Supporting information

Multi-chelation Approach Towards Natural Product-like Skeletons: One-pot Access to Nitrogen-containing Tetracyclic Framework from AlaAla Dipeptide

Kasipandi Vellaisamy, John Victor Napoleon, Ramkumar Venkatachalam and Muraleedharan Kannoth Manheri *
Department of Chemistry, Indian Institute of Technology Madras, Chennai - 600 036 India.

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General Experimental Information:

Thin-layer chromatography (TLC) was performed on 0.25 mm silica gel plates (60 F254 grade) from Merck, and were analyzed using a 254 nm UV light. The chromatographic separation was carried out on 100-200 mesh silica gel. Melting points were obtained on electro-thermal apparatus and are uncorrected. $^1$H NMR and $^{13}$C NMR spectra were recorded on Bruker Avance 500 MHz instrument, and the chemical shifts are reported in parts per million (ppm) relative to tetramethylsilane, with $J$ values in Hertz. The splitting patterns in $^1$H NMR spectra are reported as follows: s = singlet; d = doublet; t = triplet; dd = doublet of doublet; bs = broad singlet; m = multiplet. $^{13}$C NMR data are reported with the solvent peak (CDCl$_3$ = 77.0) as the internal standard. A sealed tube containing [Bu$_4$N(B$_3$H$_8$)] in CDCl$_3$ ($\delta_B$, ppm, -30.07) was used as an external reference for the $^{11}$B NMR. High-resolution mass spectra (HRMS) were recorded on a Waters Q-Tof micro$^{TM}$ spectrometer with lock spray source. Infrared spectra were recorded using a Nicolet 6700 FT-IR spectrophotometer.

The intensity data collection during X-ray crystallographic analysis was carried out on a Bruker AXS (kappa apex II) diffractometer$^1$ equipped with graphite monochromated Mo (K$_\alpha$) radiation. The data were collected for $\theta$ up to 25$^\circ$ for Mo (K$_\alpha$) radiation. $\omega$ and $\phi$ scans were employed to collect the data. The frame width for $\omega$ was set to 0.5 deg for data collection.

$^1$ Bruker (2004). APEX-II and SAINT-Plus (Version 7.06a), Bruker AXS Inc., Madison, Wisconsin, USA.
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The frames were integrated and data were reduced for Lorentz and polarization correction using SAINT-Plus. The multi-scan absorption correction\(^2\) was applied to the data. All structures were solved using SIR-92 and refined using SHELXL-97.\(^3\) The molecular and packing diagrams were drawn using ORTEP-3\(^2\) and Mercury 1.4.2. The non-hydrogen atoms were refined with anisotropic displacement parameter. All hydrogen atoms could be located in the difference Fourier map. However, the hydrogen atoms bonded to carbons were fixed at chemically meaningful positions and were allowed to ride with parent atom during the refinement.

Procedure for the preparation of compound 2: To a stirred suspension of NaBH\(_4\) (0.33 g, 8.76 mmol) in dry THF (7 mL), taken in a two-neck RB flask fitted with an addition funnel and reflux condenser at 0°C under nitrogen atmosphere, was added a solution of BocAlaAlaOMe (0.40 g, 1.46 mmol) in dry THF (3 mL) in one portion, followed by a solution of iodine (1.1 g, 4.4 mmol) in dry THF (10 mL) drop-wise. The reaction mixture was allowed to warm to room temperature and after it became colorless, the mixture was refluxed for 48 h keeping the bath temperature at 90°C (We have noticed reduction in yields on keeping the oil bath temperature below 80°C. The higher temperature mentioned (90°C) is to ensure a vigorous reflux). It was then cooled to 0°C, and methanol (~ 5 mL) was added until a clear solution was obtained. The mixture was stirred for 30 minutes, solvents and other volatiles were removed under reduced pressure to get a white paste which was dissolved in 20% aq. KOH (10 mL) and extracted with dichloromethane (3 x 10 mL). The solvent was dried (Na\(_2\)SO\(_4\)), evaporated under reduced
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pressure and the residue chromatographed on silica gel column using ethyl acetate - hexane system in a gradient mode to get compound 2 as a white solid in 45% yield (110 mg) which was crystallized from ethyl acetate.

