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Regioselective Diboron-Mediated Semireduction of Terminal Allenes

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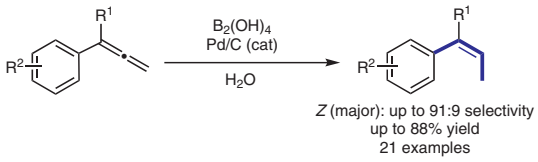

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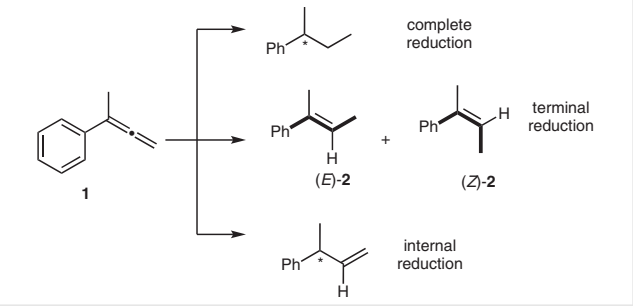
Abstract A method for the regioselective reduction of the terminal double bond of 1,1-disubstituted allenes has been developed. In the presence of a palladium catalyst, tetrahydroxydiboron and stoichiometric water, allene semireduction proceeds in high yield to afford *Z*-alkenes selectively.

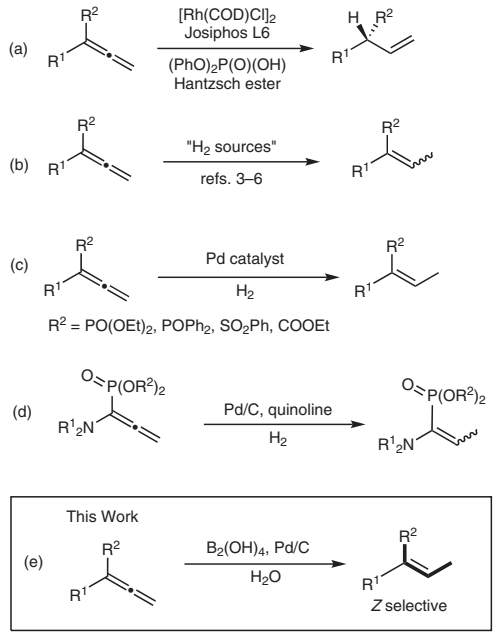
Key words diboron-mediated, allenes, hydrogenation, semireduction

Allenes are a special class of functional group because they possess unique reactivity, are important building blocks in chemical synthesis, and are a motif found in natural products.[1] Among many transformations, semireduction of allenes is challenging because of regio-, chemo- and stereoselectivity issues potentially affording up to four different products with two containing chiral centers (Scheme 1). Controlling the extent of reduction such that only 1 equivalent of molecular hydrogen adds is difficult and complete reduction leads to chiral alkanes. Successful semireduction of the terminal alkene leads to trisubstituted styrene **2**; however, the product can be confounded by a mixture of *E*- and *Z*-isomers. Furthermore, selective reduction of the internal alkene affords a chiral product bearing a terminal alkene. Toward this end, Dong and co-workers provided an approach to enantioselective internal alkene reduction using a rhodium catalyst in the presence of Josiphos ligand and Hantzsch ester as the reductant (Scheme 2a).[2] However, there are only a very limited number of investigations on the complementary terminal alkene reduction. Previously reported methods to achieve this transformation include sodium–ammonia,[3] diimide,[4] diisopropylaluminum hydride,[5] silyl-cupration/protodesilylation[6] and rhodium-catalyzed hydrogenation (Scheme 2b).[7] Unfortunately, these methods suffer from several limitations including severely narrow substrate scope, low stereoselectivity, poor yields and harsh reaction conditions. More recently, allenylphosphonates, phosphine oxides, sulfones and allenoates were shown to be efficient substrates in partial hydrogenations utilizing a [palladium(bis(arylimino)acenaphthene) (alkene)] complex (Scheme 2c).[8] In addition, α-amino vinylphosphonates were synthesized by partial reduction of the α-amino allenylphosphonates when conducted with a poisoned palladium catalyst under a hydrogen atmosphere (Scheme 2d).[9]



Scheme 1 Challenges in the reduction of allenes

Our interest in the reactivity of allenes and their conversion into motifs useful in medicinal and synthetic chemistry persuaded us to investigate diboron-mediated semireduction approaches.[10] In 2016, Stokes and co-workers reported a tetrahydroxydiboron-mediated palladium-catalyzed hydrogenation of alkenes and alkynes using water as a stoichiometric hydrogen donor to furnish the corresponding alkanes in excellent yields.[11] Furthermore, Prabhu and co-workers demonstrated that molecular hydrogen could be released from water in the presence of bis(pinacolato)diboron with toluene as a solvent.[12] The tetrahydroxydiboron/water system has been utilized in reductive

