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Asymmetric Epoxidation of *trans*-Chalcones Organocatalyzed by β-Amino Alcohols

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Cyclic and acyclic β-amino alcohols were examined as organocatalysts in the epoxidation of *trans*-chalcones with *tert*-butyl hydroperoxide as the oxidant. Primary, secondary, and tertiary β-amino alcohols are able to promote the reaction with variable activity and level of asymmetric induction. Subtle modifications to the structures of simple primary β-amino alcohol strongly influenced their efficiency in the epoxidation. They are promising catalysts that afford *trans*-chalcone epoxides in up to 52 % *ee* at room temperature.

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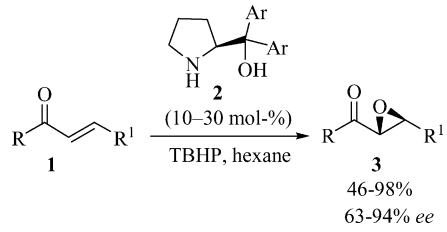
Introduction

The development of new methodologies, characterized by operational simplicity and the use of easily available catalysts, is the main target of modern organic synthesis. Asymmetric organocatalysis offers most of these advantages, as metal-free and environmentally friendly conditions have been developed for many transformations by using small organic molecules as chiral promoters.[1] Because of the great synthetic versatility and the pharmaceutical importance of enantiomerically enriched epoxides, different approaches have been disclosed to access these compounds. The asymmetric epoxidation of alkenes has been the privileged route to epoxides.[2] Most of the methods are based on metal complexes and chiral ligands such as the well-known Ti–tartrate-mediated epoxidation of allylic alcohols[3] and the chiral manganese salen catalyzed epoxidation of *cis* alkenes.[4] Organocatalyzed enantioselective epoxidation of unfunctionalized alkenes with oxaziridines,[5] chiral dioxiranes,[6] oxaziridinium salts,[7] and amines[8] were also reported. The Juliá–Colonna reaction, which was discovered more than two decades ago, can be considered one of the most efficient ways to epoxidize electron-poor alkenes.[9] Over the years, this reaction, which is promoted by homo-oligopeptides, has been intensively investigated by different groups and significant improvements have been reached in terms of practicality[10] as well as in the understanding of the mechanism of asymmetric induction.[11] Recently, notable results have been achieved in the asymmetric epoxidation of α,β-unsaturated aldehydes, a challenging transformation, which was promoted by simple *O*-protected diaryl-2-pyrrolidinemethanols in the presence of aqueous H_2O_2 as the oxidant.[12] At the same time, we found that diaryl-2-pyrrolidinemethanols **2**, which are readily accessible from L-proline, catalyzed the asymmetric epoxidation of α,β-enones by using *tert*-butyl hydroperoxide (TBHP) as the oxidant (Scheme 1).[13] The epoxy ketones were isolated in good yields and high *ee* values (up to 94 % *ee*). Improvements in the activity and the enantioselectivity of the original promoter α,α-diphenyl-L-prolinol (**2a**) were achieved by employing modified derivatives. Indeed, higher conversions and *ee* values were achieved by using electron-rich phenyl-substituted compounds **2**[13b,13c] at a significantly reduced loading (10 mol-%) with respect to commercially available **2a** employed at 30 mol-% loading.[13a]



Scheme 1. Diaryl-2-pyrrolidinmethanol-catalyzed asymmetric epoxidations of α,β-enones.

Although modifications at the phenyl ring of **2a** led to appreciable results in the epoxidation, the β-amino alcohol framework deserved a more in-depth investigation. Here, we report the study on the employment of easily available and differently substituted primary, secondary, and tertiary cyclic and acyclic β-amino alcohols as organocatalysts in the asymmetric epoxidation of chalcones. This investigation helped to shed more light on the structural requirements of

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the β-amino alcohol that is important for the catalysis, and the results provide clues for further developments and mechanistic interpretation of this oxidative system.

