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Asymmetric Michael addition of acetone to β-nitrostyrenes catalyzed by novel organocatalysts derived from D-isomannide or L-isoidide

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Abstract
Novel bifunctional organocatalysts were prepared from D-isomannide or L-isoidide in three steps. These catalysts were then evaluated in the asymmetric Michael addition of acetone to *trans*-β-nitrostyrenes. Although moderate enantioselectivities were observed, this study has highlighted that a simple chiral primary diamine can catalyze this reaction. Furthermore, the reaction was also performed with an isomannide-derived diimine which was transformed *in situ* into the active catalyst under acidic conditions leading to the best enantioselectivity.

Keywords: Organocatalysis, isomannide, isoidide, Michael addition, monothiourea, nitroalkenes

Introduction

Asymmetric organocatalysis has been revived as an important field of asymmetric synthesis since the independent work of List,[1] MacMillan,[2] and Barbas.[3] Inspired by natural enzymatic systems, successful efforts have been directed towards the development of bifunctional organocatalysts containing a Lewis-basic amine and a hydrogen bond donor able to activate both nucleophile and electrophile simultaneously.[4-6] In particular, bifunctional amine-thiourea-based catalysts have proved to be efficient in various asymmetric transformations owing to the ability of the thiourea moiety to highly activate carbonyl or nitro groups through double hydrogen-bonding interactions.[7,8] Therefore, this kind of organocatalyst has been widely studied in asymmetric nitro-Michael addition reactions.[9,10] The first asymmetric Michael addition of

ketones to *trans*-β-nitrostyrenes was performed independently by List[11] and Barbas[3] involving proline as catalyst. Since these reports, successful examples using bifunctional tertiary or secondary amine-thiourea catalysts have been reported.[12-22]

Since Tsogoeva[23] and Jacobsen[24] demonstrated that a primary amine-thiourea catalyst can act as efficient bifunctional catalyst for the asymmetric nitro Michael addition, such bifunctional organocatalysts have attracted much attention owing to their easy preparation from chiral diamines.[25-32] However, the chiral scaffold of these reported organocatalysts is limited and is mostly derived from 1,2-diaminocyclohexane and 1,2-phenylethylenediamine.

As part of an ongoing program, we were interested in the design of new bifunctional organocatalysts from original chiral building blocks, *i.e.* from D-isomannide and L-isoidide; two side-products of the starch industry. Although numerous examples of polymers containing this backbone have been reported,[33] only a few examples in the field of asymmetric catalysis have been investigated. In asymmetric organometallic catalysis, ligands derived from dianhydrohexitols have already been used to perform Diels-Alder reactions,[34] nucleophilic addition to aldehydes,[35] asymmetric allylic substitution,[36,37] hydrogen transfer reduction of prochiral ketones[38-40] and asymmetric hydrogenation of olefins.[41,42] Recently, we described the first example of organocatalysts derived from dianhydrohexitols for the asymmetric Friedel-Craft alkylation of indoles.[43] Herein, we report our preliminary results on asymmetric Michael addition of acetone to *trans*-β-nitrostyrenes catalyzed by chiral thioureas and imines organocatalysts derived from D-isomannide- or L-isoidide.

Results and Discussion

Herein, we report our preliminary results on asymmetric Michael addition of acetone to *trans*-β-nitrostyrenes catalyzed by D-isomannide- or L-isoidide-derived organocatalysts **1-8** (Figure 1).