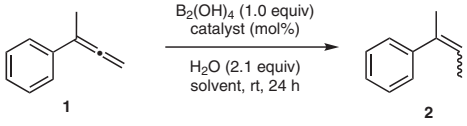


Scheme 2 Approaches toward the semireduction of allenes

amination,[13] hydrogenation of heterocycles[14] and nitro reduction in DNA.[15] Inspired by these works, we investigated the applicability of diboron reagents in the semihydrogenation of allenes to produce *Z*-alkenes (Scheme 2e).

Thus, we began our study by using tetrahydroxydiboron, water and a palladium catalyst. The initial reaction conditions provided the desired product **2** in good yield and *Z* selectivity (Table 1, entry 1). A variety of solvent conditions were subsequently screened. While methanol resulted in a very low yield (entry 2), diethyl ether and methyl *tert*-butyl ether afforded the product in good yield (entries 3, 4). Unfortunately, hexanes and THF resulted in poor yield and selectivity (entries 5, 6). Reducing the catalyst loading from 10 mol% to 5 mol% (entry 7) did not affect the yield. Next, a variety of palladium catalysts were evaluated. For example, Lindlar's catalyst and Pd(dppf)Cl_2 essentially shut down double-bond hydrogenation (entries 8, 9). However, palladium hydroxide and palladium acetate restored activity, albeit in reduced yields (entries 10, 11). Switching to other transition-metal catalysts, platinum on carbon and platinum oxide, induced an improvement in *Z*/*E* selectivity; however, these reactions suffered from poor yields and further optimization did not lead to substantial improvement (entries 12, 13). Rhodium did not afford any of the desired product (entry 14). When tetrahydroxydiboron and palladium catalyst were removed independently from the reaction, no product was observed suggesting their essential roles for the transformation (entries 15, 16). When exploring alternative diboron reagents, we found that bis(pinacolato)diboron and bis(catecholato)diboron were less effective mediators (entries 17, 18). As both dichloromethane and diethyl ether were equally efficient, we chose diethyl ether as the solvent and Pd/C as the transition-metal catalyst (entry 3). The *E*/*Z* configuration was determined using nOe experiments (see the Supporting Information). In general, additional tetrahydroxydiboron could be added to force the conversion of the reaction.

Table 1 Optimization of Reaction Conditions[a]

