

# Supporting Information

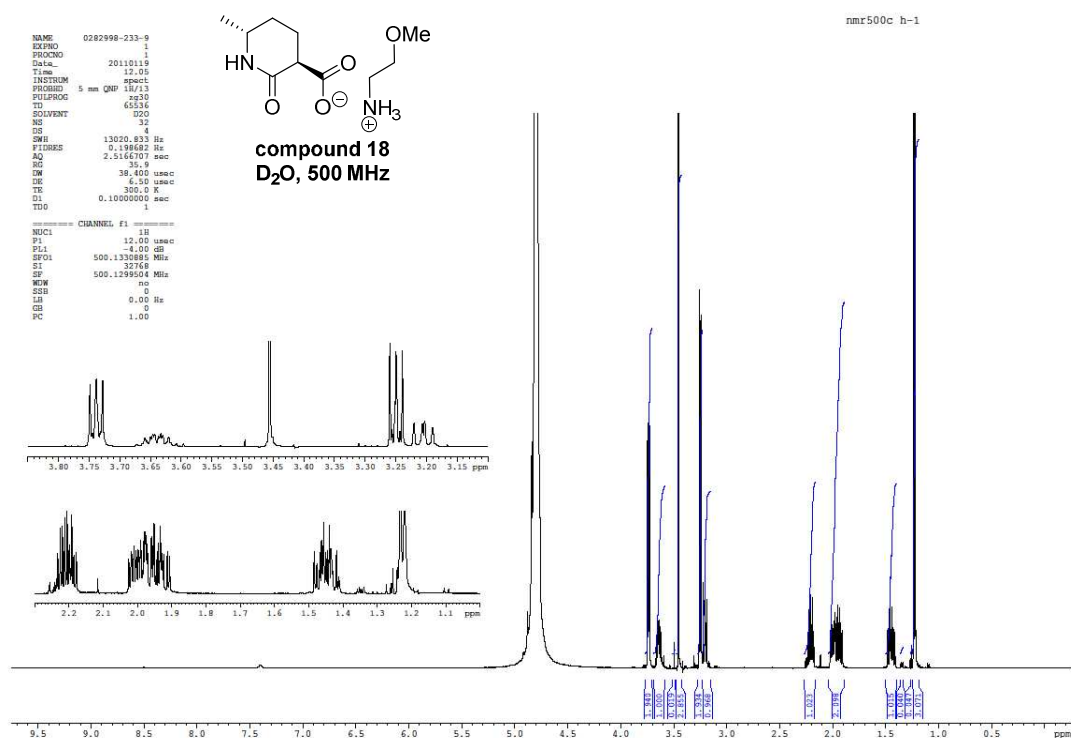
## Synthesis of ((3*R*,6*R*)-6-methylpiperidin-3-yl)methanol via Biocatalytic Transamination and Crystallization- Induced Dynamic Resolution

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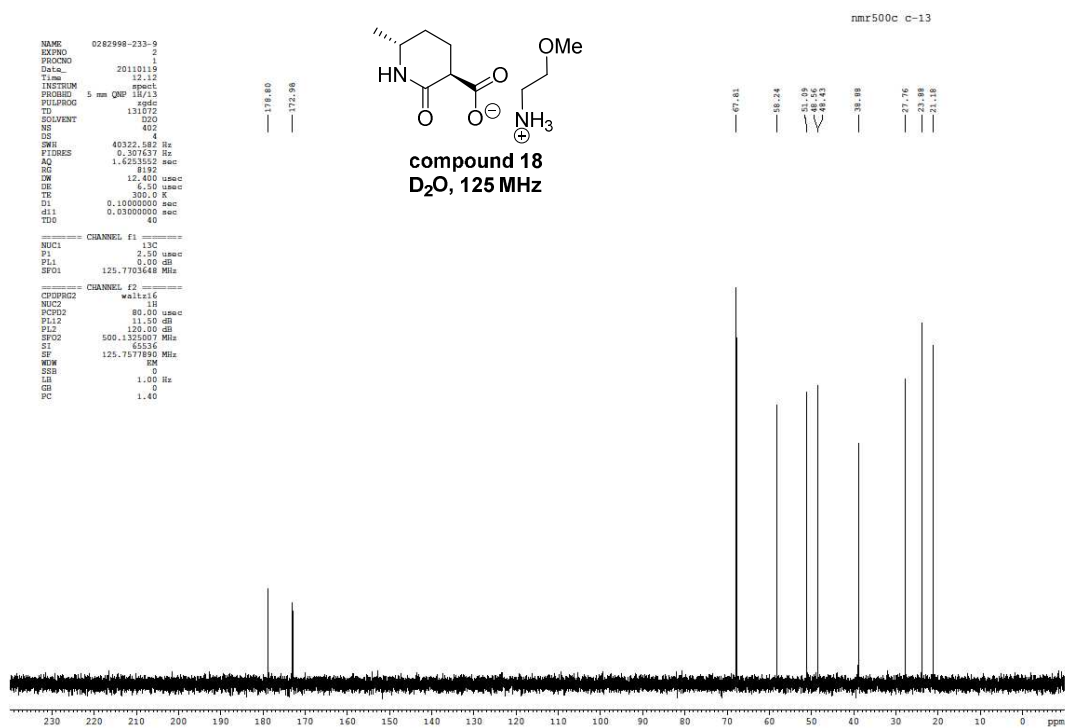
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**Figure S1. <sup>1</sup>H NMR of compound 18**



