Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Electronic Supporting Information

Studies Concerning the Electrophilic Amino-Alkene Cyclisation for the Synthesis of Bicyclic Amines

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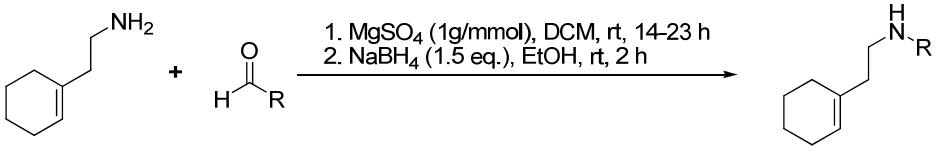
1. General Procedure for the preparation of secondary amines 1a – 1f: [1]

Suitable aldehyde (1 eq.) and 2-cyclohex-1-enyl-ethylamine (1.1 eq.) were dissolved in anhydrous DCM (3.3-10 ml/mmol). To the solution was added anhydrous $MgSO_4$ (1g/mmol) and the suspension stirred for 14-23 h at room temperature. The $MgSO_4$ was filtered-off and washed with DCM (2 x 25 ml). Combined filtrates were concentrated *in vacuo* and the residue dissolved in EtOH (3.3-10 ml/mmol). To the solution was added immediately $NaBH_4$ (1.5 eq.). The mixture was stirred for 2 h at room temperature. The reaction mixture was concentrated *in vacuo* and 3 M NaOH (5-7 ml/mmol) added. The mixture was extracted with DCM (3 x 5-10 ml/mmol). Combined organic extracts were dried over $MgSO_4$ or Na_2SO_4, filtered and the solvent removed under reduced pressure. The crude amines were purified by column chromatography as indicated below.

Table S1: Preparation of achiral secondary amines.



S1 **S2** **1a-f**

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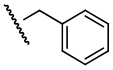
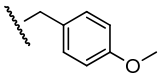
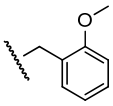
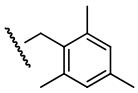
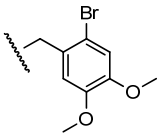
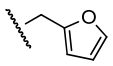
1a		77%
1b		76%
1c		95%
1d		54%
1e[2]		83%
1f		98%

[a] Isolated yield after purification by column chromatography.

N-Benzyl-2- cyclohex-1-enyl-ethylamine (1a):[3]

The *title compound* was purified by flash column chromatography (EtOAc-cyclohexane; 1:3 to 3:1) to give **1a** as a clear oil. R_f = 0.13 (EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) 7.29-7.33 (m, 4H) 7.21-7.25 (m, 1H) 5.45 (bs, 1H) 3.79 (s, 2H) 2.69 (t, J = 7.0 Hz, 2H) 2.15 (t, J = 7.0 Hz, 2H) 1.96-2.00 (m, 2H) 1.85-1.90 (m, 2H) 1.58-1.62 (m, 2 H) 1.51-1.56 (m, 2H) 1.46 (bs, 1H); ^{13}C-NMR (125.6 MHz, $CDCl_3$) δ (ppm) 140.5 (C) 135.4 (C) 128.3 (CH) 128.0 (CH) 126.8 (CH) 122.7 (CH) 53.9 (CH_2) 46.9 (CH_2) 38.3 (CH_2) 28.1 (CH_2) 25.2 (CH_2) 22.9 (CH_2) 22.4 (CH_2); IR (NaCl dep from DCM) 3354, 2923, 2834, 1645 cm^{-1}; HRMS (ES$^+$): calcd for $[C_{15}H_{22}N]^+$ 216.1752; found 216.1742.

2-Cyclohex-1-enyl-*N*-(4-methoxybenzyl)ethylamine (1b):
The *title compound* was purified by flash column chromatography (EtOAc-cyclohexane; 2:3 to 3:2) to give **1b** as a clear oil. R_f = 0.09 (EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) 7.22 (d, *J* = 8.5 Hz, 2H) 6.86 (d, *J* = 8.5 Hz, 2H) 5.45 (bs, 1H) 3.79 (s, 3H) 3.72 (s, 2H) 2.67 (t, *J* = 7.0 Hz, 2H) 2.15 (t, *J* = 7.0 Hz, 2H) 1.96-2.01 (m, 2H) 1.86-1.90 (m, 2H) 1.58-1.63 (m, 2H) 1.52-1.56 (m, 2H) 1.51 (bs, 1H); ^{13}C-NMR (125.6 MHz, $CDCl_3$) δ (ppm) 158.5 (C) 135.4 (C) 132.7 (C) 129.2 (CH) 122.6 (CH) 113.7 (CH) 55.2 (CH_3) 53.2 (CH_2) 46.8 (CH_2) 38.2 (CH_2) 28.1 (CH_2) 25.2 (CH_2) 22.9 (CH_2) 22.4 (CH_2); IR (neat) 3363, 2924, 2834, 1613, 1512 cm^{-1}; HRMS (ES$^+$): calcd for $[C_{16}H_{24}NO]^+$ 246.1858; found 246.1867.

