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# Chiral amine catalyzed enantio- and diastereoselective Michael reaction in brine

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ABSTRACT

Simple pyrrolidine-based chiral amines were synthesized and used for the Michael addition of different ketones to a variety of nitro-olefins in brine. The effect of different surfactants and acids on the yields and stereochemical outcome of the Michael adducts was studied in detail. Chiral amine **1g** was found to catalyze the formation of Michael adducts with high enantioselectivity (up to >99%), diastereoselectivity [up to 98:2 (*syn*:*anti*)] and yield (up to 94%).



## 1. Introduction

The development of organic molecules as catalysts for asymmetric organic transformations in aqueous media is a major challenge for organic chemists. Such aqua-organocatalyzed reactions have also found a great deal of application in green chemistry because of their environmentally benign and inexpensive nature. In recent years, a large number of carbon–carbon and carbon–heteroatom bond forming reactions have been reported to be catalyzed by organic molecules in aqueous media.[1]

Among the different methods of carbon–carbon bond formation, the Michael addition is of special importance and has been widely used to generate valuable building blocks in organic synthesis.[2] Among the different types of Michael donors and acceptors used for the Michael reaction, the conjugate addition of aldehydes or ketones to nitroalkenes to afford γ-nitrocarbonyl compounds containing contiguous stereocenters is of special interest mainly due to the ready availability of the starting materials, inherent simplicity of the process and the ease of transformation of the nitro group into other groups such as amines, nitrile oxides, ketones, and carboxylic acids.[3] The γ-nitrocarbonyl compounds are also key precursors of various important compounds such as alkaloids,[4] aminoacids,[5,25a] antitumorals,[6] antibiotics,[7] peptidomimetics,[8] and marine metabolites[9] among others.[10] In recent years, tremendous effort has been made in developing efficient organocatalysts for enantioselective Michael reactions.[11] Among the different organocatalysts used for Michael reactions, the cinchona alkaloid and L-proline based chiral amines,[12a–e,g–k] chiral thioureas,[13] L-prolinols,[14] and chiral sulfonamides[15] have been widely used and proven to be most efficient. However, only a few of these catalysts have been found to be effective in an aqueous medium.[1d,e,12h–j,15f] Since we are interested in developing organocatalyzed synthetic transformations in aqueous media,[16] so we planned to design simple organocatalysts for enantioselective Michael reactions in aqueous media. Herein we report the synthesis of new L-proline based chiral amines and their application as organocatalysts for the Michael addition of ketones to different nitrostyrene derivatives in brine.

## 2. Results and discussion

A series of simple pyrrolidine-based chiral amines (Fig. 1) were synthesized based on the assumption that the pyrrolidine ring should act as the catalytic site by forming an enamine with the donor ketones, while the side chain should function as the chiral induction group by appropriately orienting the nitro-olefins using suitable steric and hydrophobic interactions.

Initially, a model reaction of cyclohexanone **2** and β-nitrostyrene **3a** was performed in brine using 10 mol % of diamine catalyst **1a** containing an aromatic moiety as side chain. The aromatic moiety was supposed to enhance the hydrophobic interactions in the aqueous medium[12f,i] (Scheme 1). Brine was chosen as the solvent instead of water because it is known in the literature that in the presence of amines, nitrostyrenes can polymerize and this polymerization could be inhibited by using an electrolyte solution as the solvent.[17]

The reaction was allowed to run for 30 h and its progress was observed at regular intervals. The crude reaction mixture obtained upon extraction and concentration was purified by column chromatography to obtain pure Michael adduct **4a** in 12% yield (Table 1, entry 1). The $^1$H NMR of the product showed the presence of two diastereomers in a ratio of 94:6 (*syn*:*anti*), which was calculated from the integration of the 1H signal at $\delta$ 3.75–3.80 (*syn*) and $\delta$ 3.96–4.05 (*anti*). The chiral HPLC analysis of product **4a** gave the enantiomeric excess of the *syn* diastereomer was 80%. By comparing the HPLC data and specific rotation of the Michael adduct with that reported in literature,[13] the absolute configuration of *syn* dia-

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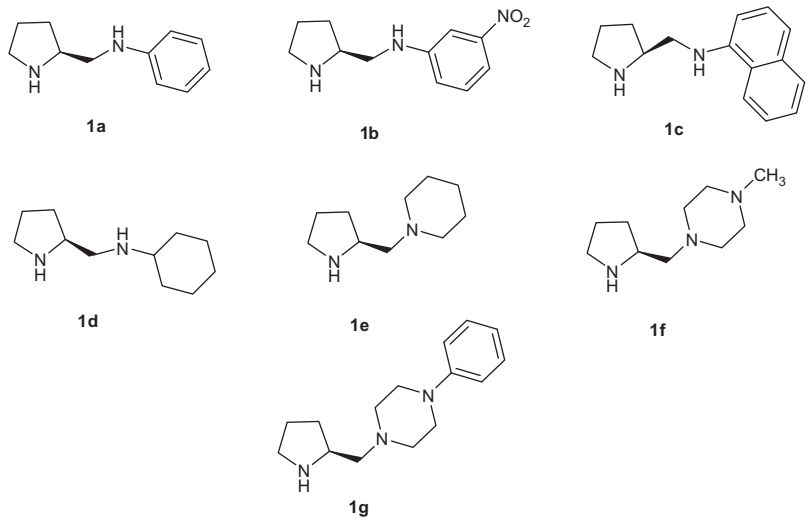
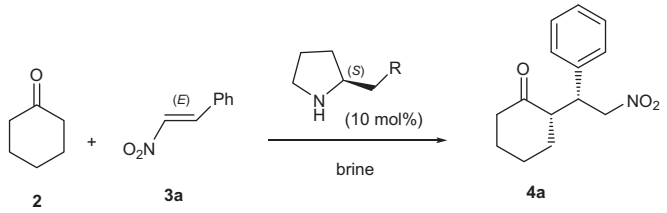



**Figure 1.** Structures of di-and triamine catalysts.




**Scheme 1.**

**Table 1**
Screening of different catalysts[a]

| Entry | Catalyst | Additive | Time (h) | Yield (%)[c] | dr[d] | ee[e] (*syn*) |
|---|---|---|---|---|---|---|
| 1 | **1a** | — | 30 | 12 | 94:6 | 80 |
| 2 | **1a** | SDS | 30 | 18 | 95:5 | 80 |
| 3[b] | **1a** | — | 24 | — | — | — |
| 4[b] | **1a** | SDS | 30 | — | — | — |
| 5 | **1b** | SDS | 2 days | 25 | 96:4 | 79 |
| 6 | **1c** | SDS | 2 days | — | — | — |
| 7 | **1d** | SDS | 20 | 48 | 94:6 | 78 |
| 8 | **1e** | SDS | 22 | 47 | 97:3 | 86 |
| 9 | **1f** | SDS | 24 | 41 | 98:2 | 81 |
| 10 | **1g** | SDS | 24 | 82 | 96:4 | 85 |
| 11[b] | **1g** | SDS | 24 | 36 | 93:7 | 82 |
| 12 | **1g** | — | 24 | 58 | 94:8 | 80 |

[a] Reaction conditions: 10 mol % of catalyst, 10 mol % of SDS, 1.25 mmol of cyclohexanone, 0.25 mmol of nitrostyrene, 0.5 mL of brine at 25 °C.
[b] Reaction was performed in water.
[c] Isolated yield.
[d] Diastereoselectivity determined from $^1$H NMR.
[e] Determined by HPLC using chiral column.

stereomer was designated as (2*S*,1′*R*). When the same reaction was carried out in water, only trace amounts of **4a** were obtained probably due to polymerization of the nitrostyrene (Table 1, entry 3).

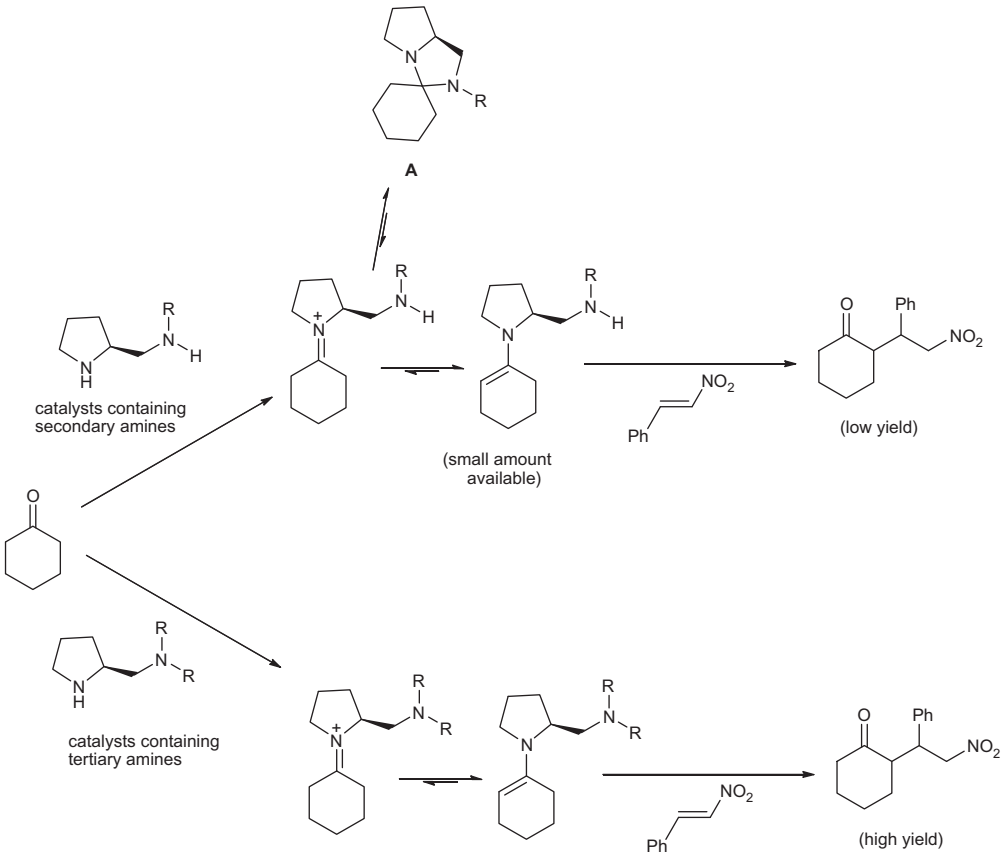
Surfactants are known to facilitate organic reactions in water, so a reaction of cyclohexanone and β-nitrostyrene catalyzed by **1a** was performed in water containing sodium dodecyl sulfate (SDS) as the surfactant. The addition of the surfactant (SDS) did not help in increasing the yield of product **4a** (Table 1, entry 4). Therefore, brine was found to be the best solvent system, while water and the water-surfactant solvent system were not a suitable medium for the organocatalytic Michael reaction. In order to determine if the surfactant had any effect on the yield of the reaction in brine, a reaction was performed with the addition of SDS. Under these conditions the Michael product **4a** was obtained in a slightly higher yield (18%), but there was no effect on its enantiomeric excess (Table 1, entry). Since the use of surfactants had a positive impact on the yields of reaction, we decided to perform further screening of the catalysts as well as optimization using a brine-SDS system. The screening of the other proline based di- and triamine catalysts **1a**–**1h** was performed using the model reaction in the brine-SDS reaction medium.

Catalyst **1b** with a nitro group on the phenyl moiety catalyzed the reaction providing **4a** in 25% yield in 2 days with a diastereomeric ratio of 96:4 (*syn*:*anti*) and enantiomeric excess of 79% (*syn*) (Table 1, entry 5). Catalyst **1c** with a naphthyl group did not catalyze the reaction, even when the reaction was run for 2 days (Table 1, entry 6). Catalysts **1d** and **1e** containing a cyclohexylamine or piperidine moiety gave **4a** in 48% and 47% yields, respectively (Table 1, entries 7–8). The Michael product **4a**, obtained as a result of catalysis by **1e**, showed a higher level of stereoselectivity; dr of 97:3 (*syn*:*anti*) and ee of 86% (*syn*). Michael reactions with catalysts **1f** and **1g** were performed which gave **4a** with similar levels of stereoselectivity; a comparatively high yield of product **4a** was obtained using catalyst **1g** (Table 1, entries 9–10). The probable reason for higher yield observed in case of catalyst **1g** seems to be hydrophobic effects provided by phenyl group.

Little to no yield was observed in the cases of secondary-secondary diamine catalysts **1a**–**1c** containing aromatic rings adjacent to the –NH group due to the formation of aminal **A** (Scheme 2). Due to the formation of **A**, the catalyst may become engaged in the cyclic form and so only a small amount of the catalyst is available to form an enamine with cyclohexanone.

From the screening of different di- and triamine catalysts, catalyst **1g** was found to be the best, affording Michael product **4a** with a yield of 82%, a dr of 96:4 (*syn*:*anti*) and an enantioselectivity of 85% in brine using SDS as the additive (Table 1, entry 1). Further optimization of the reaction conditions was performed by varying the amount of brine. The results are summarized in Table 2.