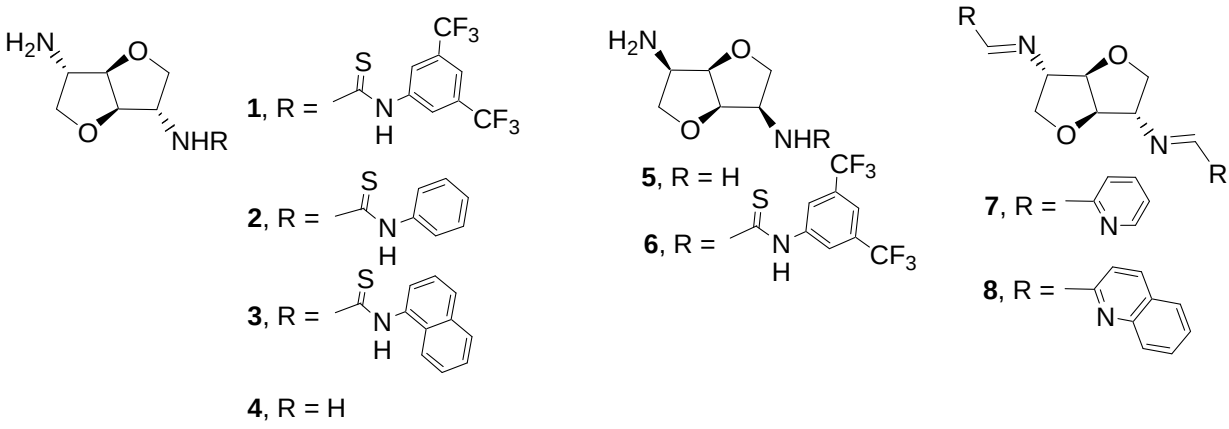
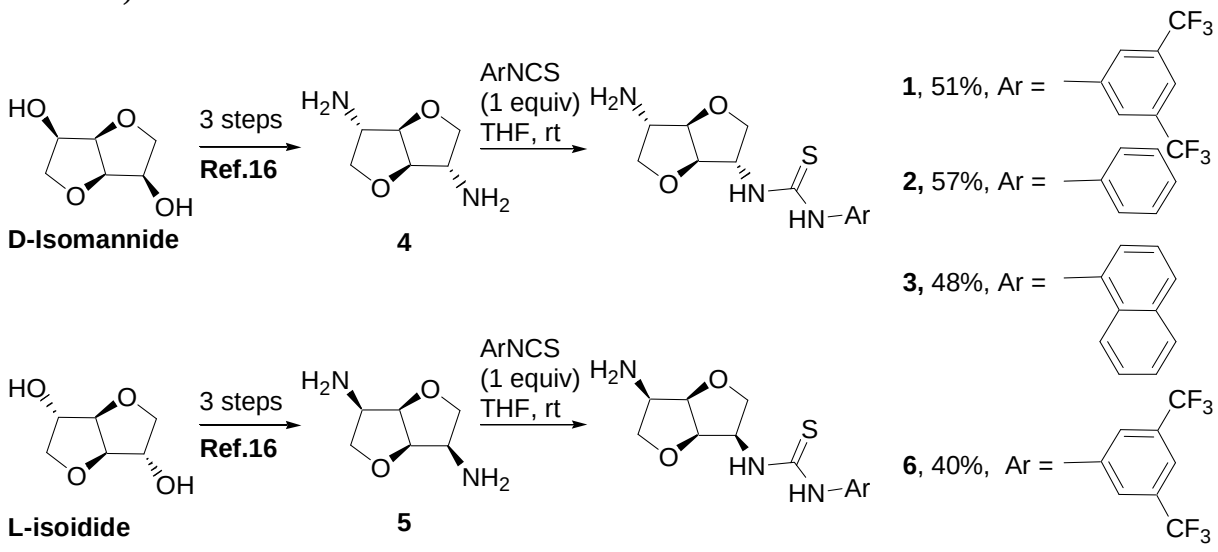


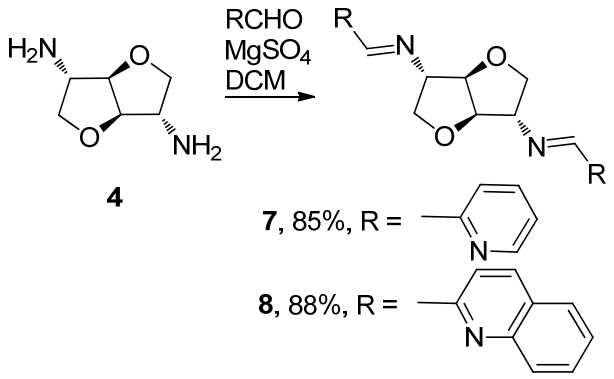
Figure 1. D-Isomannide and L-isoidide-derived organocatalysts.

Catalysts **1-3** were obtained after reaction of one equivalent of the corresponding isothiocyanate and diamine **4**, which was obtained in three steps from D-isomannide (Scheme 1). Around 10-15% of the corresponding dithioureas were also isolated. Monothiourea **6** was prepared from diamine **5** which was isolated in three steps from L-isoidide.[43] Finally, using the same conditions as preparing thioureas **1-3**, catalyst **6** was successfully obtained in 40% yield (Scheme 1).



Scheme 1. Synthesis of monothioureas **1-3** and **6**.

