Synthesis of Enantiomerically Pure Cyclopropanes from Cyclopropylboronic Acids†

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A general method for the stereocontrolled synthesis of cyclopropanes is described. Various, highly stable, enantiomerically pure alkenylboronic esters **13** have been conveniently synthesized by the direct hydroboration of alkynes **11** using the new chiral 1,3,2-dioxaborolane **15**. The high stability was also demonstrated by the selective deprotection of a *tert*-butyldimethylsilyl protecting group without hydrolyzing the boronic ester. The diastereoselective cyclopropanation of the olefins was achieved by the palladium(II) acetate catalyzed decomposition of diazomethane. This process was optimized giving cyclopropylboronic esters **20/21** in high yield (89−99%) and with good to excellent diastereomeric ratios (up to 95:5). The diastereomers were separated by means of MPLC and their configurations determined by X-ray crystallography (compound **21c**), by transformation to known cyclopropanols, and by correlation of NMR data. Treatment with $LiAlH_4$ followed by acidic hydrolysis yielded the enantiomerically pure cyclopropylboronic acid **27** for the first time and allowed the nearly quantitative recovery of the chiral auxiliary **3**. Different protocols for the Suzuki coupling reaction of compound **27** were investigated.

Introduction

Cyclopropanes have attracted considerable interest in recent years. They are also increasingly incorporated into pharmaceuticals due to their well-defined three-dimensional structure.[1] From the point of view of new synthetic targets, it is especially noteworthy that a growing number of natural products containing a cyclopropyl group have been isolated.[2] Elegant, highly selective methods for the synthesis of optically active cyclopropanes have consequently been developed in recent years.[3] Nevertheless, new, more general approaches to a wide variety of enantiomerically pure cyclopropane derivatives are still highly desirable.[4] Alkenylmetal compounds (B, Al, Si, Sn) are versatile intermediates, since after cyclopropanation they can potentially react with a variety of electrophiles.[5] Cyclopropyl boron derivatives are ideal: the starting materials are not only readily available in a stereodefined manner, but by utilizing the whole potential of boron compounds,[6] the synthesis of a plethora of different cyclopropanes should be feasible. Cyclopropylboronic esters are most convenient,[7−9] since the only carbon substituent on boron is easily displaced. In addition, boronic esters allow for the introduction of chiral auxiliaries, thus enabling diastereoselective cyclopropanations of alkenylboronic esters, a method first employed by Imai et al.[8a] and later adopted by others.[8b,c] A major setback has been the relative lability of this class of compounds; separation of diastereomers was not

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(1) (a) De Meijere, A., Ed. *Houben-Weyl, Methods in Organic Chemistry*, 4th ed.; Georg Thieme Verlag: Stuttgart, 1997; Vol. E17c. (b) Wong, H. N. C.; Hon, M.-Y.; Tse, C.-W.; Yip, Y. C.; Tanko, J.; Hudlicky, T. *Chem. Rev.* **1989**, *89*, 165−198. (c) Regitz, M.,Ed. *Houben-Weyl, Methoden in der Organischen Chemie,* 4th ed.; Georg Thieme Verlag: Stuttgart, 1989; Vol. E19. (d) Reissig, H.-U. *Top. Curr. Chem.* **1988**, *144*, 73−135. (e) Salaün, J. R. Y. *Top. Curr. Chem.* **1988**, *144*, 1−69. (f) Patai, S., Rappoport, Z., Eds. *The Chemistry of the Cyclopropyl Group*; Wiley: New York, 1987.

(2) (a) Gerwick, W. H. *Chem. Rev.* **1993**, *93*, 1807−1823. (b) Suckling, C. J. *Angew. Chem.* **1988**, *100*, 555−570; *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 537. Recent examples: Isolation of plakosides A and B: (c) Costantino, V.; Fattorusso, E.; Mangoni, A.; Di Rosa, M.; Ianaro, A. *J. Am. Chem. Soc.* **1997**, *119*, 12465−12470. Constanolactone: Isolation: (d) Nagle, D. G.; Gerwick, W. H. *Tetrahedron Lett.* **1990**, *31*, 2995−2998. (e) Nagle, D. G.; Gerwick, W. H. *J. Org. Chem.* **1994**, *59*, 7227−7237. Synthesis: (f) White, J. D.; Jensen, M. S. *J. Am. Chem. Soc.* **1995**, *117*, 6224−6233. (g) Miyaoka, H.; Shigemoto, T.; Yamada, Y. *Tetrahedron Lett.* **1996**, *37*, 7407−7408. (h) Miyaoka, H.; Shigemoto, T.; Yamada, Y. *Heterocycles* **1998**, *47*, 415−428. Halicholactone and neohalicholactone: Isolation: (i) Niwa, H.; Wakamatsu, K.; Yamada, K. *Tetrahedron Lett.* **1989**, *30*, 4543−4546. (j) Kigoshi, H.; Niwa, H.; Yamada, K.; Stout, T. J.; Clardy, J. *Tetrahedron Lett.* **1991**, *32*, 2427−2430. Synthesis: (k) Crichter, D. J.; Connolly, S.; Wills, M. *J. Org. Chem.* **1997**, *62*, 6638−6657 and references therein. Formal synthesis: (l) Mohapatra, D. K.; Datta, A. *J. Org. Chem.* **1998**, *63*, 642−646. Solandelactones: Isolation: (m) Seo, Y.; Cho, K. W.; Rho, J.-R.; Shin, J. *Tetrahedron* **1996**, *52*, 10583−10596. Fragment synthesis: (n) Varadarajan, S.; Mohapatra, D. K.; Datta, A. *Tetrahedron Lett.* **1998**, *39*, 1075−1078. (o) Barloy-Da Silva, C.; Pale, P. *Tetrahedron: Asymmetry* **1998**, *9*, 3951−3954. Related eicosanoids: (p) White, J. D.; Jensen, M. S. *J. Am. Chem. Soc.* **1993**, *115*, 2970−2971. (q) Nagasawa, T.; Handa, Y.; Onoguchi, Y.; Suzuki, K. *Bull. Chem. Soc. Jpn.* **1996**, *69*, 31−39. Callipeltoside: Isolation: (r) Zampella, A.; D'Auria, M. V.; Minale, L.; Debitus, C.; Roussakis, C. *J. Am. Chem. Soc.* **1996**, *118*, 11085−11088. Cepaciamide: Isolation: (s) Ishikuri, S.; Uchino, H.; Kanazawa, K. A. *Phytopath. Soc. Jpn.* **1992**, *58*, 456−460. Revised structure: (t) Toshima, H.; Maru, K.; Jiao, Y.; Yoshihara, T.; Ichihara, A. *Tetrahedron Lett.* **1999**, *40*, 935−938. Synthesis: (u) Toshima, H.; Maru, K.; Saito, M.; Ichihara, A. *Tetrahedron Lett.* **1999**, *40*, 939−942. FR-900848: Isolation: (v) Yoshida, M.; Ezaki, M.; Hashimoto, M.; Yamashita, M.; Shigematsu, N.; Okuhara, M.; Kohsaka, M.; Horikoshi, K. *J. Antibiot.* **1990**, *43*, 748−754. Configuration: (w) Barrett, A. G. M.; Kasdorf, K.; Tustin, G. J.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1995**, 1143−1144. Synthesis: (x) Barrett, A. G. M.; Kasdorf, K. *J. Am. Chem. Soc.* **1996**, *118*, 11030−11037. (y) Barrett, A. G. M.; Kasdorf, K. *Chem. Commun.* **1996**, 325−326. (z) Falck, J. R.; Mekonnen, B.; Yu, J.; Lai, J.-Y. *J. Am. Chem. Soc.* **1996**, *118*, 6096−6097. U-106305: Isolation and structure: (aa) Kuo, M. S.; Zielinski, J. I.; Cialdella, J. I.; Marschke, C. K.; Dupuis, M. J.; Li, G. P.; Kloosterman, D. A.; Spilman, C. H.; Marshall, V. P. *J. Am. Chem. Soc.* **1995**, *117*, 10629−10634. Synthesis: (bb) Barrett, A. G. M.; Hamprecht, D.; White, A. J. P.; Williams, D. J. *J. Am. Chem. Soc.* **1996**, *118*, 7863−7864. (cc) Charette, A. B.; Lebel, H. *J. Am. Chem. Soc.* **1996**, *118*, 10327−10328. Fragment synthesis: (dd) McDonald, W. S.; Verbicky, C. A.; Zercher, C. K. *J. Org. Chem.* **1997**, *62*, 1215−1222.

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possible, and after workup and/or further transformation only partially enantiomerically enriched cyclopropanes were isolated.

Recently,[9] we demonstrated that alkenylboronic esters **1**, which are stable on silica gel, are conveniently cyclopropanated by the Pd(II)-catalyzed decomposition of diazomethane to furnish cyclopropylboronic esters **2** (Figure 1). Bulky substituents appear ideally adapted to stabilize these dioxaborolanes.[9a] Previously, we reported[9b] that the synthesis of cyclopropylboronic esters of diol **3**[10] proved to be superior (higher diastereoselectivity; readily separable diastereomers) to the corresponding esters of pinanediol **4**[11] and 1,1,2-triphenyl-1,2-ethanediol **5**.[12] We now present a detailed account of the synthesis of a variety of enantiomerically pure cyclopropanes, demonstrating that cyclopropylboronic esters **2** are highly desirable key intermediates.

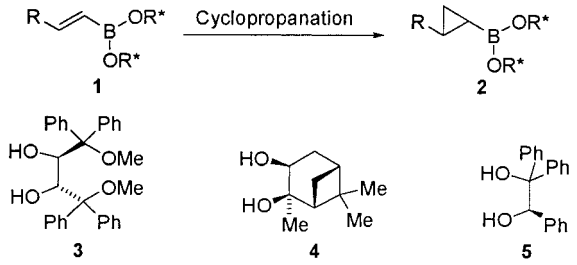
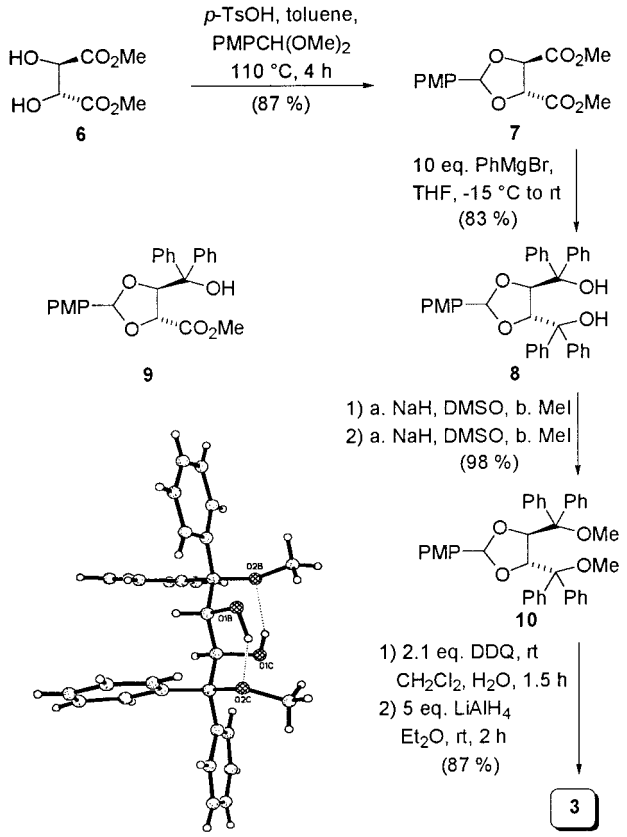


Figure 1. Synthesis of cyclopropylboronic esters **2** from enantiomerically pure alkenylboronic esters **1** (derived from diols **3**−**5**).[9]

Scheme 1. Synthesis and Structure (As Determined by X-ray Diffraction) of Diol 3



Results and Discussion

To serve as a good and reliable protecting group for boronic esters, the chiral auxiliary **3** needs to meet the following requirements: (a) diol **3** must be available on a multigram scale; (b) synthesis of alkenylboronic esters **2** should be straightforward; (c) the cyclopropanation should be highly diastereoselective; (d) the cyclopropylboronic esters **3** should be sufficiently stable so as to allow separation of the diastereomers, but (e) not so stable as to prevent further transformations; and (f) as an ideal protecting group, the recovery of diol **3** is the ultimate prerequisite.