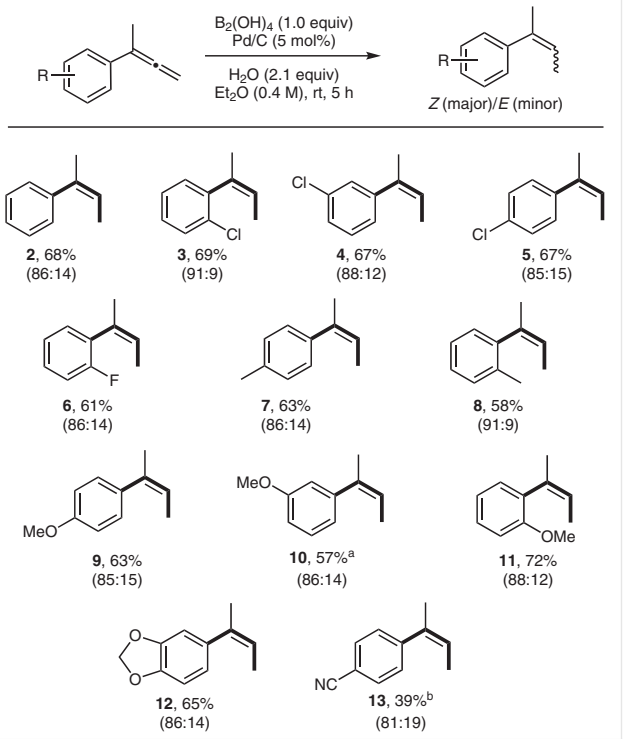


Entry	Catalyst (mol%)	Solvent	Z/E	Yield (%) (% conversion)
1	Pd/C (10)	DCM	85:15	70 (99)
2	Pd/C (10)	MeOH	81:19	18 (56)
3	Pd/C (10)	Et_2O	86:14	68 (93)
4	Pd/C (5)	MTBE	84:16	62 (82)
5	Pd/C (5)	hexanes	75:25	46 (99)
6	Pd/C (5)	THF	80:20	4 (53)
7	Pd/C (5)	DCM	85:15	69 (99)
8	Lindlar's catalyst (10)	DCM	–	0 (24)
9	Pd(dppf)Cl_2 (5)	DCM	–	0 (18)
10	Pd$(OH)_2$/C (10)	DCM	83:17	54 (73)
11	Pd$(OAc)_2$ (10)	DCM	84:16	59 (88)
12	Pt/C (5)	DCM	89:11	29 (63)
13	PtO_2 (10)	DCM	91:9	33 (80)
14	Rh/C (5)	DCM	–	0 (27)
15[b]	Pd/C (5)	DCM	–	0 (5)
16	–	DCM	–	0 (9)
17	Pd/C[c] (5)	DCM	85:15	23 (50)
18	Pd/C[d] (5)	DCM	87:13	42 (73)

[a] Reaction conditions: buta-2,3-dien-2-ylbenzene (**1**, 0.38 mmol), tetrahydroxydiboron (0.38 mmol), metal catalyst and water (0.81 mmol) were dissolved in the indicated solvent and stirred under inert atmosphere. Conversions and yields determined via ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard. MTBE = methyl *tert*-butyl ether, DCM = dichloromethane.
[b] Reaction performed without $B_2(OH)_4$.
[c] Boron source: bis(pinacolato)diboron.
[d] Boron source: bis(catecholato)diboron.

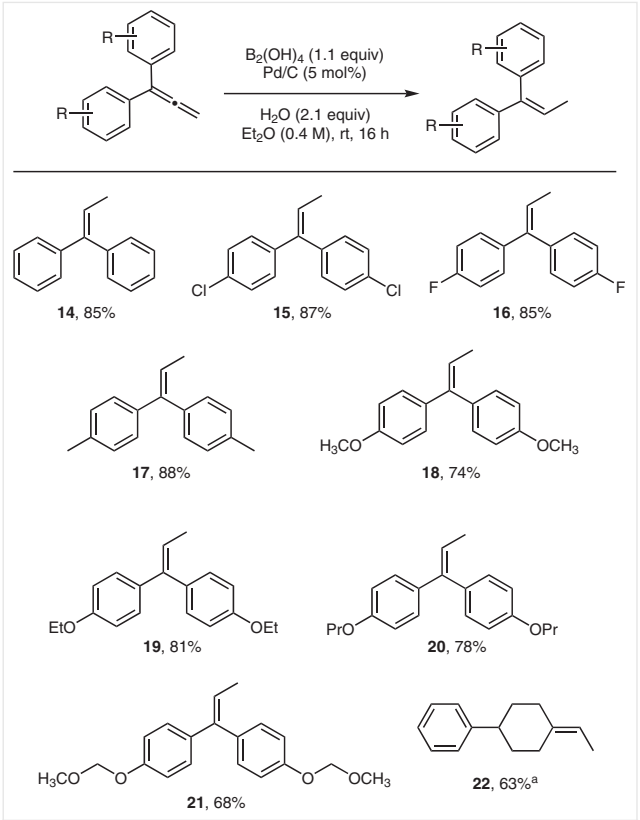
With optimized conditions in hand, a series of substrates was evaluated to determine the steric and electronic effects on the semireduction procedure (Scheme 3). Electron-withdrawing substituents such as chloro were well tolerated in the *ortho*, *meta* and *para* positions (**3**–**5**). A fluorine atom in the *ortho* position is also an efficient substrate affording alkene **6** in 61% yield. Electron-donating substituents such as methyl (**7**, **8**) or methoxy (**9**–**11**) also proved to be well-tolerated at various positions. An aryl ring with methylenedioxy substitution (**12**) also served as a

good substrate. The presence of a cyano moiety in the *para* position resulted in a small reduction in yield and selectivity (**13**). The stereoselectivity of the reaction was generally very good with 85–90% *Z* selectivity. Because the stereoisomeric products and side products have similar nonpolar properties, purification using silica gel chromatography using various solvent combinations as well as Kugelrohr distillation were unsuccessful.



Scheme 3 Substrate scope of the semireduction of 1,1-disubstituted allenes. % Yield calculated via ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard and refers to the sum of inseparable isomers. Reaction conversions were 94–100% unless stated otherwise. [a] 90% conversion. [b] 88% conversion.

