Synthesis of Borylated Hydrazino Acid Derivatives

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Abstract α-Boryl-α-hydrazinoacetic acid is a highly functionalized boron-containing building block that can be easily accessed from readily available α-borylacetaldehyde. The hydrazine motif can be converted into a variety of α-borylated azoles and diazines in a straightforward protocol. Furthermore, the carboxy group can be derivatized to afford novel organoboron compounds that should find applications in various cross-coupling transformations.

Key words hydrazinoboronates, aminoboronic acids, organoboron, borylated heterocycles, BMIADA

Organoboron compounds have found widespread applications in various fields of inquiry.1 The ability of boron to reversibly bind to heteroatom nucleophiles, combined with boric acid’s low toxicity (main metabolite of organoboron compounds, LD50 comparable to table salt) have allowed the identification of numerous boron-containing molecules as promising candidates in drug discovery.1,2 Among the many boron-containing scaffolds, borylated peptidomimetics derived from α-aminoboronic acids often display potent antitumor properties.3 As such, the synthesis of α-aminoboronics acids has been a subject of ongoing interest (Scheme 1).4

Compared to α-aminoboronic acids, α-hydrazinoboronic acids have received no attention despite the prevalence of hydrazine building blocks in organic chemistry.5 The hydrazine motif is frequently employed in the synthesis of heterocyclic scaffolds with biomedical applications.6 In addition to being versatile synthetic handles, incorporation of the hydrazine functional group in peptidic scaffolds results in aza-β-peptides, which can display new secondary structures when compared to the parental forms.7 As part of our ongoing efforts in the pursuit of unique boron-containing building blocks,8 we report the synthesis and utility of α-boryl-α-hydrazinoacetic acid 1.

Treatment of readily available α-borylacetaldehyde 2 with DBAD (di-tert-butyl azodicarboxylate) in the presence of catalytic amount of proline yielded α-boryl-α-hydrazinoacetaldehyde 3 with complete consumption of 2 (Scheme 2).9 No side products were generated based on 1H NMR

Scheme 1 Synthesis of α-aminoboronic acids: (a) Cu-catalyzed borylation of enantiopure sulfanyl imines. (b) Ugi 4CR reaction using α-boryl isocyanides with aldehydes, carboxylic acids, and ammonia. (c) Reductive amination of MIDA acyl boronates and potassium acyltrifluoroborates. (d) Rh-catalyzed amine-directed C(sp3)–H borylation. (e) Synthesis of α-boryl-α-hydrazinoacetic acid 1.
spectroscopy of the crude reaction mixture. Accordingly, we moved forward with the reaction by carrying out a Pinnick oxidation. To our delight, highly functionalized MIDA boronate 1 was isolated by filtration in 86% yield over two steps in a one-pot fashion.

**Scheme 2** Synthesis of MIDA boronate 1 via a proline-catalyzed α-amination of α-borylacetaldelyde 2 then subsequent Pinnick oxidation in one pot

With 1 in hand, we set out to explore the utility of the hydrazine moiety. Deprotection of the Boc (tert-butoxycarbonyl) group in a DCM/TFA mixture provided the free hydrazine salt in quantitative yield after 30 minutes without any signs of MIDA deprotection or protodeboronation. Upon evaporation of the solvent, reaction with 1,3-, or 1,4-electrophiles in MeCN yielded a series of N-heterocycle-substituted α-carboxy MIDA boronates 5 (Scheme 3). Reaction with acetylacetdehyde dimethyl acetal produced a 4:1 mixture of 1,5- and 1,3-substituted pyrazole 5a in quantitative yield. Condensation with acetylacetone and dibenzoylmethane gave 5b and 5c, respectively. However, the reaction to give 5c did not go to completion after 20 h, presumably due to reduced reactivity of dibenzoylmethane. Aryl keto-enamines reacted efficiently with 4 to form the corresponding 5-arylpyrazoles in high yields (5d–5f). Cyclization with arylated malondialdehydes successfully gave the corresponding 4-arylpyrazoles (5g and 5h). Pyrazolone 5i was generated when ethyl acetoacetate was used as the bis-electrophile. Similarly, methyl 2-formylbenzoate and 2-formylphenylboronic acid were suitable 1,4-electrophiles under these conditions and the reactions provided phthalazinone 5j and 1,2,3-diazaborinine 5k, respectively. Lastly, condensation with phthalic anhydride afforded a mixture of phthalazinedione 5l and N-aminophthalimide 5l’, which are separable by column chromatography.