Synthesis of Chiral Auxiliary 3. For the synthesis of diol **3**, we followed a procedure described by Nakayama and Rainier (Scheme 1).[10] Starting from dimethyl L-tartrate **6**, we first formed acetal **7** (87%) by the acid-

(3) (a) Reissig, H.-U. In *Stereoselective Synthesis of Organic Compounds/Methods of Organic Chemistry (Houben-Weyl)*, 4th ed.; Helmchen, G., Hoffmann, R. W., Mulzer, J., Schaumann, E., Eds.; Thieme: Stuttgart, 1995; Vol. E21c, pp 3179−3270. (b) Charette, A. B.; Marcoux, J.-F. *Synlett* **1995**, 1197−1207. (c) Denmark, S. E.; O'Connor, S. P. *J. Org. Chem.* **1997**, *62*, 584−594. (d) Denmark, S. E.; Christenson, B. L.; Coe, D. M.; O'Connor, S. P. *Tetrahedron Lett.* **1995**, *36*, 2215−2218. (e) Denmark, S. E.; Christenson, B. L.; O'Connor, S. P. *Tetrahedron Lett.* **1995**, *36*, 2219−2222. (f) Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307−1370. (g) Ye, T.; McKervey, M. A. *Chem. Rev.* **1994**, *94*, 1091−1160. (h) Nagasawa, T.; Handa, Y.; Onoguchi, Y.; Suzuki, K. *Bull. Chem. Soc. Jpn.* **1996**, *69*, 31−39. (i) Charette, A. B.; Juteau, H. *J. Am. Chem. Soc.* **1994**, *116*, 2651−2652. (j) Charette, A. B.; Presscott, S.; Brocha, C. *J. Org. Chem.* **1995**, *60*, 1081−1083. (k) Charette, A. B.; Lebel, H. *Org. Synth.* **1998**, *76*, 86−100 and references therein.

(4) Reissig, H.-U. *Angew. Chem.* **1996**, *108*, 1049−1051; *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 971−973.

(5) Zn: (a) Yachi, K.; Shinokubo, H.; Oshima, K. *Angew. Chem.* **1998**, *110*, 2672−2674; *Angew. Chem. Int. Ed.* **1998**, *37*, 2515−2519. Al: (b) Zweifel, G.; Clark, G. M.; Whitney, C. C. *J. Am. Chem. Soc.* **1971**, *93*, 1305−1307. Si: (c) Hirabayashi, K.; Mori, A.; Hiyama, T. *Tetrahedron Lett.* **1997**, *38*, 461−464. (d) Paquette, L. A. *Chem. Rev.* **1986**, *86*, 733−750. (e) Ukaji, Y.; Sada, K.; Inomata, K. *Chem. Lett.* **1993**, 1227−1230. Sn: (f) Seyferth, D.; Cohen, H. M. *Inorg. Chem.* **1962**, *1*, 913−916. (g) Hoffmann, R. W.; Koberstein, R. *Chem. Commun.* **1999**, 33−34. (h) Lautens, M.; Delanghe, P. H. M. *J. Org. Chem.* **1995**, *60*, 2474−2487, and ref. therein. (i) Imai, N.; Sakamoto, K.; Takahashi, H.; Kobayashi, S. *Tetrahedron Lett.* **1994**, *35*, 7045−7048. Also see ref 2z and references therein.

(6) (a) Matteson, D. S. In *Stereodirected Synthesis with Organoboranes*; Hafner, K., Rees, C. W., Trost, B. M., Lehn, J.-M., von Ragué Schleyer, P., Eds.; Springer-Verlag: Heidelberg, 1995. (b) Pelter, A.; Smith, K.; Brown, H. C. In *Borane Reagents*; Academic Press: London, 1988. (c) Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. In *Organic Synthesis via Boranes*; Wiley: New York, 1975. (d) Matteson, D. S. In *The Chemistry of the Metal−Carbon Bond*; Hartley, F., Patai, S., Eds.; Wiley: Chichester, 1987; Vol. 4. (e) Brown, H. C.; Negishi, E.; Zaidlewicz, M. In *Comprehensive Organometallic Chemistry: Organoborane Compounds in Organic Synthesis*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon Press: Oxford, 1982; Vol. 7. (f) Brown, H. C.; Jadhav, P. K. In *Asymmetric synthesis: Asymmetric hydroboration*; Morrison, J. D., Ed.; Academic Press: Orlando, 1983; Vol. 2.

(7) (a) Bubnov, Y. N.; Nesmeyanova, O. A.; Rudashevskaya, T. Y.; Mikhailov, B. M.; Kazansky, B. A. *Tetrahedron Lett.* **1971**, 2153−2156. (b) Danheiser, R. L.; Savoca, A. C. *J. Org. Chem.* **1985**, *50*, 2401−2403. (c) Fontani, P.; Carboni, B.; Vaultier, M.; Carrié, R. *Tetrahedron Lett.* **1989**, *30*, 4815−4818. (d) Fontani, P.; Carboni, B.; Vaultier, M.; Maas, G. *Synthesis* **1991**, 605−609. (e) Hildebrand, J. P.; Marsden, S. P. *Synlett* **1996**, 893−894. (f) Wang, Z.; Deng, M.-Z. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2663−2664. (g) Charette, A. B.; De Freitas-Gil, R. P. *Tetrahedron Lett.* **1997**, *38*, 2809−2812. (h) Zhou, S.-M.; Yan, Y.-L.; Deng, M.-Z. *Synlett* **1998**, 198−200.

(8) (a) Imai, H. Mineta, S. Nishida, *J. Org. Chem.* **1990**, *55*, 4986−4988. (b) Pietruszka, J.; Widenmeyer, M. *Synlett* **1997**, 977−979. (c) Zhou, S.-M.; Deng, M.-Z.; Xia, L.-J.; Tang, M.-H. *Angew. Chem.* **1998**, *110*, 3061−3063; *Angew. Chem. Int. Ed.* **1998**, *37*, 2845−2847.

(9) (a) Luithle, J. E. A.; Pietruszka, J. *Liebigs Ann./Recueil* **1997**, 2297−2302. (b) Luithle, J. E. A.; Pietruszka, J.; Witt, A. *Chem. Commun.* **1998**, 2651−2652.

(10) Nakayama, K.; Rainier, J. D. *Tetrahedron* **1990**, *46*, 4165−4170.

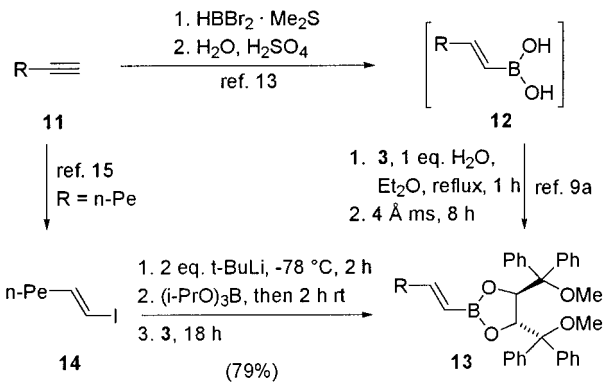
(11) (a) Matteson, D. S.; Sadhu, K. M.; Peterson, M. L. *J. Am. Chem. Soc.* **1986**, *108*, 810−819. (b) Ray, R.; Matteson, D. S. *J. Ind. Chem. Soc.* **1982**, *59*, 119−123.

(12) Devant, R.; Mahler, U.; Braun, M. *Chem. Ber.* **1988**, *121*, 397−406.

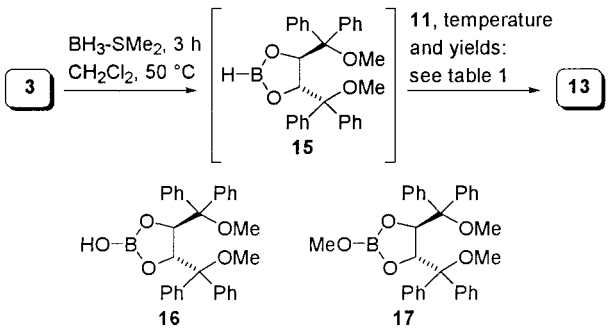
catalyzed transacetalization with anisaldehyde dimethyl acetal (PMP: *p*-methoxyphenyl). Addition of phenylmagnesium bromide gave diol **8** (83%), with minor amounts (<2%) of monoester **9** and biphenyl, side products that were easily separated. Sequential methylation (giving diether **10** in 98% yield) followed by oxidative cleavage of the acetal with 2,3-dichloro-4,5-dicyano-1,4-benzoquinone (DDQ) and subsequent reduction of the intermediate with $LiAlH_4$ furnished diol **3** (87%). Upon crystallization, suitable crystals for an X-ray structure analysis were obtained, revealing the highly stabilizing hydrogen bonds between the methoxy groups at C-1/C-4 and the hydroxy groups at C-3/C-2. Although we optimized the whole sequence by minimizing the amounts of solvents and reagents in each step and thus increasing the yield of every reaction (62% overall), the workup procedures, especially the chromatographic purifications of the intermediates, were much too time-, solvent-, and silica gel-consuming to make multigram quantities of product available. Since the amounts of side products were also minimized, starting from diester **7** (which was isolated by crystallization), all laborious purifications could be omitted and a single chromatographic separation gave diol **3**. This four-step sequence (70% yield from **7**; 61% overall) was regularly performed giving up to 35 g of product **3**. Unfortunately, we were not yet able to directly crystallize the desired diol **3** from the crude reaction mixture.

Hydroboration with Enantiomerically Pure 1,3,2-Dioxaborolanes. Alkenylboronic esters were regularly synthesized starting from alkynes **11** by a hydroboration (with $HBBr_2{-}SMe_2$ complex[13] or catecholborane[14]) hydrolysis sequence to form alkenylboronic acids that were condensed with diols. The reaction with diol **3** to ester **13** proved to be rather sluggish. One problem was the known difficulty in obtaining boronic acids (white solids) analytically pure, because of their tendency to form boroxines (oils, slightly off color).[3i,9b] Another obvious reason could be the steric bulk of diol **3**; however, similarly sterically demanding auxiliaries had not been observed to cause a problem.[9a] Finally, the highly stable hydrogen bonds that were also observed in solution might prevent the otherwise fast reaction. Surprisingly, treatment of the reagents with 1 equiv of water prior to the condensation was found to be advantageous when mixtures of boronic acid and boroxines were used. This process is still not understood, since NMR investigations at room temperature showed neither a change of the boronic acid/boroxine equilibrium nor an influence on the hydrogen bonds of diol **3**. An alternative approach that would omit the isolation of boronic acids was the employment of alkenyl iodides, e.g., **14**, that were obtained from alkynes utilizing a hydroalumination, iodination sequence.[15] By a metal−halide-exchange reaction with 2 equiv of *tert*-butyllithium followed by triisopropyl borate, an ate complex was formed[16] that was directly treated with diol **3,** giving the desired alkenylboronic ester **13a** in 79% yield (Scheme 2).

Scheme 2



Scheme 3



This was still an indirect, two-step synthesis of **13** from alkynes **11**, and the overall efficiency was moderate. Arguably, the most convenient method would be a direct hydroboration of alkynes to give alkenylboronic esters. Although this is established when performing the transformation with catechol-[14] or pinacolborane,[17] other examples, especially with chiral hydroborating reagents, are scarce.[18,19] The 1,3,2-dioxaborolane derived from pinanediol attracted considerable interest in the past, but no convenient conditions for the reaction with alkynes were reported.[17,19] Recently,[9b] we reported that the new reagent **15** was obtained by treatment of diol **3** with $BH_3{-}SMe_2$ complex in dichloromethane. However, its formation required a higher temperature than expected; the relatively sensitive 1,3,2-dioxaborolane **15** was only formed after refluxing for 4 h (Scheme 3). The hydroboration of alkynes **11** was not straightforward, since no reaction occurred at room temperature or in refluxing dichloromethane. After hydrolysis, the hydroxy compound **16** was the only isolated product whose structure was confirmed by X-ray crystallography (recrystallization from methanol gave the 1-methoxy-1,3,2-dioxaborolane **17**). The first success was achieved when the alkyne **11** was heated with the neat reagent **15** at 80 °C giving alkenylboronic esters **13**, products that are neither thermolabile[20] nor sensitive to oxidation,[21] albeit in low yield with major amounts of product **16**. Further increasing the temperature (Table 1) improved the yield of **13**

(13) (a) Brown, H. C.; Campbell, J. B., Jr. *J. Org. Chem.* **1980**, *45*, 389−395. (b) Brown, H. C.; Bhat, N. G.; Somayaji, V. *Organometallics* **1983**, *2*, 1311−1316.