**Figure S2. <sup>13</sup>C NMR of compound 18**



### Compound 3 *trans-cis* ratio determination via benzoyl derivatization and chiral LC method:

Column: Lux 3 $\mu$  Cellulose-4 Phenomenex, 4.6 x 150 mm

Temperature: 40 °C

Detector: 210 nm

Injection volume: 4  $\mu$ L

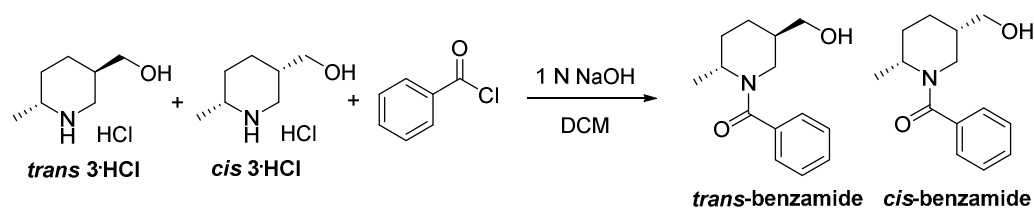
Flow Rate: 1.0 mL/min

Mobile Phase Composition: A: 0.1% H<sub>3</sub>PO<sub>4</sub>, B: acetonitrile

Gradient: 20% B to 60% B over 13 min, then to 80% B over 4.5 min, post time 5.5 min

#### Derivatization procedure:

Weighed out 41.42 mg (0.5 mmol) of Piperidinol HCl salt **3**, added 0.5 mL of 1.0 N NaOH (1.0 mmol), 0.5 mL of dichloromethane, and finally 60  $\mu$ L of benzoyl chloride (~1.5 eq). Stirred the reaction mixture for ~5 min and allowed layers to separate (until clear phases are shown). Bottom layer (org layer where the product is): 20  $\mu$ L into 2.0 mL acetonitrile. For the aqueous layer, 50  $\mu$ L into 1.0 mL acetonitrile and filtered the solution.

