



Quantum chemical study on asymmetric allylation of benzaldehyde in the presence of chiral allylboronate

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Abstract: The quantum chemical method is employed to study the modified asymmetric allylation of benzaldehyde controlled by diisopropyl D-(-)-tartrate auxiliary. All the structures are optimized completely at the B3LYP/6-31G(d,p) level. The (R)-secondary alcohol can be achieved mainly through a six-membered ring chair-like transition state structure. From the relative reaction rates theory the main product configuration predicted is in agreement with the experiment result.

Key words: Benzaldehyde, Asymmetric allylation, DFT

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INTRODUCTION

The stereocontrolled formation of the carbon-carbon bond recently is of great importance in organic synthesis. The reactions of allylmetal reagents with aldehydes are of considerable interest in quantum chemistry. Over the past decades, the product yield of enantioselective excess (%e.e.) has been improved greatly with the development of various chiral Lewis catalysts, use of which to obtain 96 %e.e. yield has been achieved by Denmark in the catalyzed allylation of benzaldehyde with monophosphoramidate.

In the asymmetric addition of aldehydes to allylboronates, modifying different chiral auxiliaries resulted in good to excellent enantioselectivity (Roush *et al.*, 1985a; Jadhav *et al.*, 1986; Brown *et al.*, 1990; Racherla and Brown, 1991). And tartrate esters modified allylboronates from several laboratories have been studied thoroughly because of its simple preparation and high enantioselectivity (Haruta *et al.*, 1982; Roush *et al.*, 1985b; Roush *et al.*, 1988; Roush *et al.*, 1990a). However, the reaction mechanism has rarely been reported owing to its complexity. Roush hypothesized a transition state structure of the asymmetric allylation (Roush *et al.*, 1990b), and

successfully explained the corresponding relationship of experimental results and product structures. Gung *et al.* (2002) suggested that n/n electronic repulsion plays only a minor role in stereodifferentiation in the allylboration reaction based on the fact that distances between the aldehydic hydrogen and the carbonyl oxygen in the transition structure and between the aldehydic oxygen and the amide carbonyl oxygen exceed the sum of van der Waals radii. This paper presents a computation of the enantioselective addition of benzaldehyde to diisopropyl D-(-)-tartrate modified allylboronate by means of the density functional theory (DFT) yielding results quite different from those of Gung *et al.* (2002). Furthermore, the conformation of products will be reported here using thermochemistry and related reaction rates theory.

METHODS AND COMPUTATIONS

In the asymmetric allylation of benzaldehyde with diisopropyl D-(-)-tartrate modified allylboronate, all modeling molecules for the intermediary states and transition states are shown in Fig.1 and Fig.2. And all the structures for the reaction are optimized

completely at the B3LYP/6-31G(d,p) (Lee *et al.*, 1988; Miehlich *et al.*, 1989) level on Gaussian 98 (Frisch *et al.*, 1998). The vibrational analysis for all the optimized structures is performed at the same computational level. Selected bond lengths and angles are summarized in Table 1. Total electron and zero-point energies E , formation energies ΔE and reaction activation energies ΔE^\ddagger corrected with zero-point vibrational energies are shown in Table 2. For comparison, the first two vibrational frequencies are also listed in Table 2. The optimized reaction intermediary states structures and transition states structures are shown in Fig.3.

RESULTS AND DISCUSSION

Transition states structures

In the reactants molecules for 1 and 2, the Mulliken electric charges of B9, O3, O10 are 0.255e, $-0.351e$ and $-0.287e$, respectively. B9 and O3 are strongly attracted to each other because of the electronic effects. And the Mulliken electric charges of C1, C2, C6, C7 and C8 are $-0.203e$, $0.196e$, $-0.323e$, $-0.210e$ and $-0.262e$ respectively. It is easier to form carbon-carbon bond of atoms C2 and C6. From the computational results we know that the bonds of C2-C6 and O3-B9 are formed at the same time to

