Structural optimization of thiourea-based bifunctional organocatalysts for the highly enantioselective dynamic kinetic resolution of azlactones

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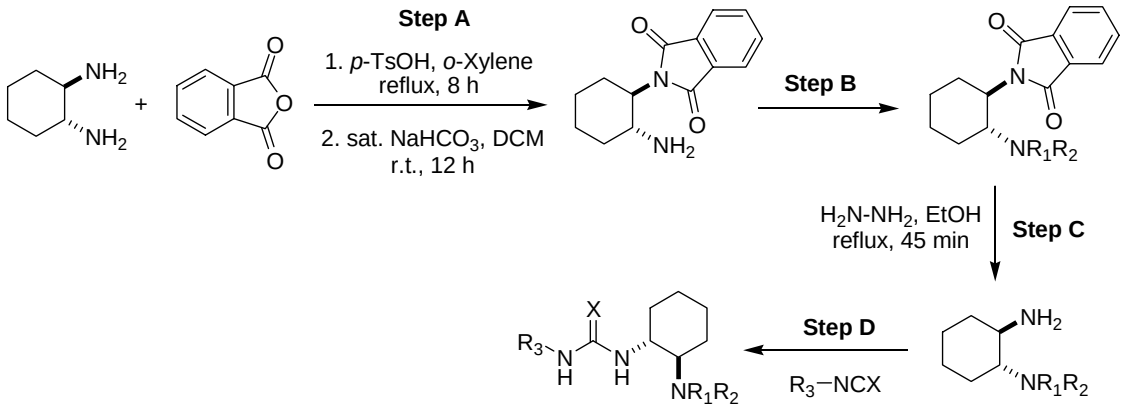
Supporting Information

General Procedures. All reactions were carried out in oven-dried or flame-dried round bottom flasks and the reactions were conducted under a positive pressure of argon, unless otherwise stated. Stainless steel syringes or cannulae were used to transfer air- and/or moisture-sensitive liquids. Chromatographic separations were performed using silica gel 60 (230-400 mesh) from MN GmbH & Co.

Materials. Commercial reagents were purchased from Sigma Aldrich, Fluka, Acros, Lancaster or NovaBioChem, and used as received. Solvents were distilled and dried prior to use following the standard procedure.[1]

Instrumentation. Nuclear magnetic resonance (^{1}H and ^{13}C) spectra were recorded on Bruker AC250 (250 MHz), Bruker AC300 (300 MHz), Bruker DPX300 (300 MHz) or Bruker DRX500 (500 MHz) NMR spectrometer. FT-IR spectra were recorded on a Perkin-Elmer 1600 Series FTIR or Perkin-Elmer Paragon 1000 FT-IR spectrometer with ATR technique. HPLC analyses were performed using Agilent 1100 Series or Merck Hitachi LaChrom HPLC instrument. Melting points were measured on a Büchi 535 Melting Point apparatus and are uncorrected. HRMS data were recorded on a Finnigan MAT 900S instrument (Δmu = 5). Optical rotations were measured using a 1 mL cell with a 1 dm path length on a Perkin-Elmer 343plus polarimeter at 20 °C.

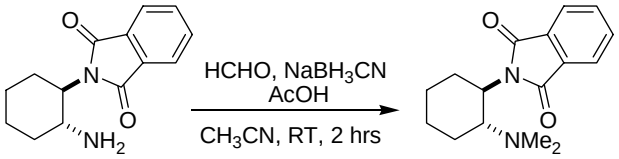
Synthesis of bifunctional catalysts 1a-g, **16-29**



Step A: Monoprotection of *trans*-1,2-diaminocyclohexane was carried out following the literature procedure of *Kaik* and *Gawronski*.[2]

Step B: Dialkylation of (1*R*,2*R*)-*N*-phthaloyl-1,2-diaminocyclohexane.

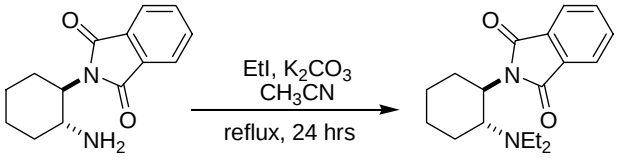
- (1*R*,2*R*)-*N*,*N*-Dimethyl-*N*′-phthaloyl-1,2-diaminocyclohexane:



To a solution of (1*R*,2*R*)-*N*-phthaloyl-1,2-diaminocyclohexane (3.28 g, 13.43 mmol) in 85 mL of acetonitrile, formaldehyde (2.02 g, 67.15 mmol) was added and the resulting mixture was stirred for 15 minutes at room temperature. $NaBH_3CN$ (1.69 g, 26.86 mmol) was then added, followed 15 minutes later by AcOH (3.9 mL, 67.15 mmol). After stirring 2 hours at room temperature, the reaction mixture was diluted with 2% CH_3OH-$CHCl_3$ (200 mL), washed with 1N NaOH (3 × 150 mL). The aqueous layer was re-extracted with $CHCl_3$ (2 × 150 mL), the combined organic layer was dried over anh. $MgSO_4$ and the solvent was removed in vacuo to obtain a yellowish white crystalline solid. This was dissolved in diethylether and the residue was filtered off. The filtrate was concentrated in vacuo to obtain pure (1*R*,2*R*)-*N*,*N*-dimethyl-*N*′-phthaloyl-1,2-diaminocyclohexane as a pale yellow crystalline solid (3.29 g, 12.08 mmol, 90% yield). mp = 124-126 °C [Lit.[2] 117-120 °C]. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.06-1.38 (m; 3H), 1.73-1.91 (m; 5H), 2.12 (s; 6H), 3.26 (dt, *J* = 3.6, 11.4 Hz; 1H), 4.07 (dt, *J* = 3.6, 11.6 Hz; 1H), 7.60-7.66 (m; 2H), 7.73-7.79 (m; 2H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 22.6, 25.0, 25.7, 30.2, 40.2, 52.2, 62.0, 122.9, 132.2, 133.5, 168.6. FT-IR (CsI): $\tilde{\nu}$ [cm^{-1}] = 3454

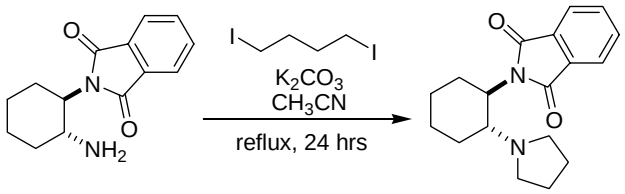
(w), 2932 (m), 2864 (w), 2830 (w), 2784 (w), 1763 (m), 1701 (s), 1611 (m), 1471 (m), 1453 (m), 1390 (s), 1372 (m), 1332 (w), 1273 (w), 1195 (w), 1141 (s), 1082 (s), 1067 (w), 1046 (m), 1018 (w), 956 (w), 906 (w), 872 (m), 848 (w), 826 (w), 794 (w), 719 (s), 640 (m). HRMS (EI): Calcd. for [$C_{16}H_{20}N_2O_2$] ([M]$^+$): 272.153 Found: 272.152.

- (1*R*,2*R*)-*N*,*N*-Diethyl-*N*′-phthaloyl-1,2-diaminocyclohexane:



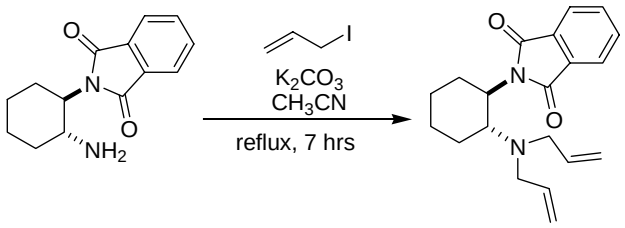
To a solution of (1*R*,2*R*)-*N*-phthaloyl-1,2-diaminocyclohexane (1.0 g, 4.1 mmol) in 20 mL abs. CH_3CN and K_2CO_3 (1.3 g, 9.4 mmol) was added ethyl iodide (1.34 g, 8.6 mmol) and the resulting mixture was heated to reflux for 24 hours. The reaction mixture was cooled to ambient temperature and the solvent was removed in vacuo. The residue was dissolved in dichloromethane (20 mL) and water (20 mL); the organic layer was separated and the aqueous layer (pH ~10) was extracted with dichloromethane (3 × 15 mL). The combined organic layer was dried over anh. Na_2CO_3 and the solvent was removed in vacuo to obtain pure (1*R*,2*R*)-*N*,*N*-diethyl-*N*′-phthaloyl-1,2-diaminocyclohexane as an off-white crystalline solid (1.21 g, 4.03 mmol, 98.5% yield). mp 132-133 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.73 (t, *J* = 7.05 Hz; 6H), 1.11-1.39 (m; 3H), 1.75-1.91 (m; 4H), 2.17-2.38 (m; 3H), 2.41-2.50 (m; 2H), 3.27 (dt, *J* = 3.71, 11.57 Hz; 1H), 4.10 (dt, *J* = 3.71, 11.24 Hz; 1H), 7.62-7.67 (m; 2H), 7.74-7.80 (m; 2H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 14.6, 24.7, 25.5, 25.9, 29.8, 43.0, 52.4, 59.0, 122.8, 132.2, 133.5, 168.8. FT-IR (CsI): $\tilde{\nu}$ [cm^{-1}] = 3456 (w), 2974 (m), 2932 (m), 2870 (w), 2813 (w), 1764 (m), 1704 (s), 1614 (w), 1468 (m), 1395 (s), 1376 (s), 1335 (w), 1298 (w), 1255 (w), 1209 (w), 1144 (m), 1112 (m), 1087 (m), 1066 (w), 1024 (m), 956 (w), 904 (m), 871 (w), 844 (w), 796 (m), 718 (s), 642 (m). HRMS (EI): Calcd. for [$C_{18}H_{24}N_2O_2$] ([M]$^+$): 300.184 Found: 300.183.

