1807. (2*S*,5*S*)-**15a:** 304 mg, 25%. – R_f (*c*-Hex/EtOAc 4:1) = 0.04. – mp: 82–84 °C. – $[\alpha]_D^{20}$ = −68.5 (*c* = 1.06, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 0.83 (s, 9 H, C(C*H*$_3$)$_3$), 1.69 (s, 1 H, N*H*), 2.91 (s, 3 H, NC*H*$_3$), 2.89 (dd, ^2J = 13.8 Hz, ^3J = 7.2 Hz, 1 H, C*H*$_2$), 3.15 (dd, ^2J = 13.8 Hz, ^3J = 3.9 Hz, 1 H, C*H*$_2$), 3.68–3.73 (m, 1 H, CH$_2$C*H*), 4.05 (d, ^4J = 1.7 Hz, 1 H, NC*H*N), 7.21–7.31 (m, 5 H, 5 × *H*$_{ar}$). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 25.3 (p, 3 × C(*C*H$_3$)$_3$), 30.7 (p, NC*H*$_3$), 35.0 (q, *C*(CH$_3$)$_3$), 38.2 (s, *C*H$_2$), 59.4 (t, CH$_2$*C*H), 82.4 (t, NC*H*N), 126.6 (t, *C*$_{ar}$H), 128.5 (t, 2 × *C*$_{ar}$H), 129.6 (t, 2 × *C*$_{ar}$H), 137.8 (q, *C*$_{ar}$), 175.2 (q, *C*=O). – IR (DRIFT): ṽ/cm^{-1} = 3368 (m), 3355 (m), 3084 (w), 3060 (w), 3030 (w), 1893 (m), 1676 (s), 1603 (w), 1477 (m), 1421 (m), 1393 (m), 1360 (m), 1341 (m), 1261 (m), 1206 (m), 1107 (m), 1078 (w), 1051 (w),

1028 (w), 1008 (w), 974 (w), 946 (w), 913 (w), 892 (m), 827 (w), 792 (w), 764 (m), 740 (m), 710 (m), 700 (m), 617 (w), 574 (w), 543 (w), 489 (m), 421 (w), 412 (w). – EI-MS *m/z* (%): 247 (1) [M^++H], 189 (100) [M^+−*t*-Bu]. – EI-HRMS ($C_{15}H_{22}N_2O$+H^+): calcd. 247.1810, found 247.1813.

(2*R*,5*S*)-5-Benzyl-3-methyl-2-(2-nitrophenyl)imidazolidin-4-one ((2*R*,5*S*)-15b) and (2*S*,5*S*)-5-benzyl-3-methyl-2-(2-nitrophenyl)imidazolidin-4-one ((2*S*,5*S*)-15b):



(2*R*,5*S*)-**15b**

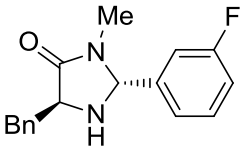


(2*S*,5*S*)-**15b**

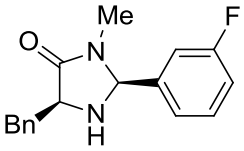
Scale: 1.12 mmol. (2*R*,5*S*)-**15b:** 135 mg, 42%. – R_f (*c*-Hex/EtOAc 1:1) = 0.10. – $[\alpha]_D^{20}$ = 58.3 (*c* = 1.03, $CHCl_3$). – ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm = 2.56 (bs, 1 H, N*H*), 2.68 (s, 3 H, CH_3), 3.01 (dd, ^2J = 13.9 Hz, ^3J = 7.1 Hz, 1 H, CH_2), 3.15 (dd, ^2J = 13.9 Hz, ^3J = 4.1 Hz, 1 H, CH_2), 3.90–3.94 (m, 1 H, CH_2C*H*), 5.55 (d, ^4J = 1.3 Hz, 1 H, NC*H*N), 7.23–7.28 (m, 3 H, 3 × H_{ar}), 7.30–7.36 (m, 3 H, 3 × H_{ar}), 7.47–7.51 (m, 1 H, H_{ar}), 7.63–7.67 (m, 1 H, H_{ar}), 7.94–7.97 (m, 1 H, H_{ar}). – ^{13}C NMR (125 MHz, $CDCl_3$): δ/ppm = 27.7 (p, N*C*H_3), 38.3 (s, *C*H_2), 59.0 (t, CH_2*C*H), 72.1 (t, NCHN), 125.2 (t, C_{ar}H), 127.0 (t, C_{ar}H), 127.2 (t, C_{ar}H), 128.7 (t, 2 × C_{ar}H), 129.4 (t, 2 × C_{ar}H), 129.6 (t, C_{ar}H), 133.9 (t, C_{ar}H), 134.6 (q, C_{ar}), 136.8 (q, C_{ar}), 149.2 (q, C_{ar}-NO_2), 174.3 (q, *C*=O). – IR (KBr): ṽ/cm^{-1} = 3458 (m), 3374 (m), 3063 (w), 3029 (w), 2923 (w), 1690 (m), 1606 (w), 1581 (w), 1528 (m), 1496 (w), 1479 (w), 1453 (m), 1401 (m), 1349 (m), 1303 (w), 1262 (w), 1097 (w), 1079 (w), 1046 (w), 999 (w), 856 (w), 827 (w), 789 (w), 746 (w), 703 (w), 487 (w). – EI-MS *m/z* (%): 312 (92) [M^++H], 293 (33), 220 (100) [M^+−C_7H_7], 91 (27) [$C_7H_7^+$]. – EI-HRMS ($C_{17}H_{17}N_3O_3$): calcd. 312.1348, found 312.1346. (2*S*,5*S*)-**15b:** 155 mg, 52%. – R_f (*c*-Hex/EtOAc 1:1) = 0.25. – $[\alpha]_D^{20}$ = −165 (*c* = 1.04, $CHCl_3$). – ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm = 2.49 (bs, 1 H, N*H*), 2.62 (s, 3 H, CH_3), 3.07 (dd, ^2J = 13.8 Hz, ^3J = 6.3 Hz, 1 H, CH_2), 3.11 (dd, ^2J = 13.8 Hz, ^3J = 4.4 Hz, 1 H, CH_2), 4.00–4.02 (m, 1 H, CH_2C*H*), 5.79 (d, ^4J = 1.2 Hz, 1 H, NC*H*N), 6.71–6.73 (m, 1 H, H_{ar}), 7.18–7.20 (m, 2 H, 2 × H_{ar}), 7.23–7.26 (m, 3 H, 3 × H_{ar}), 7.43–7.46 (m, 2 H, 2 × H_{ar}), 7.85–7.88 (m, 1 H, H_{ar}). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 27.7 (p, N*C*H_3), 38.3 (s, *C*H_2), 60.0 (t, CH_2*C*H), 71.4 (t, NCHN), 124.3 (t, C_{ar}H), 126.6 (t, C_{ar}H), 128.3 (t, C_{ar}H), 128.5 (t, 2 × C_{ar}H), 129.5 (t, C_{ar}H), 130.0 (t, 2 × C_{ar}H), 133.7 (t, C_{ar}H), 134.4 (q, C_{ar}), 137.3 (q, C_{ar}), 149.7 (q, C_{ar}-NO_2), 173.7 (q, *C*=O). – IR (KBr): ṽ/cm^{-1} = 3472 (w), 3348 (w),

