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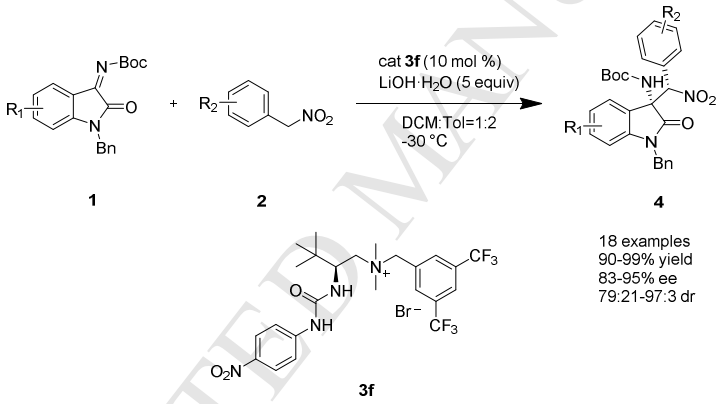

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L-tert-Leucine derived urea-ammonium salts : efficient bifunctional phase transfer catalysts for highly diastereo- and enantioselective aza-Henry reaction of isatin-derived *N*-Boc ketimines with *α*-aryl nitromethanes

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ABSTRACT

An efficient way of aza-Henry reaction between isatin-derived *N*-Boc ketimines and *α*-aryl nitromethanes catalyzed by bifunctional phase transfer catalysts with a quaternary ammonium center derived from *L-tert*-Leucine has been developed. A series of 3-substituted 3-amino-oxindoles were constructed by this catalytic protocol in excellent yields (90-99%), with high enantioselectivities (83-95%) and diastereoselectivities (79:21-97:3). The asymmetric aza-Henry reaction of *N*-Boc amidosulfones and *α*-aryl nitromethanes were also investigated and gave the corresponding products in high to excellent yields (72-97%) with high enantioselectivities (up to 99%) and diastereoselectivities (up to >99:1).

1. Introduction

The use of chiral phase transfer catalysts to catalyze asymmetric reactions has become one of the main ways of asymmetric synthesis. Previous reports in this filed indicate that, most successful catalysts are based on the skeleton of cinchona alkaloids[1, 2], chiral binaphthyls[3, 4]. Amino acids due to their inexpensive and accessible characteristics are attracting more and more attention of chemists. To our delight, a series of excellent work about amino acid-derived phase transfer catalyst has been reported by the Zhao' group in recent years. In 2013, Zhao's group report a novel class of chiral bifunctional thiourea ammonium phase-transfer catalysts and chiral bifunctional thiourea phosphonium salts[5] derived from commercially available *a*-amino acids[6] and applied to aza-Henry reaction successfully. They first imported thiourea groups into phase-transfer catalysts based on acyclic natural amino acids, and proposed a possible transition state model showed that the thiourea moiety and the quaternary ammonium or quaternary phosphonium centre both have very important influence and the H-bonding interaction and electrostatic interaction both plays a significant role in this reaction. Moreover, under the same catalytic mechanism, they alter the thiourea moiety as well as quaternary ammonium or quaternary phosphonium group on the catalysts to expand a series of reactions. In 2013 year, they reported the addition of thiols to imines reaction catalyzed by chiral bifunctional thiourea ammonium phase-transfer catalysts derived from *a*-amino acid[7] to synthesize high enantio- and diastereoselective chiral N,S-acetals. In 2017, they first applied *a*-amino acid derived thiourea phosphonium salts[8] to asymmetric Strecker reaction. The same year, they published stereoselective conjugate addition of oxindoles to electron-deficient β-haloalkenes catalyzed by quaternary ammonium salts[9]. In 2018, they reported 1,3-dipolar cycloaddition of imino esters with benzofuranone derivatives catalyzed by thiourea-ammonium salt with high enantioselectivities[10]. Encouraged by a series of excellent work of Zhao's group, we design a new kind of multiple hydrogen-bonding donors catalysts derived from *a*-amino acids and applied to a highly enantio- and diastereoselective nitro-Mannich reaction[11]. According to our and Zhao's results, we find that *a*-amino acid skeleton have a great influence on stereocontrol and reactivity in nitro-Mannich reaction. To the best of our knowledge, although a lot of successful examples of aza-Henry reaction are based on aldimines[5, 12-22], the aza-Henry reaction of ketimines[23-26] is still rarely reported owing to their low reactivity and diffcult enantiocontrol. We assume that such kind of catalysts should be well applied in aza-Henry reaction of ketimines. The aza-Henry reaction of isatin-derived ketimines is one of the most efficient and rational approach to construct 3-substituted 3-amino-2-oxindoles[27-32], which contained a stereogenic centre and have been recognized as key structures in a variety of natural products and biologically active compounds[27]. For example, the spirooxindole anti-malarial NITD609[33], the spirocyclic thioureawith p53/Hdm2 antagonist activity[34], AG-041R, a gastrin/cholecystokinin type B receptorantagonist, is effective in repairing cartilage defects[35] (Figure 1) . Recently our group

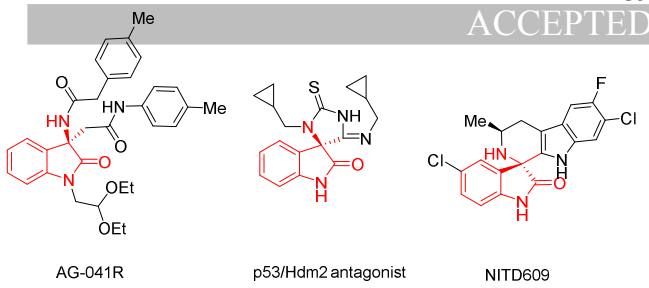


Figure 1. Examples of biologically important 3-subtituted 3-amino-2-oxindoles.

reported a novel kind of organocatalysts, cinchona alkaloid-derived phase-transfer catalysts bearing multiple hydrogen-bonding donors, and successfully applied them to this reaction with high diastereo- and enantioselectivities.[36] In spite of this, this existing catalytic system still can not effectively accommodate with some substrates with the electron-donating groups at the C6-position or different group at the C7-position. To this end, we try to develop and evaluate a series of novel bifunctional phase-transfer catalysts derived from *α*-amino acid for this reaction. In order to solve this problem, firstly we tried amino acid-derived phase transfer catalysts with multiple hydrogen bonding donors[11] and amino acid-derived bifunctional thiourea-ammonium catalysts[6] respectively in this aza-Henry reaction of isatin-derived ketimines and *α*-aryl nitromethanes but did not afford satisfied results. To our surprised, when we modify the structure of Zhao's catalyst we find that change the thiourea group to the urea group give a much better result. Encouraged by

2. Results and Discussion

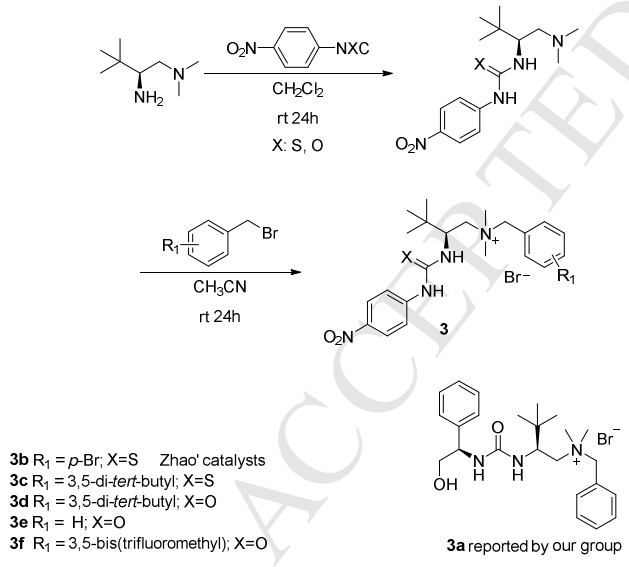


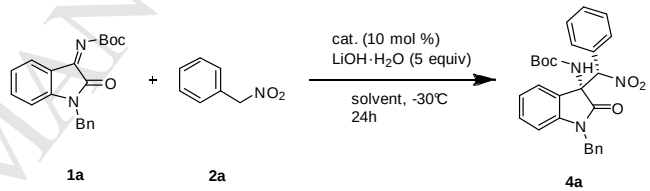
Figure 2. Synthesis of the Catalyst

better experimental results, we developed a series of chiral phase transfer catalysts with a quaternary ammonium center derived of *L-tert* Leucine and after screening, we successfully used catalyst **3f** in the aza-Henry reaction of isatin-derived N-Boc ketimines and *α*-aryl nitromethanes. To our delight, electron-donating group at C6-position and different group at the C7-position also provide the great diastereo- and enantioselectivities (up to ee 95%, dr 96:4). To our surprise, the catalyst **3d** can also successfully catalyze aza-Henry reaction with N-Boc amidosulfones *α*-aryl nitromethanes. Herein, we would like to report our results.

Starting from known (*S*)-N^1,N^1,3,3-tetramethylbutane-1,2-diamine, the catalysts can be easily prepared through the three steps reaction as outlined in Figure 2. (*S*)-N^1,N^1,3,3-tetramethylbutane-1,2-diamine was synthesized from *L-tert*-Leucine in four steps as reported.[37] Firstly, treatment of (*S*)-N^1,N^1,3,3-tetramethylbutane-1,2-diamine was transformed with isothiocyanate or isocyanate to the corresponding urea or thiourea, then urea or thiourea reacted with various benzyl bromides and afforded catalysts **3b**−**3f**.

