Tetrahedron Letters, Vol. 33, No. 8, pp. 1017-1020, 1992
Printed in Great Britain

0040-4039/92 $3.00 + .00
Pergamon Press plc

Vinylboranes are Omniphilic Dienophiles.
Some Unusual and Useful Properties of Vinylboranes in Diels-Alder Reactions

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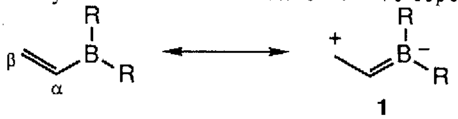
Summary: The rate of Diels-Alder reactions with vinyl-9-BBN is uniquely insensitive to diene substituent effects, and high reactivity is observed with both electron-rich and electron-poor dienes. The regioselectivity of these reactions is controlled mainly by steric effects.

We recently reported that vinyldialkylboranes are exceptionally reactive, regioselective, and *endo*-stereoselective Diels-Alder dienophiles.[1] This discovery was based on the old idea that a trivalent boron atom should behave in a fashion similar to traditional organic electron-withdrawing groups.[2] The application of this idea to vinylboranes is illustrated by the resonance structure **1**. We report here the results of rate and regiochemical studies which show that this view of the reactivity of vinylboranes is incorrect, and that vinyl-9-BBN, rather than acting as a normal electron-poor dienophile, is actually the first example of an *omniphilic* dienophile. The unusual rate and regiochemical properties of Diels-Alder reactions on vinylboranes should further enhance their synthetic utility.



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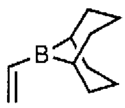
A variety of observations suggested that vinylboranes are not simple electron-poor dienophiles. While experimental and theoretical studies agree that the π delocalization in vinylboranes suggested by **1** is present, Raman, infrared, and NMR spectral studies indicate that the extent of delocalization and C-B double-bond character in vinylboranes is very limited.[3] The ^{13}C chemical shift of C_β has been the most sensitive measure of mesomeric contribution from **1**, but C_β is more shielded (electron-rich) in vinyldimethylborane than in vinylboronic esters or vinyldichloroborane, which are much less reactive dienophiles.[3a,4] The reactivity of vinylboranes with dienes is also much higher than expected from its MNDO LUMO energy.[1]

It was apparent from qualitative studies that the reactivity of vinylboranes did not respond in a normal fashion to changes in diene structure. To better understand the dienophilic character of vinylboranes, the rate of reaction of vinyl-9-BBN with an electronically diverse but sterically similar (except for cyclopentadiene) series of dienes was studied. Our results and a comparison[5] with maleic anhydride and tetracyanoethylene are shown in Table 1. Vinyl-9-BBN, maleic anhydride, and tetracyanoethylene all react at similar rates with 2-chlorobutadiene, but the latter two react faster with all of the electron rich dienes. Vinyl-9-BBN reacts at 25 °C with all of the



vinyl-9-BBN

dienes, and the rate varies by only a factor of eight in dienes ranging from 2,3-dichlorobutadiene to 2-ethoxybutadiene. The surprisingly low rate with 2-ethoxybutadiene is probably not the result of boron complexation by the ether oxygen – the rate constant for reaction of butadiene with vinyl-9-BBN was only slightly decreased to 2.5×10^{-6} $M^{-1}s^{-1}$ by the addition of 1.3 equiv of diethyl ether. Of the more reactive *s-cis* dienes, 2-*t*-butylbutadiene and cyclopentadiene, cyclopentadiene is normally much more reactive due to a unique effect of 1,4-distance,[7] but no special reactivity is observed with vinyl-9-BBN. 2-Phenylbutadiene reacted the fastest, despite the MM2 prediction (Chem3D Plus™) that its *s-trans* conformation is favored by ≈0.5 kcal.

