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Asymmetric 1,4-Addition of Oxazolones to Nitroalkenes by Bifunctional Cinchona Alkaloid Thiourea Organocatalysts: Synthesis of α,α-Disubstituted α-Amino Acids

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Abstract: An easy and simple synthetic approach to optically active α,α-quaternary α-amino acids using asymmetric organocatalysis is presented. The addition of oxazolones to nitroalkenes catalyzed by thiourea cinchona derivatives provides the corresponding α,α-quaternary α-amino acid derivatives with good yields, excellent diastereoselectivities (up to 98% *dr*), and from moderate to good enantioselectivities (up to 92% *ee*). The reaction can be performed on a large scale. The optically active oxazolone–nitroalkene addition products can be opened in a one-pot reaction to the corresponding ester–amide derivatives. Additional transformations are also presented, such as the synthesis of amino esters, amino acids, and transformation into 3,4-disubstituted pyrrolidin-2-ones.

Keywords: amino acids · organocatalysis · oxazolones · thiourea

Introduction

In the last few years, organocatalysis has proved to be a powerful tool in the development of a large number of enantioselective reactions.[1] During the development of organocatalytic methodologies, the asymmetric 1,4-conjugate additions have emerged as powerful strategies to obtain chiral organic compounds in an easy way.[2] There are two main organocatalytic activation modes for carrying out the 1,4 addition: i) a covalent strategy, which often takes place after the formation of an iminium ion by the reaction of an unsaturated carbonyl compound with a chiral amine,[3] or ii) a non-covalent activation method in which, for example, the cinchona alkaloids represent a cornerstone in the functionalization of nitroalkenes.[4] Using the former concept, we have recently reported the addition of oxazolones to α,β-unsaturated aldehydes using secondary amines as catalysts obtaining excellent enantioselectivities and good diastereoselectivies.[5] However, we believe that optically active addition products of nitroalkanes are also attractive substrates which can be used due to the numerous transformations that allow further reactions towards the nitro functionality, and also allow us to study the non-covalent method for the addition of important oxazolones to nitroalkenes. To the best of our knowledge, this reaction has been never explored before.

Peptides and proteins are an area of interest in bioorganic chemistry.[6] The synthesis of non-natural amino acids is an important target as these compounds can be incorporated into the peptide chain and might cause a dramatically change in the properties of, for example, proteins. The α,α-disubstituted quaternary α-amino acids are a particular class of non-natural amino acids of particular importance.[7] There are several reasons for the importance of these α,α-disubstituted α-amino acids; they increase the stability of proteins avoiding in vivo racemization, restrict the conformational flexibility, which is highly important for, for example, the secondary structure of proteins, and which can lead to an improvement of the resistance against chemical and enzymatic degradation.[8] Furthermore, α,α-disubstituted quaternary α-amino acids are also present in some antibiotics (for, e.g., lactacystin).[9]

The importance of α,α-disubstituted α-amino acids has caused an increased interest in the development of efficient methodologies for the asymmetric synthesis of these valuable optically active compounds. One of the synthetic challenges is to develop procedures that provide flexible and

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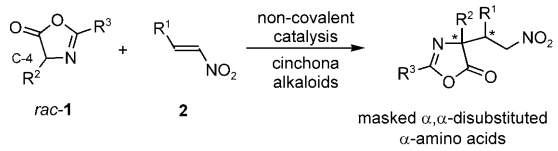
simple methods for obtaining optically active α,α-disubstituted α-amino acids and which, furthermore, give diversity in structural and electronic properties.

Several different catalytic approaches have been developed for the synthesis of optically active amino acids.[10] Thus, one classical procedure for the synthesis of α-amino acid derivatives is the Strecker reaction.[11] This reaction is well-established for the asymmetric synthesis of chiral α-substituted amino acids starting from aldimines, although the synthesis of chiral α,α-disubstituted α-amino acids using ketimines is now in progress, but shows some limitations.[12] These limitations are related to the lower reactivity and easy enolization of the ketimines, as well as the difficulties to synthesize them. A more recent approach for the preparation of optically active α,α-disubstituted α-amino acids is the alkylation of imines derived from Schiff bases with chiral phase-transfer catalysis.[13]

Oxazolones are masked amino acids, but the use of these compounds for the synthesis of amino acid derivatives is more scarce.[14] These aza species have been mainly employed as an electrophile source; for example, in the Steglich reaction which generates α,α-disubstituted amino acids by ring-opening reaction of chiral oxazolones.[15] The use of oxazolones as nucleophiles has only been shown in a few examples using metal catalysis for these funtionalizations.[16]

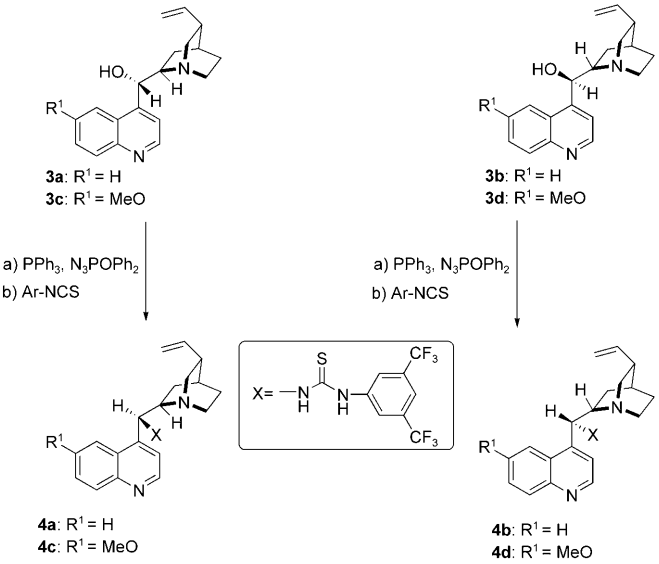
In this work we present our efforts to use the racemic oxazolones **1** as masked amino acid nucleophiles and their reaction with nitroalkenes **2** to afford the corresponding optically active addition products with two new chiral centers, in which one is a quaternary and the other a tertiary center (Scheme 1). The optically products obtained are highly funtionalized molecules, containing nitro, ester and imine groups, which allow us to create diversity-oriented synthesis using different reactions.



Scheme 1. Organocatalytic enantioselective synthesis of optically active α,α-disubstituted-α-amino acids.

Results and Discussion

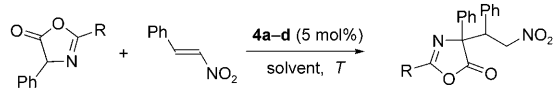
Our initial screening reactions between the oxazolone and the α,β-unsaturated nitroalkene occur in the presence of cinchona alkaloid derivatives **3** as the catalyst. Unfortunately, our preliminary results showed that only rather low enantioselectivity was obtained with this catalyst system. However, it has been found that, bifunctional thiourea cinchona alkaloid catalysts can be used with good results for reactions with nitroalkenes as electrophile partner.[17] These thiourea cinchona alkaloid catalysts **4a–d** are really accessible from commercial available cinchona alkaloids by using the method developed by Soós et al.[18] This method applies modified Mitsunobu conditions, obtaining the amine intermediate with inversion of configuration from the corresponding commercial available cinchona alcohols **3a–d**. Therefore, the catalysts **4a–d** were obtained by addition of the intermediate amine to 3,5-bis(trifluoromethyl)phenylisothiocyanate (Scheme 2). It was our hope that these catalysts might give good results for the addition of oxazolones to nitroalkenes. Table 1 presents some of the screening results, in which racemic oxazolones *rac*-**1a**,**b** are reacted with nitroalkene **2a** using catalysts **4a–d** (5 mol%).



Scheme 2. Synthesis of bifunctional thiourea catalyst **4a–d** used in this work.

The results in Table 1 show that full conversion was obtained when catalyst **4a**,**c** were used at RT with the oxazolone **1a** in toluene as the solvent, and the addition product **5a** was formed in a 90:10 diastereomeric ratio, 44 and 20% *ee*, respectively (Table 1, entries 1, 2). The enantioselectivity of the major diastereomer was increased to 74% *ee* when the temperature was decreased to −24°C using **4c** as the catalyst (Table 1, entry 3). No improvement of the enantioselectivity was obtained when lower temperature, such as −78°C, was applied. Thus, at −40°C the enantioselectivity was 58 and 68% *ee* with catalyst **4a** and **c**, respectively (Table 1, entries 4, 5). Solvents as CH_2Cl_2 and xylene did not improve the enantioselectivity (Table 1, entries 7–9). Further attempts to increase the enantioselectivity by for example, lowering the concentration (0.2 and 0.1 M) did not give any improvements (Table 1, entries 10, 11). However, a change in the structure of the nucleophile by using **1b**, a *tert*-butyl instead of *p*-tolyl as the R group (Table 1, entries 12–16) gave an increase of the enantioselectivity. The highest enantioselectivity was obtained when catalyst **4c** was used at −24°C in toluene where 83% *ee* was obtained (Table 1, entry 14).

Table 1. Screening of various reaction conditions.[a]



Entry	Cat.	T	1	Solvent	dr[b]	ee [%][c]
1	**4c**	RT	**1a**	Tol	90:10	44
2	**4a**	RT	**1a**	Tol	90:10	−20
3	**4c**	−24	**1a**	Tol	91:9	74
4	**4c**	−40	**1a**	Tol	94:6	68
5	**4a**	−40	**1a**	Tol	97:3	−58
6	**4b**	−24	**1a**	Tol	91:9	−48
7	**4c**	RT	**1a**	CH_2Cl_2	90:10	50
8	**4c**	−24	**1a**	CH_2Cl_2	83:17	52
9	**4c**	−24	**1a**	Xyl	80:20	57
10	**4c**	−24	**1a**	Tol[d]	91:9	53
11	**4c**	−24	**1a**	Tol[e]	92:8	55
12	**4a**	−30	**1b**	Tol	>95:<5	70[f]
13	**4b**	−30	**1b**	Tol	>95:<5	53[f]
14	**4c**	−24	**1b**	Tol	>95:<5	83[f]
15	**4d**	−30	**1b**	Tol	>95:<5	−54[f]
16	**4c**	−30	**1b**	Tol	>95:<5	80[f]

[a] Performed with **1** (0.20 mmol), **2** (0.21 mmol) and catalyst **4** (5 mol%) in the corresponding solvent (0.2 mL). All the reactions were stopped after 16 h, and full conversion was observed in all the cases. [b] Determined by ^{1}H NMR spectroscopy [c] Determined by chiral-stationary phase HPLC. [d] Performed at 0.2 M. [e] Performed at 0.1 M. [f] *ee* was determined by transformation to product **6b** (see below).

