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PAPER

The roles of benzoic acid and water on the Michael reactions of pentanal and nitrostyrene catalyzed by diarylprolinol silyl ether†

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The roles of benzoic acid and water on the Michael reaction of pentanal and nitrostyrene catalyzed by diarylprolinol silyl ether are revealed by density functional theory calculations. The calculations demonstrate that the benzoic acid is ready to attack the catalysts and form a hydrogen bond between the hydrogen atom of the COOH of benzoic acid and one of the N atoms of the catalyst. The complex formed from pentanal, catalyst and benzoic acid attacks nitroalkene and forms transition states. Finally, the transition states hydrolyze and the products are formed. The calculations demonstrate that the stereoselectivity is dominated by the steric hindrance of the 2-substituent groups, and the benzoic acid can increase the reaction rate evidently by decreasing the activation energies; however, H_3O^+ or strong acid may prevent the formation of the transition states between enamines and nitroalkenes. The employed solvent can decrease the activation energies and promote the proton transfer from benzoic acid onto the catalyst 2. The calculated enantiomeric excess values are in good agreement with the experimental results. These calculations also reveal that the role of benzoic acid is dependent on the sophisticated structures of the catalysts and provide a valuable index for the structural design of new catalysts and selection of additives or co-catalysts.

1. Introduction

The reported direct aldol reaction catalyzed by proline[1] stimulated extensive study on asymmetric organocatalysis. Since then, asymmetric organocatalysis reactions of aldehydes and ketones, such as the aldol reaction,[2] the Michael reaction,[3] the Mannich reaction[4] and a variety of other reactions[5–9] have been developed by using small organic molecules as the catalysts. Currently, asymmetric organocatalysis has become a hot topic in organic chemistry.[10–16]

As one of the most versatile and efficient methods for the formation of carbon–carbon bonds, Michael additions have attracted enormous attention in organic synthesis in the past decades. Among these Michael reactions, the additions of aldehydes to nitroalkenes are very useful and interesting because they can be used to prepare versatile synthetic intermediates, nitroalkenes and may generate two contiguous stereo centers in a single step. Actually, extensive experiments have been carried out and great progress has been achieved with the asymmetric versions of the Michael reaction.[17–20] In 2005, Hayashi *et al.*[21] reported that diphenylprolinol silyl ethers catalyzed the additions of simple aldehydes to nitroalkenes with much higher diastereoselectivities and enantioselectivities than the most used catalyst proline. Zheng *et al.*[22] also achieved excellent results in this reaction with modified diphenylprolinol silyl ether.

For the mechanisms of the asymmetric organocatalytic Michael additions, the established viewpoints are that the key intermediate is iminium ion or enamine.[23–25] For those reactions catalyzed by proline, theoretical and experimental studies have demonstrated that the stereochemical outcome of the products are determined by hydrogen-bonding. For those reactions catalyzed by derivatives of proline without the COOH group, the stereochemical outcomes are determined by the steric hindrance of the 2-substituent groups of the employed catalysts.[26]

However, recently more and more experiments demonstrate that the employed solvent and additives have a great impact on the reactions.[27–31] These experimental observations are not well understood. To gain further insight into the reaction mechanism of asymmetric organocatalytic Michael additions, especially on the roles of solvents and additives, we take the Michael addition between pentanal and nitrostyrene catalyzed by diarylprolinol silyl ether combined with or without benzoic acid as a model system and perform a systematic study on it. The DFT calculations demonstrate that the solvent can decrease the energy barriers of Michael reactions and the additive benzoic acid can improve the reactivity of catalysts *via* forming a complex with the catalysts or enamines. These findings are helpful for the design of new high-selectivity and reactivity catalysts and the optimization of reaction conditions.

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2. Computational details

In the Michael additions (see Fig. 1a), the catalysts (diarylprolinol silyl ether, see Fig. 1b) and pentanal dehydrate to form enamine intermediates. Subsequently, an enamine intermediate and nitrostyrene may form an addition product. Finally, the initial product is hydrolyzed, leading to the formation of the ultimate product and the regeneration of the catalyst. The second step forming the carbon–carbon bond determines the configuration of the product and is the most important step, thus, we focus on this step and localize the corresponding transition states.

B3LYP functional has been questioned for its ability to deal with weak interactions such as hydrogen bonding,[32] however, our analysis and discussion are based on the relative energies or relative activation energies, instead of total energies, thus the B3LYP functional can still provide results reliably. The reactants, catalysts, additives and the structures formed by the two different catalysts with a hydronium or a benzoic acid molecule were all optimized at the B3LYP/6-31G(d,p) level of theory. The transition state structures under neat condition or with the additive were searched using a TS approach at the same level of theory. Frequency calculations were also performed at the same level of theory and the transition state structures were identified by their modes of vibration. Solvent effects were computed using Tomasi's polarized continuum model (PCM) with UFF radii at the CPCM$_{\text{(water)}}$/B3LYP/6-31G(d,p) level of theory. All calculations were performed using the Gaussian 09 quantum chemical program package.[33]

