Synthesis of Novel Quinone Boronic Ester Derivatives via a Highly Regioselective Cr-Mediated Benzannulation Reaction and Their Application in Pd-Catalyzed Coupling Processes

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This paper describes the synthesis and reactivity of a novel class of quinone boronic esters. These compounds are prepared utilizing a highly regioselective Dötz annulation of Fischer carbene complexes with alkynylboronates. All substrates studied to date provided a single regioisomeric arylboronic ester product; the origin of this selectivity is discussed in the context of steric and electronic effects. Additionally, these compounds have been found to undergo Pd-catalyzed coupling reactions with a range of aryl and allyl halides and provides a strategy for the selective and predictable preparation of highly substituted quinones and hydroquinones. Finally, the propensity of this technique to prepare highly functionalized aromatic compounds in an expeditious fashion is demonstrated in the total synthesis of dimeric carbazole (±)-bis-*N*-dimethylbismurrayaquinone-A **33**.

Introduction

Arylboronic acids and their esters are among the most widely used synthetic intermediates in organic synthesis. In particular, their facile transformation into other functional groups[1] and their ability to undergo efficient carbon−carbon bond-forming coupling reactions[2] has kept them at the forefront of modern organic chemistry. In the context of arylboronic ester synthesis, these compounds are generally prepared through a functional group interconversion strategy from an appropriate aryl halide. Traditional approaches include metal−halogen exchange followed by addition of a trialkylborate.[3] More recently, the groups of Miyaura and Masuda have reported the palladium-catalyzed coupling reaction of aryl halides with tetraalkoxydiboranes[4] and dialkoxyboranes,[5] respectively, which provides a particularly effective route to arylboronic pinacol esters under mild conditions.

Despite the success of the aforementioned methods, they all rely on the availability of an appropriate aryl halide as a prerequisite, which can present problems when more complex and heavily functionalized arylboronic esters are required. With a view to addressing this issue, we have embarked upon a program toward the development of techniques that would provide arylboronic esters through a benzannulation protocol. Unlike conventional methods for formation of arylboronic esters, which rely on the formation of the arene−boron bond, we envisaged that our benzannulation strategy could utlilize readily available alkynyl boronate esters as precursors. In this paper, we wish to describe an account of our studies toward the application of the Dötz annulation reaction with boronate containing alkynes in the synthesis of novel arylboronic esters.[6] Additionally, we wish to report the effectiveness of these novel arylboronic esters in palladium-catalyzed carbon−carbon bond-forming reactions.

The reaction between chromium Fischer carbene complexes and alkynes was first reported by Dötz in 1975[7] and has since received considerable attention from a number of research groups.[8] It is undoubtedly one of the most widely used metal-mediated transformations in organic synthesis; a reflection of this is that even 25 years after its initial discovery it is still the subject of intense research and development with respect to both synthetic applications and mechanistic issues.[9] The importance of this reaction as a synthetic tool stems from the ability to construct highly substituted benzenoid compounds from simple starting materials in one step with a high degree of regiochemical control.[9b,10]

In the context of boron-containing alkynes, we not only anticipated that the reaction products would be versatile synthetic intermediates but also were intrigued by the potential regiochemical consequences of this benzannulation process. As outlined in Scheme 1, this cycloaddition

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(1) For the conversion of arylboronic acids to phenols, see: Webb, K. S.; Levy D. *Tetrahedron Lett.* **1995**, *36*, 5117. For their conversion to aryl halides, see: Thiebes, C. T.; Surya Prakash, G. K.; Petasis, N. A.; Olah, G. *Synlett* **1998**, 141.

(2) For comprehensive reviews, see: (a) Suzuki, A. *Pure Appl. Chem.* **1994**, *66*, 213. (b) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.

(3) Vaultier, M.; Carboni, B. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, 1995; Vol. 11, p 191.

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(6) The preliminary communication of this work has been reported: Davies, M. W.; Johnson, C. N.; Harrity, J. P. A. *Chem. Commun.* **1999**, 2107.

(7) Dötz, K. H. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 644.

(8) (a) For recent reviews, see: Dötz, K. H.; Tomuschat, P. *Chem. Soc. Rev.* **1999**, *28*, 187. (b) Wulff, W. D. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, 1995; Vol. 12, p 469. (c) Dötz, K. H. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 587.

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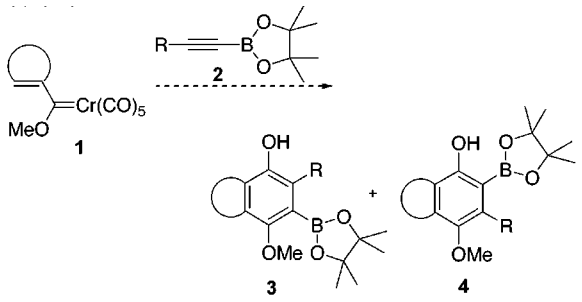
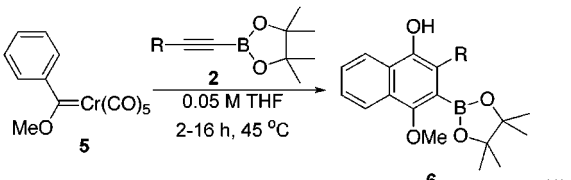
Scheme 1



reaction can, in principle, provide products **3** and **4**. It is generally understood that dialkyl-substituted alkynes undergo insertion with poor to moderate levels of regioselectivity, although electronically/sterically biased alkynes can prove to be useful exceptions. Indeed, the employment of alkynylsilanes[11] and -stannanes,[11] ethers,[10d] and amines[12] has been addressed with mixed success; alkynylsilanes are generally poorly regioselective, alkynyl ethers give good selectivity but undergo inefficient cycloaddition, and alkynylamines do not provide benzenoid products. In sharp contrast, alkynylstannanes undergo efficient benzannulation with exquisite levels of selectivity, although the products are prone to protodestannylation. Not surprisingly, therefore, although the Dötz reaction has been used extensively in total synthesis, terminal alkynes have been employed almost exclusively[13] in order to avoid such regioisomeric product mixtures since terminal alkynes react with a much higher degree of regioselective fidelity.

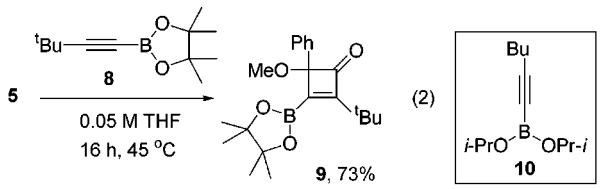
Results and Discussion

Benzannulation Regiochemistry. Initial benzannulation studies were carried out using readily available aryl Fischer carbene complexes[14] and alkynylboronates[15] of varying steric size. Consequently, we examined the cycloaddition of complex **5** with alkynes **2a**−**d** and were pleased to discover that these substrates reacted smoothly to provide arylboronate products in good yield. Additionally, and significantly, we discovered that both aryl- and alkyl-substituted alkynes provided the corresponding arylboronic ester **6** as single regioisomers (eq 1, entries 2−4). In contrast, the employment of 2-ethynyl-4,4,5,5-tetramethyl[1,3,2]dioxaborolane **2a** resulted in complete reversal of regioselectivity to provide **7a**, remarkably, with none of the corresponding regioisomer being detected by ^{1}H NMR spectroscopy. The product regiochemistry can be readily assigned by ^{1}H NMR on inspection of the phenolic −OH proton resonance, which shows a characteristic broad signal at around δ 5.0 ppm for compounds **6**, whereas regioisomer **7** shows a sharp singlet at around δ 8.2 ppm. The latter signal is presumably shifted downfield due to hydrogen bonding with the oxygen of the adjacent boronate moiety. Finally, the sterically hindered *tert*-butyl substituted alkynylboronates **8** led only to the formation of cyclobutenone **9** (eq 2). This result is in accordance with Yamashita's observations that bulky electron-deficient alkynes provide cyclobutenone products at the expense of benzannulated compounds.[10d] Nonetheless, again a single regioisomer was observed and the product displayed an analogous insertion pattern to **2b**−**d**. All attempts to use isopropoxyboronic esters such as **10** failed to furnish characterizable benzannulation products.

