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# Regio- and Stereocontrolled Access to γ-Boronated Unsaturated Amino Esters and Derivatives from (*Z*)-Alkenyl 1,2-Bis(boronates)

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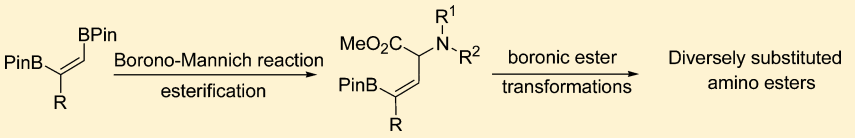
Supporting Information

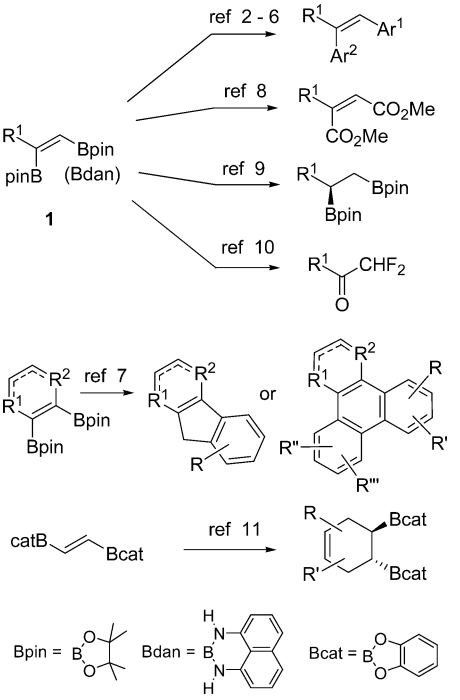



**ABSTRACT:** The Borono−Mannich reaction of (*Z*)-1-alkene-1,2-diboronic esters proceeded regioselectively at the terminal C−B bond to afford (E)-γ-boronated unsaturated amino esters in good yields. These compounds were then subjected to Suzuki couplings for the creation of diversely substituted olefinic amino acid systems. Several other functional transformations were also carried out to illustrate the synthetic utility of the Petasis products.

Alkenyl boronates constitute an important family of organoboron compounds whose utility in organic synthesis has been repeatedly illustrated.[1] Among this class of versatile intermediates, 1-alkene-1,2-diboronic esters **1** have been relatively poorly studied. Since the discovery of an efficient cis-selective route to these species by platinum-catalyzed diboration of alkynes in 1993, most of the work related to these compounds has been focused on their metal-catalyzed cross-coupling reactions.[2] Regioselective palladium Suzuki coupling at the terminal C−B bond can be followed by the introduction of a second aryl or heteroaryl moiety to afford unsymmetrical tetrasubstituted alkenes (Scheme 1).[3,4] By contrast, the use of a differently protected diboron, instead of the classical bis-(pinacolato)diboron, allowed internal selective cross coupling.[5] Other convincing examples of the interest of compounds **1** were provided by couplings with 2 equiv of the same electrophile[2a,3e,6] and annulation reactions with aromatic dihalides.[7] Much less has been reported about other aspects of their reactivity. Double carbomethoxylation,[8] enantioselective hydrogenation,[9] fluoro-deboronation,[10] and Diels−Alder cycloaddition[11] were recently described (Scheme 1), whereas, to the best our knowledge, no Borono−Mannich reactions have been hitherto carried out with the 1,2-diboronic esters as substrates.

This transformation, now referred to as the Petasis reaction, involving aldehyde or ketone, unsaturated organoborane, and amine partners, enables the preparation of a wide variety of molecules with high levels of structural diversity.[12,13] In the course of our research programs devoted to the synthesis of amino acids[14] and multicomponent assembly processes involving boronic acids or their derivatives,[15] in this article, we have investigated a new route to γ-boronated unsaturated amino esters **2** from bis(boronates) **1** (Scheme 2). These compounds may have interesting biological properties, by themselves or by their derivatives;[16] the presence of a boronate group also allows access through diverse functionalizations, for example, cross coupling, oxidation, or azidation,[1] to a number of diversely substituted amino acids or heterocycles.

**Scheme 1. Some Representative Examples of the Reactivity of 1-Alkene-1,2-diboronic Esters 1**

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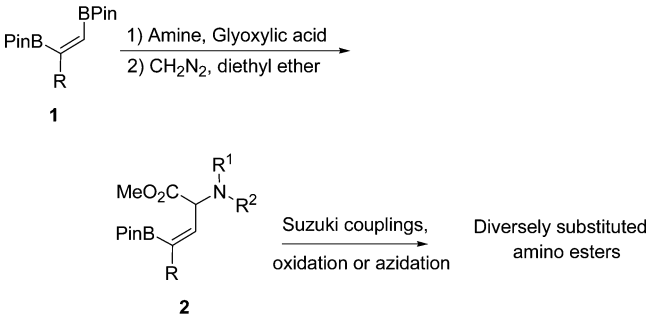
**Scheme 2. Access to Diversely Substituted Amino Esters from 1,2-Bis Boronates**




(*Z*)-Alkenyl 1,2-bis(boronates) **1** were prepared in good yields according to a known protocol[2] from the corresponding alkynes, 1-hexyne, 3-hexyne, propargyl trimethylsilane, and phenylacetylene, independently on reaction with bis(pinacolato)diboron in the presence of tetrakis(triphenylphosphine)platinum as catalyst in DMF/toluene at 80 °C for 18 h. These boronic esters **1a**−**d** were then subjected to regioselective Petasis reaction at the terminal C−B bond using different amines and glyoxylic acid in HFIP (1,1,1,3,3,3-hexafluoropropan-2-ol) at room temperature for 8 h to give the corresponding γ-boronated unsaturated amino acids. Poor results were obtained with other solvents, such as methanol or THF, as previously reported,[17] which was attributed to the positive effect of HFIP on the formation of ionic intermediates and stabilization of polarized transition states. Thus, prepared amino acids were directly subjected to esterification with an ethereal solution of $CH_2N_2$ to afford corresponding γ-boronated esters **2** with diversity (Table 1). A single isomer was present with an E stereochemistry, as evidenced from NOESY experiments; no product resulting from a double Petasis condensation was detected under these experimental conditions. Yields are moderate to good (50−69% over two steps), with the best results being generally obtained with morpholine or N-substituted piperazines (entries 1, 3, 4, and 7). The reaction also took place with (*S*)-(−)-*N*-benzyl-α-methylbenzylamine, a more sterically demanding amine than dibenzylamine, but with poor diastereoselectivity (dr 58:42) (entry 5). In addition, it should also be noted that no reaction occurred at room temperature with the primary amine, $PhCH_2NH_2$, and **1a** (entry 6) as with the tetrasubstituted bisboronate **1d** and morpholine (entry 11), whereas complex, inseparable mixtures are produced upon heating at 50 °C in HFIP for 2 h.