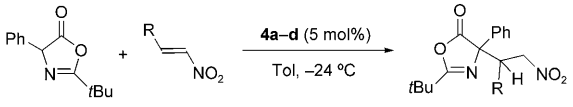
With these conditions at hand we investigated the scope of different nitroalkenes **2** and oxazolone **1b** as the nucleophile (Table 2). For every entry in the table we have checked the four catalysts **4a–d** (Scheme 2) and the best results of every reaction are shown. The reaction could be performed with aromatic substituted nitroalkenes containing electron-donating groups, allowing the synthesis of compound **5c** in a good yield, good diastereomeric ratio and acceptable 72% *ee* (Table 2, entry 2). We have also found that an electron-withdrawing group at the aromatic substituent in the nitroalkene, such as a nitro group in the *para*-position, reacts smoothly, providing **5d** with good diastereoselectivity; however, slighter lower yield and enantioselectivity were obtained (Table 2, entry 3). The reaction took also place with heteroaromatic substituents as thiophene with excellent yield, good diastereomeric ratio and enantioselectivity (Table 2, entry 4). An *ortho*-chloro substitution, as well as bulkier groups, such as naphthyl could be used obtaining the optically active products **5f** and **g** with similar good results (Table 2, entries 5, 6). Interestingly, alkyl chains in the nitroalkene could also be applied, obtaining in all the cases good yield, diastereoselectivity and slighter lower enantioselectivity, exemplified with a methyl substituent, giving the oxazolone derivative **5h** (Table 2, entry 7) and a thioether alkyl chain (**5i**) (Table 2, entry 8).

The results in Table 2, in which the electrophile—the nitroalkene—was varied, gave us interesting compounds with two stereocenters in good yield, diastereomeric ratio, and from moderate to good enantioselectivity. It should be noted that these compounds have different masked functions that could be transformed (see below).

We have also studied the addition of different oxazolones **1a–h** to nitroalkenes **2** and the results are shown in Table 3. The reaction took place with aromatic ring imine function at R^2, aromatic and alkyl groups (R^1) at C-4/2. Thus, compounds **5a** and **j** were obtained with high diastereomeric ratio and moderate to high enantioselectivities (Table 3, entries 1, 2).

Bulkier R^1 groups at C-4 in the oxazolone, such as *i*Bu, gave in one case a slightly lower diastereo- and enantioselectivity compared with the other oxazolones studied (Table 3, entry 3). Interestingly, the enantioselectivity increased up to 82% *ee* when this reaction was carried out with an *o*-Cl-C_6H_4 substituent at R^2 and only one diastereoisomer could be detected (Table 3, entry 4). The later nucleophile was additionally used for two different nitroalkenes, *p*-$MeOC_6H_4$ and thiophen-2-yl derivatives (Table 3, entries 5, 6). These reactions took placed in excellent yields, enantioselectivities up to 90% *ee* and only one diastereoisomer was obtained for both oxazolones.

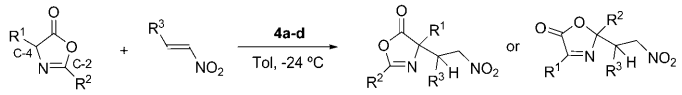
Table 2. Scope of oxazolone **1b** with nitroalkenes **2**.[a]



Entry	R	Cat.	Yield [%][b]	dr[c]	ee [%][d]
1	Ph	**4c**	65 (**5b**)	>95:<5	83[e]
2	*p*-MeO-C_6H_4	**4d**	90 (**5c**)	93:7	72
3	*p*-NO_2-C_6H_4	**4c**	65 (**5d**)	81:19	72
4	thiophen-2-yl	**4d**	91 (**5e**)	91:9	70[e]
5	*o*-Cl-C_6H_4	**4c**	80 (**5f**)	92:8	74
6	naphth-2-yl	**4c**	54 (**5g**)	>95:<5	66
7	Me	**4b**	88 (**5h**)	95:5	66
8	$MeSCH_2CH_2$-	**4d**	65 (**5i**)	>95:<5	67

[a] Performed with **1** (0.20 mmol), **2** (0.20 mmol) and catalyst **4** (5 mol%) in toluene (0.2 mL). [b] Overall yield. [c] Determined by ^{1}H NMR. [d] Determined by chiral stationary phase HPLC. [e] *ee* was determined after transformation into compound **6** (see Table 4).

Table 3. Scope of different oxazolones **1a–h** with nitroalkenes **2**.[a]



rac-**1a-h** **2** **5a** **5j-t**[20]

Entry	R^1/R^2	R^3	Cat.	Yield [%][b]	*dr*[c]	*ee* [%][d]
1	Ph/*p*-Tol	Ph	**4c**	98 (**5a**)	91:9	74
2	Me/Ph	Ph	**4c**	82 (**5j**)	93:7	66
3	*i*Bu/Ph	Ph	**4c**	93 (**5k**)	80:20	65
4	*i*Bu/*o*-Cl-Ph	Ph	**4c**	95 (**5l**)	>95:<5	82
5	*i*Bu/*o*-Cl-Ph	*p*-MeO-C_6H_4	**4d**	82 (**5m**)	>95:<5	90
6	*i*Bu/*o*-Cl-Ph	2-thienyl	**4c**	84 (**5n**)	>95:<5	80
7	*i*Bu/*o*-F-Ph	Ph	**4d**	93 (**5o**)	>95:<5	91
8[e]	*i*Bu/*o*-F-Ph	Ph	**4d**	94 (**5o**)	>95:<5	92
9	*i*Bu/*o*-F-Ph	*p*-NO_2-Ph	**4d**	91 (**5p**)	95:5	75
10	*i*Bu/*o*-F-Ph	2-thienyl	**4d**	82 (**5q**)	>95:<5	87
11	*i*Bu/*o*-F-Ph	*o*-Cl-C_6H_4	**4d**	85 (**5r**)	>95:<5	77
12	*i*Bu/*o*-F-Ph	2-Furyl	**4d**	61 (**5s**)	>95:<5	64
13	*i*Bu/*p*-NO_2-Ph	Ph	**4d**	64 (**5t**)	>95:<5	70

[a] Performed with **1** (0.20 mmol), **2** (0.21 mmol) and catalyst **3** (5 mol%) in toluene (0.2 mL). [b] Overall yield. [c] Determined by ^{1}H NMR. [d] Determined by chiral stationary phase HPLC. [e] Reaction performed at 2.0 mmol scale.

Encouraged by these results, we also introduced a fluorine substituent in the *ortho*-position of a phenyl group at R^2 (Table 3, entries 7–12). The *o*-F-C_6H_4 substituent had a positive influence on the enantioselectivity and in this case 91% *ee* was obtained (Table 3, entry 7) compared to the *o*-Cl-C_6H_4 substituent which gave 82% *ee* (Table 3, entry 4). We have also shown that this reaction could be performed in 2 mmol scale giving an excellent diastereomeric ratio and a slightly higher enantioselectivity (Table 3, entry 8). We then explored different nitroalkenes for the reaction with the *o*-F-C_6H_4-substituted oxazolone. For the nitroalkenes having a *p*-NO_2-C_6H_4 substituent (Table 3, entry 9), a heteroaromatic group (Table 3, entry 10, 12), and *o*-Cl-C_6H_4 substituent (Table 3, entry 11), the optically active addition products were formed in all cases in good yields and excellent diastereoselectivities and enantiomeric excesses from 64–87% *ee*. Finally, we explored also the effect of an electron-withdrawing group in the *para*-position of the phenyl substituent at R^2 in the oxazolone ring system. For this substrate having a nitro substituent in the *para*-position, a slightly lower enantioselectivity of the addition product **5t** was obtained (Table 3, entry 13) compared to the *o*-F- and *o*-Cl-C_6H_4 substituents (Table 3, entries 4, 7).

The absolute configuration of the two stereocenters was determined as *R*,*R* by X-ray analysis of the crystals of compound **5e** (Figure 1).[19]

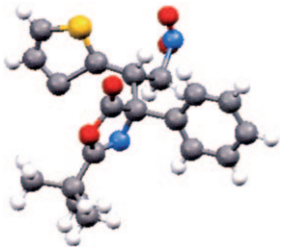


Figure 1. X-ray structure of compound **5e**.

Table 4. Ring-opening reaction of oxazolones with TMSCl.[a]

5 **6a–e**

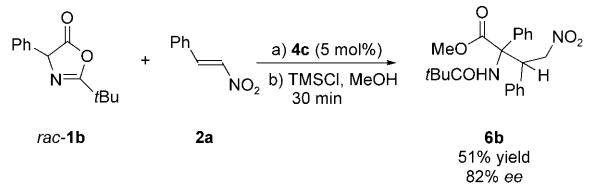
Entry	Starting material	R^1	R^2	Yield [%]
1	**5a**	Tol	Ph	99 (**6a**)
2	**5b**	*t*Bu	Ph	95 (**6b**)
3	**5c**	*t*Bu	*p*-$MeOC_6H_4$	87 (**6c**)
4	**5e**	*t*Bu	thiophene-2-yl	99 (**6d**)
5	**5g**	*t*Bu	2-naphthyl	99 (**6e**)

[a] Performed with **4** (0.20 mmol), and TMSCl (0.20 mmol) and 0.4 mL of MeOH.

Transformations of the optically active products: One of our objectives of this work was to develop new synthetic methodologies for optically active α,α-quaternary α-amino acids and their derivatives. Therefore, we decided to investigate the ring-opening reactions of some of the optically active oxazolone addition products **5a–c**,**e**,**g** by using the protocol developed by Trost et al.[16] (Table 4). This reaction was performed with TMSCl in MeOH for 30 min with complete conversion and the amino acid esters **6a–e** were obtained in very high yields. This method is compatible with oxazolones with phenyl and alkyl group at R^1 (Table 4, entries 1, 2). The reaction could also be carried out with different substituents at R^2, such as electron-donating groups (Table 4, entries 3, 4) and bulkier groups as the naphthyl ring (Table 4, entry 5). In these reaction, the corresponding products **6a–e** were obtained without loss of enantioselectivity.