We began the aza-Henry reaction of isatin-derived N-Boc ketimines **1a** and with 1.5 equiv of (nitromethyl)benzene **2a** in the presence of 10 mol % catalyst **3a** and 5 equiv LiOH·H_2O at -30 °C in $CHCl_3$ (Table 1). In initial screening of catalysts **3a-3f**, we were glad to find catalyst **3f** with 3,5-bis(trifluoromethyl) and urea group gave good enantio- and diastereoselectivity (86% ee, 92:8 dr, entries 1-6). The product configuration is in agreement with the data reported in the literature.[38] In addition, well-behaved catalyst **3a** (our previous work)[11] and **3b** (reported by Zhao's group)[6], which exhibited excellent asymmetric catalytic

Table 1. Optimization of Reaction Conditions



entry[a]	cat	solvent	yield[b] (%)	ee[c] (%)	dr[d]
1	**3a**	CHCl3	93	42	83:17
2	**3b**	CHCl3	80	60	94:6
3	**3c**	CHCl3	82	78	92:8
4	**3d**	CHCl3	99	84	91:9
5	**3e**	CHCl3	82	72	93:7
6	**3f**	CHCl3	98	86	92:8
7	**3f**	MTBE	99	87	73:27
8	**3f**	DCM	97	91	91:9
9	**3f**	Tol	99	89	93:7
10	**3f**	m-Xylene	95	87	93:7
11	**3f**	DCM:Tol (1:1)	99	82	93:7
12	**3f**	DCM:Tol (2:1)	97	89	93:7
13	**3f**	DCM:Tol (1:2)	99	94	93:7
14[e]	**3f**	DCM:Tol (1:2)	95	89	91:9
15[f]	**3f**	DCM:Tol (1:2)	90	87	89:11
16[g]	**3f**	DCM:Tol (1:2)	94	89	90:10

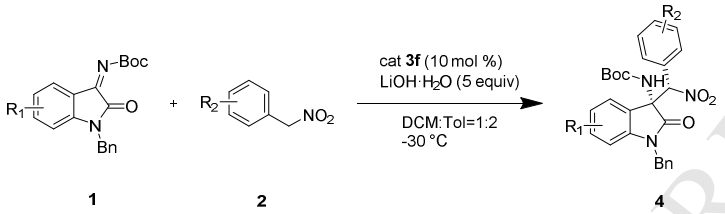
[a]Reactions were conducted at 0.1 mmol scale in 1 mL of solvent with 2a (1.5 equiv). [b]Yield of isolated product. [c]Determined by HPLC using a chiral stationary phase. [d]Determined by HPLC using a chiral stationary phase. [e] The reaction conducted at -20°C. [f]The reactions was performed with (nitromethyl)benzene 2a (1.2 equiv). [g]The reactions was performed with 3f (5 mol %).

activity in the aza-Henry reaction of nitromethane and its alkyl congeners, was also evaluated under the identical reaction conditions. However, compared with catalyst **3f**, catalyst **3a** and **3b** did not have a positive impact on the enantioselectivity (entris 1 and 2). By comparsion, the catalyst **3d** with urea group gets higher enantioselectivity than catalyst **3c** with thiourea group (entries 3 and 4), and catalyst **3f** with 3,5-

bis(trifluoromethyl)benzyl gave the best result (98% yield, 86% ee, 92:8 dr, entry 6) . In the screening of solvent (entries 7-10), dichloromethane gave higher enantioselectivity and toluene gave higher diastereoselectivity. So mixed solvent optimization was performed (entries 11-13), and a mixture of dicholoromethane and toluene (1:2) was chosen as the best solvent (99% yield, 94% ee, 93:7 dr).

Then, the optimization of reaction temperature was performed, -30 °C was chosen as the optimal temperature (entries 13 vs 14). Finally, when the loading of (nitromethyl)benzene **2a** was reduced to 1.2 equiv, high enantio- and diastereoselectivity was a little decreased (entry 15). Suprisingly, high enantio- and diastereoselectivity of the product was still achieved although the catalyst loading was reduced to 5 mol% (entry 16). After screening and optimization, the optimal reaction conditions are as follows: 1.5 equiv aryl nitromethanes in the presence of 10 mol% catalyst **3f** and 5 equiv $LiOH·H_2O$ at −30 °C in dichloromethane and toluene (1:2).

Table 2. Substrate Scope of the reaction



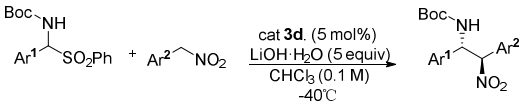
entry[a]	**1**	R_1	**2**	R_2	**4**	yield (%)[b]	ee (%)[c]	dr[d]	time (h)
1	**1a**	H	**2a**	H	**4a**	98	94	93:7	24
2	**1b**	5-F	**2a**	H	**4b**	98	90	91:9	24
3	**1c**	5-Cl	**2a**	H	**4c**	99	91	93:7	24
4	**1d**	5-Br	**2a**	H	**4d**	99	91	94:6	24
5	**1e**	5-I	**2a**	H	**4e**	97	91	97:3	24
6	**1f**	5-Me	**2a**	H	**4f**	95	91	93:7	24
7	**1g**	5-OMe	**2a**	H	**4g**	96	90	94:6	24
8	**1h**	6-F	**2a**	H	**4h**	99	90	93:7	24
9	**1i**	6-Cl	**2a**	H	**4i**	99	92	92:8	24
10	**1j**	6-Br	**2a**	H	**4j**	97	92	93:7	24
11	**1k**	6-OMe	**2a**	H	**4k**	95	93	92:8	24
12	**1l**	7-Cl	**2a**	H	**4l**	94	93	91:9	12
13	**1m**	7-Br	**2a**	H	**4m**	98	95	96:4	12
14	**1n**	7-Me	**2a**	H	**4n**	99	94	92:8	12
15	**1o**	7-CF3	**2a**	H	**4o**	98	92	92:8	12
16	**1a**	H	**2b**	*p*-Cl	**4p**	98	91	91:9	24
17	**1a**	H	**2c**	*p*-Br	**4q**	97	93	95:5	24
18	**1a**	H	**2d**	*p*-OMe	**4r**	96	94	92:8	24
19	**1a**	H	**2e**	*m*-OMe	**4s**	99	90	92:8	24
20	**1a**	H	**2f**	*o*-OMe	**4t**	95	95	79:21	24
21	**1a**	H	**2g**	*β*-naphthyl	**4u**	85	83	92:8	24

[a]Reactions were conducted at 0.1 mmol scale in 1 mL of solvent with (nitromethyl)benzene **2a** (1.5 equiv). [b]Yield of isolated product. [c]Determined by HPLC using a chiral stationary phase. [d]Determined by HPLC using a chiral stationary phase.

With optimal conditions in hand, the substrate scope of the aza-Henry reactions was investigated using *α*-aryl nitromethanes and various substituted isatin-derived ketimines as substrates, and corresponding results were show in Table 2. All corresponding products were obtained in excellent yields (85–99%) and high to excellent enantioselectivities (83–95% ee) and diastereoselectivities (79:21-97:3). Different substrates of isatin-derived *N*-Boc ketimines bearing either electron-withdrawing or electron-donating worked well. The ketimines containing different groups (F, Cl, Br, I, Me, OMe) at the C5-position reacted smoothly with **2a** could provide **4b**-**4g** in 96-99% yields, 91:9-97:3 dr and 90-91% ee. Istain-derived ketimines containing different halogen atoms (F, Cl, Br) at the C6-position reacted with **2a** provided the corresponding adducts **4h**-**4j** in 97-99% yields, 92:8-93:7 dr and 90-92% ee. Especially an electron-donating group (OMe) at the C6-position could also react efficiently with **2a** (95% yield, 92:8 dr and 93% ee). Different groups (Cl, Br, Me, CF_3) at C7-position could also provided **4l**-**4o** in 94-99% yields, 91:9-96:4 dr and 93-95% ee. It is worth noting that reactivity and stereoselectivity of substrates (**1k**-**1o**)

with the electron-donating group at the C6-position or various different groups at C6, C7-position have been solved effectively using this protocol, and corresponding product was obtanied in higher diastereo- and enantioselectivities. However, only low reactivity and stereoselectivity of substrate (**1k**-**1o**) was obtained in previous work[38,36]. Subsequently, we set out to investigate the generality of the reaction with other *α*-aryl nitromethanes. Suprisingly, aryl nitromethanes with either electron-rich or -poor groups in ortho-, meta- as well as para- position were well tolerated and corresponding products were obtained in 85-99% yields, 83-95% ee and 79:21-95:5 dr. In all cases, high to excellent yields (70−99%) and excellent ee values (90−97% ee) were obtained. Subsequently, we attempted to apply our catalytic systems in other aza-Henry reaction. When we chose *N*-Boc amidosulfones as substrates, after screening and optimization, the optimal reaction conditions are as follows: 1.2 equiv of aryl

Table 3. Substrate scope of aza-Henry reation



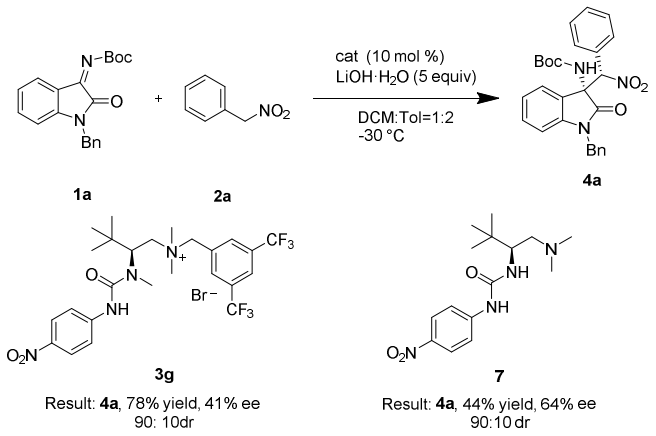
5 **2** **6**

entry[a]	**5**	Ar_1	**2**	Ar_2	**6**	yield[b] (%)	ee[c] (%)	dr[d]	time (h)
1	**5a**	Ph	**2a**	Ph	**6a**	97	98	>99:1	36
2	**5b**	*o*-FC_6H_4	**2a**	Ph	**6b**	97	91	95:5	72
3	**5c**	*o*-$MeOC_6H_4$	**2a**	Ph	**6c**	89	92	96:4	48
4	**5d**	*m*-ClC_6H_4	**2a**	Ph	**6d**	91	97	98:2	72
5	**5e**	*p*-FC_6H_4	**2a**	Ph	**6e**	94	98	>99:1	72
6	**5f**	*p*-ClC_6H_4	**2a**	Ph	**6f**	90	98	>99:1	72
7	**5g**	*p*-MeC_6H_4	**2a**	Ph	**6g**	72	95	97:3	96
8	**5h**	*p*-$MeOC_6H_4$	**2a**	Ph	**6h**	93	97	98:2	48
9	**5i**	*p*-$CF_3C_6H_4$	**2a**	Ph	**6i**	90	97	98:2	72
10	**5j**	2-furyl	**2a**	Ph	**6j**	94	93	96:4	48
11	**5k**	2-thienyl	**2a**	Ph	**6k**	96	97	98:2	48
11	**5a**	Ph	**2h**	*o*-FC_6H_4	**6l**	85	99	94:6	72
12	**5a**	Ph	**2d**	*m*-$MeOC_6H_4$	**6m**	87	97	93:7	72
13	**5a**	Ph	**2f**	*p*-BrC_6H_4	**6n**	92	95	98:2	72
14	**5a**	Ph	**2i**	*p*-MeC_6H_4	**6o**	93	98	99:1	72
15[e]	**5a**	Ph	**2e**	*p*-$MeOC_6H_4$	**6p**	80	96	98:2	72
16	**5a**	Ph	**2b**	2-naphthyl	**6q**	97	95	97:3	72

