JOC*Note*

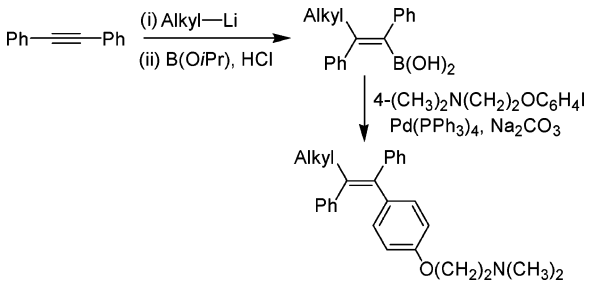
Carbolithiation of Diphenylacetylene as a Stereoselective Route to (*Z*)-Tamoxifen and Related Tetrasubstituted Olefins

Neola F. McKinley and Donal F. O'Shea*

Centre for Synthesis and Chemical Biology, School of Chemistry and Chemical Biology, University College Dublin, Belfield, Dublin 4, Ireland

donal.f.oshea@ucd.ie

Received September 21, 2006



Carbolithiation of diphenylacetylene can be exploited to generate (*E*)-1-lithio-1,2-diphenylalkyl-1-enes which can be reacted in situ with triisopropylborate to stereoselectively provide (*E*)-1,2-diphenyl-1-alkylene boronic acids. These tetrasubstituted vinylboronic acids served as versatile intermediates for the generation of tetrasubstituted olefins with retention of stereochemistry. The application of this method for the stereoselective synthesis of (*Z*)-tamoxifen and related analogues is described.

The use of (*Z*)-tamoxifen **1a** as the leading therapeutic agent for the treatment of estrogen-dependent breast cancer and other emerging clinical applications has given rise to a resurged interest in developing new selective routes to this compound class (Figure 1).[1] Notwithstanding the historical interest in

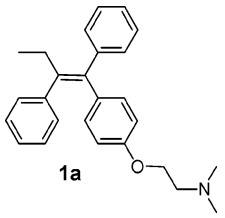
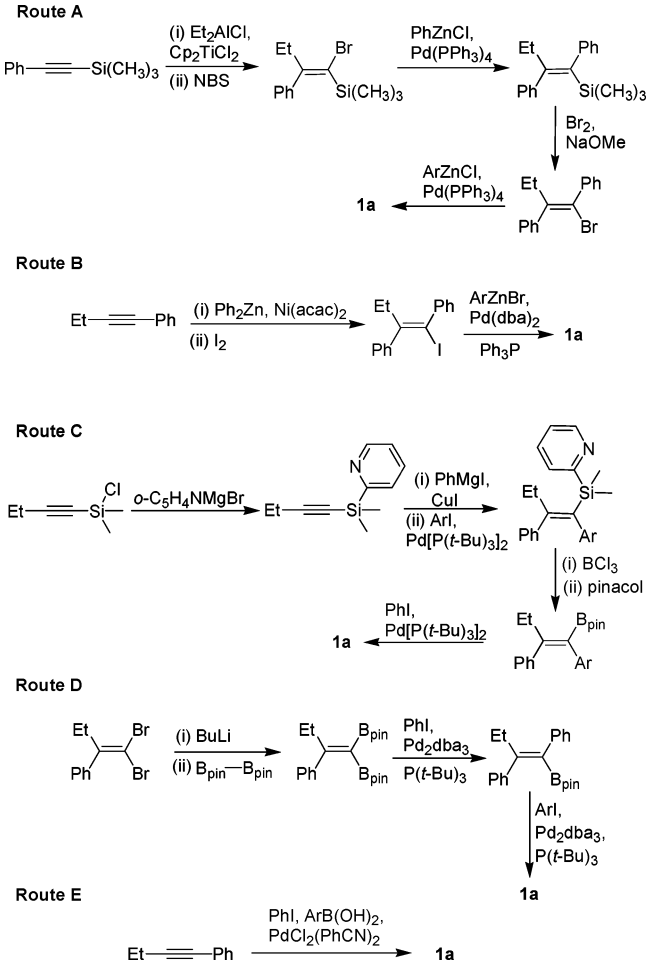


FIGURE 1. (*Z*)-Tamoxifen.

olefins such as tamoxifen, the development of concise regio- and stereoselective routes remains an ongoing challenge.[2] The majority of previously reported selective routes has utilized either carbometalation reactions or palladium-mediated cross-coupling reactions, or a combination of both, to construct the tetrasubstituted olefin.