Diimines **7** and **8** were also prepared as precursor of amine-imine organocatalysts according to Cheng *et al*.[44] They were prepared from the corresponding diamine **4** under the usual conditions (Scheme 2).

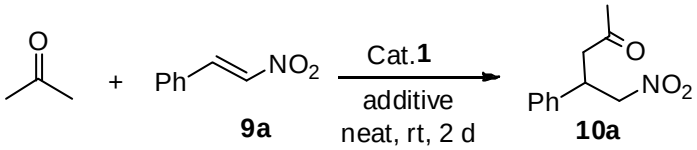


Scheme 2. Synthesis of diimine derivatives.

With these organocatalysts in hand, the Michael addition of acetone to *trans*-*β*-nitrostyrene **9a**, using 20 mol% of catalyst **1**, was evaluated without any solvent (Table 1). In these conditions, the desired product was obtained with moderate yield and poor enantioselectivity (Table 1, entry 1). To improve the reaction rate and the enantioselectivity, we investigated the effect of acidic

additives (1 equivalent related to the catalyst) on the reaction (Table 1, entries 1-9). Compared to the reaction performed without additive, in the presence of benzoic acid, the chemical yield and enantioselectivity were improved (Table 1, entries 1 and 2). With mandelic acids, both yields and *ee*s decreased (Table 1, entries 3 and 4), no matched-mismatched double diastereoselectivity effects were observed. Moreover, the chirality of the acid had no influence on the enantioselectivity; the same major isomer being formed (entries 3 and 4). In the case of 2,2,2-trichloroacetic acid (TCA), although better enantioselectivity was obtained, the product was isolated along with a side-product even after purification (Table 1, entry 5). The use of a strong acid such as trifluoroacetic acid led to deactivation of the catalyst (Table 1, entry 6). *p*-Toluenesulfonic acid was also not suitable for this asymmetric reaction (Table 1, entry 7). Finally, a weaker acid, such as acetic acid, gave the best results in terms of yield and *ee* (Table 1, entry 9). However, the use of larger amounts or less than 20 mol% of acetic acid had a dramatic effect on both yields and *ee*s (Table 1, entries 10-12).

Table 1. Catalytic asymmetric Michael addition of acetone with *trans*-β-nitrostyrene **9a** with different additives[a]



Entry	Additive (mol%)	Yield (%)[b]	*EE* (%)[c] (*R*)[d]
1	-	44	<5
2	$PhCO_2H$ (20)	77	15
3	D-Mandelic acid (20)	24	10
4	L-Mandelic acid (20)	39	8
5	TCA (20)	95[e]	27
6	TFA (20)	-	-
7	*p*-TsOH (20)	29	11
8	PhOH (20)	39	24
9	AcOH (20)	87	23
10	AcOH (75)	87	7
11	AcOH (175)	24	10
12	AcOH (10)	68	6

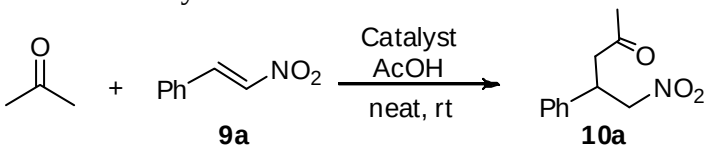
[a] Reaction conditions: **9a** (0.1 mmol), acetone (0.4 mL), **1** (20 mol%), additive at rt for 2 d.
[b] Yield of product isolated after flash chromatography.
[c] Determined by HPLC analysis (Phenomenex® Lux 5μ cellulose-2, *i*-octane/*i*-PrOH = 9/1).
[d] Absolute configuration was determined by comparison of the optical rotation with the known compounds in the literature.[45]
[e] % Conversion.

Using the optimized conditions from Table 1 (entry 9), we then explored the different organocatalysts. Among all the primary amine-thiourea-based catalysts **1-3** and **6**, catalyst **1** had the best performance, affording yields up to 87%. However, the *ee*s were all in the same range (around 25%, Table 2, entries 1-3), except for catalyst **6** which led to a racemic product (Table 2, entry 6).