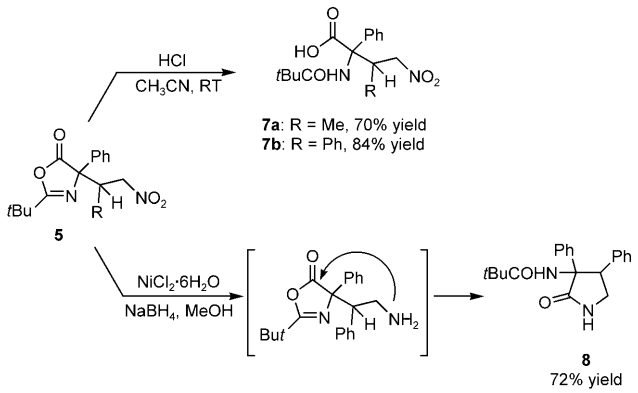
This reaction can also be carried out as a one-pot procedure by first the conjugate 1,4-addition of the oxazolone to the nitroalkene catalyzed by **4c**, followed by the direct addition of TMSCl and MeOH. This one-pot procedure allows the direct synthesis of α,α-quaternary amino acid derivatives without loss of enantioselectivity compared with the two-step procedure and **6b** was formed in moderate isolated yield (Scheme 3).

Furthermore, we were able to transform the optically active oxazolones **5** to various compounds by using different



Scheme 3. One-pot synthesis of optically active α,α-quaternary α-amino acids.

strategies. Thus, compound **5b** and **h** were transformed to the corresponding amino-acid derivatives **7a** and **b** with conc. HCl in CH_3CN in good yields (top, Scheme 4). The nitro group in **5** could also be converted to the amine intermediate by nickel boride reduction to give the 3,4-disubstituted pyrrolidin-2-one **8** by an intramolecular ring-opening of the oxazolone intermediate (bottom, Scheme 4).



Scheme 4. Different transformation of compounds **5**.

Conclusion

We have presented an easy and simple synthetic approach to optically active α,α-quaternary α-amino acids using asymmetric non-covalent organocatalysis. The addition of oxazolones to nitroalkenes catalyzed by thiourea cinchona derivatives achieved the corresponding α,α-quaternary α-amino acid derivatives with good yields, excellent diastereoselectivies, up to 98% *dr*, and from moderate to good enantioselectivities, up to 92% *ee*. The reaction can be performed in a large scale and the oxazolones could be opened in one-pot reaction to the corresponding ester–amide derivatives. Additional transformations were also presented, such as synthesis of synthesis of optically active amido esters, amido acids, and 3,4-disubstituted pyrrolidin-2-ones.

Experimental Section

General: NMR spectra were acquired on a Varian AS 400 spectrometer, running at 400 and 100 MHz for ^1H and ^{13}C, respectively, at room temperature. Chemical shifts (δ) are reported in ppm relative to residual solvent signals ($CHCl_3$, 7.26 ppm for ^1H NMR, $CDCl_3$, 77.0 ppm for ^{13}C NMR). ^{13}C NMR spectra were acquired on a broad band decoupled mode. Mass spectra were recorded on a Micromass LCT spectrometer using electrospray (ES^+) ionisation techniques. Analytical thin layer chromatography (TLC) was performed using pre-coated aluminium-backed plates (Merck Kieselgel 60 F254) and visualised by ultraviolet irradiation or $KMnO_4$ dip. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. The enantiomeric excess (*ee*) of the products was determined by chiral stationary phase HPLC (Daicel Chiralpak AD or Daicel Chiralcel OD, OJ columns).

Materials: Analytical grade solvents and nitroalkenes **2** were purchased by Aldrich and used as received. Oxazolones were prepared according to literature procedures. Flash chromatography (FC) was carried out using Iatrobeads 6RS-8060 (spherical silica gel). Racemic samples were prepared using DABCO as the catalyst. Catalyst **4a–d** were obtained in two step synthesis from cinchona commercial available catalyst.[18a]

General procedure for the addition of oxazolones to nitroalkenes: An ordinary vial equipped with a magnetic stirring bar was charged with oxazolone **1** (0.2 mmol) and the nitroalkene (0.2 mmol) in toluene (0.2 mL) at −20 °C. After 15 min the corresponding catalyst **4** was added. The stirring was maintained at −20 °C overnight and the crude reaction mixture was directly charged onto Iatrobeads and subjected to FC.

(−)-4-(2-Nitro-1-phenylethyl)-4-phenyl-2-*p*-tolyloxazol-5(4*H*)-one (5a): The title compound was obtained according to the general procedure using 5 mol% of catalyst **4c** after FC (hexane/Et_2O 5:1) as a white solid (72 mg, 90%). M.p. 129–131 °C; $[\alpha]_D^{20} = -13.5$ ($c = 0.3$ in CH_2Cl_2); ^1H NMR: $\delta = 7.79$–7.73 (m, 4H), 7.42–7.10 (m, 10H), 5.00 (dd, $J = 13.2$, 11.2, 1H), 4.46–4.37 (m, 2H), 2.35 ppm (s, 3H); ^{13}C NMR: $\delta = 176.3$, 161.5, 144.1, 135.6, 132.8, 129.6, 129.2, 129.1, 129.1, 128.8, 128.7, 128.0, 126.1, 122.3, 76.0, 75.4, 52.6, 21.7 ppm; HRMS: *m/z*: calcd for $C_{24}H_{20}N_2NaO_4$: 423.1320; found 423.1317 $[M+Na]^+$. The *ee* was determined by HPLC analysis using a Chiralpak AD column (hexane/*i*PrOH 80:20); flow rate 1.0 mL min^{-1}; $\tau_{minor} = 6.5$ min, $\tau_{major} = 16.8$ min (74% *ee*).

(−)-2-*tert*-Butyl-4-(2-nitro-1-phenylethyl)-4-phenyloxazol-5(4*H*)-one (5b): The title compound was obtained according to the general procedure using 5 mol% of catalyst **4c** after FC (hexane/Et_2O 20:1) as a white solid (48 mg, 65%). M.p. 97–99 °C; $[\alpha]_D^{20} = -52.1$ ($c = 0.7$ in CH_2Cl_2); ^1H NMR: $\delta = 7.78$ (d, $J = 7.2$ Hz, 2H), 7.48–7.31 (m, 8H), 5.09 (td, $J =$ 14.8, 4.4 Hz, 1H), 4.43–4.37 (m, 2H), 1.13 ppm (s, 9H); ^{13}C NMR: $\delta =$ 176.9, 171.4, 135.4, 132.7, 129.3 (2C), 128.9, 128.9, 128.5, 125.8, 125.7, 75.1, 74.9, 51.8, 34.1, 26.4 ppm; HRMS: *m/z*: calcd for $C_{21}H_{22}N_2NaO_4$: 389.1477; found 389.1487 $[M+Na]^+$. The *ee* was determined after transformation into the product **6b** (83% *ee*).

(−)-2-*tert*-Butyl-4-[1-(4-methoxyphenyl)-2-nitroethyl]-4-phenyl oxazol-5(4*H*)-one (5c): The title compound was obtained according to the general procedure using 5 mol% of catalyst **4d** after FC (hexane/Et_2O 9:1) as a yellow oil (71 mg, 90%). $[\alpha]_D^{20} = -50.2$ ($c = 0.9$ in CH_2Cl_2); ^1H NMR: $\delta = 7.77$–7.75 (m, 2H), 7.47–4.38 (m, 3H), 7.22 (d, $J = 8.8$ Hz, 2H), 6.84 (d, $J = 8.8$ Hz, 2H), 4.94 (dd, $J = 14.4$, 12.4 Hz, 1H), 4.38–4.33 (m, 2H), 3.76 (s, 3H), 1.16 ppm (s, 9H); ^{13}C NMR: $\delta = 177.1$, 171.4 159.8, 135.5, 129.2, 125.8, 124.4, 113.9, 75.3, 75.2, 55.2, 51.3, 34.1, 26.4 ppm; HRMS: *m/z*: calcd for $C_{22}H_{24}N_2NaO_5$: 419.1582; found 419.1582 $[M+Na]^+$. The *ee* was determined by HPLC analysis using a Chiralcel OD column (hexane/*i*PrOH 90:10); flow rate 1.0 mL min^{-1}; $\tau_{minor} = 5.4$ min, $\tau_{major} =$ 6.4 min (72% *ee*).

(+)-2-*tert*-Butyl-4-[2-nitro-1-(4-nitrophenyl)ethyl]-4-phenyl oxazol-5(4*H*)-one (5d): The title compound was obtained according to the general procedure using 5 mol% of catalyst **4c** after FC (pentane/AcOEt 9:1) as a white solid (53 mg, 65%). M.p. 152–153 °C; $[\alpha]_D^{20} = +63.4$ ($c = 1.0$ in CH_2Cl_2); ^1H NMR: $\delta = 8.23$–8.19 (m, 2H), 7.77–7.74 (m, 2H), 7.56–7.41 (m, 4H), 5.01 (dd, $J = 13.9$, 11.5 Hz, 1H), 4.51 (dd, $J = 11.5$, 4.0 Hz, 1H), 4.43 (dd, $J = 14.0$, 4.1 Hz, 2H), 1.16 ppm (s, 9H); ^{13}C NMR: $\delta =$ 176.4, 172.2, 148.1, 140.2, 134.6, 130.4, 129.7, 129.5, 125.7, 123.6, 74.6, 74.5, 51.3, 34.3, 26.5 ppm; HRMS: *m/z*: calcd for $C_{21}H_{21}N_3NaO_6$: 434.1328; found 434.1335 $[M+Na]^+$. The *ee* was determined by HPLC analysis using a Chiralcel OJ column (hexane/*i*PrOH 90:10); flow rate 1.0 mL min^{-1}; $\tau_{minor} = 22.6$ min, $\tau_{major} = 30.8$ min (72% *ee*).

(+)-2-*tert*-Butyl-4-[2-nitro-1-(thiophen-2-yl)ethyl]-4-phenyl oxazol-5(4*H*)-one (5e): The title compound was obtained according to the gen-

eral procedure using 5 mol% of catalyst **4d** after FC (hexane/Et_2O 15:1) as an inseparable mixture of diastereoisomers (91:9) (68 mg, 91%). M.p. 110–112 °C; $[\alpha]_D^{20}=+58.1$ ($c=1.0$ in CH_2Cl_2); ^{1}H NMR: $\delta=7.76$ (d, $J=7.2$ Hz, 2H), 7.48–7.41 (m, 3H), 7.26 (d, $J=5.2$ Hz, 1H), 7.04 (d, $J=2.8$ Hz, 1H), 6.96 (dd, $J=8.8$, 5.2 Hz, 1H), 4.86 (dd, $J=13.2$, 11.6 Hz, 1H), 4.75 (dd, $J=12.0$, 3.6 Hz, 1H), 4.40 (dd, $J=13.7$, 3.6 Hz, 1H), 1.22 ppm (s, 9H); ^{13}C NMR: $\delta=176.8$, 172.3, 135.0 134.7, 129.3, 129.1, 128.6, 126.9, 126.1, 125.7, 76.5, 75.2, 47.6, 34.2, 26.3 ppm; HRMS: *m/z*: calcd for $C_{19}H_{20}N_2NaO_4S$: 395.1041; found 395.1041 $[M+Na]^+$. The *ee* was determined after transformation into the product **6d** (70% *ee*). Representative ^{1}H NMR signals of the minor diastereoisomer: $\delta=7.70$ (d, $J=5.2$ Hz, 2H), 7.20 (d, $J=4.8$ Hz, 1H), 6.90 (dd, $J=8.4$, 4.8 Hz, 1H), 5.07 (dd, $J=14.0$, 12.4 Hz, 1H), 4.54–4.48 (m, 1H), 1.07 ppm (s, 9H).

