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Preparation and Diels–Alder/Cross Coupling Reactions of New 2-Boron-Substituted 1,3-Dienes

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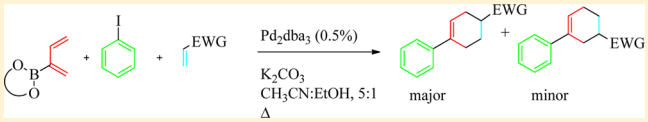
Supporting Information

ABSTRACT: Several new 2-boron substituted dienes have been prepared and characterized. Their reactivity in Diels–Alder reactions has been examined and the boron substituted cycloadducts of those cycloaddition reactions have been used in cross coupling reactions. One-pot tandem Diels–Alder/cross coupling reactions of 2-boron substituted dienes are then also reported along with some experimental evidence that these one-pot reactions are proceeding through a Pd(II)-catalyzed Diels–Alder/cross coupling reaction pathway.



INTRODUCTION

We have been interested in the preparation and reaction chemistry of metal substituted dienes for over 15 years. Initially, we prepared a number of transition metal substituted dienes[1] for these studies, but more recently, we have been interested in the investigation of silicon and boron substituted dienes.[2] In the case of boron substituted diene chemistry, we initially reported the preparation of 2-BF_3 substituted 1,3-butadienes and demonstrated that they could be used in sequential Diels–Alder/cross coupling reactions.[3] These trifluoroborate substituted dienes are stable, but their organic solvent solubility is not ideal. Preparation of more highly substituted BF_3 dienes also requires a transmetalation protocol which yields a byproduct from a side reaction of the commercially available Grignard reagent used and which has to be separated from the desired diene.[3b] To overcome these methodology challenges, we wanted to prepare additional boron substituted 1,3-dienes,[4] and we report our most recent results in this area here.[5]

RESULTS AND DISCUSSION

Preparation of New Boron Substituted 1,3-Dienes. All the new dienes reported here were obtained as white solids on a multigram scale via a simple procedure which involved preparing the Grignard reagent from chloroprene (**1**), adding this reagent to trimethoxyborane followed by the addition of acid at low temperature and finally the chelating di- or triol ligand of interest.

In 2009, we communicated this method to prepare the diethanolamine chelated boron diene (**3**) and then also reported on its subsequent Diels–Alder and cross coupling reaction chemistry.[4] Subsequent to this initial report, we have found that N-methyl diethanolamine also works well in this procedure to produce **4**, but somewhat surprisingly, N-phenyl diethanolamine fails to produce an isolable product (**5**) and only the transiently stable boronic acid diene (**2**) was observed in that case by NMR (Scheme 1).

When their ^{11}B NMR spectra were obtained, diethanolamine boronate-1,3-butadiene (**3**) (δ10.08, $(CD_3)_2SO$); δ10.46, $(CDCl_3)$) was found to have a stronger N–B bond than N-methyl diethanolamine boronate-1,3-butadiene (**4**) (δ11.31, $(CD_3)_2SO$; δ11.38, $CDCl_3$) (these ^{11}B NMR chemical shifts are similar to other reported diolamine boronates in $(CD_3)_2SO$).[6] When the temperature was raised gradually to 60 °C, there was only one boron peak in the diethanolamine boronate-1,3-butadiene (**3**) spectrum, but an extra small peak appears (δ10.43, $(CD_3)_2SO$) in N-methyl diethanolamine boronate-1,3-butadiene (**4**), which is consistent with some B–N bond dissociation (accompanied most likely by residual water coordination) at higher temperature.[7] Finally, when the similar N-donating chelator (3,3′-(methylazanediyl)-dipropanoic acid))[8] was tried, no product was detected by NMR or GC-MS.

Following this analysis of possible N and O chelating ligands for boron dienes, we examined a number of non amine containing diols and triols. Initially, we tried adding diols or triols to the transient boronic acid diene (**2**) followed by reflux or the addition of acidic dehydrating reagents such as sodium sulfate or molecular sieves, but in all cases, this resulted in diene decomposition or dimerization.[9] Attempts to prepare **7** by other groups previously by alternative routes had also noted this easy diene dimerization.[5a,10] Alternatively, we found that boronic acid diene (**2**) could be dissolved in THF and then treated with the diol or triol of interest followed by NaH (1.5 equiv) and that from these basic conditions we were able to isolate a series of new 2-boron substituted dienes (**6**–**10**) (Scheme 2) without dimerization, so we now suspect that the earlier reports of easy dimerization of **7** may have been Lewis or Bronsted acid catalyzed dimerizations. When we prepared **6**–**9** under these basic conditions, we found that we could heat these dienes for 6 h in toluene and recover them unreacted and that we saw only a trace of dimerization when they were heated for 24 h in THF. Brown and co-workers had also previously noted that when they treated bromo-alkenylboronic esters with

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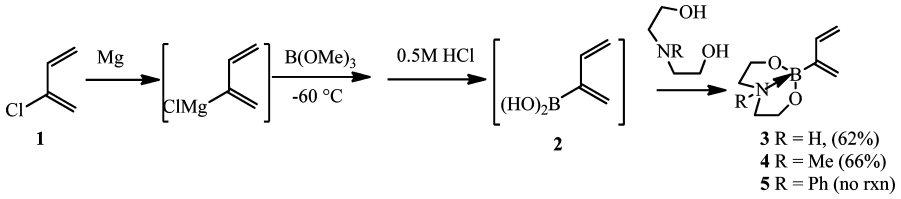
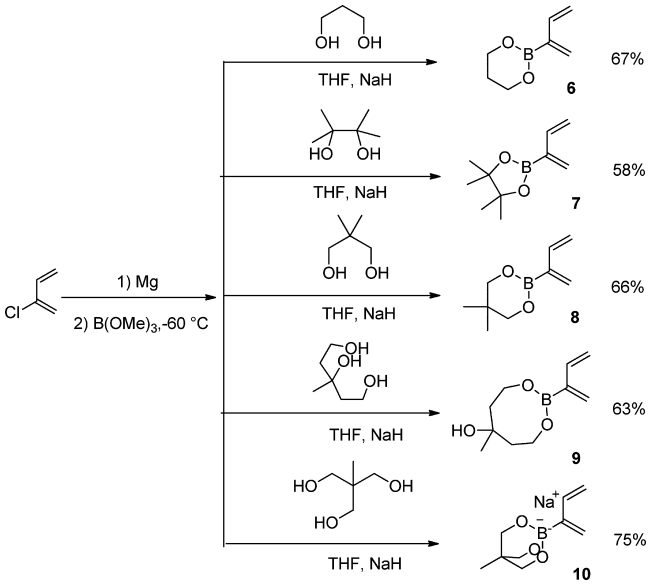
Scheme 1. Preparation of Boron Dienes Containing Diethanolamine Ligands



