

Improved procedure for the synthesis of enamines *N*-oxides

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1. General methods

All solvents were reagent grade. PE refers to light petroleum b.p. 40-60°C. Diethyl ether (Et₂O) and tetrahydrofuran (THF) were freshly distilled from sodium/benzophenone under argon. Dichloromethane (CH₂Cl₂) was freshly distilled from calcium hydride under argon. Reagents were purchased from commercial sources and used without further purification unless otherwise stated.

Products were purified by flash-chromatography^[1] (eluent composition given in parentheses).

Stationary phase	Column packing	TLC
SiO ₂	Fluorochem Davisil silica gel (35-70 µm)	Merck Kieselgel 60 F ₂₄₅₊₃₆₆
Deactivated SiO ₂	Fluorochem Davisil silica gel (35-70 µm) stirred for 2 h with 2.5 wt.-% of Et ₃ N.	Merck Kieselgel 60 F ₂₄₅₊₃₆₆ plates dipped in a 10 vol.-% Et ₃ N solution in Et ₂ O and dried before use.
Neutral Al ₂ O ₃	Acros aluminium oxide, activated, neutral, 50-200 µm	Fluka aluminium oxide on aluminium sheets F ₂₄₅ plates
Basic Al ₂ O ₃	Acros aluminium oxide, activated, basic, 50-200 µm	

¹H-NMR [CHCl₃ (7.26 ppm^[2]) internal standard in CDCl₃; benzene-d₅ (7.16 ppm^[2]) internal standard in benzene-d₆] and ¹³C-NMR [CDCl₃ (77.16 ppm^[2]) as internal standard in CDCl₃; benzene-d₆ (128.06 ppm^[2]) internal standard in benzene-d₆]: the assignments of ¹H- and ¹³C-NMR resonances refer to the IUPAC nomenclature; primed numbers belong to the side-chain. Chemical shifts (δ) quoted in ppm; integrals in accord with assignments; coupling constants (J) quoted in Hz; **Melting points** are uncorrected; **Crystal structure determination:** Diffraction data were collected on an APEX CCD area detector, using graphite monochromated MoK_α radiation (λ = 0.71073 Å), from a crystal cooled to 150 K using an open-flow nitrogen gas cryostat^[3]. The structure was solved by direct methods using *SHELXS97*^[4] and refined by full-matrix least squares using *SHELXL97*^[4]. The figure was produced using *PLATON*^[5] which was also used for structure validation.

1.1. General procedure GP1: Preparation of dry mCPBA

Following a procedure slightly modified from that of Aggarwal and coworkers^[6], commercial 3-chloroperoxybenzoic acid (Aldrich 57-86%, 30 g) was dissolved in 350 ml CH₂Cl₂ and washed with 3 × 150 mL buffer solution (410 ml 0.1 M NaOH, 250 ml 0.2 M KH₂PO₄ made up to 1 l, pH 7.5). The organic layer was dried over Na₂SO₄ and carefully evaporated under reduced pressure to give ca. 12 g mCPBA. Iodometric titration^[7] gave a purity of 82 wt.-%. (In the original literature, diethyl ether was used for the extraction. To avoid the hazard of incidental formation of dialkyl peroxides, we used CH₂Cl₂ instead. The separation of the 2

¹ Still; Kahn; Mitra, *J. Org. Chem.* **1978**, *43*, 2923-2925.

² Gottlieb; Kotlyar; Nudelman, *J. Org. Chem.* **1997**, *62*, 7512-7515.

³ Cosier; Glazer, *J. Appl. Crystallogr.* **1986**, *19*, 105-107.

⁴ Sheldrick, *Acta Crystallogr., Sect. A: Found. Crystallogr.* **2008**, *A64*, 112-122.

⁵ Spek, *J. Appl. Crystallogr.* **2003**, *36*, 7-13.

⁶ Aggarwal; Gültekin; Grainger; Adams; Spargo, *J. Chem. Soc., Perkin Trans. I* **1998**, 2771-2781.

⁷ Woodward in *Transition metals in Organic Synthesis: A practical approach*, Gibson, Ed., Oxford University Press: Oxford, **1997**.

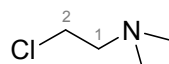
layers is slower with CH₂Cl₂ than with Et₂O. In CH₂Cl₂, the solubility of *m*CPBA is excellent but that of the 3-chlorobenzoic acid is significantly lower than in Et₂O.)

1.2. General procedure GP2: β -chloroamines from their corresponding hydrochlorides

(Following the procedure of Hickmott, Wood, and Murray-Rust, ref. [8])

The commercially available hydrochloride (20.0 mmol) was dissolved in water (10 mL) and the solution was basified by adding solid Na₂CO₃. The solution was extracted with Et₂O (4 \times 15 mL), dried (MgSO₄), and the combined organic extracts were dried (MgSO₄) and concentrated under reduced pressure. The residual oil was shown by ¹H-NMR to be the pure free amine.

1.2.1. *N*-(2-chloroethyl)-dimethylamine (**7aa**)



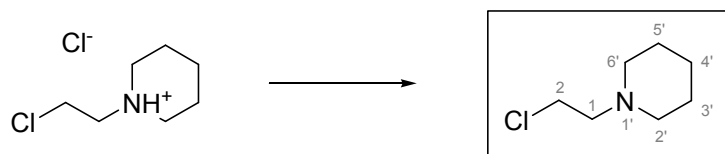
* **CARE!** β -chloroamines are known to have a high toxicity. They should be handled in a fumehood only, and with appropriate care.

(Described in literature^[8]) Prepared according to general procedure GP2, using 2-Dimethylaminoethyl chloride•HCl (2.88 g, 20 mmol) and Na₂CO₃ (4.24 g, 40 mmol). This β -chloroamine is very volatile. Therefore, concentration on the rotary evaporator (bath temperature: 30°C) was limited to a few minutes: the ¹H-NMR spectrum consequently shows the presence of some residual Et₂O. Concentration afforded 1.26g of colourless oil. Yield: 59%.

The β -chloroamine is not stable and should be stored at 0°C and used within 24h (after prolonged storage a white precipitate appears, presumably indicating internal cyclisation to the corresponding aziridinium).

¹H-NMR (CDCl₃, 270 MHz) δ_H = 3.49 (t, ³J_{2-H,1-H} = 6.8 Hz, 2-H₂) 2.57 (t, ³J_{1-H,2-H} = 6.8 Hz, 1-H₂), 2.21 (s, NMe₂); ¹³C-NMR (CDCl₃, 125 MHz) δ_H = 61.0 (C-1), 45.5 (NMe₂), 41.7 (C-2).

1.2.2. *N*-(2-chloroethyl)-piperidine (**7ca**)



* **CARE!** β -chloroamines are known to have a high toxicity. They should be handled in a fumehood only, and with appropriate care.

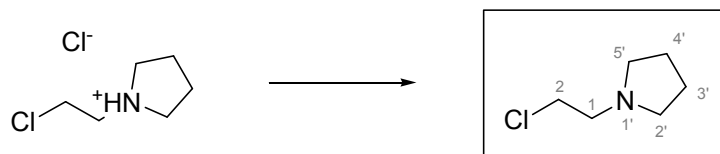
(Described in literature^[8]) Prepared according to general procedure GP2. Prepared according to general procedure GP2, using *N*-(2-Chloroethyl)piperidine•HCl (3.68 g, 20 mmol) and Na₂CO₃ (4.15 g, 40 mmol). Concentration on the rotary evaporator (bath temperature: 30°C) afforded 2.79g of colourless oil. Yield: 94%.

¹H-NMR (CDCl₃, 400 MHz) δ_H = 3.57 (t, ³J_{2-H,1-H} = 7.5 Hz, 2-H₂), 2.68 (t, ³J_{1-H,2-H} = 7.5 Hz, 1-H₂), 2.52-2.33 (m, 2'-H₂ and 6'-H₂), 1.63-1.52 (m, 3'-H₂ and 5'-H₂), 1.49-1.35 (m, 4'-H₂);

⁸ Hickmott; Wood; Murray-Rust, *J. Chem. Soc., Perkin Trans. 1* **1985**, 2033-2038.

^{13}C -NMR (CDCl_3 , 101 MHz): δ_{C} = 60.8 (C-1), 54.7 (C-2', C-6'), 41.2 (C-2), 26.0 (C-3', C-5'), 24.3 (C-4').

1.2.3. *N*-(2-chloroethyl)-pyrrolidine (**7da**)



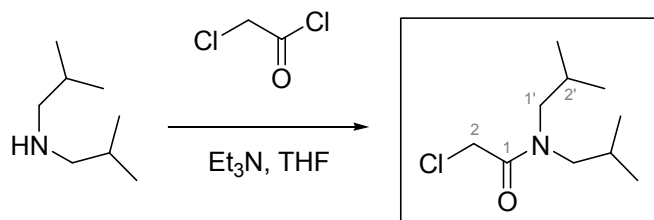
* **CARE!** β -chloroamines are known to have a high toxicity. They should be handled in a fumehood only, and with appropriate care.

(Described in literature^[8]) Prepared according to general procedure GP2, using *N*-(2-Chloroethyl)pyrrolidine•HCl (3.40 g, 20 mmol) and K_2CO_3 (4.15 g, 30 mmol). Concentration on the rotary evaporator (bath temperature: 30°C) afforded 2.47g of colourless oil. Yield: 92%.

^1H -NMR (CDCl_3 , 270 MHz) δ_{H} = 3.59 (t, $^3J_{2-\text{H},1-\text{H}}$ = 7.0 Hz, 2-H₂), 2.82 (t, $^3J_{1-\text{H},2-\text{H}}$ = 7.0 Hz, 1-H₂), 2.60-2.52 (m, 2'-H₂ and 5'-H₂), 1.82-1.75 (m, 3'-H₂ and 4'-H₂); **^{13}C -NMR** (CDCl_3 , 101 MHz): δ_{C} = 58.1 (C-1), 54.3 (C-2'/C-5'), 42.7 (C-2), 23.6 (C-3'/C-4'); **HRMS** (ESI, pos., CH_3CN), calcd. for $\text{C}_6\text{H}_{13}\text{ClN}^+$ ($[\text{M}+\text{H}]^+$): m/z = 134.0731, found: 134.0743.

1.3. α -chloroamides from α -chloroacetyl chloride

1.3.1. General procedure GP3: 2-Chloro-*N,N*-diisobutylacetamide



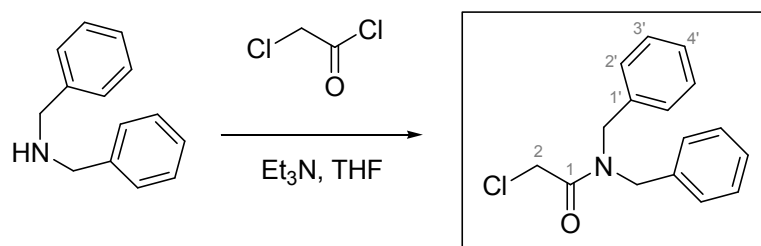
To an ice-cooled solution of α -chloroacetyl chloride (3.98 mL, 50 mmol) in Et_2O (100 mL) was added *i*-Bu₂NH (6.15 mL, 35 mmol) dropwise, followed by Et_3N (4.90 mL, 35 mmol). After stirring at room temperature for 8h, the reaction mixture was diluted with Et_2O (50 mL), washed with aq. HCl (1 M, 40 mL), then with sat. aq. NaHCO_3 (15 mL), and finally with brine (30 mL).

The organic layer was separated and dried (Na_2SO_4). Concentration *in vacuo* afforded the known amide^[9] as an amber oil (7.05 g), of sufficient purity as determined by ^1H - and ^{13}C -NMR. Yield: 98%.

IR (CHCl_3): ν = 2960, 2930, 2875, 1650, 1460, 1390, 1370, 1125, 1100 cm^{-1} ; **^1H -NMR** (CDCl_3 , 400 MHz) δ_{H} = 4.08 (s, 2-H₂), 3.20 (d, 3J = 7.6 Hz) and 3.13 (d, 3J = 7.6 Hz) (2 sets of 1'-H₂ due to anisotropy), 2.03 (spt, J = 7.1 Hz) and 1.93 (spt, J = 6.90 Hz) (2 distinct 2'-H due to anisotropy), 0.92 (d, J = 6.7 Hz, 6H) and 0.88 (d, J = 6.7 Hz, 6H) [2 sets of 2'-(CH₃)₂ due to anisotropy]; **^{13}C -NMR** (CDCl_3 , 101 MHz) δ_{C} = 167.2 (C-1), 55.8 and 53.1 (C-1'a and C-1'b), 41.5 (C-2), 27.9 and 26.4 (C-2'a and C-2'b), 20.2 (2'-Me₂); **Anal.** calcd. for $\text{C}_{10}\text{H}_{20}\text{ClNO}$: C 58.38%, H 9.80%, N 6.81%, found C 58.10%, H 9.77%, N 6.77%.

⁹ Speziale; Hamm, *J. Am. Chem. Soc.* **1956**, 78, 2556-2557.

1.3.2. 2-Chloro-*N,N*-dibenzylacetamide



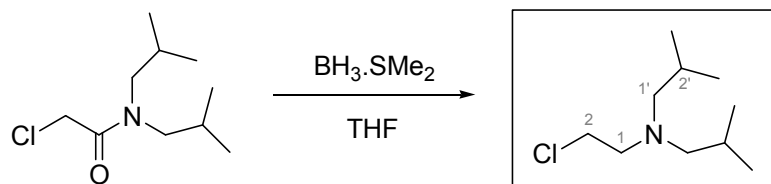
To an ice-cooled solution of α -chloroacetyl chloride (3.98 mL, 50 mmol) in THF (100 mL) was added Bn_2NH (9.61 mL, 50 mmol) dropwise, followed by Et_3N (6.97 mL, 50 mmol). After stirring at room temperature for 8h, the reaction mixture was diluted with Et_2O (100 mL), washed with aq. HCl (1 M, 75 mL), then with sat. aq. NaHCO_3 (20 mL), and finally with brine (30 mL).

The organic layer was separated and dried (Na_2SO_4). Concentration *in vacuo* afforded the known amide^[9] as an amber oil (13.11 g), of sufficient purity as determined by ^1H - and ^{13}C -NMR. Yield: 96%.

^1H -NMR (CDCl_3 , 270 MHz) δ_{H} = 7.38-7.08 (m, $2 \times \text{Ph}$), 4.57 (s) and 4.46 (s) ($2 \times \text{CH}_2\text{Ph}$), 4.10 (s, 2- H_2); ^{13}C -NMR (CDCl_3 , 101 MHz): δ_{C} = 167.4 (C-1), 136.5, 135.8 ($2 \times \text{C-1'}$), 129.2, 128.8, 128.3, 126.5 ($2 \times \text{C-2'}/\text{C-6'}$ and $2 \times \text{C-3'}/\text{C-5'}$), 128.1, 127.8 ($2 \times \text{C-4'}$), 50.4, 48.7 ($2 \times \text{CH}_2\text{Ph}$), 41.5 (C-2).

1.4. $\text{BH}_3\cdot\text{Me}_2\text{S}$ Reduction of α -chloroamides

1.4.1. General procedure GP4: *N*-(2-chloroethyl)-*N,N*-diisobutylamine (**7ea**)



* **CARE!** Dimethyl sulphide is malodorous, β -chloroamines are toxic. Work in a fumehood, neutralise glassware with commercial bleach solution.

To a solution of the amide (5.00 mmol, 1.03 g) in THF (20 mL), cooled at 0-5°C with an ice bath, was added $\text{BH}_3\cdot\text{SMe}_2$ (1.19 mL, 2.5 mmol, 2.5 eq.). After 15 min., the ice bath was removed and the mixture was stirred at r.t. overnight.

