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Theoretical investigation of the Diels–Alder reactions of unsaturated boronates†

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The Diels–Alder reactions of simple unsaturated boronates have been investigated using computational methods and the results were compared with those for the analogue dihalo- and dialkylboranes. Our results indicate that the activating effect of the boronate moiety is small. All the studied reactions are concerted normal electron-demand Diels–Alder reactions with asynchronous transition structures and weak [4 + 3] C–B secondary orbital interactions, which explains the low experimental reactivity. Both electronic and steric effects contribute to give the observed low stereo- and regioselectivities.

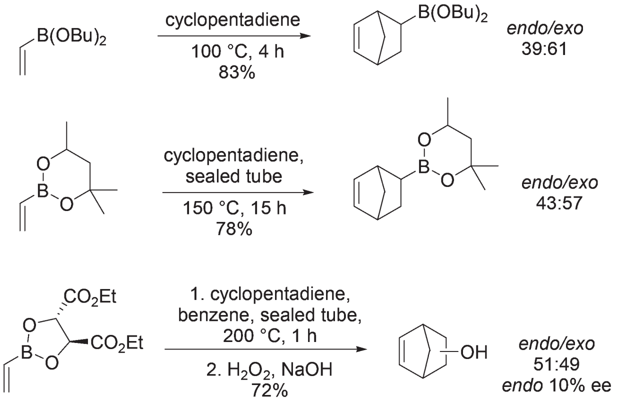
Introduction

Boron-substituted dienophiles participate in Diels–Alder reactions under thermal conditions.[1,2] Simple vinylboronates, such as the butanol,[3,4] 2-methyl-2,4-pentanediol[5] and (−)-diethyl tartrate[6] derivatives, have been shown to display modest reactivity and selectivities.[7] Scheme 1 shows the [4 + 2] cycloadditions with cyclopentadiene, a reactive cyclic 1,3-diene.

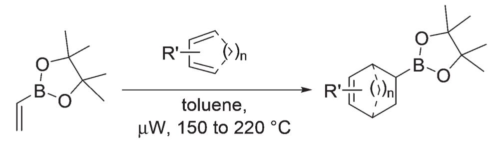
Recently, we described that the Diels–Alder reactions of pinacol vinylboronate with a variety of cyclic and acyclic dienes can be performed under microwave irradiation in short reaction times (1–6 h) to yield the boronate cycloadducts in excellent yields (>90%) (Scheme 2).[8] For example, the reaction with cyclopentadiene was complete in 1 h at 150 °C, affording the products in quantitative yield with a 38 : 62 *endo*/*exo* ratio.

The synthetically versatile cyclohexenylboronate products tolerate a wide range of reaction conditions for further elaboration of C–C, C–O and C–N bonds.

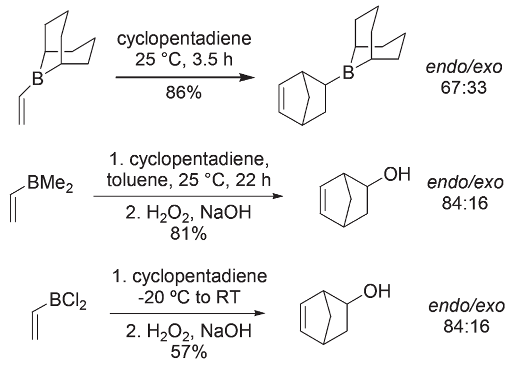
Dialkylvinylboranes react at much lower temperatures than those required for the corresponding vinylboronates and give higher *endo*-selectivities (Scheme 3). For example, 9-vinyl-9-BBN[9] and dimethylvinylborane[10] react with cyclopentadiene at room temperature. Dihalovinylboranes, such as dicholorovinylborane,[11,12] exhibit even higher reactivity. However, in contrast to vinylboronates which are more stable and can be easily



Scheme 1



Scheme 2



Scheme 3

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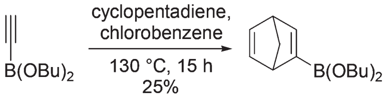


Scheme 4

manipulated and purified, alkenylboranes often have to be prepared *in situ* and the cycloadducts derivatised.

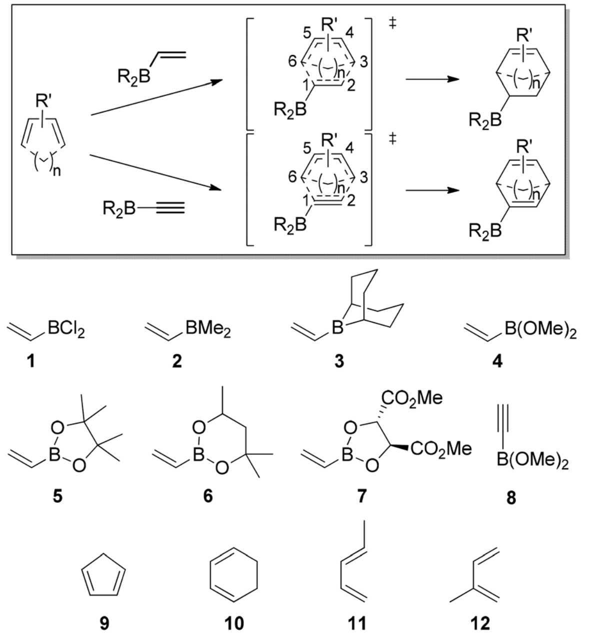
Apart from the inverse electron-demand Diels–Alder reactions recently described by Harrity and co-workers,[13] the reports on [4 + 2] cycloadditions of alkynylboronates with simple dienes are limited. For instance, Matteson described the reaction of dibutyl acetyleneboronate with cyclopentadiene to generate dibutyl norbornadien-2-boronate with 25% yield (Scheme 4).[3,14]

An early computational study suggested that the [4 + 2] cycloadditions of dialkylvinylboranes had [4 + 3] transition states.[15] We later showed that the secondary orbital interaction (SOI) with the boron atom becomes less important when the size of the alkyl groups on boron increases, which generates a decrease in the *endo*-stereoselectivity.[16,17] In general, for small alkyl groups, electronic effects appear to govern the course of the reaction, whereas for bulky ligands, steric effects dominate the regio- and stereoselectivity.

