Chiral Ureas and Thioureas Supported on Polystyrene for Enantioselective Aza-Henry Reaction in Solvent-free conditions.

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Abstract.

Novel bifunctional ureas and thioureas inmovilized on sulfonylpystyrene have been prepared as recoverable and reusable organocatalysts and used in the stereoselective aza-Henry reaction under solvent-free conditions. The activity and stereoselection of the catalysts are dependent on the length of the tether bringing the active site and the polymer, being the catalyst derived from 1,6-hexane diamine the best one. It has been also demonstrated that the supported catalysts are more effective than the homologous soluble catalysts.

Introduction

The aza-Henry reaction constitutes an important C-C forming process, which can result in the formation of two contiguous stereocenters containing nitrogen substituents. The resulting nitroamines are valuable chiral building blocks that are easily converted in 1,2-diamines[1] or α-amino substituted carbonyl derivatives,[2] and the development of asymmetric version of the reaction has attracted continuous interest.

The first asymmetric aza-Henry reaction was attempted by using chiral heterobimetallic complexes derived from binaphtol[3] or bisoxazoline-Cu(II) complexes,[4] leading to the corresponding 2-nitroamines with good yields and enantiomeric excesses (ee). More recently, chiral bifunctional thioureas derived from *trans*-1,2-cyclohexane diamine have been successfully used as organocatalysts in the enantioselective addition of nitromethane to N-phosphinoylimines[5] and N-Boc imines[6] yielding the aza-Henry products with moderate to good enantioselectivities. Ureas and thioureas attached to different chiral structures, such as alkaloids,[7] diamines,[8] carbohydrates,[9] steroids,[10] sulfinyl group,[11] triaryliminophosphoryl,[12] oxazolino thioureas,[13] guanidino thioureas,[14] and bis-thioureas[15] have been used to promote enantioselective aza-Henry reactions.

The use of chiral squaramides[16] and bisamidine triflate salts[17] has been also documented for the diastereo and enantioselective addition of nitroethane to N-Boc imines, and chiral BINOL phosphates also act as bifunctional catalysts in the addition of nitroalkanes to aldimines.[18] In a different approach, enantioselective aza-Henry reactions have been carried out from carbamate-protected imines generated *in situ* from α-amido sulfones under phase-transfer catalysis by using guanidinium,[19]

phosphonium,[20] or quaternary ammonium salts derived from cinchone,[21] and amino acids.[22]

In general, all the ureas and thioureas described until now are highly active catalysts, but methods leading to improvement of the recovering and reuse of the catalysts are desirable, and one possible solution consists on their immobilization onto a polymeric material.[23] In that way, chiral thioureas have been anchored into different functionalized polymers,[24] mesoporous silica gel,[25] and magnetic nanoparticles,[26] but to the best of our knowledge, there are not antecedents on the use of these catalysts in the enantioselective aza-Henry reaction.

Because the use of organocatalysts supported on chemically inert material made the process more sustainable and greener,[27] and based on our previous experience in the used of sulfonyl polystyrene as support,[28] we envisaged that it was possible to anchor bifunctional ureas and thioureas to be able to promote enantioselective aza-Henry reactions. The catalytic activity of these materials is dependent on a lot of parameters, including the accessibility of the reactants to the active site, whereas the recyclability and durability of the catalyst is dependent on the robustness of the bond linking the catalyst to the polymer.[23] We have prepared catalysts from sulfonylpolystyrene and bifunctional ureas and thioureas with an additional amino group because the sulfonamide group is very stable. The supported catalysts differ in the size of the tether connecting the catalyst with the sulfonyl group and the substitution pattern on the nitrogen atom in the sulfonamide.

The general approach to the catalysts is depicted in Figure 1. Essentially, the catalysts were prepared by condensation of supported chiral triamines with 3,5-bis(trifluoro methyl) phenyl isocyanate or isotiocyanate. Chiral triamines were prepared instead by reaction of 1,2- or 1,6-diamines with natural α-amino acids followed by reduction. In

our case, we chose L-valine as a source of the chiral environment because we have previously demonstrated that bifunctional ureas and thioureas derived from this amino acid are excellent organocatalysts in several enantioselective transformations.[29]