To the ice-cooled reaction mixture was carefully added aq. HCl (2 M) dropwise until a clear solution was obtained and gas evolution stopped. * The mixture was then basified by addition of aq. NaOH (2 M) and diluted with Et_2O (25 mL). The layers were separated and the aqueous layer was extracted with Et_2O (2×20 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated * *in vacuo* to afford the β -chloroamine (0.95 g) as a colourless oil. Yield: 99%.

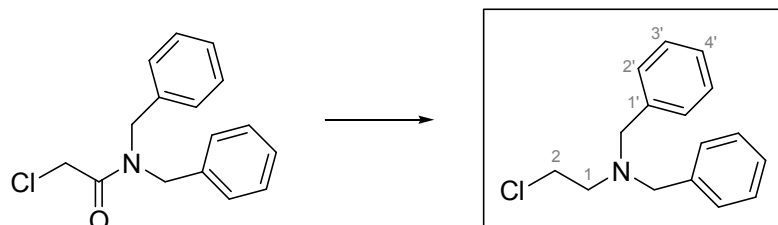
(Described in literature^[10])

^1H -NMR (CDCl_3 , 400 MHz) δ_{H} = 3.47 (t, $^3J_{2\text{-H},1\text{-H}}$ = 7.6 Hz, 2- H_2), 2.71 (t, $^3J_{1\text{-H},2\text{-H}}$ = 7.6 Hz, 1- H_2), 2.15 (d, $^3J_{1'\text{-H}_2,2'\text{-H}}$ = 7.3 Hz, 1'- H_2), 1.66 (th, $^3J_{2'\text{-H},1'\text{-H}_2} = ^3J_{2'\text{-H},2'\text{-CH}_3}$ = 6.7 Hz, 2'-H),

¹⁰ Bachman; Szmant, *J. Am. Chem. Soc.* **1946**, 68, 31-34.

0.87 (d, $^3J_{2'-\text{CH}_3, 2'-\text{H}} = 6.6$ Hz, 2'-CH₃); $^{13}\text{C-NMR}$ (CDCl₃, 67.9 MHz): $\delta_{\text{C}} = 64.5$ (C-1'), 57.5 (C-1), 42.2 (C-2), 27.1 (C-2'), 20.9 (2'-CH₃); **HRMS** (ESI, pos., CH₃CN), calcd. for C₁₀H₂₃ClN⁺ ([M+H]⁺): $m/z = 192.1514$, found: 192.1504.

1.4.2. *N*-(2-chloroethyl)-*N,N*-dibenzylamine (**7fa**)



* **CARE!** Dimethyl sulphide is malodorous, β -chloroamines are toxic. Work in a fumehood, neutralise glassware with commercial bleach solution.

To a solution of the amide (2.74 g, 10.0 mmol) in THF (20 mL), cooled at 0-5°C with an ice bath, was added BH₃.SMe₂ (2.38 mL, 25.0 mmol, 2.5 eq.). After 15 min., the ice bath was removed and the mixture was stirred at r.t. overnight.

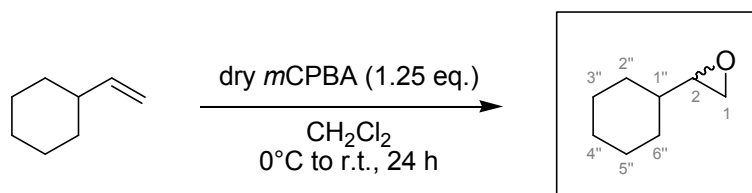
The ice-cooled reaction mixture was acidified with aq. HCl (6 M) dropwise until a clear solution was obtained and gas evolution stopped. Basification with NaOH (2 M) and extraction with Et₂O (3 × 20 mL) afforded the crude chloroamine as a mixture with the starting chloroamide (2.55 g). After flash chromatography (SiO₂, PE:Et₂O:Et₃N = 1:1:0.1), the title compound (4.75 mmol) was obtained as a pale yellow oil. Yield: 47%.

(Described in literature^[11,12])

$^1\text{H-NMR}$ (CDCl₃, 270 MHz) $\delta_{\text{H}} = 7.50$ -7.18 (m, 2 × Ph), 3.66 (s, CH₂Ph), 3.50 (t, $^3J_{2-\text{H}_2, 1-\text{H}_2} = 7.2$ Hz, 2-H₂), 2.84 (t, $^3J_{1-\text{H}_2, 2-\text{H}_2} = 7.2$, 1-H₂); $^{13}\text{C-NMR}$ (CDCl₃, 101 MHz): $\delta_{\text{C}} = 139.3$ (C-1'), 128.9, 128.5 (C-2'/C-6' and C-3'/C-5'), 127.3 (C-4'), 58.9 (CH₂Ph), 55.5 (C-1), 42.0 (C-2); **HRMS** (ESI, pos., CH₃CN), calcd. for C₁₆H₁₉ClN ([M + H]⁺): $m/z = 260.1201$, found: 260.1213.

1.5. Epoxidation of alkenes with *m*CPBA

1.5.1. General procedure GP5: Cyclohexyl oxirane (*rac.* **3c**)



To an ice-cooled solution of vinylcyclohexane (Alfa Aesar, 98+%, 2.20 g, 20.0 mmol) in anhydrous CH₂Cl₂ (100 mL) was added dried *m*CPBA (82 wt.-%, 5.26 g, 25.0 mmol). After 15 min, the ice bath was removed and the reaction stirred at room temperature for 24 h. After dilution with pentane (100 mL), the suspension was filtered over a short (3 cm) plug of Al₂O₃ (neutral, Ø = 2.5 cm). Removal of the solvents under reduced pressure afforded cyclohexyl oxirane (2.14 g) as a clear, colourless, and fruity-smelling oil. It was used without further

¹¹ Dupre; Elks; Hems; Speyer; Evans, *J. Chem. Soc.* **1949**, 500-510.

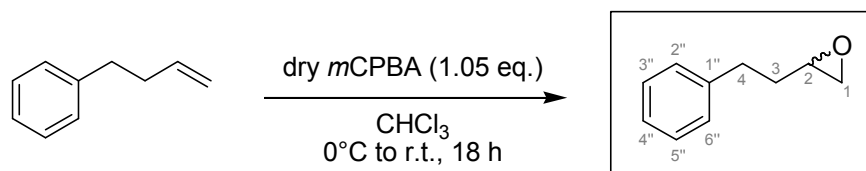
¹² Trapani; Reho; Latrofa, *Synthesis* **1983**, 1013-1014.

purification for the next step (^1H -NMR did not show any appreciable amount of contaminant). Yield: 85%.

(Described in literature^[13])

^1H -NMR (CDCl_3 , 270 MHz) $\delta_{\text{H}} = 3.00\text{--}2.85$ (m, 1-H and 2- H_{a}), 2.53 (poorly resolved dd, $J = 4.4$, $J = 3.7$, 2- H_{b}), 1.93–1.80 (m, 1 H), 1.80–1.65 (m, 4 H), 1.32–1.03 (m, 6 H); ^{13}C -NMR (CDCl_3 , 101 MHz): $\delta_{\text{C}} = 56.9$ (C-1), 46.2 (C-2), 40.5 (C-1'), 29.9, 29.0, 26.5, 25.8, 25.7 (C-2' to C-6').

1.5.2. Phenethyl oxirane (3,4-epoxybutyl benzene, *rac.* **3d**)



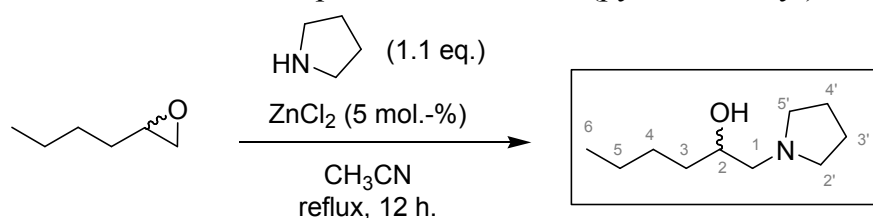
To a solution of 4-phenylbut-1-ene (Alfa Aesar, 98+%, 2.64 g, 20 mmol) in CHCl_3 (100 mL) was added dried *m*CPBA (82 wt-%, 1.25 eq., 5.26 g) at 0°C (ice bath), and the mixture stirred 30 min. at this temperature. The ice bath was then removed and the mixture was stirred further at r.t. for 18h, at which point TLC showed disappearance of the starting material. The mixture was washed with a 1:1 mixture of water and sat. aq. NaHCO_3 (2×25 mL) and pH 7 buffer (25 mL). Flash-chromatography (SiO_2 , \varnothing 2.5 cm, $h = 12$ cm, $\text{PE}:\text{Et}_2\text{O} = 10:1$, F7-15) yielded the title compound ($m = 2.21$ g) as a colourless oil. Yield: 74%.

(Described in literature^[14])

^1H -NMR (CDCl_3 , 400 MHz) $\delta_{\text{H}} = 7.34\text{--}7.27$ (m, 2''-H/6''-H), 7.24–7.18 (3''-H/5''-H and 4''-H), 2.99–2.93 (m, 2-H), 2.89–2.71 (m, 4- H_2 and 1- H^{a}), 2.48 (dd, $J = 5.0$, $J = 2.8$, 1- H^{b}), 1.95–1.79 (3- H_2); ^{13}C -NMR (CDCl_3 , 101 MHz): $\delta_{\text{C}} = 141.4$ (C-1''), 128.6 and 128.5 (C-2''/C-6'' and C-3''/C-5''), 126.1 (C-4''), 51.9 (C-2), 47.4 (C-1), 34.4 and 32.3 (C-3 and C-4).

1.6. Aminolysis of epoxides

1.6.1. General procedure GP6a: 1-(pyrrolidin-1-yl)hexan-2-ol (*rac.* **4db**)



(Described in literature^[15])

To a solution of 1,2-epoxyhexane (4.00 mL, 33.2 mmol) and pyrrolidine (Fluka, 2.86 mL, 33.2 mmol, 1.0 eq.) in CH_3CN (25 mL) was added zinc chloride (Fischer Scientific, 226 mg, 5 mol.-%). The resulting clear solution was refluxed for 12 h under an argon atmosphere. After cooling down, the mixture was diluted with AcOEt (40 mL) and the zinc chloride was removed by filtration over a short plug (3 cm) of silica gel ($\varnothing = 4.5$ cm), which was subsequently rinsed with AcOEt (2×70 mL). The organic washings were combined and the solvents were removed under reduced pressure, yielding a clear colourless oil (3.73 g), of sufficient purity to be used as such for the next steps. Yield: 66%.

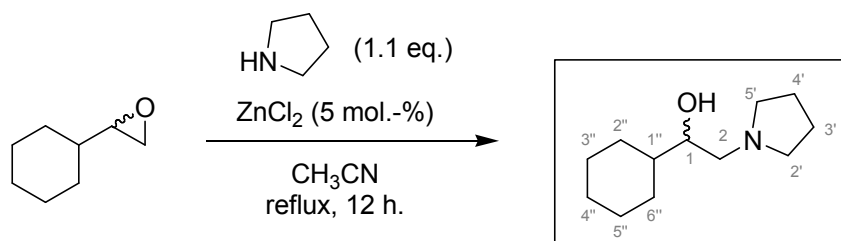
¹³ White; Doyle; Jacobsen, *J. Am. Chem. Soc.* **2001**, 123, 7194–7195.

¹⁴ Elings; Downing; Sheldon, *Eur. J. Org. Chem.* **1999**, 4, 837–846.

¹⁵ Mojtahedi; Saidi; Bolourtchian, *J. Chem. Res., Synop.* **1999**, 2, 128–129.

IR (CHCl₃): ν = 3440, 2955, 2930, 2870, 2800, 1460, 1350, 1290, 1220, 1145, 1080, 915, 770, 745 cm⁻¹; **¹H-NMR** (CDCl₃, 400 MHz): δ_H = 3.63 (dddd, $^3J_{2-H,1-H_a} = 10.6$, $^3J_{2-H,3-H_b} = 6.9$, $^3J_{2-H,3-H_b} = 4.5$, $^3J_{2-H,1-H_a} = 3.0$, 2-H), 3.59 (br. s, OH), 2.72-2.62 and 2.49-2.39 (m, 2'/5'-H₂, axial and equatorial), 2.56 (dd, $^2J_{1-H_a,1-H_b} = 11.9$, $^3J_{1-H_a,2-H} = 10.6$, 1-H_a), 2.26 (dd, $^2J_{1-H_b,1-H_a} = 11.9$, $^3J_{1-H_b,2-H} = 3.0$, 1-H_b), 1.82-1.70 (m, 3'/4'-H₂), 1.56-1.23 (m, 3-H₂, 4-H₂ and 5-H₂), 0.90 (t, $J_{6-H_3,5-H_2} = 7.1$, 6-H₃); **¹³C-NMR** (CDCl₃, 101 MHz): δ_C = 68.4 (C-2), 62.2 (C-1), 54.1 (C-2'/C-5'), 35.0 (C-3), 28.0 (C-4), 23.8 (C-3'/C-4'), 23.0 (C-5), 14.2 (C-6); **HRMS** (ESI, pos., MeOH), calc for C₁₀H₂₂NO⁺ ([M+H]⁺) m/z : 172.1696, found: 172.1686.

1.6.2. 1-cyclohexyl-2-(piperidin-1-yl)ethanol (*rac.* **4dc**)

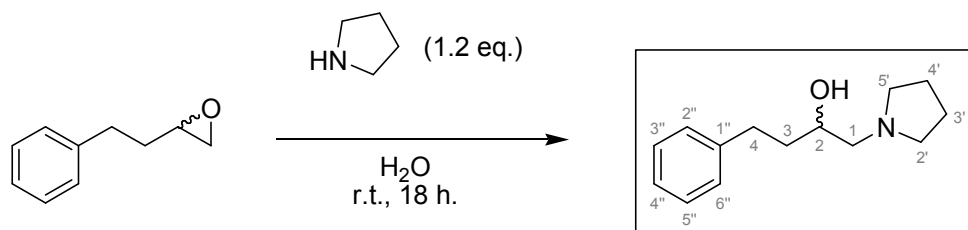


To a solution of cyclohexane oxirane (2.14 g, 17.0 mmol) and piperidine (Fluka, 98+%, 1.46 mL, 1.0 eq.) in CH₃CN (70 mL) was added zinc chloride (Fischer Scientific, 97+%, 116 mg, 5 mol.-%). The resulting clear solution was refluxed for 12 h under an argon atmosphere. After cooling down, the mixture was diluted with AcOEt (70 mL) and the zinc chloride was removed by filtration over a short plug (3 cm) of silica gel (\varnothing = 4.5 cm), which was subsequently rinsed with AcOEt (2 \times 70 mL). The organic washings were combined and the solvents were removed under reduced pressure. Flash chromatography (SiO₂; eluent PE:Et₂O:Et₃N = 1:1:0.1) of the residual oil afforded the aminoalcohol as a clear colourless oil (2.33 g). Yield: 69%.

(Described in literature^[16])

IR (CHCl₃): ν = 3440, 2925, 2850, 2795, 1450, 1350, 1310, 1260, 1220, 1110, 1050, 915, 770, 745 cm⁻¹; **¹H-NMR** (CDCl₃, 400 MHz, spectrum shows traces of Et₂O, PE and Et₃N): δ_H = 3.61 (br. s, 1-OH), 3.37 (ddd, $^3J_{2-H,1-H_a} = 10.8$, $^3J_{2-H,1''-H} = 6.4$, $^3J_{2-H,1-H_b} = 3.0$, 2-H), 2.73-2.67 and 2.47-2.37 (m, 2'/5'-H₂, axial and equatorial), 2.62 (dd, $^2J_{1-H_a,1-H_b} = 11.7$, $^3J_{1-H_a,2-H} = 10.8$, 1-H_a), 2.28 (dd, $^2J_{1-H_b,1-H_a} = 11.7$, $^3J_{1-H_b,2-H} = 3.0$, 1-H_b), 1.94-1.60 (m, 9H including 3'/4'-H₂), 1.42-0.82 (m, 6H); **¹³C-NMR** (CDCl₃, 101 MHz, spectrum shows traces of Et₂O, PE and Et₃N): δ_C = 72.0 (C-2), 59.5 (C-1), 53.9 (C-2'/C-5'), 42.4 (C-1''), 28.8 and 28.6 (C-2'' and C-6''), 26.6, 26.2, 26.1 (C-3'', C-4'', C-5''), 23.6 (C-3'/C-4'); **HRMS** (ESI, pos., CH₃CN), calcd. for C₁₂H₂₄NO⁺ ([M+H]⁺): m/z = 198.1852, found: 198.1843.