[a]Unless otherwise noted, reations were carried out with 0.1 mmol of **5a**, 0.12 mmol of **2a**, and 5 mol% of catalyst in 1.0 mL of solvent at -40°C, for 36 h . [b]Yield of isolated product. [c]Determined by HPLC using a chiral stationary phase. [d]Diastereomeric ratios determined by ^{1}HNMR.

nitromethanes, 5 mol% of catalyst **3d**, 5 equiv of $LiOH\cdot H_2O$ in $CHCl_3$, at -40 °C. To our delight, *N*-Boc amidosulfones having either electron-rich or –poor groups were well tolerated, and the position of the substituents seemed to have limited influence (Table 3). The reaction tolerates electron donating and electron withdrawing groups within the phenyl group of the nitro substrate.

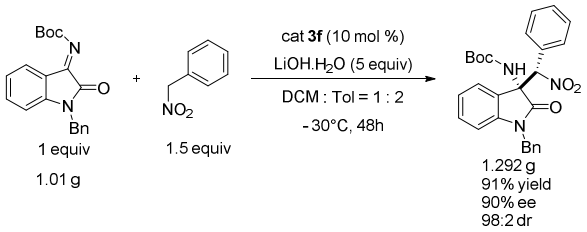
Ultimately, to investigate the mechanism of our catalyst, according to previous report[6], two control experiments were carried out (Scheme 1). Compared with catalyst **3f**, the catalyst **3g** with one block H-bond has also show lower catalytic activity and gave product **4a** with lower ee 41% and 90:10 dr. We also find that catalyst **7** without a quaternary ammonium center, gave product with lower ee 64% and 90:10 dr. These results show that the H-bond and quaternary ammonium center play a crucial role in the reaction.



Scheme 1. Control Experiment for Mechanistic Study

To demonstrate that this reaction can be operated scalability and practicality on large scale, we performed a gram scale reaction using isatin derived ketimine **1a** and 1.5 equiv of **2a**.

Surprisingly, the reaction can still react smoothly and affording the corresponding adduct in 91% yield with 90% ee and 98:2 dr (Scheme 2).



Scheme 2. Gram-scale reaction

On the basis of previous experiment results and relevant work[50], a possible transition state can be considered. We propose a model to explain the binding model of the catalyst and the substrate. The urea motif captures the isatin-derived ketimines by H-bond interaction, and the nitro group anion of the nucleophile would pair with ammonium motif by electrostatic interaction. Such an assembly would direct the nitro compound to attack from the Re face of isatin-derived ketimines.

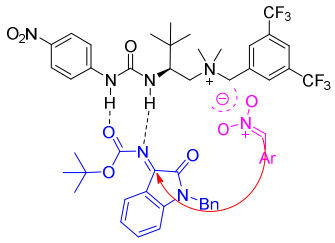


Figure 3. Proposed transition state.

3. Conclusions

In summary, we have developed a series of bifunctional phase-transfer catalysts derived from L-tert-Leucine, and successfully applied them to the aza-Henry reactions of N-Boc ketimines and amidosulfones with α-aryl nitromethanes. A variety of N-Boc ketimines and amidosulfones with α-aryl nitromethanes were investigated and corresponding products were obtained in high yields with excellent diastereo- and enantioselectivity. Detail mechanism study on this reaction, and further application of amino acid-derived bifunctional phase transfer catalysts are underway in our laboratory.

4. Experimental section

4.1. General Information.

Unless otherwise stated, all reagents were purchased from commercial suppliers and used without purification. All solvents were obtained from commercial sources and were purified according to standard procedures. For thin-layer chromatography (TLC), silica gel plates (HSGF 254) were used and compounds were visualized by irradiation with UV light. Purification of reaction products was carried out by flash column chromatography using silica gel (200-300 mesh). ^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury-300BB (300 MHz) or a Bruker NMR Spectrometer (400 MHz), Bruker NMR Spectrometer (500 MHz). All chemical shifts (δ) were given in ppm. Chemical shifts (δ ppm) are relative to the resonance of the deuterated solvent as the internal standard (CD_3OD-d_4, δ 3.31 ppm for proton NMR, δ 49.00 ppm for carbon NMR; $CDCl_3$, δ 7.26 ppm for proton NMR, δ 77.16 ppm for carbon NMR). Data are presented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet) and coupling constant in Hertz (Hz). Mass spectra were recorded on the Bruker Agilent 1290 MicrOTOF Q II. Melting points were measured on a melting point apparatus and were uncorrected. The ee values determination was carried out using chiral HPLC (Waters) with Chiracel IA-3 column, Chiracel IC-3 column Chiracel AD-H column. Optical rotations were measured on a Shanghai ShenGuang SGW-2 Polarimeter at λ = 589 nm. Optical rotations are reported as follows: $[\alpha]_D^{25}$ (c=g/100 mL, solvent).

4.2. Starting materials

(*S*)-N^1,N^1,3,3-tetramethylbutane-1,2-diamine and (*S*)-N^1,N^1,N^2, 3,3-Pentamethylbut- ane-1,2-diamine was prepared according to reported procedure.[6] Catalyst **3a** has been reported by our group.[11] Catalyst **3b** has been reported by Zhao's group.[6] All amidosulfones (**5a**-**5j**) were prepared using reported procedures from corresponding aldehydes.[39-41] All aldehydes was purchased from commercial suppliers and sued directly. All ketimines (**1a**-**1o**) were prepared using reported procedures from corresponding isatins.[42] All a-Aryl Nitromethanes (**2a**-**2g**) were prepared using reported procedures.[43]

4.3. Preparation and characterization of the chiral Catalysts.

Corresponding diamine (200 mg, 1 equiv) was dissolved in CH_2Cl_2, then added isothiocyanate or isocyanate (1.1 equiv) to the system and stirred over night at room temperature. The mixture was concentrated and purified by flash chromatography (CH_2Cl_2/MeOH = 20:1). The product (200 mg, 1 equiv) was dissolved in THF/CH_3CN (0.1 M), Then various benzyl bromide (1.2 equiv) was added, the mixture was stirred over night at room temperature, the mixture was concentrated and purified by flash chromatography (CH_2Cl_2/MeOH = 30:1).

*4.3.1 (S)-N-(3,5-di-tert-butylbenzyl)-N,N,3,3-tetramethyl-2-(3-(4-nitrophenyl)thioureido)butan-1-aminium bromide (**3c**).*

Obtained according to the general procedure. Little yellow solid, 124 mg, 44% yield, mp = 125-126 ℃, $[a]_D^{25}$ = -95.2 (c = 0.5, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.65 (s, 1H), 9.74 (d, *J* = 9.6 Hz, 1H), 8.17 – 8.02 (m, 4H), 7.67 – 7.54 (m, 1H), 7.27 (d, *J* = 2.0 Hz, 2H), 5.26 – 5.14 (m, 1H), 4.77 (d, *J* = 12.6 Hz, 1H), 4.52 (d, *J* = 12.5 Hz, 1H), 4.21 (dd, *J* = 13.5, 10.0 Hz, 1H), 3.59 (d, *J* = 13.8 Hz, 1H), 3.29 (s, 3H), 3.14 (s, 3H), 1.33 (s, 18H), 1.12 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.09, 152.48, 152.31, 145.80, 144.98, 143.10, 127.25, 125.48, 125.26, 124.25, 120.99, 67.48, 56.23, 50.96, 49.39, 37.11, 34.98, 31.34, 26.48. HRMS (ESI): calculated for $C_{30}H_{47}N_4O_2S[M\text{-}Br]^+$: 527.3414, found 527.3416.

*4.3.2.(S)-N-(3,5-di-tert-butylbenzyl)-N,N,3,3-tetramethyl-2-(3-(4-nitrophenyl)thioureido)butan-1-aminium bromide (**3d**).*

Obtained according to the general procedure. Little yellow solid, 146 mg, 51% yield, mp = 131-132 ℃, $[a]_D^{25}$ = -72.6 (c = 0.5, $CHCl_3$). ^{1}H NMR (300 MHz, CD_3OD) δ 8.18 – 8.12 (m, 2H), 7.70 – 7.60 (m, 3H), 7.45 (d, *J* = 1.8 Hz, 2H), 4.66 (dd, *J* = 27.0, 12.6 Hz, 2H), 4.25 (d, *J* = 8.8 Hz, 1H), 3.74 (d, *J* = 13.7 Hz, 1H), 3.55 (dd, *J* = 13.9, 9.1 Hz, 1H), 3.12 (s, 3H), 3.10 (s, 3H), 1.36 (s, 18H), 1.04 (s, 9H). ^{13}C NMR (101 MHz, CD_3OD) δ 156.54, 153.32, 147.23, 143.35, 128.71, 127.97, 125.91, 125.86, 118.71, 71.54, 67.44, 53.71, 37.28, 35.86, 31.74, 26.35. HRMS (ESI): calculated for $C_{30}H_{47}N_4O_3$ $[M\text{-}Br]^+$:511.3643, found 511.3640. 1.36 (s, 18H), 1.04 (s, 9H).

