A Method for the Deprotection of Alkylpinacolyl Boronate Esters

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S Supporting Information

ABSTRACT: A two-step procedure for deprotection of alkylpinacolyl boronate esters via transesterification with diethanolamine followed by hydrolysis was successfully developed with the advantages of tolerance to various functional groups, short reaction time, and ease of product isolation.



Boronic acids are important in organic synthesis because of their versatility as synthetic intermediates in the preparation of complex molecules. Their utility is exemplified by the powerful carbon–carbon bond-forming Suzuki–Miyaura coupling reaction.^{1,2} As inhibitors of serine proteases, boronic acids inhibit therapeutically relevant proteases including chymotrypsin, thrombin, dipeptidyl peptidase, HCV NS3 protease, and the proteasome.³ Indeed, the first boron-containing drug, bortezomib (Velcade), was approved by the FDA for the treatment of multiple myeloma and mantle cell lymphoma. Thus, methods for synthesizing boronic acids are vital in harnessing their full potential in a variety of applications.

Introduction of the boronyl moiety has been a subject of intense investigation. Traditionally, arylboronic acids can be obtained from electrophilic borate trapping of arylmetal intermediates from aryl halides,⁴ transmetalation of arylsilanes and stannanes,⁵ transition-metal-catalyzed coupling between aryl halides/triflates and diboron reagents,⁶ and direct boration by transition-metal-catalyzed aromatic C-H activation.^{7,8} Some boronic acids are unstable and incompatible to reaction conditions during functional group transformations; therefore, they are converted to air- and chromatography-stable boronate esters using diols such as pinanediol,⁹ cathecol,^{10,11} neopentyl glycol,^{12–16} and pinacol.^{17,18} Although these groups are usually benign to various reaction conditions, their removal has been troublesome and unpredictable.¹⁹ Recently, trifluoroborate,²⁰ *N*-methylimi-nodiacetic acid,^{21–23} and 1,8-diaminonaphthalene^{24,25} units were introduced as alternative protecting groups for boronic acids. Organotrifluoroborate salts undergo hydrolysis in the presence of silica gel to afford the corresponding boronic acids,²⁶ and more recently, a direct route to arylboronic acids was reported.27

Several deprotection methods for the removal of cyclic boronate esters are available. These include oxidative cleavage with sodium periodate,²⁸ biphasic transesterification with other boronic acids,^{28,29} transborylation with boron trichloride,^{30–32} and acidic hydrolysis.^{33,34} The yield and purity of these deprotection procedures vary greatly, notwithstanding issues that can arise from functional group incompatibilities and purification problems.





Alternatively, a solid-phase process that utilizes polystyrene—boronic acid has been developed for arylpinacolyl boronic esters.³⁵ However, this method requires acidic conditions, is time-consuming, and relies on the commercial availability of the resin. Recently, Hutton and co-workers³⁶ reported a two-step deprotection of the pinacol group via fluorinated intermediates³⁷ that is followed by trimethylsilyl chloride³⁸ or lithium hydroxide.

In the course of our work on the development of N-terminal peptidic boronic acids as protease inhibitors,³⁹ we were faced with the difficulty of removing the pinacolyl group during the initial phase of our study. The boronyl moiety in all of these cases was directly attached to alkyl groups. For example, when β -boronopinacolyl- β -phenyl benzyl ester **1e** was subjected to various deprotection conditions, either the starting material decomposed or no reaction occurred, and thus β -boronic acid **3e** was not obtained (Scheme 1).

