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Asymmetric conjugate addition of carbonyl compounds to nitroalkenes catalyzed by chiral bifunctional thioureas

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ABSTRACT

Readily available chiral thioureas derived from cyclohexane-1,2-diamine were prepared and found to be highly effective organocatalysts for the conjugate addition of aldehydes and ketones to nitroalkenes. Excellent enantioselectivities and yields were obtained for a variety of aryl and heteroaryl nitroalkenes. The base additives are essential for good yields and excellent enantioselectivities in this transformation. Based on new experimental evidence, a modified catalytic mechanism was proposed to rationalize the important role of the base additives.

1. Introduction

In recent years, asymmetric organocatalysis has emerged as a powerful tool for the synthesis of valuable chiral compounds.[1] Organocatalytic conjugate additions of aldehydes and ketones to nitroalkenes are an important strategy for asymmetric carbon–carbon bond formation.[2,3] The resulting products are readily converted to chiral γ-amino acids and to other useful compounds. Chiral primary amines, secondary amines and bifunctional organocatalysts have been used with great success.[4] Jacobsen's thiourea-primary amine organocatalysts have been reported to be highly efficient for the transformation.[3p,q] These catalysts consist of chiral cyclohexane-1,2-diamine and *tert*-leucine derivatives. The match of the multiple stereogenic centres in the catalysts is crucial for excellent enantioselectivity. Unfortunately these catalysts require tedious synthesis and are not readily available. Recently we found that chiral bifunctional sulfamide–primary amines are highly efficient catalysts for the conjugate addition of aldehydes to nitroalkenes.[5] During the study we also found that the ability for enantioselective induction is mainly governed by the cyclohexane-1,2-diamine motif of the catalysts. Therefore, we presume that structurally simplified chiral thiourea–primary amines based on cyclohexane-1,2-diamine are efficient catalysts for the reaction. Herein we report on the synthesis and application of these thiourea–primary amines in the asymmetric conjugate addition of aldehydes and ketones to nitroalkenes. The present research results provide an interesting comparison with the results obtained using Jacobsen's catalysts.

2. Results and discussion

Chiral organocatalysts **1a**–**1g** were prepared via simple procedures (Scheme 1). Compound **1b**, which has a strongly electron-withdrawing 3,5-ditrifluoromethylaryl group, was designed to investigate the effect of N-H acidity on catalytic activity. For comparison, compound **1f**, which is free of the thiourea group, and secondary amine **1g** were also prepared.

In a previous study of chiral sulfamide-primary amine catalysts, we found that the conjugate addition of aldehydes to nitroalkenes is very slow in the absence of base additives.[5] Thus, catalysts **1a**–**1g** were examined for the conjugate addition of isobutyraldehyde to nitrostyrene in the presence of DMAP (20 mol %). The results are summarized in Table 1. The reactions were monitored by GC to obtain chromatographic yields. The isolated yields of the product were obtained by flash column chromatography after the reaction. It is interesting to note that the GC yields were generally lower than the corresponding isolated yields in most cases (Table 1). We supposed that the intermediates from the product **4a** and the catalysts were formed; the intermediates were decomposed during column chromatography and an additional amount of product was released.

Catalyst **1a** provided the product **4a** with excellent yield and enantioselectivity (Table 1, entry 1).[6] Decreasing the reaction temperature did not improve enantioselectivity furthermore, but resulted in lower yields (Table 1, entry 2). Catalyst **1b** provided almost the same results as **1a** (Table 1, entry 3). The acidity of the N–H of the thiourea group seems to have a small effect on the catalytic activity and enantioselectivity in the reaction. In many other reactions with thiourea catalysts, the acidity of the N–H is crucial for the catalytic activity.[7] The enantioselective induction of the catalysts was dominated by the chiral cyclohexane-1,2-diamine motif. The additional stereogenic centre in

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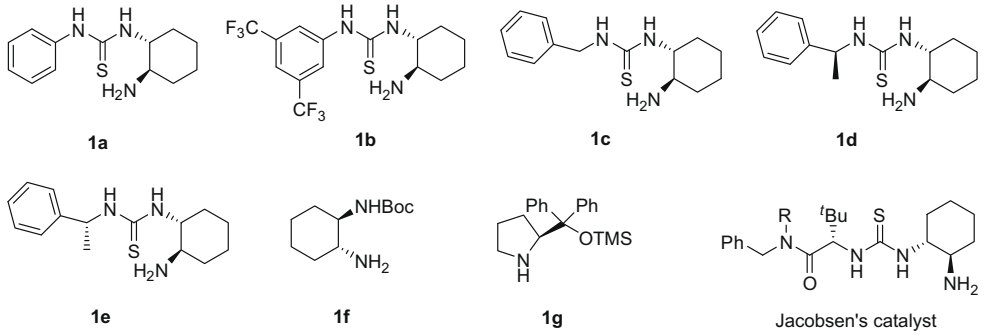
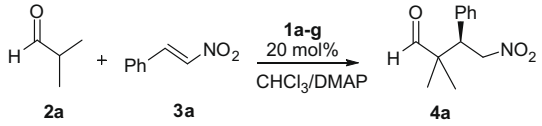


Scheme 1. Chiral organocatalysts **1a**–**1g** and Jacobsen's catalyst.

catalysts **1d** and **1e** did not have an obvious effect on the enantioselectivity (Table 1, entries 5 and 6). Catalyst **1f** afforded good enantioselectivity, however the reaction was significantly slower and gave **4a** in low yield (Table 1, entry 7). The double H-bond activation by the thiourea motif seems to be important for good catalytic activity. Prolinol silyl ether **1g** provided almost racemic **4a** in low yield (Table 1, entry 8). In the previous study, **1g** was reported to provide good enantioselectivity for the reaction in the presence of acid additives.[8] This emphasizes the importance of the match of the catalysts with the additives.

Table 1
Conjugate addition of isobutyraldehyde to *trans*-β-nitrostyrene catalyzed by **1a**–**1g**[a]



2a **3a** **4a**

Entry	Cat.	Time (h)	GC yield (%)	Isolated yield (%)	ee[b,c] (%)
1	**1a**	2	88	92	98
2[d]	**1a**	8	64	78	98
3	**1b**	2	88	92	97
4	**1c**	2	81	93	98
5	**1d**	5	69	67	98
6	**1e**	5	73	76	98
7	**1f**	26	49	52	83
8	**1g**	26	41	60	4

[a] The reactions were carried out with **1a**–**1g** (0.04 mmol), **2a** (50 μL, 0.55 mmol), **3a** (0.2 mmol) and DMAP (4.8 mg, 0.04 mmol), in $CHCl_3$ (0.3 mL) at room temperature.
[b] Ee values were determined by HPLC with a Diacel chiralpak-AD column.
[c] The absolute configuration of **4a** was determined as (*R*) by comparing the specific rotation with reported data.
[d] The reaction was carried out at 0 °C.