*4.3.3.(S)-N-benzyl-N,N,3,3-tetramethyl-2-(3-(4-nitrophenyl)ureido) butan-1-aminium bromide (**3e**).*

Obtained according to the general procedure. Little yellow solid, 178mg, 58% yield, mp = 60-61 ℃, $[a]_D^{25}$ = -24.4 (c = 0.5, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ 9.56 (s, 1H), 8.09 (d, *J* = 9.2 Hz, 2H), 7.78 (d, *J* = 9.6 Hz, 1H), 7.68 (d, *J* = 9.2 Hz, 2H), 7.51 (dd, *J* = 15.7, 6.6 Hz, 5H), 4.92 (d, *J* = 12.3 Hz, 1H), 4.68 (d, *J* = 12.5 Hz, 1H), 4.32 – 4.04 (m, 2H), 3.73 (d, *J* = 13.1 Hz, 1H), 3.23 (s, 3H), 3.12 (s, 3H), 1.07 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.47, 146.14, 133.19, 131.56, 129.69, 126.47, 125.17, 117.65, 112.56, 69.84, 53.18, 49.63, 47.14, 36.46, 26.49. HRMS (ESI): calculated for $C_{15}H_{24}N_4O_3$ $[M-Br]^+$: 399.2391, found 399.2390.

*4.3.4.(S)-N-(3,5-bis(trifluoromethyl)benzyl)-N,N,3,3-tetramethyl-2-(3-(4-nitrophenyl)ureido)butan-1-aminium bromide (**3f**).*

Obtained according to the general procedure. Little yellow solid, 137 mg, 51% yield, mp = 119-120 ℃, $[a]_D^{25}$ = -16.8 (c = 0.5, $CHCl_3$). ^1H NMR (400 MHz, MeOD) δ 8.30 (s, 2H), 8.23 (s, 1H), 8.16 – 8.12 (m, 2H), 7.67 – 7.63 (m, 2H), 4.94 (d, *J* = 12.9 Hz, 1H), 4.82 (d, *J* = 13.0 Hz, 1H), 4.30 (d, *J* = 8.8 Hz, 1H), 4.13 – 4.06 (m, 1H), 3.85 (d, *J* = 13.8 Hz, 1H), 3.76 – 3.66 (m, 1H), 3.18 (d, *J* = 8.8 Hz, 6H), 2.01 (s, 1H), 1.08 (s, 9H). ^{13}C NMR (126 MHz, DMSO) δ 154.97, 147.18, 141.21, 134.48, 131.24 (q, J = 33.3 Hz, CF_3), 130.84, 125.60, 124.64, 122.47, 117.43, 66.81, 66.21, 52.27, 49.64, 49.47, 36.57, 26.09. HRMS (ESI): calculated for $C_{24}H_{29}F_6N_4O_3$ $[M-Br]^+$:535.2138,found 535.2138

*4.3.5. (S)-N-(3,5-bis(trifluoromethyl)benzyl)-N,N,3,3-tetramethyl-2-(1-methyl-3-(4-nitrophenyl)ureido)butan-1-aminium bromide (**3g**).*

Obtained according to the general procedure. White solid, 143mg, 49% yield, mp = 201-202 ℃, $[a]_D^{25}$ = -17.2 (c = 0.5, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 2H), 8.21 (s, 1H), 8.11 (d, *J* = 9.2 Hz, 2H), 7.73 (d, *J* = 9.2 Hz, 2H), 5.07 – 4.99 (m, 2H), 4.93 (d, *J* = 12.9 Hz, 1H), 4.86 (s, 2H), 4.20 (dd, *J* = 14.3, 9.8 Hz, 1H), 3.81 (d, *J* = 14.4 Hz, 1H), 3.25 (s, 2H), 3.19 (d, *J* = 4.9 Hz, 5H), 1.11 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.78, 149.86, 146.48, 137.55, 136.21 (d, *J* = 33.8 Hz, CF_3), 134.37, 128.31, 127.99, 125.60, 123.51, 70.19, 67.42, 59.68, 52.85, 52.58, 52.19, 51.98, 51.77, 51.56, 51.34, 51.13, 50.92, 40.71, 34.71, 30.24. HRMS (ESI): calculated for $C_{25}H_{31}F_6N_4O_3[M-Br]^+$: 549.2295, found 549.2295.

4.4. General procedure for mixtures of Stereoisomers aza-Henry reaction of imines.

Without protection of inert gases, *α*-aryl nitromethanes (0.15 mmol, 1.5 equiv), TBAB (20 mol %) and imines (0.1 mmol) were dissolved in $CHCl_3$ (1 mL), the mixture was stirred at room temperature, freshly grounded K_2CO_3 (69.1 mg, 5 equiv) was added in one portion, the resulting suspention was stirred at room temperature. Until complete disappearance of the starting materials detected by TLC, 2 mL sat. aq. NH_4Cl was added, the aqueous was extracted with ethylacetate (3×5 mL), then the organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography (PE/EA).

4.5. General procedure for enantio- and diastereoselective aza-Henry reaction.

Ketimines: Without protection of inert gases, *α*-aryl nitromethane (0.15 mmol, 1.5 equiv), catalyst **3f** (10 mol%) and ketimines (0.1 mmol) were dissolved in chloroform (1 ml), the mixture was cooled to -30 °C freshly grounded $LiOH\cdot H_2O$ (20.98 mg, 5 equiv) was added in one portion, the resulting suspention was vigorously stirred at –30 °C. Until complete disappearance of the starting materialsdetected by TLC, 2 ml sat. aq. NH_4Cl was added, the aqueous was extracted with ethylacetate (3×5 mL), then the organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography (PE/EA).

Aldimines: Without protection of inert gases, *α*-Aryl nitoalkane (0.12 mmol, 1.2 equiv), amidosulfones (0.1 mmol) and catalyst **3d** (5 mol%) were dissolved in dry chloroform (1.0 mL). The mixture was cooled to –40 °C, freshly grounded $LiOH\cdot H_2O$ (20.98 mg, 5 equiv) was added in one portion, the resulting suspention was vigorously stirred at –40 °C. After 36 h, 2 mL sat. aq. NH_4Cl was added and the solution was allowed to warm to room temperature, the aqueous was extracted with ethylacetate (3×5 mL), then the organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography (PE/EA).

*4.6. Characterization data of products **4a-4u***

*4.6.1tert-butyl((R)-1-benzyl-3-((S)-nitro(phenyl)methyl)-2-oxoindo-lin-3-yl)carbamate (**4a**).*

White solid, 47.2 mg, 99% yield, mp = 69 -70 ℃, $[a]_D^{25}$ = 13.5 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 94%, dr = 93:7 [Chiralpak IA-3, hexane/*i*-PrOH = 80:20, 254 nm, 1 mL/min, Major- (t_{major} = 17.502 min, t_{minor} = 6.833 min), Minor- (t_{major} = 15.540 min, t_{minor} = 10.211 min)]. ^1H NMR (300 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.6 Hz, 1H), 7.43 – 7.35 (m, 1H), 7.24 (d, *J* = 1.3 Hz, 1H), 7.22 – 7.09 (m, 6H), 7.08 – 7.01 (m, 2H), 6.69 (d, *J* = 6.5 Hz, 2H), 6.49 (d, *J* = 7.8 Hz, 1H), 6.08 (s, 1H), 5.96 (s, 1H), 4.84 (d, *J* = 16.0 Hz, 1H), 4.45 (d, *J* = 15.8 Hz, 1H), 1.32 (s, 9H). Analytical and spectral data were in agreement with the literature data.[36]

*4.6.2.tert-butyl((R)-1-benzyl-5-fluoro-3-((S)-nitro(phenyl)methyl)-2-oxoindolin-3-yl)carbamate (**4b**).*

White solid, 48.4 mg, 98% yield, mp = 86-87 ℃, $[a]_D^{25}$ = 10 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 90%, dr = 91:9 [Chiralpak IA-3, hexane/*i*-PrOH = 80:20, 254 nm, 1 mL/min, Major- (t_{major} = 11.995 min, t_{minor} = 6.349 min), Minor- (t_{major} = 15.941 min, t_{minor} = 9.994min)]. ^1H NMR (300 MHz, $CDCl_3$) δ 7.44 – 7.39 (m, 1H), 7.39 – 7.34 (m, 1H), 7.25 – 7.11 (m, 5H), 7.11 – 7.05 (m, 2H), 6.98 – 6.83 (m, 1H), 6.68 (d, *J* = 6.4 Hz, 2H), 6.38 (dd, *J* = 8.6, 4.2 Hz, 1H), 6.06 (s, 1H), 5.88 (s, 1H), 4.81 (d, *J* = 15.9 Hz, 1H), 4.46 (d, *J* = 16.1 Hz, 1H), 1.35 (s, 9H). Analytical and spectral data were in agreement with the literature data.[36]

*4.6.3.tert-butyl((R)-1-benzyl-5-chloro-3-((S)-nitro(phenyl)methyl)-2-oxoindolin-3-yl)carbamate (**4c**).*

White solid, 50.1 mg, 99% yield, mp = 60-61 ℃, $[a]_D^{25}$ = 18 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 91%, dr = 93:7 [Chiralpak IA-3, hexane/*i*-PrOH = 80:20, 254 nm, 1 mL/min, Major- (t_{major} = 11.991 min, t_{minor} = 6.203 min), Minor- (t_{major} = 15.604 min, t_{minor} = 10.083 min)]. ^1H NMR (300 MHz, CDCl3) δ 7.59 (d, *J* = 2.1 Hz, 1H), 7.44 – 7.37 (m, 1H), 7.25 (d, *J* = 5.6 Hz, 1H), 7.21 – 7.15 (m, 3H), 7.15 – 7.11 (m, 1H), 7.10 – 7.05 (m, 2H), 6.68 (d, *J* = 6.6 Hz, 2H), 6.38 (d, *J* = 8.4 Hz, 1H), 6.04 (s, 1H), 5.91 (s, 1H), 4.78 (d, *J* = 16.0 Hz, 1H), 4.47 (d, *J* = 16.0 Hz, 1H), 1.35 (s, 9H). Analytical and spectral data were in agreement with the literature data.[36]