1.6.3. General procedure GP6b: 4-phenyl-1-(pyrrolidin-1-yl)butan-2-ol (*rac.* **4dd**)



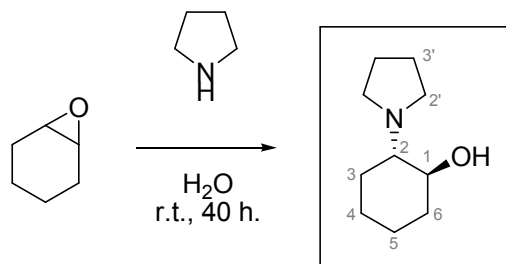
¹⁶ Miyano; Lu; Viti; Sharpless, *J. Org. Chem.* **1985**, *50*, 4350-4360.

A heterogenous mixture of 3,4-epoxybutyl benzene (5.15 g, 34.7 mmol) and pyrrolidine (3.60 mL, 41.8 mmol, 1.2 eq.) in water (18 mL) was stirred 18h at r.t. After dilution with EtOAc (35 mL), the layers were separated, and the aqueous layer was further extracted with EtOAc (3 × 20 mL). The organic extracts were combined, washed with brine (20 mL), filtered over a short plug of SiO₂, and dried (MgSO₄). Concentration under reduced pressure yielded a clear light amber oil (7.02 g), of sufficient purity to be used as such for the next steps. Yield: 92%.

R_F (SiO₂, PE:Et₂O:Et₃N = 10:1:0.1) = 0.38

IR (CHCl₃): ν = 3430, 3005, 2970, 2935, 2880, 2810, 1495, 1455, 1420, 1355, 1315, 1290, 1260, 1145, 1130, 1095, 1075, 1030, 885 cm⁻¹; **¹H-NMR** (CDCl₃, 400 MHz) δ_H = 7.32-7.14 (m, Ph), 3.67 (dddd, ³ $J_{2-H,1-Ha}$ = 10.7, ³ $J_{2-H,3-Ha}$ = 7.6, ³ $J_{2-H,3-Hb}$ = 4.4, ³ $J_{2-H,1-Hb}$ = 3.2, 2-H), 3.55 (br. s, 2-OH), 2.85 (ddd, J = 13.9, 10.0, 5.8 Hz, 4-H^a), 2.74-2.64 (m, 2'-H^a/5'-H^a and 4-H^b), 2.61 (dd, ³ $J_{1-Ha,1-Hb}$ = 11.7, ³ $J_{1-Ha,2-H}$ = 10.7, 1-H^a), 2.49-2.41 (m, 2'-H^b/5'-H^b), 2.29 (dd, ³ $J_{1-Hb,1-Ha}$ = 11.9, ³ $J_{1-Hb,2-H}$ = 3.0 Hz, 1H, 1-H^b), 1.73 (3-H₂); **¹³C-NMR** (CDCl₃, 101 MHz): δ_C = 142.5 (C-1''), 128.6 and 128.5 (C-3''/C-5'' and C-2''/C-6''), 125.9 (C-4''), 67.7 (C-2), 62.1 (C-1), 54.2 (C-2'/C-5'), 37.0 (C-3), 32.2 (C-4), 23.8 (C-3'/C-4'); **HRMS** (ESI, pos., CH₃CN), calcd. for C₁₄H₂₂NO⁺ ([M+H]⁺): m/z = 220.1696, found: 220.1690.

1.6.4. *trans*-2-(Pyrrolidin-1-yl)cyclohexanol (*rac. trans*-**4dx**)



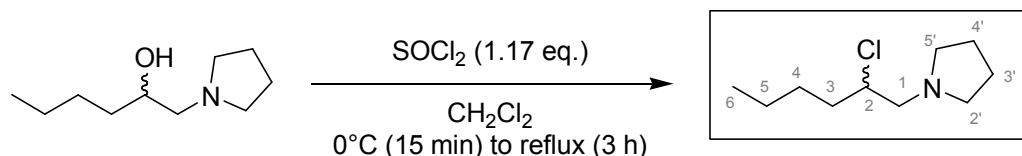
(Described in literature^[17,18])

To a mixture of cyclohexene oxide (Aldrich, 21.2 mL, 210 mmol, 1.05 eq.) and water (80 mL) was added pyrrolidine (16.6 mL, 200 mmol). After stirring at room temperature for 40 h, the mixture was diluted with EtOAc (100 mL). The layers were separated; the aqueous phase was washed with EtOAc (3 × 75 mL). The combined organic layers were washed with brine (35 mL), dried (Na₂SO₄) and concentrated at 40°C *in vacuo*, to afford the title compound (31.2 g) as an off-yellow oil, of sufficient purity to be used as such for the next steps. Yield: 92%.

¹H-NMR (CDCl₃, 400 MHz) δ_H = 4.04 (br s, OH), 3.35 (ddd, $^3J_{1-H,6-H_{ax}} \sim ^3J_{1-H,6-H_{eq}} = 9.5$, $^3J_{1-H,2-H} = 4.1$, 1-H), 2.68 (m, 2H), 2.54 (m, 2H), 2.45 (ddd, 1H, $^3J_{2-H,3-H_{ax}} = 11.0$, $^3J_{2-H,3-H_{eq}} = 9.5$, $^3J_{2-H,1-H} = 3.3$, 2-H), 2.10 (m, 1H), 1.82-1.64 (m, 7H), 1.32-1.10 (m, 4H, *one of the 3-H₂, one of the 4-H₂, one of the 5-H₂, one of the 6-H₂*); ¹³C-NMR (CDCl₃, 101 MHz): δ_C = 70.0 (C-1), 65.4 (C-2), 47.9 (2 × C-2'), 33.3 (C-6), 24.6 (2 × C-3'), 24.0, 23.4, 22.2 (C-3, C-4, C-5).

1.7. Chlorination of aminoalcohols

1.7.1. General procedure GP7: *N*-(2-chlorohexyl)pyrrolidine (*rac. 7db*)



* **CARE!** β -chloroamines are known to have a high toxicity. They should be handled in a fumehood only, and with appropriate care.

To an ice-cooled solution of 1-(pyrrolidin-1-yl)hexan-2-ol (2.58 g, 15.1 mmol) in anhydrous CH₂Cl₂ (35 mL) was added dropwise SOCl₂ (1.65 mL, 1.50 eq.). After the end of the addition, the ice bath was removed and the mixture was refluxed for 2 h. After cooling down to room temperature, the reaction mixture was poured into a mixture of ice water (50 mL) and sat. aq. NaHCO₃ (50 mL). The water phase was basified with NaOH (2 M), the layers were separated and the aqueous layer extracted with CH₂Cl₂ (3 × 50 mL). The combined organic extracts were dried (MgSO₄) and concentrated *in vacuo*. Flash-chromatography (SiO₂; eluent PE:Et₂O:Et₃N = 10:1:0.2) of the residual oil afforded the β -chloroamine as a pale amber-coloured oil (2.54 g). Yield: 89%.

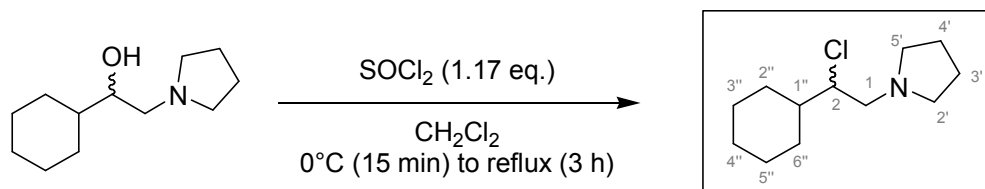
IR (CHCl₃): ν = 2960, 2935, 2875, 2800, 1465, 1380, 1355, 1315, 1295, 1245, 1145, 1105 cm⁻¹; ¹H-NMR (CDCl₃, 400 MHz) δ_H = 3.95 (dddd, $^3J_{2-H,3-H_a} = 9.2$, $^3J_{2-H,1-H_a} = 7.4$, $^3J_{2-H,3-H_b} = 5.8$, $^3J_{2-H,1-H_b} = 3.4$ Hz, 2-H), 2.78 (dd, $^2J_{1-H_a,1-H_b} = 12.7$, $^3J_{1-H_a,2-H} = 7.4$ Hz, 1-H_a), 2.67 (dd, $^2J_{1-$

¹⁷ Meguro; Asao; Yamamoto, *J. Chem. Soc., Perkin Trans. 1* **1994**, 2597-2601.

¹⁸ Chakraborti; Rudrawar; Kondaskar, *Org. Biomol. Chem.* **2004**, 2, 1277-1280.

$H_{b,1}-H_a = 12.7$, $^3J_{1-H_b,2-H} = 3.4$, $1-H_b$), 2.59-2.52 (m, $2'/5'-H_2$), 1.94-1.83 (m, $3-H_a$), 1.83-1.74 (m, $3'/4'-H_2$), 1.70-1.23 (m, $3-H_b$, $4-H_2$ and $5-H_2$), 0.92 (t, $J_{6-H_3,5-H_2} = 7.2$, $6-H_3$); $^{13}\text{C-NMR}$ (CDCl_3 , 101 MHz): $\delta_C = 63.8$ (C-1), 61.8 (C-2), 54.6 (C-2'/C-5'), 36.3 (C-3), 28.7 (C-4), 23.7 (C-3'/C-4'), 22.4 (C-5), 14.1 (C-6); **HRMS** (ESI, pos., MeOH), calc for $\text{C}_{10}\text{H}_{22}\text{ClNO}^+$ ($[\text{M}+\text{H}]^+$) m/z : 190.1357, found: 190.1353.

1.7.2. N-(2-chloro-2-cyclohexylethyl)pyrrolidine (rac. 7dc)

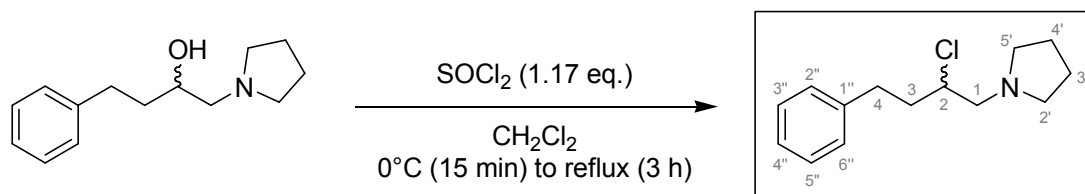


* **CARE!** β -chloroamines are known to have a high toxicity. They should be handled in a fumehood only, and with appropriate care.

Prepared according to general procedure GP7, using 1-cyclohexyl-2-(pyrrolidin-1-yl)ethanol (2.33 g, 11.8 mmol), SOCl_2 (1.0 mL, 1.17 eq.) in CH_2Cl_2 (25 mL) (reflux, 3h). Work-up and flash chromatography (SiO_2 ; eluent $\text{PE}:\text{Et}_2\text{O}:\text{Et}_3\text{N} = 10:1:0.2$), afforded the β -chloroamine as a pale amber-coloured oil (1.42 g). Yield: 56%.

IR (CHCl_3): $\nu = 2930, 2855, 2800, 1450, 1355, 1310, 1125, 895 \text{ cm}^{-1}$; **$^1\text{H-NMR}$** (CDCl_3 , 400 MHz) $\delta_H = 3.93$ (ddd, $^3J_{2-H,1-H_a} = 8.3$, $^3J_{2-H,1-H_b} = 5.0$, $^3J_{2-H,1''-H} = 3.3$, 2-H), 2.81 (dd, $^2J_{1-H_a,1-H_b} = 12.9$, $^3J_{1-H_b,2-H} = 8.3$, $1-H_a$), 2.71 (dd, $^2J_{1-H_b,1-H_a} = 12.9$, $^3J_{1-H_b,2-H} = 5.0$, $1-H_b$), 2.47-2.63 (m, $2'/5'-H_2$), 1.85-1.53 and 1.42-1.08 (m, $3'/4'-H_2$, $2''/6''-H_2$, $3''/5''-H_2$, $4''-H_2$); **$^{13}\text{C-NMR}$** (CDCl_3 , 101 MHz): $\delta_C = 67.3$ (C-2), 61.3 (C-1), 54.6 (C-2'/C-5'), 42.3 (C-1''), 30.6, 27.3, 26.4, 26.4, 26.1 (C-2'', C-3'', C-4'', C-5'', C-6''), 23.6 (C-3'/C-4'); **HRMS** (ESI, pos., CH_3CN), calcd. for $\text{C}_{12}\text{H}_{23}\text{ClN}^+$ ($[\text{M}+\text{H}]^+$): $m/z = 216.1514$, found: 216.1517.

1.7.3. 1-(2-chloro-4-phenylbutyl)pyrrolidine (rac. 7dd)



* **CARE!** β -chloroamines are known to have a high toxicity. They should be handled in a fumehood only, and with appropriate care.

Prepared according to general procedure GP7, using 4-phenyl-1-(pyrrolidin-1-yl)butan-2-ol (1.97 g, 9.0 mmol), SOCl_2 (1.0 mL, 1.52 eq.) in CH_2Cl_2 (20 mL) (reflux, 3h). Work-up and flash chromatography (SiO_2 ; eluent $\text{PE}:\text{Et}_2\text{O}:\text{Et}_3\text{N} = 10:1:0.2$), afforded the β -chloroamine as a pale amber-coloured oil (1.71 g). Yield: 80%.

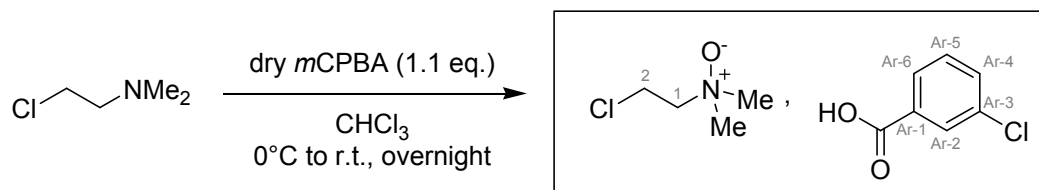
IR (CHCl_3): $\nu = 2930, 2855, 1700, 1570, 1450, 1360, 1305, 1070, 980, 895 \text{ cm}^{-1}$; **$^1\text{H-NMR}$** (CDCl_3 , 400 MHz) $\delta_H = 7.32$ -7.25 (m, $2''-H$ and $6''-H$), 7.24-7.16 ($3''-$, $4''-$ and $5''-H$), 3.92 (dddd, $^3J_{2-H,3-H_b} = 9.6$, $^3J_{2-H,1-H_a} = 7.3$, $^3J_{2-H,1-H_b} = 6.4$, $^3J_{2-H,3-H_a} = 3.1$, 2-H), 2.93 (ddd, $^2J_{4-H_a,4-H_b} = 13.9$, $^3J_{4-H_a,3-H_a} = 9.4$, $^3J_{4-H_a,3-H_b} = 4.8$, $4-H_a$), 2.79 (dd, $^2J_{1-H_a,1-H_b} = 12.6$, $^3J_{1-H_a,2-H} = 7.3$, $1-H_a$), 2.76 (ddd, $^2J_{4-H_b,4-H_a} = 13.9$, $^3J_{4-H_b,3-H_b} = 9.0$, $^3J_{4-H_b,3-H_a} = 7.3$, $4-H_b$), 2.70 (dd, $^2J_{1-H_b,1-H_a} = 12.6$, $^3J_{1-H_b,2-H} = 6.4$, $1-H_b$), 2.57-2.46 (m, $2'/5'-H_2$), 2.22 (dddd, $^2J_{3-H_a,3-H_b} = 14.2$, $^3J_{3-H_a,4-H_a} = 9.4$, $^3J_{3-H_a,4-H_b} = 7.3$, $^3J_{3-H_a,2-H} = 3.1$, $3-H_a$), 1.94 (dddd, $^2J_{3-H_b,3-H_a} = 14.2$, $^3J_{3-H_b,2-H} = 9.6$, $^3J_{3-H_b,4-H_b} = 9.0$,

$^3J_{3-H_a,4-H_b} = 4.8$, 3-H_b), 1.82-1.71 (m, 3'/4'-H₂); $^{13}\text{C-NMR}$ (CDCl₃, 101 MHz): $\delta_C = 141.3$ (C-1''), 128.7 and 128.6 (C-2''/C-6'' and C-3''/C-5''), 126.2 (C-4''), 63.6 (C-1), 60.8 (C-2), 54.6 (C-2', C-5'), 38.1 (C-3), 32.6 (C-4), 23.6 (C-3', C-4'); **HRMS** (ESI, pos., CH₃CN), calcd. for C₁₄H₂₁ClN⁺ ([M+H]⁺): $m/z = 238.1357$, found: 238.1363.

