Supporting Information

Chemo- and regioselective Pd(II)-catalyzed aminoarylation of N-allylureas providing 4-arylmethyl imidazolidinones

Sabrina Giofrè, Egle M. Beccalli,* Francesca Foschi, Concetta La Rosa, Leonardo Lo Presti, Michael S. Christodoulou

Corresponding author:
Egle Maria Beccalli: egle.beccalli@unimi.it
Contents

X-Ray Analysis ......................................................................................................................... 3

$^1$H and $^{13}$C NMR Spectra of Unknown Compounds ............................................................ 7

N-Allyl-N-cyclohexyl-N'-tosyl-urea (1d) .......................................................................................... 7

N-Allyl-N-cyclohexyl-N'-(4-chlorophenyl)urea (1e) ....................................................................... 9

N-Allyl-N-phenyl-N'-(4-chlorophenyl)urea (1f) .............................................................................. 11

N-Allyl-N-phenyl-N'-tosyl-urea (1g) .............................................................................................. 13

N-Allyl-N-phenyl-N'-'-toly-urea (1h) ........................................................................................ 15

N-But-2-en-1-yl-N-phenyl-N'-tosyl-urea (5) ................................................................................. 17

4-Benzyl-1-methyl-3-tolyl-imidazolidin-2-one (3aa) ................................................................. 21

4-(chloromethyl)-1-methyl-3-(p-tolyl)imidazolidin-2-one (4) .................................................. 23

4-Benzyl-1-methyl-3-tosyl-imidazolidin-2-one (3ba) ............................................................... 25

4-(4-Benzylxyphenyl)methyl-1-methyl-3-tosylimidazolidin-2-one (3bb) ............................. 27

4-Benzyl-1-methyl-3-(4-chlorophenyl)imidazolidin-2-one (3ca) ............................................. 29

4-(4-Benzylxyphenyl)methyl-1-methyl-3-(4-chlorophenyl)imidazolidin-2-one (3cb) ............. 31

4-Benzyl-1-cyclohexyl-3-tosyl-imidazolidin-2-one (3da) .......................................................... 33

4-(4-Benzylxyphenyl)methyl-1-cyclohexyl-3-tosylimidazolidin-2-one (3db) ..................... 35

4-Benzyl-1-cyclohexyl-3-(4-chlorophenyl)imidazolidin-2-one (3ea) ....................................... 37

4-(4-Benzylxyphenyl)methyl-1-cyclohexyl-3-(4-chlorophenyl)imidazolidin-2-one (3eb) ... 39

4-benzyl-3-(4-chlorophenyl)-1-phenylimidazolidin-2-one (3fa) ................................................. 41

4-(4-Benzylxyphenyl)methyl-1-phenyl-3-(4-chlorophenyl) imidazolidin-2-one (3fb) .......... 43

4-(4-Benzylxyphenyl)methyl-1-phenyl-3-tosylimidazolidin-2-one (3gb) ........................ 45

4-benzyl-1-phenyl-3-(p-tolyl)imidazolidin-2-one (3ha) .......................................................... 47

4-(4-Benzylxyphenyl)methyl-1-phenyl-3-tolyelimidazolidin-2-one (3hb) ............................. 49

4-phenethyl-1-phenyl-3-tosylimidazolidin-2-one (6) ............................................................... 51

4-vinyl-1-phenyl-3-tosylimidazolidin-2-one (7) ........................................................................ 53
X-Ray Analysis

Single crystal X-ray diffraction analysis of the compound 3ea

See the main text for details of the data collection. CCDC 1896769 contains supplementary crystallographic data for this paper. These can be obtained free of charge from The Cambridge Crystallographic Data Centre.

The compound is chiral and crystallizes in the centric space group \( \text{P}2_1/c \) as a racemate, with two molecules with inverse handedness per asymmetric unit (ASU). An attempt to model the structure in the non-centrosymmetric \( \text{P}2_1 \) space group with 4 independent molecules in the ASU was unsuccessful, as the least-squares refinement invariably led to a 100% correlation between \([x, y, z]\) and \([–x, –y, –z]\) coordinates. Figures S1 and S2 show the absolute configuration of the chiral centres in the asymmetric unit. The configurational descriptor of the unique stereogenic centre is C9 (R) for the molecule A and C9 (S) for the molecule B (see Figure S1 for the atom numbering).

\[\text{Figure S1.} \ \text{(a) Asymmetric unit of 3ea at RT. The crystallographic reference system is also shown. (b) Molecule A, with the atom-numbering scheme. Thermal ellipsoids of non-H atoms were drawn at the 25 \% probability level. (c) As (b), for the molecule B. The usual colour code was employed for atoms (grey: C; white: H; blue: N; red: O; green: Cl).}\]
Figure S2. Molecular structure of 3ea, with the CIP descriptors highlighted. Both symmetry-independent molecules in the asymmetric unit are shown. (a) Molecule A. (b) Molecule B.