3063 (w), 3030 (w), 2922 (w), 1709 (m), 1688 (w), 1678 (w), 1607 (w), 1529 (w). – EI-MS *m/z* (%): 312 (8) [M^++H], 220 (32) [$M^+-C_7H_7$], 117 (24), 91 (100) [$C_7H_7^+$]. – EI-HRMS ($C_{17}H_{17}N_3O_3$): calcd. 312.1348, found 312.1346.

(2*R*,5*S*)-5-Benzyl-2-(3-fluorophenyl)-3-methylimidazolidin-4-one ((2*R*,5*S*)-15c) and (2*S*,5*S*)-5-benzyl-2-(3-fluorophenyl)-3-methylimidazolidin-4-one ((2*S*,5*S*)-15c):



(2*R*,5*S*)-**15c**

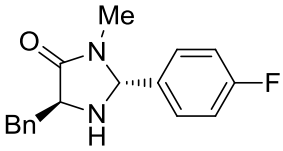


(2*S*,5*S*)-**15c**

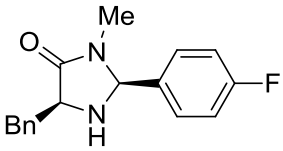
Scale: 1.12 mmol. (2*R*,5*S*)-**15c:** 89.1 mg, 28%. – R_f (*c*-Hex/EtOAc 2:1) = 0.12. – $[\alpha]_D^{20}$ = −5.45 (*c* = 1.01, $CHCl_3$). – ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm = 2.15 (bs, 1 H, N*H*), 2.59 (s, 3 H, CH_3), 2.97 (dd, ^2J = 13.8 Hz, ^3J = 7.3 Hz, 1 H, CH_2), 3.12 (dd, ^2J = 13.8 Hz, ^3J = 4.0 Hz, 1 H, CH_2), 4.02–4.07 (m, 1 H, CH_2C*H*), 4.85 (d, ^4J = 1.0 Hz, 1 H, NC*H*N), 6.93–6.96 (m, 1 H, H_{ar}), 7.00–7.06 (m, 2 H, 2 × H_{ar}), 7.23–7.26 (m, 1 H, H_{ar}). 7.28–7.36 (m, 5 H, 5 × H_{ar}). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 27.2 (p, NCH_3), 38.6 (s, CH_2), 59.8 (t, CH_2C*H*), 77.2 (t, NCHN), 113.6 (t, dubl, ^2J = 21.9 Hz, $C_{ar'}$-4), 116.3 (t, dubl, ^2J = 21.2 Hz, $C_{ar'}$-2), 122.3 (t, $C_{ar'}$-6), 126.8 (t, C_{ar}H), 128.5 (t, 2 × C_{ar}H), 129.6 (t, 2 × C_{ar}H), 130.8 (t, dubl, ^3J = 8.1 Hz, $C_{ar'}$-5), 137.4 (q, C_{ar}), 142.0 (q, dubl, ^3J = 6.1 Hz, $C_{ar'}$-1), 163.1 (q, dubl, ^1J = 247.9 Hz, $C_{ar'}$-3), 174.1 (q, *C*=O). – ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm = −112.0 (s, *F*). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3324 (s), 3084 (m), 3061 (s), 3029 (s), 2923 (s), 2866 (s), 1951 (w), 1883 (w), 1692 (s), 1614 (m), 1594 (m), 1453 (m), 1400 (m), 1359 (m), 1260 (m), 1139 (m), 1096 (m), 1030 (m), 1003 (m), 970 (m), 948 (m), 945 (m), 789 (m), 741 (m), 700 (w), 639 (w), 607 (w), 581 (w), 522 (w), 488 (w), 454 (w), 429 (w). – EI-MS *m/z* (%): 284 (9) [M^+], 193 (100) [$M^+-C_7H_7$], 138 (32) [$C_8H_9FN^+$]. – EI-HRMS ($C_{17}H_{17}FN_2O$): calcd. 284.1325, found 284.1323. (2*S*,5*S*)-**15c:** 124 mg, 39%. – R_f (*c*-Hex/EtOAc 2:1) = 0.04. – $[\alpha]_D^{20}$ = −91.2 (*c* = 1.00, $CHCl_3$). – ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm = 1.92 (bs, 1 H, N*H*), 2.55 (s, 3 H, CH_3), 3.11 (dd, ^2J = 14.0 Hz, ^3J = 4.6 Hz, 1 H, CH_2), 3.24 (dd, ^2J = 14.0 Hz, ^3J = 5.60 Hz, 1 H, CH_2), 3.86–3.89 (m, 1 H, CH_2C*H*), 5.12 (d, ^4J = 1.0 Hz, 1 H, NC*H*N), 6.43–6.46 (m, 1 H, H_{ar}), 6.66–6.69 (m, 1 H, H_{ar}), 6.98–7.03 (m, 1 H, H_{ar}). 7.20–7.24 (m, 3 H, 3 × H_{ar}), 7.28–7.33 (m, 3 H, 3 × H_{ar}). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 27.3 (p, NCH_3), 36.9 (s, CH_2), 60.2 (t, CH_2C*H*), 76.9 (t, dubl, ^4J = 1.5 Hz, NC*H*N), 113.8 (t, dubl, ^2J = 22.2 Hz, $C_{ar'}$-4), 116.5 (t, dubl, ^2J = 21.2 Hz, $C_{ar'}$-2), 122.9 (t, dubl, ^4J = 2.9 Hz, t, $C_{ar'}$-6), 127.1 (t,