(14) (a) Brown, H. C.; Gupta, S. K. *J. Am. Chem. Soc.* **1971**, *93*, 1816−1819. (b) Brown, H. C.; Gupta, S. K. *J. Am. Chem. Soc.* **1972**, *94*, 4370−4371. (c) Brown, H. C.; Gupta, S. K. *J. Am. Chem. Soc.* **1975**, *97*, 5249−5255. (d) Brown, H. C.; Chandrasekharan, J. *J. Org. Chem.* **1983**, *48*, 5080−5082.

(15) (a) Stille, J. K.; Simpson, J. H. *J. Am. Chem. Soc.* **1987**, *109*, 2138−2152. (b) Zweifel, G.; Whitney, C. C. *J. Am. Chem. Soc.* **1967**, *89*, 2753−2754.

(16) Dieck, H. A.; Heck, R. F. *J. Org. Chem.* **1975**, *40*, 1083−1090.

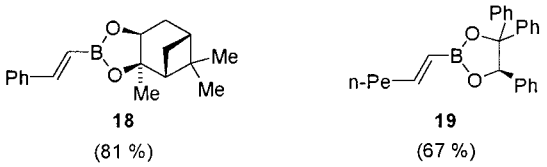
(17) Tucker, C. E.; Davidson, J.; Knochel, P. *J. Org. Chem.* **1992**, *57*, 3482−3485.

(18) Woods, W. G.; Strong, P. L. *J. Am. Chem. Soc.* **1966**, *88*, 4667−4671.

(19) (a) Ray, R.; Matteson, D. S. *J. Ind. Chem. Soc.* **1982**, *59*, 119−123. (b) Matteson, D. S.; Jesthi, P. K.; Sadhu, K. M. *Organometallics* **1984**, *3*, 1284−1288. (c) Matteson, D. S.; Sadhu, K. M.; Peterson, M. L. *J. Am. Chem. Soc.* **1986**, *108*, 810−819.

Table 1. Hydroboration of Alkynes 11 with 1,3,2-Dioxaborolane 15

product	R	yield (%)	*T* (°C)
13a	*n*-Pe	68	90
13b	*n*-Bu	70	90
13c	*t*-Bu		40−90
13d	Ph	82	120
13e	$TPSO(CH_2)_3$	83	135
13	$BzOCH_2$		100−120
13g	$MOMOCH_2$		100−120
13h	$BnOCH_2$	(31)	120
13i	$TBSOCH_2$	91	120



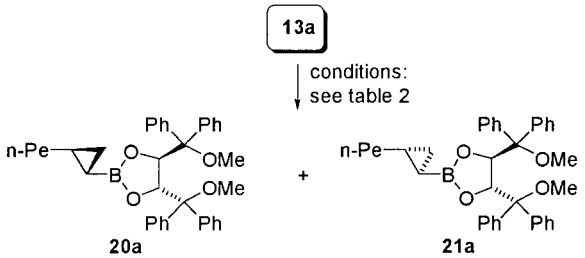
18 (81 %) **19** (67 %)

Figure 2. Esters **18** and **19** formed by direct hydroboration using enantiomerically pure 1,3,2-dioxaborolanes.[9b]

dramatically with only traces (<1%) of the regioisomers detectable. The limiting factor is the boiling point of some alkynes; e.g., to form *n*-pentyl- or *n*-butyl-substituted products **13a** or **13b**, respectively, the reaction temperature should not exceed 90 °C. In addition, it is advantageous to use 2 equiv of the low-boiling alkynes for the transformations, whereas usually 1.3−1.5 equiv was used. Unfortunately, we were not able to obtain the ester **13c**, probably due to the low boiling point of 3,3-dimethylbutyne **11c**. On the other hand, if temperatures between 100 and 135 °C were used for the transformation, e.g., alkynes **11d** or **11e**, this one-pot reaction gave alkenylboronic esters **13** in high yield and purity. Although protected propargylic alcohols were also successfully employed in this sequence, it is obvious that the choice of protecting group is crucial. Whereas the benzoyl (Bz) group or ether protecting groups (MOM, methoxymethyl; Bn, benzyl) that could easily serve to complex the reagent, thus further decreasing its reactivity, were not suitable for this transformation, silyl groups proved to be compatible. The microanalytically pure ester **13i** was isolated in high yield (91%). The benzyl-protected product **13h** was obtained as a complex, inseparable mixture of isomers and undefined side products. However, the general concept can be employed for a variety of 1,3,2-dioxaborolanes as long as the starting diol does not show any side reactions. It proved to be versatile for the transformation of pinanediol **4**[11] and 1,1,2-triphenyl-1,2-ethanediol **5**,[12] giving stable alkenylboronic esters **18** and **19** (81% and 67% yield), respectively (Figure 2).

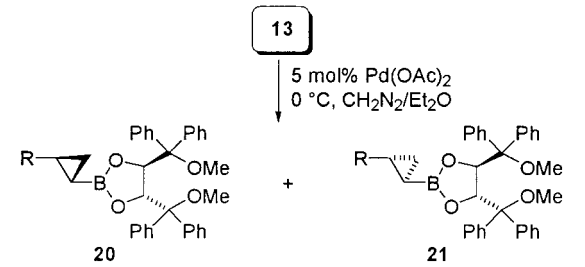
Cyclopropanation of Alkenylboronic Esters. Next we focused on the improvement of the diastereoselectivity of the cyclopropanation step. First we optimized the transformation of the *n*-pentyl-substituted olefin **13a** to the diastereomeric cyclopropylboronic esters **20a** and **21a** (Scheme 4). We found that neither Simmons−Smith conditions nor reactions with sulfur or phosphorus ylides would yield the desired cyclopropanes. $Pd(OAc)_2$-catalyzed decomposition of diazomethane in the presence of

Scheme 4



20a **21a**

Scheme 5



20 **21**

Table 2. Diastereoselective Cyclopropanation of Alkenylboronic Ester 13a with Diazomethane

entry	*T* (°C)	$Pd(OAc)_2$ (mol %)	CH_2N_2 (mL/h)	dr **(20a:21a)**
1	−15	2	60	72:28
2	−15	2	2	83:17
3	0	5	60	88:12
4	0	10	2	91:9
5	0	30	2	92:8
6	0	50	60	97:3
7	0	5[a]	2	93:7

[a] Catalyst was pretreated in an ultrasonic bath.

the olefin was the method of choice. To get high diastereomeric ratios (dr), it was observed that the important requirement was a fast decomposition of diazomethane. Conditions favoring this fast reaction, relatively high reaction temperature (0 °C), high concentration of $Pd(OAc)_2$ (up to 50 mol %), and slow addition of diazomethane (2 mL/h) would lead to an increased selectivity (Table 2). Instead of using more than reasonable amounts of "catalyst" (Table 2, entry 6), it was advantageous to pretreat it in an ultrasonic bath, guaranteeing a fine distribution (Table 2, entry 7). These conditions did not only give a high selectivity (93:7, compared to 72:28 (Table 2, entry 1) as previously reported[9a]), but it also minimized the formation of polymethylene, a side product that regularly led to deactivation of the catalysts. The strong influence of temperature and amount of catalyst are in contrast to our observations made with the more reactive alkenylboronic esters derived from tartric acid derivatives.[8b]

With these conditions, we performed all cyclopropanations of alkenylboronic esters **13a**−**e**,**i** (Scheme 5 and Table 3) and obtained the desired cyclopropanes **20** and **21** in high yield (89% to 99%) and with good selectivity (up to 95:5). The diastereoisomers were purified by flash-column chromatography to yield analytically pure compounds, and the diastereomers were separated by means of MPLC (the minor diastereomer **21e** could not be fully separated). The only exception was the transformation of the silyl-protected boronic ester **13i**. The combination of low selectivity and difficulty in diastereomer separation presented a problem.

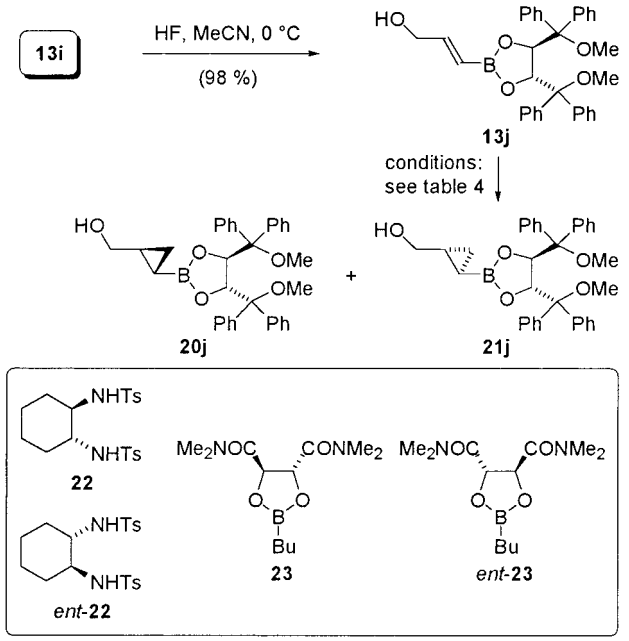
(20) (a) Matteson, D. S. *J. Am. Chem. Soc.* **1960**, *82*, 4228−4233. (b) Matteson, D. S.; Schaumberg, G. D. *J. Org. Chem.* **1966**, *31*, 726−731.

(21) (a) Johnson, J. R.; Van Campen, M. G., Jr. *J. Am. Chem. Soc.* **1938**, *60*, 121−124. (b) Korcek, S.; Watts, G. B.; Ingold, K. U. *J. Chem. Soc., Perkin Trans. 2* **1972**, 242−248.

Table 3. Cyclopropanation of Alkenes 13

starting material	product	yield (%) (**20** + **21**)	dr (**20**:**21**)
13a	**20a** + **21a**	99	93:7
13b	**20b** + **21b**	98	89:11
13c[9a]	**20c** + **21c**	95	87:13
13d	**20d** + **21d**	93	86:14
13e	**20e** + **21e**	89	95:5
13i	**20i** + **21i**	90	70:30

Scheme 6



In view of the high synthetic potential of cyclopropylboronic esters derived from propargylic alcohols, we looked for an alternative. The high stability of our boronic esters allowed us to easily desilylate ester **13i**, using either hydrofluoric acid in acetonitrile or concentrated hydrochloric acid in ethanol (Scheme 6). This deprotection furnished alkenylboronic ester **13j** in 98% or 76% yield, respectively. Cyclopropanation (Table 4) using the usual conditions gave—relative to the silylated compound **13i**—an increased selectivity (**20j**/**21j** 80:20; 98% yield). For the first time, we were also able to perform a diastereoselective Simmons–Smith-type (Et_2Zn, CH_2I_2) cyclopropanation (94% yield) of one of our highly sterically demanding alkenylboronic esters, demonstrating the importance of a free hydroxy group for this type of reaction. Although the selectivity was low, it was interesting to note that it was reversed (**20j**/**21j** 36:64). With these results, we next investigated whether a matched/mismatched interaction could be observed when a chiral ligand **22** or *ent*-**22**[22] was added. Indeed, when performing the cyclopropanation as described by Denmark et al.,[3c] we got in good yield (90–91%) the products **20j** and **21j**, with bissulfonamide **22** in a 20:80 ratio and with the enantiomeric ligand *ent*-**22** as a 60:40 mixture. Although the Charette protocol[3k] using the chiral modifier **23** or *ent*-**23** could not be successfully employed—after 72 h the conversion was not complete—the results in Table 4 indicate that a matched/mismatched interaction is observed. Summing up, we found two complementary, selective approaches to either of the diastereomers **20j** and **21j**, providing a good access to these versatile building blocks.