SCHEME 1. Stereoselective Routes to (*Z*)-Tamoxifen 1a (Ar = *p*-$C_6H_4O(CH_2)_2N(CH_3)_2$)



The first of these routes exploited a carbometalation of phenyl(trimethylsilyl)acetylene with diethylaluminum chloride/titanocene dichloride to yield an organometallic intermediate, which was reacted with *N*-bromosuccinimide (NBS) to generate 1,2-diphenyl-but-1-enyl-trimethyl-silane (Scheme 1, route A).[3] This was subsequently converted in two steps to analogues of **1a**. Alternative routes have used Ni-catalyzed carbozincation of 1-phenyl-1-butyne, followed by addition of iodine to generate the (*Z*)-iodoalkene, which could be converted to **1a** by a Pd-catalyzed cross-coupling reaction with an arylzinc bromide (route B).[4] An alkynyl(2-pyridyl)silane (derived from but-1-ynyl-chloro-dimethyl-silane) has been utilized to effect a regio- and stereoselective carbomagnesation/cross-coupling sequence to generate the 1,2-diaryl-1-butenyl(2-pyridyl)silane. Subsequent conversion to an alkenylboronate ester and Suzuki−Miyaura coupling yielded **1a** (route C).[5] Route D exploited a geminal

(1) (a) Jordan, V. C. *Nat. Rev. Drug Discovery* **2003**, *2*, 205. (b) Harper, M. J. K.; Walpole, A. L. *Nature* **1996**, *212*, 87. (c) Knox, A. J. S.; Meegan, M. J.; Lloyd, D. G. *Curr. Top. Med. Chem.* **2006**, *6*, 217. (d) Lloyd, D. G.; Meegan, M. J. *IDrug* **2000**, *3*, 3177. (e) Perez-Gracia, J. L.; Carrasco, E. M. *Gynecol. Oncol.* **2002**, *84*, 201.

(2) Reiser, O. *Angew. Chem., Int. Ed.* **2006**, *45*, 2838.

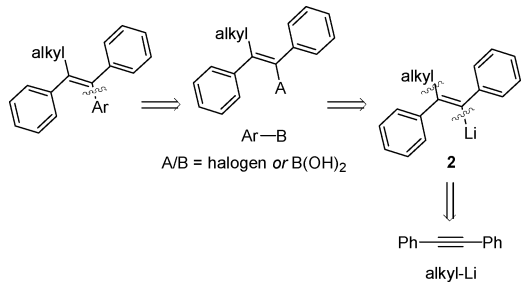
(3) Miller, R. B.; Al-Hassan, M. I. *J. Org. Chem.* **1985**, *50*, 2121.

(4) Stüdemann, T.; Knochel, P. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 93.

(5) Itami, K.; Kamei, T.; Toshida, J. *J. Am. Chem. Soc.* **2003**, *125*, 14670.

10.1021/jo061949s CCC: $33.50
Published on Web 11/11/2006

SCHEME 2. Retrosynthetic Analysis of a Carbolithiation Route to Tetrasubstituted Olefins

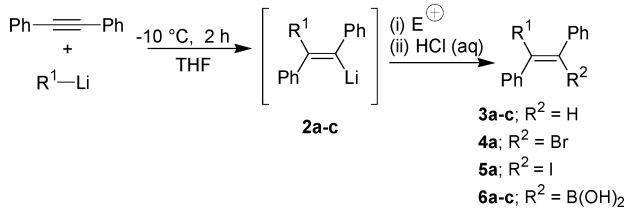


diborylation of 2,2-dibromo-1-ethyl-vinyl-benzene with bis-(pinacolato)diboron generating the 1,1-diboryl-1-alkene, which underwent successive cross-couplings with two different aryl iodides to afford **1a**.[6] The three-component coupling of 1-phenyl-1-butyne with iodobenzene and an arylboronic acid has provided **1a** in the most direct manner to date (route E).[7]