We next turned our attention towards the derivatization of the carboxyl functional group (Scheme 4). Methylation of the carboxylic acid with TMSCHN gave the methyl ester in good yield (6a). Activation of the acid with HATU and subsequent reduction of the activated ester with NaBH₄ gave β-hydrazino alcohol 6b. Similarly, borylated exadi-azole 6c could be synthesized using a one-pot HATU-mediated coupling protocol adapted from our previous report. Activation of the carboxylic acid with DIC in the presence of 4-nitrobenzyl alcohol provided the corresponding 4-nitro-benzyl ester 6d in excellent yield. Additionally, redox-active ester 6e could be synthesized on a 1-g scale in good yield using N-hydroxyphthalimide as the nucleophile. Reaction with DPPA (diphenylphosphoryl azide) under mild heat provided triazolidine 6f via the Curtius rearrangement. This represents one of the few examples of a boronate that is attached to a carbon atom with the oxidation state of an aldehyde. Subsequent N-alkylation of 6f with 4-nitrobenzyl bromide gave 6g, the structure of which was confirmed by single crystal X-ray diffraction (Figure 1).

In conclusion, we have developed a straightforward synthesis of α-carboxy-α-hydrazino MIDA boronate 1 using a column-free protocol from readily available aldehyde 2. The highly functionalized building block was used to access a variety of boro-methylated heterocycles and carboxy derivatives. The resulting borylated compounds 5 and 6 have...
Miyaura cross-coupling and decarboxylative cross-coupling possess considerable potential in transition-metal-catalyzed Suzuki–Miyaura cross-coupling and decarboxylative cross-coupling to access value-added products.

All solvents and reagents were purchased from commercial sources and used as received unless otherwise stated. HPLC grade MeCN, hexane, and i-PrOH were purchased from MilliporeSigma and used as received. THF was distilled from NaN-benzophenone ketyl prior to use. Aaryl keto-enamines,12 malondialdehydes,13 and 2aza were synthesized according to literature procedures. Flash column chromatography was carried out using Silicycle 230–400 mesh silica gel. Thin-layer chromatography was performed on Merck Aluminum-backed TLC Silica gel 60 F254 and visualized using a UV lamp (254 nm) and curcumin stain. Reverse-phase chromatography was carried out using Biotage SNAP ultra C18 on a Teledyne-Isco Combiflash system.1H, 13C, and 19F NMR spectra were recorded on Bruker 400 MHz and 500 MHz spectrometers at 23 ºC unless otherwise stated.1H NMR chemical shifts are referenced to residual protonated solvent peak (MeCN-d3; δ = 1.94 ppm; DMSO-d6; δ = 2.50 ppm).13C NMR chemical shifts are referenced to the corresponding solvent peaks (MeCN-d3; δ = 118.2 ppm; DMSO-d6; δ = 39.5 ppm). Carbon atoms exhibiting significant line broadening brought about by boron substituents were not reported due to quadrupolar relaxation.13F NMR chemical shifts are referenced to an external standard of CFCl3 (δ = 0.0 ppm). HRMS were obtained on a VG 70-2505 (double focusing) mass spectrometer at 70 eV or on an AB/Sciex Qstar mass spectrometer with ESI or DART sources, MS/MS and accurate mass capabilities. Low-resolution mass spectra (ESI) were collected on an Agilent Technologies 1200 series HPLC paired to a 6130 Mass Spectrometer. FTIR analysis was carried out on a Bruker Alpha Platinum ATP spectrometer and peaks below 1500 cm–1 are not reported. Melting points were measured uncorrected utilizing a Mel-Temp capillary melting point apparatus.