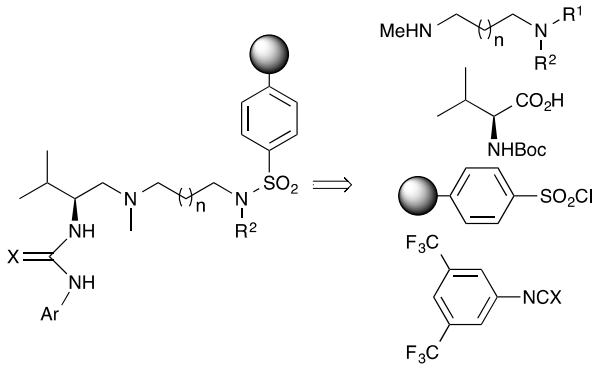
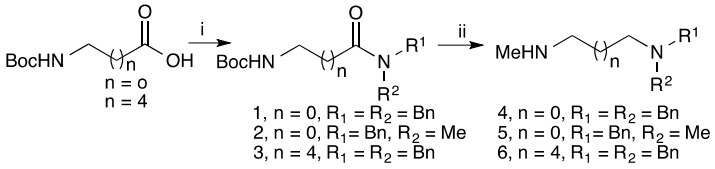


Figure 1. Proposed synthesis of supported catalysts.

Results and discussion

Starting ethylene diamine and 1,6-hexane diamine derivatives with different substituents at the nitrogen atoms were prepared, in two steps and good yields, from Boc-glycine and N-Boc amino hexanoic acid,[30] respectively, as summarized in Scheme 1.

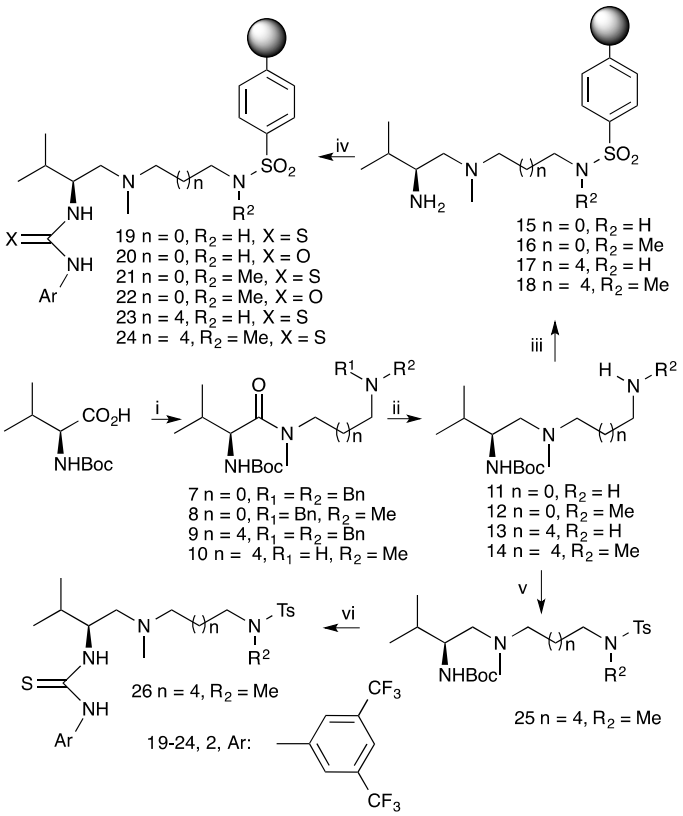


Scheme 1. : (i) 1. $ClCO_2Et$, NMM, THF, 0 ºC, then Bn_2NH for **1** and **3**, or BnNHMe for **2**. (ii) LAH, THF, reflux.

Reaction of N-Boc protected amino acids with dibenzylamine or benzyl methylamine lead to amides **1**-**3**, which were transformed into N-methyl amines **4**-**6** by reduction with lithium aluminum hydride in THF at reflux.

Supported catalysts **19**-**24** were prepared as summarized in Scheme 2. The reaction of a mixture of N-Boc-L-valine and DCC with diamines **4**-**6** or the commercially available 1,6-N,N´-dimethyl hexane diamine in DCM lead to N-Boc-L-valinamides **7**-**9** and **10**, respectively. These were transformed into triamines **11**-**14** by sequential quimioselective reduction of the amide function with LAH in THF at 0 ^{o}C, followed by hydrogenolysis of the benzyl groups in the presence of palladium on carbon or Perlman´s catalyst.

The covalent immobilization onto the polystyrene resin was done by reacting triamines **11**-**14** with chlorosulfonyl polystyrene and triethylamine in DCM at rt for 4 days leading to supported materials that were transformed into **15**-**18** by deprotection with trifluoroacetic acid in DCM for 6 h at rt, in good yields. Finally, **15** and **16**, which differ in the substitution pattern on the nitrogen of the sulfonamide, were transformed into thioureas **19** and **21** by condensation with 3,5-bis(trifluromethyl) isothiocyanate, whereas ureas **20** and **21** were also obtained from the same supported amines by reaction with 3,5-bis(trifluromethyl) isocyanate. In the same way, thioureas **23** and **24** result in the reaction of **17** and **18**, respectively, with the corresponding isothiocyanate. For comparative purposes, we also prepared the tosyl thiourea **26**, unsupported homologous of **24**, from triamine **14** by tosylation to **25** followed by deprotection and condensation with 3,5-bis(trifluromethyl) isothiocyanate.