Table 4. Cyclopropanation of Alkene 13j

conditions	yield (%) (**20j** + **21j**)	dr (**20j**:**21j**)
CH_2N_2, $Pd(OAc)_2$, Et_2O, 0 °C	98	80:20
Et_2Zn, CH_2I_2, ZnI_2, CH_2Cl_2, 0 °C	94	36:64
Et_2Zn, CH_2I_2, ZnI_2, **22**, CH_2Cl_2, 0 °C	90	20:80
Et_2Zn, CH_2I_2, ZnI_2, *ent*-**22**, CH_2Cl_2, 0 °C	91	60:40
Et_2Zn, CH_2I_2, **23**, CH_2Cl_2, 0 °C	*a*	60:40
Et_2Zn, CH_2I_2, *ent*-**23**, CH_2Cl_2, 0 °C	*b*	30:70

[a] 50% conversion of alkenylboronic ester **13j**. [b] 78% conversion of alkenylboronic ester **13j**.

Table 5. Diagnostic ^{1}H NMR Chemical Shifts of Cycloclopropylboronic Esters 20 and 21 (500 MHz, $CDCl_3$)

major diastereomer			minor diastereomer		
entry	2′-H	3′-H_{trans}	entry	2′-H	3′-H_{trans}
20a	0.26	0.31	**21a**	0.57	−0.06
20b	0.26	0.31	**21b**	0.57	−0.06
20c	0.49	0.20	**21c**	0.59	−0.26
20d	1.36	0.80	**21d**	1.74	0.43
20e	0.25	0.30	**21e**	0.58	−0.05
20i	0.65	0.43	**21i**	0.99	0.08
20j	0.64	0.41	**21j**	1.00	0.06

In the preceding tables, the absolute configuration of the major or minor diastereomers was assigned without any comment. Previously,[9a] a chemical correlation via the synthesis of the corresponding, known cyclopropanols unequivocally allowed the assignment. With these results and the characteristic, diagnostic ^{1}H NMR shifts for the 2′-H and the 3′-H_{trans} protons of the cyclopropane moiety, new cyclopropylboronic esters **20** or **21** were easily classified (Table 5). Whereas in all major diastereomers **20**, the 2′-H protons show a distinct high-field shift relative to the minor diastereomer **21**, the 3′-H_{trans} protons show a (relative) downfield shift. A last proof was the X-ray structure of the minor diastereomer **21c** (Figure 3), confirming the assignment.

The X-ray structures of **21c** and especially of the corresponding alkenylboronic ester **13c** are not only good evidence for the identity of the compounds, but also served as a tool for rationalizing the stereochemical outcome of the cyclopropanation step. It is obvious that the conformation of the 1,3,2-dioxaborolane ring with its bulky substituents is always very similar, and it is reasonable to assume that the same holds true for the reactive conformation. With the substituents blocking three quadrants, one face of attack should be favored. However, this cannot directly explain the difference of selectivity when ester **13j** is cyclopropanated under different conditions. A simple MM2 calculation[23] starting with the X-ray data from olefin **13c** and replacing the *tert*-butyl group with a hydroxymethyl group was performed (Figure 3, bottom). From these calculations, it was obvious that the depicted conformation is approximately 8 kJ/mol more stable than a different conformer with the hydroxyalkyl chain showing up. We believe that the conformation of the side chain is essential for the selectivity, with the cyclopropanating reagent derived from diazomethane attacking the double bond from the opposite face (broad arrow, major diastereomer). On the other hand, it is well established that the Simmons–

(22) Takahashi, H.; Kawakita, T.; Ohno, M.; Yoshioka, M.; Kobayashi, S. *Tetrahedron* **1992**, *48*, 5691–5700.

(23) The MM2 tool in CS Chem3D Pro 4.0 1997 from CambridgeSoft Corp. was used.

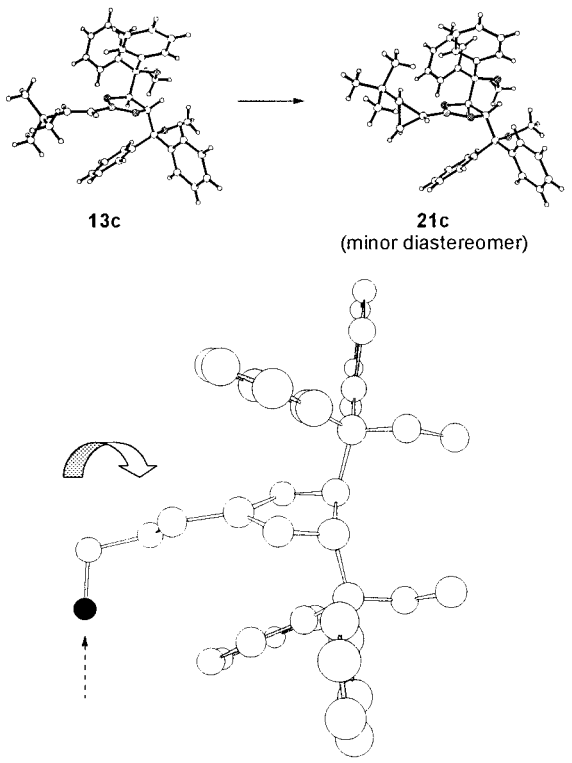
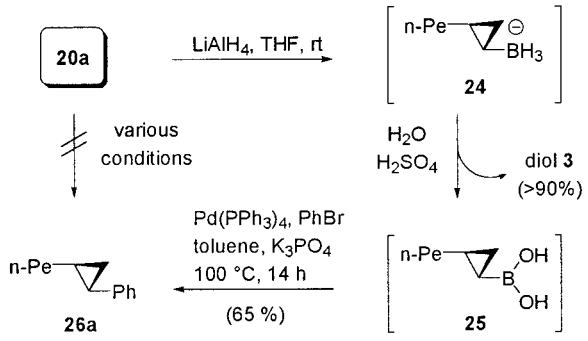


Figure 3. (Top) structures of **13c** and **21c** by X-ray diffraction. (Bottom) Chem3D[23] projection of **13j**, rationalizing the major reaction pathway (see text).

Scheme 7



Smith reagent will first form a complex between the hydroxy group (dotted arrow) and the carbenoid being delivered. This would obviously give a totally different conformation since an attack from the lower face would be more likely.

Suzuki-Type Couplings of Cyclopropylboronic Ester 20a. One of the most important transformations of cyclopropylboronic esters is their potential in C−C bond formations. Apart from the one-carbon homologation developed by Matteson et al.,[8a,24] the Suzuki coupling is the most prominent method to achieve the coupling between cyclopropyl boron compounds and aryl,[7e−f,8b] alkenyl,[7h,8c] or cyclopropyl halides.[7g] We were not surprised to find that under various reported conditions the direct coupling of our stable cyclopropylboronic ester **20a** did not succeed (Scheme 7). In analogy to our previously reported results,[9a] it was necessary to first form an ate complex before further transformations were possible. Although reactions with methyllithium are possible and

(24) Luithle, J. E. A.; Pietruszka, J. Unpublished results.

Scheme 8

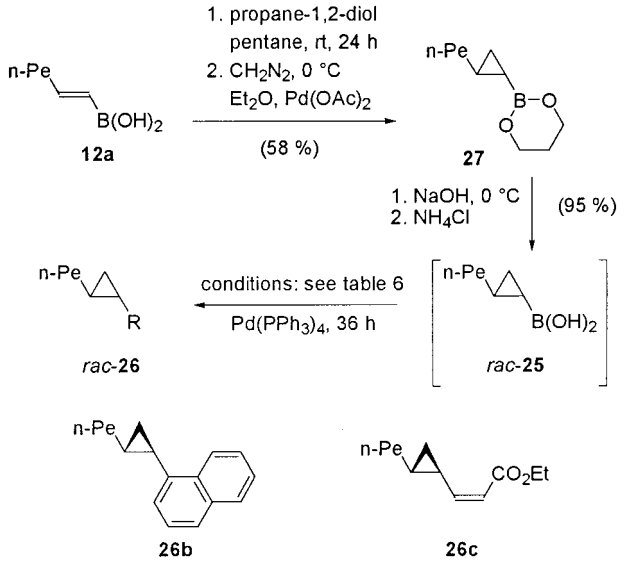


Table 6. Cyclopropylboronic Acid 25 (or *rac*-25) in Suzuki Reactions[a]

entry	product	halide	solvent	base	*T* (°C)	yield[b] (%)
1	**26a**	PhI	THF	10% KOH	50	− (<10)
2	**26a**	PhI	THF	10% KOH	70	51 (>98)
3	**26a**	PhI	hexane	10% KOH	50	− (66)
4	**26a**	PhI	toluene	10% KOH	100	71 (>98)
5	**26a**	PhBr	DME	2 equiv of KO-*t*-Bu	80	74 (>98)
6	**26b**	1-naphthyl bromide	THF	10% KOH	70	66 (>98)
7	**26b**	1-naphthyl bromide	toluene	3 equiv of K_3PO_4	100	48 (70)
8	**26b**	1-naphthyl bromide	DME	2 equiv of KO*t*Bu	80	77 (>98)
9	**26c**	ethyl (*Z*)-3-bromo acrylate	toluene	3 equiv of K_3PO_4	100	65 (>98)

[a] All reactions were performed with $Pd(PPh_3)_4$ as catalyst; the mixtures were left for 36 h at the temperature given. [b] Isolated product; turnover of reaction given in parentheses was determined by GLC.

proceed well, we found it more convenient to use $LiAlH_4$. The reaction to give compound **24** was fast, and subsequent hydrolysis with diluted sulfuric acid gave the boronic acid **25**. A fast filtration through a pad of silica was essential to separate boronic acid **25** from diol **3**, allowing the diol to be recovered in near-quantitative yield (always >90%). The crude boronic acid was directly used for the Suzuki coupling, employing the conditions described by Deng et al.[7f] Surprisingly, the yield was relatively low (65%), although monitoring of all our reactions by GLC indicated complete conversion of phenyl bromide.

For a more detailed investigation, we synthesized racemic cyclopropylboronic acid *rac*-**25** from ester **27**[7e] (Scheme 8). We then compared the different coupling protocols to form cyclopropanes *rac*-**26** and later repeated the "best conditions" with enantiomerically pure acid **25** (Table 6). It was obvious to us that even when a complete conversion of the phenyl halide (Table 6, entries 1−5) was possible (temperatures at 70 °C or above; entries 2, 4, and 5, **26a** in up to 74% yield), another side product was formed. Changing to 1-naphthyl bromide (Table 6, entries 6−8) not only underlined the superiority of the

conditions developed by Marsden[7e] (Table 6, entry 8, **26b** in 77% yield), but also allowed the isolation of naphthalene as the only side product in 10−30% yield, thus explaining the relatively low yield obtained before. Potassium phosphate remained the base of choice for relatively labile olefins such as ethyl (*Z*)-3-bromoacrylate (Table 6, entry 9, **26c** in 65% yield).

Conclusion

Highly stable, enantiomerically pure cyclopropylboronic esters **20** and **21** have been synthesized by a simple two-step protocol from alkynes **11** in high yield, utilizing the new hydroborating reagent **15** and the palladium-catalyzed decomposition of diazomethane in the cyclopropanation step. The high stability was demonstrated by a selective silyl group protection without decomposition of the boronic ester moiety. A rationale for the selectivity based on X-ray crystal structures has been proposed. In addition, by employing Suzuki conditions we were able to transform cyclopropylboronic ester **20a** into enantiomerically pure cyclopropanes **26**, showing that these stable boronic esters are ideal, general intermediates for cyclopropane chemistry.

