PAPER

Alkylhalovinylboranes: a new class of Diels–Alder dienophiles†

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The Diels–Alder reactions of alkylhalovinylboranes have been investigated theoretically and experimentally. Alkylhalovinylboranes presented higher reactivity than the corresponding dialkylvinylboranes. Although *endo/exo* selectivities were high for the reactions with cyclopentadiene, facial selectivities for the chiral analogues were low. Our results demonstrate that the replacement of an alkyl group on the boron atom by a halogen increases the dienophilicity considerably.

Introduction

In the past decades, Singleton and others have extensively explored the synthetic utility of alkenyl-, alkynyl- and dienylboranes in Diels–Alder reactions.[1–18] Given that many variations of the Diels–Alder reaction of vinylboranes have been developed, it is surprising that there is only one precedent in the use of chiral vinylboranes in asymmetric [4 + 2] cycloaddition reactions. This Diels–Alder reaction was based on the use of dialkylvinylborane **1**, derived from (+)-camphene, with 2-phenyl-1,3-butadiene (Scheme 1).[8] However, although the yield of the oxidized products and the *para* regioselectivity were high, the enantiomeric excess of the major regioisomer was lower than 10%.

One of the main goals of our group is to develop new chiral unsaturated boron compounds that exhibit high reactivity and selectivity as dienophiles in Diels–Alder reactions. Such compounds have a tremendous potential as precursors of chiral building blocks in asymmetric synthesis.

Initially, we thought that dialkylvinylboranes **2–6** shown in Scheme 2 would be good candidates because the stereocenters are directly bonded to the boron atom, and therefore closer to the prochiral olefin than in the derivative of (+)-camphene (**1**).[19] Furthermore, compounds **2–4** could be readily synthesized from commercial optically pure terpenes (+)-α-pinene, (+)-2-carene and (+)-3-carene.[20,21] For that purpose, we tested the reaction sequence shown in Scheme 3 for (+)-α-pinene, analogous to that developed previously by

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Singleton for (+)-camphene (Scheme 1),[8] consisting of hydroboration, transmetallation, Diels–Alder reaction and oxidation. *In situ* preparation of intermediates **7**, **2** and **8** under inert atmosphere would avoid the manipulation of the labile boranes. Unfortunately, although numerous reactions were tested for the three chiral terpenes with different reagents and reaction conditions, we failed to detect the presence of the desired products.[22] By monitoring the reaction by ^{1}H NMR under inert atmosphere we observed that, although the hydroboration step occurred efficiently, transmetallation of the dialkylhaloboranes did not go to completion. We managed to avoid this difficulty by generating the monohaloborane free of dimethylsulfide *in situ* with trihaloborane and triethylsilane.[23] Nevertheless, when using this method we could not detect the formation of product **9** either, possibly due to the competitive dimerization of the vinylboranes[6] and the protodeboronation of the cycloadducts.
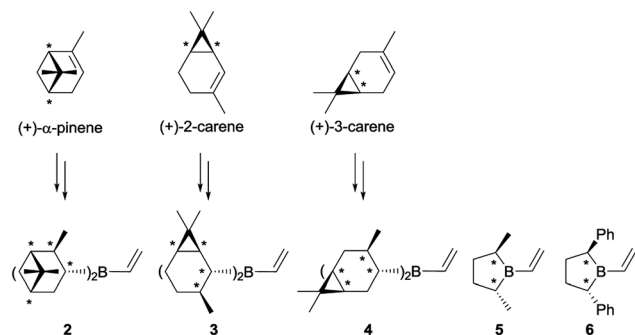
Alternative use of cyclohexene as an achiral model of starting alkene, to generate dicyclohexylvinylborane (**10**), also gave negative results. These initial results demonstrated that dialkylvinylboranes with secondary carbons attached to the boron atom, such as **2–4** and **10**, are highly congested, which complicates their synthesis and the course of their Diels–Alder reactions.[19]
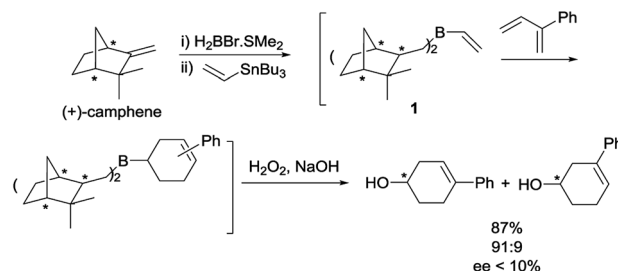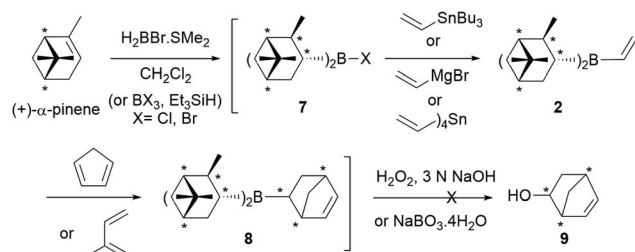

Scheme 1 Synthesis and Diels–Alder reaction of chiral dialkylvinylborane **1**.