Results and Discussion

In our previous studies, organocatalyst **2b** was identified as the most effective promoter (Figure 1).[13c] The aromatic substitution pattern was maintained and the aliphatic ring was modified for the synthesis of cyclic compounds **4a** and **5a**, which were obtained as reported in the literature,[13c,14] starting from the corresponding commercially available L-amino acids.

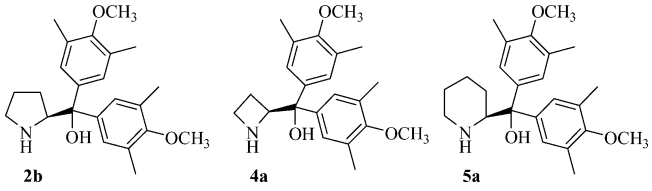
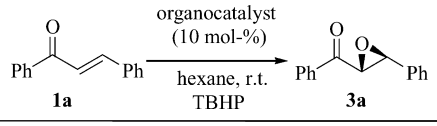


Figure 1. Modified cyclic amino alcohols employed in the epoxidation.

The epoxidation of model compound *trans*-chalcone (**1a**; R = R[1] = Ph) was carried out by employing compounds **4a** and **5a** under standard conditions[13c] (Table 1).

Table 1. Epoxidation of **1a** with catalysts **2b**, **4a**, and **5a** and TBHP.[a]



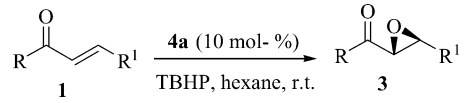
Entry	Catalyst	Time [h]	Yield **3a** [%][b]	*ee* **3a** [%][c]
1[d]	**2b**	110	93	89
2	**4a**	112	33	85
3	**5a**	118	48	75

[a] Molar ratios: **1a**/catalyst/TBHP, 1:0.10:1.4. [b] Isolated products after flash chromatography. [c] Determined by HPLC analysis on Chiralcel OD column. Absolute configuration (α*R*,β*S*) was determined by comparison of the HPLC retention times with those in the literature. [d] Yield and *ee* values as reported in ref.[13c].

Azetidinol derivative **4a** afforded (α*R*,β*S*)-**3a** in low yield but in fairly good enantioselectivity (Table 1, Entry 2). Six-membered ring catalyst **5a** proved to be more active than **4a** but significantly less enantioselective (Table 1, Entry 3). These results clearly showed that ring size is crucial for the epoxidation to proceed and the pyrrolidine ring ensured the highest conversion and asymmetric induction.

Although less active compound, **4a** yielded **3a** in good asymmetric induction (Table 1, Entry 2). Further experiments were then carried out to better ascertain the performance of **4a** with respect to **2b** in the epoxidation of different *trans*-chalcones (Table 2). In all the examples,[15] catalyst **4a** proved to be rather less effective than **2b**, but the enantioselectivity was marginally decreased.

Table 2. Epoxidation of **1** with catalyst **4a** and TBHP.[a]



Entry	R	R[1]	Time [h]	Yield **3** [%][b]	*ee* **3** [%][c]
1	Ph	Ph	112	33 (93)	85 (89)
2	4-BrC_6H_4	Ph	165	45 (98)	82 (86)
3	3-$CH_3C_6H_4$	Ph	142	46 (87)	86 (89)
4	Ph	4-CNC_6H_4	144	21 (65)	85 (86)
5	Ph	4-$CH_3C_6H_4$	141	22 (80)	82 (86)
6	Ph	2-ClC_6H_4	117	10 (70)[d]	60 (69)[d]

[a] Molar ratios: **1**/**4a**/TBHP, 1:0.10:1.4. [b] Isolated products after flash chromatography. Yields in parenthesis refer to those reported in ref.[13c] by using catalyst **2b**. [c] Determined by HPLC analysis on Chiralcel OD and Chiralpack AD columns. The *ee* values in parentheses refer to those reported in ref.[13c] by using catalyst **2b**. Absolute configuration (α*R*,β*S*) was determined by comparison of the HPLC retention times with those in the literature. [d] The reaction was carried out by using catalyst **2b** (15 mol-%).[13c]

The ability to catalyze the epoxidation of **1a** by a variety of commercially available primary β-amino alcohols, and among them, acyclic compounds structurally retaining the *gem*-diphenyl carbinol group, was then studied (Table 3).