3. Results and discussion

3.1 Michael additions

As shown in Fig. 2, the enamine intermediates derived from pentanal and each catalyst can be present in four different conformers (IM1, IM2, IM3 and IM4), which originate from the two possible configurations (*E* or *Z*) of the enamine double bond, and from the *syn* or *anti* orientations of the enamine double bond relative to the 2-substituent groups in the pyrrolidine ring. Each enamine intermediate has two faces (Re and Si) and can approach a nitrostyrene from two different directions (above or below the plane of N–C═C of the nitrostyrene), so there are sixteen mathematically possible reaction pathways for each catalyst. However, the Re face of the enamine intermediate is effectively shielded by the bulky 2-substituent group of the pyrrolidine ring of the catalyst, in other words, only the Si face of the enamine intermediate can approach nitrostyrene. Test calculations show that when the Re face attacks the nitrostyrene, no transition state is located for most intermediates or even is a transition state obtained, the corresponding activation energy being much higher than those of the ones formed by the attack of the Si face on the nitrostyrene; further calculations by rotating the dihedral angle along the reaction coordinate reach the same conclusions. Thus, the possible reaction pathways reduce from sixteen to eight. The stereochemical outcome of the product of the reaction depends on the approach of the enamine intermediate to nitrostyrene (Fig. 2). For instance, if the *E*-configuration enamine IM1, with the double bond *syn* to the 2-substituent group of the pyrrolidine ring, attacks from the above face of the nitrostyrene, the reaction generates a product with *S* configuration; if the enamine IM1 attacks from the below face of the nitrostyrene, a *R* configurational product is obtained.

The calculated relative energies (Δ*E*) of the enamine conformers are reported in Table 1 and the optimized structures are provided in S1.† The results in Table 1 show that the first two enamines of the two different catalysts containing an *E* configuration of the double bond are more stable than the two *Z* configurational enamines. The enamine IM4 (IM4′) is ruled out due to the highest relative energy in the following calculations.

The approach of the remaining three intermediates to the two different faces of nitrostyrene can lead to six different reaction

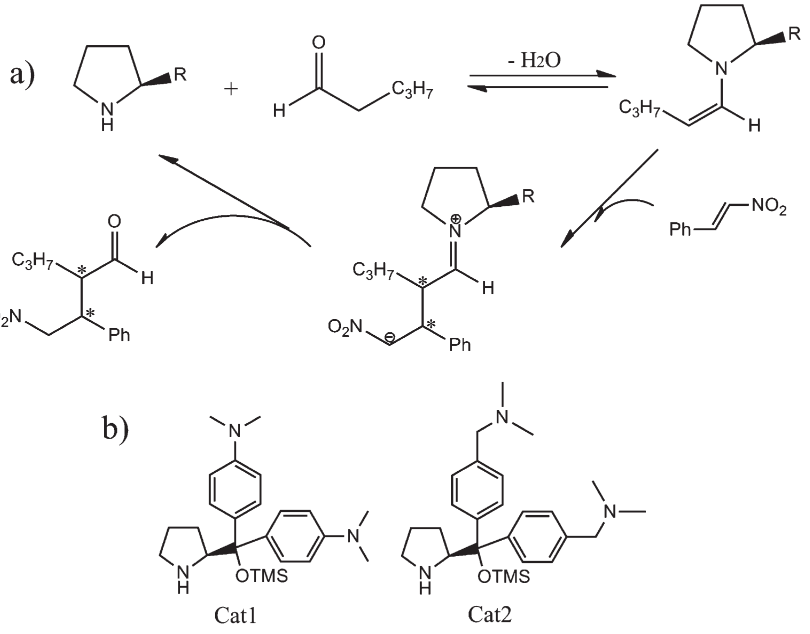

Fig. 1 (a) Key steps involved in asymmetric Michael additions of pentanal and nitrostyrene. (b) Catalysts: diarylprolinol silyl ether.