Results and discussion

The aims of this study were to extend the scope of the existing theoretical studies on Diels–Alder reactions of boron-activated dienophiles. In particular, we wanted to rationalise the experimental reactivity and selectivity of simple unsaturated boronates as Diels–Alder dienophiles and to compare the results with those for unsaturated dihalo- and dialkylboranes. Also, we aimed to analyse whether the reactions were normal or inverse electron-demand Diels–Alder reactions. To our knowledge, no reports on theoretical studies for the Diels–Alder reactions of alkenylboronates have been described to date. In addition, only the mechanisms of the cycloadditions of alkynylboronates to tetrazines and furans,[13e] sydnones[13j] and 2-pyrones[13n] have been computationally investigated. We have theoretically studied the Diels–Alder reaction of boron-activated alkenes and alkynes with different substituents on the boron atom (Scheme 5).[18] We have chosen varied substituents on boron (compounds **1–8**) to study and compare the reactivity and selectivity in the reaction with cyclopentadiene.[19] In addition, we have studied the Diels–Alder reactions of pinacol vinylboronate (**5**) with four different dienes: cyclopentadiene, cyclohexadiene, *trans*-piperylene and isoprene (compounds **9–12**). The results are summarised in Tables 1–4 and Fig. 1–3.[20]

We initially carried out conformational searches for the reactants, the transition structures (TSs) and the products to locate the global minima at the B3LYP/6-31G* level of theory.[21] The conformers thus obtained were characterised by computing the frequencies. The molecular orbitals of the reactants were calculated to analyse the frontier molecular orbital interactions. Intrinsic reaction coordinate (IRCs) calculations were run to verify the connectivity between reactants, TSs and products. To examine the more important interactions in the TSs (C_1–C_6, C_2–C_3 and C_6–B) we performed natural bond orbital calculations and Wiberg bond indexes (WBIs) were analysed. Free energies in solution were computed on the structures optimized in the gas phase at the B3LYP/6-31G* level of theory with the polarisable continuum model (PCM) using toluene and dichloromethane as solvents ($\varepsilon_{\mathrm{DCM}}$ = 8.93, $\varepsilon_{\mathrm{Toluene}}$ = 2.38).[22] Finally, theoretical results were compared with the experimental results described in the literature and the reactivity and selectivity patterns were analysed.[23] All the calculations were run with Gaussian 03.[24]



Scheme 5

All the studied reactions were computed to be normal electron-demand Diels–Alder reactions, governed by the $\mathrm{HOMO_{diene}}$–$\mathrm{LUMO_{dienophile}}$ interaction (Table 1). For boronates **4–8**, this observation differed from previous results for the reactions with tetrazines[13e] and 2-pyrones,[13n] which suggested that alkynylboronates might perform as inverse electron demand dienophiles. Fig. 1 shows the shapes, the energies and the coefficients of the FMOs of some of the studied dienophiles. As anticipated, the LUMOs of the boron activated dienophiles under study are localised on the carbon–carbon double bond of the vinyl group, with higher coefficients for C_2 than for C_1 (0.36–0.52 for C_2 and 0.16–0.39 for C_1) and also on the boron atom (0.25–0.42). Boronates **4–8** also exhibit less significant coefficients on the oxygen atoms attached to boron (0.14–0.21). The topological properties of the LUMOs of **1–8** provide a rationale to explain the activation of the boron-substituted dienophiles and the non-classical [4 + 3] secondary orbital interaction between the boron atom of the borane and C_6 in the diene in the transition structures of the Diels–Alder

Table 1 Selected distances and Wiberg Bond Indexes for the transition structures of the Diels–Alder reactions of boron-substituted dienophiles and energy gaps between the FMOs of the reactants