In order to circumvent this issue, we investigated a transesterification procedure with diethanolamine (DEA) to form an sp³hybridized boron \cdot DEA adduct, which is then hydrolyzed to yield a boronic acid derivative. Indeed, a few examples of pinacol deprotection with DEA have been reported, but most of these are arylboronic esters.^{40–42} To date, only two examples of successful alkylpinacolyl boronate ester deprotection involving transesterification and hydrolysis to produce boron-containing amino acid analogues have been disclosed.^{43,44} In some cases, an acidic resin, long reaction time, or distillation was necessary to effectively provide the boronic acid moiety. Because there has not been a

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Scheme 2. Two-Step Protocol for the Boronic Ester Deprotection



comprehensive investigation of the boryl pinacolate deprotection with DEA, we explored the generality of a two-step protocol in the deprotection of alkylpinacolyl boronate esters. Herein, we report a simple and efficient deprotection method of pinacolyl boronate esters.

We initially employed an arylboronic ester as our test case (Scheme 2). Treatment of pinacolylphenylboronic ester with DEA in ether afforded the DEA boronate product, which was filtered and subsequently treated with 0.1 M HCl for 20 min to provide phenylboronic acid in 99% yield. Having established the deprotection procedure, we investigated whether a one-pot deprotection method was possible with pinacolyl boronate ester substrates.⁴⁵ However, none of these studies (changing solvents, biphasic solutions, sequential addition of reagents, etc.) was successful. Thus, we elected to pursue the two-step transesterification/hydrolysis using a variety of pinacolyl- β -alkylboronic esters. As shown in Table 1, transesterification of the pinacol group with DEA efficiently proceeded in up to 97% isolated yield. It should be noted that not only did this reaction occur in a short amount of time (<30 min) but the purification was a simple filtration as the DEA boronate product precipitated in the ethereal solution. For example, unhindered substrates containing benzyl or methyl esters provided compounds 2a,b in good yields (entries 1 and 2). Introduction of substituents on the β -position with a phenyl or methyl group was also effective (entries 3-7). In addition, cyclic and acyclic ketones as well as nitriles underwent the transesterification smoothly (entries 8-11). All the isolated compounds 2a-l were white solids, stable to atmospheric conditions, and had long shelf lives. These compounds were characterized by ¹H, ¹³C, and ¹¹B NMR and high-resolution mass spectroscopy. Introduction of DEA produced desirable effects: the formation of a "boron-ate" species that is stable to oxidation and an adduct that is insoluble in ether. sp³-hybridized boron complexes are reported to be stable and resistant to air oxidation. 20,22 To further confirm the tetracoordination on boron, the single-crystal X-ray diffraction data for 2b was solved. As shown in Figure 1, boron adopts a tetrahedral geometry similar to what is observed in aryl. DEA boronates.

With the diethanolamine derivatives in hand, hydrolysis to the corresponding boronic acids was performed using a biphasic solution of 0.1 M HCl and ether. As expected, the boronic acid products were readily formed within minutes. For example, esters **3a,b**, amides **3f,g**, ketone **3i**, and nitrile **3j** were isolated as white solids in moderate to excellent yields (Table 1). However, in some cases, we experienced difficulty in isolating the desired alkylboronic acids. This was not surprising as some boronic acids are known to be unstable, undergoing facile decomposition in polar protic media via protodeboronation, oxidation, and/or polymerization.^{46–49} To test whether boronic acids were formed but decomposed during the reaction and/or workup, the DEA boronates were subjected to a biphasic solution of 0.1 M HCl and hexanes in the presence of 2 equiv of pinacol. We hypothesized that DEA boronates **2** undergo rapid hydrolysis



NOTE

Figure 1. X-ray crystal structure of 2b.

Scheme 3. Rapid Hydrolysis and Subsequent Trapping of 2



under acidic aqueous conditions as previously observed, and the unstable alkylboronic acids 3 are subsequently trapped as the boron pinacolyl esters 1 (Scheme 3). Indeed, when the in situ hydrolysis-trapping protocol was performed, the pinacol boronate esters were achieved in excellent yields (Table 1).

In conclusion, a two-step deprotection protocol for alkyl pinacolyl boronic esters via DEA-protected boronates was successfully developed with the advantages of tolerance to various functional groups, short reaction time, and ease of product isolation. Moderate to excellent yields were achieved for stable boronic acid products.