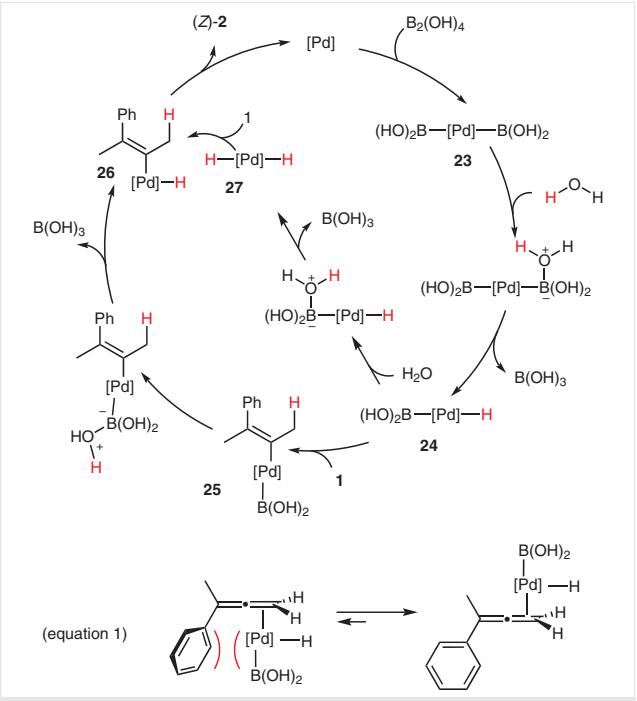
We also investigated a series of symmetrical, diaryl-substituted allenes (Scheme 4). These substrates resulted in much improved isolated yields, although longer reaction times (16 h) and a slight increase in the amount of tetrahydroxydiboron used (1.1 equiv instead of 1.0) were required. For example, 1,1-diphenylallene reacted to afford **14** in 85% yield. Electron-withdrawing groups such as chloro and fluoro produced the corresponding products **15**, **16** in high yields. Electron-donating groups such as methyl or alkyl ethers also afforded high yields (**17**–**20**). The current method is also compatible with protecting groups such as methoxymethyl (**21**). Finally, an alkyl-substituted allene was tested and was reduced in good yield (**22**).



Scheme 4 Semireduction of 1,1-diarylallenes. Complete conversion was observed, and isolated yields are reported. [a] ^{1}H NMR yield.

The proposed catalytic cycle for allene semireduction is illustrated in Scheme 5.[11] First, palladium inserts into the B–B bond of tetrahydroxydiboron to generate intermediate **23**. A water molecule acts as a Lewis base to form a tetracoordinate boron and a proton is then transferred to palladium forming **24** and releasing boric acid. We suspect that the stereoselectivity of the reaction is governed by the initial contact between the metal and allene, affording the *Z* configuration preferentially (Scheme 5, equation 1). Thus, the palladium hydride complex coordinates to allene **1** on the less sterically hindered side, i.e. on the side opposite of the phenyl ring. Palladium insertion on the allene yields **25**. Then, a second molecule of water coordinates to the boron atom, and the intermediate undergoes another hydrogen atom transfer to form palladium hydride complex **26**. Alternatively, dihydride formation could precede migratory insertion to generate **27**. Finally, reductive elimination of **26** forms the reduced product and regenerates the active catalyst.

In conclusion, we have developed a method for the regioselective semireduction of terminal allenes to form *Z*-alkenes. The protocol utilizes a diboron-mediated activation of water to generate catalytically competent palladium hydride for the reduction. The products generated could be



Scheme 5 Proposed catalytic cycle

useful as commodity materials for further chemical transformation.

Tetrahydroxydiboron was donated by AllyChem and used as received. Commercially available substrates, 1,3,5-trimethoxybenzene, palladium on carbon (10 wt %, type 487, dry, Alfa Aesar, A12012.09), bromoform, sodium hydride, sodium hydroxide, methyltriphenylphosphonium bromide, benzyltriethylammonium chloride, *n*-butyllithium and ethylmagnesium bromide were purchased and used as received. THF, DMF and DCM were dried using the PureSolv MD solvent purification system by Innovative Technology. TLC analyses were performed using aluminum-backed silica gel F_{254} plates from SiliCycle Inc. Chromatographic purification was performed using SiliaFlash P60 40–63 µm, 60 Å silica gel from SiliCycle Inc. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ using an Agilent MR-400 MHz or a Varian Inova 400 MHz spectrometer. All spectra were internally referenced to $CDCl_3$ or TMS. Chemical shifts are reported in δ ppm. Ratios of isomeric products were measured by integration of ^{1}H NMR signals from the alkene or methyl protons. NMR yields were determined using 1,3,5-trimethoxybenzene as an internal standard. ESI-HRMS were acquired with an Agilent 6220 LC-ESI-TOF or a Thermo Scientific Q Exactive Orbitrap mass spectrometer. Atmospheric solids analysis probe (ASAP)-HRMS were acquired with a Micromass Ultima Q-TOF API mass spectrometer.