- 2-{(1*R*,2*R*)-2-(Pyrrolidin-1-yl)cyclohexyl}isoindoline-1,3-dione:



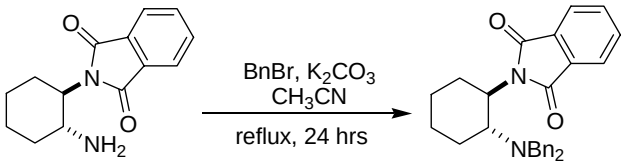
The general procedure described above was followed on the same scale. Product contaminated with unreacted 1,4-diiodo-butane was obtained as a thick yellow liquid which solidified on standing at room temperature. Unreacted 1,4-diiodo-butane was removed by drying in high vacuum (10^{-5} mbar) at 60°C to obtain pure product as a yellow solid (1.21 g, 4.06 mmol, 99% yield). mp 93-95 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.19-1.38 (m; 3H), 1.42-1.55 (m; 4H), 1.78-1.94 (m; 4H), 2.13-2.27 (m; 1H), 2.46-2.60 (m; 4H), 3.50-3.57 (m; 1H), 4.09 (dt, *J* = 3.90, 11.72 Hz; 1H), 7.62-7.69 (m; 2H), 7.74-7.82 (m; 2H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 23.8, 23.9, 25.1, 25.8, 30.2, 47.3, 53.6, 57.7, 122.9, 132.2, 133.5, 168.7. FT-IR (CsI): $\tilde{\nu}$ [cm^{-1}] = 3452 (w), 2932 (s), 2856 (m), 2802 (w), 1764 (s), 1699 (s), 1612 (w), 1467 (m), 1389 (s), 1370 (s), 1332 (m), 1284 (w), 1116 (m), 1077 (s), 1017 (m), 1002 (w), 957 (w), 903 (m), 870 (m), 796 (w), 718 (s), 639 (m). HRMS (EI): Calcd. for [$C_{18}H_{22}N_2O_2$] ([M]$^+$): 298.168 Found: 298.168.

- (1*R*,2*R*)-*N*,*N*-Diallyl-*N*'-phthaloyl-1,2-diaminocyclohexane:



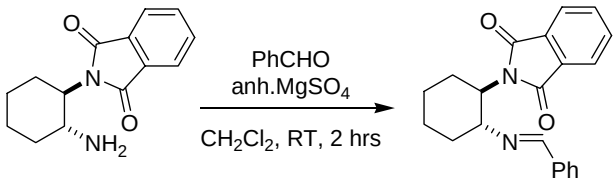
The general procedure described above was followed on a 2.50 mmol scale. Product was obtained as a pale brown solid (410 mg, 1.27 mmol, 51% yield). mp 83-85 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.14-1.36 (m; 3H), 1.79-1.98 (m; 4H), 2.23-2.43 (m; 1H), 2.78 (m; 2H), 3.16-3.19 (m; 1H), 3.22-3.25 (m; 1H), 3.37 (m; 1H), 4.14 (m; 1H), 4.89-5.00 (m; 4H), 5.29-5.55 (m; 2H), 7.67-7.72 (m; 2H), 7.78-7.83 (m; 2H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 24.6, 25.2, 25.8, 29.8, 52.2, 52.5, 58.5, 100.8, 116.0, 122.8, 133.6, 137.4, 168.6. FT-IR (CsI): $\tilde{\nu}$ [cm^{-1}] = 3074 (w), 2928 (m), 2855 (w), 2807 (w), 1765 (m), 1704 (s), 1466 (w), 1446 (w), 1416 (w), 1389 (s), 1369 (s), 1115 (w), 1021 (w), 994 (w), 915 (w), 869 (w), 846 (w), 717 (s).

- (1*R*,2*R*)-*N*,*N*-Dibenzyl-*N*'-phthaloyl-1,2-diaminocyclohexane:



The general procedure described above was followed on a 1.86 mmol scale. Product was obtained as a pale brown solid (690 mg, 1.63 mmol, 87% yield). mp 120-122 °C [Lit.[2] 123-127 °C]. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.22-1.40 (m; 3H), 1.78-1.87 (m; 5H), 2.15-2.32 (m; 2H), 3.28-3.37 (m; 1H), 3.33 (d, *J* = 13.4 Hz, 2H), 3.75 (d, *J* = 13.4 Hz; 2H), 4.30 (dt, *J* = 3.7, 11.7 Hz; 1H), 7.00-7.03 (m; 4H), 7.07-7.15 (m; 4H), 7.72-7.88 (m; 4H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 24.3, 25.2, 25.8, 29.5, 51.4, 53.3, 57.7, 122.9, 126.6, 127.9, 128.9, 130.4, 133.6, 139.8), 165.3. FT-IR (CsI): [cm^{-1}] =3059 (w), 3024 (w), 2928 (m), 2855 (w), 2802 (w), 1766 (m), 1705 (vs), 1610 (w), 1492 (m), 1465 (m), 1452 (m), 1386 (s), 1369 (s), 1330 (m), 1103 (m), 1075 (m), 1019 (m), 904 (w), 870 (w), 848 (w), 747 (m), 718 (s), 698 (s), 637 (w).

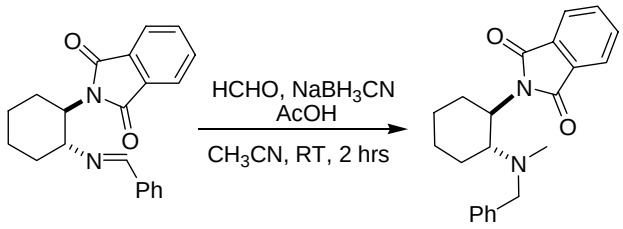
- 2-{(1*R*,2*R*)-2-(*N*-Benzyl-*N*-methylamino)cyclohexyl}isoindoline-1,3-dione:



A solution of (1*R*,2*R*)-*N*-phthaloyl-1,2-diaminocyclohexane (1.0 g, 4.09 mmol) in 25 mL of abs. dichloromethane was stirred with anh. $MgSO_4$ (985 mg, 8.18 mmol) and benzaldehyde (434 mg, 4.09 mmol) for 2 hours at room temperature. $MgSO_4$ was then filtered off and the solvent was removed in vacuo to obtain pure 2-{(1*R*,2*R*)-2-(benzylideneamino)cyclohexyl}isoindoline-1,3-dione as an off-white crystalline solid (1.32 g, 3.97 mmol, 97% yield). mp 135-136 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.47-1.61 (m; 2H), 1.71-1.92 (m; 5H), 2.22-2.36 (m; 1H), 4.08 (dt, *J* = 4.41, 9.68 Hz; 1H), 4.45 (dt, *J* = 3.81, 9.68 Hz; 1H), 7.24-7.34 (m; 3H), 7.49-7.63 (m; 4H), 7.70-7.80 (m; 2H), 8.21 (s; 1H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 24.1, 25.5 28.7, 34.1, 55.6, 69.3, 122.9, 128.0, 128.3, 130.4, 131.7, 133.6, 136.1, 160.7, 168.4. FT-IR (KBr) $\tilde{\nu}$ [cm^{-1}] = 3459 (w), 3063 (w), 3029 (w), 2943 (m), 2920 (s), 2851 (s), 1768 (s), 1703 (s), 1649 (s), 1582 (w), 1450 (m), 1392 (s), 1371 (s), 1330 (w), 1250 (w), 1170 (m), 1155 (m), 1098 (s), 1075 (m), 1045 (m), 1016 (m), 967 (w), 944

(w), 909 (m), 870 (m), 858 (w), 836 (m), 788 (m), 752 (s), 716 (s), 692 (s), 639 (m). HRMS (EI): Calcd. for [$C_{21}H_{20}N_2O_2$] ([M]$^+$): 332.153 Found: 332.152.

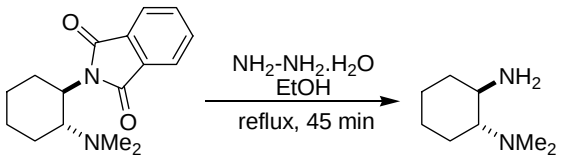
- 2-{(1*R*,2*R*)-2-(*N*-benzyl-*N*-methylamino)cyclohexyl}isoindoline-1,3-dione:



To a solution of 2-{(1*R*,2*R*)-2-(benzylideneamino)cyclohexyl}isoindoline-1,3-dione (500 mg, 1.5 mmol) in 25 mL of acetonitrile, $NaBH_3CN$ (189 mg, 3.0 mmol) was added and the resulting mixture was stirred for 15 minutes at room temperature. Formaldehyde (90 mg, 3.0 mmol) was then added, followed 15 minutes later by AcOH (0.35 mL, 6.0 mmol). After stirring the mixture for 2 hours at room temperature, the reaction mixture was diluted with 2% CH_3OH-$CHCl_3$ (25 mL), washed with 1N NaOH (3 × 50 mL). The aqueous layer was re-extracted with $CHCl_3$ (3 × 50 mL). The combined organic layer was dried over anh. $MgSO_4$ and the solvent was removed in vacuo to obtain a yellowish white semisolid. This was taken in diethylether and the white residue was filtered off. The filtrate was concentrated in vacuo to obtain pure 2-{(1*R*,2*R*)-2-(*N*-benzyl-*N*-methylamino)cyclohexyl}isoindoline-1,3-dione as a thick yellowish liquid (512 mg, 1.47 mmol, 98% yield). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.25-1.44 (m; 3H), 1.78-1.89 (m; 3H), 1.98-2.02 (m; 1H), 2.04 (s; 3H), 2.20-2.33 (m; 1H), 3.38-3.47 (m; 1H), 3.42 (d, *J* = 13.3 Hz; 1H), 3.57 (d, *J* = 13.3 Hz; 1H), 4.20 (dt, *J* = 3.85, 11.6 Hz; 1H), 6.87-7.07 (m; 5H), 7.65-7.71 (m; 2H), 7.77-7.82 (m; 2H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 24.1, 25.2, 25.7, 30.0, 36.0, 52.2, 58.3, 62.2, 122.9, 126.3, 127.7, 128.1, 132.1, 133.5, 134.0, 168.6. HRMS (EI): Calcd. for [$C_{22}H_{24}N_2O_2$] ([M]$^+$): 348.184 Found: 348.184.

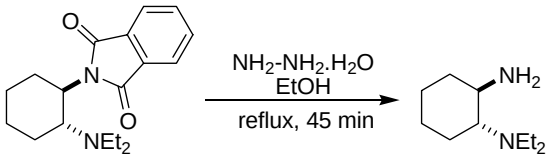
Step C: Deprotection of phthalimide:

- (1*R*,2*R*)-*N*,*N*-Dimethyl-1,2-diaminocyclohexane:



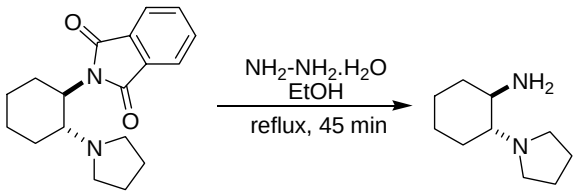
A solution of (1*R*,2*R*)-*N*,*N*-dimethyl-*N*′-phthaloyl-1,2-diaminocyclohexane (2.25 g, 8.28 mmol) in 10 mL ethanol was refluxed with hydrazine monohydrate (1.04 g, 20.7 mmol) for 0.5 hr. The reaction mixture was then cooled to room temperature and diethyl ether was added to it to precipitate phthaloyl hydrazide completely. The white solid was filtered and the filtrate was evaporated to afford (1*R*,2*R*)-*N*,*N*-dimethyl-1,2-diaminocyclohexane as light yellow oil (1.06 g, 7.45 mmol, 90% yield). This was used in the following step without further purification. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.89-1.17 (m; 4H), 1.53-1.67 (m; 3H), 1.80-1.95 (m; 2H), 1.99 (br s; 2H, NH_2), 2.12 (s; 6H, NCH_3), 2.46 (dt, *J* = 4.1, 10.15 Hz; 1H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 20.4, 24.9, 25.4, 35.0, 40.0, 51.2, 69.6.