1.8. General procedure GP8: *N*-oxidation of tertiary β -chloroamines with *m*CPBA

Dried *m*CPBA (prepared according to GP1 and titrated according to ref. [7], usually containing 5-15% residual chlorobenzoic acid, 1.1-1.5 eq.) was dissolved in CH₂Cl₂ (to obtain an approximately 0.2 M solution). To this solution, cooled with an ice-brine bath, was added the amine slowly (approximately 1 mL/min) via syringe. The mixture was then stirred while being allowed to warm up to room temperature. After 2 to 12 h, consumption of the starting amine was completely as shown by TLC of a basified aliquot of the reaction mixture (Eluent PE/Et₂O/Et₃N: 1:1:0.1). The solvent was removed under reduced pressure to yield quantitative amounts of the *m*-chlorobenzoic acid salt (**8**) of the β -chloroamine *N*-oxide as a brown oil. In all cases, excess *m*-chlorobenzoic acid was the main contaminant; the excess of *m*-chlorobenzoic acid was assessed by $^1\text{H-NMR}$ to be between 0.2 and 0.7 eq. The highly hygroscopic nature of these salts (**8**) limits their suitability for combustion analysis.

1.8.1. *N*-(2-chloroethyl)-dimethylamine *N*-oxide (3-chlorobenzoic acid salt) (**8aa**)

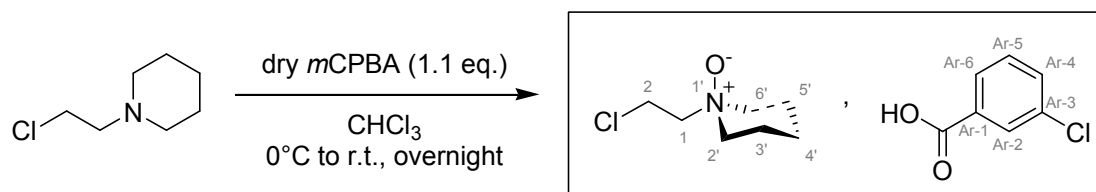


Prepared according to general procedure GP8. (Contains approx. 0.70 eq. excess *m*-chlorobenzoic acid, based on the $^1\text{H-NMR}$ integrations of the aromatic signals.)

IR (CHCl₃): $\nu = 3005, 1700, 1575, 1475, 1430, 1290, 1260, 1145, 1070, 905, 850\text{ cm}^{-1}$; **$^1\text{H-NMR}$** (CDCl₃, 270 MHz) $\delta_H = 10.40$ (br. s, OH), 8.05 (t, $^4J_{\text{Ar}2-\text{H}, \text{Ar}4-\text{H}} = ^4J_{\text{Ar}2-\text{H}, \text{Ar}6-\text{H}} = 1.5\text{ Hz}$, Ar2-H), 7.94 (dt, $^3J_{\text{Ar}6-\text{H}, \text{Ar}5-\text{H}} = 7.8\text{ Hz}$, $^4J_{\text{Ar}6-\text{H}, \text{Ar}2-\text{H}} = ^4J_{\text{Ar}6-\text{H}, \text{Ar}4-\text{H}} = 1.5\text{ Hz}$, Ar6-H)*, 7.48 (ddd, $^2J_{\text{Ar}4-\text{H}, \text{Ar}5-\text{H}} = 7.8\text{ Hz}$, $^3J_{\text{Ar}4-\text{H}, \text{Ar}6-\text{H}} \sim ^3J_{\text{Ar}4-\text{H}, \text{Ar}2-\text{H}} \sim 1.5\text{ Hz}$, Ar4-H)*, 7.35 (t, $^2J_{\text{Ar}5-\text{H}, \text{Ar}4-\text{H}} = ^2J_{\text{Ar}5-\text{H}, \text{Ar}6-\text{H}} = 7.8\text{ Hz}$, Ar5-H), 4.14 (t, $^3J_{2-\text{H}_2, 1-\text{H}_2} = 5.8\text{ Hz}$, 2-H₂), 3.98 (t, $^3J_{1-\text{H}_2, 2-\text{H}_2} = 5.8\text{ Hz}$, 1-H₂), 3.56 (s, NMe₂); **$^{13}\text{C-NMR}$** (CDCl₃, 100 MHz): $\delta_C = 169.7$ (CO₂H), 134.5, 134.3 (Ar-1, Ar-3), 132.4, 130.1, 129.6, 128.0 (Ar-2, Ar-4, Ar-5, Ar-6), 71.1 (C-1), 58.5 (NMe₂), 36.4 (C-2) **HRMS** (ESI, pos., CH₃CN), calc for C₄H₁₁ClNO⁺ ([M+H]⁺) m/z : 124.0524, found: 124.0522.

*The spectroscopic data does not allow unequivocal differentiation of 4' vs. 6'.

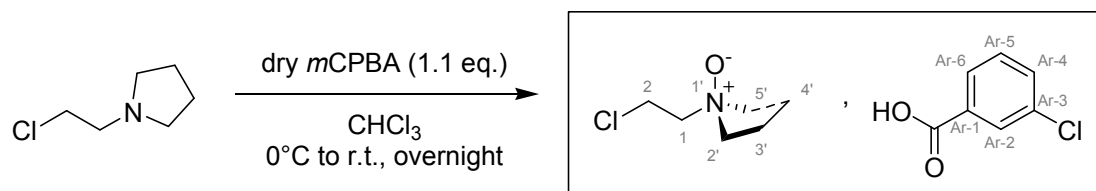
1.8.2. *N*-(2-chloroethyl)-piperidine *N*-oxide (3-chlorobenzoic acid salt) (**8ca**)



Prepared according to general procedure GP8. (Contains approx. 0.45 eq. excess *m*-chlorobenzoic acid, based on the ^1H -NMR integrations of the aromatic signals.)

IR (CHCl_3): $\nu = 3005, 2970, 1700, 1570, 1430, 1290, 1265, 940, 905, 850 \text{ cm}^{-1}$; **^1H -NMR** (CDCl_3 , 270 MHz) $\delta_{\text{H}} = 8.04$ (t, $^4J_{\text{Ar2-H}, \text{Ar4-H}} = ^4J_{\text{Ar2-H}, \text{Ar6-H}} = 1.6 \text{ Hz}$, Ar2-H), 7.93 (dt, $^3J_{\text{Ar6-H}, \text{Ar5-H}} = 7.8 \text{ Hz}$, $^4J_{\text{Ar6-H}, \text{Ar2-H}} = ^4J_{\text{Ar6-H}, \text{Ar4-H}} = 1.6 \text{ Hz}$, Ar6-H)*, 7.46 (ddd, 1H, $^2J_{\text{Ar4-H}, \text{Ar5-H}} = 7.8 \text{ Hz}$, $^3J_{\text{Ar4-H}, \text{Ar6-H}} \sim ^3J_{\text{Ar4-H}, \text{Ar2-H}} \sim 1.6 \text{ Hz}$, Ar4-H)*, 7.34 (t, $^2J_{\text{Ar5-H}, \text{Ar4-H}} = ^2J_{\text{Ar5-H}, \text{Ar6-H}} = 7.8 \text{ Hz}$, Ar5-H), 4.13-4.20 (m, 2-H₂), 4.05-4.12 (m, 1-H₂), 3.91-4.01 (m, 2H) and 3.23-3.39 (m, 2H) (2'-H₂ and 6'-H₂, presumably splitted into axial and equatorial signals), 2.22-2.39 (m, 2H), 1.68-1.88 (m, 3H) and 1.41-1.61 (m, 1H) (3'-H₂, 4'-H₂, 5'-H₂, presumably respectively splitted into axial and equatorial signals); **^{13}C -NMR** (CDCl_3 , 100 MHz): $\delta_{\text{C}} = 169.8$ (CO_2H), 134.9, 134.3 (Ar-1, Ar-3), 132.1, 130.0, 129.5, 128.0 (Ar-2, Ar-4, Ar-5, Ar-6), 69.2 (C-1), 65.5 (C-2', C-6'), 36.1 (C-2), 21.7 and 21.0 (C-3', C-4', C-5'); **HRMS** (ESI, pos., CH_3CN), $\text{C}_7\text{H}_{15}\text{ClNO}$ ($[\text{M}+\text{H}]^+$) calc: 164.0837 ; found: 164.0829. *The spectroscopic data does not allow unequivocal differentiation of 4' vs. 6'.

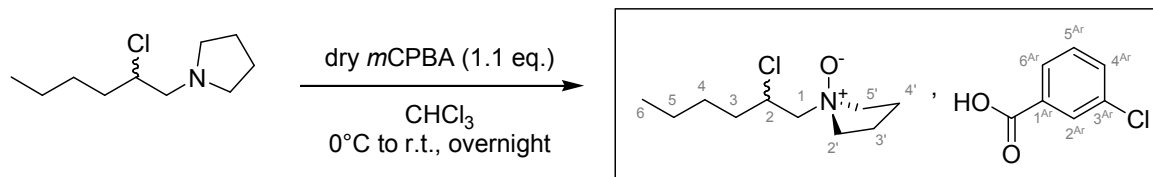
1.8.3. *N*-(2-chloroethyl)-pyrrolidine *N*-oxide (3-chlorobenzoic acid salt) (**8da**)



Prepared according to general procedure GP8. (Contains approx. 0.20 eq. excess *m*-chlorobenzoic acid, based on the ^1H -NMR integrations of the aromatic signals.)

IR (CHCl_3): $\nu = 3015, 2400, 1700, 1570, 1455, 1360, 1305, 1070, 985, 895 \text{ cm}^{-1}$; **^1H -NMR** (CDCl_3 , 400 MHz) $\delta_{\text{H}} = 8.03$ (t, 1H, $^4J_{\text{Ar2-H}, \text{Ar4-H}} = ^4J_{\text{Ar2-H}, \text{Ar6-H}} = 1.8 \text{ Hz}$, Ar2-H), 7.92 (dt, 1H, $^3J_{\text{Ar6-H}, \text{Ar5-H}} = 7.8 \text{ Hz}$, $^4J_{\text{Ar6-H}, \text{Ar2-H}} = ^4J_{\text{Ar6-H}, \text{Ar4-H}} = 1.3 \text{ Hz}$, Ar6-H), 7.44 (ddd, 1H, $^2J_{\text{Ar4-H}, \text{Ar5-H}} = 7.8 \text{ Hz}$, $^3J_{\text{Ar4-H}, \text{Ar6-H}} \sim ^3J_{\text{Ar4-H}, \text{Ar2-H}} \sim 1.6 \text{ Hz}$, Ar4-H), 7.32 (t, 1H, $^2J_{\text{Ar5-H}, \text{Ar4-H}} = ^2J_{\text{Ar5-H}, \text{Ar6-H}} = 7.8 \text{ Hz}$, Ar5-H), 4.24-4.12 (m, 6H, 1-H₂, 2-H₂, 2'-H and 5'-H), 3.46-3.32 (m, 2H, 2'-H and 5'-H), 2.56-2.44 (m, 2H, 3'-H and 4'-H), 2.17-2.06 (m, 2H, 3'-H and 4'-H); **^{13}C -NMR** (CDCl_3 , 101 MHz): $\delta_{\text{C}} = 169.9$ (Ar CO_2), 135.6, 134.2 (Ar-1, Ar-3), 131.8, 129.9, 129.5, 127.9 (Ar-2, Ar-4, Ar-5, Ar-6), 68.2 (C-2', C-5'), 67.6 (C-1), 37.2 (C-2), 21.5 (C-3', C-4'); **HRMS** (ESI, pos., CH_3CN), calcd. for $\text{C}_{14}\text{H}_{27}\text{N}_2\text{O}_2$ ($[\text{M} + \text{H}]^+$): $m/z = 150.0680$, found: 150.0694; **Anal.** matches the hemihydrate of the expected salt, with the stoichiometry deduced from the NMR: calcd. for $\text{C}_6\text{H}_{12}\text{ClNO} \cdot (\text{C}_7\text{H}_5\text{ClO}_2)_{1.20} \cdot (\text{H}_2\text{O})_{0.50}$: C 49.91%, H 5.53%, N 4.04%, found C 49.77%, H 5.51%, N 3.91%.

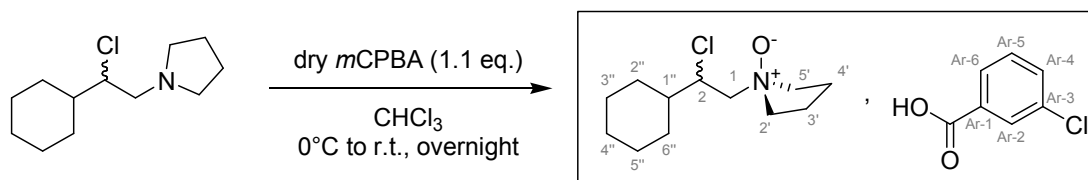
1.8.4. *N*-(2-chloro-2-cyclohexylethyl)pyrrolidine *N*-oxide, 3-chlorobenzoic acid salt (*rac.* **8db**)



Prepared according to general procedure GP8. (Contains approx. 0.38 eq. excess *m*-chlorobenzoic acid, based on the ^1H -NMR integrations of the aromatic signals.)