This substance crystallizes in very thin needles, which also give very low diffraction intensities. After various attempts, we eventually managed to obtain X-ray quality crystals by slow evaporation (~ 1 month) from CH$_3$CN at room temperature. The crystalline material is highly elastic and has a fibrous appearance. We cut a sample with a needle habit, transparent, with dimensions 0.800 x 0.100 x 0.050 mm from a larger agglomerate using a blade (Figure S3). It showed pleochroism under polarized light (from colourless to green-light blue). After polishing by mechanical ablation in a drop of perfluorinated oil, we mounted it on the diffractometer to carry out the data collection.

Figure S3. Sample used for the present structural determination.

The resolution of the overall data collection is quite low (~ 1 Å), as at higher Bragg angles the count statistics was too low to be meaningful. Consequently, the present structural analysis suffers of various drawbacks (poor data-to-parameter ratio, low resolution), which result in a general low precision of the geometrical parameters (bond lengths, angles) and high agreement factors. However, the purpose of the present work was to secure the molecular connectivity, and particularly to determine whether the 4-chlorobenzyl substituent is connected either to oxygen or nitrogen of the imidazolidin-2-one ring. In this respect, the experiment was successful, as the data are fully consistent with the model shown in Figures S1-S2.
Figure S4. Crystal packing of 3ea at RT, as seen as wires-stick molecular representations (a) along the \(a\) cell axis; (b) the \(b\) cell axis; (c) the \(c\) cell axis. Colour code as in Figure 1. H atoms are omitted for clarity. The crystallographic reference system is also shown.

Figure S4 shows the main packing motifs of 3ea. No strong hydrogen bond donors are present: only C–H···O contacts with distance H···acceptor lower than the sum of the van der Waals radii and favourable geometries are set up (Table S1, Figure S5). “A” molecules exploit the phenyl C19A–H19A···O1A contact to form CH···O hydrogen-bonded infinite chains with translation-related images of themselves along the \(a\) axis. “B” molecules form an analogue, parallel chain-like arrangement, using the phenyl C21B–H21B···O1B contact. Parallel chains of “A” and “B” molecules are cross-linked through C9A–H9A···O1B and C9B–H9B···O1A contacts, C9 being the asymmetric ternary carbon (see above). No significant halogen-bonded contacts are set up.

Table 1. Short intermolecular C–H···O halogen bonded contacts with \(d_{H···O} < 3.0\) Å and \(120^\circ \leq \alpha_{CHO} \leq 180^\circ\) in 3ea at room temperature. Distances are expressed in Å and angles in degrees. Estimated standard deviations are given in parentheses.

<table>
<thead>
<tr>
<th>C–H···O</th>
<th>(d_{C–H})</th>
<th>(d_{H···O})</th>
<th>(d_{C···O})</th>
<th>(\alpha_{CHO})</th>
<th>symmetry</th>
</tr>
</thead>
<tbody>
<tr>
<td>C19A–H19A···O1A</td>
<td>0.93</td>
<td>2.53</td>
<td>3.35(2)</td>
<td>147</td>
<td>1+x, y, z</td>
</tr>
<tr>
<td>C21B–H21B···O1B</td>
<td>0.93</td>
<td>2.57</td>
<td>3.36(2)</td>
<td>143</td>
<td>1+x, y, z</td>
</tr>
<tr>
<td>C9A–H9A···O1B</td>
<td>0.98</td>
<td>2.41</td>
<td>3.36(1)</td>
<td>162</td>
<td>1+x, y, z</td>
</tr>
<tr>
<td>C9B–H9B···O1A</td>
<td>0.98</td>
<td>2.42</td>
<td>3.35(1)</td>
<td>158</td>
<td>x, y, z</td>
</tr>
</tbody>
</table>
Figure S5. Short CH···O contacts in the parallel chains of A and B molecules of 3ea at room temperature, as viewed down the c axis. See Table 1 for geometrical parameters.