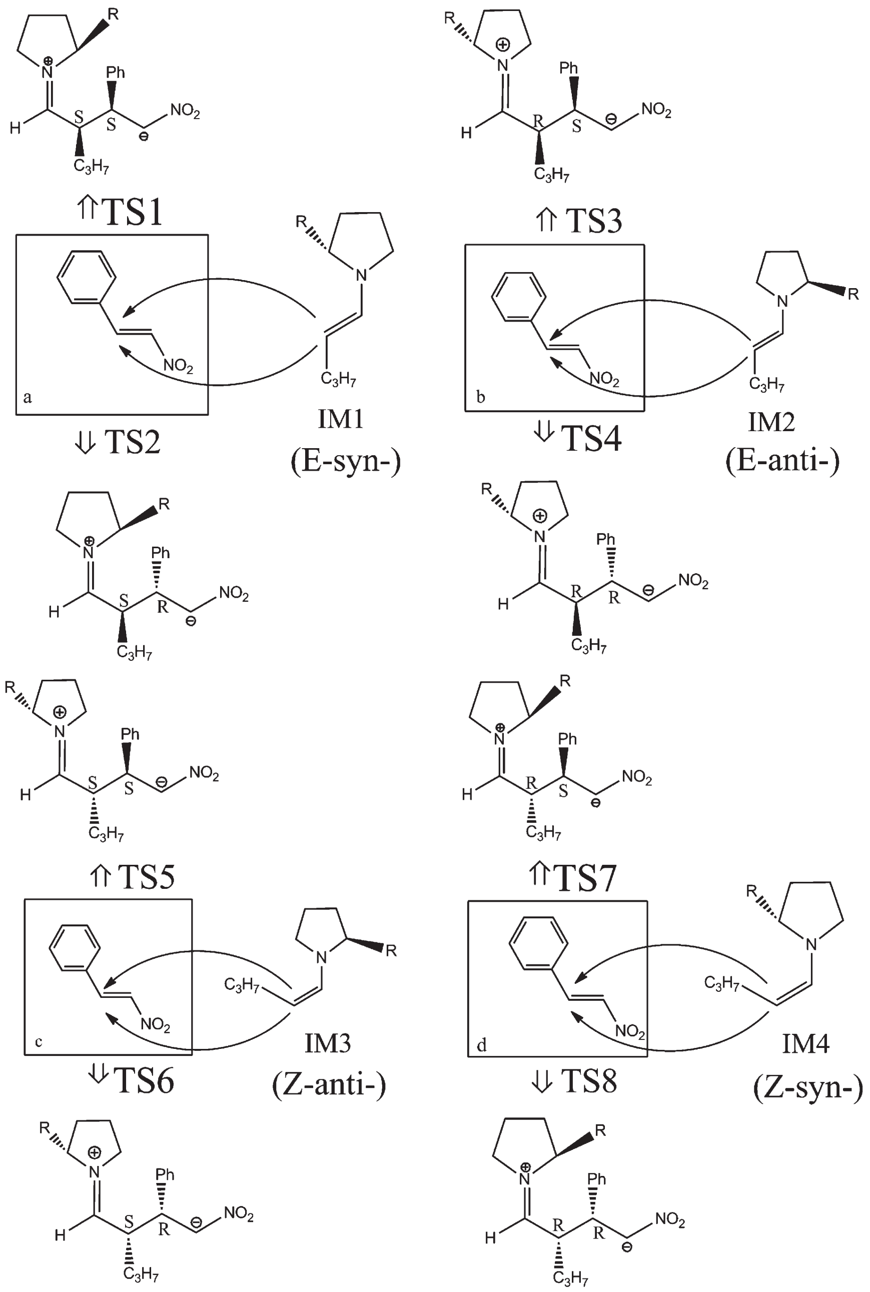

Fig. 2 The possible reaction pathways of pentanal and nitrostyrene catalyzed by diarylprolinol silyl ether.

Table 1 The calculated relative energies (ΔE, in kcal mol^{-1}) of enamine conformers formed by the two different catalysts with pentanal at the B3LYP/6-31G(d,p) level of theory

Enamine	Conformer	ΔE^a	Enamine	Conformer	ΔE^b
IM1	*E-syn-*	2.25	IM1′	*E-syn-*	2.20
IM2	*E-anti-*	0.00	IM2′	*E-anti-*	0.00
IM3	*Z-anti-*	2.96	IM3′	*Z-anti-*	2.80
IM4	*Z-syn-*	8.09	IM4′	*Z-syn-*	8.01

[a] The relative energies are given relative to Cat1-IM2. [b] The relative energies are given relative to Cat2-IM2′.

pathways for each catalyst. We located the six transition states (TS1–TS6); the calculated activation barriers of the transition states are given in Table 2, and the optimized structures are shown in Fig. 3.

As seen in Table 2, for the Cat1, other transition states are higher in energy than TS3, demonstrating that the corresponding pathways are disadvantageous. The two lowest energy transition states TS2 and TS3 are formed from different enamine intermediates, demonstrating that the configurations of the intermediates play an important role in the Michael reactions. For the lowest energy enamine intermediate IM2 (*E-anti-*), when it approaches the above face of the nitrostyrene, it leads to the product with (2*R*,3*S*)-configuration. On the contrary, by approaching the below face, it leads to the product with (2*R*,3*R*)-configuration. Evidently, the approaching direction of the enamine intermediate is significant in the Michael reactions. The

Table 2 The calculated activation barriers (ΔG, in kcal mol^{-1}) and relative activation barriers ($\Delta\Delta G$, in kcal mol^{-1}) of the transition states for the Michael reaction between pentanal and nitrostyrene catalyzed by the two different catalysts with or without benzoic acid in the gas-phase at the B3LYP/6-31G(d,p) level and in the solvent-phase at the CPCM$_{(\text{water})}$/B3LYP/6-31G(d,p) level

				Gas-phase		Solvent-phase	
Catalyst	TS	IM	Chirality	ΔG	$\Delta\Delta G$	$\Delta G'$	$\Delta\Delta G'$
Cat1	TS1	*E-syn*	2*S*,3*S*	30.34	4.95	28.70	4.12
	TS2	*E-syn*	2*S*,3*R*	28.05	2.66	27.69	3.11
	TS3	*E-anti*	2*R*,3*S*	25.39	0.00	24.58	0.00
	TS4	*E-anti*	2*R*,3*R*	28.13	2.74	25.81	1.23
	TS5	*Z-anti*	2*S*,3*S*	29.23	3.84	27.57	2.99
	TS6	*Z-anti*	2*S*,3*R*	30.70	5.31	27.67	3.09
Cat2	TS1′	*E-syn*	2*S*,3*S*	31.58	4.62	28.64	3.05
	TS2′	*E-syn*	2*S*,3*R*	28.93	1.97	26.84	1.25
	TS3′	*E-anti*	2*R*,3*S*	26.96	0.00	25.59	0.00
	TS4′	*E-anti*	2*R*,3*R*	30.10	3.14	28.45	2.86
	TS5′	*Z-anti*	2*S*,3*S*	29.68	2.72	27.47	1.88
	TS6′	*Z-anti*	2*S*,3*R*	31.53	4.57	28.02	2.43
Cat2-H_3O^+	TS1″	*E-syn*	2*S*,3*S*	37.62	6.64	32.36	6.98
	TS2″	*E-syn*	2*S*,3*R*	31.99	1.01	28.25	2.87
	TS3″	*E-anti*	2*R*,3*S*	30.98	0.00	25.38	0.00
	TS4″	*E-anti*	2*R*,3*R*	33.10	2.12	25.68	0.30
	TS5″	*Z-anti*	2*S*,3*S*	34.49	3.51	29.39	4.01
	TS6″	*Z-anti*	2*S*,3*R*	36.16	5.18	29.16	3.78
Cat2-benzoic acid	TS1‴	*E-syn*	2*S*,3*S*	32.76	6.15	29.09	4.11
	TS2‴	*E-syn*	2*S*,3*R*	30.70	4.09	28.32	3.34
	TS3‴	*E-anti*	2*R*,3*S*	26.61	0.00	24.98	0.00
	TS4‴	*E-anti*	2*R*,3*R*	29.51	2.90	25.36	0.38
	TS5‴	*Z-anti*	2*S*,3*S*	30.98	4.37	29.24	4.26
	TS6‴	*Z-anti*	2*S*,3*R*	32.68	6.07	30.74	5.76