*4.6.4.tert-butyl((R)-1-benzyl-5-bromo-3-((S)-nitro(phenyl)methyl)-2-oxoindolin-3-yl)carbamate (**4d**).*

White solid, 54.6 mg, 99% yield, mp = 55-56 ℃, $[a]_D^{25}$ = 22 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 91%, dr = 94:6 [Chiralpak IA-3, hexane/*i*-PrOH =80:20, 254 nm, 1 mL/min, Major - (t_{major} = 13.330 min, t_{minor} = 7.011 min), Minor - (t_{major} = 16.954 min, t_{minor} = 15.893 min)]. ^{1}H NMR (300 MHz, CDCl3) δ 7.71 (d, *J* = 2.0 Hz, 1H), 7.44 – 7.37 (m, 1H), 7.35 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.24 (s, 1H), 7.22 (s, 1H), 7.19 (s, 1H), 7.18 – 7.16 (m, 1H), 7.14 (d, *J* = 1.5 Hz, 1H), 7.13 – 7.04 (m, 3H), 6.68 (d, *J* = 6.5 Hz, 2H), 6.33 (d, *J* = 8.4 Hz, 1H), 6.03 (s, 1H), 5.92 (s, 1H), 4.77 (d, *J* = 16.0 Hz, 1H), 4.47 (d, *J* = 16.0 Hz, 1H), 1.35 (s, 9H). Analytical and spectral data were in agreement with the literature data.[36]

*4.6.5.tert-butyl((R)-1-benzyl-5-iodo-3-((S)-nitro(phenyl)methyl)-2-oxoindolin-3-yl)carba mate (**4e**).*

White solid, 58.3 mg, 97% yield, mp = 99-100 ℃, $[a]_D^{25}$ = 41.2 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 91%, dr = 97:3 [Chiralpak IA-3, hexane/*i*-PrOH = 80:20, 254 nm, 1 mL/min, Major - (t_{major} = 11.897 min, t_{minor} = 10.394 min), Minor - (t_{major} = 19.406 min, t_{minor} = 11.170 min)]. ^{1}H NMR (300 MHz, $CDCl_3$)) δ 7.85 (d, *J* = 1.7 Hz, 1H), 7.54 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.46 – 7.36 (m, 1H), 7.25 – 7.11 (m, 5H), 7.09 – 7.02 (m, 2H), 6.72 – 6.62 (m, 2H), 6.23 (d, *J* = 8.3 Hz, 1H), 6.01 (s, 1H), 5.93 (s, 1H), 4.76 (d, *J* = 15.9 Hz, 1H), 4.45 (d, *J* = 16.0 Hz, 1H), 1.35 (s, 9H). Analytical and spectral data were in agreement with the literature data.[36]

*4.6.6.tert-butyl((R)-1-benzyl-5-methyl-3-((S) nitro(phenyl)methyl)-2-oxoindolin-3-yl)carbamate (**4f**).*

White solid, 46.7 mg, 95% yield, mp = 93-94 ℃, $[a]_D^{25}$ = 28.4 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 91%, dr = 92:8 [Chiralpak IA-3, hexane/*i*-PrOH = 80:20, 254 nm, 1 mL/min, Major- (t_{major} = 17.729 min, t_{minor} = 6.270 min), Minor- (t_{major} = 14.179min, t_{minor} = 8.838 min)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 – 7.37 (m, 1H), 7.36 – 7.32 (m, 1H), 7.23 – 7.18 (m, 2H), 7.17 – 7.14 (m, 2H), 7.14 – 7.12 (m, 1H), 7.08 – 7.00 (m, 3H), 6.70 (d, *J* = 6.3 Hz, 2H), 6.37 (d, *J* = 8.0 Hz, 1H), 6.07 (s, 1H), 5.98 (s, 1H), 4.78 (d, *J* = 15.9 Hz, 1H), 4.44 (d, *J* = 15.9 Hz, 1H), 2.36 (s, 3H), 1.33 (s, 9H). Analytical and spectral data were in agreement with the literature data.[36]

*4.6.7.tert-butyl((R)-1-benzyl-5-methoxy-3-((S)-nitro(phenyl)methyl) -2-oxoindolin-3-yl)carbamate (**4g**).*

White solid, 49.5 mg, 98% yield, mp = 117-118 ℃, $[a]_D^{25}$ = 35.2 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 90%, dr=94:6 [Chiralpak IA-3, hexane/*i*-PrOH = 80:20, 254 nm, 1 mL/min, Major- (t_{major} = 21.460 min, t_{minor} = 7.349 min), Minor- (t_{major} = 19.203 min, t_{minor} = 12.636min)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 – 7.34 (m, 1H), 7.24 – 7.18 (m, 2H), 7.18 – 7.11 (m, 4H), 7.10 – 7.03 (m, 2H), 6.76 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.68 (d, *J* = 6.5 Hz, 2H), 6.37 (d, *J* = 8.6 Hz, 1H), 6.06 (s, 1H), 5.96 (d, *J* = 4.4 Hz, 1H), 4.79 (d, *J* = 15.9 Hz, 1H), 4.43 (d, *J* = 16.0 Hz, 1H), 3.80 (s, 3H), 1.33 (s, 9H). Analytical and spectral data were in agreement with the literature data.[36]

*4.6.8.tert-butyl((R)-1-benzyl-6-fluoro-3-((S)-nitro(phenyl)methyl)-2-oxoindolin-3-yl)carbamate (**4h**).*

White solid, 48.7 mg, 99% yield, mp = 88-89 ℃, $[a]_D^{25}$ = 11.2 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 90%, dr = 93:7 [Chiralpak IA-3, hexane/*i*-PrOH = 80:20, 254 nm, 1 mL/min, Major- (t_{major} = 12.360 min, t_{minor} = 5.801 min), Minor- (t_{major} = 14.887 min, t_{minor} = 8.423)]. ^{1}H NMR (500 MHz, CDCl3) δ 7.58 – 7.52 (m, 1H), 7.43 – 7.38 (m, 1H), 7.24 – 7.13 (m, 5H), 7.07 (d, *J* = 7.5 Hz, 2H), 6.84 – 6.78 (m, 1H), 6.69 (d, *J* = 6.8 Hz, 2H), 6.22 (d, *J* = 8.6 Hz, 1H), 6.06 (s, 1H), 5.95 (s, 1H), 4.81 (d, *J* = 15.9 Hz, 1H), 4.44 (d, *J* = 15.8 Hz, 1H), 1.35 (s, 9H). Analytical and spectral data were in agreement with the literature data.[36]

*4.6.9.tert-butyl((R)-1-benzyl-6-chloro-3-((S)-nitro(phenyl)methyl)-2-oxoindolin-3-yl)carbamate (**4i**).*

White solid, 50.2 mg, 99% yield, mp = 74-75 ℃, $[a]_D^{25}$ = 20 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 92%, dr = 92:8 [Chiralpak IA-3, hexane/*i*-PrOH = 80:20, 254 nm, 1 mL/min, Major- (t_{major} = 11.290 min, t_{minor} = 5.610 min), Minor- (t_{major} = 15.221 min, t_{minor} = 7.508)]. ^{1}H NMR (500 MHz, CDCl3) δ 7.52 (d, *J* = 8.0 Hz, 1H), 7.44 – 7.39 (m, 1H), 7.25 – 7.19 (m, 3H), 7.19 – 7.14 (m, 2H), 7.14 – 7.06 (m, 3H), 6.71 (d, *J* = 6.7 Hz, 2H), 6.50 (s, 1H), 6.02 (d, *J* = 41.7 Hz, 2H), 4.81 (d, *J* = 16.0 Hz, 1H), 4.45 (d, *J* = 15.9 Hz, 1H), 1.36 (s, 9H).Analytical and spectral data were in agreement with the literature data.[36]

*4.6.10.tert-butyl((R)-1-benzyl-6-bromo-3-((S)-nitro(phenyl)methyl)-2-oxoindolin-3-yl)carbamate (**4j**).*

White solid, 53.4 mg, 97% yield, mp = 74-75 ℃, $[a]_D^{25}$ = 23.2 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 92%, dr = 93:7 [Chiralpak IA-3, hexane/*i*-PrOH = 80:20, 254 nm, 1 mL/min, Major- (t_{major} = 11.588 min, t_{minor} = 5.736 min), Minor- (t_{major} = 15.897 min, t_{minor} = 7.610)]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (dd, *J* = 17.6, 7.8 Hz, 2H), 7.28 (d, *J* = 1.4 Hz, 1H), 7.25 – 7.19 (m, 3H), 7.19 – 7.14 (m, 2H), 7.08 (d, *J* = 7.6 Hz, 2H), 6.70 (d, *J* = 7.2 Hz, 2H), 6.64 (d, *J* = 1.2 Hz, 1H), 6.04 (s, 1H), 5.92 (s, 1H), 4.79 (d, *J* = 16.0 Hz, 1H), 4.45 (d, *J* = 16.0 Hz, 1H), 1.35 (s, 9H). Analytical and spectral data were in agreement with the literature data.[36]

*4.6.11.tert-buty((R)-1-benzyl-6-methoxy-3-((S)-nitro(phenyl)methyl)-2-oxoindolin-3-yl)carbamate (**4k**).*

White solid, 53.6 mg, 97% yield, mp = 74-75 ℃, $[a]_D^{25}$ = 16 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 92%, dr = 93:8 [Chiralpak IA-3, hexane/i-PrOH = 80:20, 254 nm, 1 mL/min, Major- (t_{major} = 20.787 min, t_{minor} = 7.153 min), Minor- (t_{major} = 19.369 min, t_{minor} = 9.655)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (d, J = 8.4 Hz, 1H), 7.43 – 7.35 (m, 1H), 7.30 (d, J = 6.9 Hz, 1H), 7.24 – 7.12 (m, 5H), 7.08 (d, J = 8.1 Hz, 2H), 6.67 (d, J = 6.8 Hz, 2H), 6.60 (dd, J = 8.4, 2.3 Hz, 1H), 6.07 (s, 1H), 5.91 (s, 1H), 4.82 (d, J = 16.0 Hz, 1H), 4.42 (d, J = 16.4 Hz, 1H), 3.73 (s, 3H), 1.34 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.29, 161.50, 153.52, 145.21, 134.80, 130.48, 129.98, 128.64, 128.36, 128.01, 127.35, 126.80, 126.44, 116.43, 106.66, 97.64, 93.08, 81.01, 77.30, 77.04, 76.79, 63.65, 55.37, 53.45, 44.43, 31.59, 28.14, 22.66, 14.11. HRMS (ESI): calculated for $C_{30}H_{47}N_4O_3[M+H]^+$: 504.2129, found 504.2128.