In order to compare the activity of the organocatalysts with that of compound **2a**, the reactions were carried out by using 30 mol-% of the promoter. β-Amino alcohols having one chiral center, respectively bearing the amino or the hydroxy groups (Table 3, Entries 1 and 2), led to the formation of the epoxide in low yield and *ee*. The substitution at the chiral carbon center binding the amino group played a major role in controlling the asymmetric induction. When two chiral centers were present in the amino alcohol (Table 3, Entries 3–5), a sterically rigid scaffold as in catalysts **9** and **10** is necessary to assure a beneficial effect in the conversion and more importantly in the *ee* with respect to compound **8**. Moreover, *trans*-**10** proved to be significantly more enantioselective than *cis*-**9**. Acyclic catalysts **11a**–**d** bearing the diphenyl carbinol group afforded (α*R*,β*S*)-**3a** in low-to-modest yield and low *ee*, although a moderate influence on the asymmetric induction was displayed by the substituent at the chiral center (Table 3, Entries 6–9). It is interesting to note that catalyst activity was reduced in the absence of the hydroxy group as in the case of compound **11e** (Table 3, Entry 10), which was significantly less active than catalyst **11a** (Table 3, Entry 6). This result confirmed the importance of the OH group in the catalysis as previously observed for diaryl pyrrolidinemethanols.[13] Then, trifluoroacetic acid was added as a cocatalyst with the use of **11e**, but the epoxidation did not proceed (Table 3, Entry 11). A similar result was achieved in the presence of 15 mol-% of *p*-toluensulfonic acid (Table 3, Entry 12). These findings suggest that even in the presence of a primary amine as a catalyst, the epoxidations of chalcones do not seem to proceed through iminium formation,[16] as

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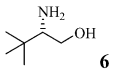
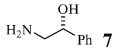
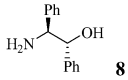
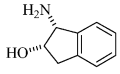
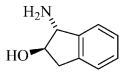
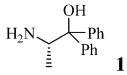
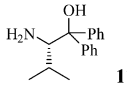
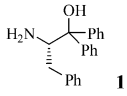
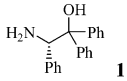
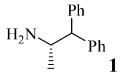
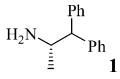
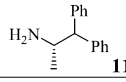
Table 3. Epoxidation of **1a** with primary β-amino alcohols and TBHP.[a]

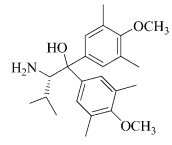
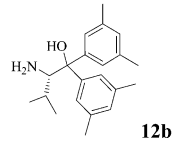
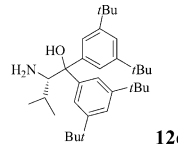
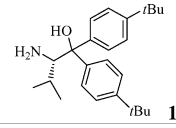
Entry	Catalyst	Time [h]	Yield **3a**[%][b]	*ee* **3a**[%][c]
1	 **6**	168	20	19 (α*S*,β*R*)
2	 **7**	192	22	7 (α*R*,β*S*)
3	 **8**	238	25	racemic
4	 **9**	120	37	19 (α*R*,β*S*)
5	 **10**	118	30	34 (α*R*,β*S*)
6	 **11a**	140	37	racemic
7	 **11b**	172	41	22 (α*R*,β*S*)
8	 **11c**	192	14	15 (α*R*,β*S*)
9	 **11d**	214	28	6 (α*R*,β*S*)
10	 **11e**	138	21	racemic
11[d]	 **11e**	160	<5	-
12[e]	 **11e**	138	12	racemic