IR (CHCl_3): $\nu = 3000, 2965, 2875, 1700, 1570, 1455, 1430, 1365, 1290, 1240, 1145, 1070, 985, 905 \text{ cm}^{-1}$; **^1H -NMR** (CDCl_3 , 400 MHz) $\delta_{\text{H}} = 9.95$ (br. s, OH), 8.04 (t, 1H, $^4J_{\text{Ar}2\text{-H}, \text{Ar}4\text{-H}} = ^4J_{\text{Ar}2\text{-H}, \text{Ar}6\text{-H}} = 1.6 \text{ Hz}$, Ar2-H), 7.93 (dt, 1H, $^3J_{\text{Ar}6\text{-H}, \text{Ar}5\text{-H}} = 7.8 \text{ Hz}$, $^4J_{\text{Ar}6\text{-H}, \text{Ar}2\text{-H}} = ^4J_{\text{Ar}6\text{-H}, \text{Ar}4\text{-H}} = 1.6 \text{ Hz}$, Ar6-H), 7.46 (ddd, 1H, $^2J_{\text{Ar}4\text{-H}, \text{Ar}5\text{-H}} = 7.8 \text{ Hz}$, $^3J_{\text{Ar}4\text{-H}, \text{Ar}6\text{-H}} \sim ^3J_{\text{Ar}4\text{-H}, \text{Ar}2\text{-H}} \sim 1.6 \text{ Hz}$, Ar4-H), 7.34 (t, 1H, $^2J_{\text{Ar}5\text{-H}, \text{Ar}4\text{-H}} = ^2J_{\text{Ar}5\text{-H}, \text{Ar}6\text{-H}} = 7.8 \text{ Hz}$, Ar5-H), 4.90 (dddd, $^3J_{2\text{-H}_1, 1\text{-H}_b} = 8.4$, $^3J = 8.1$, $^3J = 5.1$, $^3J_{2\text{-H}_1, 1\text{-H}_a} = 1.2$, 2-H), 4.81 (dd, $^3J_{1\text{-H}_a, 1\text{-H}_b} = 13.9$, $^3J_{1\text{-H}_a, 2\text{-H}} = 1.2$, 1-H_a), 4.53-4.45 (m), 4.11-4.03 (m) and 3.46-3.36 (m) (2'-H₂ and 5'-H₂, diastereotopic and splitted into axial and equatorial signals), 3.48 (dd, $^3J_{1\text{-H}_b, 1\text{-H}_a} = 13.9$, $^3J_{1\text{-H}_b, 2\text{-H}} = 8.4$, 1-H_b), 2.55-2.42 (m) and 2.21-2.02 (m) (3'-H₂ and 4'-H₂, diastereotopic and splitted into axial and equatorial signals), 1.93-1.75 (m, 3-H₂, diastereotopic), 1.55-1.42 (m, 4-H₂, diastereotopic), 1.40-1.21 (m, 5-H₂, diastereotopic), 0.85 (t, $J_{6\text{-H}_3, 5\text{-H}_2} = 7.3$, 6-H₃); **^{13}C -NMR** (CDCl_3 , 101 MHz): $\delta_{\text{C}} = 169.9$ (ArCO₂), 135.2, 134.3 (Ar-1, Ar-3), 132.0, 130.0, 129.5, 128.0 (Ar-2, Ar-4, Ar-5, Ar-6), 73.1 (C-1), 69.5 and 67.1 (C-2', C-5'), 55.6 (C-2), 36.9 (C-3); 28.0, 22.3, 22.1 and 20.5 (C-4, C-5 and C-3'/C-4'), 13.9 (C-6); **HRMS** (ESI, pos., MeOH), calc for $\text{C}_{10}\text{H}_{21}\text{ClNO}^+$ ($[\text{M}+\text{H}]^+$) m/z : 206.1306, found: 206.1309.

1.8.5. *N*-(2-chloro-2-cyclohexylethyl)pyrrolidine *N*-oxide, 3-chlorobenzoic acid salt (*rac.* **8dc**)

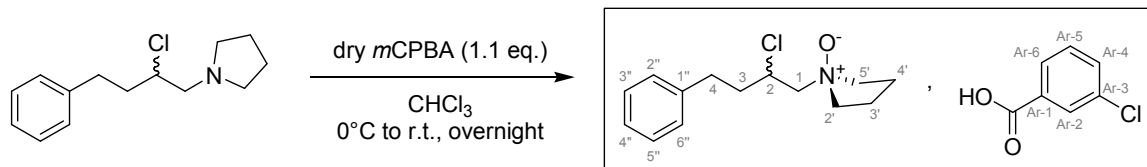


Prepared according to general procedure GP8. (Contains approx. 0.45 eq. excess *m*-chlorobenzoic acid, based on the ^1H -NMR integrations of the aromatic signals.)

IR (CHCl_3): $\nu = 3000, 2935, 2860, 1700, 1570, 1450, 1425, 1360, 1290, 1240, 1070, 905 \text{ cm}^{-1}$; **^1H -NMR** (CDCl_3 , 400 MHz) $\delta_{\text{H}} = 8.78$ (br. s, OH), 8.04 (t, 1H, $^4J_{\text{Ar}2\text{-H}, \text{Ar}4\text{-H}} = ^4J_{\text{Ar}2\text{-H}, \text{Ar}6\text{-H}} = 1.6 \text{ Hz}$, Ar2-H), 7.94 (dt, 1H, $^3J_{\text{Ar}6\text{-H}, \text{Ar}5\text{-H}} = 7.8 \text{ Hz}$, $^4J_{\text{Ar}6\text{-H}, \text{Ar}2\text{-H}} = ^4J_{\text{Ar}6\text{-H}, \text{Ar}4\text{-H}} = 1.6 \text{ Hz}$, Ar6-H), 7.46 (ddd, 1H, $^2J_{\text{Ar}4\text{-H}, \text{Ar}5\text{-H}} = 7.8 \text{ Hz}$, $^3J_{\text{Ar}4\text{-H}, \text{Ar}6\text{-H}} \sim ^3J_{\text{Ar}4\text{-H}, \text{Ar}2\text{-H}} \sim 1.6 \text{ Hz}$, Ar4-H), 7.34 (t, 1H, $^2J_{\text{Ar}5\text{-H}, \text{Ar}4\text{-H}} = ^2J_{\text{Ar}5\text{-H}, \text{Ar}6\text{-H}} = 7.8 \text{ Hz}$, Ar5-H), 4.84 (ddd, $^3J_{2\text{-H}_1, 1\text{-H}_b} = 7.8$, $^3J_{2\text{-H}_1, 1\text{-H}_a} = 3.1$, $^3J_{2\text{-H}_1, 1\text{-H}_a} = 1.0$, 2-H), 4.77 (dd, $^3J_{1\text{-H}_a, 1\text{-H}_b} = 13.9$, $^3J_{1\text{-H}_a, 2\text{-H}} = 1.0$, 1-H_a), 4.59-4.49 (m, 1H), 4.07-3.99 (m, 1H) and 3.45-3.34 (m, 2H) (2'-H₂ and 5'-H₂, diastereotopic and splitted into axial and equatorial signals), 3.47 (dd, $^3J_{1\text{-H}_b, 1\text{-H}_a} = 13.9$, $^3J_{1\text{-H}_b, 2\text{-H}} = 8.0$, 1-H_b), 2.56-2.41 (m, 2H) and 2.21-2.02 (m, 2H) (3'-H₂ and 4'-H₂, diastereotopic and splitted into axial and equatorial signals), 1.86-1.58 and 1.38-1.02 (m, 3'/4'-H₂, 2''/6''-H₂, 3''/5''-H₂, 4''-H₂); **^{13}C -NMR** (CDCl_3 , 101 MHz): $\delta_{\text{C}} = 169.9$ (ArCO₂), 135.3, 134.3 (Ar-1, Ar-3), 132.0, 130.0, 129.5, 127.9 (Ar-2, Ar-4, Ar-5, Ar-6), 72.2 (C-1), 69.5 and 67.0 (C-2', C-5'), 60.7 (C-2), 44.2 (C-1''), 29.7, 27.4, 26.0, 26.0 and 25.8 (C-2'', C-3'', C-4'', C-5'', C-6''), 22.3 and 20.6 (C-3',

C-4'); **HRMS** (ESI, pos., CH₃CN), calcd. for C₁₂H₂₃ClNO⁺ ([M+H]⁺): *m/z* = 232.1463, found: 232.1472.

1.8.6. 1-(2-chloro-4-phenylbutyl)pyrrolidine *N*-oxide, 3-chlorobenzoic acid salt (*rac.* **8dd**)



Prepared according to general procedure GP8. (Contains approx. 0.25 eq. excess *m*-chlorobenzoic acid, based on the ¹H-NMR integrations of the aromatic signals.)

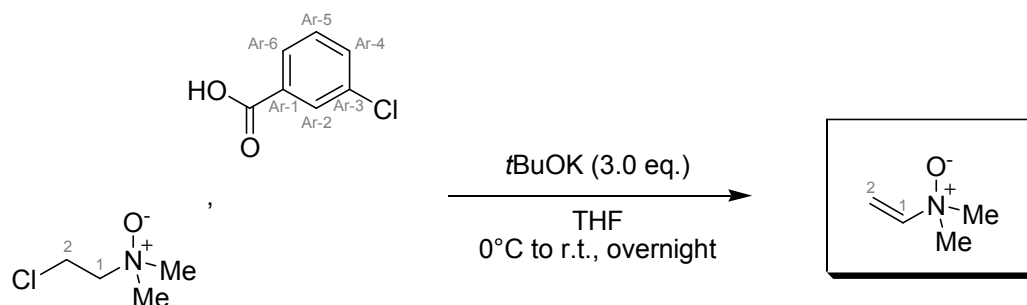
IR (CHCl₃): ν = 3000, 1700, 1570, 1495, 1455, 1430, 1365, 1290, 1255, 1145, 1070, 905 cm⁻¹; **¹H-NMR** (CDCl₃, 400 MHz) δ_H = 8.03 (t, 1H, ⁴J_{Ar2-H, Ar4-H} = ⁴J_{Ar2-H, Ar6-H} = 1.6 Hz, Ar2-H), 7.92 (dt, 1H, ³J_{Ar6-H, Ar5-H} = 7.8 Hz, ⁴J_{Ar6-H, Ar2-H} = ⁴J_{Ar6-H, Ar4-H} = 1.6 Hz, Ar6-H), 7.45 (ddd, 1H, ²J_{Ar4-H, Ar5-H} = 7.8 Hz, ³J_{Ar4-H, Ar6-H} ~ ³J_{Ar4-H, Ar2-H} ~ 1.6 Hz, Ar4-H), 7.33 (t, 1H, ²J_{Ar5-H, Ar4-H} = ²J_{Ar5-H, Ar6-H} = 7.8 Hz, Ar5-H), 7.26-7.20 (m, 2''-H and 6''-H), 7.20-7.14 (3''-, 4''- and 5''-H), 4.90 (dddd, ³J_{2-H, 3-H_b} = 9.1, ³J_{2-H, 1-H_b} = 8.0, ³J_{2-H, 3-H_a} = 4.6, ³J_{2-H, 1-H_a} = 1.3, 2-H), 4.86 (dd, ²J_{1-H_a, 1-H_b} = 13.9, ³J_{1-H_a, 2-H} = 1.3, 1-H_a), 4.51-4.39 (m, 1H) and 4.11-3.94 (m, 1H) and 3.45-3.34 (m, 2H) (2'-H₂ and 5'-H₂, diastereotopic and presumably splitted into axial and equatorial signals), 3.52 (dd, ²J_{1-H_b, 1-H_a} = 13.9, ³J_{1-H_b, 2-H} = 8.0 Hz, 1-H_b), 2.91 (ddd, ²J_{4-H_a, 4-H_b} = 13.8, ³J_{4-H_a, 3-H_a} = 9.9, ³J_{4-H_a, 3-H_b} = 5.0 Hz, 4-H_a), 2.81 (ddd, ²J_{4-H_b, 4-H_a} = 13.8, ³J_{4-H_b, 3-H_b} = 9.5, ³J_{4-H_b, 3-H_a} = 6.5 Hz, 4-H_b), 2.55-2.42 (m, 2H) and 2.14-2.04 (m, 2H) (3'-H₂, 4'-H₂, diastereotopic and presumably splitted into axial and equatorial signals), 2.25 (dddd, ²J_{3-H_a, 3-H_b} = 13.9, ³J_{3-H_a, 4-H_a} = 9.9, ³J_{3-H_a, 4-H_b} = 6.5 Hz, ³J_{3-H_a, 2-H} = 4.6 Hz, 3-H_a), 2.15 (dddd, ²J_{3-H_b, 3-H_a} = 13.9, ³J_{3-H_b, 4-H_b} = 9.5, ³J_{3-H_b, 2-H} = 9.1, ³J_{3-H_b, 4-H_a} = 5.4, 3-H_b); **¹³C-NMR** (CDCl₃, 101 MHz): δ_C = 170.0 (ArCO₂), 140.2 (C-1''), 135.8, 134.2 (Ar-1, Ar-3), 131.7, 130.0, 129.4, 127.9 (Ar-2, Ar-4, Ar-5, Ar-6), 128.7 and 128.6 (C-2''/C-6'' and C-3''/C-5''), 126.4 (C-4''), 73.0 (C-1), 69.5, 67.2 (C-2' and C-5', diastereotopic), 55.1 (C-2), 38.7 (C-4), 32.1 (C-3), 22.3, 20.6 (C-3' and C-4', diastereotopic); **HRMS** (ESI, pos., MeOH), calc for C₁₄H₂₁ClNO⁺ ([M+H]⁺) *m/z*: 254.1306, found: 254.1304; as a minor peak beside C₁₄H₂₀NO⁺ ([M-Cl]⁺) *m/z*: 218.1539, found: 218.1549.

1.9. General procedure GP9: Enamine *N*-oxides by dehydrochlorination of β-chloroamine *N*-oxides

To a suspension of KO^tBu (4 eq.) in THF (0.6 M), cooled with an ice-brine bath to -5-0°C, was added dropwise via syringe a solution of the *m*-chlorobenzoic acid salt of β-chloroamine *N*-oxide (obtained by GP8) in THF (0.2 M). The mixture was then stirred while being allowed to warm up to room temperature. After 7 to 12 h, consumption of the starting amine was complete as shown by TLC (SiO₂, Eluent CH₂Cl₂/MeOH: 80/20, staining with a 5 wt.% solution of 2,3,5-Triphenyltetrazolium chloride in *i*PrOH). The THF was removed under reduced pressure. The resulting solid was triturated in CH₂Cl₂ (potassium chlorobenzoate is only sparingly soluble in CH₂Cl₂) and filtered over plug of Celite®, or alternatively triturated in CH₂Cl₂/MeOH (80/20) and filtered over a short plug of neutral alumina (potassium chlorobenzoate does not elute on alumina). Concentration under reduced pressure afforded the crude enamine *N*-oxide, which was further purified by flash chromatography (SiO₂,

CH₂Cl₂/MeOH from 95/5 to 70/30). This afforded enamine *N*-oxides as crystalline products, that rapidly became oily if exposed to atmospheric moisture. (In which case co-evaporation with CHCl₃ at the rotary evaporator removed most residual MeOH and water and yielded a crystalline product again.) The highly hygroscopic nature of these compounds limits their suitability for combustion analysis. Typical yield: 55-65% based on the starting β -chloroamine *N*-oxide salt.

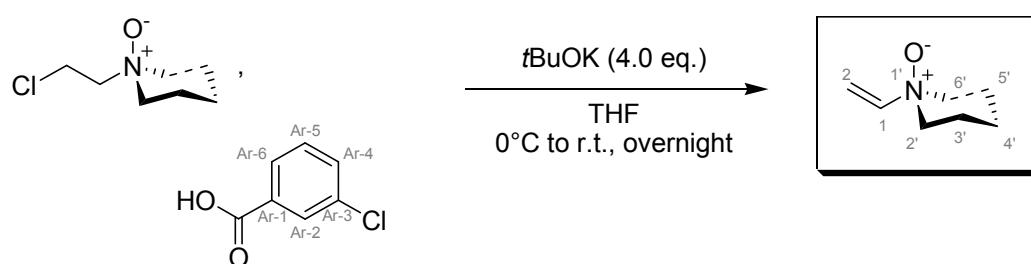
1.9.1. *N,N*-Dimethylvinylamine *N*-oxide (**1aa**)



Prepared according to GP9, starting from KO^tBu (6.72 g, 60.0 mmol, 3 eq.) and **8aa** (5.98 g, 20.0 mmol). After 7h, work-up followed by chromatography (SiO₂, CH₂Cl₂/MeOH gradient from 90:10 to 70:30) and co-evaporation with CHCl₃ at the rotary evaporator to remove excess MeOH afforded **1aa** (1.06 g) as a crystalline product. Yield: 60%. (Described in literature^[19])

IR (CHCl₃): ν = 3660, 3630, 3205, 2915, 2500, 1650, 1455, 1390, 1360, 1075, 1040, 1015, 960, 900 cm⁻¹; **¹H-NMR** (CDCl₃, 400 MHz) δ_H = 6.46 (dd, ³*J*_{1-H,2-Htrans} = 14.8 Hz, ³*J*_{1-H,2-Hcis} = 7.7 Hz, 1-H), 5.890 (dd, ³*J*_{2-Htrans,1-H} = 14.8 Hz, ³*J*_{2-Htrans,2-Hcis} = 2.0 Hz, 2-Htrans), 5.19 (dd, ³*J*_{2-Hcis,1-H} = 7.7 Hz, ³*J*_{2-Hcis,2-Htrans} = 2.0 Hz, 2-Hcis), 3.30 (s, NMe₂); **¹³C-NMR** (CDCl₃, 101 MHz): δ_C = 148.1 (C-1), 107.8 (C-2), 60.0 (NMe₂); **HRMS** (EI, positive), calc for C₄H₉NO⁺ ([M]⁺) *m/z*: 87.0684, found: 87.0679.

