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Enantioselective synthesis of cyclic allylboronates by Mo-catalyzed asymmetric ring-closing metathesis (ARCM). A one-pot protocol for net catalytic enantioselective cross metathesis

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This work is dedicated to our colleague and friend, Professor Robert H. Grubbs, for his groundbreaking contributions to organometallic chemistry and catalytic metathesis

Abstract—Mo-catalyzed asymmetric ring-closing metathesis (ARCM) reactions are used to synthesize cyclic allylboronates of high optical purity (89% ee to >98% ee). A one-pot procedure involving formation of allylboronates, Mo-catalyzed ARCM and functionalization of the optically enriched cyclic allylboronates constitutes net asymmetric cross metathesis (ACM). Structural modification of ARCM products include reactions with aldehydes to afford optically enriched compounds that bear quaternary carbon centers with excellent diastereoselectivity. These studies emphasize the significance of the availability of chiral Mo-based complex as a class of chiral metathesis catalysts that frequently complement one another in terms of reactivity and selectivity.

1. Introduction

Catalytic enantioselective olefin metathesis allows efficient access to a range of optically enriched organic molecules that cannot be readily synthesized by alternative methods.[1] Accordingly, research in these laboratories has focused on the design and development of effective chiral complexes for asymmetric olefin metathesis.[1] We have disclosed the synthesis, characterization and activity of a number of chiral Mo-based alkylidenes (see Chart 1) that readily promote asymmetric ring-closing (ARCM)[2] and ring-opening metathesis (AROM)[3] reactions. We recently outlined the synthesis of supported chiral catalysts[4] (e.g., **5** in Chart 1) as well as practical procedures involving in situ preparation and use of related Mo complexes.[5] Applications to enantioselective synthesis of biologically active compounds are beginning to emerge.[6]

One area of research that poses a challenging task, but is of high potential in enantioselective organic synthesis, relates to the development of catalytic asymmetric cross metathesis (ACM) reactions.[7] Discovery of a direct catalytic ACM (**i**→**ii**, Scheme 1) is yet to be realized. However, an alternative approach, one that involves a one-pot operation and the intermediacy of cyclic allylboronates,[8] is illustrated in Scheme 1. Thus, formation of allylboronate **iii**, followed by catalytic ARCM may afford cyclic **iv** which can then be functionalized to afford net ACM products (e.g., **ii** after oxidation). Such a strategy provides opportunities for stereoselective formation of additional C–C bonds through reaction of **iv** with different electrophiles (e.g., carbonyl-containing compounds).

Herein we report an approach to net ACM which involves the intermediacy of optically enriched cyclic allylboronates formed through Mo-catalyzed ARCM. The present protocol offers an efficient route for the preparation of synthetically versatile organic molecules of high optical purity (up to >98% ee). Research outlined further underlines the significance of the modular character of high oxidation state Mo-based complexes that has led to the availability of a class of chiral catalysts for enantioselective olefin metathesis.[1a,b,9]