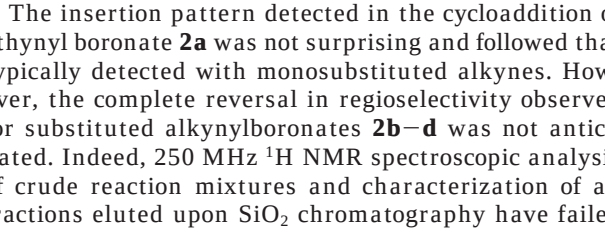


Entry	Alkyne	R	Product
1	**2a**	H	**7a; 50%**
2	**2b**	Me	**6b; 53%**
3	**2c**	Bu	**6c; 73%**
4	**2d**	Ph	**6d; 64%**

(1)



The insertion pattern detected in the cycloaddition of ethynyl boronate **2a** was not surprising and followed that typically detected with monosubstituted alkynes. However, the complete reversal in regioselectivity observed for substituted alkynylboronates **2b**−**d** was not anticipated. Indeed, 250 MHz ^{1}H NMR spectroscopic analysis of crude reaction mixtures and characterization of all fractions eluted upon SiO_2 chromatography have failed to identify in all cases any minor regioisomers.[16] Three possible rationales can be put forward for the high selectivity observed in the insertion of the boronate group in alkynes **2b**−**d** in the more hindered position adjacent to the MeO group. In general, regiochemical insertion appears to be sterically controlled and is proposed to be determined during the formation of a η^1,η^3-vinylcarbene intermediate.[17] Indeed, as outlined in Figure 1, the insertion may simply be sterically controlled and therefore follows traditional patterns where the boronate unit



(2)

(9) For recent discussions on the reaction mechanism, see: (a) Barluenga, J.; Aznar, F.; Gutiérrez, I.; Martín, A.; García-Granda, S.; Amparo Llorca-Baragaño *J. Am. Chem. Soc.* **2000**, *122*, 1314. (b) Waters, M. L.; Bos, M. E.; Wulff, W. D. *J. Am. Chem. Soc.* **1999**, *121*, 6403. (c) Waters, M. L.; Brandvold, T. A.; Isaacs, L.; Wulff, W. D.; Rheingold, A. L. *Organometallics* **1998**, *17*, 429. (d) Hsung, R. P.; Quinn, J. F.; Weisemberg, B. A.; Wulff, W. D.; Yap, G. P. A.; Rheingold, A. L. *Chem. Commun.* **1997**, 615. (e) Gross, M. F.; Finn, M. G. *J. Am. Chem. Soc.* **1994**, *116*, 10921. (e) Wulff, W. D.; Bax, B. M.; Brandvold, T. A.; Chan, K. S.; Gilbert, A. M.; Hsung, R. P.; Mitchell, J.; Clardy, J. *Organometallics* **1994**, *13*, 102. (f) Bos, M. E.; Wulff, W. D.; Miller, R. A.; Chamberlin, S.; Brandvold, T. A. *J. Am. Chem. Soc.* **1991**, *113*, 9293.

(10) For studies on the regioselectivity of the benzannulation reaction see: (a) Wulff, W. D.; Tang, P. C.; McCallum, J. S. *J. Am. Chem. Soc.* **1981**, *103*, 7677. (b) Dötz, K. H.; Muhlemeier, J.; Schubert, U.; Orama, O. *J. Organomet. Chem.* **1983**, *247*, 187. (c) Wulff, W. D.; Chan, K. S.; Tang, P. C. *J. Org. Chem.* **1984**, *49*, 2293. (d) Yamashita, A.; Toy, A. *Tetrahedron Lett.* **1986**, *27*, 3471.

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(13) The utilization of an intramolecular cycloaddition strategy can prove to be an effective solution to this problem: Semmelhack, M. F.; Bozell, J. J.; Keller, L.; Sato, T.; Spiess, E. J.; Wulff, W.; Zask, A. *Tetrahedron* **1985**, *41*, 5803.

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(15) (a) Brown, H. C.; Bhat, N. G.; Srebnik, M. *Tetrahedron Lett.* **1988**, *29*, 2631. (b) For a review of alkynylboronates, see: Negishi, E. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon: Oxford, 1983; Vol. 7, p 337.

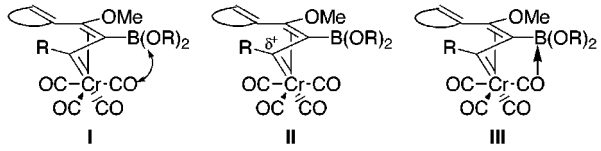


Figure 1. Rationale for the regiochemical insertion.

is acting as the less sterically demanding group (**I**).[18] Alternatively, the vinylcarbene intermediate **II** may be electronically more favored than its regioisomer due to the instalment of the electron-withdrawing boronate unit away from the electrophilic carbene carbon atom, or alternatively, through lone-pair stabilization at this site by the adjacent O-heteroatom. Finally, a model proposed by Wulff to explain the contrasteric insertion of alkynylstannanes in the benzannulation process may be invoked whereby the regiochemistry is controlled by a Lewis acid/base interaction [CO → $B(OR)_2$] in the metallohexatriene intermediate, thus directing regiochemical insertion via **III**.[11]

We were surprised to find that minor quantities of deboronated cycloaddition products were generated in the reactions outlined in eq 1. Although the origin of these compounds has not been unambiguously established, it likely arises from the protodeboronation of **2** by the phenolic product (probably as the chromium tricarbonyl arene complexes in the first instance) followed by the annulation of the corresponding terminal alkyne. Indeed, the hydrolysis of alkynylboronates to the parent alkyne in the presence of mild proton donors has been described by Brown and co-workers.[15a] A number of factors pointed to this conclusion: (1) The deboronated products are isolated with identical regiochemistry to those resulting from the corresponding terminal alkyne annulation. (2) Small quantities of 1-hexyne were recovered from the volatile material isolated from the reaction mixture outlined in eq 1, entry 3, providing circumstantial evidence for this notion. (3) The arylboronic acid products are remarkably robust to deboronation. For example, an ether solution of these compounds show minimal decomposition (and <5% deboronation by 250 MHz ^{1}H NMR) after stirring for 24 h in the presence of 0.1 M aqueous HNO_3.

Preparation of Quinone Boronic Esters. The direct oxidation of the hydroquinones formed in the Dötz reaction provides a facile and routine method for the isolation of the corresponding quinones. Indeed, we were pleased to find that the CAN oxidation of our arylboronic esters proceeded smoothly and provided the corresponding quinone boronic esters as stable orange crystalline solids or oils. In addition, these quinones represent a novel class of boronic esters that clearly hold great potential as synthetic intermediates (see later). We investigated the scope of the benzannulation process for the direct synthesis of quinone boronic esters after CAN oxidation of the crude reaction mixture, and the results are summarized in Table 1.

The reaction appeared to tolerate both polar and nonpolar solvents, although THF gave consistently higher yields and was used throughout the remainder of the study. Promotion of the reaction using dry state conditions[19] (entry 3) was not successful and served only to provide deboronated quinone **14b** albeit in high yield. This result served to confirm the acid lability of the alkynylboronate substrates, since the hydroquinone products were found to be stable under these conditions. In extending the reaction to the furan complex **12**, we found that higher reaction temperatures and longer reaction times were required for complete conversion and resulted in the recovery of larger quantities of deboronated products (entries 6 and 7, Table 1). Nonetheless, quinones **17a** and **18a** were again isolated as single regioisomers. Finally, the cyclohexenyl complex **13** was found to participate smoothly in the cycloaddition process providing the corresponding quinone **19a** in high yield (entry 8, Table 1).