Scheme 2 Chiral dialkylvinylboranes with secondary carbons attached to boron.

Scheme 3 One-pot synthesis of chiral dialkylvinylborane **2**, followed by Diels–Alder reaction and oxidation. The same procedure was tested for (+)-2-carene and (+)-3-carene and cyclohexene.

To circumvent these problems, it occurred to us that alkylhalovinylboranes would represent an interesting alternative to dialkylvinylboranes because the boron atom would be less sterically hindered and more electron deficient, which should ultimately increase the reactivity in Diels–Alder reactions (Fig. 1).[24] In this paper, we present the results of a theoretical study of the Diels–Alder reactions of a number of alkylhalovinylboranes with cyclopentadiene, together with the experimental development of a one-pot procedure that includes the synthesis of the dienophiles, the Diels–Alder reaction and the oxidation of the products.

Results and discussion

Model studies with cyclohexene vinylborane derivatives

To validate our hypothesis, we first performed a comparative study of the reactivity of dicyclohexylvinylborane (**10**), chlorocyclohexylvinylborane (**11a**) and bromocyclohexylvinylborane (**11b**), derived from cyclohexene as achiral models of the dienophiles. Initially, we investigated the Diels–Alder reactions of vinylboranes **10**, **11a** and **11b** with cyclopentadiene, a highly

Fig. 1 Dialkylvinylboranes and alkylhalovinylboranes.

reactive and easily accessible diene, with theoretical methods. Due to the absence of chiral centres in the alkyl moiety, only *endo* and *exo* attacks should be considered, which, in turn, would give rise to diastereomeric products as racemic mixtures. After oxidation, racemic *endo* and *exo* alcohols **9** might arise.
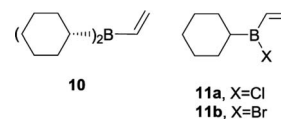
All calculations were performed with the Gaussian 09 package.[25] We carried out thorough conformational analyses to locate the lowest energy geometry for all the structures under study. Final geometry optimizations were carried out using the B3LYP hybrid functional together with the 6-31G* basis set. The selection of this level of theory was based on existing records in the literature for the modelling of Diels–Alder reactions.[19,26–32] Additionally, solvent effects in dichloromethane ($\varepsilon = 8.93$) and heptane ($\varepsilon = 1.91$) were calculated for the most stable geometries of reagents, transition structures (TSs), and products using the Polarized Continuum Model of Self-Consistent Reaction Field method (PCM method).[33,34] Furthermore, the molecular orbitals (MOs) of reagents were calculated to analyse the Frontier molecular orbital interactions and Natural Bond Orbitals (NBOs) analysis of TSs were performed using Wiberg bond indices for interpreting most relevant electronic interactions.[35–38] Finally, we performed Intrinsic Reaction Coordinate calculations (IRC) to verify if the TSs were directly connected to the reactants and the products.

Fig. 2 shows the correlation diagrams for the Diels–Alder reactions of vinylboranes **10**, **11a**, and **11b** with cyclopentadiene. Analysis of MOs of the reagents shows that all Diels–Alder reactions under study are of normal electron-demand dominated by the HOMO$_{diene}$–LUMO$_{dienophile}$ interaction. As expected, the LUMOs of the vinylboranes have large
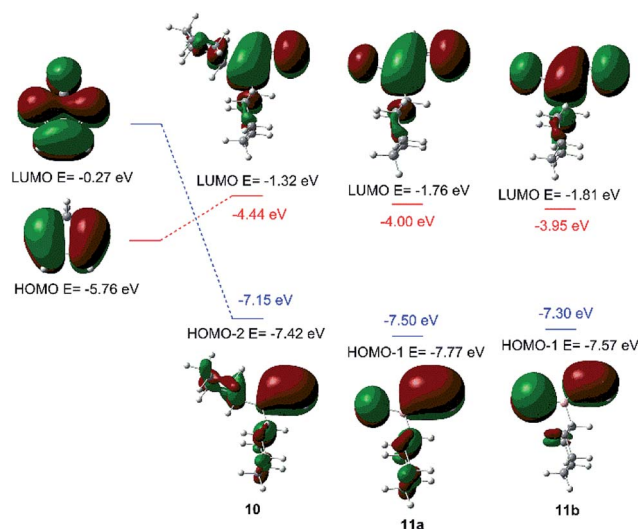