- (1*R*,2*R*)-*N*,*N*-Diethyl-1,2-diaminocyclohexane:



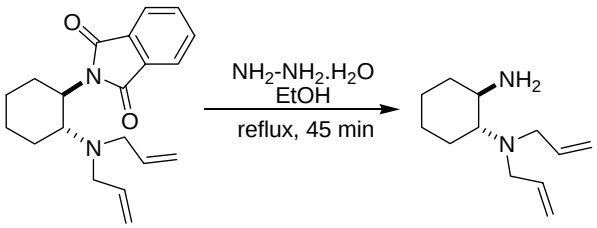
The general procedure as above was followed, on 2.02 mmol scale in 8 mL ethanol. Product was isolated as pale yellow oil (325 mg, 1.91 mmol, 95% yield). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 7.1 Hz; 6H), 0.93-0.98 (m; 3H), 1.45-1.63 (m; 3H), 1.77-1.87 (m; 3H), 1.92-2.00 (m; 1H), 2.12-2.23 (m; 2H), 2.36-2.50 (m; 3H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 14.8, 22.9, 24.9, 25.8, 34.9, 43.1, 51.0, 66.1.

- (1*R*,2*R*)-2-(Pyrrolidin-1-yl)cyclohexanamine:



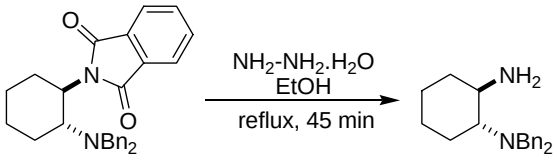
The general procedure described above was followed on 2.18 mmol scale in 6 mL ethanol. Product was isolated as pale yellow oil (325 mg, 1.93 mmol, 89% yield). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.95-1.22 (m; 4H), 1.55-1.91 (m; 10H), 2.16-2.26 (m; 1H), 2.40-2.53 (m; 5H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 21.4, 23.6, 24.9, 25.4, 34.8, 47.0, 52.6, 65.1.

- (1*R*,2*R*)-*N*,*N*-Diallyl-1,2-diaminocyclohexane:



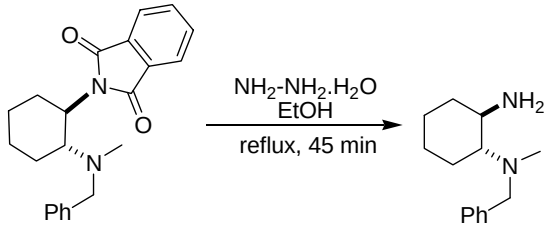
The general procedure described above was followed on 1.23 mmol scale in 15 mL ethanol. Product was isolated as brown oil (210 mg, 1.08 mmol, 88% yield). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 1.05-1.26 (m; 4H), 1.62-1.99 (m; 6H), 2.15-2.33 (m; 1H), 2.53-2.64 (m; 1H), 2.87 (m; 2H) 3.23-3.30 (m; 2H), 5.05-5.18 (m; 4H), 5.73-5.86 (m; 2H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 22.9, 25.1, 25.8, 35.0, 51.3, 52.6, 65.3, 116.2, 137.8.

- (1*R*,2*R*)-*N*,*N*-Dibenzyl-1,2-diaminocyclohexane:



The general procedure described above was followed on 660 µmol scale in 20 mL ethanol. Product was isolated as pale brown oil (186 mg, 632 µmol, 96% yield). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.82-1.31 (m; 4H), 1.61-1.85 (m; 4H), 1.89-2.03 (m; 2H), 2.13 (m; 1H), 2.65 (dt, *J* = 4.0, 10.2 Hz; 1H), 3.35 (d; 2H), 3.80 (d; 2H), 7.21-7.45 (m; 10H).

- (1*R*,2*R*)-*N*-Benzyl-*N*-methylcyclohexane-1,2-diamine:



The general procedure described as above was followed on 2.50 mmol scale in 5 mL ethanol. Product was obtained as an yellow oil (530 mg, 2.43mmol, 97% yield). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.95-1.08 (m; 3H), 1.57-1.92 (m; 7H), 2.07 (s; 3H), 2.10-2.15 (m; 1H), 2.60 (dt, *J* = 4.1, 10.13 Hz; 1H), 3.38 (d, *J* = 13.07 Hz; 1H), 3.60 (d, *J* = 13.07 Hz; 1H), 7.12-7.17 (m; 5H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 21.9, 24.9, 25.5, 34.9, 36.2, 51.2, 57.9, 69.3, 126.6, 128.0, 128.4, 140.1.

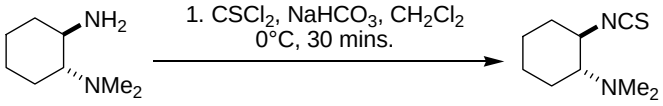
Step D: Formation of (thio)ureas:

The iso(thio)cyantes used for the synthesis of catalysts **1a-g**, **17-22**, **24-26** are commercially available and those for the catalysts **27-29** were prepared following the literature procedure by *Jacobsen* et al.[3] and used directly without isolation and purification.

Compound **16** was synthesized following the literature procedure.[4]

The isothiocyanate used for the synthesis of catalyst **23** was prepared according to the following procedure:

- (1*R*,2*R*)-2-Isothiocyanato-*N*,*N*-dimethylcyclohexanamine:

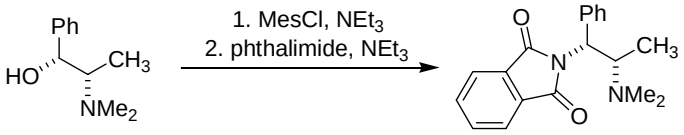


Saturated aqueous sodium bicarbonate (10 mL) was added to a solution of (1*R*,2*R*)-*N*,*N*-dimethyl-1,2-diaminocyclohexane (240 mg, 1.69 mmol) in 10 mL of dichloromethane and the resulting biphasic mixture was cooled to 0°C. Thiophosgene (140 µL, 1.86 mmol) was added to the organic (lower) phase by syringe. The resulting mixture was vigorously stirred at 0°C for 30 mins. The reaction mixture was then diluted with dichloromethane (20 mL) and the organic phase was separated. The aqueous phase was extracted with dichloromethane (5 × 15 mL). The combined organic layer was dried over anh. Na_2SO_4 and concentrated under

reduced pressure to afford (1*R*,2*R*)-2-isothiocyanato-*N*,*N*-dimethylcyclohexanamine as an orange-brown semisolid which was used directly in the following step without purification.

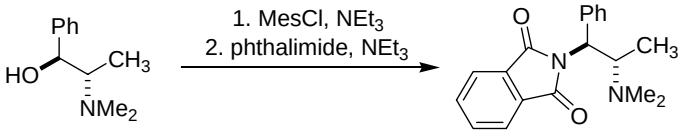
Synthesis of precursors for the bifunctional catalyst 9 and **10**

- (1*R*, 2*S*)-1-Phenyl-1-phthalimido-2-dimethylaminopropane:



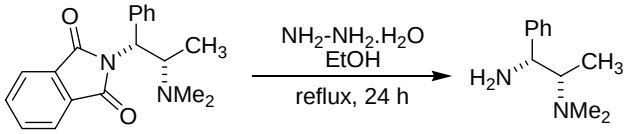
A general procedure published by *Dieter et al.* was followed.[5] To a solution of 1.79 g (10.0. mmol) (+)-*N*-methylephedrine and 4.18 mL (30.0 mmol) of triethylamine in 40 mL of dry THF a solution of 1.37 mL (20.0 mmol) Methanesulphonyl chloride in 20 mL of dry THF was added at 0 °C under an inert atmosphere over a period of 30 minutes. After complete addition, stirring was maintained for one hour at 0 °C and for another hour at room temperature. The solvent was removed *in vacuo* and the resulting residue was suspended in 80 mL of dry benzene. After addition of 2.81 mL (20.0 mmol) triethylamine and 1.47 g (10.0 mmol) of pththalimide the mixture was heated to reflux under an inert atmosphere for 12 hours. After cooling to room temperature, 15 mL of a 15 % sodium hydroxide solution were added, the organic layer was separated and was washed with 30 mL of brine. After drying over anhydrous K_2CO_3 and removal of the solvent *in vacuo*, the resulting residue was recrystallized from diethylether to yield the desired product as colourless plates (2.34 g, 7.6 mmol, 76 % yield). mp 151 - 154 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.86 (d, 3H), 2.13 (s, 6H), 4.12 – 4.22 (m, 1H) 5.13 (d, 1H) 7.15 – 7.24 (m, 3H), 7.47 – 7.51 (m, 2H),7.55 - 7.58 (m, 2H), 7.67 -7.70 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 8.4, 39.9, 56.6, 57.5, 123.2, 127.7, 128.3, 128.9, 131.7, 133.9, 138.9, 168.3. FT-IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3216 (w, br), 3057 (w), 3027 (w), 2971 (m), 2933 (m), 2871 (w), 2830 (m), 2780 (m), 1771 (m), 1706 (vs), 1610 (m), 1581 (m), 1493 (m), 1467 (s), 1452 (s), 1382 (vs), 1348 (vs), 1328 (s), 1265 (m), 1167 (m), 1157 (m), 1136 (m), 1105 s), 1087 (m), 1072 (s), 1051 (s), 965 (w), 900 (m), 882 (s), 792 (m), 778 (w), 773 (w), 715 (vs), 704 (vs), 698 (vs), 647 (s), 618 (m).

- (1*S*, 2*S*)-1-Phenyl-1-phthalimido-2-dimethylaminopropane:



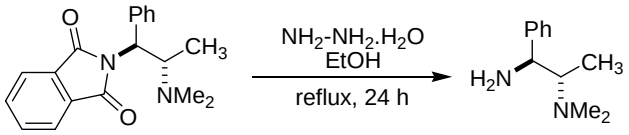
The same procedure described above was followed for the synthesis. The starting material was prepared according to a literature known procedure by *Davies et al.*[6] The reaction was performed on a 10 mmol scale. The product was isolated as a colorless solid. Yield: 1.54 g (5.1 mmol, 51 %). mp 131 - 134 °C. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.81 (d, 3H), 2.22 (s, 6H), 4.14 – 4.24 (m, 1H), 5.16 (d, 1H), 7.28 – 7.38 (m, 4H), 7.63 – 7.69 (m, 3H), 7.78 – 7.81 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 8.4, 39.9, 56.6, 58.8, 122.9, 127.9, 128.6, 129.3, 132.1, 133.5, 138.7, 168.5. FT-IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3029, 2969, 2934, 2869, 2824, 2781 (all w), 1765 (w), 1706 (s), 1466 (w), 1454 (w), 1386, 1367, 1331 (all m), 1145, 1105, 1076, 1051, 906, 884, (all w), 716, 699 (both m).