Scheme 2. *Reagents and conditions*: (i) DCC, CH_2Cl_2, diamines **4-6** for **7-9** or $MeNH(CH_2)_6NHMe$ for **10**, 0 ºC to rt. (ii) 1. LAH, THF, 0 ºC, 1h. 2. H_2, $Pd(OH)_2$-C, MeOH for **11** and **13**; H_2, Pd/C, MeOH for **12** and **14**. (iii) 1. Sulfonyl chloride, polymer bound, CH_2Cl_2, Et_3N, rt, 4 days. 2. TFA, CH_2Cl_2, rt, 18 h. (iv) 3,5-$(CF_3)_2C_6H_3NCX$, CH_2Cl_2, 0 ^oC to rt 24h. (v) TsCl, Et_3N, CH_2Cl_2, 0 ^oC to rt. (vi) 1. TFA, CH_2Cl_2, rt, 6h. 2. 3,5-$(CF_3)_2C_6H_3NCS$, CH_2Cl_2, 0 ^oC to rt 24h.

The supported materials were characterized by IR spectroscopy, and the analytical data allowed the calculation of effective functionalization *f* (urea or thiourea contents per gram of resin) of the functionalized polymer, that varied from *f* = 0.95 for **19** to *f* = 1.11 for **22**.[31]

For comparison of the activity of the different catalysts, and optimization of the reaction conditions, we studied the reaction of N-Boc-benzaldimine **29a** with nitromethane, and the results are collected in Table 1. Initially, we test the influence

of the solvent in the reaction catalyzed by 5 mol% of thiourea **24** at rt (entries 1-4 in Table 1), observing that the reaction rate decreased when increasing the polarity of the solvent, but both the yield and the enantioselectivity increased. Fortunately, searching for greener conditions, **24** (10 mol%) was able to catalyze the reaction under solvent-free conditions, leading to the addition product **30a** with excellent yield (95%) and enantioselectivity (98/2 er) after only 3 h of reaction (entry 5).

These results are comparable with those obtained in homogeneous reaction conditions by employing urea **27** and thiourea **28**[32] as soluble catalysts, although in these cases the time decreased to 1h and 8h for the reactions without solvent or in DCM, respectively (entries 6-8 in Table 1). The catalytic activity of the supported ureas and thioureas derived from 1,2-ethylene diamine (**19**-**22**) is moderate. In neat conditions, both the yields and the enantioselection are lesser than the obtained with **24** (compare entry 5 versus 9-12 in Table 1). Moreover, thioureas **19** and **21** gave better results than ureas **20** and **22** (compare entries 9 versus 10 and 11 versus 12), and N-methyl-substituted derivatives **21** and **22** are better catalysts that unsubstituted sulfonamides **19** and **20**. This behavior parallels that of thioureas derived from 1,6-hexane diamine, being better catalyst N-methyl substituted derivative **24** than supported unsubstituted sulfonamide **23** (compare entry 5 versus 13).

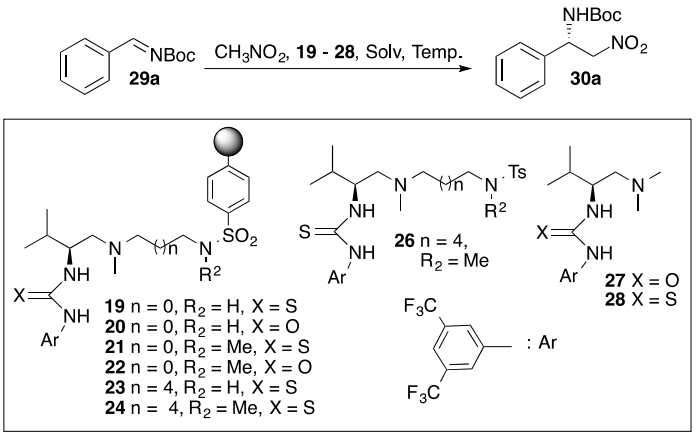


Table 1. Screening of thiourea catalysts and optimization of enantioselective aza-Henry reaction conditions of N-Boc-imine **29a** with nitromethane.

