DOI: 10.1002/chem.200902796

Synthesis of Benzo- and Naphthoquinonyl Boronic Acids: Exploring the Diels–Alder Reactivity

Marcos Veguillas,[a] Maria C. Redondo,[a] Isabel García,[b] María Ribagorda,*[a] and M. Carmen Carreño*[a]

Abstract: Substituted 2-quinonyl boronic acids have been synthesised from 1,4-dimethoxy aromatic derivatives in two steps: regiocontrolled boronation and oxidative demethylation. The study of their dienophilic behaviour evidenced that the boron substituent significantly increases the reactivity and triggers an efficient domino process in which the Diels–Alder reaction was followed by a protodeboronation or dehydroboronation, depending on the substitution on both the quinone and diene partners. The boronic acid acts as a temporary controller, opening a direct access to *trans*-fused *meta*-regiosomeric adducts when 3-methyl-substituted 2-quinonyl boronic acids react with dienes with a substituent at C-1. A particularly valuable synthetic result was obtained in the reaction between 3,6-dimethyl-2-quinonyl boronic acid and piperylene under an oxygen atmosphere; *trans*-fused 8a-hydroxy-2,4a,8-trimethyl tetrahydronaphthoquinone was formed directly, in excellent yield and in a highly diastereoselective manner.

Keywords: boron · Diels–Alder reactions · quinones · regioselectivity · fused adducts

Introduction

Boranes, boronic acids and their esters are widely used in organic synthesis, mainly as the precursors of alcohols and as intermediates in Suzuki–Miyaura couplings.[1] Besides these applications, dienyl and alkenyl boron derivatives have been shown to participate in Diels–Alder reactions, in which they act as dienes and dienophiles, respectively. Thus, 1-dialkoxyboryl-substituted 1,3-butadienes[2] react with typical dienophiles and azadienophiles to give to allyl boronic esters,[3] which in turn react with aldehydes to give highly functionalised cyclohexenes (Vaultier tandem sequence).[2b,4] The C-2-boron-substituted 1,3-butadienyl derivatives[5] afforded alkenyl boron cycloadducts that have been also used in subsequent palladium cross-coupling reactions.[6] β-Boronoacrolein pinacolates[7] and their imino analogues[8] behave as oxa- and azadienes to afford to dihydropyran or piperidine heterocycles, respectively. Alkenyl boranes[9] and boronates[10] are reactive dienophiles giving highly regio- and endo-selective cycloadditions.[11] Diels–Alder reactions catalysed by internal and external boron Lewis acids have also been reported. For instance, a boronate-substituted acrylanilide[12] is able to act as an internal Lewis acid, and activates the dienophile by coordination of the boron with the amide carbonyl. In situ generated aryloxy boronate esters of juglone[13] were shown to improve both the reactivity and regioselectivity of cycloadditions.

Although quinones are well recognised as highly reactive and synthetically useful dienophiles in [4+2] cycloadditions, the effect on Diels–Alder reactions of a boron substituent placed at the dienophilic double bond had not been investigated.[14] The structure of quinone Diels–Alder adducts is a recurrent building block for the synthesis of complex molecular targets.[15,16] Controlling the regioselectivity of cycloadditions with quinones is an essential task en route to the synthesis of these targets, including naturally occurring quinones and other complex secondary metabolites.[17] Lewis[18] and Brønsted[19] acid catalysts are known to improve the regioselectivity of cycloadditions with unsymmetrical quinones

[a] M. Veguillas, M. C. Redondo, Dr. M. Ribagorda, Prof. Dr. M. Carmen Carreño
Departamento de Química Orgánica (C-I)
Universidad Autónoma de Madrid Cantoblanco
28049 Madrid (Spain)
Fax: (+34) 914973966
E-mail: maria.ribagord@uam.es
carmen.carrenno@uam.es

[b] Dr. I. García
Laboratory of Glyconanotechnology, CIC biomaGUNE
Parque Tecnológico de San Sebastián, Paseo Miramón 182
20009 San Sebastián (Spain)

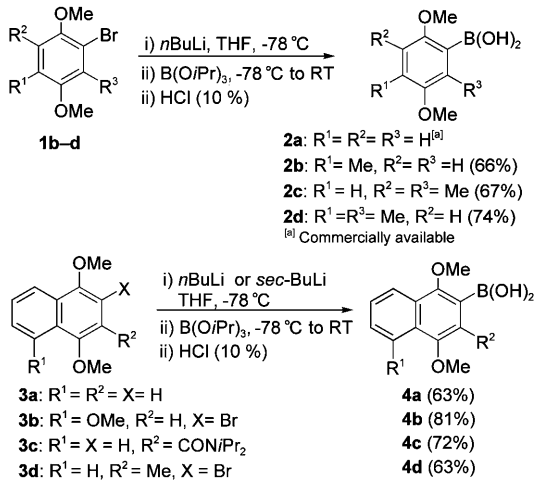
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.200902796.

by coordination (or protonation) with the least sterically hindered or the most basic carbonyl group of the quinones. Some asymmetric catalysts have been reported to promote highly enantio- and regioselective reactions with quinones.[19,20] The regiochemistry of the Diels–Alder reaction can also be controlled by remote substituents in benzo-,[21] naphtho-[22] and 1,4-phenanthrenequinones.[23] In these cycloadditions, Lewis acid catalysts are also used to improve the regioselectivity. The introduction of a substituent such as a Cl or Br atom (X) at the quinone dienophilic double bond has been used with the double aim of controlling regioselectivity and recovering the quinone skeleton after the cycloaddition by HX elimination.[24] Sulfoxides[25] have also been used to this end. With enantiopure sulfinyl quinones, we have reached excellent regio- and stereochemical control in the cycloadditions, en route to synthetically interesting targets such as helicenequinones[26] and natural angucyclinones.[27]

In connection with this project devoted to extend the applications of quinones in synthesis,[25,26] we decided to investigate the unknown affect of a boron substitutent on these dienophiles. In a preliminary investigation, we found that a boronic acid group placed at C-2 of a 3-methyl-substituted quinone skeleton produced a dramatic increase of the dienophilic reactivity. Full control of the regiochemical and final stereochemical course of the Diels–Alder reactions is exerted by the metal substituent, which is lost in the course of the reaction.[28] These interesting findings prompted us to extend the study of the dienophilic behaviour of 2-quinonyl boronic acids to other quinones. Herein, we report the preparation of substituted 2-quinonyl boronic acids and the study of their Diels–Alder reactions. Our previous work is also discussed in detail, including results not described in the preliminary communication. Combined, this work has allowed us to establish the advantages and limitations of using the $B(OH)_2$ substituent as a control element in these cycloadditions.

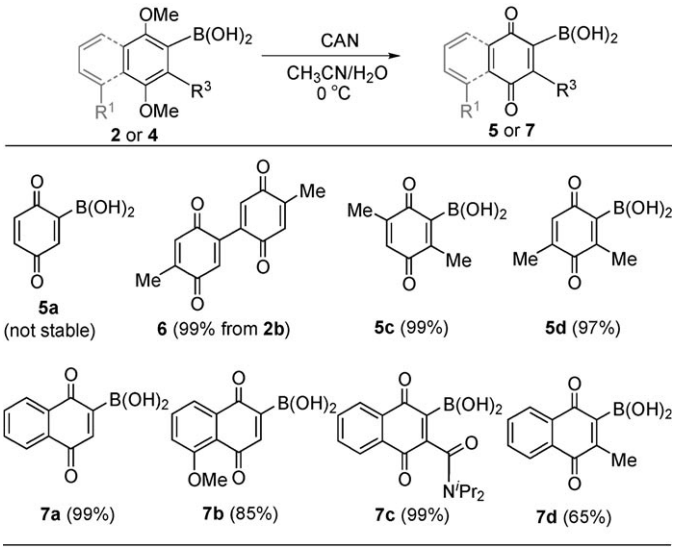
Results and Discussion

Prior to our work, there was only one synthetic approach to 2-boron-substituted quinones, reported by Harrity and coworkers in 1999.[29] They described the synthesis of 2-naphthoquinonyl boronic esters (and other fused heterocyclic analogues) using a Dötz benzannulation of Fischer chromium carbene complexes with 2-substituted 1-alkynylboronates, followed by oxidation of the most electron-rich aromatic ring. In our case, we decided to use dimethoxy-substituted phenyl and naphthyl derivatives **1** and **3** as starting materials, which could be easily transformed into the boronic acids **2** and **4** by the conventional *ortho*-lithiation or Br–Li exchange/boronation protocol.[30] Further oxidative demethylation with ammonium cerium(IV) nitrate (CAN) would yield the corresponding quinones. Thus, starting from bromodimethoxy benzenes **1b–d**[31] bromo–lithium exchange, followed by reaction with $B(OiPr)_3$ and hydrolysis (HCl, 10%) afforded the phenyl boronic acids **2b–d**[32], isolated pure in 66–74% yield (Scheme 1).



Scheme 1. Synthesis of phenyl boronic acids **2b–d** and naphthyl boronic acids **4a–d**.

The naphthyl boronic acid **4a** and the diisopropyl amide derivative **4c** were synthesised in 69 and 72% yield, respectively, by *ortho*-metallation/boronation of **3a** and **3c**. The bromo–lithium exchange/boronation process was used to transform 2-bromonaphthalene derivatives **3b** and **3d** into **4b** and **4d**, in 81 and 63% yield, respectively. CAN oxidation of commercially available 2,5-dimethoxyphenyl boronic acid (**2a**) led to the formation of the benzoquinone derivative **5a**, which was not stable enough to be isolated and could only be detected by ^1H NMR spectroscopy. The electron-withdrawing effect of the $B(OH)_2$ substituent must destabilise the quinonic system by decreasing the quinone/hydroquinone redox potential. Attempted CAN oxidation of 4-methyl-2,5-dimethoxyphenyl boronic acid (**2b**) to the boron-bearing quinone was also unsuccessful. Instead, 4,4′-dimethyl-1,1′-bicyclohexa-3,6-diene-2,2′,5,5′-tetraone (**6**)[33] was formed in an almost quantitative yield and in a regiocontrolled manner, probably due to the initial deboronation of **2b**, followed by coupling of the intermediate radicals and evolution to the final product by oxidative demethylation. Fortunately, the oxidative demethylation of 3,6- and 3,5-dimethyl-2,4-dimethoxyphenyl boronic acids **2c** and **d** was successfully achieved by reaction with CAN in CH_3CN/H_2O at 0°C. Under these conditions, pure benzoquinonyl boronic acids **5c** and **5d** were obtained as stable yellow-crystalline solids in excellent yields (99 and 97%, Scheme 2). The oxidative demethylation of the dimethoxynaphthyl boronic acids **4** also occurred with good to excellent yields, leading to the naphthoquinones **7a–d**. The stability of **7a–d** was dependent on the substitution. For instance, 2-naphthoquinonyl boronic acids **7a–c** could be isolated as orange solids, but had to be used immediately after preparation because the initial crystals turned dark on standing. Conversely, 3-

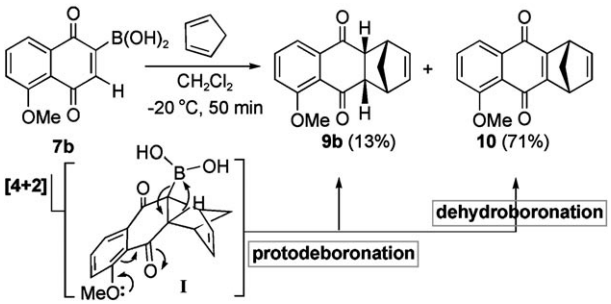


Scheme 2. Synthesis of 2-benzo and 2-naphthoquinonyl boronic acids **5** and **7**.

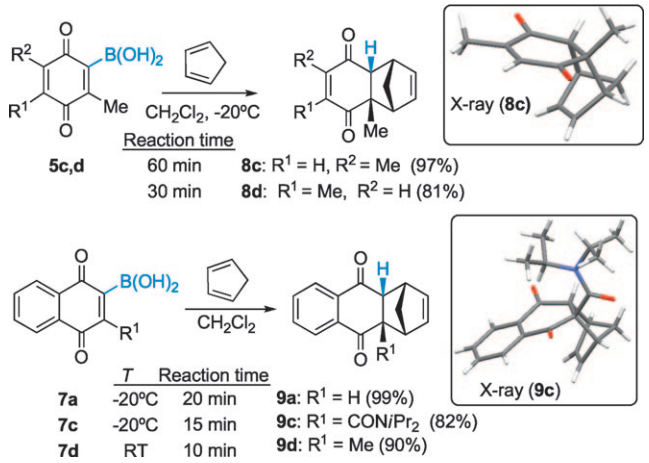
methyl-naphthoquinonyl boronic acid (**7d**) was a stable yellow-crystalline solid.