Experimental Section

General Methods. The silyl-protected alkynes **11e** and **11i** were prepared according to literature procedures.[25] All reagents were used as purchased from commercial suppliers without further purification. The reactions were carried out using standard Schlenk techniques under a dry nitrogen atmosphere. Glassware was oven-dried at 150 °C overnight. Solvents were dried and purified by conventional methods prior to use; diethyl ether and THF were freshly distilled from sodium/benzophenone. **Caution:** The generation and handling of diazomethane requires special precaution.[26] Flash-column chromatography: Merck silica gel 60, 0.040−0.063 mm (230−400 mesh). Preparative MPLC: packed column (49 × 500 mm), LiChroprep, Si60 (15−25 μm), and UV detector (259 nm). ^{13}C NMR signals were assigned by means of C−H and H−H COSY spectra. Microanalysis: performed at the Institut für Organische Chemie, Universität Stuttgart.

Preparation of (2*R*,3*R*)-1,4-Dimethoxy-1,1,4,4-tetraphenyl-2,3-butandiol (3). For the synthesis of acetal **7** we followed the procedure described previously,[10] starting from dimethyl tartrate **6** (111.4 g, 0.625 mol), anisaldehyde dimethyl acetal[27] (120.8 g, 0.663 mol), and *p*-toluenesulfonic acid (130 mg, 0.75 mmol) in toluene (320 mL). The product was recrystallized from petroleum ether/diethyl ether, giving product **7** as a colorless solid in 87% yield (137.1 g, 0.463 mol).

The phenylmagnesium bromide was prepared in the conventional manner in 2 L three-neck round-bottom flask from Mg turnings (24.3 g, 1.0 mol) and phenyl bromide (105 mL, 1.0 mol) in THF (280 mL). After the mixture was cooled to −15 °C, the diester **7** (29.62 g, 0.1 mol) in THF (180 mL) was carefully added. The reaction mixture was allowed to warm to room temperature. After TLC indicated consumption of the starting material, the mixture was diluted with diethyl ether and hydrolyzed with aqueous NH_4Cl solution. Separation of the organic layer followed by extraction of the aqueous layer with diethyl ether, washing the combined organic extracts with saturated aqueous $NaHCO_3$, drying over anhydrous $MgSO_4$, and removing of the solvent under reduced pressure gave a yellow oil (83.5 g). Purification by flash column chromatography (2 kg silica gel, petroleum ether/ethyl acetate 15:1 to 7:1) could give diol **8** in 83% yield and compound **9** in traces (<2%); however, the crude product could also be directly converted to ether **10**.

A solution of the yellow oil in DMSO (100 mL) was treated with 20 mL of a solution of dimsyl anion (prepared from 0.3 mol of NaH and 60 mL of DMSO) at room temperature. To the resulting brown mixture was added methyl iodide (7.5 mL, 0.12 mmol) after 30 min. Within 30 min, the solution had changed to pale yellow. This procedure was repeated (in some cases twice when TLC indicated the incomplete conversion to product **10**). Addition of diethyl ether and H_2O was followed by repeated extraction of the aqueous layer with diethyl ether. The etheral layer was washed with water and brine to remove remaining DMSO. After the mixture was dried over anhydrous $MgSO_4$, the solvent was removed under reduced pressure to give a yellow oil. Again, flash-column chromatography (1000 g of silica gel per 20 mmol of product; petroleum ether/ethyl acetate 19:1) could give product **10** in 99% yield (starting from pure diol **8**), but we prefer to perform the final deprotection with the crude product.

Crude dioxolane **10** was dissolved in CH_2Cl_2/H_2O (17:1), DDQ (30.47 g, 0.11 mol) was added in portions at room temperature, and immediate formation of DDQH was observed (color change to orange/red and formation of precipitate). After 2 h, TLC indicated complete consumption of starting material. The mixture was diluted with CH_2Cl_2 and filtered through a pad of Celite. The filtrate was washed with saturated aqueous $NaHCO_3$, and the combined aqueous layers were extracted with CH_2Cl_2. The extracts were dried ($MgSO_4$), and the solvent was removed under reduced pressure. The yellow oil was dissolved in dry diethyl ether (120 mL) and slowly added to a stirred suspension of $LiAlH_4$ (8.38 g, 0.22 mol) in diethyl ether (120 mL) at room temperature. The mixture was kept at ambient temperature by cooling with a water bath. After 2 h, the suspension was diluted with diethyl ether (100 mL) and the reaction quenched by sequential addition of H_2O (10 mL), NaOH (15%, 10 mL), and H_2O (30 mL). The precipitate was filtered off and the solid thoroughly washed with diethyl ether. The filtrate was dried over $MgSO_4$ and the solution concentrated in vacuo. The resulting yellow oil was purified by flash-column chromatography (1500 g of silica gel, petroleum ether/ethyl acetate 93:7). Diol **3** (31.67 g, 70 mmol) was obtained in 70% yield (from diester **7**) as a colorless, analytically pure solid. Crystallization from petroleum ether/MeOH at −20 °C gave colorless crystals, sufficient for X-ray analysis.

(2*R*,3*R*)-1,4-Dimethoxy-1,1,4,4-tetraphenyl-2,3-butandiol (3): mp = 76−79 °C; $[\alpha]^{21}_D$ = +66.6 (*c* 1.5, $CHCl_3$); IR (film) 3554, 3427 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.74 (br, 2 H, O*H*), 3.16 (s, 6 H, OMe), 4.71 (d, *J* = 3.7 Hz, 2 H, 2-H/3-H), 7.20−7.31 (m, 16 H, Ar-H), 7.41−7.44 (m, 4 H, Ar-H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 53.5 (OMe), 71.1 (C-2/C-3), 85.2 (C-1/C-4), 127.2, 127.3, 127.8, 127.9, 128.0, 128.7, 141.2, 142.5 (Ar-C). Anal. Calcd for $C_{30}H_{30}O_4$ (454.56): C, 79.27; H, 6.65. Found: C, 78.98; H, 6.60.

(4*R*,3*R*)-5-(Hydroxy(diphenyl)methyl)-4-methyloxycarbonyl-2-(4-methoxyphenyl)-1,3-dioxolane (9): mp = 119−121 °C; $[\alpha]^{21}_D$ = +45.5 (*c* 2.0, $CHCl_3$); IR (film) 3456, 3027, 1748 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.99 (s, 1 H, O*H*), 3.37 (s, 3 H, OMe), 3.80 (s, 3 H, OMe), 4.64 (d, *J* = 6.9 Hz, 1 H, 5-H or 4-H), 5.35 (d, *J* = 6.9 Hz, 1 H, 4-H or 5-H), 6.00 (s, 1 H, 2-H), 6.91 (d, *J* = 8.6 Hz, 2 H, Ar-H), 7.20−7.57 (m, 12 H, Ar-H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 52.3 (OMe), 55.3 (OMe), 76.4, 78.1 (C-4/C-5), 82.9 (*C*Ph_2OH), 106.7 (C-2), 113.7, 126.2, 127.3, 127.4, 127.6, 128.2, 128.3, 129.3, 142.3, 144.6, 160.6 (Ar-C), 169.8 (C=O). Anal. Calcd for $C_{25}H_{24}O_6$ (420.46): C, 71.42; H, 5.75. Found: C, 71.51; H, 5.80.

Preparation of Alkenylboronic Ester 13a from Vinyl Iodide 14. Under an atmosphere of nitrogen vinyl iodide,[15] **14** (224 mg, 1.00 mmol) was dissolved in diethyl ether (1 mL) and cooled to −78 °C. After addition of *t*-BuLi (1.35 mL of a 1.5 M solution in hexane, 2 mmol), a white precipitate formed. Stirring was continued, and after 30 min triisopropyl borate (188 mg, 231 μL, 1.00 mmol) was syringed into the mixture, which was then allowed to warm to room temperature. The

(25) Toshima, K.; Ohta, K.; Ohashi, A.; Nakamura, T.; Nakata, M.; Tatsuta, K.; Matsumura, S. *J. Am. Chem. Soc.* **1995**, *117*, 4822−4831.

(26) (a) Lombardi, P. *Chem. Ind. (London)* **1990**, 708. (b) Moss, S. *Chem. Ind. (London)* **1994**, 122. (c) Moore, J. A.; Reed, D. E. *Organic Syntheses*; Wiley: New York, 1973; Collect. Vol. V, pp 351−355.

(27) Evans, M. E. *Carbohydr. Res.* **1972**, *21*, 473−475.

ate complex was quenched with diol **3** (340 mg, 0.75 mmol), and the reaction mixture was left at ambient temperature for 18 h. Diethyl ether was added, and the organic layer was washed with saturated aqueous NH_4Cl, H_2O, and brine and dried over $MgSO_4$. The solution was concentrated under reduced pressure and the residue subjected to flash-column chromatography on silica gel, eluting with pentane/diethyl ether (10:1 to 4:1), yielding product **13a** (330 mg, 0.59 mmol, 79%). All data were in full agreement to those previously published.[9a]

General Procedure for the Preparation of Alkenylboronic Esters 13 via Direct Hydroboration of Alkynes 11. Diol **3** (1 equiv) was carefully dried at 50 °C under reduced pressure for 1 h. Under an atmosphere of nitrogen, CH_2Cl_2 (1 mL/2 mmol of diol **3**) was added and the solution cooled to 0 °C. $BH_3{-}SMe_2$ complex (1.2 equiv of a 12 M solution in dimethyl sulfide) was added dropwise with vigorous stirring, followed by refluxing the mixture for 4 h. The solvent was removed, the reagent cooled to 0 °C, and alkyne **11** (1.5 equiv) slowly added. The flask was closed with a septum, slowly heated to the temperature indicated (Table 1), and kept at this temperature for 12 h. After the mixture was cooled to room temperature, standard workup (see above or ref 9) followed, giving analytically pure alkenylboronic esters **13**. Yields for compounds **13a**, **13b**, and **13d** are given in Table 1; all analytical data are in full agreement to those previously published.[9a]

(4*R*,5*R*)-2-[(*E*)-2-[3-*tert*-Butyl(diphenyl)siloxypropyl]-ethenyl]-4,5-bis[methoxy(diphenyl)methyl]-1,3,2-dioxaborolane (13e):[28] yield 83%; white foam; softening range = 60−75 °C; $[\alpha]^{20}_D = -46.6$ (*c* 1.1, $CHCl_3$); IR (film) 3056, 3027, 1380, 1077 cm^{-1}; MS (EI, 70 eV) *m*/*z* 786 (<0.1) [M^+], 754 (0.8) [$(M - MeOH)^+$], 197 (100) [$(Ph_2COMe)^+$]; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.94 (s, 9 H, Me_3C), 1.46 (m_c, 2 H, 2″-H), 1.98 (m_c, 2 H, 1″-H), 2.92 (s, 6 H, OMe), 3.49 (t, J = 6.5 Hz, 2 H, 3″-H), 4.95 (dt, J = 17.9, 1.5 Hz, 1 H, 1′-H), 5.24 (s, 2 H, 4-H and 5-H), 6.10 (dt, J = 17.9, 6.5 Hz, 1 H, 2′-H), 7.12−7.33 (m, 26 H, Ar-H), 7.54 (m_c, 4 H, Ar-H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 18.9 (Me_3C), 26.6 (Me_3C), 30.7 (C-2″), 31.5 (C-1″), 51.5 (OMe), 62.8 (C-3″), 77.2 (C-4/C-5), 83.2 (CPh_2OMe), 117.9 (C-1′), 127.0 (2×), 127.2, 127.3 (2×), 127.4, 127.5, 128.2, 129.3, 129.5, 133.7, 135.0, 135.2, 140.9, 141.2 (Ar-C), 153.2 (C-2′). Anal. Calcd for $C_{51}H_{55}BO_5Si$ (786.88): C, 77.85; H, 7.05. Found: C, 77.72; H, 7.13.