2-Cyclohex-1-enyl-*N*-(2-methoxybenzyl)ethylamine (1c):
The *title compound* was purified by flash column chromatography (EtOAc-cyclohexane; 2:3 to 1:0 to EtOAc-MeOH; 9:1) to give **1c** as a clear oil. R_f = 0.33 (EtOAc-MeOH; 9:1); ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 7.20-7.23 (m, 2H) 6.90 (t, *J* = 7.5 Hz, 1H) 6.85 (d, *J* = 8.0 Hz, 1H) 5.44 (bs, 1H) 3.82 (s, 3H) 3.78 (s, 2H) 2.65 (t, *J* = 7.0 Hz, 2H) 2.14 (t, *J* = 7.0 Hz, 2H) 1.94-2.01 (m, 2H) 1.82-1.88 (m, 2H) 1.64 (bs, 1H), 1.50-1.62 (m, 4H); ^{13}C-NMR (100.5 MHz, $CDCl_3$) δ (ppm) 157.6 (C) 135.5 (C) 129.7 (CH) 128.6 (C) 128.0 (CH) 122.4 (CH) 120.3 (CH) 110.1 (CH) 55.1 (CH_3) 49.3 (CH_2) 46.8 (CH_2) 38.3 (CH_2) 28.0 (CH_2) 25.2 (CH_2) 22.9 (CH_2) 22.5 (CH_2); IR (neat) 3411, 3065, 3046, 2998, 2926, 2855, 2834, 1665, 1641, 1601 cm^{-1}; HRMS (ES$^+$): calcd for $[C_{16}H_{24}NO]^+$ 246.1858; found 246.1861.

2-Cyclohex-1-enyl-*N*-(2,4,6-trimethylbenzyl)ethylamine (1d):
The *title compound* was purified by flash column chromatography (EtOAc-cyclohexane; 1:4 to 1:0) to give **1d** as a clear oil. R_f = 0.42 (EtOAc); ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 6.82 (s, 2H) 5.44 (bs, 1H) 3.72 (s, 2H) 2.75 (t, *J* = 7.0 Hz, 2H) 2.33 (s, 6H) 2.24 (s, 3H) 2.15 (t, *J* = 7.0 Hz, 2H) 1.94-2.00 (m, 2H) 1.86-1.91 (m, 2H) 1.50-1.63 (m, 4H) 1.10 (bs, 1H); ^{13}C-NMR (100.5 MHz, $CDCl_3$) δ (ppm) 136.8 (C) 136.2 (C) 135.5 (C) 134.0 (C) 128.9 (CH) 122.7 (CH) 47.5 (CH_2, both N*C*H$_2$CH$_2$ and NCH$_2$*C*H$_2$Ar, as confirmed by HSQC) 38.2 (CH_2) 28.1 (CH_2) 25.2 (CH_2) 23.0 (CH_2) 22.5 (CH_2) 20.8 (CH_3) 19.4 (CH_3); IR (neat) 3321, 3000, 2922, 2856, 2834, 2731, 2670, 1666, 1614, 1581 cm^{-1}; HRMS (ES$^+$): calcd for $[C_{18}H_{28}N]^+$ 258.2222; found 258.2216.