The study of the Diels–Alder reactions of the quinonyl boronic acids **5c**, **5d** and **7a–d** was initiated by using cyclopentadiene as a model diene. Addition of the freshly distilled diene to a solution of 3,6-dimethyl-2-benzoquinonyl boronic acid (**5c**) in CH_2Cl_2 afforded the Diels–Alder adduct **8c** in 97% yield after 1 h at RT. The structure of **8c** corresponded to a protodeboronated *endo* adduct, as confirmed by X-ray diffraction[34] (Scheme 3). 4,6-Dimethyl-2-benzoquinonyl boronic acid (**5d**) also reacted with cyclopentadiene under very mild conditions (CH_2Cl_2, −20 °C, 30 min) and the protodeboronated *endo* adduct **8d** was isolated in 81% yield. The short reaction times and mild conditions used were evidence of a significant increase of the dienophilic reactivity in the presence of the $B(OH)_2$ group, if compared with the boron-free quinone analogues.[35] 2-Naphthoquinonyl boronic acids **7a**, **7c** and **7d** also reacted with cyclopentadiene, affording the protodeboronated *endo* adducts **9a**, **9c** and **9d** in excellent yields. The structure of **9c** was secured by X-ray diffraction[36] (Scheme 3). Although the increase of the quinone dienophilic reactivity is significant in all cases, the most impressive increase corresponded to 3-methyl-2-naphthoquinonyl boron derivative **7d**; the reaction with cyclopentadiene was completed in 10 min at RT to afford **9d** in 90% yield. The analogous cycloaddition using the boron-free 2-methyl-naphthoquinone only occurred in the presence of Lewis acids.[37] All of these protodeboronated adducts were formed directly in the reaction vessel before any workup, as evidenced from the direct formation of **9a** when the reaction between **7a** and cyclopentadiene was carried out in an NMR tube (CD_2Cl_2). These results suggested that the boron substituent at the quinone triggers an efficient domino process in which the Diels–Alder reaction is followed by a fast protodeboronation step.

When 5-methoxy-2-naphthoquinonyl boronic acid (**7b**) was treated with cyclopentadiene at −20 °C, the corresponding *cis*-protodeboronated adduct **9b** was formed in 13% yield, together with 71% of the dehydroboronated product, characterised as 1,4-dihydro-9,10-anthraquinone (**10**) (Scheme 4). Compound **10** could be formed by oxidation of



Scheme 4. Reaction of **7b** with cyclopentadiene.

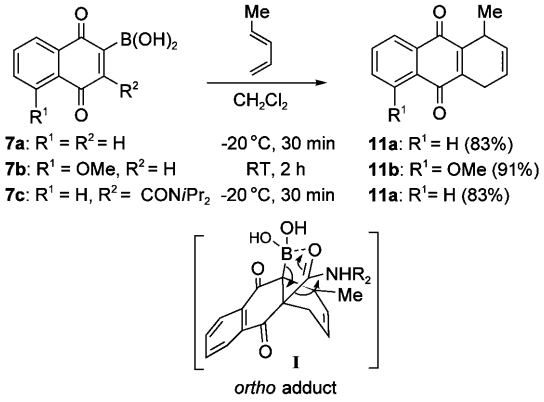


Scheme 3. Reactions of **5c** and **d** and **7a**, **c** and **d** with cyclopentadiene and X-ray structures of **8c** and **9c**.

9b, facilitated by the presence of the electron-rich methoxy-substituted ring. To disregard this mechanism, we carried out the cycloaddition between **7b** and cyclopentadiene under an argon atmosphere and showed the formation of the same mixture of **9b** and **10**. Moreover, compound **9b** was shown to be stable under atmospheric conditions. A plausible explanation for the formation of **10** could be a protodeboronation process facilitated by the lower acidity of the boron vicinal hydrogen atom in the initially formed Diels–Alder adduct **I**, if compared with the undetected adduct resulting from naphthoquinone **7a**. This must be due to the electron-donating effect of the OMe group on the system, which suffers a spontaneous dehydroboronation to recover the quinone double bond in **10**. The evolution observed from **7b**, evidenced that the final result of the overall sequence was dependent on the nature of the substituents

surrounding the conjugated carbonyl groups, both in the dienophile and in the initially formed Diels–Alder adduct.

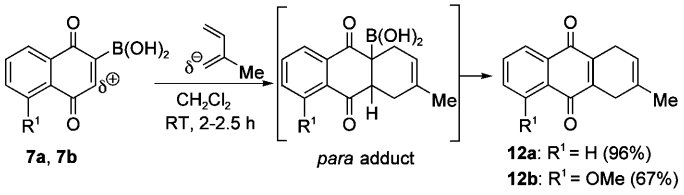
This influence was also evident in the reactions of naphthoquinonyl boronic acids **7** with acyclic dienes. Thus, when *trans*-piperylene was submitted to reaction with **7a** or **7b**, both with a hydrogen atom at C-3, the products isolated corresponded to the 1,4-dihydro-9,10-anthraquinone derivatives **11a** and **11b**, a result of the [4+2] cycloaddition/dehydroboronation process, isolated in 83 and 91% yield, respectively (Scheme 5). The regiochemistry of **11b** indicated that



Scheme 5. Reactions of 2-naphthoquinonyl boronic acids **7a–c** with piperylene.

the *ortho* adduct was formed initially, as expected on the basis of a regiochemical control exerted by the $B(OH)_2$ substituent. Surprisingly, the product resulting from the reaction between 3-*N*,*N*-diisopropylcarbamoyl-2-naphthoquinonyl boronic acid (**7c**) and piperylene was also identified as 1-methyl-1,4-dihydro-9,10-anthraquinone (**11a**) and was isolated in 83% yield. In this case, a favoured intramolecular association between the boron atom and the basic oxygen atom of the amide group[12,38] could be facilitating the boron elimination process to recover the quinone double bond.

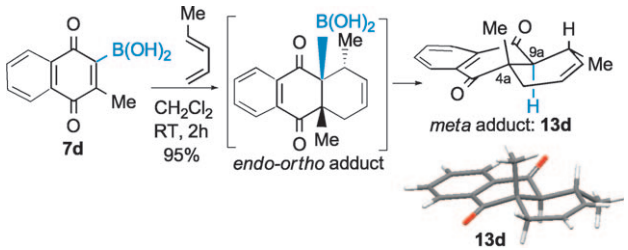
Similarly, the reaction of naphthoquinonyl boronic acids **7a** and **7b** with isoprene afforded the dehydroboronated dihydroanthraquinones **12a** and **12b** in 96 and 67% yield, respectively (Scheme 6). The regiochemistry of **12b** also suggested that the boronic acid is controlling the regiochemical course of the initial cycloaddition, to form the expected *para* adduct, which yielded **12b** after dehydroboronation.



Scheme 6. Reactions of 2-naphthoquinonyl boronic acids **7a** and **b** with isoprene.

Compound **7c** did not react with isoprene, even after long reaction times.

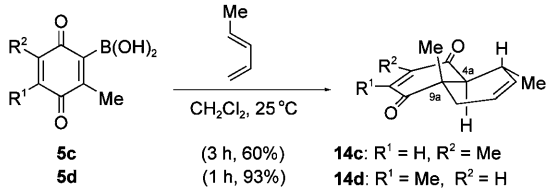
Benzoquinonyl boronic acids **5c** and **5d** and the naphthoquinonyl derivative **7d**, which has a methyl substituent at C-3 of the dienophilic double bond, also reacted with acyclic dienes, but the fate of the initially formed adducts was unexpected. The reaction between 3-methyl-2-naphthoquinonyl boronic acid (**7d**) and piperylene was complete within 2 h at RT affording, exclusively, the protodeboronated adduct **13d** in 95% yield. The structure of **13d** was confirmed by X-ray diffraction (Scheme 7).[39] Three aspects of this reaction are



Scheme 7. Reaction of **7d** with piperylene and X-ray structure of *trans*-fused **13d**.

noteworthy. First, the mild conditions used and short reaction time required revealed again the high reactivity of the dienophile if compared with boron-free 2-methylnaphthoquinone. Reaction of the boron-free analogue with piperylene only occurred under high-pressure conditions at 150 °C, to produce a complex mixture, from which the *ortho* adduct was isolated in a poor yield (27%).[40] Second, the exclusive formation of the 1,4a-dimethyl-substituted derivative **13d** indicated that the regiochemistry of the cycloaddition was fully controlled by the boron substituent, the *endo-ortho* adduct formed initially, before protodeboronation, facilitated the transformation into the product. This result opens an easy access to the *meta* adducts, which are not favoured in cycloadditions between 1-substituted dienes and 2-alkyl-substituted quinones. Third, the *trans* relative configuration of the C-4a and C-9a stereogenic centres in **13d** indicated that the Diels–Alder reaction was followed by a *trans*-protodeboronation process occurring in situ. The *trans*-fused quinone cycloadducts are only accessible from the *cis-endo* Diels–Alder adducts, directly formed from quinones by treatment with strong bases or acids,[35b,41] which generally give different *trans*/*cis* mixtures.[42] Thus, the boronic acid is acting as a temporary controller and opens up a straightforward access to the *trans*-fused *meta*-regiosomeric cycloadducts under very mild reaction conditions.

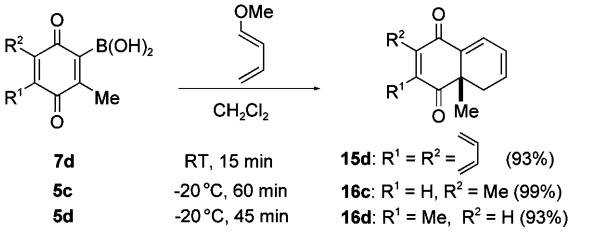
Dimethyl-substituted benzoquinonyl boronic acids **5c** and **5d** behave similarly in the reactions with *trans*-piperylene. Once again, the boronic acid directed the regiochemical outcome of the reaction and promoted the formation of the *trans*-fused *meta*-adducts **14c** and **14d** in 60 and 93% yield, respectively, over short reaction times (Scheme 8). To obtain such a high yield of **14c**, the reaction between piperylene



Scheme 8. Reactions of **5c** and **5d** with piperylene.

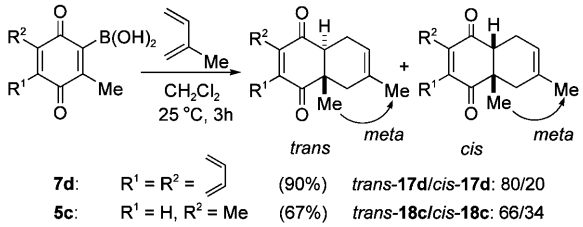
and **5c** had to be performed under rigorous inert-atmosphere conditions (Argon or N_2) otherwise variable amounts of a hydroxyl-substituted product **30** (see below) were formed when air was present. A comparison of the reactivity of **5c** and **5d** with that reported for 2,5-[43,44] and 2,6-dimethyl benzoquinones,[13,45] evidenced that the boron-free quinones are much less reactive, only giving good yields of the piperylene adducts when working at high temperatures, in the presence of Li salts ($LiClO_4$ or LiOTf) or Lewis acids catalysts. The major regioisomers formed from the boron-lacking quinones under thermal conditions are the *ortho* adducts. The regiochemical course could be inverted to favour the *para* adducts in the presence of catalysts. In any case, the *meta* adducts are generally obtained as minor components. Regarding the stereochemistry, all of these cycloadditions followed Alder's rule, to give the undetected *endo-cis* structures, transformed in situ into the *trans* systems. Thus, our methodology opens a direct and straightforward access to the *trans*-fused *meta*-regioisomers. To disregard a catalysed reaction by some boron species,[46] we tested the reaction of 2,6-dimethyl benzoquinone with piperylene in CH_2Cl_2 at RT, in the presence of $PhB(OH)_2$. Under these conditions no cycloadduct was detected, even after three days.