C_{ar}H), 128.8 (t, 2 × C_{ar}H), 129.8 (t, 2 × C_{ar}H), 130.5 (t, dubl, ^3J = 8.1 Hz, $C_{ar'}$-5), 136.5 (q, C_{ar}), 141.2 (q, dubl, ^3J = 6.5 Hz, $C_{ar'}$-1), 163.0 (q, dubl, ^1J = 247.7 Hz, $C_{ar'}$-3), 174.2 (q, *C*=O). – ^{19}F NMR (400 MHz, $CDCl_3$): δ/ppm = −111.6 (s, *F*). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3465 (m), 3339 (m), 3085 (m), 3062 (m), 3029 (m), 2923 (m), 2855 (m), 1689 (m), 1614 (m), 1595 (m), 1548 (w), 1484 (m), 1443 (m), 1402 (m), 1365 (m), 1335 (m), 1262 (m), 1180 (w), 1139 (m), 1098 (m), 1030 (w), 1003 (w), 955 (w), 913 (w), 882 (w), 788 (m), 746 (m), 701 (m), 597 (m), 521 (w), 484 (w), 454 (w), 430 (w). – EI-MS *m/z* (%): 284 (8) [M^+], 193 (100) [M^+−C_7H_7], 43 (52) [$C_2H_3O^+$]. – EI-HRMS ($C_{17}H_{17}FN_2O$): calcd. 284.1325, found 284.1323.

(2*R*,5*S*)-5-Benzyl-2-(4-fluorophenyl)-3-methylimidazolidin-4-one ((2*R*,5*S*)-15d) and (2*S*,5*S*)-5-benzyl-2-(4-fluorophenyl)-3-methylimidazolidin-4-one ((2*S*,5*S*)-15d):



(2*R*,5*S*)-**15d**

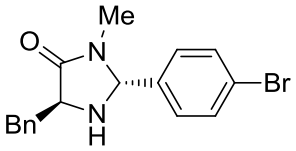


(2*S*,5*S*)-**15d**

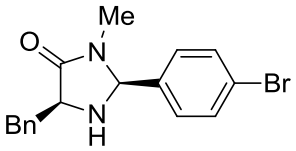
Scale: 1.12 mmol. (2*R*,5*S*)-**15d:** 101 mg, 32%. – R_f (*c*-Hex/EtOAc 1:1) = 0.28. – $[\alpha]_D^{20}$ = −8.98 (*c* = 1.08, $CHCl_3$). – ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm = 2.14 (bs, 1 H, N*H*), 2.58 (s, 3 H, CH_3), 2.98 (dd, ^2J = 13.8 Hz, ^3J = 7.3 Hz, 1 H, CH_2), 3.14 (dd, ^2J = 13.8 Hz, ^3J = 4.0 Hz, 1 H, CH_2), 4.06–4.08 (m, 1 H, CH_2C*H*), 4.85 (d, ^4J = 1.7 Hz, 1 H, NC*H*N), 7.06–7.08 (m, 2 H, 2 × H_{ar}), 7.22–7.28 (m, 3 H, 3 × H_{ar}), 7.30–7.33 (m, 4 H, 4 × H_{ar}). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 27.1 (p, N*C*H_3), 38.7 (s, *C*H_2), 60.0 (t, CH_2*C*H), 77.0 (t, N*C*HN), 116.1 (t, dubl, ^2J = 21.9 Hz, $C_{ar'}$-3, $C_{ar'}$-5), 126.7 (t, C_{ar}H), 128.4 (t, 2 × C_{ar}H), 128.5 (t, dubl, ^3J = 8.6 Hz, $C_{ar'}$-2, $C_{ar'}$-6), 129.6 (t, 2 × C_{ar}H), 135.1 (q, dubl, ^4J = 3.1 Hz, $C_{ar'}$-1), 137.5 (q, C_{ar}), 163.1 (q, dubl, ^1J = 249 Hz, C_{ar}-F), 174.1 (q, *C*=O). – ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm = −112.0 (s, *F*). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3474 (m), 3327 (m), 3062 (m), 3029 (m), 2922 (m), 1695 (s), 1605 (s), 1510 (s), 1479 (m), 1432 (s), 1400 (s), 1357 (m), 1263 (m), 1224 (s), 1157 (m), 1030 (w), 1029 (w), 1014 (w), 998 (w), 841 (m), 743 (w), 702 (w), 555 (w), 502 (w), 488 (w). – EI-MS *m/z* (%): 284 (9) [M^+], 193 (100) [M^+−C_7H_7], 58 (36) [$C_2H_4NO^+$], 43 (99) [$C_2H_3O^+$]. – EI-HRMS ($C_{17}H_{17}FN_2O$): calcd. 284.1325, found 284.1322. (2*S*,5*S*)-**15d:** 139 mg, 43%. – R_f (*c*-Hex/EtOAc 1:1) = 0.10. – $[\alpha]_D^{20}$ = −117 (*c* = 1.12, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.82 (bs, 1 H, N*H*), 2.53 (s, 3 H, CH_3), 3.11 (dd, ^2J = 14.0 Hz, ^3J = 4.7 Hz, 1 H, CH_2), 3.26 (dd, ^2J = 14.0 Hz, ^3J = 5.6 Hz, 1 H, CH_2), 3.86–3.88 (m,

1 H, CH_2CH), 5.12 (d, ^4J = 1.2 Hz, 1 H, NC*H*N), 8.76–8.79 (m, 2 H, 2 × H_{ar}), 8.91–8.95 (m, 2 H, 2 × H_{ar}), 7.21–7.24 (m, 2 H, 2 × H_{ar}), 7.28–7.33 (m, 3 H, 3 × H_{ar}). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 27.2 (p, NCH_3), 36.9 (s, CH_2), 60.3 (t, CH_2CH), 76.8 (t, NCHN), 115.9 (t, dubl, ^2J = 21.7 Hz, $C_{ar'}$-3, $C_{ar'}$-5), 126.9 (t, $C_{ar}H$), 128.8 (t, 2 × $C_{ar}H$), 128.9 (t, dubl, ^3J = 8.9 Hz, $C_{ar'}$-2, $C_{ar'}$-6), 129.8 (t, 2 × $C_{ar}H$), 134.4 (q, dubl, ^4J = 2.5 Hz, $C_{ar'}$-1), 136.7 (q, C_{ar}), 163.2 (q, dubl, ^1J = 249 Hz, C_{ar}-F), 174.2 (q, C=O). – ^{19}F NMR (376 MHz, $CDCl_3$): δ/ppm = −111.8 (s, *F*). – IR (DRIFT): $\tilde{\nu}$/cm^{-1} = 3330 (w), 3062 (w), 2930 (w), 2879 (m), 1926 (w), 1695 (s), 1604 (m), 1509 (m), 1496 (m), 1443 (m), 1400 (m), 1364 (m), 1314 (m), 1299 (m), 1263 (m), 1218 (m), 1163 (m), 1098 (m), 1076 (m), 1002 (m), 936 (w), 923 (w), 875 (m), 793 (m), 763 (w), 742 (m), 702 (m), 641 (w), 604 (m), 566 (m), 553 (m), 504 (m), 485 (w), 432 (w), 422 (w), 412 (w). – EI-MS *m/z* (%): 284 (9) [M^+], 193 (100) [M^+−C_7H_7]. – EI-HRMS ($C_{17}H_{17}FN_2O$): calcd. 284.1325, found 284.1328.

