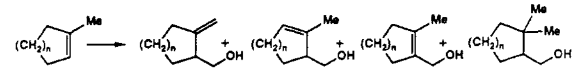
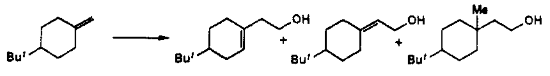
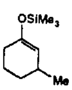
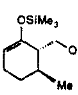
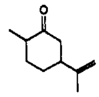
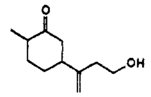
Table I. Reaction of Formaldehyde–Organoaluminum Complexes with Olefins

entry	olefin	reagent	conditions (°C, h)	products (ratio)
				
1	a, n = 1	CH_2=O·MAPH[a]	-78, 1	61% (100 : 0 : 0 : 0)[e]
2		CH_2=O·$AlMe_2Cl$[b]	0, 0.17	73% (75 : 25 : 0 : 0)
3	b, n = 2	CH_2=O·MAPH[a]	-78, 1	80% (100 : 0 : 0 : 0)[e]
4		CH_2=O·$AlMe_2Cl$[b]	0, 0.17	92% (41 : 59 : 0 : 0)
5		CH_2=O·$AlMe_3$[c]	25, 0.25	56% (7 : 0 : 25 : 68)
				
6		CH_2=O·MAPH[a]	-78, 1	71% (100 : 0 : 0)[e]
7		CH_2=O·$AlMe_3$[c]	25, 0.25	71% (44 : 21 : 35)
8		CH_2=O·MAPH[a]	0, 0.5	 71%
9		CH_2=O·MAPH[a]	0, 0.5	 90%
				
10		CH_2=O·MAPH[a]	0, 0.5	86%
11		CH=$_2$O·$AlMe_2Cl$[d]	25, 1	3%[f]

[a] The CH_2=O·MAPH complex (3 equiv) was prepared by treatment of trioxane (1 equiv) with MAPH (3 equiv) at 0 °C for 1 h and subsequently reacted with olefins under the indicated conditions. [b] See ref 4a. [c] See ref 4b. [d] This ene reaction was carried out according to ref 4a. [e] The ene reactions at higher temperature (~0 °C) showed similar selectivities. [f] Complex reaction mixtures were formed.

aldehyde by the troublesome thermal depolymerization of paraformaldehyde.

Supplementary Material Available: Representative experimental procedures for ene and aldol reactions with the CH_2=O·MAPH complex and table of five additional ene reactions (2 pages). Ordering information is given on any current masthead page.

High Reactivity, Regioselectivity, and Endo Stereoselectivity of Vinylboranes in Diels–Alder Reactions

Daniel A. Singleton* and Jose P. Martinez

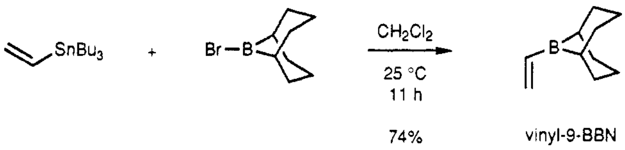
Department of Chemistry, Texas A&M University
College Station, Texas 77843

Received May 31, 1990

Chemists have long believed that a trivalent boron atom, with its empty p orbital, should behave in a fashion similar to that of traditional organic electron-withdrawing groups.[1] This idea is synthetically attractive when applied to the activation of Diels–Alder dienophiles, because the product boron compounds can be transformed into alcohol, ketone, amine, or alkane products, none of which can usually be produced by a direct Diels–Alder reaction. However, Diels–Alder reactions on vinylboron derivatives are very rare and the known examples do not exhibit either high reactivity or general synthetic utility. In 1963, Matteson[2] reported the reaction of vinylboronic esters with cyclopentadiene at 90–100 °C and isoprene at 130–140 °C. Vinyldichloroborane reacts with cyclopentadiene in low yield at 80 °C.[3,4] In an evaluation of ketene equivalents, Evans reported the low reactivity of vinylboronic esters with 1,3-cyclohexadiene derivatives, with long reaction times at 200 °C required.[5] Due to the necessarily strenuous reaction conditions, other examples are lacking.

We were interested in experimentally assessing how a *dialkyl*boron group compares to carbonyl groups in its effects on reactivity. The recent utilization of diarylboron groups in anion chemistry[6,7] made it surprising that there were no reports of successful[8] Diels–Alder reactions on vinyl*boranes*. We report here that a dialkylboron group is dramatically more activating than esters and boronic esters in normal Diels–Alder reactions and that vinylboranes are exceptionally reactive, regioselective, and stereoselective dienophiles. We anticipate that excellent synthetic applicability should result.

