Synthesis of Functionalized Azabicycloalkane Amino Acids as Dipeptide Mimics

Leonardo Manzoni,*a Laura Belvisi,b Eliana DiCarlo,c Alessandra Forni,a Donatella Invernizzi,b Carlo Scolastico*b
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Abstract: Functionalized bicyclic lactams serve as building blocks for the synthesis of conformationally constrained peptides. A route to these building blocks is described based on the stereoselective alkylation of an appropriate azabicycloalkane; all possible diastereoisomers can be obtained stereoselectively.

Key words: peptidomimetics, alkylations, lactams, bicyclic compounds, diastereoselective synthesis

The synthesis of conformationally restricted amino acids and their utilization in the synthesis of peptide conformation mimics, such as β-turn mimics, has been of considerable interest.1 Azabicyclo[X.3.0]alkane amino acids are particularly attractive constrained dipeptide mimics because of their ability to serve as conformationally fixed surrogates of peptide turn secondary structures.2 This has created a demand for efficient synthetic approaches towards such molecules and many methods for their synthesis have been introduced.3–6 While studying peptide secondary structure mimics, we have synthesized several 5,5-, 6,5-, 7,5-, and 8,5-fused 1-aza-2-oxobicyclic compounds, diastereoselective synthesis

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base and benzyl or allyl bromide yielded the alkyl derivatives 5–8 after reduction with NaBH4 (Figure 1).

The stereoselectivity and the yield of the reaction can be modulated using different bases or additives (Table 1). In the case of the enolate derived from 3 with LiHMDS and NaHMDS the major isomer isolated was the 3R isomer 5a; the yields can be increased by adding DMPU as co-solvent. The stereoselectivity is totally reversed when a bicoordinating Lewis acid such as MgBr2·Et2O is added to the reaction mixture. In this case the main product is the 3S isomer 5b. By contrast, the benzylation of 4 affords the 3S isomer 7b selectively, independently of the reaction conditions. A similar behavior can be observed with allyl bromide as the alkylating reagent.

The excellent results obtained for trans-fused bicyclic lactams encouraged us to extend the protocol to the cis series. Thus, imines 9 and 10 were obtained from the known lactams 11 and 12, respectively, using the same procedure reported above. As observed in the trans series, due to the

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Steric and electronic factors in compounds 9 and 10, the reaction with the base was regioselective, only the proton at C3 was removed, and there was no epimerization at C9 or C10.

As shown in Table 2, the alkylation with benzyl bromide conducted with LiHMDS on imine 9, proceeded with moderate yields but with low stereoselectivity affording the 3S isomer 13b as the major product (Table 2, entry 1). It is well known that the reactivity of alkali enolates is strongly dependent on their coordination. The best results were obtained when the cation is solvated, thus, when the reaction was performed in the presence of a polar aprotic solvent such as DMPU, a slight effect on the yield and a dramatic effect on the stereoselectivity (diastereomeric ra-