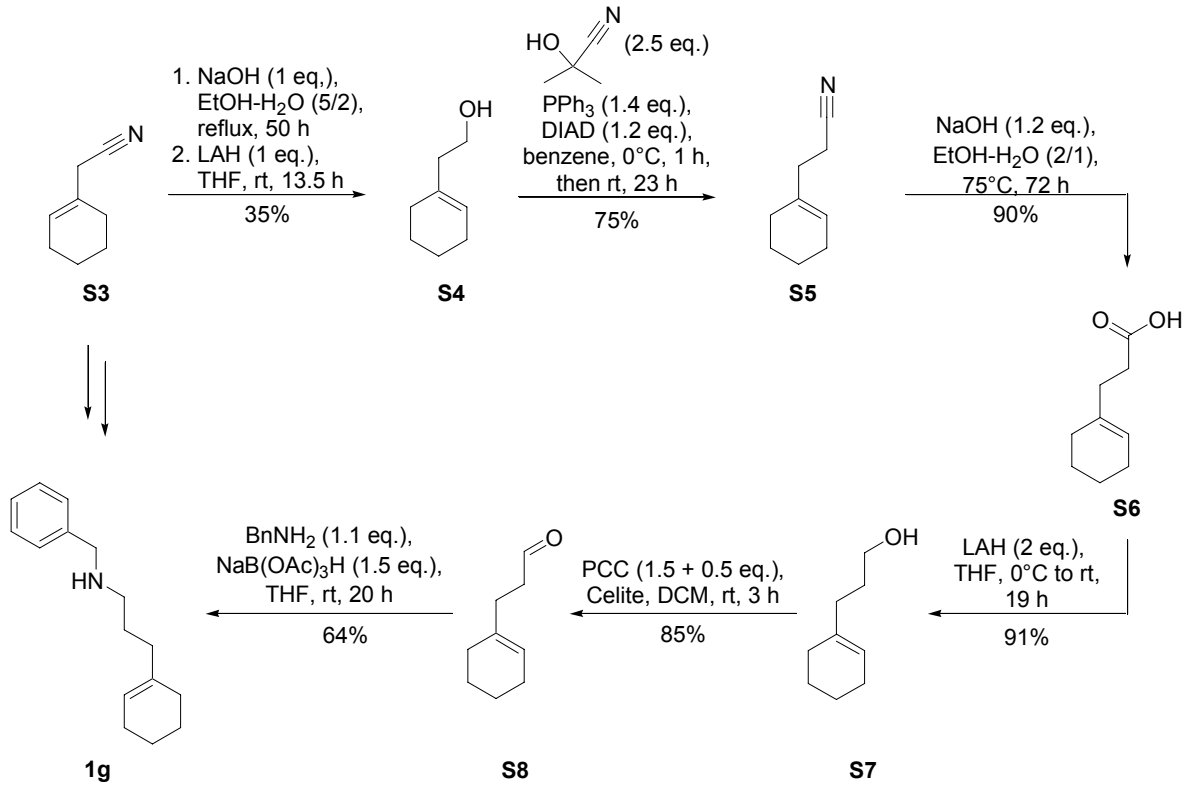
2-Cyclohex-1-enyl-*N*-(furan-2-ylmethyl)ethylamine (1e):
The *title compound* was purified by flash column chromatography (EtOAc-cyclohexane; 1:3 to 1) to give **1e** as a clear oil. R_f = 0.36 (EtOAc); ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 7.34 (dd, *J* = 1.0 Hz, *J* = 2.0 Hz, 1H) 6.29 (dd, *J* = 2.0 Hz, *J* = 3.0 Hz, 1H) 6.15 (dd, *J* = 1.0 Hz, *J* = 3.0 Hz, 1H) 5.44 (bs, 1H) 3.77 (s, 2H) 2.66 (t, *J* = 7.0 Hz, 2H) 2.13 (t, *J* = 7.0 Hz, 2H) 1.95-2.01 (m, 2H) 1.84-1.89 (m, 2H) 1.51-1.62 (m, 4H) 1.41 (bs, 1H); ^{13}C-NMR (100.5 MHz, $CDCl_3$) δ (ppm) 154.1 (C) 141.6 (CH) 135.3 (C) 122.7 (CH) 110.0 (CH) 106.6 (CH) 46.7 (CH_2) 46.1 (CH_2) 38.2 (CH_2) 28.0 (CH_2) 25.2 (CH_2) 22.9 (CH_2) 22.4 (CH_2); IR (neat) 3320, 3114, 3044, 2995, 2922, 2834, 2654, 1666, 1598, 1506 cm^{-1}; HRMS (ES$^+$): calcd for $[C_{13}H_{20}NO]^+$ 206.1545; found 206.1537.

***N*-(2-Bromo-4,5-dimethoxybenzyl)-2-cyclohex-1-enylethylamine (1f):**
The *title compound* was purified by flash column chromatography (EtOAc-cyclohexane; 2:3 to 4:1) to give **1f** as a clear oil. R_f = 0.07 (EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) 6.99 (s, 1H) 6.91 (s, 1H) 5.46 (bs, 1H) 3.86 (s, 3H) 3.84 (s, 3H) 3.77 (s, 2H) 2.67 (t, *J* = 7.0 Hz, 2H) 2.15 (t, *J* = 7.0 Hz, 2H) 1.95-2.00 (m, 2H) 1.85-1.89 (m, 2H) 1.63 (bs, 1H) 1.57-1.62 (m, 2H) 1.51-1.55 (m, 2H); ^{13}C-NMR (125.6 MHz, $CDCl_3$) δ (ppm) 148.5 (C) 148.3 (C) 135.2 (C) 131.5 (C) 122.9 (CH) 115.6 (CH) 113.7 (C) 113.2 (CH) 56.2 (CH_3) 56.0 (CH_3) 53.6 (CH_2) 46.7 (CH_2) 38.3 (CH_2) 28.0 (CH_2) 25.2 (CH_2) 22.9 (CH_2) 22.5 (CH_2); IR (neat) 3357.

2995, 2924, 2836, 1644, 1603, 1504 cm^{-1}; HRMS (ES^+): calcd for $[C_{17}H_{25}NO_2Br]^+$ 354.1069; found 354.1051.

2. Synthesis of *N*-benzyl-3-cyclohex-1-enylpropan-1-amine (1g):

The synthesis of 3-cyclohex-1-enylpropan-1-ol (**S7**) had previously been reported by Crotti *et al*.[4] The preparation of cyclohex-1-enylethanol (**S4**) following this report resulted in partial isomerization of the double bond. Hence cyclohex-1-enylethanol (**S4**) was prepared by saponification of the nitrile **S3**[5] and subsequent reduction with LAH.[6] The alcohol **S4** was converted to the nitrile **S5** by Mitsunobu-reaction, using conditions that have been reported by Fukuyama *et al*.[7] Saponification of the nitrile **S5** and reduction of the free acid **S6** was carried out similarly to the reported procedure by Crotti *et al*..[4] The alcohol **S7** was oxidized to the aldehyde **S8** under standard conditions using PCC/celite, followed by reductive amination to give the secondary amine **1g**. Conditions for the reductive amination using $NaBH(OAc)_3$ were previously described by Abdel-Magid *et al*.[8]



Scheme S1: Synthesis of secondary amine 1g.