α-Boryl-a-hydrazinoacetic Acid 1
To a stirred suspension of 2 (1.00 g, 5.03 mmol, 1 equiv) in MeCN (50 mL) were added di-tert-butyl azodicarboxylate (1.39 g, 6.03 mmol, 1.2 equiv) and l-proline (145 mg, 1.26 mmol, 25 mol%). The mixture was stirred at rt for 16 h. Cyclohexene (5.1 mL, 50.3 mmol, 10 equiv), NaH2PO4·H2O (6.94 g, 50.3 mmol, 10 equiv), NaClO2 (1.36 g, 15.1 mmol, 3 equiv), and water (30 mL) were subsequently added. The mixture was stirred at rt for 6 h. Upon completion of reaction as indicated by 1H NMR spectroscopy, the organic layer was removed from the biphasic mixture in vacuo. MeCN (10 mL) was added, then the mixture was cooled for 1 h in a 4 ºC fridge. The mixture was filtered, then the filter cake was washed with water (20 mL) and Et2O (50 mL) to afford 1 (1.93 g, 4.33 mmol, 86%) as a colorless solid; mp 207–210 ºC.

IR (neat): 3173, 2979, 1799, 1773, 1726, 1714, 1662, 1524 cm–1.
1H NMR (500 MHz, 333 K, DMSO-d6): δ = 8.12 (br s, 1 H), 4.37 (s, 1 H), 4.27 (d, J = 17.5 Hz, 1 H), 4.21 (d, J = 17.0 Hz, 1 H), 4.00 (d, J = 17.5 Hz, 1 H), 3.95 (d, J = 17.0 Hz, 1 H), 3.16 (s, 3 H), 1.43 (s, 9 H), 1.40 (s, 9 H).
13C NMR (126 MHz, 333 K, DMSO-d6): δ = 173.6, 168.0, 167.7, 80.7, 80.2, 62.7, 46.3, 27.7, 27.5.
19F NMR (160 MHz, 333 K, DMSO-d6): δ = 9.8.

α-Boryl-a-hydrazinoacetaldehyde 3
To a stirred suspension of 2 (0.400 g, 2.01 mmol, 1 equiv) in MeCN (10 mL) were added di-tert-butyl azodicarboxylate (0.555 g, 2.41 mmol, 1.2 equiv) and l-proline (58 mg, 0.50 mmol, 25 mol%). The mixture was stirred at rt for 16 h. The mixture was diluted with MeCN (100 mL) and loaded onto Celite. The volatiles were removed in vacuo, then
the residue was purified by normal-phase column chromatography (mixture hexanes/acetone) to afford 3 (0.656 g, 1.53 mmol, 76%) as a colorless solid; mp 120-122 °C.

IR (neat): 3274, 2932, 2861, 1772, 1717, 1685, 1500 cm⁻¹.

Hydrazine Condensation; General Procedure
To a 1-dram vial containing 1 (44.5 mg, 0.11 mmol, 1 equiv) was added DCM (0.5 mL) and TFA (0.5 mL). The mixture was stirred for 30 min at rt. To rt was removed in vacuo, then MeCN (1 mL) was added. The stirring solution was added the appropriate electrophile (1–1.1 equiv), then the mixture was stirred at rt or 50 °C for 16 h. The mixture was poured onto Celite, then the volatiles were removed in vacuo, and MeCN (1 mL) was added. The mixture was stirred at rt or 50 °C for 16 h. The mixture was washed with MeCN (1 mL) to afford the corresponding products upon removal of solvents. Alternatively, if the product precipitated from the mixture, then the mixture was filtered, and the filter cake was washed with MeCN (1 mL) to afford the corresponding products.

2-(5-Methyl-1H-pyrrozol-1-yl)-2-(MIDA-boryl)acetic Acid (5a)
The reaction was carried out according to the general procedure using acetylacetaldheyde dimethyl acetal (14.6 mL, 0.11 mmol, 1.1 equiv) at rt and purified by reversed-phase column chromatography to afford 5a (29.2 mg, 0.099 mmol, 99%) as a colorless solid; mp 176–180 °C (decomp.).


11B NMR (500 MHz, MeCN-d₃): δ = 7.80–7.78 (m, 2 H), 7.51–7.49 (m, 3 H), 7.44–7.42 (m, 4 H), 7.38–7.36 (m, 1 H), 6.77 (s, 1 H), 4.86 (s, 1 H), 4.21 (d, J = 17.0 Hz, 1 H), 4.09–3.99 (m, 3 H), 3.04 (s, 3 H).

