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Preparation of 2-BF_3-Substituted 1,3-Dienes and Their Diels–Alder/Cross-Coupling Reactions

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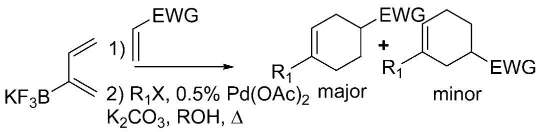
ABSTRACT



2-BF_3-substituted 1,3-butadienes with potassium and tetrabutylammonium counterions have been prepared in gram quantities from chloroprene via a simple synthetic procedure. The potassium salt of this new main group element substituted diene has been characterized by ^{1}H, ^{13}C, ^{11}B, and ^{19}F NMR. Diels–Alder reactions of these dienes with ethyl acrylate and methyl vinyl ketone are reported, as well as subsequent Pd-catalyzed cross-coupling reactions of those Diels–Alder adducts.

Reports of main group element substituted 1,3-dienes and their reaction chemistry are still fairly rare in organic chemistry. 2-Triethylsilyl-1,3-butadiene and a few of its Diels−Alder reactions were reported by Ganem and Batt in 1978.[1] Fleming and co-workers reported 1-trimethylsilyl-1,3-butadiene in 1976[2] and its Diels−Alder dimerization in 1981.[3] Paquette and Daniels reported some 2-silyl-substituted 1,3-cyclohexadienes in 1982 but none of their Diels−Alder chemistry.[4] Silyl-substituted diene chemistry was reviewed in 1993.[5] Although not containing a diene carbon to silicon bond, related 2-trimethylsilyloxy-1,3-dienes have also been transmetalated to zirconium.[6] A 2-phenylseleno and 2-trialkylstannyl-1,3-butadiene and their Diels−Alder reactions were reported by Bates and co-workers in 1987.[7] Much less has been reported previously about aluminum-substituted 1,3-dienes. Eisch[8] and Hoberg[9] reported the preparation of alumina-1,3-cyclopentadienes decades ago, but very little has been done with them synthetically.[10]

Most work reported with main group substituted dienes has been done with the 1-(dialkoxyboryl)-1,3-butadienes (**1**), sometimes termed 1,3-dienyl-1-boronates. These compounds were reported by Vaultier in 1987,[11] and numerous reports of their Diels−Alder chemistry have appeared from the laboratories of Vaultier,[12−15] Lallemand,[13,15−18] and others.[19−21] Most of these reports use the dienylboronates in [4 + 2]/allylation tandem reactions (**1−4**), and this sequence is now often called the Vaultier tandem sequence (Scheme 1).

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(1) Batt, D. G.; Ganem, B. *Tetrahedron Lett.* **1978**, 3323.
(2) Fleming, I.; Percival, A. *J. Chem. Soc., Chem. Commun.* **1976**, 681.
(3) Carter, M. J.; Fleming, I.; Percival, A. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2415.
(4) Daniels, R. G.; Paquette, L. A. *Organometallics* **1982**, *1*, 1449.
(5) Luh, T. Y.; Wong, K. T. *Synthesis-Stuttgart* **1993**, 349−370.
(6) Ganchegui, B.; Bertus, P.; Szymoniak, J. *Synlett* **2001**, 123.
(7) Bates, G. S.; Fryzuk, M. D.; Stone, C. *Can. J. Chem.* **1987**, *65*, 2612.
(8) Eisch, J. J. Kaska., W. C. *J. Am. Chem. Soc.* **1966**, *88*, 2976.
(9) Hoberg, H.; Krausegoing, R. *J. Organomet. Chem.* **1977**, *127*, C29.
(10) Fang, H. Y.; Zhao, C. J.; Li, G. T.; Xi, Z. F. *Tetrahedron* **2003**, *59*, 3779.
(11) Vaultier, M.; Truchet, F.; Carboni, B.; Hoffmann, R. W.; Denne, I. *Tetrahedron Lett.* **1987**, *28*, 4169.
(12) Garnier, L.; Plunian, B.; Mortier, J.; Vaultier, M. *Tetrahedron Lett.* **1996**, *37*, 6699.
(13) Lallemand, J. Y.; Six, Y.; Ricard, L. *Eur. J. Org. Chem.* **2002**, 503.
(14) Mazal, C.; Vaultier, M. *Tetrahedron Lett.* **1994**, *35*, 3089.
(15) Six, Y.; Lallemand, J. Y. *Tetrahedron Lett.* **1999**, *40*, 1295.
(16) Ohanessian, G.; Six, Y.; Lallemand, J. Y. *Bull. Soc. Chim. Fr.* **1996**, *133*, 1143.
(17) Renard, P. Y.; Lallemand, J. Y. *Tetrahedron: Asymmetry* **1996**, *7*, 2523.
(18) Renard, P. Y.; Lallemand, J. Y. *Bull. Soc. Chim. Fr.* **1996**, *133*, 143.
(19) Wang, X. B. *J. Chem. Soc., Chem. Commun.* **1991**, 1515.
(20) Zhang, A.; Kan, Y.; Jiang, B. *Tetrahedron* **2001**, *57*, 2305.
(21) Gao, X. R.; Hall, D. G. *Tetrahedron Lett.* **2003**, *44*, 2231.