(2*R*,5*S*)-5-Benzyl-2-(4-bromophenyl)-3-methylimidazolidin-4-one ((2*R*,5*S*)-15e) and (2*S*,5*S*)-5-benzyl-2-(4-bromophenyl)-3-methylimidazolidin-4-one ((2*S*,5*S*)-15e):



(2*R*,5*S*)-**15e**

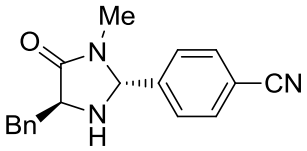


(2*S*,5*S*)-**15e**

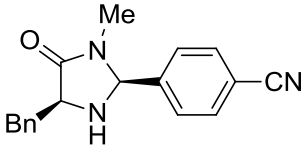
Scale: 1.12 mmol. (2*R*,5*S*)-**15e:** 151 mg, 39%. – R_f (*c*-Hex/EtOAc 3:1) = 0.10. – $[\alpha]_D^{20}$ = 18.5 (*c* = 2.05, $CHCl_3$). – ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm = 2.10 (bs, 1 H, N*H*), 2.56 (s, 3 H, CH_3), 2.97 (dd, ^2J = 13.7 Hz, ^3J = 7.2 Hz, 1 H, CH_2), 3.12 (dd, ^2J = 13.7 Hz, ^3J = 4.1 Hz, 1 H, CH_2), 4.03–4.06 (m, 1 H, CH_2CH), 4.81 (d, ^4J = 1.7 Hz, 1 H, NC*H*N), 7.08–7.12 (m, 2 H, 2 × H_{ar}), 7.22–7.33 (m, 5 H, 5 × H_{ar}), 7.47–7.51 (m, 2 H, 2 × H_{ar}). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 27.1 (p, NCH_3), 38.6 (s, CH_2), 60.0 (t, CH_2CH), 77.1 (t, NCHN), 123.3 (q, C_{ar}-Br), 126.8 (t, $C_{ar}H$), 128.4 (t, 2 × $C_{ar}H$), 128.5 (t, 2 × $C_{ar}H$), 129.6 (t, 2 × $C_{ar}H$), 132.3 (t, 2 × $C_{ar}H$), 137.4 (q, C_{ar}), 138.4 (q, C_{ar}), 174.1 (q, C=O). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3468 (w), 3323 (w), 3084 (w), 3060 (w), 3028 (w), 2921 (w), 1701 (m), 1591 (w), 1484 (m), 1453 (m), 1430 (m), 1399 (m), 1355 (w), 1275 (w), 1092 (w), 1072 (w), 1030 (w), 1010 (w), 824 (w), 750 (w), 487 (w). – EI-MS *m/z* (%): 346/344 (10/9) [M^+], 255/253 (100/57) [M^+−C_7H_7], 200/198 (20/30). – EI-HRMS ($C_{17}H_{17}BrN_2O$): calcd. 344.0524, found 344.0522. (2*S*,5*S*)-**15e:** 174 mg, 45%. – R_f (*c*-Hex/EtOAc 3:1) = 0.03. – $[\alpha]_D^{20}$ = −87.9 (*c* = 0.97, $CHCl_3$). – ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm = 1.86 (bs, 1 H, N*H*), 2.53 (s, 3 H, CH_3),

3.09 (dd, ^2J = 14.0 Hz, ^3J = 4.7 Hz, 1 H, CH_2), 3.26 (dd, ^2J = 14.0 Hz, ^3J = 5.5 Hz, 1 H, CH_2), 3.86–3.89 (m, 1 H, CH_2CH), 5.10 (d, ^4J = 1.1 Hz, 1 H, NC*H*N), 6.64–6.67 (m, 2 H, 2 × H_{ar}), 7.19–7.23 (m, 2 H, 2 × H_{ar}), 7.29–7.33 (m, 3 H, 3 × H_{ar}), 7.36–7.38 (m, 2 H, 2 × H_{ar}). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 27.2 (p, NCH_3), 36.8 (s, CH_2), 60.2 (t, CH_2CH), 76.7 (t, NCHN), 123.5 (q, C_{ar}-Br), 127.0 (t, C_{ar}H), 128.8 (t, 2 × C_{ar}H), 128.9 (t, 2 × C_{ar}H), 129.9 (t, 2 × C_{ar}H), 132.1 (t, 2 × C_{ar}H), 136.6 (q, C_{ar}), 137.6 (q, C_{ar}), 174.1 (q, *C*=O). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3471 (w), 3333 (w), 3085 (w), 3061 (w), 3028 (w), 2921 (w), 2854 (w), 1702 (m), 1591 (w), 1546 (w), 1483 (w), 1425 (w), 1398 (w), 1335 (w), 1294 (w), 1274 (w), 1095 (w), 1073 (w), 1010 (w), 822 (w), 741 (w), 701 (w), 606 (w), 488 (w), 405 (w). – EI-MS *m/z* (%): 346/344 (9/12) [M^+], 255/253 (98/100) [$M^+-C_7H_7$], 200/198 (17/30), 91 (30) [$C_7H_7^+$]. – EI-HRMS ($C_{17}H_{17}BrN_2O$): calcd. 344.0524, found 344.0527.

