Supporting Information

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General Methods and Materials

**General:** All biotransformations were carried out in HEPES buffer (100 mM pH 10.9) unless otherwise stated and were incubated at 30 °C and 200 rpm. ¹H and ¹³C NMR spectra were recorded on a Bruker DPX 400 or Bruker AV(III)500 spectrometer (400 MHz for ¹H and 100.3 MHz for ¹³C) in CDCl₃ or D₂O. The chemical shifts are reported in ppm with the residual solvent referenced to 7.26 ppm/77.23 ppm (¹H/¹³C CDCl₃) and 4.79 ppm (¹H D₂O) respectively. Coupling constants (J) are reported in Hz and refer to the observed peak multiplicities. ¹³C ppm values are rounded up and reported to one decimal place. GC-FID analysis was performed on a Bruker Trace 1310 series GC equipped with an autosampler and chiral sil Dex CB (25 m x 0.25 mm x 0.25 mm) column. Mass spectra were recorded on a Bruker MicroTOF II spectrometer (ESI).

**Materials:** Commercially available reagents were used throughout without further purification. Reagents were purchased from Sigma Aldrich, Acros and Merck Millipore. Commercially available ATA 256 was a gift from Codexis®.

**Analytical biotransformation of Ketones 7-9 with ATA 256 and amine donors 4-5.** Commercially available (S)-selective ATA 256 (2.5 mg/mL) was rehydrated in HEPES buffer (1 mL, 100 mM, pH 10.9) containing PLP (1 mM) and amines 4-5 (60 mM from a 500 mM stock in HEPES buffer). For comparison, isopropylamine was also tested under the same reaction conditions. The ketone substrate was added (20 mM from a 500 mM stock in DMSO) and the reaction pH adjusted to 10.9. The mixture was incubated at 30° C for 48 hours in a shaking incubator (200 rpm). The reactions were analysed by GC-FID following extraction of the basified (pH 12 adjusted with conc. NaOH) solution (500 µL) with EtOAc (1 x 750 µL) and derivatisation (10 µL Ac₂O, 10 µL TEA).

**Preparative scale biotransformation of acetophenone 8 with ATA 256 and cadaverine 4 (1,5-diaminopropane)** Commercially available (S)-selective ATA 256 (2.5 mg/mL) was rehydrated in HEPES buffer (10 mL, 100 mM, pH 10.9) containing PLP (1 mM) and cadaverine (150 mM from a 500 mM stock in HEPES buffer). To this was added acetophenone (50 mM from a 500 mM stock in DMSO) and the mixture was incubated at 30° C for 48 hours in a shaking incubator (200 rpm). The mixture was then adjusted to pH 4.0 and extracted with diethyl ether (30 mL). The aqueous solution was then adjusted to pH 12 and extracted with diethyl ether (30 ml x 2). The combined organic fractions were reduced in vacuo and dissolved in ethyl acetate (5 mL).
and filtered through a small plug of silica, which was washed with a further portion of ethyl acetate (5 ml). The solvent was combined and concentrated in vacuo to give (S)-methylbenzylamine (39 mg, 64 % yield). $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.37 – 7.19 (m, 5H), 4.11 (q, $J = 6.6$ Hz, 1H), 1.70 – 1.58 (m, 2H), 1.39 (d, $J = 6.6$ Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 147.8, 128.5, 126.8, 125.7, 51.4, 25.7. In accordance with literature data. $^{[1]}$

**Analytical scale biotransformation of 1-aminoindane 15 with ATA 256 and isotripiperideine 14**

Commercially available (S)-selective ATA 256 (2.5 mg/mL) was rehydrated in HEPES buffer (1 mL, 100 mM, at pH 8.0, 9.0 10.0 and 10.9) containing PLP (1 mM) and isotripiperideine 14 (40 mM from a 125 mM stock in HEPES buffer). To this was added 1-aminoindane 15 (20 mM from a 500 mM stock in DMSO) and the mixture incubated at 30 °C for 48 hours in a shaking incubator (200 rpm). The reactions were analysed by GC-FID following extraction of the basified (pH 12 adjusted with conc. NaOH) solution (500 µL) with EtOAc (1 x 750 µL) and derivatisation (10 µL Ac$_2$O, 10 µL TEA).

**Synthesis of $\alpha$-Tripiperideine 12$^{[2,3]}$**

$N$-Chlorosuccinimide (3.29 g, 24.66 mmol, 1.05 eq) was stirred in Et$_2$O (25 mL) and cooled in an ice-bath. Piperidine (2.32 mL, 23.49 mmol) was then added slowly over 5 minutes and left to stir at room temperature for two hours. The mixture was filtered and the resulting filtrate washed with water and dried with MgSO$_4$ and reduced in vacuo to approx. 1/3 volume (without heating)* to give 1-chloropiperidine as a crude yellow oil. This oil was dissolved in EtOH (15 mL) and to this was added potassium hydroxide (3.1 g, 55 mmol). This mixture was then refluxed for a further two hours, filtered, and the solvent removed in vacuo to give a thick yellow oil $\Delta^1$-piperideine (1.33g, 15.97 mmol, 68% over two steps). $^1$H NMR (300 MHz, Chloroform-$d$) $\delta$ 3.16 – 3.03 (m, 3H), 2.83 – 2.72 (m, 3H), 2.05 – 1.91 (m, 3H), 1.76 – 1.60 (m, 9H), 1.60 – 1.47 (m, 6H), 1.32 – 1.20 (m, 3H); $^{13}$C NMR (75 MHz, Chloroform-$d$) $\delta$ 82.0, 46.5, 29.3, 25.9, 22.4; (m/z) calculated C$_{13}$H$_{27}$N$_3$ [M] 249.2205; found 249.2135.