highest energy transition state is TS6 formed by the highest energy IM3 (*Z-anti*), which is 5.31 kcal mol^{-1} higher in energy than TS3. It thus can be concluded that the stability of the enamine intermediate plays an important role in the Michael reactions. The products formed by TS3 (2*R*,3*S*) and TS2 (2*S*,3*R*) are a pair of enantiomers. Their energy difference of 2.66 kcal mol^{-1} corresponds to an enantiomeric excess (ee) in favor of the (2*R*,3*S*)-configurational product of 97.8% ee. It should be noted that the product resulting from the hydrolysis of TS4 is only a little less than that of TS2, thus, the relative concentration of the main product from TS3 should roughly decrease a percent. Even so, the calculated excess value is a little larger than the experimental value of 93%.[22]

For the Cat2, similarly the two lowest energy transition states TS2′ and TS3′ are formed from different enamine intermediates, demonstrating that the configurations of the intermediates play an important role in the Michael reactions. TS2′ is 1.97 kcal mol^{-1} higher in energy than TS3′. The highest energy transition state TS1′ formed by IM1′ (*E-syn*), is 4.62 kcal mol^{-1} higher in energy than TS3′. The products formed from TS3′ (2*R*,3*S*) and TS2′ (2*S*,3*R*) are a pair of enantiomers. Their energy difference of 1.97 kcal mol^{-1} corresponds to an enantiomeric excess of 93%. Similarly to the reactions catalyzed by Cat1, there is also an important by-product with (2*S*,3*S*)-configuration from TS5′, thus the relative concentration of the main product from TS3′ will decrease slightly.

3.2 Solvent effect

The gas-phase results in Table 2 only consider the interactions among reactants and catalysts. Although these results can also provide valuable insights into the reaction mechanisms, the reactions are actually taking place in the liquid phase and the employed solvent should play a role on the reactions. As shown in Table 2, the activation energies of TS2 and TS3 decrease from 28.05 and 25.39 kcal mol^{-1} in the gas-phase to 27.69 and 24.58 kcal mol^{-1} in water, respectively, and the relative energy of them increases from 2.66 to 3.12 kcal mol^{-1}. For Cat2, the calculations show that the activation energies of TS2′ and TS3′ decrease from 28.93 and 26.96 kcal mol^{-1} in the gas-phase to 26.84 and 25.59 kcal mol^{-1} in water, respectively, and the relative energy of them decreases from 1.97 to 1.25 kcal mol^{-1}. Table 2 also shows that the activation energies and their differences for the Michael reactions in water, a closer and more real model to the actual reaction system, are all smaller than those in gas phase. These results demonstrate that the employed solvent can evidently increase the reaction rate by decreasing the activation barriers and modify the selectivity to some degree by changing the differences in activation energies.

3.3 The role of the benzoic acid

It has been reported that the additives such as water, acids, and bases can affect either or both reactivity and enantioselectivity in transformations catalyzed by amine-based catalysts.[34–36] Zheng *et al.*[22] experimentally found that the benzoic acid can increase the rate of reaction between aldehydes and nitroalkene and the effect of the benzoic acid on the reaction rate is different for two different catalysts although they are highly similar in structure. To reveal why the benzoic acid can substantially modify the rate