The formation of the racemic compound can be explained by the proximity of the two nitrogen group in the 'endo'-position which perhaps give rise to a strong intramolecular hydrogen bond either between the thiourea moiety and the oxygen of the bicycle or between the primary amine and the thiourea groups.[46]

The same stereochemical outcome was observed with the chiral primary diamine **5** (Table 2, entry 5). Surprisingly, the simple diamine catalyst **4** gave promising results in terms of both yield and *ee* (Table 2, entry 4). Although some examples using secondary or secondary-tertiary diamines as catalysts for this reaction have been reported,[47,48] to the best of our knowledge, a successful example with a chiral primary diamine has not yet been described. Finally, the asymmetric reaction was also performed in solvents such as toluene, $CHCl_3$, DCM and MTBE, but the reaction rate dramatically decreased in all cases.

Table 2. Catalytic asymmetric Michael addition of acetone with *trans*-β-nitrostyrene **9a** with different catalysts[a]



9a **10a**

Entry	Catalyst	Time (h)	Yield[b] (%)	*EE*[c] (%)
1	**1**	48	87	23
2	**2**	48	43	26
3	**3**	48	34	28
4	**4**	48	65	40
5	**5**	48	36	<5
6	**6**	48	58	<5
7	**7**	48	34	37
8	**8**	48	39	59

[a] Reaction conditions: **9a** (0.1 mmol), acetone (0.4 mL), catalyst **1-9** (20 mol%), AcOH (20 mol%.

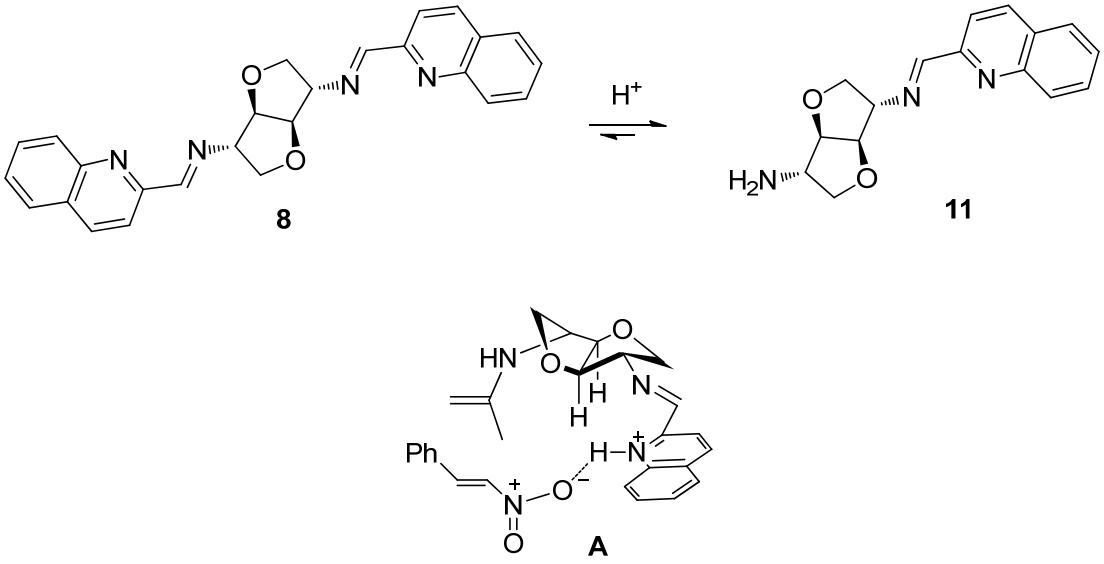
[b] Yield of product isolated after flash chromatography.

[c] Determined by HPLC analysis (Phenomenex® Lux 5μ cellulose-2, *i*-octane/*i*-PrOH = 9/1).

With the diimine catalysts **7** and **8**, some catalytic effect was observed. We think that, in the presence of acetic acid, the diimines are likely to be transformed *in situ* into primary amine-

imines which might be potential catalysts, as demonstrated by Cheng *et al*.[44] With the quinoline-derived diimine catalyst **8**, we assumed that the pre-catalyst **8** led to the catalyst **11**, able to both activate the nucleophile and electrophile. The activation of the nitro group is possible by a hydrogen-bonding interaction after *in situ* formation of the quinolinium cation (intermediate A, Scheme 3). In that case, the *ee* reached 59% (Table 2, entry 9). The difference in the *ee* observed between that obtained from pre-catalyst diimines **7** and **8** is probably attributed to the presence of the second aromatic ring in compound **8** which likely induced additional steric hindrance (Table 2, entries 7 and 8). Our attempts to perform the synthesis of the pure amino-imine **11** to test its reactivity on the catalytic reaction were unsuccessful as the organocatalyst could not be obtained pure even after chromatography on deactivated silica gel.