Scheme 2. Preparation of Boron Dienes Containing Diol and Triol Ligands

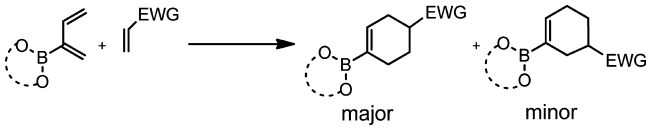


alkenyl lithium reagents under basic conditions they could also isolate the dienes, which they subsequently proto-deboronated or oxidized.[11]

Initially, we had thought we might be able to determine whether or not the boron in one of these dienes was three or four coordinate from differences in their ^{1}H or ^{13}C NMR spectra, but they proved to all be very similar. Dienes (**6**–**10**) show C_1 and H_1 resonances (d_6-DMSO) from 116.9 to 119.7 and 4.82–5.09, C_3 and H_3 from 144.6 to 145.5 and 6.18–6.32, and C_4 and H_4 from 112.4 to 113.2 and H_{4trans} 5.36–5.50, H_{4cis} 4.65–4.71. Dienes (**6**–**9**) exhibit interesting ^{11}B NMR resonances. In $CDCl_3$ (dried over molecular sieves) where they are sparingly soluble and we filter samples into the NMR tubes, they have ^{11}B NMR spectra typical of 3 coordinate boron (δ25–30 ppm).[12] When we obtain NMR spectra from those same samples of material but in d_6-DMSO, all the ^{11}B resonances occur at 1–6 ppm, so we believe they are all 4 coordinate in this solvent[13] as a result of the basic reaction conditions used to prepare them and traces of NaOH that may be present or traces of water that are more prevalent in d_6-DMSO than $CDCl_3$. Dienes (**6**, **8**, and **9**) all appear to exist as a mixture of *s-cis* and *s-trans* conformers in solution at 25 °C, since we see NOESY cross peaks between H_3 as well as H_4 protons and the H_1 protons. Dienes (**7** and **10**), on the other hand, only show NOESY cross peaks between H_3 and the H_1 protons indicating that *s-cis* to *s-trans* interconversion is not as rapid for those 2 dienes.

Diels–Alder Reactions of Boron Substituted Dienes. Diels–Alder reactions of diene (**3**) were reported in our earlier communication.[4] We noted at that time that this diene was the most reactive of any transition element or main group element substituted diene that we had prepared to this point. The enhanced Diels–Alder reactivity was consistent with a relatively high calculated diene HOMO energy of −6.00 eV for this boron substituted diene as compared to −12.58 eV for a 2-BF_3 substituted 1,3-butadiene.[4] New dienes reported here (**4** and **6**–**10**) were also examined for their reactivity in Diels–Alder chemistry (Scheme 3). The diene obtained from the N-methyl

Scheme 3. Diels–Alder Reactions of Boron Dienes



diethanolamine (**4**) proved to be slightly less reactive than its diethanolamine counterpart (**3**), and where we thought it might have even better organic solvent solubility than **3**, we found them to be virtually identical and both highly soluble.[4] Whereas **3** had reacted completely with N-phenylmaleimide in 0.25 h at 20 °C ($t_{1/2}$ < 4 min @ −10 °C), **4** required 2 h to go to completion (Table 1, entry 1). Similarly, where **3** reacted with ethyl acrylate and N-phenyl citraconimide after 6 h and 8 h of reflux to provide products in 84% and 95% isolated yields with 16.4 and 4:1 regioisomeric ratios, **4** required 20 h of reflux to provide the cycloadducts (**12** and **13**) in 90% and 75% yields with reduced (3:1) regioselectivities (Table 1, entries 2 and 3). Dienes (**6**–**9**), which all contain 3 coordinate boron in dry solvents, failed to produce any product when reacted with N-phenylmaleimide at 20 °C for 20 h in THF. Switching to toluene reflux yielded just trace amounts of product when heated with N-phenylmaleimide with the exception of diene **6** which did produce about a 50% yield of cycloadduct after 10 h of reflux. The other diene, which contained four coordinate boron from a triol ligand (**10**), reacted well with N-phenylmaleimide at 20 °C (Table 1, entry 4) and N-phenylcitraconimide (Table 1, entry 6) but produced a poor yield of cycloadduct with ethyl acrylate (Table 1, entry 5).