Catalyst **1a** was selected for further optimization. The results of the solvent screening are listed in Table 2. Although excellent enantioselectivities were obtained in most solvents tested, the reaction yields were highly variable. Acetone could also be used as the reaction solvent, and no adduct from acetone and nitrostyrene was observed (Table 2, entry 8). MeOH and DMF had a detrimental effect on the yield and enantioselectivity (Table 2, entries 10 and 11). It is interesting to note that water was found to be a suitable solvent for the reaction. Excellent enantioselectivity and good yield were achieved (Table 2, entry 12). Catalyst **1a** and nitrostyrene are almost insoluble in water, and tiny 'oil' droplets floating on water were formed during the reaction. The 'on water' effect was highly possible in this case.[9] Finally chloroform was identified as the best solvent concerning excellent enantioselectivity, good yield and short reaction time (Table 2, entry 5).

The influence of additives was studied further and the results are summarized in Table 3. The reaction provided excellent enantioselectivity in the absence of any additives, however the yield was rather low (Table 3, entry 1). Jacobsen et al. reported that the conjugate addition of aldehydes to nitroalkenes was achieved with excellent yields and enantioselectivities, using the thiourea–primary amines as the catalysts and 500 mol % water as the additive.[3q] We examined the **1a**-catalyzed reaction under the reaction conditions used by Jacobsen et al., however no substantial improvement was observed concerning the yield and enantioselectivity (Table 3, entry 2). It should be noted that the structure of **1a** is highly similar with that of Jacobsen's catalysts. The great difference in the catalytic behaviours cannot be rationalized at

Table 2
Solvent screening for **1a**-catalyzed addition of isobutyraldehyde to *trans*-β-nitrostyrene[a]

Entry	Solvent	Yield[b] (%)	ee (%)
1	*n*-Hexane	42	95
2	Toluene	61	94
3	Et_2O	54	96
4	CH_2Cl_2	55	97
5[c]	$CHCl_3$	92	98
6	EtOAc	68	94
7	THF	54	91
8	Acetone	63	93
9	CH_3CN	75	92
10	Methanol	50	92
11	DMF	29	81
12[d]	H_2O	83	94

[a] The reactions were carried out with **1a** (0.04 mmol), **2a** (50 μL, 0.55 mmol), **3a** (0.2 mmol) and DMAP (4.8 mg, 0.04 mmol) in the solvent (0.3 mL) at room temperature for 6 h.
[b] Isolated yields.
[c] Reaction time was 2 h.
[d] Reaction time was 24 h.

Table 3
Effect of additives on the reaction[a]

Entry	Additive	Time (h)	Yield[b] (%)	ee (%)
1	—	24	35	97
2[c]	H_2O	24	31	98
3	PhCOOH	6	21	96
4	HOAc	6	10	96
5	DMAP	2	92	98
6	DABCO	3	88	97
7	Imidazole	3	71	97
8	TEA	3	75	96
9	DIPEA	3	86	97
10	Sparteine	3	31	96

[a] The reactions were carried out with **1a** (0.04 mmol), **2a** (50 μL, 0.55 mmol), **3a** (0.2 mmol) and additive (0.04 mmol) in chloroform (0.3 mL) at room temperature.
[b] Isolated yields.
[c] The reaction was carried out with **1a** (0.04 mmol), **2a** (50 μL, 0.55 mmol), **3a** (0.2 mmol) and water (18 mg, 1 mmol) in dichloromethane (0.3 mL) at room temperature.

the present stage. Benzoic acid and acetic acid showed the detrimental effect on the yield (Table 3, entries 3 and 4). Most of base additives gave excellent yields and enantioselectivities (Table 3, entries 5–9). DMAP was identified as the best additive (Table 3, entry 5). In the case of sparteine (Table 3, entry 10), a large amount of polymerized product of nitrostyrene was formed.[5]

Interesting results were obtained by monitoring the reaction with GC (Fig. 1). While benzoic acid was used as the additive, the reaction was almost stopped after 0.5 h and the conversion was not increased during the prolonged reaction time. However, in the presence of DMAP, the reaction proceeded until all the nitrostyrenes were consumed. The deactivation of the catalyst in the presence of acid additives was supposed to result in the observed low yield. LC–MS analysis of the reaction mixture showed a prominent peak at m/z 453 with DMAP as the additive, however a prominent peak at m/z 467 was observed with benzoic acid as the additive.

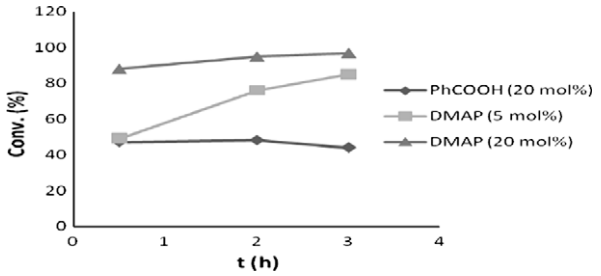
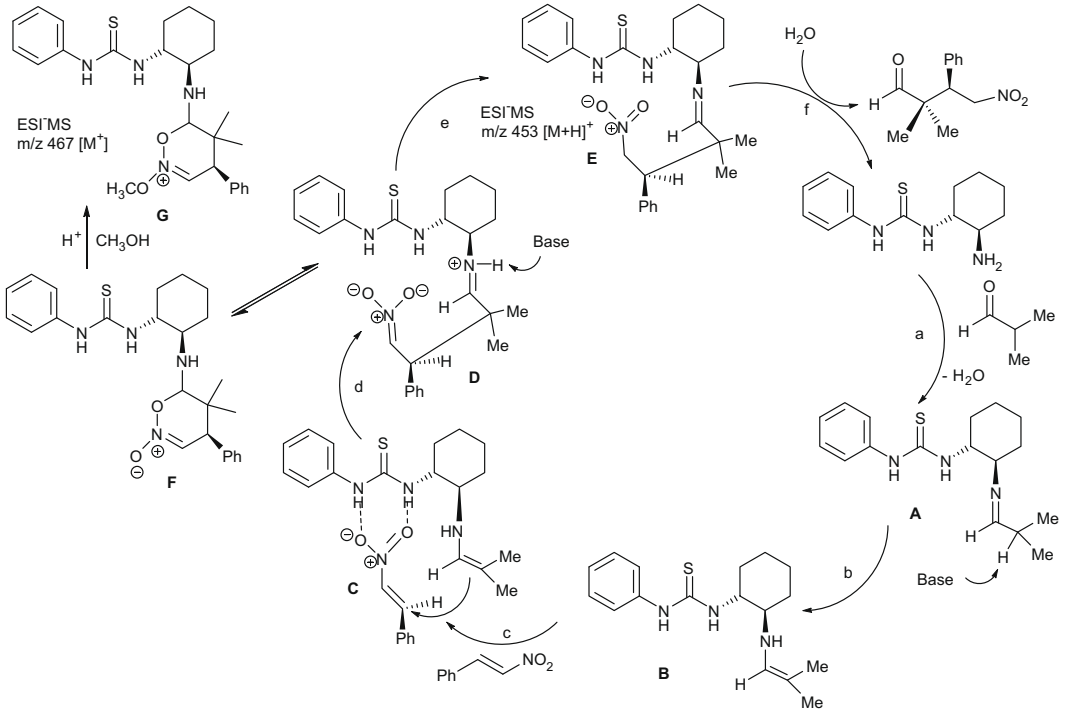


Figure 1. Conversion–reaction time curves in the presence of PhCOOH and DMAP.