(2*R*,5*S*)-5-Benzyl-3-methyl-2-(4-cyanophenyl)imidazolidin-4-one ((2*R*,5*S*)-15f) and (2*S*,5*S*)-5-benzyl-3-methyl-2-(4-cyanophenyl)imidazolidin-4-one ((2*S*,5*S*)-15f):



(2*R*,5*S*)-**15f**

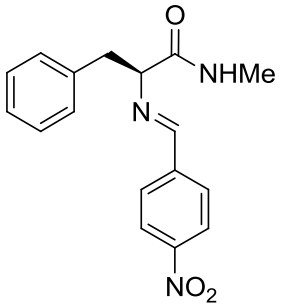


(2*S*,5*S*)-**15f**

Scale: 1.12 mmol. (2*R*,5*S*)-**15f:** 124 mg, 38%. – R_f (*c*-Hex/EtOAc 1:1) = 0.14. – $[\alpha]_D^{20}$ = 27.6 (*c* = 0.99, $CHCl_3$). – ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm = 2.16 (bs, 1 H, N*H*), 2.58 (s, 3 H, CH_3), 3.00 (dd, ^2J = 13.9 Hz, ^3J = 7.0 Hz, 1 H, CH_2), 3.12 (dd, ^2J = 13.9 Hz, ^3J = 4.2 Hz, 1 H, CH_2), 4.02–4.05 (m, 1 H, CH_2CH), 4.89 (d, ^4J = 1.0 Hz, 1 H, NC*H*N), 7.24–7.32 (m, 5 H, 5 × H_{ar}), 7.34–7.36 (m, 2 H, 2 × H_{ar}). 7.66–7.68 (m, 2 H, 2 × H_{ar}). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 27.2 (p, NCH_3), 38.5 (s, CH_2), 60.0 (t, CH_2CH), 76.8 (t, NCHN), 113.2 (q, C_{ar}-CN), 118.1 (q, *C*N), 126.9 (t, C_{ar}H), 127.5 (t, 2 × C_{ar}H), 128.5 (t, 2 × C_{ar}H), 129.5 (t, 2 × C_{ar}H), 132.9 (t, 2 × C_{ar}H), 137.0 (q, C_{ar}), 144.5 (q, C_{ar}), 174.0 (q, *C*=O). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3328 (w), 3086 (w), 3061 (w), 3029 (w), 3003 (w), 2922 (m), 2855 (w), 2229 (m), 1689 (m), 1607 (w), 1496 (m), 1478 (m), 1430 (m), 1400 (m), 1366 (w), 1330 (w), 1276 (w), 1204 (w), 1095 (w), 1030 (w), 1018 (w), 999 (w), 843 (w), 754 (w), 702 (w), 566 (w), 528 (w). – EI-MS *m/z* (%): 291 (7) [M^+], 200 (100) [$M^+-C_7H_7$], 145 (22), 58 (23), 43 (68) [$C_2H_3O^+$]. – EI-HRMS ($C_{18}H_{17}N_3O$): calcd. 291.1372, found 291.1368. (2*S*,5*S*)-**15f:** 149 mg, 46%. – R_f (*c*-Hex/EtOAc 1:1) = 0.05. – $[\alpha]_D^{20}$ = −144 (*c* = 1.04, $CHCl_3$). – ^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm = 2.12 (bs, 1 H, N*H*), 2.53 (s, 3 H, CH_3), 2.95 (dd,

^2J = 13.8 Hz, ^3J = 7.0 Hz, 1 H, CH_2), 3.08 (dd, ^2J = 13.8 Hz, ^3J = 4.2 Hz, 1 H, CH_2), 3.95–4.07 (m, 1 H, CH_2CH), 4.84 (d, ^4J = 1.6 Hz, 1 H, NC*H*N), 7.20–7.26 (m, 5 H, 5 × H_{ar}), 7.29–7.32 (m, 2 H, 2 × H_{ar}). 7.60–7.64 (m, 2 H, 2 × H_{ar}). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 27.3 (p, NCH_3), 37.1 (s, CH_2), 60.1 (t, CH_2CH), 76.6 (t, NCHN), 113.3 (q, C_{ar}-CN), 118.1 (q, *C*N), 126.9 (t, C_{ar}H), 128.0 (t, 2 × C_{ar}H), 128.8 (t, 2 × C_{ar}H), 129.9 (t, 2 × C_{ar}H), 132.7 (t, 2 × C_{ar}H), 136.6 (q, C_{ar}), 144.0 (q, C_{ar}), 173.9 (q, *C*=O). – IR (KBr): ṽ/cm^{-1} = 3347 (w), 3055 (w), 2967 (w), 2933 (w), 2837 (w), 2225 (w), 1951 (w), 1828 (w), 1681 (m), 1608 (w), 1487 (w), 1451 (w), 1338 (w), 1264 (w), 1205 (w), 1153 (w), 1099 (w), 1074 (w), 1005 (w), 936 (w), 908 (w), 848 (w), 811 (w), 780 (w), 450 (w), 731 (w), 698 (w), 645 (w), 616 (w), 573 (w), 533 (w), 511 (w), 482 (w), 453 (w), 433 (w), 411 (w). – EI-MS *m/z* (%): 291 (8) [M^+], 200 (100) [M^+−C_7H_7], 145 (20). – EI-HRMS ($C_{18}H_{17}N_3O$): calcd. 219.1372, found 291.1374.

(S,E)-*N*-methyl-2-((4-nitrobenzylidene)amino)-3-phenylpropanamide (16):

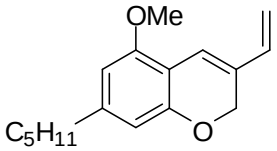


(*S*)-Phenylalanine-*N*-methylamide **13** (714 mg, 4.01 mmol, 1.00 equiv), 4-nitrobenzaldehyde (618 mg, 4.01 mmol, 1.00 equiv), $FeCl_3$ (130 mg, 801 µmol, 0.20 equiv) and molecular sieves (3 Å) were suspended in THF (10 mL) and stirred at room temperature for 3 d. The reaction mixture was filtered and diluted with 10% Na_2CO_3-solution, extracted with dichloromethane (4 × 20 mL) and dried over Na_2SO_4, and the solvent was evaporated.

823 mg, 66%. R_f = 0.40 (*n*-Hex/EtOAc 1:1 + 5% triethylamine). – mp: 150–152 °C. – $[\alpha]_D^{20}$ = 0.87 (*c* = 1.03, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 2.90 (d, ^3J = 4.4 Hz, 3 H, CH_3), 2.97 (dd, ^2J = 13.5 Hz, ^3J = 10.1 Hz, 1 H, CH_2), 3.47 (dd, ^2J = 13.5 Hz, ^3J = 3.1 Hz, 1 H, CH_2), 4.02 (dd, ^3J = 10.1 Hz, ^3J = 3.1 Hz, 1 H, C*H*-CH_2), 6.82–6.87 (m, 1 H, N*H*), 7.05 (d, ^4J = 1.4 Hz, 1 H, 2-H_{ar}), 7.07 (d, ^4J = 1.9 Hz, 1 H, 6-H_{ar}), 7.14–7.23 (m, 3 H, 3-H_{ar}, 4-H_{ar}, 5-H_{ar}), 7.57 (s, 1 H, C*H*=N), 7.75 (d, ^3J = 8.8 Hz, 2 H, 2-$H_{ar'}$, 6-$H_{ar'}$), 8.24 (d, ^3J = 8.8 Hz, 2 H, 3-$H_{ar'}$, 5-$H_{ar'}$). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 26.0 (p, CH_3), 41.1 (s, CH_2), 75.4 (t, *C*H-CH_2), 123.9 (t, $C_{ar'}$-3, $C_{ar'}$-5), 126.7 (t, C_{ar}-4), 128.3 (t, C_{ar}-2, C_{ar}-6), 128.8 (t, C_{ar}-3, C_{ar}-5), 130.0 (t, $C_{ar'}$-2, $C_{ar'}$-6), 137.1 (q, C_{ar}-1), 140.5 (q, $C_{ar'}$-1), 149.3 (q, $C_{ar'}$-4), 160.3 (t, *C*H=N), 172.1 (q, *C*=O). – IR (DRIFT): ṽ/cm^{-1} = 3237 (w), 3078 (w), 2950 (w), 1825 (w), 2882 (w), 1652 (m), 1600 (m), 1571 (m), 1520 (s), 1494 (w), 1454 (w), 1415 (w), 1384 (w),