Reactions of **7d**, **5c** and **5d** were also carried out with 1-methoxy-1,3-butadiene and led to compounds **15d**, **16c** and **16d** in excellent yields after very short reaction times. In this case, the domino sequence, including the Diels–Alder reaction and protodeboronation, was followed by elimination of MeOH (Scheme 9), which generated directly 1,9a-dihydro anthraquinone (**15d**) or the 4a,5-dihydro-1,4-naphthoquinone derivatives **16b** and **16c**, with an angular methyl substituent. The regiochemical course of the initial cycloaddition, deduced from the position of the double bond generated in the elimination, was also directed by the $B(OH)_2$ group through the intermediate formation of an undetected *ortho* adduct.



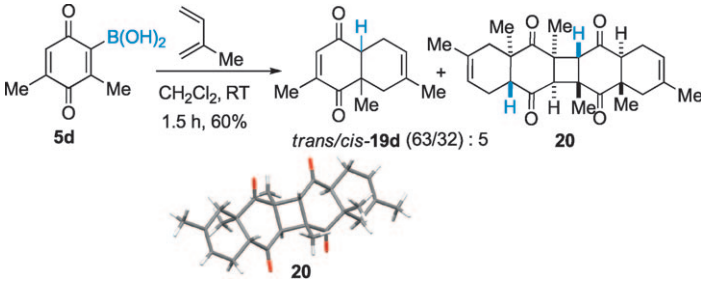
Scheme 9. Reactions of **7d**, **5c** and **5d** with 1-methoxy-1,3- butadiene.

The cycloadditions of **7d** and **5c** with isoprene also occurred in a highly regioselective manner, to give the *meta* regioisomer exclusively after protodeboronation. Although the regiochemistry was fully controlled by the boronic acid, in these cases the spontaneous protodeboronation process gave a mixture of *trans*- and *cis*-fused adducts **17d** (80:20) and **18c** (66:34)[47] from **7d** and **5c**, respectively (Scheme 10). Diels–Alder reaction of 2,5-dimethylbenzoquinone and isoprene had been reported to occur only in toluene at reflux to give a 50:50 mixture of regioisomeric *meta*/*para-cis* adducts after 36 h.[43]



Scheme 10. Reactions of 3-methyl-2-quinonyl boronic acids **7d** and **5c** with isoprene.

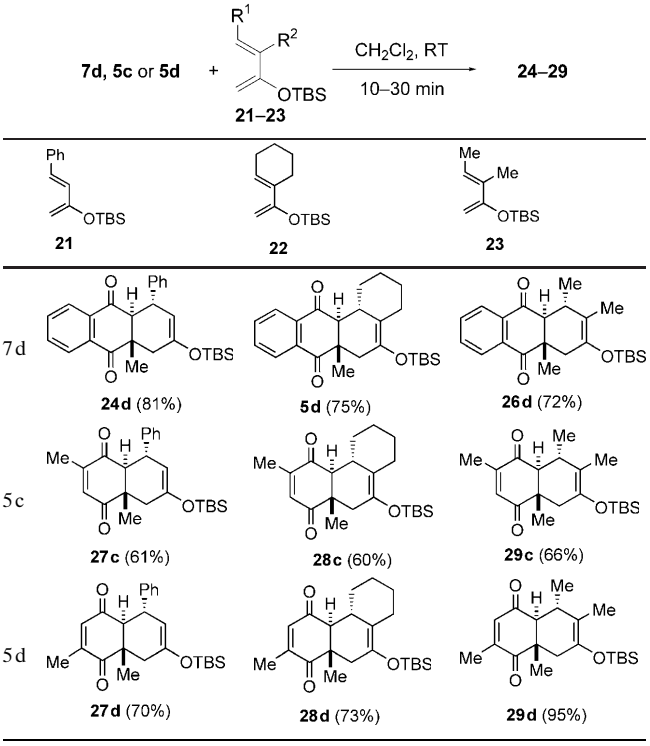
The reaction between 3,5-dimethyl-substituted-2-quinonyl boronic acid (**5d**) and isoprene allowed the isolation of a 63:32:5 mixture of *trans*-**19d**, *cis*-**19d** and **20** as determined by ^1H NMR spectroscopy (Scheme 11). Although we could not isolate them in a diastereomerically pure form, to our surprise, the crystallisation of the mixture from EtOAc/*n*-hexane gave a good quality single crystal of **20** from which the unequivocal structure was established by X-ray diffraction analysis (Scheme 11).[48]



Scheme 11. Reaction of dimethylquinonyl boronic acid **5d** with isoprene and X-ray structure of dimer **20**.

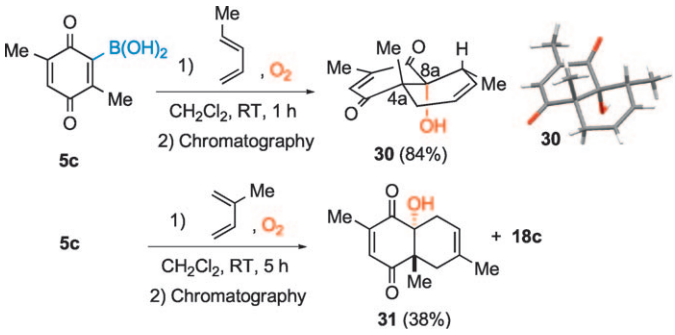
To clarify the effect of the substitution pattern of the diene on the stereochemical outcome of the protodeboronation step (*trans*/*cis* ratio) we investigated the reactions of **7d**, **5c** and **5d** with highly substituted dienes **21–23**. The results obtained are summarised in Table 1. Reaction with 1-phenyl-3-trimethylsilyloxybutadiene (**21**) or 1,2,3-trisubtitued dienes **22** and **23** also proceeded under very mild con-

Table 1. Diels–Alder reactions of **7d**, **5c** and **5d** with 1,3-disubtituted and 1,2,3-trisubstituted-1,3-butadiene derivatives **21–23**.



ditions (CH_2Cl_2, RT) in very short reaction times. All of the adducts formed (**24–29**) corresponded to the protodeboronated *trans*-fused structures and were obtained with good to excellent yields (60–95%) (Table 1). These results provided evidence for the regiochemical control exerted by the $B(OH)_2$ group in the dienophile and the cooperating effect of the C-1 and C-3 substituents in the diene partners. Moreover, the exclusive formation of the *trans*-fused adducts revealed that the stereochemistry of the protodeboronation is controlled by the C-1 substitution of the diene. These results show the generality and potential utility of quinonyl boronic acids as dienophiles.

Taking into consideration the reactivity observed for these quinonyl boronic acids, and given the power of the organoboron compounds to incorporate different functionalities into organic substrates, we tried to further functionalise the resulting quinone adducts. Assuming the initial formation of an α-boro ketone from the cycloaddition between the quinonyl boronic acid and the diene, we decided to carry out a series of experiments to trap the initially formed boron-containing adduct. With this aim, a solution of cyclopentadiene or piperylene in CH_2Cl_2 was added to a previously prepared solution of boronic acid **7a** or **5c** CH_2Cl_2 containing different electrophiles (*p*-nitro- or *p*-fluorobenzaldehyde, *N*-bromosuccinimide). In all cases, the adducts **9a** (Scheme 3) or **14c** (Scheme 8) and/or complex reaction mixtures were detected. All of these attempts to trap the intermediate boron derivative failed probably due to the extremely rapid elimination or protodeboronation process occurring after the Diels–Alder reaction. Based on the above observations of the reaction between **5c** and piperylene in the presence of air, we decided to run this reaction in CH_2Cl_2, at room temperature in a flask fitted with a bubbling oxygen balloon. Under these conditions, derivative **30** was formed exclusively, and could be isolated in 84% yield after chromatographic purification. The structure and stereochemistry of **30**, an *all-trans* 8a-hydroxy-2,4a,8-trimethyl-substituted naphthoquinone-derived *meta* adduct, was confirmed by X-ray diffraction (Scheme 12).[49]



Scheme 12. Reactions of **5c** with piperylene or isoprene under an oxygen atmosphere and X-ray structure of **30**.

Considering the synthetic interest of this result, a direct access to angularly hydroxyl-substituted systems,[50] we decided to investigate the generality of the process. When isoprene was used as the diene, the reaction with **5c** under an oxygen atmosphere gave the hydroxy derivative **31**, together with the protodeboronated adduct **18c** in a 40:60 ratio. Compound **31** was isolated pure in 38% as a 94:6 mixture of *trans*- and *cis*-fused angularly hydroxy-substituted adducts. We also tried to obtain the hydroxy derivatives by reaction between **5d** or **7d** and piperylene under an oxygen atmosphere, unfortunately only the *trans* adducts **14d** and **13d** were obtained, respectively.

Regio- and stereochemistry of the reactions: mechanistic aspects: The high dienophilic reactivity observed for 2-quinonyl boronic acids must be a consequence of the electron-withdrawing effect of the $B(OH)_2$ group, which must decrease the LUMO energy of the C-2=C-3 quinonic double bond, thus decreasing the HOMO–LUMO energy gap.[51] The electron-withdrawing effect of the boron substituent can be deduced from the ^{13}C NMR shifts of the methyl-substituted β-carbon atom of boronic acid **5d** or the corresponding pinacolate ester, which are deshielded relative to the β-carbon atom of the boron-free quinone analogues (Figure 1). This is also reinforced by the formation of a hydrogen bond between the boronic acid and the C-1 carbonyl group (**TS1** in Scheme 13), evident in the X-ray of quinone **5d**.[52]

The activating effect of the hydrogen bond was also evidenced from the results of the cycloaddition between the pinacol ester derived from boronic acid **5d** and cyclopentadiene. The pinacolate, obtained by treatment of **2d** with pi-

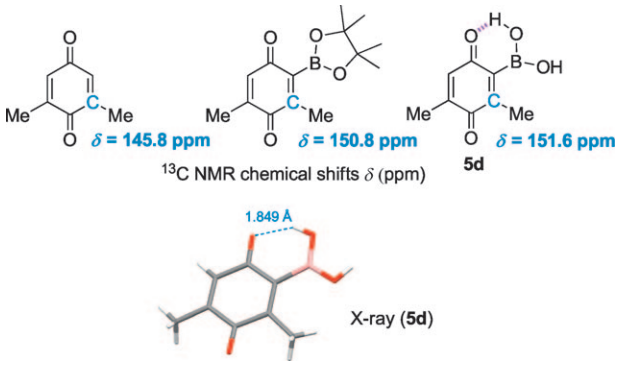
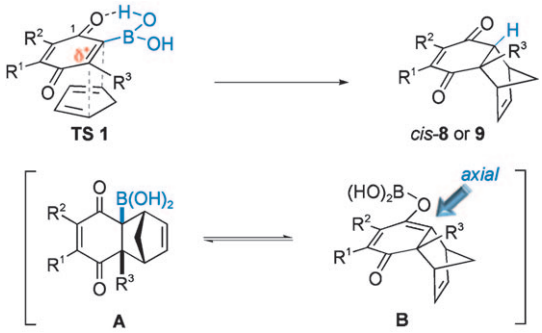


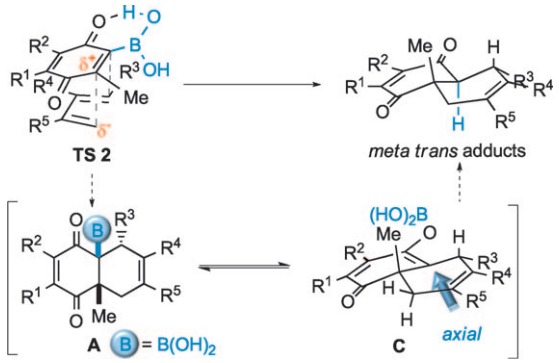
Figure 1. ^{13}C NMR chemical shifts of selected carbon atoms and X-ray structure of **5d**.



Scheme 13. Regio- and stereochemical course of the domino Diels–Alder reactions and protodeboronation of quinonyl boronic acids **5c–d**, **7a**, **7c** and **7d** with cyclopentadiene.