*4.6.12.tert-butyl((R)-1-benzyl-7-chloro-3-((S)-nitro(phenyl)methyl)-2-oxoindolin-3-yl)carbamate (**4l**).*

White solid, 50.5 mg, 99% yield, mp = 74-75 ℃, $[a]_D^{25}$ = 12.8 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 93%, dr = 91:9 [Chiralpak IA-3, hexane/i-PrOH = 80:20, 254 nm, 1 mL/min, Major- (t_{major} = 16.840 min, t_{minor} =6.361 min), Minor- (t_{major} = 15.441 min, t_{minor} = 8.660)]. ^{1}H NMR (500 MHz, CDCl3) δ 7.46

– 7.40 (m, 2H), 7.29 – 7.27 (m, 1H), 7.25 – 7.21 (m, 2H), 7.17 – 7.14 (m, 3H), 7.10 – 7.06 (m, 1H), 7.03 (d, *J* = 7.7 Hz, 2H), 6.78 (s, 2H), 6.06 (s, 1H), 6.02 (s, 1H), 5.17 – 4.83 (m, 2H), 1.35 (s, 9H). Analytical and spectral data were in agreement with the literature data.[36]

*4.6.13.tert-butyl((R)-1-benzyl-7-bromo-3-((S)-nitro(phenyl)methyl)-2-oxoindolin-3-yl)carbamate (**4m**).*

White solid, 54.3 mg, 98% yield, mp = 76-77 ℃, $[a]_D^{25}$ = 16.4 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 95%, dr = 96:4 [Chiralpak IC-3, hexane/*i*-PrOH = 80:20, 254 nm, 1 mL/min, Major- (t_{major} = 11.115 min, t_{minor} = 9.713 min), Minor- (t_{major} = 20.131 min, t_{minor} = 22.413)]. ^{1}H NMR (300 MHz, $CDCl_3$)) δ 7.49 – 7.39 (m, 3H), 7.31 – 7.26 (m, 1H), 7.25 – 7.21 (m, 1H), 7.18 – 7.10 (m, 3H), 7.06 – 6.97 (m, 3H), 6.79 – 6.69 (m, 2H), 6.03 (s, 1H), 6.00 (s, 1H), 5.09 (d, *J* = 16.7 Hz, 1H), 4.98 (d, *J* = 16.7 Hz, 1H), 1.35 (s, 9H). Analytical and spectral data were in agreement with the literature data.[36]

*4.6.14.tert-butyl((R)-1-benzyl-7-methyl-3-((S)-nitro(phenyl)methyl)-2-oxoindolin-3-yl)carbamate (**4n**).*

White solid, 43.9 mg, 90% yield, mp = 71-72 ℃, $[a]_D^{25}$ = 29.6 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 94%, dr = 92:8 [Chiralpak AD-H, hexane/*i*-PrOH = 80:20, 254 nm, 1 mL/min, Major - (t_{major} = 33.219 min, t_{minor} = 8.496 min), Minor - (t_{major} = 36.065 min, t_{minor} = 39.560)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 – 7.40 (m, 1H), 7.37 – 7.26 (m, 2H), 7.23 (d, *J* = 7.6 Hz, 1H), 7.18 – 7.11 (m, 3H), 7.08 – 7.01 (m, 4H), 6.67 (d, *J* = 3.8 Hz, 2H), 6.08 (s, 1H), 6.04 (s, 1H), 4.94 – 4.74 (m, 2H), 2.05 (d, *J* = 2.8 Hz, 4H), 1.35 (s, 9H). Analytical and spectral data were in agreement with the literature data.[36]

*4.6.15.tert-butyl(R)-1-benzyl-3-((S)-nitro(phenyl)methyl)-2-oxo-7-(trifluoromethyl)indolin-3-yl)car-bamate (**4o**).*

White solid, 52.7 mg, 98% yield, mp = 52-53 ℃, $[a]_D^{25}$ = 24.4 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 92%, dr = 92:8 [Chiralpak IA-3, hexane/*i*-PrOH = 80:20, 254 nm, 1 mL/min, Major- (t_{major} = 11.172 min, t_{minor} = 5.048 min), Minor- (t_{major} = 10.039 min, t_{minor} = 6.275)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (dd, *J* = 7.8, 4.2 Hz, 2H), 7.47 – 7.40 (m, 1H), 7.28 (d, *J* = 2.4 Hz, 1H), 7.25 – 7.21 (m, 2H), 7.16 – 7.11 (m, 3H), 6.96 (dd, *J* = 8.3, 1.1 Hz, 2H), 6.79 (s, 1H), 6.05 (s, 1H), 5.98 (s, 1H), 4.85 – 4.66 (m, 2H), 1.35 (s, 9H). Analytical and spectral data were in agreement with the literature data.[36]

*4.6.16.tert-butyl((R)-1-benzyl-3-((S)-(4-chlorophenyl)(nitro)methyl)-2-oxoindolin-3-yl)caramate (**4p**).*

White solid, 50.6 mg, 99% yield, mp = 74-75 ℃, $[a]_D^{25}$ = 46 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 91%, dr = 91:8 [Chiralpak IA-3, hexane/*i*-PrOH = 80:20, 254 nm, 1 mL/min, Major- (t_{major} = 23.641 min, t_{minor} = 6.568 min), Minor- (t_{major} = 21.613 min, t_{minor} = 11.171)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 (d, *J* = 6.4 Hz, 1H), 7.30 – 7.26 (m, 1H), 7.25 – 7.20 (m, 3H), 7.16 – 7.10 (m, 3H), 6.94 (d, *J* = 8.6 Hz, 2H), 6.72 (dd, *J* = 6.4, 2.7 Hz, 2H), 6.56 (d, *J* = 7.8 Hz, 1H), 6.06 (s, 1H), 5.98 (s, 1H), 4.92 (d, *J* = 15.8 Hz, 1H), 4.41 (d, *J* = 15.8 Hz, 1H), 1.32 (s, 9H). Analytical and spectral data were in agreement with the literature data.[36]

*4.6.17.tert-butyl((R)-1-benzyl-3-((S)-(4-bromophenyl)(nitro)methyl)-2-oxoindolin-3-yl)carbamate (**4q**).*

White solid, 55 mg, 99% yield, mp = 66-67 ℃, $[a]_D^{25}$ = 32.4 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 93%, dr = 95:4 [Chiralpak IA-3, hexane/*i*-PrOH = 80:20, 254 nm, 1 mL/min, Major- (t_{major} = 24.683 min, t_{minor} = 6.616 min), Minor- (t_{major} = 22.483 min, t_{minor} = 10.684)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 – 7.50 (m, 1H), 7.32 – 7.29 (m, 1H), 7.29 – 7.26 (m, 2H), 7.25 – 7.20 (m, 3H), 7.14 (d, *J* = 7.6, 1.0 Hz, 1H), 6.91 – 6.84 (m, 2H), 6.72 (dd, *J* = 6.4, 2.9 Hz, 2H), 6.56 (d, *J* = 7.8 Hz, 1H), 6.05 (s, 1H), 5.96 (s, 1H), 4.93 (d, *J* = 15.8 Hz, 1H), 4.41 (d, *J* = 15.8 Hz, 1H), 1.32 (s, 9H). Analytical and spectral data were in agreement with the literature data.[36]

*4.6.18.tert-butyl((R)-1-benzyl-3-((S)-(4-methoxyphenyl)(nitro)meth-yl)-2-oxoindolin-3-yl)carbamate (**4r**).*

White solid, 49.7 mg, 99% yield, mp = 52-53 ℃, $[a]_D^{25}$ = 20.8 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 94%, dr = 92:8 [Chiralpak IA-3, hexane/*i*-PrOH = 80:20, 254 nm, 1 mL/min, Major- (t_{major} = 18.630 min, t_{minor} = 7.132 min), Minor- (t_{major} = 20.159 min, t_{minor} = 11.272)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 – 7.47 (m, 1H), 7.31 – 7.27 (m, 1H), 7.25 – 7.21 (m, 1H), 7.20 – 7.14 (m, 2H), 7.13 – 7.08 (m, 2H), 6.94 – 6.88 (m, 2H), 6.70 – 6.66 (m, 2H), 6.64 (s, 2H), 6.51 (d, *J* = 7.7 Hz, 1H), 6.01 (s, 1H), 5.97 (d, *J* = 10.3 Hz, 1H), 4.95 (d, *J* = 16.0 Hz, 1H), 4.39 (d, *J* = 15.6 Hz, 1H), 3.76 (s, 3H), 1.31 (s, 9H). Analytical and spectral data were in agreement with the literature data.[36]

*4.6.19.tert-butyl((R)-1-benzyl-3-((S)-(3methoxyphenyl)(nitro) methyl) - 2- oxoindolin-3-yl) carbamate (**4s**).*

White solid, 48.5 mg, 97% yield, mp = 61-62 ℃, $[a]_D^{25}$ = 18 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 90%, dr = 92:8 [Chiralpak IA-3, hexane/*i*-PrOH = 80:20, 254 nm, 1 mL/min, Major- (t_{major} = 15.569 min, t_{minor} = 7.446 min), Minor- (t_{major} = 16.730 min, t_{minor} = 8.528)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 – 7.35 (m, 1H), 7.35 – 7.26 (m, 1H), 7.21 (d, *J* = 8.1 Hz, 1H), 7.18 – 7.05 (m, 5H), 6.76 (dd, *J* = 8.6, 2.6 Hz, 1H), 6.70 (s, 1H), 6.68 (s, 1H), 6.37 (d, *J* = 8.6 Hz, 1H), 6.06 (s, 1H), 5.95 (s, 1H), 4.79 (d, *J* = 15.9 Hz, 1H), 4.44 (d, *J* = 16.0 Hz, 1H), 3.80 (s, 3H), 1.34 (s, 9H). Analytical and spectral data were in agreement with the literature data.[36]