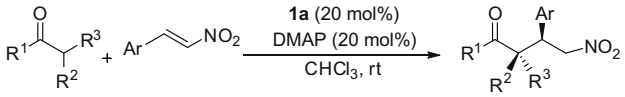
Based on the present experimental observation and previous suggestions, an improved catalytic mechanism was proposed (Scheme 2).[3q,5] Imine intermediate **A** is generated from catalyst **1a** and isobutyraldehyde. The tautomerization of **A** is promoted by the base additive and provides the enamine **B**. The formation of hydrogen bond between the nitro group and the thiourea group (intermediate **C**) activates nitrostyrene towards the attack of the enamine. The resulting intermediate **D** is transformed into **E** after the proton transfer. Intermediate **E** is hydrolyzed to give the product and regenerate the catalyst **1a**. The MS peak at m/z 453 corresponds to intermediate **E** ($M+H^+$). The intermediate **D** probably undertakes an intramolecular addition to give 1,2-oxazine-N-oxide (intermediates **F**).[3q,5,10] Then **F** is further converted to the intermediate **G** (m/z 467) in the presence of acid and methanol ($MeOH/H_2O$ is used as the eluting solvent for LC–MS analysis). The formation of intermediate **G** was further supported by mixing **4a**, **1a** and benzoic acid in $CDCl_3/CD_3OD$ and by analyzing the mixture with LC–MS. A prominent MS peak at m/z 470, corresponding to the replacement of CH_3O with CD_3O, was observed. The generation of intermediate **F** is proposed to result in the catalyst deactivation. The acid additives promote the transformation of **D** to **F**, however base additives promote the transformation of **D** to **E** by removing the proton from the iminium cation.

The application scope of **1a** was examined in the reaction of a range of aldehydes and ketones with β-aryl-nitroethenes. The results are summarized in Table 4. Excellent enantioselectivities and yields were achieved for the conjugate addition of isobutyraldehyde to various β-aryl-nitroethenes (Table 4, entries 1–10). The substitution of the electron-withdrawing group on the phenyl ring accelerated the reaction (Table 4, entry 6). 2-Furanyl-nitroethene and 2-thiophenyl-nitroethene afforded excellent yields and enantioselectivities (Table 4, entries 7 and 8). *trans*-β-Styryl-nitroethene gave the 1,4-addition product with excellent enantioselectivity, however in low yield (Table 4, entry 9). 1-Naphthyl-nitroethene also provided excellent enantioselectivity and yield. The conjugate addition of propionaldehyde and butyraldehyde to β-nitrostyrene provided two diastereoisomers (dr = 2/1) with moderate yields and excellent enantioselectivities (Table 4, entries 11 and 12). The conjugate addition of acetone afforded moderate yield and enantioselectivity (Table 4, entries 13). Low yield and enantioselectivity were obtained when cyclopentanone was used (Table 4, entry 14). The reaction of methoxyacetone occurred regioselectively



Scheme 2. Proposed catalytic mechanism.

Table 4
Conjugate addition of aldehydes and ketones to β-aryl-nitroethenes catalyzed by **1a**[a]



Entry	Aldehyde or ketone	Ar	Product	Time (h)	Yield[b] (%)	ee[c] (%)
1	$(CH_3)_2CHCHO$ **2a**	Ph **3a**	**4a**	2	92	98
2	$(CH_3)_2CHCHO$ **2a**	*p*-$CH_3OC_6H_5$ **3b**	**4b**	3	93	97
3	$(CH_3)_2CHCHO$ **2a**	*p*-$CH_3C_6H_5$ **3c**	**4c**	9	96	98
4	$(CH_3)_2CHCHO$ **2a**	*p*-ClC_6H_5 **3d**	**4d**	2.5	90	97
5	$(CH_3)_2CHCHO$ **2a**	*m*-ClC_6H_5 **3e**	**4e**	2	83	98
6	$(CH_3)_2CHCHO$ **2a**	*p*-$NO_2C_6H_5$ **3f**	**4f**	1	85	97
7	$(CH_3)_2CHCHO$ **2a**	2-Furanyl **3g**	**4g**	1	90	97
8	$(CH_3)_2CHCHO$ **2a**	2-Thiophenyl **3h**	**4h**	2	98	95
9	$(CH_3)_2CHCHO$ **2a**	PhCH=CH **3i**	**4i**	9	43	96
10	$(CH_3)_2CHCHO$ **2a**	1-Naphthyl **3j**	**4j**	5	96	95
11	CH_3CH_2CHO **2b**	Ph **3a**	**4k**	2.5	75	96/97 (2:1)[d]
12	$CH_3(CH_2)_2CHO$ **2c**	Ph **3a**	**4l**	6	50	95/96 (2:1)[d]
13	CH_3COCH_3 **2d**	Ph **3a**	**4m**	23	59	78
14	$(CH_2)_4CO$ **2e**	Ph **3a**	**4n**	45	27	54/52 (2:1)[d]
15	$CH_3OCH_2COCH_3$ **2f**	Ph **3a**	**4o**	22	80	41/62 (2:1)[d]

[a] The reactions were carried out with **1a** (0.04 mmol), **2a–f** (0.55 mmol), **3a–j** (0.2 mmol) and DMAP (0.04 mmol) in chloroform (0.3 mL) at room temperature.
[b] Isolated yields.
[c] Determined by chiral HPLC.
[d] The diastereoisomeric ratio in parentheses was determined by HPLC.

at the α-methoxymethylene side and provided the adduct in good yield, however with low enantioselectivity and diastereoselectivity (Table 4, entry 15).

3. Conclusion

In conclusion, we have found that readily available chiral thioureas derived from cyclohexane-1,2-diamine are highly effective organocatalysts for the conjugate addition of aldehydes to nitroalkenes. Excellent enantioselectivities and yields were obtained for a variety of aryl and heteroaryl nitroalkenes. The catalysts are also applicable for ketones, however in lower enantioselectivities and yields. The use of base additives in the transformation is essential for good yield and excellent enantioselectivity. This new experimental observation sheds light on the exact function of base additives.

4. Experimental

4.1. General method

^1H NMR and ^{13}C NMR spectra were recorded on Bruker AVANCE 400 spectrometer. Chemical shifts of protons are reported in parts per million downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($CHCl_3$: δ 7.26). Chemical shifts of carbon are referenced to the carbon resonances of the solvent ($CHCl_3$: δ 77.0 and CH_3OH: δ 46.0). Peaks are labelled as singlet (s), doublet (d), triplet (t), quartet (q) and multiplet (m). Optical rotations were measured on a Perkin Elmer digital polarimeter. Melting points were measured on a WRS-2A melting point apparatus and are uncorrected. The mass spectroscopic data were obtained at the Thermo DSQII and Agilent 6120 mass spectrometer. The high-resolution mass spectroscopic data were obtained at the Thermo MAT 95XP mass spectrometer. Infrared (IR) spectra were recorded on a Bruker Tensor 37 spectrophotometer. Data are represented as follows: frequency of absorption (cm^{-1}), and intensity of absorption (vs = very strong, s = strong, m = medium, w = weak). Enantiomeric excesses were determined by HPLC using a Daicel Chiralcel AD-H OD-H, column and eluting with a hexane/*i*-PrOH solution.