[a] Molar ratios: **1a**/catalyst/TBHP, 1:0.30:1.4. [b] Isolated products after flash chromatography. [c] Determined by HPLC analysis on Chiralcel OD column. Absolute configuration (α*R*,β*S*) was determined by comparison of the HPLC retention times with those in the literature. [d] TFA (30 mol-%) was added. [e] *p*-Toluensulfonic acid (15 mol-%) was added.

reported for the epoxidation of enals organocatalyzed by secondary amines[12,17] and anilines.[18,19] The most efficient catalyst **11b** was then modified at the phenyl ring to study the impact on the activity (Table 4).

Promoter **12a** bearing the previously optimized aromatic moiety, when used in the epoxidation, afforded the epoxide in low yield but greatly enhanced *ee* (Table 4, Entry 1).[20] Compound **12b** lacking the *p*-methoxy groups proved to be far more active, and the epoxide was isolated in satisfactory yield and improved *ee* relative to those of compound **11b** (Table 4, Entry 2). Catalyst **12c** having sterically hindered *tert*-butyl groups in the *meta* positions of the phenyl rings led to a poor result (Table 4, Entry 3). Thus, the size of the substituents in the *meta* positions plays a relevant role in the control of the enantioselectivity. Finally, catalyst **12d**

Table 4. Epoxidation of **1a** with modified catalysts of type **11b** and TBHP.[a]

Entry	Catalyst	Time [h]	Yield **3a**[%][b]	*ee* **3a** [%][c]
1	 **12a**	120	21	52
2	 **12b**	165	58	35
3	 **12c**	163	32	14
4	 **12d**	160	36	22

[a] Molar ratios: **1a**/catalyst/TBHP, 1:0.30:1.4. [b] Isolated products after flash chromatography. [c] Determined by HPLC analysis on Chiralcel OD column. Absolute configuration (α*R*,β*S*) was determined by comparison of the HPLC retention times with those in the literature.

bearing *p*-*tert*-butyl groups, which was scarcely soluble in the reaction mixture, had a comparable performance to unmodified compound **11b** (Table 4, Entry 4). It appears that in the series of acyclic primary β-amino alcohols **12a**–**d**, which are structurally similar to secondary cyclic catalysts **2**, the type of substitution at the phenyl ring remarkably affected the level of enantiocontrol. Both *meta* and *para* substituents seem to equally influence the asymmetric induction, but in a less predictable way as previously observed in modified catalyst of type **2**.

Some secondary β-amino alcohols were examined in the epoxidation of **1a** (Table 5). The introduction of a methyl or a benzyl group in compound **13** and **14** was detrimental for the activity and the enantioselectivity (Table 5, Entries 1 and 2). Cycloesan *N*-benzylated catalyst **15**, which is a γ-amino alcohol, was slightly more active and enantioselective than **13** and **14** (Table 5, Entry 3). It is important to point out how acyclic secondary compounds **13** and **14** are very poor catalysts relative to structurally similar cyclic secondary α,α-L-diphenyl prolinol (**2a**; Table 5, Entry 4). Moreover, their performance is significantly inferior to that of parent primary amino alcohol **11b** (Table 3, entry 7). Then, *O*-methylated catalyst **2c** was employed in the epoxidation of **1a** to afford the product in poor yield, but satisfactory *ee* (Table 5, Entry 5).