The Michael reaction without brine was very slow and gave product **4a** with a yield of 65%, dr of 92:8 (*syn*:*anti*) and ee of 83% after 3 days (Table 2, entry 1). The addition of 0.1 mL of brine to the reaction mixture reduced the reaction time to 34 h along with a slight increase in the yield and stereoselectivity of product **4a** (Table 2, entry 2). Increasing the amount of brine to 0.5 mL in-




**Scheme 2.** The plausible reason of low yields observed in case of secondary–secondary diamine catalysts.

**Table 2**
Variation of amount of brine[a]

| Entry | **2** (equiv) | Brine (mL) | Time (h) | Yield[b] | dr[c] (*syn*:*anti*) | ee[d] |
|---|---|---|---|---|---|---|
| 1 | 5 | — | 3 days | 65 | 92:8 | 83 |
| 2 | 5 | 0.1 | 34 | 71 | 94:6 | 85 |
| 3 | 5 | 0.25 | 24 | 76 | 94:6 | 84 |
| 4 | 5 | 0.5 | 24 | 82 | 96:4 | 85 |
| 5 | 5 | 0.75 | 24 | 81 | 94:6 | 82 |

[a] Reaction conditions: 10 mol % of catalyst, 10 mol % of SDS, 0.25 mmol of nitrostyrene at 25 °C.
[b] Isolated yield.
[c] Determined from $^1$H NMR.
[d] Determined by HPLC using a chiral column.

**Table 3**
Variation of the amount of cyclohexanone[a]

| Entry | **2** (equiv) | Brine (mL) | Time (h) | Yield[b] | dr[c] (*syn*:*anti*) | ee[d] (*syn*) |
|---|---|---|---|---|---|---|
| 1 | 3 | 0.5 | 2 days | 74 | 94:6 | 86 |
| 2 | 5 | 0.5 | 24 | 82 | 96:4 | 85 |
| 3[e] | 5 | 0.5 | 24 | 81 | 93:7 | 84 |
| 4 | 10 | 0.5 | 20 | 82 | 94:6 | 85 |

[a] Reaction conditions: 10 mol % of catalyst, 10 mol % of SDS, 0.25 mmol of nitrostyrene, 0.5 mL of brine at 25 °C.
[b] Isolated yield.
[c] Determined from $^1$H NMR.
[d] Determined by HPLC using a chiral column.
[e] 20 mol % of SDS were used.

creased the yield of **4a** to 82% and also reduced the reaction time to 24 h (Table 2, entries 3–4). Using an excess amount of brine (0.75 mL) resulted in a lower yield and enantioselectivity of product **4a** (Table 2, entry 5).

Next, the amount of cyclohexanone and catalyst was varied by fixing the amount of brine to 0.5 mL. The results are summarized in Tables 3 and 4, respectively.

Decreasing the amount of cyclohexanone decreased the yield of **4a** as well as increasing the reaction time (Table 3, entry 1). Increasing the amount of cyclohexanone slightly lowered the reaction rate (Table 3, entry 4). Any variation of the catalyst loading from 10 mol % did not give better results (Table 4).

Thus our standard conditions consisted of using 10 mol % of catalyst **1g**, 10 mol % of SDS, 5 equiv of cyclohexanone, 0.5 mL of brine, and 0.25 mmol of nitrostyrene at 25 °C. We next planned to screen different surfactants in order to study their effects on the yield and stereoselectivity of the Michael reaction. A variety

**Table 4**
Variation in the catalyst loading[a]

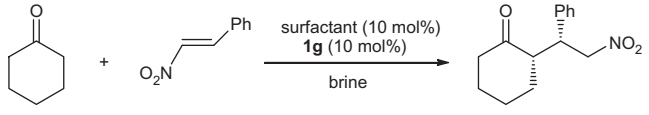
| Entry | Catalyst loading (mol %) | Time (h) | Yield[b] (%) | dr[c] (*syn*:*anti*) | ee[d] |
|---|---|---|---|---|---|
| 1 | 5 | 36 | 62 | 93:7 | 79 |
| 2 | 10 | 24 | 81 | 93:7 | 84 |
| 3 | 20 | 16 | 85 | 96:4 | 80 |

[a] Reaction conditions: 1.25 mmol of cyclohexanone, 0.25 mmol of nitrostyrene, 10 mol % of SDS, 0.5 mL of brine at 25 °C.
[b] Isolated yield.
[c] Determined from $^1$H NMR.
[d] Determined by HPLC using a chiral column.

of cationic, anionic, and non-ionic surfactants were screened. The results are summarized in Table 5.

The use of both cationic and anionic surfactants (except SDS) as additives yielded the Michael product **4a** in low yield (Table 5, en-

**Table 5**
Screening of different surfactants[a]




2a 3a 4a

| Entry | Surfactant | Time (h) | Yield[b] (%) | dr[c] (*syn*:*anti*) | ee[d] (*syn*) |
|---|---|---|---|---|---|
| 1 | HTPB | 28 | 34.41 | 93:7 | 80 |
| 2 | TTPB | 21 | 26.46 | 92:8 | 80 |
| 3 | DTPB | 22 | 18.18 | 93:7 | 77 |
| 4 | HTAB | 36 | 31 | 93:7 | 78 |
| 5 | TTAB | 36 | 35 | 93:7 | 82 |
| 6 | DTAB | 36 | 33.70 | 93:7 | 79 |
| 7 | Triton X-100 | 24 | 41.07 | 90:10 | 80 |
| 8 | CHAPS | 28 | 22.56 | 90:10 | 82 |
| 9 | Tween-20 | 19 | 86 | 95:5 | 87 |
| 10 | Tween-80 | 24 | 73 | 93:7 | 82 |
| 11 | SDS | 24 | 82 | 95:5 | 85 |
| 12 | SDBS | 24 | 31.0 | 95:5 | 84 |
| 13 | AOT | 28 | 41.72 | 91:8 | 84 |
| 14 | HPyBr | 30 | 46.91 | 91:9 | 80 |

[a] Reaction conditions: 10 mol % of catalyst, 10 mol % of surfactant, 1.25 mmol of cyclohexanone, 0.25 mmol of nitrostyrene, 0.5 mL of brine at 25 °C.
[b] Isolated Yield.
[c] Diastereoselectivity determined from $^1$H NMR.
[d] Determined by HPLC using a chiral column.

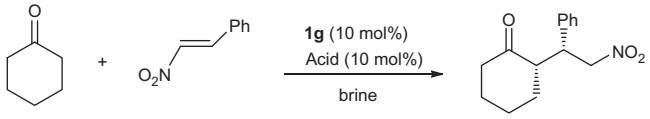
tries 1–6). High stereoselectivity was observed with anionic surfactant SDBS (Table 5, entry 12). However, the non-ionic surfactant Tween-20 yielded the Michael product **4a** with the highest yield and stereoselectivity (Table 5, entry 9). The yield and enantioselectivity of **4a** were found to be better when using the non-ionic surfactant Tween-20 than SDS (Table 5, entries 9 and 11).

The organocatalytic reactions in aqueous media were found to proceed with high stereoselectivity and yield when performed in the presence of an acid as the co-catalyst. This observation was made in the aldol reaction catalyzed by (*S*)-prolinamide, where the aldol products were obtained with high enantioselectivity and diastereoselectivity when reaction was performed in the presence of acids as co-catalysts.[16] We also observed that the pH of the reaction mixture could control the overall stereoselectivity of aldol product. In general, high stereoselectivity of the aldol product was observed when the pH of the reaction mixture was 4.5 ± 0.2.[16] As a result we planned to investigate the role of acids as co-catalysts in the Michael reaction of cyclohexanone and *trans*-β-nitrostyrene in brine. A number of acid co-catalysts were screened for the reaction. The results showed that the product was obtained with excellent enantioselectivity and diastereoselectivity with all acid additives (Table 6).

The highest yield of 90% and enantioselectivity of 89% of **4a** were observed with trichloroacetic acid (TCA) (Table 6, entry 3). A similar yield was also observed with benzoic acid but with slightly lower enantioselectivity (Table 6, entry 6). A good range of enantioselectivity and diastereoselectivity of **4a** were observed with TFA and 2-chlorobenzoic acid but with moderate yields (Table 6, entries 1 and 4). The product was obtained in low yield but high stereoselectivity with 2,4-dinitrophenol (DNP), acetic acid, and *p*-toluenesulfonic acid (TsOH) additives (Table 6, entries 2, 5 and 7).

No Michael product was formed with trifluoromethanesulfonic acid (TfOH), even after 30 h (Table 6, entry 8). This may be due to the strong ion-pair formation which results in inactivation of the catalyst. Since the use of brine had a clear advantage over water as evident from Table 1 (Table 1, entries 2, 4 and 10–11), we next

**Table 6**
Screening of different acid additives[a]




2a 3a 4a

| Entry | Acid | Time (h) | Yield[b] (%) | dr[c] (*syn*:*anti*) | ee[d] |
|---|---|---|---|---|---|
| 1 | TFA | 24 | 72 | 94:6 | 84 |
| 2 | DNP | 28 | 53 | 96:4 | 85 |
| 3 | TCA | 12 | 90 | 96:4 | 89 |
| 4 | 2-Chlorobenzoic acid | 24 | 77 | 95:5 | 84 |
| 5 | Acetic acid | 24 | 67 | 92:8 | 83 |
| 6 | Benzoic acid | 16 | 90 | 92:8 | 87 |
| 7 | TsOH | 24 | 61 | 93:7 | 83 |
| 8 | TfOH | 30 | — | — | — |

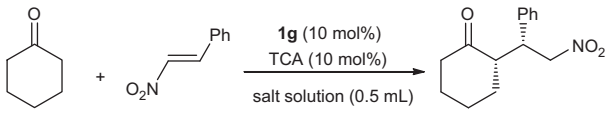
[a] Reaction conditions: 10 mol % of catalyst, 10 mol % of acid, 1.25 mmol of cyclohexanone, 0.25 mmol of nitrostyrene, 0.5 mL of brine at 25 °C.
[b] Isolated Yield.
[c] Diastereoselectivity determined from $^1$H NMR.
[d] Determined by HPLC using a chiral column.

decided to study the effect of other salt solutions on the yield and stereoselectivity of Michael product **4a**. The results are summarized in Table 7.

In all of the salt solutions, the Michael addition proceeded with excellent level of enantioselectivity but with slight differences in the yield of the Michael adduct (Table 7). A lower yield and stereoselectivity of Michael product were observed when the Michael reaction was performed in KCl and KBr solutions in comparison to NaCl and NaBr solutions (Table 7, entries 1–2 and 3–4). A moderate yield was obtained in saturated LiCl solution (Table 7, entry 6). Similar levels of stereoselectivity and yield were observed in both NaCl and NaBr solutions (Table 7, entries 1 and 2) but from an economical point of view, NaCl is more inexpensive and largely available. As a result, a saturated solution of NaCl (brine) was used as solvent for further screening of different substrates to explore the scope and limitation of the organocatalytic transformation.

Thus, the optimization of the reaction conditions gave the two best conditions, one using a Tween-20 surfactant (A) (Table 5, entry 9) and the other using TCA as the co-catalyst (B) (Table 6, entry 3). Since the results obtained using both conditions were comparable, we decided to screen the substrates using both sets of conditions.

**Table 7**
Screening of different salt solutions[a]




| Entry | Salt solution (satd) | Time (h) | Yield[b] (%) | dr[c] (*syn*:*anti*) | ee[d] |
|---|---|---|---|---|---|
| 1 | NaCl | 12 | 90 | 94:6 | 89 |
| 2 | NaBr | 12 | 88 | 95:5 | 89 |
| 3 | KCl | 12 | 82 | 84:16 | 87 |
| 4 | KBr | 12 | 80 | 86:14 | 86 |
| 5 | $NH_4Cl$ | 12 | 82 | 88:12 | 85 |
| 6 | LiCl | 12 | 74 | 92:8 | 84 |

[a] Reaction conditions: 10 mol % of catalyst, 10 mol % of TCA, 1.25 mmol of cyclohexanone, 0.25 mmol of nitrostyrene, 0.5 mL of salt solution at 25 °C.
[b] Isolated Yield.
[c] Diastereoselectivity determined from $^1$H NMR.
[d] Determined by HPLC using a chiral column.

Conditions A: 10 mol % of catalyst **1g**, 10 mol % of TCA (trichloroacetic acid), 5 equiv of cyclohexanone, 0.25 mmol of nitrostyrene and 0.5 mL of brine at 25 °C (Table 6, entry 3).

Conditions B: 10 mol % of catalyst **1g**, 10 mol % of Tween-20 surfactant, 5 equiv of cyclohexanone, 0.25 mmol of nitrostyrene and 0.5 mL of brine at 25 °C (Table 5, entry 9).

Conditions A gave slightly better results than conditions B, but since the differences in stereoselectivity and yield were very small, we decided to select both conditions to explore the scope of catalyst **1g**. The results are summarized in Table 8.