Cyclohex-1-enylethanol (S4):[4]

2-Cyclohex-1-enylacetonitrile (**S3**) (2.6 ml, 20 mmol, 1 eq.) was dissolved in a mixture of EtOH-H_2O (28 ml, 5:2) and NaOH (800 mg, 20 mmol, 1 eq.) was added solid. After all NaOH was dissolved the mixture was heated to reflux for 50 h. Solvent was removed under reduced pressure and the residue partioned between H_2O (100 ml) and Et_2O (100 ml). Aqueous layer was extracted with Et_2O (100 ml). Organic extracts were disposed of, the aqueous layer was acidified to pH ~ 1 with conc. HCl and extracted with Et_2O (4 x 100 ml). Combined organic extracts were washed with brine (50 ml), dried over $MgSO_4$ and the solvent removed under reduced pressure. The crude 2-cyclohex-1-enylacetic acid was subjected to the next reaction without further purification.

LAH (790 mg, 20 mmol, 1 eq.) was suspended in anhydrous THF (20 ml). The crude 2-cyclohex-1-enylacetic acid was added, as a solution in anhydrous THF (10 ml) in a dropwise fashion at room temperature. The mixture was stirred for 13.5 h and subsequently cooled to 0°C and quenched by careful addition of H_2O (20 ml) followed by 20% H_2SO_4 (20 ml). The mixture was transferred to a separating funnel and extracted with EtOAc (2 x 100 ml). Combined organic extracts were washed with brine (40 ml), dried over $MgSO_4$ and the solvent removed under reduced pressure. The crude product **S4** was purified by column chromatography (pentane-Et_2O; 7:3) to give pure product (889 mg, 35% yield) as a clear oil. R_f = 0.33 (pentane-Et_2O; 7:3); ^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) 5.51 (bs, 1H) 3.64 (t, J = 6.0 Hz, 2H) 2.19 (t, J = 6.0 Hz, 2H) 1.97-2.03 (m, 2H) 1.91-1.96 (m, 2H) 1.60-1.65 (m, 2H) 1.53-1.58 (m, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ (ppm) 134.0 (C) 124.2 (CH) 60.2 (CH_2) 41.1 (CH_2) 28.0 (CH_2) 25.2 (CH_2) 22.8 (CH_2) 22.3 (CH_2); IR (neat) 3356, 2926, 1643 cm^{-1}.

3-Cyclohex-1-enylpropannitrile (S5):[3]
A mixture of cyclohex-1-enylethanol (**S4**) (3.1 g, 24.6 mmol, 1 eq.), PPh_3 (9.00 g, 34.3 mmol, 1.4 eq.) and acetone cyanohydrin (5.6 ml, 61.5 mmol, 2.5 eq.) were added to benzene (140 ml) at room temperature. The mixture was cooled to 0°C and DIAD (5.8 ml, 29.52 mmol, 1.2 eq.) added as a solution in benzene (15 ml + 5 ml rinse) by means of a syringe in a dropwise fashion. Mixture was stirred at 0°C for 1 h and subsequently for 23 h at room temperature. Solvent was removed under reduced pressure and the residue filtered through a pad of silica (cHex-EtOAc; 19/1) the solvent removed under reduced pressure and the obtained residue subjected to column chromatography (cHex-EtOAc; 100:0 to 19:1) to give **S5** as a clear oil (2.51 g, 75% yield). R_f = 0.53 (cHex-EtOAc; 4:1); ^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) 5.51 (bs, 1H) 2.40 (t, J = 7.5 Hz, 2H) 2.24 (t, J = 7.5 Hz, 2H) 1.97-2.02 (m, 2H) 1.88-1.92 (m, 2H) 1.59-1.64 (m, 2H) 1.51-1.56 (m, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ (ppm) 133.8 (C) 123.6 (CH) 119.5 (C) 33.2 (CH_2) 27.7 (CH_2) 25.0 (CH_2) 22.5 (CH_2) 22.0 (CH_2) 15.9 (CH_2); IR (neat) 3367, 2927, 2858, 2842, 2245, 1644 cm^{-1}.

3-Cyclohex-1-enylpropanoic acid (S6):[3]
3-Cyclohex-1-enylpropanenitrile (**S5**) (400 mg, 2.96 mmol, 1 eq.) was dissolved in a mixture of EtOH-H_2O (4.5 ml, 2:1). To the solution was added NaOH (0.142 g, 3.56 mmol, 1.2 eq.) and the mixture heated to 75°C for 72 h, TLC indicated consumption of starting material. Solvent was removed under reduced pressure and the residue partioned between H_2O (20 ml) and Et_2O (20 ml). Ether layer was disposed of, aqueous layer was acidified to pH ~ 1 using conc. HCl and extracted with Et_2O (4 x 25 ml). Combined org. layers were dried over $MgSO_4$.and the solvent removed under reduced pressure. Desired product (411 mg, 90% yield) was obtained in pure form without further purification as a low melting white solid. The product crystallized upon storage at 5°C to give X-ray quality crystals. M.pt. < 30°C; ^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) 5.44 (bs, 1H), 2.46 (t, J = 7.5 Hz, 2H) 2.26 (t, J = 7.5 Hz, 2H) 1.95-2.01 (m, 2H) 1.90-1.95 (m, 2H) 1.60-1.64 (m, 2H) 1.52-1.57 (m, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ (ppm) 179.7 (C) 135.8 (C) 121.7 (CH) 32.61 (CH_2) 32.60 (CH_2) 28.3 (CH_2) 25.5 (CH_2) 22.9 (CH_2) 22.4 (CH_2) ; IR (CH_2Cl_2) 3365, 2924, 1701 cm^{-1}; HRMS (ES$^-$): calcd for $[C_9H_{13}O_2]^-$ 153.0916; found 153.0909.