EXPERIMENTAL SECTION

General Procedure for the Synthesis of DEA-Protected Boronic Esters 2a–l. To a solution of pinacolyl boronic ester 1 (1.7 mmol) in ether was added diethanolamine (0.199 g, 1.9 mmol). After a few minutes, a white precipitate formed, and the reaction was allowed to continue until the starting material was completely consumed as monitored by TLC (\sim 30 min). The precipitate was then filtered, washed with ether, and dried to afford the desired product 2.

8-(3-(Benzyloxy)-3-oxopropyl)hexahydro-1,3,2-oxazaborolo-[2,3-*b***]-1,3,2-oxazaborol-4-ium-8-uide (2a):** white solid (0.305 g, 85% yield); mp 159.7–161.6 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.43–7.27 (m, 5H), 6.16 (s, 1H), 5.08 (s, 2H), 3.95 (m, 2H), 3.81 (m, 2H), 3.15–3.00 (m, 2H), 2.76–2.65 (m, 2H), 2.60–2.48 (m, 2H), 0.81–0.56 (m, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 179.3, 136.1, 128.7, 128.3, 128.0, 66.3, 63.3, 51.3, 29.8; the signal for the carbon directly attached to boron was not observed due to quadrupolar relaxation; ¹¹B NMR (160 MHz, CDCl₃) δ 11.26; HRMS (ESI+) calcd for C₁₄H₂₁BO₄ [M + H]⁺ 278.1558, found 278.1532.

8-(3-Methoxy-3-oxopropyl)hexahydro-1,3,2-oxazaborolo-[**2,3-***b*]-**1,3,2-oxazaborol-4-ium-8-uide (2b):** white solid; 72% yield; mp 147.3–148.4 °C; ¹H NMR (500 MHz, CD₃Cl) δ 6.39 (s, 1H), 4.00 (td, *J* = 5.3, 9.6, 2H), 3.92–3.81 (m, 2H), 3.65 (s, 3H), 3.26–3.14 (m, 2H), 2.86–2.73 (m, 2H), 2.53–2.45 (m, 2H), 0.77–0.60 (m, 2H); ¹³C NMR (125 MHz, CD₃Cl) δ 180.1, 63.3, 51.71, 51.3, 29.4; ¹¹B NMR (160 MHz, CD₃Cl) δ 11.25; HRMS (ESI+) calcd for C₈H₁₇BNO₄ [M + H]⁺ 202.1245, found 202.1243.

8-(3-Methoxy-3-oxo-1-phenylpropyl)hexahydro-1,3,2-oxazaborolo[2,3-b]-1,3,2-oxazaborol-4-ium-8-uide (2c): white solid;

				EWG_0.1M		
		12-4	ether, rt	2a-k	о́н 3а-к	
		I a-K	purified	by filtration		
entry		substrate	2	% yield of 2^{b}	3	% yield of 3^{b}
1	1a	pinB	⊕N [×] B [©] OBn	85	HO _B OBn OH	95
2	1b	pinB OCH3	⊕N-B,© H-N-COCH3	72	HO HO HO HO HO	90
3	1c	pinB OCH ₃	Ph O Ph O Ph O O Ph O OCH_3 $H^{-}N^{-B} O$	88	HO HO B OH	92 ^{<i>c</i>}
4	1d	Ph O pinB O ^t Bu	⊕ N ⁻ B,⊖ H 0'Bu	75	HO HO HO HO HO H	96 ^c
5	1e	Ph O pinB OBn	$ \begin{array}{c} Ph & O \\ \swarrow & \downarrow \\ \oplus & N \\ H \end{array} \\ \begin{array}{c} O \\ \oplus \\ O \\ \end{array} \\ O \\ O$	84	HO _B OH	90 ^c
6	1f	pinB NHBn	$(\mathbf{H}_{3}) (\mathbf{H}_{3}) (\mathbf{H}_{3}$	65	HO, B HO, B OH	98
7	1g	pinB NHBn	Ph O O H N-B O H O NHBn	68	HO, Ph O HO, NHBn OH	69 ^c
8	1h	pinB		79	HO HO ^B O	79 ^c
9	1i	pinB Ph O	$ \begin{array}{c} Ph & O \\ O & H \\ H \\ H \\ H \\ O \\ \end{array} $	80	HO. B HO. B OH	82
10	1j	pinB	⊕N ^{−B} ⊙ H [−] O	76	HO _N B OH	31
11	1k	Ph pinB CN	O Ph CN B O CN H CN	97	HO _B CN	89 ^c