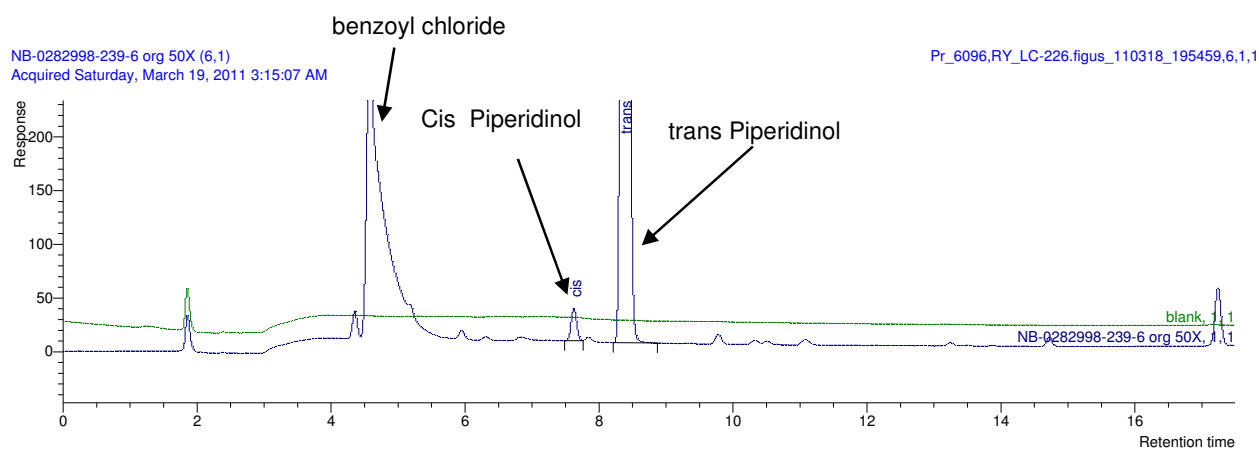


Diluent for org fraction: pure acetonitrile

Diluent for aq fraction: 50/50 MeCN/H<sub>2</sub>O v/v%

Peak Name	RT
Cis-benzamide	7.63 min
Trans-benzamide	8.39 min

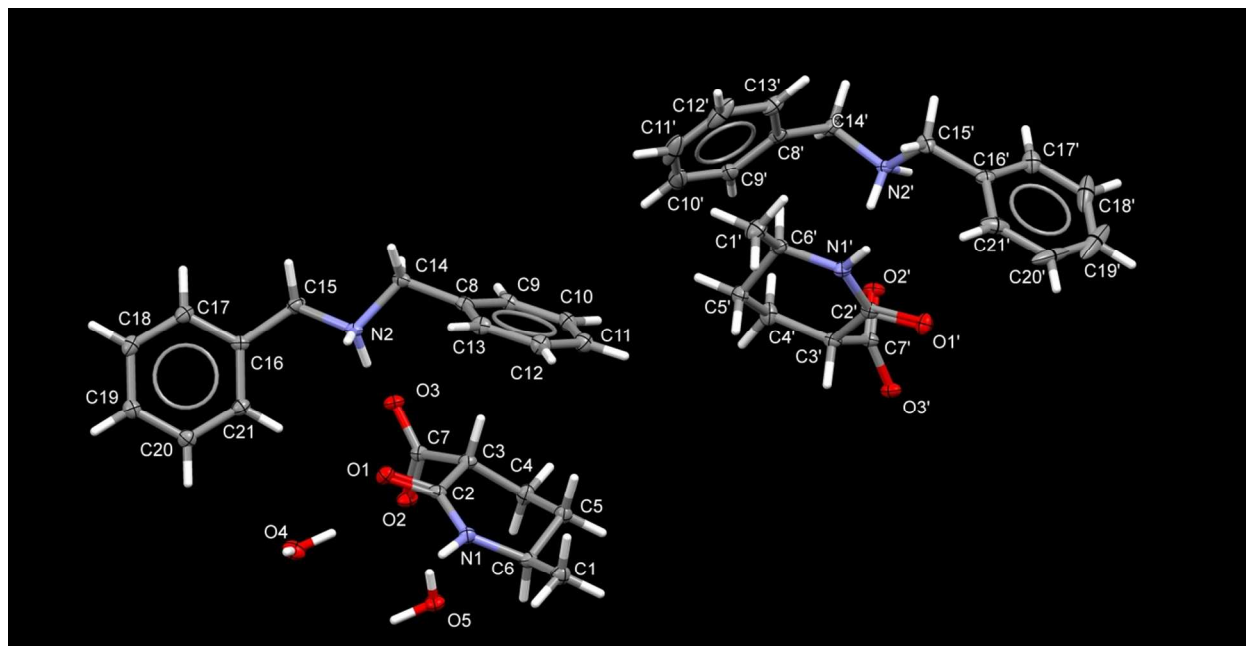
Figure S3: Typical chromatograph for Piperidinol HCl salt after derivatization