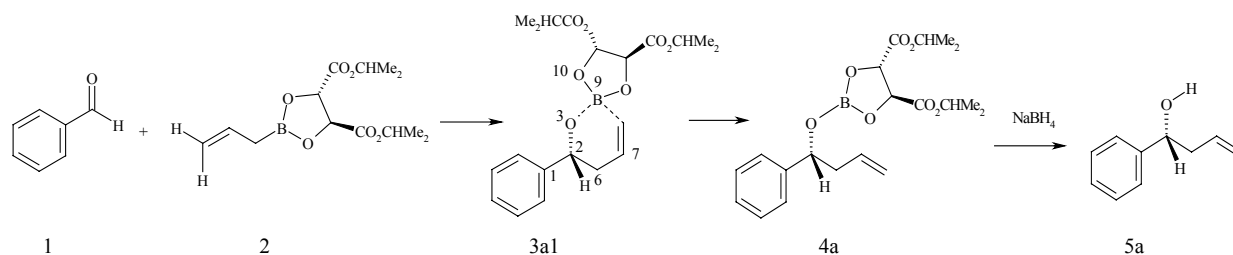


Fig.1 Asymmetric allylation route of benzaldehyde

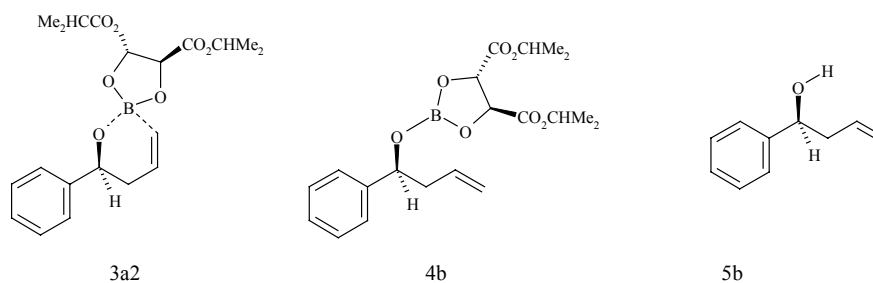


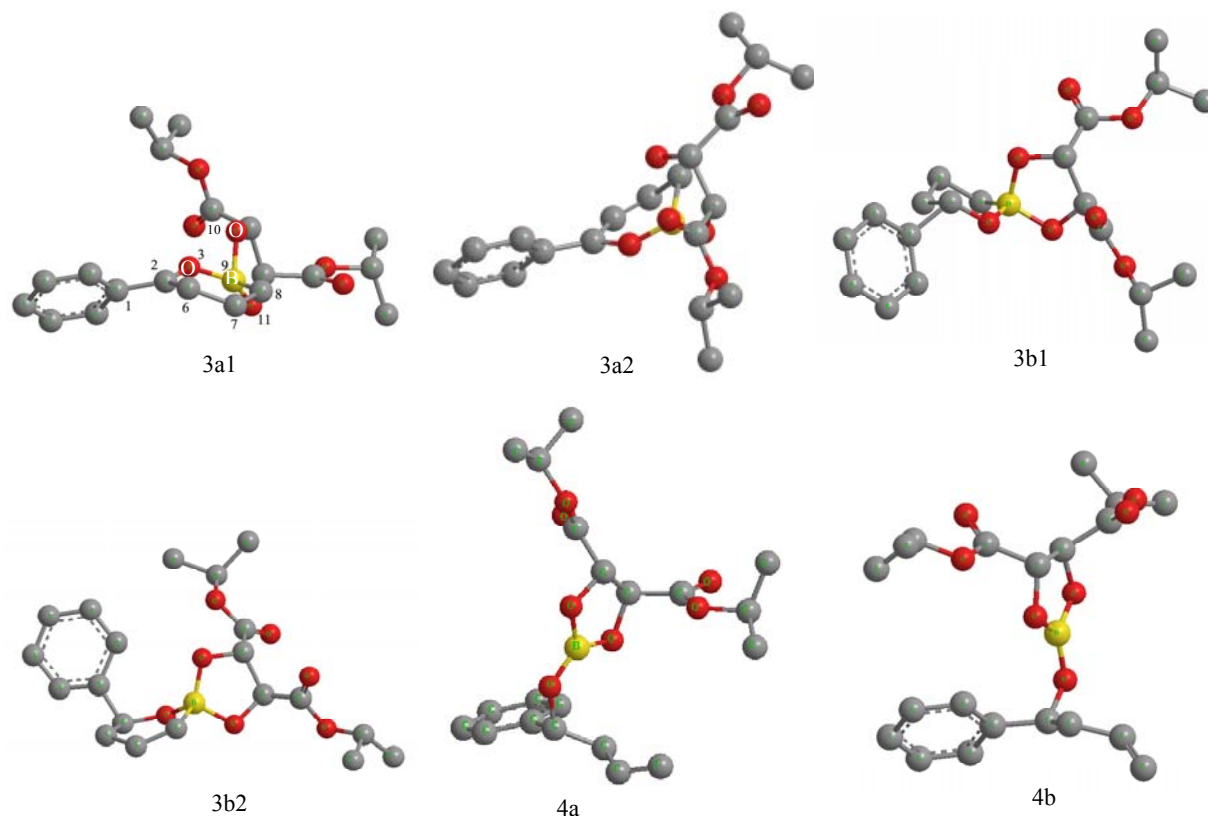
Fig.2 Other possible compounds in the allylation