The variation in rate through the series was only a factor of ≈420, compared to >200,000 with maleic anhydride. A wide range of other dienes, including hexachlorocyclopentadiene and methyl 2,4-pentadienoate, also exhibit good reactivity with vinyl-9-BBN. Although *ambiphilic* reagents favoring reaction with both electron-rich and electron-poor species are known for many reactions, including a recent report of an ambiphilic diene for Diels-Alder reactions,[8] the high and relatively invariant reactivity of vinylboranes with electron-rich, electron-poor, and *unactivated* dienes leads us to describe vinylboranes as *omniphilic* dienophiles.

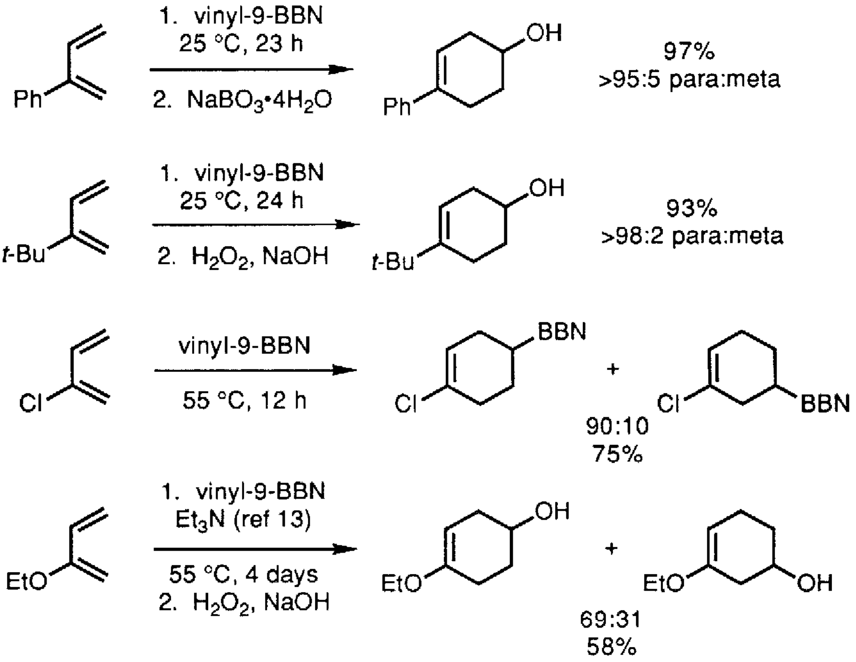
Table 1. Diene Structure vs Reactivity for Vinyl-9-BBN and Maleic Anhydride

diene	k (25 °C, $M^{-1}s^{-1}$) vinyl-9-BBN	k_{rel} (25 °C) vinyl-9-BBN	k_{rel} (25 °C) maleic anhydride[a]	k_{rel} (20 °C) tetracyanoethylene[b]
2,3-dichlorobutadiene	1.1×10^{-6}	0.34	0.0047	
2-chlorobutadiene	4.3×10^{-6}	1.3	0.1 (5.3×10^{-6} $M^{-1}s^{-1}$)	0.002 (10×10^{-6} $M^{-1}s^{-1}$)[c]
butadiene	3.2×10^{-6} [d]	1	1	1
isoprene	3.0×10^{-6} [d]	0.94	3	45
2-(m)ethoxybutadiene[e]	5.3×10^{-7}	0.17	10	1750
2-phenylbutadiene	2.3×10^{-4}	72	8.8[f]	191
2-*t*-butylbutadiene	4.0×10^{-5}	13	28	
cyclopentadiene	6.5×10^{-5}	22	1160	2.1×10^{6}

[a]Calculated from data in ref 9, except where noted.[9] [b]Ref 7, except where noted. [c]See ref 10.[10] [d]Ref 1. [e]2-Ethoxybutadiene for vinyl-9-BBN, 2-methoxybutadiene for maleic anhydride and tetracyanoethylene. [f]Ref 6, relative rate at 30 °C.