2. Optically pure cyclic allylboronates by Mo-catalyzed kinetic resolution

We began our investigation by examining the possibility of

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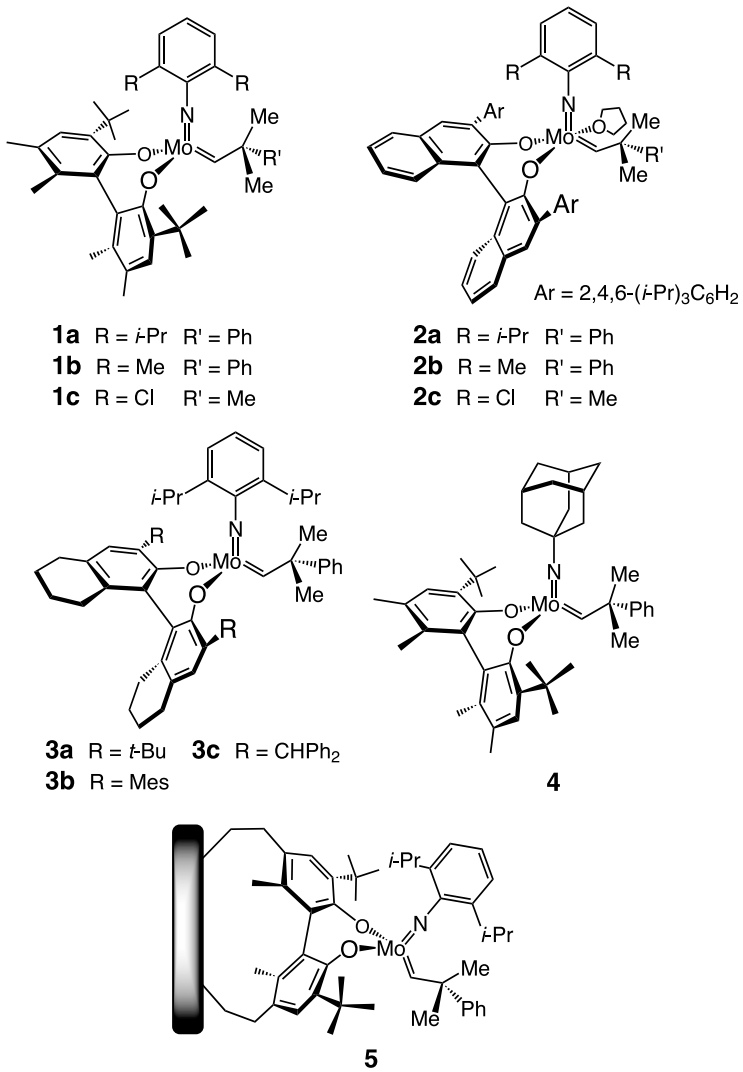
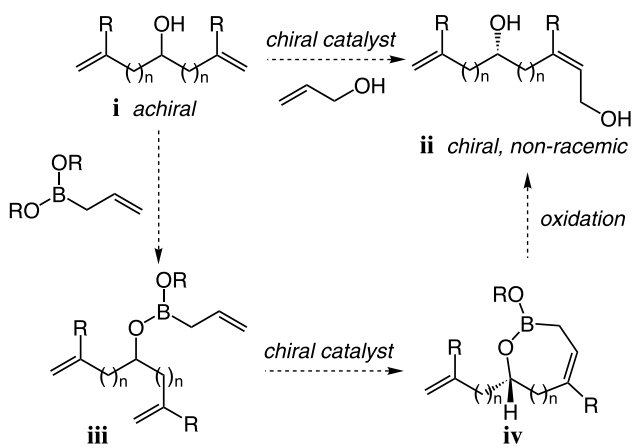


Chart 1. Representative chiral Mo catalysts for olefin metathesis.

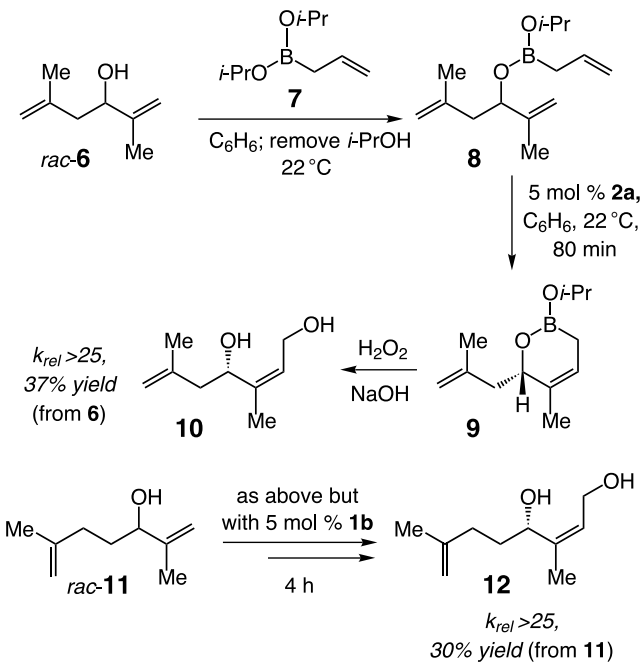
the one-pot Mo-catalyzed strategy shown in Scheme 1 to effect kinetic resolution of dienes **6** and **11** (Scheme 2). As illustrated in Scheme 2, treatment of *rac*-diene **6** with one equivalent of allyl boronate **7** in benzene at 22 °C results in the smooth formation of a solution of triene **8** (400 MHz ^{1}H NMR analysis). Since high oxidation state Mo complexes are sensitive to unprotected alcohols, *i*-PrOH generated in the course of the formation of **8** must be removed in vacuo before the addition of chiral metathesis catalysts. Screening studies indicated that in the presence of 5 mol% **2a** (see Chart 1), ARCM proceeds smoothly to afford **9** (~50% conv. after 80 min). The resulting cyclic allylboronate can be directly (not isolated) subjected to oxidation conditions (H_2O_2, NaOH) to afford optically pure **10** in 37% overall isolated yield (>30:1 *Z*/*E*; maximum theoretical yield=50%). In a similar fashion *rac*-**11** is converted, by the one-pot protocol, to stereosiomerically pure **12** in 35% yield. It should be noted that catalytic ARCM of the allylboronate derived from *rac*-**11** proceeds most selectively in the presence of chiral complex **1b** (vs. **2a** for *rac*-**6**; see below for additional discussion).