4.2. Typical procedure for the preparation of thioureas 1a–1e[11,12]

A 50-mL round-bottomed flask was charged with benzylamine (1.07 g, 10.0 mmol), triethylamine (2.42 g, 24.0 mmol) and THF (10 mL). The mixture was cooled with an ice bath under a N_2 atmosphere. Carbon disulphide (760 mg, 10 mmol) was added to the reaction mixture by syringe pump over 0.5 h. After the addition was completed, the mixture was stirred at room temperature for 1 h. The reaction mixture was cooled under an ice bath and tosyl chloride (2.28 g, 12 mmol) was added. The reaction mixture was warmed to room temperature and was stirred for 0.5 h. Next 1 M hydrochloride (10 mL) and MTBE (10 mL) were added to the mixture. The aqueous layer was separated and extracted with MTBE (10 mL). The combined organic layer was dried over Na_2SO_4. After the solvent was evaporated under vacuum, the residue was passed through a silica plug, which was washed with hexane. After the solvent was evaporated, the crude benzyl isothiocyanate was obtained.

A solution of benzyl isothiocyanate (745 mg, 5 mmol) in 10 mL CH_2Cl_2 was added dropwise to a solution of a (1*R*,2*R*)-cyclohexane-1,2-diamine (570 mg, 5 mmol) in CH_2Cl_2 (10 mL). The reaction solution was stirred at room temperature for 4 h. After the solvent was evaporated, the residue was purified by column chromatography (petroleum ether/$CHCl_3$ = 1/1–0/100) to afford thiourea **1c** (536 mg, 72% yield).

4.3. Spectroscopic data of thiourea 1

4.3.1. 1-[(1*R*,2*R*)-2-Aminocyclohexyl]-3-phenylthiourea 1a

Prepared from phenyl isothiocyanate and (1*R*,2*R*)-cyclohexane-1,2-diamine (77% yield). Yellow solid, mp: 54–57 °C; $[\alpha]_D^{24} = +11.0$ (*c* 1.0, CH_3OH); ^1H NMR (400 MHz, $CDCl_3$) δ: 7.27–7.07 (m, 5H, Ar–H), 4.13–4.09 (m, 1H, CH), 2.46–2.42 (m, 1H, CH), 1.97–1.86 (m, 2H, CH_2), 1.65–1.63 (m, 2H, CH_2), 1.21–1.11 (m, 4H, $2CH_2$); ^{13}C NMR

(100 MHz, CD_3OD) δ: 179.5, 136.9, 127.1, 123.5, 122.6, 58.8, 52.7, 32.3, 29.6, 23.1, 22.9; MS (ESI, M+1): 250; IR (thin film) ν/cm^{-1}: 3272 (m), 3028 (w), 2925 (s), 2852 (m), 1533 (vs), 1496 (s), 1446 (m), 1330 (s), 1141 (m), 941 (m), 709 (s).

4.3.2. 1-[(1*R*,2*R*)-2-Aminocyclohexyl]-3-[3,5-bis(trifluoromethyl) phenyl] thiourea 1b

Prepared from 3,5-bis(trifluoromethyl) phenyl isothiocyanate and (1*R*,2*R*)-cyclohexane-1,2-diamine (yield: 95%). Yellow solid, mp: 69–71 °C; $[\alpha]_D^{24} = -3.0$ (*c* 1.0, CH_3OH); ^1H NMR (400 MHz, CD_3OD) δ: 8.11 (s, 2H, Ar–H), 7.52 (s, 1H, Ar–H), 4.21–4.16 (m, 1H, CH), 2.61–2.59 (m, 1H, CH), 2.03–1.91 (m, 2H, CH_2), 1.69–1.67 (m, 2H, CH_2), 1.31–1.14 (m, 4H, $2CH_2$); ^{13}C NMR (100 MHz, CD_3OD) δ: 179.0, 140.4, 129.7, 129.3, 123.1, 121.0, 120.4, 108.7, 60.2, 53.8, 31.6, 29.5, 23.9, 23.7; MS (ESI, M+1): 386; IR (thin film) ν/cm^{-1}: 2939 (m), 1544 (w), 1474 (w), 1384 (m), 1278 (s), 1178 (m), 1133 (s), 968 (w), 886 (w), 681 (m).

4.3.3. 1-[(1*R*,2*R*)-2-Aminocyclohexyl]-3-benzylthiourea 1c

Prepared from benzylamine and (1*R*,2*R*)-cyclohexane-1,2-diamine (yield: 72%). Yellow solid, mp: 114–115 °C; $[\alpha]_D^{24} = -16.0$ (*c* 1.0, CH_3OH); ^1H NMR (400 MHz, CD_3OD) δ: 7.33–7.25 (m, 5H, Ar–H), 4.09–4.01 (m, 1H, CH), 2.50–2.47 (m, 1H, CH), 2.01–1.94 (m, 2H, CH_2), 1.74–1.71 (m, 2H, CH_2), 1.33–1.15 (m, 4H, $2CH_2$); ^{13}C NMR: (100 MHz, CD_3OD) δ: 181.8, 137.5, 128.0, 127.0, 126.8, 60.2, 54.8, 34.2, 31.6, 24.3, 24.1; IR (thin film) ν/cm^{-1}: 3338 (m), 2935 (m), 2856 (m), 1568 (s), 1515 (vs), 1444 (m), 1372 (s), 1274 (vs), 1211 (m), 829 (m), 620 (s); MS (ESI, M+1): 264; HRMS (ESI) calcd for $C_{14}H_{21}N_3S_1$ $(M+1)^+$: 264.1534, found: 264.1531.

4.3.4. 1-[(1*R*,2*R*)-2-Aminocyclohexyl]-3-[(*S*)-1-phenylethyl] thiourea 1d

Prepared from (*S*)-1-phenylethylamine and (1*R*,2*R*)-cyclohexane-1,2-diamine (yield: 90%). Yellow liquid, $[\alpha]_D^{24} = +5.0$ (*c* 1.0, CH_3OH); ^1H NMR (400 MHz, CD_3OD) δ: 7.31–7.21 (m, 5H, Ar–H), 4.09–3.97 (m, 1H, CH), 2.46–2.41 (m, 1H, CH), 1.93–1.86 (m, 2H, CH_2), 1.68–1.65 (m, 2H, CH_2), 1.47 (d, J = 6.8 Hz, 3H, CH_3), 1.28–1.22 (m, 4H, $2CH_2$); ^{13}C NMR (100 MHz, CD_3OD) δ: 142.1, 137.4, 127.8, 126.5, 125.1, 125.0, 124.2, 58.1, 53.1, 32.0, 30.0, 23.1, 22.9, 18.5; IR (thin film) ν/cm^{-1}: 3257 (m), 2930 (s), 2857 (m), 1543 (s), 1449 (m), 1333 (m), 1157 (w), 1090 (w); MS (ESI, M+1): 278.