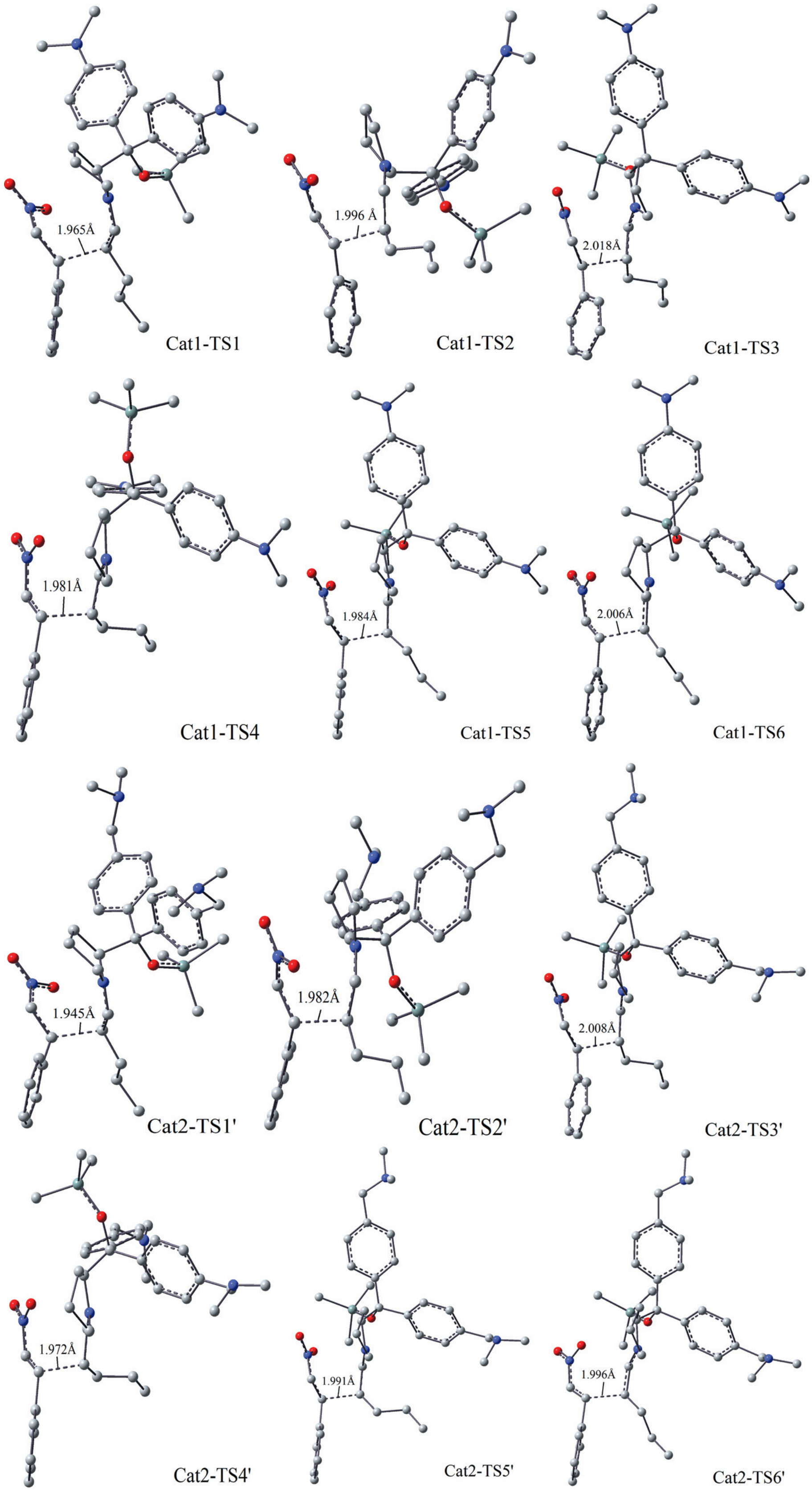

Fig. 3 The optimized structures of different transition states for the Michael reactions of pentanal and nitrostyrene at the B3LYP/6-31G(d,p) level of theory.

Table 3 The key bond lengths (in Å) of the complexes formed between the two different catalysts and a hydronium and the corresponding complexation energies (Δ*E*, in kcal mol^{-1}) in the gas-phase at the B3LYP/6-31G(d,p) level and the solvent-phase at the $CPCM_{(water)}$/B3LYP/6-31G(d,p) level

	Gas phase			Solvent phase		
	d(N–H)	*d*(O–H)	Δ*E*	*d*(N–H)	*d*(O–H)	Δ*E*
I	1.041	1.773	−84.63	1.050	1.719	−43.08
II	1.050	1.685	−102.55	1.048	1.721	−54.68
III	1.042	1.748	−83.26	1.052	1.707	−48.57
IV	1.048	1.712	−90.10	1.051	1.726	−49.16

I: The N on dimethylamine group of the Cat1 with H_3O^+. II: The N on pyrrolidine of the Cat1 with H_3O^+. III: The N on dimethylamine group of the Cat2 with H_3O^+. IV: The N on pyrrolidine of the Cat2 with H_3O^+.

Table 4 The key bond lengths (in Å) of the complexes formed between the two different catalysts and a benzoic acid molecule and the corresponding complexation energies (Δ*E*, in kcal mol^{-1}) in the gas-phase at the B3LYP/6-31G(d,p) level and the solvent-phase at the $CPCM_{(water)}$/B3LYP/6-31G(d,p) level

	Gas phase			Solvent phase		
	d(N–H)	*d*(O–H)	Δ*E*	*d*(N–H)	*d*(O–H)	Δ*E*
I	1.763	1.006	−10.69	1.704	1.018	−8.97
II	1.579	1.048	−18.32	1.489	1.084	−15.98
III	1.669	1.024	−13.70	1.155	1.385	−11.33
IV	1.684	1.020	−14.19	1.628	1.036	−13.12

I: The N on dimethylamine group of the Cat1 with a benzoic acid molecule. II: The N on pyrrolidine of the Cat1 with a benzoic acid molecule. III: The N on dimethylamine group of the Cat2 with a benzoic acid molecule. IV: The N on pyrrolidine of the Cat2 with a benzoic acid molecule.

of Michael additions and has different effects on the two catalysts, a detailed study has been undertaken.