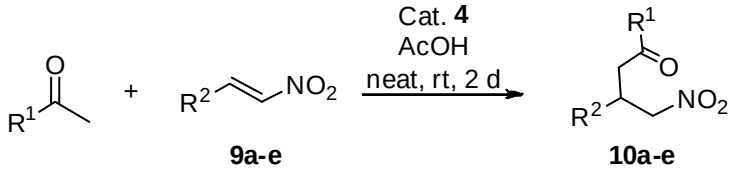
The asymmetric Michael addition was then performed with other substrates **9b-e** to expand upon the scope of this reaction (Table 3). The reaction was carried out with catalyst **4** which afforded the best results in terms of both yields and enantioselectivities under the optimal conditions.



Scheme 3. Possible transition state A.

The reaction between different nitrostyrenes which had either electron-withdrawing groups or electron-donating groups were studied. The corresponding adducts were isolated in moderate to good yields and with *ee*s in the similar range to those obtained previously (*ca.* 40% *ee*) (Table 3, entries 1-4). However, when the naphthyl nitroolefin **9e** was used, the *ee* of product **10e** was only 24% (Table 3, entry 5). Furthermore, with our catalytic system, the Michael addition of aromatic ketones, such as acetophenone, was unsuccessful contrary to the Xu's catalysts.[31]

Table 3. The scope of catalytic asymmetric Michael addition of ketones with *trans*-β-nitrostyrenes **9a**-e[a]



Entry	R^1	R^2	Product	Yield[b] (%)	*EE*[c] (%)
1	Me	Ph	**10a**	65	40
2	Me	4-ClC_6H_4	**10b**	62	37
3	Me	4-Tol	**10c**	63	39
4	Me	4-$MeOC_6H_4$	**10d**	51	40
5	Me	Naphth-1-yl	**10e**	72	24
6	Ph	Ph	-	-	-

[a] Reaction conditions: **9a-e** (0.1 mmol), acetone (0.4 mL), **4** (20 mol%), AcOH (20 mol%).
[b] Yield of product isolated after flash chromatography.
[c] Determined by HPLC analysis (Phenomenex® Lux 5μ cellulose-2, *i*-octane/*i*-PrOH = 9/1).

Conclusions

In conclusion, we have developed a new series of organocatalysts derived from D-isomannide and L-isoidide, which have shown their ability to catalyze for the first time the asymmetric Michael addition of acetone to *trans*-β-nitroolefins. Although moderate enantioselectivities and yields were observed, this study has shown that the reaction can be catalyzed by a simple chiral primary diamine. On the other hand, the use of a chiral diimine in acidic conditions led to the best enantioselectivity, however, the reaction rate was low. Owing to their ease of preparation from D-isomannide even on large scale, these catalysts are ideal candidates for wider studies in this area. To determine the stereochemical outcome using the diimine catalyst and to improve the reaction rate, further investigations are in progress in our laboratory and the results will be reported in due course.

Experimental Section

General. Unless otherwise noted, solvents and starting materials were obtained from commercial suppliers. All chemicals used were of reagent grade without further purification before use. ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance (200 or 400 MHz for ^1H, and 50 or 100

MHz for ^{13}C) in $CDCl_3$, MeOH-d_4, DMSO-d_6 or acetone-d_6. Chemical shifts were recorded in ppm (δ) relative to $CHCl_3$ on 7.26 or TMS on 0.00 for ^1H NMR and 77.0 for ^{13}C NMR, to MeOH on 3.31 for ^1H NMR and 49.0 for ^{13}C NMR, to DMSO on 2.50 for ^1H NMR and 39.5 for ^{13}C NMR, to acetone on 2.05 for ^1H NMR and 29.8 for ^{13}C NMR. Melting points were determined on a Reichert Thermoval apparatus and are uncorrected. Optical rotations values were recorded using a Perkin-Elmer 343 polarimeter. FT-IR spectra were performed on a Nicolet AVATAR 370 DTGS Thermo Electron Corporation apparatus and band positions are given in cm^{-1}. High resolution mass spectra were recorded on a Waters Micromass® GCT Premier™. Diamines **4** and **5** were prepared according to the procedure described in the literature.[43]

General procedure for the synthesis of catalysts 1-3 and 6. To a stirred solution of diamine **4** (0.5 mmol) in THF (8 mL) was slowly added isothiocyanate (0.5 mmol) in THF (2.5 mL). After stirring at rt for 2 h, the reaction mixture was concentrated, and the residue was purified by column chromatography (eluent: DCM/MeOH: 10/1 to 5/1) to afford monothioureas **1-3** and **6.**