IR (neat): 3374, 3146, 2982, 2262, 1748, 1607, 1511 cm⁻¹.

2-(3,5-Diphenyl-1H-pyrrozol-1-yl)-2-(MIDA-boryl)acetic Acid (5c)
The reaction was carried out according to the general procedure using 1,3-diphenylpropane-1,3-dione (14.5 μL, 0.11 mmol, 1 equiv) at 50 °C and purified by reversed-phase column chromatography to afford 5c (10.2 mg, 0.024 mmol, 24%) as a colorless solid; mp 208–213 °C.


13C NMR (126 MHz, MeCN-d₃): δ = 173.4, 169.1, 168.9, 147.7, 142.3, 105.8, 65.1, 65.0, 48.0, 13.4, 11.1.

11B NMR (128 MHz, MeCN-d₃): δ = 10.6.


2-(3,5-Dimethyl-1H-pyrrozol-1-yl)-2-(MIDA-boryl)acetic Acid (5b)
The reaction was carried out according to the general procedure using (E)-3-(dimethylamino)-1-(1H-pyrrozol-2-yl)-1-prop-2-en-1-one (18.4, 0.105 mmol, 1.05 equiv) at rt and purified by reversed-phase column chromatography to afford 5b (33.9 mg, 0.095 mmol, 95%) as a colorless solid; mp 165–168 °C.

IR (neat): 3274, 2932, 2861, 1772, 1717, 1557 cm⁻¹.

11B NMR (500 MHz, MeCN-d₃): δ = 7.97 (d, J = 2.0 Hz, 1 H), 7.49–7.46 (m, 3 H), 7.38–7.36 (m, 2 H), 6.36 (d, J = 1.5 Hz, 1 H), 4.86 (s, 1 H), 4.28 (d, J = 17.0 Hz, 1 H), 4.09–3.99 (m, 3 H), 3.04 (s, 3 H).

IR (neat): 3029, 2799, 2475, 1769, 1670, 1553 cm⁻¹.


13C NMR (126 MHz, MeCN-d₃): δ = 173.0, 169.0, 168.8, 146.1, 139.4, 131.3, 129.8, 129.8, 129.8, 107.1, 65.1, 64.9, 47.9.

11B NMR (128 MHz, MeCN-d₃): δ = 10.8.


2-(5-Phenyl-1H-pyrrozol-1-yl)-2-(MIDA-boryl)acetic Acid (5d)
The reaction was carried out according to the general procedure using (E)-3-(dimethylamino)-1-phenylprop-2-en-1-one (18.4, 0.105 mmol, 1.05 equiv) at rt and purified by reversed-phase column chromatography to afford 5d (33.9 mg, 0.095 mmol, 95%) as a colorless solid; mp 165–168 °C.

IR (neat): 3274, 2932, 2861, 1772, 1717, 1553 cm⁻¹.

11B NMR (500 MHz, MeCN-d₃): δ = 7.52 (d, J = 2.0 Hz, 1 H), 7.49–7.46 (m, 3 H), 7.38–7.36 (m, 2 H), 6.36 (d, J = 1.5 Hz, 1 H), 4.86 (s, 1 H), 4.28 (d, J = 17.0 Hz, 1 H), 4.09–3.99 (m, 3 H), 3.04 (s, 3 H).


2-(3,5-Dimethyl-1H-pyrrozol-1-yl)-2-(MIDA-boryl)acetic Acid (5e)
The reaction was carried out according to the general procedure using (E)-3-(dimethylamino)-1-(1H-pyrrozol-2-yl)-1-prop-2-en-1-one (18.1 mg, 0.11 mmol, 1.1 equiv) at rt and purified by reversed-phase column chromatography to afford 5e (33.9 mg, 0.098 mmol, 98%) as a brown solid; mp 170–175 °C (decomp.).

IR (neat): 3374, 3146, 2982, 2626, 1748, 1607, 1511 cm⁻¹.