			Distances (Å) (Wiberg Bond Indexes, WBIs)			ΔE (eV)	
Diene	Dienophile	Transition structure	C_2–C_3	C_1–C_6	C_6–B	$HOMO_{diene}$–$LUMO_{dienophile}$	$HOMO_{dienophile}$–$LUMO_{diene}$
9	**1**	*endo*	2.03 (0.48)	2.62 (0.19)	3.01 (0.07)	3.55	7.81
		exo	2.05 (0.46)	2.63 (0.20)	3.05 (0.06)		
	2	*endo*	2.07 (0.46)	2.51 (0.23)	2.83 (0.10)	4.56	7.19
		exo	2.08 (0.44)	2.53 (0.24)	2.90 (0.07)		
	3	*endo*	2.07 (0.46)	2.52 (0.23)	2.95 (0.09)	4.45	7.20
		exo	2.08 (0.44)	2.54 (0.23)	2.97 (0.07)		
	4	*endo*	2.07 (0.45)	2.47 (0.25)	3.00 (0.03)	5.34	6.76
		exo	2.09 (0.44)	2.45 (0.28)	2.96 (0.03)		
	5	*endo*	2.09 (0.44)	2.43 (0.28)	2.98 (0.03)	5.38	6.82
		exo	2.11 (0.43)	2.43 (0.29)	2.95 (0.03)		
	6	*Re–endo*	2.10 (0.44)	2.42 (0.28)	2.96 (0.03)	5.62	6.58
		Si–endo	2.11 (0.43)	2.41 (0.29)	2.98 (0.03)		
		Re–exo	2.12 (0.43)	2.41 (0.29)	2.95 (0.03)		
		Si–exo	2.12 (0.42)	2.41 (0.29)	2.96 (0.03)		
	7	*Re–endo*	2.08 (0.45)	2.46 (0.27)	2.92 (0.05)	5.08	6.98
		Si–endo	2.08 (0.45)	2.46 (0.27)	2.97 (0.04)		
		Re–exo	2.09 (0.44)	2.47 (0.27)	2.91 (0.04)		
		Si–exo	2.09 (0.44)	2.47 (0.27)	2.92 (0.04)		
	8		1.99 (0.46)	2.62 (0.22)	3.00 (0.04)	5.63	7.18
10	**5**	*endo*	2.12 (0.42)	2.49 (0.26)	2.91 (0.04)	5.22	6.63
		exo	2.14 (0.41)	2.47 (0.27)	3.04 (0.02)		
11	**5**	*ortho–endo*	2.02 (0.49)	2.60 (0.25)	2.99 (0.04)	5.62	6.64
		meta–endo	2.14 (0.42)	2.40 (0.30)	2.82 (0.05)		
		ortho–exo	2.04 (0.47)	2.57 (0.26)	3.01 (0.03)		
		meta–exo	2.15 (0.41)	2.38 (0.31)	2.83 (0.03)		
12	**5**	*meta–endo*	2.09 (0.44)	2.50 (0.27)	2.82 (0.05)	5.81	6.68
		para–endo	2.09 (0.44)	2.50 (0.26)	2.86 (0.05)		
		meta–exo	2.12 (0.43)	2.45 (0.29)	2.88 (0.03)		
		para–exo	2.11 (0.43)	2.49 (0.27)	2.92 (0.03)		

reactions. The energies of the LUMOs of the dienophiles are in agreement with the experimentally observed reactivity trends in the reactions with cyclopentadiene. As the ability to donate electron density of the substituents on boron of the dienophile increases (chlorine < carbon < oxygen), the LUMO coefficient on the boron atom decreases and the energy of this molecular orbital increases. As a result, the $HOMO_{diene}$–$LUMO_{dienophile}$ gap increases in *ca.* 1 eV from dichloroborane **1** to dialkylboranes **2** and **3** and finally to boronates **4–8**, decreasing the reactivity. Furthermore, the difference between the coefficients on the carbon atoms of the dienophile becomes less significant, which would lead to lower asynchronicities and poorer regioselectivities in reactions with non-symmetrical dienes.

IRC calculations demonstrated that all studied Diels–Alder reactions are concerted since the transition structures are connected directly to the reactants and the products. However, the transition structures are highly asynchronous (distances C_1–C_6: 2.38–2.63 Å and C_2–C_3: 1.99–2.15 Å) (Table 1 and Fig. 2 and 3). Except for alkynylboronate **8**, for the series of the organoboron dienophiles, the degree of asynchronicity increases with the electron-attracting character of the ligands on boron. For the reactions with cyclopentadiene (**9**), dienophile **1** shows a difference between distances C_1–C_6 and C_2–C_3 of *ca.* 0.60 Å, dialkylvinylboranes **2** and **3** of 0.45 Å and vinylboronates **4–7** of 0.4–0.3 Å. These data suggest that when the asynchronicity decreases, the activation free energy increases, which has precedents in the literature.[25] The asynchronicity can be understood in terms of the FMO theory. The higher LUMO coefficient for C_2 relative to C_1 of the dienophile suggests that C_2 is more electrophilic. As a consequence, in the transition structures overlap with the diene is more effective at C_2, the interaction C_2–C_3 is stronger and the distance is shorter. Visualisation of the normal modes corresponding to the imaginary frequencies calculated for the transition structures also evidences that bond formation is more advanced at C_2 (C_2–C_3 bond), although there is some degree of bond formation at C_1 (C_1–C_6 bond). Despite the high degree of asynchronicity, all transition structures show classical [4 + 2] character and weak non-classical [4 + 3] C_6–B SOIs (distances: 2.82–3.05 Å and WBIs: 0.10–0.02). For the reactions with cyclopentadiene, the Wiberg bond indexes between C_6 and the boron atom are higher for the TSs corresponding to the reactions of dichloroborane **1** and dialkylboranes **2** and **3**. Also, for these dienophiles the C_6–B WBIs are higher in *endo* TSs, which explains the experimental *endo* selectivity of the Diels–Alder reactions. These results indicate that the lower *endo* selectivity observed in the reaction with **3** might be a consequence of the steric effects produced by carbon skeleton of the 9-BBN. The [4 + 3] C_6–B SOIs for the TSs of the reactions of vinylboronates **4–7** with cyclopentadiene (**9**) are very weak and of the same magnitude for the *endo* and *exo* TSs (C_6–B distances: 2.91–3.00 Å, WBIs: 0.05–0.03), which suggests that the low *exo* selectivity

Table 2 Calculated free energy barriers and selectivities for the Diels–Alder reactions of boron-substituted dienophiles