The previously unknown 9-vinyl-9-borabicyclo[3.3.1]nonane (vinyl-9-BBN)[9] was easily synthesized by treatment of a 1.0 M solution of *B*-bromo-9-BBN in methylene chloride with 1 equiv of vinyltributyltin, followed by distillation of the reaction mixture [bp 28–30 °C (0.25 mm)]. Vinyl-9-BBN can be kept for weeks in a freezer under an inert atmosphere and is extremely pyrophoric.



The reactions of vinyl-9-BBN with some simple dienes are summarized in Table I. In contrast to the reactions of butadiene or isoprene with methyl acrylate,[10] nitroethylene,[11] phenyl vinyl sulfone,[12] dibutyl vinylboronate,[2] or even vinylboronic esters substituted with a second electron-withdrawing group,[13] all requiring prolonged heating at 100–150 °C, the Diels–Alder reactions of vinyl-9-BBN with butadiene and isoprene were both >80% complete in a day at 25 °C! Based on the bimolecular rate constant determined by NMR (Table I), vinyl-9-BBN is 200 times more reactive than methyl acrylate with butadiene.[14] Vinyl-9-BBN is still less reactive than Lewis acid complexed dienophiles[10] and α,β-unsaturated Fischer carbene complexes,[15] but among simple neutral substituents, the activating effect of a dialkylboron

---

(1) Matteson, D. S. *J. Am. Chem. Soc.* **1960**, *82*, 4228.

(2) Matteson, D. S.; Waldbillig, J. O. *J. Org. Chem.* **1963**, *28*, 366.

(3) Coindard, G.; Braun, J. *Bull. Chim. Soc. Fr.* **1972**, 817.

(4) In our hands, acid-catalyzed reactions of dienes in the presence of dihalovinylboranes are a severe problem.

(5) Evans, D. A.; Scott, W. L.; Truesdale, L. K. *Tetrahedron Lett.* **1972**, 121. Evans, D. A.; Golob, A. M.; Mandel, N. S.; Mandel, G. S. *J. Am. Chem. Soc.* **1978**, *100*, 8170.

(6) Pelter, A.; Buss, D.; Colclough, E. *J. Chem. Soc., Chem. Commun.* **1987**, 297. Pelter, A.; Singaram, B.; Williams, L.; Wilson, J. W. *Tetrahedron Lett.* **1983**, *24*, 623.

(7) Cooke, M. P., Jr.; Widener, R. K. *J. Am. Chem. Soc.* **1987**, *109*, 931.

(8) Reference 3 reports a failed attempt.

(9) In all cases, ^1H and ^{13}C NMR and mass spectral data were consistent with the assigned structures. The "para" regiochemistry of **2** was established by oxidation (H_2O_2/NaOH and then pyridinium dichromate) and *p*-toluenesulfonic acid catalyzed equilibration to a mixture of 4-methyl-2-cyclohexenone and 4-methyl-3-cyclohexenone. See: Kinney, W. A.; Crouse, G. D.; Paquette, L. A. *J. Org. Chem.* **1983**, *48*, 4986. The stereochemistry and regiochemistry of **4–9** were assigned after oxidation to the corresponding alcohols. ^1H-Decoupling experiments on the alcohols corresponding to **4** and **5** established connectivity consistent only with 5-methyl-3-cyclohexenol isomers. The 5-methyl-3-cyclohexenol isomer corresponding to **4** was assigned the cis stereochemistry on the basis of coupling constants to the carbinol proton of 11.5, 9.7, 5.6, and 3.5 Hz. The 1,2,3,5,6,7,8,8a-octahydronaphthalen-2-ol corresponding to **6** was assigned the given stereochemistry on the basis of coupling constants to the carbinol proton of 11.6, 9.3, 5.3, and 3.4 Hz. The carbinol protons of the minor alcohol isomers corresponding to **5** and **7** were located 0.16 and 0.19 ppm downfield from those of the major isomers, respectively, and both displayed four smaller, incompletely resolvable coupling constants totaling ≈18 Hz.

(10) Inukai, T.; Kojima, T. *J. Org. Chem.* **1967**, *32*, 872.

(11) Kaplan, R. B.; Shechter, H. *J. Org. Chem.* **1961**, *26*, 982.