4.3.5. 1-[(1*R*,2*R*)-2-Aminocyclohexyl]-3-[(*R*)-1-phenylethyl] thiourea 1e

Prepared from (*R*)-1-phenylethylamine and (1*R*,2*R*)-cyclohexane-1,2-diamine (yield: 77%). Yellow liquid, $[\alpha]_D^{24} = -30.0$ (*c* 1.0, CH_3OH); ^1H NMR (400 MHz, CD_3OD) δ: 7.31–7.21 (m, 5H, Ar–H), 4.09–3.97 (m, 1H, CH), 2.46–2.41 (m, 1H, CH), 1.93–1.86 (m, 2H, CH_2), 1.68–1.65 (m, 2H, CH_2), 1.47 (d, J = 6.8 Hz, 3H, CH_3), 1.28–1.22 (m, 4H, $2CH_2$); ^{13}C NMR (100 MHz, CD_3OD) δ: 142.1, 137.4, 127.8, 126.5, 125.1, 125.0, 124.2, 58.1, 53.1, 32.0, 30.0, 23.1, 22.9, 18.5; MS (ESI, M+1): 278; IR (thin film) ν/cm^{-1}: 3257 (m), 2930 (s), 2857 (m), 1543 (s), 1449 (m), 1333 (m), 1157 (w), 1090 (w).

4.4. Typical procedure for the conjugate addition of aldehydes to nitroalkenes

A mixture of *trans*-β-nitrostyrene (30.0 mg, 0.2 mmol), **1a** (10.0 mg, 0.04 mmol), DMAP (4.8 mg, 0.04 mmol), isobutyraldehyde (50 μL, 0.55 mmol) and chloroform (0.3 mL) in a 5 mL flask was stirred at room temperature for 2 h. After the evaporation of the solvent under vacuum, the residue was separated by flash chromatography over silica gel (petroleum ether/ethyl acetate = 10/1) to give **4a** as a colourless oil (40.7 mg, 92% yield).

4.5. Spectroscopic data of conjugate addition products 4

4.5.1. (*R*)-2,2-Dimethyl-4-nitro-3-phenyl-butanal 4a

The title compound was prepared from *trans*-β-nitrostyrene and isobutyraldehyde according to the representative procedure. $[\alpha]_D^{24} = +7.0$ (*c* 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ: 9.51 (s, 1H, CHO), 7.31–7.24 (m, 5H, Ar–H), 4.85 (dd, ^2J(H,H) = 12.9 Hz, ^3J(H,H) = 11.1 Hz, 1H, CH_2), 4.68 (dd, ^2J(H,H) = 12.9 Hz, ^3J(H,H) = 4.2 Hz, 1H, CH_2), 3.78 (dd, ^3J(H,H) = 11.1 Hz, ^3J(H,H) = 4.2 Hz, 1H, CH), 1.14 (s, 3H, CH_3), 1.01 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 204.0, 135.2, 129.0, 128.6, 128.0, 76.3, 48.5, 48.2, 21.7, 19.0; MS (EI): m/z = 221 (M^+), 187, 170, 159, 145, 117, 105, 91, 77, 72; IR (thin film) ν/cm^{-1}: 2925 (w), 1726 (m), 1638 (m), 1556 (s), 1456 (w), 1380 (m), 705 (m). The enantiomeric excess was determined by HPLC with Chiralpak AD-H column at 208 nm (hexane/^{i}-PrOH = 98/2, 0.5 mL/min; $t_{R(major)}$ = 24.9 min, $t_{R(minor)}$ = 25.9 min).

4.5.2. (*R*)-3-(4-Methoxyphenyl)-2,2-dimethyl-4-nitrobutanal 4b

The title compound was prepared from *trans*-1-methoxy-4-(2-nitrovinyl) benzene and isobutyraldehyde according to the representative procedure. $[\alpha]_D^{25} = -3.0$ (*c* 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ: 9.51 (s, 1H, CHO), 7.11 (d, ^3J(H,H) = 8.7 Hz, 2H, 3,5-Ar–H), 6.84 (d, ^3J(H,H) = 8.7 Hz, 2H, 2,6-Ar–H), 4.81 (dd, ^2J(H,H) = 12.6 Hz, ^3J(H,H) = 11.4 Hz, 1H, CH_2), 4.66 (dd, ^2J(H,H)= 12.6 Hz, ^3J(H,H) = 4.2 Hz, 1H, CH_2), 3.79 (s, 3H, OCH_3), 3.74 (dd, ^3J(H,H) = 11.4 Hz, ^3J(H,H) = 4.5 Hz, 1H, CH), 1.13 (s, 3H, CH_3), 1.01 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 204.3, 159.3, 130.1, 127.1, 114.1, 76.5, 55.2, 48.3, 47.9, 21.5, 18.9; MS (EI): m/z = 251 (M^+), 180, 135, 134, 121, 119, 91; HRMS (EI) calcd for $C_{13}H_{17}O_4N_1$ (M^+): 251.1152, found: 251.1150; IR (thin film) ν/cm^{-1}: 2927 (w), 1725 (m), 1611 (w), 1556 (vs), 1514 (s), 1465 (w), 1380 (m), 1252 (m), 1033 (w), 836 (w). The enantiomeric excess was determined by HPLC with Chiralpak OD-H column at 208 nm (hexane/^{i}-PrOH = 75/25, 0.8 mL/min; $t_{R(major)}$ = 15.0 min, $t_{R(minor)}$ = 21.1 min).

4.5.3. (*R*)-2,2-Dimethyl-4-nitro-3-(4-tolyl)-butanal 4c

The title compound was prepared from *trans*-1-methyl-4-(2-nitrovinyl) benzene and isobutyraldehyde according to the representative procedure. $[\alpha]_D^{25} = -5.0$ (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ: 9.53 (s, 1H, CHO), 7.13 (d, ^3J(H,H) = 8.0 Hz, 2H, Ar–H), 7.07 (d, ^3J(H,H) = 8.0 Hz, 2H, Ar–H), 4.82 (dd, ^2J(H,H) = 12.8 Hz, ^3J(H,H) = 11.2 Hz, 1H, CH_2), 4.67 (dd, ^2J(H,H) = 12.8 Hz, ^3J(H,H) = 4.0 Hz, 1H, CH_2), 3.74 (dd, ^3J(H,H) = 11.2 Hz, ^3J(H,H) = 4.0 Hz, 1H, CH), 2.32 (s, 3H, CH_3), 1.12 (s, 3H, CH_3), 1.00 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 204.4, 137.9, 132.1, 129.4, 128.9, 76.4, 48.2, 48.1, 21.6, 21.0, 18.9; MS (EI): m/z = 235 (M^+), 173, 164, 118, 105, 119, 91; IR (thin film) ν/cm^{-1}: 2973 (w), 2925 (w), 1726 (m), 1556 (vs), 1516 (w), 1381 (m), 1120 (w), 824 (w). The enantiomeric excess was determined by HPLC with Chiralpak OD-H column at 208 nm (hexane/^{i}-PrOH = 75/25, 0.8 mL/min; $t_{R(major)}$ = 12.2 min, $t_{R(minor)}$ = 17.0 min).