11B NMR (500 MHz, MeCN-d₃): δ = 9.51 (br s), 7.47 (d, J = 2.0 Hz, 1 H), 6.90–6.89 (m, 1 H), 6.38 (d, J = 2.0 Hz, 1 H), 6.27–6.25 (m, 1 H), 6.24–6.23 (m, 1 H), 5.06 (s, 1 H), 4.29 (d, J = 16.5 Hz, 1 H), 4.10–4.01 (m, 3 H), 3.02 (s, 3 H).

2-[5-(Furan-2-yl)-1H-pyrazol-1-yl]-2-(MIDA-boryl)acetic Acid (5f)
The reaction was carried out according to the general procedure using (E)-3-(dimethylamino)-1-(furan-2-yl)prop-2-en-1-one (18.2 mg, 0.011 mmol, 1 equiv) at rt and purified by reversed-phase column chromatography to afford 5f (28.4 mg, 0.067 mmol, 67%) as a colorless solid; mp 158–161 °C.

IR (neat): 3127, 2969, 2541, 1909, 1770, 1736, 1639, 1575 cm⁻¹.
1H NMR (500 MHz, DMSO-d₆): δ = 5.36 (br s, 1 H), 4.66 (br s, 1 H), 4.44 (d, J = 17.0 Hz, 1 H), 4.27 (d, J = 16.5 Hz, 1 H), 4.16–4.11 (m, 2 H), 3.06 (s, 3 H), 2.10 (s, 3 H).
13C NMR (126 MHz, DMSO-d₆): δ = 172.8, 172.0, 168.8, 168.4, 158.3 (q, J = 36.6 Hz), 145.7, 115.5 (q, J = 292.8 Hz), 87.1, 63.7, 63.4, 47.1, 13.2.
19F NMR (376 MHz, DMSO-d₆): δ = –74.7.

2-(MIDA-Boryl)-2-(1-oxophthalazin-2(1H)-yl)acetic Acid (5j)
The reaction was carried out according to the general procedure using methyl 2-formylbenzoate (18.1 mg, 0.11 mmol, 1 equiv) at rt and purified by filtration to afford 5j (28.1 mg, 0.078 mmol, 78%) as a colorless solid; mp 235–236 °C (decomp.).

IR (neat): 3072, 3013, 2982, 1780, 1754, 1722, 1674, 1524 cm⁻¹.
1H NMR (400 MHz, DMSO-d₆): δ = 12.9 (s, 1 H), 8.45 (s, 1 H), 8.26 (dd, J = 7.8 Hz, 1 H), 7.97–7.96 (m, 2 H), 7.91–7.87 (m, 1 H), 5.39 (s, 1 H), 4.50 (d, J = 17.2 Hz, 1 H), 4.28 (d, J = 16.8 Hz, 1 H), 4.20–4.14 (m, 2 H), 3.13 (s, 3 H).
13C NMR (126 MHz, DMSO-d₆): δ = 172.7, 169.0, 168.8, 158.8, 137.2, 133.7, 132.1, 129.2, 126.8, 126.8, 125.9, 63.8, 63.5, 47.7.
19F NMR (376 MHz, DMSO-d₆): δ = –74.7.
HRMS (ESI): m/z [M – CF₃CO₂H₂]– calcd for C₁₄H₁₄B₂N₃O₇: 357.0888; found: 357.0891.

2-(1-Hydroxybenzeno[d][1,2,3]diazaborinin-2(1H)-yl)-2-(MIDA-boryl)acetic Acid-Trifluoroacetic Acid (5k)
The reaction was carried out according to the general procedure using 2-formylphenylboronic acid (15.0 mg, 0.1 mmol, 1 equiv) at rt and purified by filtration to afford 5k (23.2 mg, 0.049 mmol, 49%) as a colorless solid; mp >250 °C.