Palladium-Catalyzed Coupling Reactions. Having an efficient route to novel quinone containing boronic esters in hand, we next turned our attention to the synthetic elaboration of these intermediates. We had found that these compounds rapidly oxidized in the presence of basic hydrogen peroxide to provide the corresponding hydroxyquinones.[6] However, we were keen to develop carbon−carbon bond-forming functionalization of these intermediates and specifically uncover suitable conditions for the Suzuki coupling reaction of these compounds with aryl halides. We were aware of the potential for electron-deficient arylboronic esters to readily undergo protodeboronation[20] and therefore decided to investigate the scope of this coupling process under nonaqueous basic conditions.[21]

We investigated a range of conditions for the coupling of quinone **15a** with common coupling partners aryl bromides and aryl triflates. $Pd(Ph_3P)_4$ was found to be a poor catalyst system and provided undesired **15b** as the major product from both aryl triflates and bromides (entries 1−3, Table 2).[22] Indeed, it appears that aryl triflates do not react smoothly in the coupling process under the conditions outlined in Table 2, giving predominantly deboronated material **15b**. The optimum conditions for the coupling process of quinone **15a** with bromobenzene were found using 5 mol % of $PdCl_2$(dppf) as catalyst,[23] the solvent of choice being dioxane, leading to a 98% yield of the desired quinone (entry 5, Table 2). The reaction also proceeded efficiently at lower catalyst

(16) We are currently attempting to independently prepare the alternative regioisomers so that an accurate assessment of regioselectivity by more sensitive chromatographic techniques can be employed. The regiochemistry of **7a** was definitively assigned by NOE experiment (see the Supporting Information for details). The regiochemistry of compounds **6c** and **9** was elucidated by X-ray crystal structure analysis (see ref 6); all other regiochemical assignments are inferred from the shift values of the phenolic hydroxyls as discussed in the text.

(17) (a) Hofmann, P.; Hämmerle, M. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 908. (b) Hofmann, P.; Hämmerle, M, Unfried, G. *New J. Chem.* **1991**, *15*, 761.

(18) We assume that the boronate unit is small in comparison to an alkyl/aryl substituent since it bears an O−B−O array that centers on an sp^2-hybridized boron atom. Yamashita has demonstrated that a correlation exists between substituent *A* value and benzannulation regiochemistry;[10d] however, we have not been able to locate literature *A* values for the boronic ester moiety and therefore anticipate that we will have to ascertain these data experimentally.

(19) (a) Harrity, J. P. A.; Kerr, W. J.; Middlemiss, D. *Tetrahedron Lett.* **1993**, *34*, 2995. (b) Harrity, J. P. A.; Kerr, W. J.; Middlemiss, D. *Tetrahedron* **1993**, *49*, 5565.

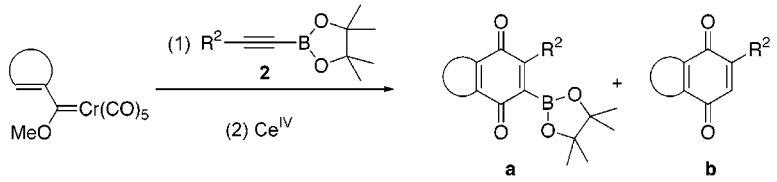
(20) For a discussion, see: Zhang H.; Chan, K. S. *Tetrahedron Lett.* **1996**, *37*, 1043 and references therein.

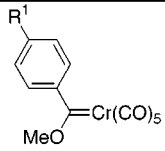
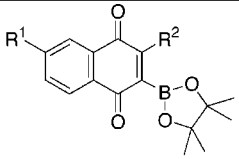
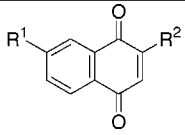
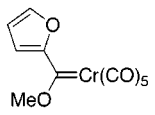
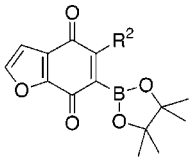
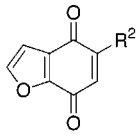
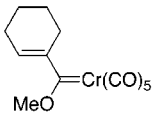
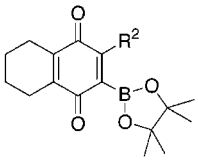
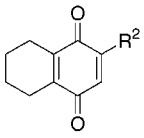
(21) Watanabe, T.; Miyaura, N.; Suzuki, A. *Synlett* **1992**, 207.

(22) Control reactions in the absence of Pd catalyst showed rapid conversion of the quinone boronic esters to the appropriate protodeboronated material; therefore, efficient transition metal catalyzed coupling is essential to minimize formation of protodeboronated byproducts.

(23) Hayashi, T.; Konishi, M.; Kobori, Y.; Kumada, M.; Higuchi, T.; Hirotsu, K. *J. Am. Chem. Soc.* **1984**, *106*, 158.

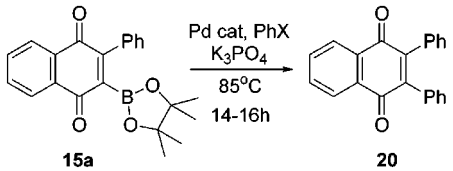
Table 1. Synthesis of Quinone Boronic Esters



Entry	Complex	R^2	Conditions[a]	Boronic Ester, % Yield	Protodeboronation, % Yield
					
1	R^1=H **5**	Bu	A	**14a**; 66	**14b**; 6
2	R^1=H **5**	Bu	B	**14a**; 62	**14b**; 35
3	R^1=H **5**	Bu	C	**14a**; 0	**14b**; 84
4	R^1=H **5**	Ph	A	**15a**; 57	**15b**; 12
5	R^1=Me **11**	Ph	D	**16a**; 45	**16b**; 15
					
6	**12**	Bu	D	**17a**; 47	**17b**; 30
7	**12**	Ph	D	**18a**; 35	**18b**; 42
					
8	**13**	Ph	D	**19a**; 83	**19b**; 14

[a] Reaction conditions: reaction mixtures were heated in 0.05 M solvent with 3 equiv of alkyne until complete consumption of starting complex was observed. The crude reaction mixture was then dissolved in ether and stirred for 0.5 h with 0.5 M Ce(IV) in 0.1 M aq HNO_3. Key: (A) THF, 45 °C; (B) hexane 45 °C; (C) SiO_2, 45 °C; (D) THF, 65 °C.

Table 2. Optimization of Pd-Catalyzed Coupling of Quinone Boronic Ester 15a[a]

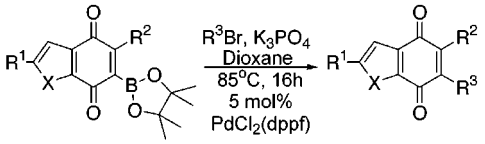


entry	X	catalyst	solvent	**20**, % yield[b]	
1	OTf	$Pd(PPh_3)_4$	DMF		(48)
2	Br	$Pd(PPh_3)_4$	DMF	15	(85)
3	Br	$Pd(PPh_3)_4$	dioxane		(63)
4	OTf	$PdCl_2$(dppf)	dioxane	17	(61)
5	Br	$PdCl_2$(dppf)	dioxane	98	(0)
6	Br	$PdCl_2$(dppf)	DMF	38[c]	(0)
7	Br	$PdCl_2$(dppf)	dioxane	80[d]	(18)
8	Br	$PdCl_2$(dppf)/dppf	dioxane		(90)

[a] Reaction conditions: a solution of **15a**, PhX (2 equiv), K_3PO_4 (3 equiv), and catalyst (5 mol %) in a 0.025 M solution of the appropriate solvent was heated until the starting material was consumed. [b] Yields in parentheses refer to protodeboronated material **15b**. [c] Isolated from a complex reaction mixture. [d] 2 mol % catalyst used in this case.

loadings (entry 7, Table 2) although the coupling process was generally more capricious. Finally, it was found that the addition of a catalyst equivalent of dppf had an adverse effect on the coupling reaction, again furnishing considerable quantities of deboronated starting material (entry 8, Table 2).