Optimization Reactions; General Procedure

Diboron reagent and catalyst were weighed into a 1 dram vial containing a micro stir bar and fitted with a septum. After purging with argon, solvent (1.0 mL) was added, followed by buta-2,3-dien-2-ylbenzene (**1**) (0.050 g, 0.38 mmol, 1.0 equiv) and water (15 µL). The reaction mixture was stirred at room temperature for 24 h. After 24 h, the reaction solution was diluted with DCM (1.0 mL) and filtered through a pipet with a small plug of Celite. The Celite plug was rinsed thoroughly with DCM. An internal standard, 1,3,5-trimethoxybenzene, was added and the solution was concentrated in vacuo. $CDCl_3$ was added and the yield was determined by quantitative NMR analysis.

But-2-en-2-ylbenzene (2); Typical Procedure for Semireductions

Tetrahydroxydiboron (35 mg, 0.38 mmol, 1.0 equiv) and Pd/C (20 mg, 0.019 mmol, 0.050 equiv) were weighed into a 1 dram vial containing a micro stir bar and fitted with a septum. After purging with argon, Et_2O (1.0 mL) was added, followed by buta-2,3-dien-2-ylbenzene (**1**) (0.050 g, 0.38 mmol, 1.0 equiv) and water (0.015 mL, 0.8 mmol, 2.1 equiv). The reaction mixture was stirred at room temperature for 5 h. Upon completion, the reaction solution was diluted with Et_2O (1.0 mL) and filtered through a pipet with a small plug of Celite. The Celite plug was rinsed thoroughly with Et_2O. An internal standard, 1,3,5-trimethoxybenzene, was added and the solution was concentrated in vacuo. $CDCl_3$ was added and the yield was determined by quantitative NMR analysis.

Reaction scale: 0.384 mmol; NMR yield: 68%; *Z*/*E* = 86:14.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.15 (m, 5 H, 5 H), 5.85 (qq, *J* = 6.8, 1.4 Hz, 1 H), 5.55 (qq, *J* = 6.9, 1.5 Hz, 1 H), 2.04–2.01 (m, 3 H, 3 H), 1.79 (dq, *J* = 6.9, 1.1 Hz, 3 H), 1.59 (dq, *J* = 6.9, 1.6 Hz, 3 H); data consistent with literature values.[16]

1-(But-2-en-2-yl)-2-chlorobenzene (3)

Reaction scale: 0.304 mmol; NMR yield: 69%; *Z*/*E* = 91:9.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.07 (m, 4 H, 4 H), 5.61 (qq, *J* = 6.7, 1.5 Hz, 1 H), 5.47 (qq, *J* = 6.7, 1.4 Hz, 1 H), 1.98–1.95 (m, 3 H, 3 H), 1.76 (dq, *J* = 6.8, 1.1 Hz, 3 H), 1.39 (dq, *J* = 6.8, 1.6 Hz, 3 H); data consistent with literature values.[16]

1-(But-2-en-2-yl)-3-chlorobenzene (4)

Reaction scale: 0.298 mmol; NMR yield: 67%; *Z*/*E* = 88:12.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.04 (m, 4 H, 4 H), 5.87 (qq, *J* = 6.8, 1.4 Hz, 1 H), 5.58 (qq, *J* = 6.9, 1.5 Hz, 1 H), 2.01–1.98 (m, 3 H, 3 H), 1.79 (dq, *J* = 6.8, 1.0 Hz, 3 H), 1.58 (dq, *J* = 7.0, 1.6 Hz, 3 H); data consistent with literature values.[16]

1-(But-2-en-2-yl)-4-chlorobenzene (5)

Reaction scale: 0.304 mmol; NMR yield: 67%; *Z*/*E* = 85:15.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33–7.09 (m, 4 H, 4 H), 5.84 (qq, *J* = 6.9, 1.4 Hz, 1 H), 5.57 (qq, *J* = 6.9, 1.5 Hz, 1 H), 2.01–1.98 (m, 3 H, 3 H), 1.78 (dq, *J* = 6.9, 1.1 Hz, 3 H), 1.58 (dq, *J* = 6.9, 1.6 Hz, 3 H); data consistent with literature values.[16]

1-(But-2-en-2-yl)-2-fluorobenzene (6)

Reaction scale: 0.310 mmol; NMR yield: 61%; *Z*/*E* = 86:14.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.27–6.96 (m, 4 H, 4 H), 5.68 (qq, *J* = 6.8, 1.5 Hz, 1 H), 5.67 (qq, *J* = 6.8, 1.5 Hz, 1 H), 2.02–2.01 (m, 3 H, 3 H), 1.79 (dq, *J* = 6.8, 1.2 Hz, 3 H), 1.50 (dq, *J* = 6.8, 1.6 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 160.9, 158.4, 131.5, 130.6, 130.6, 128.5, 128.4, 124.3, 123.9, 123.9, 115.8, 115.6, 24.8, 24.7, 15.0, 14.98.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –115.46.