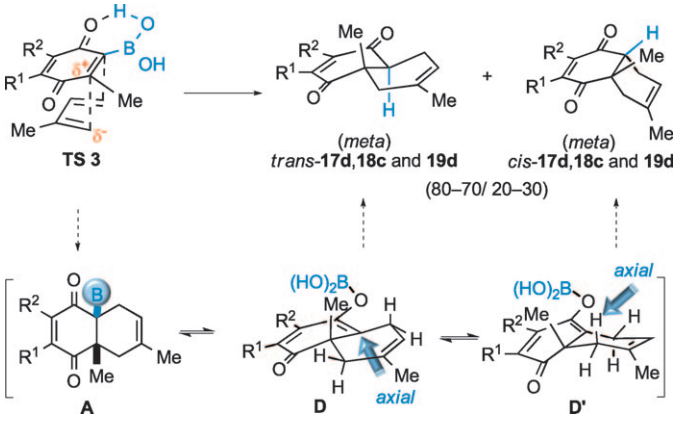
nacol followed by CAN oxidation, reacted with cyclopentadiene after 1.5 h at reflux in CH_2Cl_2. No reaction occurred under the conditions in which the free boronic acid **5d** evolved in 30 min (CH_2Cl_2, −20 °C), even over extended reaction time (overnight). The origin of the efficient regiocontrol exerted by the boronic acid can also be due to these features because the values of the coefficient of the C-1 carbonyl group of the LUMO orbital become larger and the dienophilic double bond of the quinone is polarised, as shown in Scheme 13. The regiochemistry is that expected, taking into account the substitution of the diene partners. A plausible explanation of the formation of *cis*- or *trans*-fused adducts from the reactions with 3-substituted 2-quinonyl boronic acids is also summarised in Schemes 13–15. The evolution of the initially formed cyclopentadiene *endo* adduct **A** (resulting from the *endo* approach shown as **TS1**, through the boron enolate intermediate **B**) could explain the formation of compounds **8** and **9** after protonation and loss of the boron group (Scheme 13). ^{11}B NMR spectroscopy was used to monitor the reaction between **7d** and cyclopentadiene in CD_2Cl_2 and revealed the formation of a signal appearing at $\delta = 19.1$ ppm, which was assigned to boroxine ($B_3O_6H_3$), the formation of which could favour the protonation of **B**.[53] When cyclopentadiene was the diene, the rigid and concave-shaped boron enolate **B** could only suffer protonation from the external face, in the axial direction. As such *endo* adducts **8** and **9** were observed.

The exclusive formation of the *trans*-fused adducts **13b**, **14c**, **14d** and **24–29** from piperylene or 1,3- or 1,2,3-substituted dienes **21–23** can be explained from the stereoselective axial protonation of the boron enolate **C**, from the less-hindered bottom face of the half-chair conformation (Scheme 14). This must be the most stable situation since the C-1 (or C-8) R^3 group is in the *pseudo*-equatorial position. This approach justifies why the *trans*-protodeboronation only occurred stereoselectively in the adducts resulting from dienes having a substituent at C-1.



Scheme 14. Regio- and stereochemical course of the domino Diels–Alder reactions and protodeboronation of quinonyl boronic acids with 1-substituted acyclic dienes.

In the case of the reaction between quinonyl boronic acids **5c**, **5d** and **7d** and isoprene, the major formation of *trans*-fused adducts can be explained in a similar way, through the axial protonation of the boron enolate **D** (Scheme 15). The minor *cis*-fused adducts could result from the axial protonation of the half-chair conformation **D′**. The relative stability of the **D** (*pseudo*-axial Me) and **D′** (*pseudo*-axial C=O) conformers must not be very different, thus explaining the formation of a mixture of *cis*- and *trans*

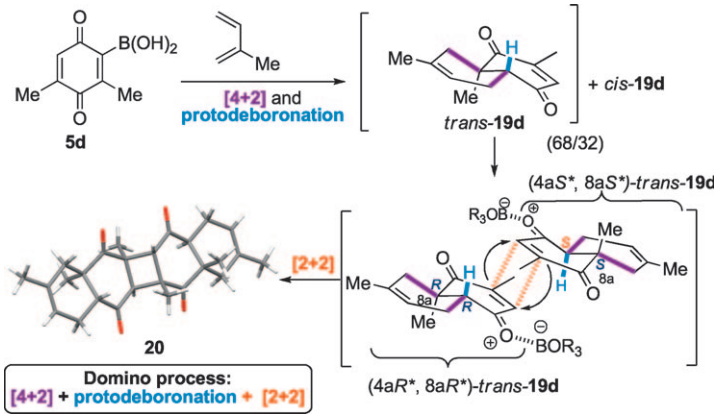


Scheme 15. Regio- and stereochemical course of the domino Diels–Alder reactions and protodeboronation of quinonyl boronic acids with piperylene.

adducts from the protodeboronation on the bottom and top faces of **D** and **D′**, respectively.

The stereoselective formation of the pentacyclic compound **20** obtained in the reaction between 3,5-dimethylbenzoquinone derivative **5d** and isoprene, was not easy to explain. Its structure corresponded to a dimer of *trans*-**19d**, the formation of which was also observed in the dark, thus disregarding a photochemically allowed [2+2] cycloaddition as a mechanistic pathway to explain the formation of the cyclobutane ring. To improve the final yields of **20**, we effected the reaction between **5d** and isoprene under different conditions, however, the relative amounts of *trans*-**19d**, *cis*-**19d** and **20** remained constant, even after extended reaction times. To explain the formation of **20**, we propose a one-pot, domino sequence including a Diels–Alder cycloaddition between **5d** and isoprene, followed by a *trans* protodeboronation and a catalysed [2+2] cycloaddition involving the methyl-substituted cross-conjugated C-2=C-3 double bond of *trans*-**19d**, which leads to the cyclobutane ring.[54,55] Most likely, some of the boron species present in the reaction medium could catalyse the stepwise sequence. In the overall process six new C–C bonds were formed in a highly stereoselective manner.

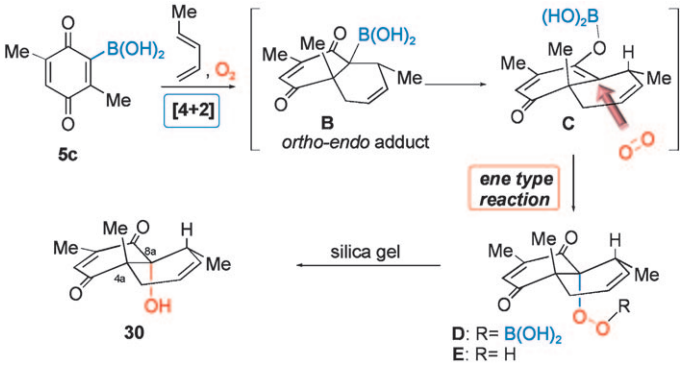
A detailed analysis of the X-ray structure shown in Scheme 16 revealed that the pentacyclic compound **20** must arise exclusively through the reaction between the pair of



Scheme 16. Plausible formation and X-ray structure of dimer **20**.

enantiomers (4a*R**, 8a*R**)-*trans*-**19d** and (4a*S**, 8a*S**)-*trans*-**19d**. Both enantiomers must approach each other from the less-hindered face (opposite to the 8a-axial methyl substituent) giving a sole *meso* diastereoisomer **20** with S_2 symmetry.

A mechanistic explanation of the isolation of hydroxyl derivative **30** from the reaction between **5c** and piperylene in the presence of oxygen was not evident. A detailed analysis of the ^{1}H NMR spectrum of the crude mixture prior to chromatographic purification revealed the presence of a broad singlet at $\delta = 8.35$ ppm, which was assigned to the hydrogen atom of hydroperoxide **E** shown in Scheme 17.[50] After



Scheme 17. Mechanistic proposal to justify the formation of hydroxy derivative **30**.

column chromatography the isolated product showed a broad singlet at $\delta = 2.10$ ppm, which was assigned to the angular OH of **30**. The direct oxidation of the initial boron-containing *ortho-endo*-adduct **B**, could be disregarded due to the *trans* disposition between the 8a-OH and the 4a-methyl substituents. We also could disregard the formation of **30** from the protodeboronated adduct **14c** because it remained unchanged in the presence of oxygen in CH_2Cl_2. Thus, we assumed that once the initial *ortho-endo*-adduct **B** was formed in the Diels–Alder reaction of **5c** and piperylene, the evolution to the boron enolate **C** (favoured by the Lewis acidity of the boron atom in **B** and its proximity to the carbonyl group) could be followed by reaction with oxygen. A stereoselective ene-type reaction occurring from the less-hindered face of the intermediate **C** could explain the formation of **D**, protodeboronation of which would yield intermediate hydroperoxide **E**, further reduced to the OH derivative **30** by the SiO_2 used in the chromatographic purification.

Conclusion

We have reported the synthesis of a series of substituted 2-quinonyl boronic acids by regiocontrolled boronation/oxidation of 1,4-dimethoxybenzene derivatives, in good to excellent yields. The study of their Diels–Alder reactions with different dienes evidenced the following features:

1) The boron substituent dramatically increased the dienophilic reactivity of the quinones, if compared with the analogous boron-free quinone derivatives. The most impressive increase corresponds to the systems with a methyl substituent at the dienophilic double bond; Diels–Alder reactions of quinones **5c**, **5d** and **7d** were complete in very short reaction times and under very mild reaction conditions.
2) In all cases, the initially formed adducts spontaneously lose the boron substituent in a domino process to give different products, the structures of which are dependent on the nature of the C-3 substituent of the quinonyl bor-

onic acid and the cyclic or acyclic nature of the diene, as well as the presence or absence of a C-1 substituent in the diene.

3) The boronic acid acts as a temporary regiocontrol element, affording regioisomeric adducts not directly available from the boron-free quinones.

All of these features combined make 2-quinonyl boronic acids useful dienophiles, providing a direct synthetic access to otherwise elusive polycyclic quinone adducts. Another noteworthy observation of this study is the efficient formation of the *trans*-fused hydroxy derivative **30** from reaction between **5c** and piperylene, working under an oxygen atmosphere. Further studies of this process are currently ongoing.

Experimental Section

General:[56] ^{1}H, ^{13}C and ^{11}B NMR spectra were recorded on a AV-300 Bruker instrument using $CDCl_3$ or [D_6]acetone as solvent at 300, 75 and 96 MHz, respectively. A DRX-500 Bruker instrument was used to record ^{1}H and ^{13}C NMR spectra at 500 MHz. Chemical shifts are reported in ppm relative to $CDCl_3$ ($\delta = 7.27$ ppm) and [D_6]acetone ($\delta = 2.09$ ppm). In the ^{13}C NMR spectra of boron-containing compounds, a typical ^{13}C signal is missing, which corresponds to the carbon directly linked to the boron atom. A HP 5985 Hewlett-Packard instrument was used to measure HRMS at 70 eV. All reactions were monitored by thin-layer chromatography, which was performed on precoated sheets of silica gel 60 and flash column chromatography was performed with silica gel 60 (230–400 mesh) (Merck). Eluting solvents are indicated in the text. Cyclopentadiene was freshly distilled before use. The apparatus for inert-atmosphere experiments was flame dried under a stream of dry argon. Trimethylsilyloxybutadienes **21**, **22** and **23** were prepared by following standard procedure.[57,58]

General procedure A for the synthesis of the phenylboronic acids: A solution of *n*BuLi (1.56 mmol, 2.5 M in hexane) was added dropwise to a stirred solution of the corresponding 1,4-dimethoxy aromatic compound (1.30 mmol) in THF (7.42 mL) under argon at −78 °C. The mixture was stirred at this temperature for 5 min and then B(O*i*Pr)$_3$ (3.25 mmol) was added dropwise at −78 °C. After 10 min the mixture was allowed to warm to RT and was stirred overnight. The mixture was acidified with hydrochloric acid 10% (~2 mL) and then extracted with Et_2O (2×10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (eluent indicated in each case).

Compound ***2b***:[59] Following the general procedure A, the reaction of 2-bromo-5-methyl-1,4-dimethoxybenzene (300 mg, 1.30 mmol) in THF (6 mL) with *n*BuLi (0.57 mL, 1,43 mmol, 2.5 M in hexane) and B(O*i*Pr)$_3$ (0.9 mL, 3.89 mmol) gave **2b**, which was isolated after flash column chromatography (hexane/EtOAc, 6:1) as white solid (169 mg, 66%). M.p. 108–110 °C.