Table 3. Coupling Reactions of Quinone Boronic Esters[a]

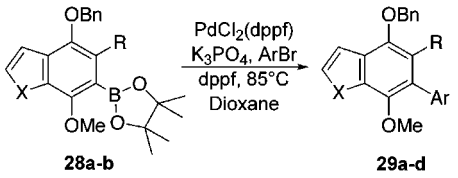


entry	R^1	R^2	X	R^3	product, % yield
1	H	Ph	CH=CH	*p*-$MeOC_6H_4$	**21**, 74
2	H	Ph	CH=CH	*p*-$CF_3C_6H_4$	**22**, 80
3	H	Bu	O	C_6H_5	**23**, 96
4	H	Bu	O	*p*-$CF_3C_6H_4$	**24**, 97
5	Me	Bu	CH=CH	C_6H_5	**25**, 82
6	Me	Ph	CH=CH	C_6H_5	**26**, 88
7	H	Ph	CH=CH	CH_2=$CHCH_2$	**27**, 67

[a] Reaction conditions: See Table 2, entry 5.

Having uncovered conditions for the efficient Suzuki coupling of **15a** with bromobenzene, we briefly explored the scope of the coupling process with respect to quinone boronic esters and arylbromides (Table 3). We have found that these coupling reactions take place with good to

Table 4. Coupling Reactions of Hydroquinone Boronic Esters[a]



28a-b **29a-d**

entry	X	R	Ar	reaction time (h)	**29**, % yield[b]
1	CH=CH	Bu	C_6H_5	16[c]	**a**, 9 (69)
2	CH=CH	Bu	C_6H_5	16	**a**, 39 (45)
3	CH=CH	Bu	C_6H_5	72	**a**, 69 (23)
4	CH=CH	Bu	C_6H_5	72[d]	**a**, 83 (10)
5	CH=CH	Bu	*p*-$MeOC_6H_4$	40	**b**, 0 (96)
6	CH=CH	Bu	*p*-$CF_3C_6H_4$	72	**c**, 64 (36)
7	O	Ph	C_6H_5	72	**d**, 33 (64)

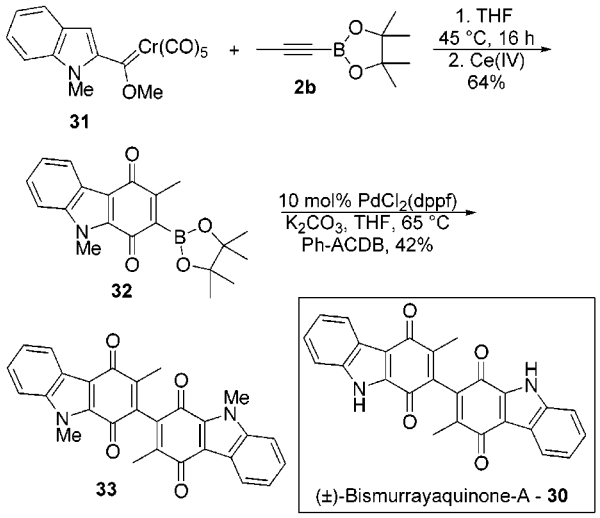
[a] Reaction conditions: a solution of **28**, PhX (2 equiv), K_3PO_4 (3 equiv), dppf (5 mol %), and $PdCl_2$(dppf) (5 mol %) in a 0.025 M solution of dioxane heated until the starting material was consumed. [b] Yields in parentheses refer to recovered starting material. [c] No dppf added. [d] 10 mol % dppf added.

excellent levels of efficiency with electron-rich and electron-deficient aryl bromides. Importantly, as exemplified in entries 3−5, *this protocol permits the assembly of unsymmetrical quinone products in high yield as single regioisomers using the two-step boronate annulation/coupling strategy*. Moreover, these products would constitute the *minor* regioisomers resulting from the traditional benzannulation of the corresponding disubstituted acetylenes and, therefore, contribute greatly to the scope of this cycloaddition technique. In addition to aryl bromides, this method was found to be readily extended to allyl bromide substrates as exemplified by the example in entry 7 of Table 3.

Having confirmed the synthetic potential of quinone boronates, we investigated the Suzuki coupling reaction of hydroquinone boronic esters. We found these substrates slowly underwent aerobic oxidation to the corresponding quinones and therefore protected the phenolic −OH as a benzyl ether for convenience before undertaking the Pd-catalyzed reactions.[24] These compounds were isolated as stable crystalline solids and could be stored indefinitely under N_2 at low temperature.

Once again, a range of coupling conditions was investigated, the results of which are summarized in Table 4. We were concerned that the highly substituted boronic ester substrates would participate sluggishly in the coupling process. Indeed, the reactions proceeded very slowly and led to poor yields of desired product. The Pd catalyst appeared to be precipitating from solution during the extended reaction times and we therefore added a catalyst equivalent of dppf ligand. We were pleased to find that this slight modification permitted good to excellent yields of coupled products to be obtained, although long reaction times were still required (compare entries 2 and 3, Table 4). Notably, unlike the reactions of the quinone boronic esters, protodeboronation proceeded very slowly and the crude reaction mixtures were generally free of byproducts. Overall, we found the reaction to tolerate electron withdrawing groups on the aryl coupling partner, but electron rich aryl halides did not participate in the coupling reaction in a satisfactory manner. Indeed, as exemplified in entry 5, Table 4 the only isolated compound from the reaction between hydroquinone **28a** and 4-methoxy bromobenzene after 40 h at 85 °C was a 96% recovery of starting material.

Scheme 2



Both Tables 3 and 4 illustrate the power of this sequential annulation/coupling protocol for the synthesis of unsymmetrical quinones and hydroquinones with reliable and predictable regiochemistry and with very high levels of regioselectivity. In the case of quinone boronic esters, the coupling process appears to be viable for electron-rich and -poor aromatic bromides as well as allylic bromides, although the corresponding hydroquinone coupling reactions require further optimization.

Oxidative Coupling Reactions. The effectiveness of quinone boronic esters in metal-catalyzed coupling reactions prompted us to investigate their participation in oxidative coupling reactions. We envisaged that this technique would hold great potential for the highly convergent and selective preparation of symmetrical quinone dimers, given the broad scope of Fischer carbene complexes that participate in the benzannulation reaction with both alkyl- and aryl-substituted alkynylboronates.

In an effort to exemplify this strategy, we investigated the benzannulation of known indolyl complex **31**[25] with propynylboronate **2b**, which provided quinone **32** as a dark red powder in good yield following in situ oxidation. Once again, a single regioisomer was detected which was isolated from the reaction mixture by trituration in hexane. The oxidative-coupling step was carried out in the presence of phenyl acrylate dibromide (Ph-ACDB) according to the protocol of Tamao[26] and furnished the symmetrical quinone dimer **33**, a close analogue of carbazole alkaloid (±)-bismurrayaquinone-A **30**,[27] in moderate yield (Scheme 2).

(24) Benzylation of the hydroquinones was carried out as follows: Hydroquinone dissolved in THF was treated with 2 equiv of KH at 25 °C followed by benzyl bromide and 0.2 equiv of tetra-*n*-butylammonium iodide and the reaction mixture stirred for 2 h. The product was isolated after aqueous workup and chromatographic purification. Spectroscopic data for compounds **28a** and **28b** can be found in the Supporting Information.

(25) Bauta, W. E.; Wulff, W. D.; Pavkovic, S. F.; Zaluzec, E. J. *J. Org. Chem.* **1989**, *54*, 3249

(26) Yamaguchi, S.; Ohno, S.; Tamao, K. *Synlett* **1997**, 1199.

(27) (a) Ito, C.; Thoyama, Y.; Omura, M.; Kajiura, I.; Furukawa, H. *Chem. Pharm. Bull.* **1993**, *41*, 2096. (b) Bringmann, G.; Ledermann, A.; Stahl, M.; Gulden, K.-P. *Tetrahedron*, **1995**, *51*, 9353. (c) Murphy, W. S.; Bertrand, M. *J. Chem. Soc., Perkin Trans. 1* **1998**, 4115.