Suzuki Cross Coupling Reactions of Boron Substituted Diels–Alder Cycloadducts and Tandem Diels–Alder/Cross Coupling Reactions. A variety of cross coupling reactions of the boron substituted cycloadducts of the diethanolamine boron diene (**3**) were reported in our earlier communication.[4] Initially, here we just took the N-methyl diethanolamine cycloadduct (**11**), as well as the triol boronate substituted cycloadduct (**14**), and cross coupled them with iodobenzene using conditions analogous to those we had used for cycloadducts of **3** (Scheme 4) (Table 2, entries 1 and 2). We then performed Diels–Alder reactions to produce **12** and **13**, but rather than stop to purify those cycloadducts, we just took the crude products on into the cross coupling reaction and found that this approach also produced organic cycloadducts (**18** and **19**) in good yields for the 2 steps (Table 2, entries 3

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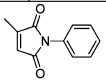
Table 1. Diels–Alder Reactions of Dienes

Entry	Diene	Product	Dienophile	Temp (°C)	Solvent	Time (h)	Yield (%)	Major:Minor
1	4	11	 N-Phenyl maleimide	20	$CHCl_3$	2	90	NA
2	4	12	 Ethyl acrylate	110	Toluene	20	90	3:1
3	4	13	 N-Phenyl citraconimide	110	Toluene	20	75	3:1
4	10	14	N-Phenyl maleimide	20	Toluene	3	92	NA
5	10	15	Ethyl acrylate	110	Toluene	12	40 (NMR)	2:1
6	10	16	N-Nhenyl citraconimide	110	Toluene	12	80 (NMR)	2:1

Scheme 4. Cross Coupling Reactions of Boron Substituted Diels–Alder Cycloadducts

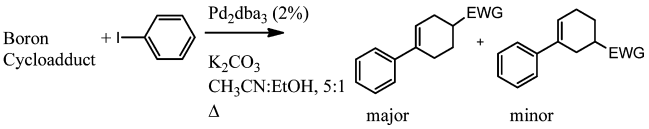
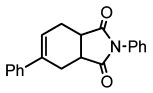
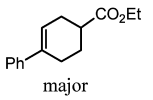
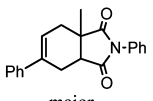


Table 2. Results of Cross Coupling Reactions

Entry	Cycloadduct (#)	Yield (%)	Isomer Ratio	Product (#)
1)	11	92	NA	 17
2)	14	86	NA	17
3)	12	68*	3:1	 major 18
4)	13	60*	1.3:1	 major 19

*Yield reported is cumulative for 2 steps, the Diels–Alder reaction followed by the cross coupling reaction.

Scheme 5. Tandem Diels–Alder/Cross Coupling Reactions of Boron Substituted Dienes

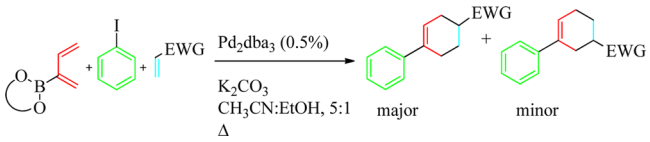
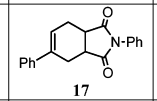
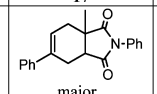
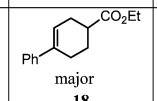


Table 3. Tandem Diels–Alder/Suzuki Cross Coupling Reactions

Entry	Diene	Dienophile	Product	%Yield /Isomer Ratio
1	6		 17	73/NA
2	6		 major 19	83/2:1
3	10		19	78/2:1
4	10		 major 18	63/3:1
5	8		19	65/2:1
6	9		19	72/2:1

and 4; avg yield of 82% per step for **18** and 78% per step for **19**).

The success with the no purification two-step approach to produce **18** and **19** led us to try one-pot tandem reactions combining boron substituted diene, dienophile, and iodobenzene (Scheme 5). Surprisingly, these one-pot reactions worked very well for 3 out of 4 of the boron substituted dienes (**6**, **8**, and **9**), which had failed to react in Diels–Alder chemistry previously (Table 3, entries 1, 2, 5, and 6) and these reactions worked well for triol boronate substituted diene (**10**) (Table 3, entries 3 and 4). These reactions failed for the pinacol boron diene (**7**) and the two diethanolamine boron dienes (**3** and **4**) resulting instead in diene decomposition.

We thought of several possible mechanistic pathways which could be used to explain the observation of Diels–Alder/cross coupled products here under these conditions where we had seen no Diels–Alder products from thermal reactions of several of these dienes and dienophiles earlier. One possibility (labeled path 1 below) would be that oxidative addition of iodobenzene occurred followed by transmetalation and reductive elimination to produce 2-phenyl-1,3-butadiene (**20**). Diene (**20**) would

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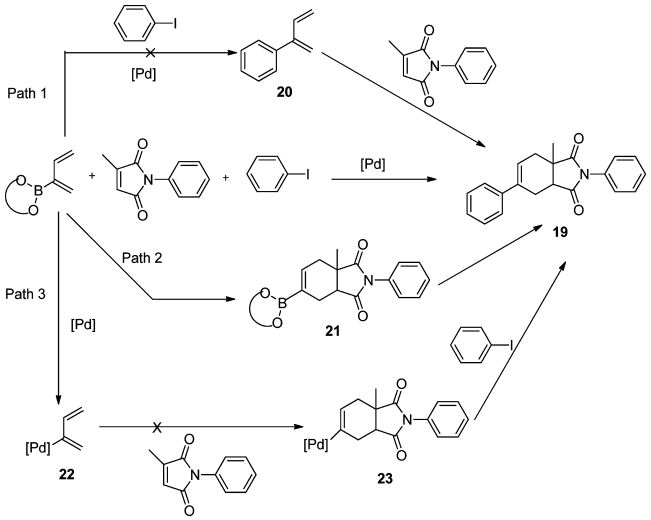
then simply undergo a thermal or Pd-catalyzed Diels–Alder reaction with N-phenylcitraconimide to produce **19**. However, we saw no traces of **20** by ^{1}H NMR, and when we treated dienes (**6**, **8**, **9**, and **10**) with these reaction conditions less the dienophile, N-phenylcitraconimide, we isolated no diene (**20**) and instead just observed boron substituted diene decomposition.