## Crystal data and structure refinement for Compound 20 (CCDC 1417569)

A single crystal grown from acetonitrile and water by slow evaporation was selected for single crystal X-ray data analysis. The crystal was a small colorless lathe with dimensions of 0.02mm x 0.13mm x 0.34mm. Data collection was performed at 100K on an Oxford Gemini system with a Cu radiation source. The unit cell was determined to be orthorhombic in space group  $P2_12_12_1$  with two independent ion pairs in the asymmetric unit of the crystal lattice along with two molecules of water. Crystallographic data is summarized in Table 1. Absolute configuration was established by reference to the known chiral center at the C6 position and supported by anomalous-dispersion effects in diffraction measurements on the crystal. Results confirmed that the stereochemistry of Compound 20 was 3R, 6R. Figure 1 shows an ORTEP representation of Compound 20 with thermal ellipsoid set at the 30% probability level. Full structural details have been deposited with the Cambridge Crystallographic Data Centre (CCDC 1417569).

**Figure S4:** ORTEP representation of Compound **20** with thermal ellipsoids set at the 30% probability level.

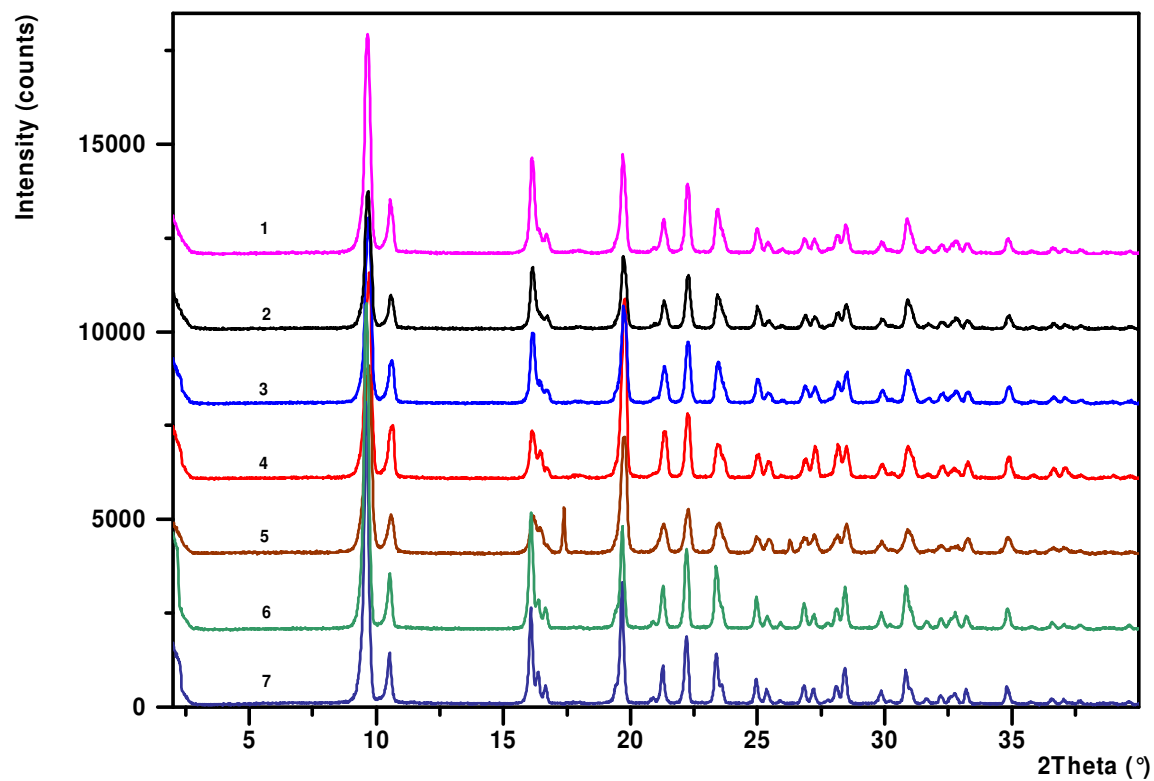


**Table S1.** Crystal data and structure refinement for Compound **20**

Empirical formula	C <sub>14</sub> H <sub>16</sub> N, C <sub>7</sub> H <sub>10</sub> N O <sub>3</sub> , H <sub>2</sub> O	
Formula weight	372.46	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P2 <sub>1</sub> 2 <sub>1</sub> 2 <sub>1</sub>	