1351 (s), 1291 (w), 1233 (w), 1149 (w), 1107 (w), 4087 (w), 4043 (w), 1005 (w), 987 (w), 929 (w), 852 (m), 832 (w), 775 (w), 753 (w), 735 (w), 704 (m), 691 (w), 673 (w), 585 (w), 524 (w), 507 (w), 490 (w). – EI-MS (70 eV) *m/z* (%): 311 (10) [M^+], 253 (100) [$C_{16}H_{17}N_2O^+$], 220 (33) [$M^+-C_7H_7$], 163 (99) [$C_{10}H_{12}NO^+$], 91 (37) [$C_7H_7^+$]. – EI-HRMS ($C_{17}H_{17}N_3O_3$): calcd. 311.1268, found 311.1270. – $C_{17}H_{17}N_3O_3$ (311.1): calcd. C 65.58, H 5.50, N 13.50, found. C 65.01, H 5.28, N 13.77.

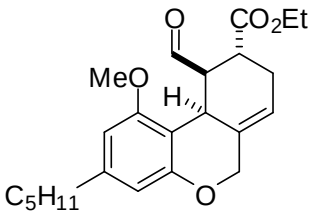
5-Methoxy-7-pentyl-3-vinyl-2*H*-chromene (17):



Methyltriphenylphosphonium bromide (1.68 g, 4.61 mmol, 2.00 equiv) in THF (45 mL) was cooled to −78 °C and *n*-BuLi (1.48 mL, 3.69 mmol, 1.60 equiv, 2.5 M in *n*-hexane) was added slowly. It was stirred for 30 min at −78 °C before it was warmed to 0 °C. After being stirred for 30 min the suspension of the Wittig reagent was cooled again to −78 °C and 5-methoxy-7-pentyl-2*H*-chromene-3-carbaldehyde (600 mg, 2.30 mmol, 1.00 equiv) in THF (6 mL) was added. The suspension was stirred for 30 min at −78 °C and 30 min at room temperature. After that, ethanol (1.5 mL) was added, the solvent was removed, and the product was purified by flash column chromatography (*c*-Hex/EtOAc 50:1).

533 mg, 90%. R_f = 0.40 (*c*-Hex/EtOAc 50:1). – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 0.89 (t, ^3J = 7.0 Hz, 3 H, CH_3), 1.31–1.34 (m, 4 H, CH_2), 1.58–1.61 (m, 2 H, CH_2), 2.52 (t, ^3J = 7.7 Hz, 2 H, CH_2), 3.83 (s, 3 H, OCH_3), 4.89 (s, 2 H, O-CH_2), 5.05 (d, $^3J_{trans}$ = 17.8 Hz, 1 H, CH=C$H_{2,trans}$), 5.10 (d, $^3J_{cis}$ = 11.0 Hz, 1 H, CH=C$H_{2,cis}$), 6.26 (s, 1 H, H_{ar}), 6.33 (s, 1 H, H_{ar}), 6.47 (dd, $^3J_{trans}$ = 17.8 Hz, $^3J_{cis}$ = 11.0 Hz, 1 H, CH=C$H_{2,trans}$), 6.70 (s, 1 H, CH). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 14.0 (p, CH$_3$), 22.5 (s, CH$_2$), 30.8 (s, CH$_2$), 31.5 (s, CH$_2$), 36.85 (s, CH$_2$), 55.6 (p, OCH$_3$), 64.8 (s, O-CH$_2$), 103.9 (t, C_{ar}H), 108.4 (t, C_{ar}H), 109.6 (q, C_{ar}-CH), 112.0 (s, CH=CH$_2$), 118.7 (t, C_{ar}-CH), 128.1 (q, C-CH), 135.2 (t, CH=CH$_2$), 145.0 (q, C_{ar}-CH$_2$), 154.4 (q, C_{ar}-O), 155.4 (q, C_{ar}-OCH$_3$). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 2955 (m), 2930 (m), 2855 (w), 1630 (w), 1612 (m), 1600 (m), 1568 (m), 1462 (m), 1428 (w), 1390 (w), 1361 (w), 1288 (w), 1227 (w), 1190 (m), 1144 (w), 1111 (m), 1056 (w), 1024 (w), 985 (w), 944 (w), 884 (w), 820 (w). – EI-MS *m/z* (%): 259 (17) [M^++H], 258 (100) [M^+], 202 (23), 201 (25) [$C_{13}H_{13}O_2^+$], 69 (21), 43 (57) [$C_3H_7^+$]. – EI-HRMS ($C_{17}H_{22}O_2$): calcd. 258.1620, found 258.1617. – $C_{17}H_{22}O_2$ (258.2): calcd. C 79.03, H 8.58, found C 79.16, H 8.20.

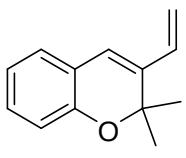
Ethyl 10-formyl-1-methoxy-3-pentyl-8,9,10,10a-tetrahydro-6*H*-benzo[*c*]chromene-9-carboxylate (19):



(*E*)-Ethyl-4-oxobut-2-enoate (**18**, 25.8 mg, 194 µmol, 1.00 equiv) was added to a solution of 1,3-bis(3,5-bis-(trifluoromethyl)phenyl)thiourea (19.4 mg, 38.7 µmol, 0.20 equiv) in CH_2Cl_2 (1 mL). It was stirred for 5 min, before 5-methoxy-7-pentyl-3-vinyl-2*H*-chromene (**17**, 50.0 mg, 194 µmol, 1.00 equiv), dissolved in methanol (1 mL), was added. The resulting mixture was stirred for 2 d at rt. For workup, the reaction mixture was diluted with Et_2O (2 mL), and the organic phase was washed with brine (5 mL) and dried over sodium sulfate. The solvent was removed under reduced pressure and the product was purified by flash column chromatography (*c*-Hex/EtOAc 30:1).