Diene	Dienophile	Transition structure	$\Delta G^{\neq}$ (kcal mol^{-1})			Experimental selectivity	Calculated selectivity		
			Gas phase	Dichloromethane	Toluene		Gas phase	Dichloromethane	Toluene
9	**1**	*endo*	27.74	9.87	10.27	*endo*/*exo* 84 : 16[11]	63 : 37	83 : 17	78 : 22
		exo	28.00	10.66	10.92				
	2	*endo*	31.82	13.81	13.46	*endo*/*exo* 84 : 16[10]	65 : 35	81 : 19	79 : 21
		exo	32.18	14.66	14.24				
	3	*endo*	32.06	15.49	15.08	*endo*/*exo* 67 : 33[9]	45 : 55	44 : 56	44 : 56
		exo	31.94	15.35	14.93				
	4	*endo*	33.68	17.32	16.93	*endo*/*exo* 39 : 61[3]	26 : 74	32 : 68	26 : 74
		exo	32.90	16.76	16.17				
	5	*endo*	33.61	18.21	17.61	*endo*/*exo* 38 : 62[8]	26 : 74	24 : 76	23 : 77
		exo	32.73	17.23	16.58				
	6	*Re*–*endo*	33.62	19.32	18.65	*endo*/*exo* 43 : 57[5]	31 : 69	30 : 70	31 : 69
		Si–*endo*	33.78	18.92	18.19				
		Re–*exo*	32.99	18.66	17.91	*Re*/*Si* *endo* n.d.	55 : 45	38.62	37.63
		Si–*exo*	33.03	18.17	17.56	*exo* n.d.	51 : 49	36 : 64	40 : 60
	7	*Re*–*endo*	32.53	15.37	15.34	*endo*/*exo* 51 : 49[6]	35 : 65	42 : 58	34 : 66
		Si–*endo*	32.08	15.58	15.46				
		Re–*exo*	31.82	14.96	14.98	*Re*/*Si* *endo* 55 : 45[6]	38 : 62	55 : 45	53 : 47
		Si–*exo*	31.55	18.71	14.56	*exo* 50 : 50[6]	43 : 57	39 : 61	39 : 61
	8	—	32.26	19.34	18.58	—	—	—	—
10	**5**	*endo*	37.52	22.39	21.75	*endo*/*exo* 75 : 25[8]	63 : 37	68 : 32	68 : 32
		exo	38.05	23.14	22.50				
11	**5**	*ortho*–*endo*	33.29	16.07	15.42	*endo*/*exo* 39 : 61[8]	38 : 62	61 : 39	59 : 41
		meta–*endo*	34.11	17.67	17.17				
		ortho–*exo*	32.81	16.51	15.79	*ortho*/*meta* 54 : 46[8]	70 : 30	83 : 17	84 : 16
		meta–*exo*	33.63	18.06	17.31				
12	**5**	*meta*–*endo*	33.39	15.84	15.34	*meta*/*para* 33 : 67[8]	37 : 63	60 : 40	59 : 41
		para–*endo*	32.35	16.65	16.09				
		meta–*exo*	32.21	17.41	16.84				
		para–*exo*	31.91	16.80	16.29				

Table 3 Calculated free energy barriers and selectivities for the Diels–Alder reactions of boron-substituted dienophiles after optimisation in toluene

Diene	Dienophile	Transition structure	$\Delta G^{\neq}$ toluene (kcal mol^{-1})	Experimental selectivity	Calculated selectivity in toluene
9	**1**	*endo*	25.57	*endo*/*exo*: 84 : 16[11]	77 : 23
		exo	25.88		
	2	*endo*	29.26	*endo*/*exo*: 84 : 16[10]	74 : 26
		exo	29.90		
	3	*endo*	30.89	*endo*/*exo*: 67 : 33[9]	49 : 51
		exo	30.88		
	4	*endo*	32.64	*endo*/*exo*: 39 : 61[3]	29 : 71
		exo	31.96		
11	**5**	*ortho*–*endo*	30.28	*endo*/*exo*: 39 : 61[8]	53 : 47
		meta–*endo*	31.53		
		ortho–*exo*	30.53	*ortho*/*meta*: 54 : 46[8]	74 : 26
		meta–*exo*	31.34		
12	**5**	*meta*–*endo*	29.98	*meta*/*para*: 33 : 67[8]	47 : 53
		para–*endo*	30.19		
		meta–*exo*	30.11		
		para–*exo*	29.74		

observed in the Diels–Alder reactions is a result of the greater steric hindrance in the *endo* TSs. The selectivities of the reactions of pinacol vinylboronate (**5**) with 1,3-cyclohexadiene (**10**), *trans*-piperylene (**11**) and isoprene (**12**) seem to result from a fine combination of electronic and steric effects. Although the WBIs C_6–B for such reactions are small (0.05–0.03), the interactions are slightly stronger for the *endo* TSs. For 1,3-cyclohexadiene (**10**), this result explains the observed *endo*-selectivity. The geometries of the TSs for the reaction with *trans*-piperylene (**11**) suggest that the *exo*-selectivity might originate from steric effects.

The computed energy barriers in solution were considerably lower than in the gas phase, probably owing to the greater stabilisation of the TSs relative to the reactants (Table 2). For vinylboranes **1**–**7**, when the electron-attracting character of the ligands on boron increases, the activation free energy decreases. In general, gas-phase calculations reproduced the experimental *endo*/*exo* selectivities reasonably well for all the

Table 4 Calculated global properties of reactants

	Global properties					
Dienophile/diene	η	μ	ω	$\Delta N_{\max}$	N	N'
1	0.2159	−0.1891	2.25	0.876	0.44	1.04
2	0.2300	−0.1591	1.50	0.691	0.67	1.66
3	0.2265	−0.1613	1.56	0.712	0.64	1.65
4	0.2431	−0.1367	1.05	0.562	0.96	2.09
5	0.2470	−0.1371	1.04	0.555	0.97	2.03
6	0.2465	−0.1284	0.91	0.521	1.10	2.28
7	0.2415	−0.1458	1.20	0.604	0.84	1.87
8	0.2689	−0.1393	0.98	0.518	1.02	1.67
9	0.2017	−0.1107	0.83	0.549	1.21	3.37
10	0.1884	−0.1113	0.89	0.591	1.12	3.53
11	0.2036	−0.1182	0.93	0.580	1.07	3.13
12	0.2120	−0.1212	0.94	0.572	1.06	2.94