Fig. 2 Correlation diagrams for the Diels–Alder reaction of vinylboranes **10**, **11a**, and **11b** with cyclopentadiene. Energy gaps are shown in red and blue.
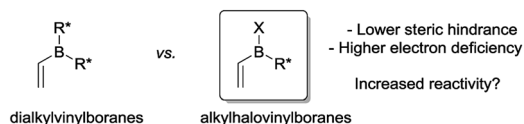
coefficients on the two carbon atoms of the carbon–carbon double bond of the vinyl group, and also on the boron atoms. This feature promotes the non-classical [4 + 3] secondary orbital interaction (SOI) between the boron atom of vinylboranes and C1 of the diene, resulting in an increase in the observed *endo*-selectivity. Both FMOs of haloalkylvinylboranes **11a** and **11b** also show important coefficients in the halogen atoms too. The presence of the halogen attached to the boron atom lowers the LUMO energy significantly (*ca.* 0.5 eV) and, therefore, the energy gap for the HOMO$_{diene}$–LUMO$_{dienophile}$ interaction of **11a** and **11b** is lower than the value obtained for **10**, which suggests greater reactivity for alkylhalovinylboranes with respect to the corresponding dialkylvinylborane.[39]

Fig. 3 shows the optimized geometries of the most stable conformers for the TSs for the Diels–Alder reaction of vinyl-boranes **10**, **11a**, and **11b** with cyclopentadiene, with the carbon–carbon and C6–B bond distances (in Å) and Wiberg bond indices in parentheses. C6–B distances are approximately 3.1 Å and NBOs of 0.08 and 0.06 indicating that the SOI [4 + 3] are weak. In the IRC studies no intermediate structures between reagents and TSs and between TSs and products were found, confirming that the Diels–Alder reactions under study are concerted. Although in these reactions all bonds are formed and broken in a single stage, all TSs are asynchronous with carbon–carbon distances approximately of 2.0 Å for C2–C3 and 2.6 Å for C1–C6.[40,41] As shown in Fig. 3, the dienophile portion of the structures corresponding to **11a** and **11b** adopts the same conformation in all TSs, the halogen attached to the boron atom is anti relative to the adjacent axial hydrogen atom of the

Table 1 Calculated activation free energies and *endo/exo* selectivities for the Diels–Alder reaction of vinylboranes **10**, **11a**, and **11b** with cyclopentadiene. Relative activation free energies are shown in parenthesis

	Vinylborane	$\Delta G^{\ddagger}$, kcal mol^{-1} ($\Delta G^{\ddagger}_{rel}$)		*endo/exo*
		endo	*exo*	
Gas phase	**10**	32.28 (0.00)	32.39 (0.12)	55 : 45
	11a	30.10 (0.00)	30.22 (0.12)	55 : 45
	11b	27.22 (0.00)	27.34 (0.12)	55 : 45
Heptane	**10**	16.52 (0.00)	16.73 (0.21)	59 : 41
	11a	12.71 (0.00)	13.25 (0.54)	71 : 29
	11b	10.62 (0.00)	11.01 (0.38)	65 : 35

cyclohexyl group and the double bond is eclipsed with the boron–halogen bond. Table 1 shows the activation free energies ($\Delta G^{\ddagger}$) calculated in the gas phase and heptane of the three systems derived from cyclohexene. As expected, the relative energies of the TSs in the gas phase are considerable higher than in solution. However, in both cases the reactions of **11a** and **11b** have lower activation free energies than those for **10**, which in principle indicates higher reactivity for the alkylhalo-vinylborane compounds relative to the dialkylvinylborane counterpart. Also, *endo* TSs were computed to be more stable than the *exo* isomers for all systems. Selectivity calculations were performed at 298 K using the Boltzmann equation with the activation free energies calculated for the TSs. The selectivity values obtained for **10**, **11a** and **11b** are shown in Table 1. For alkylhalovinylboranes **11a** and **11b**, the *endo/exo* selectivity is significantly higher in solution than the gas phase. The computed energies of the products also suggested that the reactions under study are exergonic (see the ESI†).

Encouraged by these promising results, we then studied and optimised the reaction sequence shown in Scheme 4. Many experiments were performed using different reaction times and temperatures, as well as number of equivalents and modes of addition of reagents. Fortunately, our hypothesis, which was supported by the calculations, proved to be correct and we managed to obtain the expected products. Initial reaction of trichloroborane with one equivalent of triethylsilane in the presence of 1.1 equivalents of cyclohexene readily gave dichloroborane, which subsequently hydroborated the starting
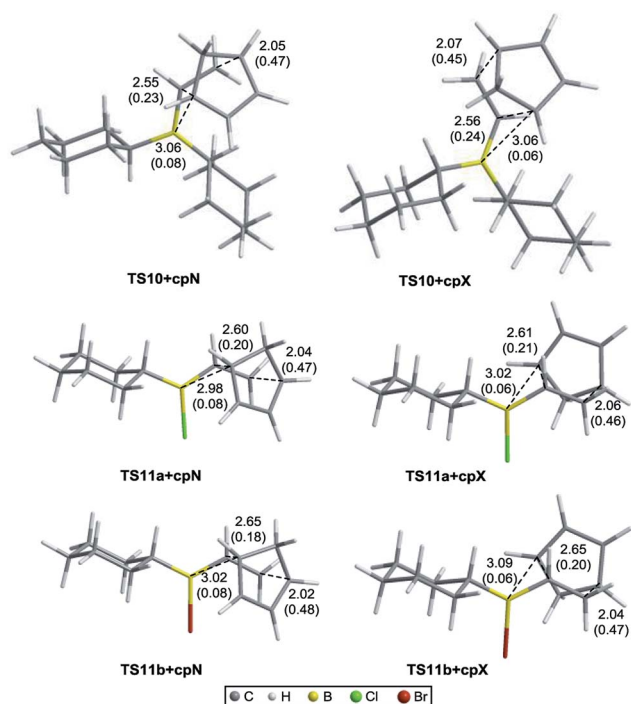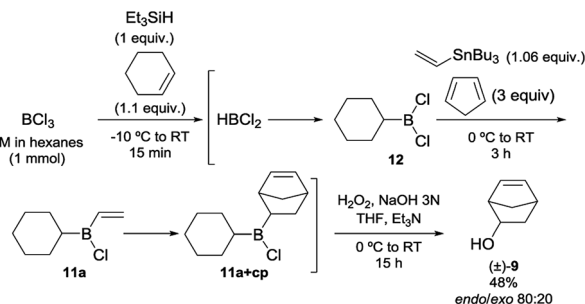