1.9.2. *N*-Vinylpiperidine *N*-oxide (**1ca**)



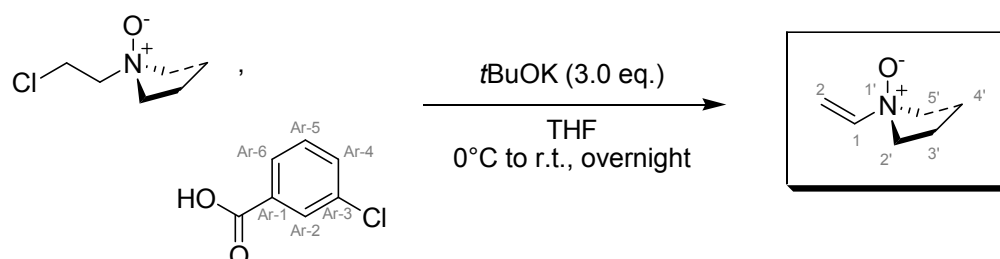
Prepared according to GP9, starting from KO^tBu (761 mg, 6.80 mmol, 4 eq.) and **8ca** (662 mg, 1.70 mmol). After 7h, work-up followed by chromatography (SiO₂, CH₂Cl₂/MeOH gradient from 90:10 to 70:30) and co-evaporation with CHCl₃ at the rotary evaporator to remove excess MeOH afforded **1ca** (133 mg) as a crystalline product. Yield: 62%.

IR (CHCl₃): ν = 2935, 2500, 1645, 1445, 1355, 1265, 1015, 955, 915 cm⁻¹; **¹H-NMR** (CDCl₃, 270 MHz) δ_H = 6.37 (dd, ³*J*_{1-H,2-Htrans} = 14.8 Hz, ³*J*_{1-H,2-Hcis} = 7.8 Hz, 1-H), 5.98 (dd, ³*J*_{2-Htrans,1-H} = 14.8 Hz, ³*J*_{2-Htrans,2-Hcis} = 1.5 Hz, 2-Htrans), 5.21 (dd, ³*J*_{2-Hcis,1-H} = 7.8 Hz, ³*J*_{2-Hcis,2-Htrans} = 1.5 Hz, 2-Hcis), 3.25 (ddd, ²*J*_{2'/6'-Hax,2'/6'-Heq} = ³*J*_{2'/6'-Hax,3'/5'-Hax} = 11.2, ³*J*_{2'/6'-Hax,3'/5'-Heq} = 3.1, 2'-H_{ax} and 6'-H_{ax}), 3.18 (ddd, ²*J*_{2'/6'-Heq,2'/6'-Hax} = 11.2, ³*J*_{2'/6'-Heq,3'/5'-Hax} = ³*J*_{2'/6'-Heq,3'/5'-Heq} = 4.2, 2'-

¹⁹ Krouwer; Richmond, *J. Org. Chem.* **1978**, *43*, 2464-2466.

H_{eq} and 6'-H_{eq}), 2.42 (app. dddt, $^2J_{3'/5'-H_{ax}, 3'/5'-H_{eq}} = 14.5$, $^3J_{3'/5'-H_{ax}, 4'-H_{ax}} = 11.5$, $^3J_{3'/5'-H_{ax}, 2'/6'-H_{ax}} = 11.1$, $^3J_{3'/5'-H_{ax}, 2'/6'-H_{eq}} = ^3J_{3'/5'-H_{ax}, 4'-H_{eq}} = 3.9$, 3'-H_{ax} and 5'-H_{ax}), 1.77 (app. dtt, $^2J_{4'-H_{eq}, 4'-H_{ax}} = 13.4$, $^3J_{4'-H_{eq}, 3'/5'-H_{eq}} = 4.2$, $^3J_{4'-H_{eq}, 3'/5'-H_{ax}} = 3.9$, 4'-H_{eq}), 1.64 (app. dtt, $^2J_{3'/5'-H_{eq}, 3'/5'-H_{ax}} = 14.5$, $^3J_{3'/5'-H_{eq}, 2'/6'-H_{eq}} = ^3J_{3'/5'-H_{eq}, 4'-H_{eq}} = 4.2$, $^3J_{3'/5'-H_{eq}, 2'/6'-H_{ax}} = ^3J_{3'/5'-H_{eq}, 4'-H_{ax}} = 3.1$, 3'-H_{eq} and 5'-H_{eq}), 1.39 (app. dtt, $^2J_{4'-H_{ax}, 4'-H_{eq}} = 13.4$, $^3J_{4'-H_{ax}, 3'/5'-H_{ax}} = 11.5$, $^3J_{4'-H_{ax}, 3'/5'-H_{eq}} = 3.9$, 4'-H_{ax}); ¹³C-NMR (CDCl₃, 126 MHz): δ_C = 148.3 (C-1), 108.8 (C-2), 66.6 (C-2'/6'), 22.1 (C-4'), 21.0 (C-3'/5'); HRMS (ESI, pos., CH₃CN), calcd. for C₇H₁₄NO ([M + H]⁺): *m/z* = 128.1070, found: 128.1067; Main peak is the homoconjugate dimer: calcd. for C₁₄H₂₇N₂O₂ ([2 × M + H]⁺): *m/z* = 255.2067, found: 250.2067.

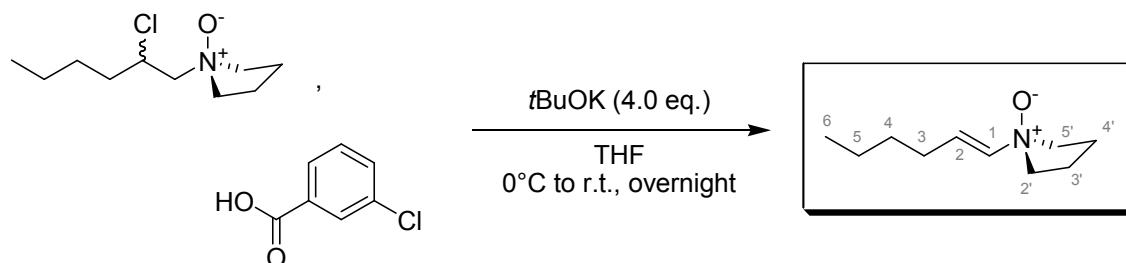
1.9.3. *N*-Vinylpyrrolidine *N*-oxide (**1da**)



Prepared according to GP9, starting from KO^tBu (4.04 g, 36.0 mmol, 3 eq.) and **8da** (4.04 g, 12.0 mmol). After 7h, work-up followed by chromatography (SiO₂, CH₂Cl₂/MeOH gradient from 90:10 to 70:30) and co-evaporation with CHCl₃ at the rotary evaporator to remove excess MeOH afforded **1da** (807 mg) as a crystalline product. Yield: 60%.

IR (CHCl₃): ν = 3200, 2915, 2500, 1650, 1455, 1390, 1360, 1295, 1075, 1040, 1015, 960, 900 cm⁻¹; ¹H-NMR (CDCl₃, 270 MHz) δ_H = 6.45 (dd, $^3J_{1-H, 2-H_{trans}} = 14.7$ Hz, $^3J_{1-H, 2-H_{cis}} = 7.7$ Hz, 1-H), 6.03 (dd, $^3J_{2-H_{trans}, 1-H} = 14.7$ Hz, $^3J_{2-H_{trans}, 2-H_{cis}} = 1.5$ Hz, 2-H_{trans}), 5.26 (dd, $^3J_{2-H_{cis}, 1-H} = 7.7$ Hz, $^3J_{2-H_{cis}, 2-H_{trans}} = 1.5$ Hz, 2-H_{cis}), 3.48-3.38 (m, 4H), 2.65-2.54 (m, 2H), 2.08-2.00 (m, 2H); ¹³C-NMR (CDCl₃, 126 MHz): δ_C = 145.5 (C-1), 109.6 (C-2), 69.3 (C-2'/5'), 22.0 (C-3'/4'); HRMS (ESI, pos., CH₃CN), calcd. for C₆H₁₁NNaO ([M + Na]⁺): *m/z* = 136.0733, found: 136.0739; Homoconjugate dimer is a much stronger peak: calcd. for C₁₂H₂₃N₂O₂ ([2 × M + H]⁺): *m/z* = 227.1754, found: 227.1746.

1.9.4. *N*-(2-cyclohexylvinyl)pyrrolidine *N*-oxide (**1db**)

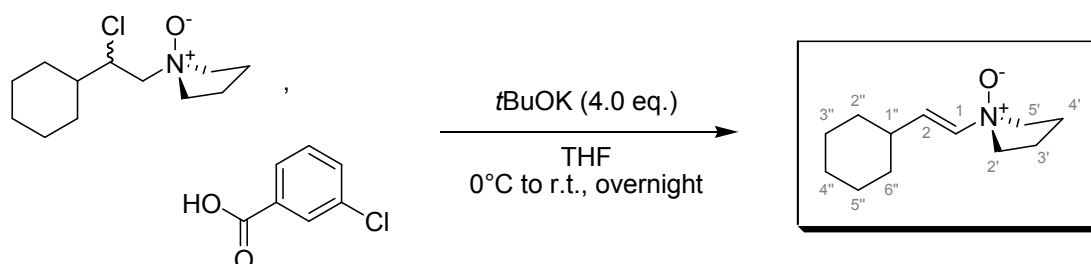


Prepared according to GP9, starting from KO^tBu (449 mg, 4.00 mmol, 4 eq.) and **8db** (422 mg, 1.00 mmol). After 7h, work-up followed by chromatography (SiO₂, CH₂Cl₂/MeOH gradient from 90:10 to 80:20) afforded **1db** (98 mg) as an oil. Yield: 58%.

IR (CHCl₃): ν = 2960, 2930, 2875, 1450, 1260, 950, 920, 910 cm⁻¹; ¹H-NMR (CDCl₃, 500 MHz) δ_H = 6.43 (dt, $^3J_{2-H, 1-H} = 13.3$, $^3J_{2-H, 3-H_2} = 7.3$, 2-H), 6.11 (dt, $^3J_{1-H, 2-H} = 13.3$, $^4J_{1-H, 3-H_2} = 1.4$, 1-H), 3.48-3.22 (m, 2'-/5'-H₂), 2.55-2.43 (m, 2H) and 2.03-1.93 (m, 2H) (3'-H₂, 4'-H₂, splitted into axial and equatorial), 2.07 (td, $^3J_{3-H_2, 2-H} \sim ^3J_{3-H_2, 4-H_2} = 7.3$, $^4J_{3-H_2, 1-H} = 1.4$, 3-H₂),

1.41-1.33 (m, 2H) and 1.33-1.23 (m, 2H) (4-H₂ and 5-H₂), 0.84 (t, $^3J_{6\text{-H}_3,5\text{-H}_2}=7.2$, 6-H₃); ^{13}C -NMR (CDCl₃, 101 MHz): $\delta_{\text{C}} = 138.7$ (C-1), 126.6 (C-2), 69.7 (C-2', C-5'), 30.9 (C-3), 28.5 (C-4), 22.3 (C-5), 22.0 (C-3', C-4'), 13.9 (C-6); HRMS (ESI, pos., MeOH), calc for C₁₀H₂₀NO⁺ ([M+H]⁺) m/z : 170.1539, found: 170.1552. Main peak: calc for C₂₀H₃₉N₂O₂⁺ ([2×M+H]⁺) m/z : 339.3006, found: 339.3009.

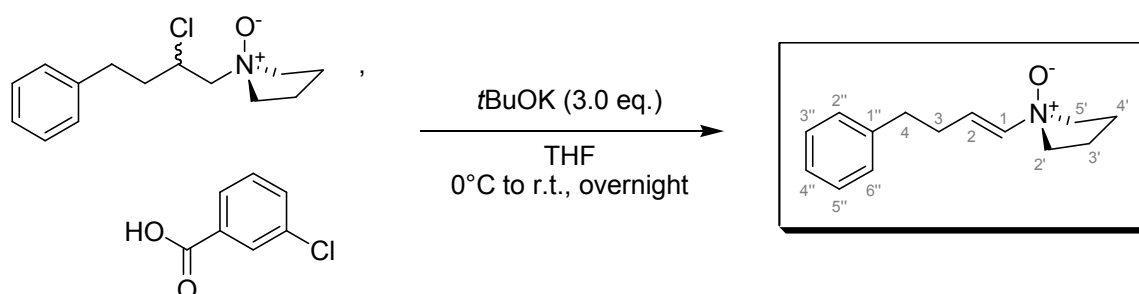
1.9.5. *N*-(2-cyclohexylvinyl)pyrrolidine *N*-oxide (**1dc**)



Prepared according to GP9, starting from KO^tBu (224 mg, 4 eq.) and **8dc** (229 mg, 0.50 mmol). After 7h, work-up followed by chromatography (SiO₂, CH₂Cl₂/MeOH gradient from 90:10 to 80:20) and co-evaporation with CHCl₃ at the rotary evaporator to remove excess MeOH afforded **1dc** (55.0 mg) as a crystalline product. Yield: 56%.

IR (CHCl₃): $\nu = 2960, 2935, 2870, 1450, 1265, 950, 915, 905\text{ cm}^{-1}$; ^1H -NMR (CDCl₃, 400 MHz): $\delta_{\text{H}} = 6.37$ (dt, $^3J_{2\text{-H},1\text{-H}} = 13.4$, $^3J_{2\text{-H},3\text{-H}_2} = 7.2$, 2-H), 6.06 (dt, $^3J_{1\text{-H},2\text{-H}} = 13.4$, $^4J_{1\text{-H},3\text{-H}_2} = 1.1$, 1-H), 3.45-3.29 (m, 2'-/5'-H₂), 2.55-2.41 (m, 2H) and 2.10-1.92 (m, 3H) (3'-H₂/4'-H₂, splitted into axial and equatorial, and 1''-H), 1.76-1.57 (m, 5H) and 1.30-1.02 (m, 5H) (2''-H₂/6''-H₂, 3''-H₂/5''-H₂, 4''-H₂); ^{13}C -NMR (CDCl₃, 101 MHz): $\delta_{\text{C}} = 137.0$ (C-1), 131.9 (C-2), 69.5 (C-2', C-5'), 37.6 (C-1''), 32.5 (C-2''/C-6''), 25.9 (C-4''), 25.8 (C-3''/C-5''), 21.8 (C-3', C-4'); HRMS (ESI, pos., CH₃CN), calcd. for C₁₂H₂₂NO⁺ ([M+H]⁺): $m/z = 196.1696$, found: 196.1746 main peak is ([2M+H]⁺): 391.3326).

1.9.6. *N*-(4-phenylbuten-1-yl)pyrrolidine *N*-oxide (**1dd**)



Prepared according to GP9, starting from KO^tBu (10.0 g, 3 eq.) and **8dd** (13.3 g, 28.8 mmol). After 7h, work-up followed by chromatography (SiO₂, CH₂Cl₂/MeOH gradient from 90:10 to 70:30) and co-evaporation with CHCl₃ at the rotary evaporator to remove excess MeOH afforded **1dd** (3.91 g) as a crystalline product. Yield: 67%.