Analytical data of 2: Rf (EtOAc-hexane, 1:1), 0.45; Mp. 155-157°C; [α]D25 = +135.18° (c = 1, CHCl3); 1H NMR (500 MHz) CDCl3: δ 4.46 - 4.37 (m, 1H, α-C9H), 4.02 (b+s, 1H, C7Hb); 3.84 - 3.65 (m, 4H, C12H, C2H, C8Hb, C11Hb), 3.48 - 3.38 (m, 3H, C8Hb, C7Hb, C5H), 3.30 (dd, 1H, C11Ha, J = 8.5, 7.0, Hz), 2.79 (brs, -OH), 2.61 (dd, 1H, C4Hb, J = 11.75 Hz), 2.53-2.46 (m, 1H, C2Hb), 2.15 (s, 3H, N-CH3), 1.36 (d, 3H, 13-CH3, J = 6.5 Hz), 1.17 (d, 3H, 6-CH3, J = 5.5 Hz), 1.12 (d, 3H, 3-CH3, J = 6.5 Hz), 1.07 (d, 3H, 10-CH3, J = 6.5 Hz) ppm; 13C NMR (125 MHz) CDCl3: δ 161.8 (C=O), 69.7 (C(7)H2), 63.6 (C(8)H2), 63.0 (C(5)H), 56.0 (C(2)H), 52.3 (C(4)H2), 51.3 (C(12)H), 49.0 (C(9)H), 47.4 (C(11)H2), 34.2 (N-CH3), 19.9 (C(13)H3), 14.9 (C(10)H3), 10.2 (C(3)H3), 9.8 (C(6)H3) ppm; 11B NMR (128 MHz, CDCl3, 22°C, decoupled; reference Bu4NB3H8 set at -30.07 ppm): δ = 9.04, -10.5, -16.6 ppm; IR (neat): 3465, 2974, 2364, 2313, 1570, 1457, 1380, 1163, 1189, 1094, 993 cm⁻¹; HRMS (ESI) exact mass calcd. for C14H33B3N4O3 (M⁺·H) 337.2754, found 337.2757; Crystal Data: C14H33B3N4O3, Mr = 337.87, orthorhombic, P212121, a =10.7127(15) Å, b = 11.6890(16) Å, c =15.5054(17) Å, α=β=γ=90°, Volume = 1941.6(4) Å³, Z = 4, Dₐ = 1.156 mg/m³.
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$^1$H NMR spectrum of compound 1
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$^{13}$C NMR spectrum of compound 1
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$^{1}$H NMR spectrum of Compound 2

![NMR spectrum](image-url)
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$^1$H NMR spectrum of the compound 2 (expanded)
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$^{13}$C NMR spectrum of the compound 2

125 MHz; CDCl$_3$
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DEPT 135 NMR spectrum of the compound 2

NMR spectrum details:
- NMR spectrometers: 125 MHz; CDCl₃
- Acquisition parameters:
  - SCPS: 5 mm, FABRO BRL
  - Delay (τ): 10.25
  - TR: 10.00
  - Number of scans: 1
  - Other parameters:
    - δ values: 63.12, 62.88, 56.20, 56.21, 51.32, 51.34, 47.39, 34.11, 34.11, 28.03

Chemical shifts and assignments:
- C1: 63.12
- C2: 62.88
- C3: 56.20
- C4: 56.21
- C5: 51.32
- C6: 51.34
- C7: 47.39
- C8: 34.11
- C9: 34.11
- C10: 28.03

Other notes:
- Figure inset: Structure of compound 2 with labeled atoms.
- Additional parameters:
  - δ values: 0, 1.00, 1.40
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**COSY spectrum of compound 2**
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COSY spectrum of the compound 2 (expanded)
HSQC spectrum of the compound 2

500 MHz; CDCl₃
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HSQC spectrum of the compound 2 (expanded)
Supporting information

HMBC spectrum of the compound 2
Supporting information

HMBC spectrum of the compound 2 (expanded)
Supporting information

HMBC spectrum of the compound 2 continued …
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$^{11}$B (Proton decoupled) NMR spectrum of the compound 2

Bu$_4$N(B$_3$H$_8$) Reference peak

128 MHz; CDCl$_3$
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$^{11}$B (Proton coupled) NMR spectrum of the compound 2

Bu$_4$N (B$_3$H$_8$) Reference peak
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TGA profile of 2 in Nitrogen atmosphere
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TGA profile of 2 under aerial conditions