Our goal was to develop a new two-step route to **1a** and related derivatives in which the medicinal effects of structural variations in the alkyl and substituted aryl ring could be explored in a combinatorial fashion. We aimed to utilize intermolecular carbolithiation as our strategic transformation, as it has been shown to be an effective tool for organic synthesis.[8] Retrosynthetic analysis of a carbolithiation route reveals two inexpensive commercially available starting materials: diphenylacetylene and alkyllithium (Scheme 2).

The carbolithiation of diphenylacetylene was first reported in the 1960s, but its application to targeted synthetic methodology has not been previously described.[9,10] It has been shown that the carbolithiation of diphenylacetylene occurs by a syn addition to the triple bond, but a rapid isomerization through ion pair formation under specific reaction conditions can generate the thermodynamically more stable vinyllithium species **2** with a *trans*-diphenyl geometry.[11] It was anticipated that the intermediates **2** produced from this carbolithiation could be transformed in situ into either vinylboronic acids or vinyl halides by trapping with suitable electrophiles. The second step would be a Pd-catalyzed Suzuki−Miyaura cross-coupling reaction of the vinylboronic acids with aryl halides or reaction of the vinyl halides with an arylboronic acid. We envisage that for future combinatorial library generation the substituted vinylboronic acids would be more useful intermediate building blocks, but as we were in the position to compare the two complementary approaches, both were investigated. In contrast to other previously reported approaches, our starting material would be a symmetrical alkyne, which negates issues of carbometalation regioselectivity.

TABLE 1. Carbolithiation of Diphenylacetylene



	R^1	electrophile	R^2	product	isomer ratio	yield (%)[a]
1	Et	MeOH	H	**3a**	96:4[b,c]	57
2	Bu	MeOH	H	**3b**	96:4[b,c]	54
3	hexyl	MeOH	H	**3c**	96:4[b,c]	53
4	Et	Br(CH$_2$)$_2$Br	Br	**4a**	99:1[d,e]	31
5	Et	I(CH$_2$)$_2$I	I	**5a**	99:1[d,e]	30
6	Et	B(O^{i}Pr)$_3$	B(OH)$_2$	**6a**	–[f]	52
7	Bu	B(O^{i}Pr)$_3$	B(OH)$_2$	**6b**	–[f]	54
8	hexyl	B(O^{i}Pr)$_3$	B(OH)$_2$	**6c**	–[f]	51

[a] Isolated purified yield. [b] Determined by ^{1}H NMR of the crude product mixture. [c] *E*/*Z* ratio. [d] Determined by ^{1}H NMR after column chromatography purification. [e] *Z*/*E* ratio. [f] ^{1}H NMR of precipitated boronic acid indicated a single *E* stereoisomer, but because of the potential for boronic acid/boroxane mixtures in the spectra, the presence of small quantities of the *Z* isomer could not be totally ruled out.[12]

An extensive study of reaction conditions for the carbolithiation of diphenylacetylene was undertaken to identify an optimal stereochemical outcome for a series of alkyllithiums (ethyl, *n*-butyl, and *n*-hexyllithium). The carbolithiation selectivity was first assessed by protonating the lithiated intermediates **2a**−**c** with methanol, and the crude reaction products were analyzed by ^{1}H NMR. Encouragingly, it was found that the reaction of ethyl, *n*-butyl, and *n*-hexyllithium with diphenylacetylene in THF at −10 °C for 2 h, followed by treatment with methanol, generated the (*E*)-alkylstilbenes **3a**−**c** with excellent 96:4 *E*/*Z* stereoselectivity (Table 1, entries 1−3).