The thus obtained esters **2** were engaged in Suzuki−Miyaura cross-coupling reactions with different aromatic halides in the presence of [1,1′-bis(diphenylphosphino)ferrocene]-dichloropalladium(II) and potassium phosphate tribasic monohydrate in THF/$H_2O$ at reflux.[18] The corresponding esters **3** were obtained in good (60−89%) yields (Table 2), with no significant influence being noticed on the basis of the nature of the aromatic ring substituent (entries 5 and 6, 8 and 9). Heteroaromatic halide can be used with similar efficiency (entry 3). The coupling reactions proceeded with retention of configuration to afford the Z isomers as single products except in the case of 2-bromo toluene, which gave a 58:42 mixture of geometrical isomers.

The synthetic utility of the amino esters **2** was also demonstrated by several transformations of the boronic ester group (Scheme 3). For example, oxidation of **2a** with sodium perborate in THF/water afforded γ-oxo α-aminoester **4** in 74% yield, whereas the copper-catalyzed reaction with sodium azide in methanol gave alkenylazide **5**.[19] In addition, a one-pot procedure, which avoided the need to isolate this potentially unstable species, was employed to synthesize 4-aryl-1,2,3-triazole **6** directly from **2a** and phenylacetylene in an overall yield of 36%.[19,20]

In conclusion, a regioselective Petasis reaction has been performed for the first time at the terminal C−B bond of (*Z*)-1-alkene-1,2-diboronic esters. The resulting amino esters were then subjected to Suzuki coupling with the second boronate moiety to give the corresponding amino esters. This protocol provides an opportunity not only for the conversion of bisboronates into Petasis/Suzuki products but also to other functionalized amino esters derivatives by exploiting the versatility of the boronic ester group.

## EXPERIMENTAL SECTION

**General Information and Materials.** All commercially available chemicals were used without further purification. Tetrahydrofuran (THF), diethylether, and 1,1,1,3,3,3-hexafluoropropan-2-ol (HFIP) were used as received. Analytical thin-layer chromatography was performed on silica gel 60 F254 plates. The compounds were characterized by $^1$H, $^{13}$C, and $^{11}$B NMR techniques. $^1$H and $^{13}$C spectra were recorded in $CDCl_3$ (internal standard: 7.26 ppm, $^1$H; 77.00 ppm, $^{13}$C) and $^{11}$B NMR chemical shifts to external $BF^3{\cdot}OEt_2$ (0.0 ppm). High-resolution mass spectra (HMRS) were recorded on a micro-TOF-Q II mass analyzer or Q-TOF 2 using positive ion electrospray. Compounds **1a**,[10] **1b**,[3d] **1c**,[2b] and **1d**[3b] were prepared according to a known protocol.[2] The ethereal solution of $CH_2N_2$ was generated from *N*-nitroso-*N*-methylurea according to the literature.[21]

**General Procedure for Petasis Reaction.** Glyoxylic acid monohydrate (0.33 mmol) and amine (0.33 mmol) were added to a stirred solution of bispinacolate ester **1** (0.3 mmol) in hexafluoropropan-2-ol (2 mL) under an argon atmosphere at room temperature. The reaction mixture was stirred for 8 h. The solvent was removed under reduced pressure to give a residue that was directly used for the further esterification reaction. To a solution of the crude acid in diethylether (5 mL) at 0 °C was added a solution of $CH_2N_2$ in ether[21] until the persistence of yellow color. After 2 h, the solvent was evaporated, and the resulting residue was purified by column chromatography (230−400 mesh silica gel, EtOAc in cyclohexane) to afford γ-boronated unsaturated amino esters **2** in 50−69% yield (over two steps) (Table 1).

*Methyl 4-(4,4,4,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(morpholino)-oct-3-enoate* ***2a***. Seventy six milligrams (69%). Colorless oil, $R_f$ = 0.25 (EtOAc/cyclohexane 20:80). $^1$H NMR (300 MHz, $CDCl_3$): δ 5.96 (d, *J* = 9.8 Hz, 1H), 4.32 (d, *J* = 9.8 Hz, 1H), 3.73 (t, *J* = 4.3 Hz, 4H), 3.69 (s, 3H), 2.59−2.48 (m, 4H), 2.24−2.07 (m, 2H,), 1.41−1.21 (m, 4H), 1.27 (s, 12H), 0.86 (t, *J* = 7.0 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 171.8, 140.4 (br), 136.7, 83.4, 69.1, 66.7, 51.9, 51.0, 36.4, 31.7, 24.8, 24.7, 22.2, 13.9. $^{11}$B NMR (96 MHz, $CDCl_3$): δ 30.0 (br s). HRMS (ESI+): *m*/*z* (M + H)$^+$ calcd for $C_{19}H_{35}NO_5{}^{11}B$, 368.26083; found, 368.2608.

*Methyl 2-Dibenzylamino-4-(4,4,4,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-oct-3-enoate* ***2b***. Seventy two milligrams (50%). Colorless oil, $R_f$ = 0.40 (EtOAc/cyclohexane 30:70). $^1$H NMR (300 MHz, $CDCl_3$): δ 7.39−7.40 (m, 4H), 7.29−7.26 (m, 4H), 7.20−7.19 (m, 2H), 6.16 (d, *J* = 9.3 Hz, 1H), 4.74 (d, *J* = 9.3 Hz, 1H), 3.76 (s, 4H), 3.69 (s, 3H), 2.26−2.11 (m, 2H), 1.42−1.29 (m, 4H), 1.09 (s, 6H), 1.05 (s, 6H), 0.91 (t, *J* = 7.0 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 173.2, 139.8, 137.7, 128.7, 128.0, 126.6, 83.0, 63.2, 54.9, 51.4, 36.5, 31.9, 26.9, 24.6, 24.4, 22.3, 14.0 (C α to boron not visible). $^{11}$B NMR (96 MHz, $CDCl_3$): δ 30.4 (br s). HRMS (ESI+): *m*/*z* (M + H)$^+$ calcd for $C_{29}H_{41}NO_4{}^{11}B$, 478.31286; found, 478.3129.