Table 1. Substrate Scope of the Two-Step Transesterification/Hydrolysis of Pinacolyl Boronate Esters^a

^{*a*} Each reaction was performed at least twice. Conditions: 1 (1 equiv), DEA (1.1 equiv), ether, rt, \sim 30 min followed by 0.1 M HCl (20 min). ^{*b*} Isolated yield. ^{*c*} Product was isolated as the pinacol ester.

88% yield; mp 188.7–189.9 °C; ¹H NMR (500 MHz, CD₃Cl) δ 7.29–6.98 (m, 5H), 5.65 (s, 1H), 4.01–3.88 (m, 2H), 3.87–3.78 (m, 2H), 3.62 (s, 3H), 3.12–3.01 (m, 1H), 3.00–2.89 (m, 2H), 2.76–2.64 (m, 3H), 2.32 (dd, *J* = 5.5, 8.1 Hz, 1H); ¹³C NMR (125 MHz, CD₃Cl) δ 177.9, 147.34, 128.2, 127.8, 124.5, 63.4, 63.2, 51.7, 51.5, 51.4, 37.0; ¹¹B NMR (160 MHz, CD₃Cl) δ 11.25; HRMS (ESI+) calcd for C₁₄H₂₁BNO₄ [M + H]⁺ 278.1558, found 278.1543.

8-(3-*tert*-Butoxy-3-oxo-1-phenylpropyl)hexahydro-1,3, 2-oxazaborolo[2,3-*b*]-1,3,2-oxazaborol-4-ium-8-uide (2d): white solid; 75% yield; mp 186.5–187.7 °C; ¹H NMR (500 MHz, CD₃Cl) δ 6.01 (s, 1H), 4.03–3.91 (m, 2H), 3.89–3.81 (m, 2H), 3.22–3.11 (m, 1H), 3.02–2.94 (m, 1H), 2.94–2.84 (m, 1H), 2.79–2.68 (m, 2H), 2.61 (dd, *J* = 4.8, 17.2 Hz, 1H), 2.27 (dd, *J* = 4.6, 8.9 Hz, 1H), 1.39 (s, 9H). ¹³C NMR (125 MHz, CD₃Cl) δ 155.7, 131.8, 128.0, 127.8, 124.2, 80.3, 77.3, 77.0, 76.7, 63.4, 63.2, 51.3, 51.20, 38.5, 28.0. ¹¹B NMR (160 MHz, CD₃Cl) δ 10.38. HRMS (ESI+) Calculated for C₁₇H₂₇BNO₄ [M+H]⁺: 320.2028, found: 320.2006.

8-(3-Oxo-3-phenoxy-1-phenylpropyl)hexahydro-1,3,2-oxazaborolo[2,3-*b***]-1,3,2-oxazaborol-4-ium-8-uide (2e):** white solid; 84% yield; mp 173.9–174.8 °C; ¹H NMR (400 MHz, CD₃CN) δ 7.41–6.99 (m, 9H), 4.96 (s, 3H), 3.82–3.70 (m, 2H), 3.67–3.49 (m, 2H), 3.01–2.85 (m, 1H), 2.82–2.60 (m, 6H), 2.34 (dd, J = 5.8, 9.8 Hz, 1H); 13 C NMR (100 MHz, CD₃CN) δ 174.7, 128.3, 128.0, 127.7, 127.6, 124.0, 117.3, 105.0, 65.2, 62.4, 51.2, 51.0, 36.7; 11 B NMR (160 MHz, CD₃Cl) δ 10.86; HRMS (ESI+) calcd for C₂₀H₂₅BNO₄ [M + H]⁺ 354.1871, found 354.1878.