- (1*R*, 2*S*)-1-Amino-2-dimethylamino-1-phenylpropane:



To a stirred solution of 1.00 g (3.24 mmol) of the phthaloyl protected material in 35 mL ethanol 1.04 mL (20.5 mmol) of hydrazine hydrate was added and the mixture heated to reflux. After 24 hours, the colourless precipitate was filtered off and the filtrate was evaporated to dryness. The residue was taken up in 10 mL of diethyl ether and the solid was filtered off. The solvent of the filtrate was removed again and the resulting (1*R*, 2*S*)-1-Amino-2-dimethylamino-1-phenylpropane was collected as a light yellow oil (445 mg, 2.33 mmol, 72 %). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.91 (d, 3H), 1.78 (br s, 2H), 2.30 (s, 6H), 2.44 – 2.52 (m, 1H), 4.22 (d, 1H), 7.29 – 7.34 (m, 5H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 10.0, 42.9, 56.5, 65.8, 126.5, 126.8, 128.1, 138.7. EI-MS (70 eV): m/z = 161 (1), 145 (2), 132 (2), 117 (5), 104 (20), 72 (100), 56 (10).

- (1*S*, 2*S*)-1-Amino-2-dimethylamino-1-phenylpropane:



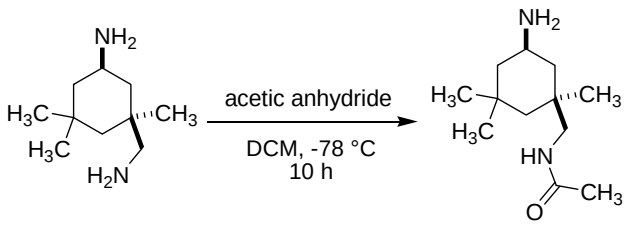
The same procedure as described above was followed on a 1.44 mmolar scale. The desired product was obtained as a light yellow oil (200 mg, 1.12 mmol, 78 %). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.58 (d, *J* = 6.6 Hz, 3H) 1.95 (br s, 2H), 2.28 (s, 6H), 2.58 – 2.68 (m, 1H), 3.68 (d, *J* = 10.0 Hz, 1H), 7.23 – 7.36 (m, 5H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 7.0, 40.0, 59.3, 65.0, 127.1, 127.8, 128.3, 144.4. EI-MS (70 eV): m/z = 161 (1), 145 (2), 132 (2), 117 (5), 104 (20), 72 (100), 56 (10).

Synthesis of the bifunctional catalysts 12 and 13

Catalyst **12**[7] and **13**[8] were synthesized according to the literature procedure.

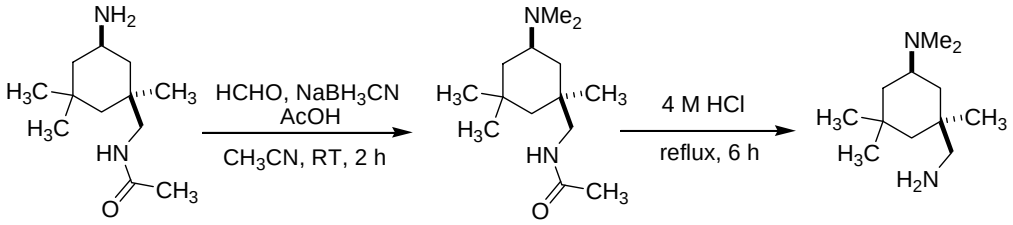
Synthesis of precursors for the bifunctional catalyst 14

- *N*-[{(1*S*,5*R*)-5-Amino-1,3,3-trimethylcyclohexyl}methyl]acetamide:



To a solution of (1*R*,3*S*)-3-(aminomethyl)-3,5,5-trimethylcyclohexanamine (1.00 mL, 920 mg, 5.40 mmol) in DCM (8.00 mL) at -78 °C was added dropwise over 1 h acetic anhydride (511 µL, 552 mg, 5.40 mmol) in DCM (8.00 mL) and stirred for 10 h (-78 °C → rt). The solvent was removed under reduced pressure and the colorless residue dissolved in water (3.00 mL). It was extracted with DCM (3 × 15.0 mL), then the aqueous layer brought to pH 10 by addition of NaOH and extracted again with DCM (3 × 15.0 mL). The organic layers of the second extraction were joined, dried over $MgSO_4$ and the solvent removed under reduced pressure to yield the mono-acetylated amine as a colorless highly viscous liquid (995 mg, 4.67 mmol, 87 %). bp 65 °C (3 mbar). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.82-1.18 (m; 13H), 1.44-1.65 (m; 2H), 1.76 (s; 3H), 1.83 (s; 1H), 2.81 (d; 2H), 2.96-3.15 (m; 1H), 7.81 (t(br)). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 23.4, 23.6, 27.9, 31.9, 35.1, 36.3, 43.8, 45.5, 47.2, 50.0, 53.2, 170.3.

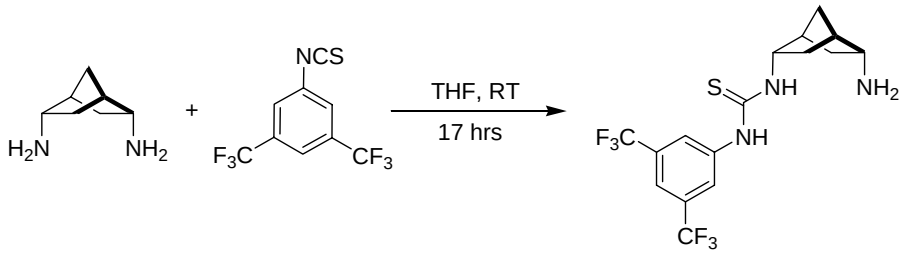
- (1*R*,3*S*)-3-(Aminomethyl)-*N*,*N*,3,5,5-pentamethylcyclohexanamine:



To a solution of *N*-[{(1*S*,5*R*)-5-amino-1,3,3-trimethylcyclohexyl}methyl]acetamide (500 mg, 2.35 mmol) in CH_3CN (12.5 mL) was added successively in 15 min intervals formaldehyde (37 % aqueous solution, 954 µL, 11.8 mmol), $NaBH_3CN$ (261 mg, 4.71 mmol) and acetic acid (634 µL). It was stirred at rt for 2 h, then 2 % MeOH in DCM (30.0 mL) added and washed with NaOH (1 M, 3 × 50.0 mL). It was dried over Na_2SO_4 and the solvent removed under reduced pressure. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.90-1.10 (m; 12H), 1.15-1.25 (m; 1H), 1.46-1.62 (m; 2H), 2.00 (2s; 6H), 2.27 (s; 3H), 2.53-2.66 (m; 1H), 2.90 (m; 2H), 5.67 (t(br); 1H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 23.6, 27.8, 31.7, 36.1, 36.2, 37.3, 41.1, 41.2, 47.7, 53.6, 55.4, 170.3. FT-IR (ATR) [cm^{-1}] $\tilde{\nu}$ = 3291 (m(br)), 2949 (s(br)), 1651, 1553, 1458, 1372 (all s), 1287, 1214 (both m), 1151, 1097 (both w), 1036 (m), 919, 840 (both w), 730 (m). The crude product was refluxed with HCl (4 M, 37.0 mL) for 6 h, before NaOH (4 M, 40.0 mL) was added. The aqueous phase was extracted with 5 % MeOH in DCM (3 × 50.0 mL), the organic phase dried over Na_2SO_4 and the solvent removed under reduced pressure. The product was isolated as a colorless liquid (278 mg, 1.40 mmol, 60 % over two steps). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.84-1.08 (m; 12H), 1.13-1.22 (m; 1H), 1.40-1.60 (m; 2H), 2.26 (s; 6H), 2.36 (s; 2H), 2.53-2.66 (m; 1H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 23.4, 27.9, 31.7, 35.6, 36.2, 36.9, 41.2, 41.5, 47.7, 56.6, 58.0. FT-IR (ATR) [cm^{-1}] $\tilde{\nu}$ = 3262 (s(br)), 2925 (s(br)), 1547, 1462, 1362, 1254 (all s), 848 (w).

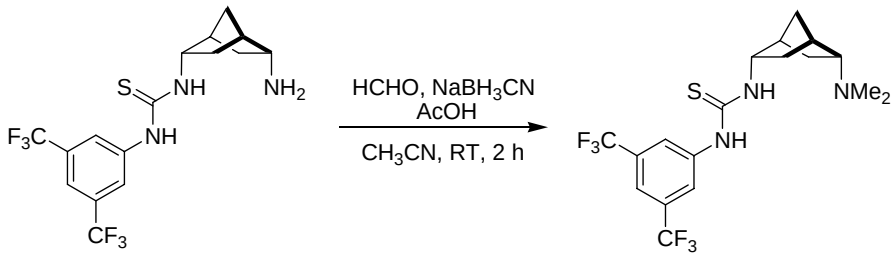
Synthesis of bifunctional catalyst 15

- 1-[(1*S*,2*S*,4*S*,5*S*)-5-Aminobicyclo[2.2.1]hept-2-yl)-3-[3,5-bis(trifluoromethyl)phenyl]-thiourea:



To a suspension of (1*S*,2*S*,4*S*,5*S*)-2,5-diamino-bicyclo[2.2.1]heptane (DIANANE)[9] (89 mg, 0.71 mmol) in absolute THF (2 mL) was added 3,5-bis(trifluoromethyl)phenyl isothiocyanate (103 µL, 0.56 mmol) dropwise and the resulting solution was stirred under argon atmosphere for 17 h. The solution was then concentrated in vacuo to obtain a pale yellow solid. Purification by column chromatography on silica gel ($CHCl_3$/MeOH(ammonia saturated) = 5:1 as eluant) gave the desired thiourea as a white solid (119 mg, 0.30 mmol, 42% yield). $[\alpha]_{546}^{20}$ = +64.1 °, $[\alpha]_{589}^{20}$ = +53.8 ° (c = 0.88, acetonitrile). mp 175°C. ^{1}H-NMR (300 MHz, CD_3OD): δ = 1.08 (dd; 1H), 1.49-1.55 (m; 1H), 1.55 (s; 2H), 1.80-1.89 (m; 1H), 1.89-2.01 (m; 1H), 2.16 (s; 1H), 2.59 (s; 1H), 3.32-3.35 (m; 1H), 4.51 (br. s; 1H), 7.61 (s; 1H), 8.17 (s; 2H). NH-signals could not be detected. ^{13}C-NMR (75 MHz, CD_3OD): δ = 27.8, 31.7, 38.9, 42.2, 44.1, 53.7, 57.3, 117.6, 123.5, 124.8, 132.6, 143.4, 182.8. FT-IR (CsI): $\tilde{\nu}$ [cm^{-1}] = 3394 (m), 3287 (m), 2967 (m), 1605 (s), 1470 (w), 1384 (s), 1349 (m), 1279 (s), 1179 (s), 1130 (m), 975 (w), 890 (m), 707 (m), 682 (m). HR-ESI-MS (EI): Calcd. for [$C_{16}H_{18}F_6N_3S$] ([M+H^+]): 398.113 Found: 398.112. Elemental Analysis: Anal. Calcd. for $C_{16}H_{17}F_6N_3S$: C 48.36, H 4.31, N 10.57 Found: C 48.25, H 4.51, N 10.36.