Scheme 1. Catalytic asymmetric CM and a one-pot multistep alternative.

3. Enantioselective synthesis of cyclic allylboronates by Mo-catalyzed ARCM

With the feasibility of the general approach described in Scheme 1 substantiated through our investigation of the Mo-catalyzed kinetic resolutions shown in Scheme 2, we turned our attention to the possibility of achieving net ACM through one-pot desymmetrizations of achiral substrates.



[a]Enantioselectivities determined through chiral GLC analysis (α-dex)

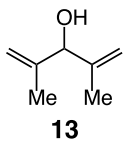
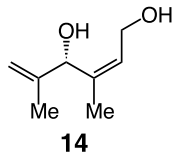
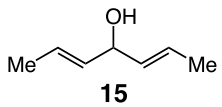
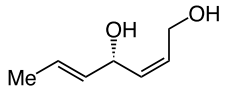
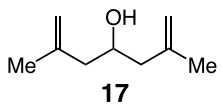
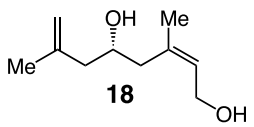
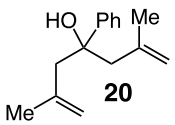
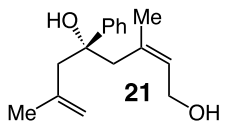
Scheme 2. Catalytic kinetic resolution through ARCM/oxidation (net asymmetric CM)[a].

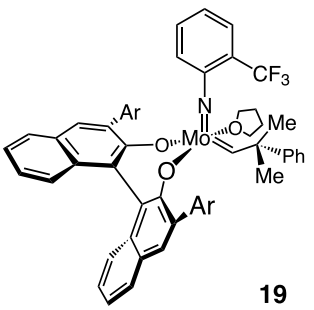
The results of these investigations are summarized in Table 1. Treatment of diene **13** with 1 equiv. of allylboronate **7** (Scheme 2), removal of *i*-PrOH in vacuo and treatment with chiral binaphtholate-based Mo complex **2a** (Chart 1) leads to formation of the desired cyclic allylboronate (cf. **9**, Scheme 2) which is directly oxidized to afford **14** in >98% ee and 57% overall isolated yield.[10] Catalytic enantioselective desymmetrization of allylic alcohol **15** is promoted by dichloroimido complex **1c** to deliver **16** in optically pure form and 58% yield after silica gel chromatography. As the data in entry 3 of Table 1 indicate, one-pot desymmetrization of homoallylic alcohol **17** in the presence of 5 mol% *o*-(trifluoromethyl)phenylimido complex **19** leads to the formation of **18** in 89% ee and 64% isolated yield. Net Mo-catalyzed ACM with tertiary homoallylic alcohol **20** is less efficient and proceeds to ~80% conv. in the presence of 5 mol% of a variety of Mo catalysts; the highest enantioselectivity is obtained with adamantylimido complex **4** (Chart 1) to generate **21** in >98% ee and 38% isolated yield (from **20**).

Several issues regarding the experiments summarized in Table 1 are worthy of note:

(1) An underlining feature of the present catalytic method is that in each of the cases described above a different chiral Mo complex is used to obtain optimal levels of reactivity and selectivity. This should not be viewed as a drawback of the protocol. As we have described in detail elsewhere,[1a,b] the identity of the optimal chiral metathesis catalyst should not be generalized; the availability of a class of catalysts increases the possibility of obtaining the most desirable conversion and enantioselectivities. If **1a** were the only available chiral complex, high selectivities would be feasible in

Table 1. Mo-catalyzed one-pot net ACM reactions[a]

Entry	Substrate	Product	Catalyst	Time (h)	Conv. (%);[b] yield (%)[c]	ee (%)[d]
1	 **13**	 **14**	**2a**	12	78; 57	>98
2	 **15**	 **16**	**1c**	1	90; 58	>98
3	 **17**	 **18**	**19**	14	80; 64	>89
4	 **20**	 **21**	**4**	24	80; 38[e]	>98