Are vinylboranes in fact "inverse electron demand" dienophiles, as suggested by the greater reactivity of 2-chlorobutadiene over 2-ethoxybutadiene? For such small changes in rate, it is impossible to separate electronic and conformational effects on the reactivity of the dienes. To test the electronic preference of vinylboranes more carefully, a σ–ρ study using 2-arylbutadienes was undertaken. The relative reactivities of the 2-arylbutadienes at 25 °C were determined by competition for a deficiency of vinyl-9-BBN, with the ratio of products determined after oxidation to the corresponding alcohols. Because 2-phenylbutadiene, 2-*para*-methoxyphenylbutadiene, and 2-*para*-chlorophenylbutadiene *all reacted at identical rates*, within an ≈5% error limit, no further 2-arylbutadienes were studied. The reaction constant ρ was -0.01 ± 0.10. For comparison, the normal electron demand reaction of maleic anhydride with 1-arylbutadienes had a ρ of -0.685,[11] and the inverse electron demand reaction of substituted cinnamaldehydes with octyl vinyl ether had a ρ of +0.71.[12] Although minimal substituent effects would be expected for reactions with unactivated dienophiles such as ethylene, the absence of substituent effects with the highly reactive vinylboranes is both unprecedented and extraordinary.[13]

The electronically unusual nature of Diels-Alder reactions of vinylboranes is also displayed in the regioselectivity of these reactions. A 93:7 ratio of "para" and "meta" products had been observed in the reaction of vinyl-9-BBN with isoprene, which was comparable in selectivity to the best of dienophiles.[1] The regioselectivity is >98:2, >95:5, and 90:10 para:meta with 2-*t*-butylbutadiene, 2-phenylbutadiene, and 2-chlorobutadiene. However, surprisingly low selectivity (68:32) was observed with 2-ethoxybutadiene.[14] The last result is inconsistent with our previous FMO explanation of the high regioselectivity of vinylboranes. Instead, models suggest that there can be a steric interaction between the bulky bicyclo[3.3.1]nonane group and substituents in the 2-position of the diene in the *endo* transition state leading to the meta isomer. The regiochemical observations are consistent with this steric effect playing the largest role in the regioselectivity of vinyl-9-BBN. The regioselectivity with 2-ethoxybutadiene is disappointing, but considering the high regioselectivity observed with 2-*t*-butylbutadiene, greater regioselectivity may be observed with bulky 2-alkoxy substituents.



The reactivity and regioselectivity of vinylboranes cannot be explained by a polarization of vinylboranes as depicted in **1**, but the origin of the high reactivity of vinylboranes remains unknown. There is ≈7 kcal greater stability associated with a boron on an sp^2 carbon than on an sp^3 carbon,[15] so these reactions should be less exothermic than normal Diels-Alder reactions. Calculations indicate that a BH_2 should be among the best substituents for stabilizing adjacent radicals,[16] so it is possible that a dialkylboron group accelerates Diels-Alder reactions by stabilizing a concerted but *biradicaloid*[17] transition state. However, many other radical stabilizing groups, such as vinyl and phenyl, are not good activating groups for dienophiles, and even a biradicaloid transition state should be subject to substituent effects.

From a synthetic standpoint, the omniphilicity of vinylboranes should result in a very broad range of utility. We are continuing to study these intriguing dienophiles.

Acknowledgment. Acknowledgment is made to The Robert A. Welch Foundation for support of this research.

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(4) Preliminary studies indicate that vinyldimethylborane is very similar in reactivity to vinyl-9-BBN.

(5) Methyl acrylate and acryloyl chloride show a similar pattern of reactivity to maleic anhydride. The relative rates at 25 °C for the reaction of butadiene, isoprene, and cyclopentadiene with methyl acrylate are 1,[6a] 2.16,[6a] and 780,[6b] respectively, and with acryloyl chloride are 1,[1] 6,[6c] and 1400,[6b] respectively.

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(13) We considered several more-complex mechanisms which might have explained the lack of substituent effects, but none was consistent with the observation of clean second-order kinetics.

(14) The regioselectivity is not affected by the presence of THF or stoichiometric triethylamine, though the rate is decreased somewhat by the latter. Catalytic triethylamine is necessary to inhibit an unusual rearrangement of the minor product of the 2-ethoxybutadiene reaction. The details of this rearrangement will be published elsewhere.

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(Received in USA 11 November 1991)