- 1-[3,5-Bis(trifluoromethyl)phenyl]-3-[(1*S*,2*S*,4*S*,5*S*)-5-(dimethylamino)bicyclo [2.2.1]hept-2-yl]thiourea (**15**):

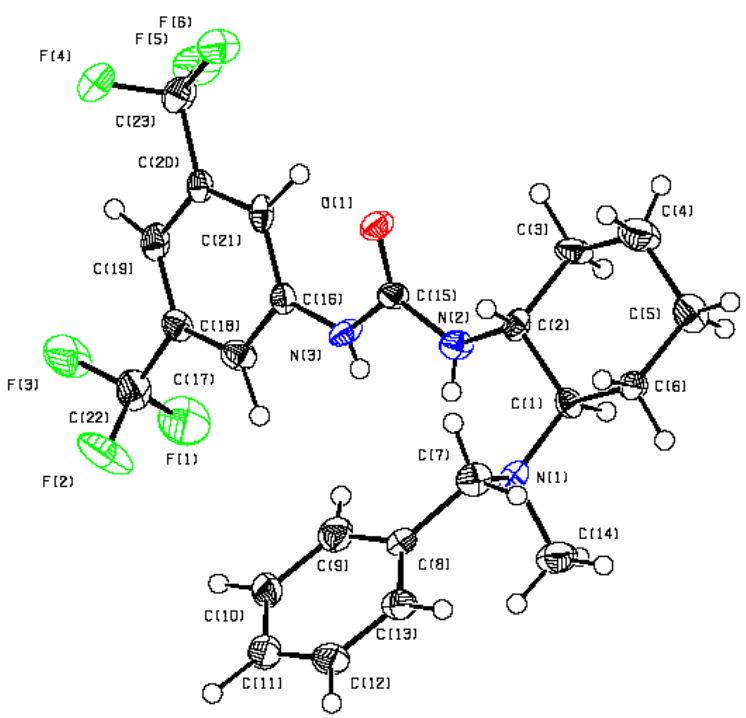


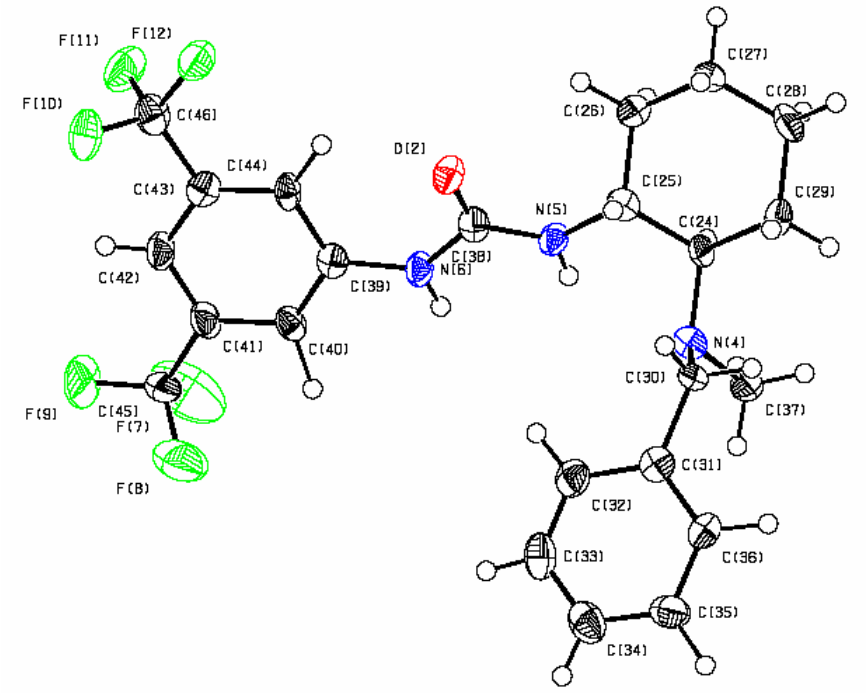
To a solution of 1-[(1*S*,2*S*,4*S*,5*S*)-5-aminobicyclo[2.2.1]hept-2-yl)-3-[3,5-bis(trifluoromethyl)phenyl]-thiourea (74 mg, 0.190 mmol) in 2.5 mL of acetonitrile, formaldehyde (76 µL, 0.93 mmol) was added and the resulting mixture was stirred for 15 minutes at room temperature. $NaBH_3CN$ (23.4 mg, 0.37 mmol) was then added, followed 15 minutes later by AcOH (51.0 µL, 67.15 mmol). After stirring 2 hours at room temperature, the reaction mixture was diluted with 2% CH_3OH-$CHCl_3$ (3 mL) and washed with 1N NaOH (4 × 4 mL). The organic layer was dried over anh. $NaSO_4$ and the solvent was removed in vacuo to obtain pure 1-[3,5-bis(trifluoromethyl)phenyl]-3-[(1*S*,2*S*,4*S*,5*S*)-5-(dimethyl-amino)bicyclo [2.2.1]hept-2-yl]thiourea **15** as a pale yellow solid (42 mg, 0.10 mmol, 52% yield). $[\alpha]_{405}^{20}$ = -90.1 °$[\alpha]_{546}^{20}$ = -49.0 °, $[\alpha]_{589}^{20}$ = -40.9 ° (c = 0.88, $CHCl_3$). mp 54°C. ^{1}H-NMR (300 MHz, CD_3OD): δ = 1.24-1.28 (m; 1H), 1.45-1.60 (m; 1H), 1.56 (s; 2H), 1.65-1.74 (m; 1H), 1.88-1.98 (m; 1H), 2.21 (s; 6H), 2.29 (s; 1H), 2.33 (s; 1H), 2.65 (s; 1H), 4.59 (br s; 1H), 7.62 (s; 1H), 8.11 (s; 2H). NH-signals could not be detected. ^{13}C-NMR (75 MHz, CD_3OD): δ = 28.0, 29.2, 38.5, 41.4, 41.8, 45.1, 57.4, 70.4, 117.7, 123.7, 124.8, 132.7, 143.2, 182.7. FT-IR (CsI): $\tilde{\nu}$ [cm^{-1}] = 3519 (s), 3288 (s), 3195 (m), 1590 (s), 1474 (w), 1387 (m), 1350 (m), 1280 (m), 1181 (m), 1135 (m), 887 (w), 682 (m). HR-ESI-MS (EI): Calcd. for [$C_{18}H_{22}F_6N_3S$] ([M+H^+]): 426.144 Found: 426.143. Elemental Analysis: Anal. Calcd. for $C_{18}H_{21}F_6N_3S \cdot ½H_2O$: C 49.76, H 5.10, N 9.67 Found: C 49.50, H 5.32, N 9.45.

ORTEP view of the catalysts 1f-g, 5a, 9, 17, 18, 20, 26a-b

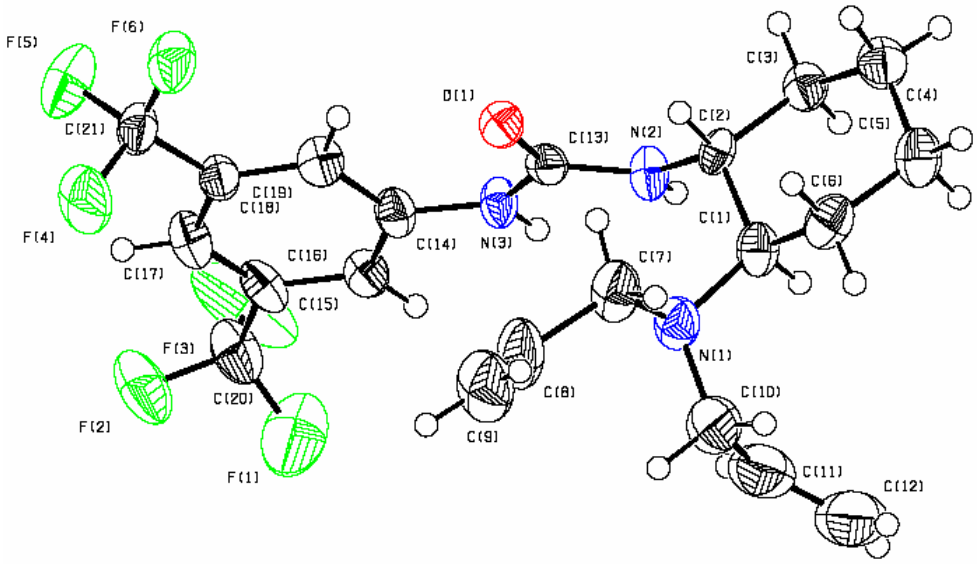
All ORTEP show thermal ellipsoid with 50 % probability.