*Methyl 4-(4,4,4,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(pyridin-4-yl)piperazino-oct-3-enoate* ***2c***. Seventy six milligrams (57%). Colorless oil, $R_f$ = 0.30 (EtOAc/cyclohexane 30:70). $^1$H NMR (300 MHz, $CDCl_3$): δ 8.18 (d, *J* = 3.9 Hz, 1H), 7.46 (t, *J* = 7.4 Hz, 1H), 6.64−


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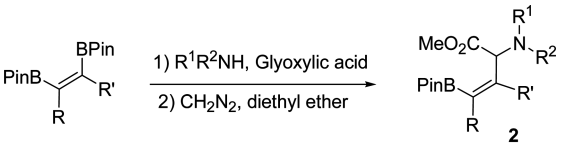
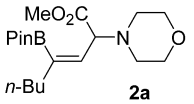
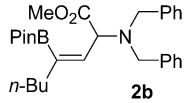
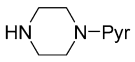
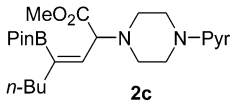
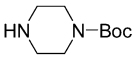
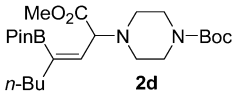
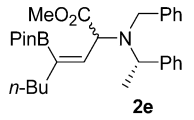
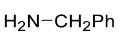
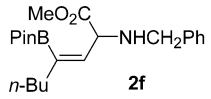
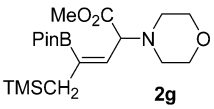
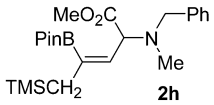
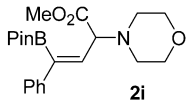
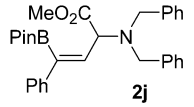
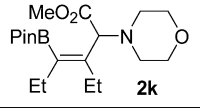
**Table 1. Borono–Mannich Route to γ-Boronated Unsaturated Amino Esters 2**




**1a** R = *n*-Bu, R' = H
**1b** R = $CH_2TMS$, R' = H
**1c** R = Ph, R' = H
**1d** R = R' = Et

| entry | R | R' | amine | product | yield (%)[a] |
|---|---|---|---|---|---|
| 1 | n-Bu | H |  |  **2a** | 69 |
| 2 | *n*-Bu | H |  |  **2b** | 50 |
| 3 | *n*-Bu | H |  |  **2c** | 57 |
| 4 | *n*-Bu | H |  |  **2d** | 63 |
| 5 | *n*-Bu | H |  |  **2e** | 58[b] |
| 6 | *n*-Bu | H |  |  **2f** | nr |
| 7 | $TMSCH_2$ | H |  |  **2g** | 60 |
| 8 | $TMSCH_2$ | H |  |  **2h** | 53 |
| 9 | Ph | H |  |  **2i** | 53 |
| 10 | Ph | H |  |  **2j** | 54 |
| 11 | Et | Et |  |  **2k** | nr |

[a]Yields are calculated over two steps after purification by column chromatography. [b]Mixtures of two diastereomers (58:42).

6.59 (m, 2H), 5.99 (d, $J$ = 9.8 Hz, 1H), 4.40 (d, $J$ = 9.8 Hz, 1H), 3.72 (s, 3H,), 3.57 (t, $J$ = 4.9 Hz, 4H), 2.66–2.53 (m, 4H), 2.18–2.02 (m, 2H), 1.41–1.26 (m, 4H), 1.26 (s, 12H), 0.87 (t, $J$ = 7.2 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 172.2, 147.8, 137.5, 137.2, 113.2, 107.0, 83.4, 68.9, 51.9, 50.4, 45.1, 36.5, 31.8, 24.8, 24.7, 22.3, 13.9. $^{11}$B NMR (96 MHz, $CDCl_3$): $\delta$ 29.8 (br s). HRMS (ESI+): $m/z$ (M + H)$^+$ calcd for $C_{24}H_{39}N_3O_4{}^{11}B$, 444.30336; found, 444.3037.

*Methyl 4-(4,4,4,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-2-[4-(1,1-dimethylethoxy)carbonyl]piperazino-oct-3-enoate* ***2d.*** Eighty eight milligrams (63%). Colorless oil, $R_f$ = 0.30 (EtOAc/cyclohexane 30:70).


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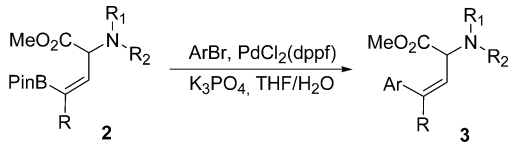
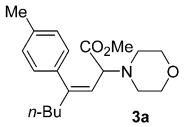
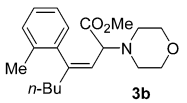
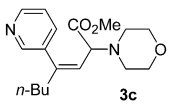
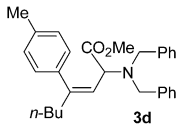
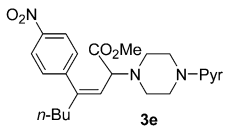
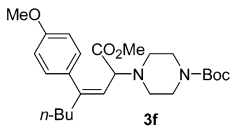
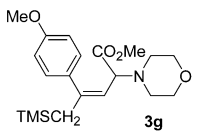
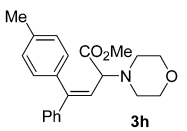
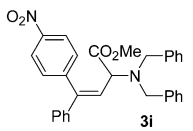
**Table 2. Suzuki Couplings with γ-Boronated Unsaturated Amino Esters 2**




| entry | boronate | Ar | product | yield (%)[a] |
|---|---|---|---|---|
| 1 | **2a** | 4-$MeC_6H_4$ |  **3a** | 75 |
| 2 | **2a** | 2-$MeC_6H_4$ |  **3b** | 60 |
| 3 | **2a** | 3-Pyr |  **3c** | 82 |
| 4 | **2b** | 4-$MeC_6H_4$ |  **3d** | 86 |
| 5 | **2c** | 4-$NO_2C_6H_4$ |  **3e** | 82 |
| 6 | **2d** | 4-$MeOC_6H_4$ |  **3f** | 89 |
| 7 | **2g** | 4-$MeOC_6H_4$ |  **3g** | 80 |
| 8 | **2i** | 4-$MeC_6H_4$ |  **3h** | 80 |
| 9 | **2j** | 4-$NO_2C_6H_4$ |  **3i** | 78 |

[a]Yields are calculated after purification by column chromatography.

$^1$H NMR (300 MHz, $CDCl_3$): δ 5.90 (d, $J$ = 9.7 Hz, 1H), 4.29 (d, $J$ = 9.7 Hz, 1H), 3.65 (s, 3H), 3.41−3.39 (m, 4H), 2.56−2.40 (m, 4H), 2.23−207 (m, 2H), 1.40 (s, 9H), 1.34−1.22 (m, 4H), 1.22 (s, 12H), 0.93 (t, $J$ = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 172.0, 154.6, 139.8 (br), 137.1, 83.3, 79.4, 68.5, 51.7, 50.2, 43.0 (br), 36.4, 31.7, 28.3, 24.7, 24.6, 22.2, 13.8. $^{11}$B NMR (96 MHz, $CDCl_3$): δ 30.2 (br s). HRMS (ESI+): $m/z$ (M + Na)$^+$ calcd for $C_{24}H_{43}N_2O_6{}^{11}BNa$, 489.31119; found, 489.3112.