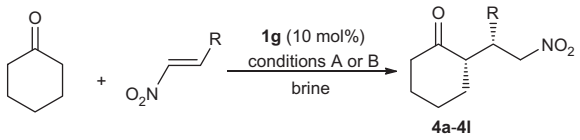
In general, reaction rates were faster under condition A (TCA as an additive) compared to conditions B (Tween-20 as an additive) albeit with similar yields but with slightly different stereoselectivities. The highest enantioselectivity of >99% was observed with 4-chloro substituted nitrostyrene under both reaction conditions A and B (Table 8, entries 11–12). Excellent enantioselectivity and diastereoselectivity were also observed with 2-naphthyl (under conditions A) (Table 8, entry 7) and 4-methoxy substituted nitrostyrenes (under conditions A and B) (Table 8, entries 19–20). Moderate levels of enantioselectivity were observed with 4-methyl (condition A), 3,4-dimethoxy, (conditions A and B) and 1-naphthyl (conditions B) substituted nitrostyrenes (Table 8, entries 3, 5, 6, and 10).

Different cyclic and acyclic ketones were screened by employing catalyst **1g** under conditions A and B to afford Michael products with moderate to excellent enantioselectivity (Table 9). Low enantioselectivity was observed with acetone as the donor in both conditions A and B (Table 9, entries 1–2). Excellent enantioselectivity was observed with 3-pentanone (Table 9, entries 3–4). Moderate enantioselectivity and diastereoselectivity were observed with cyclopentanone under both conditions (Table 9, entries 5–6). To further explore the scope of catalyst **1g**, 4-substituted cyclohexanones were next selected as the Michael donors. The Michael reaction of 4-substituted cyclohexanones led principally to chiral adducts with the formation of three carbon stereocenters. Despite the numerous numbers of organocatalytic processes for the Michael additions of carbonyl compounds to nitroolefins, catalytically stereoselective versions involving such types of ketones are rare.[18] We thus decided to perform the Michael reactions of 4-substituted cyclohexanones with different nitrostyrenes under both conditions A and B. The results are summarized in Table 9.

In general, moderate to good level of enantioselectivity was observed with all substrates under both conditions A and B. The highest enantioselectivity (of major isomer) was observed with Michael product **4r**, formed by the addition of 2-chloro nitrostyrene to 4-methyl substituted cyclohexanone (under both conditions A and B) (Table 9, entries 9–10). Good enantioselectivity was observed with other Michael products **4q**, **4s**, **4t**, **4u** under both conditions (Table 9, entries 7–8 and 11–16,). Good enantioselectivity was also observed with product **4v** formed by the addition of 4-*tert*-butylcyclohexanone to nitrostyrene (Table 9, entries 17–18).

Nitro-diene[14b,25] was also used as the Michael acceptor using catalyst **1g** under both reaction conditions (Scheme 3). Interestingly, the 1,6-addition adduct was not observed, and only the 1,4-addition product **4w** was formed with very good enantioselectivity and diastereoselectivity, thus highlighting the broad utility of the catalyst with structurally different substrates.

**Table 8**
Screening of different nitrostyrene derivatives[a]

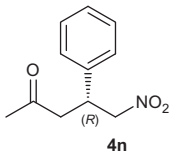
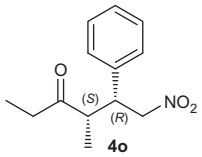
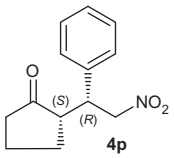
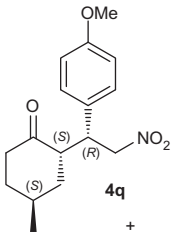
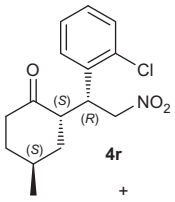
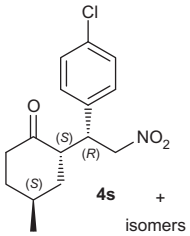
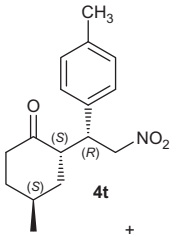
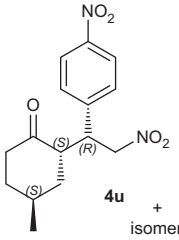


**4a-4l**

| Entry | Product R = | A or B | Time (h) | Yield[b] (%) | dr[c] (*syn*:*anti*) | ee[d] (*syn*) |
|---|---|---|---|---|---|---|
| 1 | Ph **4a** | A | 12 | 90 | 96:4 | 89 |
| 2 | | B | 19 | 86 | 95:5 | 87 |
| 3 | 4-MePh **4b** | A | 10 | 86 | 95:5 | 88 |
| 4 | | B | 14 | 84 | 95:5 | 77 |
| 5 | 3,4-$(MeO)_2$Ph **4c** | A | 8 | 89 | 93:7 | 87 |
| 6 | | B | 12 | 82 | 92:8 | 79 |
| 7 | 2-Naphthyl **4d** | A | 10 | 87 | 97:3 | 97 |
| 8 | | B | 13 | 90 | 98:2 | 89 |
| 9 | 1-Naphthyl **4e** | A | 12 | 89 | 86:14 | 78 |
| 10 | | B | 14 | 92 | 87:13 | 83 |
| 11 | 4-ClPh **4f** | A | 9 | 93 | 91:9 | >99 |
| 12 | | B | 10 | 88 | 90:10 | >99 |
| 13 | 4-FPh **4g** | A | 10 | 90 | 91:9 | 76 |
| 14 | | B | 13 | 92 | 92:8 | 78 |
| 15 | Cyclohexyl **4h** | A | 14 | 80 | 57:43 | 76 |
| 16 | | B | 17 | 78 | 58:42 | 75 |
| 17 | 2-Thienyl **4i** | A | 12 | 88 | 86:14 | 78 |
| 18 | | B | 16 | 84 | 85:15 | 78 |
| 19 | 4-MeOPh **4j** | A | 10 | 89 | 93:7 | 94 |
| 20 | | B | 14 | 89 | 92:8 | 93 |
| 21 | 4-$NO_2$-Ph **4k** | A | 8 | 91 | 75:25 | 75 |
| 22 | | B | 12 | 86 | 74:26 | 74 |
| 23 | 2-ClPh **4l** | A | 14 | 88 | 95:5 | 84 |
| 24 | | B | 17 | 84 | 94:6 | 84 |

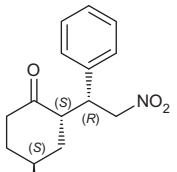
[a] Conditions A: 10 mol % of catalyst, 10 mol % of TCA, 1.25 mmol of cyclohexanone, 0.25 mmol of nitroalkene, 0.5 mL of salt solution at 25 °C. Conditions B: 10 mol % of catalyst, 10 mol % of Tween-20, 1.25 mmol of cyclohexanone, 0.25 mmol of nitroalkene, 0.5 mL of salt solution at 25 °C.
[b] Isolated yield.
[c] Diastereoselectivity determined from $^1$H NMR.
[d] Determined by HPLC using a chiral column.

**Table 9**
Screening of different ketone derivatives[a]

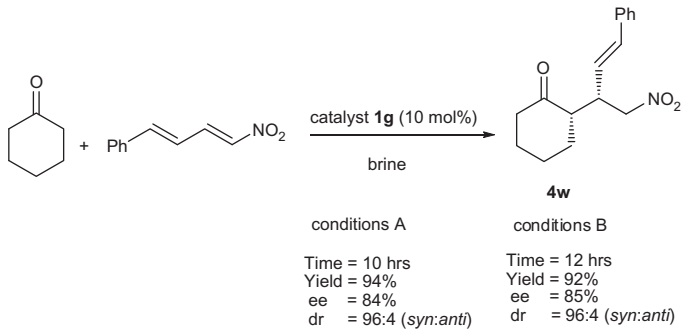
| Entry | Product | A or B | Time (h) | Yield[b] (%) | dr[c] | ee[d] (%) |
|---|---|---|---|---|---|---|
| 1 |  **4n** | A | 28 | 74 | — | 25 |
| 2 | | B | 30 | 79 | — | 27 |
| 3 |  **4o** | A | 3 days | 64 | 97:3 | 87 |
| 4 | | B | 4 days | 58 | 96:4 | 87 |
| 5 |  **4p** | A | 2 days | 69 | 70:30 | 52 |
| 6 | | B | 2.5 days | 75 | 72:28 | 51 |
| 7 |  **4q** + isomers | A | 16 | 89 | — | 79 |
| 8 | | B | 18 | 90 | — | 79 |
| 9 |  **4r** + isomers | A | 14 | 82 | — | 89 |
| 10 | | B | 16 | 84 | — | 88 |
| 11 |  **4s** + isomers | A | 14 | 77 | — | 81 |
| 12 | | B | 19 | 81 | — | 81 |
| 13 |  **4t** + isomers | A | 17 | 82 | — | 77 |
| 14 | | B | 20 | 85 | — | 77 |
| 15 |  **4u** + isomers | A | 18 | 71 | — | 82 |
| 16 | | B | 18 | 76 | — | 86 |

(*continued on next page*)

**Table 9** (*continued*)

| Entry | Product | A or B | Time (h) | Yield[b] (%) | dr[c] | ee[d] (%) |
|---|---|---|---|---|---|---|
| 17 |  | A | 14 | 94 | — | 78 |
| 18 | **4v** + isomers | B | 17 | 88 | — | 79 |

[a] Conditions A: 10 mol % catalyst 1 g, 10 mol % TCA (trichloroacetic acid), 1.25 mmol of cyclohexanone, 0.25 mmol nitrostyrene and 0.5 mL of brine at 25 °C. Conditions B: 10 mol % catalyst **1g**, 10 mol % Tween-20, 1.25 mmol of cyclohexanone, 0.25 mmol nitrostyrene and 0.5 mL of brine at 25 °C.
[b] Isolated yield.
[c] Determined from $^1$H NMR.
[d] Determined from HPLC using chiral columns.




**Scheme 3.** Michael reaction of cyclohexanone and a nitrodiene.

## 3. Conclusions

In conclusion, we have successfully demonstrated that very simple chiral amines can efficiently catalyze an enantioselective and diastereoselective Michael reaction in brine. The catalyst developed is capable of promoting efficient conjugate additions of cyclic and acyclic ketones to a wide range of nitro-olefins. Moreover, the methodology developed is very simple, environmentally benign, and highly enantioselective.

## 4. Experimental

### 4.1. General

NMR spectra were obtained at 300 MHz (JEOL AL-300) and 500 MHz (Bruker Avanced 500 MHz) for $^1$H NMR and at 75 MHz (JEOL AL-300) and 100 MHz (Bruker Avanced 400 MHz) for $^{13}$C NMR with $Me_4Si$ (in $CDCl_3$) as the internal standard. Chemical shifts are reported in $\delta$ values relative to TMS and coupling constants ($J$) are expressed in Hz. Spectroscopic patterns are designated as s = singlet; d = doublet; dd = doublet of doublets; q = quartet; t =triplet; br = broad; m = multiplet. When necessary, assignments were aided by DEPT-135 experiments. IR spectra were obtained with FT-IR Bruker (270–30) spectrophotometer and Varian 660-IR FT-IR spectrometer and reported in wave numbers ($cm^{-1}$). Mass spectra were recorded on JEOL-MSD-300, Bruker Esquire 300 LC Mass spectrometer and JEOL AccuTOF DART mass spectrometer. Optical rotations were noted on JASCO DIP-360 digital polarimeter. Analytical thin-layer chromatography (TLC) was performed on either (i) aluminum sheets pre-coated with silica gel 60F254 (Merck, India) or (ii) glass plates (7.5 × 2.5 cm) coated with silica gel GF-254 (Spectrochem India) containing 13% calcium sulfate as binder and various combinations of dichloromethane and methanol were used as eluents. Visualization of the spots was accomplished by exposing to UV light or iodine vapors. Column chromatography was performed on Spectrochem silica gel (60–120 mesh) using an increasing concentration of methanol in dichloromethane as the eluent.

### 4.2. General procedure for the synthesis of catalysts 1a–g

First, the protonated L-prolinamides were synthesized according to the literature.[16a] The deprotonation of these protonated L-prolinamides was carried with $Na_2CO_3$. The deprotonated L-prolinamides were further reduced into the corresponding di- and triamines by using $BH_3$ as the reducing agent.

### 4.3. Synthesis of (*S*)-2-(*N*-alkyl/arylaminometh-1-yl)pyrrolidine

To a stirred solution of (*S*)-2-(alkyl/arylcarbamoyl)pyrrolidinium bromide (0.184 mmol) in water (1.5 mL), was slowly added a saturated solution of sodium carbonate in water until the effervescence ceased and a clear solution was obtained. The mixture was extracted with chloroform (3 × 10 mL) and the combined organic layer was dried over anhydrous sodium sulfate, filtered, and distilled to give the product (*S*)-2-(alkyl/arylcarbamoyl)pyrrolidine with 72–89% yield.