catalyst 1f





catalyst 1g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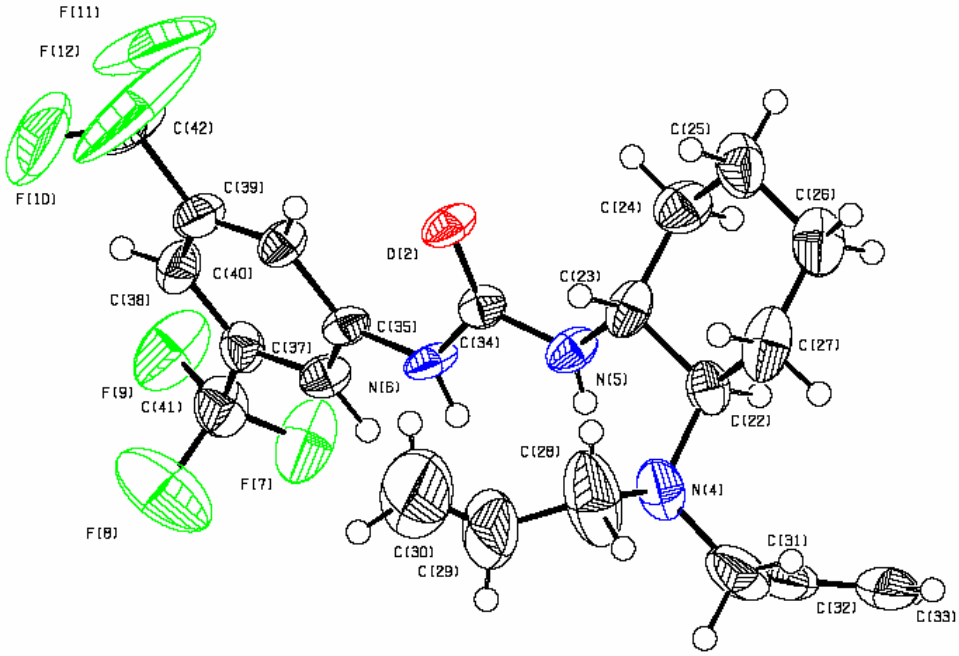
C(12)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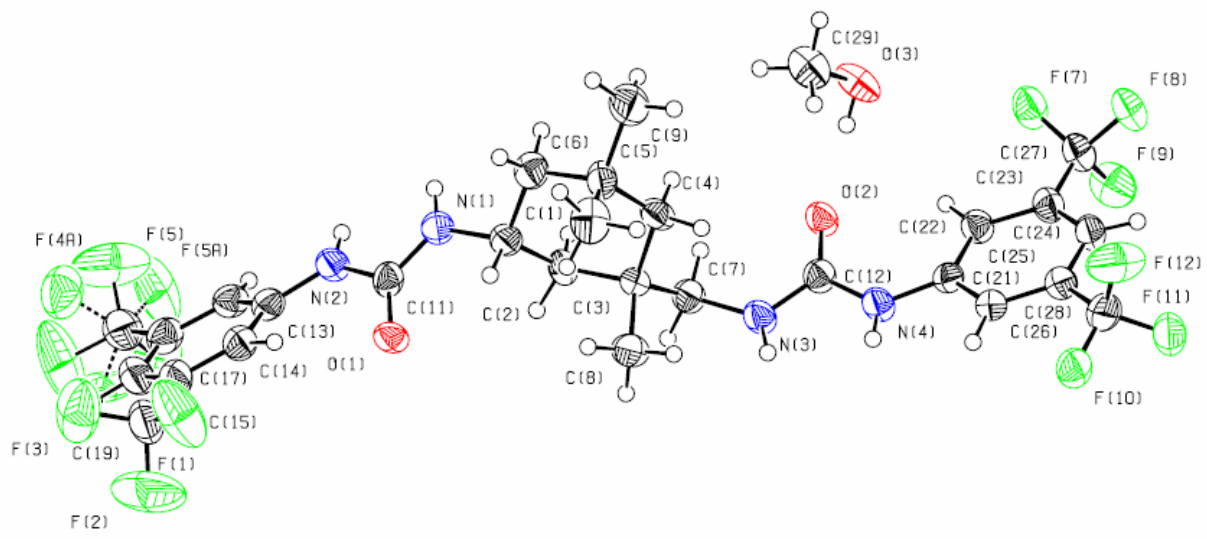
C(33)

catalyst 5a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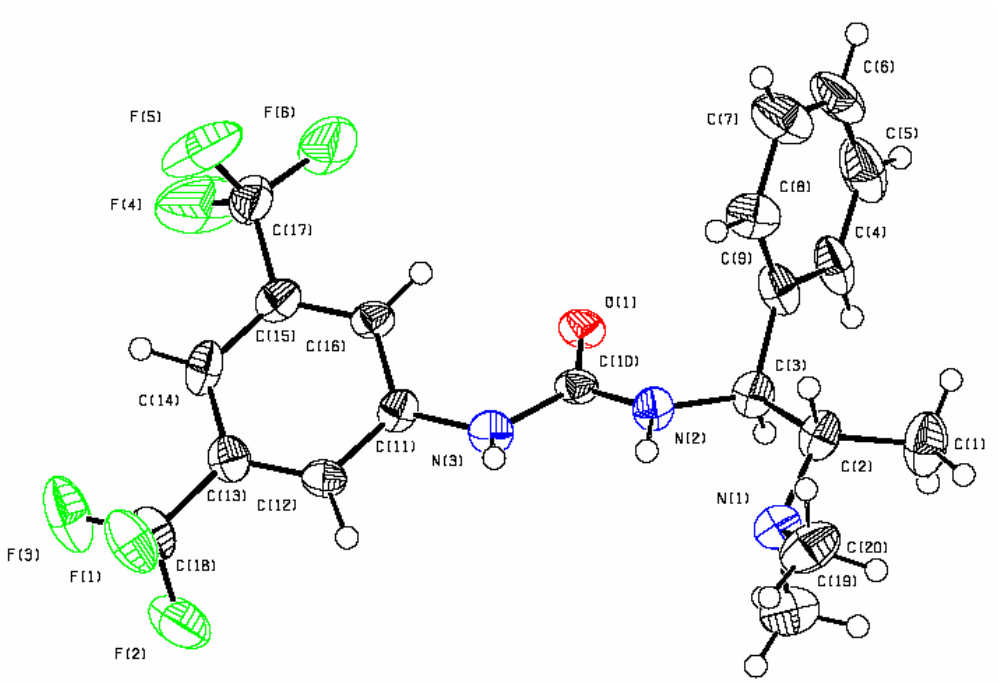
catalyst 9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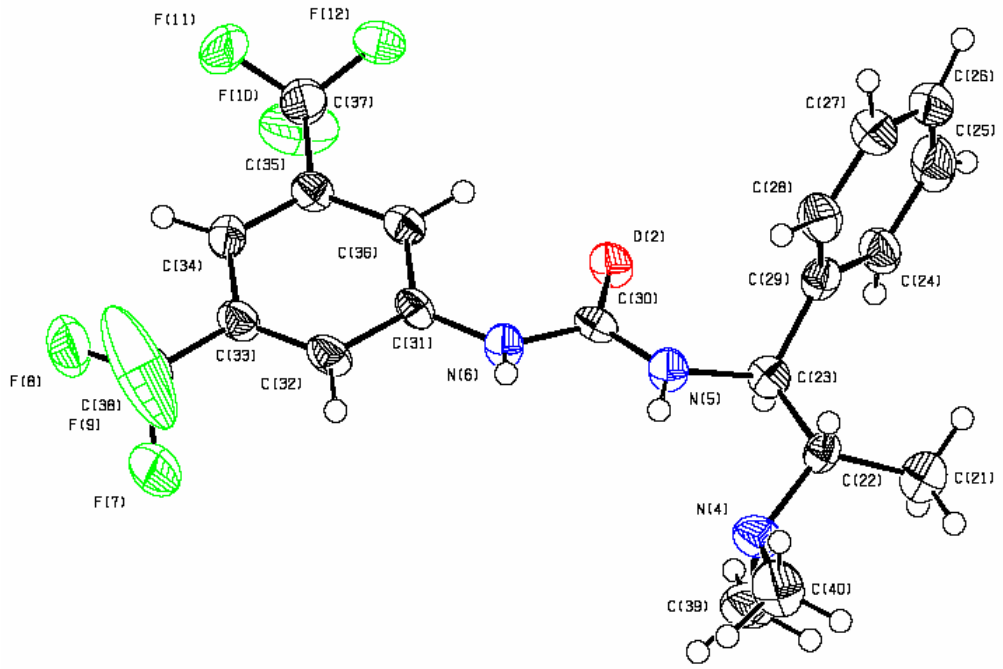
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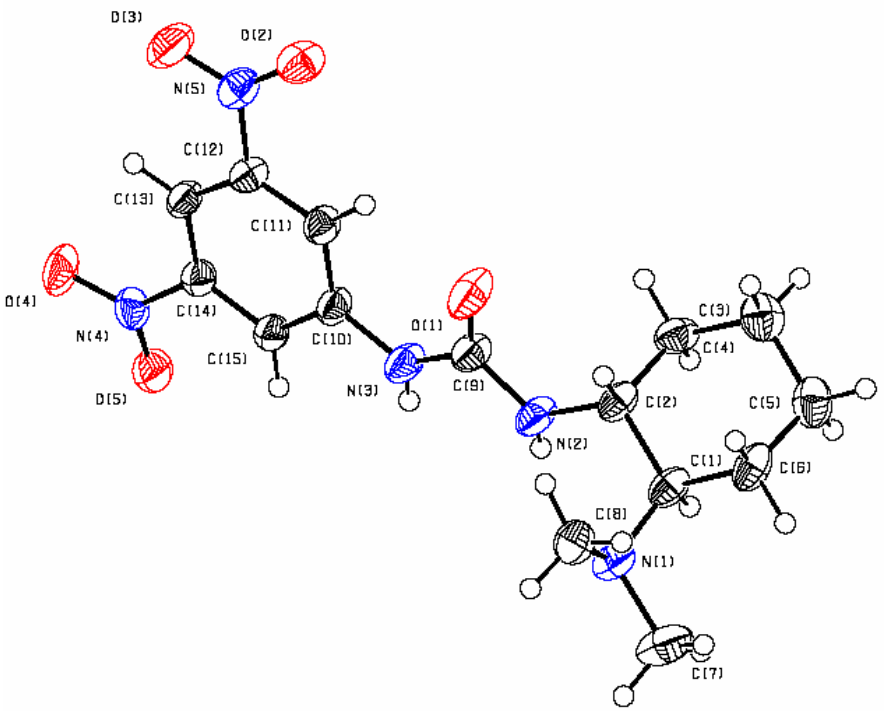
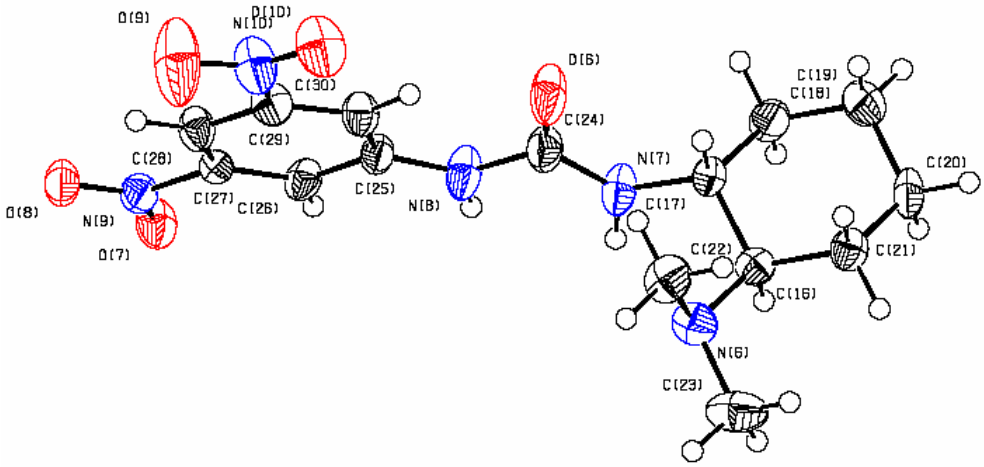
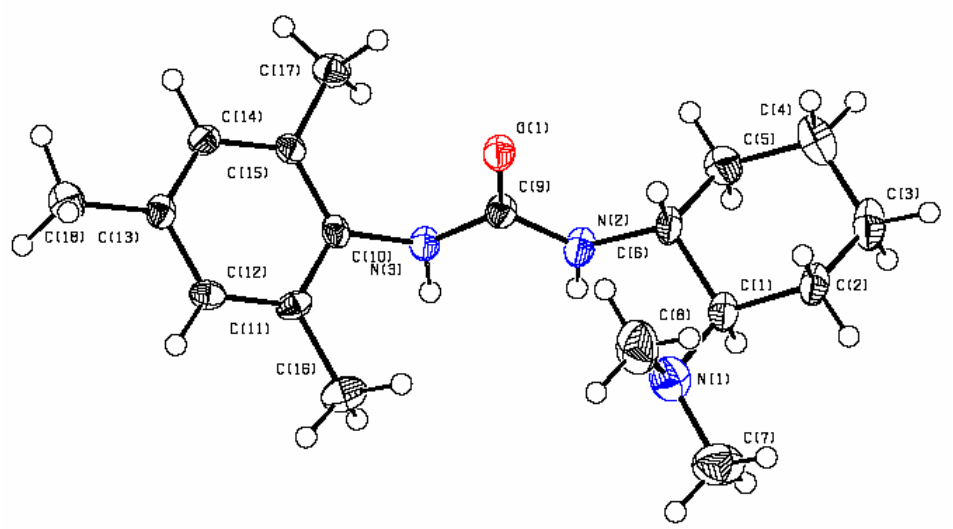
C(32)
N(6)
N(5)
C(23)
F(8)
C(38)
F(9)
F(7)
C(22)
C(21)
N(4)
C(40)
C(39)
C(26)
C(27)
C(25)
C(28)
C(29)
C(24)