30.4 mg, 41%. R_f (*c*-Hex/EtOAc 30:1) = 0.09. – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 0.89 (t, ^3J = 6.9 Hz, 3 H, CH_2-CH_2-CH_3), 1.29–1.36 (m, 3 H, CH_2), 1.33 (t, ^3J = 7.1 Hz, 3 H, O-CH_2-CH_3), 1.56–1.64 (m, 3 H, CH_2), 2.24–2.33 (m, 1 H, 8-*H*), 2.53 (t, ^3J = 7.7 Hz, 2 H, CH_2-CH_2-C_{ar}), 2.57–2.65 (m, 1 H, 8-*H*), 3.41 (dd, ^3J = 7.5 Hz, ^4J = 2.7 Hz, 1 H, 9-*H*), 3.80–3.82 (m, 1 H, 10a-*H*), 3.83 (s, 3 H, OCH_3), 3.89 (dd, ^3J = 4.8 Hz, ^4J = 2.7 Hz, 1 H, 10-*H*), 4.13–4.21 (m, 1 H, 6-*H*), 4.29–4.34 (m, 1 H, 6-*H*), 4.33 (q, ^3J = 7.1 Hz, 2 H, O-CH_2-CH_3), 5.75–5.78 (m, 1 H, 7-*H*), 6.33 (d, ^4J = 1.3 Hz, 1 H, H_{ar}), 6.38 (d, ^4J = 1.3 Hz, 1 H, H_{ar}), 9.19 (s, 1 H, C*H*O). – ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 14.0 (p, CH_2-CH_2-*C*H_3), 14.3 (p, O-CH_2-*C*H_3), 22.5 (s, *C*H_2), 22.7 (s, *C*-8), 30.1 (t, *C*-10a), 30.8 (s, *C*H_2), 31.5 (s, *C*H_2), 36.0 (s, *C*H_2), 38.4 (t, *C*-9), 48.3 (t, *C*-10), 55.3 (p, O*C*H_3), 60.9 (s, O-CH_2), 70.4 (s, *C*-6), 103.9 (t, *C*-4), 108.3 (q, *C*-10b), 110.1 (t, *C*-2), 125.2 (t, *C*-7), 132.0 (q, *C*-6a), 143.7 (q, *C*-3), 157.8 (q, *C*-4a), 157.9 (q, *C*-1), 174.5 (q, *C*$O_2CH_2CH_3$), 202.8 (t, *C*HO). – IR (KBr): ṽ/cm^{-1} = 2931 (m), 2856 (w), 1719 (s), 1616 (m), 1578 (m), 1459 (m), 1425 (m), 1376 (w), 1329 (w), 1289 (w), 1198 (m), 1167 (m), 1109 (m), 1037 (m), 925 (w), 828 (w). – EI-MS *m/z* (%): 387 (24) [M^++H], 386 (100) [M^+], 313 (65) [M^+−$CO_2C_2H_5$], 283 (45) [M^+−$CO_2C_2H_5$−OCH_3]. – EI-HRMS ($C_{23}H_{30}O_5$): calcd. 386.2093, found 386.2091.

2,2-Dimethyl-3-vinyl-2*H*-chromene (20):

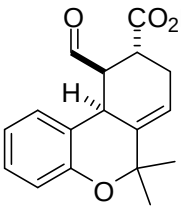


Methyltriphenylphosphoniumbromide (3.15 g, 8.65 mmol, 2.00 equiv) in THF (40 mL) was cooled to −78 °C and *n*-BuLi (1.48 mL, 3.69 mmol, 1.60 equiv, 2.5 M in *n*-hexane) was added

slowly. It was stirred for 30 min at −78 °C before it was warmed to 0 °C. After being stirred for 30 min the suspension of the Wittig reagent was cooled again to −78 °C and 2,2-dimethyl-2*H*-chromene-3-carbaldehyde (970 mg, 4.33 mmol, 1.00 equiv) in THF (10 mL) was added. The suspension was stirred for 30 min at −78 °C and 30 min at room temperature. After that, ethanol (5 mL) was added, the solvent was removed, and the product was purified by flash column chromatography (*c*-Hex/EtOAc 50:1).

858 mg, 80%. R_f = 0.37 (*n*-Hex/EtOAc 50:1). – ^{1}H NMR (250 MHz, $CDCl_3$): δ/ppm = 1.41 (s, 6 H, 2 × CH_3), 5.06 (dd, $^3J_{cis}$ = 11.0 Hz, ^5J = 1.5 Hz, 1 H, CH-C$H_{2,\ cis}$), 5.46 (dd, $^3J_{trans}$ = 17.3 Hz, ^5J = 1.5 Hz, 1 H, CH-C$H_{2,\ trans}$), 6.18 (ddd, $^3J_{trans}$ = 17.3 Hz, $^3J_{cis}$ = 11.0 Hz, ^4J = 1.0 Hz, 1 H, C*H*-CH_2), 6.37 (s, 1 H, C*H*), 6.70 (d, ^3J = 7.9 Hz, 1 H, 5-H_{ar}), 6.78 (dd, ^3J = 7.5 Hz, ^4J = 1.2 Hz, 1 H, 7-H_{ar}), 6.92 (dd, ^3J = 7.5 Hz, ^4J = 1.8 Hz, 1 H, 8-H_{ar}), 7.00 (dd, ^3J = 7.9 Hz, ^4J = 1.8 Hz, 1 H, 6-H_{ar}).

Ethyl 10-formyl-6,6-dimethyl-8,9,10,10a-tetrahydro-6*H*-benzo[*c*]chromene-9-carboxylate (21)

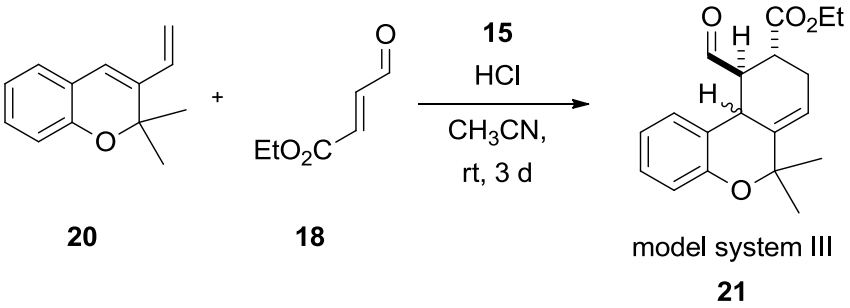


(*E*)-Ethyl-4-oxobut-2-enoate (**18**, 2.26 mL, 2.41 g, 18.8 mmol, 1.00 equiv) was added to a solution of diene **20** (3.50 g, 18.8 mmol, 1.00 equiv) in CH_2Cl_2 (60 mL) and the solution was stirred overnight at rt. After evaporation of the solvent, the crude product was purified by flash column chromatography (*c*-Hex/EtOAc 30:1).