Table 1 Reaction Conditions for the Alkylation of Compounds 3 and 4

<table>
<thead>
<tr>
<th>Entry</th>
<th>Imine</th>
<th>Base</th>
<th>T (°C)</th>
<th>R Products</th>
<th>Yield (%)</th>
<th>Ratio a/b (3R/3S)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3</td>
<td>LiHMDS</td>
<td>–78 → r.t.</td>
<td>CH3Ph</td>
<td>5a/5b</td>
<td>56</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>LiHMDS/DMPU</td>
<td>–78 → r.t.</td>
<td>CH3Ph</td>
<td>5a/5b</td>
<td>86</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>LiHMDS</td>
<td>–50</td>
<td>CH3Ph</td>
<td>5a/5b</td>
<td>89</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>NaHMDS</td>
<td>–78 → r.t.</td>
<td>CH3Ph</td>
<td>5a/5b</td>
<td>55</td>
</tr>
<tr>
<td>5</td>
<td>3</td>
<td>NaHMDS/DMPU</td>
<td>–78 → r.t.</td>
<td>CH3Ph</td>
<td>5a/5b</td>
<td>81</td>
</tr>
<tr>
<td>6</td>
<td>3</td>
<td>KHMDS</td>
<td>–78 → r.t.</td>
<td>CH3Ph</td>
<td>5a/5b</td>
<td>24</td>
</tr>
<tr>
<td>7</td>
<td>3</td>
<td>LiHMDS/Mg(^{2+})</td>
<td>–78 → r.t.</td>
<td>CH3Ph</td>
<td>5a/5b</td>
<td>43</td>
</tr>
<tr>
<td>8</td>
<td>3</td>
<td>LiHMDS/Mg(^{2+})</td>
<td>–50 → 20</td>
<td>CH3Ph</td>
<td>5a/5b</td>
<td>43</td>
</tr>
<tr>
<td>9</td>
<td>3</td>
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<td>CH3Ph</td>
<td>5a/5b</td>
<td>33</td>
</tr>
<tr>
<td>10</td>
<td>3</td>
<td>LiHMDS</td>
<td>–78 → r.t.</td>
<td>CH2CH=CH2</td>
<td>6a/6b</td>
<td>75</td>
</tr>
<tr>
<td>11</td>
<td>3</td>
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<td>–50</td>
<td>CH2CH=CH2</td>
<td>6a/6b</td>
<td>90</td>
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<td>12</td>
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<td>–78 → r.t.</td>
<td>CH2CH=CH2</td>
<td>6a/6b</td>
<td>78</td>
</tr>
<tr>
<td>13</td>
<td>3</td>
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<td>–78 → r.t.</td>
<td>CH2CH=CH2</td>
<td>6a/6b</td>
<td>55</td>
</tr>
<tr>
<td>14</td>
<td>3</td>
<td>LiHMDS/Mg(^{2+})</td>
<td>–50 → 20</td>
<td>CH2CH=CH2</td>
<td>6a/6b</td>
<td>45</td>
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<tr>
<td>15</td>
<td>4</td>
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<td>–78 → r.t.</td>
<td>CH3Ph</td>
<td>7a/7b</td>
<td>53</td>
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<td>16</td>
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<td>CH3Ph</td>
<td>7a/7b</td>
<td>82</td>
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<td>17</td>
<td>4</td>
<td>NaHMDS</td>
<td>–78 → r.t.</td>
<td>CH3Ph</td>
<td>7a/7b</td>
<td>81</td>
</tr>
<tr>
<td>18</td>
<td>4</td>
<td>NaHMDS</td>
<td>–50 → 20</td>
<td>CH3Ph</td>
<td>7a/7b</td>
<td>73</td>
</tr>
<tr>
<td>19</td>
<td>4</td>
<td>NaHMDS/DMPU</td>
<td>–78 → r.t.</td>
<td>CH3Ph</td>
<td>7a/7b</td>
<td>59</td>
</tr>
<tr>
<td>20</td>
<td>4</td>
<td>LiHMDS/Mg(^{2+})</td>
<td>–78 → r.t.</td>
<td>CH3Ph</td>
<td>7a/7b</td>
<td>68</td>
</tr>
<tr>
<td>21</td>
<td>4</td>
<td>LiHMDS</td>
<td>–78 → r.t.</td>
<td>CH2CH=CH2</td>
<td>8a/8b</td>
<td>67</td>
</tr>
<tr>
<td>22</td>
<td>4</td>
<td>LiHMDS</td>
<td>–50</td>
<td>CH2CH=CH2</td>
<td>8a/8b</td>
<td>67</td>
</tr>
<tr>
<td>23</td>
<td>4</td>
<td>LiHMDS/Mg(^{2+})</td>
<td>–78 → r.t.</td>
<td>CH2CH=CH2</td>
<td>8a/8b</td>
<td>20</td>
</tr>
</tbody>
</table>

\(^a\) Base was added at –78 °C, then bromide was added at the reported temperature.