Fig. 3 Optimized geometries of the TSs for the Diels–Alder reaction of vinylboranes **10**, **11a**, and **11b** with cyclopentadiene, with carbon–carbon and C6–B bond distances (in Å) and Wiberg bond indices in parentheses.

Scheme 4 One-pot synthesis of chlorocyclohexylvinylborane (**11a**), followed by Diels–Alder reaction and oxidation.
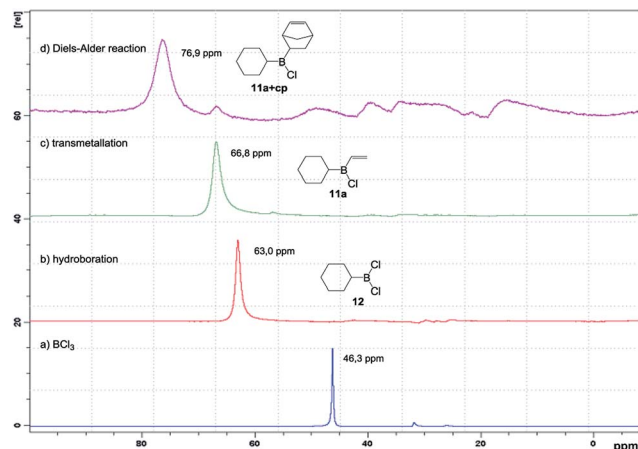
**Fig. 4** ^{11}B NMR of the consecutive steps of the synthetic sequence.

alkene, giving rise to dichlorocyclohexylborane (**12**). Simultaneous addition of one equivalent of tributylvinyltin and three equivalents of cyclopentadiene successively generated the desired dienophile **11a** and cycloadduct (**11a+cp**). Final oxidation of the reaction mixture conducted to 5-norbornen-2-ol (**9**) in 48% global yield with 80 : 20 *endo/exo* selectivity. The consecutive steps of the synthetic sequence were monitored by ^{11}B NMR under inert atmosphere (Fig. 4), which allowed the optimization of the reaction conditions.

Studies with chiral terpene vinylborane derivatives

Having accomplished the proof of concept with the achiral models, we then turned our attention to the Diels–Alder reactions of chiral alkylhalovinylboranes derived from (−)-α-pinene, (+)-2-carene, (+)-3-carene as starting alkenes. To increase the structural diversity of the ligands, we also included (−)-myrtenol, which has the same carbon skeleton as (−)-α-pinene and allows the preparation synthetic derivatives **13–15** due to the presence of the hydroxymethyl group (for synthetic procedures see the ESI†). We figured that the presence of a heteroatom or an aromatic ring in the side chain of the dienophile would introduce further steric and electronic features, which in turn might contribute to reduce the conformational flexibility and, therefore, increase the stereoselectivity of the cycloaddition.
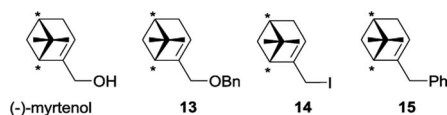
The Diels–Alder reactions of the resulting alkylhalovinylboranes **16–22** with cyclopentadiene were first studied theoretically (Scheme 5). In these cases, four diasteromeric Diels–Alder cycloadducts might arise from the *endo* and *exo* attacks of the diene to both faces of the double bond of the chiral alkylhalovinylborane (*Re* and *Si*). Upon oxidation such compounds would be converted into two diastereomeric pairs of enantiomers.
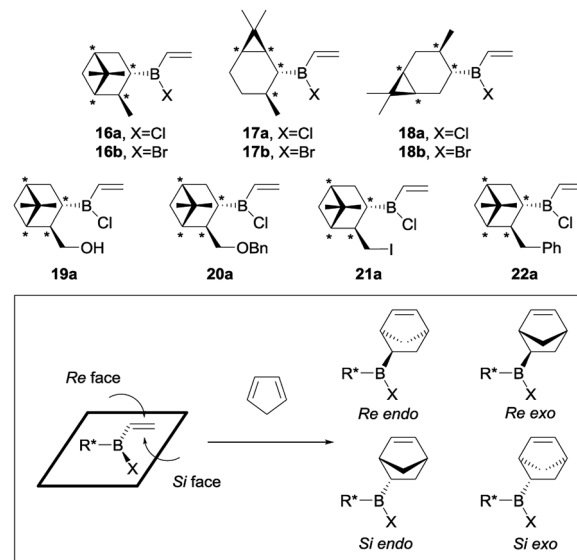
Scheme 5 Diels–Alder reactions of chiral alkylhalovinylboranes **16–22** with cyclopentadiene.