It is well-known that benzoic acid is a moderate organic acid. Accordingly, there may exit hydronium in the reaction system and this kind of ion may affect the reactions. There are three N atoms in the catalyst (see Fig. 1b), and these N atoms may strongly interact with hydronium due to their lone pair of electrons. We thus examined the structures formed between the two different catalysts and a hydronium in the gas- and solvent-phases. The two N atoms on the 2-substituent group should have the same properties for each catalyst, thus only one N atom of the 2-substituent group and the N atom on the pyrrolidine ring are considered. The main bond lengths and the relative energies are given in Table 3, the optimized complex structures are shown in S2.†

The calculated results show that, for Cat1, the lowest energy structure occurs when the hydronium approaches the nitrogen on the pyrrolidine ring both in the gas- and solvent-phase. However, for Cat2, whether the hydronium approaches the N of the pyrrolidine ring or the N of the dimethylamine group of the side chain, the complex structures have nearly the same energies. The complexation energies are all remarkably negative as shown in Table 3. These results indicate that hydronium can modify the function of the catalysts by forming complexes with the catalysts and the effect of the hydronium is dependent on the structures of the employed catalyst. These results are in agreement with the experimental observations that the acidic additives can accelerate the formation of enamine.[36]

For Cat1, as the complexation energy (−54.68 kcal mol^{-1}) resulting from the approaching of hydronium to the nitrogen of the pyrrolidine ring is evidently larger (absolute value) than that of the approach of hydronium to the nitrogen of the dimethylamine group of the side chain (−43.08 kcal mol^{-1}), the hydronium may mainly modify the formation rate of enamines. However, the corresponding complexation energies are nearly equal (−48.57 and −49.16 kcal mol^{-1}) for Cat2, thus, the hydronium may modify the formation rates for both the enamines and the later transition states. Since here we only focus on the carbon–carbon formation step, only the role of hydronium on Cat2 is considered below.

We located the six transition states of the Michael reaction of pentanal and nitrostyrene catalyzed by Cat2 with a hydronium. The calculated activation energies of the transition states are given in Table 2 and the optimized structures are shown in ESI S3.† The calculated results demonstrate that the activation energies of the mentioned transitions states with a hydronium are all evidently higher than the activation energies of the corresponding transition states without a hydronium attached. Thus, these pathways should be ruled out, and indicate that the acceleration effect of the added benzoic acid should be achieved *via* other pathways. Considered that benzoic acid is a moderate organic acid and the main species in the reaction system is the two reactants, the benzoic acid should be in molecular form, not in ion form. We thus studied the structures formed by the two different catalysts with a benzoic acid molecule. The main bond lengths and the complexation energies are given in Table 4.

As seen in Table 4, for Cat1, the O–H and H–N bonds of the structures formed by the catalyst and a benzoic acid molecule change slightly in the solvent-phase compared with the corresponding bonds in the gas-phase. The O–H and N–H bonds of the complex only change slightly from 1.006 and 1.763 Å into 1.018 and 1.704 Å. The large difference between the two complexation energies (−15.98 *vs.* −8.97 kcal mol^{-1}) demonstrates that the benzoic acid is much more ready to approach the nitrogen on pyrrolidine of the Cat1 and thus may mainly modify the formation rate of the enamines. However, for Cat2, both the O–H and N–H bonds in the solvent-phase have a great transformation compared with the bonds in the gas-phase. The length of the O–H bond increases from 1.024 into 1.385 Å, while the length of the N–H bond decrease from 1.669 into 1.155 Å. In fact, the hydrogen atom on the COOH group of benzoic acid has been transferred directly to the N of the dimethylamine group of Cat2 in water. Naturally, the benzoic acid molecule exerts a different effect on the electronic configuration of the two catalysts, and thus the complexes formed between the different catalysts and the benzoic acid molecule have different properties. These calculated results also support the experimental observations that the benzoic acid has a different effect on the reactivity of the two structurally similar catalysts. The complexation energies are all negative and more than 8.00 (absolute value) kcal mol^{-1}, demonstrating that the benzoic acid may form a complex with the catalyst or as-formed enamines. Thus, the reactions should take place between the nitrostyrene and the enamine with a benzoic acid attached, instead of between the nitrostyrene and the pure enamine.

In addition, the large complexation energies resulting from the interactions between the nitrogen on the pyrrolidine of the two catalysts and a benzoic acid molecule imply that even in the absence of an amino group on the 2-substituent group, benzoic acid should also have an impact on the reaction by modifying the formation rate of the enamines. These results are in agreement with recent experimental observations.[37]

Of course, it is also possible for the other reactant nitrostyrene to be activated by benzoic acid, or the two catalysts *via* hydrogen bonding.[38] We performed additional calculations. The results are reported in the ESI S3.† The results show that the complex energies (absolute value) resulting from the hydrogen bonding between nitrostyrene and benzoic acid, or the two catalysts are evidently smaller than the corresponding values between benzoic acid and the two catalysts. In other words, benzoic acid is more ready to form a complex with the two catalysts than with nitrostyrene. Thus, this kind of hydrogen bonding was not considered in the following calculations.

Based on the findings calculated above, we located the transition states formed by enamines with benzoic acid attached and nitrostyrene. The calculated activation barriers of the transition states are given in Table 2, and the optimized structures are shown in Fig. 4.

From Table 2, it is found that the activation barrier of the lowest-energy transition state (TS3‴) is 24.98 kcal mol^{-1}, which is less than the activation barrier of TS3 (25.59 kcal mol^{-1} in solvent phase) catalyzed by Cat2 only. Moreover, all other transition states with a benzoic acid molecule attached have relatively low activation barriers, compared to those catalyzed by Cat2 only. The decreasing activation energies from 25.59 kcal mol^{-1} (without benzoic acid) to 24.98 kcal mol^{-1} (with benzoic acid) may lead to rate acceleration of nearly three times for the formation of the corresponding transition state. These results validate the experimental observations that Cat2 with added benzoic acid has a better catalytic effect than Cat2 only. Since the benzoic acid can also modify the formation rate of the enamine,[37] the overall rate acceleration may be different from this calculated value. The calculated energy difference of 3.34 kcal mol^{-1} between TS2‴ and TS3‴ in the solvent-phase corresponds to an enantiomeric excess of 99%.