(4*R*,5*R*)-2-[(*E*)-2-[3-*tert*-Butyl(dimethyl)siloxymethyl]-ethenyl]-4,5-bis[methoxy(diphenyl)methyl]-1,3,2-dioxaborolane (13i): yield 91%; white foam; softening range = 59−65 °C; $[\alpha]^{20}_D = -60.2$ (*c* 2.6, $CHCl_3$); IR (film) 3048, 3010, 1351, 1063 cm^{-1}; MS (EI, 70 eV) *m*/*z* 602 (0.8) [$(M - MeOH)^+$], 197 (100) [$(Ph_2COMe)^+$]; ^1H NMR ($CDCl_3$, 500 MHz) δ −0.07 (s, 6 H, Me_2Si), 0.80 (s, 9 H, Me_3C), 2.93 (s, 6 H, OMe), 4.01 (dd, J = 3.6, 2.0 Hz, 2 H, 1″-H), 5.27 (dt, J = 17.9, 2.0 Hz, 1 H, 1′-H), 5.27 (s, 2 H, 4-H and 5-H), 6.18 (dt, J = 17.9, 3.6 Hz, 1 H, 2′-H), 7.18−7.30 (m, 20 H, Ar-H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ −5.3 (Me_2Si), 18.4 (Me_3C), 25.9 (Me_3C), 51.8 (OMe), 64.5 (C-1″), 77.6 (C-4/C-5), 83.4 (CPh_2OMe), 115.3 (C-1′), 127.2, 127.3 (2×), 127.4, 127.8, 128.4, 128.5, 129.7, 141.1, 141.5 (Ar-C), 151.6 (C-2′). Anal. Calcd for $C_{39}H_{47}BO_5Si$ (634.68): C, 73.80; H, 7.46. Found: C, 73.54; H, 7.61.

(4*R*,5*R*)-2-Hydroxy-4,5-bis[methoxy(diphenyl)methyl]-1,3,2-dioxaborolane (16): white foam; softening range = 120−135 °C; $[\alpha]^{20}_D = -125.7$ (*c* 0.56, $CHCl_3$); IR (film) 3437, 3089, 3059, 1384, 1077 cm^{-1}; MS (CI, CH_4) *m*/*z* 462 (4) [$(M - H_2O)^+$], 197 (100) [$(Ph_2COMe)^+$]; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.91 (s, 6 H, OMe), 3.31 (s, 1 H, O*H*), 5.19 (s, 2 H, 4-H and 5-H), 7.17−7.34 (m, 20 H, Ar-H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 51.8 (OMe), 76.5 (C-4/C-5), 83.3 (CPh_2OMe), 127.4, 127.5, 127.6, 127.8, 128.2, 129.6, 140.9, 141.0 (Ar-C). Anal. Calcd for $C_{30}H_{29}BO_5$ (480.36): C, 75.01; H, 6.09. Found: C, 74.87; H, 6.21.

(4*R*,5*R*)-2-Methoxy-4,5-bis[methoxy(diphenyl)methyl]-1,3,2-dioxaborolane (17): colorless crystals obtained by the attempted crystallization of compound **16** from MeOH; mp = 129−130 °C; $[\alpha]^{20}_D = -106.0$ (*c* 1.8, $CHCl_3$); IR (film) 3058, 1405, 1076 cm^{-1}; MS (CI, CH_4) *m*/*z* 494 (0.3) [M^+], 462 (0.7) [$(M - MeOH)^+$], 197 (100) [$(Ph_2COMe)^+$]; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.95 (s, 6 H, OMe), 3.18 (s, 3 H, BO*Me*), 5.21 (s, 2 H, 4-H and 5-H), 7.18−7.35 (m, 20 H, Ar-H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 51.8 (OMe), 52.3 (BO*Me*), 76.1 (C-4/C-5), 83.4 (CPh_2OMe), 127.3, 127.4, 127.5, 127.8, 128.2, 129.6, 141.0, 141.1, 141.2, 141.3 (Ar-C). Anal. Calcd for $C_{31}H_{31}BO_5$ (494.39): C, 75.31; H, 6.32. Found: C, 75.25; H, 6.35.

(4*R*,5*R*)-2-[(*E*)-2-{Hydroxymethyl}ethenyl]-4,5-bis-[methoxy(diphenyl)methyl]-1,3,2-dioxaborolane (13j). (A) HF (0.25 mL in 5 mL of MeCN) was slowly added to a stirred solution of alkenylboronic ester **13i** (200 mg, 0.32 mmol) in MeCN (5 mL) at room temperature. After 20 min, TLC indicated complete conversion of starting material. The crude product was obtained after dilution with H_2O, extraction with CH_2Cl_2, washing the organic layer with brine, drying over anhydrous $MgSO_4$, and evaporation of the solvent. Flash-column chromatography on silica gel, eluting with petroleum ether/diethyl ether (10:1 to 3:1), yielded a colorless foam (161 mg, 0.31 mmol, 98%).

(B) Alkenylboronic ester **13i** (5.67 g, 8.74 mol) was dissolved in EtOH (100 mL), concentrated HCl (1.45 mL) in EtOH (20 mL) was slowly added, and the solution was stirred at room temperature for 2 h. The mixture was diluted with diethyl ether and H_2O, the aqueous layer was extracted with diethyl ether, and the combined organic layer was washed with saturated aqueous $NaHCO_3$. After being dried over $MgSO_4$, the mixture was filtered, the solvent evaporated, and the crude product subjected to flash-column chromatography (see above): yield 3.44 g (6.62 mmol, 76%); softening range = 80−86 °C; $[\alpha]^{20}_D = -85.8$ (*c* 1.0, $CHCl_3$); IR (film) 3420, 3042, 3010, 1361, 1063 cm^{-1}; MS (EI, 70 eV) *m*/*z* 520 (>1) [M^+], 488 (2) [$(M - MeOH)^+$], 197 (100) [$(Ph_2COMe)^+$]; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.21 (t, J = 6.0 Hz, 1 H, O*H*), 2.97 (s, 6 H, OMe), 4.03 (ddd, J = 6.0, 4.2, 1.9 Hz, 2 H, 1″-H), 5.27 (dt, J = 18.1, 1.9 Hz, 1 H, 1′-H), 5.32 (s, 2 H, 4-H and 5-H), 6.29 (dt, J = 18.1, 4.2 Hz, 1 H, 2′-H), 7.21−7.35 (m, 20 H, Ar-H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 51.8 (OMe), 64.4 (C-1″), 77.7 (C-4/C-5), 83.3 (CPh_2-OMe), 116.2 (C-1′), 127.2, 127.3, 127.5, 127.8, 128.4, 129.7, 141.1, 141.3 (Ar-C), 151.2 (C-2′). Anal. Calcd for $C_{33}H_{33}BO_5$ (520.42): C, 76.16; H, 6.39. Found: C, 75.84; H, 6.41.

General Procedure for the Cyclopropanation of Alkenylboronic Esters 13 with Diazomethane. Alkenylboronic ester **13** (1 equiv) was dissolved in diethyl ether (1 mL/mmol **13**) and 5 mol % $Pd(OAc)_2$ added. The suspension was treated for 2 min in an ultrasonic bath. After the mixture was cooled to 0 °C, diazomethane[26] (50 mL/mmol **13** of an approximately 0.5 M solution in diethyl ether) was slowly (2 mL/min) added by means of a syringe pump.[29] Unreacted diazomethane was destroyed by stirring the reaction mixture vigorously. Filtration through Celite and evaporation of the solvent under reduced pressure, followed by chromatographic purification, led to analytically pure cyclopropylboronic esters **20/21**. The diastereomeric ratios and yields are given in Table 3. Analytical data for cyclopropanes **20a**−**d**/**21a**−**d** were in full agreement with those previously published.[9a]

(4*R*,5*R*,1′*S*,2′*S*)-2-[2-{3-*tert*-Butyl(diphenyl)siloxypropyl}-cyclopropyl]-4,5-bis[methoxy(diphenyl)methyl]-1,3,2-dioxaborolane (20e) and (4*R*,5*R*,1′*R*,2′*R*)-2-[2-{3-*tert*-Butyl-(diphenyl)siloxypropyl}cyclopropyl]-4,5-bis[methoxy(diphenyl)methyl]-1,3,2-dioxaborolane (21e). After flash-column chromatography (petroleum ether/diethyl ether 10:1) a white foam (yield 89%) was isolated; by MPLC (1% EtOAc in petroleum ether) only the major, second eluted diastereomer

(28) The attempted crystallization from the crude mixture failed; the only product isolated was (4*R*,5*R*)-2-*tert*-butyldimethylsiloxy-4,5-bis[methoxy(diphenyl)methyl]-1,3,2-dioxaborolane **27** as single crystals (suitable for X-ray crystallographic analysis), probably derived by the deprotection of alkyne **11i** with the boric acid derivative **16**.

(29) For the safe handling of diazomethane with the help of a syringe-pump, all tubing, fittings, and joints were made from Teflon; metals *must* be omitted.

20e could be obtained in pure form (the ^{1}H NMR data for the cyclopropyl group of compound **21e** in Table 5 were determined from the mixture): softening range = 55−60 °C; $[\alpha]^{20}_D = -34.9$ (*c* 1.1, $CHCl_3$); IR (film) 3067, 1370, 1077 cm^{-1}; MS (EI, 70 eV) *m*/*z* 768 (<1) [(M − MeOH)$^+$], 743 (<1) [(M − *t*-Bu)$^+$], 197 (100) [(Ph_2COMe)$^+$]; ^{1}H NMR ($CDCl_3$, 500 MHz) δ −0.88 (ddd, J = 9.2, 6.0, 5.4 Hz, 1 H, 1′-H), 0.07 (ddd, J = 9.2, 5.0, 3.0 Hz, 1 H, 3′-H_{cis}), 0.25 (m_c, 1 H, 2′-H), 0.30 (ddd, J = 9.1, 6.0, 3.0 Hz, 1 H, 3′-H_{trans}), 0.89−0.97 (m, 1 H, 1″-H_a), 0.96 (s, 9 H, Me_3C), 1.19−1.27 (m, 1 H, 1″-H_b), 1.45 (tt, J = 7.5, 6.5 Hz, 2 H, 2″-H), 2.93 (s, 6 H, OMe), 3.54 (m_c, 2 H, 3″-H), 5.18 (s, 2 H, 4-H and 5-H), 7.18−7.34 (m, 26 H, Ar-H), 7.57−7.59 (m, 4 H, Ar-H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ ∼−0.4 (C-1′), 11.5 (C-3′), 18.0 (C-2′), 18.9 (Me_3C), 26.7 (Me_3C), 31.3 (C-1″), 32.4 (C-2″), 51.5 (OMe), 63.5 (C-3″), 76.5 (C-4/C-5), 83.0 (CPh_2OMe), 122.9, 127.0, 127.2, 127.3, 127.5, 128.2, 129.2, 129.5, 133.8, 135.3, 141.0, 141.2 (Ar-C). Anal. Calcd for $C_{52}H_{57}BO_5Si$ (800.90): C, 77.98; H, 7.17. Found: C, 77.90; H, 7.36.

(4*R*,5*R*,1′*S*,2′*S*)-2-[2-[*tert*-Butyl(dimethyl)siloxymethyl]-cyclopropyl]-4,5-bis[methoxy(diphenyl)methyl]-1,3,2-dioxaborolane (20i) and (4*R*,5*R*,1′*R*,2′*R*)-2-[(*E*)-2-[*tert*-Butyl-(dimethyl)siloxymethyl]cyclopropyl]-4,5-bis[methoxy(diphenyl)methyl]-1,3,2-dioxaborolane (21i). After flash-column chromatography (petroleum ether/diethyl ether 10:1), a white foam (yield 90%) was isolated; by MPLC (1% EtOAc in petroleum ether) the diastereoisomers **20i** and **21i** could be partially separated. The analytical data for the minor diastereoisomer **21i** were obtained from the mixture: IR (film) 3059, 3026, 1387, 1077 cm^{-1}; MS (FAB, NBA + NaI) *m*/*z* 671 (5) [(M + Na)$^+$], 197 (100) [(Ph_2COMe)$^+$]. Anal. Calcd for $C_{40}H_{49}BO_5$ (648.71): C, 74.06; H, 7.61. Found: C, 73.90; H, 7.70.