(12) Carr, R. V. C.; Paquette, L. A. *J. Am. Chem. Soc.* **1980**, *102*, 853.

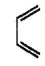
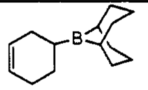
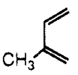
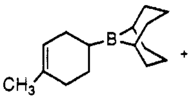
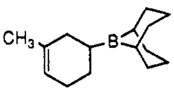
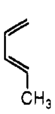
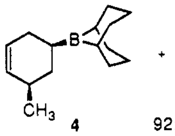
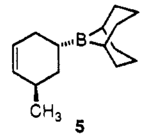
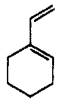
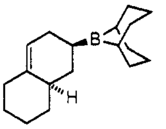
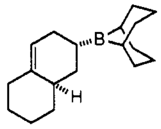
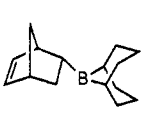
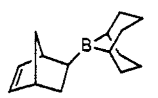
(13) Martinez-Fresneda, P.; Vaultier, M. *Tetrahedron Lett.* **1989**, *30*, 2929.

(14) A value of 1.6×10^{-8} M^{-1} s^{-1} for the reaction of 1,3-butadiene with methyl acrylate at 25 °C may be extrapolated from literature data.[10]

(15) Wulff, W. D.; Yang, D. C. *J. Am. Chem. Soc.* **1983**, *105*, 6726.

0002-7863/90/1512-7423$02.50/0

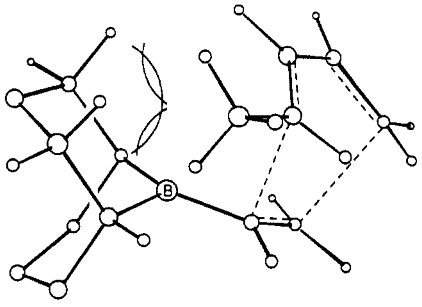
Table I. Rate Constants, Products, and Yields for Diels–Alder Reactions with Vinyl-9-BBN

Diene	Rate Constant ($M^{-1}s^{-1}$) or Rxn Conditions	Isolated Yield[a]	Product(s) and Ratio[b]
	3.2±0.4x10^{-6} (25 °C)	82%	 1
	3.0±0.6x10^{-6} (25 °C)	79%	 +  2 93:7 3
	4.6±0.5x10^{-7} (25 °C)	71%[c]	 +  4 92:8 5
	48 h, 55 °C[d]	72%	 +  6 96:4 7
	3.5 h, 25 °C[d]	86%	 +  8 2:1 9

[a] General procedure: A neat mixture of vinyl-9-BBN and 1.5–3 equiv of diene was allowed to react at 25 °C until the reaction was estimated to be >95% complete, followed by fractional vacuum distillation. [b] See ref 9. [c] After 5 days at 25 °C, the reaction mixture was heated to 70 °C for 26 h. [d] The reaction times were convenient and were not minimized or optimized.

group is approached only by acyl and sulfonyl halides.[10]

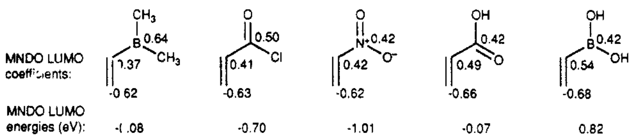
The regioselectivity in these reactions is outstanding and displays an intriguing feature. With isoprene, vinyl-9-BBN formed the normal "para" isomer **2** with selectivity comparable to that of methyl acrylate/$AlCl_3$ (95:5),[17] and significantly greater than that of the corresponding reactions of methyl acrylate (70:30)[18] or dibutyl vinylboronate (75:25).[5] In contrast, with *trans*-piperylene there was regiospecific formation of the normally disfavored[18] meta isomers **4** and **5**. The relatively low rate of this reaction, at first surprising since *trans*-piperylene would normally react faster than butadiene with electron-deficient dienophiles,[19] is as expected from known partial rate factors with the ortho product excluded.[20] Molecular mechanics calculations using Houk's fixed transition state method suggest that both the endo and exo transition states leading to the normal ortho isomer are sterically hindered by the bulky bicyclo[3.3.1]nonane group, as depicted in **10**.[21] This steric effect also results in the regiospecific formation of the 2-substituted octahydronaphthalenes **6** and **7** from 1-vinylcyclohexene, while the corresponding reaction of methyl acrylate/diethylaluminum chloride afforded a 69:15:12:4 mixture with the two 1-substituted octahydronaphthalene isomers being major.[22] Use of less hindered vinylboranes may result in a normal pattern of regioselectivity.