8-(4-(Benzylamino)-4-oxobutan-2-yl)hexahydro-1,3,2-oxazaborolo[2,3-*b***]-1,3,2-oxazaborol-4-ium-8-uide (2f):** white solid; 65% yield; mp 127.5–128.6 °C; ¹H NMR (500 MHz, CD₃Cl) δ 7.77 (s, 1H), 7.41–7.10 (m, 5H), 6.00 (s, 1H), 4.39 (d, *J* = 5.7 Hz, 2H), 4.04–3.77 (m, 4H), 3.35–3.01 (m, 2H), 2.82–2.68 (m, 2H), 2.49–2.10 (m, 2H), 0.99 (d, *J* = 6.1 Hz, 3H), 0.94 (dd, *J* = 9.1, 17.7 Hz, 1H); ¹³C NMR (125 MHz, CD₃Cl) δ 177.3, 138.0, 128.8, 127.6, 127.6, 63.5, 63.4, 51.5, 51.3, 43.7, 40.8, 17.3; ¹¹B NMR (160 MHz, CD₃Cl) δ 11.37; HRMS (ESI+) calcd for C₁₅H₂₄BN₂O₃ [M + H]⁺ 291.1874, found 291.1890.

8-(3-(Benzylamino)-3-oxo-1-phenylpropyl)hexahydro-1,3, 2-oxazaborolo[2,3-*b*]-1,3,2-oxazaborol-4-ium-8-uide (2g): white solid; 68% yield; mp 197.3–198.2 °C; ¹H NMR (500 MHz, CD₃Cl) δ 7.34–7.19 (m, 10H), 7.08–7.01 (m, 1H), 6.04 (s, 1H), 4.39 (d, *J* = 5.7 Hz, 2H), 4.02–3.76 (m, 4H), 3.33–3.19 (m, 1H), 3.10–2.62 (m, 2H), 2.53–2.19 (m, 2H); ¹³C NMR (125 MHz, CD₃Cl) δ 176.7, 148.1, 137.9, 128.8, 128.2, 127.9, 127.6, 124.4, 63.6, 63.5, 51.4, 43.8, 40.2; ¹¹B NMR (160 MHz, CD₃Cl) δ 11.03; HRMS (ESI+) calcd for C₂₀H₂₆BN₂O₃ [M + H]⁺ 353.2031, found 353.2034.

8-(3-Oxocyclopentyl)hexahydro-1,3,2-oxazaborolo[2,3-*b*]-1, 3,2-oxazaborol-4-ium-8-uide (2h): white solid; 79% yield; mp 201.4–202.1 °C; ¹H NMR (500 MHz, CD₃CN) δ 5.13 (s, 1H), 3.88–3.77 (m, 3H), 3.73–3.63 (m, 3H), 3.16–3.03 (m, 3H), 2.82– 2.73 (m, 3H), 2.13–2.07 (m, 1H), 2.06–1.97 (m, 2H), 1.92–1.77 (m, 3H), 1.67–1.55 (m, 1H), 1.24–1.11 (m, 1H); ¹³C NMR (125 MHz, CD₃Cl) δ 171.2, 63.4, 63.3, 52.3, 42.2, 39.9, 31.1, 26.2; ¹¹B NMR (160 MHz, CD₃Cl) δ 11.56; HRMS (ESI+) calcd for C₉H₁₇BNO₃ [M + H]⁺ 198.1296, found 198.1308.

