Allylboration of Alkenes with Allyldihaloboranes

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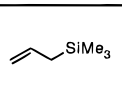
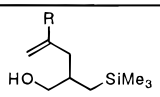
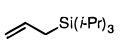
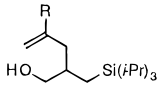
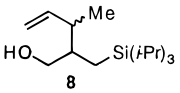
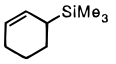
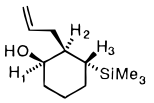
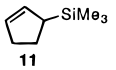
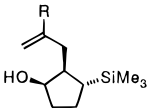
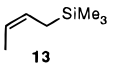
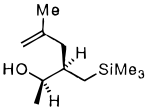
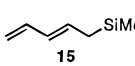
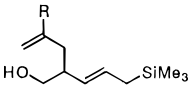
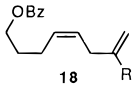
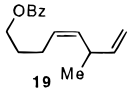
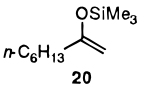
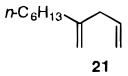
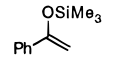
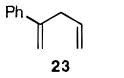
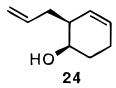
Chemists have exerted considerable effort to develop carbometalations of alkenes that would complement the well-developed areas of hydrometalations (e.g., hydroboration) or organometal additions to carbonyls. There has been great success with electron-deficient alkenes (e.g., cuprate chemistry) and isolated alkynes,[1] but much less general progress has been made with the carbometalation of unactivated and electron-rich alkenes. Examples include polymerizations, intramolecular cyclizations,[2] additions to allylic alcohols or amines,[3] and uncatalyzed[4] and catalyzed[5] additions to terminal and highly strained alkenes.[6] Carbometalations with allylic reagents are often more facile—simple allyl Grignards and zincs can undergo metallo−ene additions to monosubstituted and strained alkenes.[4,7] Due to problems with selectivity and efficiency, these reactions have found best utility in intramolecular examples.[8] Allylic boranes can also effect carbometalations of alkynes and specialized alkenes.[9] However, the low reactivity of the allylboranes employed (usually triallylborane) has been a critically limiting feature. Triallylborane reacts rapidly with alkoxyacetylenes and methylcyclopropene, but much more slowly with alkynes and allenes in reactions troubled by the instability of the initial products. Vinyl ethers are also moderately reactive with triallylborane, forming 1,4-dienes at 110−140 °C in variable yields.[10]

We report here the carbometalation of alkenes with allyldihaloboranes. These electrophilic boranes are highly reactive allylborating reagents and react with electron-rich alkenes regio- and stereospecifically in high yields.

The previously unreported allyldichloroborane (**1**) can be generated in hexanes solution by the reaction of BCl_3 with allyltributyltin (0 °C, <15 min), as indicated by the clean appearance of ^{1}H NMR peaks at δ 5.85 (d of d of t, 1 H), 5.02 (d, 1 H), 4.99 (d, 1 H), and 2.40 (br d, 2 H). Although **1** could not be isolated, it decomposes only slowly in solution over the course of 2−3 days at 25 °C. Methallyldichloroborane (**2**) was generated similarly. Crotyldichloroborane (**3**) was generated as a undetermined mixture of *cis* and *trans* isomers (based on a complex ^{1}H NMR pattern centered at δ 5.5), with no observable 3-boryl-1-butene isomer, from either purified *trans*-crotyltributylstannane or an ∼1:1:1 mixture of *trans*,*cis*, and 3-buten-2-yl isomers. The NMR observation of allyldibromoborane (**4**) from the reaction of BBr_3 with allylic stannanes

Table 1. Allylborations with Allyldihaloboranes

substrate	borane, conditions[a]	product[b]	yield
	**1**, 8 h[e]		R = H 83%
	2, 24 h[e]		R = Me 93%
	**1**, 12 h[e]		R = H 82%
	2, 24 h[e]		R = Me 87%
		7	
	3, 12 h[e]		76% (65:35 mixture)
		8	
	**1**, 18 h[e]		70% (single isomer)
9		**10**	
	**1**, 24 h[e]		R = H 67%
11	**2**, 12 h[e]	**12**	R = Me 64%
	**2**, 6 h[e]		64% (single isomer)
13		**14**	
	**1**, 90 min[e]		R = H 78%
15	**2**, 2 h[e]	**16**	R = Me 80%
	**1**, 20 min[c,d]		R = H 76%
17	**2**, 1 h[c,d]	**18**	R = Me 87%
	3, 1 h[c,d]		85%
		19	
	**1**, 2 h[c]		76%
20		**21**	
	**1**, 2 h[c]		72%
22		**23**	
	1, 0 °C, 1 h[f]	**23**	78%
	**4**, -20 °C, 90 min[e]		62%
		24	

[a] Unless otherwise noted, the reaction was carried out at 25 °C for the indicated time. The substrate was added to a solution of the indicated allylborane at either −45 or 0 °C before warming to 25 °C. [b] See ref 12 for stereochemical assignments. [c] Worked up by addition of excess NaOH or pyridine or triethylamine and then stirring with aqueous $NaHCO_3$. [d] The crude product was benzoylated with benzoyl chloride/pyridine. [e] Worked up by treatment with H_2O_2/excess NaOH. [f] Worked up by treatment with anhydrous NaOAc followed by refluxing in HOAc for 1 h.