*4.6.20.tert-butyl((R)-1-benzyl-3-((S)-(2-methoxyphenyl) (nitro)methyl) -2-oxoindolin-3-yl)carbamate (**4t**).*

White solid, 47.4 mg, 95% yield, mp = 64-65 ℃, $[a]_D^{25}$ = 57.6 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 95%, dr = 79:21 [Chiralpak IA-3, hexane/*i*-PrOH = 80:20, 254 nm, 1 mL/min, Major- (t_{major} = 11.137 min, t_{minor} = 7.631 min), Minor- (t_{major} = 8.870 min, t_{minor} = 8.276)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 – 7.36 (m, 1H), 7.35 – 7.30 (m, 2H), 7.23 – 7.19 (m, 1H), 7.19 – 7.12 (m, 3H), 7.10 – 7.02 (m, 1H), 6.97 – 6.84 (m, 2H), 6.83 – 6.75 (m, 3H), 6.72 (s, 1H), 6.66 (d, *J* = 7.1 Hz, 1H), 6.53 (d, *J* = 7.8 Hz, 1H), 6.32 (s, 1H), 4.94 (d, *J* = 16.0 Hz, 1H), 4.45 (d, *J* = 15.8 Hz, 1H), 3.72 (s, 3H), 1.29 (s, 9H). Analytical and spectral data were in agreement with the literature data.[36]

*4.6.21.tert-butyl((R)-1-benzyl-3-((S)-naphthalen-2-yl(nitro)methyl)-2-oxoindolin-3-yl)carbamate (**4u**).*

White solid, 52.2 mg, 99% yield, mp = 82-83 ℃, $[a]_D^{25}$ = 80 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 83%, dr = 92:8 [Chiralpak IA-3, hexane/*i*-PrOH = 80:20, 254 nm, 1 mL/min, Major- (t_{major} = 25.432 min, t_{minor} = 7.215 min), Minor- (t_{major} = 20.976 min, t_{minor} = 20.277)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83

– 7.76 (m, 1H), 7.70 – 7.66 (m, 1H), 7.66 – 7.62 (m, 1H), 7.60 (dd, *J* = 8.5, 2.8 Hz, 2H), 7.57 – 7.51 (m, 2H), 7.51 – 7.44 (m, 1H), 7.29 – 7.26 (m, 1H), 7.22 (dd, *J* = 10.8, 1.3 Hz, 1H), 7.16 (dd, *J* = 7.6, 1.0 Hz, 1H), 7.04 – 6.88 (m, 3H), 6.69 – 6.55 (m, 2H), 6.45 (d, *J* = 7.8 Hz, 1H), 6.36 (d, *J* = 7.4 Hz, 2H), 6.25 (s, 1H), 6.05 (s, 1H), 4.89 (d, *J* = 16.0 Hz, 1H), 4.30 (d, *J* = 15.9 Hz, 1H), 1.32 (s, 9H). Analytical and spectral data were in agreement with the literature data.[36]

4.7. Characterization data of products ***6a-6p***

*4.7.1 tert-butyl (1S,2R)-2-nitro-1,2-diphenylethyl carbamate (**6a**).*

White solid, 33.1 mg, 97% yield, mp = 200-202 ℃, $[a]_D^{25}$ = 80 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 98%, dr >99:1 [Chiralpak IA-3, hexane/*i*-PrOH = 90:10, 210 nm, 1.0 mL/min, Major- (t_{major} = 18.14 min., t_{minor} = 15.99 min), Minor- (t_{major} = 25.92 min, t_{minor} = 12.52 min)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 – 7.52 (m, 2H), 7.49 – 7.40 (m, 3H), 7.37 – 7.29 (m, 3H), 7.28 (d, *J* = 1.9 Hz, 1H), 5.82 – 5.58 (m, 2H), 4.84 (s, 1H), 1.26 (s, 9H). Analytical and spectral data were in agreement with the literature data.[44]

*4.7.2 tert-butyl(1S,2R)-1-(2-fluorophenyl)-2-nitro-2-phenylethyl carbamate (**6b**).*

White solid, 35.1 mg, 97% yield, mp = 181-183 ℃, $[a]_D^{25}$ = 54.4 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 91%, dr = 95:5 [Chiralpak IC-3, hexane/EtOH = 16:1, 210 nm, 0.5 mL/min, Major- (t_{major} = 12.17 min, t_{minor} = 13.13 min), Minor- (t_{major} = 17.92 min, t_{minor} = 15.15 min)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 – 7.59 (m, 2H), 7.46 – 7.39 (m, 4H), 7.38 – 7.29 (m, 1H), 7.17 – 7.13 (m, 1H), 7.13 – 7.07 (m, 1H), 5.91 – 5.82 (m, 2H), 5.06 (s, 1H), 1.22 (s, 9H). Analytical and spectral data were in agreement with the literature data.[44]

4.7.3 tert-butyl (1S,2R)-1-(2-methoxyphenyl)-2-nitro-2-phenylethyl carbamate ***(6c).***

White solid, 33.1 mg, 89% yield, mp = 185-187 ℃, $[a]_D^{25}$ = 27.2 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 92%, dr = 96:4 [Chiralpak IA-3, hexane/*i*-PrOH = 90:10, 210 nm, 1.0 mL/min, Major- (t_{major} = 8.99 min, t_{minor} = 28.42 min), Minor- (t_{major} = 10.50 min, t_{minor} = 18.63 min)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (s, 2H), 7.40 (s, 3H), 7.35 – 7.28 (m, 2H), 7.00 – 6.89 (m, 2H), 6.04 – 5.94 (m, 1H), 5.87 – 5.75 (m, 1H), 5.58 – 5.47 (m, 1H), 3.98 (s, 3H), 1.20 (s, 9H). Analytical and spectral data were in agreement with the literature data.[43]

*4.7.4.tert-butyl (1S,2R)-1-(3-chlorophenyl)-2-nitro-2-phenylethyl carbamate (**6d**)*

White solid, 34.2 mg, 91% yield, mp = 192-194 ℃, $[a]_D^{25}$ = 18.7 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 97%, dr = 98:2 [Chiralpak IA-3, hexane/*i*-PrOH = 90:10, 210 nm, 1.0 mL/min, Major- (t_{major} = 12.16 min, t_{minor} = 13.43 min), Minor- (t_{major} = 15.89 min, t_{minor} = 9.78 min)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (dd, *J* = 7.4, 1.9 Hz, 2H), 7.48 – 7.38 (m, 3H), 7.37 – 7.28 (m, 3H), 7.26 – 7.19 (m, 1H), 5.81 – 5.54 (m, 2H), 4.85 (s, 1H), 1.26 (s, 9H). Analytical and spectral data were in agreement with the literature data.[43]

*4.7.8.tert-butyl (1S,2R)-1-(4-fluorophenyl)-2-nitro-2-phenylethyl carbamate (**6e**).*

White solid, 33.9 mg, 94% yield, mp = 191-193 ℃, $[a]_D^{25}$ = 22 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 98%, dr >99:1 [Chiralpak IA-3, hexane/EtOH = 95:5, 230 nm, 1.0 mL/min, Major- (t_{major} =14.48min, t_{minor} =13.90 min), Minor- (t_{major} = 16.82 min, t_{minor} = 26.62 min)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 – 7.51 (m, 2H), 7.46 – 7.39 (m, 3H), 7.34 (dd, *J* = 8.6, 5.2 Hz, 2H), 7.10 – 7.00 (m, 2H), 5.83 – 5.53 (m, 2H), 4.89 (s, 1H), 1.26 (s, 9H). Analytical and spectral data were in agreement with the literature data.[45]

*4.7.9. tert-butyl (1S,2R)-1-(4-chlorophenyl)-2-nitro-2-phenylethyl carbamate (**6f**).*

White solid, 34.3 mg, 90% yield, mp = 196-197 ℃, $[a]_D^{25}$ = 21.2 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 98%, dr >99:1 [Chiralpak AD-H, hexane/*i*-PrOH = 90:10, 214 nm, 1.0 mL/min, Major- (t_{major} = 21.66 min, t_{minor} = 34.58 min), Minor- (t_{major} = 32.26 min., t_{minor} = 23.78 min)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 7.2, 2.3 Hz, 2H), 7.47 – 7.40 (m, 3H), 7.39 – 7.31 (m, 4H), 5.83 – 5.61 (m, 2H), 4.77 (d, *J* = 8.9 Hz, 1H), 1.25 (s, 9H). Analytical and spectral data were in agreement with the literature data.[45]

*4.7.10. tert-butyl (1S,2R)-2-nitro-2-phenyl-1-(p-tolyl)ethyl carbamate (**6g**).*

White solid, 25.7 mg, 72% yield, mp = 190-192 ℃, $[a]_D^{25}$ = 32.8 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 95%, dr = 97:3 [Chiralpak AD-H, hexane/*i*-PrOH = 90:10, 210 nm, 1.0 mL/min, Major- (t_{major} = 16.36 min, t_{minor} = 14.88 min), Minor- (t_{major} = 25.02 min, t_{minor} = 11.38 min)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62 – 7.54 (m, 2H), 7.46 – 7.36 (m, 3H), 7.26 (d, *J* = 0.5 Hz, 1H), 7.22 (s, 1H), 7.17 (d, *J* = 8.1 Hz, 2H), 5.80 – 5.58 (m, 2H), 4.76 (d, *J* = 9.1 Hz, 1H), 2.34 (s, 3H), 1.24 (s, 9H). Analytical and spectral data were in agreement with the literature data.[44]

*4.7.11.tert-butyl (1S,2R)-1-(4-methoxyphenyl)-2-nitro-2-phenylethyl carbamate (**6h**).*