η: chemical hardness (in au), μ: electronic chemical potential (in au), ω: global electrophilicity (in eV), $\Delta N_{\max}$: the maximum amount of electronic charge that the system might accept (in e) and N and N': nucleophilicity (computed as $1/\omega$ and $\text{HOMO}_{\text{Nu}}-\text{HOMO}_{\text{TCE}}$ respectively, in eV).

systems under study. The calculated *endo*-selectivities were *ca.* 20% lower than the experimental values for **1–3** and 10% lower for boronates **4–7**. The reaction that presented the greatest error was the reaction of vinyl-9-BBN (**3**) with cyclopentadiene (**9**), probably due to the small difference in energy of the TSs corresponding to the *endo* and *exo* pathways.

In addition, vinylboronates **6** and **7** with stereogenic centers two bonds away from boron were predicted to show no appreciable facial diastereoselectivity, which in the case of **7** agreed with the experimental findings (Table 2).[26] The calculated *Re*/*Si* ratios are roughly 50 : 50 both in the gas-phase and in solution. We postulate that the low *Re*/*Si* stereoselectivity of these reactions is probably due to the fact that the stereogenic centers are too far from the reacting carbons (C_1 and C_2) of the dienophiles. As a result, the substituents of the stereogenic centers do not block any of the faces of the double bond of the dienophile effectively and therefore they do not have any influence on the approximation of the diene.

A comparison of the calculated free energies of activation for the Diels–Alder reactions of pinacol vinylboronate (**5**) allowed us to compare the reactivity of the dienes, observing that cyclopentadiene (**9**) is the most reactive diene, followed by isoprene (**12**), *trans*-piperylene (**11**) and 1,3-cyclohexadiene (**10**), which agrees with the relative experimental reactivities.[27]

With regard to the regiochemistry, FMO theory correctly predicted that the *para* regioisomer would be slightly favoured for isoprene (**12**) based on the coefficients of the HOMO of the diene. The coefficients of the terminal carbons of *trans*-piperylene (**11**) are very similar, which suggested low *ortho*/*meta* selectivity. Calculated free energy barriers for the Diels–Alder reactions of vinylboronate **5** with isoprene (**12**) accurately predicted the *meta*/*para* selectivity in the gas-phase, but in solution the ratio was inverted. Similarly, for the reaction with

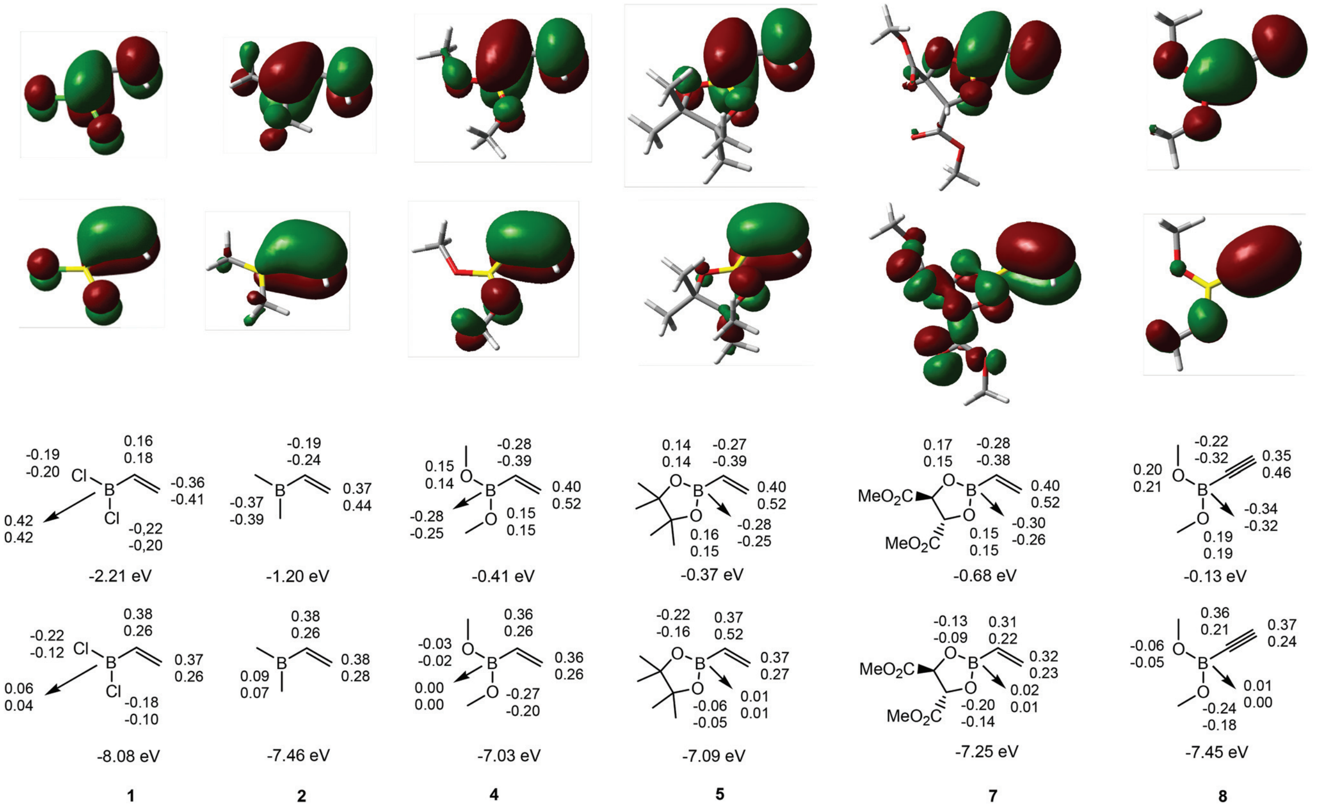


Fig. 1 B3LYP/6-31G* FMO shapes, energies and coefficients of selected boron-substituted dienophiles (top: LUMOs, bottom: HOMOs).