4.5.4. (*R*)-3-(4-Chlorophenyl)-2,2-dimethyl-4-nitrobutanal 4d

The title compound was prepared from *trans*-1-chloro-4-(2-nitrovinyl) benzene and isobutyraldehyde according to the representative procedure. $[\alpha]_D^{24} = +3.0$ (*c* 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ: 9.48 (s, 1H, CHO), 7.32 (t, ^3J(H,H) = 2.4 Hz, 1H, 2-Ar–H), 7.29 (t, ^3J(H,H) = 2.4 Hz, 1H, 6-Ar–H), 7.15 (t, ^3J(H,H) = 2.4 Hz, 1H, 3-Ar–H), 7.12 (t, ^3J(H,H) = 2.4 Hz, 1H, 5-Ar–H), 4.82 (dd, ^2J(H,H) = 13.2 Hz, ^3J(H,H) = 11.4 Hz, 1H, CH_2), 4.68 (dd, ^2J(H,H) = 13.2 Hz, ^3J(H,H) = 4.2 Hz, 1H, CH_2), 3.77 (dd, ^3J(H,H) = 11.4 Hz, ^3J(H,H) = 4.2 Hz, 1H, CH), 1.13 (s, 3H, CH_3), 1.01 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 203.5, 134.0, 133.9, 130.3, 128.8, 76.1, 48.2, 48.0, 21.8, 19.0; MS (EI): m/z = 255 (M^+),

193, 184, 140, 138, 125, 103, 77, 72; HRMS (EI) calcd for $C_{12}H_{14}O_3N_1Cl_1$ (M^+): 255.0657, found: 255.0658; IR (thin film) ν/cm^{-1}: 2926 (w), 1728 (m), 1556 (s), 1494 (w), 1378 (m), 1094 (w), 835 (w). The enantiomeric excess was determined by HPLC with Chiralpak OD-H column at 208 nm (hexane/^{i}-PrOH = 75/25, 0.8 mL/min; $t_{R(major)}$ = 13.5 min, $t_{R(minor)}$ = 20.0 min).

4.5.5. (*R*)-3-(3-Chlorophenyl)-2,2-dimethyl-4-nitrobutanal 4e

The title compound was prepared from *trans*-1-chloro-3-(2-nitrovinyl) benzene and isobutyraldehyde according to the representative procedure. $[\alpha]_D^{24} = +10.0$ (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.51 (s, 1H, CHO), 7.29–7.10 (m, 4H, Ar–H), 4.83 (dd, ^2J(H,H) = 13.2 Hz, ^3J(H,H) = 11.2 Hz, 1H, CH_2), 4.69 (dd, ^2J(H,H) = 13.2 Hz, ^3J(H,H) = 4.0 Hz, 1H, CH_2), 3.77 (dd, ^3J(H,H) = 11.2 Hz, ^3J(H,H) = 4.0 Hz, 1H, CH), 1.15 (s, 3H, CH_3), 1.03 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 203.7, 137.7, 134.6, 130.0, 129.3, 128.4, 127.3, 76.1, 48.2, 48.1, 21.8, 18.9; MS (EI): *m*/*z* = 255 (M^+), 193, 166, 138, 125, 103, 77, 72; HRMS (ESI) calcd for $C_{12}H_{14}O_3N_1Cl_1$ ($M-H)^-$: 254.0584, found: 254.0586; IR (thin film) ν/cm^{-1}: 2975 (w), 1726 (s), 1556 (vs), 1478 (w), 1435 (w), 1379 (m), 1085 (w), 703 (m). The enantiomeric excess was determined by HPLC with Chiralpak OD-H column at 208 nm (hexane/^{i}-PrOH = 75/25, 0.8 mL/min; $t_{R(major)}$ = 15.0 min, $t_{R(minor)}$ = 22.7 min).

4.5.6. (*R*)-2,2-Dimethyl-4-nitro-3-(4-nitrophenyl)-butanal 4f

The title compound was prepared from *trans*-1-nitro-4-(2-nitrovinyl) benzene and isobutyraldehyde according to the representative procedure. $[\alpha]_D^{24} = +10.0$ (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.48 (s, 1H, CHO), 8.21 (d, ^3J(H,H) = 8.7 Hz, 2H, 3, 5-Ar–H), 7.42 (d, ^3J(H,H) = 8.7 Hz, 2H, 2, 6-Ar–H), 4.90 (t, $^{2,3}J$(H,H) = 13.5 Hz, 1H, CH_2), 4.77 (dd, ^2J(H,H) = 13.5 Hz, ^3J(H,H) = 3.9 Hz, 1H, CH_2), 3.94 (dd, ^3J(H,H) = 13.5 Hz, ^3J(H,H) = 3.9 Hz, 1H, CH), 1.17 (s, 3H, CH_3), 1.06 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 203.3, 147.8, 143.5, 130.4, 124.1, 76.1, 48.6, 48.3, 22.3, 19.4; MS (EI): *m*/*z* = 267 $(M+1)^+$, 220, 204, 190, 177, 164, 149, 129, 115, 103, 91, 77; HRMS (EI) calcd for $C_{12}H_{15}O_5N_2$ $(M+1)^+$: 267.0975, found: 267.0973; IR (thin film) ν/cm^{-1}: 2923 (w), 1725 (m), 1604 (w), 1556 (s), 1522 (s), 1377 (w), 1348 (s), 858 (m), 703 (w). The enantiomeric excess was determined by HPLC with Chiralpak OD-H column at 208 nm (hexane/^{i}-PrOH = 75/25, 0.8 mL/min; $t_{R(major)}$ = 25.9 min, $t_{R(minor)}$ = 39.7 min).

4.5.7. (*R*)-3-(Furan-2-yl)-2,2-dimethyl-4-nitrobutanal 4g

The title compound was prepared from *trans*-2-(2-nitrovinyl) furan and isobutanaldehyde according to the representative procedure. $[\alpha]_D^{25} = -20.5$ (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.50 (s, 1H, CHO), 7.36 (s, 1H, Ar–H), 6.30 (s, 1H, Ar–H), 6.21 (d, ^3J(H,H) = 3.0 Hz, 1H, Ar–H), 4.75 (dd, ^2J(H,H) = 12.6 Hz, ^3J(H,H) = 11.1 Hz, 1H, CH_2), 4.57 (dd, ^2J(H,H) = 12.6 Hz, ^3J(H,H) = 3.6 Hz, 1H, CH_2), 3.92 (dd, ^3J(H,H) = 11.1 Hz, ^3J(H,H) = 3.6 Hz, 1H, CH), 1.18 (s, 3H, CH_3), 1.05 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 203.7, 149.9, 142.9, 110.7, 109.9, 75.2, 48.5, 42.5, 21.5, 19.4; MS (EI): *m*/*z* = 211 (M^+), 181, 164, 149, 121, 94, 81; IR (thin film) ν/cm^{-1}: 2925 (w), 1728 (m), 1557 (s), 1376 (m), 1148 (m), 740 (m). The enantiomeric excess was determined by HPLC with Chiralpak OD-H column at 208 nm (hexane/^{i}-PrOH = 75/25, 0.8 mL/min; $t_{R(major)}$ = 9.7 min, $t_{R(minor)}$ = 14.3 min).