(−)-2-*tert*-Butyl-4-[1-(2-chlorophenyl)-2-nitroethyl]-4-phenyl oxazol-5(4*H*)-one (5f): The title compound was obtained according to the general procedure using 5 mol% of catalyst **4c** after FC (pentane/AcOEt 9:1) as a colorless oil (64 mg, 80%). $[\alpha]_D^{20}=-41.2$ ($c=0.5$ in CH_2Cl_2); ^{1}H NMR: $\delta=7.84$–7.79 (m, 2H), 7.51–7.39 (m, 4H), 7.32 (dd, $J=7.2$, 2.3 Hz, 1H), 7.28–7.19 (m, 2H), 5.27 (dd, $J=11.5$, 3.9 Hz, 1H), 4.92 (dd, $J=13.7$, 11.7 Hz, 1H), 4.48 (dd, $J=13.9$, 4.0 Hz, 1H), 1.25 ppm (s, 9H); ^{13}C NMR: $\delta=175.9$, 171.9, 136.1, 135.7, 131.3, 130.7, 129.9, 129.3, 129.3, 128.3, 126.4, 125.9, 75.5, 74.6, 46.1, 34.2, 26.5 ppm; HRMS: *m/z*: calcd for $C_{21}H_{21}ClN_2NaO_4$: 423.1088; found 423.1088 $[M+Na]^+$. The *ee* was determined by HPLC analysis using a Chiralcel OD column (hexane/*i*PrOH 98:2); flow rate 1.0 mL min^{-1}; $\tau_{major}=6.5$ min, $\tau_{minor}=7.3$ min (74% *ee*).

(−)-2-*tert*-Butyl-4-[1-(naphthalen-2-yl)-2-nitroethyl]-4-phenyl oxazol-5(4*H*)-one (5g): The title compound was obtained according to the general procedure using 5 mol% of catalyst **4c** after FC (hexane/Et_2O 15:1) as a white solid (45 mg, 54%). M.p. 74–76 °C; $[\alpha]_D^{20}=-84.0$ ($c=0.5$ in CH_2Cl_2); ^{1}H NMR: $\delta=7.85$–7.80 (m, 6H), 7.51–7.25 (m, 6H), 5.15 (dd, $J=13.6$ 11.6 Hz, 1H), 4.60 (dd, $J=11.6$, 4 Hz, 1H), 4.49 (dd, $J=13.6$, 4.0 Hz, 1H), 1.07 ppm (s, 9H); ^{13}C NMR: $\delta=176.9$, 171.5, 135.4, 133.2, 132.7, 130.2, 129.3, 129.2, 128.8 (2C), 128.3, 127.9, 127.6, 126.6, 126.5, 125.8, 75.2 (2C), 51.9, 34.1, 26.3 ppm; HRMS: *m/z*: calcd for $C_{25}H_{24}N_2NaO_4$: 439.1633; found 439.1636 $[M+Na]^+$. The *ee* was determined by HPLC analysis using a Chiralpak AD column (hexane/*i*PrOH 90:10); flow rate 1.0 mL min^{-1}; $\tau_{major}=5.4$ min, $\tau_{minor}=5.9$ min (66% *ee*).

(+)-2-*tert*-Butyl-4-(1-nitropropan-2-yl)-4-phenyloxazol-5(4*H*)-one (5h): The title compound was obtained according to the general procedure using 5 mol% of catalyst **4b** after FC (pentane/AcOEt 9:1) as a white solid (53 mg, 88%). M.p. 150–152 °C; $[\alpha]_D^{20}=+46.7$ ($c=1.0$ in CH_2Cl_2); ^{1}H NMR: $\delta=7.61$ (d, $J=8.1$ Hz, 2H), 7.46–7.34 (m, 3H), 4.27 (dd, $J=12.7$, 10.7 Hz, 1H), 4.18 (dd, $J=12.8$, 3.5 Hz, 1H), 3.30–3.20 (m, 1H), 1.35 (s, 9H), 0.99 ppm (d, $J=6.6$ Hz, 3H); ^{13}C NMR: $\delta=177.8$, 172.0, 135.6, 129.1, 129.0, 125.6, 77.1, 74.6, 40.8, 34.5, 26.9, 12.7 ppm; HRMS: *m/z*: calcd for $C_{16}H_{20}N_2NaO_4$: 327.1321; found 327.1307 $[M+Na]^+$. The *ee* was determined by HPLC analysis using a Chiralcel OJ column (hexane/*i*PrOH 90:10); flow rate 1.0 mL min^{-1}; $\tau_{minor}=5.0$ min, $\tau_{major}=5.8$ min (66% *ee*).

(+)-2-*tert*-Butyl-4-[4-(methylthio)-1-nitrobutan-2-yl]-4-phenyl oxazol-5(4*H*)-one (5i): The title compound was obtained according to the general procedure using 5 mol% of catalyst **4d** after FC (pentane/AcOEt 9:1) as a colorless oil (47 mg, 65%). $[\alpha]_D^{20}=+61.3$ ($c=1.0$ in CH_2Cl_2); ^{1}H NMR: $\delta=7.62$–7.60 (m, 2H), 7.45–7.35 (m, 3H), 4.32 (dd, $J=8.4$, 5.7 Hz, 2H), 3.40–3.26 (m, 1H), 2.61–2.43 (m, 2H), 2.05 (s, 3H), 1.66–1.60 (m, 2H), 1.34 ppm (s, 9H); ^{13}C NMR: $\delta=177.9$, 171.8, 135.5, 129.1, 129.0, 125.9, 75.3, 75.0, 44.3, 44.3, 34.4, 31.1, 28.2, 26.8 ppm; HRMS: *m/z*: calcd for $C_{18}H_{24}N_2NaO_4S$: 387.1354; found 387.1357 $[M+Na]^+$. The *ee* was determined by HPLC analysis using a Chiralpak AD column (hexane/*i*PrOH 98:2); flow rate 1.0 mL min^{-1}; $\tau_{minor}=6.8$ min, $\tau_{major}=7.5$ min (67% *ee*).

(+)-4-Methyl-2-(2-nitro-1-phenylethyl)-2-phenyloxazol-5(2*H*)-one (5j): The title compound was obtained according to the general procedure using 5 mol% of catalyst **4c** after FC (hexane/Et_2O 5:1) as a white solid (53 mg, 82%). M.p. 150–152 °C; $[\alpha]_D^{20}=+50.0$ ($c=0.4$ in CH_2Cl_2); ^{1}H NMR: $\delta=7.63$–7.61 (m, 2H), 7.46–7.27 (m, 8H), 4.93 (dd, $J=13.3$, 11.2 Hz, 1H), 4.59 (dd, $J=13.6$, 4.4 Hz, 1H), 4.43 (dd, $J=11.2$, 4.4 Hz, 1H), 1.90 ppm (s, 3H); ^{13}C NMR: $\delta=164.5$, 160.1, 135.7, 131.5, 129.7, 129.5, 129.1, 128.7, 128.6, 125.9, 105.6, 74.9, 53.0, 13.4 ppm; HRMS: *m/z*: calcd for $C_{18}H_{16}N_2NaO_4$: 347.1007; found 347.1011 $[M+Na]^+$. The *ee* was determined by HPLC analysis using a Chiralpak AD column (hexane/*i*PrOH 90:10); flow rate 1.0 mL min^{-1}; $\tau_{minor}=7.0$ min, $\tau_{major}=9.0$ min (66% *ee*).

(+)-4-Isobutyl-2-(2-nitro-1-phenylethyl)-2-phenyloxazol-5(2*H*)-one (5k): The title compound was obtained according to the general procedure using 5 mol% of catalyst **4c** after FC (pentane/AcOEt 9:1) as a colorless oil (68 mg, 93% as a mixture of diastereoisomers). $[\alpha]_D^{20}=+27.4$ ($c=0.5$ in CH_2Cl_2); ^{1}H NMR: $\delta=7.67$–7.61 (m, 2H), 7.44 (m, 3H), 7.37–7.16 (m, 5H), 4.92 (dd, $J=13.3$, 11.4 Hz, 1H), 4.60 (dd, $J=13.5$, 4.2 Hz, 1H), 4.45 (dd, $J=11.1$, 4.2 Hz, 1H), 2.21–2.08 (m, 2H), 1.85–1.73 (m, 1H), 0.69–0.63 ppm (m, 6H); ^{13}C NMR: $\delta=164.7$, 162.5, 136.2, 131.8, 129.6, 129.4, 129.0, 128.8, 128.8, 125.9, 105.8, 75.3, 52.9, 36.2, 26.1, 22.3, 22.1 ppm; HRMS: *m/z*: calcd for $C_{21}H_{22}N_2NaO_4$: 389.1477; found 389.1480 $[M+Na]^+$. The *ee* was determined by HPLC analysis using a Chiralpak AD column (hexane/*i*PrOH 98:2); flow rate 1.0 mL min^{-1}; $\tau_{minor}=10.1$ min, $\tau_{major}=11.3$ min (65% *ee*).

(+)-2-(2-Chlorophenyl)-4-isobutyl-2-(2-nitro-1-phenylethyl) oxazol-5(2*H*)-one (5l): The title compound was obtained according to the general procedure using 5 mol% of catalyst **4c** after FC (pentane/AcOEt 9:1) as a colorless oil (76 mg, 95%). $[\alpha]_D^{20}=+35.6$ ($c=0.5$ in CH_2Cl_2); ^{1}H NMR: $\delta=7.53$ (dd, $J=9.4$, 8.1 Hz, 2H), 7.35 (t, $J=7.7$ Hz, 1H), 7.32–7.21 (m, 6H), 5.34 (dd, $J=10.5$, 4.4 Hz, 1H), 4.91 (dd, $J=13.4$, 10.7 Hz, 1H), 4.56 (dd, $J=13.5$, 4.5 Hz, 1H), 2.20–2.16 (m, 2H), 1.88–1.76 (m, 1H), 0.70 (d, $J=6.8$ Hz, 3H), 0.68 ppm (d, $J=6.8$ Hz, 3H); ^{13}C NMR: $\delta=164.4$, 163.6, 133.8, 132.6, 132.5, 132.2, 131.2, 129.7, 129.0, 128.5, 128.4, 127.5, 106.0, 75.6, 48.9, 36.4, 26.3, 22.5, 22.4 ppm; HRMS: *m/z*: calcd for $C_{21}H_{21}ClN_2NaO_4$: 423.1088; found 423.1103 $[M+Na]^+$. The *ee* was determined by HPLC analysis using a Chiralcel OD column (hexane/*i*PrOH 90:10); flow rate 1.0 mL min^{-1}; $\tau_{minor}=10.2$ min, $\tau_{major}=13.2$ min (82% *ee*).