HRMS (ESI+): *m*/*z* $[M]^+$ calcd for $C_{10}H_{10}F$: 150.0845; found: 150.0797.

1-(But-2-en-2-yl)-4-methylbenzene (7)

Reaction scale: 0.277 mmol; NMR yield: 63%; *Z*/*E* = 86:14.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28 (d, *J* = 8.0 Hz, 2 H), 7.19–7.15 (m, 2 H), 7.12 (d, *J* = 8.2 Hz, 2 H, 2 H), 5.85 (qq, *J* = 6.8, 1.4 Hz, 1 H), 5.56 (qq, *J* = 6.9, 1.5 Hz, 1 H), 2.37 (s, 3 H), 2.34 (s, 3 H), 2.05–2.02 (m, 3 H, 3 H), 1.81 (dq, *J* = 7.0, 1.1 Hz, 3 H), 1.63 (dq, *J* = 6.9, 1.6 Hz, 3 H); data consistent with literature values.[17]

1-(But-2-en-2-yl)-2-methylbenzene (8)

Reaction scale: 0.173 mmol; NMR yield: 58%; *Z*/*E* = 91:9.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.22–7.08 (m, 4 H), 7.02–6.98 (m, 4 H), 5.54 (qq, *J* = 6.7, 1.5 Hz, 1 H), 5.36 (qq, *J* = 6.7, 1.5 Hz, 1 H), 2.26 (s, 3 H), 2.20 (s, 3 H), 1.94–1.91 (m, 3 H), 1.91–1.89 (m, 3 H), 1.76 (dq, *J* = 6.8, 1.1 Hz, 3 H), 1.35 (dq, *J* = 6.7, 1.6 Hz, 3 H); data consistent with literature values.[18]

1-(But-2-en-2-yl)-4-methoxybenzene (9)

Reaction scale: 0.312 mmol; NMR yield: 63%; *Z*/*E* = 85:15.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31 (d, *J* = 8.9 Hz, 2 H), 7.14 (d, *J* = 8.8 Hz, 2 H), 6.89 (d, *J* = 8.8 Hz, 2 H), 6.84 (d, *J* = 8.8 Hz, 2 H), 5.78 (qq, *J* = 6.9, 1.4 Hz, 1 H), 5.53 (qq, *J* = 6.9, 1.5 Hz, 1 H), 3.81 (s, 3 H), 3.80 (s, 3 H), 2.03–2.00 (m, 3 H, 3 H), 1.78 (dq, *J* = 6.8, 1.0 Hz, 3 H), 1.61 (dq, *J* = 6.9, 1.5 Hz, 3 H); data consistent with literature values.[19]

1-(But-2-en-2-yl)-3-methoxybenzene (10)

Reaction scale: 0.312 mmol; NMR yield: 57%; *Z*/*E* = 86:14.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.27–7.17 (m, 1 H, 1 H), 6.80–6.72 (m, 3 H, 3 H), 5.86 (qq, *J* = 6.9, 1.4 Hz, 1 H), 5.54 (qq, *J* = 6.9, 1.5 Hz, 1 H), 3.80 (s, 3 H), 3.79 (s, 3 H), 2.03–1.97 (m, 3 H, 3 H), 1.78 (dq, *J* = 6.9, 1.1 Hz, 3 H), 1.60 (dq, *J* = 6.9, 1.6 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 159.5, 143.6, 136.9, 129.2, 121.9, 120.7, 114.0, 111.8, 55.3, 25.5, 15.0.

HRMS (ESI+): *m*/*z* $[M + H]^+$ calcd for $C_{11}H_{15}O$: 163.1123; found: 163.1130.

1-(But-2-en-2-yl)-2-methoxybenzene (11)

Reaction scale: 0.156 mmol; NMR yield: 72%; *Z*/*E* = 88:12.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26–7.21 (m, 1 H, 1 H), 7.10 (dd, *J* = 7.4, 1.8 Hz, 1 H), 7.04 (dd, *J* = 7.4, 1.8 Hz, 1 H), 6.96–6.82 (m, 2 H, 2 H), 5.60 (qq, *J* = 6.7, 1.5 Hz, 1 H), 5.54 (qq, *J* = 6.7, 1.4 Hz, 1 H), 3.82 (s, 3 H), 3.81 (s, 3 H), 2.00–1.95 (m, 3 H, 3 H), 1.76 (dq, *J* = 6.8, 1.1 Hz, 3 H), 1.45 (dq, *J* = 6.7, 1.5 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 156.6, 134.9, 131.0, 130.1, 128.0, 122.6, 120.6, 111.0, 55.6, 24.6, 14.9.