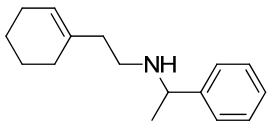
3-Cyclohex-1-enylpropan-1-ol (S7):[3, 9]
LAH (175 mg, 4.6 mmol, 2 eq.) was suspended in anhydrous THF (5 ml) and the suspension cooled to 0°C. 3-Cyclohex-1-enylpropanoic acid (**S6**) (355 mg, 2.3 mmol, 1 eq.) was added as a solution in anhydrous THF (5 ml). The mixture was stirred for 19 h, during which time it slowly reached room temperature. The reaction was carefully quenched with H_2O (5 ml) and further with 10% H_2SO_4 (5 ml). The mixture was transferred to a separating funnel and was extracted with Et_2O (3 x 20 ml). Combined organic extracts were washed with brine (20 ml),

dried over $MgSO_4$ and the solvent removed under reduced pressure. The crude product was purified by column chromatography (pentane-Et_2O; 7:3) to give **S7** (294 mg, 91% yield) as a clear oil. R_f = 0.47 (cHex-EtOAc; 1:1); ^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) 5.42 (bs, 1H) 3.61 (t, *J* = 6.5 Hz, 2H) 1.94-2.02 (m, 4H) 1.89-1.94 (m, 2H) 1.63-1.71 (m, 3H) 1.58-1.62 (m, 2H) 1.50-1.56 (2H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ (ppm) 137.3 (C) 121.2 (CH) 62.8 (CH_2) 34.3 (CH_2) 30.5 (CH_2) 28.2 (CH_2) 25.2 (CH2) 22.9 (CH_2) 22.5 (CH_2); IR (neat) 3343, 2927, 1643 cm^{-1}; MS (ES$^-$): found 139.0697.

3-Cyclohex-1-enylpropanal (S8):[9]
3-Cyclohex-1-enylpropan-1-ol (**S7**) (280 mg, 2 mmol, 1 eq.) was dissolved in DCM (20 ml). To the solution was added celite (647 mg) and PCC (647 mg, 3 mmol, 1.5 eq.). Suspension was stirred for 2 h at room temperature. TLC indicated unreacted staring material, which lead to further addition of PCC (216 mg, 1 mmol, 0.5 eq.) and celite (216 mg). The suspension was stirred for 1 h, the solvent removed under reduced pressure and the residue resuspended in Et_2O (20 ml) and filtered through a pad of celite. The solvent was removed under reduced pressure and the crude material immediately subjected to column chromatography (pentane-Et_2O; 19:1) to give aldehyde **S8** (235 mg, 85% yield) as a clear oil. R_f = 0.49 (pentane-Et_2O; 4:1); ^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) 9.74 (t, *J* = 2.0 Hz, 1H) 5.40 (bs, 1H) 2.50 (dt, *J* = 2.0 Hz, *J* = 7.5 Hz, 2H) 2.25 (t, *J* = 7.5 Hz, 2H) 1.93-1.99 (m, 2H) 1.87-1.92 (m, 2H) 1.57-1.63 (m, 2H) 1.50-1.55 (m, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ (ppm) 202.6 (CH) 135.7 (C) 121.8 (CH) 41.8 (CH_2) 30.1 (CH_2) 28.4 (CH_2) 25.1 (CH_2) 22.8 (CH_2) 22.3 (CH_2); IR (neat) 3372, 2925, 2853, 2716, 1725, 1652 cm^{-1}.

***N*-Benzyl-3-cyclohex-1-enylpropan-1-amine (1g):**
3-Cyclohex-1-enylpropanal (**S8**) (274 mg, 1.98 mmol, 1 eq.) was dissolved in anhydrous THF (25 ml) under an atmosphere of N_2. Benzylamine (238 µl, 2.18 mmol, 1.1 eq.) was added at room temperature and the solution stirred for 30 min. $NaBH(OAc)_3$ (630 mg, 2.97 mmol, 1.5 eq.) was added in one portion and the suspension stirred for 20 h at room temperature. The mixture was concentrated under reduced pressure and subsequently partioned between 3 M NaOH (25 ml) and Et_2O (40 ml). The aqueous layer was extracted with Et_2O (2 x 40 ml). Combined organic layers were dried over $MgSO_4$ and the solvent removed under reduced pressure. The crude was subject to column chromatography (cHex-EtOAc; 4:1 to 0:1) to give pure product (290 mg, 64% yield) as a clear oil. R_f = 0.43 (MeOH-EtOAc; 1:9); ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 7.30-7.31 (m, 4H) 7.21-7.26 (m, 1H) 5.37 (bs, 1H) 3.78 (s, 2H) 2.16 (t, *J* = 7.0 Hz, 2H) 1.96 (t, *J* = 7.0 Hz, 4H) 1.87-1.93 (m, 2H) 1.57-1.65 (m, 4H) 1.49-1.56 (m, 2H) 1.43 (bs, 1H); ^{13}C-NMR (100.5 MHz, $CDCl_3$) δ (ppm) 140.5 (C) 137.4 (C) 128.3 (CH) 128.0 (CH) 126.8 (CH) 121.0 (CH) 54.0 (CH_2) 49.2 (CH_2) 35.7 (CH_2) 28.2 (CH_2) 28.0 (CH_2) 25.2 (CH_2) 23.0 (CH_2) 22.5 (CH_2); IR (neat) 3419, 3062, 3027, 2926, 28.34, 1945, 1871, 1807, 1668, 1553 cm^{-1}; HRMS (ES$^+$): calcd for $[C_{16}H_{24}N]^+$ 230.1909; found 230.1916.