\(^b\) Ratio determined by \(^1\)H NMR spectroscopy.

\(^c\) Ratio determined by HPLC.
tio 17:83 in favor of the 3S stereoisomer), were observed (Table 2, entry 2).

Changing the counterion from lithium to sodium affected both the yield, which increased to 81%, and the diastereoselectivity toward the 3S isomer 13b (Table 2, entry 3).

When KHMDS was used as the base, a high diastereoselectivity in favor of the 3S isomer 13b was observed, accompanied by only a moderate yield (Table 2, entry 4).

A dramatic effect both on the yield and on the stereoselectivity was observed when the enolate was generated with LiHMDS in the presence of a bicoordinating Lewis acid such as MgBr2·Et2O (Table 2, entry 5). The 3S isomer 13b was obtained in 72% yield and 9:91 diastereoisomeric ratio.

In contrast to what was observed for the 6,5-fused trans series, the addition of a Lewis acid did not reverse the stereochemistry. This behavior could be explained by postulating that the preferred conformation of the enolate was not affected by the presence of a Lewis acid or at least was the same with or without coordinating metals. The allylation of 9 gave the same results: the presence of MgBr2·Et2O enhanced the diastereoisomeric ratio although with a moderate drop in yield (Table 2, entries 6 and 7). In contrast, the benzylation of 10 afforded selectively the 3R isomer 15a in good yield and diastereoisomeric ratio. The only effect of the Lewis acid was to enhance the yield (Table 2, entries 8 and 9).

The stereochemical outcome of the alkylation reaction can be assigned, as in the case of the trans series, by invoking a pseudo-axial attack onto the lowest energy conformers obtained from ab initio calculation for the bicyclic intermediate enolates. The preferred conformations of the enolates derived from 9 and 10 feature a pseudo-chair conformation for the bicyclic ring (Figure 2). If pseudo-axial attack is hypothesized the products should be the 3S isomer 13b and 3R isomer 15a, respectively.

The pure isomer 13b was obtained by recrystallization from diethyl ether and its absolute configuration was assigned by X-ray structure analysis (Figure 3).13

The conformation of the fused five- and six-membered rings of isomer 13b was determined according to the Cremer and Pople puckering analysis.14 The conformation of the five-membered ring is very near an envelope with atom C7 as the flap [$q_2 = 0.404(2) \text{ Å}, \varphi_2 = 76.6(3)^\circ$, $q_3$ being the puckering amplitude and $\varphi_3$ the phase angle]. The six-membered ring adopts a conformation intermediate between envelope, with C5 as the flap, and half-chair, with C5 pointing up and C4 pointing down with respect to the mean plane of the ring [the puckering parameters in