Entry[a]	Catalyst, (mol %)	Solvent	t (h)	T (ºC)	Yield (%)[b]	Er[c]
1	**24** (5%)	toluene	10	rt	72	94:6
2	**24** (5%)	CH_2Cl_2	24	rt	76	94:6
3	**24** (5%)	THF	20	rt	86	94:6
4	**24** (5%)	MeCN	24	rt	88	96:4
5	**24** (10%)	neat	3	rt	95	98:2
6	**27** (10%)	neat	1	rt	99	96:4
7	**28** (10%)	CH_2Cl_2	8	rt	84	96:4
8	**28** (10%)	neat	1	rt	85	98:2
9	**19** (10%)	neat	32	rt	45	91:9
10	**20** (10%)	neat	48	rt	34	83:17
11	**21** (10%)	neat	28	rt	72	93:7
12	**22** (10%)	neat	24	rt	68	85:15
13	**23** (10%)	neat	3	rt	85	95:5
14	**23** (5%)	neat	5	rt	80	95:5
15	**23** (2%)	neat	24	rt	78	95:5
16	**24** (5%)	neat	5	rt	93	98:2
17	**24** (2%)	neat	16	rt	85	97:3
18	**24** (5%)	neat	6	0	88	97:3
19	**24** (5%)	neat	15	-18	89	97:3
20	**26** (5%)	neat	3	rt	84	96:4

[a] Reactions were conducted at 0.3 mmol scale in 0.1 mL of nitromethane (6 equiv). [b] Isolated yield. [c] Enantiomeric ratio determined by HPLC analysis using a chiral column, and absolute configuration was determined by comparison of the HPLC retention time with that of literature data.

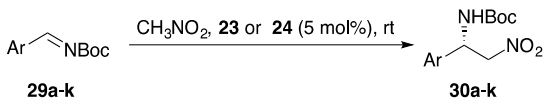
Otherwise a comparison of the results obtained with the supported catalysts derived from ethylene diamine (**19**-**22**) and 1,6-hexane diamine (**23**, **24**) showed that both the yields and enantioselectivities increased with the size of the length of the tether connecting the catalytic structure and the polymer. The effect of the amount of

catalyst in the reaction was examined by using supported thioureas **23** and **24**, and the results shown that the catalysts loading could be reduced to 2 mol% without affecting the enantioselectivity for **23** and slightly decreasing for **24**, but in both cases, at expenses of decreasing the yields, and increasing the reaction time (compare entries 13-15 and 5, 16-17 in Table 1). It is interesting to note that supported thiourea **24** provided better yield and enantioselectivity than the soluble tosyl thiourea **26** with the same functionality (compare entries 16 and 20).

In order to increase the enantioselection, the effect of the temperature was also studied, but not improvement in the er was observed when the reactions were carried out at 0 ^{o}C or -18 ^{o}C (entries 18, and 19).

After the optimization studies, we decide that the best reaction conditions consisted in using 5 mol% of supported catalysts **23** or **24**, without solvent and performing the reactions at rt. Under these conditions, we tested the generality of the reaction of nitromethane with different N-Boc aldimines **29a-k**, which differ in the electronic nature of the aryl group (Scheme 3 and Table 2).

From the data collected in Table 2 it was observed that, as a general trend, catalyst **24** was better than **23**, yielding the addition products in higher yields and enantioselectivities except for imines **29b** and **29f** with substituents with strong withdrawing effect, or imine **29j** derived from 1-naphtaldehyde.



Scheme 3. Enantioselective aza-Henry reaction with different aldimines.

Table 2. Enantioselective aza-Henry reaction of nitromethane with aldimines **29a-k** in the presence of catalyst **23** and **24**.