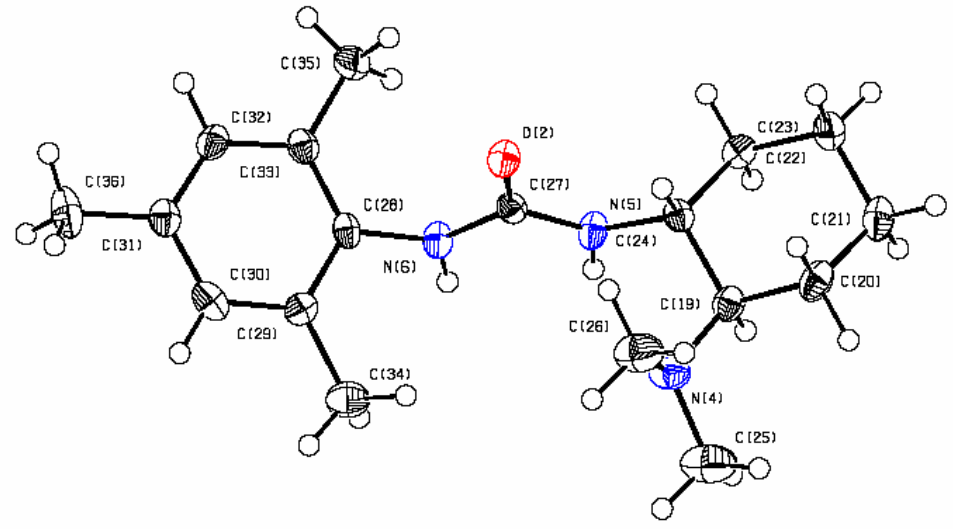
catalyst 17


O(3)
O(2)
N(5)
C(12)
C(13)
C(11)
O(4)
N(4)
C(14)
C(15)
C(10)
O(5)
O(1)
N(3)
C(9)
C(3)
C(4)
C(2)
C(5)
N(2)
C(1)
C(6)
C(8)
N(1)
C(7)

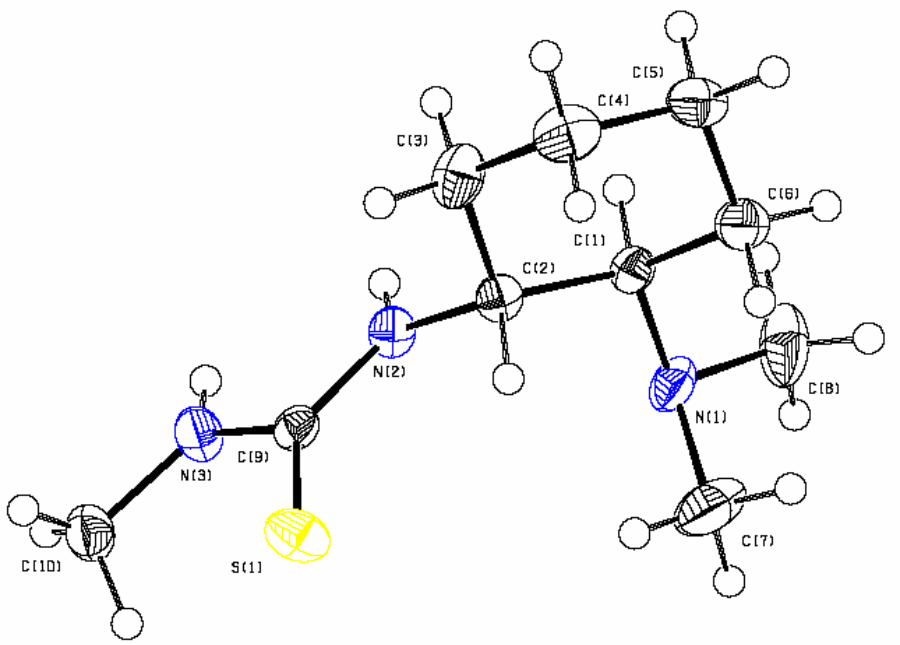

O(9)
N(10)
O(10)
C(30)
C(29)
C(28)
C(27)
C(26)
O(8)
N(9)
O(7)
C(25)
N(8)
O(6)
C(24)
N(7)
C(17)
C(19)
C(18)
C(20)
C(22)
C(21)
C(16)
N(6)
C(23)

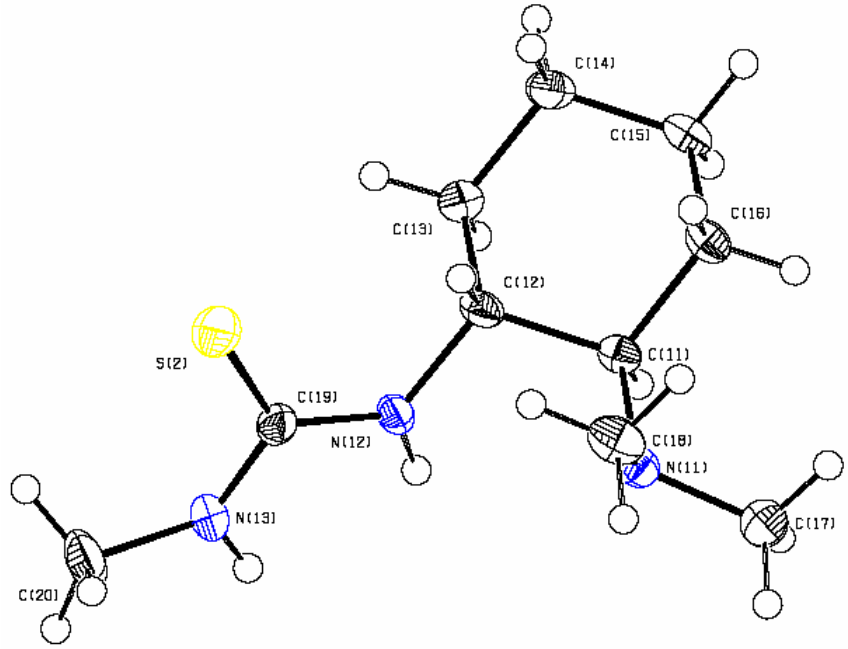
catalyst 18


C(17)
C(14)
C(15)
C(18)
C(13)
C(12)
C(11)
C(16)
C(10)
N(3)
O(1)
C(9)
N(2)
C(6)
C(4)
C(5)
C(3)
C(1)
C(2)
C(8)
N(1)
C(7)