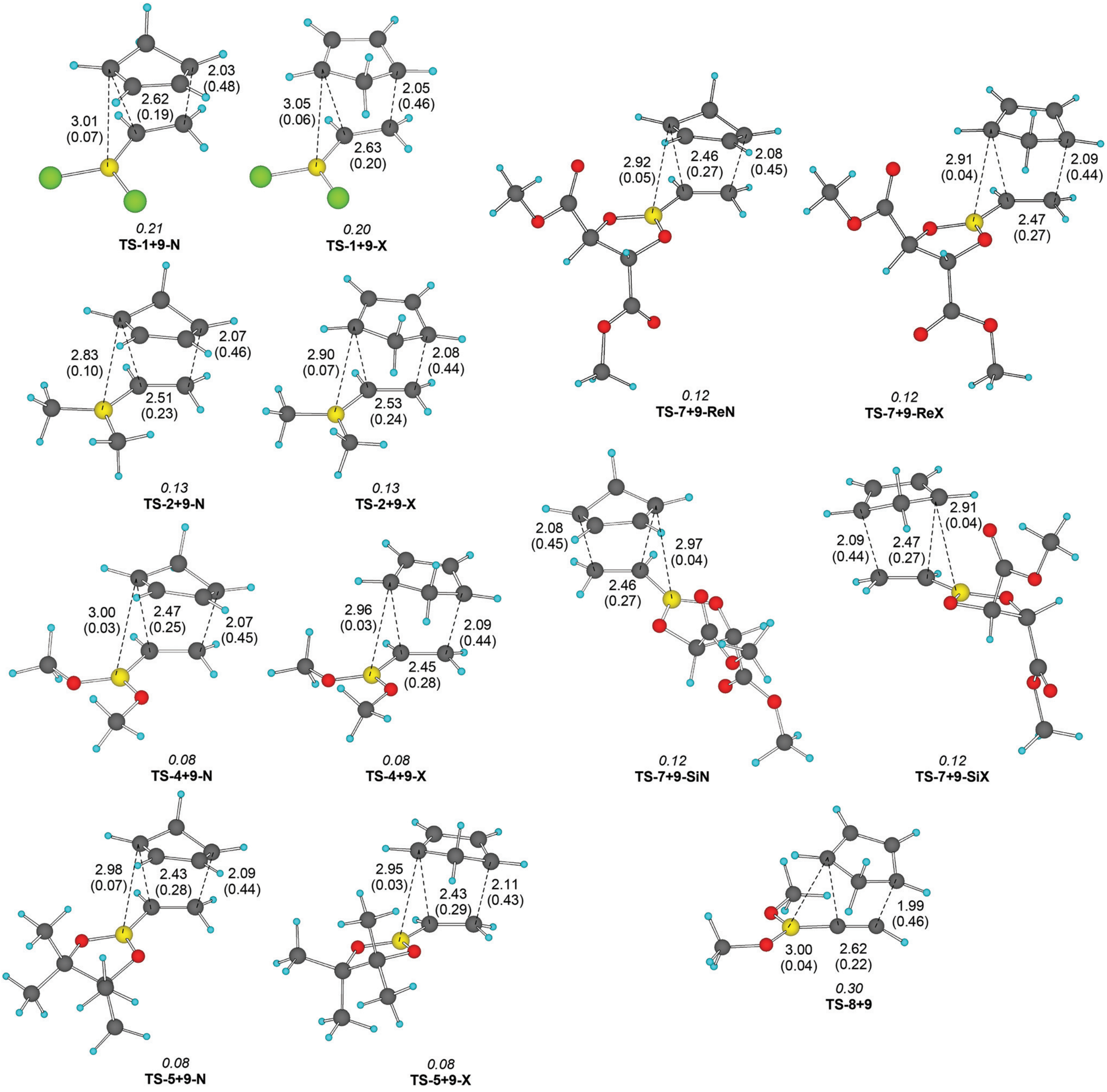


Fig. 2 B3LYP/6-31G* optimized geometries for the transition structures of the Diels–Alder reactions of selected boron-substituted dienophiles with cyclopentadiene (**9**) with selected distances in Å and Wiberg bond indexes in parentheses and charge transfer in italics (in *e*).

trans-piperylene (**11**), the *ortho*/*meta* regioselectivity computed in the gas-phase correlated well with the experimental data, while calculations in solution overestimated the *ortho* selectivity. Probably, dienes **11** and **12** show the greater disagreement between selectivities calculated in the gas phase and in solution (*ca.* 23%) because the corresponding TSs have higher differences in charge transfer (Fig. 2 and 3).