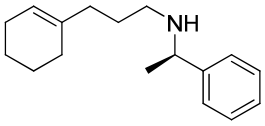
3. Synthesis of *rac*-2-cyclohex-1-enyl-*N*-(1-phenylethyl)ethylamine (1h):[10]



1h

Acetophenone (233 µl, 2 mmol, 1 eq.) and 2-cyclohex-1-enyl-ethanamine (**S1**) (278 µl, 2 mmol, 1 eq.) were combined in anhydrous DCM (7 ml) under an atmosphere of N_2. To the mixture was added glacial AcOH (115 µl, 2 mmol, 1 eq.) and $NaBH(OAc)_3$ (593 mg, 2.8 mmol, 1.4 eq.) at room temperature. The mixture was stirred for 72 h at room temperature, then poured into 3 M NaOH (20 ml) and extracted with Et_2O (3 x 25 ml). Combined organic extracts were dried over $MgSO_4$ and the solvent removed under reduced pressure. The crude product was subject to column chromatography (cHex-EtOAc; 9:1 to 1:1) to give pure product **1h** (337 mg, 73% yield) as a clear oil. R_f = 0.20 (EtOAc); ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 7.27-7.33 (m, 4H) 7.20-7.25 (m, 1H) 5.43 (bs, 1H) 3.75 (q, *J* = 6.5 Hz, 1H) 2.45-2.60 (m, 2H) 2.10 (t, *J* = 7.0 Hz, 2H) 1.94-2.01 (m, 2H) 1.79-1.84 (m, 2H) 1.48-1.61 (m, 5H) 1.34 (d, *J* = 6.5 Hz, 3H); ^{13}C-NMR (100.5 MHz, $CDCl_3$) δ (ppm) 145.8 (C) 135.4 (C) 128.3 (CH) 126.7 (CH) 126.4 (CH) 122.6 (CH) 58.2 (CH) 45.3 (CH_2) 38.3 (CH_2) 28.0 (CH_2) 25.2 (CH_2) 24.2 (CH_3) 22.9 (CH_2) 22.4 (CH_2); IR (neat) 3369, 2924, 2835, 1643 cm^{-1}; HRMS (ES$^+$): calcd for $[C_{16}H_{24}N]^+$ 230.1909; found 230.1902; Anal. Calcd. for $C_{16}H_{23}N$: C (83.79) H (10.11) N (6.11), Found: C (83.55) H (10.17) N (6.07).

4. Synthesis of (*R*)-3-cyclohex-1-enyl-*N*-(1-phenylethyl)propan-1-amine (1i):[10]



1i

3-Cyclohex-1-enylpropanal (**S8**) (195 mg, 1.41 mmol, 1 eq.) was dissolved in anhydrous THF under an atmosphere of N_2. (*R*)-(+)-α-Methyl-benzylamine (197 µl, 1.55 mmol, 1.1 eq.) was added by means of a syringe and the mixture stirred for 30 min at room temperature prior to addition of $NaBH(OAc)_3$ (448 mg, 2.11 mmol, 1.5 eq.). Mixture was stirred at room temperature for 22 h. Solvent was removed under reduced pressure and the residue partioned between Et_2O (30 ml) and 3 M NaOH (20 ml). Aqueous layer was extracted with Et_2O (2 x 30 ml), combined organic layers were dried over $MgSO_4$, solvent removed under reduced pressure. The crude material was subjected to column chromatography (cHex-EtOAc; 3:1) to give **1i** (239 mg, 70% yield) as a pale yellow oil. $[\alpha]_D$ = +47.95 (c 0.1, $CHCl_3$); R_f = 0.16 (EtOAc); ^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) 7.28-7.33 (m, 4H), 7.20-7.25 (m, 1H) 5.36 (bs, 1H) 3.74 (q, *J* = 6.6 Hz, 1H) 2.38-2.50 (m, 2H) 1.85-1.97 (m, 6H) 1.55-1.61 (3H) 1.48-1.55 (3H) 1.34 (d, *J* = 6.6 Hz, 3H) 1.20-1.33 (bs, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ (ppm) 145.9 (C) 137.4 (C) 128.3 (CH) 126.7 (CH) 126.5 (CH) 120.9 (CH) 58.3 (CH) 47.5 (CH_2) 35.7 (CH_2) 28.2 (CH_2) 28.1 (CH_2) 25.2 (CH_2) 24.3 (CH_3) 23.0 (CH_2) 22.5 (CH_2); IR (NaCl dep from DCM) 3338, 3060, 3025, 2925, 2856, 2835, 1663, 1604 cm^{-1}. HRMS (ES$^+$): calcd for $[C_{17}H_{26}N]^+$ 244.2065; found 244.2055.