4.5.8. (*R*)-2,2-Dimethyl-4-nitro-3-(thiophen-2-yl) butanal 4h

The title compound was prepared from *trans*-2-(2-nitrovinyl) thiophene and isobutanaldehyde according to the representative procedure. $[\alpha]_D^{25} = +13.0$ (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.52 (s, 1H, CHO), 7.23–7.22 (m, 1H, 5-Ar–H), 6.95 (dd, ^3J(H,H) = 5.1 Hz, ^3J(H,H) = 3.6 Hz, 1H, 4-Ar–H), 6.91 (dd, ^3J(H,H) = 3.6 Hz, ^4J(H,H) = 0.9 Hz, 1H, 3-Ar–H), 4.76–4.62 (m, 2H, CH_2), 4.14 (dd, ^3J(H,H) = 10.5 Hz, ^3J(H,H) = 4.5 Hz, 1H, CH), 1.22 (s, 3H, CH_3), 1.08 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 203.8, 138.0, 128.1, 127.2, 125.7, 78.1, 48.7, 44.3, 21.9, 19.2; MS (EI): *m*/*z* = 227 (M^+), 207, 180, 165, 156, 110, 97, 84; IR (thin film) ν/cm^{-1}: 2925 (w), 1725 (m), 1557 (s), 1433 (w), 1378 (m), 882 (w), 704 (m). The enantiomeric excess was determined by HPLC with Chiralpak OD-H column at 208 nm (hexane/ ^{i}-PrOH = 75/25, 0.8 mL/min; $t_{R(major)}$ = 12.8 min, $t_{R(minor)}$ = 19.9 min).

4.5.9. (*R*)-*E*-2,2-Dimethyl-3-(nitromethyl)-5-phenylpent-4-enal 4i

The title compound was prepared from (1*E*,2*E*)-4-nitrobuta-1,3-dienyl benzene and isobutyraldehyde according to the representative procedure. $[\alpha]_D^{24} = -5.0$ (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.52 (s, 1H, CHO), 7.35–7.26 (m, 5H, Ar–H), 6.53 (d, ^3J(H,H) = 15.6 Hz, 1H, =CH), 6.02 (dd, ^3J(H,H) = 10.2 Hz, ^3J(H,H) = 15.6 Hz, 1H, =CH), 4.52 (dd, ^3J(H,H) = 4.0 Hz, ^2J(H,H) = 12.0 Hz, 1H, CH_2), 4.45 (dd, ^3J(H,H) = 4.0 Hz, ^2J(H,H) = 12.0 Hz, 1H, CH_2), 3.28 (dt, ^3J(H,H) = 4.0 Hz, ^3J(H,H) = 10.2 Hz, 1H, CH), 1.17 (s, 3H, CH_3), 1.16 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 203.8, 136.3, 136.0, 128.6, 128.2, 126.6, 122.9, 47.8, 47.2, 21.0, 19.1; MS (EI): *m*/*z* = 247 (M^+), 200, 157, 129, 115, 104, 91, 77; HRMS (EI) calcd for $C_{14}H_{17}O_3N_1$ $(M)^+$: 247.1203, found: 247.1206; IR (thin film) ν/cm^{-1}: 2974 (w), 1723 (m), 1554 (s), 1450 (w), 1380 (m), 972 (m), 887 (w), 749 (m). The enantiomeric excess was determined by HPLC with Chiralpak OD-H column at 208 nm (hexane/ ^{i}-PrOH = 80/20, 0.8 mL/min; $t_{R(major)}$ = 15.4 min, $t_{R(minor)}$ = 16.5 min).

4.5.10. (*R*)-2,2-Dimethyl-3-(naphthalene-1-yl)-4-nitrobutanal 4j

The title compound was prepared from *(E)*-1-(2-nitrovinyl)naphthalene and isobutyraldehyde according to the representative procedure. White solid, mp: 103–104 °C; $[\alpha]_D^{24} = +87.0$ (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.59 (s, 1H, CHO), 8.23 (d, ^3J(H,H) = 8.4 Hz, 1H, Ar–H), 7.86 (d, ^3J(H,H) = 8.0 Hz, 1H, Ar–H), 7.81 (d, ^3J(H,H) = 8.0 Hz, 1H, Ar–H), 7.59 (dd, ^3J(H,H) = 8.4 Hz, ^3J(H,H) = 7.2 Hz,1H, Ar–H), 7.53–7.41 (m, 3H, Ar–H), 5.03–4.91 (m, 2H, CH_2), 4.88–4.85 (m, 1H, CH), 1.21 (s, 3H, CH_3), 0.97 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 204.4, 133.0, 132.9, 132.3, 129.1, 128.8, 126.8, 126.0, 125.0,124.9, 122.1, 77.0, 49.1, 40.3, 21.7, 18.8; MS (EI): *m*/*z* = 271 (M^+), 200, 154, 141; HRMS (EI) calcd for $C_{16}H_{17}O_3N_1$ $(M-H)^-$: 270.1130, found: 270.1136; IR (thin film) ν/cm^{-1}: 2971 (w), 2815 (w), 1717 (m), 1551 (vs), 1471 (w), 1433 (w), 1377 (m), 796 (m), 782 (m). The enantiomeric excess was determined by HPLC with Chiralpak OD-H column at 208 nm (hexane/^{i}-PrOH = 75/25, 1.0 mL/min; $t_{R(major)}$ = 9.3 min, $t_{R(minor)}$ = 10.4 min).

4.5.11. (2*R*/2*S*,3*R*)-2-Methyl-4-nitro-3-phenylbutanal 4k

The title compound was prepared from *trans*-β-nitrostyrene and propionaldehyde according to the representative procedure. $[\alpha]_D^{29} = +6.0$ (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) signals corresponding to the major diastereomer δ: 9.69 (s, 1H, CHO), 7.32–7.13 (m, 5H, Ar–H), 4.82–4.63 (m, 2H, CH_2), 3.86–3.76 (m, 1H, CH), 2.81–2.74 (m, 1H, CH), 1.21 (d, ^3J(H,H) = 7.2 Hz, 3H, CH_3); signals corresponding to the minor diastereomer δ: 9.51 (s, 1H, CHO), 7.32–7.13 (m, 5H, Ar–H), 4.82–4.63 (m, 2H, CH_2), 3.86–3.76 (m, 1H, CH), 2.81–2.74 (m, 1H, CH), 1.00 (d, ^3J(H,H) = 7.2 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 202.3, 136.6, 130.9, 129.0, 128.0, 78.1, 48.7, 44.0, 12.0; MS (EI): *m*/*z* = 207 (M^+), 160, 145, 131, 117, 104, 91, 77; IR (thin film) ν/cm^{-1}: 3032 (w), 2973 (w), 2929 (w), 1724 (m), 1603 (w), 1555 (s), 1456 (m), 1377 (m), 702 (m). The enantiomeric excess and diastereomeric ratio were determined by HPLC with Chiralpak OD-H column at 208 nm (hexane/^{i}-PrOH = 80/20, 0.8 mL/min; signals corresponding to the major diastereomer: $t_{R(major)}$ = 25.1 min, $t_{R(minor)}$ = 19.1 min; signals

corresponding to the minor diastereomer: $t_{R(major)}$ = 28.8 min, $t_{R(minor)}$ = 23.0 min).

4.5.12. (2*R*/2*S*,3*R*)-2-Ethyl-4-nitro-3-phenylbutanal 4l

The title compound was prepared from *trans*-β-nitrostyrene and butyraldehyde according to the representative procedure. $[\alpha]_D^{25} = +6.0$ (*c* 1.0, $CHCl_3$); MS (EI): *m*/*z* = 221 (M^+), 175, 145, 131, 117, 105, 104, 91, 77; IR (thin film) ν/cm^{-1}: 2956 (w), 2926 (m), 2360 (w), 1718 (m), 1555 (s), 1496 (m), 1379 (m), 701 (m). The enantiomeric excess and diastereomeric ratio were determined by HPLC with Chiralpak OD-H column at 208 nm (hexane/^{i}-PrOH = 80/20, 0.8 mL/min).