To a completely dry 10 mL round bottomed flask, $NaBH_4$ (80 mg or 2.1 mmol) and dry THF (5 mL) were added and stirred for 5–10 min at 0 °C followed by the addition of (*S*)-2-(alkyl/arylcarba-

moyl)pyrrolidine (0.525 mmol). The reaction mixture was again stirred for 10–15 min and then a boron trifluoride:etherate (1:1) solution (4.68 equiv) was added slowly to the reaction mixture using a dropping funnel. The mixture was again stirred for 3 h at 0 °C and then refluxed for 10–12 h followed by quenching with methanol at room temperature until the effervescence ceased. The solvent was distilled on a water bath under reduced pressure. The residue was cooled to 0 °C and 6 M HCl (10 mL) was added to it. The resulting mixture was refluxed for 1 h in an oil bath and cooled to room temperature. The mixture was washed with ethyl acetate (2 × 8 mL) and ether (2 × 8 mL) to remove any organic impurities. The mixture was again cooled to 0 °C and a chilled solution of 4 M NaOH was added slowly to it with stirring until it attained a pH in the range of 9–10. The aqueous solution was extracted with dichloromethane (3 × 30 mL) and the organic extract was dried over anhydrous sodium sulfate and distilled to obtain (*S*)-2-(*N*-alkyl/arylaminometh-1-yl)pyrrolidine in 62–79% yield.

#### 4.3.1. (*S*)-2-(*N*-Phenylaminometh-1-yl)pyrrolidine[27] 1a

Yield, 77%; dark yellow liquid; $R_f$ 0.22 (methanol/chloroform, 6:94); IR (KBr); 1506, 1603, 3332 $cm^{-1}$; $[\alpha]_D^{20} = +18.6$ (*c* 0.72, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 1.40–1.53 (m, 1H, $CH_2$), 1.66–1.98 (m, 3H, $CH_2$), 2.55–2.65 (br s, 1H, NH), 2.81–3.0 (m, 3H, $CH_2$), 3.13–3.22 (m, 1H, $CH_2$), 3.34–3.44 (m, 1H, CH), 3.95–4.20 (br, 1H, NH), 6.60–6.70 (m, 3H, ArH), 7.12–7.24 (m, 2H, ArH); $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 25.5 (−ve), 29.4 (−ve), 46.3 (−ve), 48.3 (−ve), 57.7 (+ve), 112.9 (+ve), 117.2 (+ve), 129.1 (+ve), 148.4.

#### 4.3.2. (*S*)-2-(*N*-3-Nitrophenylaminometh-1-yl)pyrrolidine 1b

Yield, 62%; brown liquid; $R_f$ 0.20 (methanol/chloroform, 6:94), MS (Q-TOF) (*m*/*z*): 222.1257 ($M^+$); IR (KBr); 1527, 1622, 3420 $cm^{-1}$; $[\alpha]_D^{20} = +16.7$ (*c* 0.61, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 1.44–1.58 (m, 1H, $CH_2$), 1.67–2.09 (m, 3H, $CH_2$), 2.24 (br s, 1H, NH), 2.90–3.08 (m, 3H, $CH_2$), 3.13–3.27 (m, 1H, $CH_2$), 3.38–3.54 (m, 1H, CH), 4.71 (br s, 1H, NH), 6.87–6.90 (m, 1H, ArH), 7.21–7.28 (m, 1H, ArH), 7.38 (s, 1H, ArH), 7.48–7.50 (d, 1H, *J* = 8.1 Hz, ArH); $^{13}C$ NMR ($CDCl_3$, 75 MHz) ; 25.3, 29.1, 46.0, 47.1, 57.7, 106.1, 111.7, 118.9, 129.6, 149.1, 149.3.

#### 4.3.3. (*S*)-2-(*N*-Naphth-1-ylaminometh-1-yl)pyrrolidine 1c

Yield, 78%; dark brown sticky liquid; $R_f$ 0.54 (methanol/chloroform, 6:94), MS (Q-TOF) (*m*/*z*): 227.1406 ($M^+$); HRMS calcd for $C_{15}H_{19}N_2$ ($M^+$+H): 227.1548, found 227.1548; IR (KBr): 1474, 1581, 3047, 3366 $cm^{-1}$; $[\alpha]_D^{20} = +17.9$ (*c* 0.65, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 1.40–1.50 (m, 1H, $CH_2$), 1.60–1.69 (m, 1H, $CH_2$), 1.72–1.80 (m, 1H, $CH_2$), 1.82–1.90 (m, 1H, $CH_2$), 2.80–2.94 (m, 2H, $CH_2$), 3.09–3.16 (m, 1H, $CHCH_2NH$), 3.25–3.32 (m, 1H, $CHCH_2NH$), 3.45–3.53 (m, 1H, CH), 3.60 (br s, 1H, NH), 5.19 (br s, 1H, NH), 6.50–6.59 (d, 1H, *J* = 7.4 Hz, ArH,), 7.16–7.23 (m, 1H, ArH), 7.28–7.31 (m, 1H, ArH), 7.39–7.41 (m, 2H, ArH), 7.73–7.75 (d, 1H, *J* = 6.78 Hz), 7.95–7.98 (m, 1H, ArH); $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 25.4, 29.3, 46.1, 48.0, 57.4, 104.0, 117.0, 120.5, 123.5, 124.50, 125.5, 125.6, 126.5, 128.3, 134.2, 143.6.

#### 4.3.4. (*S*)-2-(*N*-Cyclohexylaminometh-1-yl)pyrrolidine[19] 1d

Yield, 75%; dark yellow liquid; $R_f$ 0.41 (methanol/chloroform, 6:94), MS (Q-TOF) (*m*/*z*): 183.1758 ($M^+$); IR (KBr): 2929, 3434 $cm^{-1}$; $[\alpha]_D^{20} = +14.45$ (*c* 0.78, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 0.97–1.25 (m, 5H, $CH_2$),1.30–1.46 (m, 1H, $CH_2$), 1.52–2.06 (m, 9H, $CH_2$ and NH), 2.44–2.50 (m, 1H, CH), 2.55–2.65 (m, 1H, $CHCH_2NH$), 2.75–2.83 (m, 1H, $CHCH_2NH$), 2.96–3.10 (m, 2H, $CH_2$), 3.28–3.40 (m, 1H, CH), 3.69 (br s, 1H, NH); $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 25.0, 25.6, 26.1, 29.6, 31.0, 33.3, 46.1, 47.2, 51.2, 57.0, 58.6.

#### 4.3.5. (*S*)-1-(Pyrrolidin-2-ylmethyl)piperidine[20] 1e

Yield, 63%; dark yellow liquid; $R_f$ 0.22 (methanol/chloroform, 6:94), MS (DART) (*m*/*z*): 169.24 ($M^+$); IR (KBr): 1456, 3296 $cm^{-1}$; $[\alpha]_D^{20} = +18.3$ (*c* 0.84, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 1.28–2.12 (m, 10H, $CH_2$), 2.27–2.59 (m, 6H, $CH_2$), 2.88–4.0 (m, 3H, $CH_2$ and CH), 3.49 (br s, 1H, NH); $^{13}C$ NMR ($CDCl_3$, 75 MHz,): $\delta$ 24.1, 25.6, 26.7, 27.8, 47.4, 54.2, 56.3, 59.8.

#### 4.3.6. (*S*)-1-Methyl-4-(pyrrolidin-2-ylmethyl)piperazine 1f

Yield, 62%; dark yellow liquid; $R_f$ 0.15 (methanol/chloroform, 6:94), MS (DART) (*m*/*z*): 184.20 ($M^+$); HRMS (ESI) calcd for $C_{10}H_{22}N_3$ ($M^+$+H): 184.1814, found 184.1807; IR (KBr): 1415, 3494 $cm^{-1}$; $[\alpha]_D^{20} = +17.1$ (*c* 0.83, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 1.22–1.41 (m, 1H, $CH_2$), 1.65–1.99 (m, 3H, $CH_2$), 2.25–2.30 (s, 3H, $NCH_3$), 2.32–2.72 (m, 10H, $CH_2$), 2.85–2.96 (m, 1H, $CH_2$), 2.98–3.10 (m, 1H, $CH_2$), 3.29–3.39 (m, 1H, CH), 3.51 (br s, 1H, NH); $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 24.6, 29.6, 45.7, 45.9, 53.3, 55.0, 55.4, 62.8, 77.4.

#### 4.3.7. (*S*)-1-Phenyl-4-(pyrrolidin-2-ylmethyl)piperazine 1g

Yield, 72%; dark brown thick liquid; $R_f$ 0.19 (methanol/chloroform, 6:94), MS (DART) (*m*/*z*): 246.21 ($M^+$); HMRS (ESI) calcd for $C_{15}H_{24}N_3$ ($M^+$+H) 246.1970, found 246.1965; IR (KBr): 1497, 1599, 3421 $cm^{-1}$; $[\alpha]_D^{20} = +17.0$ (*c* 0.77, $CHCl_3$); $^1H$ NMR ($CDCl_3$, 300 MHz,): $\delta$ 1.37–1.51 (m, 1H, $CH_2$), 1.72–1.85 (m, 2H, $CH_2$), 1.91–2.10 (m, 1H, $CH_2$), 2.30–2.45 (m, 2H, $CH_2$), 2.49–2.65 (m, 2H, $CH_2$), 2.69–2.80 (m, 2H, $CH_2$), 2.93–3.11 (m, 2H, $CH_2$), 3.13–3.29 (m, 4H, $CH_2$), 3.28–3.53 (m, 2H, CH and NH), 6.80–6.95 (m, 3H, ArH), 7.20–7.31 (m, 2H, ArH); $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 24.5, 29.5, 45.0, 45.6, 49.0, 53.4, 55.6, 62.3, 115.9, 119.6, 129.0, 151.2.

### 4.4. General procedure for the organocatalyzed asymmetric Michael reaction of cyclohexanone with *trans*-β-nitrostyrene in brine[21]

To a brine solution (0.5 mL), diamine **1g** (6.12 mg, 0.025 mmol) and trichloroacetic acid (2.5 μL, 0.025 mmol) were added at 25 °C and the mixture stirred for 2 min. Cyclohexanone (129 μL, 1.25 mmol) and *trans*-β-nitrostyrene (37.2 mg, 0.25 mmol) were then added to the brine and the reaction mixture was stirred for 24 h. The brine phase was extracted with ethyl acetate (3 × 8 mL) and organic extracts were dried over anhydrous $Na_2SO_4$, filtered, and concentrated to obtain a crude reaction mixture. The diastereoselectivity was determined by $^1H$ NMR analysis of the crude Michael product after short column chromatography purification. The enantiomeric excess (ee) of the Michael product was determined by chiral HPLC analyses. The relative and absolute configurations of the products were determined by comparison with the known $^1H$ NMR, chiral HPLC analysis, and specific rotation values.

#### 4.4.1. (*S*)-2-((*R*)-2′-Nitro-1′-phenylethyl)cyclohexanone 4a[12i]

Yield: 90%; white solid; mp 121–123 °C; $R_f$ 0.33 (ethyl acetate/hexane, 20:80); IR (KBr): 1349, 1551, 1699 $cm^{-1}$; *syn*/*anti* = 96:4; $[\alpha]_D^{20} = -27.8$ (*c* 0.87, $CHCl_3$); enantiomeric excess of *syn* diastereomer: 89%, determined by HPLC (Diacel chiralpak AS-H, hexane/*i*-PrOH 85:15, flow rate 0.5 mL/min, $\lambda$ = 208 nm); $t_R$ (*syn*, minor) = 25.01 min, $t_R$ (*syn*, major) = 36.47 min; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 1.19–1.29 (m, 1H, $CH_2$), 1.53–1.80 (m, 4H, $CH_2$), 2.05–2.19 (m, 1H, $CH_2$), 2.36–2.55 (m, 2H, $CH_2$), 2.63–2.76 (m, 1H, CH), 3.75–3.80 (dd, 0.96H (*syn*), $J_1$ = 9.9 Hz, $J_2$ = 4.5 Hz, $CHCH_2NO_2$), 3.96–4.05 (dd, 0.04H (*anti*), $J_1$ = 9.9 Hz, $J_2$ = 4.5 Hz, $CHCH_2NO_2$), 4.59–4.67 (m, 1H, $CHCH_2NO_2$), 4.91–4.96 (m, 1H, $CHCH_2NO_2$), 7.14–7.17 (m, 2H, ArH), 7.23–7.35 (m, 3H, ArH); $^{13}C$

NMR ($CDCl_3$, 75 MHz): $\delta$ 25.0, 28.5, 29.7, 33.2, 42.7, 43.9, 52.5, 78.9, 127.7, 128.1, 128.9, 137.7, 211.9.