IR (CHCl₃): $\nu = 2975, 2465, 1720, 1680, 1660, 1625, 1605, 1560, 1495, 1455, 1380, 1265, 1240, 1030, 945\text{ cm}^{-1}$; ^1H -NMR (CDCl₃, 500 MHz) $\delta_{\text{H}} = 7.29$ -7.24 (m, 2''-H/6''-H), 7.19-7.13 (m, 3''-H/5''-H and 4''-H), 6.49 (dt, $^3J_{2\text{-H},1\text{-H}} = 13.3$, $^3J_{2\text{-H},3\text{-H}_2} = 7.5$, 2-H), 6.03 (dt, $^3J_{1\text{-H},2\text{-H}} = 13.3$, $^4J_{1\text{-H},3\text{-H}_2} = 1.4$, 1-H), 3.42-3.36 (m, 2H) and 3.29-3.22 (m, 2H) (2'-/5'-H₂, splitted into axial and equatorial), 2.74 (t, $^3J_{4\text{-H}_2,3\text{-H}_2} = 7.5$, 4-H₂), 2.42 (qd, $^3J_{3\text{-H}_2,2\text{-H}} = ^3J_{3\text{-H}_2,4\text{-H}_2} = 7.5$,

$^4J_{3\text{-H}_2,1\text{-H}} = 1.4$, 3-H₂), 2.55-2.46 (m, 2H) and 2.01-1.92 (m, 3H) (3'-H₂/4'-H₂, splitted into axial and equatorial); ^{13}C -NMR (CDCl₃, 101 MHz): $\delta_{\text{C}} = 140.9$ (C-1''), 139.4 (C-1), 128.5 and 128.4 (C-2''/C-6'' and C-3''/C-5''), 126.2 (C-4''), 125.3 (C-2), 69.6 (C-2'/C-5'), 35.0 (C-4), 30.5 (C-3), 21.8 (C-3'/C-4'); **HRMS** (ESI, pos., CH₃CN), calc for C₁₄H₂₀NO⁺ ([M+H]⁺) m/z : 218.1539, found: 218.1556.

Crystal structure determination: The asymmetric unit of this structure contains four independent molecules, and their pseudosymmetric relationship leads to systematic weaknesses in the diffraction dataset. Two of the molecules exhibit disorder in their phenyl rings, while the other two molecules have disorder of their oxygen atoms (attached to N).

The phenyl ring disorder affects the 2,3,5,6 positions and this was modelled by allowing elongated ellipsoids to model a torsional mode of disorder. A model which allowed up to three alternative sites for each affected atom shows no advantages. These ellipsoids lead to a number of checkCIF Alerts but these are consistent with the model being used.

The disorder of the two oxygen atoms O21 and O31 was modelled by using two alternative sites for each atom and then refining occupancies competitively. Similarity restraints were applied among the molecules and disorder components and the N—O distances were restrained to be equal within 0.01 Å. The occupancies converged to around 0.5. The final N—O distances of around 1.39 Å are close to values in the literature (1.36 ± 0.03 Å for trimethylamine *N*-oxide).^[20]

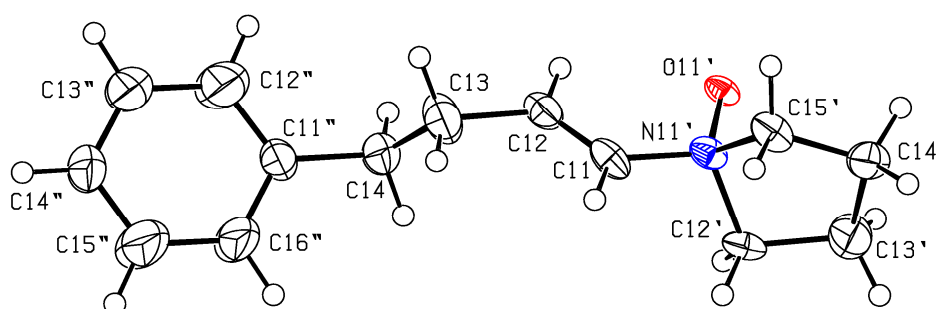
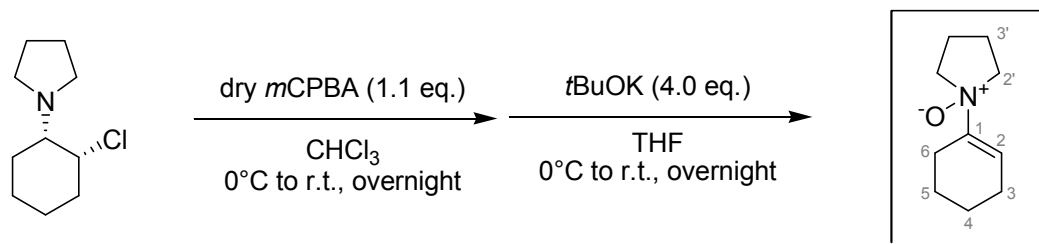


Figure 1. Crystal structure of **1dd** at 150(2)K.

²⁰ Maia; Peguy; Perez, *Acta Crystallogr., Sect. B: Struct. Sci.* **1981**, B37, 1858-1862.

1.9.7. *cis*-1-(2-chlorocyclohexyl)pyrrolidine *N*-oxide (**1dx**)

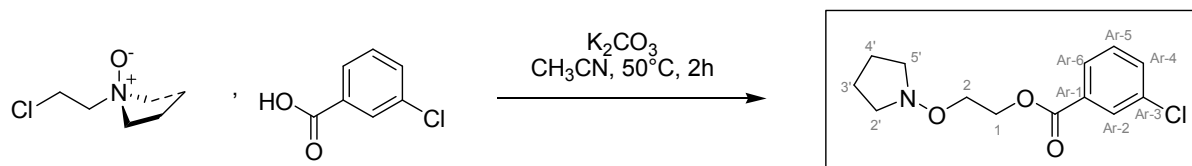


To a solution of *m*CPBA in CH_2Cl_2 (0.2 M, 3.20 mL) at 0°C was added the *cis* β -chloroamine *cis*-**7dx** (100 mg, 0.533 mmol). The mixture was stirred 8h at room temperature, the concentrated *in vacuo*. The residual oil was dissolved in THF (5 mL) and added dropwise to a suspension of K_{Ot}Bu (240 mg, 2.13 mmol, 4 eq.) in THF (5 mL) at 0°C , then the reaction mixture was allowed to warm up to room temperature slowly and stirred for 7 h. The THF was removed under reduced pressure. The resulting gel was triturated in $\text{CH}_2\text{Cl}_2/\text{MeOH}$ and filtered over plug of celite. Concentration under reduced pressure afforded the crude enamine *N*-oxide, which was further purified by flash chromatography (SiO_2 , $\text{CH}_2\text{Cl}_2/\text{MeOH}$ from 95/5 to 70/30). This afforded the enamine *N*-oxide **1dx** contaminated with approx. 1.70 eq. of 3-chlorobenzoic acid as a clear, colourless oil (126 mg). Yield: 55% based on the starting β -chloroamine.

(In an attempt to remove the 3-chlorobenzoic acid by chromatography on basic alumina, partial decomposition was observed leading to a mixture of enamine *N*-oxide **1dx** with an other unidentified compound showing *inter alia* 2 signals in the olefinic regions of the ^1H - and ^{13}C -NMR spectra.) **^1H -NMR** (CDCl_3 , 400 MHz) $\delta_{\text{H}} = 8.04$ (t, 1H, $^4J_{\text{Ar2-H, Ar4-H}} = ^4J_{\text{Ar2-H, Ar6-H}} = 1.8$ Hz, Ar2-H), 7.93 (dt, 1H, $^2J_{\text{Ar4-H, Ar5-H}} = 7.8$ Hz, $^3J_{\text{Ar4-H, Ar6-H}} \sim ^3J_{\text{Ar4-H, Ar2-H}} \sim 1.3$ Hz, Ar6-H), 7.40 (ddd, 1H, $^2J_{\text{Ar4-H, Ar5-H}} = 7.8$ Hz, $^3J_{\text{Ar4-H, Ar6-H}} \sim ^3J_{\text{Ar4-H, Ar2-H}} \sim 1.6$ Hz, Ar4-H), 7.30 (t, 1H, $^2J_{\text{Ar5-H, Ar4-H}} = ^2J_{\text{Ar5-H, Ar6-H}} = 7.8$ Hz, Ar5-H), 6.34 (tt, $^3J_{2\text{-H}_2, 3\text{-H}_2} = 4.1$, $^4J_{2\text{-H}_2, 6\text{-H}_2} = 1.2$, 2-H), 4.34-4.26 (m), 3.49-3.39 (m) ($2'\text{-H}_2$ and $5'\text{-H}_2$), 2.65-2.51 (m, 4H) and 2.21-2.08 (m, 4H) ($2'\text{-H}_2/5'\text{-H}_2$, 6-H₂ and 3-H₂), 1.85-1.70 (m, 2H) and 1.62-1.54 (m, 2H) (4-H₂ and 5-H₂); **^{13}C -NMR** (CDCl_3 , 120 MHz): $\delta_{\text{C}} = 170.3$ (ArC=O₂), 145.0 (C-1), 138.3, 134.0 (Ar-1, Ar-3), 131.0, 129.9, 129.2, 127.8 (Ar-2, Ar-4, Ar-5, Ar-6), 121.1 (C-2), 65.8 (C-2', C-5'), 45.1 (C-6), 24.4, 22.6, 21.2 (C-3, C-4, C-5), 21.4 (C-3', C-4'); **HRMS** (ESI, pos., CH_3CN), calc for $\text{C}_{10}\text{H}_{18}\text{NO}^+$ ($[\text{M}+\text{H}]^+$) m/z : 168.1383, found: 168.1372.

1.10. General procedure GP10: Forced “Owari-type” rearrangement

1.10.1.2-(pyrrolidin-1-yloxy)ethyl 3-chlorobenzoate (**12da**)

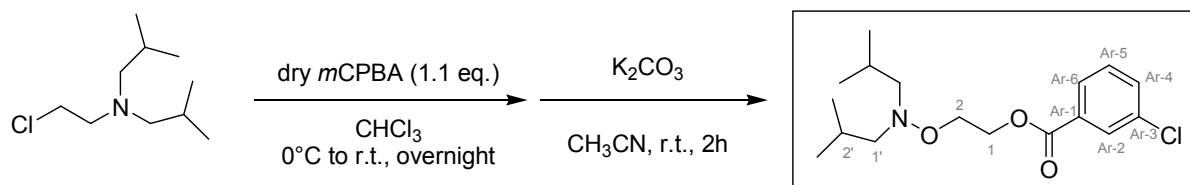


To a solution of **8da** (2.53 g, 7.50 mmol) in CH_3CN (100 mL) was added K_2CO_3 (3.11 g, 22.5 mmol, 3.0 eq.). The suspension was stirred for 2h at 50°C . After cooling down to room temperature, the mixture was diluted with EtOAc (20 mL), filtered over Kieselguhr, and

concentrated under reduced pressure. The residual oil was purified by flash chromatography (SiO₂, PE:Et₂O = 5:1) to yield **12da** (1.36 g) as a yellow oil. Yield: 67%.

IR (CHCl₃): ν = 2955, 2875, 1715, 1575, 1455, 1390, 1365, 1295, 1130, 1085, 1075, 900 cm⁻¹; **¹H-NMR** (CDCl₃, 400 MHz) δ_H = 8.03 (t, 1H, $^4J_{Ar2-H, Ar4-H} = ^4J_{Ar2-H, Ar6-H} = 1.8$ Hz, Ar2-H), 7.94 (dt, 1H, $^2J_{Ar4-H, Ar5-H} = 7.8$ Hz, $^3J_{Ar4-H, Ar6-H} \sim ^3J_{Ar4-H, Ar2-H} \sim 1.3$ Hz, Ar6-H), 7.52 (ddd, 1H, $^2J_{Ar4-H, Ar5-H} = 7.8$ Hz, $^3J_{Ar4-H, Ar6-H} \sim ^3J_{Ar4-H, Ar2-H} \sim 1.6$ Hz, Ar4-H), 7.38 (t, 1H, $^2J_{Ar5-H, Ar4-H} = ^2J_{Ar5-H, Ar6-H} = 7.8$ Hz, Ar5-H), 4.51 (m, 2-H₂), 3.99 (m, 1-H₂), 3.04-2.97 (m, 2'-H₂ and 5'-H₂), 1.87-1.68 (br. s., 3'-H₂ and 4'-H₂); **¹³C-NMR** (CDCl₃, 120 MHz): δ_C = 165.5 (ArCO₂), 134.6, 132.1 (Ar-1, Ar-3), 133.1, 129.9, 129.8, 127.9 (Ar-2, Ar-4, Ar-5, Ar-6), 70.2 (C-2), 63.8 (C-1), 57.0 (C-2', C-5'), 22.1 (C-3', C-4'); **HRMS** (ESI, pos., CH₃CN), calcd. for C₁₃H₁₇ClNO₃ ([M + H]⁺): m/z = 270.0891, found: 270.0890; **Anal.** calcd. for C₁₃H₁₆ClNO₃: C 57.89%, H 5.98%, N 5.19%, found C 57.64%, H 5.94%, N 5.17%.

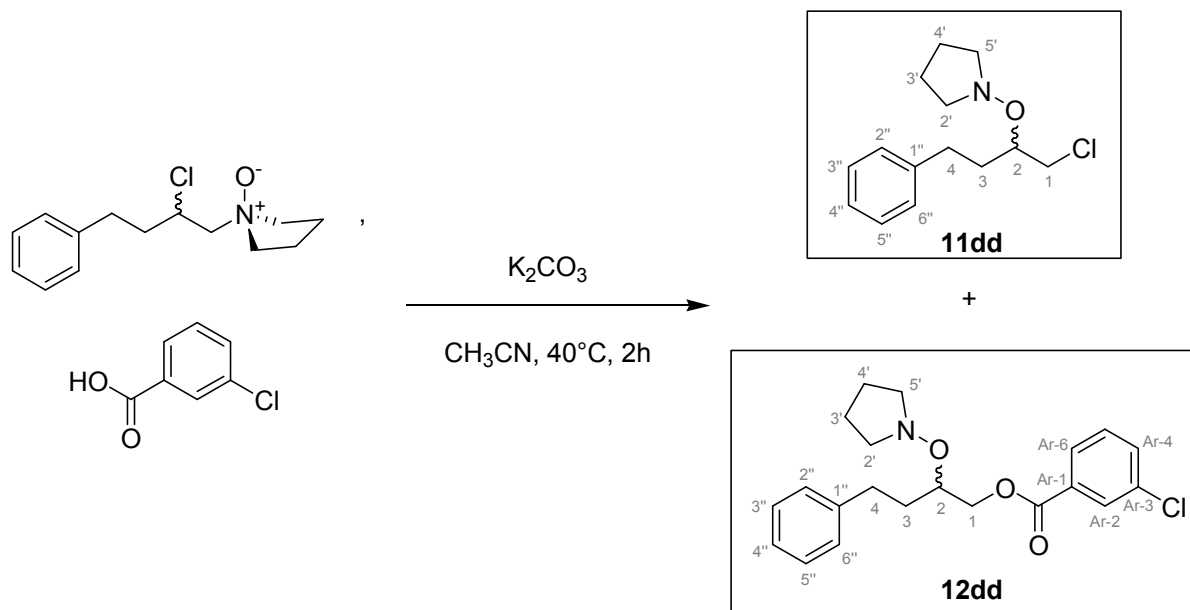
1.10.2.2-(diisobutylaminoxy)ethyl 3-chlorobenzoate (**12ea**)



To a solution of *N*-(2-chloroethyl)-*N,N*-diisobutylamine (192 mg, 1.00 mmol) in CH₂Cl₂ was added dropwise a solution of dried *m*CPBA (0.2 M in CH₂Cl₂, 5.5 mL, 1.1 eq.) at 0°C. The mixture was stirred over night at room temperature and concentrated under vacuum to afford a mixture of β -chloroamine *N*-oxide and the corresponding Owari-rearrangement product **12ea**. This mixture was dissolved in CH₃CN (10 mL), K₂CO₃ (415 mg, 3 eq.) was added, and the resulting suspension was stirred for 2 h at room temperature, then concentrated *in vacuo*. Flash-chromatography of the resulting oil (SiO₂, PE:Et₂O = 5:1) afforded **12ea** (186 mg) as a yellow oil. Yield: 57%.