**Table 2** Reaction Conditions for the Alkylation of Compounds 9 and 10

<table>
<thead>
<tr>
<th>Entry</th>
<th>Imine</th>
<th>Base</th>
<th>T (°C)ᵃ</th>
<th>R</th>
<th>Products</th>
<th>Yield (%)</th>
<th>Ratio a/b (3R/3S)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9</td>
<td>LiHMDS</td>
<td>–78→r.t.</td>
<td>CH2Ph</td>
<td>13a/13b</td>
<td>60</td>
<td>39:61</td>
</tr>
<tr>
<td>2</td>
<td>9</td>
<td>LiHMDS/DMPU</td>
<td>–78→r.t.</td>
<td>CH2Ph</td>
<td>13a/13b</td>
<td>69</td>
<td>17:83</td>
</tr>
<tr>
<td>3</td>
<td>9</td>
<td>NaHMDS</td>
<td>–78→r.t.</td>
<td>CH2Ph</td>
<td>13a/13b</td>
<td>81</td>
<td>23:77</td>
</tr>
<tr>
<td>4</td>
<td>9</td>
<td>KHMDS</td>
<td>–78→r.t.</td>
<td>CH2Ph</td>
<td>13a/13b</td>
<td>58</td>
<td>7:93</td>
</tr>
<tr>
<td>5</td>
<td>9</td>
<td>LiHMDS/Mg²⁺</td>
<td>–78→r.t.</td>
<td>CH2Ph</td>
<td>13a/13b</td>
<td>72</td>
<td>9:91</td>
</tr>
<tr>
<td>6</td>
<td>9</td>
<td>LiHMDS</td>
<td>–78→r.t.</td>
<td>CH2CH=CH2</td>
<td>14a/14b</td>
<td>63</td>
<td>10:90</td>
</tr>
<tr>
<td>7</td>
<td>9</td>
<td>LiHMDS/Mg²⁺</td>
<td>–78→r.t.</td>
<td>CH2CH=CH2</td>
<td>14a/14b</td>
<td>42</td>
<td>&lt;2:98</td>
</tr>
<tr>
<td>8</td>
<td>10</td>
<td>LiHMDS</td>
<td>–78→r.t.</td>
<td>CH2Ph</td>
<td>15a/15b</td>
<td>30</td>
<td>&gt;98:&lt;2</td>
</tr>
<tr>
<td>9</td>
<td>10</td>
<td>LiHMDS/Mg²⁺</td>
<td>–78→r.t.</td>
<td>CH2Ph</td>
<td>15a/15b</td>
<td>40</td>
<td>&gt;99:&lt;1</td>
</tr>
</tbody>
</table>

ᵃ Base was added at –78 °C, then bromide was added at the reported temperature.

ᵇ Ratio determined by ¹H NMR spectroscopy.
this case are $Q = 0.490(2)$ Å, $\phi = 43.4(1)^\circ$, $f = 225.0(3)^\circ$. The puckering analysis on the fused rings of the (3S,6S,9S)-diastereoisomer previously reported, which differs from 13b only for the configuration at C6, indicated an intermediate twisted-envelope conformation and an almost perfect envelope with C2 as the flap for the five- and six-membered rings, respectively [$q_2 = 0.297(4)$ Å, $\phi_2 = 242(1)^\circ$, $Q = 0.469(4)$ Å, $\phi = 65(1)^\circ$].

The conformational differences observed in the azabicyclo moiety of the two diastereoisomers, together with the different spatial disposition of the tert-butoxycarbonyl, benzyl, and benzylamino groups, can be ascribed to their different crystal packing.

On the basis of an absolute stereogenic center of the molecule, as shown in Figure 3, the X-ray structure of compound 13b clearly indicated that the benzyl group is cis to the tert-butoxycarbonyl group, which implied a 3S configuration.

In conclusion we have found a new versatile method for the functionalization of the C3 position of azabicycloalkanes based on a stereoselective alkylation of a Schiff base amide enolate. With this method it is possible to obtain the desired functionalized azabicycloalkane by changing the base and/or adding coordinating metals to the reaction mixture.

All chemicals and solvents were of reagent grade and were used without further purification. Solvents were dried by standard procedures and reactions requiring anhydrous conditions were performed under N$_2$ or Ar. Optical rotations were measured in a cell of 1 dm path length and 1 mL capacity on a Perkin-Elmer 241 polarimeter. $^1$H and $^{13}$C NMR spectra were recorded at 300 K on a Bruker AVANCE-400 or Bruker AC-300 or AC-200 spectrometer. Chemical shifts are expressed in ppm relative to TMS as internal standard.
MS were determined with a VG 7070 EQ-HF apparatus. TLC was carried out with precoated Merck F254 silica gel plates. Flash chromatography was carried out with Macherey-Nagel silica gel 60 (230–400 mesh). Elemental analyses were performed by the staff of the microanalytical laboratory of our department.