R_f (*c*-Hex/EtOAc 5:1) = 0.40. – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 1.24 (s, 3 H, 6-CH_3), 1.25 (t, ^3J = 7.1 Hz, 3 H, $CO_2CH_2CH_3$), 1.49 (s, 3 H, 6-CH_3), 2.21 (m_c, 1 H, 8-H_A), 2.58 (ddd, ^2J = 19.2 Hz, $^3J_{8,9}$ = 3.1 Hz, $^3J_{8,7}$ = 3.1 Hz, 1 H, 8-H_B), 3.29 (dd, $^3J_{9,8}$ = 7.1 Hz, $^3J_{9,10}$ = 2.9 Hz, 1 H, 9-H), 3.45 (dd, $^3J_{10,10a}$ = 4.9 Hz, $^3J_{10,9}$ = 2.9 Hz, 1 H, 10-H), 3.76 (m_c, 1 H, 10a-H), 4.18 (m_c, 2 H, $CO_2CH_2CH_3$), 5.70 (dd, $^3J_{7,8A}$ = 7.1 Hz, $^3J_{7,8B}$ = 3.1 Hz, 1 H, 7-H), 6.78 (dd, $^3J_{4,3}$ = 8.1 Hz, $^4J_{4,2}$ = 1.1 Hz, 1 H, 4-H), 6.89 (dd, $^3J_{2,1}$ = 7.6 Hz, $^3J_{2,3}$ = 7.4 Hz, 1 H, 2-H), 7.09 (ddd, $^3J_{3,4}$ = 8.1 Hz, $^3J_{3,2}$ = 7.4 Hz, $^4J_{3,1}$ = 1.5 Hz, 1 H, 3-H), 7.16 (d, $^3J_{1,2}$ = 7.6 Hz, 1 H, 1-H), 9.07 (s, 1 H, C*H*O). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.3 (p, CH_2CH_3), 22.9 (s, C-8), 25.6 (p, 6-CH_3), 25.9 (p, 6-CH_3), 30.7 (t, C-10a), 37.9 (t, C-9), 51.0 (t, C-10), 61.1 (s, CH_2CH_3), 76.2 (q, C-6), 118.1 (t, C-4), 120.0 (t, C-7), 121.2 (t, C-2), 122.0 (q, C-10b), 127.3 (t, C-3), 128.1 (t, C-1), 137.0 (q, C-6a), 154.0 (q, C-4a), 173.9 (q, CO_2Et), 202.5 (t, CHO). – IR (KBr): ṽ/cm^{-1} = 3062 (w), 2981 (m), 2934 (m), 2907 (m), 2836 (m), 2737

(w), 1722 (s), 1608 (w), 1584 (m), 1487 (s), 1455 (s), 1384 (m), 1367 (m), 1340 (w), 1305 (m), 1261 (s), 1239 (s), 1190 (s), 1140 (s), 1094 (m), 1052 (m), 1034 (m), 939 (m), 912 (w), 890 (w), 862 (w), 817 (w), 757 (s), 702 (w), 527 (w). – EI-MS (70 eV): *m/z* (%) = 315 (4) [M^++H], 314 (19) [M^+], 300 (17) [M^++H−CH_3], 299 (49) [M^+−CH_3], 226 (16), 225 (100), 197 (15), 43 (19). – EI-HRMS ($C_{12}H_{12}O_2$): calcd. 314.1518, found 314.1517. – $C_{19}H_{22}O_4$ (314.2): calcd. C 72.09, H 7.05, found C 72.42, H 7.09.

We also tested imidazolidinone catalysts **15** on a model system **20** without the pentyl chain, but bearing two geminal methyl groups, also typical for the THC scaffolds.



Scheme S1: Catalyst screening on model system III.

Table S1: Summarized results of catalyst screening on model system **20**.

Entry	Catalyst		*cis*-**21**	
			Yield [%]	ee [%]
1	*t*-Bu	(2*R*,5*S*)-**15a**	19	−41
2		(2*S*,5*S*)-**15a**	14	−73
3	*o*-NO_2-C_6H_4	(2*R*,5*S*)-**15b**	21	n.d.
4		(2*S*,5*S*)-**15b**	n.d.	−13
5	*m*-F-C_6H_4	(2*R*,5*S*)-**15c**	22	−7
6		(2*S*,5*S*)-**15c**	27	−4
7	*p*-F-C_6H_4	(2*R*,5*S*)-**15d**	18	−31
8		(2*S*,5*S*)-**15d**	27	−4
9	*p*-CN-C_6H_4	(2*R*,5*S*)-**15e**	16	−53
10		(2*S*,5*S*)-**15e**	21	−4
11	$(CH_3)_2$	(5*R*)-**15g**	30	+59

References

1. Yan, Z.; Cai, X.; Yang, X.; Song, B.; Chen, Z.; Bhadury, S. P.; Hu, D.; Jin, L.; Xue, W.; Lu, P. *Chin. J. Chem.* **2009,** *27,* 593–601. doi:10.1002/cjoc.200990097
2. Hernández-Rodríguez, M.; Avila-Ortiz, C. G.; del Campo, J. M.; Hernández-Romero, D.; Rosales-Hoz, M. J.; Juaristi, E. *Aust. J. Chem.* **2008,** *61,* 364–375. doi:10.1071/CH08116
3. Breuzard, J. A. J.; Tommasino, M. L.; Touchard, F.; Lemaire, M.; Bonnet, M. C. *J. Mol. Catal. A: Chem.* **2000,** *156,* 223–232. doi:10.1016/S1381-1169(99)00401-X
4. Sibi, M. P.; Itoh, K. *J. Am. Chem. Soc.* **2007,** *129,* 8064–8065. doi:10.1021/ja071739c
5. MacMillan, D. W. C. Enantioselective transformations of α,β-unsaturated aldehydes by a wide variety of reactions using imidazolidinone enantiomers as chiral organic catalysts. Patent WO 2003002491, January, 9, 2003.