(1) Normant, J. F.; Alexakis, A. *Synthesis* **1981**, 841. Negishi, E. *Acc. Chem. Res.* **1987**, *20*, 65−72.
(2) Shaughnessy, K. H.; Waymouth, R. M. *J. Am. Chem. Soc.* **1995**, *117*, 5873−4. Negishi, E.; Jensen, M. D.; Kondakov, D. Y.; Wang, S. *J. Am. Chem. Soc.* **1994**, *116*, 8404. Zhang, Y.; Negishi, E. *J. Am. Chem. Soc.* **1989**, *111*, 3454.
(3) Richey, H. G., Jr.; Erickson, W. F.; Heyn, A. S. *Tetrahedron Lett.* **1971**, *48*, 2183−2186. Eisch, J. J.; Merkley, J. H.; Galle, J. E. *J. Am. Chem. Soc.* **1979**, *101*, 1148−1155. See also: Hoveyda, A. H.; Xu, Z.; Morken, J. P.; Houri, A. F. *J. Am. Chem. Soc.* **1991**, *113*, 8950.
(4) Lehmkuhl, H. *Bull. Chim. Soc. Fr. II* **1981**, 87−95.
(5) Dzhemilev, U. M.; Vostrikova, O. S. *J. Organomet. Chem.* **1985**, *285*, 43−51. Hoveyda, A. H.; Xu, Z. *J. Am. Chem. Soc.* **1991**, *113*, 5079. Takahashi, T.; Seki, T.; Nitto, Y.; Saburi, M.; Rousset, C. J.; Negishi, E. *J. Am. Chem. Soc.* **1991**, *113*, 6266−6268.
(6) Nakamura, E.; Nakamura, M.; Miyachi, Y.; Koga, N.; Morokuma, K. *J. Am. Chem. Soc.* **1993**, *115*, 99.
(7) Lehmkuhl, H. In *Organometallics in Organic Synthesis*; De Meijere, A., Dieck, T., Eds.; Springer-Verlag: New York, 1987; pp 185−202. Nakamura, M.; Arai, M.; Nakamura, E. *J. Am. Chem. Soc.* **1995**, *117*, 1179−1180. Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207−2293.
(8) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 38−52.
(9) For reviews, see: Mikhailov, B. M. *Russ. Chem. Rev.* **1976**, *45*, 557. Bubnov, Y. N. *Pure Appl. Chem.* **1987**, *59*, 895.
(10) Mikhailov, B. M.; Bubnov, Y. N. *Zh. Obshch. Khim.* **1971**, *41*, 2039.

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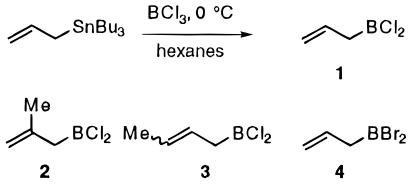
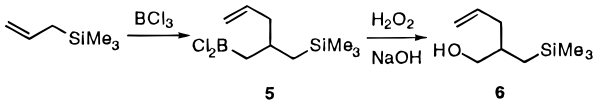
had been previously reported,[11] although **4** was most conveniently generated from allyltrimethylsilane (−20 °C, 15 min).

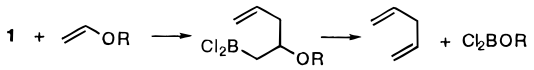


The most striking observation was the facility of the allylborations of allylic silanes. This was discovered when the reaction of BCl_3 with allyltrimethylsilane, an independent synthesis of **1**, afforded **6** after oxidative workup. Although **1** could be observed as an intermediate by NMR, it appeared to allylborate the allyltrimethylsilane to form **5** at a rate comparable to that of its formation.



The allylborations of allylic silanes are uniformly regiospecific, affording after oxidation alcohols derived from addition of the boryl group distally to the silyl group (Table 1).[12,13] The additions to (trimethylsilyl)cyclohexene and (trimethylsilyl)-cylopentene (**9** and **11**) in each case produce a single isomeric product, derived from a *syn* allylboration, *anti* to the silyl group. The reaction of pure *cis*-crotyltrimethylsilane (**13**) with **2** afforded a single isomeric product, while a 47:53 *cis*/*trans* mixture of crotylsilanes afforded a 47:53 mixture of the product from the pure *cis* and a diastereomeric product. Together, these results indicate the stereospecificity of the reaction.