*Methyl 2-(S)-Benzyl-α-methylbenzylamino-4-(4,4,4,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-oct-3-enoate* ***2e***. Eighty five milligrams (58%). Colorless oil, $R_f$ = 0.29 (EtOAc/cyclohexane 8:92). Mixture of 2 diastereomers (55:45). $^1$H NMR (400 MHz, $CDCl_3$): δ 7.45−7.43 (m, 3H), 7.36−7.15 (m, 7H), 6.16 (d, $J$ = 9.3 Hz, 0.55H), 6.00 (d, $J$ = 9.1 Hz, 0.45H), 4.93 (d, $J$ = 9.2 Hz, 0.45H), 4.86 (d, $J$ = 9.4 Hz, 0.55H), 4.12−4.06 (m, 1H), 3.98 (d, $J$ = 15.2 Hz, 0.55H), 3.93 (d, $J$ = 15.4 Hz, 0.55H), 3.89 (d, $J$ = 15.4 Hz, 0.45H), 3.81 (d, $J$ = 15.2 Hz, 0.45H), 3.65 (s, 3 × 0.45H), 3.47 (s, 3 × 0.55H), 2.20−2.04 (m, 2H), 1.40 (d, $J$ = 7.2 Hz, 3 × 0.45H), 1.38 (d, $J$ = 7.4 Hz, 3 × 0.55H), 1.34−1.25 (m, 4H), 1.19 (s, 12 × 0.45H), 1.16 (s, 12 × 0.55H), 0.89 (t, $J$ = 7.1 Hz, 3 × 0.45H), 0.88 (t, $J$ = 7.0 Hz, 3 × 0.55H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 174.1, 173,6, 144.35, 143.8, 141.9, 141.7, 139.7, 139.2, 136.6 (br), 128.2, 128.1, 127.95, 127.9, 127.85, 127.8, 126.55, 126.5, 126.3, 126.1, 83.0, 83.0, 62.8, 62.5, 59.0, 58.35, 51.7, 51.6, 51.4, 51.2, 36.4, 36.2, 31.8, 31.6, 24.7, 24.5, 24.4, 22.3, 22.2, 16.9, 14.0. $^{11}$B NMR (96 MHz, $CDCl_3$): δ 30.0 (br s). HRMS (ESI+): $m/z$ (M + H)$^+$ calcd for $C_{30}H_{43}NO_4{}^{11}B$, 492.3285; found, 492.3279.

*Methyl 4-(4,4,4,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(morpholino)-5-(trimethylsilyl)-pent-3-enoate* ***2g***. Seventy one milligrams (60%). Colorless oil, $R_f$ = 0.25 (EtOAc/cyclohexane 10:90). $^1$H NMR (300 MHz, $CDCl_3$): δ 5.80 (d, $J$ = 9.9 Hz, 1H), 4.47 (d, $J$ = 9.9 Hz, 1H), 3.74 (t, $J$ = 4.0 Hz, 4H), 3.68 (s, 3H), 2.60−2.46 (m, 4H), 1.67 (s, 2H), 1.25 (s, 6H), 1.24 (s, 6H), −0.05 (s, 9H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 171.9, 137.2 (br),135.1, 83.5, 69.0, 66.7, 51.8, 51.0, 26.6, 24.9, −1.5. $^{11}$B NMR (96 MHz, $CDCl_3$): δ 29.7 (br s). HRMS (ESI+): $m/z$ (M + Na)$^+$ calcd for $C_{19}H_{36}NO_5{}^{11}BNaSi$, 420.23535; found, 420.2351.

*Methyl 2-Benzyl(methy)amino-4-(4,4,4,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-(trimethylsilyl)-pent-3-enoate* ***2h***. Sixty nine milligrams (53%). Colorless oil, $R_f$ = 0.15 (EtOAc/cyclohexane 3:97). $^1$H NMR (400 MHz, $CDCl_3$): δ 7.40−7.19 (m, 5H), 5.97 (d, $J$ = 9.6 Hz, 1H), 4.73 (d, $J$ = 9.6 Hz, 1H), 3.76−3.54 (m, 2H), 3.73 (s, 3H), 2.21 (s, 3H), 1.73 (s, 2H), 1.23 (s, 6H), 1.21 (s, 6H), 0.00 (s, 9H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 173.1, 139.2 (br), 136.1, 129.2, 128.1, 126.9, 83.3, 67.0, 58.5, 51.6, 38.7, 26.6, 24.9, 24.8, −1.5 (C α to boron not visible). $^{11}$B NMR (96 MHz, $CDCl_3$): δ 29.6 (br s). HRMS (ESI+): $m/z$ (M + H)$^+$ calcd for $C_{23}H_{39}{}^{11}BNO_4Si$, 432.27414; found, 432.2738.

*Methyl 4-(4,4,4,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(morpholino)-4-phenyl-but-3-enoate* ***2i***. Sixty two milligrams (53%). Colorless oil, $R_f$ = 0.30 (EtOAc/cyclohexane 20:80). $^1$H NMR (400 MHz, $CDCl_3$): δ 7.42−7.22 (m, 5H), 6.40 (d, $J$ = 9.9 Hz, 1H), 4.32 (d, $J$ = 9.9 Hz, 1H), 3.78−3.74 (m, 4H), 3.74 (s, 3H), 2.67−2.54 (m, 4H), 1.35 (s, 6H), 1.34 (s, 6H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 171.3, 141.3, 138.2, 128.7, 128.3, 127.3, 126.6, 84.1, 70.0, 66.8, 52.1, 51.3, 24.9, 24.7. $^{11}$B NMR (96 MHz, $CDCl_3$): δ 30.3 (br s). HRMS (ESI+): $m/z$ (M + Na)$^+$ calcd for $C_{21}H_{30}{}^{11}BNO_5Na$, 410.21147; found, 410.2112.

*Methyl 2-Dibenzylamino-4-(4,4,4,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-phenyl-but-3-enoate* ***2j***. Eighty one milligrams (54%). Colorless oil, $R_f$ = 0.15 (EtOAc/cyclohexane 3:97). $^1$H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, $J$ = 7.8 Hz, 4H), 7.33−7.24 (m, 8H,), 7.21−7.15 (m, 3H), 6.53 (d, $J$ = 9.3 Hz, 1H), 4.73 (d, $J$ = 9.5 Hz, 1H), 3.81 (s, 4H), 3.69 (s, 3H), 1.09 (s, 6H), 1.06 (s, 6H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 172.4, 142.2, 139.9, 139.5, 137.1 (br), 128.7, 128.15, 128.10, 127.4, 126.8, 126.7, 83.7, 63.7, 55.0, 51.6, 24.6, 24.5. $^{11}$B NMR (96 MHz, $CDCl_3$): δ 30.3 (br s). HRMS (ESI+): $m/z$ (M + H)$^+$ calcd for $C_{31}H_{37}NO_4{}^{11}B$, 498.28156; found, 498.2809.

**General Procedure for Suzuki Coupling.** To a solution of ester **2** (0.14 mmol) in THF (1.2 mL) and water (30 μL) under an argon atmosphere were added [1,1′-bis (diphenyl phosphino)ferrocene]-dichloropalladium(II) (0.0028 mmol), potassium phosphate tribasic monohydrate (0.42 mmol), and arylbromide (0.28 mmol) at room temperature. The reaction mixture was heated at reflux for 8 h, cooled to room temperature, and diluted with water. The aqueous layer was extracted with $Et_2O$ (2 × 15 mL). The combined organic extracts were dried over $MgSO_4$ and evaporated under vacuum. The residue was purified by column chromatography (230−400 mesh silica gel, EtOAc in cyclohexane) to give ester **3** in 69−89% yield (Table 2).