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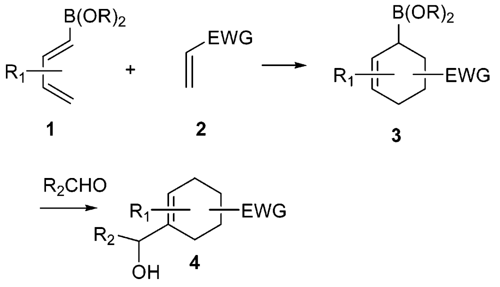
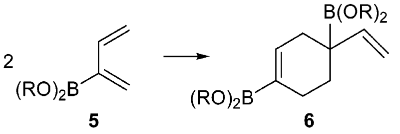
Scheme 1. Reactions of 1, 3-Dienyl-1-boronates



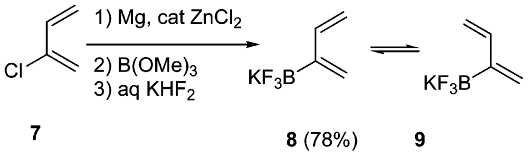
In general, the regioselectivities and *endo*/*exo* selectivities of the Diels−Alder reactions of these 1,3-dienyl-1-boronates are in the 4−9:1 range. One report also exists of a Suzuki coupling of a 1,3-dienyl-1-boronate (**1**).[22]

In contrast to the 1,3-dienyl-1-boronates, few report the preparation and Diels−Alder chemistry of 1,3-dienyl-2-boronates (**5**).[23,24] The Diels−Alder chemistry of this class of compounds has presumably been limited by their propensity to dimerize (**6**) even at room temperature.[25] Renaud and co-workers have recently reported a clever enyne ring-closing metathesis reaction involving boronate-substituted alkynes, which leads to more highly functionalized 1,3-dienyl-2-boronates, but many of these compounds also proved unstable and prone to dimerization.[26]

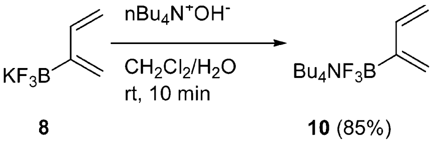


Because so much is now known about cross-coupling/transmetalation reactions of boron-, aluminum-, and silicon-substituted alkenyl compounds, we were convinced that when we found a synthetic route to stable compounds in the 1,3-dienyl-2-main group element family, then these compounds would prove useful to synthetic organic chemists. Our experience in transition metal dienyl complex chemistry had also been that 2-metal-substituted 1,3-dienes were vastly superior to 1-metal-substituted 1,3-dienes[27,28] both in rate enhancement and stereoselectivity, so we expected the same to be true for main group susbstituted dienes if we could develop this chemistry. Our preliminary results in this area are outlined below.

Boron Diene Preparation. Potassium organotrifluoroborates were first introduced as alternatives to boronic esters and acids in 1995.[29] Since then, many have reported on their utility and advantages, such as atom economy compared to boronic acids and esters, their ease of purification and disposal, their monomeric rather than trimeric nature, and their air stability.[30] Given the reported stability and utility of this class of compounds, we recently set out to prepare the first 1,3-dienyl-2-trifluoroborates. We chose to prepare the butadiene initially and used a route that involved preparing the Grignard reagent of chloroprene (**7**), [31,32] followed by its quenching with trimethylborate ($B(OMe)_3$) and aqueous KHF_2. This new boron-substituted dienyl (**8**) is a white, air-stable solid and shows no propensity to dimerize.[33] It has now been prepared on a several-gram scale (78%), characterized by ^1H, ^{13}C, ^{11}B, and ^{19}F NMR, and appears by NOESY to be predominantly in a solution conformation close to *s-trans* (**9**).