8-(3-Oxo-1,3-diphenylpropyl)hexahydro-1,3,2-oxazaborolo-[**2,3-***b*]**-1,3,2-oxazaborol-4-ium-8-uide (2i):** white solid; 72% yield; mp 170.0–171.4 °C; ¹H NMR (400 MHz, CD₃CN) δ 7.98–6.96 (m, 8H), 3.87–3.71 (m, 2H), 3.67–3.52 (m, 2H), 3.46–3.28 (m, 2H), 3.03–2.89 (m, 1H), 2.88–2.74 (m, 1H), 2.75–2.64 (m, 2H), 2.56–2.45 (m, 1H); ¹³C NMR (125 MHz, CD₃Cl) δ 199.4, 148.0, 137.2, 133.3, 128.6, 128.3, 128.1, 124.5, 63.5, 63.3, 51.5, 51.3, 43.3, 24.8; ¹¹B NMR (160 MHz, CD₃Cl) δ 11.32; HRMS (ESI+) calcd for C₁₉H₂₃BNO₃ [M + H]⁺ 324.1766, found 324.1777.

8-(2-Cyanoethyl)hexahydro-1,3,2-oxazaborolo[2,3-*b***]-1,3, 2-oxazaborol-4-ium-8-uide (2j):** White solid, 76% yield; mp 218.6–220.4 °C; ¹H NMR (400 MHz, CD₃CN) δ 3.81 (td, *J* = 9.3, 5.4 Hz, 1H), 3.74 – 3.63 (m, 1H), 3.23 – 3.04 (m, 1H), 2.84 – 2.69 (m, 1H), 2.20 (dd, *J* = 16.1, 7.8 Hz, 1H), 0.75 – 0.61 (m, 1H). ¹³C NMR (100 MHz, CD₃CN) δ 117.3, 62.5, 51.2, 12.5. ¹¹B NMR (160 MHz, CD₃Cl) δ 11.28. HRMS (ESI+) Calculated for C₇H₁₄BN₂O₂ [M+H]: 169.1148, found: 169.1165.

8-(2-Cyano-1-phenylethyl)hexahydro-1,3,2-oxazaborolo-[**2,3-***b***]-1,3,2-oxazaborol-4-ium-8-uide (2k):** white solid; 97% yield; mp 147.5–148.9 °C; ¹H NMR (500 MHz, CD₃CN) δ 7.34–7.07 (m, 6H), 4.86 (s, 1H), 3.82–3.71 (m, 3H), 3.67–3.61 (m, 1H), 3.56 (dt, *J* = 4.8, 9.9 Hz, 1H), 3.04–2.94 (m, 1H), 2.74–2.61 (m, 7H), 2.18 (t, *J* = 8.3 Hz, 1H), 2.14 (s, 1H); ¹³C NMR (125 MHz, CD₃CN) δ 145.3, 128.1, 128.0, 124.9, 117.4, 62.6, 62.5, 51.3, 51.2, 19.6; ¹¹B NMR (160 MHz, CD₃CN) δ 10.47; HRMS (ESI+) calcd for C₁₃H₁₆BN₂O₂ [M + H]⁺ 243.1310, found 243.1335.

8-Phenylhexahydro-1,3,2-oxazaborolo[2,3-b]-1,3,2-oxazaborol-4-ium-8-uide (2l): white solid; 88% yield; mp 215.1– 217.5 °C; ¹H NMR (400 MHz, CD₃CN) δ 7.55–7.15 (m, 2H), 3.97 (td, J = 9.3, 5.4 Hz, 1H), 3.93–3.81 (m, 1H), 3.28–3.14 (m, 1H), 2.90–2.78 (m, 1H); ¹³C NMR (100 MHz, CD₃CN) δ 132.5, 126.9, 126.7, 63.1, 51.1; ¹¹B NMR (160 MHz, CD₃CN) δ 10.55; HRMS (ESI+) calcd for C₁₀H₁₅BNO₂ [M + H]⁺ 192.1196, found 192.1204.