Compound ***4a***: Following the general procedure A, the reaction of **3a** (100 mg, 0.53 mmol) with *n*BuLi (0.21 mL, 0.54 mmol, 2.5 M in hexane) and B(O*i*Pr)$_3$ (0.15 mL, 1.35 mmol) gave **4a**, which was isolated after flash column chromatography (EtOAc/hexane, 1:2) as white solid (78 mg, 63%). M.p. 105–107 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.31$–8.28 (m, 1H), 8.07–8.04 (m, 1H), 7.60–7.54 (m, 2H), 7.15 (s, 1H), 6.55 (s, 2H), 4.04 (s, 3H), 4.01 ppm (s, 3H); ^{13}C NMR (75MHz, $CDCl_3$): $\delta = 157.2$, 151.8, 128.8, 127.4, 126.7, 126.5, 122.6, 122.0, 107.1, 63.7, 55.6 ppm; ^{11}B NMR (96 MHz, $CDCl_3$): $\delta = 29.5$ ppm; MS (EI): *m*/*z* (%): 232 (8) $[M]^+$, 188 (61), 173 (100); HRMS: *m*/*z* calcd for $C_{12}H_{13}BO_4$: 232.0907 $[M]^+$; found: 232.1160.

Compound ***4b***: Following the general procedure A, the reaction of 2-bromo-1,4,5-trimethoxynaphthalene (350 mg, 1.18 mmol) with *n*BuLi (0.51 mL, 1.29 mmol, 2.5 M in hexane) and B(O*i*Pr)$_3$ (554 mg, 2.94 mmol) gave **4b**, isolated pure after flash column chromatography (hexane/EtOAc, 6:1) as white solid (250 mg, 81%). M.p. 122–124 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.83$ (dd, $J = 8.5$, 0.8 Hz, 1H), 7.60 (t, $J = 8.1$ Hz, 1H), 7.38 (s, 1H), 7.10 (d, $J = 7.8$ Hz, 1H), 4.16 (s, 9H), 4.13 (s, 9H), 4.11 ppm (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 157.2$, 157.1, 157.1, 156.6, 153.0, 152.9, 130.2, 129.9, 126.4, 126.4, 126.2, 120.2, 114.7, 114.4, 109.4, 107.6, 107.4, 63.1, 63.0, 60.0, 56.3, 56.2, 56.1, 20.6, 13.8 ppm; MS (EI): *m*/*z* (%): 315 (48) $[M]^+$, 272 (14), 215 (100); HRMS: *m*/*z* calcd for $C_{19}H_{25}NO_3$: 315.1834 $[M]^+$; found: 315.0392.

Compound ***3c***: 1,4-Dimethoxy-2-naphthoic acid (1.7 g, 7.30 mmol) was dissolved in thionyl chloride (6.1 mL) and stirred at room temperature for 15 h. Excess thionyl chloride was then removed in vacuo to afford the acid chloride as a brown solid in quantitative yield. The crude product was dissolved in benzene (8.7 mL) and *N*,*N*-4-dimethylaminopyridine (DMAP) (10 mol%) and diisopropylamine (1.5 mL, 10.9 mmol) were added dropwise at 0 °C. After stirring at 0 °C for 1 h, the solvent was removed under pressure and the residue was dissolved in CH_2Cl_2 (50 mL). The organic layer was washed with water, dried over $MgSO_4$ and filtered. The solvent was removed in vacuo and the crude product was purified by flash column chromatography (hexane/EtOAc, 4:1) to give **3c** as a pale yellow solid (2 g, 85%). M.p. 122–124 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.26$–8.23 (m, 1H), 8.11–8.08 (m, 1H), 7.59–7.48 (m, 2H), 6.59 (s, 1H), 3.99 (s, 3H), 3.97 (s, 3H), 3.82 (sept, $J = 6.8$ Hz, 1H), 3.56 (sept, $J = 6.8$ Hz, 1H), 1.64 (d, $J = 6.8$ Hz, 3H), 1.63 (d, $J = 6.8$ Hz, 3H), 1.21 (d, $J = 6.7$ Hz, 3H), 1.06 ppm (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 168.6$, 152.1, 144.8, 128.5, 127.1, 126.7, 126.3, 125.8, 122.2, 122.1, 101.8, 62.6, 55.7, 51.1, 45.6, 21.0, 20.8, 20.4, 20.2 ppm; MS (EI): *m*/*z* (%): 315 (48) $[M]^+$, 272 (14), 215 (100); HRMS: *m*/*z* calcd for $C_{19}H_{25}NO_3$: 315.1834 $[M]^+$; found: 315.0392.

Compound ***4c***: A solution of *sec*-BuLi (1.0 mL, 1.43 mmol, 1.4 M in hexane), was added dropwise to a stirred solution of **3c** (300 mg, 0.95 mmol) in THF (14 mL) under argon at −78 °C. The mixture was stirred at room temperature for 2 h and then B(O*i*Pr)$_3$ (0.22 mL, 1.9 mmol) was added dropwise at −78 °C. After 10 min the mixture was allowed to warm to RT and was stirred overnight. The mixture was acidified with dilute hydrochloric acid and then extracted with EtOAc. The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by flash column chromatography (hexane/EtOAc, 2:1). The product was obtained as a white solid (246 mg, 72%). M.p. 132–134 °C; ^{1}H NMR (300 MHz, cdcl3): $\delta = 8.12$–8.08 (m, 2H), 7.60–7.56 (m, 2H), 6.76 (brs, 2H), 3.98 (s, 3H), 3.95 (s, 3H), 3.48 (m, 2H), 1.62 (d, $J = 6.8$ Hz, 6H), 1.08 ppm (d, $J = 6.8$ Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 170.5$, 159.1, 147.8, 130.7, 130.1, 128.3, 128.0, 127.0, 122.9, 199.7, 63.8, 62.8, 51.9, 46.2, 20.2 (2C), 20.1 ppm (2C); ^{11}B NMR (96 MHz, $CDCl_3$): $\delta = 28.9$ ppm; MS (ES): *m*/*z* (%): 359 (8) $[M]^+$, 360 (100) $[M+1]^+$; HRMS: *m*/*z* calcd for $C_{19}H_{26}NO_5$: 359.1904 $[M]^+$; found: 359.1898.

Compound ***6***:[59] The reaction of **2b** (25 mg, 0.13 mmol) with CAN (280 mg, 0.51 mmol) in aqueous MeCN gave **7a** as an orange solid (39 mg, 99%). M.p. 179–182 °C.

General procedure B for the synthesis of 2-naphtho and benzoquinonyl boronic acids: An aqueous solution (5 mL) of CAN (0.55 g, 1.00 mmol) was added slowly to a solution of the corresponding 1,4-dimethoxy aromatic boronic acid (0.4 mmol) in MeCN (5 mL) at 0 °C. After stirring for 30 min, the organic solvent was evaporated and the mixture was extracted with EtOAc (2×5 mL). The combined extracts were washed with water (2×5 mL) and brine (2×5 mL), dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The crude product was used in next step without further purification.

Compound ***5c***: Following the general procedure B, the reaction of **2c** (220 mg, 1.04 mmol) with CAN (1.38 g, 2.51 mmol) in aqueous CH_3CN gave **5c** as a yellow solid (187 mg, 100%). M.p. 118–120 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 6.65$ (q, $J = 1.5$ Hz, 1H), 6.64 (s, 2H), 2.37 (s, 3H), 2.04 ppm (d, $J = 1.5$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 195.1$, 187.7, 157.4, 146.7, 133.8, 15.9, 15.1 ppm; ^{11}B NMR (96 MHz, $CDCl_3$): $\delta =$

28.3 ppm; MS (ES): *m/z* (%): 181.12 (3) $[M+1]^+$; HRMS: *m/z* calcd for $C_8H_9BO_4$: 180.0594 $[M+1]^+$; found: 181.1219.

Compound ***7a***: Following the general procedure B, the reaction of **4a** (60 mg, 0.26 mmol) with CAN (339 mg, 0.62 mmol) in aqueous MeCN gave **7a** as an orange solid (51 mg, 100%). M.p. 106–108°C; ^{1}H NMR (300 MHz, [D$_6$]acetone): δ=8.14–8.08 (m, 2H), 7.81–7.78 (m, 2H), 7.58 (s, 1H), 6.25 ppm (s, 2H); ^{13}C NMR (75 MHz, [D$_6$]acetone): δ=190.9, 184.7, 145.9, 134.2, 134.0, 132.4, 132.3, 126.2, 125.7 ppm; ^{11}B NMR (96 MHz, [D$_6$]acetone): δ=27.8 ppm; MS (ES): *m/z* (%): 203 (25) $[M+1]^+$, 189 (29), 61 (100); HRMS: *m/z* calcd for $C_{10}H_7BO_4$: 202.0437 $[M]^+$; found: 202.0550.

Compound ***7b***: Following the general procedure B, the reaction of **4b** (94 mg, 0.360 mmol) with CAN (473 mg, 0.864 mmol) in aqueous MeCN gave **7b** as an orange solid (53 mg, 63%). M.p. decomposes above 140°C; ^{1}H NMR (300 MHz, CDCl$_3$): δ=7.77–7.69 (m, 2H), 7.44 (s, 1H), 7.34 (dd, *J*=7.9, 1.0 Hz, 1H), 6.25 (brs, 2H), 4.02 ppm (s, 3H); ^{13}C NMR (75 MHz, CDCl$_3$): δ=191.5, 184.3, 159.6, 149.8, 135.2, 134.2, 120.2, 119.4, 118.3, 56.5 ppm; ^{11}B NMR (96 MHz, CDCl$_3$): δ=27.5 ppm; MS (ES): *m/z* (%): 227 (100), 205 (40); HRMS: *m/z* calcd for $C_{11}H_7O_3$: 187.0395 $[M]^+$; found: 187.0606.

Compound ***7c***: Following the general procedure B, the reaction of **4c** (50 mg, 0.14 mmol) with CAN (183 mg, 0.33 mmol) in aqueous MeCN gave **7c** as an orange solid (46 mg, 100%). M.p. 136–138°C; ^{1}H NMR (300 MHz, CDCl$_3$): δ=8.14–8.07 (m, 2H), 7.84–7.78 (m, 2H), 6.96 (brs, 2H), 3.52 (sept, *J*=6.8 Hz, 2H), 3.52 (sept, *J*=6.8 Hz, 2H), 3.46 (d, *J*=6.8 Hz, 6H), 1.19 ppm (d, *J*=6.8 Hz, 6H); ^{13}C NMR (75 MHz, CDCl$_3$): δ=191.1, 182.7, 165.7, 152.2, 134.5 (2C), 132.2, 131.3, 126.7, 126.5, 52.0, 46.6, 20.0 (2C), 19.9 ppm (2C); ^{11}B NMR (96 MHz, CDCl$_3$): δ=28.2 ppm; MS (ES): *m/z* (%): 329 (7) $[M]^+$, 330 (100) $[M+1]^+$; HRMS: *m/z* calcd for $C_{10}H_7BO_4$: 329.1435 $[M]^+$; found: 329.1558.

General procedure C for Diels–Alder reactions: The appropriate diene (0.6–0.8 mmol) was added to a solution of the corresponding 2-benzo- or naphthoquinonylboronic acid (0.2 mmol) in CH_2Cl_2 (3 mL). The resulting mixture was stirred at temperature *T* during the time indicated in each case. Water (3 mL) was added and the mixture was extracted with CH_2Cl_2 (3×3 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed in vacuo.

Compound ***9a***:[60] Following the general procedure C, the reaction of **7a** (60 mg, 0.30 mmol) with cyclopentadiene (98 mL, 1.18 mmol) gave **9a** as a pale yellow solid (67 mg, 100%). Reaction time: 20 min, *T*: −20°C.