IR (neat): 3312, 2982, 1780, 1754, 1722, 1674, 1524 cm⁻¹.
1H NMR (500 MHz, DMSO-d₆): δ = 8.26 (d, J = 7.5 Hz, 1 H), 7.99 (s, 3 H), 7.72–7.71 (m, 2 H), 7.61–7.58 (m, 1 H), 4.84 (s, 1 H), 4.46 (d, J = 17.0 Hz, 1 H), 3.95 (d, J = 17.0 Hz, 1 H), 3.11 (s, 3 H).
13C NMR (126 MHz, DMSO-d₆): δ = 172.8, 172.0, 168.8, 168.4, 158.3 (q, J = 36.6 Hz), 145.7, 115.5 (q, J = 292.8 Hz), 87.1, 63.7, 63.4, 47.1, 13.2.
19F NMR (376 MHz, DMSO-d₆): δ = –74.7.
HRMS (ESI): m/z [M – CF₃CO₂H₂]– calcd for C₁₄H₁₄B₂N₃O₇·CF₃CO₂H: 356.1096; found: 356.1102.
NaBH₄ (11.3 mg, 0.3 mmol, 3 equiv) was added to the solution, then (45.6 mg, 0.12 mmol, 1.2 equiv) in MeCN (1 mL) was added. The mixture was stirred at rt for 15 min. After addition of MeOH (0.1 mL), the mixture was stirred for 20 h. The mixture was filtered then loaded onto Celite, and the volatiles were removed in vacuo. The residue was subjected to reverse-phase column chromatography to afford 5f (38.5 mg, 0.084 mmol, 84%) as a colorless solid; mp 115–117 °C.

IR (neat): 3411, 2981, 2962, 2906, 1768, 1705 cm⁻¹.
1H NMR (500 MHz, MeCN-d₃): δ = 8.18–8.14 (m, 1 H), 7.96–7.95 (m, 1 H), 7.87–7.85 (m, 2 H), 5.57 (s, 1 H), 4.26 (d, J = 17.0 Hz, 1 H), 4.12 (d, J = 17.5 Hz, 1 H), 3.98 (d, J = 17.6 Hz, 1 H), 3.96 (d, J = 17.5 Hz, 1 H), 3.47 (s, 1 H).
13C NMR (126 MHz, MeCN-d₃): δ = 173.5, 169.1, 169.0, 159.6, 150.4, 134.2, 133.5, 127.9, 125.2, 125.1, 65.1, 64.5, 48.6.
11B NMR (128 MHz, MeCN-d₃): δ = 10.9.

Di-tert-butyl [(MIDA-boryl)[5-(phenylamino)-1,3,4-oxadiazol-2-yl]methyl]hydrazine-1,2-dicarboxylate (6c)
To a stirred suspension of 1 (44.5 mg, 0.1 mmol, 1 equiv) and HATU (41.8 mg, 0.11 mmol, 1.1 equiv) in MeCN (1 mL) was added DIPEA (52.3 μL, 0.3 mmol, 3 equiv). The mixture was stirred at rt for 15 min. N-Phenylhydrazinecarboxothioamide (18.4 mg, 0.11 mmol, 1.1 equiv) was added to the solution, then the mixture was stirred at rt for 30 min. TSCI (41.9 mg, 0.22 mmol, 2 equiv) was added, then the mixture was stirred at rt for 4 h. After 4 h, another aliquot of TSCI (19.1 mg, 0.1 mmol, 1 equiv) and DIPEA (52.3 μL, 0.3 mmol, 3 equiv) were added, then the mixture was stirred at rt for 10 h. The mixture was loaded onto Celite, then the volatiles were removed in vacuo. The residue was subjected to reverse-phase column chromatography to afford 6c (38.2 mg, 0.068 mmol, 68%) as a colorless solid; mp 157–158 °C.

IR (neat): 3328, 2982, 2936, 1778, 1740, 1700, 1515 cm⁻¹.
1H NMR (500 MHz, MeCN-d₃): δ = 7.92–7.88 (m, 4 H), 7.17–7.02 (br, 1 H), 5.10 (br s, 1 H), 4.14–3.99 (m, 4 H), 3.28 (s, 3 H), 1.44 (overlapped, 18 H).
13C NMR (126 MHz, MeCN-d₃): δ = 165.8, 168.4, 163.1, 136.3, 129.6, 124.9, 82.1, 65.0, 64.3, 47.9, 28.4, 28.1.
11B NMR (128 MHz, MeCN-d₃): δ = 10.3.
Di-tert-butyl 1-[(1,3-Dioxoisooisinol-2-yl)oxy]-1-(MIDA-boryl)-2-oxoethyl]hydrazine-1,2-dicarboxylate (6e)