We have also prepared the tetra *n*-butylammonium (TBA) salt of the BF_3 substituted diene (**10**) (85%).[34] TBA salts of other trifluoroborates have been shown to improve cross-coupling yields considerably, presumably as a result of their greater organic solvent solubility.[35] The bulkier ammonium salt should also increase organic solvent solubility of this class of dienes and may drive their solution conformation more toward *s-cis* and increase their Diels−Alder reactivity.



Diels−Alder/Cross-Coupling. We have begun to explore the tandem reaction chemistry of these dienyl trifluoroborates (**8** and **10**). We first tried Diels−Alder reactions of diene (**8**) with ethyl acrylate and methyl vinyl ketone (MVK) and found that boron-containing cycloadducts (**11**−**14**) could be isolated in high yield. Those cycloadducts (**11**−**14**) could then subsequently be cross-coupled using Pd catalysis to yield organic cycloadducts (**15**, **16**) (Scheme 2).

We then performed a series of tandem Diels−Alder/cross-coupling reactions without isolating and characterizing boron intermediates as shown in Table 1. We first heated the boron diene (**8** or **10**) and dienophile then added $Pd(OAc)_2$ (0.5

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[22] Tivola, P. B.; Deagostino, A.; Prandi, C.; Venturello, P. *Org. Lett.* **2002**, *4*, 1275.

[23] (a) Brown, H. C.; Bhat, N. G.; Iyer, R. R. *Tetrahedron Lett.* **1991**, *32*, 3655. (b) Guennouni, N.; Rasset-Deloge, C.; Carboni, B.; Vaultier, M. *Synlett* **1992**, 581.

[24] Kamabuchi, A.; Miyaura, N.; Suzuki, A. *Tetrahedron Lett.* **1993**, *34*, 4827.

[25] Carreaux, F.; Posseme, F.; Carboni, B.; Arrieta, A.; Lecea, B.; Cossio, F. P. *J. Org. Chem.* **2002**, *67*, 9153.

[26] Renaud, J.; Graf, C. D.; Oberer, L. *Angew. Chem., Int. Ed.* **2000**, *39*, 3101.

[27] Hayes, B. L.; Adams, T. A.; Pickin, K. A.; Day, C. S.; Welker, M. E. *Organometallics* **2000**, *19*, 2730.

[28] Hayes, B. L. Ph. D. Dissertation, Wake Forest, 2000.

[29] Vedejs, E.; Chapman, R. W.; Fields, S. C.; Lin, S.; Schrimpf, M. R. *J. Org. Chem.* **1995**, *60*, 3020.

[30] Molander, G. A.; Biolatto, B. *J. Org. Chem.* **2003**, *68*, 4302.

[31] Nunomoto, S.; Yamashita, Y. *J. Org. Chem.* **1979**, *44*, 4788.

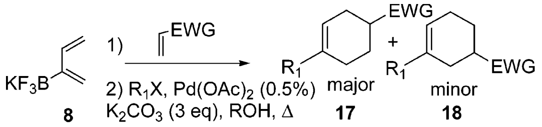
[32] Fleming, F. F.; Jiang, T. *J. Org. Chem.* **1997**, *62*, 7890.

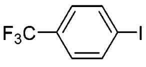
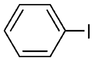
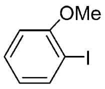
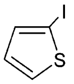
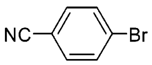
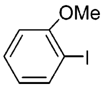
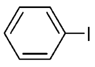
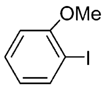
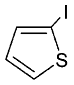
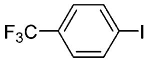
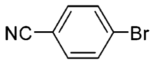
[33] Molander, G. A.; Dehmel, F. *J. Am. Chem. Soc.* **2004**, *126*, 10313.

[34] Batey, R. A.; Quach, T. D. *Tetrahedron Lett.* **2001**, *42*, 9099.

[35] Thadani, A. N.; Batey, R. A. *Tetrahedron Lett.* **2003**, *44*, 8051.