5. Experimental directions for X-ray crystallography

Crystals were grown according to experimental procedures outlined in the text. Data were collected using a Bruker SMART APEX CCD area detector diffractometer at 100 K (**2a**: eva27, **1b**·HBr: eva30, **9a**·HCl: eva32, **12a**: eva36, **S6**: eva40), or 293K (**2h**·HCl: eva45, **2i**·HCl: eva46). A full sphere of reciprocal space was scanned by phi-omega scans. Pseudo-empirical absorption correction based on redundant reflections was performed by the program SADABS (X-1). The structures were solved by direct methods using SHELXS-97 (X-2) and refined by full matrix least-squares on F^2 for all data using SHELXL-97 (X-3).

The treatment of the hydrogen atoms varied from compound to compound, depending on the quality of the dataset. For **2a**: eva27 and **1b**·HBr: eva30, all hydrogen atoms were located in the difference Fourier map and allowed to refine freely. In **12a**: eva36 and **2i**·HCl: eva46, hydrogen atoms were added at calculated positions and refined using a riding model. Their isotropic temperature factors were fixed to 1.2 times (1.5 times for methyl groups) the equivalent isotropic displacement parameters of the carbon atom the H-atom is attached to. In the remaining compounds hydrogen atoms attached to carbon were treated as in **12a**: eva36 and **2i**·HCl: eva46, and hydrogen atoms attached to nitrogen or oxygen were treated as in **2a**: eva 27 and **1b**·HBr: eva30. Anisotropic thermal displacement parameters were used for all non-hydrogen atoms. In **12a**: eva36 the refinement of the absolute structure parameter did not converge properly. Since the crystal had grown from a solution of the racemic mixture the absolute structure parameter was fixed to 0.5. In **S6**: eva40, the two disorder parts were restrained to have the same shape using SADI commands. In **2i**·HCl: eva46 DELU (rigid bond) restraints were applied to all thermal displacement parameters.

(X-1) Sheldrick, G.M. SADABS, Bruker AXS Inc., Madison, WI 53711, 2000.

(X-2) Sheldrick, G. M., SHELXS-97, University of Göttingen 1997.

(X-3) Sheldrick, G. M., SHELXL-97-2, University of Göttingen 1997.

6. X-Ray-structure of 2a

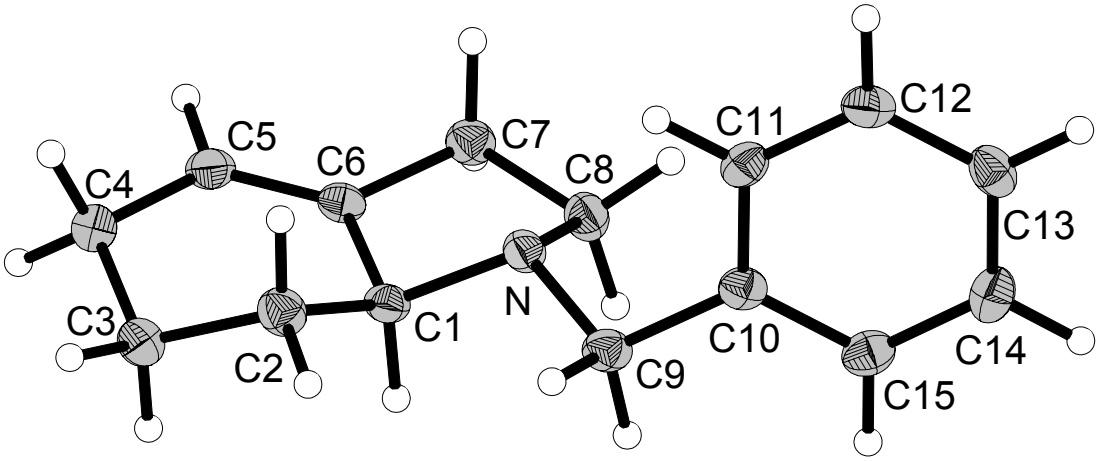


Figure S1: X-Ray Structure of 2a, thermal ellipsoid drawn on the 50% level. (X-ray depicted using Mercury 1.4)

Compound **2a**; Molecular formula: $C_{15}H_{19}N$; Formula weight: 213.31 $gmol^{-1}$; Crystal system: Triclinic; Unit cell dimensions: a = 5.8108(8) Å, α = 68.858(3)°; b = 10.4031(15) Å, β = 87.535(3)°; c = 10.8646(15) Å, γ = 79.418(3)°; Volume: 601.95(15) $Å^3$; Temperature: 100(2) K; Space group: P–1; Number of formula units in unit cell (Z): 2; Reflections collected: 6448; Independent reflections: 2129 [R(int) = 0.0348]; Final R indices [I>2sigma(I)]: R1 = 0.0370, wR2 = 0.0885; R indices (all data): R1 = 0.0461, wR2 = 0.0934.