IR (CHCl₃): ν = 2960, 2930, 2870, 1720, 1470, 1430, 1260, 1135, 1075 cm⁻¹; **¹H-NMR** (CDCl₃, 500 MHz) δ_H = 8.03 (t, $^3J_{Ar2-H, Ar4-H} = ^3J_{Ar2-H, Ar6-H} = 1.5$, Ar2-H), 7.94 (dt, $^2J_{Ar6-H, Ar5-H} = 8.0$, $^3J_{Ar6-H, Ar2-H} = ^3J_{Ar6-H, Ar4-H} = 1.5$, Ar6-H), 7.53 (app ddd, $^2J_{Ar4-H, Ar5-H} = 8.0$, $^3J_{Ar4-H, Ar2-H} \sim ^3J_{Ar4-H, Ar6-H} = 1.5$, Ar4-H), 7.38 (t, $^2J_{Ar5-H, Ar4-H} = ^2J_{Ar5-H, Ar6-H} = 8.0$ Hz, Ar5-H), 4.44 (t, $^3J_{1-H_2, 2-H_2} = 4.9$ Hz, 1-H₂), 4.02 (t, $^3J_{2-H_2, 1-H_2} = 4.9$ Hz, 2-H₂), 2.45 (br. d, $^3J_{1'-H_2, 2'-H} = 6.8$ Hz, 1'-H₂), 1.84 (apparent hept., $^3J_{2'-H_2, 2'-CH_3} = ^3J_{2'-H, 1'-H} = 6.8$ Hz, 2'-H), 0.94 [d, $^3J_{2'-CH_3, 2'-H} = 6.8$ Hz, 2'-CH₃]₄; **¹³C-NMR** (CDCl₃, 125 MHz): δ_C = 165.4 (ArCO₂), 134.6, 132.0 (C-Ar1, C-Ar3), 133.1, 130.0, 129.8, 127.9 (Ar-2, Ar-4, Ar-5, Ar-6), 70.8 (C-2), 67.6 (C-1'), 63.9 (C-1), 26.3 (C-2'), 21.1 (2'-CH₃); **HRMS** (ESI, pos., CH₃CN), calcd. for C₁₇H₂₇ClNO₃⁺ ([M+H]⁺): m/z = 328.1674, found: 328.1698.

1.10.3.1-chloro-4-phenyl-2-(pyrrolidin-1-yloxy)butane (**11dd**) and 4-phenyl-2-(pyrrolidin-1-yloxy)butyl 3-chlorobenzoate (**12dd**)



To a solution of **8dd** (225 mg, 0.50 mmol) in CH_3CN (7 mL) was added K_2CO_3 (207 mg, 1.50 mmol, 3.0 eq.). The suspension was stirred for 2h at $40^\circ C$. After cooling down to room temperature, the mixture was diluted with EtOAc (10 mL), filtered over Kieselguhr, and concentrated under reduced pressure. The residual oil was purified by flash chromatography (SiO_2 , PE:Et₂O = 5:1) to yield a first fraction of **11dd** (12.5 mg; 10%) as a light brown oil (this sample was unstable. NMR after 1 day at room temperature showed significant decomposition to unidentified species. The main peak in ESI-MS was $[M-Cl]^+$, expectably indicating that the opening of the ‘Owari’ oxazetidinium intermediate by chloride anions is a reversible process) and a second fraction of **12dd** (109 mg; 58%) as a light brown oil.

11dd: 1H -NMR ($CDCl_3$, 500 MHz) δ_H = 7.32-7.26 (m, 2''-H/6''-H), 7.22-7.16 (m, 3''-H/5''-H and 4''-H), 3.79 (ddt, $^3J_{2-H,3-H_b}$ = 8.3, $^3J_{2-H,1-H_a}$ = 5.2, $^3J_{2-H,3-H_a}$ = 4.5, $^3J_{2-H,1-H_b}$ = 3.5, 2-H), 3.73 (dd, $^2J_{1-H_a,1-H_b}$ = 11.0, $^3J_{1-H_a,2-H}$ = 5.2, 1-H_a), 3.67 (dd, $^2J_{1-H_b,1-H_a}$ = 11.0, $^3J_{1-H_b,2-H}$ = 3.5, 1-H_b), 3.05-2.91 (m, 2'-H₂/5'-H₂), 2.77 (ddd, $^2J_{4-H_a,4-H_b}$ = 13.9, $^3J_{4-H_a,3-H_a}$ = 9.3, $^3J_{4-H_a,3-H_b}$ = 5.8, 4-H_a), 2.63 (ddd, $^2J_{4-H_b,4-H_a}$ = 13.9, $^3J_{4-H_b,3-H_b}$ = 9.5, $^3J_{4-H_b,3-H_a}$ = 7.0, 4-H_b), 1.90 (dddd, $^2J_{3-H_a,3-H_b}$ = 14.2, $^3J_{3-H_a,4-H_a}$ = 9.3, $^3J_{3-H_a,4-H_b}$ = 7.0, $^3J_{3-H_a,2-H}$ = 4.5, 3-H_a), 1.86 (dddd, $^2J_{3-H_b,3-H_a}$ = 14.2, $^3J_{3-H_b,4-H_b}$ = 9.5, $^3J_{3-H_b,2-H}$ = 8.3, $^3J_{3-H_b,4-H_a}$ = 5.8, 3-H_b), 1.87-1.69 (m, 3'-H₂/4'-H₂); ^{13}C -NMR ($CDCl_3$, 68 MHz): δ_C = 128.5 (C-2''/6'', C-3''/5''), 126.0 (C-4''), 80.0 (C-2), 57.4 (broad, C-2'/C-5'), 46.2 (C-1), 32.7 (C-3), 31.9 (C-4), 22.1 (C-3'/C-4'), C-1'' was not observed due to very poor signal/noise ratio; HRMS (ESI, pos., CH_3CN), calcd. for $C_{14}H_{20}NO^+$ ($[M-Cl]^+$): m/z = 218.1539, found: 218.1552.

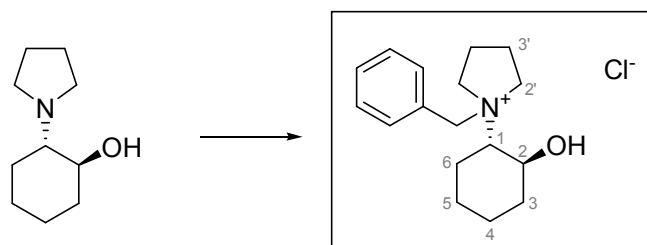
12dd: 1H -NMR ($CDCl_3$, 500 MHz) δ_H = 8.02 (t, $^3J_{Ar2-H,Ar4-H}$ = $^3J_{Ar2-H,Ar6-H}$ = 1.5, Ar2-H), 7.92 (dt, $^2J_{Ar6-H,Ar5-H}$ = 8.0, $^3J_{Ar6-H,Ar2-H}$ = $^3J_{Ar6-H,Ar2-H}$ = 1.5, Ar6-H), 7.53 (app ddd, $^2J_{Ar4-H,Ar5-H}$ = 8.0, $^3J_{Ar4-H,Ar2-H}$ ~ $^3J_{Ar4-H,Ar6-H}$ = 1.5, Ar4-H), 7.38 (t, $^2J_{Ar5-H,Ar4-H}$ = $^2J_{Ar5-H,Ar6-H}$ = 8.0 Hz, Ar5-H), 7.32-7.26 (m, 2''-H/6''-H), 7.24-7.17 (m, 3''-H/5''-H and 4''-H), 4.51 (dd, $^2J_{1-H_a,1-H_b}$ = 11.4, $^3J_{1-H_a,2-H}$ = 4.4, 1-H_a), 4.40 (dd, $^2J_{1-H_b,1-H_a}$ = 11.4, $^3J_{1-H_b,2-H}$ = 4.9, 1-H_b), 3.94 (ddt, $^3J_{2-H,3-H_a}$ = 8.5, $^3J_{2-H,1-H_b}$ = 4.9, $^3J_{2-H,1-H_a}$ = $^3J_{2-H,3-H_b}$ = 4.4, 2-H), 3.05-2.94 (m, 2'-H₂/5'-H₂), 2.83 (ddd, $^2J_{4-H_a,4-H_b}$ = 13.9, $^3J_{4-H_a,3-H_b}$ = 9.8, $^3J_{4-H_a,3-H_a}$ = 5.2, 4-H_a), 2.69 (ddd, $^2J_{4-H_b,4-H_a}$ = 13.9, $^3J_{4-H_b,3-H_a}$ =

9.6, $^3J_{4-H_b,3-H_b} = 6.8$, 4- H_b), 1.95 (dddd, $^2J_{3-H_a,3-H_b} = 14.2$, $^3J_{3-H_a,4-H_b} = 9.6$, $^3J_{3-H_a,2-H} = 8.5$, $^3J_{3-H_a,4-H_a} = 5.2$, 3- H_a), 1.87 (dddd, $^2J_{3-H_b,3-H_a} = 14.2$, $^3J_{3-H_b,4-H_a} = 9.8$, $^3J_{3-H_b,4-H_b} = 6.8$, $^3J_{3-H_b,2-H} = 4.4$, 3- H_b), 2.03-1.66 (m, 3'- H_2 /4'- H_2); $^{13}\text{C-NMR}$ (CDCl_3 , 125 MHz): $\delta_C = 165.5$ (ArCO_2), 141.9 (C-1''), 134.7, 132.2 (Ar-1, Ar-3)^a, 133.1 (Ar-4)^b, 129.8 (Ar-5, Ar-2)^b, 128.6 (C-2''/6'', C-3''/5'')^b, 127.9 (Ar-6)^b, 126.1 (C-4'')^b, 78.6 (C-2), 66.0 (C-1)^b, 57.2 (broad, C-2'/C-5')^b, 32.56 (C-3)^b, 32.00 (C-4)^b, 22.04 (C-3'/C-4')^b; **HRMS** (ESI, pos., CH_3CN), calcd. for $\text{C}_{21}\text{H}_{25}\text{ClNO}_3^+$ ($[\text{M}+\text{H}]^+$): $m/z = 374.1517$, found: 374.1522.

^a Assignment confirmed by HMBC crosspeaks – ^b Assignment confirmed by HMQC crosspeaks

2. Other procedures

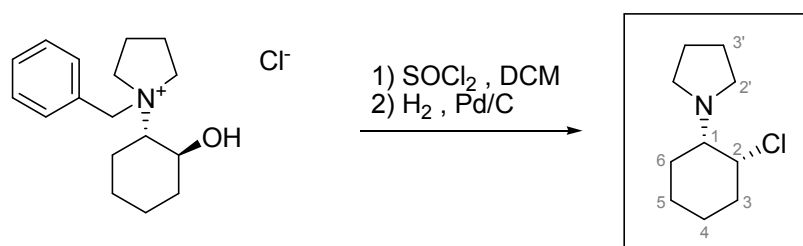
2.1.1. *trans*-1-benzyl-1-(2-hydroxycyclohexyl)pyrrolidinium chloride (*rac. trans-13*)



To a solution of aminoalcohol (10 mmol, 1.69 g) in toluene (20 mL) was added benzyl chloride (1.15 mL, 10 mmol, 1 eq.). The mixture was refluxed for 12 h. After cooling to room temperature, the mixture was concentrated *in vacuo* and recrystallized from Et_2O to yield the β -hydroxyammonium chloride (1.71 g, 58%) as white crystals.

IR (CHCl_3): $\nu = 3255$, 2940, 1460, 1220, 1075, 1000, 775, 710 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) $\delta_H = 7.72$ -7.67 (m, Bn-2/Bn-6), 7.46-7.36 (m, Bn-3/Bn-5 and Bn-4), 6.68 (d, $^3J_{1\text{-OH},1\text{-H}} = 7.0$, 1-OH), 5.14 (d, $^2J = 12.7$) and 4.56 (d, $^2J = 12.7$) (PhCH_2N); 4.39-4.27 (m), 4.13-4.00 (m), 3.83-3.73 (m) and 3.65-3.54 (m) (2'- H_2 and 5'- H_2 , diastereotopic and splitted into axial and equatorial signals), 4.26-4.16 (m, 2-H), 3.48-3.39 (m, 1-H), 2.25-1.99 (m, 3H), 1.95-1.77 (m, 2H), 1.76-1.48 (m, 4H), 1.47-1.12 (m, 3H) (3- H_2 , 4- H_2 , 5- H_2 , 6- H_2 , 3'- H_2 and 4'- H_2); $^{13}\text{C-NMR}$ (CDCl_3 , 101 MHz): $\delta_C = 133.2$ and 129.3 (Bn-2/6 and Bn-3/5), 130.6 (Bn-4), 129.0 (Bn-1), 78.8 (broad, C-1), 69.7 (C-2), 64.3 and 60.9 (C2' and C-5', diastereotopic), 60.5 (PhCH_2N), 36.5 (C-6), 27.5, 25.6, 24.2, 22.9, 21.6 (C-3, C-4, C-5, C-3' and C-4'); **HRMS** (ESI, pos., CH_3CN), calc for $\text{C}_{17}\text{H}_{26}\text{NO}^+$ ($[\text{M}]^+$) m/z : 260.2009, found: 260.2020.

2.1.2. *cis*-1-(2-chlorocyclohexyl)pyrrolidine (*rac. cis-7dx*)



The starting β -hydroxyammonium chloride (592 mg, 2 mmol) was dissolved in CHCl_3 (10 mL) and the solution was cooled with an ice-water bath. Thionyl chloride (0.19 mL, 2.6 eq.) was added dropwise. The mixture was stirred over night, then the excess thionyl chloride was destroyed by adding MeOH (5 mL) at 0°C . After stirring for 1 h, then volatiles were removed *in vacuo*. (NMR analysis at this point showed a complex mixture of products) The residual oil was dissolved in MeOH (10 mL), and K_2CO_3 (3 g) was added. The mixture was degassed by 2 cycles of vacuum/ N_2 -flushings, then Palladium on charcoal (10% wt., 5 mol-%, 106 mg) was added. The mixture was degassed again by 2 cycles of vacuum/ N_2 -flushings, then a balloon of hydrogen gas was fitted to the flask and the reaction was left to stir at room temperature over 12h. After filtration over celite, concentration *in vacuo* and flash-chromatography (PE:Et₂O = 5:1), the *cis* β -chloroamine *cis*-**7dx** was obtained (112 mg) as a clear oil. Yield: 30%.

IR (CHCl_3): $\nu = 3395, 2940, 2865, 2780, 1650, 1445, 1375, 1355, 1270, 1215, 1160, 1130, 885, 770 \text{ cm}^{-1}$; **$^1\text{H-NMR}$** (CDCl_3 , 400 MHz) $\delta_{\text{H}} = 4.45$ (br. s, 2-H), 2.70-2.52 (2'-H₂/5'-H₂), 2.15-2.01 (m, 1-H and 3-H_a), 1.91-1.60 (m, 9H), 1.54-1.41 (m, 1H) and 1.37-1.17 (m, 1H) (3-H_b, 4-H₂, 5-H₂, 6-H₂, 3'-H₂, 4'-H₂); **$^{13}\text{C-NMR}$** (CDCl_3 , 101 MHz): $\delta_{\text{C}} = 67.7$ (C-2), 62.0 (C-1), 51.7 (C-2'/C-5'), 33.5 (C-3), 23.3 (C-3'/C-4'), 26.1, 24.8, 19.6 (C-4, C-5, C-6); **HRMS** (ESI, pos., CH_3CN), calc for $\text{C}_{10}\text{H}_{19}\text{ClN}^+$ ($[\text{M}+\text{H}]^+$) m/z : 188.1201, found: 188.1203.

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