Finally, some tertiary β-amino alcohols were employed as catalysts in the epoxidation of **1a** (Table 6). *N*-Methyl L-pyrrolidinol (**16**) gave epoxide **3a** in 17% yield and 7% *ee*

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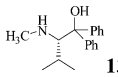
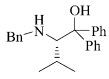
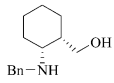
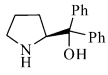
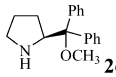
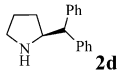
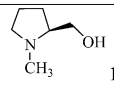
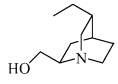
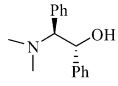
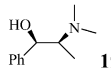
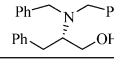
Table 5. Epoxidation of **1a** with secondary β-amino alcohols and TBHP.[a]

Entry	Catalyst	Time [h]	Yield **3a** [%][b]	*ee* **3a** [%][c]
1	 **13**	234	18	racemic
2	 **14**	218	9	racemic
3	 **15**	123	21	15 (α*R*,β*S*)
4[d]	 **2a**	94	72	75 (α*R*,β*S*)
5	 **2c**	97	14	63 (α*R*,β*S*)
6[d]	 **2d**	140	22	23 (α*R*,β*S*)

[a] Molar ratios: **1/4a**/TBHP, 1:0.30:1.4. [b] Isolated products after flash chromatography. [c] Determined by HPLC analysis on Chiralcel OD column. [d] Yields and *ee* values refer to those reported in ref.[13a]

(Table 6, Entry 1). More sterically hindered tertiary amino alcohol **17** proved to be inactive under the same conditions (Table 6, Entry 2). Although compound **18**, the *N*,*N*-dimethyl derivative of catalyst **8**, furnished traces of the product, it proved to be slightly more enantioselective than primary amino alcohol **8** (Table 6, Entry 3). (–)-*N*-methyl ephedrine (**19**) afforded a similar result in comparison to catalyst **18** (Table 6, Entry 4). Finally, acyclic compound **20** gave the product in slightly better yield but in racemic form (Table 6, Entry 5).

Table 6. Epoxidation of **1a** with tertiary β-amino alcohols and TBHP.[a]

Entry	Catalyst	Time [h]	Yield **3a** [%][b]	*ee* **3a** [%][c]
1	 **16**	195	17	7 (α*S*,β*R*)
2	 **17**	206	5	racemic
3	 **18**	200	5	13 (α*R*,β*S*)
4	 **19**	160	5	7 (α*R*,β*S*)
5	 **20**	141	14	racemic

[a] Molar ratios: **1/4a**/TBHP, 1:0.30:1.4. [b] Isolated products after flash chromatography. [c] Determined by HPLC analysis on Chiralcel OD column.

Upon analysis of the data in Tables 1–6, a picture emerges in which the epoxidation of *trans*-chalcone can be promoted with variable efficiency by primary, secondary, and tertiary β-amino alcohols. In addition to these observations, epoxidation was prevented in the presence of a primary amine and an acid as cocatalyst (Table 3, Entries 11 and 12). These data further confirm and generalize our hypothesis that the β-amino alcohol plays the role of a bifunctional catalyst according to the catalytic cycle proposed in Figure 2.

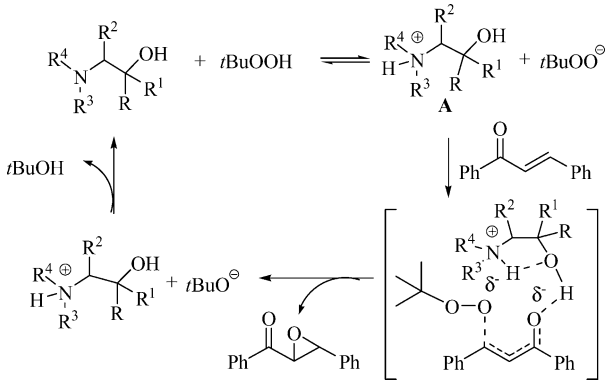


Figure 2. Proposed catalytic cycle for β-amino alcohols catalyzed epoxidation.

TBHP first undergoes deprotonation by the β-amino alcohol, which thus generates the active catalytic species, that is, the ammonium **A**/*tert*-butyl peroxyanion ion pair. The hydroxy group of the promoter then activates and orientates *trans*-chalcone through hydrogen bonding with its carbonyl group for the nucleophilic 1,4-addition of the *tert*-butyl peroxy anion according to the accepted mechanism for the Weitz–Scheffer epoxidation.[21] On the basis of the proposed catalytic cycle, the basicity of the amine and hydrogen bonding interactions are fundamental in regulating the activity of the promoters.