Table 1 Selected bonds lengths (nm) and bonds angles ($^\circ$)

Compounds	C2-O3 (nm)	C8-B9 (nm)	C7-C8 (nm)	C6-C7 (nm)	C2-C6 (nm)	O3-B9 (nm)	C1-C2-O3 ($^\circ$)	C6-C7-C8 ($^\circ$)
1	0.1233	—	—	—	—	—	—	—
2	—	0.1541	0.1470	0.1330	—	—	—	—
3a1	0.1352	0.1600	0.1420	0.1390	0.1850	0.1830	114.04	121.43
3a2	0.1360	0.1601	0.1470	0.1360	0.1860	0.1850	108.79	120.64
3b1	0.1342	0.1620	0.1430	0.1390	0.1860	0.1860	114.64	121.28
3b2	0.1334	0.1640	0.1430	0.1390	0.1900	0.1870	121.16	120.69
4a	0.1441	0.4310	0.1330	0.1480	0.1500	0.1890	112.30	123.80
4b	0.1442	0.5050	0.1330	0.1480	0.1520	0.1890	113.39	123.68
5a	0.1424	—	0.1330	0.1480	0.1530	—	108.43	123.88
5b	0.1424	—	0.1330	0.1480	0.1530	—	108.42	123.88

Table 2 Total energies E ($\times 2625.5$ kJ/mol), formation energies ΔE (kJ/mol), activation energies ΔE^\ddagger (kJ/mol) and the first two vibrational frequencies ν (cm^{-1})

Compounds	E	ΔE	ΔE^\ddagger	ν_1	ν_2
1	-406.2984	-	-	77.4	194.3
2	-778.8532	-	-	6.7	9.3
1+2	-1185.1582	-17.3283	-	46.3	63.8
3a1	-1185.1474	-	28.40	-339.8	3.1
3a2	-1185.1442	-	36.76	-325.2	3.8
3b1	-1185.1437	-	38.07	-651.9	8.7
3b2	-1185.1416	-	43.58	-573.9	11.5
4a	-1185.1496	5.2510	-	8.8	13.9
4b	-1185.1483	8.6642	-	12.7	15.8

**Fig.3** Optimized reaction transition state and intermediary state structures

consist of a six-membered ring transition state structure. Roush *et al.* (1990b) hypothesized that the allylation can be accomplished through a six-membered ring chair-like transition state structure. We were able to obtain both of chair and boat-twist transition structures after optimization with OPT=QST3 on B3LYP/6-31G(d,p), and which confirmed later by vibrational analysis with Freq (Norian) at the same level (Fig.3).

The molecules 3a1 and 3a2 can produce easily the R-chiral alcohols, with the 3a1 being a chair transition state structure in which the bonds lengths of C2-O3, C8-B9, C7-C8, C6-C7 and O3-B9 are 0.1352 nm, 0.1600 nm, 0.1420 nm, 0.1390 nm, 0.1850 nm and 0.1830 nm, and the bonds angles of C1-C2-O3 and C6-C7-C8 are 114.04° and 121.43° respectively, but the only one imaginary frequency is -339.8 cm^{-1} . In the boat-twist transition state structure of 3a2, the

bonds lengths of C2-O3, C8-B9, C7-C8, C6-C7 and O3-B9 are 0.1360 nm, 0.1601 nm, 0.1470 nm, 0.1360 nm, 0.1850 nm, and the bonds angles of C1-C2-O3 and C6-C7-C8 are 108.79° and 120.64° respectively, and the only one vibrational frequency is -325.2 cm^{-1} . It is obvious that the bond length of C2-O3 both in 3a1 and 3a2 is longer than that of molecule 1. The lengthening bond of C8-B9 decreases its bond energy. And the single bond of C7-C8 is shortened because of the delocalization of the double bond of C6-C7. Changes of the bonds lengths, angles and dihedrals caused the formation of two new unstable bonds of O3-B9 and C2-C6 at the same time. From the results in Table 2, the total energy of chair structure 3a1 is lower than that of the boat-twist structure 3a2 by 8.36 kJ/mol. Therefore, the chair-like transition state structure of 3a1 is more stable.