Table 1. Tandem Diels−Alder/Cross-Coupling Reactions of Boron Dienes[a]

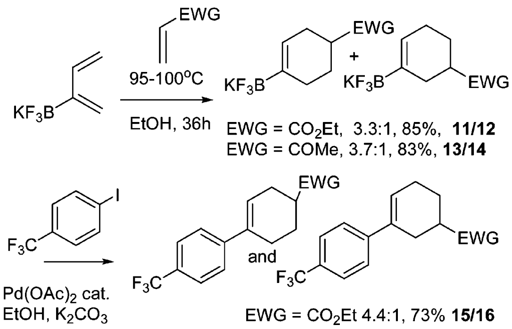


Entry	Diene	α,β Unsaturated Carbonyl	Aryl Halide	Products	Ratios	Yields
1)	**8**	$CH_2{=}CHCO_2Et$		**15/16**	2.9:1	62
2)	**8**	$CH_2{=}CHCO_2Et$	“*	**15/16**	3.1:1	64
3)	**8**	$CH_2{=}CHCO_2Et$		**17/18a**	2.5:1	60
4)	**8**	$CH_2{=}CHCO_2Et$		**17/18b**	3.9:1	50
5)	**8**	$CH_2{=}CHCO_2Et$		**17/18c**	3.8:1	55
6)	**8**	$CH_2{=}CHCO_2Et$#		**17/18d**	5.7:1	60
7)	**11**	$CH_2{=}CHCO_2Et$		**17/18b**	2.3:1	53
8)	**8**	$CH_2{=}CHCOMe$		**17/18e**	2.7:1	56
9)	**8**	$CH_2{=}CHCOMe$		**17/18f**	5.1:1	48
10)	**8**	$CH_2{=}CHCOMe$		**17/18g**	5.2:1	50
11)	**8**	$CH_2{=}CHCOMe$	“*	**17/18h**	4.8:1	54
12)	**8**	$CH_2{=}CHCOMe$		**17/18h**	2.8:1	57
13)	**8**	$CH_2{=}CHCOMe$#		**17/18i**	3.9:1	41

[a] Notes: (∗) reactions run in a microwave; (#) 1.5% Pd cat used.

mol %), 3 equiv K_2CO_3, and refluxed in EtOH or MeOH for 5 h. The sequence appears useful for unsubstituted phenyl halides (entries 3 and 8), phenyl halides substituted by electron-donating (entries 4, 7, and 9) or -withdrawing groups (entries 1, 2, 6, 12, and 13), and heteroaromatic halides (entries 5, 10, and 11). The yields for this tandem sequence are generally slightly higher for acrylate rather than MVK adducts (entries 1−7 versus 8−13). Phenyl halides with electron-withdrawing groups (entries 1, 2, 6, 12, and 13) typically produce products in 5−10% higher isolated yield than those with electron-donating groups (entries 4, 7, and 9). The preference for the para over meta regioisomer in these initial experiments ranges from 3 to 5:1. We wondered if the tetrabutylammonium counterion might have some effect on isolated yields (due to increased solubility) or regiochemical outcomes (due to steric effects), but comparison of entries 4 and 7 indicates dienes **8** and **11** are almost identical in product outcome. Performing these reactions in a commercial microwave reactor drastically reduces the time required and produces a product in almost identical yield and regiochemistry to the one obtained from a classical thermal reaction (entries 1 and 2 and 10 and 11) Even in its limited form, Table 1 demonstrates that **8** or **11** can serve as a synthon for a host of 2-substituted-1,3-butadienes. We have not worried about regiochemistry here in these early studies, since we ultimately plan to transmetalate boron dienes to Rh prior to cycloadditions and we have already demonstrated that low valent transition-metal-substituted dienes participate in Diels−Alder reactions with excellent regio- and stereoselectivity.[36]

Scheme 2. Sequential Diels−Alder/Cross-Coupling



In summary, we have prepared new, stable, monomeric dienyl trifluoroborates in high yield and find that they readily participate in Diels−Alder/cross-coupling tandem reactions. We will report the transition-metal-catalyzed reaction chemistry of these main group element substituted dienes in due course.

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(36) Welker, M. E. *Curr. Org. Chem.* **2001**, *5*, 785.

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Supporting Information Available: Experimental procedures and characterization data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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