Conclusions

In conclusion, we have demonstrated the effectiveness of alkynylboronates in the rapid assembly of highly functionalized aromatic boronic esters. The high regioselectivity observed in this reaction is surprising and may be rationalized by a combination of steric and electronic factors in the case of substituted alkynyl boronic esters. In contrast, the terminal alkynylboronate shows a complete reversal of selectivity that is consistent with regioselective insertion through steric control.

The product quinone and hydroquinone boronic esters have been shown to undergo Pd-catalyzed coupling reactions. The investigation of more diverse coupling partners and the application of this methodology in target-orientated synthesis is currently underway in our laboratories, and we believe that this methodology is complementary to, and in many cases holds significant advantages over, the Dötz annulation of internal alkyne substrates for the preparation of highly substituted hydroquinone and quinone containing compounds.

Experimental Section

General Procedures. Infrared (IR) spectra were recorded on a Perkin-Elmer Paragon 100 FTIR spectophotometer, ν_{max} in cm^{-1}. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). ^1H NMR spectra were recorded on a Bruker AC-250 (250 MHz). Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CHCl_3$, δ 7.27 ppm; CH_2Cl_2, δ 5.32 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet, app = apparent), coupling constants (Hz), and assignment. ^{13}C NMR spectra were recorded on a Bruker AC-250 (62.9 MHz) or AMX-400 (100.6 MHz) with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent as the internal reference ($CDCl_3$, δ 77.0 ppm; CD_2Cl_2, δ 53.8 ppm). Elemental analysis was performed using a Perkin-Elmer 2400 CHN elemental analyzer. High-resolution mass spectra were obtained using a Kratos MS 80 spectrometer supported by a DS 90 data system. All reactions were conducted in flame-dried glassware under an inert atmosphere of dry nitrogen. All reagents were used as received unless otherwise stated. Tetrahydrofuran and dioxane were distilled from sodium metal/benzophenone ketyl; hexane was distilled from sodium metal. All complexes[14] and alkynylboronates[15] were prepared following literature procedures.

Representative Experimental Procedure for Benzannulation Reactions. 2-Butyl-4-methoxy-3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)naphthalen-1-ol 6c. The typical experimental procedure was as exemplified by benzannulation of complex **5** and alkyne **2c**. To a solution of **5** (102 mg, 0.327 mmol) in THF (6.4 mL) was added alkyne **2c** (204 mg, 0.980 mmol) via syringe under nitrogen. The reaction mixture was stirred at 45 °C for 14 h and concentrated by rotary evaporation. Purification of the resulting residue by silica gel chromatography provided boronate ester **6c** (85 mg, 73%), which was crystallized from hexanes to provide an amber solid. Mp = 116−116.5 °C. ^1H NMR (250 MHz, $CDCl_3$): δ 0.96 (3H, t, J = 7.3 Hz, CH_3CH$_2$), 1.42 (12H, s, CH_3), 1.47−1.72 (4H, m, CH$_2$CH$_2$CH$_3$), 2.73 (2H, app t, J = 7.9 Hz, C=CCH_2), 3.91 (3H, s, CH_3O), 4.93 (1H, br s, O*H*), 7.39−7.53 (2H, m, Ar-*H*) 7.95−8.03 (1H, m, Ar-*H*), 8.05−8.13 (1H, m, Ar-*H*). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 14.1, 24.7, 24.9, 30.2, 33.0, 63.5, 84.0, 121.6, 122.0, 124.3, 125.2, 125.9, 126.6, 144.4, 153.9. FTIR: 3445 (br), 2991 (m), 2977 (m), 1662(m), 1142 (s) cm^{-1}. Anal. Calcd for $C_{21}H_{29}BO_4$: C, 70.80; H, 8.20. Found: C, 70.67; H, 8.36.

4-Methoxy-2-methyl-3-(4,4,5,5-tetramethyl[1,3,2]dioxaborolan-2-yl)naphthalen-1-ol 6b. Following the representative procedure, **6b** was isolated as a cream-colored solid. Mp = 187.1−190.9 °C**.** ^1H NMR (250 MHz, $CDCl_3$): δ 1.44 (12H, s, CH_3), 2.38 (3H, s, Ar-CH_3), 3.93 (3H, s, CH_3O), 4.95 (1H, br s, O*H*), 7.38−7.51 (2H, m, Ar-*H*), 7.95−8.12 (2H, m, Ar-*H*). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 15.2, 24.9, 63.6, 84.3, 119.3, 121.7, 122.0, 125.1, 125.9, 126.5, 126.8, 144.9, 153.8. FTIR: 3596 (br), 2981 (m), 2936 (m), 1662 (m), 1141 (s) cm^{-1}. HRMS: calcd for $C_{18}H_{23}BO_4$ 314.1689, found 314.1680.

4-Methoxy-2-phenyl-3-(4,4,5,5-tetramethyl[1,3,2]-dioxaborolan-2-yl)naphthalen-1-ol 6d. Following the representative procedure, **6d** was isolated as an orange oil. ^1H NMR (250 MHz, $CDCl_3$): δ 1.11 (12H, s, CH_3), 3.98 (3H, s, CH_3O), 5.32 (1H, br s, O*H*), 7.37−7.54 (7H, m, Ar-*H*), 8.01−8.10 (1H, m, Ar-*H*), 8.19−8.27 (1H, m, Ar-H). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 24.6, 63.5, 83.9, 121.9, 122.9, 123.5, 126.0, 126.1, 126.2, 127.6, 128.1, 129.1, 130.7, 136.9, 144.2, 153.0. FTIR: 3544 (br s), 3065 (w), 2982 (m), 2938 (m), 1663 (m), 1296 (s) cm^{-1}. HRMS: calcd for $C_{23}H_{25}BO_4$ 376.1846, found 376.1859.

4-Methoxy-2-(4,4,5,5-tetramethyl[1,3,2]dioxaborolan-2-yl)naphthalen-1-ol 7a. Following the representative procedure, **7a** was isolated as a clear oil. ^1H NMR (250 MHz, $CDCl_3$): δ 1.40 (12H, s, CH_3), 3.97 (3H, s, CH_3O), 6.85 (1H, s, Ar-*H*), 7.45−7.59 (2H, m, Ar-*H*), 8.15−8.29 (2H, m, Ar-*H*), 8.32 (1H, s, O*H*). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 24.9, 55.7, 84.5, 106.4, 121.8, 123.0, 125.1, 125.7, 127.4, 129.1, 148.2, 155.9. FTIR: 3421 (br), 2999 (m), 2982 (m), 1633 (m), 1139 (s) cm^{-1}. HRMS: calcd for $C_{17}H_{21}BO_4$ 300.1533, found 300.1518.

2-*tert*-Butyl-4-methoxy-4-phenyl-3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)cyclobut-2-enone 9. Following the representative procedure, **9** was isolated as a pale green crystalline solid. Mp = 112−114 °C. ^1H NMR (250 MHz, $CDCl_3$): δ 1.17 (12H, s, CH_3C(O)), 1.20 (9H, s, CH_3C), 3.32 (3H, s, CH_3O), 7.16−7.31 (3H, m, Ar-*H*), 7.35−7.44 (2H, m, Ar-*H*). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 24.6, 28.0, 33.2, 53.3, 84.9, 102.0, 126.4, 128.0, 128.3, 138.0, 175.2. FTIR: 3051 (w), 2976 (m), 1756 (s) cm^{-1}. Anal. Calcd for $C_{21}H_{29}BO_4$: C, 70.80; H, 8.20. Found: C, 70.71; H, 8.22.