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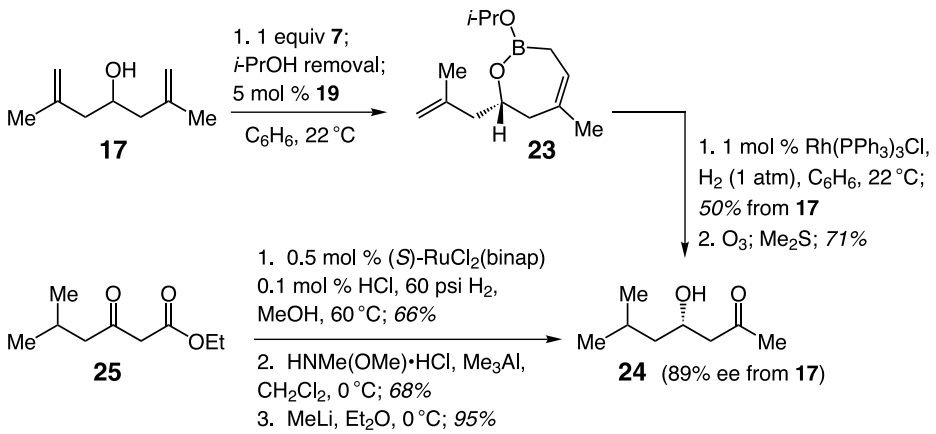
Ar = 2,4,6-(*i*-Pr)$_3$C$_6$H$_3$

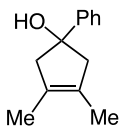
[a] Conditions: 5 mol% chiral catalyst, C_6H_6, 22 °C.
[b] Conversions determined through 400 MHz ^{1}H NMR analysis.
[c] Isolated yields of purified products (overall from starting diene).
[d] Determined by GLC (entries 1–3, α-dex column) and HPLC (entry 4, chiral OJ column).
[e] 40% of tetrasubstituted olefin **22** also formed.



Scheme 3. Mo-catalyzed conversiton of diene **17** to optically pure β-hydroxyketone **24**.

net ACM with *rac*-**11** (Scheme 2); other transformations shown here would proceed with similar levels of efficiency but with significantly lower selectivities.

(2) The lower efficiency of the catalytic ARCM involving tertiary alcohol **20** is likely due to inefficient formation of the acyclic allylboronate intermediate (cf. **iii** in Scheme 1). As a result, cyclic tertiary alcohol **22**, bearing a tetrasubstituted olefin, is formed as a significant byproduct (40% yield). This observation indicates that not only is chiral alkylimido complex **4** capable of promoting the formation of tetrasubstituted olefins by RCM but also that sterically congested alcohols may be viewed as viable substrates for this class of chiral metathesis catalysts. Studies to investigate and exploit such attributes of chiral Mo complex **4** are underway.



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4. Functionalization and synthetic utility of optically enriched allylboronates

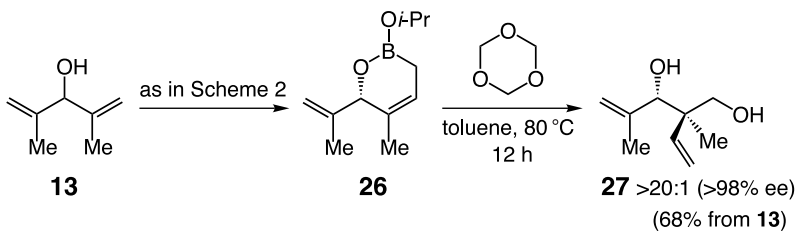
The allylboronates obtained in the Mo-catalyzed ARCM reactions discussed above can be functionalized in a variety of manners (in addition to oxidations). One example is shown in Scheme 3. Regioselective Rh-catalyzed hydrogenation[11] of cyclic boronate **23** (89% ee; see entry 3 in Table 1), followed by ozonolytic cleavage of the trisubstituted cyclic olefin leads to the formation of the acetate aldol adduct **24**. Conversion of **25** to the same compound based on previously reported protocols,[12] as illustrated in Scheme 3, secures the stereochemical identity of the major enantiomer in the catalytic ARCM.[13]

Optically enriched allylboronates are attractive because they can serve as effective nucleophiles. The example shown in Scheme 4 is illustrative. Treatment of optically pure **26**, obtained from catalytic ARCM of the allyboronate derived from **13**, with trioxane in toluene at 80 °C leads to the formation of diol **27** as a single enantiomer and diastereomer (68% overall yield from **13**). The facile synthesis and stereoselective formation of the quaternary carbon center[14] in **27** augurs well for the utility of cyclic allylboronates generated by catalytic ARCM reactions.[15,16]