Solvation effects are of reduced importance in the stabilization of charged and polar species when hexane is used as the solvent. A more realistic idea on the basicity of secondary cyclic amines would be gained by considering the intrinsic basicity rather than the solution basicity. Intrinsic basicity of cyclic amines has been estimated by experimental and calculated gas-phase proton affinities.[22] Solvent leveling effects on the pK_{BH^+} measured in water (Table 7) for the four-, five-, and six-membered cyclic amines would not be expected in hexane. As a result, meaningful differences in the basicities of the amines can be predicted by evaluation of the proton affinities, and the four-membered ring amine is the least basic. Detectable differences in calculated pK_{BH^+} values were estimated in aprotic acetonitrile, which is a less polar solvent than water (Table 7).[23]

By taking this into account, the data reported in Tables 1 and 2 are more easily rationalized. Indeed, four-membered catalyst **4a** appeared significantly less active than catalysts **2b** and **5a**, whereas better performances are displayed by compounds **2b** and **5a**, whose basic properties become closer (Table 7).

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Table 7. Calculated and experimental gas-phase proton affinities and pK_{BH^+} values for cyclic amines.

Entry	PA(G3)[a]	PA(exp)[b]	pK_{BH^+}[c]
	936.3	932.1	11.29 (16.9)[d]
	946.3	938.8	11.27 (17.5)[d]
	948.1	943.4	11.22 (17.2)[d]

[a] Values given in kJ/mol as reported in ref.[22] [b] Values given in kJ/mol as reported in ref.[22] [c] Values in water as reported in ref.[22] [d] Calculated pK_{BH^+} in acetonitrile.

In solution, direct interactions between functional groups in a molecule are generally masked by the interfering presence of functional groups of the solvent. Apart from the gas phase, hexane can be considered an inert medium, where intra- and intermolecular hydrogen bonding interactions of a functionalized molecule are exalted and play a decisive role in affecting physical properties and eventually chemical activity. In the present study, we disclosed that simple primary β-amino alcohols catalyze the epoxidation of *trans*-chalcone and the enantioselectivity can be tuned to achieve an encouraging level.

The formation of the ion pair in hexane as the active species (Figure 2) deserves some considerations: (i) On going from tertiary to primary amino alcohols, ion-pairing interactions increase as stronger localized charged ammonium ions are formed that can better stabilize the unsolvated *tert*-butyl peroxyanion. (ii) Increasing alkyl substitution at the ammonium ion would preclude an optimized electrostatic interaction with the anion and give rise to a steric destabilization of the ion pair. This would explain the higher activity generally assured by primary and secondary cyclic amino alcohols with respect to acyclic secondary and tertiary amino alcohols, which form a looser and more sterically crowded ion pair. Moreover, the possibility of intramolecular hydrogen-bonding interactions between charged N–H and the vicinal oxygen atom of the hydroxy group would block the conformation of the β-hydroxy ammonium ion and impart steric rigidity to the ion pair, which thus influences the level of enantioselectivity. This would account for the remarkable difference observed in the enantioselectivities for the epoxidation of **1a** by promoters **2c** and **2d** (Table 5, Entries 5 and 6).[24] Finally, the key role of the hydroxy group in the catalyst is consistent with an intermolecular hydrogen-bonding interaction with the oxygen atom of the enone carbonyl group, which activates the enone towards 1,4-addition of the peroxyanion while directing and placing the partners in close proximity to react. Indeed, **2a** is the most active and enantioselective catalyst in comparison to **2c**,**d** (Table 5, Entry 4).[25]