To a stirred suspension of 1 (1.2 g, 2.70 mmol, 1 equiv), N-hydroxypthalimide (484 mg, 2.97 mmol, 1.1 equiv), and DMAP (33 mg, 0.27 mmol, 10 mol%) in DCM (20 mL) and MeCN (7 mL) was added DIC (0.464 mL, 2.97 mmol, 1.1 equiv). The mixture was stirred at rt for 14 h. The mixture was filtered then loaded onto Celite, then the volatiles were removed in vacuo. The residue was subjected to normal-phase column chromatography to afford 6e (1.02 g, 1.73 mmol, 64%) as a colorless solid; mp 155–158 °C.

IR (neat): 3328, 2982, 2936, 1778, 1740, 1700, 1515 cm⁻¹.

1H NMR (500 MHz, MeCN-d₃): δ = 7.92–7.88 (m, 4 H), 7.17–7.02 (br, 1 H), 5.10 (br s, 1 H), 4.14–3.99 (m, 4 H), 3.28 (s, 3 H), 1.44 (overlapped, 18 H).

13C NMR (126 MHz, MeCN-d₃): δ = 166.8, 168.4, 163.1, 136.3, 129.6, 124.9, 82.1, 65.0, 64.3, 47.9, 28.4, 28.1.

11B NMR (128 MHz, DMSO-d₆): δ = 10.3.


Di-tert-butyl 3-(MIDA-boryl)-5-oxo-1,2,4-triazolidine-1,2-dicarboxylate (6f)

To a stirred suspension of 2 (2.4 g, 5.39 mmol, 1 equiv) in MeCN (36 mL) at rt was added DIPEA (2.07 mL, 11.86 mmol, 2.2 equiv) and DPPA (1.28 mL, 5.93 mmol, 1.1 equiv). The mixture was stirred at 50 °C for 1.5 h. The mixture was cooled and loaded onto Celite, then the volatiles were removed in vacuo. The residue was subjected to normal-phase column chromatography to afford 6f (1.53 g, 3.46 mmol, 64%) as a colorless solid; mp 172–177 °C (decomp.).

IR (neat): 3328, 2982, 2936, 1778, 1740, 1700, 1515 cm⁻¹.

1H NMR (500 MHz, MeCN-d₃): δ = 6.16 (br s, 1 H), 5.05 (s, 1 H), 4.07–4.03 (m, 2 H), 3.94–3.88 (m, 2 H), 3.07 (s, 3 H), 1.47 (s, 9 H), 1.45 (s, 9 H).

13C NMR (126 MHz, MeCN-d₃): δ = 168.7, 167.9, 158.8, 153.9, 84.6, 83.7, 63.7, 63.4, 47.1, 28.2, 28.1.

11B NMR (128 MHz, MeCN-d₃): δ = 8.9.


Di-tert-butyl 3-(MIDA-boryl)-4-(4-nitrobenzyl)-5-oxo-1,2,4-triazolidine-1,2-dicarboxylate (6g)

To a stirred suspension of 6f (100 mg, 0.23 mmol, 1 equiv), K₂CO₃ (63.6 mg, 0.46 mmol, 2 equiv), and TBAB (7.3 mg, 0.023 mmol, 10 mol%) in DCM (20 mL) and MeCN (7 mL) was added K₂CO₃ (1.53 g, 3.46 mmol, 64%) using chiral HPLC. The Taylor lab (University of Toronto) is thanked for assistance with e.r. determination of 6d using chiral HPLC. The Taylor lab (University of Toronto) is thanked for FTIR instrument accommodation. Members of the Yudin lab are thanked for valuable discussions.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0040-1706046.

Conflict of Interest

The authors declare no conflict of interest.

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References


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(10) Based on separation by HPLC on a chiral stationary phase column (see Supporting Information), the e.r. of 6d, and thus 1 by correlation, was determined to be 60:40. Due to the almost racemic nature of 1, e.r. determination of derivatives 5 and 6 were not measured.