After optimising the transition structures of these reactions in toluene, results were closer to those obtained in the gas-phase, fitting the experimentally obtained regioselectivities more accurately (Table 3). These results motivated us to study other reactions in solution. For reasons of computational cost, we only reoptimised the structures for the reactions that had considerable differences between the selectivity calculated in the gas-phase and in solution, such as the reactions of dienes **11** and **12** with pinacol vinylboronate (**5**), and also for the reactions of cyclopentadiene (**9**) with vinyl-9-BBN (**3**) and the smaller dienophiles **1**, **2** and **4** (Table 3). The free energy barriers obtained after geometry optimisation in toluene were 1 to 3 kcal mol^{-1} lower than those obtained in the gas-phase but the geometries varied slightly. In general, the calculated *endo*/*exo* selectivities were between those obtained in the gas-phase

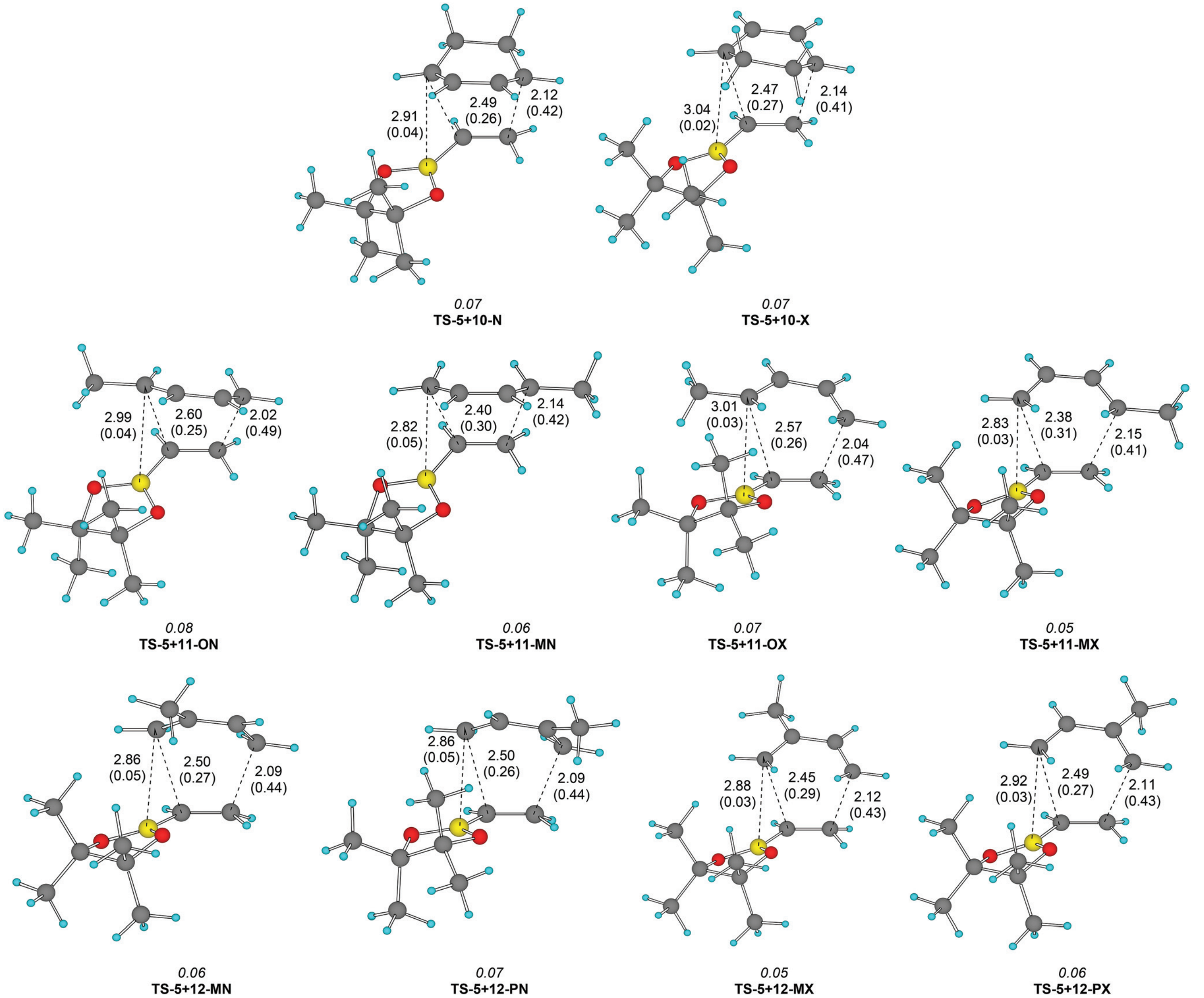


Fig. 3 B3LYP/6-31G* optimized geometries for the transition structures of the Diels–Alder reactions of pinacol vinylboronate (**5**) with cyclohexadiene, *trans*-piperylene and isoprene (**10–12**) with selected distances in Å and Wiberg bond indexes in parentheses and charge transfer in italics (in e).

and those obtained with single-point energies in solution (Table 2). The systems for which the selectivity obtained with the single-point calculations reproduced correctly the experimental value (dienophiles **1**, **2** and **4** with diene **9**) did not show a significant change. The same occurred for the reaction between vinyl-9-BBN (**3**) and cyclopentadiene (**9**). The reactions for which the selectivity in solution differed considerably with the experimental results (dienes **11** and **12** with vinylboronate **5**) showed better agreement with the experimental data, similar to the gas-phase value.