*Methyl 4-(4-Methylphenyl)-2-(morpholino)-oct-3-enoate* ***3a***. Thirty five milligrams (75%). Colorless oil, $R_f$ = 0.40 (EtOAc/cyclohexane 10:90). $^1$H NMR (300 MHz, $CDCl_3$): δ 7.14 (d, $J$ = 7.9 Hz, 2H), 7.02 (d, $J$ = 7.9 Hz, 2H), 5.48 (d, $J$ = 9.9 Hz, 1H), 3.73 (s, 3H), 3.69 (t, $J$ = 4.5 Hz, 4H), 3.52 (d, $J$ = 9.9 Hz, 1H), 2.58−2.45 (m, 2H),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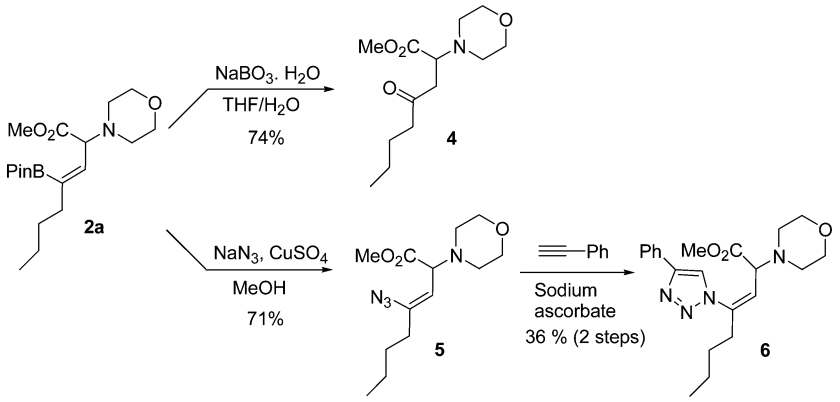
**Scheme 3. Synthetic Transformations of γ-Boronated Unsaturated Amino Ester 2a**




2.38−2.26 (m, 4H), 2.36 (s, 3H), 1.33−1.22 (m, 4H), 0.84 (t, $J$ = 7.0 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 171.8, 149.3, 136.9, 136.8, 128.9, 128.0, 120.0, 67.9, 66.7, 52.0, 50.9, 39.4, 29.8, 22.2, 21.2, 13.8. HRMS (ESI+): $m/z$ (M + Na)$^+$ calcd for $C_{20}H_{29}NO_3Na$, 354.20451; found, 354.2042.

*Methyl 4-(2-Methylphenyl)-2-(morpholino)-oct-3-enoate* ***3b***. Twenty milligrams (60%). Colorless oil, $R_f$ = 0.40 (EtOAc/cyclohexane 30:70). Mixture of 2 diastereomers (58:42). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.22−7.12 (m, 3H), 6.93 (d, $J$ = 6.9 Hz, 0.4H), 6.92 (d, $J$ = 6.6 Hz, 0.6H), 5.58 (d, $J$ = 9.6 Hz, 0.4H), 5.56 (d, $J$ = 10 Hz, 0.6H), 3.73−3.68 (m, 4H), 3.71 (s, 3 × 0.4H), 3.68 (s, 3 × 0.6H), 3.28 (d, $J$ = 9.6 Hz, 0.4H), 3.23 (d, $J$ = 9.9 Hz, 0.6H), 2.56−2.47 (m, 2H), 2.33−2.23 (m, 4H), 2.23 (s, 3 × 0.4), 2.15 (s, 3 × 0.6H), 1.43−1.29 (m, 4H), 0.88 (t, $J$ = 7.0 Hz, 3 × 0.6H), 0.86 (t $J$ = 7.1 Hz, 3 × 0.4). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 171.7, 171.6, 148.6, 148.6, 139.4, 139.0, 135.5, 134.1, 130.0, 129.5, 128.0, 127.1, 127.0, 125.2, 125.1, 121.2, 120.8, 68.4, 68.3, 66.7, 51.7, 51.7, 51.1, 51.05, 38.6, 38.2, 29.6, 29.4, 22.4, 22.2, 19.2, 18.9, 13.8. HRMS (ESI+): $m/z$ (M + Na)$^+$ calcd for $C_{20}H_{29}NO_3Na$, 354.20451; found, 354.2047.

*Methyl 4-(Pyridin-3-yl)-2-(morpholino)-oct-3-enoate* ***3c***. Thirty seven milligrams (82%). Colorless oil, $R_f$ = 0.15 (EtOAc/cyclohexane 40:60). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 8.54 (d, $J$ = 3.6 Hz, 1H), 8.50 (s, 1H), 7.49 (dt, $J$ = 1.9, 7.8 Hz, 1H), 7.30 (dd, $J$ = 4.9, 7.5 Hz, 1H), 5.65 (d, 1H, $J$ = 10 Hz), 3.72 (s, 3H), 3.68 (t, $J$ = 4.6 Hz, 4H), 3.42 (d, $J$ = 10 Hz, 1H), 2.49 (dt, $J$ = 4.9, 9.5 Hz, 2H), 2.41−2.26 (m, 4H), 1.36−1.22 (m, 4H), 0.85 (t, $J$ = 7.0 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 171.4, 149.0, 148.5,145.2, 135.7, 135.5, 123.1, 122.7, 67.7, 66.7, 52.0, 50.8, 39.0, 29.6, 22.0, 13.7. HRMS (ESI+): $m/z$ (M + H)$^+$ calcd for $C_{18}H_{27}N_2O_3$, 319.20162; found, 319.2017.

*Methyl 2-Dibenzylamino-4-(4-methylphenyl)-oct-3-enoate* ***3d***. Fifty three milligrams (86%). Colorless oil, $R_f$ = 0.25 (EtOAc/cyclohexane 1:99). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.19−7.16 (m, 10H), 7.0 (s, 4H), 5.69 (d, $J$ = 9.8 Hz, 1H), 4.07 (d, $J$ = 9.8 Hz, 1H), 3.69 (s, 3H), 3.66 (s, 4H), 2.45−2.40 (m, 2H), 2.33 (s, 3H,), 1.31−1.28 (m, 4H), 0.86 (t, $J$ = 7.0 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 173.4, 147.6, 139.6, 136.9, 136.4, 128.7, 128.0, 127.9, 126.6, 120.1, 60.6, 54.9, 51.4, 39.3, 30.1, 22.2, 21.1, 13.9. HRMS (ESI+): $m/z$ (M + H)$^+$ calcd for $C_{30}H_{36}NO_2$, 442.2746; found, 442.2742.