Treatment of **2a** with either dibromoethane or diiodoethane gave the corresponding trisubstituted vinyl halides **4a** and **5a**, respectively, also with excellent stereoselectivity (entries 4 and 5). The reaction of **2a**−**c** with triisopropyl borate and subsequent hydrolysis with aqueous acid provided the three vinylboronic acids **6a**−**c** in good isolated yields following direct precipitation from the reaction mixture. ^{1}H NMR analysis of isolated **6a**−**c** showed only one stereoisomer, but the presence of trace amounts of the other isomer could not be ruled out due to the potential for boronic acid/boroxane mixtures in the spectra (Table 1, entries 6−8).[12] To prove the stereochemical assignment of the double bond, solid-state evidence was sought and suitable crystals of **6a** were grown by the slow evaporation of a chloroform solution at room temperature. Compound **6a** crystallized as the *E*-isomer in monoclinic space group *C*2/*c* with the two phenyl rings trans to each other (Supporting Information).

The scope of the Suzuki−Miyaura cross-coupling of the vinyl halides **4a** and **5a** with a suitably functionalized arylboronic acid and the vinylboronic acids **6a**−**c** with the corresponding aryl bromide and iodide was next investigated. It was found that the reaction of **4a** and **5a** with 4-[2-(dimethylamino)ethoxy]-phenylboronic acid[7] under standard cross-coupling reaction

(6) Shimizu, M.; Nakamaki, C.; Shimono, K.; Schelper, M.; Kurahashi, T.; Hiyama, T. *J. Am. Chem. Soc.* **2005**, *127*, 12506.

(7) (a) Zhou, C.; Emrich, D. E.; Larock, R. C. *Org. Lett.* **2003**, *5*, 1579. (b) Zhou, C.; Larock, R. C. *J. Org. Chem.* **2005**, *70*, 3765.

(8) (a) Hogan, A.-M. L.; O'Shea, D. F. *J. Am. Chem. Soc.* **2006**, *128*, 10360. (b) Hogan, A.-M. L.; O'Shea, D. F. *Org. Lett.* **2006**, *8*, 3769. (c) Cottineau, B.; O'Shea, D. F. *Tetrahedron Lett.* **2005**, *46*, 1935. (d) Kessler, A.; Coleman, C. M.; Charoenying, P.; O'Shea, D. F. *J. Org. Chem.* **2004**, *69*, 7836. (e) Coleman, C. M.; O'Shea, D. F. *J. Am. Chem. Soc.* **2003**, *125*, 4054. (f) Clayden, J. *Organolithiums: Selectivity for Synthesis*; Pergamon Press: Oxford, U.K., 2002; pp 273−335.

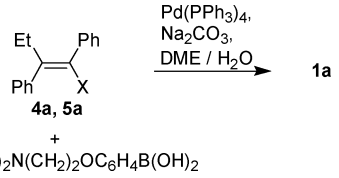
(9) Mulvaney, J. E.; Gardlund, Z. G.; Gardlund, S. L. *J. Am. Chem. Soc.* **1963**, *85*, 3897.

(10) Carbolithiation of ether-substituted alkynes has provided a stereoselective route to tetrasubstituted alkenes: Hojo, M.; Murakami, Y.; Aihara, H.; Sakuragi, R.; Baba, Y.; Hosomi, A. *Angew. Chem., Int. Ed.* **2001**, *40*, 621.

(11) Bauer, W.; Feigel, M.; Müller, G.; von Ragué Schleyer, P. *J. Am. Chem. Soc.* **1988**, *110*, 6033.

(12) Bruns, S.; Sinnwell, V.; Voss, J. *Magn. Reson. Chem.* **2003**, *41*, 269.