Such C–C bond forming reactions are less feasible with the corresponding cyclic siloxanes that can also be obtained through Mo-catalyzed ARCM reactions.[17] Although Mo-catalyzed ARCM of allylsiloxanes allows access to products shown in Scheme 2 and Table 1 through oxidations of the C–Si bonds, the present method offers a more attractive option. This preference is for two reasons: (i) C–Si oxidation is generally less efficient than those of C–B bonds and with allylsilane compounds such processes can occur with low regioselectivity. (ii) In contrast to the one pot procedure described herein, installation of the silyl ether and its subsequent oxidation must be carried out in separate vessels, thus reducing the efficiency of the overall protocol.

5. Conclusions

In summary, we disclose an efficient catalytic enantioselective method for the preparation of synthetically



Scheme 4. Diastereo- and enantioselective synthesis of quarternary carbons.

versatile cyclic allylboronates through ring-closing metathesis. The products obtained after functionalization of the optically enriched allylboronates can be considered as products of catalytic ACM reactions. Design and development of additional effective catalysts that promote a wide variety of metathesis reactions and applications to the synthesis of biologically active molecules continue in these laboratories.

6. Experimental

6.1. General

Infrared (IR) spectra were recorded on a Nicolet 210 spectrophotometer, ν_{max} is in cm^{-1}. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). ^1H NMR spectra were recorded on Varian GN-400 (400 MHz), and Varian Gemini 2000 (400 MHz) spectrometers. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 7.26, C_6D_6: δ 7.15). Data are reported as follows: chemical shift, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, br=broad, m=multiplet), coupling constants (Hz), integration, and assignment. ^{13}C NMR spectra were recorded on Varian GN-400 (100 MHz), and Varian Gemini 2000 (100 MHz) spectrometers with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent as the internal reference ($CDCl_3$: δ 77.2 ppm, C_6D_6: δ 128.1 ppm). Enantiomer ratios were determined by chiral GLC (Supelco alphadex 120 column (30 m×0.25 mm)) or chiral HPLC analysis (Chiral Technologies chiracel OJ (0.46 cm×25 cm)) in comparison with authentic racemic materials.

All reactions were conducted in oven- (135 °C) and flame-dried glassware under an inert atmosphere of dry nitrogen. Solvents were purified under a positive pressure of dry argon by a modified Innovative Technologies purification system. Benzene and toluene were purged with argon before being passed through activated copper and alumina columns. Tetrahydrofuran, and diethyl ether are purged with Ar before being passed through activated alumina columns. Olefin-free pentane was generated by allowing (commercial grade) pentane to stir in the presence of concentrated sulfuric acid (20 mL per L of pentane) for 24 h. The pentane was poured over fresh concentrated sulfuric acid. The process was repeated until the acid layer remained colorless for 48 h. The pentane was separated, washed with water, dried over Na_2SO_4, filtered, purged with Ar and then passed through activated copper and alumina columns. All handling of the molybdenum catalysts was performed in a glove box under nitrogen atmosphere. All substrates were rigorously dried by repeated azeotropic distillation using anhydrous benzene (3 times) prior to use.