20i (major diastereomer): softening range = 54−60 °C; $[\alpha]^{21}_D = -44.3$ (*c* 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ −0.64 (ddd, J = 9.5, 6.0, 5.4 Hz, 1 H, 1′-H), −0.01 (s, 3 H, Me), 0.00 (s, 3 H, Me), 0.34 (ddd, J = 9.5, 5.2, 3.4 Hz, 1 H, 3′-H_{cis}), 0.43 (ddd, J = 7.9, 6.0, 3.4 Hz, 1 H, 3′-H_{trans}), 0.65 (m_c, 1 H, 2′-H), 0.84 (s, 9 H, Me_3C), 2.99 (s, 6 H, OMe), 3.08 (dd, J = 10.5, 7.0 Hz, 1 H, 1″-H_a), 3.59 (dd, J = 10.5, 4.7 Hz, 1 H, 1″-H_b), 5.25 (s, 2 H, 4-H and 5-H), 7.23−7.34 (m, 20 H, Ar-H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ −5.3 (Me), −5.2 (Me), −3.2 (C-1′), 9.6 (C-3′), 18.4 (Me_3C), 20.0 (C-2′), 26.0 (Me_3C), 51.7 (OMe), 66.9 (C-1″), 77.6 (C-4/C-5), 83.3 (CPh_2OMe), 127.2, 127.4, 127.7, 128.4, 129.7, 141.2, 141.4 (Ar-C). **21i** (minor diastereomer): ^{1}H NMR ($CDCl_3$, 500 MHz) δ −0.63 (ddd, J = 9.8, 5.9, 5.7 Hz, 1 H, 1′-H), −0.03 (s, 3 H, Me), −0.02 (s, 3 H, Me), 0.08 (m_c, 1 H, 3′-H_{trans}), 0.27 (ddd, J = 9.8, 5.2, 3.4 Hz, 1 H, 3′-H_{cis}), 0.84 (s, 9 H, Me_3C), 0.99 (m_c, 1 H, 2′-H), 3.00 (s, 6 H, OMe), 3.07 (dd, J = 10.6, 7.0 Hz, 1 H, 1″-H_a), 3.57 (dd, J = 10.6, 4.9 Hz, 1 H, 1″-H_b), 5.26 (s, 2 H, 4-H and 5-H), 7.24−7.37 (m, 20 H, Ar-H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ −5.6 (Me), −5.5 (Me), −3.2 (C-1′), 9.8 (C-3′), 18.4 (Me_3C), 20.0 (C-2′), 26.0 (Me_3C), 51.7 (OMe), 67.1 (C-1″), 77.7 (C-4/C-5), 83.3 (CPh_2-OMe), 127.1, 127.3, 127.4, 128.3, 129.7, 141.2, 141.4 (Ar-C).

(4*R*,5*R*,1′*S*,2′*S*)-2-[2-(Hydroxymethyl)cyclopropyl]-4,5-bis[methoxy(diphenyl)methyl]-1,3,2-dioxaborolane (20j) and (4*R*,5*R*,1′*R*,2′*R*)-2-[2-(Hydroxymethyl)cyclopropyl]-4,5-bis[methoxy(diphenyl)methyl]-1,3,2-dioxaborolane (21j). After flash-column chromatography (petroleum ether/ethyl acetate 4:1) a white foam (yield 98%) was isolated: IR (film) 3392, 3058, 1387, 1076 cm^{-1}; MS (FAB, NBA + NaI) *m*/*z* 557 (35) [(M + Na)$^+$], 197 (100) [(Ph_2COMe)$^+$]. Anal. Calcd for $C_{34}H_{55}BO_5$ (534.45): C, 76.41; H, 6.60. Found: C, 76.31; H, 6.72.

By MPLC (20% EtOAc in petroleum ether) the diastereomers **20j** and **21j** could be separated. **20j** (major, second eluted diastereomer): mp = 135−136 °C; $[\alpha]^{20}_D = -89.8$ (*c* 2.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ −0.72 (ddd, J = 9.6, 6.2, 5.4 Hz, 1 H, 1′-H), 0.24 (ddd, J = 9.6, 5.2, 3.6 Hz, 1 H, 3′-H_{cis}), 0.41 (ddd, J = 7.7, 6.2, 3.6 Hz, 1 H, 3′-H_{trans}), 0.64 (m_c, 1 H, 2′-H), 1.04 (br, 1 H, O*H*), 2.93 (s, 6 H, OMe), 3.13−3.18 (m, 1 H, 1″-H_a), 3.19−3.25 (m, 1 H, 1″-H_b), 5.21 (s, 2 H, 4-H and 5-H), 7.17−7.28 (m, 20 H, Ar-H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ ∼−2.0 (C-1′), 9.4 (C-3′), 20.4 (C-2′), 51.7 (OMe), 67.8 (C-1″), 77.5 (C-4/C-5), 83.3 (CPh_2OMe), 127.2, 127.3, 127.5, 127.8, 128.4, 129.7, 141.2, 141.2 (Ar-C). **21j** (minor, first eluted diastereomer): softening range = 85−88 °C; $[\alpha]^{20}_D = -117.7$ (*c* 0.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ −0.72 (ddd, J = 9.7, 6.0, 5.6 Hz, 1 H, 1′-H), 0.06 (ddd, J = 7.7, 6.0, 3.6 Hz, 1 H, 3′-H_{trans}), 0.20 (ddd, J = 9.7, 5.2, 3.6 Hz, 1 H, 3′-H_{cis}), 0.98−1.03 (m, 2 H, 2′-H and O*H*), 2.94 (s, 6 H, OMe), 3.08−3.13 (m, 1 H, 1″-H_a), 3.23−3.27 (m, 1 H, 1″-H_b), 5.21 (s, 2 H, 4-H and 5-H), 7.17−7.28 (m, 20 H, Ar-H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ ∼−2.0 (C-1′), 9.6 (C-3′), 20.9 (C-2′), 51.7 (OMe), 67.8 (C-1″), 77.5 (C-4/C-5), 83.3 (CPh_2OMe), 127.2, 127.3, 127.5, 127.8, 128.4, 129.7, 141.2, 141.2 (Ar-C).

Cyclopropanation of Alkenylboronic Ester 13j Utilizing Modified Simmons−Smith Conditions. (A) To a stirred solution of alkenylboronic ester **13j** (100 mg, 0.19 mmol) in CH_2Cl_2 (2 mL) was added diethylzinc (211 μL of a 1 M solution in hexane) at 0 °C. After 10 min, the mixture was transferred to a second flask containing freshly prepared ZnI_2 (from 97.5 mg iodine and 192 μL diethyl zinc solution (1 M in hexane)) in CH_2Cl_2 (4 mL). The suspension was stirred for 5 min at 0 °C and was then added to a third flask with a preformed reagent [31 μL (0.38 mmol) CH_2I_2 dissolved in CH_2Cl_2 (8 mL) and treated with diethylzinc solution (192 μL of a 1 M solution in hexane) at 0 °C] for the cyclopropanation. Stirring was continued for 12 h at room temperature. After the reaction was quenched with saturated aqueous NH_4Cl, the aqueous layer was extracted with diethyl ether. The combined organic layer was dried over $MgSO_4$ and the solvents were removed under reduced pressure. The crude product was purified by flash-column chromatography (see above): yield 97 mg (0.18 mmol, 94%), dr **20j**/**21j** 36:64.

(B) The same protocol was followed, but bis(sulfonamide) **22**[22] (8.1 mg, 0.02 mmol) was added to the alkenylboronic ester **13j** before addition of diethylzinc: yield 92 mg (0.17 mmol, 90%), dr **20j**/**21j** 20:80.

(C) Same protocol as above (B), but with bis(sulfonamide) ***ent*-22**: yield 93 mg (0.17 mmol, 91%), dr **20j**/**21j** 60:40.

(D) Dioxaborolane **23** was prepared from butylboronic acid (6.2 mg, 0.06 mmol) and l-(+)-*N*,*N*,*N*′,*N*′-tetramethyltartramide[30] (14.7 mg, 0.07 mmol) in CH_2Cl_2 (1 mL) in the presence of $MgSO_4$ (200 mg). The resulting solution was filtered under an atmosphere of nitrogen into a flask containing alkenylboronic ester **13j** (26.4 mg, 0.05 mmol). The resulting solution was syringed into a third flask with the freshly prepared Simmons−Smith reagent (from 26 μL of CH_2I_2 dissolved in 1 mL of CH_2Cl_2 and 160 μL of 1 M diethylzinc solution) at 0 °C. After 72 h at room temperature, NMR indicated only 50% conversion to the product (dr **20j**/**21j** 60:40).

(E) Same protocol as above (D), but with D-(−)-*N*,*N*,*N*′,*N*′-tetramethyltartramide. Conversion after 72 h: 78% (dr **20j**/**21j** 30:70).

Synthesis of Cyclopropylboronic Acid *rac*-25. A stirred solution of 1-heptyne (8.53 mL, 65 mmol) in CH_2Cl_2 (20 mL) was cooled to 0 °C. Dibromoborane−dimethyl sulfide complex (13.55 g, 58 mmol) in CH_2Cl_2 (24 mL) was slowly added. After 4 h at room temperature, the green solution was carefully transferred into a cooled solution of 10% aqueous NaOH (90 mL) and the mixture stirred for 15 min at 0 °C. Saturated aqueous NH_4Cl (150 mL) was added, and a voluminous white precipitate formed. CH_2Cl_2 was removed under reduced pressure. The boronic acid **12a** was filtered with suction and washed extensively with ice−water. The colorless solid was directly used without any further purification. To a slurry of the boronic acid in pentane (40 mL) was added 1,3-propanediol (4.33 mL, 60 mmol). After 48 h, the aqueous layer was separated. The organic layer was dried over $MgSO_4$ and the product distilled to yield a colorless oil (9.19 g, 50 mmol, 87%).

(30) (a) Seebach, D.; Kalinowski, H.-O.; Bastani, B.; Crass, G.; Daum, H.; Dörr, H.; DuPreez, N. P.; Ehrig, V.; Langner, W.; Nüssler, C.; Oei, H.-A.; Schmidt, M. *Helv. Chim. Acta* **1977**, *60*, 301−325. (b) Seebach, D.; Kalinowski, H.-O.; Langer, W.; Crass, G.; Wilka, E.-M. *Organic Syntheses*; Wiley: New York, 1990; Collect. Vol. VII, pp 41−50.

2-[(*E*)-1-Hepten-1-yl]-1,3,2-dioxaborinane: bp = 105 °C (15 Torr); IR (film) 2928, 2857, 1325 cm^{-1}; MS (EI, 70 eV) *m/z* 182 (17) [M^+], 154 (10) [$(M - C_2H_4)^+$], 139 (17) [$(M - C_3H_7)^+$], 126 (100) [$(M - C_4H_8)^+$]; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.85 (t, J = 6.9 Hz, 3 H, 7′-H), 1.21−1.31 (m, 4 H, 5′-H and 6′-H), 1.35−1.61 (m, 2 H, 3′-H), 1.93 (m_c, 2 H, 5-H), 2.07−2.11 (m, 2 H, 3′-H), 4.00 (m_c, 4 H, 4-H and 6-H), 5.29 (dt, J = 17.8, 1.2 Hz, 1 H, 1′-H), 6.47 (dt, J = 17.8, 6.5 Hz, 1 H, 2′-H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.0 (C-7′), 22.5 (C-5′ or C-6′), 27.4 (C-5), 28.2 (C-4′), 31.4 (C-6′ or C-5′), 35.5 (C-3′), 61.6 (C-4 and C-6), ∼124.9 (br, C-1′), 151.7 (C-2′). Anal. Calcd for $C_{10}H_{19}BO_2$ (182.07): C, 65.97; H, 10.52. Found: C, 65.87; H, 10.67.

The olefin (6.66 g, 36.6 mmol) was dissolved in diethyl ether (10 mL), and $Pd(OAc)_2$ (165 mg, 0.74 mmol) was added. A solution of diazomethane in diethyl ether (600 mL) was carefully added. The excess diazomethane was destroyed by vigorously stirring the mixture. The suspension was filtered through a pad of Celite, the solvent removed under reduced pressure, and the residue distilled. The product (4.70 g, 24.0 mmol, 65%) was obtained as a colorless oil.