As an example, the optimized geometries of the most stable conformers for the TSs for the Diels–Alder reaction of vinylborane **16a** with cyclopentadiene are depicted in Fig. 5. Tables 2 and 3 present the activation free energies ($\Delta G^{\ddagger}$) and the stereoselectivities calculated in the gas phase and heptane for the Diels–Alder reactions of chiral alkylhalovinylboranes. In general terms, all [4 + 2] cycloadditions of chiral alkylhalovinylboranes present the same features as the reactions of cyclohexylhaloboranes **11a** and **11b**:

- Normal electron demand Diels–Alder reactions (HOMO$_{diene}$–LUMO$_{dienophile}$ ~4 eV).

- LUMOs of the dienophiles show high coefficients on the C–C double bond, the boron and the halogen atoms.

- Concerted reactions with asynchronous TSs with classical [4 + 2] character and weak C–B [4 + 3] SOI (C$_2$–C$_3$, C$_1$–C$_6$ and C$_6$–B distances 2.0, 2.6, and 3.0 Å respectively).

- $\Delta G^{\ddagger}$ in heptane 13–15 kcal mol^{-1} for chloroalkylboranes and 11 kcal mol^{-1} for bromoalkylboranes.
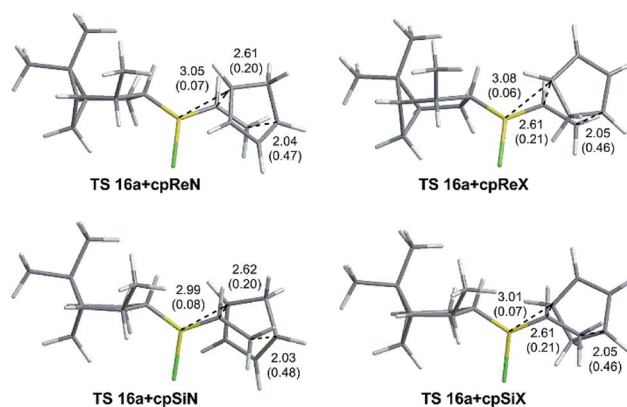

Fig. 5 Optimized geometries of the TSs for the Diels–Alder reaction of vinylboranes **16a** with cyclopentadiene with the carbon–carbon and C6–B bond distances (in Å) and Wiberg bond indices in parentheses.

Table 2 Calculated activation free energies for the Diels–Alder reaction of alkylhalovinylboranes **16–22** with cyclopentadiene. Relative activation free energies are shown in parenthesis

| | Vinylborane | $\Delta G^{\ddagger}$, kcal mol^{-1} ($\Delta G^{\ddagger}_{rel}$) | | | |
		Re endo	Re exo	Si endo	Si exo
Gas phase	**16a**	29.89(0.78)	29.79(0.68)	29.23(0.12)	29.11(0.00)
	16b	27.32(0.42)	27.43(0.52)	26.90(0.00)	26.91(0.01)
	17a	30.09(0.51)	30.37(0.78)	29.58(0.00)	29.68(0.10)
	17b	28.40(1.04)	27.72(0.35)	27.50(0.13)	27.37(0.00)
	18a	29.18(0.00)	29.44(0.26)	30.36(1.18)	30.05(0.87)
	18b	27.31(0.30)	27.02(0.00)	27.71(0.69)	27.54(0.53)
	19a	30.80(2.03)	28.76(0.00)	30.25(1.49)	29.78(1.02)
	20a	29.97(0.00)	30.64(0.67)	30.58(0.61)	30.78(0.80)
	21a	31.64(0.69)	31.56(0.60)	31.17(0.22)	30.95(0.00)
	22a	29.30(0.74)	29.37(0.81)	28.56(0.00)	28.87(0.31)
Heptane	**16a**	13.43(0.46)	14.07(1.11)	12.96(0.00)	13.48(0.52)
	16b	11.46(0.50)	11.67(0.71)	10.96(0.00)	11.20(0.24)
	17a	13.56(0.23)	13.97(0.63)	13.34(0.00)	13.72(0.38)
	17b	11.65(0.27)	11.53(0.15)	11.40(0.02)	11.38(0.00)
	18a	12.99(0.00)	13.50(0.51)	13.16(0.16)	13.57(0.58)
	18b	10.86(0.00)	11.14(0.28)	11.26(0.40)	11.06(0.21)
	19a	13.71(0.83)	12.88(0.00)	13.79(0.91)	13.82(0.93)
	20a	15.40(1.38)	14.02(0.00)	14.02(0.00)	14.48(0.46)
	21a	16.00(0.92)	16.54(1.47)	15.08(0.00)	15.69(0.61)
	22a	14.67(1.10)	15.15(1.59)	13.56(0.00)	14.07(0.51)