Monothiourea 1. Prepared according to the general procedure to provide the product **1** as a solid in 51% yield, mp: 94-95 ^oC; $[\alpha]_D^{20}$ = + 36.5 (*c* 0.96, DCM); ^1H NMR (400 MHz, $CDCl_3$) 8.94 (br s, 1H), 7.90 (s, 2H), 7.62 (s, 1H), 7.34 (br s, 1H), 4.81 (d, *J* 4.3 Hz, 1H), 4.73 (br s, 1H), 4.44 (d, *J* 4.3 Hz, 1H), 4.05-4.01 (m, 1H), 3.92 (dd, *J* 9.7, 4.1 Hz, 1H), 3.81 (d, *J* 9.7 Hz, 1H), 3.74-3.68 (m, 1H), 3.58-3.56 (m, 1H), 2.68 (br s, 2H).

Monothiourea 2. Prepared according to the general procedure to provide the product **2** as a solid in 57% yield, mp: 78.8-80.5 ^oC; $[\alpha]_D^{20}$ = + 47.4 (*c* 1.16, DCM). IR (ATR, cm^{-1}): 3250, 2933, 2872, 1593, 1526, 1495, 1449, 1313, 1242, 1061, 900, 842, 758, 693, 470; ^1H NMR (200 MHz, $CDCl_3$) 8.48 (s, 1H), 7.47-7.38 (m, 2H), 7.33-7.21 (m, 3H), 6.24 (dm, *J* 5.8 Hz, 1H), 4.86 (br s, 1H), 4.75 (d, *J* 4.2 Hz, 1H), 4.29 (d, *J* 4.2 Hz, 1H), 3.97 (dd, *J* 10.0, 4.6 Hz, 1H), 3.91 (dd, *J* 9.4, 4.6 Hz, 1H), 3.75 (dd, *J* 10.0, 2.0 Hz, 1H), 3.67 (dd, *J* 9.4, 2.2 Hz, 1H), 3.52-3.48 (m, 1H), 1.66 (s, 2H). ^{13}C NMR (50 MHz, $CDCl_3$) 180.5, 136.2, 130.1, 127.2, 124.9, 89.1, 86.0, 75.1, 71.8, 61.5, 58.0. HRMS *m/z* calcd for $C_{13}H_{18}N_3O_2S$ $[M+H]^+$ = 280.1118, found 280.1120.

Monothiourea 3. Prepared according to the general procedure to provide the product **3** as a solid in 48% yield, mp: 160.7-161.5 ^oC, $[\alpha]_D^{20}$ = + 5.23 (*c* 1.51, THF), IR (film, cm^{-1}): 3358, 3056, 2947, 2880, 1712, 1541, 1398, 1272, 1056, 919, 777; ^1H NMR (400 MHz, MeOH-d_4) 7.94-7.91 (m, 2H), 7.87-7.85 (m, 1H), 7.57-7.47 (m, 4H), 4.89 (s, 2H), 4.70 (d, *J* 3.3 Hz, 1H), 4.30 (d, *J* 3.8 Hz, 1H), 3.98 (dd, *J* 9.8, 5.3 Hz, 1H), 3.93 (dd, *J* 9.8, 4.8 Hz, 1H), 3.69-3.65 (m, 2H). ^{13}C NMR (100 MHz, MeOH-d_4) δ 183.8, 136.1, 135.0, 131.5, 129.5, 129.0, 127.8, 127.5, 126.8, 126.4, 123.7, 88.9, 87.8, 74.3, 72.8, 62.8, 58.6. HRMS *m/z* calcd for $C_{17}H_{20}N_3O_2S$ $[M+H]^+$ = 330.1276, found 330.1261.