6.1.1. (4*R*)-Diol 10. To a round bottom flask was added *rac*-dieneol **6** (150 mg, 1.19 mmol, 1.0 equiv.), diisopropoxyallylboronate **7** (202 mg, 1.19 mmol, 1.0 equiv.) and benzene (12.0 mL) (in a glovebox). The resulting mixture was allowed to stir for 16 h at 22 °C. At this time, benzene was removed in vacuo to afford the desired mixed boronate as a colorless oil (222.0 mg, 0.940 mmol). Analysis of the ^1H NMR spectrum showed complete removal of isopropanol by absence of ^1H resonance at 4.04 ppm. A portion of the resulting oil (11.8 mg, 0.050 mmol) was dissolved in 0.50 mL of benzene and chiral complex (*R*)-**2a** (2.9 mg, 0.03 mmol, 0.05 equiv.) was added. The mixture was allowed to stir at 22 °C for 80 minutes. At this time, the reaction vessel was removed from the glovebox, and the reaction was quenched by exposure of the solution to air.[18] The unpurified mixture was dissolved in THF (500 μL) and ethanol (500 μL). To this stirring solution was added aqueous NaOH (500 μL of a 3.8 M solution) and H_2O_2 (500 μL of a 30% aqueous solution). The mixture was allowed to stir at 22 °C for 2 h during which the solution changed in color from dark brown to light yellow. After 2 h, the solution was washed with 5.0 mL of Et_2O. The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The resulting light yellow oil was dissolved in 2 mL of hexanes and purified by silica gel chromatography (1:1 hexanes/Et_2O) to afford diol **10** as a colorless oil (3.7 mg, 0.023 mmol, 46%). R_f=0.1 (1:1 hexanes/Et_2O). IR (neat): 3377 (s), 2974 (m), 2930 (m), 1652 (w), 1445 (m), 1381 (m), 1060 (s), 1023 (s), 872 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 5.55 (t, J=8.2 Hz, 1H, C=C*H*CH_2OH), 4.89 (m, 1H, CH_AH_B=C), 4.81 (m, 1H, CH_AH_B=C), 4.66 (dd, J=9.2, 5.1 Hz, 1H, C*H*OH), 4.26 (dd, J=12.7, 8.5 Hz, 1H, CH_AH_BOH), 4.08 (dd, J=12.5, 6.0 Hz, 1H, CH_AH_BOH), 2.36 (dd, J=13.6, 8.7 Hz, 1H, CH_AH_BCHOH), 2.19 (dd, J=13.6, 4.9 Hz, 1H, CH_AH_BCHOH), 1.78 (s, 6H, $-CH_3$). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 142.2, 141.0, 126.2, 113.9, 67.7, 58.0, 43.8, 22.5, 18.4; HRMS calcd for $C_9H_{16}O_2Na$: 179.1048. Found: 179.1046.

6.1.2. (4*R*)-Diol 12. R_f=0.1 (1:1 hexanes/Et_2O). IR (neat): 3327 (s), 3068 (w), 2943 (s), 1652 (m), 1628 (m), 1451 (s), 1376 (m), 1067 (m), 1004 (s), 891 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 5.54 (dd, J=6.8, 6.8 Hz, 1H, C=C*H*CH_2OH), 4.74 (m, 1H, CH_AH_B=C), 4.71 (m, 1H, CH_AH_B=C), 4.52 (t, J=6.8 Hz, 1H, C*H*OH), 4.25 (dd, J=12.8, 8.4 Hz, 1H, CH_AH_BOH), 4.06 (ddd, J=12.8, 6.4, 1.2 Hz, 1H, CH_AH_BOH), 3.70 (br s, 2H, –OH), 2.03 (m, 2H, CH_2C=CH_2), 1.81 (m, 1H, CH_AH_BCHOH), 1.76 (s, 3H, $-CH_3$), 1.74 (s, 3H, $-CH_3$), 1.62 (m, 1H, CH_AH_BCHOH); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 145.3, 141.4, 126.2, 110.3, 69.7, 58.1, 34.1, 32.9, 22.7, 18.3; HRMS calcd for $C_{10}H_{18}O_2Na$: 193.1204. Found: 193.1208.

6.1.3. (4*R*)-Diol 14. R_f=0.1 (1:1 hexanes/Et_2O). IR (neat): 3376 (br s), 2971 (m), 2921 (s), 2853 (m), 1721 (m), 1658 (m), 1449 (m), 1381 (m), 1256 (w), 1230 (w), 1060 (s), 1017 (s), 994 (s), 903 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 5.64 (dd, J=6.6, 6.6 Hz, 1H, C=C*H*CH_2OH), 5.10 (s, 1H, C=CH_AH_B), 4.95 (s, 1H, C=CH_AH_B), 4.91 (s, 1H, C*H*OH), 4.32 (dd, J=12.4, 8.2 Hz, 1H, CH_AH_BOH), 4.14 (dd, J=12.4, 6.0 Hz, 1H, CH_AH_BOH), 2.06 (br s, 2H, –O*H*), 1.66 (s, 3H, $-CH_3$) 1.64 (s, 3H, $-CH_3$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 145.0, 139.4, 127.5, 110.8, 73.4, 58.5, 19.4, 18.4; HRMS calcd for $C_8H_{14}O_2Na$: 165.0891. Found: 165.0891.