Representative Experimental Procedure for Preparation of Quinone Boronates. 2-Butyl-3-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)[1,4]naphthoquinone 14a. The typical experimental procedure was as exemplified by benzannulation of complex **5** and alkyne **2c**. To a solution of **5** (100 mg, 0.320 mmol) in THF (6.4 mL) was added alkyne **2c** (195 mg, 0.940 mmol) via syringe under nitrogen. The reaction mixture was stirred at 45 °C for 14 h and concentrated by rotary evaporation. The residue was dissolved in 5 mL of ether and treated with 8 equiv of 0.5 M ceric ammonium nitrate in 0.1 M $HNO_{3(aq)}$. The reaction mixture was stirred at room temperature for 30 min and quenched with water. The product was extracted with ether, and purification of the resulting residue by silica gel chromatography provided quinone **14b**[28] (4 mg, 6%) and boronate ester **14a** (71 mg, 66%) as a yellow oil. ^1H NMR (250 MHz, $CDCl_3$): δ 0.93 (3H, t, J = 7.3 Hz, CH_3CH$_2$), 1.40 (12H, s, CH_3), 1.43−1.58 (4H, m, CH$_2$CH$_2$CH$_3$), 2.55 (2H, app t, J = 7.3 Hz, C=CCH_2), 7.63−7.71 (2H, m, Ar-*H*), 7.95−8.09 (2H, m, Ar-*H*). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 13.9, 23.2, 24.8, 30.6, 32.3, 84.9, 125.9, 126.4, 132.1, 132.4, 133.4, 133.5, 156.1, 184.5, 188.1. FTIR: 3072 (w), 2959 (m), 2931 (m), 2872 (m), 1662 (s), 1596 (m) cm^{-1}. HRMS: calcd for $C_{20}H_{25}BO_4$ 339.1882, found 339.1879.

2-Phenyl-3-(4,4,5,5-tetramethyl[1,3,2]dioxaborolan-2-yl)[1,4]naphthoquinone 15a. Following the representative procedure, **15b**[19b] and **15a** were isolated as yellow solids. **15a**. Mp = 140.7−141.4 °C. ^1H NMR (250 MHz, $CDCl_3$): δ 1.18 (12H, s, CH_3), 7.40−7.47 (5H, m, Ar-*H*), 7.70−7.79 (2H, m, Ar-*H*), 8.04−8.16 (2H, m, Ar-*H*). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 24.6, 85.0, 125.9, 126.8, 127.9, 129.3, 129.7, 132.1, 132.4, 133.7, 133.8, 134.4, 152.9, 183.9, 188.2. FTIR: 3012 (w), 2924 (m), 1662 (s), 1596 (m) cm^{-1}. Anal. Calcd for $C_{22}H_{21}BO_4$: C, 73.36; H, 5.88. Found: C, 73.21; H, 5.82.

6-Methyl-3-phenyl-2-(4,4,5,5-tetramethyl[1,3,2]-dioxaborolan-2-yl)[1,4]naphthoquinone 16a. Following

(28) Yamashita A.; Ayako, S.; Schaub, R. G.; Bach, M. K.; White, G. J.; Toy, A. *J. Med. Chem.* **1990**, *33*, 775.

the representative procedure, **16b**[29] and **16a** were isolated as yellow solids. **16a**. Mp = 177.3−178.2 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.18 (12H, s, CH_3), 2.50 (3H, s, ArCH_3), 7.40−7.45 (5H, m, Ar-*H*), 7.51−7.56 (1H, m, Ar-*H*), 7.89−7.91 (1H, m, Ar-*H*), 7.97 (1H, d, J = 7.9 Hz). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 21.9, 24.6, 85.0, 126.2, 127.1, 128.0, 129.2, 129.7, 130.2, 132.0, 134.5, 144.8, 152.7, 184.2, 188.1. FTIR: 2983 (m), 2930 (w), 1664 (s), 1645 (s), 1605 (s) cm^{-1}. HRMS: calcd for $C_{23}H_{23}BO_4$ 374.1689, found 374.1682. Anal. Calcd for $C_{23}H_{23}BO_4$: C, 73.82; H, 6.19. Found: C, 73.77; H, 6.15.

5-Butyl-6-(4,4,5,5-tetramethyl[1,3,2]dioxaborolan-2-yl)-benzo[*b*]furan-4,7-dione 17a. Following the representative procedure, **17b**[28] and **17a** were isolated as yellow oils. **17a**. ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.85 (3H, t, J = 7.0 Hz, CH_3-CH_2), 1.34 (12H, s, CH_3), 1.35−1.47 (4H, m, CH_2CH_2CH$_3$), 2.44 (2H, app t, J = 7.9 Hz, C=CCH_2), 6.73 (1H, d, J = 1.8 Hz, C_3H), 7.57 (1H, d, J = 1.8 Hz, C_2H)). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 13.9, 23.1, 24.8, 29.8, 32.6, 85.0, 107.9, 127.9, 147.5, 151.2, 154.7, 178.6, 182.7. FTIR: 2959 (m), 2872 (m), 1660 (s), 1575 (w) cm^{-1}. HRMS: calcd for $C_{18}H_{23}BO_5$ 329.1679, found 329.1674. Anal. Calcd for $C_{18}H_{23}BO_5$: C, 65.48; H, 7.02. Found: C, 65.27; H, 7.12.

5-Phenyl-6-(4,4,5,5-tetramethyl[1,3,2]dioxaborolan-2-yl)benzo[*b*]furan-4,7-dione 18a. Following the representative procedure, **18b** and **18a** were isolated as yellow solids. **18a**. Mp = 180.0−182 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.15 (12H, s, CH_3), 6.86 (1H, d, J = 1.8 Hz, C_3H), 7.34−7.44 (5H, m, Ar-*H*), 7.69 (1H, d, J = 1.8 Hz, C_2H). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 24.5, 85.1, 108.2, 127.9, 128.0, 129.3, 129.8, 133.7, 147.9, 151.1, 151.6, 178.3, 182.1. FTIR: 2978 (w), 1659 (s) cm^{-1}. Anal. Calcd for $C_{20}H_{19}BO_5$: C, 68.60; H, 5.47. Found: C, 68.25; H, 5.51. **18b**. Mp = 146−148 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 6.74 (1H, s, C_6H), 6.84 (1H, d, J = 1.8 Hz, C_3H), 7.30−7.50 (5H, m, Ar-*H*), 7.67 (1H, d, J = 1.8 Hz, C_2H). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 108.5, 128.5, 128.6, 129.5, 130.0, 132.7, 132.8, 147.0, 148.1, 151.0, 175.2, 181.9. FTIR: 3125 (m), 1656 (s), 1565 (m) cm^{-1}. HRMS: calcd for $C_{14}H_8O_3$ 224.0473, found 224.0463.

2-Phenyl-3-(4,4,5,5-tetramethyl[1,3,2]dioxaborolan-2-yl)-5,6,7,8-tetrahydro[1,4]naphthoquinone 19a. Following the representative procedure, **19b** and **19a** were isolated as yellow oils. **19a**. ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.16 (12H, s, CH_3), 1.64−1.74 (4H, m, Cy-*H*), 2.40−2.50 (4H, m, Cy-*H*), 7.32−7.40 (5H, m, Ar-*H*). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 21.0, 21.2, 22.4, 22.8, 24.5, 84.8, 127.9, 129.2, 129.6, 134.3, 142.4, 142.8, 150.5, 186.2, 190.6. FTIR: 3054 (w), 2983 (m), 2942 (m), 2865 (w), 1644 (s), 1628 (m), 1131 (s) cm^{-1}. HRMS: calcd for $C_{22}H_{25}BO_4$ 364.1846, found 364.1835. **19b**. ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.64−1.78 (4H, m, Cy-*H*), 2.39−2.56 (4H, m, Cy-*H*), 6.78 (1H, s, C=C*H*), 7.31−7.52 (5H, m, Ar-*H*). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 21.0, 21.2, 22.4, 22.9, 128.4, 129.2, 129.7, 132.4, 133.3, 142.2, 142.7, 145.6, 186.6, 187.6. FTIR: 3056 (w), 2938 (m), 2862 (w), 1650 (s), 1213 (s) cm^{-1}. HRMS: calcd for $C_{16}H_{14}O_2$ 238.0994, found 238.0989.