(−)-2-(2-Chlorophenyl)-4-isobutyl-2-[1-(4-methoxyphenyl)-2-nitroethyl]oxazol-5(2*H*)-one (5m): The title compound was obtained according to the general procedure using 5 mol% of catalyst **4d** after (pentane/AcOEt 9:1) as a colorless oil (70 mg, 82%). $[\alpha]_D^{20}=-21.4$ ($c=0.5$ in CH_2Cl_2); ^{1}H NMR: $\delta=7.57$–7.50 (m, 2H), 7.35 (td, $J=7.9$, 1.7 Hz, 1H), 7.31–7.25 (m, 1H), 7.16 (d, $J=8.7$ Hz, 2H), 6.80 (d, $J=8.8$ Hz, 2H), 5.28 (dd, $J=10.7$, 4.5 Hz, 1H), 4.85 (dd, $J=13.2$, 10.8 Hz, 1H), 4.52 (dd, $J=13.3$, 4.5 Hz, 1H), 3.75 (s, 3H), 2.22–2.18 (m, 2H), 1.92–1.80 (m, 1H), 0.72 (d, $J=6.8$ Hz, 3H), 0.70 ppm (d, $J=6.7$ Hz, 3H); ^{13}C NMR: $\delta=164.1$, 163.3, 159.7, 133.6, 132.5, 132.2, 130.9, 130.6, 128.2, 127.3, 123.6, 114.1, 105.9, 75.6, 55.1, 47.9, 36.2, 26.1, 22.3, 22.1 ppm; HRMS: *m/z*: calcd for $C_{22}H_{23}ClN_2NaO_5$: 453.1193; found 453.1194 $[M+Na]^+$. The *ee* was determined by HPLC analysis using a Chiralpak AD column (hexane/*i*PrOH 90:10); flow rate 1.0 mL min^{-1}; $\tau_{major}=8.6$ min, $\tau_{minor}=14.0$ min (90% *ee*).

(+)-2-(2-Chlorophenyl)-4-isobutyl-2-[2-nitro-1-(thiophen-2-yl)ethyl]oxazol-5(2*H*)-one (5n): The title compound was obtained according to the general procedure using 5 mol% of catalyst **4c** after FC (pentane/AcOEt 9:1) as a colorless oil (68 mg, 84%). $[\alpha]_D^{20}=+29.5$ ($c=0.2$ in CH_2Cl_2); ^{1}H NMR: $\delta=7.55$ (ddd, $J=15.6$, 7.9, 1.5 Hz, 2H), 7.37 (td, $J=7.9$, 1.7 Hz, 1H), 7.29 (td, $J=7.7$, 1.3 Hz, 1H), 7.23 (dd, $J=5.1$, 1.0 Hz, 1H), 6.98 (dd, $J=3.7$, 1.0 Hz, 1H), 6.92 (dd, $J=5.1$, 3.5 Hz, 1H), 5.65 (dd, $J=10.5$, 4.3 Hz, 1H), 4.77 (dd, $J=13.3$, 10.5 Hz, 1H), 4.55 (dd, $J=13.3$, 4.3 Hz, 1H), 2.33–2.21 (m, 2H), 1.98–1.88 (m, 1H), 0.78–0.75 ppm (m, 6H); ^{13}C NMR: $\delta=164.1$, 163.5, 133.6, 133.2, 132.4, 132.2, 131.1, 128.8, 128.2, 127.3, 127.1, 126.7, 105.2, 76.7, 44.4, 36.3, 26.1, 22.2, 22.2 ppm; HRMS: *m/z*: calcd for $C_{19}H_{19}ClN_2NaO_4$: 429.0652; found 429.0645 $[M+Na]^+$. The *ee* was determined by HPLC analysis using a Chiralpak AD column (hexane/*i*PrOH 90:10); flow rate 1.0 mL min; $\tau_{minor}=8.1$ min^{-1}, $\tau_{major}=10.8$ min (80% *ee*).

(−)-2-(2-Fluorophenyl)-4-isobutyl-2-(2-nitro-1-phenylethyl)oxazol-5(2*H*)-one (5o): The title compound was obtained according to the general procedure using 5 mol% of catalyst **4d** after FC (pentane/AcOEt 9:1) as a colorless oil (71 mg, 93%). $[\alpha]_D^{20}=-38.2$ ($c=1.0$ in CH_2Cl_2); ^{1}H NMR: $\delta=7.22$ (m, 9H), 4.96–4.83 (m, 2H), 4.61 (dd, $J=12.5$, 3.6 Hz, 1H), 2.23–2.09 (m, 2H), 1.84–1.72 (m, 1H), 0.66 (d, $J=6.7$ Hz, 3H), 0.63 ppm (d,

J=6.7 Hz, 3H); ^{13}C NMR: δ=164.4, 163.4, 159.4 (d, J(C,F)=252.0 Hz), 131.9 (d, J(C,F) = 8.5 Hz), 131.8, 129.5, 128.8, 127.3 (d, J(C,F)=2.4 Hz), 124.6 (d, J(C,F)=3.6 Hz), 123.5 (d, J(C,F)=11.1 Hz), 117.2 (d, J(C,F)= 22.1 Hz), 104.5 (d, J(C,F)=6.1 Hz), 75.5, 50.3, 50.2, 36.2, 26.2, 22.3, 22.1 ppm; HRMS: m/z: calcd for $C_{21}H_{21}FN_2NaO_4$: 407.1383; found 407.1399 $[M+Na]^+$. The *ee* was determined by HPLC analysis using a Chiralcel OD column (hexane/*i*PrOH 90:10); flow rate 1.0 mL min^{-1}; τ_{major}=9.8 min, τ_{minor}=12.0 min, (92% *ee*).

(−)-2-(2-Fluorophenyl)-4-isobutyl-2-[2-nitro-1-(4-nitrophenyl)ethyl]oxazol-5(2*H*)-one (5p): The title compound was obtained according to the general procedure using 5 mol% of catalyst **4d** after FC (pentane/AcOEt 9:1) as a colorless oil (78 mg, 91%). $[\alpha]_D^{20}=-31.0$ (c=1.0 in CH_2Cl_2); ^{1}H NMR: δ=8.15 (d, J=8.8 Hz, 2H), 7.51–7.41 (m, 3H), 7.38 (td, J=7.7, 1.6 Hz, 1H), 7.22 (ddd, J=11.3, 8.3, 0.9 Hz, 1H), 7.16 (td, J=7.7, 1.0 Hz, 1H), 5.00–4.88 (m, 2H), 4.65 (dd, J=13.2, 3.7 Hz, 1H), 2.33–2.19 (m, 2H), 1.94–1.82 (m, 1H), 0.71 (d, J=6.7 Hz, 3H), 0.68 ppm (d, J=6.7 Hz, 3H); ^{13}C NMR: δ=164.2, 163.8, 159.3 (d, J(C,F)=251.8 Hz), 148.0, 139.5, 132.3 (d, J(C,F)=8.0 Hz), 130.6, 127.3, 124.8 (d, J(C,F)=3.3 Hz), 123.8, 123.0 (d, J(C,F)=11.1 Hz), 117.3 (d, J(C,F)=22.0 Hz), 104.0 (d, J(C,F)=5.9 Hz), 74.9, 49.9, 36.3, 26.2, 22.2, 22.0 ppm; HRMS: m/z: calcd for $C_{21}H_{20}FN_3NaO_6$: 452.1234; found 452.1248 $[M+Na]^+$. The *ee* was determined by HPLC analysis using a Chiralpak AD column (hexane/*i*PrOH 95:5); flow rate 1.0 mL min^{-1}; τ_{major}=17.2 min, τ_{minor}=22.4 min (75% *ee*).

(−)-2-(2-Fluorophenyl)-4-isobutyl-2-[2-nitro-1-(thiophen-2-yl)ethyl]oxazol-5(2*H*)-one (5q): The title compound was obtained according to the general procedure using 5 mol% of catalyst **4d** after FC (pentane/AcOEt 9:1) as a colorless oil (64 mg, 82%). $[\alpha]_D^{20}=-31.6$ (c=1.0 in CH_2Cl_2); ^{1}H NMR: δ=7.51–7.41 (m, 2H), 7.25–7.13 (m, 3H), 6.98 (dd, J=3.6, 1.1 Hz, 1H), 6.92 (dd, J=5.1, 3.5 Hz, 1H), 5.19 (dd, J=10.7, 4.2 Hz, 1H), 4.80 (ddd, J=13.3, 10.7, 0.6 Hz, 1H), 4.61 (dd, J=13.4, 4.2 Hz, 1H), 2.26 (dd, J=7.0, 0.8 Hz, 2H), 1.96–1.84 (m, 1H), 0.70–0.66 ppm (m, 6H); ^{13}C NMR: δ=164.4, 163.6, 159.5 (d, J(C,F)=251.7 Hz), 133.3, 132.1 (d, J(C,F)=8.5 Hz), 128.9, 127.3 (d, J(C,F)=2.4 Hz), 127.2, 126.7, 124.8 (d, J(C,F)=3.6 Hz), 123.1 (d, J(C,F)=11.3 Hz), 117.3 (d, J(C,F)=22.0 Hz), 104.0 (d, J(C,F)=6.3 Hz), 76.8, 45.8, 36.3, 26.2, 22.2 ppm (2C); HRMS: m/z: calcd for $C_{19}H_{19}FN_2NaO_4S$: 413.0947; found 413.0959 $[M+Na]^+$. The *ee* was determined by HPLC analysis using a Chiralcel OD column (hexane/*i*PrOH 95:5); flow rate 1.0 mL min^{-1}; τ_{major}=10.3 min, τ_{minor}= 11.7 min (87% *ee*).