*Potentially hazardous/explosive

**Conversion of $\Delta^1$-Piperideine 13 to Isotripiperideine 14$^{[2,3,4]}$**

$\Delta^1$-piperideine (1 g, 4.01 mmol) was dissolved in acetone (2 mL) and the solution was left to crystallise over 5 days at -20 °C. The resulting crystals were washed with water and Et$_2$O to give clear crystals of isotripiperideine 14 (810 mg, 3.25 mmol) suitable for x-ray crystallographic analysis. $^1$H NMR (500 MHz, Chloroform-$d$) $\delta$ 3.77 – 3.67 (m, 1H), 3.15 –
3.08 (m, 2H), 2.67 – 2.51 (m, 3H), 1.98 – 1.69 (m, 8H), 1.68 – 1.46 (m, 4H), 1.39 – 1.14 (m, 5H), 0.96 (m, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 82.0, 81.2, 64.2, 48.0, 48.0, 45.7, 43.7, 29.8, 28.7, 27.7, 26.5, 26.2, 25.4, 23.4, 23.4; (m/z) calculated for C$_{15}$H$_{27}$N$_3$ [M+H] 250.2278; found 250.2277.
$^1$H and $^{13}$C NMR spectra

**Tripiperideine**

$^1$H NMR (300 MHz, Chloroform-$d$) $\delta$ 3.16 – 3.03 (m, 3H), 2.83 – 2.72 (m, 3H), 2.05 – 1.91 (m, 3H), 1.76 – 1.60 (m, 9H), 1.60 – 1.47 (m, 6H), 1.32 – 1.20 (m, 3H).

**Tripiperideine**

$^{13}$C NMR (75 MHz, Chloroform-$d$) $\delta$ 82.04, 46.48, 29.28, 25.89, 22.42.
Isotriptiprileine

$^1$H NMR (500 MHz, Chloroform-$d$) δ 3.76 – 3.66 (m, 1H), 3.14 – 3.07 (m, 2H), 2.66 – 2.50 (m, 3H), 2.16 (s, 6H), 1.97 – 1.68 (m, 8H), 1.67 – 1.45 (m, 4H), 1.38 – 1.13 (m, 5H), 1.01 – 0.85 (m, 1H).

$^{13}$C NMR (101 MHz, Chloroform-$d$) δ 81.95, 81.16, 64.18, 48.02, 47.94, 45.72, 43.72, 29.79, 28.66, 27.67, 26.48, 26.18, 25.37, 23.44, 23.40.
**Figure S1:** Overlay of spectra from the large-scale reaction of acetophenone 8 with ATA256 employing cadaverine 4 as the amine donor showing the presence of the trimeric by-product. A) Purified large scale reaction showing (S)-methylbenzylamine. B) Synthesised and purified isotripterideine 14. C) Crude NMR of large scale enzyme reaction, showing both isotripterideine 14 and (S)-methylbenzylamine before purification.

**Crystal Data** for C$_{15}$H$_{27}$N$_{3}$ ($M$=249.39 g/mol): monoclinic, space group C2/c (no. 15), $a$ = 10.06270(12) Å, $b$ = 16.75395(15) Å, $c$ = 16.98045(18) Å, $\beta$ = 97.0391(10)$^\circ$, $V$ = 2841.16(5) Å$^3$, $Z$ = 8, $T$ = 120(2) K, $\mu$(CuK$\alpha$) = 0.531 mm$^{-1}$, $D_{\text{calc}}$ = 1.166 g/cm$^3$, 36653 reflections measured (10.312$^\circ$ ≤ 2$\Theta$ ≤ 148.41$^\circ$), 2871 unique ($R_{\text{int}}$ = 0.0341, $R_{\text{sigma}}$ = 0.0099) which were used in all calculations. The final $R_1$ was 0.0560 (I > 2$\sigma$(I)) and $wR_2$ was 0.1651 (all data). Single crystals of C$_{15}$H$_{27}$N$_{3}$ 14 were obtained as detailed above. A suitable crystal (0.408 × 0.266 × 0.205mm) was selected and mounted in fomblin film on a MiTeGen micromount on a Rigaku Oxford Diffraction single source SuperNova TitanS2 diffractometer, using Cu-K$\alpha$ radiation ($\lambda$ = 1.54184 Å). The crystal was kept at 120(2) K during data collection. Using Olex2,$^5$ the structure was solved with the olex2.solve$^6$ structure solution program using Charge Flipping and refined with the ShelXL$^7$ refinement package using Least Squares minimisation; (CCDC 1471632).

**References**

[2] E. Gravel, E. Poupon, R. Hocquemiller, *Tetrahedron*, **2006**, *62*, 5248–5253. It is worth noting that our $^1$H MNR data for compound 14 is not fully consistent with the data reported in this manuscript.