10

The endo stereoselectivity observed in the reactions of piperylene and 1-vinylcyclohexene with vinyl-9-BBN was also much greater than that observed with the common neutral dienophiles.[23] The 1-vinylcyclohexene reaction is particularly notable for being much more stereoselective with vinyl-9-BBN than with methyl acrylate/diethylaluminum chloride. However, the endo stereoselectivity with cyclopentadiene was relatively low. The role of steric effects in the latter case is uncertain.[24]

The high regioselectivity and endo stereoselectivity in these reactions were predictable from FMO theory.[25] MNDO calculations[26] place a greater difference in vinylic LUMO coefficients (relating to regioselectivity[27]) and a much greater LUMO coefficient on boron (relating to endo stereoselectivity[23a]) in dimethylvinylborane than on the corresponding atoms in acrylic acid, vinylboronic acid, acryloyl chloride, and nitroethylene. The high reactivity of vinylboranes was more surprising;[28] dimethylvinylborane's LUMO, from MNDO calculations, is about equal in energy to that of acrylic acid and 0.6 and 0.9 eV higher than that of acryloyl chloride and nitroethylene, respectively.



Coupling the high reactivity, regioselectivity, and endo stereoselectivity of Diels–Alder reactions on vinylboranes with the synthetic versatility of the products should allow a significant extension of the variety of structures easily available from the Diels–Alder reaction. We are continuing to study the intriguing reactivity and selectivity effects in these reactions and the possibility of enantioselective reactions using chiral boranes.

Acknowledgment is made to the Robert A. Welch Foundation and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

---

(16) The availability of appropriate kinetic data for comparison is limited, and the relative reactivity is diene dependent. We have measured a bimolecular rate constant of 3.1×10^{-6} M^{-1} s^{-1} at 25 °C for the reaction of acryloyl chloride with butadiene. For the reaction of ethylenesulfonyl chloride with butadiene at 50 °C, see: Snyder, H. R.; Anderson, H. V.; Hallada, D. P. *J. Am. Chem. Soc.* **1951**, *73*, 3258.

(17) Inukai, T.; Kojima, T. *J. Org. Chem.* **1966**, *31*, 1121.

(18) For example, the reaction of *trans*-piperylene with methyl acrylate forms an 86:14 ratio of ortho and meta isomers.[20]

(19) Craig, D.; Shipman, J. J.; Fowler, R. B. *J. Am. Chem. Soc.* **1961**, *83*, 2885.

(20) Inukai, T.; Kojima, T. *J. Org. Chem.* **1967**, *32*, 869.

(21) (a) Brown, F. K.; Houk, K. N. *J. Am. Chem. Soc.* **1985**, *107*, 1971. (b) Structure **10** was created by adding a methyl group to the structure calculated for butadiene, with some hydrogens removed for clarity. The distance between interacting hydrogen atoms in **10** is 1.9 Å.

(22) The stereochemistries of the products were not assigned.

(23) (a) Güner, O. F.; Ottenbrite, R. M.; Shillady, D. D.; Alston, P. V. *J. Org. Chem.* **1988**, *53*, 5348 and references therein. (b) Claims of regiospecificity or complete endo stereoselectivity abound in the literature, but are often later refuted. For examples, see ref 5 and 20, compared to references therein. Also, the reaction of isoprene with phenyl vinyl sulfone was reported to afford a single regioisomer, but in our hands affords a 75:25 mixture of regioisomers.

(24) In preliminary studies, we have observed higher endo stereoselectivity (>4:1) in the reaction of cyclopentadiene with the less hindered 1-vinyl-3-methylborolane. These studies will be reported in due course.

(25) Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*; Wiley: New York, 1976.

(26) Program MOPAC QCPE 455.

(27) For a discussion of the application of FMO theory to the regioselectivity of Diels–Alder reactions, and its limitations, see: Kahn, S. D.; Pau, C. F.; Overman, L. E.; Hehre, L. E. *J. Am. Chem. Soc.* **1986**, *108*, 7381.

(28) For a correlation of Diels–Alder reactivity with the HOMO(diene)-LUMO(dienophile) energy gap, see: Sustmann, R. *Pure Appl. Chem.* **1974**, *40*, 569.