6.1.4. (4*R*)-Diol 16. R_f=0.1 (1:1 hexanes/Et_2O). IR (neat): 3394 (s), 2953 (s), 2924 (s), 2853 (m), 1729 (m), 1474 (m), 1367 (m), 1099 (s), 1022 (s), 802 (m) cm^{-1}; ^1H NMR

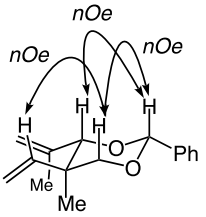
($CDCl_3$, MeOD 400 MHz): δ 5.73–5.68 (m, 2H, C=C*H*CHOH), 5.64–5.53 (m, 2H, C*H*=CHCHOH), 4.93 (t, J=7.6 Hz, 1H, C*H*OH), 4.35–4.30 (dd, J=12.8, 7.2 Hz, 1H, CH_AH_BOH), 4.23–4.18 (dd, J=12.8, 6.4 Hz, 1H, CH$_A$$H_B$OH), 1.71 (dd, J=6.8 Hz, 3H, $-CH_3$); ^{13}C NMR ($CDCl_3$, MeOD 100 MHz): δ 133.5, 132.4, 130.0, 127.1, 68.7, 58.2, 18.2; HRMS calcd for $C_7H_{13}O_2$: 129.0916. Found: 129.0918.

6.1.5. (5*R*)-Diol 18. R_f=0.1 (1:1 hexanes/Et_2O). IR (neat): 3323 (s), 3075 (w), 2967 (s), 2934 (s), 2916 (m), 1658 (w), 1628 (m), 1445 (s), 1376 (m), 1068 (m), 1046 (w), 1024 (s), 997 (s), 890 (m), 669 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.76 (dd, J=8.2, 7.1 Hz, 1H, C=C*H*CH$_2$OH), 4.92 (m, 1H, CH_AH$_B$=C), 4.83 (m, 1H, CH$_A$$H_B$=C) 4.17 (dd, J=11.8, 8.2 Hz, 1H, CH_AH$_B$OH), 3.92 (dd, J=11.8, 7.0 Hz, 1H, CH$_A$$H_B$OH), 3.84 (ddt, J=9.7, 6.4, 2.7 Hz, 1H, C*H*OH), 2.51 (dd, J=13.5, 9.7 Hz, 1H, CH$_2$C=CCH_AH$_M$-CHOH), 2.23 (d, J=6.4 Hz, 2H, *CH*$_2$CHOH), 2.02 (dd, J=13.5, 2.7 Hz, 1H, CH$_2$C=CCH$_A$$H_M$CHOH), 1.81 (s, 3H, $-CH_3$), 1.79 (s, 3H, $-CH_3$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 142.5, 127.0, 114.1, 113.4, 65.8, 57.9, 46.7, 39.5, 24.0, 22.5; HRMS calcd for $C_{10}H_{18}O_2Na$: 193.1204. Found: 193.1205.

6.1.6. (5*R*)-Diol 21. R_f=0.1 (1:1 hexanes/Et_2O). IR (neat): 3384 (s), 3067 (w), 3027 (w), 2960 (s), 2921 (s), 2869 (m), 1709 (m), 1636 (m), 1446 (s), 1370 (s), 1070 (m), 996 (m), 889 (m) 701 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.42 (d, J=7.1 Hz, 2H, Ar–H), 7.31 (dd, J=7.3, 7.1 Hz, 2H, Ar–H), 7.22 (dd, J=7.3, 7.2 Hz, 1H, Ar–H), 5.63 (dd, J=6.6, 6.6 Hz, 1H, C=C*H*CH$_2$OH), 4.89 (m, 1H, CH_AH$_B$=C), 4.77 (m, 1H, CH$_A$$H_B$=C), 4.06 (dd, J=11.7, 8.1 Hz, 1H, CH_AH$_B$OH), 3.86 (dd, J=11.7, 7.3 Hz, 1H, CH$_A$$H_B$OH), 2.82 (dd, J=13.6, 3.5 Hz, 2H, CH_2COH), 2.60 (d, J=13.4 Hz, 1H, CH_AH$_B$COH), 2.51 (d, J=13.4 Hz, 1H, CH$_A$$H_B$COH), 1.30 (s, 3H, $-CH_3$), 1.28 (s, 3H, $-CH_3$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 145.8, 142.4, 137.0, 128.5, 128.2, 126.9, 125.7, 116.6, 74.4, 58.5, 51.4, 46.0, 26.1, 24.4; HRMS calcd for $C_{16}H_{22}O_2Na$: 269.1517. Found: 269.1515.