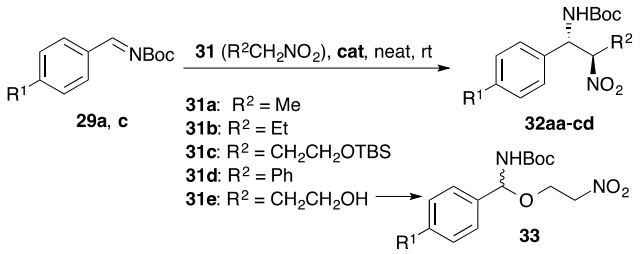
Entry[a]	Ar	Catalyst	t (h)	Product Yield (%)[b]	Er[c]
1	C_6H_5	**23**	5	**30a** (88)	95:5
2	C_6H_5	**24**	5	**30a** (93)	98:2
3	*p*-$NO_2C_6H_4$	**23**	2	**30b** (81)	95:5
4	*p*-$NO_2C_6H_4$	**24**	2	**30b** (78)	95:5
5	*p*-ClC_6H_4	**23**	3	**30c** (70)	95:5
6	*p*-ClC_6H_4	**24**	2	**30c** (88)	97:3
7	*o*-ClC_6H_4	**24**	2	**30d** (90)	94:6
8	*m*-ClC_6H_4	**24**	2	**30e** (82)	96:4
9	*p*-$CF_3C_6H_4$	**23**	2	**30f** (95)	98:2
10	*p*-$CF_3C_6H_4$	**24**	3	**30f** (89)	97:3
11	*p*-$MeOC_6H_4$	**23**	10	**30g** (73)	92:8
12	*p*-$MeOC_6H_4$	**24**	5	**30g** (91)	97:3
13	*p*-MeC_6H_4	**23**	6	**30h** (73)	94:6
14	*p*-MeC_6H_4	**24**	5	**30h** (96)	95:5
15	1-naphtyl	**23**	4	**30j** (98)	94:6
16	1-naphtyl	**24**	4	**30j** (91)	94:6
17	2-naphtyl	**23**	5	**30i** (70)	95:5
18	2-naphtyl	**24**	2	**30i** (93)	96:4
19	2-furyl	**23**	2	**30k** (67)	88:12
20	2-furyl	**24**	2	**30k** (73)	91:9
21[d]	C_6H_5	**23**	6	**30a** (83)	95:5 (100:0)[f]
22[d]	C_6H_5	**24**	6	**30a** (85)	96:4 (100:0)[f]
23[e]	C_6H_5	**24**[g]	16	**30a** (82)	97:3 (100:0)[f]

[a] The reactions were carried out with imines **29a-k** (0.3 mmol) and nitromethane (6 equiv) at room temperature in the presence of catalyst **23** or **24** (0.05 equiv). [b] Isolated yield after chromatography. [c] Enantiomeric ratio determined by HPLC analysis using a chiral column and absolute configuration was determined by comparison of the HPLC retention time with that of literature data. [d] Reaction performed with 3 mmol of imine. [e] Reaction performed with 6 mmol of imine. [f] Numbers in parenthesis indicated the er after recrystallization in hexane-EtOAc, and 100:0 means that only one enantiomer was detected in the HPLC trace. [g] Only 2 mol% of catalyst was used.

Otherwise, the reactions occurred in high yields (67-96%) and enantioselection (88:12 to 98:2 er) independently of the donating or withdrawing character of the substituent at the aromatic ring, including aldimine **29k** with a heteroaromatic substituent.

On the light of these results, we decide to scale-up the reaction (entries 21-23 in Table 2). Both catalysts **23** and **24** were able to promote the reaction of 0.567 g (3 mmol) of benzaldimine **29a** with nitrometane yielding the addition product in excellent yield and 95:5 or 96:4 er, respectively. A single recrystallization leaded nitroamine **30a** enantiomerically pure (entries 21, 22 in Table 2). Similar results were obtained increasing the amount of aldimine **29a** to 6 mmol, and using only 2 mol% of catalyst **24**, although at expenses to increase the reaction time to 16 h. (entry 23 in Table 2).

The generality of the reaction was extended to different nitroalkanes searching for stereoselective aza-Henry reaction. To this end, N-Boc imines derived from benzaldehyde (**29a**) and 4-chlorobenzaldehyde (**29c**) were reacted with different nitroalkanes (**31a-e**) in the presence of 5 mol% of catalysts **23** and **24** (Scheme 4), and the results are summarized in Table 3.



Scheme 4. Diastereo- and enantioselective aza-Henry reaction.

The reaction of imines with nitroalkanes **31a-d** yielded the known *anti*-addition products as major diastereoisomers with stereoselectivities that are dependent on the nature of the nitroalkane. Thus, nitroethane (**31a**) or nitropropane (**31b**) provided the addition products with good diastereoselectivity and very good enantioselectivity (entries 1-3 in Table 4), but phenyl nitromethane (**31d**) leaded to **32ad** in good

diastereoselectivity and poor enantioselection (entry 5).[33] Both diastereo- and enantioselection slightly improved when the reaction was carried out at 0 ^{o}C. In these conditions N-Boc-4-chloro benzaldimine (**29c**) yielded **32cd**[17b] with excellent diastereoselection but poor enantioselection when reacted with phenyl nitromethane (entry 7 in Table 4). In an attempt to prepare 2-nitro-3-aminopropanol derivatives, we reacted 2-nitroethanol (**31e**) with imine **29a**, but the ethanol derivative behaved as nucleophile by the hydroxyl group leading to the N,O-acetal **33** in excellent yield as a racemic mixture (entry 8 in Table 3). The use of the protected nitroalcohol **31c** as a nucleophile allowed the isolation of the aza-Henry product **32ac** in good yield, although with poor diastereoselectivity and moderate enantioselectivity (entry 4 in Table 3).