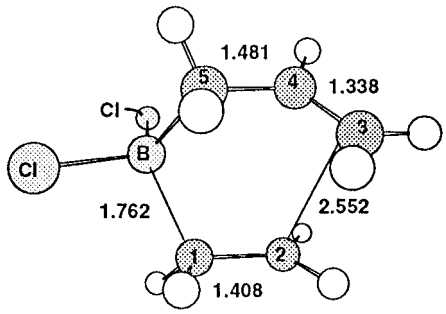
The allylborations of vinyl and silyl enol ethers readily afford 1,4-dienes. These can be understood as arising from an initial allylboration followed by elimination of the β-alkoxy- or β-(silyloxy)borane. The allylboration of dihydropyran (**17**) with



1−**3** afforded purely the *cis* products, consistent with a *syn* allylboration (as observed above) followed by an *anti* elimination. The allylboration of phenylacetylene also produced a 1,4-diene after protodeboronation. The instability of adducts obtained from the allylboration of alkynes with triallylborane[9] is not a problem here, and the reaction with **1** is much more efficient.

While the dienylsilane **15** reacts readily and regiospecifically with **1** and **2**, simple dienes failed to react faster than the decomposition of the allyldichloroboranes. However, the more electrophilic **4** appears to be much more reactive. In a promising initial result, the reaction of **4** with 1,3-cyclohexadiene afforded **24** regiospecifically after oxidation.

Ab initio calculations provide several insights into these reactions. RHF calculations with a 6-31G* basis set predict the transition structure **25**[14] for the reaction of **1** with ethylene. The chairlike cyclic six-membered transition structure is consistent with the allylically rearranged products observed with **3** (cf, **8** and **19**) and with the stereospecificity of the reactions. The addition is highly asynchronous, and **25** is polarized. The advanced bonding of C_1 with B results in a relatively high positive charge on C_2 compared to ethylene (0.21 e difference in Mulliken charges). Thus, donor substituents on C_2 accelerate the reaction and control the regiochemistry.



25

The combination of the high reactivity and selectivity of allyldihaloboranes with the versatility of the borane adducts should significantly extend the range of products available from carbometalations of alkenes.

Acknowledgment. We thank the NIH and The Robert A. Welch Foundation for support of our programs.

JA961616K

(11) Harston, P.; Wardell, J. L.; Marton, D.; Tagliavini, G.; Smith, P. J. *Inorg. Chim. Acta* **1989**, *162*, 245−50.

(12) The stereochemistry of **12** (R = Me) was assigned from an X-ray crystal structure of the corresponding 3,5-dinitrobenzoate, and **12** (R = H) was assigned from a similarity of its ^{1}H NMR spectrum to that of **12** (R = Me). The stereochemistry of **10** was assigned from an H2−H3 coupling of 12.4 Hz and the lack of any large coupling to H1 (all <5 Hz). For **18** (R = H), **18** (R = Me), and **19**, the complex AB pattern in the ^{1}H NMR of the internal double bond could be simulated using a vinylic vicinal coupling constant of 10 Hz, indicative of the *Z* stereochemistry. The structure of **18** (R = H) was further confirmed by hydrolysis to the known alcohol (Andrews, G. D. *Macromolecules* **1984**, *17*, 1624−1626). The stereochemistry of **24** was assigned from a similarity of its NMR spectrum to that of the known *cis*-2-methyl-3-cyclohexen-1-ol (Singleton, D. A.; Martinez, J. P.; Watson, J. V.; Ndip, G. M *Tetrahedron* **1992**, *48*, 5831). The stereochemistry of **14** could only be speculatively assigned on the basis of the stereospecificity of the reaction (see text) and the observation of syn addition in the other reactions.

(13) In a typical procedure, 1.47 g (4.3 mmol) of allyltributyltin was added slowly to 3.5 mL (3.5 mmol) of a 1.0 M solution of BCl_3 in hexanes at −78 °C, and the mixture was warmed to 25 °C for 30 min. The mixture was then cooled to −45 °C, and 0.325 g (2.0 mmol) of **9** was added. The reaction was then allowed to warm slowly to 25 °C and stirred for 18 h. In the workup there were added successively 5 mL of 3 M aqueous NaOH, 5 mL of 30% aqueous H_2O_2, and 5 mL of THF to the cooled mixture, which was then stirred at 25 °C overnight. After a normal ethereal extraction, chromatography of the residue on a 0.75 in. × 14 in. silica gel column with 6% EtOAc in hexanes as eluent afforded 0.295 g (70%) of **10**.

(14) E = −1138.21609. Structure **25** is fully optimized and exhibited one imaginary frequency. The predicted activation energy is 31.0 kcal/mol. For comparison calculations on simple ene reactions, see: Loncharich, R. J.; Houk, K. N. *J. Am. Chem. Soc.* **1987**, *109*, 6947.