#### 4.4.2. (*S*)-2-((*R*)-2′-Nitro-1′-*p*-tolylethyl)cyclohexanone 4b[22a]

Yield: 86%; white sticky solid; $R_f$ 0.36 (ethyl acetate/hexane, 20:80); MS (*m*/*z*): 283.8 ($M^+$+Na); IR ($CHCl_3$): 1379, 1551, 1707 $cm^{-1}$; *syn*/*anti* = 95:5; $[\alpha]_D^{20} = -29.4$ (*c* 0.91, $CHCl_3$); enantiomeric excess of *syn* diastereomer: 88%, determined by HPLC (Diacel chiralpak AS-H, hexane/*i*-PrOH 90:10, flow rate 0.8 mL/min, $\lambda$ = 254 nm); $t_R$ (*syn*, minor) = 11.47 min, $t_R$ (*syn*, major) = 16.40 - min; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 1.15–1.35 (m, 1H, $CH_2$), 1.48–1.85 (m, 4H, $CH_2$), 2.02–2.16 (m, 1H, $CH_2$), 2.31 (s, 3H, $CH_3$), 2.35–2.53 (m, 2H, $CH_2$), 2.61–2.73 (m, 1H, CH), 3.62–3.78 (m, 0.95H (*syn*), $CHCH_2NO_2$), 3.89–4.01 (m, 0.05H (*anti*), $CHCH_2NO_2$, 4.57–4.64 (dd, 1H, $J_1$ = 12.15 Hz, $J_2$ = 9.9 Hz, $CHCH_2NO_2$), 4.88–4.94 (dd, 1H, $J_1$ = 12.3 Hz, $J_2$ = 4.5 Hz, $CHCH_2NO_2$), 7.03–7.06 (d, 2H, *J* = 8.1 Hz, ArH), 7.11–7.14 (d, 2H, *J* = 8.4 Hz, ArH). $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 21.0, 24.9, 28.4, 33.1, 42.6, 43.5, 52.5, 79.0, 128.0, 129.5, 134.6, 137.4, 212.0.

#### 4.4.3. (*S*)-2-((*R*)-1′-(3″,4″-Dimethoxyphenyl)-2′-nitroethyl) cyclohexanone 4c[22b]

Yield: 89%; white solid; mp 125–126 °C; $R_f$ 0.34 (ethyl acetate/hexane, 20:80); MS (*m*/*z*): 330.0 ($M^+$+Na); IR ($CHCl_3$): 1310, 1550, 1706 $cm^{-1}$; *syn*/*anti* = 93:7; $[\alpha]_D^{20} = -33.8$ (*c* 0.78, $CHCl_3$); enantiomeric excess of *syn* diastereomer: 87%, determined by HPLC (Diacel chiralpak AS-H, hexane/*i*-PrOH 90:10, flow rate 1.0 mL/min, $\lambda$ = 254 nm); $t_R$ (*syn*, minor) = 24.79 min, $t_R$ (*syn*, major) = 43.87 min; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 1.19–1.35 (m, 1H, $CH_2$), 1.50–1.92 (m, 4H, $CH_2$), 2.06–2.17 (m, 1H, $CH_2$), 2.32–2.56 (m, 2H, $CH_2$), 2.60–2.77 (m, 1H, CH), 3.64–3.77 (m, 1H, $CHCH_2NO_2$), 3.79–3.94 (2s, 6H, 2× $OCH_3$), 4.56–4.68 (dd, 1H, $J_1$ = 12.45 Hz, $J_2$ = 9.9 Hz, $CHCH_2NO_2$), 4.83–4.97 (dd, 1H, $J_1$ = 12.15 Hz, $J_2$ = 4.8 Hz, $CHCH_2NO_2$), 6.66–6.72 (m, 2H, ArH), 6.78–6.82 (m, 1H, ArH); $^{13}$C NMR ($CDCl_3$, 300 MHz): $\delta$ (*syn* + *anti* isomers) 24.9, 27.2, 28.4, 30.2, 33.0, 42.6, 43.5, 52.7, 53.7, 55.7, 55.90, 55.9, 78.9, 111.4, 111.5, 120.1, 120.3, 130.1, 148.4, 149.1, 211.9.

#### 4.4.4. (*S*)-2-((*R*)-1′-Naphthalen-2″-yl-2′-nitro-ethyl)-cyclohexanone 4d[12i]

Yield: 87%; light brown solid; mp 115–117 °C; $R_f$ 0.40 (ethyl acetate/hexane, 20:80); MS (*m*/*z*): 319.9 ($M^+$+Na); IR ($CHCl_3$): 1379, 1550, 1707 $cm^{-1}$; *syn*/*anti* = 97:3; $[\alpha]_D^{20} = -37.3$ (*c* 0.91, $CHCl_3$); enantiomeric excess of *syn* diastereomer: 97%, determined by HPLC (Diacel chiralpak AS-H, hexane/*i*-PrOH 70:30, flow rate 0.8 mL/min, $\lambda$ = 254 nm); $t_R$ (*syn*, minor) = 9.59 min, $t_R$ (*syn*, major) = 16.27 min; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 1.18–1.35 (m, 1H, $CH_2$), 1.49–1.78 (m, 4H, $CH_2$), 2.01–2.18 (m, 1H, $CH_2$), 2.31–2.57 (m, 2H, $CH_2$), 2.74–2.85 (m, 1H, CH), 3.92–3.98 (m, 0.97H (*syn*), $CHCH_2NO_2$), 4.12–4.24 (m, 0.03H (*anti*), $CHCH_2NO_2$), 4.68–4.76 (dd, 1H, $J_1$ = 12.4 Hz, $J_2$ = 9.9 Hz, $CHCH_2NO_2$), 4.98–5.04 (dd, 1H, $J_1$ = 12.4 Hz, $J_2$ = 4.5 Hz, $CHCH_2NO_2$), 7.25–7.29 (m, 1H, ArH), 7.44–7.51 (m, 2H, ArH), 7.63 (s, 1H, ArH), 7.75–7.83 (m, 3H, ArH); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 24.9, 28.4, 33.3, 42.7, 44.1, 52.5, 78.8, 125.2, 126.1, 126.4, 127.6, 127.8, 128.8, 132.8, 133.3, 135.1, 211.8.

#### 4.4.5. (*S*)-2-((*R*)-1′-(Naphthalen-1″-yl)-2′-nitroethyl)cyclohexanone 4e[23]

Yield: 89%; brown solid; mp 110–112 °C; $R_f$ 0.41 (ethyl acetate/hexane, 20:80); MS (*m*/*z*): 319.8 ($M^+$+Na); IR ($CHCl_3$): 1341, 1550, 1706.5 $cm^{-1}$; *syn*/*anti* = 86:14; $[\alpha]_D^{20} = -72.2$ (*c* 0.79, $CHCl_3$); enantiomeric excess of *syn* diastereomer: 78%, determined by HPLC (Diacel chiralpak AS-H, hexane/*i*-PrOH 70:30, flow rate 0.8 mL/min, $\lambda$ = 254 nm); $t_R$ (*syn*, minor) = 10.88 min, $t_R$ (*syn*, major) =14.53 min; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 1.17–1.37 (m, 1H, $CH_2$), 1.40–1.78 (m, 4H, $CH_2$), 2.01–2.17 (m, 1H, $CH_2$), 2.37–2.57 (m, 2H, $CH_2$), 2.75–3.03 (brs, 1H, CH), 4.61–4.82 (brs, 0.86H (*syn*), $CHCH_2NO_2$), 4.83–4.99 (m, 1H, $CHCH_2NO_2$), 5.01–5.09 (dd, 1H, $J_1$ = 12.45 Hz, $J_2$ = 4.5 Hz, $CHCH_2NO_2$), 5.19–5.29 (brs, 0.14H (*anti*), $CHCH_2NO_2$), 7.30–7.60 (m, 4H, ArH), 7.60–7.79 (d, 1H, *J* = 8.1 Hz, ArH), 7.84–7.87 (m, 1H, ArH), 8.08–8.25 (brs, 1H, ArH); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (*syn* + *anti* isomers) 25.0, 25.2, 27.2, 28.6, 33.2, 36.8, 42.0, 42.8, 52.9, 53.7, 74.8, 78.7, 122.34, 122.7, 123.5, 124.9, 125.3, 125.8, 126.5, 126.7, 128.2, 129.0, 132.3, 134.0, 134.6, 210.3, 212.2.

#### 4.4.6. (*S*)-2-((*R*)-1′-(4″-Chlorophenyl)-2′-nitroethyl)cyclohexanone 4f[12i]

Yield: 93%; white solid; mp 125–126 °C; $R_f$ 0.38 (ethyl acetate/hexane, 20:80); MS (*m*/*z*): 303.8 ($M^+$+Na); IR ($CHCl_3$): 1379, 1551, 1707 $cm^{-1}$; *syn*/*anti* = 91:9; $[\alpha]_D^{20} = -40.2$ (*c* 0.91, $CHCl_3$); enantiomeric excess of *syn* diastereomer: >99%, determined by HPLC (Diacel chiralpak AS-H, hexane/*i*-PrOH 90:10, flow rate 1.0 mL/min, $\lambda$ = 254 nm); $t_R$ (*syn*, minor) = 13.23 min, $t_R$ (*syn*, major) = 19.79 - min; $^1$H NMR ($CDCl_3$, 300 MHz,): $\delta$ 1.13–1.35 (m, 1H, $CH_2$), 1.50–1.81 (m, 4H, $CH_2$), 2.0–2.19 (m, 1H, $CH_2$), 2.31–2.55 (m, 2H, $CH_2$), 2.60–2.72 (m, 1H, CH), 3.70–3.83 (m, 0.91H (*syn*), $CHCH_2NO_2$), 3.85–3.99 (m, 0.09H (*anti*), $CHCH_2NO_2$), 4.56–4.64 (dd, 1H, $J_1$ = 12.6 Hz, $J_2$ = 9.9 Hz, $CHCH_2NO_2$), 4.90–4.96 (dd, 1H, $J_1$ = 12.6 Hz, $J_2$ = 4.5 Hz, $CHCH_2NO_2$), 7.10–7.14 (m, 2H, ArH), 7.26–7.31 (m, 2H, ArH); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 25.0, 28.4, 33.1, 42.7, 43.3, 52.3, 78.5, 129.1, 129.5, 129.8, 133.5, 136.2, 211.5.

#### 4.4.7. (*S*)-2-((*R*)-1′-(4″-Fluorophenyl)-2′-nitroethyl)cyclohexanone 4g[12i]

Yield: 90%; brown solid; mp 69–70 °C; $R_f$ 0.34 (ethyl acetate/hexane, 20:80); MS (*m*/*z*): 287.8 ($M^+$+Na); IR ($CHCl_3$): 1379, 1551, 1708 $cm^{-1}$; *syn*/*anti* = 91:9; $[\alpha]_D^{20} = -30.4$ (*c* 0.82, $CHCl_3$); enantiomeric excess of *syn* diastereomer: 76%, determined by HPLC (Diacel chiralpak AS-H, hexane/*i*-PrOH 90:10, flow rate 1.0 mL/min, $\lambda$ = 254 nm); $t_R$ (*syn*, minor) = 14.82 min, $t_R$ (*syn*, major) = 20.88 - min; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 1.17–1.30 (m, 1H, $CH_2$), 1.47–1.85 (m, 4H, $CH_2$), 2.03–2.16 (m, 1H, $CH_2$), 2.31–2.54 (m, 2H, $CH_2$), 2.60–2.73 (m, 1H, CH), 3.74–3.79 (m, 0.91H (*syn*), $CHCH_2NO_2$), 3.88–3.99 (m, 0.09H (*anti*), $CHCH_2NO_2$), 4.55–4.63 (dd, 1H, $J_1$ =12.45 Hz, $J_2$ = 9.9 Hz, $CHCH_2NO_2$), 4.90–4.95 (dd, 1H, $J_1$ = 12.6 Hz, $J_2$ = 4.5 Hz, $CHCH_2NO_2$), 6.97–7.04 (m, 2H, ArH), 7.12–7.17 (m, 2H, ArH); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (*syn* + *anti* isomers): 25.0, 26.9, 28.4, 33.1, 42.6, 43.2, 52.5, 78.8, 115.7, 115.9, 129.7, 129.8, 133.4, 133.5, 160.4, 163.7, 211.6.

#### 4.4.8. (*S*)-2-((*R*)-1′-Cyclohexyl-2′-nitroethyl)cyclohexanone 4h[12i]

Yield: 80%; white liquid; $R_f$ 0.28 (ethyl acetate/hexane, 20:80); MS (*m*/*z*): 275.8 ($M^+$+Na); IR ($CHCl_3$): 1379, 1550, 1707 $cm^{-1}$; *syn*/*anti* = 57:43; $[\alpha]_D^{20} = -16.8$ (*c* 0.68, $CHCl_3$); enantiomeric excess of *syn* diastereomer: 76%, determined by HPLC (Diacel chiralpak AD-H, hexane/*i*-PrOH 95:5, flow rate 1.0 mL/min, $\lambda$ = 214 nm); $t_R$ (*syn*, major) = 7.55 min, $t_R$ (*syn*, minor) = 8.35 min; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 0.83–1.44 (m, 6H, CyH), 1.48–1.84 (m, 8H, CyH), 1.90–2.0 (m, 1H, CyH), 2.02–2.20 (m, 2H, CyH), 2.22–2.90 (m, 4H, CyH and $CHCH_2NO_2$), 4.29–4.40 (m, 1.43H (*syn* + *anti*), $CHCH_2NO_2$), 4.61–4.68 (dd, 0.57H (*syn*), $J_1$ = 13.9 Hz, $J_2$ = 6 Hz, $CHCH_2NO_2$); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (*syn* + *anti* isomers) 25.1, 25.3, 26.2, 26.3, 26.4, 27.4, 27.8, 29.6, 29.8, 30.0, 31.0, 31.4, 32.3, 38.9, 39.0, 39.9, 42.1, 42.6, 43.6, 50.6, 50.8, 75.9.