7. X-Ray-structure of 1b·HBr.

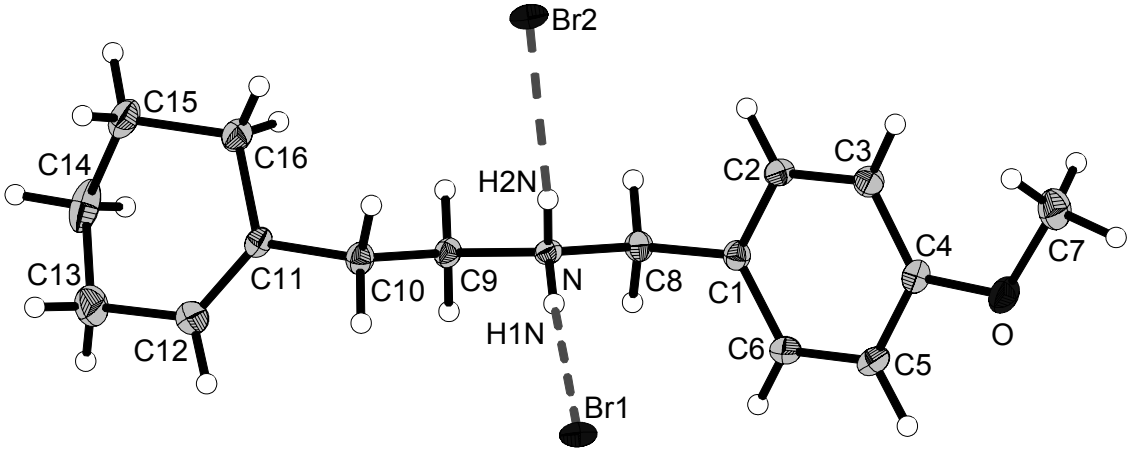


Figure S2: X-Ray Structure of 1b·HBr, thermal ellipsoid drawn on the 50% level. (X-ray depicted using Mercury 1.4)

Compound **1b** HBr; Molecular formula: $C_{16}H_{24}NOBr$; Formula weight: 326.27 $gmol^{-1}$; Crystal system: Monoclinic; Unit cell dimensions: a = 29.078(7) Å, α = 90°; b = 4.8656(12) Å, β = 96.268(5)°; c = 22.535(5) Å, γ = 90°; Volume: 3169.3(13) $Å^3$; Temperature: 100(2) K; Space group: C2/c; Number of formula units in unit cell (Z): 8; Reflections collected: 32279; Independent reflections: 4257 [R(int) = 0.0307]; Final R indices [I>2sigma(I)]: R1 = 0.0255, wR2 = 0.0626; R indices (all data): R1 = 0.0296, wR2 = 0.0645.

8. X-Ray-structure of S6

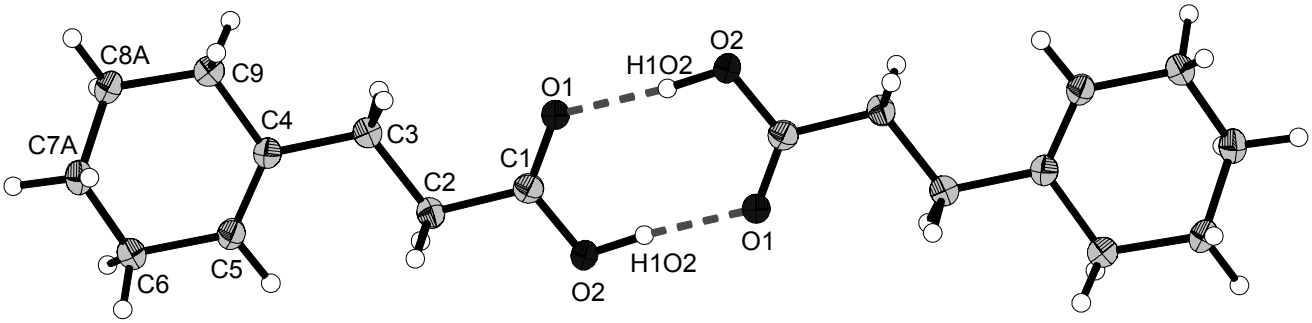


Figure S3: X-Ray Structure of S6, thermal ellipsoid drawn on the 50% level. Unit cell contained three different types of molecule S6, of which one contained disorder (not shown). (X-ray depicted using Mercury 1.4)

Compound **S6**; Molecular formula: $C_9H_{14}O_2$; Formula weight: 154.20 $gmol^{-1}$; Crystal system: Triclinic; Unit cell dimensions: a = 7.3608(7) Å, α = 103.092(2)°; b = 12.1760(11) Å, β = 93.820(2)°; c = 15.1409(14) Å, γ = 100.303(2)°; Volume: 1292.3(2) $Å^3$; Temperature: 100(2) K; Space group: P–1; Number of formula units in unit cell (Z): 6; Reflections collected: 19207; Independent reflections: 4122 [R(int) = 0.0327]; Final R indices [I>2sigma(I)]: R1 = 0.0353, wR2 = 0.0810; R indices (all data): R1 = 0.0431, wR2 = 0.0850.

9. References

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[3] For a different route, including characterization, see the supporting information of: D. Solé, Y. Concho, A. Llebaria, J. M. Moretó, and A. Delgado, *J. Org. Chem.*, 1996, **61**, 5895.
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[10] For a different route, including characterization, see: Z.-H. Shao, F.-Z. Peng, B.-K. Zhu, Y.-Q. Tu and H.-B. Zhang, *Chin. J. Chem.*, 2004, **22**, 727.