TABLE 2. Synthesis of (*Z*)-Tamoxifen from 4a and 5a



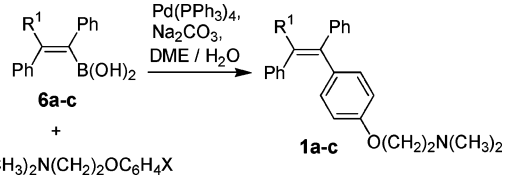
entry	substrate	X	product	*Z*/*E*[a]	yield (%)[b]
1	**4a**	Br	**1a**	98:2	67
2	**5a**	I	**1a**	98:2	73

[a] Determined by ^{1}H NMR of the crude product mixture. [b] Isolated purified yield.

conditions ($Pd(PPh_3)_4$ catalyst, Na_2CO_3, DME/H_2O, reflux) provided the desired product **1a** in a 67% and 73% yield, respectively, with a *Z*/*E* selectivity of 98:2 for both reactions (Table 2).

When the coupling partners were reversed, the reaction of vinylboronic acid **6a** with the substituted aryl bromide (BrC_6H_4O-$(CH_2)_2N(CH_3)_2$) provided **1a** in a 65% yield but a lower *Z*/*E* selectivity of 90:10 (Table 3, entry 1). We were pleased to discover that an improved 73% yield and 98:2 *Z*/*E* selectivity were obtained by using the more reactive aryl iodide in the reaction (entry 2). It was also possible to generate the alkyl chain extended tamoxifen analogues **1b** and **1c** in good yields and high selectivities by reaction with the substituted aryl iodide (entries 3 and 4).

TABLE 3. Reaction of 1,2-Diphenyl-1-alkylene Boronic Acids 6a−c with Aryl Halides



entry	substrate	R^1	X	product	*Z*/*E*[a]	yield (%)[b]
1	**6a**	Et	Br	**1a**	90:10	65
2	**6a**	Et	I	**1a**	98:2	73
3	**6b**	Bu	I	**1b**	98:2	62
4	**6c**	Hex	I	**1c**	95:5	68

[a] Determined by ^{1}H NMR of the crude product mixture. [b] Isolated purified yield.

As it is known that the reactions of sterically hindered boronic acids often suffer from competing formation of protodeboronation byproducts, the crude product mixtures were examined for the generation of **3a**−**c**.[13] In each case, no protodeboronation products were observed but 1,2-diphenyl-ketones **7a**−**c** were observed in very low yields; for example, **7a** was isolated in 5% yield from the cross-coupling reaction of **6a** (Figure 2).

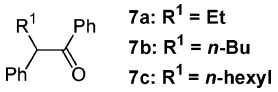


FIGURE 2. Cross-coupling byproduct.

These byproducts could be viewed as a formal oxidation of the boronic acid to generate a 1,2-diphenyl-alkyl-1-en-1-ol which would equilibrate to the ketone **7a**.[14] Indeed, the reaction of **6a** with hydrogen peroxide under basic conditions did generate **7a**, and subjecting **6a** to the coupling reaction conditions in the absence of aryl halide increased the isolated yield of **7a** to 22%. Compound **7a** was not formed from the reactions of the vinyl halides **4a** or **5a** with the substituted arylboronic acid.

In summary, a concise highly stereoselective two-step synthesis of tetrasubstituted alkenes with specific application to tamoxifen and related analogues has been described. The synthesis from commercially available starting materials of the key trisubstituted vinylboronic acids allows variation of the alkyl group and the use of cross-coupling chemistry to insert the final aryl ring. The application of these vinylboronic acids for tetrasubstituted olefin library generation is currently being explored.