Puckering analysis (D. Cremer & J.A. Pople, J.Amer.Chem.Soc., 97, (1975), 1354-1358), shows that the imidazolidin-2-one ring of both the enantiomers is not completely planar. The configurational descriptors (Molecule A: Q = 0.214 Å, \( \varphi \) = 116.52°; Molecule B: Q = 0.210 Å, \( \varphi \) = 296.42°) are invariably compatible with a slight distortion toward a half-chair conformation. Both cyclohexyl rings, on the other hand, assume regular chair conformations, with puckering descriptors Q = 0.583 Å, \( \theta \) = 2.24°, \( \varphi \) = 253.20° (Molecule A) and Q = 0.539 Å, \( \theta \) = 0.59°, \( \varphi \) = 245.19° (Molecule B).

A \( \sim 124 \text{ Å}^3 \) large void space is present in the unit cell. It might potentially allocate solvent molecules, and it has likely a strong hydrophobic nature, as it is bounded by cyclohexyl substituents and chlorine atoms (Figure S6). Indeed, due to the poor diffracting ability of this substance, and consequently to poor intensity statistics, we cannot exclude the presence of partially or totally disordered solvent in this cavity. However, the highest Fourier residuals are smaller than +0.4/-0.3 e/Å³, and localized in close proximity of the chlorine atoms. Any attempt to locate meaningful solvent residual inside the cavity were unsuccessful.

Figure S6. Crystal packing of 3ea viewed down the b axis. The void space among cyclohexyl units, potentially able to allocate solvents, is highlighted as blue circles.
$^1$H and $^{13}$C NMR Spectra of Unknown Compounds

$N$-Allyl-$N$-cyclohexyl-$N'$-tosyl-urea (1d)
$N$-Allyl-$N$-cyclohexyl-$N'$(4-chlorophenyl)urea (1e)
$N$-Allyl-$N$-phenyl-$N'$-(4-chlorophenyl)urea (1f)
N-Allyl-N-phenyl-N'-tosyl-urea (1g)
N-Allyl-N-phenyl-N’-tolyl-urea (1h)
$N$-But-2-en-1-yl-N-phenyl-N$'$-tosyl-urea (5)
1-(But-3-en-1-yl)-1-phenyl-3-(p-tolyl)urea (8)
4-Benzyl-1-methyl-3-tolyl-imidazolidin-2-one (3aa)
4-(chloromethyl)-1-methyl-3-(p-tolyl)imidazolidin-2-one (4)
4-Benzyl-1-methyl-3-tosyl-imidazolidin-2-one (3ba)
4-(4-Benzylxyphenyl)methyl-1-methyl-3-tosylimidazolidin-2-one (3bb)
4-Benzyl-1-methyl-3-(4-chlorophenyl)imidazolidin-2-one (3ca)
4-(4-Benzyloxyphenyl)methyl-1-methyl-3-(4-chlorophenyl)imidazolidin-2-one (3cb)
4-Benzyl-1-cyclohexyl-3-tosyl-imidazolidin-2-one (3da)
4-(4-Benzylxoyphenyl)methyl-1-cyclohexyl-3-tosylimidazolidin-2-one (3db)
4-Benzyl-1-cyclohexyl-3-(4-chlorophenyl)imidazolidin-2-one (3ea)
4-(4-Benzylxoyphenyl)methyl-1-cyclohexyl-3-(4-chlorophenyl)imidazolidin-2-one (3eb)
4-benzyl-3-(4-chlorophenyl)-1-phenylimidazolidin-2-one (3fa)
4-(4-Benzoyloxyphenyl)methyl-1-phenyl-3-(4-chlorophenyl) imidazolidin-2-one (3fb)
4-(4-Benzylxyphenyl)methyl-1-phenyl-3-tosylimidazolidin-2-one (3gb)
4-benzyl-1-phenyl-3-(p-tolyl)imidazolidin-2-one (3ha)
4-(4-Benzyloxyphenyl)methyl-1-phenyl-3-tolylimidazolidin-2-one (3hb)
4-phenethyl-1-phenyl-3-tosylimidazolidin-2-one (6)
4-vinyl-1-phenyl-3-tosylimidazolidin-2-one (7)
1,4-diphenyl-3-(p-tolyl)-1,3-diazepan-2-one (9)