Table 3 Calculated stereoselectivities for the Diels–Alder reaction of alkylhalovinylboranes **16–22** with cyclopentadiene

	Vinylborane	endo/exo	endo Re/Si	exo Re/Si	Re/Si
Gas phase	**16a**	45 : 55	25 : 75	24 : 76	25 : 75
	16b	51 : 49	33 : 67	29 : 71	31 : 69
	17a	56 : 44	30 : 70	24 : 76	27 : 73
	17b	38 : 62	18 : 82	36 : 64	29 : 71
	18a	57 : 43	88 : 12	73 : 27	82 : 18
	18b	39 : 61	66 : 34	71 : 29	69 : 31
	19a	9 : 91	29 : 71	85 : 15	80 : 20
	20a	70 : 30	74 : 26	56 : 44	68 : 32
	21a	42 : 58	31 : 69	27 : 73	29 : 71
	22a	60 : 40	23 : 77	30 : 70	26 : 74
Heptane	**16a**	72 : 28	31 : 69	27 : 73	30 : 70
	16b	59 : 41	30 : 70	31 : 69	31 : 69
	17a	66 : 34	41 : 59	40 : 60	40 : 60
	17b	47 : 53	40 : 60	44 : 56	42 : 58
	18a	68 : 32	57 : 43	53 : 47	56 : 44
	18b	53 : 47	66 : 34	47 : 53	57 : 43
	19a	28 : 72	53 : 47	83 : 17	74 : 26
	20a	43 : 57	9 : 91	68 : 32	43 : 57
	21a	73 : 27	18 : 82	19 : 81	18 : 82
	22a	70 : 30	14 : 86	14 : 86	14 : 86

Computed *endo/exo* stereoselectivities are higher for the chloro analogues than for the bromo counterparts and vary considerably (from 28 : 72 to 72 : 28 in heptane). Likewise, *Re/Si* facial selectivities are variable, ranging from 74 : 26 for **19a** to 14 : 86 for **22a**. Since the free energies of the four TSs are within 1 kcal mol^{-1} for most systems, none of the approximations would be clearly favoured and all cycloadducts would be formed, albeit in different amounts. Both electronic, steric and stereoelectronic effects seem to contribute to give the computed

reactivities and selectivities. As found before, in all TSs the vinylborane portion adopts the same conformation in which the halogen attached to the boron atom and the hydrogen of the vicinal carbon adopt a antiperiplanar relationship and the double bond is eclipsed with the boron–halogen bond.
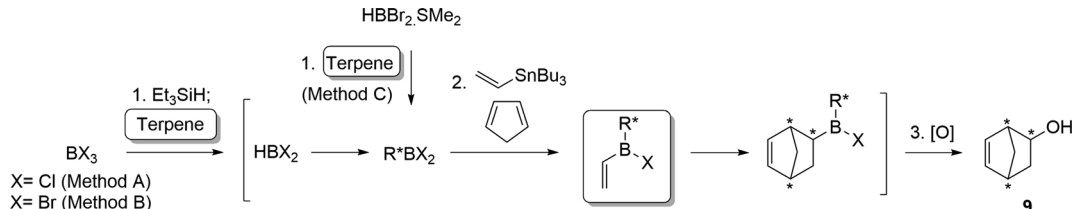
As a consequence the substituents of the carbon backbone (for instance, methyls for **16–18**) block preferentially one face of the dienophile and the attack of the diene occurs from the other face.

As an example, in the TSs of the vinylborane derived from (−)-α-pinene (**16a**), the methyl shields the *Re* face, making the *Si endo* approximation more favourable (Fig. 5). The same situation is observed for the derivatives of (+)-2-carene (**17**), while for the (+)-3-carene counterparts (**18**) the facial selectivity is reversed because the methyl group is on the other side of the molecule and, therefore, steric clashes would make the attack of the *Si* face more difficult. The synthetic analogues derived from (−)-myrtenol **21a** and **22a** were predicted to give the highest *endo/exo* and *Re/Si* facial stereoselectivities.

Since the reactions conditions had already been optimised using cyclohexene as the starting alkene (Scheme 4), we next investigated the use of the chiral terpenes and synthetic derivatives as staring materials. The reaction sequences were first investigated using (+)-3-carene and different reagents as the boron source: BCl$_3$ (1 M in hexanes), BBr$_3$ and HBBr$_2$·SMe$_2$ (1 M in CH$_2$Cl$_2$). The reoptimised reaction conditions for the consecutive steps of the synthetic sequences were then used with the chiral terpenes and derivatives (Table 4).