[Graph showing TGA profile]
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HRMS (ESI) showing $[M^+-H]$ peak
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HRMS (ESI) showing the \([\text{M+Na}]^+\) peak
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Table 1. Crystal data of compound 2

<table>
<thead>
<tr>
<th>Identification code</th>
<th>Compound (2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empirical formula</td>
<td>C_{14}H_{33}B_{3}N_{4}O_{3}</td>
</tr>
<tr>
<td>Formula weight</td>
<td>337.87</td>
</tr>
<tr>
<td>Temperature</td>
<td>298(2) K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>0.71073 Å</td>
</tr>
<tr>
<td>Crystal system, space group</td>
<td>Orthorhombic, P2(1)2(1)2(1)</td>
</tr>
</tbody>
</table>
| Unit cell dimensions | a = 10.7127(15) Å, alpha = 90 deg  
                           b = 11.6890(16) Å, beta=90deg  
                           c = 15.5054(17) Å, gamma = 90 deg |
| Volume              | 1941.6(4) Å³ |
| Z, Calculated density | 4, 1.156 Mg/m³ |
| Absorption coefficient | 0.078 mm⁻¹  |
| F(000)              | 736          |
| Crystal size        | 0.42 x 0.28 x 0.10 mm |
| Theta range for data collection | 2.58 to 28.15 deg |
| Limiting indices    | -9<=h<=14, -15<=k<=7, -14<=l<=16 |
| Reflections collected / unique | 8309/4201[R(int)=0.0301] |
| Completeness to theta | 25.00 94.7 % |
| Absorption correction | None                                   |
| Max. And min. transmission | 0.9923 and 0.9681 |
| Refinement method   | Full-Matrix least-squares on F²  |
| Data / restraints / parameters | 4201 / 0 / 227 |
| Goodness-of-fit on F² | 1.024            |
| Final R indices [I>2sigma (I)] | R1 = 0.0500, wR2 = 0.1143 |
| R indices (all data) | R1 = 0.0797, wR2 = 0.1285 |
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**Isolation and characterization of the intermediate A** (presented in Figure 4).

0.5g (1.8 mmol) of BocAlaAlaOMe was subjected to reduction using 0.4 g (10.8 mmol) of sodium borohydride and 0.9 g of iodine (3.5 mmol) according to the procedure discussed in page 3. The residue after work up was chromatographed on silica gel using ethyl acetate-hexanes solvent system in a gradient mode to get 32 mg (7%) of the intermediate A. The structure of this compound was confirmed by X-ray diffraction analysis of its crystals obtained from ethyl acetate solution.
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Table 2. Crystal data of intermediate A (CCDC number 778722).

<table>
<thead>
<tr>
<th>Identification code</th>
<th>Compound A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empirical formula</td>
<td>C_{11}H_{27}B_{2}N_{2}O_{3}</td>
</tr>
<tr>
<td>Formula weight</td>
<td>246.16</td>
</tr>
<tr>
<td>Temperature</td>
<td>298(2) K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>0.71073 Å</td>
</tr>
<tr>
<td>Crystal system, space group</td>
<td>Orthorhombic, P2(1)2(1)2(1)</td>
</tr>
</tbody>
</table>
| Unit cell dimensions| a = 10.3002(5) Å, alpha = 90 deg  
b = 22.7449(10) Å, beta = 90 deg  
c = 6.6083(2) Å, gamma = 90 deg |
| Volume              | 1548.17(11) Å³ |
| Z, Calculated density | 4, 1.056 Mg/m³³ |
| Absorption coefficient | 0.074 mm⁻¹ |
| F(000)              | 544        |
| Crystal size        | 0.28 x 0.25 x 0.17 mm |
| Theta range for data collection | 2.67 to 28.26 deg |
| Limiting indices    | -11<=h<=13, -29<=k<=30, -8<=l<=8 |
| Reflections collected / unique | 11064 / 3644 [R(int) = 0.0335] |
| Completeness to theta | 25.00 99.8 % |
| Absorption correction | None |
| Max. And min. transmission | 0.9875 and 0.9796 |
| Refinement method   | Full-Matrix least-squares on F² |
| Data / restraints / parameters | 3644 / 0 / 178 |
| Goodness-of-fit on F² | 1.029 |
| Final R indices [I>2sigma (I)] | R1 = 0.0657, wR2 = 0.1717 |
| R indices (all data) | R1 = 0.1280, wR2 = 0.2040 |