#### 4.4.9. (*S*)-2-((*S*)-1′-Thien-2″-yl-2′-nitro-ethyl)-cyclohexanone 4i[12i]

Yield: 88%; dark brown solid; mp 69–71 °C; $R_f$ 0.34 (ethyl acetate/hexane, 20:80); MS (*m*/*z*): 275.7 ($M^+$+Na); IR ($CHCl_3$): 1378, 1552, 1706 $cm^{-1}$; *syn*/*anti* = 86:14; $[\alpha]_D^{20} = -32.2$ (*c* 0.88, $CHCl_3$);

enantiomeric excess of *syn* diastereomer: 78%, determined by HPLC (Diacel chiralpak AS-H, hexane/*i*-PrOH 95:5, flow rate 0.5 mL/min, $\lambda$ = 254 nm); $t_R$ (*syn*, minor) = 38.17 min, $t_R$ (*syn*, major) = 48.03 - min; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 1.22–1.40 (m, 1H, $CH_2$), 1.53–1.77 (m, 2H, $CH_2$), 1.79–1.98 (m, 2H, $CH_2$), 2.07–2.23 (m, 1H, $CH_2$), 2.28–2.55 (m, 2H, $CH_2$), 2.61–2.78 (m, 1H, CH), 4.08–4.25 (m, 1H, $CHCH_2NO_2$), 4.61–4.68 (dd, 1H, $CHCH_2NO_2$, $J_1$ = 12.6 Hz, $J_2$ = 9.3 Hz), 4.86–4.92 (m, 1H, $CHCH_2NO_2$), 6.86–6.94 (m, 2H, ArH), 7.20–7.26 (m, 1H, ArH); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (*syn* + *anti* isomers) 25.0, 28.2, 32.7, 39.3, 42.2, 42.5, 53.3, 53.5, 79.1, 124.9, 125.17, 126.6, 126.7, 126.9, 140.5, 211.1.

#### 4.4.10. (*S*)-2-((*R*)-1′-(4″-Methoxyphenyl)-2′-nitroethyl)cyclohexanone 4j[12i]

Yield: 89%; brown solid; mp 107–109 °C; $R_f$ 0.31 (ethyl acetate/hexane, 20:80); MS (*m*/*z*): 299.9 ($M^+$+Na); IR ($CHCl_3$): 1380, 1551, 1706 $cm^{-1}$; *syn*/*anti* = 93:7; $[\alpha]_D^{20} = -22.3$ (*c* 0.94, $CHCl_3$); enantiomeric excess of *syn* diastereomer: 94%, determined by HPLC (Diacel chiralpak AD-H, hexane/*i*-PrOH 80:20, flow rate 0.5 mL/min, $\lambda$ = 254 nm); $t_R$ (*syn*, minor) = 17.92 min, $t_R$ (*syn*, major) = 21.71 - min; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 1.14–1.32 (m, 1H, $CH_2$), 1.47–1.85 (m, 4H, $CH_2$), 2.01–2.18 (m, 1H, $CH_2$), 2.30–2.54 (m, 2H, $CH_2$), 2.60–2.71 (m, 1H, CH), 3.66–3.78 (m, 1H, $CHCH_2NO_2$), 3.79 (s, 3H, $OCH_3$), 4.54–4.61 (dd, 1H, $J_1$ = 12.3 Hz, $J_2$ = 9.9 Hz, $CHCH_2NO_2$), 4.88–4.93 (dd, 1H, $J_1$ = 12.3 Hz, $J_2$= 4.5 Hz, $CHCH_2NO_2$), 6.82–6.86 (m, 2H, ArH), 7.06–7.09 (m, 2H, ArH); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (*syn* + *anti* isomers) 24.9, 28.4, 30.1, 33.1, 42.3, 42.6, 43.1, 52.6, 53.7, 55.2, 79.1, 114.1, 114.3, 129.1, 129.4, 159.0, 212.0.

#### 4.4.11. (*S*)-2-((*R*)-1′-(4″-Nitrophenyl)-2′-nitroethyl)cyclohexanone 4k[24]

Yield: 91%; brown solid; mp 107–109 °C; $R_f$ 0.28 (ethyl acetate/hexane, 20:80); MS (*m*/*z*): 314.9 ($M^+$+Na); IR ($CHCl_3$): 1348, 1379, 1521, 1552, 1707 $cm^{-1}$; *syn*/*anti* = 75:25; $[\alpha]_D^{20} = -22.4$ (*c* 0.94, $CHCl_3$); enantiomeric excess of *syn* diastereomer: 75%, determined by HPLC (Diacel chiralpak IB, hexane/*i*-PrOH 90:10, flow rate 0.5 mL/min, $\lambda$ = 254 nm); $t_R$ (*syn*, minor) = 63.25 min, $t_R$ (*syn*, major) = 68.75 min; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 1.16–1.46 (m, 1H, $CH_2$), 1.50–1.98 (m, 4H, $CH_2$), 2.0–2.21 (m, 1H, $CH_2$), 2.24–2.58 (m, 2H, $CH_2$), 2.64–2.88 (m, 1H, CH), 3.85–4.01 (m, 0.75H (*syn*), $CHCH_2NO_2$), 4.02- 4.13 (m, 0.25H (*anti*), $CHCH_2NO_2$), 4.88–5.02 (m, 2H, $CHCH_2NO_2$), 7.38–7.49 (m, 2H, ArH), 8.16–8.22 (m, 2H, ArH); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (*syn* + *anti* isomers) 25.1, 27.3, 28.3, 30.6, 33.2, 42.3, 42.7, 43.3, 43.7, 52.2, 53.4, 76.4, 77.9, 123.9, 124.1, 129.3, 129.5, 145.5, 146.0, 147.5, 210.8.

#### 4.4.12. (*S*)-2-((*R*)-1′-(2″-Chlorophenyl)-2′-nitroethyl)cyclohexanone 4l[12i]

Yield: 88%; yellow liquid; $R_f$ 0.36 (ethyl acetate/hexane, 20:80); MS (*m*/*z*): 303.8 ($M^+$+Na); IR ($CHCl_3$): 1379, 1551, 1707 $cm^{-1}$; *syn*/*anti* = 95:5; $[\alpha]_D^{20} = -23.2$ (*c* 0.84, $CHCl_3$); enantiomeric excess of *syn* diastereomer: 84%, determined by HPLC (Diacel chiralpak AS-H, hexane/*i*-PrOH 99:1, flow rate 1 mL/min, $\lambda$ = 211 nm); $t_R$ (*syn*, minor) = 26.69 min, $t_R$ (*syn*, major) = 34.03 min; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 1.22–1.45 (m, 1H, $CH_2$), 1.53–1.87 (m, 4H, $CH_2$), 2.05–2.18 (m, 1H, $CH_2$), 2.33–2.56 (m, 2H, $CH_2$), 2.83–2.99 (m, 1H, CH), 4.02–4.37 (m, 0.95H (*syn*), $CHCH_2NO_2$), 4.60–4.72 (m, 0.05H (*anti*), $CHCH_2NO_2$), 4.88–4.92 (m, 2H, $CHCH_2NO_2$), 7.16–7.28 (m, 3H, ArH), 7.35–7.41 (m, 1H, ArH); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (*syn* + *anti* isomers) 25.2, 28.5, 33.0, 40.9, 42.7, 51.7, 77.4, 127.3, 128.8, 129.4, 130.3, 134.5, 135.4, 211.5.

#### 4.4.13. (*R*)-5-Nitro-4-phenyl-pentan-2-one 4n[12i]

Yield: 74%; white solid; mp 81–83 °C; $R_f$ 0.18 (ethyl acetate/hexane, 20:80); IR (KBr): 1383, 1546, 1715 $cm^{-1}$; $[\alpha]_D^{20} = -4.6$ (*c* 0.91, $CHCl_3$); enantiomeric excess: 25% determined by HPLC (Diacel chiralpak AS-H, hexane/*i*-PrOH 80:20, flow rate 0.5 mL/min, $\lambda$ = 225 nm); $t_R$ (minor) = 39.32 min, $t_R$ (major) = 48.69 min; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 2.11 (s, 3H, $CH_3$), 2.90–2.92 (d, 2H, $J$ = 6 Hz, $CH_2CO$), 3.90–4.05 (m, 1H, $CHCH_2NO_2$), 4.55–4.72 (m, 2H, $CHCH_2NO_2$), 7.15–7.37 (m, 5H, ArH); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 30.4, 39.0, 46.1, 79.4, 127.4, 127.9, 129.1, 138.8, 205.4.

#### 4.4.14. (4*S*,5*R*)-4-Methyl-6-nitro-5-phenylhexan-3-one 4o[26]

Yield: 64%; light yellow liquid; $R_f$ 0.28 (ethyl acetate/hexane, 20:80), *syn*/*anti* = 97:3; IR (KBr): 1384, 1551, 1699 $cm^{-1}$; $[\alpha]_D^{20} = -35.4$ (*c* 0.81, $CHCl_3$); enantiomeric excess of *syn* diastereomer: 87%, determined by HPLC (Diacel chiralpak IB, hexane/*i*-PrOH 99:1, flow rate 1.0 mL/min, $\lambda$ = 220 nm); $t_R$ (*syn*, major) = 20.21 min, $t_R$ (*syn*, minor) = 25.71 min; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 0.95–0.98 (d, 2.7H, $J$ = 7.2 Hz, $CHCH_3$), 1.04–1.09 (t, 2.7H, $J$ = 7.2 Hz, $CH_2CH_3$), 1.17–1.20 (d, 0.3H, $J$ = 7.2 Hz, $CHCH_3$), 1.23–1.28 (t, 0.3H, $J$ = 7.2 Hz, $CH_2CH_3$), 2.26–250 (m, 1H, $CH_2CH_3$), 2.53–2.70 (m, 1H, $CH_2CH_3$), 2.92–3.05 (m, 1H, $CHCH_3$), 3.63–3.82 (m, 0.97H (*syn*), CHAr, 4.08–4.17 (m, 0.03H (*anti*), CHAr), 4.52–4.84 (m, 2H, $CH_2NO_2$), 7.12–7.21 (m, 2H, ArH), 7.22–7.40 (m, 3H, ArH); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 7.6, 16.3, 35.4, 46.0, 48.3, 78.3, 127.8, 127.9, 128.9, 129.0, 137.6, 213.6.

#### 4.4.15. (*S*)-2-((*R*)-2′-Nitro-1′-phenyl-ethyl)-cyclopentanone 4p[12i]

Yield: 69%; dark brown liquid; $R_f$ 0.35 (ethyl acetate/hexane, 20:80), *syn*/*anti* = 70:30; IR (KBr): 1382, 1552, 1733 $cm^{-1}$; $[\alpha]_D^{20} = -29.9$ (*c* 0.78, $CHCl_3$); enantiomeric excess of *syn* diastereomer: 52%, determined by HPLC (Diacel chiralpak AS-H, hexane/*i*-PrOH 90:10, flow rate 0.5 mL/min, $\lambda$ = 211 nm); $t_R$ (*syn*, minor) = 26.29 min, $t_R$ (*syn*, major) = 35.50 min; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 1.39–1.53 (m, 1H, $CH_2$), 1.55–1.98 (m, 4H, $CH_2$), 2.05–2.22 (m, 1H, $CH_2$), 2.28–2.55 (m, 1H, CH), 3.62–3.76 (m, 0.7H (*syn*), CHAr), 3.76–3.88 (m, 0.3H (*anti*), CHAr), 4.62–4.78 (m, 0.7H, $CH_2NO_2$), 4.95–5.07 (m, 0.7H, $CH_2NO_2$), 5.20–5.40 (m, 0.6H, $CH_2NO_2$), 7.02–7.49 (m, 5H, ArH); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (*syn* + *anti* isomers) 20.2, 20.5, 26.9, 28.2, 38.6, 39.2, 43.9, 44.1, 50.4, 51.4, 77.4, 77.9, 78.2, 127.8, 127.9, 128.3, 128.4, 128.8, 128.9, 129.0, 137.7, 218.51.