**Lactams 3, 4, 9, and 10; General Procedure**
A solution of NCbz-protected lactam (1.07 mmol) in MeOH (11 mL) containing 10% Pd/C (cat.) was stirred overnight under H2. The catalyst was then removed by filtration through a pad of celite and washed with MeOH. The filtrate was concentrated under reduced pressure. The crude was dissolved in anhyd CH2Cl2 (11 mL) containing 10% Pd/C (cat.) was stirred overnight under H2. The solution was filtered through a pad of celite and washed with CH2Cl2. The solvent was removed under reduced pressure. After 24 h at r.t. the mixture was filtered through a pad of celite and washed with CH2Cl2. The solvent was removed under reduced pressure. The crude was dissolved in anhyd CH2Cl2 (11 mL) and anhyd Et3N (299 mL) and distilled benzaldehyde (217 mL) was added and stirred for 3–5 h. H2O (2 mL) was added and the mixture was extracted with EtOAc (3×2 mL). The combined organic layers were dried over Na2SO4 and concentrated under reduced pressure. The crude was dissolved in MeOH (4 mL) and NaBH4 (2 mmol) was added in small portions. The mixture was stirred for 3–5 h. H2O (2 mL) was added and the mixture was extracted with EtOAc (7:3), and the crude was purified by flash chromatography (hexane–EtOAc, 7:3).

**Yield: 90% (2 steps); white solid.**

**1H NMR (200 MHz, CDCl3):** δ = 1.31 (s, 9 H, t-Bu), 1.70–2.27 (m, 10 H), 3.78 (m, 1 H, CHN), 3.97 (dd, J = 7.5, 7.5 Hz, 1 H, CHN=CHPh), 4.35 (m, 1 H, CH(COO-But)), 7.41 (m, 2 H, Ar), 7.37 (m, 5 H, Ar), 8.22 (s, 1 H, N=CHPh).

**13C NMR (50.3 MHz, CDCl3):** δ = 172.0, 167.2, 163.4, 136.4, 130.8, 129.2, 128.7, 128.5, 81.1, 69.3, 61.3, 58.6, 58.5, 35.1, 33.0, 32.7, 32.5, 28.2, 27.4, 27.1.

**FAB-MS:** m/z calcld for C20H27N2O3 [M + 1]+: 343.43; found: 343.
Anal. Calcld for C20H27N2O3: C, 70.77; H, 7.93; N, 7.85.

**Alkylation; General Procedure A**
To a solution of imine (0.2 mmol) in anhyd THF (2 mL) under an Ar atmosphere, cooled to −78 °C, base (0.3 mmol) was added and the temperature was adjusted according to Table 1. After 20 min alkyl bromide was added and the solution was stirred for 3–5 h. H2O (2 mL) was added and the mixture was extracted with EtOAc (3×2 mL). The combined organic layers were dried over Na2SO4 and concentrated under reduced pressure. The crude was dissolved in MeOH (4 mL) and NaBH4 (2 mmol) was added in small portions. After 15 min the solvent was evaporated under reduced pressure and the crude was purified by flash chromatography (hexane–EtOAc, 7:3).

**Yield: 94% (2 steps); white solid.**

**1H NMR (200 MHz, CDCl3):** δ = 1.42 (s, 9 H, t-Bu), 1.45–2.41 (m, 10 H), 4.03 (m, 1 H, CHN), 4.21 (m, 1 H, CHN=CHPh), 4.51 (m, 1 H, CH(COO-But)), 7.37 (m, 5 H, Ar), 8.22 (s, 1 H, N=CHPh).

**13C NMR (50.3 MHz, CDCl3):** δ = 172.1, 167.1, 162.3, 136.4, 130.8, 129.2, 128.7, 128.5, 81.1, 72.9, 61.3, 58.6, 58.5, 35.1, 33.0, 32.7, 32.5, 28.2, 27.4, 27.1.

**FAB-MS:** m/z calcld for C20H27N2O3 [M + 1]+: 357.21; found: 357.
Anal. Calcld for C20H27N2O3: C, 70.76; H, 7.92; N, 7.86. Found: C, 70.77; H, 7.93; N, 7.85.