Experimental Section

(*Z*)-Tamoxifen (1a). [2-(4-Iodo-phenoxy)-ethyl]-dimethyl-amine (0.058 g, 0.20 mmol) and $Pd(PPh_3)_4$ (0.012 g, 0.01 mmol) were added to a Schlenk tube. The tube was evacuated and backfilled three times, and DME (4 mL) was added. The reaction mixture was stirred at room temperature under N_2 in the dark for 20 min. Sodium carbonate (0.021 g, 0.20 mmol), water (1 mL), and **6a** (0.10 g, 0.40 mmol) were added, and the reaction was heated at reflux under N_2 for 18 h. The reaction mixture was cooled to room temperature, and the solvent was removed under reduced pressure. The product was extracted into diethylether, washed with brine, and concentrated. Column chromatography on silica gel gave the product as a colorless solid (0.054 g, 73% yield, mp 95−97 °C). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.90 (t, J = 7.5 Hz, 3H), 2.26 (s, 6H), 2.42 (q, J = 7.5 Hz, 2H), 2.67 (t, J = 5.7 Hz, 2H), 3.91 (t, J = 5.7 Hz, 2H), 6.54 (d, J = 6.7 Hz, 2H), 6.75 (d, J = 6.7 Hz, 2H), 7.10−7.36 (m, 10H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 12.6, 28.0, 44.7, 57.2, 64.5, 112.4, 125.0, 125.5, 126.8, 127.1, 128.4, 130.8, 134.6, 137.2, 140.3, 141.4, 142.8, 155.6. IR (KBr disk, cm^{-1}) 2252, 1606. ES-MS: *m*/*z* 372.3 $[M + H]^+$. HRMS: calcd for $C_{26}H_{30}NO$, 372.2327; found, 372.2318 $[M + H]^+$.

{2-[4-(1,2-Diphenyl-hex-1-enyl)-phenoxy]-ethyl}-dimethyl-amine (1b). [2-(4-Iodo-phenoxy)-ethyl]-dimethyl-amine (0.038 g, 0.13 mmol) and $Pd(PPh_3)_4$ (0.008 g, 0.007 mmol) were added to a Schlenk tube. The tube was evacuated and refilled with N_2 three times, and DME (4 mL) was added. The reaction mixture was stirred at room temperature under N_2 in the dark for 20 min. Sodium carbonate (0.014 g, 0.13 mmol), water (1 mL), and **6b** (0.075 g, 0.27 mmol) were added, and the reaction was heated at reflux under N_2 for 18 h. The reaction mixture was cooled to room temperature, and the solvent was removed under reduced pressure. The product was extracted into diethylether, washed with brine, and concentrated. Column chromatography on silica gel gave the product as a colorless solid (0.032 g, 62% yield, mp 67−68 °C). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.74 (t, J = 7.2 Hz, 3H), 1.16 (m, 4H), 2.28 (s, 6H), 2.37 (m, 3H), 2.62 (t, J = 5.8 Hz, 2H), 3.90 (t, J = 5.8 Hz, 2H), 6.54 (d, J = 8.8 Hz, 2H), 6.74 (d, J = 8.8 Hz, 2H), 7.10−7.16 (m, 6H), 7.19−7.36 (m, 4H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 14.1, 23.0, 31.4, 35.9, 46.1, 58.5, 65.9, 113.6, 126.2, 126.7, 128.1, 128.3, 129.7, 129.8, 132.0, 135.8, 138.7, 140.4, 143.0, 144.0, 157.0. IR (neat, cm^{-1}) 2954, 2856, 2363, 1604. ES-MS: *m*/*z* 400.5 $[M + H]^+$. HRMS: calcd for $C_{28}H_{34}NO$, 400.2640; found, 400.2628 $[M + H]^+$.

{2-[4-(1,2-Diphenyl-oct-1-enyl)-phenoxy]-ethyl}-dimethyl-amine (1c). [2-(4-Iodo-phenoxy)-ethyl]-dimethyl-amine (0.047 g,

(13) (a) Suzuki, A. *Pure Appl. Chem.* **1994**, *66*, 213. (b) Brown, S. D.; Armstrong, R. W. *J. Am. Chem. Soc.* **1996**, *118*, 6331.

(14) For examples of oxidation byproducts with arylboronic acids, see: (a) Yin, J.; Rainka, M. P.; Zhang, X.-X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 1162. (b) Adamo, C.; Amatore, C.; Ciofini, I.; Jutand, A.; Lakmini, H. *J. Am. Chem. Soc.* **2006**, *128*, 6829.