Representative Experimental Procedure for Pd-Catalyzed Couplings of Quinone Boronates. 2,3-Diphenyl-[1,4]naphthoquinone 20. The typical experimental procedure was as exemplified by coupling of quinone **15a** with bromobenzene. A solution of quinone **15a** (34 mg, 0.094 mmol) and bromobenzene (30 mg, 0.189 mmol) in dioxane (3.8 mL) was treated with potassium phosphate (60 mg, 0.283 mmol) and dichloro[1,1′-bis(diphenylphosphino)ferrocene]palladium-(II) dichloromethane adduct (3.9 mg, 0.0048 mmol) and heated at 85 °C for 16 h. The reaction mixture was diluted with water (5 mL) and extracted with DCM (3 × 5 mL). The organic layer was washed with brine, dried over $MgSO_4$, and purified chromatographically to provide quinone **20** (29 mg, 98%), which had spectroscopic and physical characteristics identical to those of authentic material.[19b]

2-(4-Methoxyphenyl)-3-phenyl[1,4]naphthoquinone 21. Following the representative procedure, quinone **21** was isolated as a orange oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ 3.76 (3H, s, CH_3O), 6.75 (2H, d, J = 8.8 Hz, Ar-*H*), 7.00 (2H, d, J = 8.8 Hz, Ar-*H*), 7.06−7.12 (2H, m, Ar-*H*), 7.21−7.29 (3H, m, Ar-*H*), 7.74−7.82 (2H, m, Ar-*H*), 8.14−8.22 (2H, m, Ar-*H*). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 55.2, 113.2, 125.3, 126.5, 126.6, 127.7, 128.1, 130.6, 132.2, 132.3, 133.6, 133.7, 133.8, 145.1, 145.3, 159.5, 184.7, 185.0. FTIR: 3054 (w), 2960 (m), 2936 (m), 1664 (s), 1289 (s) cm^{-1}. HRMS: calcd for $C_{23}H_{16}O_3$ 340.1099, found 340.1094.

2-Phenyl-3-(4-trifluoromethylphenyl)[1,4]naphthoquinone 22. Following the representative procedure, quinone **22** was isolated as a yellow solid. Mp = 126.0−127.4 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.01−7.08 (2H, m, Ar-*H*), 7.16−7.29 (5H, m, Ar-*H*), 7.49 (2H, d, J = 8.2 Hz, Ar-*H*) 7.77−7.85 (2H, m, Ar-*H*), 8.15−8.24 (2H, m, Ar-*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 124.6 (q, J = 3.8 Hz, *C*H−C−CF_3), 126.6 (q, J = 272.4 Hz, *C*F_3), 126.7, 126.8, 127.8, 128.6, 129.7 (q, J = 32.0 Hz, *C*-CF_3), 130.4, 130.9, 131.9, 132.0, 132.5, 134.0, 134.1, 137.0, 144.3, 146.4, 184.3, 184.4. FTIR: 2962 (m), 1665 (s), 1597 (m), 1324 (s), 1128 (s) cm^{-1}. HRMS: calcd for $C_{23}H_{13}FO_2$ 378.0867, found 378.0858.

5-Butyl-6-phenyl-benzo[*b*]furan-4,7-dione 23. Following the representative procedure, quinone **23** was isolated as an yellow solid. Mp = 68.0−69.6 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.76 (3H, t, J = 7.0 Hz, CH_3CH$_2$), 1.13−1.43 (4H, m, CH_2CH_2), 2.36 (2H, app t, J = 8.1 Hz, C=CCH_2), 6.87 (1H, d, J = 1.8 Hz, C_3H), 7.12−7.20 (2H, m, Ar-*H*), 7.39−7.49 (3H, m, Ar-*H*, C_2H), 7.68 (1H, d, J = 1.8 Hz, C_2H). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 13.6, 22.9, 27.5, 32.0, 108.0, 128.2, 128.5, 129.2, 132.7, 135.5, 143.27, 146.6, 150.9, 152.3, 175.5, 183.0. FTIR: 3065 (w), 2962 (m), 2933 (m), 1668 (s), 1572 (m), 1362 (m), 1143 (m) cm^{-1}. Anal. Calcd for $C_{18}H_{16}O_3$: C, 77.12; H, 5.75. Found: C, 76.83; H, 5.81.

5-Butyl-6-(4-trifluoromethylphenyl)benzo[*b*]furan-4,7-dione 24. Following the representative procedure, quinone **24** was isolated as a yellow solid. Mp = 80.0−81.3 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.77 (3H, t, J = 7.0 Hz, CH_3CH$_2$), 1.13−1.43 (4H, m, CH_2CH_2), 2.36 (2H, app t, J = 7.3 Hz, C=CCH_2), 6.89 (1H, d, J = 1.8 Hz, C_3H), 7.31 (2H, d, J = 7.9 Hz, Ar-*H*), 7.68−7.75 (3H, m, Ar-*H*, C_2H). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 13.6, 22.9, 27.6, 32.0, 108.2, 124.0 (q, J = 272.3 Hz, *C*F_3), 125.2 (q, J = 3.8 Hz, *C*HCCF_3), 128.4, 129.8, 130.6 (q, J = 32.4 Hz, *C*-CF_3), 136.5, 142.0, 147.2, 148.1, 150.7, 174.9, 182.5. FTIR: 3152 (w), 3132 (w), 2962 (m), 2873 (m), 1669 (s), 1172 (s), 1126 (s) cm^{-1}. Anal. Calcd for $C_{19}H_{15}F_3O_3$: C, 65.52; H, 4.34. Found: C, 65.73; H, 4.59.

3-Butyl-6-methyl-2-phenyl[1,4]naphthoquinone 25. Following the representative procedure, quinone **25** was isolated as a yellow oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.76 (3H, t, J = 7.3 Hz, CH_3CH$_2$), 1.14−1.47 (4H, m, CH_2CH_2CH$_3$), 2.42 (2H, app t, J = 7.3 Hz, C=CCH_2), 2.50 (3H, s, Ar-CH_3), 7.16−7.23 (2H, m, Ar-*H*), 7.39−7.57 (4H, m, Ar-*H*), 7.90−8.01 (2H, m, Ar-*H*). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 13.7, 21.9, 22.9, 24.6, 27.9, 31.8, 126.7, 128.1, 128.3, 128.9, 129.9, 132.2, 133.8, 134.4, 144.6, 146.2, 148.1, 184.5, 185.8. FTIR: 3058 (w), 2861 (w), 1661 (s), 1601 (s), 1300 (s) cm^{-1}. HRMS: calcd for $C_{21}H_{20}O_2$ 304.1463, found 304.1464.

6-Methyl-2,3-diphenyl[1,4]naphthoquinone 26. Following the representative procedure, quinone **26** was isolated as a yellow crystalline solid which had identical spectroscopic and physical characteristics to authentic material.[19b]

2-Allyl-3-phenyl-[1,4]naphthoquinone 27. Following the representative procedure, quinone **27** was isolated as a yellow solid. Mp = 88.1−89.5 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 3.16 (2H, dt, J = 6.4, 1.5 Hz, CH_2), 4.87 (1H, ddd, J = 17.1, 1.5, 1.5 Hz, C=CH_a), 4.94 (1H, ddd, J = 10.1, 1.5, 1.5 Hz, C=CH_b), 5.76 (1H, ddt, J = 17.1, 10.1, 6.4 Hz, *H*C=CH$_2$), 7.18−7.28 (2H, m, Ar-*H*), 7.38−7.51 (3H, m, Ar-*H*), 7.68−7.80 (2H, m, Ar-*H*), 8.06−8.19 (2H, m, Ar-*H*). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 32.5, 117.0, 126.4, 126.6, 128.1, 128.6, 129.0, 132.1, 132.2, 133.2, 133.7, 133.8, 134.6, 145.2, 146.9, 184.6, 185.1. FTIR: 3064 (w), 2991 (w), 2929 (w), 1665 (s), 1596 (m), 1294 (s) cm^{-1}. HRMS: calcd for $C_{19}H_{14}O_2$ 274.0994, found 274.0980. Anal. Calcd for $C_{19}H_{14}O_2$: C, 83.19; H, 5.14. Found: C, 82.73; H, 4.88.