Monothiourea 6. Prepared from diamine **5** according to the general procedure to provide the product **6** as a yellow solid in 40% yield, mp: 115.6-117.5 ^oC, $[\alpha]_D^{20}$ = + 3.1 (*c* 1.5, $CHCl_3$), ^1H NMR (400 MHz, MeOH-d_4) 8.26 (s, 2H), 7.63 (s, 1H), 5.06-5.00 (m, 1H), 4.72 (dd, *J* 5.1, 4.2 Hz, 1H), 4.55 (dd, *J* 4.6, 4.2 Hz, 1H), 4.35 (dd, *J* 8.2, 7.9 Hz, 1H), 4.12 (dd, *J* 8.2, 7.5 Hz, 1H), 3.65 (ddd, *J* 9.5, 7.5, 4.6 Hz, 1H), 3.55 (dd, *J* 8.8, 8.6 Hz, 1H), 3.49 (dd, *J* 9.5, 8.6 Hz, 1H). ^{13}C

NMR (100.6 MHz, MeOH-d_4) 182.9, 143.2, 132.7 (q, *J* 33.2 Hz), 124.8 (q, *J* 271.6 Hz), 123.2, 117.8, 83.9, 83.4, 73.6, 72.6, 59.4, 56.6. HRMS *m/z* calcd for $C_{15}H_{16}F_6N_3O_2S$ $[M+H]^+$ = 416.0867, found 416.0858.

General procedure for the synthesis of catalysts 7-8

To a solution of diamine **4** (200 mg, 1.39 mmol) in dry DCM (8 mL) was added anhydrous $MgSO_4$ (332.4 mg) and the aldehyde (2.77 mmol). The resulting mixture was stirred for 16 h at rt. The $MgSO_4$ was filtered off. After evaporation of the solvent, the product was recrystallized in Et_2O.

Diimine 7. Prepared according to the general procedure to provide the product **7** as a solid in 85% yield, mp: 122.3-123.3 ^oC; $[\alpha]_D^{20}$ = + 6.9 (*c* 0.82, $CHCl_3$). IR (ATR, cm^{-1}): 2880, 2851, 1644, 1585, 1565, 1468, 1436, 1282, 1087, 1067, 1049, 991, 955, 905, 819, 772, 614. ^1H NMR (400 MHz, $CDCl_3$) 8.66 (d, *J* 4.9 Hz, 2H), 8.47 (s, 2H), 8.02 (d, *J* 7.9 Hz, 2H), 7.74 (td, *J* 7.7, 1.6 Hz, 2H), 7.33 (dd, *J* 7.6, 4.8 Hz, 2H), 4.80 (s, 2H), 4.24-4.20 (m, 2H), 3.95 (dd, *J* 11.1, 4.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9, 154.1, 149.5, 136.5, 125.0, 121.5, 89.0, 75.8, 74.0.

Diimine 8. Prepared according to the general procedure to provide the product **8** as a solid in 88% yield, mp: 145.1-146.5 ^oC; $[\alpha]_D^{20}$ = + 11.6 (*c* 1.0, $CHCl_3$). IR (ATR, cm^{-1}): 3052, 2901, 2872, 1638, 1589, 1556, 1495, 1454, 1422, 1205, 1099, 1066, 1046, 972, 886, 825, 739. ^1H NMR (200 MHz, $CDCl_3$) 8.65 (s, 2H), 8.16-8.12 (m, 6H), 7.87-7.71 (m, 4H), 7.63-7.54 (m, 2H), 4.87 (s, 2H), 4.34-4.29 (m, 2H), 4.29-4.23 (m, 2H), 4.03 (d, *J* 1.8 Hz, 1H), 3.99 (d, *J* 1.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) 163.4, 154.4, 147.8, 136.5, 129.9, 129.7, 128.9, 127.7, 127.6, 118.5, 89.0, 75.9, 74.2. HRMS *m/z* calcd for $C_{26}H_{23}N_4O_2$ $[M+H]^+$ = 423.1821, found 423.1817.

General procedure for Michael addition of ketones to nitrostyrenes

To a solution of catalyst (0.02 mmol) and AcOH (0.02 mmol) in 0.4 mL of ketone in a Schlenk tube was added after 30 min nitrostyrene (0.1 mmol). The reaction was kept stirring for 2 d. The mixture was introduced into a flash column chromatography with *c*-hexane/EtOAc (4/1, v/v) as eluent to afford the product.