*Methyl 4-(4-Nitrophenyl)-2-(pyridin-4-yl)piperazino-oct-3-enoate* ***3e***. Fifty milligrams (82%). Colorless oil, $R_f$ = 0.25 (EtOAc/cyclohexane 20:80). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 8.21 (d, $J$ = 8.7 Hz, 2H), 8.17−8.15 (m, 1H), 7.49−7.42 (m, 1H,), 7.36 (d, $J$ = 8.7 Hz, 2H), 6.65−6.58 (m, 2H), 5.72 (d, $J$ = 10.0 Hz, 1H), 3.75 (s, 3H), 3.56−3.49 (m, 4H), 3.47 (d, $J$ = 10.0 Hz, 1H), 2.64−2.57 (m, 2H), 2.47−2.40 (m, 4H), 1.35−1.25 (m, 4H), 0.87 (t, $J$ = 6.6 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 171.4, 159.2, 147.9, 147.1, 146.6, 137.5, 129.2, 123.5, 122.9, 113.4, 107.0, 67.6, 52.1, 50.3, 45.1, 38.9, 29.7, 22.1, 13.8. HRMS (ESI+): $m/z$ (M + H) $^+$ calcd for $C_{24}H_{31}N_4O_4$, 439.23453; found, 439.2342.

*Methyl 4-(4-Methoxyphenyl)-2-[4-(1,1-dimethylethoxy)carbonyl]-piperazino-oct-3-enoate* ***3f***. Fifty six milligrams (89%). Colorless oil $R_f$ = 0.15 (EtOAc/cyclohexane 10:90). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.08 (d, $J$ = 8.7 Hz, 2H), 6.87 (d, $J$ = 8.7 Hz, 2H), 5.49 (d, $J$ = 10.0 Hz, 1H), 3.81 (s, 3H), 3.72 (s, 3H), 3.56 (d, $J$ = 9.9 Hz, 1H), 3.40 (t, $J$ = 4.5 Hz, 4H), 2.49−2.39 (m, 2H), 2.39−2.29 (m, 2H), 2.29−2.19 (m, 2H), 1.42 (s, 9H), 1.34−1.21 (m, 4H), 0.84 (t, $J$ = 7.0 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 172.1, 158.7, 154.6, 148.5, 132.2, 129.3, 120.5, 113.5, 79.6, 67.6, 55.2, 51.9, 50.3, 43.0 (br), 39.4, 29.8, 28.4, 22.1, 13.8. HRMS (ESI+): $m/z$ (M + H)$^+$ calcd for $C_{25}H_{39}N_2O_5$, 447.2859; found, 447.2858.

*Methyl 2-(Morpholino)-4-(4-methoxyphenyl)-5-(trimethylsilyl)-pent-3-enoate* ***3g***. Forty two milligrams (80%). Colorless oil, $R_f$ = 0.39 (EtOAc/cyclohexane 10:90). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.17 (d, $J$ = 8.7 Hz, 2H), 6.86 (d, $J$ = 8.8 Hz, 2H), 5.29 (d, $J$ = 10.1 Hz, 1H), 3.82 (s, 3H), 3.74 (s, 3H), 3.70−3.67 (m, 4H), 3.62 (d, $J$ = 10.1 Hz, 1H), 2.55−2.45 (m, 2H), 2.33−2.23 (m, 2H), 1.91 (s, 2H), −0.17 (s, 9H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 172.2, 158.8, 146.2, 133.3, 129.6, 118.1, 113.4, 68.0, 66.9, 55.2, 51.8, 50.9, 31.0, −1.5. HRMS (ESI+): $m/z$ (M + Na)$^+$ calcd for $C_{20}H_{31}NO_4SiNa$, 400.19201; found, 400.1913.

*Methyl 4-(4-Methylphenyl)-2-(morpholino)-4-phenyl-but-3-enoate* ***3h***. Thirty nine milligrams (80%). Colorless oil, $R_f$ = 0.40 (EtOAc/cyclohexane 10:90). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.30−7.25 (m, 5H), 7.21 (d, $J$ = 7.8 Hz, 2H), 7.10 (d, $J$ = 7.9 Hz, 2H), 6.15 (d, $J$ = 10.1 Hz, 1H), 3.77−3.72 (m, 5H), 3.76 (s, 3H), 2.65−2.58 (m, 2H), 2.44−2.38 (m, 2H), 2.40 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 171.4, 148.0, 141.5, 137.5, 135.7, 129.7, 129.0, 128.2, 128.0, 127.5, 122.2, 68.3, 66.8, 52.1, 51.1, 21.3. HRMS (ESI+): $m/z$ (M + Na)$^+$ calcd for $C_{22}H_{25}NO_3Na$, 374.17321; found, 374.1736.

*Methyl 2-Dibenzylamino-4-(4-nitrophenyl)-4-phenyl-but-3-enoate* ***3i***. Fifty four milligrams (78%). Colorless oil, $R_f$ = 0.35 (EtOAc/cyclohexane 7:93). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.03 (d, $J$ = 8.7 Hz, 2H), 7.35−7.17 (m, 17H), 6.43 (d, $J$ = 9.8 Hz, 1H), 4.10 (d, $J$ = 9.8 Hz, 1H), 3.86 (d, $J$ = 13.7 Hz, 2H), 3.83 (s, 3H), 3.72 (d, $J$ = 13.7 Hz, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 172.2, 147.0, 145.6, 144.8, 140.7, 139.0, 130.4, 128.7, 128.4, 128.3, 128.2, 127.6, 127.0, 124.6, 123.4, 60.4, 55.0, 51.8. HRMS (ESI+): $m/z$ (M + Na)$^+$ calcd for $C_{31}H_{28}N_2O_4Na$, 515.19468; found, 515.1948.

**Oxidation of Boronate 2a.** Sodium perborate monohydrate (45 mg, 0.45 mmol) was added to a stirred solution of ester **2a** (50 mg, 0.14 mmol) in THF (2 mL) and water (2 mL) at room temperature. The reaction mixture was stirred during 12 h and then diluted with water. The aqueous layer was extracted with $Et_2O$ (2 × 5 mL). The combined organic extracts were dried over $MgSO_4$ and evaporated under vacuum. The resulting residue was purified by column chromatography (230−400 mesh silica gel, EtOAc/cyclohexane, 1:9 to 1:2) to afford γ-keto amino ester **4** (26 mg) in 74% yield as a colorless oil.

*Methyl 2-(Morpholino)-4-oxo-octanoate* ***4***. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 3.77−3.73 (m, 1H), 3.67 (s, 3H), 3.67−3.61 (m, 4H), 2.99 (dd, $J$ = 17.0, 9.2 Hz, 1H), 2.75−2.64 (m, 2H), 2.56−2.47 (m, 2H), 0.86 (t, $J$ = 7.4 Hz, 2H), 1.49 (quint, $J$ = 7.4 Hz, 2H), 1.24 (hex, $J$ = 7.4 Hz, 2H), 0.84 (t, $J$ = 7.3 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 207.3, 169.8, 65.9, 61.9, 50.7, 49.2, 41.8, 40.6, 24.7, 21.25, 12.8. HRMS (ESI+): $m/z$ (M + Na)$^+$ calcd for $C_{13}H_{23}NO_4Na$, 280.1525; found, 280.1523.