Unit cell dimensions	a = 8.7278(3) Å	α = 90°
	b = 9.6635(4) Å	β = 90°
	c = 46.6791(18) Å	γ = 90°
Volume	3937.0(3) Å <sup>3</sup>	
Z	8	
Density (calculated)	1.257 Mg/m <sup>3</sup>	
Absorption coefficient	0.705 mm <sup>-1</sup>	
F(000)	1600.0	
Crystal size	0.02 x 0.13 x 0.34 mm <sup>3</sup>	
Theta range for data collection	3.7846 to 66.4567°.	
Index ranges	-10 ≤ h ≤ 9, -11 ≤ k ≤ 8, -55 ≤ l ≤ 54	
Reflections collected	15078	
Independent reflections	6503 [R(int) = 0.0587]	
Completeness to theta = 66.500°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.989 and 0.867	
Refinement method	Full-matrix least-squares on F <sup>2</sup>	
Data / restraints / parameters	6503 / 6 / 492	
Goodness-of-fit on F <sup>2</sup>	1.043	
Final R indices [I > 2σ(I)]	R1 = 0.0507, wR2 = 0.1182	
R indices (all data)	R1 = 0.0605, wR2 = 0.1216	
Absolute structure parameter	0.1(2)	
Largest diff. peak and hole	0.268 and -0.229 e.Å <sup>-3</sup>	

### Figure S5: X-ray powder diffractions (XRPD) of compound **18**

The XRPD patterns of seven samples of MEA salts **18** are essentially identical. The two extra peaks in XRPD pattern of sample 5 is due to the cis isomer, since the sample is 89% d.e.

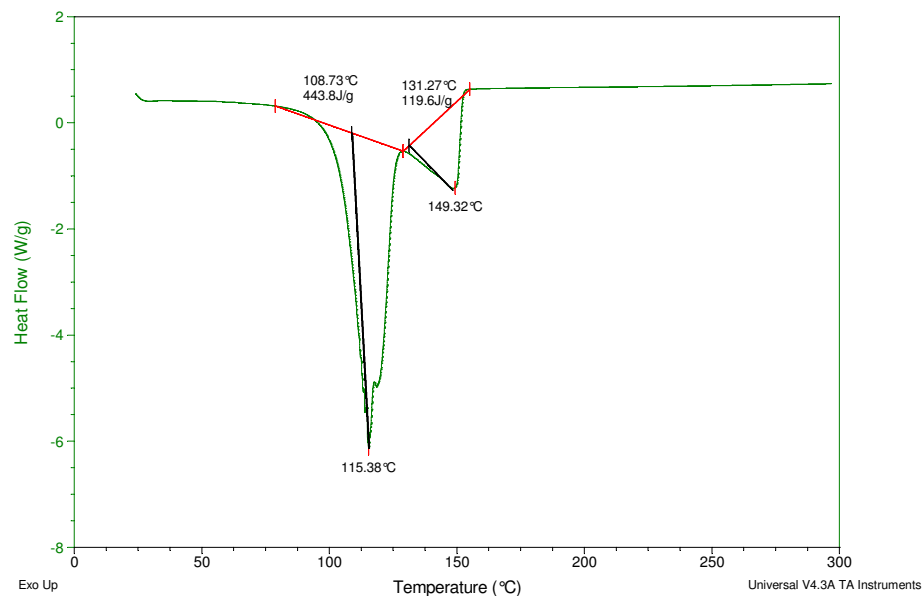


**Figure S6: Differential scanning calorimetry (DSC) and Thermogravimetric analysis (TGA) of compound 18**

Sample: Methoxyethylamine salt of acid I  
Size: 4.3540 mg  
Method: Ramp  
Comment: DSC-3, N2, open, 10cpm