**Alkylation; General Procedure B**
To a solution of imine (0.2 mmol) in anhyd THF (2 mL) and DMPU (5 mmol) under an Ar atmosphere, cooled to −78 °C, base (0.3 mmol) was added and the temperature was adjusted according to Table 1. After 20 min alkyl bromide was added and the solution was stirred for 3–5 h. H2O (2 mL) was added and the mixture was extracted with EtOAc (3×2 mL). The combined organic layers were dried over Na2SO4 and concentrated under reduced pressure. The crude was dissolved in MeOH (4 mL) and NaBH4 (2 mmol) was added in small portions. After 15 min the solvent was evaporated under reduced pressure and the crude was purified by flash chromatography.

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After 15 min the solvent was evaporated under reduced pressure and the crude was purified by flash chromatography (hexane–EtOAc, 7:3).

(3R,6S,9S)-1-Aza-2-oxo-3-benzylamino-3-benzyl-9-(tert-butoxycarbonyl)bicyclo[4.3.0]nonane (5a)

\[ [\alpha]_D^{19} = -107.1 (c = 1.05, \text{CHCl}_3). \]

1H NMR (300 MHz, CDCl3): \( \delta = 0.51 \text{ (m, 1 H), 1.03 \text{ (m, 1 H), 1.49 (s, 9 H, -Bu), 1.61–2.20 (m, 23 H), 2.81 \text{ (d, } J = 12.8 \text{ Hz, 1 H, PhCHH})}, 3.23 \text{ (d, } J = 12.8 \text{ Hz, 1 H, PhCH}_2\text{CH)}}] , 3.60 \text{ (m, 1 H, CHN)}, 3.74 \text{ (d, } J = 11.9 \text{ Hz, 1 H, PhCH(NH)}) , 3.88 \text{ (d, } J = 11.9 \text{ Hz, 1 H, PhCH(NH)}) , 4.41 \text{ (dd, } J = 8.6 \text{, 8.6 Hz, 1 H, CH(COO-CBu)}, 7.19–7.40 \text{ (m, 10 H, Ar))}.

FAB-MS: \( m/z \) calec for C\(_{23}\)H\(_{34}\)N\(_2\)O\(_3\): 397.57; found: 397.

Calc. For C\(_{23}\)H\(_{34}\)N\(_2\)O\(_3\): C, 72.36; H, 8.89; N, 7.29. Found: C, 72.24; H, 8.73; N, 7.36.

Anal. Calc. For C\(_{23}\)H\(_{34}\)N\(_2\)O\(_3\): C, 72.53; H, 8.88; N, 7.25. Found: C, 72.54; H, 8.87; N, 7.25.

(3R,6S,9S)-1-Aza-2-oxo-3-benzylamino-3-benzyl-9-(tert-butoxycarbonyl)bicyclo[4.3.0]nonane (5b)

Mp 104–106 °C; \([\alpha]_D^{19} = -37.0 (c = 1.05, \text{CHCl}_3)\).

1H NMR (300 MHz, CDCl3): \( \delta = 1.51 \text{ (s, 9 H, -Bu), 1.65–2.12 (m, 7 H), 2.26 (m, 1 H), 2.93 \text{ (d, } J = 13.1 \text{ Hz, 1 H, PhCHCH}_2\text{CH)}}] , 3.17 \text{ (d, } J = 12.0 \text{ Hz, 1 H, PhCHCH(NH)}) , 3.88 (d, J = 12.0 Hz, 1 H, PhCHCH(NH)), 4.41 (dd, J = 8.6, 8.6 Hz, 1 H, CH(COO-CBu)), 7.20–7.37 (m, 10 H, Ar).

FAB-MS: \( m/z \) calec for C\(_{24}\)H\(_{34}\)N\(_2\)O\(_3\): 399.57; found: 399.

Calc. For C\(_{24}\)H\(_{34}\)N\(_2\)O\(_3\): C, 72.33; H, 8.78; N, 7.44. Found: C, 72.45; H, 8.83; N, 7.46.

(3R,6S,9S)-1-Aza-2-oxo-3-benzylamino-3-allyl-9-(tert-butoxycarbonyl)bicyclo[4.3.0]nonane (6a)

\([\alpha]_D^{19} = -37.3 (c = 1.00, \text{CHCl}_3)\).