With respect to path 2, this pathway could have occurred for diene (**10**), since it will react thermally with N-phenylcitraconimide and no catalyst is required (Table 1, entry 6). However, when dienes (**6**, **8**, and **9**) were heated under these reaction conditions with Pd(0) with N-phenylcitraconimide, we saw no cycloadducts (**21**) and the dienes decomposed, so we do not believe path 2 is being catalyzed by Pd(0) for those dienes. However, when those dienes were heated in CH_3CN for 18 h with dienophile and a Pd(II) source (Pd-$(CH_3CN)_2Cl_2$), we did see evidence for the formation of boron substituted cycloadducts (**21**) by ^{1}H NMR and MS, but we could not isolate those boron cycloadducts like we could some others here. A Pd(II) catalyzed Diels–Alder reaction[14] to produce **21** followed by cross coupling to produce **19** would fit these observations as a route from dienes **6**, **8**, and **9** to **19**.



Finally, we investigated path 3 as a possibility via a palladium substituted diene (**22**) as an intermediate.[15] When palladium (0) was added to diene (**6**) in CD_3CN and no attempts were made to exclude oxygen, we see a new set of diene peaks grow in over 1.5 h at 50 °C. We postulated that these peaks were due to the formation of a 2-Pd(II) substituted 1,3-diene (**22**).[16] This postulate is further corroborated by the observation that when diene (**6**) is added to $Pd(CH_3CN)_2Cl_2$ or $Pd(PPh_3)_2Cl_2$ in CD_3CN these same diene peaks are observed in less than 1 min. However, when this diene which is formed in the presence of Pd is treated with iodobenzene and N-phenylcitraconimide and heated to 50 °C for 12 h in CD_3CN, we observe no change in the ^{1}H NMR, no product **19**, nor any new peaks which might be attributed to a Pd substituted cycloadduct (**23**). To summarize, Pd(II) appears to catalyze a Diels–Alder reaction between boron dienes and N-phenylcitraconimide. Having a Pd(II) complex present with a Pd–Ph bond appears critical, since adding Ph-I to a solution containing **22** does not lead to product, i.e., we assume the products we are seeing here are coming from a Pd(0) to Pd(II) cycle rather than a Pd(II) to Pd(IV) cycle.

CONCLUSION

We have prepared six new 2-boron substituted 1,3 dienes. We found that preparing these dienes under basic reaction conditions allows them to be isolated as monomers and alleviates previous complications that were noted as facile Diels–Alder dimerization of diene **7**. We found that boron substituted dienes where the boron was 4 coordinate participated readily in Diels–Alder reactions, whereas the boron dienes with 3 coordinate boron were unreactive. Where boron substituted Diels–Alder cycloadducts were isolated, they could be used in cross coupling reactions. Lastly, we discovered that 3 dienes, which were unreactive in thermal Diels–Alder chemistry, participated in tandem Diels–Alder/cross coupling reactions which appear to be Pd(II) catalyzed.

EXPERIMENTAL SECTION

General. The ^{1}H NMR were recorded on a 500 MHz spectrometer and a 300 MHz spectrometer operating at 500.13 MHz and 300.13 MHz, respectively. ^{13}C NMR were recorded on a 300 MHz spectrometer and a 500 MHz spectrometer operating at 75.48 MHz and 125.77 MHz, respectively. Chemical shifts were reported in parts per million (δ) relative to tetramethylsilane (TMS), or the residual proton resonances in the deuterated solvents: chloroform ($CDCl_3$)

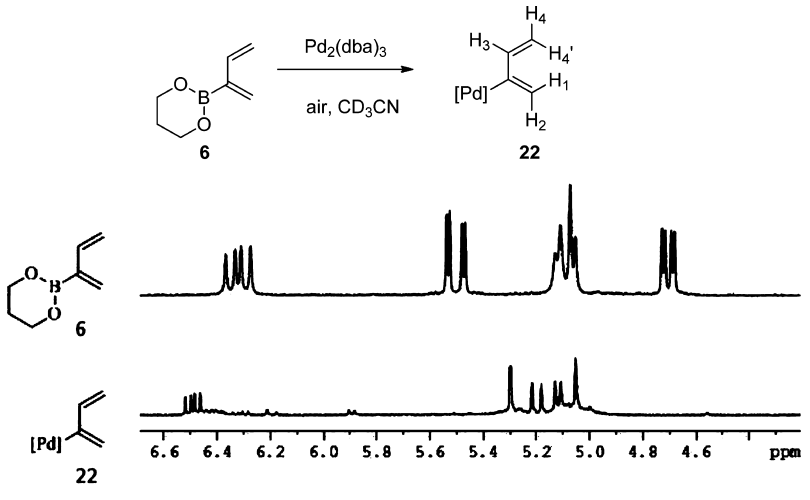


Figure 1. Comparison of NMR chemical shifts of boron substituted diene (**6**) and palladium substituted diene (**22**) in CD_3CN.

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and dimethyl sulfoxide (DMSO). Coupling constants (J values) were reported in hertz (Hz).

All reactions were carried out under an inert atmosphere unless otherwise noted. Flash chromatography was performed using thick-walled glass chromatography columns and ultrapure silica gel. Ether and pentane were distilled over Na. Absolute ethanol and methanol were used without further purification. THF was purchased in the form of solvent kegs and purified using the centrally located solvent dispensing system developed by J. C. Meyer. Deuterated solvents were dried over molecular sieves. Magnesium sulfate, magnesium small turnings, iodobenzene, 4-iodobenzotrifluoride, 2-iodoanisole, 4-iodoanisole, ethyl acrylate, *N*-phenylmaleimide, and methyl *N*-phenylmaleimide were used as received. 2-Chloro-1,3-butadiene, 50% in xylene (Chloroprene) was purchased from Pfaltz & Bauer, Inc and used as received.