#### 4.4.16. (2*S*,4*S*)-2-((*R*)-1′-(4″-Methoxyphenyl)-2′-nitroethyl)-4-methylcyclohexanone 4q[18]

Yield: 89%; white liquid; $R_f$ 0.32 (ethyl acetate/hexane, 20:80); MS (*m*/*z*): 313.8 ($M^+$+Na); IR ($CHCl_3$): 1380, 1551, 1708 $cm^{-1}$; $[\alpha]_D^{20} = -32.3$ (*c* 0.78, $CHCl_3$); enantiomeric excess of major diastereomer: 80%, determined by HPLC (Diacel chiralpak AS-H, hexane/*i*-PrOH 90:10, flow rate 0.5 mL/min, $\lambda$ = 254 nm); $t_R$ (minor) = 32.95 min, $t_R$ (major) = 73.31 min; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 0.87–0.89 (d, 0.88H, $J$ = 6.6 Hz, $CH_3$), 0.96–0.98 (d, 2.12H, $J$ = 6.6 Hz, $CH_3$), 1.28–1.70 (m, 3H, $CH_2$), 1.84–2.11 (m, 2H, $CH_2$), 2.38–2.51 (m, 2H, $CH_2$ and CH), 2.54–2.70 (m, 1H, CH), 3.55–3.76 (m, 1H, CHAr), 3.77 (s, 3H, $OCH_3$), 4.40–4.65 (m, 1.56H, $CH_2NO_2$), 4.78–4.90 (m, 0.44H, $CH_2NO_2$), 6.77–6.83 (m, 2H, ArH), 7.0–7.06 (m, 2H, ArH); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (all isomers) 19.5, 21.0, 26.5, 32.3, 34.4, 36.4, 37.8, 38.6, 41.2, 42.2, 43.2, 43.4, 50.3, 55.2, 79.3, 114.3, 114.5, 128.9, 129.01, 129.2, 159.2, 213.2.

#### 4.4.17. (2*S*,4*S*)-2-((*R*)-1′-(2″-Chlorophenyl)-2′-nitroethyl)-4-methylcyclohexanone 4r[18]

Yield: 82%; light yellow liquid; $R_f$ 0.37 (ethyl acetate/hexane, 20:80); MS (*m*/*z*): 317.8 ($M^+$+Na); IR ($CHCl_3$): 1379, 1553, 1709 $cm^{-1}$; $[\alpha]_D^{20} = -55.4$ (*c* 0.96, $CHCl_3$); enantiomeric excess of major diastereomer: 89%, determined by HPLC (Diacel chiralpak AD-H, hexane/*i*-PrOH 98:2, flow rate 0.5 mL/min, $\lambda$ = 254 nm); $t_R$ (minor) = 34.32 min, $t_R$ (major) = 43.24 min; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 0.99–1.01 (d, 0.81H, $J$ = 6.3 Hz, $CH_3$), 1.07–1.10 (d, 0.39H, $J$ = 6.6 Hz, $CH_3$), 1.14–1.16 (d, 1.74H, $J$ = 6.9 Hz, $CH_3$), 1.45–

1.70 (m, 2H, $CH_2$), 1.72–1.90 (m, 1H, $CH_2$), 2.0–2.35 (m, 2H, $CH_2$), 2.41–2.75 (m, 2H, $CH_2$ and CH), 2.94–3.30 (m, 1H, CH), 4.25–4.55 (m, 1H, CHAr), 4.82–5.04 (m, 2H, $CH_2NO_2$), 7.35–7.38 (m, 3H, ArH), 7.49–7.52 (m, 1H, ArH); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (all isomers) 18.7, 20.8, 26.8, 32.2, 34.0, 36.2, 37.9, 38.5, 40.8, 42.0, 48.6, 50.3, 127.3, 127.4, 128.8, 128.9, 130.3, 134.5, 135.2, 211.8, 212.4.

#### 4.4.18. (2*S*,4*S*)-2-((*R*)-1′-(4″-Chlorophenyl)-2′-nitroethyl)-4-methylcyclohexanone 4s[18]

Yield: 82%; light yellow solid; mp 70–72 °C; $R_f$ 0.37 (ethyl acetate/hexane, 20:80), IR (KBr): 1378, 1553, 1710 cm$^{-1}$; $[\alpha]_D^{20} = -37.4$ (*c* 0.91, $CHCl_3$); enantiomeric excess of major diastereomer: 81%, determined by HPLC (Diacel chiralpak OD-H, hexane/*i*-PrOH 90:10, flow rate 0.5 mL/min, $\lambda$ = 208 nm); $t_R$ (minor) = 33.32 min, $t_R$ (major) = 41.65 min; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 0.81–0.89 (d, 0.78H, *J* = 6.6 Hz, $CH_3$), 0.95–1.02 (d, 2.26H, *J* = 6.9 Hz, $CH_3$), 1.35–1.45 (m, 1H, $CH_2$), 1.55–1.72 (m, 2H, $CH_2$), 1.80–2.10 (m, 2H, $CH_2$), 2.25–2.55 (m, 2H, $CH_2$ and CH), 2.60–2.77 (m, 1H, CH), 3.65–3.80 (m, 1H, CHAr), 4.50–4.98 (m, 2H, $CH_2NO_2$), 7.07–7.11 (m, 2H, ArH), 7.24–7.32 (m, 2H, ArH); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 19.1, 26.5, 32.2, 34.2, 37.8, 38.4, 43.3, 43.4, 49.5, 51.15, 78.8, 129.1, 129.3, 129.3, 129.6, 135.8.

#### 4.4.19. (2*S*,4*S*)-2-((*R*)-1′-(*p*-Tolylethyl)-2′-nitroethyl)-4-methylcyclohexanone 4t[18]

Yield: 82%; light yellow liquid; $R_f$ 0.37 (ethyl acetate/hexane, 20:80); MS (*m*/*z*): 297.8 ($M^+$+Na); IR ($CHCl_3$): 1379, 1552, 1709 cm$^{-1}$; $[\alpha]_D^{20} = -40.1$ (*c* 0.72, $CHCl_3$); enantiomeric excess of major diastereomer: 77%, determined by HPLC (Diacel chiralpak IB, hexane/*i*-PrOH 95:5, flow rate 0.5 mL/min; $\lambda$ = 254 nm); $t_R$ (minor) = 23.90 min, $t_R$ (major) = 26.55 min; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 0.83–0.89 (d, 0.75H, *J* = 6.3 Hz, $CH_3$), 0.94–1.01 (d, 2.25H, *J* = 6.6 Hz, $CH_3$), 1.30–1.54 (m, 2H, $CH_2$), 1.57–1.72 (m, 1H, $CH_2$), 1.85–2.14 (m, 2H, $CH_2$), 2.32 (s, 3H, Ar–$CH_3$), 2.39–2.55 (m, 2H, $CH_2$ and CH), 2.65–2.82 (m, 1H, CH), 3.62–3.83 (m, 1H, CHAr), 4.52–4.70 (m, 1.69H, $CH_2NO_2$), 4.72–5.01 (m, 0.31H, $CH_2NO_2$), 7.02–7.06 (m, 2H, ArH), 7.09–7.15 (m, 2H, ArH); $^{13}$C NMR: ($CDCl_3$, 75 MHz): $\delta$ (all isomers) 19.4, 20.9, 21.0, 26.4, 32.2, 34.4, 36.4, 37.8, 38.5, 41.2, 42.1, 43.5, 43.7, 50.1, 51.3, 79.0, 79.2, 127.8, 128.0, 129.5, 129.7, 134.1, 137.6, 213.1.

#### 4.4.20. (2*S*,4*S*)-2-((*R*)-1′-(4″-Nitrophenyl)-2′-nitroethyl)-4-methylcyclohexanone 4u[18]

Yield: 71%; dark yellow liquid; $R_f$ 0.30 (ethyl acetate/hexane, 20:80); MS (*m*/*z*): 305.7 ($M^+$); IR ($CHCl_3$): 1378, 1520, 1709 cm$^{-1}$; $[\alpha]_D^{20} = -32.3$ (*c* 0.78, $CHCl_3$); enantiomeric excess of major diastereomer: 80%, determined by HPLC (Diacel chiralpak AD-H, hexane/*i*-PrOH 95:5, flow rate 1.5 mL/min, $\lambda$ = 254 nm); $t_R$ (major) = 62.42 -min, $t_R$ (minor) = 67.30 min; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 0.83–0.89 (d, 0.52H, *J* = 6.6 Hz, $CH_3$), 0.93–0.98 (d, 0.55H, *J* = 6.6 Hz, $CH_3$), 0.99–1.04 (d, 1.93H, *J* = 6.6 Hz, $CH_3$), 1.32–1.46 (m, 2H, $CH_2$), 1.52–1.76 (m, 1H, $CH_2$), 1.85–2.10 (m, 2H, $CH_2$), 2.30–2.57 (m, 2H, $CH_2$ and CH), 2.70–2.85 (m, 1H, CH), 3.80–3.97 (m, 0.87H, CHAr), 3.98–4.04 (m, 0.13H, CHAr), 4.56–4.72 (m, 0.89H, $CH_2NO_2$), 4.75–4.90 (m, 0.96H, $CH_2NO_2$), 4.92–5.03 (m, 0.15H, $CH_2NO_2$) 7.32–7.40 (m, 2H, ArH), 8.10–8.25 (m, 2H, ArH); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 18.7, 26.6, 33.8, 38.3, 43.7, 48.7, 78.2, 124.1, 124.2, 129.1, 129.5, 145.14, 147.6, 211.59.

#### 4.4.21. (2*S*,4*S*)-2-((*R*)-1′-(Phenyl)-2′-nitroethyl)-4-*tert*-butylcyclohexanone 4v[18]

Yield: 94%; white solid; mp 94–96 °C; $R_f$ 0.32 (ethyl acetate/hexane, 20:80); MS (*m*/*z*): 326.0 ($M^+$+Na); IR ($CHCl_3$): 1379, 1553, 1710 cm$^{-1}$; $[\alpha]_D^{20} = -47.9$ (*c* 0.72, $CHCl_3$); enantiomeric excess of major diastereomer: 78%, determined by HPLC (Diacel chiralpak AS-H, hexane/*i*-PrOH 98:2, flow rate 0.5 mL/min, $\lambda$ = 208 nm); $t_R$ (minor) = 24.02 min, $t_R$ (major) = 36.40 min; $^1$H NMR $CDCl_3$, 300 MHz): $\delta$ 0.77 (s, 4H, $(CH_3)_3$), 0.81 (s, 2H, $(CH_3)_3$), 0.92 (s, 2H, $(CH_3)_3$), 0.97 (s, 1H, $(CH_3)_3$), 1.35–1.90 (m, 4H, $CH_2$), 2.05–2.20 (m, 1H, $CH_2$), 2.30–2.88 (m, 3H, $CH_2$ and CH), 3.74–3.95 (m, 0.7H, CHAr), 3.97–4.07 (m, 0.3H, CHAr), 4.52–4.77 (m, 1.2H, $CH_2NO_2$), 4.90–5.07 (m, 0.8H, $CH_2NO_2$), 7.18–7.46 (m, 5H, ArH); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (all isomers) 26.9, 27.1, 27.3, 27.4, 27.5, 27.9, 29.1, 29.5, 30.8, 32.2, 32.3, 32.4, 34.2, 38.9, 40.8, 41.2, 41.5, 42.0, 43.3, 44.0, 44.1, 46.6, 46.9, 47.2, 51.5, 51.9, 52.7, 76.5, 78.7, 79.0, 127.4, 127.6, 128.0, 128.1, 128.3, 128.6, 128.8, 129.0, 136.6, 137.8, 213.7.

#### 4.4.22. (*E*)-(*S*)-2-((*S*)-1′-Nitro-4′-phenylbut-3′-en-2′-yl)cyclohexanone 4w[25]

Yield: 94%; brown solid; mp 96–98 °C; $R_f$ 0.44 (ethyl acetate/hexane, 20:80); MS (*m*/*z*): 295.8 ($M^+$+Na); IR ($CHCl_3$): 1380, 1550, 1707 cm$^{-1}$; *syn*/*anti* = 87:13; $[\alpha]_D^{20} = -45.4$ (*c* 0.91, $CHCl_3$); enantiomeric excess of *syn* diastereomer: 84%, determined by HPLC (Diacel chiralpak AS-H, hexane/*i*-PrOH 90:10, flow rate 1.0 mL/min, $\lambda$ = 254 nm); $t_R$ (*syn*, minor) = 10.82 min, $t_R$ (syn, major) = 15.44 min; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 1.37–1.51 (m, 1H, $CH_2$), 1.60–1.80 (m, 2H, $CH_2$), 1.82–1.99 (m, 1H, $CH_2$), 2.01–2.26 (m, 2H, $CH_2$), 2.31–2.65 (m, 3H, $CH_2$ and CH), 3.15–3.24 (m, 0.13H (*anti*), $CHCH_2NO_2$), 3.27–3.45 (m, 0.87H (*syn*), $CHCH_2NO_2$), 4.50–4.79 (m, 2H, $CHCH_2NO_2$), 5.93–6.14 (dd, 1H, $J_1$ = 15.75 Hz, $J_2$ = 9.2 Hz, Ar–CH=C–H, 6.45–6.52 (m, 1H, Ar–CH=C–H), 7.23–7.35 (m, 5H, ArH); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ (*syn* + *anti* isomers) 25.0, 28.0, 29.6, 32.5, 41.8, 42.6, 51.6, 78.0, 125.6, 126.4, 126.4, 127.9, 128.5, 134.4, 136.2, 211.2.