HRMS (ESI+): *m*/*z* $[M + H]^+$ calcd for $C_{11}H_{15}O$: 163.1123; found: 163.1128.

5-(But-2-en-2-yl)benzo[*d*][1,3]dioxole (12)

Reaction scale: 0.287 mmol; NMR yield: 65%; *Z*/*E* = 86:14.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.93–6.63 (m, 3 H, 3 H), 5.93 (s, 2 H), 5.91 (s, 2 H), 5.75 (qq, *J* = 6.9, 1.4 Hz, 1 H), 5.51 (qq, *J* = 6.9, 1.5 Hz, 1 H), 2.00–1.95 (m, 3 H, 3 H), 1.76 (dq, *J* = 6.9, 1.1 Hz, 3 H), 1.59 (dq, *J* = 6.9, 1.6 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 147.4, 146.0, 136.5, 135.9, 121.7, 121.4, 108.8, 108.1, 101.0, 25.7, 15.1.

HRMS (ESI+): *m*/*z* $[M + H]^+$ calcd for $C_{11}H_{13}O_2$: 177.0916; found: 177.0924.

4-(But-2-en-2-yl)benzonitrile (13)

Reaction scale: 0.161 mmol; NMR yield: 39%; *Z*/*E* = 81:19.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63 (d, *J* = 8.1 Hz, 2 H), 7.57 (d, *J* = 6.8 Hz, 2 H), 7.44 (d, *J* = 8.4 Hz, 2 H), 7.29 (d, *J* = 8.4 Hz, 2 H), 5.99 (qq, *J* = 6.1, 1.2 Hz, 1 H), 5.66 (qq, *J* = 6.8, 1.3 Hz, 1 H), 2.04–2.01 (m, 3 H, 3 H), 1.83 (dq, *J* = 6.9, 1.1 Hz, 3 H), 1.58 (dq, *J* = 7.0, 1.5 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 147.0, 135.4, 132.1, 129.0, 123.9, 119.2, 110.2, 25.0, 15.0.

HRMS (ESI+): *m*/*z* $[M + H]^+$ calcd for $C_{11}H_{12}N$: 158.0964; found: 158.0982.

Prop-1-ene-1,1-diyldibenzene (14)

Reaction scale: 0.260 mmol; yield: 43 mg (85%); colorless solid; R_f = 0.39 (hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41–7.32 (m, 2 H), 7.33–7.14 (m, 8 H), 6.17 (q, *J* = 7.0 Hz, 1 H), 1.76 (d, *J* = 7.0 Hz, 3 H); data consistent with literature values.[20]

4,4′-(Prop-1-ene-1,1-diyl)bis(chlorobenzene) (15)

Reaction scale: 0.061 mmol; yield: 14 mg (87%); colorless oil; R_f = 0.52 (5% EtOAc in hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35 (d, *J* = 8.6 Hz, 2 H), 7.23 (d, *J* = 8.7 Hz, 2 H), 7.15–7.08 (m, 4 H), 6.16 (q, *J* = 7.1 Hz, 1 H), 1.75 (d, *J* = 7.1 Hz, 3 H); data consistent with literature values.[21]

4,4′-(Prop-1-ene-1,1-diyl)bis(fluorobenzene) (16)

Reaction scale: 0.22 mmol; yield: 43 mg (85%); colorless oil; R_f = 0.36 (hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.21–7.11 (m, 4 H), 7.11–7.04 (m, 2 H), 7.00–6.91 (m, 2 H), 6.11 (q, *J* = 7.0 Hz, 1 H), 1.76 (d, *J* = 7.0 Hz, 3 H); data consistent with literature values.[22]

4,4′-(Prop-1-ene-1,1-diyl)bis(methylbenzene) (17)

Reaction scale: 0.23 mmol; yield: 45 mg (88%); colorless oil; R_f = 0.40 (hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.22–7.16 (m, 2 H), 7.15–7.05 (m, 6 H), 6.12 (q, *J* = 7.0 Hz, 1 H), 2.40 (s, 3 H), 2.33 (s, 3 H), 1.77 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 142.3, 140.6, 137.3, 136.5, 136.5, 130.1, 128.9, 128.9, 127.3, 123.2, 21.4, 21.2, 15.8.

HRMS (ESI+): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{19}$: 223.1487; found: 223.1478.