6.1.7. Diol 27. Paraformaldehyde (42 mg, 1.0 mmol) was added (while stirring) to a solution of boronate **26** (7.8 mg, 0.050 mmol) in toluene (200 μL). The resulting mixture was placed under nitrogen and heated to 80 °C (temperature controlled oil bath) for 12 h. At this time, the solution was allowed to cool to 22 °C, and volatiles were removed in vacuo to afford a viscous black oil. The resulting black oil was dissolved in MeOH (1.0 mL of a solution of MeOH (5.0 mL) at 0 °C (ice bath) and acetyl chloride (100 μL, 1.4 mmol)) was added slowly with vigorous stirring (*caution*: highly exothermic) and then allowed to stand at 22 °C for 5 minutes. Evaporation of volatiles (3 times) resulted in the removal of volatile boron-derived impurities. The resulting black oil was dissolved in a 0.5 mL of 1:1 hexanes/Et_2O and purified by silica gel chromatography (1:1 hexanes /Et_2O) to give **27** as a colorless oil (6.6 mg, 0.043 mmol, 85%). R_f=0.1 (1:1 hexanes/Et_2O). IR (neat): 3386 (s), 3075 (w), 2974 (s), 2924 (s), 2873 (m), 1728 (w), 1652 (m), 1457 (m), 1426 (m), 1375 (m), 1161 (w), 1037 (s), 1013 (m), 912 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.92 (dd, J=17.6, 11.0 Hz, 1H, C*H*=CH$_2$), 5.20 (d, J=17.2 Hz, 1H, CH=CH_AH$_B$), 5.17 (d, J=12.3 Hz, 1H, CH=CH$_A$$H_B$), 5.00 (s, 2H, CH$_3$C=C$H_2$), 4.20 (s, 1H, C*H*OH), 3.66 (m, 2H, *CH*$_2$OH), 1.79 (s, 3H, CH$_3$) 1.06 (s, 3H, CH$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.0, 141.8, 114.9, 113.9, 81.2, 70.4, 46.0, 21.3, 16.3; HRMS calcd for $C_9H_{16}O_2Na$: 179.1048. Found: 179.1043.

6.1.8. Benzylidene acetal derived from diol 27 (for proof of relative stereochemistry). To a solution of diol **27** (5.0 mg, 0.032 mmol) in benzene (300 μL) was added benzaldehyde (16 μL, 0.16 mmol, 5.0 equiv.) and 100 μL of a solution consisting of 1.0 mL CH_2Cl_2, 3.0 mg pTsOH·H_2O, 0.10 μL MeOH (to dissolve p-TsOH). The resulting mixture was placed under N_2 atmosphere and heated to 100 °C (temperature controlled oil bath) for 10 h. The solution was allowed to cool to ambient temperature and was loaded directly onto a silica gel column (eluted with 100:1 hexanes/Et_2O) to give **28** as a colorless oil (6.8 mg, 0.28 mmol, 87%). R_f=0.9 (10:1 hexanes/Et_2O). IR (neat): 3081 (m), 3062 (m), 3024 (m), 2967 (s), 2917 (s), 2848 (s), 1734 (w), 1646 (m), 1457 (s), 1407 (s), 1394 (s), 1350 (s), 1300 (m), 1224 (m), 1174 (m), 1099 (s), 1029 (s), 979 (m), 916 (m), 752 (m), 696 (s), 658 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.53 (dd, J=8.1, 1.8 Hz, 2H, Ar–H), 7.37 (m, 3H, Ar–H), 5.74 (dd, J=17.0, 11.3 Hz, 1H, C*H*=CH$_2$), 5.56 (s, 1H, Ar–C*H*(O)O), 5.18 (s, 1H, CH_AH$_B$=CH), 5.14 (dd, J=7.1, 1.1 Hz, 1H, CH$_A$$H_B$=CH), 5.02 (m, 1H, C$H_AH_B$=C), 4.96 (m, 1H, CH$_A$$H_B$=C), 4.21 (s, 1H, C*H*–C=CH$_2$), 3.85 (d, J=11.4 Hz, 1H, CH_AH$_B$O), 3.69 (d, J=11.2 Hz, 1H, CH$_A$$H_B$ O), 1.76 (s, 3H, $-CH_3$) 1.27 (s, 3H, $-CH_3$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 142.3, 140.9, 138.7, 129.0, 128.4, 126.4, 115.5, 113.5, 101.8, 86.1, 77.2, 40.6, 21.9, 15.6; HRMS calcd for $C_{16}H_{20}O_2Na$: 267.1361. Found: 267.1359.



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