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## References

1. (a) Gruttadauria, M.; Giacalone, F.; Notoa, R. *Adv. Synth. Catal.* **2009**, *351*, 33–57; (b) Paradowska, J.; Stodulski, M.; Mlynarski, J. *Angew. Chem., Int. Ed.* **2009**, *48*, 4288–4297; (c) Mlynarski, J.; Paradowska, J. *Chem. Soc. Rev.* **2008**, *37*, 1502–1511; (d) Yong, B. H.; Some, S.; Oh, J. S.; Lee, Y. S.; Song, C. E. *Chem. Commun.* **2011**, *47*, 9621–9623; (e) Lina, J.; Tiana, H.; Jianga, Y.-J.; Huanga, W.-B.; Zheng, L.-Y.; Zhang, S.-Q. *Tetrahedron: Asymmetry* **2011**, *22*, 1434–1440.
2. (a) Tokoroyama, T. *Eur. J. Org. Chem.* **2010**, 2009–2016; (b) Sulzer-Mosse, S.; Alexakis, A. *Chem. Commun.* **2007**, 3123–3135; (c) Roca-Lopez, D.; Sadaba, D.; Delso, I.; Herrera, R. P.; Tejero, T. Merino *P. Tetrahedron: Asymmetry* **2010**, *21*, 2561–2601; (d) Chauhan, P.; Chimni, S. S. *RSC Adv.* **2012**, *2*, 6117–6134.
3. Berner, O. M.; Tedeschi, L.; Enders, D. *Eur. J. Org. Chem.* **2002**, 1877–1894.
4. (a) Ikeda, S.; Shibuya, M.; Kanoh, N.; Iwabuchi, Y. *Org. Lett.* **2009**, *11*, 1833–1836; (b) Zou, W.; Vembaiyan, K.; Bhasin, M.; Williams, D. T. *Carbohydr. Res.* **2009**, *344*, 2144–2150; (c) Pansare, S. V.; Lingampally, R.; Kirby, R. L. *Org. Lett.* **2010**, *12*, 556–559.
5. Nakamura, A.; Lectard, S.; Hashizume, D.; Hamashima, Y.; Sodeoka, M. *J. Am. Chem. Soc.* **2010**, *132*, 4036–4037.
6. Szanto, G.; Hegedus, L.; Mattyasovszky, L.; Simon, A.; Bitter, I.; Toth, G.; Toke, L.; Kadas, I. *Tetrahedron* **2009**, *65*, 8412–8417.
7. Andrey, O.; Vidonne, A.; Alexakis, A. *Tetrahedron Lett.* **2003**, *44*, 7901–7904.
8. Yu, Z.; Liu, X.; Zhou, L.; Lin, L.; Feng, X. *Angew. Chem., Int. Ed.* **2009**, *48*, 5195–5198.
9. Hong, B.-C.; Kotame, P.; Tsai, C.-W.; Liao, J.-H. *Org. Lett.* **2010**, *12*, 776–779.
10. (a) Elsner, P.; Jiang, H.; Nielsen, J. B.; Pasi, F.; Jorgensen, K. A. *Chem. Commun.* **2008**, 5827–5829; (b) Karthikeyan, T.; Sankararaman, S. *Tetrahedron: Asymmetry* **2008**, *19*, 2741–2745; (c) Ruiz, N.; Reyes, E.; Vicario, J. L.; Badia, D.; Carrillo, L.; Uria, U. *Chem. Eur. J.* **2008**, *14*, 9357–9367; (d) Krayer, M.; Ptaszek, M.; Kim, H.-J.; Meneely, K. R.; Fan, D.; Secor, K.; Lindsey, J. S. *J. Org. Chem.* **2010**, *75*, 1016–1039.
11. (a) Zhang, Y.; Wang, W. *Catal Sci. Technol.* **2012**, *2*, 42–53; (b) Roca-Lopez, D.; Sadaba, D.; Delso, I.; Herrera, R. P.; Tejero, T.; Merino, P. *Tetrahedron: Asymmetry* **2010**, *21*, 2561–2601; (c) Enders, D.; Wang, C.; Liebich, J. X. *Chem. Eur. J.* **2009**, *15*, 11058–11076; (d) Krishna, P. R.; Sreeshailam, A.; Srinivas, R. *Tetrahedron* **2009**, *65*, 9657–9672.
12. (a) Gogoi, S.; Zhao, C.-G.; Ding, D. *Org. Lett.* **2009**, *11*, 2249–2252; (b) Moon, H. W.; Cho, M. J.; Kim, D. Y. *Tetrahedron Lett.* **2009**, *50*, 4896–4898; (c) Dong, L.-T.;

Lu, R.-J.; Du, Q.-S.; Zhang, J.-M.; Xuan, Y.-N.; Yan, M. *Tetrahedron* **2009**, *65*, 4124–4129; (d) Luo, G.; Zhang, S.; Duan, W.; Wang, W. *Synthesis* **2009**, 1564–1572; (e) Tan, B.; Zhang, X.; Chua, P. J.; Zhong, G. *Chem. Commun.* **2009**, 779–781; (f) Breslow, R. *Acc. Chem. Res.* **2004**, *37*, 471–478; (g) Pansare, S. V.; Pandya, K. *J. Am. Chem. Soc.* **2006**, *128*, 9624–9625; (h) Mase, N.; Watanabe, K.; Yoda, H.; Takabe, K.; Tanaka, F.; Barbas, C. F., III *J. Am. Chem. Soc.* **2006**, *128*, 4966–4967; (i) Vishnumaya; Singh, V. K. *Org. Lett.* **2007**, *9*, 1117–1119; (j) Alza, E.; Cambeiro, X. C.; Jimeno, C.; Pericas, M. A. *Org. Lett.* **2007**, *9*, 3717–3720; (k) Luo, S.; Mi, X.; Liu, S.; Xua, H.; Cheng, J.-P. *Chem. Commun.* **2006**, 3687–3689.

13. (a) Kimmel, K. L.; Robak, M. T.; Ellman, J. A. *J. Am. Chem. Soc.* **2009**, *131*, 8754–8755; (b) Lu, H.-H.; Wang, X.-F.; Yao, C.-J.; Zhang, J.-M.; Wu, H.; Xiao, W.-J. *Chem. Commun.* **2009**, 4251–4253; (c) Enders, D.; Hoffman, K. *Eur. J. Org. Chem.* **2009**, 1665–1668; (e) Zhang, X.-J.; Liu, S.-P.; Lao, J.-H.; Du, G.-J.; Yan, M.; Chan, A. S. C. *Tetrahedron: Asymmetry* **2009**, *20*, 1451–1458; (f) Dong, X.-Q.; Teng, H.-L.; Wang, C.-J. *Org. Lett.* **2009**, *11*, 1265–1268; (g) Rabalakos, C.; Wulff, W. D. *J. Am. Chem. Soc.* **2008**, *130*, 13524–13525; (h) Hynes, P. S.; Stranges, D.; Stupple, P. A.; Guarna, A.; Dixon, D. *J.Org. Lett.* **2007**, *9*, 2107–2110; (i) Cao, Y.; Cao, Y.-J.; Lai, Y.-Y.; Wang, X.; Lia, Y.-J.; Xiao, W.-J. *Tetrahedron Lett.* **2007**, *48*, 21–24.
14. (a) Sulzer-Moss, S.; Alexakis, A.; Mareda, J.; Bollot, G.; Bernardinelli, G.; Filinchuk, Y. *Chem. Eur. J.* **2009**, *15*, 3204–3220; (b) Belot, S.; Massaro, A.; Tenti, A.; Mordini, A.; Alexakis, A. *Org. Lett.* **2008**, *10*, 4557–4560; (c) Vesely, J.; Ibrahem, I.; Rios, R.; Zhao, G.; Zhao, G.-L.; Xu, Y.; Cordova, A. *Tetrahedron Lett.* **2007**, *48*, 2193–2198; (d) Rios, R.; Vesely, J.; Sunden, H.; Ibrahem, I.; Zhao, G.-L.; Cordova, A. *Tetrahedron Lett.* **2007**, *48*, 5835–5839; (e) Li, H.; Zu, L.; Xie, H.; Wang, J.; Jiang, W.; Wang, W. *Org. Lett.* **2007**, *9*, 1833–1835; (f) Massa, A.; Utsumi, N.; Barbas, C. F., III *Tetrahedron Lett.* **2009**, *50*, 145–147.
15. (a) Wang, J.; Li, H.; Zu, L.; Wang, W. *Adv. Synth. Catal.* **2006**, *348*, 425–428; (b) Wang, J.; Li, H.; Lou, B.; Zu, L.; Guo, H.; Wang, W. *Chem. Eur. J.* **2006**, *12*, 4321–4332; (c) Cao, C.-L.; Sun, X.-L.; Zhou, J.-L.; Tang, Y. *J. Org. Chem.* **2007**, *72*, 4073–4076; (d) Ni, B.; Zhang, Q.; Headley, A. D. *Tetrahedron: Asymmetry* **2007**, *18*, 1443–1447; (e) Ni, B.; Zhang, Q.; Dhungana, K.; Headley, A. D. *Org. Lett.* **2009**, *11*, 1037–1040; (f) Rasappan, R.; Reiser, O. *Eur. J. Org. Chem.* **2009**, 1305–1308; (g) Kano, T.; Tanaka, Y.; Maruoka, K. *Tetrahedron Lett.* **2006**, *47*, 3039–3041; (h) Zu, L.; Wang, J.; Li, H.; Wang, W. *Org. Lett.* **2006**, *8*, 3077–3079.
16. (a) Chimni, S. S.; Singh, S.; Mahajan, D. *Tetrahedron: Asymmetry* **2008**, *19*, 2276–2284; (b) Chimni, S. S.; Singh, S.; Kumar, A. *Tetrahedron: Asymmetry* **2009**, *20*, 1722–1724; (c) Kumar, A.; Singh, S.; Kumar, V.; Chimni, S. S. *Org. Biomol. Chem.* **2011**, *9*, 2731–2742.
17. Carter, M. E.; Nash, J. L.; Drueke, J. W.; Schwietert, J. W.; Butler, G. B. *J. Polym. Sci., Polym. Chem. Ed.* **1978**, *16*, 937–959. and references therein.
18. (a) Chen, J.-R.; Lai, Y.-Y.; Lu, H.-H.; Wang, X.-F.; Xiao, W.-J. *Tetrahedron* **2009**, *65*, 9238–9242; (b) Luo, S.; Zhang, L.; Mi, X.; Qiao, Y.; Chang, J.-P. *J. Org. Chem.* **2007**, *72*, 9350–9352.
19. (a) Akahane, Y.; Inomata, K.; Endo, Y. *Heterocycles* **2011**, *82*, 1727–1737; (b) Chauhan, P.; Chimni, S. S. *Adv. Synth. Catal.* **2011**, *353*, 3203–3212; (c) Enders, D.; Wang, C.; Greb, A. *Adv. Synth. Catal.* **2010**, *352*, 987–992; (d) Li, Z.-B.; Luo, S.-P.; Guo, Y.; Xia, A.-B.; Xu, D.-Q. *Org. Biomol. Chem.* **2010**, *8*, 2505–2508.
20. Chowdhury, R.; Ghosh, S. K. *Org. Lett.* **2009**, *11*, 3270–3273.
21. This is a procedure for conditions A. In conditions B, after completion of reaction, the solvent and reactants were distilled under vaccum on a water bath and the remaining crude mixture was chromatographed on a column.
22. (a) Chen, J.-R.; Cao, Y.-J.; Zou, Y.-Q.; Tan, F.; Fu, L.; Zhu, X.-Y.; Xiao, W.-J. *Org. Biomol. Chem.* **2010**, *8*, 1275–1279; (b) Ban, S.-R.; Xie, H.-Y.; Zhu, X.-X.; Li, Q.-S. *Eur. J. Org. Chem.* **2011**, *32*, 6413–6417.
23. Li, P.; Wang, L.; Zhang, Y.; Wang, G. *Tetrahedron* **2008**, *64*, 7633–7638.
24. Xu, D.-Z.; Liu, Y.; Li, H.; Wang, Y. *Tetrahedron* **2010**, *66*, 8899–8903.
25. (a) Li, Z.-B.; Luo, S.-P.; Guo, Y.; Xia, A.-B.; Xu, D.-Q. *Org. Biomol. Chem.* **2010**, *8*, 2505–2508; (b) Belot, S.; Quintard, A.; Krause, N.; Alexakis, A. *Adv. Synth. Cat.* **2010**, *352*, 667–695; (c) Tsakos, M.; Kokotos, C. G. *Eur. J. Org. Chem.* **2012**, *2012*, 576–580; (d) Ma, H.; Liu, K.; Zhang, F.-G.; Zhu, C.-L.; Nie, J.; Ma, J.-A. *J. Org. Chem.* **2010**, *75*, 1402–1409.
26. Almasi, D.; Alonso, D. A.; Najera, C. *Tetrahedron: Asymmetry* **2006**, *17*, 2064–2068.
27. Edwards, C. W.; Shipton, M. R.; Alcock, N. W.; Clase, H.; Wills, M. *Tetrahedron* **2003**, *59*, 6473–6480.