Representative Experimental Procedure for Pd-Catalyzed Couplings of Hydroquinone Boronates. 1-Ben-

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zyloxy-2-butyl-4-methoxy-3-phenylnaphthalene 29a. The typical experimental procedure was as exemplified by coupling of hydroquinone **28a** with bromobenzene. A solution of hydroquinone **28a** (175 mg, 0.39 mmol) and bromobenzene (124 mg, 0.79 mmol) in dioxane (15 mL) was treated with potassium phosphate (250 mg, 1.18 mmol), dichloro[1,1′-bis(diphenylphosphino)ferrocene]palladium(II) dichloromethane adduct (16 mg, 0.022 mmol), and (diphenylphosphino)ferrocene (11 mg, 0.020 mmol) and heated at 85 °C for 72 h. The reaction mixture was diluted with water (5 mL) and extracted with DCM (3 × 5 mL). The organic layer was washed with brine, dried over $MgSO_4$, and purified chromatographically to provide hydroquinone **29a** (107 mg, 69%) as a clear oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.72 (3H, t, J = 7.3 Hz, CH_3CH$_2$), 1.30−1.43 (4H, m, CH$_2$CH_2), 2.66 (2H, app t, J = 8.3 Hz, C=CCH_2), 3.57 (3H, s, CH_3O) 5.10 (2H, s, PhCH_2O), 7.36−7.58 (10H, m, Ar-*H*), 7.59−7.66 (2H, m, Ar-*H*), 8.13−8.22 (2H, m, Ar-*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.5, 22.8, 27.4, 32.6, 61.5, 76.2, 122.3, 122.8, 125.5, 126.2, 127.0, 127.5, 127.9, 128.0, 128.5, 128.6, 130.2, 131.8, 132.9, 137.2, 137.7, 148.7, 149.8. FTIR: 3034 (w), 2960 (m), 2872 (m), 1587 (m), 1348 (s), 1324 (s) cm^{-1}. HRMS: calcd for $C_{28}H_{28}O_2$ 396.2089, found 396.2090.

1-Benzyloxy-2-butyl-4-methoxy-3-(4-trifluoromethylphenyl)naphthalene 29c. Following the representative procedure, hydroquinone **29c** was isolated as a white solid. Mp = 96.1−96.9 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.67 (3H, t, J = 7.3 Hz, CH_3CH$_2$), 1.05−1.38 (4H, m, CH$_2$CH_2), 2.57 (2H, app t, J = 8.0 Hz, C=CCH_2), 3.52 (3H, s, CH_3O) 5.05 (2H, s, C=CCH_2O), 7.37−7.62 (9H, m, Ar-*H*), 7.73 (2H, d, J = 8.2 Hz, Ar-*H*), 8.07−8.18 (2H, m, Ar-*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.6, 22.8, 27.4, 32.6, 61.7, 76.2, 122.4, 122.8, 124.8 (q, J = 3.0 Hz, *C*HCCF$_3$), 125.8, 126.5, 127.0 (q, J = 271.6 Hz, *C*F$_3$), 127.4, 127.5, 128.0, 128.6, 128.8, 129.2 (q, J = 32.4 Hz, *C*CF$_3$), 130.7, 131.2, 131.4, 137.6, 141.2, 149.0, 149.8. FTIR: 3033 (w), 2959 (m), 2933 (m), 1586 (m), 1348 (s), 1126 (s) cm^{-1}. HRMS: calcd for $C_{29}H_{27}F_3O_2$ 464.1963, found 464.1950.

4-Benzyloxy-7-methoxy-5,6-diphenylbenzo[*b*]furan 29d. Following the representative procedure, hydroquinone **29d** was isolated as a white crystalline solid. Mp = 111.6−112.3 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 3.90 (3H, s, OCH_3), 4.70 (2H, s, PhCH_2), 6.88 (1H, d, J = 2.1 Hz, C$_3$*H*), 7.02−7.27 (15H, m, Ar-*H*), 7.64 (1H, d, J = 2.1 Hz, C$_2$*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 60.8, 75.4, 104.8, 122.5, 126.1, 126.2, 127.2, 127.3, 127.8, 128.0, 128.2, 129.9, 130.6, 131.1, 131.4, 136.6, 136.9, 137.1, 139.1, 144.7, 146.9. FTIR: 3085 (w), 3033 (m), 2939 (m), 1733 (s) 1601 (m), 1463 (s), 1338 (s) cm^{-1}. Anal. Calcd for $C_{28}H_{22}O_3$: C, 82.74; H, 5.46. Found: C, 82.54; H, 5.52.

3,9-Dimethyl-2-(4,4,5,5-tetramethyl[1,3,2]dioxaborolan-2-yl)-9*H*-carbazole-1,4-dione 32. To a solution of **31** (288 mg, 0.788 mmol) in THF (16.0 mL) was added alkyne **2b** (392 mg, 2.360 mmol) under nitrogen. The reaction mixture was stirred at 45 °C for 16 h and concentrated by rotary evaporation. The residue was dissolved in 10 mL of ether and treated with 8 equiv of 0.5 M ceric ammonium nitrate in 0.1 M $HNO_{3(aq)}$. The reaction mixture was stirred at room temperature for 30 min and the reaction quenched with water. The crude material was extracted with CH_2Cl_2, filtered through a pad of silica gel, and triturated with hexanes to provide quinone **32** (166 mg, 64%) as an orange solid. Mp = 177.7−178.5 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.41 (12H, s, CH_3), 2.19 (3H, s, CH_3C=C), 4.10 (3H, s, CH_3N), 7.30−7.44 (3H, m, Ar-*H*), 8.24−8.30 (1H, m, Ar-*H*)). ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.6, 24.9, 31.6, 84.8, 110.8, 116.4, 123.0, 123.5, 124.3, 126.5, 133.9, 139.1, 152.3, 183.6, 184.3. FTIR: 2977 (m), 1638 (s) 1358 (s) cm^{-1}. HRMS: calcd for $C_{20}H_{22}BNO_4$ 351.1642, found 351.1635.

Bis-*N*-dimethylbismurrayaquinone-A 33. To a solution of **32** (249 mg, 0.690 mmol) in THF (10.0 mL) were added potassium carbonate (490 mg, 3.545 mmol), ethyl 2,3-dibromo-3-phenyl propionate (239 mg, 0.700 mmol) and dichloro[1,1′-bis(diphenylphosphino)ferrocene]palladium(II) dichloromethane adduct (58 mg, 0.007 mmol), and the reaction mixture was stirred at 65 °C for 16 h. The reaction mixture was diluted with water (75 mL) and extracted with DCM (3 × 75 mL). The organic layer was washed with water, dried over $MgSO_4$, and convcentrated to a deep red solution. The crude product was precipitated from solution with hexane and recrystallized from acetone to provide quinone **33** (67 mg, 42%) as a poorly soluble dark red solid. ^{1}H NMR (400 MHz, CH_2Cl_2): δ 2.02 (3H, s, CH_3C=C), 4.12 (3H, s, CH_3N), 7.32−7.54 (3H, m, Ar-*H*), 8.29 (1H, d, J = 8.0 Hz, Ar-*H*). ^{13}C NMR (100 MHz, CH_2Cl_2): δ 13.9, 32.1, 111.5, 117.0, 123.2, 123.9, 124.8, 127.1, 134.0, 137.9, 139.9, 145.7, 179.6, 182.6. FTIR: 1641 (s) 1523 (m) cm^{-1}. HRMS: calcd for $C_{28}H_{20}N_2O_4$ 448.1423, found 448.1404.

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Supporting Information Available: ^{1}H and ^{13}C spectra for select compounds and ^{1}H NOE NMR of compound **7a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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