1H NMR (300 MHz, CDCl3): \( \delta = 1.47 \text{ (s, 9 H, -Bu), 1.50 (m, 1 H), 1.76 (m, 1 H), 1.88–2.19 (m, 3 H), 2.18 (m, 1 H), 2.26–2.43 (m, 3 H), 2.54 (m, 1 H), 3.61 (m, 1 H, CHN), 3.61 (d, J = 11.7 Hz, 1 H, PhCH(NH)) , 3.70 (d, J = 11.7 Hz, 1 H, PhCH(NH)H), 4.43 (dd, J = 8.6, 8.6 Hz, 1 H, CH(COO-CBu)), 5.11 (m, 2 H, CH=CH\(_2\)), 5.90 (m, 1 H, CH=CH\(_2\)), 7.20–7.37 (m, 5 H, Ar))

FAB-MS: \( m/z \) calec for C\(_{23}\)H\(_{33}\)N\(_2\)O\(_3\): 385.51; found: 385.

Calc. For C\(_{23}\)H\(_{33}\)N\(_2\)O\(_3\): C, 71.75; H, 8.73; N, 7.29. Found: C, 71.92; H, 8.93; N, 7.30.

(3R,6S,9S)-1-Aza-2-oxo-3-benzylamino-3-allyl-9-(tert-butoxycarbonyl)bicyclo[4.3.0]nonane (6b)

\([\alpha]_D^{19} = -54.0 (c = 1.00, \text{CHCl}_3)\).

1H NMR (300 MHz, CDCl3): \( \delta = 1.45 \text{ (s, 9 H, -Bu), 1.63–1.98 (m, 8 H), 2.12 (m, 1 H), 2.29 (m, 1 H), 2.49 (m, 1 H, CH(CH=CH)=CH)}] , 2.58 (m, 1 H, CH=CH(CH=CH)), 3.68 (d, J = 11.6 Hz, 1 H, PhCH(NH)-H), 3.73 (d, J = 11.6 Hz, 1 H, PhCH(NH)), 4.07 (m, 1 H, CHN), 4.53 (dd, J = 8.3, 3.8 Hz, 1 H, CH(COO-CBu)), 5.14 (m, 2 H, CH=CH\(_2\)), 5.88 (m, 1 H, CH=CH\(_2\)), 7.26–7.42 (m, 5 H, Ar).

Calc. For C\(_{24}\)H\(_{35}\)N\(_2\)O\(_3\): C, 72.48; H, 8.92; N, 7.31.

FAB-MS: \( m/z \) calec for C\(_{24}\)H\(_{35}\)N\(_2\)O\(_3\): 399.54; found: 399.

Calc. For C\(_{24}\)H\(_{35}\)N\(_2\)O\(_3\): C, 72.48; H, 8.92; N, 7.31. Found: C, 72.49; H, 8.93; N, 7.31.

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PhCH\(_2\)NH), 4.49 (dd, \(J = 8.3, 4.4\) Hz, 1 H, PhCOO-Bu), 4.79 (m, 1 H, CHN), 5.16 (m, 2 H, CH=CH\(_2\)), 5.86 (m, 1 H, CH=CH\(_2\)), 7.20–7.40 (m, 5 H, Ar).

\(^1^C\)NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 174.4, 171.4, 141.1, 134.5, 128.7, 128.3, 126.8, 118.7, 111.4, 80.7, 67.0, 62.8, 62.5, 58.5, 57.5, 47.1, 44.7, 40.3, 35.5, 33.1, 29.7, 28.0, 26.8, 22.7.

FAB-MS: \(m/z\) calcd for C\(_{34}\)H\(_{41}\)O\(_3\)N: [M + 1\(^+\)]: 545.29; found: 545.

Calcd: C, 74.74; H, 8.09; N, 6.42. Found: C, 74.78; H, 8.09; N, 6.25.

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References