General Procedure for Preparing Boron Substituted Dienes. A mixture of magnesium (1.0 g, 41.1 mmol), 1,2-dibromoethane (0.5 mL,5.3 mmol), and THF (10 mL) was refluxed under nitrogen for 15 min to activate the magnesium. To the mixture, anhydrous zinc chloride (0.6 g, 4.1 mmol) in THF (60 mL) was added and reflux was continued for another 15 min. 2-Chloro-1,3-butadiene (4.9 mL, 25 mmol) (density 0.915 g/mL, 50% in xylene) and 1,2-dibromoethane (0.95 g, 5 mmol) in THF (30 mL) were added dropwise over a period of 30 min. This addition was controlled so as to bring the mixture into a gentle reflux. The color of the contents changed gradually from grayish-white to greenish-black. The mixture was heated to reflux for an additional 30 min after completion of the addition. The Grignard reagent thus obtained was immediately added dropwise to a solution of trimethoxyborane (4.25 mL, 38.5 mmol) in THF (25 mL) using a double-ended needle. The addition was controlled in such a way that the internal temperature of the mixture was maintained below −60 °C all the time. After completion of the addition, the solution was allowed to warm to room temperature quickly. The cloudy gray-colored reaction mixture was stirred for 1 h . To the resulting mixture at room temperature, 0.5 M HCl (100 mL) was added. The reaction mixture was extracted with Et_2O (2 × 75 mL). The combined colorless clear organic layers were dried over $MgSO_4$, and the volatiles were removed by rotovap (30 °C, 20 Torr) to yield diene boronic acid (**2**). We have already reported previously on how to use diene **2** to make **3**.[4]

Preparation of 1,3-Butadiene-2-*N*-methyl Diethanolamine Borate (4). Follow the general procedure to obtain boronic acid (**2**), then the boronic acid was added at once to a solution of *N*-methyl diethanolamine (0.8 equiv, 22.5 mmol, 2.68 g) dissolved in THF (100 mL). Sodium sulfate (8 g) was added and refluxed for 6 h. At the end of the reaction, the flask was cooled to room temperature. Solid Na_2SO_4 was separated from the solution by filtration. The solution was reduced by 150 mL using a rotary evaporator. Pentane (10 mL) was added to precipitate the product, and product **4** was obtained as white solid following filtration, washing with cold pentane, and drying under vacuum. (2.70 g, 14.9 mmol, 66%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.58 (dd, J = 17.6, 10.7 Hz,), 5.58 (m, 1H), 5.52−5.55 (m, 2H), 4.95 (dd, J = 10.9, 2.6 Hz, 1H), 4.09 (m, 2H), 3.99 (m, 2H), 3.09 (m, 2H), 2.96 (m, 2H), 2.62 (s, 3H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 143.5, 124.0, 113.6, 61.5, 59.8, 45.7; ^{11}B NMR (96 MHz, $(CD_3)_2SO$) δ 11.31, $CDCl_3$ δ 11.38; HRMS (TOF ESI) $[M + Na]^+$ calcd for $C_9H_{16}BNO_2Na$: 204.1172, found 204.1172.

Preparation of 1,3-Butadiene-(2-propane-1,3-diol)-borate (6). Follow the general procedure to obtain diene boronic acid (**2**). The dried diene boronic acid was added at once to a solution of propane-1,3-diol (0.7 equiv, 17.5 mmol, 1.33 g) dissolved in THF (100 mL). Sodium hydride (1.5 equiv, 37.5 mmol, 0.086 g) was added slowly to the mixture at room temperature. The solvent was removed by rotovap after 2 h. Dry THF (3 × 100 mL) was added to dissolve and wash the solid. The solid was removed by filtration, and all the solution was removed by rotary evaporation and high vacuum to obtain the white solid product (**6**) (1.62 g, 11.73 mmol, 67%): ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 6.32 (dd, J = 17.3, 10.5 Hz, 1H), 5.50 (dd, J = 17.3,3.8 Hz, 1H), 5.16−5.02 (m, 2H), 4.70 (dd, J = 10.5, 3.8 Hz, 1H), 3.62 (m, 2H), 3.50 (td, J = 11.0, 2.6 Hz, 2H), 1.61 (m, 1H), 1.04 (dt, J = 12.2, 2.6 Hz, 1H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 145.5, 113.1, 112.4, 60.4, 30.0; ^{11}B NMR (96 MHz, $(CD_3)_2SO$) δ 2.53, $CDCl_3$ δ 26.30; HRMS (Magnetic Sector EI) calcd for $C_7H_{11}BO_2$: 138.0852, found 138.08522.

Preparation of 1,3-Butadiene-(2-pinacol)-borate (7). Follow the general procedure to obtain diene boronic acid (**2**). The dried diene boronic acid was added at once to a solution of pinacol (0.7 equiv, 17.5 mmol, 2.07 g) dissolved in THF (100 mL). Sodium hydride (1.5 equiv, 37.5 mmol, 0.086 g) was added slowly to the mixture at room temperature. The solvent was removed by rotovap after 2 h. Dry THF (2 × 100 mL), followed by dry diethyl ether (2 × 100 mL), was added to dissolve and wash the solid. The solid was removed by filtration and the solvent was removed by rotary evaporation and high vacuum to yield the white solid product (**7**) (1.83 g, 10.15 mmol, 58%): ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 6.28 (dd, J = 17.5, 10.6 Hz, 1H), 5.40 (dd, J = 17.5, 3.4 Hz, 1H), 5.08 (d, J = 6.3 Hz, 1H), 4.81 (d, J = 6.3, Hz, 1H), 4.71 (dd, J = 10.6, 3.4 Hz, 1H), 1.00 (s, 6H), 0.86 (s, 6H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 145.7, 116.5, 112.9, 76.5, 26.7, 25.3; ^{11}B NMR (96 MHz, $(CD_3)_2SO$) δ 5.97, $CDCl_3$ δ 29.88; HRMS (Magnetic Sector EI) calcd for $C_{10}H_{17}BO_2$: 180.1322, found: 180.13217.