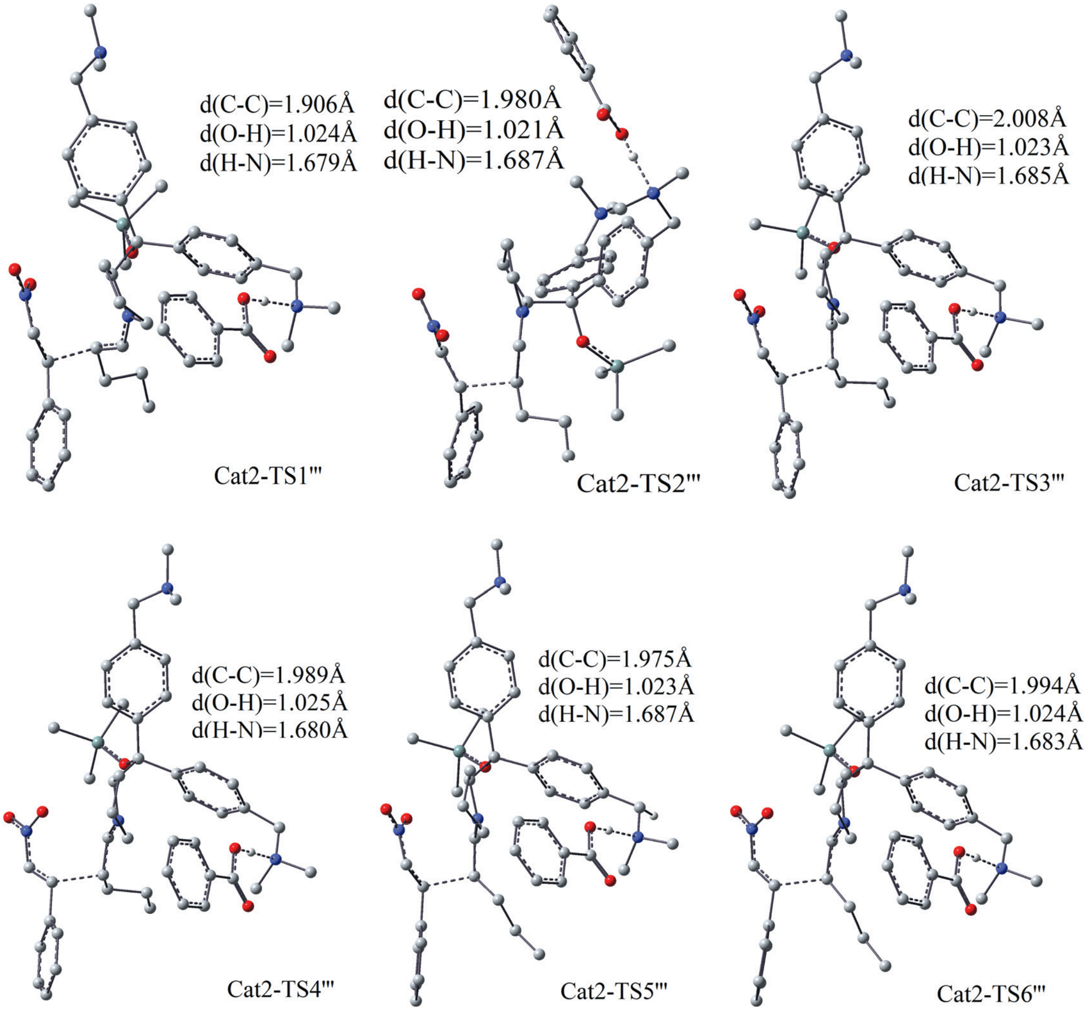

Fig. 4 The optimized structures and the key bond lengths of the transition states in Michael reactions between pentanal and nitrostyrene catalyzed by Cat2 with benzoic acid attached at the B3LYP/6-31G(d,p) level of theory.

3.4 Discussion

From Tables 3 and 4, it is evident that the complexation energies between the catalysts and hydronium are much larger than those between the catalysts and benzoic acid. The scan of the potential energy surfaces demonstrates that it is a spontaneous process for hydronium to approach the nitrogen of the catalysts. In other words, as long as there exists hydronium, it will modify the reactivity of the employed amine-based catalysts. Considering the experimental observations that strong acid will dissociate in water and lead to the formation of hydronium, and our theoretical finding that the activation energies of the mentioned transitions states with a hydronium are all evidently higher than the activation energies of the corresponding transition states without a hydronium attached, it can be safe to conclude that strong acid is not advantageous to the formation of the corresponding transition states. These calculated findings are in good agreement with the experimental observations that the reactions of aldehydes and nitrostyrene catalyzed by diarylprolinol silyl ether lead to product in trace and little yield using CF_3COOH[22] and CCl_3COOH[36] as additive, respectively.

4. Conclusions

The roles of benzoic acid and water on the Michael reactions of pentanal and nitrostyrene catalyzed by two different diarylprolinol silyl ethers have been investigated by using the density functional theory. The results demonstrate that the stereoselectivity is dominated by the steric hindrance of the 2-substituent groups of the catalysts and the introduction of benzoic acid can increase the reaction rate by modifying the properties of the employed catalyst, thus decreasing the activation energies of the corresponding reactions. The calculations also demonstrate that the added strong acid does not have a positive role on the formation of the transition states. The effect of an additive is dependent on the structures of the catalysts. These calculations can rationalize the experimental observations and provide a valuable index for the structural design of new catalysts and selection of additives or co-catalysts.