(−)-2-[1-(2-Chlorophenyl)-2-nitroethyl]-2-(2-fluorophenyl)-4-isobutyloxazol-5(2*H*)-one (5r): The title compound was obtained according to the general procedure using 5 mol% of catalyst **4d** after FC (pentane/AcOEt 9:1) as a colorless oil (71 mg, 85%). $[\alpha]_D^{20}=-36.0$ (c=1.0 in CH_2Cl_2); ^{1}H NMR: δ=7.55–7.15 (m, 8H), 5.70 (dd, J=10.8, 4.3 Hz, 1H), 4.91 (dd, J=13.6, 11.0 Hz, 1H), 4.68 (dd, J=13.8, 4.4 Hz, 1H), 2.26–2.12 (m, 2H), 1.85–1.73 (m, 1H), 0.68 (d, J=6.7 Hz, 3H), 0.63 ppm (d, J=6.7 Hz, 3H); ^{13}C NMR: δ=164.4, 163.6, 159.5 (d, J(C,F)=252.6 Hz), 136.7, 132.1 (d, J(C,F)=8.6 Hz), 130.5, 130.1, 129.9, 128.3, 127.4 (d, J(C,F)=2.5 Hz), 127.1, 124.6 (d, J(C,F)=3.7 Hz), 123.1 (d, J(C,F)=11.1 Hz), 117.4 (d, J(C,F)=22.0 Hz), 104.7 (d, J(C,F)=5.9 Hz), 75.4, 45.3, 36.2, 26.3, 22.1, 22.0 ppm; MS: calcd for $C_{21}H_{20}ClFN_2NaO_4$: 441.0993; found 441.1004 $[M+Na]^+$. The *ee* was determined by HPLC analysis using a Chiralpak AD column (hexane/*i*PrOH 95:5); flow rate 1.0 mL min^{-1}; τ_{minor}=8.7 min, τ_{major}=10.0 min (77% *ee*).

(−)-2-(2-Fluorophenyl)-2-[1-(furan-2-yl)-2-nitroethyl]-4-isobutyl oxazol-5(2*H*)-one (5s): The title compound was obtained according to the general procedure using 5 mol% of catalyst **4d** after FC (pentane/AcOEt 9:1) as a colorless oil (46 mg, 61%). $[\alpha]_D^{20}=-25.6$ (c=1.0 in CH_2Cl_2); ^{1}H NMR: δ=7.51–7.42 (m, 2H), 7.33 (brs, 1H), 7.26–7.17 (m, 2H), 6.28 (brs, 2H), 5.00 (dd, J=10.7, 3.7 Hz, 1H), 4.87 (dd, J=13.5, 10.7 Hz, 1H), 4.56 (dd, J=13.5, 3.9 Hz, 1H), 2.34–2.24 (m, 2H), 1.95 (sept, J=6.8 Hz, 1H), 0.83–0.79 ppm (m, 6H); ^{13}C NMR: δ=164.2, 163.5, 159.5 (d, J(C,F)=252.0 Hz), 132.1 (d, J(C,F)=8.5 Hz), 127.2 (d, J(C,F)=2.4 Hz), 124.8 (d, J(C,F)=3.6 Hz), 122.7 (d, J(C,F)=11.1 Hz), 117.3 (d, J(C,F)= 22.0 Hz), 111.1, 110.6, 104.0, 74.2, 44.6, 36.3, 26.0, 22.4, 22.2 ppm; HRMS: m/z: $C_{19}H_{19}FN_2NaO_5$: 397.1176; found 397.1165 $[M+Na]^+$. The *ee* was determined by HPLC analysis using a Chiralpak AD column (hexane/*i*PrOH 90:10); flow rate 1.0 mL min^{-1}; τ_{major}=7.2 min, τ_{minor}=9.0 min (64% *ee*).

(−)-4-Isobutyl-2-(2-nitro-1-phenylethyl)-2-(4-nitrophenyl)oxazol-5(2*H*)-one (5t): The title compound was obtained according to the general procedure using 5 mol% of catalyst **4d** after FC (pentane/AcOEt 9:1) as a white solid (53 mg, 64%). M.p. 129–133 °C; $[\alpha]_D^{20}=-35.6$ (c=1.0 in CH_2Cl_2); ^{1}H NMR: δ=8.32–8.26 (m, 2H), 7.82–7.77 (m, 2H), 7.34–7.28 (m, 3H), 7.13–7.15 (m, 2H), 4.87 (dd, J=13.4, 10.3 Hz, 1H), 4.58 (dd, J= 13.5, 4.8 Hz, 1H), 4.43 (dd, J=10.3, 4.9 Hz, 1H), 2.26–2.15 (m, 2H), 1.85 (sept, J=6.4 Hz, 1H), 0.72 (d, J=6.7 Hz, 3H), 0.69 ppm (d, J=6.7 Hz, 3H); ^{13}C NMR: δ=163.9, 163.8, 148.4, 142.8, 131.3, 129.4, 129.1, 128.9, 127.4, 124.0, 105.0, 74.9, 52.7, 36.3, 26.0, 22.3, 22.1 ppm; HRMS: m/z: $C_{21}H_{21}N_3NaO_6$: 434.1328; found 434.1301 $[M+Na]^+$. The *ee* was determined by HPLC analysis using a Chiralpak AD column (hexane/*i*PrOH 90:10); flow rate 1.0 mL min^{-1}; τ_{major}=14.2 min, τ_{minor}=18.5 min (70% *ee*).

General procedure for the ring opening of oxazolones with TMSCl:[16a] An ordinary vial equipped with a magnetic stirring bar was charged with MeOH (0.20 mL) and the corresponding oxazolone **5** (0.1 mmol). Then, TMSCl (0.1 mmol) was added in one portion. The stirring was maintained at room temperature until consumption of the starting material. Then, the solvent was evaporated and the product was obtaining pure without further purification.

(+)-Methyl 2-(4-methylbenzamido)-4-nitro-2,3-diphenylbutanoate (6a): The title compound was obtained according to the general procedure starting from **5a** as a colorless oil (43 mg, 99%). $[\alpha]_D^{20}=+4.8$ (c=1.0 in CH_2Cl_2); ^{1}H NMR: δ=7.72 (d, J=8.0 Hz, 2H), 7.56 (d, J=7.6 Hz, 1H), 7.43 (t, J=7.2 Hz, 1H), 7.38–7.20 (m, 5H), 5.33 (dd, J=14.0, 2.4 Hz, 1H), 5.24 (dd, J=11.2, 2.0 Hz, 1H), 5.01 (dd, J=14.0, 11.6 Hz, 1H), 3.66 (s, 3H), 2.44 ppm (s, 3H); ^{13}C NMR: δ=171.5, 166.3, 142.8, 135.1, 134.7, 130.9, 127.5, 129.3, 129.2, 128.7, 128.5, 127.1, 126.2, 77.9, 53.9, 49.1, 21.5 ppm; HRMS: m/z: calcd for $C_{25}H_{24}N_2NaO_5$: 455.1582; found 455.1570 $[M+Na]^+$. The *ee* was determined by HPLC analysis using a Chiralcel OD column (hexane/*i*PrOH 90:10); flow rate 1.0 mL min$^-$; τ_{minor}=8.9 min, τ_{major}=10.9 min (74% *ee*).

(−)-Methyl 4-nitro-2,3-diphenyl-2-(pivalamido)butanoate (6b): The title compound was obtained according to the general procedure starting from **5b** as a white solid (38 mg, 95%). M.p. 72–75 °C; $[\alpha]_D^{20}=-10.0$ (c= 0.2 in CH_2Cl_2); ^{1}H NMR: δ=7.35–7.12 (m, 10H), 7.08 (brs, 1H), 5.16 (dd, J=16.4, 2.4 Hz, 1H), 5.04 (dd, J=11.6, 2.8 Hz, 1H), 4.75 (dd, J= 14.0, 11.6 Hz, 1H), 3.56 (s, 3H), 1.20 ppm (s, 9H); ^{13}C NMR: δ=177.5, 171.6, 135.3, 134.7, 129.3, 129.1, 128.7, 128.6, 128.5, 125.8, 77.7, 67.7, 53.6, 48.5, 39.4, 27.5 ppm; HRMS: m/z: calcd for $C_{22}H_{26}N_2NaO_5$: 421.1739; found 421.1737 $[M+Na]^+$. The *ee* was determined by HPLC analysis using a Chiralcel OD column (hexane/*i*PrOH 90:10); flow rate 1.0 mL min^{-1}; τ_{major}=6.5 min, τ_{minor}=7.5 min (83% *ee*).

(−)-Methyl 3-(4-methoxyphenyl)-4-nitro-2-phenyl-2-(pivalamido)butanoate (6c): The title compound was obtained according to the general procedure starting from **5c** as a colorless oil (37 mg, 87%). $[\alpha]_D^{20}=-1.3$ (c=0.7 in CH_2Cl_2); ^{1}H NMR: δ=7.42–7.35 (m, 5H), 7.17 (brs, 1H), 7.10 (d, J=8.8 Hz, 2H), 6.84 (d, J=8.8 Hz, 2H), 5.20 (dd, J=14.0, 2.4 Hz, 1H), 5.08 (dd, J=12.0, 2.4 Hz, 1H), 4.78 (dd, J=14.0, 12.0 Hz, 1H), 3.79 (s, 3H), 3.63 (s, 3H), 1.29 ppm (s, 9H); ^{13}C NMR: δ=177.4, 171.7, 159.6, 135.4, 130.3, 129.0, 128.4, 126.4, 125.8, 113.9, 77.9, 67.8, 55.2, 53.7, 47.9, 39.4, 27.5 ppm; HRMS: m/z: calcd for $C_{23}H_{28}N_2NaO_6$: 451.1845; found 451.1840 $[M+Na]^+$. The *ee* was determined by HPLC analysis using a Chiralcel OD column (hexane/*i*PrOH 90:10); flow rate 1.0 mL min^{-1}; τ_{minor}=8.6 min, τ_{major}=10.1 min (58% *ee*, starting from a sample of 58% *ee*).

(+)-Methyl 4-nitro-2-phenyl-2-(pivalamido)-3-(thiophen-2-yl)butanoate (6d): The title compound was obtained according to the general procedure starting from **5e** as a white solid (40 mg, 99%). M.p. 150–153 °C; $[\alpha]_D^{20}=+40.7$ (c=0.3 in CH_2Cl_2); ^{1}H NMR: δ=7.43–7.25 (m, 7H), 6.50 (dd, J=4.8, 3.6 Hz, 1H), 6.91 (d, J=2.8 Hz, 1H), 5.49 (dd, J=11.2, 2.0 Hz, 1H), 5.22 (dd, J=14.0, 2.0 Hz, 1H), 4.68 (dd, J=13.6, 11.6 Hz, 1H), 3.62 (s, 3H), 1.31 ppm (s, 9H); ^{13}C NMR: δ=177.8, 171.7, 137.2, 135.0, 129.5, 128.8, 128.6, 126.8, 126.7, 125.9, 79.7, 67.9, 54.2, 45.6, 39.7, 27.7 ppm; HRMS: m/z: calcd for $C_{20}H_{24}N_2NaO_5S$: 427.1303; found

427.1302 $[M+Na]^+$. The *ee* was determined by HPLC analysis using a Chiralcel OD column (hexane/*i*PrOH 98:2); flow rate 1.0 mL min^{-1}; $\tau_{major}=9.5$ min, $\tau_{minor}=10.7$ min (70% *ee*).