Compound ***9c***: Following the general procedure C, the reaction of **7c** (40 mg, 0.12 mmol) with cyclopentadiene (41 mL, 0.48 mmol) gave **9c** as a pale yellow solid (35 mg, 82%). Reaction time: 15 h, *T*: −20°C. M.p. 120–122°C; ^{1}H NMR (300 MHz, CDCl$_3$): δ=8.02–7.94 (m, 2H), 7.71–7.68 (m, 2H), 5.86 (brs, 2H), 3.92 (brs, 1H), 3.51 (sept, *J*=6.4 Hz, 1H), 3.43 (m, 1H), 3.35 (d, *J*=3.5 Hz, 1H), 3.27 (sept, *J*=6.4 Hz, 1H), 1.81 (d, *J*=13.7 Hz, 1H), 1.61 (d, *J*=13.7 Hz, 1H), 1.47 (d, *J*=7.3 Hz, 3H), 1.38 (d, *J*=7.3 Hz, 3H), 1.00 (d, *J*=6.4 Hz, 3H), 0.68 ppm (d, *J*=6.4 Hz, 3H); ^{13}C NMR (75 MHz, CDCl$_3$): δ=197.1, 194.1, 169.3, 137.7, 135.6, 135.1, 134.5, 134.2, 126.9, 126.7, 64.6, 56.5, 56.1, 50.9 (2C), 48.5, 46.5, 29.6, 20.2 (2C), 20.0, 18.7 ppm; MS (EI): *m/z* (%): 351.2 (8.5) $[M]^+$, 285 (56), 185 (56), 200 (100); HRMS: *m/z* calcd for $C_{22}H_{25}NO_3$: 351.1834 $[M]^+$; found: 351.1819.

Compound ***9b***: Following the general procedure C, the reaction of **7b** (100 mg, 0.43 mmol) with cyclopentadiene (142 mL, 1.72 mmol) gave a 18:82 mixture of **9b** and **10**. Reaction time: 50 min, *T*: −20°C. Purification by flash column chromatography (hexane/EtOAc, 5:1) gave **9b** as a yellow oil (14 mg, 13%) ^{1}H NMR (300 MHz, CDCl$_3$): δ=7.61–7.52 (m, 2H), 7.20 (dd, *J*=8.0, 1.6 Hz , 1H), 6.05 (dd, *J*=5.9, 3.0 Hz, 1H), 5.98 (dd, *J*=5.9, 3.0 Hz, 1H), 3.93 (s, 3H), 3.62–3.55 (m, 2H), 3.47–3.44 (m, 2H), 1.56 (dt, *J*=8.7, 1.7 Hz , 1H), 1.48 ppm (d, *J*=8.7 Hz, 1H); ^{13}C NMR (75 MHz, CDCl$_3$): δ=198.5, 197.0, 158.9, 136.3, 135.5, 134.6, 118.8, 117.1, 56.4, 51.4, 50.3, 48.8, 48.4, 48.1 ppm; MS (EI): *m/z* (%): 254 (9) $[M]^+$, 240 (20), 66 (100); HRMS: *m/z* calcd for $C_{16}H_{14}O_3$: 254.0943 $[M]^+$; found: 254.0481.

Compound ***10***:[61] Following the above procedure, purification by flash column chromatography gave **10** (76 mg, 71%) as a yellow solid. M.p. 141–143°C.

Compound ***11a***: Following the general procedure C, the reaction of **7a** (60 mg, 0.30 mmol) with *trans*-piperylene (0.12 mL, 1.2 mmol) gave **11a** as a pale yellow solid (55 mg, 83%). Reaction time: 30 min, *T*: −20°C. M.p. 68–70°C; ^{1}H NMR (300 MHz, CDCl$_3$): δ=8.11–8.06 (m, 2H), 7.75–7.70 (m, 2H), 5.85 (m, 2H), 3.64 (m, 1H), 3.35 (ddd, *J*=24.5, 5.0, 3.6 Hz, 1H), 3.35 (ddd, *J*=24.5, 6.3, 2.4 Hz, 1H), 1.26 ppm (s, 1H); ^{13}C NMR (75 MHz, CDCl$_3$): δ=184.7, 184.2, 146.5, 141.7, 133.5, 133.4, 132.3, 132.0, 130.0, 126.3, 126.1, 121.3, 29.3, 24.6, 22.0 ppm; MS (EI): *m/z* (%): 224 (51) $[M]^+$, 222 (63), 209 (100); HRMS: *m/z* calcd for $C_{15}H_{12}O_2$: 224.0837 $[M]^+$; found: 224.0834.

Compound ***11b***:[61] Following the general procedure C, the reaction of **7b** (110 mg, 0.47 mmol) with *trans*-piperylene (129 μL, 1,90 mmol) gave **11b** after flash column chromatography (hexane/EtOAc, 6:1) as a yellow solid. (110 mg, 91%). Reaction time: 120 min, *T*: −20°C. M.p. 138–140°C.

Compound ***12a***: Following the general procedure C, the reaction of **7a** (40 mg, 0.19 mmol) with isoprene (75 mL, 0.76 mmol) gave **12a** as a white solid (41 mg, 96%). Reaction time: 2 h, *T*: 25°C. M.p. 124–126°C; ^{1}H NMR (300 MHz, CDCl$_3$): δ=8.12–8.08 (m, 2H), 7.73–7.70 (m, 2H), 5.57–5.54 (m, 1H), 3.29–3.22 (m, 2H), 3.17–3.11 (m, 2H), 1.82 ppm (s, 3H); ^{13}C NMR (75 MHz, CDCl$_3$): δ=184.6, 184.5, 141.8, 141.6, 133.5, 132.1, 132.1, 132.0, 130.1, 126.4, 126.2, 116.8, 26.1, 26.6, 22.9 ppm; MS (EI): *m/z* (%): 224 (2) $[M]^+$, 223 (17), 194 (63), 166 (39), 165 (100); HRMS: *m/z* calcd for $C_{15}H_{12}O_2$: 224.0837 [M]$^+$; found: 224.0713.

Compound ***12b***: Following the general procedure C, the reaction of **7b** (30 mg, 0.13 mmol) with isoprene (39 mL, 0.39 mmol) gave **12b** after flash column chromatography (hexane/EtOAc, 10:1) as an orange solid (22 mg, 67%). Reaction time: 2.5 h, *T*: 25°C. M.p. 144–146°C; ^{1}H NMR (300 MHz, CDCl$_3$): δ=7.75 (dd, *J*=7.6, 0.9 Hz, 1H), 7.64 (t, *J*=8.0 Hz, 1H), 7.27 (dd, *J*=8.4, 0.8 Hz, 1H), 5.61–5.44 (m, 1H), 4.01 (s, 3H), 3.19 (m, 2H), 3.10 (m, 2H), 1.80 ppm (s, 3H); ^{13}C NMR (75 MHz, CDCl$_3$): δ=184.7, 183.8, 159.4, 143.3, 139.5, 134.4, 134.3, 130.3, 120.0, 119.0, 117.5, 116.7, 56.4, 29.2, 25.3, 22.9 ppm. MS (EI): *m/z* (%): 254 (2) $[M]^+$, 252 (98), 165 (100), 152 (41); HRMS: *m/z* calcd for $C_{16}H_{14}O_3$: 254.0953 $[M]^+$; found: 254.0959.

Compound ***24d***: Following the general procedure C, the reaction of **7d** (35 mg, 0.16 mmol) with 2-[(*tert*-butyldimethylsilyl)oxy]-4-phenyl-1,3-butadiene (59 mg, 0.23 mmol) gave **24d** after flash column chromatography (hexane/EtOAc, 50:1) as a colourless oil (57 mg, 81%). Reaction time: 30 min, *T*: −20°C. ^{1}H NMR (300 MHz, CDCl$_3$): δ=8.01–7.97 (m, 1H), 7.75–7.70 (m, 1H), 7.65–7.53 (m, 2H), 7.34 (brs, 1H) 7.32 (brs, 1H), 7.25–7.16 (m, 2H), 7.14–7.08 (m, 1H), 4.09 (t, *J*=2.4 Hz, 1H), 3.24 (d, *J*=9.8 Hz, 1H), 2.82 (d, *J*=17.7 Hz, 1H), 2.28 (dd, *J*=17.7, 1.1 Hz, 1H), 1.25 (s, 3H), 0.87 (s, 9H), 0.09 (s, 3H), 0.08 ppm (s, 3H); ^{13}C NMR (75 MHz, CDCl$_3$: δ=200.7, 197.1, 147.4, 145.2, 136.1, 134.24, 133.9, 132.5, 128.9, 128.2, 127.3, 126.3, 126.2, 106.8, 57.2, 50.1, 39.3, 37.9, 25.6, 20.4, 18.0, −4.1, −4.34 ppm; MS (EI): *m/z* (%): 433 (100) $[M+1]^+$, 315 (100); HRMS: *m/z* calcd for $C_{27}H_{33}O_3Si$: 433.2199 $[M]^+$; found: 433.1990.

Compound ***25d***: Following the general procedure C, the reaction of **7d** (26 mg, 0.12 mmol) with 1-(1-cyclohexenyl)-1-[(*tert*-butyldimethylsilyl)oxy]-ethene (40 mg, 0.17 mmol) gave **25d** after flash column chromatography (hexane/EtOAc, 55:1) as a colourless oil (37 mg, 75%). Reaction time: 5 min, *T*: −20°C. ^{1}H NMR (300 MHz, CDCl$_3$): δ=8.10–8.02 (m, 1H), 7.98–7.91 (m, 1H), 7.75–7.69 (m, 2H), 2.97 (m, 1H), 2.83–2.65 (m, 3H), 2.35–2.23 (m, 2H), 1.84–1.72 (m, 2H), 1.65–1.45 (m, 2H), 1.31–1.18 (m, 1H), 1.16 (s, 3H), 0.98 (s, 9H), 0.87–0.75 (m, 1H), 0.17 ppm (brs, 6H); ^{13}C NMR (75 MHz, CDCl$_3$: δ=201.1, 198.1, 137.9, 136.3, 134.1, 133.9, 132.7, 127.3, 126.0, 115.8, 56.6, 48.7, 38.2, 35.3, 34.6, 26.7, 26.1, 25.9, 25.8, 20.2, 18.2, −3.7, −3.8 ppm; MS (FAB$^+$): *m/z* (%): 410 (100) $[M]^+$, 409 (58), 353 (29); HRMS: *m/z* calcd for $C_{25}H_{32}O_4Si$: 410.2277 $[M]^+$, found: 410.2286.

Compound ***(26d)***: Following the general procedure C, the reaction of **7d** (28 mg, 0.13 mmol) with 2-[(*tert*-butyldimethylsilyl)oxy]-3,4-dimethyl-1,3-butadiene (39 mg, 0.18 mmol) gave **26d** after flash column chromatography (hexane/EtOAc, 55:1) as a colourless oil (36 mg, 72%). Reaction

time: 5 min, *T*: −20 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.10–8.03 (m, 1H), 8.00–7.93 (m, 1H), 7.77–7.70 (m, 2H), 2.78–2.92 (m, 2H), 2.75–2.64 (m, 1H), 2.30 (d, J = 17.3 Hz, 1H), 1.66 (t, J = 1.16 Hz, 1H), 1.18–1.16 (m, 6H), 0.98 (s, 9H), 0.17 (s, 3H), 0.16 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 201.1, 198.1, 140.0, 136.3, 134.1, 133.9, 132.7, 127.2, 126.0, 113.3, 57.8, 49.1, 38.2, 31.4, 25.8, 20.2, 19.9, 13.5, −3.8 ppm; MS (ES): *m*/*z* (%): 384 (16) $[M]^+$, 369 (100), 351 (18), 327 (15); HRMS: *m*/*z* calcd for $C_{23}H_{32}O_3Si$: 384.2121 $[M]^+$; found: 384.2138.

*Compound (**27c**)*: Following the general procedure C, the reaction of **5c** (70 mg, 0.40 mmol) with 2-[(*tert*-butyldimethylsilyl)oxy]-4-phenyl-1,3-butadiene (203 mg, 0.78 mmol) gave **27c** after flash column chromatography (hexane/EtOAc, 25:1) as a yellow oil (94 mg, 61%). Reaction time: 30 min, *T*: −20 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.28–7.07 (m, 5H), 6.37 (q, J = 1.4 Hz, 1H), 4.68 (t, J = 2.4 Hz, 1H), 3.95 (m, 1H), 3.08 (d, J = 10.0 Hz, 1H), 2.61 (dt, J = 17.6, 2.4 Hz, 1H), 2.18 (dd, J = 17.6, 1.6 Hz, 1H), 1.87 (d, J = 1.4 Hz, 3H), 1.19 (s, 3H), 0.88 (s, 9H), 0.05 (s, 3H), 0.04 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 202.8, 199.1, 151.6, 147.5, 144.8, 134.3, 128.9, 128.2, 126.4, 106.8, 57.7, 50.4, 39.0, 37.7, 25.6, 20.6, 17.9, 16.1, −4.2, −4.3 ppm; MS (ES): *m*/*z* (%): 398 (100) $[M+2]^+$, 397 (52) $[M+1]^+$.