White solid, 34.6 mg, 93% yield, mp = 191-193 ℃, $[a]_D^{25}$ = 25.6 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 97%, dr = 98:2 [Chiralpak IA-3, hexane/*i*-PrOH = 90:10, 210 nm, 1.0 mL/min, Major- (t_{major} = 20.38 min, t_{minor} = 65.56 min), Minor- (t_{major} = 36.25 min, t_{minor} = 22.29 min)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 – 7.54 (m, 2H), 7.46 – 7.38 (m, 3H), 7.32 – 7.26 (m, 1H), 6.97 – 6.84 (m, 3H), 5.72 (dd, *J* = 23.3, 9.5 Hz, 2H), 4.75 (d, *J* = 9.0 Hz, 1H), 3.80 (s, 3H), 1.25 (s, 9H). Analytical and spectral data were in agreement with the literature data.[44]

*4.7.12. tert-butyl (1S,2R)-2-nitro-2-phenyl-1-(4(trifluoromethyl)-phenyl) ethyl]carbamate (**6i**).*

White solid, 36.9 mg, 90% yield, mp = 191-193 ℃, $[a]_D^{25}$ = 31.2 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 97%, dr = 95:5 [Chiralpak IA-3, hexane/*i*-PrOH = 95:5, 210 nm, 1.0 mL/min, Major- (t_{major} = 37.70 min, t_{minor} = 24.99 min), Minor - (t_{major} = 44.09 min., t_{minor} = 33.22 min)]. ^{1}H NMR (300 MHz, $CDCl_3$)δ 7.63 (d, *J* = 8.2 Hz, 2H), 7.58 – 7.53 (m, 2H), 7.52 – 7.46 (m, 2H), 7.46 – 7.40 (m, 3H), 5.86 – 5.65 (m, 2H), 4.82 (d, *J* = 8.9 Hz, 1H), 1.26 (s, 9H). Analytical and spectral data were in agreement with the literature data.[45]

*4.7.13. tert-butyl (1S,2R)-1-(furan-2-yl)-2-nitro-2-phenylethyl carba-mate (**6j**).*

White solid, 31.2 mg, 94% yield, mp = 163-165 ℃, $[a]_D^{25}$ = 89.2 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee =93%, dr = 96:4 [Chiralpak IC-3, hexane/*i*-PrOH = 98:2, 210 nm, 1.0 mL/min, Major- (t_{major} = 22.60 min, t_{minor} = 35.46 min), Minor- (t_{major} = 47.18 min, t_{minor} = 41.18 min)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 – 7.49 (m, 1H), 7.46 – 7.34 (m, 3H), 6.34 (s, 1H), 5.82 (s, 1H), 4.87 (s, 1H), 1.26 (s, 9H). Analytical and spectral data were in agreement with the literature data.[44]

*4.7.14. tert-butyl ((1R,2R)-2-nitro-2-phenyl-1-(thiophen-2-yl)ethyl)carbamate (**6k**)*

White solid, 34.7 mg, 99% yield, mp = 165-166 ℃, $[a]_D^{25}$ = 42.5 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee =97%, dr = 98:2 [Chiralpak IC-3, hexane/EtOH = 16:1 , 210 nm, 0.5 mL/min, Major- (t_{major} = 14.380 min, t_{minor} = 16.068 min), Minor- (t_{major} = 21.715 min, t_{minor} = 19.196 min)]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 – 7.51 (m, 2H), 7.45 – 7.37 (m, 3H), 7.28 (dd, *J* = 5.1, 0.9 Hz, 1H), 7.06 (d, *J* = 3.4 Hz, 1H), 6.96 (dd, *J* = 5.0, 3.6 Hz, 1H), 6.00 – 5.91 (m, 1H), 5.86 (d, *J* = 9.4 Hz, 1H), 4.80 (d, *J* = 8.3 Hz, 1H), 1.28 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.06, 140.40, 131.47, 130.26, 128.87, 128.63, 127.08, 126.42, 125.80, 94.55, 80.62, 52.62, 28.07. HRMS (ESI): calculated for $C_{17}H_{20}N_2O_4S$ $[M+Na]^+$: 371.1041, found 371.1039.Analytical and spectral data were in agreement with the literature data.[44]

*4.7.14. tert-butyl (1S,2R)-2-(2-fluorophenyl)-2-nitro-1-phenylethyl carbamate (**6l**).*

White solid, 30.6 mg, 85% yield, mp = 175-176 ℃, $[a]_D^{25}$ = 43.2 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 99%, dr = 94:6 [Chiralpak IA-3, hexane/*i*-PrOH = 90:10, 210 nm, 0.5 mL/min, Major- (t_{major} = 34.79 min, t_{minor} = 18.33 min), Minor- (t_{major} =28.33min, t_{minor} =20.26min)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 – 7.75 (m, 1H), 7.37 (s, 6H), 7.22 (d, *J* = 7.5 Hz, 1H), 7.16 – 7.08 (m, 1H), 6.21 (d, *J* = 10.4 Hz, 1H), 5.72 (s, 1H), 4.90 (d, *J* = 9.2 Hz, 1H), 1.23 (s, 9H). Analytical and spectral data were in agreement with the literature data.[44]

*4.7.75. tert-butyl (1S,2R)-2-(3-methoxyphenyl)-2-nitro-1-phenylethyl carbamate (**6m**).*

White solid, 32.5mg, 87% yield, mp = 179-181 ℃, $[a]_D^{25}$ = 29.2 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 97%, dr = 93:7 [Chiralpak IA-3, hexane/*i*-PrOH = 90:10, 210 nm, Major- (t_{major} = 42.36 min, t_{minor} = 21.51 min), Minor- (t_{major} = 23.19 min, t_{minor} = 17.15 min)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 – 7.32 (m, 6H), 7.32 – 7.28 (m, 1H), 7.15 – 7.09 (m, 2H), 7.00 – 6.93 (m, 1H), 5.79 – 5.63 (m, 2H), 4.77 (d, *J* = 9.0 Hz, 1H), 3.82 (s, 3H), 1.27 (s, 9H). Analytical and spectral data were in agreement with the literature data.[44]

*4.7.16 tert-butyl (1S,2R)-2-(4-bromophenyl)-2-nitro-1-phenylethyl) carbamate (**6n**).*

White solid, 38.8mg, 92% yield, mp = 169-171 ℃, $[a]_D^{25}$ = 39.6 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 95%, dr = 98:2 [Chiralpak IA-3, hexane/*i*-PrOH = 90:10, 210 nm, 1.0 mL/min, Major- (t_{major} = 16.23 min, t_{minor} = 20.65 min), Minor- (t_{major} = 43.47 min, t_{minor} = 13.22 min)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (dd, J = 27.3, 7.9 Hz, 4H), 7.35 (s, 5H), 5.69 (d, J = 32.1 Hz, 2H), 4.85 (s, 1H), 1.27 (s, 9H). Analytical and spectral data were in agreement with the literature data.[44]

*4.7.17 tert-butyl (1S,2R)-2-nitro-1-phenyl-2-(p-tolyl)ethyl carbamate (**6o**).*

White solid, 33.2mg, 93% yield, mp = 184-186 ℃, $[a]_D^{25}$ = 37.2 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 98%, dr = 99:1 [Chiralpak IA-3, hexane/*i*-PrOH = 90:10, 210 nm, 1.0 mL/min, Major- (t_{major} = 17.38 min, t_{minor} = 15.31 min), Minor- (t_{major} = 26.97 min, t_{minor} = 11.73 min)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 (d, *J* = 8.1 Hz, 2H), 7.27 (s, 4H), 7.20 – 7.09 (m, 2H), 5.63 (t, *J* = 15.2 Hz, 2H), 4.81 (s, 1H), 2.28 (d, *J* = 5.8 Hz, 3H), 1.17 (d, *J* = 6.0 Hz, 9H). Analytical and spectral data were in agreement with the literature data.[44]

*4.7.18. tert-butyl (1S,2R)-2-(4-methoxyphenyl)-2-nitro-1-phenylethyl carbamate (**6p**).*

White solid, 29.7 mg, 80% yield, mp = 181-182 ℃, $[a]_D^{25}$ = 30.5 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 96%, dr = 98:2 [Chiralpak IA-3, hexane/*i*-PrOH = 90:10, 210nm, 1.0 mL/min, Major- (t_{major} = 23.73 min, t_{minor} = 19.25 min), Minor- (t_{major} = 39.97 min, t_{minor} = 15.59 min)]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 – 7.46 (m, 2H), 7.39 – 7.29 (m, 5H), 6.95 – 6.88 (m, 2H), 5.76 – 5.58 (m, 2H), 4.81 – 4.70 (m, 1H), 3.82 (s, 3H), 1.29 – 1.24 (m, 9H). Analytical and spectral data were in agreement with the literature data.[44]

*4.7.19. tert-butyl (1S,2R)-2-(naphthalen-2-yl)-2-nitro-1-phenylethyl carbamate (**6q**).*

White solid, 38.1 mg, 97% yield, mp = 183-185 ℃, $[a]_D^{25}$ = 25.6 (c = 0.5, $CHCl_3$). Enantiomeric excess and diastereomer ratio were established by HPLC analysis, ee = 95%, dr = 97:3 [Chiralpak IA-3, hexane/*i*-PrOH = 90:10, 210 nm, 1.0 mL/min, Major- (t_{major} = 31.65 min, t_{minor} = 26.50 min),Minor- (t_{major} = 36.84 min., t_{minor} =15.03 min)]. ^{1}H NMR (300 MHz, $CDCl_{3[}$) δ 8.03 (s, 1H), 7.95 – 7.82 (m, 3H), 7.69 (d, *J* = 8.7 Hz, 1H), 7.58 – 7.50 (m, 2H), 7.37 (d, *J* = 6.8 Hz, 5H), 5.97 (d, *J* = 9.9 Hz, 1H), 5.85 – 5.69 (m, 1H), 4.80 (d, *J* = 8.5 Hz, 1H), 1.16 (s, 9H). Analytical and spectral data were in agreement with the literature data.[44]

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1. A series of bifunctional APT catalysts derived from *L*-*tert*-Leucine
2. excellent yields, high diastereo- and enantioselectivities (ee 83-95%; dr 79:21-97:3).
3. this catalyst can also catalyze aza-Henry reaction with N-Boc amidosulfones.