(+)-Methyl 3-(naphthalen-2-yl)-4-nitro-2-phenyl-2-(pivalamido)butanoate (6e): The title compound was obtained according to the general procedure starting from **5g** (44 mg, 99%). M.p. 60–63 °C; $[\alpha]_D^{20}=+6.0$ ($c=0.3$ in CH_2Cl_2); ^{1}H NMR: $\delta=7.84$–7.65 (m, 4H), 7.51–7.39 (m, 7H), 7.29 (dd, $J=8.8$, 1.6 Hz, 1H), 7.15 (brs, 1H), 5.35–5.30 (m, 2H), 4.98 (dd, $J=14.4$, 12.0 Hz, 1H), 3.65 (s, 3H), 1.30 ppm (s, 9H); ^{13}C NMR: $\delta=177.6$, 171.6, 135.3, 133.1, 132.9, 132.2, 129.1, 128.9, 128.6, 128.3, 127.8, 127.6, 126.6, 126.5, 125.9, 77.8, 53.7, 48.6, 39.4, 27.5 ppm; HRMS: *m*/*z*: calcd for $C_{25}H_{24}N_2NaO_5$: 471.1895; found 471.1879 $[M+Na]^+$. The *ee* was determined by HPLC analysis using a Chiralcel OD column (hexane/*i*PrOH 90:10); flow rate 1.0 mL min^{-1}; $\tau_{major}=10.6$ min, $\tau_{minor}=15.2$ min (66% *ee*).

General procedure for the ring opening of the oxazolones with HCl: An ordinary vial equipped with a magnetic stirring bar was charged with CH_3CN (0.30 mL) and the corresponding oxazolone **5** (0.1 mmol). Then, HCl conc. (0.5 mmol) was added in one portion. The stirring was maintained at room temperature until consumption of the starting material. Then, the solvent was evaporated and the crude reaction mixture was directly charged onto Iatrobeads and subjected to FC.

(+)-3-Methyl-4-nitro-2-phenyl-2-pivalamidobutanoic acid (7a): The title compound was obtained according to the general procedure after FC (pentane/AcOEt 2:1) as a white solid (23 mg, 70%). M.p. 146–150 °C; $[\alpha]_D^{20}=+41.7$ ($c=1.0$ in CH_2Cl_2); ^{1}H NMR: $\delta=10.55$ (brs, 1H), 7.52–7.27 (m, 5H), 4.77 (dd, $J=13.6$, 2.0 Hz, 1H), 4.26–4.00 (m, 1H), 3.66–3.53 (m, 1H), 1.25 (s, 9H), 1.06 ppm (d, $J=6.7$ Hz, 3H); ^{13}C NMR: $\delta=179.8$, 173.2, 135.0, 128.9, 128.6, 125.7, 79.6, 68.6, 39.5, 39.2, 27.3, 14.5 ppm; HRMS: *m*/*z*: calcd for $C_{16}H_{21}N_2NaO_5$: 345.1426; found 345.1415 $[M+Na]^+$.

(−)-4-Nitro-2,3-diphenyl-2-(pivaloyl)butanoic acid (7b): The title compound was obtained according to the general procedure after FC (pentane/AcOEt 2:1) as a white solid (32 mg, 84%). M.p. 169–173 °C; $[\alpha]_D^{20}=-29.3$ ($c=1.0$ in EtOAc); ^{1}H NMR: $\delta=7.49$–7.27 (m, 8H), 7.17–7.15 (m, 2H), 7.03 (brs, 1H), 5.15 (dd, $J=13.8$, 2.3 Hz, 1H), 5.06–4.92 (m, 1H), 4.69 (t, $J=12.6$ Hz, 1H), 1.17 ppm (s, 9H); ^{13}C NMR: $\delta=179.2$, 172.5, 134.4, 134.1, 129.6, 128.9, 128.8, 128.7, 128.7, 126.2, 77.4, 67.6, 48.5, 39.4, 27.3 ppm; HRMS: *m*/*z*: calcd for $C_{21}H_{24}N_2NaO_5$: 407.1583; found 407.1579 $[M+Na]^+$.

(+)-*N*-(2-Oxo-3,4-diphenylpyrrolidin-3-yl)pivalamide (8): To a solution of **5b** (20 mg, 0.05 mmol) and $NiCl_2{\cdot}6H_2O$ (12 mg, 0.05 mmol) in EtOH (0.5 mL) was added $NaBH_4$ (19 mg, 0.5 mmol) at room temperature. The reaction was stirred for 2 h before quenched with sat. aq. solution of NH_4Cl (5 mL). The reaction was extracted with CH_2Cl_2 (2×5 mL), the organic layer was dried over $MgSO_4$ and filtered though a pad of Celite-Iatrobeads. The solvent was eliminated in vacuo to afford **8** (12 mg, 72%). $[\alpha]_D^{20}=+8.8$ ($c=0.5$ in CH_2Cl_2); ^{1}H NMR: $\delta=7.19$–7.03 (m, 6H), 6.72 (d, $J=8.0$ Hz, 2H), 6.59 (d, $J=7.2$ Hz, 2H), 6.28 (brs, 1H), 5.98 (brs, 1H), 4.94 (dd, $J=10.4$, 8.0 Hz, 1H), 3.60 (d, $J=8.4$ Hz, 1H), 3.45 (d, $J=10.4$ Hz, 1H), 1.23 ppm (s, 9H); ^{13}C NMR: $\delta=179.1$, 174.5, 136.1, 135.4, 129.0, 128.6, 128.4, 127.9, 127.4, 126.4, 126.3, 77.2, 47.8, 42.2, 39.1, 29.7, 27.5 ppm; HRMS: *m*/*z*: calcd for $C_{21}H_{24}N_2NaO_2$: 359.1735; found 359.1730 $[M+Na]^+$.

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[1] For recent reviews on organocatalysis, see e.g.: a) P. I. Dalko, L. Moisan, *Angew. Chem.* **2004**, *116*, 5248; *Angew. Chem. Int. Ed.* **2004**, *43*, 5138; b) A. Berkessel, H. Gröger, *Asymmetric Organocatalysis*, VCH, Weinheim, **2004**; c) Special issue No. 8 on organocatalysis *Acc. Chem. Res.* **2004**, *37*; d) J. Seayed, B. List, *Org. Biomol. Chem.* **2005**, *3*, 719; e) B. List, J.-W. Yang, *Science* **2006**, *313*, 1584; f) B. List, *Chem. Commun.* **2006**, 819; g) M. J. Gaunt, C. C. C. Johansson, A. McNally, N. C. Vo, *Drug Discovery Today* **2007**, *12*, 8; h) P. I. Dalko, *Enantioselective Organocatalysis*, Wiley-VCH, Weinheim, **2007**; i) Special issue No. 12 on organocatalysis *Chem. Rev.* **2007**, *107*: j) S. E. Denmark, G. L. Beutner, *Angew. Chem.* **2008**, *120*, 1584; *Angew. Chem. Int. Ed.* **2008**, *47*, 1560; k) A. Dondoni, A. Massi, *Angew. Chem. Int. Ed.* **2008**, *47*, 463; l) P. Melchiorre, M. Marigo, A. Carlone, G. Bartoli, *Angew. Chem.* **2008**, *120*, 6232; *Angew. Chem. Int. Ed.* **2008**, *47*, 6138; m) X. Xu, W. Wang, *Org. Biomol. Chem.* **2008**, *6*, 2037.

[2] For general reviews of organocatalytic conjugate addition, see: a) S. B. Tsogoeva, *Eur. J. Org. Chem.* **2007**, 1701; b) D. Almasi, D. A. Alonso, C. Nájera, *Tetrahedron: Asymmetry* **2007**, *18*, 299; c) J. L. Vicario, D. Badía, L. Carrillo, *Synthesis* **2007**, 2065.

[3] For recent reviews on conjugated additions using iminium-ion activation see e.g.: a) S. B. Tsogoeva, *Eur. J. Org. Chem.* **2007**, 1701; b) D. Almasi, D. A. Alonso, C. Najera, *Tetrahedron: Asymmetry* **2007**, *18*, 299. For examples see e.g.: c) K. A. Ahrendt, C. J. Borths, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2000**, *122*, 4243; d) M. Marigo, J. Fránzen, T. B. Poulsen, W. Zhuang, K. A. Jørgensen, *J. Am. Chem. Soc.* **2005**, *127*, 6764; e) S. Brandau, A. Landa, J. Franzén, M. Marigo, K. A. Jørgensen, *Angew. Chem.* **2006**, *118*, 4411; *Angew. Chem. Int. Ed.* **2006**, *45*, 4305; f) H. Gotoh, R. Masui, H. Ogino, M. Shoji, Y. Hayashi, *Angew. Chem.* **2006**, *118*, 7007; *Angew. Chem. Int. Ed.* **2006**, *45*, 6853; g) S. Mayer, B. List, *Angew. Chem.* **2006**, *118*, 4299; *Angew. Chem. Int. Ed.* **2006**, *45*, 4193; h) W. Wang, H. Li, J. Wang, L. Zu, *J. Am. Chem. Soc.* **2006**, *128*, 10354; i) R. Rios, H. Sundén, I. Ibrahem, G. Zhao, L. Eriksson, A. Córdova, *Tetrahedron Lett.* **2006**, *47*, 8547; j) S. Brandau, E. Maerten, K. A. Jørgensen, *J. Am. Chem. Soc.* **2006**, *128*, 14986; k) Y. K. Chen, M. Yoshida, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2006**, *128*, 9328; l) I. Ibrahem, R. Rios, J. Vesely, G. Zhao, A. Córdova, *Chem. Commun.* **2007**, 849; m) J. Vesely, I. Ibrahem, G. Zhao, R. Rios, A. Córdova, *Angew. Chem.* **2007**, *119*, 792; *Angew. Chem. Int. Ed.* **2007**, *46*, 778; n) S. Bertelsen, P. Dinér, R. L. Johansen, K. A. Jørgensen, *J. Am. Chem. Soc.* **2007**, *129*, 1536; o) P. Dinér, M. Nielsen, M. Marigo, K. A. Jørgensen, *Angew. Chem.* **2007**, *119*, 2029; *Angew. Chem. Int. Ed.* **2007**, *46*, 1983; p) A. Carlone, G. Bartoli, M. Bosco, L. Sambri, P. Melchiorre, *Angew. Chem.* **2007**, *119*, 4588; *Angew. Chem. Int. Ed.* **2007**, *46*, 4504; q) I. Ibrahem, R. Rios, J. Vesely, P. Hammar, L. Eriksson, F. Himo, A Cordova, *Angew. Chem.* **2007**, *119*, 4591; *Angew. Chem. Int. Ed.* **2007**, *46*, 4507; r) E. Maerten, S. Cabrera, A. Kjærsgaard, K. A. Jørgensen, *J. Org. Chem.* **2007**, *72*, 8893; s) H. Gotoh, H. Ishikawa, Y. Hayashi, *Org. Lett.* **2007**, *9*, 5307; t) S. Fustero, D. Jiménez, J. Moscardo, S. Catalán, C. del Pozo, *Org. Lett.* **2007**, *9*, 9905; u) S. Lee, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2007**, *129*, 15438; v) V. Wascholowski, K. R. Knudsen, C. E. T. Mitchell, S. V. Ley, *Chem. Eur. J.* **2008**, *14*, 6155; w) I. Ibrahem, P. Hammar, J. Vesely, R. Rios, L. Eriksson, A. Córdova, *Adv. Synth. Catal.* **2008**, *350*, 1875; x) I. Ibrahem, G.-L. Zhao, R. Rios, J. Vesely, H. Sundén, P. Dziedzic, A. Córdova, *Chem. Eur. J.* **2008**, *14*, 7867.