Table 3. Stereoselective aza-Henry reactions with representative nitroalkanes.

Entry[a]	**Reactants**	**Catalyst (mol %)**	**t (h)**	**Product (%)**[b]	**Dr**[c]	**Er**[d]
1	**29a/31a**	**23** (5%)	3	**32aa** (81)	83/17	91:9
2	**29a/31a**	**24** (5%)	2	**32aa** (94)	82/18	93:7
3	**29a/31b**	**24** (5%)	3	**32ab** (78)	88/12	97:3
4	**29a/31c**	**24** (5%)	8	**32ac** (77)	56/44	88:12
5	**29a/31d**	**24** (5%)	3	**32ad** (93)	87/13	69:31
6[e]	**29a/31d**	**24** (5%)	3	**32ad** (71)	91/9	71:29
7[e]	**29c/31d**	**24** (5%)	20	**32cd** (60)	96/4	66:34
8	**29a/31e**	**24** (5%)	2	**33** (88)	-	50/50

[a] The reactions were carried out with imines (0.3 mmol) and nitroalkanes (6 equiv) at room temperature in the presence of catalyst (0.05 equiv). [b] Isolated yield after chromatography. [c] Diastereomeric and enantiomeric ratio determined by chiral HPLC. [d] Values refer to the major anti diastereosiomers. [e] Reaction performed at 0 ^{o}C.

Finally, the recyclability of the supported catalysts was tested for **23** and **24** in the reaction of N-Boc benzaldimine with nitromethane at rt under solvent-free conditions,

and 5 mol% of catalysts. The reaction time (6 h) was maintained constant in each cycle, the catalyst used was recovered by filtration, washed, and used in the next cycle. Supported catalyst **23** was used three times affording aza-Henry product **30a** without loss of activity and enantiocontrol (entries 1-3 in Table 4). Catalyst **24** was recycled five times, maintaining the enantioselection, but it means that the activity slightly decreased for the fifth cycle, although the IR spectrum and analytical data of the recovered material did not show any difference with the starting catalyst.

Table 4. Recyclability of catalyst **23** and **24** under the optimized conditions.[a]

Entry	Catalyst	t (h)	Yield (%)[b]	Er[c]
1	**23** (cycle 1)	6	88	95:5
2	**23** (cycle 2)	6	89	95:5
3	**23** (cycle 3)	6	86	95:5
4	**24** (cycle 1)	6	82	98:2
5	**24** (cycle 2)	6	84	96:4
6	**24** (cycle 3)	6	88	97:3
7	**24** (cycle 4)	6	86	98:2
8	**24** (cycle 5)	6	74	96:4

[a] Reactions were performed with 3 mmol imine **29a** and 6 equiv of nitromethane at rt in the presence of 5 mol% of catalyst. [b] Isolated yield after column chromatography.[c] Determined by chiral HPLC.

Conclusions

In summary, we have prepared novel supported bifunctional ureas and thioureas on a matrix of sulfonylpolystyrene in few steps from cheap and commercially accessible materials. These materials have been employed as stereoselective organocatalysts in the aza-Henry reaction, under solvent free conditions, leading to the addition products with moderate diastereoselectivity and excellent enantioselectitity. The activity and enantioselection of the catalysts is dependent on the length of the tether connecting the urea or thiourea functionality with the polymer, and the best results were obtained for catalyst **24**, derived from 1,6-hexane diamine. Catalysts **23** and **24** can be recycled

for three or five times, respectively, without loss of enantioselection and slight decrease in the activity.

Experimental part

General

^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra were recorded in $CDCl_3$ as solvent. Chemical shifts for protons are reported in ppm from TMS with the residual $CHCl_3$ resonance as internal reference. Chemical shifts for carbons are reported in ppm from TMS and are referenced to the carbon resonance of the solvent. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constants in Hertz, and integration. Specific rotations were measured on a Perkin–Elmer 341 digital polarimeter using a 5-mL cell with a 1-dm path length, and a sodium lamp, and concentration is given in g per 100 mL. Infrared spectra were recorded on a Perkin–Elmer Spectrum One FT–IR spectrometer and are reported in frequency of absorption (only the structurally most important peaks are given). Melting points were obtained with open capillary tubes and are uncorrected. Flash chromatography was carried out using silica gel (230–240 mesh). TLC analysis was performed on glass-backed plates coated with silica gel 60 and an F_{254} indicator, and visualized by either UV irradiation or by staining with phosphomolybdic acid solution. Chiral HPLC analysis was performed on a JASCO HPLC system (JASCO PU-2089 pump and UV-2075 UV/Vis detector) and on Hewlett–Packard 1090 Series II instrument equipped with a quaternary pump, using a Daicel Chiralcel OD, Chiralcel OJ, Chiralpak AD-H, Chiralpak AS-H or Chiralpak IA analytical columns (250 x 4.6 mm). UV detection was monitored at 220 or at 254 nm. Elemental analyses were carried out at the Elemental Analysis Center of the Complutense University of Madrid, using a Perkin Elmer 2400 CHN analyzer.