2-(*trans*-2-Pentylcyclopropyl)-1,3,2-dioxaborinane (27): bp = 117−119 °C (15 Torr); IR (film) 2924, 2854, 1347 cm^{-1}; MS (EI, 70 eV) *m/z* 196 (17) [M^+], 168 (26) [$(M - C_2H_4)^+$], 139 (51) [$(M - C_4H_9)^+$], 126 (100) [$(M - C_5H_{10})^+$]; ^1H NMR ($CDCl_3$, 500 MHz) δ −0.61 (ddd, J = 9.3, 6.0, 5.4 Hz, 1 H, 1′-H), 0.24 (ddd, J = 9.3, 5.0, 3.0 Hz, 1 H, 3′-H_{cis}), 0.52 (ddd, J = 9.2, 6.0, 3.0 Hz, 1 H, 3′-H_{trans}), 0.79 (m_c, 1 H, 2-H′), 0.85 (t, J = 7.3 Hz, 3 H, 5″-H), 1.11 (m_c, 1 H, 1″-H_a), 1.20−1.30 (m, 5 H, 1″-H_b, 3″-H and 4″-H), 1.31−1.38 (m, 2 H, 2″-H), 1.87 (m_c, 2 H, 5-H), 3.90 (m_c, 4 H, 4-H and 6-H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 3.4 (br, C-1′), 11.0 (C-3′), 14.1 (C-5″), 17.8 (C-2′), 22.6 (C-5′ or C-6′), 27.4 (C-5), 29.4 (C-2″), 31.7 (C-3″ or C-4″), 35.3 (C-1″), 61.5 (C-4 and C-6). Anal. Calcd for $C_{11}H_{21}BO_2$ (196.09): C, 67.37; H, 10.79. Found: C, 67.33; H, 10.94.

The cyclopropyl boronic ester **27** (1.25 g, 6.38 mmol) was added dropwise to a cooled solution of 10% aqueous NaOH (50 mL). The mixture stirred for 15 min at 0 °C. Saturated aqueous NH_4Cl (100 mL) was added, and a voluminous white precipitate formed. The boronic acid ***rac*-25** was filtered with suction and washed extensively with ice−water. The colorless solid ***rac*-25** (940 mg) was directly used for further transformations without purification.

***trans*-2-Pentylcyclopropylboronic acid (*rac*-25):** MS (EI, 70 eV) *m/z* 414 (3) [$(3M - 3H_2O)^+$] (cyclic trimer), 156 (5) [M^+], 138 (8) [$(M - H_2O)^+$], 86 (46) [$(M - C_5H_{10})^+$]; ^1H NMR (THF-d_8, 500 MHz) δ −0.65 (dt, J = 9.3, 6.0, 5.4 Hz, 1 H, 1-H), 0.20 (ddd, J = 9.3, 5.0, 2.8 Hz, 1 H, 3-H_{cis}), 0.57 (ddd, J = 7.6, 6.0, 2.8 Hz, 1 H, 3-H_{trans}), 0.83 (m_c, 1 H, 2-H), 0.89 (t, J = 7.2 Hz, 3 H, 5′-H), 1.19−1.24 (m, 2 H, 1′-H), 1.28−1.34 (m, 4 H, 3′-H and 4′-H), 1.37−1.43 (m, 2 H, 2′-H), 6.40 (s, 2 H, O*H*); ^{13}C NMR (THF-d_8, 125 MHz) δ 4.8 (br, C-1), 11.9 (C-3), 14.7 (C-5′), 18.8 (C-2), 23.9 (C-3′ or C-4′), 30.8 (C-2′), 33.1 (C-3′ or C-4′), 36.9 (C-1′); HRMS (EI, 70 eV) calcd for $C_{24}H_{45}B_3O_3$ 414.3648 [M^+], found 414.3648.

(1*S*,2*S*)-2-Pentylcyclopropylboronic Acid (25). Cyclopropylboronic ester **20a** (2.03 g, 3.53 mmol) in THF (5 mL) was stirred at 0 °C. $LiAlH_4$ (402 mg, 10.6 mmol) was carefully added and the mixture kept at 0 °C for 1 h, after which time TLC indicated the complete consumption of starting material. Dilution with diethyl ether (25 mL) was followed by treatment with 10% sulfuric acid (20 mL). The aqueous layer was quickly extracted with petroleum ether. The combined organic layer was washed with brine, and the solution was directly subjected to flash-column chromatography (silica gel, eluting with petroleum ether/diethyl ether 4:1−1:1). The diol **3** (1.57 g, 3.45 mmol, 98%) was recovered, and the crude boronic acid **25** (460 mg) was used for Suzuki couplings without further purification.

Suzuki Couplings: "Best Conditions" for the Preparation of Cyclopropanes 26. (A) Synthesis of 1-Aryl-2-pentylcyclopropanes 26a,b. Cyclopropylboronic acid **25** (1.1 equiv) was dissolved in DME (10 mL/mmol **25**). After addition of $Pd(PPh_3)_4$ (3 mol %) and KO-*t*-Bu (2 mL/mmol **25** of a 1 M solution in *t*-BuOH), the mixture was carefully deoxygenated by a freeze technique. Phenyl bromide (1 equiv) was added. After 36 h at 80 °C, the mixture was treated with H_2O and extracted with diethyl ether. The organic layer was washed with brine and dried ($MgSO_4$), the solvent removed under reduced pressure, and the crude product purified by means of MPLC (petroleum ether). **(B) Synthesis of Cyclopropane 26c.** Cyclopropylboronic acid **25** (1.1 equiv) was dissolved in toluene (10 mL/mmol **25**). After addition of $Pd(PPh_3)_4$ (3 mol %) and K_3PO_4 (4 equiv), the mixture was carefully deoxygenated. Ethyl (*Z*)-3-bromoacrylate (1 equiv) was added. After 36 h at 100 °C, the mixture was treated with H_2O and extracted with diethyl ether. The organic layer was washed with brine and dried ($MgSO_4$), the solvent removed under reduced pressure, and the crude product purified by means of MPLC (petroleum ether).

(1*S*,2*S*)-1-Phenyl-2-pentylcyclopropane (26a): yield 74%; colorless oil; $[\alpha]^{20}_D$ = +73.9 (*c* 1.0, $CHCl_3$); IR (film) 3048, 3023 cm^{-1}; MS (EI, 70 eV) *m/z* 188 (31) [M^+], 117 (59) [$(M - C_5H_{11})^+$], 104 (100) [$(M - C_6H_{12})^+$], 91 (20) [$(C_7H_7)^+$]; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.77 (ddd, J = 8.5, 5.7, 4.6 Hz, 1 H, 3-H_{cis}), 0.89 (ddd, J = 8.5, 4.8, 4.6 Hz, 1 H, 3-H_{trans}), 0.91 (t, J = 7.0 Hz, 3 H, 5′-H), 1.07 (dtdd, J = 8.5, 6.5, 5.7, 4.4 Hz, 1 H, 2-H), 1.29−1.34 (m, 4 H, 3′-H and 4′-H), 1.35−1.41 (m, 2 H, 1′-H), 1.41−1.52 (m, 2 H, 2′-H), 1.62 (ddd, J = 8.5, 4.8, 4.4 Hz, 1 H, 1-H), 7.06 (m_c, 2 H, Ar-H), 7.14 (m_c, 1 H, Ar-H), 7.26 (m_c, 2 H, Ar-H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.1 (C-5′), 16.2 (C-3), 22.7 (C-3′ or C-4′), 23.2 (C-1), 23.9 (C-2), 29.1 (C-2′), 31.7 (C-4′ or C-3′), 34.4 (C-1′), 125.1, 125.5, 128.2, 144.1 (Ar-C). Anal. Calcd for $C_{14}H_{20}$ (188.31): C, 89.29; H, 10.71. Found: C, 89.38; H, 10.71.

(1*S*,2*S*)-1-(1-Naphthyl)-2-pentylcyclopropane (26b): yield 77%; colorless oil; $[\alpha]^{20}_D$ = +31.3 (*c* 1.5, $CHCl_3$); IR (film) 3048 cm^{-1}; MS (EI, 70 eV) *m/z* 238 (72) [M^+], 167 (100) [$(M - C_5H_{11})^+$], 154 (35) [$(M - C_6H_{12})^+$], 141 (19) [$(C_{11}H_{10})^+$]; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.82 (ddd, J = 8.5, 5.4, 4.4 Hz, 1 H, 3-H_{cis}), 0.85 (t, J = 7.0 Hz, 3 H, 5′−H), 0.95 (ddd, J = 8.4, 5.2, 4.4 Hz, 1 H, 3-H_{trans}), 1.08 (dtdd, J = 8.4, 6.5, 5.4, 4.8 Hz, 1 H, 2-H), 1.24−1.38 (m, 4 H, 3′-H and 4′-H), 1.40 (m_c, 1 H, 1′-H_a), 1.46−1.54 (m, 2 H, 2′-H), 1.68 (m_c, 1 H, 1′-H_b), 2.07 (ddd, J = 8.5, 5.2, 4.8 Hz, 1 H, 1-H), 7.19 (m_c, 1 H, Ar-H), 7.34 (m_c, 1 H, Ar-H), 7.48 (m_c, 2 H, Ar-H), 7.65 (m_c, 1 H, Ar-H), 7.82 (m_c, 1 H, Ar-H), 8.43 (m_c, 1 H, Ar-H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.7 (C-3), 14.1 (C-5′), 20.8 (C-1), 21.1 (C-2), 22.7 (C-3′ or C-4′), 29.2 (C-2′), 31.8 (C-4′ or C-3′), 34.5 (C-1′), 123.4, 124.4, 125.5, 125.8, 126.3, 127.9, 128.5, 133.3, 133.4, 139.4 (Ar-C). Anal. Calcd for $C_{18}H_{22}$ (238.37): C, 90.70; H, 9.30. Found: C, 90.71; H, 9.42.

Ethyl (1*S*,2*S*)-(*Z*)-3-(2-pentylcyclopropyl)acrylate (26c): yield 65%; colorless oil; $[\alpha]^{20}_D$ = −64.9 (*c* 1.7, $CHCl_3$); IR (film) 2958, 2926, 2856, 1717, 1632, 1184 cm^{-1}; MS (EI, 70 eV)) *m/z* 210 (4) [M^+], 181 (1) [$(M - C_2H_5)^+$], 165 (9) [$(M - C_2H_5O)^+$], 125 (19) [$(M - C_2H_5) - (C_4H_8)^+$], 111 (100) [$(M - C_2H_5) - (C_4H_8)^+$]; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.70 (ddd, J = 8.5, 4.5, 4.4 Hz, 1 H, 11-H_a), 0.79 (ddd, J = 8.1, 5.9, 4.4 Hz, 1 H, 11-H_b), 0.87 (t, J = 7.1 Hz, 3 H, 10-H), 0.85−0.94 (m, 1 H, 5-H), 1.22−1.41 (m, 8 H, 6-H, 7-H, 8-H, and 9-H), 1.28 (t, J = 7.0 Hz, 3 H, C*H*$_3$CH$_2$O), 2.63 (dddd, J = 11.2, 8.1, 4.5, 4.1 Hz, 1 H, 4-H), 4.17 (m_c, 2 H, CH$_3$C*H*$_2$O), 5.47 (t, J = 11.2 Hz, 1 H, 3-H), 5.62 (d, J = 11.2 Hz, 1 H, 2-H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.1 (C-10), 14.3 (*C*H$_3$CH$_2$O), 16.4 (C-11), 19.9 (C-4), 22.6 (C-8 or C-9), 23.7 (C-5), 28.9 (C-7), 31.6 (C-8 or C-9), 33.3 (C-6), 59.6 (*C*H$_2$O), 116.1 (C-2), 155.1 (C-3), 167.3 (C-1). Anal. Calcd for $C_{13}H_{22}O_2$ (210.31): C, 74.24; H, 10.54. Found: C, 74.05; H, 10.65.

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Supporting Information Available: ^{13}C NMR data for compounds **7**, **8**, and **10**; analytical data for compounds **11e**, **18**, **19**, and **27**; crystallographic data for compounds **3**, **13c**, **21c**, and **27**; $^{1}H/^{13}C$ NMR spectra of compounds **13a**,**j**, **20a**, **21a**, **20j**, **21j**, and **26a**−**c**. This material is available free of charge via the Internet at http://pubs.acs.org.

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