Preparation of 1,3-Butadiene-(2-(2′,2′-dimethyl-propane-1,3-diol))-borate (8). Follow the general procedure to obtain diene boronic acid (**2**). The dried diene boronic acid was added at once to a solution of 2,2-dimethylpropane-1,3-diol (0.7 equiv, 17.5 mmol, 1.82 g) dissolved in THF (100 mL). Sodium hydride (1.5 equiv, 37.5 mmol, 0.086 g) was added slowly to the mixture at room temperature. The solvent was removed by rotovap after 2 h. Dry THF (2 × 100 mL) followed by dry diethyl ether (2 × 100 mL) was added to dissolve and wash the solid. The solid was removed by filtration and the solvent was removed by rotary evaporation to obtain the white solid product (**8**) (1.92 g, 11.55 mmol, 66%): ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 6.30 (dd, J = 17.5, 10.6 Hz, 1H), 5.40 (dd, J = 17.5, 3.7 Hz, 1H), 5.02 (m, 2H), 4.66 (dd, 10.6, 3.8 Hz, 1H), 3.13 (s, 4H), 0.91 (s, 3H), 0.54 (s, 3H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 145.6, 119.0, 112.3, 32.1, 24.0, 22.7; ^{11}B NMR (96 MHz, $(CD_3)_2SO$) δ 2.62, $CDCl_3$ δ 25.98; HRMS (Magnetic Sector EI) calcd for $C_9H_{15}BO_2$: 166.1165, found: 166.11652.

Preparation of Sodium 2-(Buta-1,3-dien-2-yl)-6-methyl-1,3,2-dioxaborocan-6-borate (9). Follow the general procedure to obtain diene boronic acid (**2**). The dried diene boronic acid was added at once to a solution of 3-methylpentane-1,3,5-triol (0.7 equiv, 2.34 g,17.5 mmol) dissolved in THF (100 mL). Sodium hydride (1.5 equiv, 37.5 mmol, 0.086 g) was added slowly to the mixture at room temperature. The solvent was removed by rotovap after 2 h. Dry acetone (2 × 100 mL) was added to dissolve and wash the solid. The solid was removed by filtration, and the solvent was removed by rotary evaporation and high vacuum to obtain the white solid product (**9**) (2.15 g, 11.03 mmol, 63%): ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 6.21 (dd, J = 17.6, 10.7 Hz, 1H), 5.45 (dd, J = 17.6, 3.9 Hz, 1H), 4.97 (d, J = 6.4 Hz, 1H), 4.82 (d, J = 6.4 Hz, 1H), 4.64 (dd, J = 10.7, 3.9 Hz, 1H), 3.70 (m, 2H), 3.39 (m, 2H), 1.38 (t, J = 5.7 Hz, 4H), 0.97 (s, 3H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 145.2, 116.5, 112.3, 64.3, 56.3, 41.4, 34.2; ^{11}B NMR (96 MHz, $(CD_3)_2SO$) δ 4.42; $CDCl_3$ δ 26.20; HRMS (Magnetic Sector EI) calcd for $C_{10}H_{16}BNO_3$: 195.1192, found: 195.1192.

Preparation of Sodium 1-(Buta-1,3-dien-2-yl)-4-methyl-2,6,7-trioxa-1-borabicyclo(2,2,2) octan-1-uide (10). Follow the general procedure to obtain diene boronic acid (**2**). The dried diene boronic acid was added at once to a solution of 2-(hydroxymethyl)-2-methylpropane-1,3-diol (0.7 equiv, 2.10 g,17.5 mmol) dissolved in THF (100 mL). Sodium hydride (1.5 equiv, 37.5 mmol, 0.086 g) was added slowly to the mixture at room temperature. The solvent was removed by rotovap after 2 h. Dry acetone (3 × 100 mL) was added to dissolve and wash the solid. The solid was removed by filtration, and the solvent was removed by rotary evaporation and high vacuum to obtain the white solid product (**10**) (2.68 g, 13.13 mmol, 75%): ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 6.18 (dd, J = 17.1, 10.5 Hz, 1H), 5.40 (dd, J = 17.1, 3.8 Hz, 1H), 4.90 (m, 2H), 4.65 (dd, J = 10.5, 3.8 Hz, 1H), 3.49 (s, 6H), 0.43 (s, 3H); ^{13}C NMR (300, MHz, $(CD_3)_2SO$) δ 144.5, 118.0, 113.0, 73.1, 34.4, 16.3; ^{11}B NMR (96 MHz, $(CD_3)_2SO$) δ

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1.10; HRMS (TOF ESI) calcd for $C_9H_{14}BNaO_3$ $[M+H]^+$: 205.1012, found: 205.1012.

General Procedure for Diels–Alder Reactions. Diene and dienophile (1:5) were dissolved in the solvent indicated in Table 1 and were allowed to react for the indicated time at the indicated temperature. The Diels–Alder adducts were then typically precipitated by the addition of pentane, vacuum filtered, and dried under high vacuum.

Preparation of Cycloadduct 11. Diene (**4**) (0.181 g, 1 mmol) and dienophile *N*-phenylmaleimide (0.865 g, 5 mmol) were dissolved in chloroform (15 mL) in a round-bottom flask at room temperature. After stirring for 2 h, the product (**11**) was obtained by precipitation as a white powder (0.318 g, 0.90 mmol, 90%) following addition of pentane (50 mL), vacuum filtration, and drying under high vacuum: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (t, J = 7.6 Hz, 2H), 7.35 (t, J = 7.4 Hz,1H), 7.23 (d, J = 7.6 Hz, 2H), 6.35 (m, 1H), 3.98 (m, 4H), 3.21 (m, 2H), 3.05 (m, 2H), 2.81 (m, 2H), 2.69 (m, 2H), 2.44 (s, 3H), 2.38 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.4, 179.8, 132.5, 132.2, 129.0, 128.8, 126.2, 62.0, 61.7, 60.9, 60.4, 46.4, 39.7,39.5, 26.5, 24.8; Anal. calcd for $C_{19}H_{23}N_2O_4B$ C 64.38, H 6.54; Found: C 63.73, H 6.43. HRMS (Magnetic Sector ^{17}EI) calcd for $C_{19}H_{23}BN_2O_4$ M^+ = 354.1751, found: 354.1751.