ESI mass spectra were obtained on a Agilent 5973 inert GC/MS system. Commercially available organic and inorganic compounds were used without further purification. Solvents were dried and stored over microwave–activated 4 Å molecular sieves.

General procedure to enantioselective Aza-Henry reaction using immobilized catalysts. To a mixture of Boc-imine **29** (0.3 mmol) and catalyst (0.015 mmol, 0.05 eq), nitromethane (0.1 mL, 1.8 mmol, 6 equiv) was added and the reaction mixture was stirred at rt in a wheaton vial until consumption of the starting material. The catalyst was filtered off and washed with CH_2Cl_2 (3 x 1 mL). After solvent removal under reduced pressure, the crude mixture was purified by flash column chromatography to afford the corresponding product. The enantiomeric excess was determined by chiral-phase HPLC analysis using mixtures of hexane/isopropanol as eluent.

General procedure to enantioselective Aza-Henry reaction using homogeneous catalysts. To a mixture of Boc-imine **29a** (62 mg, 0.3 mmol) and catalyst **26** (10 mg, 0.015 mmol, 0.05 eq), nitromethane (0.1 mL, 1.8 mmol, 6 equiv) was added and the reaction mixture was stirred at rt in a wheaton vial until consumption of the starting material. After solvent removal under reduced pressure, the crude mixture was purified by flash column chromatography to afford the corresponding product. The enantiomeric excess was determined by chiral-phase HPLC analysis using mixtures of hexane/isopropanol as eluent.

Recyclability of the supported thiourea catalysts in aza-Henry reaction. At the end of the aza-Henry reaction between Boc-imine **29a** and nitromethane, the catalysts were filtered and washed with CH_2Cl_2. After being dried under vacuum, the supported catalysts were reused directly without further purification.

***tert*-Butyl (*S*)-(1-phenyl) 2-nitroethylcarbamate (30a).**[34] Obtained according to the general procedure, using N-Boc-imine **29a** (62 mg, 0.3 mmol), nitromethane (0.1 mL, 1.8 mmol) and thiourea **24** (15 mg, 0.015 mmol). The crude reaction mixture was purified by flash column chromatography (hexane/ethyl acetate: 8:1) to yield compound **30a** (78 mg, 0.28 mmol, 93%). Colorless solid. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 1.44 (s, 9H, C$\underline{H}_3$), 4.71 (m, 1H, C$\underline{H}$HN), 4.85 (m, 1H, CH$\underline{H}$N), 5.29 (m, 1H, C$\underline{H}$N), 5.35 (br. s, 1H, N$\underline{H}$); 7.31-7.39 (m, 5H, $\underline{H}$ar). HPLC (Chiralpak AD-H, hexano/isopropanol 90:10, 1mL/min, λ= 210 nm) t_R = 18.5 min (mayor, *S*), 20.3 min (minor, *R*). (er 98:2).

***tert*-Butyl (*S*)-1-(4-nitrophenyl)-2-nitroethylcarbamate (30b).**[34] Obtained according to the general procedure, using N-Boc-imine **29b** (75 mg, 0.3 mmol), nitromethane (0.1 mL, 1.8 mmol) and thiourea **24** (15 mg, 0.015 mmol). The crude reaction mixture was purified by flash column chromatography (hexane/ethyl acetate: 8:1) to yield compound **30b** (73 mg, 0.24 mmol, 78%). Colorless solid.^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.43 (s, 9H), 4.79 (m, 1H, C$\underline{H}$HN), 4.89 (m, 1H, CH$\underline{H}$N), 5.50 (m, 1H, C$\underline{H}$N), 5.70 (br. s, 1H, N$\underline{H}$), 7.53 (d, *J* = 8.7 Hz, 2H, $\underline{H}$ar), 8.22 (d, *J* = 8.7 Hz, 2H, $\underline{H}$ar). HPLC (Chiralpak AD-H, hexane/*iso*-propanol = 90:10, 254 nm, 1.0 mL/min): t_R = 32.4 min (major, *S*), 74.8 min (minor, *R*). (er 95:5).