Although primary amines are expected to be poorer promoters on the basis of pK_{BH^+} values, their activity can be significantly modulated by structural modifications (Tables 3 and 4). A contribution to the changeable activity of primary β-amino alcohols as catalysts in the epoxidation of *trans*-chalcone could be ascribed to the intramolecular hydrogen bonding formed in the corresponding β-hydroxy ammonium ions. Indeed, it has been proved, both experimentally and by calculations, that gas-phase proton affinities in structurally different primary β-amino alcohols are related to the dihedral θ angle (CO–CN) with a maximum value for $\theta = 0°$ and a minimum value for $\theta = 180°$.[26] This has been interpreted as the change in the internal hydrogen-bonding interaction of the β-hydroxy ammonium ion.[27]

Therefore, to serve as active and enantioselective promoters basicity, electrostatic interactions, as well as intra- and intermolecular hydrogen-bonding interactions, have to be considered in the catalysis provided by β-amino alcohols. To better understand the structure of the ammonium ions involved in the ion pair, we then investigated the gas-phase ammonium conformers of promoters **2b**, **4a**, **5a**, **12a** by using B3LYP density functional theory (Gaussian 03W, 6-31G* basis set).[28]

The lowest-energy conformers **I** and **II** of the most enantioselective catalysts **2b** and **4a** show the intramolecular hydrogen bond between the oxygen atom of the OH group with the N–H bond from the same side of the ring plane. Conformers **III** and **IV**, where the hydrogen bonding is with the N–H bond on the opposite side of the ring plane, proved to be 3.6 and 8.5 kJ/mol less stable than **I** and **II**, respectively (Figure 3). The energetic differences observed suggest that conformers **I** and **II** are likely involved in the ion pair during the epoxidation, which thus leads to a high level of enantioselectivity.

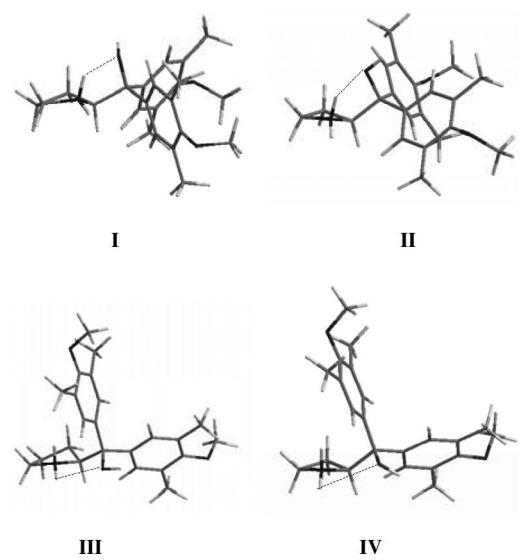

Figure 3. Calculated ammonium conformers of **2b** (**I**–**III**) and **4a** (**II**–**IV**).

Again, catalysts **5a** shows the most stable conformer **V** to have hydrogen bonding between the oxygen atom of the OH group with the N–H bond on the same side of the ring plane, but a smaller energy difference of 1.4 kJ/mol with the less stable conformer **VII** is observed (Figure 4).

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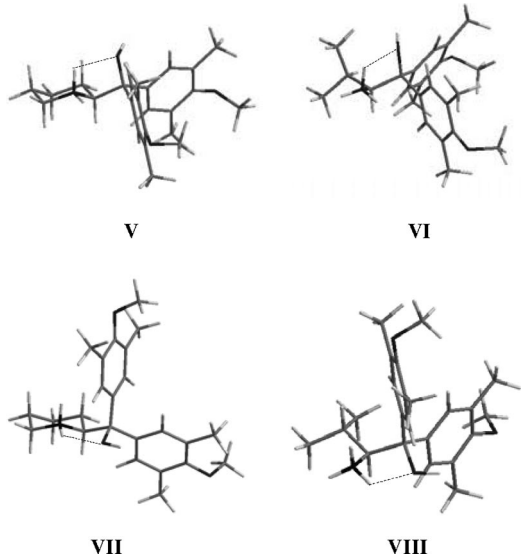

Figure 4. Calculated ammonium conformers of **5a** (**V**–**VII**) and **12a** (**VI**–**VIII**).