4,4′-(Prop-1-ene-1,1-diyl)bis(methoxybenzene) (18)

Reaction scale: 0.12 mmol; yield: 23 mg (74%); white solid; R_f = 0.52 (10% EtOAc in hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.14 (d, *J* = 8.9 Hz, 2 H), 7.10 (d, *J* = 8.8 Hz, 2 H), 6.90 (d, *J* = 8.8 Hz, 2 H), 6.79 (d, *J* = 8.9 Hz, 2 H), 6.02 (q, *J* = 7.0 Hz, 1 H), 3.84 (s, 3 H), 3.79 (s, 3 H), 1.75 (d, *J* = 7.0 Hz, 3 H); data consistent with literature values.[23]

4,4′-(Prop-1-ene-1,1-diyl)bis(ethoxybenzene) (19)

Reaction scale: 0.18 mmol; yield: 41 mg (81%); white solid; mp 67–72 °C; R_f = 0.64 (10% EtOAc in hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.13 (d, *J* = 8.9 Hz, 2 H), 7.09 (d, *J* = 8.8 Hz, 2 H), 6.89 (d, *J* = 8.8 Hz, 2 H), 6.78 (d, *J* = 8.9 Hz, 2 H), 6.02 (q, *J* = 7.0 Hz, 1 H), 4.09–3.97 (m, 4 H), 1.75 (d, *J* = 7.0 Hz, 3 H), 1.46–1.37 (m, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 158.0, 157.9, 141.6, 136.1, 132.5, 131.3, 128.4, 122.1, 114.1, 114.1, 63.5, 63.5, 15.8, 15.1, 15.0.

HRMS (ESI+): *m*/*z* $[M + H]^+$ calcd for $C_{19}H_{23}O_2$: 283.1693; found: 283.1692.

4,4′-(Prop-1-ene-1,1-diyl)bis(propoxybenzene) (20)

Reaction scale: 0.094 mmol; yield: 23 mg (78%); white solid; mp 30–34 °C; R_f = 0.27 (5% EtOAc in hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.12 (d, *J* = 8.9 Hz, 2 H), 7.08 (d, *J* = 8.8 Hz, 2 H), 6.89 (d, *J* = 8.8 Hz, 2 H), 6.78 (d, *J* = 8.9 Hz, 2 H), 6.01 (q, *J* = 7.0 Hz, 1 H), 3.95 (t, *J* = 6.5 Hz, 2 H), 3.90 (t, *J* = 6.6 Hz, 2 H), 1.88–1.76 (m, 4 H), 1.75 (d, *J* = 7.0 Hz, 3 H), 1.07 (t, *J* = 7.4 Hz, 3 H), 1.02 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 158.2, 158.1, 141.6, 136.1, 132.5, 131.3, 128.5, 122.1, 114.1, 114.1, 69.6, 69.6, 22.8, 22.8, 15.9, 10.8, 10.7.

HRMS (ESI+): *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{27}O_2$: 311.2006; found: 311.1984.

4,4′-(Prop-1-ene-1,1-diyl)bis((methoxymethoxy)benzene) (21)

Reaction scale: 0.14 mmol; yield: 31 mg (68%); viscous colorless oil; R_f = 0.30 (15% EtOAc in hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.15 (d, *J* = 8.9 Hz, 2 H), 7.10 (d, *J* = 8.9 Hz, 2 H), 7.04 (d, *J* = 8.9 Hz, 2 H), 6.93 (d, *J* = 8.9 Hz, 2 H), 6.05 (q, *J* = 7.0 Hz, 1 H), 5.21 (s, 2 H), 5.16 (s, 2 H), 3.52 (s, 3 H), 3.48 (s, 3 H), 1.76 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 156.3, 156.2, 141.4, 137.3, 133.8, 131.3, 128.5, 122.8, 115.9, 115.9, 94.6, 94.6, 56.2, 56.1, 15.8.

HRMS (ESI+): *m*/*z* $[M + Na]^+$ calcd for $C_{19}H_{22}NaO_4$: 337.1410; found: 337.1385.

(4-Ethylidenecyclohexyl)benzene (22)

Reaction scale: 0.27 mmol; NMR yield: 63%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.14 (m, 5 H), 5.22 (qt, *J* = 6.7, 1.7 Hz, 1 H), 2.75 (br d, *J* = 13.4 Hz, 1 H), 2.67 (tt, *J* = 12.2, 3.5 Hz, 1 H), 2.30 (br d, *J* = 13.2 Hz, 1 H), 2.18 (br t, *J* = 13.2 Hz, 1 H), 2.01–1.90 (m, 2 H), 1.85 (br t, *J* = 13.5 Hz, 1 H), 1.61 (dt, *J* = 6.7, 1.7 Hz, 3 H), 1.57–1.40 (m, 2 H); data consistent with literature values.[24]

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Supporting Information

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