[4] Reviews of cinchona alkaloids: a) K. Kacprzak, J. Gawroński, *Synthesis* **2001**, 961; b) S. France, D. J. Guerin, S. J. Miller, T. Leckta, *Chem. Rev.* **2003**, *103*, 2985; c) S.-K. Tian, Y. Chen, J. Hang, L. Tang, P. McDaid, L. Deng, *Acc. Chem. Res.* **2004**, *37*, 621; d) N. M. R. Hoffmann, J. Frakenpoh, *Eur. J. Org. Chem.* **2004**, 4293. Reviews about asymmetric addition of nucleophiles to nitroalkenes: e) O. M. Berner, L. Tedeschi, D. Enders, *Eur. J. Org. Chem.* **2002**, 1877; f) N. Krause, A. Hoffmman-Röder, *Synthesis* **2001**, 171; g) M. P. Sibi, S. Manyem, *Tetrahedron* **2000**, *56*, 8033.

[5] a) S. Cabrera, E. Reyes, J. Alemán, A. Milelli, K. A. Jørgensen, *J. Am. Chem. Soc.* **2008**, *130*, 12031; b) One example of a TMS-enolate

of a tertiary amino lactone adding to an α,β-unsatuarated aldehyde in enantioselective organo-cascade catalysis has been reported: Y. Huang, A. M. Walji, C. H. Larsen, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2005**, *127*, 15051.

[6] J. Venkatraman, S. C. Shankaramma, P. Balaram, *Chem. Rev.* **2001**, *101*, 3131.

[7] For reviews on synthesis of α,α-disubstituted α-amino acids see e.g.: a) C. Cativiela, M. D. Díaz-de-Villegas, *Tetrahedron: Asymmetry* **1998**, *9*, 3517; b) C. Cativiela, M. D. Díaz-de-Villegas, *Tetrahedron: Asymmetry* **2000**, *11*, 3517; c) Y. Ohfune, T. Shinada, *Eur. J. Org. Chem.* **2005**, 5127; d) H. Vogt, S. Bräse, *Org. Biomol. Chem.* **2007**, *5*, 406.

[8] a) M. C. Khosla, K. Stachowiak, R. R. Smeby, F. M. Bumpus, F. Piriou, K. Lintner, S. Fermandjian, *Proc. Natl. Acad. Sci. USA* **1981**, *78*, 757; b) S. J. O'Connon, Z. Liu, *Synlett* **2003**, 2135; c) M. Tanaka, *Chem. Pharm. Bull.* **2007**, *55*, 349.

[9] a) A. Takahashi, H. Naganawa, D. Ikeda, Y. Okami, *Tetrahedron* **1991**, *47*, 3621; b) T. Kan, Y. Kawamoto, T. Asakawa, T. Furuta, T. Fukuyama, *Org. Lett.* **2008**, *10*, 168.

[10] For a recent review on catalytic asymmetric synthesis of α-amino acids see: C. Nájera, J. M. Sansano, *Chem. Rev.* **2007**, *107*, 4584.

[11] a) H. Gröger, *Chem. Rev.* **2003**, *103*, 2795; b) T. Vilaivan, W. Bhanthumnavin, Y. Sritana-Anant, *Curr. Org. Chem.* **2005**, *9*, 1315.

[12] For a highlight on the Strecker reaction, see: S. J. Connon, *Angew. Chem.* **2008**, *120*, 1194; *Angew. Chem. Int. Ed.* **2008**, *47*, 1176.

[13] For the enantioselective synthesis of amino acids by phase-transfer catalysis with achiral Schiff base esters see: a) M. J. O'Donnell, *Acc. Chem. Res.* **2004**, *37*, 506. For recent reviews on phase-transfer catalysis, see: b) T. Ooi, K. Maruoka, *Angew. Chem.* **2007**, *119*, 4300; *Angew. Chem. Int. Ed.* **2007**, *46*, 4222; c) T. Hashimoto, K. Maruoka, *Chem. Rev.* **2007**, *107*, 5656.

[14] J. S. Fisk, R. A. Mosey, J. J. Tepe, *Chem. Soc. Rev.* **2007**, *36*, 1432, see also ref. [2d].

[15] J. C. Ruble, G. C. Fu, *J. Am. Chem. Soc.* **1998**, *120*, 11532.

[16] a) B. M. Trost, X. Ariza, *J. Am. Chem. Soc.* **1999**, *121*, 10727; b) B. M. Trost, K. Dogra, *J. Am. Chem. Soc.* **2002**, *124*, 7256; c) B. M. Trost, C. Jakel, B. Plietker, *J. Am. Chem. Soc.* **2003**, *125*, 4438.

[17] For a recent review about bifunctional cinchona alkaloid based thiourea catalysis, see: a) S. J. Connon, *Chem. Commun.* **2008**, 2499. For thiourea catalysis, see: b) M. S. Taylor, E. N. Jacobsen, *Angew. Chem.* **2006**, *118*, 1550; *Angew. Chem. Int. Ed.* **2006**, *45*, 1520; c) S. J. Connon, *Chem. Eur. J.* **2006**, *12*, 5418. For an account of multi-functional thioureas, see: d) H. Miyabe, Y. Takemoto, *Bull. Chem. Soc. Jpn.* **2008**, *81*, 785. For recent examples of cinchona thiourea catalysis, see: e) G. Tárkányi, P. Király, S. Varga, B. Vakulya, T. Soós, *Chem. Eur. J.* **2008**, *14*, 6078; f) J. M. Andrés, R. Manzano, R. Pedrosa, *Chem. Eur. J.* **2008**, *14*, 5116; g) A. Peschiulli, Y. Gunko, S. J. Connon, *J. Org. Chem.* **2008**, *73*, 2454; h) T. Mandal, C. G. Zhao, *Angew. Chem.* **2008**, *120*, 7828; *Angew. Chem. Int. Ed.* **2008**, *47*, 7714; i) B. Han, Q. P. Lin, X. Tian, X. F. Xiong, J. G. Deng, Y. C. Chen, *Chem. Eur. J.* **2008**, *14*, 8094; j) W.-M. Zhou, H. Liu, D.-M. Ming, *Org. Lett.* **2008**, *10*, 2817; k) J. Wang, H. Xie, H. Li, L. Zu, W. Wang *Angew. Chem.* **2008**, *120, 4245; Angew. Chem. Int. Ed.* **2008**, 47, 4177; *Angew. Chem. Int. Ed.* **2008**, *47*, 4177; l) Z. Zhang, P. Schreiner, *Synthesis* **2007**, 2559; m) P. Dinér, M. Nielsen, S. Bertelsen, B. Niess, K. A. Jorgensen, *Chem. Commun.* **2007**, 3646; n) N. Martin, J. A. Nolwenn L. Ozores, B. List, *J. Am. Chem. Soc.* **2007**, *129*, 8976; o) Y.-J. Cao, H.-H. Lu, Y.-Y. Lai, L.-Q. Lu, W.-J. Xiao, *Synthesis* **2006**, 3795; p) M. P. Lalonde, Y. Chen, E. N. Jacobsen, *Angew. Chem.* **2006**, *118*, 6514; *Angew. Chem. Int. Ed.* **2006**, *45*, 6366; q) A. E. Mattson, A. M. Zuhl, T. E. Reynolds, K. A. Scheidt, *J. Am. Chem. Soc.* **2006**, *128*, 4932; r) Y. Hoashi, T. Yabuta, P. Yuan, H. Miyabe, Y. Takemoto, *Tetrahedron* **2006**, *62*, 365; s) R. P. Herrera, V. Sgarzani, L. Bernardi, A. Ricci, *Angew. Chem.* **2005**, *117*, 6734; *Angew. Chem. Int. Ed.* **2005**, *44*, 6576; t) S. McCooey, S. J. Connon, *Angew. Chem.* **2005**, *117*, 6525; *Angew. Chem. Int. Ed.* **2005**, *44*, 6367; u) J. Wang, H. Li, Hao, W. Duan, L. Zu, W. Wang, *Org. Lett.* **2005**, *7*, 4713; v) J. Ye, D. J. Dixon, P. S. Hynes, *Chem. Commun.* **2005**, 4481; w) G. Dessole, R. Herrera, A. Ricci, *Synlett* **2004**, 2374; x) Y. Hoashi, T. Yabuta, Y. Takemoto, *Tetrahedron Lett.* **2004**, *45*, 9185; y) A. Berkessel, M. Albrecht, S. Mukherjee, C. Santanu, F. Cleemann, T. Mueller, J. Lex, *Chem. Commun.* **2005**, 1898.

[18] a) B. Vakulya, S. Varga, A. Csámpi, T. Soós, *Org. Lett.* **2005**, *7*, 1967; b) See also for Mitsunobu reaction by using HN_3 as nitrogen source: B.-J. Li, L. Jiang, M. Liu, Y.-C. Chen, L.-S. Ding, Y. Wu, *Synlett* **2005**, 603.

[19] CCDC 682909 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif

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