*Compound (**28c**)*: Following the general procedure C, the reaction of **5c** (60 mg, 0.33 mmol) with 1-(1-cyclohexenyl)-1-[(*tert*-butyldimethylsilyl)oxy]-ethene (159 mg, 0.67 mmol) gave **28c** after flash column chromatography (hexane/EtOAc, 25:1) as a yellow oil (71 mg, 57%). Reaction time: 5 min, *T*: −20 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.28–7.07 (m, 5H), 6.37 (q, J = 1.41 Hz, 1H), 4.68 (t, J = 2.4 Hz, 1H), 3.95 (m, 1H), 3.08 (d, J = 10.1 Hz, 1H), 2.61 (dt, J = 17.6, 2.4 Hz, 1H), 2.18 (dd, J = 17.6, 1.6 Hz, 1H), 1.87 (d, J = 1.4 Hz, 3H), 1.19 (s, 3H), 0.88 (s, 9H), 0.05 (s, 3H), 0.04 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 202.8, 199.1, 151.6, 147.5, 144.8, 134.3, 128.9, 128.2, 126.4, 106.8, 57.7, 50.4, 39.0, 37.7, 25.6, 20.6, 17.9, 16.1, −4.2, −4.3 ppm. MS (FAB$^+$): *m*/*z* (%): 374 (100) $[M]^+$, 373 (65), 317 (22); HRMS: *m*/*z* calcd for $C_{22}H_{34}O_3Si$: 374.2777 $[M]^+$; found: 374.2283.

*Compound (**29c**)*: Following the general procedure C, the reaction of **5c** (40 mg, 0.22 mmol) with 2-[(*tert*-butyldimethylsilyl)oxy]-3,4-dimethyl-1,3-butadiene (94 mg, 0.44 mmol) gave **29c** after flash column chromatography (hexane/EtOAc, 40:1) as a yellow oil (51 mg, 66%). Reaction time: 15 min, *T*: −20 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.42 (q, J = 1.4 Hz, 1H), 2.70–2.54 (m, 2H), 2.51 (d, J = 16.9 Hz, 1H), 2.14 (d, J = 16.9 Hz, 1H), 2.02 (d, J = 1.4 Hz, 3H), 1.62 (br s, 3H), 1.15–1.04 (m, 6H), 0.96 (s, 9H), 0.13 (s, 3H), 0.12 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 203.2, 200.2, 151.4, 140.0, 134.3, 113.3, 76.5, 58.2, 49.4, 38.0, 31.0, 25.8, 20.1, 19.6, 18.2, 16.2 ppm. MS (FAB$^+$): *m*/*z* (%): 348 (100) $[M]^+$, 291 (63); HRMS: *m*/*z* calcd for $C_{20}H_{32}O_3Si$: 348.2121 $[M]^+$; found: 348.2119.

*Compound (**30**)*: Following the general procedure C, the reaction of **5c** (70 mg, 0.39 mmol) with piperylene (117 μL, 1.17 mmol) under an O_2 atmosphere gave **30** as a yellow solid (72 mg, 84%) after flash column chromatography (hexane/EtOAc, 5:1). Reaction time: 60 min, *T*: 25 °C. M.p. 84–86 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.44 (q, J = 1.5 Hz, 1H), 5.81–5.57 (m, 1H), 5.46–5.30 (m, 1H), 3.06–2.79 (m, 1H), 2.72–2.51 (m, 1H), 2.15 (m, 3H), 2.05 (d, J = 1.6 Hz, 3H), 1.14 (d, J = 7.1 Hz, 3H), 1.08 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 202.1, 199.1, 148.7, 134.5, 128.7, 122.7, 79.7, 52.5, 31.0, 28.8, 20.6, 16.2, 14.3 ppm; MS (EI): *m*/*z* (%): 220 (13) $[M]^+$, 202 (42), 109 (81), 68 (100); HRMS: *m*/*z* calcd for $C_{13}H_{16}O_3$: 220.1099 $[M]^+$; found: 220.1097.

*Compound **31***: Following the general procedure C, the reaction of **5c** (25 mg, 0.14 mmol) with isoprene (55.6 μL, 0.55 mmol) under an O_2 atmosphere gave **31** as a yellow solid (12 mg, 38%) after flash column chromatography (hexane/EtOAc, 6:1). Reaction time: 5 h, *T*: 25 °C. M.p.: 110–112 °C; ^{1}H NMR (300 MHz $CDCl_3$): δ = 6.50 (q, J = 1.4 Hz, 1H), 5.50 (m, 1H), 2.66 (d, J = 16.6 Hz, 2H), 2.21 (m, 2H), 2.05 (d, J = 1.4 Hz, 3H), 1.76 (s, 3H), 1.07 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 202.2, 198.0, 147.5, 135.4, 132.1, 114.8, 76.8, 51.2, 33.9, 30.1, 23.5, 21.8, 16.1 ppm; MS (EI): *m*/*z* (%): 220 (4) [M]$^+$, 202 (64), 187 (60), 159 (100); HRMS: *m*/*z* calcd for $C_{13}H_{16}O_3$: 220.1099; found: 220.1110 [M$^+$].

Copies of the ^{1}H and ^{13}C NMR spectra and X-ray crystallography data are available in the Supporting Information.

Acknowledgements

We thank MICINN (grant no. CTQ2008-04691), Comunidad de Madrid (CM)/UAM (CCG08-UAM/PPQ-3980), Comunidad de Madrid (Grant SOLGEMAC-S2009/ENE-1617 and CM (grant no. S2009/ENE-1617) for financial support. M. C. Redondo thanks MEC for a Juan de la Cierva contract and M.V. for a FPU fellowship.

[1] a) *Boronic Acids: Preparation and Applications in Organic Synthesis and Medicine* (Ed.: D. G. Hall), Wiley-VCH, Weinheim, **2005**; b) N. Miyaura, A. Suzuki, *Chem. Rev.* **1995**, *95*, 2457–2483.

[2] a) A. Hercouet, F. Berrée, C. H. Lin, L. Toupet, B. Carboni, *Org Lett.* **2007**, *9*, 1717–1720; b) X. Gao, D. G. Hall, *Tetrahedron Lett.* **2003**, *44*, 2231–2235; c) J. Y. Lallemand, Y. Six, L. Ricard, *Eur. J. Org. Chem.* **2002**, 503–513; d) A. Zhang, Y. Kan, B. Jiang, *Tetrahedron* **2001**, *57*, 2305–2309; e) R. A. Batey, A. Thadani, A. J. J. Lough, *Chem. Commun.* **1999**, 475–476; f) Y. Six, J. Y. Lallemand, *Tetrahedron Lett.* **1999**, *40*, 1295–6590; g) P. Y. Renard, Y. Six, J. Y. Lallemand, *Tetrahedron Lett.* **1997**, *38*, 6589–6590; h) P. Y. Renard, J. Y. Lallemand, *Tetrahedron: Asymmetry* **1996**, *7*, 2523–2524; i) L. Garnier, B. Plunian, J. Mortier, M. Vaultier, *Tetrahedron Lett.* **1996**, *37*, 6699–6700.

[3] a) A. Zhang, Y. Kan, B. Jiang, *Tetrahedron* **2001**, *57*, 2305–2309; b) X. B. Wang, *J. Chem. Soc. Chem. Commun.* **1991**, 1515–1517.

[4] M. Vaultier, F. Truchet, B. Carboni, R. W. Hoffmann, I. Denne, *Tetrahedron Lett.* **1987**, *28*, 4169–4172.

[5] a) J. Renaud, C. D. Graf, L. Oberer, *Angew. Chem.* **2000**, *112*, 3231–3234; *Angew. Chem. Int. Ed.* **2000**, *39*, 3101–3104; b) A. Kamabuchi, N. Miyaura, A. Suzuki, *Tetrahedron Lett.* **1993**, *34*, 4827–4829.

[6] For Diels–Alder reactions with potassium 1,3-dienyl-2-trifluoroborates, see: a) S. De, C. Day, M. E. Welker, *Tetrahedron* **2007**, *63*, 10939–10948; b) S. De, M. E. Welker, *Org Lett.* **2005**, *7*, 2481–2484.

[7] X. Gao, D. G. Hall, A. Favre, M. Deligny, F. Carreaux, B. Carboni, *Chem. Eur. J.* **2006**, *12*, 3132–3142 and references therein.

[8] B. B. Touré, D. G. Hall, *Angew. Chem.* **2004**, *116*, 2035–2038; *Angew. Chem. Int. Ed.* **2004**, *43*, 2001–2004.

[9] a) Y-K. Lee, D. A. Singleton, *J. Org. Chem.* **1997**, *62*, 2255–2258; b) D. A. Singleton, K. Kim, J. P. Martinez, *Tetrahedron Lett.* **1993**, *34*, 3071–3074; c) D. A. Singleton, J. P. Martínez, J. V. Watson, G. D. Ndip, *Tetrahedron* **1992**, *48*, 5831–5838; d) D. A. Singleton, J. P. Martinez, G. M. Ndip, *J. Org. Chem.* **1992**, *57*, 5768–5771; e) D. A. Singleton, J. P. Martinez, *J. Am. Chem. Soc.* **1990**, *112*, 7423–7424.

[10] D. S. Matteson, J. O. Waldbillig, *J. Org. Chem.* **1963**, *28*, 366–368.

[11] For the intramolecular Diels–Alder reaction, see: a) R. A. Batey, A. N. Thadani, A. J. Lough, *J. Am. Chem. Soc.* **1999**, *121*, 450–451; b) G. Lorvelec, M. Vaultier, *Tetrahedron Lett.* **1998**, *39*, 5185–5188; c) R. A. Batey, D. Lin, Wong, C. L. S. Hayhoe, *Tetrahedron Lett.* **1997**, *38*, 3699–3702.

[12] a) J. W. J. Kennedy, D. G. Hall, *J. Organomet. Chem.* **2003**, *680*, 263–270; b) J. W. J. Kennedy, D. G. Hall, *Synlett* **2002**, 0477–0479.

[13] a) K. Krohn, J. Micheel, M. Zukowski, *Tetrahedron* **2000**, *56*, 4753–4758; b) T. R. Kelly, A. Whiting, N. S. Chandrakumar, *J. Am. Chem. Soc.* **1986**, *108*, 3510–3512.

[14] For the synthesis and applications of metal-substituted quinones, see: B. G. Vong, E. A. Theodorakis in *Science of Synthesis Houben-Weyl Methods of Molecular Transformations, Vol. 28* (Ed.: A. G. Griesbeck), Thieme, Stuttgart, **2006**, pp. 13–29.

[15] For reviews, see a) E. J. Corey, *Angew. Chem.* **2002**, *114*, 1724–1741; *Angew. Chem. Int. Ed.* **2002**, *41*, 1650–1667; b) K. C. Nicolaou, S. A. Snyder, T. Montagnon, G. Vassilikogiannakis, *Angew. Chem.* **2002**, *114*, 1742–1773; *Angew. Chem. Int. Ed.* **2002**, *41*, 1668–1698; c) M. C. Carreño, A. Urbano, *Synlett* **2005**, 1–25; d) K. Krohn, *Angew. Chem.* **1986**, *98*, 788–805; *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 790–807.

[16] For recent examples, see: a) K. C. Nicolaou, Y. H. Lim, J. Becker, *Angew. Chem.* **2009**, *121*, 3496–3500; *Angew. Chem. Int. Ed.* **2009**, *48*, 3444–3448; b) A. A. Boezio, E. R. Jarvo, B. M. Lawrence, E. N. Jacobsen, *Angew. Chem.* **2005**, *117*, 6200–6204; *Angew. Chem. Int.*

Ed. **2005**, *44*, 6046–6050; c) M. E. Layton, C. A. Morales, M. D. Shair, *J. Am. Chem. Soc.* **2002**, *124*, 773–775; d) J. D. White, Y. Choi, *Org. Lett.* **2000**, *2*, 2373–2376.