**Azidation of Boronate 2a.** Sodium azide (12 mg, 0.18 mmol) and copper sulfate (15 mg, 0.095 mmol) were added to a stirred solution of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boronic ester **2a** (56 mg, 0.15 mmol) in MeOH (2 mL) at room temperature. The reaction mixture was stirred during 24 h and then diluted with water. The aqueous layer was extracted with $CH_2Cl_2$ (2 × 5 mL). The combined organic extracts were dried over $MgSO_4$ and evaporated under vacuum. The resulting residue was purified by column chromatography (230−400 mesh silica gel, EtOAc/cyclohexane, 1:9 to 1:4) to afford γ-azido amino ester **5** (30 mg) in 71% yield as a colorless oil.

*Methyl 2-(Morpholino)-4-azido-oct-3-enoate* ***5***. $^1$H NMR (400 MHz, $CDCl_3$): δ 4.74 (d, *J* = 9.5 Hz, 1H), 3.95 (d, *J* = 9.5 Hz, 1H), 3.67 (t, *J* = 4.6 Hz, 4H), 3.66 (s, 3H), 2.56−2.49 (m, 2H), 2.45−2.38 (m, 2H), 2.26 (t, *J* = 7.5 Hz, 2H), 1.47 (quint, *J* = 7.5 Hz, 2H), 1.32 (hex, *J* = 7.5 Hz, 2H), 0.87 (t, *J* = 7.3 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 171.3, 141.2, 109.2, 66.8, 65.35, 52.0, 50.9, 32.2, 29.4, 21.9, 13.7. HRMS (ESI+): *m*/*z* $(M-N_2 + Na)^+$ calcd for $C_{13}H_{22}N_2O_3Na$, 277.1528; found, 277.1530.

**One-Pot Access to Triazole 6.** Sodium azide (9 mg, 0.13 mmol) and copper sulfate (11 mg, 0.07 mmol) were added to a stirred solution of ester **2a** (40 mg, 0.11 mmol) in MeOH (2 mL) at room temperature. The reaction mixture was stirred during 24 h. Sodium ascorbate (11 mg, 0.05 mmol) and phenylacetylene (12 mg, 0.12 mmol) were added, and the reaction mixture was stirred for 24 h and then diluted with water. The aqueous layer was extracted with $CH_2Cl_2$ (2 × 5 mL). The combined organic extracts were dried over $MgSO_4$ and evaporated under vacuum. The resulting residue was purified by column chromatography (230−400 mesh silica gel, EtOAc/cyclohexane, 1:9 to 1:2) to afford γ-triazolyl amino ester **6** (15 mg) in 36% yield (two steps) as a colorless oil.

*Methyl 2-Morpholino)-4-(4-phenyl-1H-1,2,3-triazol-1-yl)-oct-3-enoate* ***6***. $^1$H NMR (400 MHz, $CDCl_3$): δ 8.01 (s, 1H), 7.80 (d, *J* = 7.1 Hz, 2H), 7.39 (t, *J* = 7.3 Hz, 2H), 7.29 (d, *J* = 7.4 Hz, 1H), 5.71 (d, *J* = 9.4 Hz, 1H), 3.75−3.70 (m, 1H), 3.69 (s, 3H), 3.65 (t, *J* = 4.4 Hz, 4H), 2.63 (t, *J* = 7.3 Hz, 2H), 2.70−2.43 (m, 4H), 1.37−1.26 (m, 4H), 0.83 (t, *J* = 7.1 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 169.9, 147.3, 141.9, 130.1, 129.0, 128.4, 125.7, 120.7, 66.6, 65.4, 52.0, 50.6, 35.9, 28.8, 21.9, 13.7. HRMS (ESI+): *m*/*z* $(M + H)^+$ calcd for $C_{21}H_{28}N_4O_3Na$, 407.2059; found, 407.2054.

## ■ ASSOCIATED CONTENT

### Supporting Information

$^1$H, $^{13}$C, and $^{11}$B NMR spectra of compounds **2a**−**i**. NOESY NMR spectrum of compound **2b**. $^1$H and $^{13}$C spectra of compounds **3**−**6**. This material is available free of charge via the Internet at http://pubs.acs.org.

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### Notes

The authors declare no competing financial interest.

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## ■ REFERENCES


(1) *Boronic acids: Preparation, Applications in Organic Synthesis and Medicine*, 2nd ed.; Hall, D. G., Ed.; Wiley VCH: Weinheim, Germany, 2011.

(2) (a) Ishiyama, T.; Matsuda, N.; Miyaura, N.; Suzuki, A. *J. Am. Chem. Soc.* **1993**, *115*, 11018. (b) Ishiyama, T.; Matsuda, N.; Murata, M.; Ozawa, F.; Suzuki, A.; Miyaura, N. *Organometallics* **1996**, *15*, 713.

(3) (a) Ishiyama, T.; Yamamoto, M.; Miyaura, N. *Chem. Lett.* **1996**, *25*, 1117. (b) Brown, S. D.; Armstrong, R. W. *J. Org. Chem.* **1997**, *62*, 7076. (c) Yavari, K.; Moussa, S.; Ben Hassine, B.; Retailleau, P.; Voituriez, A.; Marinetti, A. *Angew. Chem., Int. Ed.* **2012**, *51*, 6748. (d) Mace, A.; Tripoteau, F.; Zhao, Q.; Gayon, E.; Vrancken, E.; Campagne, J.-M.; Carboni, B. *Org. Lett.* **2013**, *15*, 906.

(4) For intramolecular versions, see: (a) Carson, M. W.; Giese, M. W.; Coghlan, M. J. *Org. Lett.* **2008**, *10*, 2701. (b) Yoshida, H.; Asatsu, Y.; Mimura, Y.; Ito, Y.; Oshita, J.; Takaki, K. *Angew. Chem., Int. Ed.* **2011**, *50*, 9676.

(5) Iwadate, N.; Sugimone, M. *J. Am. Chem. Soc.* **2010**, *132*, 2548.

(6) Baldoli, C.; Bossi, A.; Giannini, C.; Licandro, E.; Maiorana, S.; Perdicchia, D.; Schiavo, M. *Synlett* **2005**, 1137.

(7) (a) Shimizu, M.; Tomioka, Y.; Nagao, I.; Kadowaki, T.; Hiyama, T. *Chem.—Asian J.* **2012**, *7*, 1644 and references therein. (b) Lin, Q. X.; Ho, T. L. *Tetrahedron* **2013**, *69*, 2996.

(8) Yamamoto, Y. *Adv. Synth. Catal.* **2010**, *352*, 478.