General Procedure for the Deprotection of DEA-boronate Compound 2. To a solution of DEA-boronate 2 (1.1 mmol) in ether was added 0.1 M HCl. After about 20 min as judged by TLC, the reaction was extracted with ether ($3 \times$), washed with brine ($1 \times$), and dried with sodium sulfate, and the organic solvent was removed under reduced pressure. Evaporation of residual solvent provided the analytically pure product as white solid. Because of their facile dehydration, boronic acids tend to provide inconsistent melting points.⁵⁰ Therefore, the melting points for boronic acids were not taken.

(3-(Benzyloxy)-3-oxopropyl)boronic acid (3a): white solid; 95% yield; ¹H NMR (500 MHz, CD₃Cl) δ 7.45–7.22 (m, 5H), 5.13 (s, 2H), 2.53 (t, *J* = 7.2 Hz, 2H), 1.12 (t, *J* = 7.0 Hz, 2H); ¹³C NMR (125 MHz, CD₃Cl) δ 175.15, 136.02, 128.68, 128.35, 66.58, 28.69, 24.84; ¹¹B NMR (160 MHz, CD₃Cl) δ 31.59; HRMS (ESI+) calcd for C₁₀H₁₃BO₄Cl [M + Cl]⁺ 243.0601, found 243.0619.

(3-Methoxy-3-oxopropyl)boronic acid (3b): white solid; 90% yield; ¹H NMR (500 MHz, CD₃Cl) δ 3.66 (s, 3H), 2.48 (t, *J* = 7.2 Hz, 2H), 1.11 (t, *J* = 7.2 Hz, 2H); ¹³C NMR (125 MHz, CD₃Cl) δ 175.9, 51.9, 28.4, 10.4; ¹¹B NMR (160 MHz, CD₃Cl) δ 31.49; HRMS (ESI+) calcd for C₄H₁₀BO₄ [M + H]⁺ 133.0672, found 133.0665.

(4-(Benzylamino)-4-oxobutan-2-yl)boronic acid (3f): white solid; 98% yield; ¹H NMR (500 MHz, CD₃OD) δ 7.39–7.16 (m, 5H), 4.37 (q, *J* = 14.9 Hz, 2H), 2.32 (d, *J* = 8.3 Hz, 2H), 1.51–1.34 (m, 1H), 0.92 (d, *J* = 7.4 Hz, 3H); ¹³C NMR (125 MHz, CD₃OD) δ 176.3, 138.4, 128.2, 127.3, 127.0, 43.2, 39.6, 14.3; ¹¹B NMR (160 MHz, CD₃OD) δ 26.96; HRMS (ESI+) calcd for C₁₁H₂₀BN₂O₃ [M + NH₄] 239.1561, found 239.1568.

(3-(Benzylamino)-3-oxo-1-phenylpropyl)boronic acid (3g): white solid; 69% yield; ¹H NMR (500 MHz, CD₃OD) δ 7.29–6.97 (m, 10H), 4.50–4.22 (m, 2H), 2.80–2.74 (m, 1H), 2.72–2.43 (m, 2H); ¹³C NMR (125 MHz, CD₃OD) δ 176.7, 148.1, 137.9, 128.8, 128.2, 127.9, 127.7, 127.6, 124.4, 43.8, 40.2; ¹¹B NMR (160 MHz, CD₃OD) δ 25.39; HRMS (ESI+) calcd for C₁₆H₁₉BNO₃ [M + H]⁺ 284.1453, found 284.1478.

(2-Cyanoethyl)boronic acid (3j): white solid; 31% yield; ¹H NMR (500 MHz, (CD₃)₂CO) δ 2.42 (t, *J* = 5 Hz, 2H), 1.08 (t, *J* = 5 Hz, 2H); ¹³C NMR (125 MHz, CD₃Cl) δ 120.8, 11.3; ¹¹B NMR (160 MHz, (CD₃)₂CO) δ 18.89; HRMS (ESI+) calcd for C₃H₆BNO₂Cl [M + Cl]⁺ 134.0186, found 134.0180.

ASSOCIATED CONTENT

Supporting Information. ¹H, ¹³C, and ¹¹B NMR spectra of new compounds and CIF file for **2b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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