(+)-Longifolene and (−)-camphene with exocyclic double bonds, which generate primary alkylhalovinylboranes **23** and **24** respectively, were also included in the experimental study (Scheme 6).
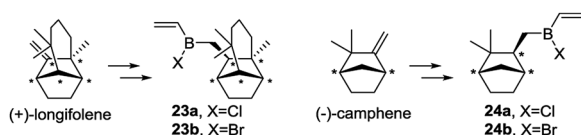
Table 4 Experimental results for the tandem hydroboration, transmetallation, Diels–Alder reaction with cyclopentadiene and oxidation for chiral terpenes and synthetic derivatives

Terpene/vinylborane	Method[a]	Global yield (%)	endo/exo	endo Re/Si (R/S)	exo Re/Si (R/S)	Re/Si
(+)-α-Pinene/**16′a**[b]	A	51	80 : 20	53 : 47	50 : 50	51 : 49
(+)-(2)-Carene/**17a**	A	34	76 : 24	30 : 70	48 : 52	39 : 61
(+)-(3)-Carene/**18a**	A	54	79 : 21	62 : 38	48 : 52	55 : 45
(−)-Myrtenol/**19a**	A	21	76 : 24	48 : 52	50 : 50	49 : 51
13/20a	A	27	78 : 22	47 : 53	44 : 56	46 : 54
14/21a	A	24	79 : 21	45 : 55	45 : 55	45 : 55
15/22a	A	26	78 : 22	47 : 53	50 : 50	49 : 51
(+)-Longifolene/**23a**	A	42	79 : 21	44 : 56	50 : 50	47 : 53
(−)-Camphene/**24a**	A	41	78 : 22	48 : 52	52 : 48	50 : 50
(+)-α-Pinene/**16′b**[b]	B	36	90 : 10	50 : 50	50 : 50	50 : 50
(+)-(2)-Carene/**17b**	B	35	91 : 9	49 : 51	50 : 50	50 : 50
(+)-(3)-Carene/**18b**	B	32	93 : 7	48 : 52	50 : 50	49 : 51
13/20b	B	27	86 : 14	48 : 52	50 : 50	49 : 51
15/22b	B	30	96 : 4	45 : 55	50 : 50	48 : 52
(+)-Longifolene/**23b**	B	32	91 : 9	47 : 53	50 : 50	49 : 51
(−)-Camphene/**24b**	B	28	93 : 7	50 : 50	50 : 50	50 : 50
(+)-(2)-Carene/**17b**	C	10	60 : 40	45 : 55	50 : 50	48 : 52
(+)-(3)-Carene/**18b**	C	23	74 : 26	50 : 50	49 : 51	50 : 50

[a] Method A: (1) BCl₃ (1 M in hexanes, 1 mL), Et₃SiH (1 equiv.), alkene (1.1 equiv.), −10 °C to RT, 1 h; (2) tributilvinylstannane (1 equiv.), cyclopentadiene (5 equiv.), 0 °C to RT, 3 h; (3) THF (3 mL), Et₃N (1 mL), NaOH 3 N (3 mL), H₂O₂ 30% (3 mL), 0 °C to RT, 15 h. Method B: (1) CH₂Cl₂ (1 mL), BBr₃ (1 mmol), Et₃SiH (1 equiv.), alkene (1.1 equiv.), −40 °C to RT, 2 h; (2) same as Method A, 5 h; (3) same as Method A. Method C: (1) HBBr₂·SMe₂ (1 M in CH₂Cl₂, 1 mL), alkene (1.1 equiv.), −10 °C to reflux, 2 h; (2) tributilvinylstannane (1 equiv.), cyclopentadiene (5 equiv.), 0 °C to reflux, 5 h, then RT, 15 h; (3) same as Method A, 4 h. [b] Compounds **16′a** and **16′b** are the enantiomers of **16a** and **16b**, respectively.

Based on the literature, and the results of our theoretical calculations, we assumed that different reactivities would be observed for boron trichloride and tribromide (Methods A and B). However, only differences in reactivity were observed in the initial steps, which had to be initiated at −40 °C for boron tribromide to avoid that temperatures increased and secondary reactions took place. ¹¹B NMR indicated that transmetallation and Diels–Alder reactions occurred at similar rates. On the other hand, when HBBr₂·SMe₂ was used (Method C), much lower reactivity was observed, probably due to the lower electron deficiency on boron of the dimethyl sulfide complexes of the reacting species in the studied sequence. As a consequence, reaction times and temperatures had to be increased and yields dropped considerably perhaps as a result of secondary reactions.

In general, global yields for chiral terpenes and synthetic derivatives were comparable to those previously obtained with achiral cyclohexene, although much lower numbers were obtained for HBBr₂·SMe₂ and consequently only (+)-(2)- and (+)-(3)-carene were tested with Method C.