5-Nitro-4-phenylpentan-2-one (10a).[17,24] Colorless solid, mp: 94.4-95.4 ^oC (lit.,[17] mp: 90-92 ^oC), 65% yield, $[\alpha]_D^{20}$ - 0.95 (*c* 0.75, $CHCl_3$) 40% *ee* (Pure *R* enantiomer lit. $[\alpha]_D^{20}$ – 2.1 [*c* 0.80, $CHCl_3$)[45]], [Phenomenex® Lux 5μ cellulose-2, isooctane/*i*-PrOH = 90/10, Flow rate = 0.90 mL/min, UV = 220 nm, t_R = 28.35 min (major) and 30.40 min], ^1H NMR (200 MHz, $CDCl_3$) 7.34-7.20 (m, 5H), 4.69 (dd, *J* 12.3, 6.8 Hz, 1H), 4.60 (dd, *J* 12.3, 7.7 Hz, 1H), 4.02-3.99 (m, 1H), 2.91 (d, *J* 7.4 Hz, 2H), 2.11 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) 205.3, 138.8, 129.0, 127.9, 127.3, 79.4, 46.1, 39.0, 30.3.

4-(4-Chlorophenyl)-5-nitropentan-2-one (10b). Colorless solid, mp: 77.1-78.2 ^oC (lit.,[49] mp: 89-91 ^oC), 62% yield, 37% *ee* [Phenomenex® Lux 5μ cellulose-2, isooctane/*i*-PrOH = 90/10, Flow rate = 1.0 mL/min, UV = 210 nm, t_R = 43.92 min (major) and 50.10 min], ^1H NMR (200 MHz, $CDCl_3$) 7.33-7.27 (m, 2H), 7.19-7.14 (m, 2H), 4.69 (dd, *J* 12.5, 6.8 Hz, 1H), 4.57 (dd, J_1 =

12.5, 7.8 Hz, 1H), 4.06-3.92 (m, 1H), 2.89 (d, *J* 6.9 Hz, 2H), 2.13 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) 204.9, 137.3, 133.7, 129.2, 128.8, 79.1, 45.9, 38.4, 30.3.

5-Nitro-4-*p*-tolylpentan-2-one (10c). Colorless solid, mp: 61.0-62.8 °C (lit.,[49] mp: 70-72 °C), 63% yield, 39% *ee* [Phenomenex® Lux 5μ cellulose-2, isooctane/*i*-PrOH = 90/10, Flow rate = 0.90 mL/min, UV = 210 nm, t_R = 25.43 min (major) and 28.58 min], ^{1}H NMR (200 MHz, $CDCl_3$) 7.16-7.07 (m, 4H), 4.68 (dd, *J* 12.4, 7.2 Hz, 1H), 4.57 (dd, *J* 12.4, 7.2 Hz, 1H), 4.04-3.90 (m, 1H), 2.90 (d, *J* 7.1 Hz, 2H), 2.31 (s, 3H), 2.11 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) 205.5, 137.6, 135.7, 129.7, 127.2, 79.6, 46.2, 38.7, 30.4, 21.0.

4-(4-Methoxy-phenyl)-5-nitro-pentan-2-one (10d). Colorless solid, 51% yield, 40% *ee* [Phenomenex® Lux 5μ cellulose-2, isooctane/*i*-PrOH = 90/10, Flow rate = 0.90 mL/min, UV = 210 nm, t_R = 43.92 min (major) and 50.10 min], ^{1}H NMR (200 MHz, $CDCl_3$) 7.17-7.10 (m, 2H), 6.89-6.82 (m, 2H), 4.67 (dd, *J* 12.3, 6.9 Hz, 1H), 4.55 (dd, *J* 12.3, 7.5 Hz, 1H), 4.03-3.89 (m, 1H), 3.78 (s, 3H), 2.89 (d, *J* 7.2 Hz, 2H), 2.12 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) 205.5, 159.1, 130.6, 128.4, 114.4, 79.7, 55.2, 46.3, 38.4, 30.4.

4-(Naphthalen-1-yl)-5-nitropentan-2-one (10e). 72% yield, 24% *ee* [Phenomenex® Lux 5μ cellulose-2, isooctane/*i*-PrOH = 90/10, Flow rate = 1.0 mL/min, UV = 210 nm, t_R = 27.35 min (major) and 36.53 min], ^{1}H NMR (200 MHz, $CDCl_3$) 8.17 (d, *J* 8.6 Hz, 1H), 7.91-7.86 (m, 1H), 7.79 (d, *J* 8.0 Hz, 1H), 7.62-7.30 (m, 4H), 5.02-4.87 (m, 1H), 4.80 (s, 1H), 4.77 (d, *J* 1.6 Hz, 1H), 3.21-2.99 (m, 2H), 2.14 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) 205.5, 134.7, 134.1, 130.8, 129.2, 128.5, 126.9, 126.1, 125.2, 123.6, 122.2, 78.8, 46.0, 33.4, 30.2.

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