DSC

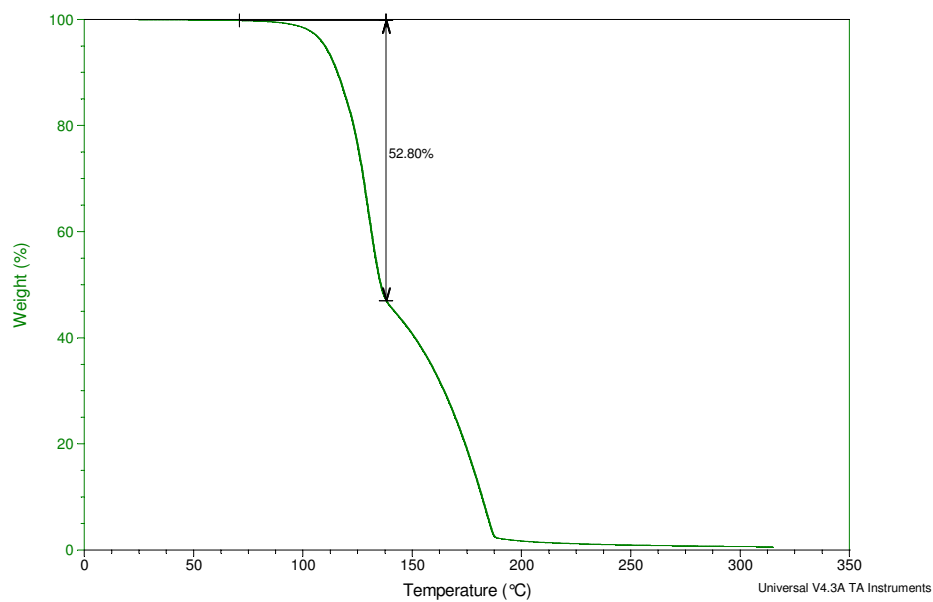
File: 282998-178-4 methoxyethylamine salt o...  
Operator: RP  
Run Date: 14-Sep-2010 17:46  
Instrument: 2920 DSC V2.6A

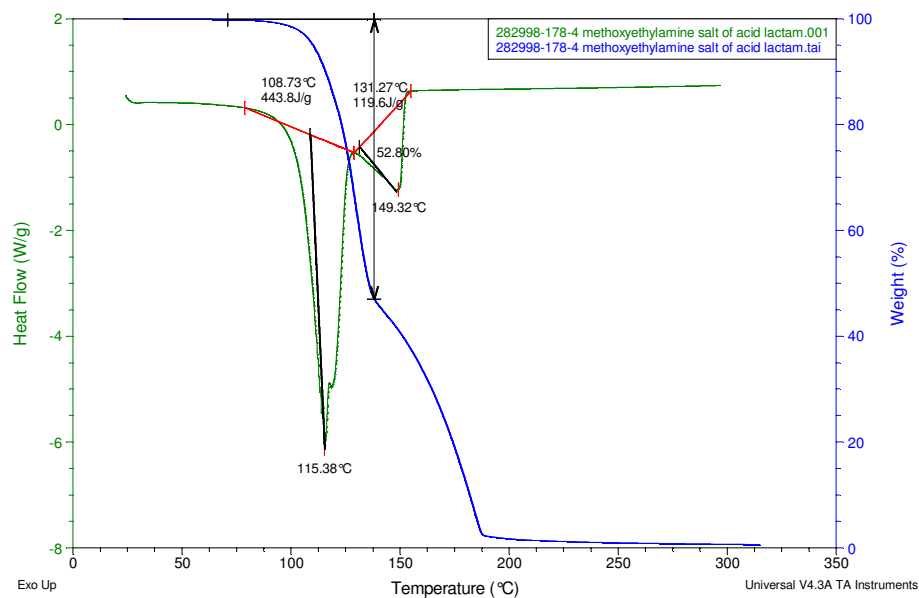


Sample: Methoxyethylamine salt of acid lactam  
Size: 8.6530 mg  
Comment: TG-1, 10 cpm, N2

TGA

File: 282998-178-4 methoxyethylamine salt o...  
Operator: RP  
Run Date: 14-Sep-2010 17:23  
Instrument: TGA 7





MEA salt sample: KF: 0.73 wt%, IPAc: 0.02 wt%

### **Summary:**

All samples contain the same crystalline form, except sample 5, which is known to have lower purity compared to the other samples. The TGA and DSC data showed that the crystal melts at 109 °C and decomposes immediately after melting. The low solvent content of the samples suggests that the analyzed samples contain anhydrous crystalline form.