Signals corresponding to the major diastereoisomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.70 (d, 1H, ^3J(H,H) = 2.4 Hz, CHO), 7.33–7.14 (m, 5H, Ar–H), 4.79–4.58 (m, 2H, CH_2), 3.82–3.77 (m, 1H, CH), 2.69–2.66 (m, 1H, CH), 0.86–0.81 (t, ^3J(H,H) = 7.5 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 202.8, 136.7, 128.9, 128.1, 127.8, 78.5, 42.7 29.7, 20.4, 10.7; $t_{R(minor)}$ = 16.3 min, $t_{R(major)}$ = 19.2 min.

Signals corresponding to the minor diastereoisomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.46 (d, 1H, ^3J(H,H) = 2.4 Hz, CHO), 7.33–7.14 (m, 5H, Ar–H), 4.79–4.58 (m, 2H, CH_2), 3.82–3.77 (m, 1H, CH), 2.61–2.53 (m, 1H, CH), 1.02–0.97 (t, ^3J(H,H) = 7.5 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 202.9, 136.7, 128.9, 128.1, 127.9, 77.8, 44.1, 29.7, 20.6, 11.5; $t_{R(minor)}$ = 17.2 min, $t_{R(major)}$ = 27.9 min).

4.5.13. (*S*)-5-Nitro-4-phenylpentan-2-one 4m

The title compound was prepared from *trans*-β-nitrostyrene and acetone according to the representative procedure. $[\alpha]_D^{25} = -1.7$ (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.35–7.20 (5H, m, Ar–H), 4.70 (1H, dd, ^3J(H,H) = 12.3 Hz, ^3J(H,H) = 6.90 Hz, CH_2), 4.60 (1H, dd, ^3J(H,H) = 12.3 Hz, ^3J(H,H) = 7.8 Hz, CH_2), 4.01 (1H, m, CH), 2.92 (2H, d, ^3J(H,H) = 7.0 Hz, CH_2), 2.13 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 205.4, 138.8, 129.1, 127.9, 127.4, 79.5, 46.1, 39.0, 30.4; MS (EI): *m*/*z* = 207 (M^+), 191, 167, 133, 91, 84; IR (thin film) ν/cm^{-1}: 3040 (w), 2950 (w), 1715 (s), 1546 (vs), 1384 (s), 1362 (m), 758 (w), 696 (w). The enantiomeric excess was determined by HPLC with Chiralpak AS-H column at 208 nm (hexane/^{i}-PrOH = 75/25, 1.0 mL/min; $t_{R(major)}$ = 12.2 min, $t_{R(minor)}$ = 16.6 min).

4.5.14. (*S*)-2-[2-Nitro-1-phenylethyl]cyclopentanone 4n

The title compound was prepared from *trans*-β-nitrostyrene and cyclopentanone according to the representative procedure. $[\alpha]_D^{25} = -3.3$ (*c* 1.3, $CHCl_3$); IR (thin film) ν/cm^{-1}: 3031 (w), 2983 (w), 2880 (w), 1730 (s), 1552 (vs), 1159 (m), 785 (m), 697 (w); MS (EI): *m*/*z* = 233, 186, 158, 129, 115, 104, 91, 77. The enantiomeric excess and diastereomeric ratio were determined by HPLC with Chiralpak AS-H column at 208 nm (hexane/^{i}-PrOH = 75/25, 0.8 mL/min).

Signals corresponding to the major diastereoisomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.34–7.30 (3H, m, Ar–H), 7.19–7.16 (2H, m, Ar–H), 5.02–5.00 (2H, m, CH_2), 3.86–3.81 (1H, m, CH), 2.55–2.49 (1H, m, CH), 2.34–1.43 (6H, m, $3CH_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 219.1, 137.4, 129.0, 128.5, 128.0, 78.3, 51.4, 44.0, 39.3, 27.0, 20.6; $t_{R(minor)}$ = 14.0 min, $t_{R(major)}$ = 16.0 min.

Signals corresponding to the minor diastereoisomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.34–7.30 (3H, m, ArH), 7.19–7.16 (2H, m, ArH), 5.33 (1H, dd, ^3J(H,H) = 12.9 Hz, ^3J(H,H) = 5.6 Hz, CH_2), 4.71 (1H, dd, ^3J(H,H) = 12.8 Hz, ^3J(H,H) = 9.9 Hz, CH_2), 3.73–3.67 (1H, m, CH), 2.43–2.36 (1H, m, CH), 2.34–1.43 (6H, m, $3CH_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 218.5, 137.7, 128.9, 128.0, 127.9, 78.3, 50.5, 44.2, 38.7, 28.3, 20.3; $t_{R(minor)}$ = 12.3 min, $t_{R(major)}$ = 22.1 min.

4.5.15. (*S*)-1-Methoxy-5-nitro-4-phenylpentan-2-one 4o

The title compound was prepared from *trans*-β-nitrostyrene and 1-methoxypropan-2-one according to the representative procedure. $[\alpha]_D^{25} = +1.2$ (*c* 0.7, $CHCl_3$); MS (EI): *m*/*z* = 237 (M^+), 194, 147, 117, 104, 91, 77; IR (KBr) ν/cm^{-1}: 2930 (w), 2830 (w), 1715 (m), 1556 (s), 1382 (m), 1109 (m), 763 (w), 703 (m). The enantiomeric excess and diastereomeric ratio were determined by HPLC with Chiralpak AS-H column at 208 nm (hexane/^{i}-PrOH = 75/25, 0.86 mL/min).

Signals corresponding to the major diastereoisomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.35–7.28 (3H, m, Ar–H), 7.25–7.21 (2H, m, Ar–H), 4.93 (1H, dd, ^3J(H,H) = 12.8, ^3J(H,H) = 8.3 Hz, CH_2), 4.65 (1H, dd, ^3J(H,H) = 12.8 Hz, ^3J(H,H) = 6.8 Hz, CH_2), 3.93–3.80 (2H, m, CH_2), 3.45 (3H, s, OCH_3), 1.78 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.9, 134.5, 129.0, 128.5, 128.4, 86.4, 76.5, 59.8, 46.3, 26.4; $t_{R(minor)}$ = 14.9 min, $t_{R(major)}$ = 19.7 min.

Signals corresponding to the minor diastereoisomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.35–7.28 (3H, m, Ar–H), 7.25–7.21 (2H, m, Ar–H), 4.86 (1H, dd, ^3J(H,H) = 13.1 Hz, ^3J(H,H) = 5.5 Hz, CH_2), 4.72 (1H, dd, ^3J(H,H) = 13.1 Hz, ^3J(H,H) = 8.6 Hz, CH_2), 3.93–3.80 (2H, m, CH_2), 3.38 (3H, s, OCH_3), 2.04 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 208.1, 135.4, 129.1, 128.9, 128.1, 88.2, 76.5, 59.8, 45.9, 26.2; $t_{R(minor)}$ = 13.8 min, $t_{R(major)}$ = 26.5 min.

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