Acknowledgements

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References

1 B. List, R. A. Lerner and C. F. Barbas, *J. Am. Chem. Soc.*, 2000, **122**, 2395–2396.
2 W. Notz, F. Tanaka and C. F. Barbas, *Acc. Chem. Res.*, 2004, **37**, 580–591.
3 O. M. Berner, L. Tedeschi and D. Enders, *Eur. J. Org. Chem.*, 2002, 1877–1894.
4 B. List, *J. Am. Chem. Soc.*, 2000, **122**, 9336–9337.
5 X. F. Liu, H. M. Li and L. Deng, *Org. Lett.*, 2005, **7**, 167–169.
6 M. P. Sibi and M. Hasegawa, *J. Am. Chem. Soc.*, 2007, **129**, 4124–4125.
7 S. Brandes, B. Niess, M. Bella, A. Prieto, J. Overgaard and K. A. Jørgensen, *Chem.–Eur. J.*, 2006, **12**, 6039–6052.
8 M. P. Brochu, S. P. Brown and D. W. C. MacMillan, *J. Am. Chem. Soc.*, 2004, **126**, 4108–4019.
9 S. Bertelsen, N. Halland, S. Bachmann, M. Marigo, A. Braunton and K. A. Jørgensen, *Chem. Commun.*, 2005, 4821–4823.
10 P. I. Dalko and L. Moisan, *Angew. Chem., Int. Ed.*, 2001, **40**, 3726–3748.
11 C. Allemann, R. Gordillo, F. R. Clemente, P. H. Y. Cheong and K. Houk, *Acc. Chem. Res.*, 2004, **37**, 558–569.
12 P. I. Dalko and L. Moisan, *Angew. Chem., Int. Ed.*, 2004, **43**, 5138–5175.
13 J. Seayad and B. List, *Org. Biomol. Chem.*, 2005, **3**, 719–724.
14 B. List, *Chem. Commun.*, 2006, 819–824.
15 P. Melchiorre, M. Marigo, A. Carlone and G. Bartoli, *Angew. Chem., Int. Ed.*, 2008, **47**, 6138–6171.
16 L. W. Xu, L. Li and Z. H. Shi, *Adv. Synth. Catal.*, 2010, **352**, 243–279.
17 T. Ishii, S. Fujioka, Y. Sekiguchi and H. Kotsuki, *J. Am. Chem. Soc.*, 2004, **126**, 9558–9559.
18 W. Wang, J. Wang and H. Li, *Angew. Chem., Int. Ed.*, 2005, **44**, 1369–1371.
19 R. Husmann, M. Jörres, G. Raabe and C. Bolm, *Chem.–Eur. J.*, 2010, **16**, 12549–12552.
20 C. Yu, J. Qiu, F. Zheng and W. H. Zhong, *Tetrahedron Lett.*, 2011, **52**, 3298–3302.
21 Y. Hayashi, H. Gotoh, T. Hayashi and M. Shoji, *Angew. Chem., Int. Ed.*, 2005, **44**, 4212–4215.
22 Z. L. Zheng, B. L. Perkins and B. Ni, *J. Am. Chem. Soc.*, 2010, **132**, 50–51.
23 M. P. Patil and R. B. Sunoj, *Chem.–Asian J.*, 2009, **4**, 714–724.
24 M. P. Patil, A. K. Sharma and R. B. Sunoj, *J. Org. Chem.*, 2010, **75**, 7310–7321.
25 P. H. Cheong, C. Y. Legault, J. M. Um, N. Çelebi-Ölçüm and K. N. Houk, *Chem. Rev.*, 2011, **111**, 5042–5137.
26 J. Q. Zhao and L. H. Gan, *Eur. J. Org. Chem.*, 2009, 2661–2665.
27 N. Mase, R. hayumanavan, F. Tanaka and C. F. Barbas, *Org. Lett.*, 2004, **6**, 2527–2530.
28 S. V. Pansare and K. Pandya, *J. Am. Chem. Soc.*, 2006, **128**, 9624–9625.
29 Y. Hayashi, T. Itoh, M. Ohkubo and H. Ishikawa, *Angew. Chem., Int. Ed.*, 2008, **47**, 4722–4724.
30 B. Tan, D. Zhu, L. H. Zhang, P. J. Chua, X. F. Zeng and G. F. Zhong, *Chem.–Eur. J.*, 2010, **16**, 3842–3848.
31 S.-e. Syu, T.-T. Kao and W. W. Lin, *Tetrahedron*, 2010, **66**, 891–897.
32 H. L. Woodcock, H. F. Schaefer and P. R. Schreiner, *J. Phys. Chem. A*, 2002, **106**, 11923–11931.
33 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski and D. J. Fox, *GAUSSIAN 09 (Revision A.01)*, Gaussian Inc., Wallingford CT, 2009.
34 P. M. Pihko, K. M. Laurikainen, A. Usano, A. I. Nyberg and J. A. Kaavi, *Tetrahedron*, 2006, **62**, 317–328.
35 N. Zotova, A. Franzke, A. Armstrong and D. G. Blackmond, *J. Am. Chem. Soc.*, 2007, **129**, 15100–15101.
36 K. Patora-Komisarska, M. Benohoud, H. Ishikawa, D. Seebach and Y. Hayashi, *Helv. Chim. Acta*, 2011, **94**, 719–745.
37 P. Dinér, M. Nielsen, M. Marigo and K. A. Jørgensen, *Angew. Chem., Int. Ed.*, 2007, **46**, 1983–1987.
38 M. Arnó, R. J. Zaragozá and L. R. Domingo, *Tetrahedron*, 2007, **18**, 157–164.