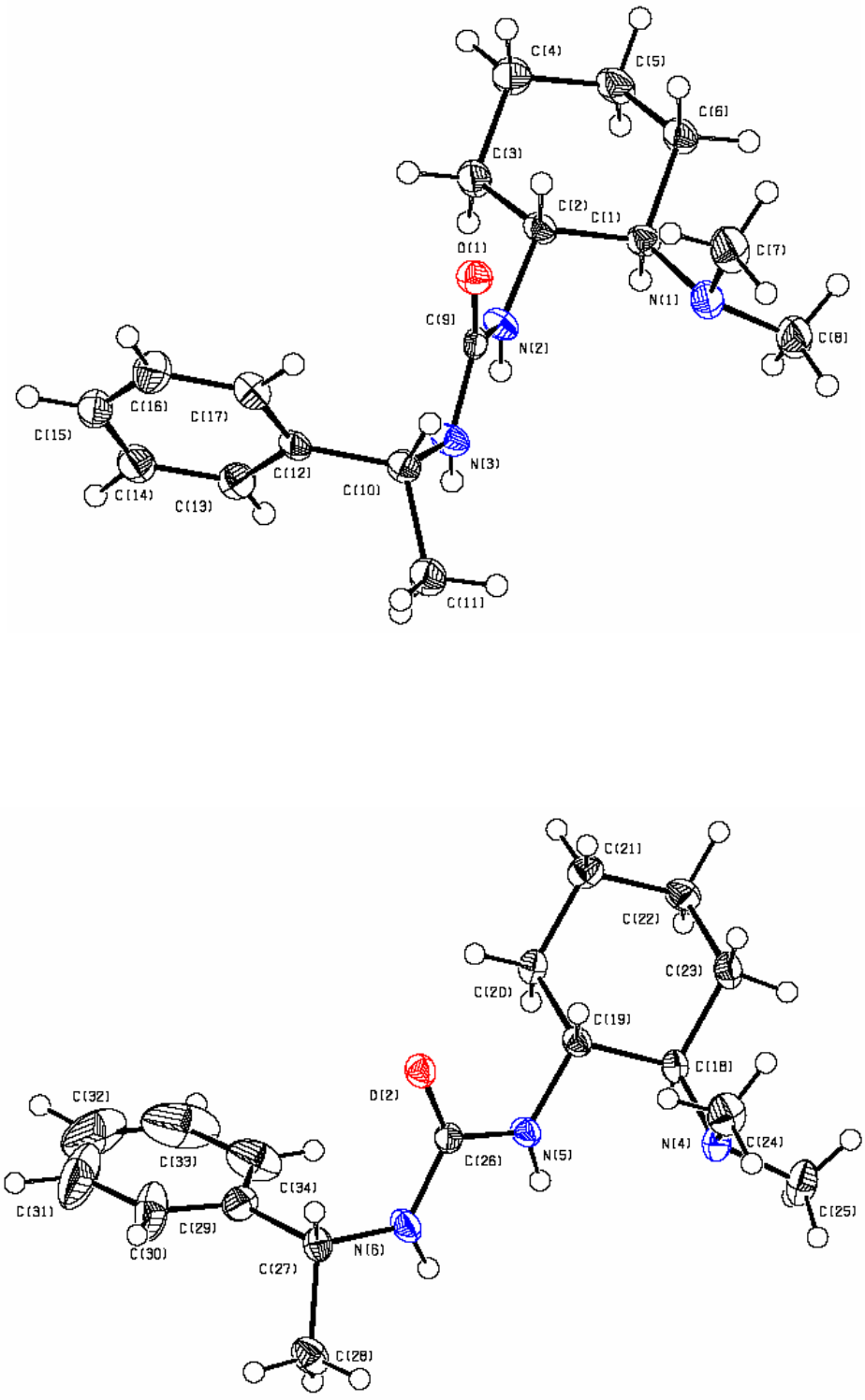

C(35)
C(32)
C(33)
C(36)
C(31)
C(30)
C(29)
C(34)
C(28)
N(6)
O(2)
C(27)
N(5)
C(24)
C(23)
C(22)
C(21)
C(20)
C(19)
C(26)
N(4)
C(25)

catalyst 20

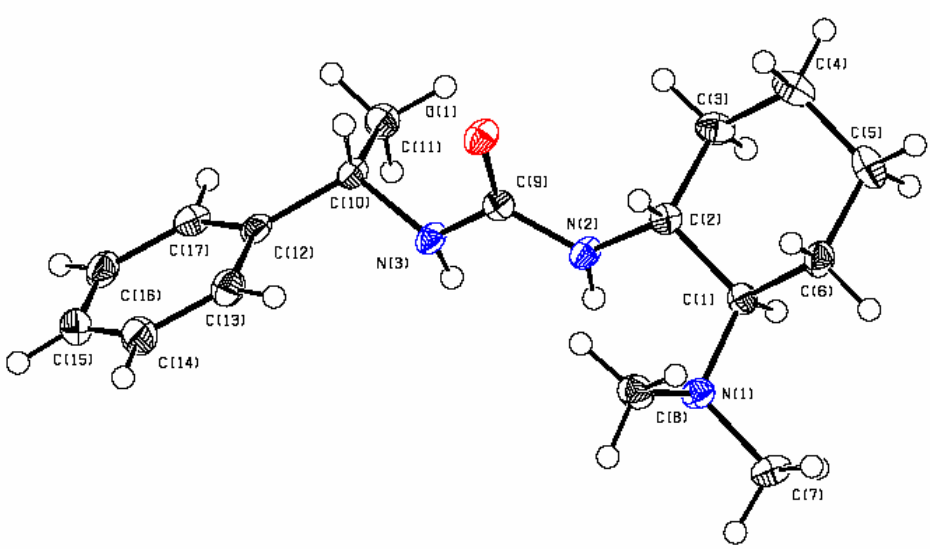

C(5)
C(4)
C(3)
C(6)
C(1)
C(2)
N(2)
C(8)
N(1)
C(9)
N(3)
C(7)
C(10)
S(1)


C(14)
C(15)
C(16)
C(13)
C(12)
S(2)
C(11)
C(19)
N(12)
C(18)
N(11)
N(13)
C(17)
C(20)

catalyst 26a



catalyst 26b



X-ray crystallographic data of the catalysts 1f-g, 5a, 9, 17, 18, 20, 26a-b

Data Collection: Nonius-Kappa-CCD diffractometer, Mo-K_α-radiation (λ = 0.71073 Å), graphite monochromator, φ-ω-scans, 2 Θ limits [°]: 2-54.

	1f	**1g**	**5a**
Formula	$C_{23}H_{25}F_6N_3O$ $\cdot(CH_3)_2CHOH$	$C_{21}H_{25}F_6N_3O$	$C_{28}H_{28}F_{12}N_4O_2$ $\cdot CH_3OH$
*M*r [g·mol^{-1}]	533.55	449.44	712.59
Cryst. dimens [mm^3]	0.35 × 0.18 × 0.15	0.35 × 0.21 × 0.17	0.20 × 0.20 × 0.06
Cryst. syst.	monoclinic	triclinic	orthorhombic
Space group	$P2_1$	$P\bar{1}$	$P2_12_12_1$
a [Å]	14.2234(7)	9.384(1)	10.0545(8)
b [Å]	8.9069(5)	9.969(1)	15.094(1)
c [Å]	21.523(1)	12.623(1)	21.397(2)
α [°]	90	81.56(1)	90
β [°]	90.890(2)	89.69(1)	90
γ [°]	90	71.13(1)	90
V [Å^3]	2726.3(3)	1104.2(2)	3247.3(4)
ρ_{calcd} [g·cm^{-3}]	1.300	1.352	1.458
Z	4	2	4
Temperature [K]	100(2)	293(2)	100(2)
Unique reflns.	6269	4749	3913
Obsd. reflns. [$I > 2\sigma(I)$]	2709	2757	1750
*R*1 (obsd. reflns.)	0.075	0.067	0.048
ω*R*2 (obsd. reflns.)	0.111	0.149	0.091
ρ_{fin} (max) [e·Å^{-3}]	0.255	0.420	0.295
CCDC depository no.	605365	605366	605367

	9	**17**	**18**
Formula	$C_{20}H_{21}F_6N_3O$	$C_{15}H_{21}N_5O_5 \cdot CH_3OH \cdot H_2O$	$C_{18}H_{29}N_3O$
*M*r [g·mol^{-1}]	433.40	752.79	303.44
Cryst. dimens [mm^3]	0.32 × 0.22 × 0.20	0.30 × 0.30 × 0.20	0.30 × 0.20 × 0.10
Cryst. syst.	monoclinic	monoclinic	orthorhombic
Space group	$P2_1$	$P2_1$	$P2_12_12_1$
a [Å]	10.578(1)	8.1767(6)	11.8168(3)
b [Å]	18.519(2)	22.874(2)	16.6626(6)
c [Å]	11.153(1)	10.1933(6)	18.2008(5)
α [°]	90	90	90
β [°]	100.72(1)	108.158(3)	90
γ [°]	90	90	90
V [Å^3]	2146.7(4)	1811.5(2)	3583.7(2)
ρ_{calcd} [g·cm^{-3}]	1.341	1.380	1.125
Z	4	2	8
Temperature [K]	293(2)	100(2)	100(2)
Unique reflns.	4834	4031	4342
Obsd. reflns. [$I > 2\sigma(I)$]	2571	2818	2550
*R*1 (obsd. reflns.)	0.063	0.059	0.052
ω*R*2 (obsd. reflns.)	0.116	0.157	0.084
ρ_{fin} (max) [e·Å^{-3}]	0.285	0.679	0.198
CCDC depository no.	605368	605369	605370

	20	**26a**	**26b**
Formula	$C_{10}H_{21}N_3S$	$C_{17}H_{27}N_3O$	$C_{17}H_{27}N_3O$
*M*r [g·mol^{-1}]	215.36	289.42	289.42
Cryst. dimens [mm^3]	0.50 × 0.40 × 0.40	0.48 × 0.38 × 0.38	0.30 × 0.20 × 0.10
Cryst. syst.	orthorhombic	monoclinic	orthorhombic
Space group	$P2_12_12_1$	$P2_1$	$P2_12_12_1$
a [Å]	11.5762(4)	8.7335(2)	9.1661(4)
b [Å]	12.7340(4)	22.1650(6)	11.3191(6)
c [Å]	16.3923(6)	9.9252(3)	15.5757(8)
α [°]	90	90	90
β [°]	90	101.774(1)	90
γ [°]	90	90	90
V [Å^3]	2416.4(1)	1880.88(9)	1616.0(1)
ρ_{calcd} [g·cm^{-3}]	1.184	1.022	1.190
Z	8	4	4
Temperature [K]	100(2)	100(2)	293(2)
Unique reflns.	5270	3892	2021
Obsd. reflns. [$I > 2\sigma(I)$]	4141	3012	1677
*R*1 (obsd. reflns.)	0.035	0.039	0.034
ω*R*2 (obsd. reflns.)	0.066	0.082	0.068
ρ_{fin} (max) [e·Å^{-3}]	0.214	0.210	0.132
CCDC depository no.	605371	605372	605373

References:

1. W. L. F. Armarego, C. L. L. Chai, *Purification of Laboratory Chemicals*, 5th Ed.; Butterworth Heinemann: Oxford, 2003.
2. M. Kaik, J. Gawronski, *Tetrahedron: Asymmetry*, 2003, **14**, 1559.
3. P. Vachal, E. N. Jacobsen, *J. Am. Chem. Soc.* 2002, **124**, 10012.
4. C. J. Salomon, E. Breuer, *J. Org. Chem.* 1997, **62**, 3858.
5. R. K. Dieter, N. Deo, B. Lagu, J. W. Dieter, *J. Org. Chem.*, 1992, **57**, 1663.
6. S. J. Coote, S. G. Davies, C. L. Goodfellow, K. H.Sutton, D. Middlemiss, A. K. Naylor, *Tetrahedron: Asymmetry*, 1990, **1**, 817.
7. H. Brunner, P. Schmidt, *Eur. J. Org. Chem.*, 2000, 2119.
8. J. Wang, H. Li, X. Yu, L. Zu, W. Wang, *Org. Lett.*, 2005, **7**, 4293.
9. A. Berkessel, M. Schröder, C. A. Sklorz, S. Tabanella, N. Vogl, J. Lex, J.-M. Neudörfl *J. Org. Chem.* 2004, **69**, 3050.