Finally, to get a more detailed idea of the activating effect of the different boron moieties and the polarity of the reactions under study, we computed the global properties of the dienophiles and the dienes and the charge transfer (Table 4 and Fig. 2 and 3).[28] Within these properties, the global electrophilicity (ω) can be used to classify compounds as strong electrophiles ($\omega > 1.50$), moderate electrophiles (ω in the range 1.50–0.80) and marginal electrophiles (nucleophiles, $\omega < 0.80$). Dichlorovinylborane **1** and dialkylvinylboranes **2** and **3** show electrophilicity values of 2.25, 1.50 and 1.56 eV respectively and therefore can be classified as strong electrophiles.[28] On the other hand, boronates **4–8** are moderate electrophiles since their electrophilicity ranges from 1.20 to 0.91 eV. Among the vinylboronates series, the higher electrophilicity power of the tartrate derived analogue (ω = 1.20 eV) evidences the electron-withdrawing effect exerted by the methyl ester groups, which is in line with the lower energy of the LUMO of this dienophile. In addition, vinylboronate **6** and alkynylboronate **8** exhibit the lowest electrophilicity indexes (ω = 0.91 and 0.98 eV respectively), the later being higher than the one reported for pinacol 1-propynylboronate (ω = 0.83 eV).[13e] The significant differences in electrophilicity, and also in $\Delta N_{\max}$, of the dienophiles suggest that charge transfer from the diene should be higher for the Diels–Alder reactions of dichlorovinylborane **1** and dialkylvinylboranes **2** and **3** and therefore the polar character of these processes should be more significant. As a consequence, the reaction rates should be higher.[29] In contrast, unsaturated boronates **4–8** display lower differences in electrophilicity and in $\Delta N_{\max}$ with the diene which means the corresponding reactions should be less polar. The calculated charge transfer values from the diene support these observations for the reactions of cyclopentadiene (**9**) with vinylboron dienophiles **1–7** (Fig. 2). Figures are around 0.20*e* for dichlorovinylborane (**1**), 0.13*e* for dimethylvinylborane (**2**) and 0.08*e* for vinylboronates **4** and **5**. Higher values are observed for tartrate vinylboronate (**7**) (~0.12*e*). However, alkynylboronate **8** presents a very high charge transfer of 0.30*e*, much higher than those computed for the other boron-activated dienophiles studied herein and than the ones reported for other Diels–Alder reactions of alkynylboronates.[13e] These calculations suggest that the reactions of dichlorovinylborane (**1**) and alkynylboronate **8** should be classified as polar Diels–Alder reactions (*P*-DA), while those of dialkylvinylboranes and vinylboronates would have non-polar character (*N*-DA).[29] The former reactions can thus be viewed as polar type Michael addition and therefore the charge transfer for **8** cannot be compared to those for the vinyl analogues to predict changes in activation energies.

Regarding the cycloadditions of pinacol vinylboronate (**5**), dienes **9–12** show similar ω values, between 0.94 eV for isoprene and 0.83 eV for cyclopentadiene, while the nucleophilicities *N* decrease in the order cyclopentadiene (1.21 eV) > 1,3-cyclohexadiene (1.12 eV) > *trans*-piperylene (1.07 eV) ~ isoprene (1.06 eV). However, when the nucleophilicity is calculated as $\mathrm{HOMO_{Nu}}$–$\mathrm{HOMO_{TCE}}$ (N') a different trend is observed: 1,3-cyclohexadiene (3.53 eV) > cyclopentadiene (3.37 eV) > *trans*-piperylene (3.13 eV) > isoprene (2.94 eV). Computed charge transfer is 0.08*e* for cyclopentadiene (**9**), 0.07*e* for cyclohexadiene (**10**), 0.08–0.05*e* for *trans*-piperylene (**11**) and 0.07–0.05 for isoprene (**12**). These data suggest that care should be also exercised in comparing Diels–Alder reactions of vinylboronates with different dienes because charge transfer and nucleophilicity trends might not always give a good estimation of relative reaction rates.[30] Nevertheless, analysis of global properties provides a complementary approach to FMO, giving interesting results which might promote further investigation on the subject.

Conclusions

In this study we have investigated the Diels–Alder reactions of boron-activated dienophiles with different dienes using computational methods. In general, calculations in the gas-phase and in solution reproduced the experimental reactivities and selectivities. For the reactions with cyclopentadiene, the reactivity decreases in the order: dichlorovinylborane > dialkylvinylboranes > vinylboronates and the *endo*-stereoselectivity decreases in the order: dichlorovinylborane ~ dimethyvinylborane > vinyl-9-BBN > vinylboronates. For the studied vinylboronates the reactions are slightly *exo*-selective. The relative reactivity can be understood by considering the activation of the carbon–carbon double bond of the dienophile, which is in line with the electronic properties of the substituents attached to the boron atom. The *endo*/*exo* selectivities arise from a fine combination of electronic and steric effects. As the electron-attracting character of the ligands on boron decreases, the [4 + 3] C–B interactions become weaker and the stereoselectivity is dominated by steric effects. For the reactions of pinacol vinylboronate, the reactivity decreases in the order: cyclopentadiene > isoprene > *trans*-piperylene > 1,3-cyclohexadiene and the *endo*-stereoselectivity decreases in the order: 1,3-cyclohexadiene > *trans*-piperylene ~ cyclopentadiene. The fact that [4 + 3] C–B interactions for *endo* transition structures are stronger than those corresponding to the *exo* transition structures suggests that for cyclopentadiene and *trans*-piperylene the *endo* modes of attack are disfavoured for steric repulsions. The calculated regioselectivities for the reactions with non-symmetrical dienes both in the gas-phase and after optimisation in toluene reproduced the experimental results.

Although the activating effect of the boronate moiety is only moderate, all the studied reactions were computed to be normal electron-demand Diels–Alder reactions. Global properties of the dienophiles and the dienes and the charge transfer for the reactions of vinylboronates were also computed and the reactions classified as non-polar Diels–Alder reactions (*N*-DA). In general, the higher the electrophilicity of the boron-activated dienophile, the higher the charge transfer to cyclopentadiene and hence the lower the activation barrier. Methanol alkynylboronate did not fit into this picture, probably because the reaction falls into the polar Diels–Alder reaction category (*P*-DA). Furthermore, charge transfer values of the Diels–Alder reactions of pinacol vinylboronate with different dienes did not correlate well with activation energies and neither did the nucleophilicities of the dienes. The analysis of the results obtained in this theoretical study allowed us to gain better knowledge of the studied Diels–Alder reactions and will assist the development of new related reactions in our laboratories.

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