As already discussed above, for 3b1 and 3b2 which can produce the S-chiral alcohols, the chair transition state of 3b1 is more stable than that of 3b2 because of the 5.51 kJ/mol difference.

Regarding the chair-like transition structures 3a1 and 3b1, the activation energy for 3a1 is lower by 9.67 kJ/mol. We observed that the starting points for 3a1, 3b1, 3a2 and 3b2 are the highest points in the energy curve with IRC (Dewar *et al.*, 1985; Dewar and Reynolds, 1986) (Calcfc, Maxpoints=12) on B3LYP/6-31G(d,p).

Intermediary states structures

The intermediary states 4a and 4b are stable because their lowest vibrational frequencies are 8.8 cm^{-1} and 12.7 cm^{-1} respectively and no imaginary frequencies were found. In molecule structure 4a, the bonds lengths of C1-C2, C2-O3 and O3-B9 are 0.1501 nm, 0.1441 nm and 0.1890 nm, and the bonds angles of C1-C2-O3 and C6-C7-C8 are 112.3° and 123.8°. The data on 4b from Table 1 is very similar to data on 4a with the exception of dihedrals B9-O3-C2-C6 57.8°, -58.9° and C8-B9 bond length 0.4310 nm, 0.5050 nm. And 4a is more stable than 4b because their relative energies are 5.25 kJ/mol and 8.66 kJ/mol respectively based on the optimized energies of compounds 1 with 2.

The reaction energies relationships are described in Fig.4.

Theoretic calculation of enantioselective yield

Based on the relative reaction rates theory, the

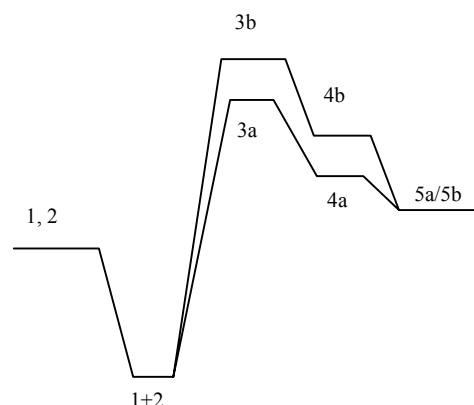


Fig.4 Energies relationships for the allylation of benzaldehyde

ratio of rate constants for the parallel reactions equals to the ratio of products concentrations, also equals to the ratio of enantioselective yield. From which we can estimate the reaction enantioselectivity by comparing the ratio value.

From the Arrhenius equation

$$k = A e^{-E_a/RT}$$

We can get

$$\frac{k_R}{k_S} = \frac{A_R e^{-E_{aR}/RT}}{A_S e^{-E_{aS}/RT}} \quad (1)$$

where k_R and k_S are reaction rate constants of R and S enantiomers; E_{aR} and E_{aS} are reaction activation energies of R and S enantiomers; R is the gas constant ($8.314\text{ J}/(\text{mol}\cdot\text{K})$); T is the reaction temperature.

Definition of enantioselective excess

$$\%e.e. = \frac{[R] - [S]}{[R] + [S]} \times 100\% \quad (2)$$

where [R] and [S] are the products concentrations of R and S enantiomers.

Use the results discussed yields the following equation

$$\%e.e. = \frac{|k_R - k_S|}{k_R + k_S} \times 100\% \quad (3)$$

So, by combining the computational data (Table 2) with the Eq.(3) we can conclude that the main product is R-chiral alcohol for the asymmetric allylation of benzaldehyde which is in agreement with the experimental results (78 %e.e.) (Roush *et al.*, 1985b).

CONCLUSION

In the asymmetric allylation of benzaldehyde with diisopropyl D-(-)-tartrate, the chiral intermediary states can be obtained mainly from a six-membered ring chair-like transition state based on the density functional theory. The agreement of the main product structure predicted from relative reaction rates theory with the experimental result indicates that the application of DFT in asymmetric allylation of benzaldehyde is feasible.

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