Finally, conformers **VI** and **VIII** of the flexible acyclic catalyst **12a** are almost comparable, as they have an energy difference of 0.6 kJ/mol. In the case of catalysts **5a** and **12a**, all ammonium conformers **V**–**VIII** are reasonably active in the epoxidation, which thus affords an average result in terms of asymmetric induction.

Conclusions

We studied the catalytic performance of easily accessible primary, secondary, and tertiary β-amino alcohols in the asymmetric epoxidation of *trans*-chalcones. They are able to catalyze the transformation with variable efficiency. In terms of activity and enantioselectivity, we confirmed that secondary pyrrolidine-based compounds are the best promoters in comparison to four- and six-membered ring analogues. Moreover, we disclosed that primary β-amino alcohols, straightforwardly available in one step from L-amino acid esters, are able to catalyze the epoxidation. Subtle modifications to the substitution pattern of the skeleton of primary β-amino alcohols were found to deeply influence the outcome of the reaction and encouraging levels of asymmetric induction were achieved. The influence of tunable properties such as hydrogen-bonding interactions and steric and electronic effects has been recognized; hence, these factors will have to be carefully taken into account for future catalyst development.

Experimental Section

General Details: All reactions requiring dry or inert conditions were conducted in flame-dried glassware under a positive pressure of argon. THF was freshly distilled before use from $LiAlH_4$. Reactions were monitored by thin-layer chromatography (TLC) on Merck silica gel plates (0.25 mm) and visualized by UV light or by phosphomolybdic acid/ethanol spray test. Flash chromatography was performed on Merck silica gel (60, particle size: 0.040–0.063 mm). ^1H and ^{13}C NMR spectra were recorded with Bruker DRX 400 and 300 spectrometers at room temperature in $CDCl_3$ as solvent. Chemical shifts for protons are reported by using residual $CHCl_3$ as internal reference (δ = 7.26 ppm). Carbon spectra were referenced to the shift of the ^{13}C signal of $CDCl_3$ (δ = 77.0 ppm). Optical rotations were performed with a Jasco Dip-1000 digital polarimeter by using the Na lamp. FTIR spectra were recorded as a thin film on KBr plates by using Bruker Vector 22 spectrometer and absorption maxima are reported in wavenumber (cm^{-1}). MS (ESI) was performed by using a Bio-Q triple quadrupole mass spectrometer (Micromass, Manchester, UK) equipped with an electrospray ion source. Melting points are uncorrected. All commercially available reagents were purchased from Aldrich. Petroleum ether (PE) refers to light petroleum ether. *trans*-Chalcones that were not commercially available were prepared by aldol condensation by using standard conditions. Hexane of HPLC grade, stored under preactivated molecular sieves (4 Å), was used as solvent for the epoxidation. Compound **5a** was prepared according to the literature.[29] Compounds **13**, **14**, and **18** were synthesized and characterized by comparison of NMR spectra with previously reported data.[30] Absolute configuration of the predominant enantiomer of epoxides was determined by comparison with the HPLC retention times by using Daicel Chiralcel OD and Daicel Chiralpak AD columns, as reported in the literature.[13,31]

General Procedure for the Epoxidation of *trans*-Chalcone: TBHP (5–6 M decane solution, 37 μL, 0.21 mmol) was added to a stirred solution of the β-amino alcohol (0.045 mmol) and *trans*-chalcone (31.2 mg, 0.150 mmol) in hexane (0.300 mL) at room temperature. Strirring was maintained for the indicated time (monitoring by TLC) in the Tables. The crude reaction mixture was directly purified by flash chromatography on silica gel (PE/diethyl ether, 99:1) to provide the epoxy ketone.

Supporting Information (see footnote on the first page of this article): Experimental procedures and characterization of products **4a**, **5a**, **12a**–**d**; computational data of conformers **I**–**VIII**.

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