Preparation of Cycloadduct 12. Diene (**4**) (0.181 g, 1 mmol) and dienophile ethyl acrylate (0.500 g, 5 mmol) were dissolved in chloroform (10 mL) in a round-bottom flask and refluxed for 6 h. The white product was precipitated with pentane (150 mL) and obtained by vacuum filtration followed by drying under high vacuum (0.252 g, 0.90 mmol, 90%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.05 (m, 1H), 4.07 (q, J = 7.2 Hz, 2H), 3.97 (m, 2H), 3.90 (m, 2H), 3.01 (m, 3H), 2.67 (m, 2H), 2.55 (s, 3H), 2.44 (m, 1H), 2.24 (m, 1H), 2.09 (m, 2H), 1.93 (m, 1H), 1.57 (m, 1H), 1.25 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) Major isomer: δ 176.6, 130.2, 62.0, 60.3, 59.8, 46.3, 39.7, 28.7, 27.0, 25.9, and 14.1; Minor isomer's peaks found: δ 177.0, 131.4, 59.9, 59.1, 59.0, 46.4, 40.1, 30.2, 25.6, and 25.2; HRMS (TOF ESI) calcd for $C_{14}H_{24}BNO_4Na$ $[M+Na]^+$: = 304.1696, found: 304.1696.

Preparation of Cycloadduct 13. Diene (**4**) (0.181 g, 1 mmol) and dienophile 2-methyl-*N*-phenylmaleimide (0.500 g, 5 mmol) were dissolved in chloroform (10 mL) in a round-bottom flask and refluxed for 6 h. The white product (**13**) was precipitated with pentane (150 mL) and obtained by vacuum filtration followed by drying under high vacuum (0.276 g, 0.75 mmol, 75%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 (t, J = 7.8 Hz, 2H), 7.36 (t, J = 7.2 Hz, 1H), 7.22 (d, J = 7.8 Hz, 2H), 6.33 (m, 1H), 3.97 (m, 4H), 3.04 (m, 2H), 2.87 (m, 2H), 2.78 (m, 3H), 2.40 (s, 3H), 2.39 (m, 1H), 2.05 (dt, J = 15.0, 7.0 Hz, 1H), 1.46 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ Major isomer: 182.6, 179.0, 132.6, 132.3, 129.0, 128.2, 126.1, 61.8, 60.9, 60.4, 47.3, 46.6, 44.2, 35.5, 26.3, 25.3, 25.2. HRMS (TOF ESI) calcd for $C_{20}H_{25}BN_2O_4$: 368.1907, found: 368.19075.

Preparation of Cycloadduct 14. Diene (**10**) (0.204 g, 1 mmol) and dienophile *N*-phenylmaleimide (0.865 g, 5 mmol) were dissolved in toluene (15 mL) in a round-bottom flask at room temperature. After stirring for 2 h, the product (**14**) was obtained by precipitation as a white powder (0.347 g, 0.92 mmol, 92%) by addition of pentane (50 mL), vacuum filtration, and drying under high vacuum: ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 7.43 (m, 2H), 7.37 (m, 1H), 7.26 (m, 2H), 5.64 (m, 1H), 3.49 (s, 6H), 3.03 (m, 1H), 2.92 (m, 1H), 2.19 (m, 4H), 0.44 (s, 3H); ^{13}C NMR (75 MHz, $(CD_3)_2SO$) δ 179.8, 179.7, 132.8, 128.8, 128.6, 127.9, 127.2, 73.3, 72.6, 34.5, 26.4, 23.6, 16.3 (one sp^3 C signal is apparently obscured by the DMSO C resonance); HRMS (TOF ESI) calcd for $C_{19}H_{21}NO_5B$: $[M\text{-}Na+H]^+$ = 355.1597, found 355.1591.

General Procedure for Stepwise Suzuki Cross Coupling Reactions. Boron substituted cycloadducts and iodoaromatic compounds were added to a N_2 flushed flask with $Pd_2(dba)_3$ and K_2CO_3 in acetonitrile and ethanol (30 mL). The mixture was refluxed for 36 h and cooled to room temperature. The solution was filtered through silica gel with CH_3CN to remove catalysts. The filtrate was washed with water (50 mL) and the aqueous extracted with Et_2O (4 × 50 mL). The combined organic layers were dried over $MgSO_4$, and volatiles were removed by rotary evaporation. The resulting cross-coupled cycloadduct residue was purified by silica flash chromatography (ethyl ether:hexane = 1:1). Optimization of conditions: 2% $Pd_2(dba)_3$ [Tris(dibenzylideneacetone)dipalladium (0)], acetonitrile:ethanol = 5:1, boron cycloadduct:iodoaromatic compounds = 1:2, K_2CO_3 (3 equiv). Reaction time: 36 h.

Preparation of 2,5-Diphenyl-3*a*,4,7,7*a*-tetrahydro-1*H*-isoindole-1,3(2*H*)-dione (17) from 11. Following the general procedure, iodobenzene (0.204 g, 1 mmol) and **11** (0.177 g, 0.5 mmol) were added along with $Pd_2(dba)_3$ (10 mg, 0.01 mmol) and K_2CO_3 (0.207 g, 1.5 mmol) to a flask under N_2 (30 mL acetonitrile and ethanol). The flask was heated and refluxed for 36 h and worked up as described in the general procedure. The resulting brown oily crude product mixture was subjected to flash chromatography to yield the cross coupled product (**17**) as a white solid (0.139 g, 0.46 mmol, 92%). ^{1}H NMR data were identical to that previously reported.[3a]