Facial selectivities (Re/Si) and resulting enantiomeric ratios and absolute configurations (R/S) of the products of oxidation (endo- and exo-5-norbornen-2-ol, **9**) were determined by ¹H NMR using a methodology developed in our group that involves the use of (S)-(+)-O-acetylmandelic acid as chiral derivatising agent.[42,43] Endo-selectivities were good to excellent. In particular, bromovinylboranes obtained with BBr₃ (Method B) gave endo/exo ratios higher than 86 : 14, with vinylborane **22b** derived from synthetic analogue **15** displaying the best endo-selectivity (endo/exo 96 : 4). When BCl₃ was used, (+)-α-pinene-derived vinylborane **16′a** showed the highest endo-selectivity (endo/exo 80 : 20). Disappointingly, facial selectivities were low. The chlorovinylborane derived from (+)-2-carene **17a** exhibited the highest chiral induction (Re/Si 30/70 for the major endo diastereoisomer). Although we hoped to get better enantiomeric ratios, such value is considerably higher than those obtained for other Diels–Alder reactions of boron-substituted dienophiles

Scheme 6 (+)-Longifolene and (−)-camphene and derived alkylhalovinylboranes **23** and **24**.
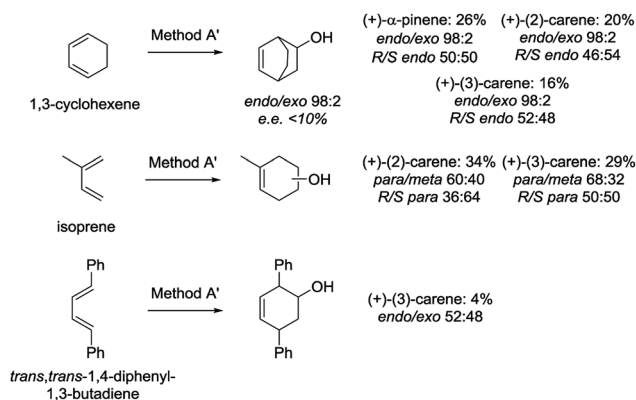
Scheme 7 Diels–Alder reactions of alkylchlorovinylboranes **16′a–18a** with other dienes.

(ee < 10%), such as the one of dialkylvinylborane **1**, derived from (+)-camphene, with 2-phenyl-1,3-butadiene (Scheme 1).[8,44,45]

As can be observed in Tables 3 and 4, experimental *endo*-selectivities for the Diels–Alder reactions of chlorovinylboranes were correctly predicted by the theoretical calculations. In contrast, computed *endo*-selectivities for bromovinylboranes were lower than those for chlorovinylboranes and than the experimental values. In general, experimental facial selectivities were in accordance to the ones computed in the theoretical study. In addition, the calculations predicted that activation free energies for bromovinylboranes would be 2 kcal mol⁻¹ lower than those for the chloro counterparts. However, experimental yields were comparable, and in some cases lower to those obtained with chlorovinylboranes. We believe that this is caused by the great reactivity of BBr$_3$, which decomposes rapidly during manipulation and generates experimental difficulties.

To determine the scope of the studied reactions, we performed preliminary experiments for the Diels–Alder reactions of alkylchlorovinylboranes **16′a–18a** with other dienes (1,3-cyclohexene, isoprene and *trans,trans*-1,4-diphenyl-1,3-butadiene) (Scheme 7).

Reaction conditions were the same as for cyclopentadiene (Method A, Table 4), except that the transmetallation-Diels–Alder reaction step was carried out at reflux for 5 h (Method A′). Global yields for 1,3-cyclohexene and isoprene were lower than those obtained with cyclopentadiene (16–34%) and poor for *trans,trans*-1,4-diphenyl-1,3-butadiene. Furthermore, the *endo/exo* selectivity for 1,3-cyclohexene was excellent (*endo/exo* 98 : 2), while the *para/meta* regioselectivity for isoprene above 60 : 40. In general, enantiomeric excesses for both dienes were <10%, except for the reaction of isoprene with the chlorovinylborane derived form (+)-(2)-carene **17a** (*R/S para* 36 : 64). This indicates that more experiments should be performed to optimise the reaction conditions.

Conclusions

In this investigation we explored the synthesis and the Diels–Alder reactivity of alkylhalovinylboranes with computational and experimental methods. We verified the viability of our initial postulate that the replacement of an alkyl group in

dialkylvinylboranes by a halogen on the boron atom of the dienophile increases the reactivity of the vinylborane significantly. Overall, experimental results were in line with those predicted by theoretical calculations. Alkylhalovinylboranes displayed high *endo/exo* selectivities, in particular for bromovinylboranes. Unfortunately, in general enantioselectivities obtained for the oxidized products were low. However, the highest value obtained with (+)-2-carene-derived chlorovinylborane (**17a**) was much higher than those described in the literature for Diels–Alder reactions of other boron-substituted dienophiles. This work contributes to a little-explored area of study, as is the use of chiral vinylboranes in asymmetric cycloaddition reactions. Finally, this novel example of the use of alkylhalovinylboranes in synthesis highlights the practical potential of such organoboron species, which may be applied to other transformations.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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