[17] See, for instance: a) K. C. Nicolaou, G. Vassilikogiannakis, W. Magerlein, R. Kranich, *Angew. Chem.* **2001**, *113*, 2543–2547; *Angew. Chem. Int. Ed.* **2001**, *40*, 2482–2486; b) J. D. White, N. S. Cutshall, T. S. Kim, H. Shin, *J. Am. Chem. Soc.* **1995**, *117*, 9780–9781; c) E. J. Corey, R. L. Danheiser, S. Chandrasekaran, P. Siret, G. E. Keck, J. L. Gras, *J. Am. Chem. Soc.* **1978**, *100*, 8031–8034.

[18] a) R. L. Nunes, L. W. Bieber, *Tetrahedron Lett.* **2001**, *42*, 219–221; b) J. Tou, W. Reusch, *J. Org. Chem.* **1980**, *45*, 5012–5014.

[19] For a recent example, see: L. Pingfan, J. N. Payette, H. Yamamoto, *J. Am. Chem. Soc.* **2007**, *129*, 9536–9537.

[20] a) E. R. Jarvo, B. M. Lawrence, E. N. Jacobsen, *Angew. Chem.* **2005**, *117*, 6197–6200; *Angew. Chem. Int. Ed.* **2005**, *44*, 6043–6046; b) D. H. Ryu, E. J. Corey, *J. Am. Chem. Soc.* **2004**, *126*, 4800–4802; c) D. A. Evans, J. Wu, *J. Am. Chem. Soc.* **2003**, *125*, 10162–10163; d) T. R. Kelly, A. Whiting, N. S. Chandrakumar, *J. Am. Chem. Soc.* **1986**, *108*, 3510–3512.

[21] a) G. A. Kraus, J. Li, M. S. Gordon, J. H. Jensen, *J. Am. Chem. Soc.* **1993**, *115*, 5859–5860.

[22] a) K. Krohn, *Tetrahedron Lett.* **1980**, *21*, 3557–3560; b) R. K. Boeckman T. M. Dolak, K. O. Culos, *J. Am. Chem. Soc.* **1978**, *100*, 7098–7100; c) T. R. Kelly, J. Vaya, L. Ananthasubramanian, *J. Am. Chem. Soc.* **1980**, *102*, 5983–5984; d) T. R. Kelly, J. W. Gillard, Jr., R. N. Goerner, J. M. Lyding, *J. Am. Chem. Soc.* **1977**, *99*, 5513–5514.

[23] G. A. Kraus, N. Zhang, J. K. Wei, J. H. Jensen, *Eur. J. Org. Chem.* **2005**, 3040–3044.

[24] R. Hawley, J. G. Bauman, H. Rapoport, *J. Org. Chem.* **1985**, *50*, 1569–1573.

[25] a) M. C. Carreño, M. Ribagorda, A. Somoza, A. Urbano, *Chem. Eur. J.* **2007**, *13*, 879–890; b) M. C. Carreño, M. Ribagorda, A. Somoza, A. Urbano, *Angew. Chem.* **2002**, *114*, 2879–2881; *Angew. Chem. Int. Ed.* **2002**, *41*, 2755–2757; c) G. A. Kraus, S. H. Woo, *J. Org. Chem.* **1985**, *50*, 114–116.

[26] a) M. C. Carreño, Á. Enríquez, S. García-Cerrada, M. J. Sanz-Cuesta, A. Urbano, F. Maseras, A. Nonell-Canals, *Chem. Eur. J.* **2008**, *14*, 603–620; b) M. C. Carreño, M. González-López, A. Urbano, *Chem. Commun.* **2005**, 611–613; c) M. C. Carreño, S. García-Cerrada, A. Urbano, *Chem. Eur. J.* **2003**, *9*, 4118–4131.

[27] a) M. C. Carreño, C. Di Vitta, A. Urbano, *Chem. Eur. J.* **2000**, *6*, 906–913; b) M. C. Carreño, A. Urbano, J. Fischer, *Angew. Chem.* **1997**, *109*, 1695–1697; *Angew. Chem. Int. Ed.* **1997**, *36*, 1621–1623.

[28] For a preliminary communication, see: M. C. Redondo, M. Veguillas, M. Ribagorda, M. C. Carreño, *Angew. Chem.* **2009**, *121*, 376–380; *Angew. Chem. Int. Ed.* **2009**, *48*, 370–374.

[29] a) M. W. Davies, C. N. Johnson, J. P. A. Harrity, *J. Org. Chem.* **2001**, *66*, 3525–3532; b) M. W. Davies, C. N. Johnson, J. P. A. Harrity, *Chem. Commun.* **1999**, 2107–2108.

[30] a) A. N. Nesmeyanov, R. A. Sokolik, *Methods of Elemento-Organic Chemistry, Vol. 1*, North-Holland, Amsterdam, **1967**; b) A. Pelter, K. Smith, H. C. Brown, *Borane Reagents*, Academic Press, London, **1988**.

[31] When not commercially available, the bromo derivatives were obtained by regioselective bromination of adequately substituted hydroquinones or 1,4-dimethoxyaromatic derivatives with *N*-bromosuccinimide (see the Supporting Information).

[32] Compound **2a** is commercially available.

[33] P. Jacob, P. S. Callery, A. T. Shulgin, Jr., N. Castagnoli, *J. Org. Chem.* **1976**, *41*, 3627–3629.

[34] CCDC-690061 (**8c**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. M_r $C_{13}H_{14}O_2$; unit cell parameters: $a=6.4479(6)$, $b=8.1944(7)$, $c=9.9567(10)$ Å; $\alpha=87.441(4)°$, $\beta=85.376(4)°$ and $\gamma=86.453(4)°$; space group $P\bar{1}$.

[35] a) 2,5-Dimethyl benzoquinone reacted with cyclopentadiene under reflux in benzene in 1.5 h, see: K. Alder, F. H. Flock, H. Beumling, *Chem. Ber.* **1960**, *93*, 1896–1899; b) reaction of 2,6-dimethylbenzoquinone and cyclopentadiene in MeOH at RT was completed in 45 h, see: C. Liu, D. J. Burnell, *J. Org. Chem.* **1997**, *62*, 3683–3697.

[36] CCDC-748451 (**9c**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. M_r $C_{22}H_{25}NO_3$; unit cell parameters: $a=7.7078(8)$, $b=23.610(3)$, $c=10.1924(8)$ Å; $\beta=90.515(3)°$; space group $P2_1/c$.

[37] Y.-F. Ji, Z.-M. Zong, X.-Y. Wei, G.-Z. Tu, L. Xu, L.-T. He, *Synth. Commun.* **2003**, *33*, 763–772.

[38] M. P. Hughes, B. D. Smith, *J. Org. Chem.* **1997**, *62*, 4492–4499.

[39] CCDC-690060 (**13d**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. M_r $C_{16}H_{16}O_2$; unit cell parameters: $a=8.109(3)$, $b=8.130(3)$ and $c=10.793(5)$ Å; $\alpha=99.06(3)°$, $\beta=110.20(3)°$ and $\gamma=107.72(2)°$; space group $P\bar{1}$.

[40] A. K. Bhattacharya, B. Miller, *J. Org. Chem.* **1983**, *48*, 2412–2418.

[41] K. Hayakawa, K. Ueyama, K. Kanematsu, *J. Org. Chem.* **1985**, *50*, 1963–1969.

[42] The equilibration of the initially formed *cis* adducts of the reaction between 2,6 or 2,5-dimethylbenzoquinone with sodium (*E*)-3,5-hexanodienoate also gave *trans*-fused cycloadducts: P. A. Grieco, K. Yoshida, P. Garner, *J. Org. Chem.* **1983**, *48*, 3137–3139.

[43] J. B. Hendrickson, V. Singh, *J. Chem. Soc. Chem. Commun.* **1983**, 837–838.

[44] a) J. Augé, R. Gil, S. Kalsey, N. Lubin-Germain, *Synlett* **2000**, 877–879; b) W.-S. Chung, J.-Y. Wang, *J. Chem. Soc. Chem. Commun.* **1995**, 971–972.

[45] a) P. A. Grieco, J. J. Nunes, M. D. Gaul, *J. Am. Chem. Soc.* **1990**, *112*, 4595–4596; b) Z. Stojanac, R. A. Dickinson, N. Stojanac, R. J. Woznow, Z. Valenta, *Can. J. Chem.* **1975**, *53*, 616–618.

[46] K. Ishihara, H. Yamamoto, *Eur. J. Org. Chem.* **1999**, 527–538.

[47] For a detailed configurational assignment of *trans*/*cis* adducts see the Supporting Information of reference [28]; see also a) H. W. Thompson, D. J. Long, *J. Org. Chem.* **1988**, *53*, 4201–4209; b) F. Bohlmann, W. Mathar, H. Schwarz, *Chem. Ber.* **1977**, *110*, 2028–2045.

[48] CCDC-690062 (**20**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. M_r $C_{26}H_{32}O_4$; unit cell parameters: $a=10.3410(10)$, $b=7.6410(8)$, $c=26.680(3)$ Å; space group *Pbca*.

[49] CCDC-748452 (**30**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. M_r $C_{13}H_{16}O_3{\cdot}H_2O$; unit cell parameters: $a=12.1146(8)$, $b=11.0495(8)$, $c=8.9789(5)$ Å; $\beta=93.429(2)°$; space group $P2_1/c$.

[50] For a stepwise synthesis of similar angularly hydroxysubstituted systems, see: K. Hayakawa, K. Ueyama, K. Kanematsu, *J. Org. Chem.* **1985**, *50*, 1963–1969.

[51] I. Fleming, *Frontier Orbitals and Organic Chemical Reactions*, Wiley, New York, **1976**.

[52] CCDC-754824 (**5d**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. M_r $C_8H_9BO_4$; unit cell parameters: $a=8.1967(6)$, $b=17.9782(12)$, $c=5.5969(4)$ Å; $\beta=95.239(3)°$; space group $P2_1/c$.

[53] ^{11}B NMR spectroscopy monitoring of the reaction between **7d** and cyclopentadiene in CD_2Cl_2 revealed the formation of a species appearing at $\delta=19.1$ ppm, which was assigned to boroxine $B_3O_6H_3$, see: R. A. Baber, N. C. Norman, A. G. Orpen, J. Rossi, *New J. Chem.* **2003**, *27*, 773–775. Water is generated in situ from the boronic acid–boroxine equilibrium, see: H. R. Snyder, M. S. Konecky, W. J. Lennarz, *J. Am. Chem. Soc.* **1958**, *80*, 3611–3615.

[54] For catalysed [2+2] cycloadditions, see: a) E. Lee-Ruff in *The Chemistry of Cyclobutanes, Vol. 1* (Eds.: Z. Rappoport, J. F. Lieb-

man), Wiley, New York, **2005**, pp. 281–355; b) E. Lee-Ruff, G. Mladenova, *Chem. Rev.* **2003**, *103*, 1449–1483.
[55] For [2+2] cycloadditions catalysed by oxazaborolidine, see: H. Butenschön, *Angew. Chem.* **2008**, *120*, 3544–3547; *Angew. Chem. Int. Ed.* **2008**, *47*, 3492–3495, and references therein.
[56] See, for instance: E. Ruijter, H. Schültingkemper, L. A. Wessjohann, *J. Org. Chem.* **2005**, *70*, 2820–2823.
[57] For the synthesis and characterisation data of quinonyl boronic acids and adducts not included in the Experimental Section, see the Supporting Information of reference [28].
[58] M. Yoshida, Y. Shoji, K. Shishido, *Org. Lett.* **2009**, *11*, 1441–1443.
[59] B. Love, J. Bonner-Stewart, L. A. Forrest, *Synthesis* **2009**, 813–817.
[60] L. A. Paquette, F. Bellamy, M. C. Bohm, R. Gleiter, *J. Org. Chem.* **1980**, *45*, 4913–4921.
[61] M. C. Carreño, J. L. Garcia Ruano, A. Urbano, *J. Org. Chem.* **1992**, *57*, 6870–6876.
[62] M. C. Carreño, J. L. García Ruano, M. A. Toledo, A. Urbano, C. Z. Remor, V. Stefani, J. Fischer, *J. Org. Chem.* **1996**, *61*, 503–509.

Received: October 9, 2009
Published online: February 19, 2010