0.16 mmol) and $Pd(PPh_3)_4$ (0.009 g, 0.008 mmol) were added to a Schlenk tube. The tube was evacuated and refilled with N_2 three times, and DME (4 mL) was added. The reaction mixture was stirred at room temperature under N_2 in the dark for 20 min. Sodium carbonate (0.017 g, 0.16 mmol), water (1 mL), and **6c** (0.10 g, 0.32 mmol) were added, and the reaction was heated at reflux under N_2 for 18 h. The reaction mixture was cooled to room temperature, and the solvent was removed under reduced pressure. The product was extracted into diethylether, washed with brine, and concentrated. Column chromatography on silica gel chromatography gave the product as a colorless solid (0.047 g, 68% yield, mp 66−67 °C). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.79 (t, J = 7.0 Hz, 3H), 1.12 (m, 8H), 2.28 (s, 6H), 2.37 (m, 2H), 2.62 (t, J = 5.8 Hz, 2H), 3.91 (t, J = 5.8 Hz, 3H), 6.54 (d, J = 8.8 Hz, 2H), 6.75 (d, J = 8.8 Hz, 2H), 7.10−7.22 (m, 6H), 7.24−7.36 (m, 4H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 14.0, 22.5, 28.8, 29.3, 31.5, 35.8, 45.9, 58.3, 65.7, 113.4, 125.9, 126.5, 127.8, 128.1, 129.5, 129.6, 131.8, 135.6, 138.4, 140.3, 142.8, 143.8, 156.8. IR (neat, cm^{-1}) 3051, 2856, 1606, 1508. ES-MS: *m*/*z* 428.5 [M + H]$^+$. HRMS: calcd for $C_{30}H_{38}NO$, 428.2953; found, 428.2961 [M + H]$^+$.

(*E*)-1,2-Diphenyl-1-butene Boronic Acid (6a). Diphenylacetylene (0.60 g, 3.36 mmol) in THF (2 mL) at −10 °C was treated dropwise with ethyllithium (1.10 mL of 1.48 M solution in dibutylether, 1.68 mmol) and stirred for a further 2 h. The reaction mixture was cooled to −78 °C and treated with triisopropyl borate (1.8 mL, 7.6 mmol). The reaction was allowed to warm to room temperature, and HCl (5 mL of 2 M solution) was added. THF was removed under reduced pressure, and the resulting precipitate formed was filtered and washed with cold pentane (25 mL) to give the product as a colorless solid (0.216 g, 51% yield, mp 83−85 °C). ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 0.73 (t, J = 7.4 Hz, 3H), 2.26 (q, J = 7.4 Hz, 2H), 7.17−7.20 (m, 4H), 7.23−7.34 (m, 4H), 7.40−7.42 (m, 2H), 7.55 (s, 2H). ^{13}C NMR (DMSO-d_6, 75 MHz) δ: 14.2, 26.2, 126.2, 127.4, 128.5, 128.6, 128.6, 128.7, 143.4, 144.2, 146.0. ^{11}B NMR (DMSO-d_6) δ: 19.3. IR (KBr disk, cm^{-1}) 2520, 2263, 1596. ES-MS: *m*/*z* 251.2 [M − H]$^-$. HRMS: calcd. for $C_{16}H_{16}BO_2$, 251.1244; found, 251.1543 [M − H]$^-$.

(*E*)-1,2-Diphenyl-1-hexene Boronic Acid (6b). Diphenylacetylene (0.60 g, 3.36 mmol) in THF (2 mL) at −10 °C was treated dropwise with *n*-butyllithium (1.0 mL of 1.70 M solution in hexanes, 1.68 mmol) and stirred for a further 2 h. The reaction mixture was cooled to −78 °C and treated with triisopropyl borate (2.3 mL, 10.1 mmol). The reaction was allowed to warm to room temperature, and HCl (5 mL of 2 M solution) was added. THF was removed under reduced pressure, and the resulting precipitate was filtered and washed with cold pentane (25 mL) to give the product as a colorless solid (0.25 g, 54% yield, mp 85−87 °C). ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 0.63 (t, J = 7.0 Hz, 3H), 1.08 (m, 4H), 2.25 (t, J = 7.0 Hz, 2H), 7.17−7.19 (m, 4H), 7.22−7.32 (m, 4H), 7.33−7.41 (m, 2H), 7.53 (s, 2H). ^{13}C NMR (DMSO-d_6, 125 MHz) δ: 14.4, 22.5, 31.1, 32.6, 126.1, 127.3, 128.4, 128.6, 128.6, 128.7, 143.4, 144.5, 144.6. ^{11}B NMR (DMSO-d_6) δ: 19.7. IR (KBr disk, cm^{-1}) 2508, 2360, 1571. ES-MS: *m*/*z* 279.3 [M − H]$^-$. HRMS calcd. for $C_{18}H_{20}BO_2$, 279.1556; found, 279.1561 [M − H]$^-$.