(9) Mazuela, J.; Norrby, P. O.; Andersson, P. G.; Pàmies, O.; Diéguez, M. *J. Am. Chem. Soc.* **2011**, *133*, 13634.

(10) Ramirez, J.; Fernandez, E. *Synthesis* **2005**, 1698.

(11) Singleton, D. A.; Redman, A. M. *Tetrahedron Lett.* **1994**, *35*, 509.

(12) For recent reviews on the Petasis three-component coupling reaction, see: (a) Candeias, N. R.; Montalbano, F.; Cal, P. M. S. D.; Gois, P. M. P. *Chem. Rev.* **2010**, *110*, 6169. (b) Batey, R. A. In *Boronic Acids: Preparation and Applications in Organic Synthesis, Medicine and Materials*, 2nd ed.; Hall, D. G., Ed.; Wiley-VCH: Weinheim, Germany, 2011; pp 427−477. (c) Carboni, B.; Berrée, F. In *Science of Synthesis: Multicomponent Reactions*; Müller, T. J. G., Ed; Thieme: New York, 2013; Vol 5, pp 219−259.

(13) For recent selected examples, see: (a) Norsikian, S.; Soule, J. F.; Cannillo, A.; Guillot, R.; Tran Huu Dau, M. E.; Beau, J. M. *Org. Lett.* **2012**, *14*, 544. (b) Le Quement, S. T.; Flagstad, T.; Mikkelsen, R. J.; Hansen, M. R.; Givskov, M. C.; Nielsen, T. E. *Org. Lett.* **2012**, *14*, 640. (c) Li, Y.; Xu, M. H. *Org. Lett.* **2012**, *14*, 2062. (d) Han, W. Y.; Wu, Z. J.; Zhang, X. M.; Yuan, W. C. *Org. Lett.* **2012**, *14*, 976. (e) Mizuta, S.; Onomura, O. *RSC Adv.* **2012**, *2*, 2266. (f) Ascic, E.; Le Quement, S. T.; Ishoey, M.; Daugaard, M.; Nielsen, T. E. *ACS Comb. Sci.* **2012**, *14*, 253. (g) Frauenlob, R.; Garcia, C.; Bradshaw, G. A.; Burke, H. M.; Bergin, E. *J. Org. Chem.* **2012**, *77*, 4445. (h) Chrzanowska, M.; Grajewska, A.; Meissner, Z.; Rozwadowska, M.; Wiatrowska, I. *Tetrahedron* **2012**, *68*, 3092. (i) Ghosal, P.; Shaw, A. K. *J. Org. Chem.* **2012**, *77*, 7627. (j) Cannillo, A.; Norsikian, S.; Retailleau, P.; Dau Tran Huu, M. E.; Iorga, B. I.; Beau, J. M. *Chem.—Eur. J.* **2013**, *19*, 9127. (k) Han, W. Y.; Zuo, J.; Zhan, X. M.; Yuan, W. C. *Tetrahedron* **2013**, *69*, 537.

(14) (a) Sharma, G. V. M; Reddy, N. Y.; Ravi, R.; Sreenivas, B.; Sridhar, G.; Chatterjee, D.; Kunwar, A. C.; Hofmann, H. J. *Org. Biomol. Chem* **2012**, *10*, 9191. (b) Sharma, G. V. M; Kodeti, S. R.; Dutta, S. K.; Velaparthi, S.; Narsimulu, K.; Anjaiah, G.; Basha, S. J.; Kunwar, A. C. *Chem.—Eur. J.* **2012**, *18*, 16046. (c) Sharma, G. V. M; Yadav, T. A.; Choudhary, M.; Kunwar, A. C. *J. Org. Chem.* **2012**, *77*, 6834. (d) Sharma, G. V. M; Sridhar, T.; Reddy, P. P.; Kunwar, A. C. *Eur. J. Org. Chem.* **2013**, 3543.

(15) (a) Berrée, F.; Gernigon, N.; Hercouet, A.; Lin, C. H.; Carboni, B. *Eur. J. Org. Chem.* **2009**, 329. (b) Tripoteau, F.; Verdelet, T.; Hercouet, A.; Carreaux, F.; Carboni, B. *Chem.—Eur. J.* **2011**, *17*, 13670. (c) Vovard-Le Bray, C.; Klein, H.; Dixneuf, P. H.; Macé, A.; Berrée, F.; Carboni, B.; Derien, S. *Adv. Synth. Catal.* **2012**, *354*, 1919.

(16) (a) Touchet, S.; Carreaux, F.; Carboni, B.; Bouillon, A.; Boucher, J.-L. *Chem. Soc. Rev.* **2011**, *40*, 3895. (b) Smoum, R.; Rubinstein, A.; Dembitsky, V. M.; Srebnik, M. *Chem. Rev.* **2012**, *112*, 4156.

(17) Jourdan, H.; Gouhier, G.; Van Hijfte, L.; Angibaud, P.; Piettre, S. R. *Tetrahedron Lett.* **2005**, *46*, 8027.

(18) For recent reviews, see: (a) Valente, C.; Organ, M. G. In *Boronic Acids: Preparation, Applications in Organic Synthesis and Medicine*, 2nd ed.; Hall, D. G., Ed.; Wiley VCH: Weinheim, Germany, 2011; pp 213−262. (b) Carboni, B.; Carreaux, F. In *Cross-Coupling and Heck-Type Reactions*; Larhed, M., Wolfe, J. P., Molander, G., Eds.; Georg Thieme: Stuttgart, Germany, 2012; pp 265−322. (c) Lennox, A. J.; Lloyd-Jones, G. C. *Angew. Chem., Int. Ed.* **2013**, *52*, 7362. (d) Lennox, A. J.; Lloyd-Jones, G. C. *Chem. Soc. Rev.* **2014**, *43*, 412−443.

(19) Tao, C. Z.; Cui, X.; Li, J.; Liu, A. X.; Liu, L.; Guo, Q. X. *Tetrahedron Lett.* **2007**, *48*, 3525.
(20) For some recent examples of this one-pot process, see: (a) Akula, H. K.; Lakshman, M. K. *J. Org. Chem.* **2012**, *77*, 8896. (b) Happ, B.; Schaefer, J.; Friebe, C.; Goerls, H.; Winter, A.; Hager, M. D.; Popp, J.; Dietzek, B.; Schubert, U. S. *Synthesis* **2012**, 2287. (c) Clouser, C.; Chauhan, J.; Bess, M. A.; Oploo, J. L.; Zhou, D.; Dimick-Gray, S.; Mansky, L. M.; Patterson, S. E. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 6642. (d) Mukherjee, N.; Ahammed, S.; Bhadra, S.; Ranu, B. C. *Green Chem.* **2013**, *15*, 389.
(21) Because of its explosiveness and toxicity, diazomethane was directly generated in diethyl ether and used without further purification after simple decantation, see: Arndt, F. *Org. Synth.* **1935**, *15*, 3; *Org. Synth.* **1943**, *II*, 165.


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