Preparation of Ethyl-4-phenyl cyclohex-3-enecarboxylate (18) from 12 without Isolation of 12. Diene (**4**) (0.090 g, 0.5 mmol) and dienophile ethyl acrylate (0.250 g, 2.5 mmol) were dissolved in chloroform (5 mL) in a round-bottom flask and refluxed for 6 h. The flask was cooled to room temperature. Iodobenzene (0.204 g, 1 mmol) was added along with $Pd_2(dba)_3$ (10 mg, 0.01 mmol) and K_2CO_3 (0.207 g, 1.5 mmol) to the crude product in the flask under N_2 (30 mL acetonitrile and ethanol). The flask was heated and refluxed for 36 h and worked up as described in the general procedure. The resulting brown oily crude product mixture was subjected to flash chromatography to yield the cross-coupled product (**18**) as a light yellow oil (0.082 g, 0.34 mmol, 68%). ^{1}H NMR data were identical to that previously reported.[3a] Major isomer:minor isomer = 3:1

Preparation of 3*a*-Methyl-2,6-diphenyl-3*a*,4,7,7*a*-tetrahydro-1*H*-isoindole-1,3(2*H*)-dione (19) from 13 without isolation of 13. Diene (**4**) (0.090 g, 0.5 mmol) and dienophile 2-methyl-*N*-phenylmaleimide (0.250 g, 2.5 mmol) were dissolved in chloroform (5 mL) in a round-bottom flask and refluxed for 6 h. The flask was cooled to room temperature. 4-Iodobenzene (0.204 g, 1 mmol) was added along with $Pd_2(dba)_3$ (10 mg, 0.1 mmol) and K_2CO_3 (0.207 g, 1.5 mmol) to a flask under N_2 (30 mL acetonitrile and ethanol). The flask was heated and refluxed for 36 h and worked up as described in the general procedure. The resulting brown oily crude product mixture was subjected to flash chromatography to yield the cross-coupled product (**19**) as a white solid (0.095 g, 0.3 mmol, 60%). ^{1}H NMR data were identical to that previously reported.[3a] Major isomer:minor isomer = 1.3:1.

General Procedures for Tandem Diels–Alder/Suzuki Cross Coupling Reactions. Diene and dienophile (1:4) were added to an N_2 flushed high-pressure resistant thick-walled tube with $Pd_2(dba)_3$ and K_2CO_3 in acetonitrile and ethanol (5 mL). Iodobenzene was added. The mixture was sealed and heated for 24 h and cooled to room temperature. The solution was filtered through silica gel with CH_3CN to remove catalysts. The filtrate was washed with water (50 mL) and the aqueous extracted with Et_2O (4 × 50 mL). The combined organic layers were dried over $MgSO_4$ and volatiles were removed by rotary evaporation. The final product was purified by silica flash chromatography (ethyl acetate:hexane = 6:1).

Tandem Diels–Alder/Suzuki Cross Coupling Reactions. *Entry 1 of Table 3: Preparation of 17.* Diene (**6**) (0.10 g, 0.72 mmol) and *N*-phenylmaleimide (0.50 g, 2.88 mmol) (1:4) were used along with iodobenzene (0.59 g, 2.88 mmol) (diene:iodobenzene = 1:4) and catalysts as described in the general procedure. After heating, workup, and chromatography (ethyl acetate:hexane = 4:1), **17** was obtained as a white powder (0.16 g, 0.52 mmol, 73%). ^{1}H NMR data were identical to that previously reported.[3a]

Entry 2 of Table 3: Preparation of 19. Diene (**6**) (0.10 g, 0.72 mmol) and 2-methyl-*N*-phenylmaleimide (0.54 g, 2.88 mmol) (1:4) were used along with iodobenzene (0.29 g, 1.44 mmol) (diene:iodobenzene = 1:2) and catalysts as described in the general procedure. After heating, workup, and chromatography, **19** was obtained as a white powder (0.19 g, 0.60 mmol, 83%). ^{1}H NMR was identical to that previously reported.[4] Major isomer:minor isomer = 2:1.

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*Entry 3 of Table 3: Preparation of **19***. Diene (**10**) (0.10 g, 0.49 mmol) and 2-methyl-*N*-phenylmaleimide (0.37 g, 1.96 mmol) (1:4) were used along with iodobenzene (0.20 g, 0.98 mmol) (diene:iodobenzene = 1:2) and catalysts according to the general procedure. After heating, workup, and chromatography, **19** was obtained as a white powder (0.12 g, 0.38 mmol, 78%). ^{1}H NMR was identical to that previously reported.[4]

*Entry 4 of Table 3: Preparation of **18***. Diene (**10**) (0.10 g, 0.49 mmol) and ethyl acrylate (0.098 g, 0.98 mmol) (1:2) were used along with iodobenzene (0.20 g, 0.98 mmol) (diene:iodobenzene = 1:2) and catalysts according to the general procedure. After heating, workup, and chromatography (ethyl ether:hexane = 1:1), **18** was obtained as a light yellow oil (0.071 g, 0.31 mmol, 63%). ^{1}H NMR data was identical to that previously reported.[3a] Major isomer:minor isomer = 3:1.

*Entry 7 of Table 3: Preparation of **19***. Diene (**8**) (0.10 g, 0.60 mmol) and 2-methyl-*N*-phenylmaleimide (0.45 g, 2.40 mmol) (1:4) were used along with iodobenzene (0.50 g, 2.4 mmol) (diene:iodobenzene = 1:4) and catalysts according to the general procedure. After heating, workup, and chromatography, **19** was obtained as a white powder (0.125 g, 0.39 mmol, 65%). ^{1}H NMR was identical to that previously reported.[4]

*Entry 8 of Table 3: Preparation of **19***. Diene (**9**) (0.10 g, 0.46 mmol) and 2-methyl-*N*-phenylmaleimide (0.34 g, 1.83 mmol) (1:4) were used along with iodobenzene (0.37 g, 1.83 mmol) (diene:iodobenzene = 1:4) and catalysts as described in the general procedure. After heating, workup, and chromatography, **19** was obtained as a white powder (0.10 g, 0.33 mmol, 72%). ^{1}H NMR was identical to that previously reported.[4]

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra of all novel compounds produced. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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