(*E*)-1,2-Diphenyl-1-octene Boronic Acid (6c). Diphenylacetylene (0.60 g, 3.36 mmol) in THF (2 mL) at −10 °C was treated dropwise with *n*-hexyllithium (0.80 mL of 2.10 M solution in hexane, 1.68 mmol) and stirred for a further 2 h. The reaction mixture was cooled to −78 °C and treated with triisopropyl borate (2.3 mL, 10.1 mmol). The reaction was allowed to warm to room temperature, and HCl (5 mL of 2 M solution) was added. THF was removed under reduced pressure, and the resulting precipitate was filtered and washed with cold pentane (25 mL) to give the product as a colorless solid (0.26 g, 51% yield, mp 79−81 °C). ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 0.72 (t, J = 7.6 Hz, 3H), 0.99 (m, 8H), 2.24 (t, J = 7.63 Hz, 2H), 7.17−7.41 (m, 10H), 7.55 (s, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 14.5, 22.6, 28.7, 29.0, 31.5, 32.8, 126.2, 127.3, 128.4, 128.5, 128.6, 128.7, 143.4, 144.5, 144.7. ^{11}B NMR (DMSO-d_6) δ: 20.0. IR (KBr disk, cm^{-1}) 2528, 2260, 1602. ES-MS: *m*/*z* 308.3 [M + H]$^+$. HRMS calcd. for $C_{20}H_{24}BO_2$, 307.1869; found, 307.1884 [M + H]$^+$.

1,2-Diphenyl-butan-1-one (7a). 6a (0.20 g, 0.80 mmol) was treated at room temperature with a solution of saturated sodium bicarbonate (15 mL) and 30% hydrogen peroxide (3.3 mL) for 2 h. The reaction solution was then extracted with diethyl ether (3 × 20 mL), and the organic layers were combined, washed with brine (20 mL), dried over sodium sulfate, and reduced. The resulting yellow oil was purified by column chromatography on silica gel yielding the product as a colorless solid (0.032 g, 17% yield, mp 48−49 °C). ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 0.91 (t, J = 7.15 Hz, 3H), 1.85 (m, 1H), 2.19 (m, 1H), 4.46 (t, J = 7.15 Hz, 1H), 7.22−7.23 (m, 1H), 7.29−7.33 (m, 4H), 7.39−7.42 (m, 2H), 7.48−7.51 (m, 1H), 7.97−7.99 (m, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz) 12.5, 27.4, 55.7, 127.2, 128.5, 128.7, 128.9, 129.1, 133.0, 137.3, 139.9, 200.3. IR (KBr disk, cm^{-1}) 1657, 1523. ES-MS: *m*/*z* 247.2 [M + Na]$^+$.

Acknowledgment. We thank Dr. D. Rai and Dr. H. Mueller-Bunz for analytical services. This work was funded under the Program for Research in Third-Level Institutions administered by the HEA.

Supporting Information Available: Experimental procedures for **3a**−**c**, **4a**, and **5a**, ^{1}H and ^{13}C spectra for **1a**−**c**, **3a**−**c**, **4a**, **5a**, **6a**−**c**, and **7a**, and X-ray crystallographic data for **6a** (CCDC 612612). This material is available free of charge via the Internet at http://pubs.acs.org.

JO061949S