***tert*-Butyl (*S*)-1-(4chlorophenyl)-2-nitroethylcarbamate (30c).**[34] Obtained according to the general procedure, using N-Boc-imine **29c** (72 mg, 0.3 mmol), nitromethane (0.1 mL, 1.8 mmol) and thiourea **24** (15 mg, 0.015 mmol). The crude reaction mixture was purified by flash column chromatography (hexane/ethyl acetate: 8:1) to yield compound **30c** (79 mg, 0.26 mmol, 88%). Colorless solid. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 1.44 (s, 9H, C$\underline{H}_3$), 4.66 (dd, *J* = 5.0Hz, 12.6 Hz, 1H, C$\underline{H}$HN), 4.79 (m, 1H, CH$\underline{H}$N), 5.30 (m, 1H, C$\underline{H}$N), 5.38 (br s, 1H, N$\underline{H}$), 7.25 (d, J= 8.5Hz, 2H,

Har), 7.36 (d, J= 8.5Hz, 2H, Har). HPLC (Chiralpak AD-H column, hexane/*iso*-propanol = 95:5, 220nm, 1.0 mL/min): t_R = 31.7 min (major, *S*), 43.6 min (minor, *R*). (er 96:4).

(S)-*tert*-Butyl-1-(2-chlorophenyl)-2-nitroethylcarbamate (30d).[34] Obtained according to the general procedure, using N-Boc-imine **29d** (72 mg, 0.3 mmol), nitromethane (0.1 mL, 1.8 mmol) and thiourea **24** (15 mg, 0.015 mmol). The crude reaction mixture was purified by flash column chromatography (hexane/ethyl acetate: 8:1) to yield compound **30d** (81 mg, 0.27 mmol, 90%). Colorless solid. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.44 (s, 9H, CH_3), 4.79 (m, 1H, CHHN), 4.86 (m, 1H, CHHN), 5.73 (m, 1H, CHN), 5.75 (br. s, 1H, NH), 7.30-7.40 (m, 4H, Har). HPLC (Chiralpak AD-H, hexane/*iso*-propanol = 90:10, 210 nm, 1.0 mL/min): t_R = 14.0 min (major, *S*), 21.0 min (minor, *R*). (er 94:6).

***tert*-Butyl (*S*)-1-(3-chlorophenyl)-2-nitroethylcarbamate (30e).**[34] Obtained according to the general procedure, using N-Boc-imine **29e** (72 mg, 0.3 mmol), nitromethane (0.1 mL, 1.8 mmol) and thiourea **24** (15 mg, 0.015 mmol). The crude reaction mixture was purified by flash column chromatography (hexane/ethyl acetate: 8:1) to yield compound **30e** (83 mg, 0.28 mmol, 92%). Colorless solid.^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.43 (s, 9H, CH_3), 4.69 (m, 1H, CHHN), 4.81 (m, 1H, CHHN), 5.35 (m, 1H, CHN), 5.47 (br s, 1H), 7.20-7.30 (m, 4H, Har). HPLC (Chiralpak AD-H column hexane/*iso*-propanol = 90:10, 210nm, 1.0 mL/min): t_R = 12.5 min (major, *S*), 16.7 min (minor, *R*). (er 96:4).

***tert*-Butyl (*S*)-1-(4-trifluoromethylphenyl)-2-nitroethylcarbamate (30f).**[22] Obtained according to the general procedure, using N-Boc-imine **29f** (82 mg, 0.3 mmol), nitromethane (0.1 mL, 1.8 mmol) and thiourea **24** (15 mg, 0.015 mmol). The crude reaction mixture was purified by flash column chromatography (hexane/ethyl

acetate: 8:1) to yield compound **30f** (73 mg, 0.27 mmol, 89%). Colorless solid. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 1.44 (s, 9H, C$\underline{H}_3$), 4.74 (d, J= 11.8Hz, 1H, C$\underline{H}$HN), 4.86 (m, 1H, CH$\underline{H}$N), 5.43 (m, 1H, C$\underline{H}$N), 5.43 (br s, 1H, N$\underline{H}$), 7.46 (d, J = 8.0 Hz, 2H, $\underline{H}$ar), 7.66 (d, J = 8.0 Hz, 2H, $\underline{H}$ar). HPLC (Chiralpak AD-H, hexane/*iso*-propanol = 90:10, 210 nm, 1.0 mL/min): t_R =10.5 min (major, *S*), 16.7 min (minor, *R*) (er 97:3).

***tert*-Butyl (*S*)-1-(4-methoxyphenyl)-2-nitroethylcarbamate (30g).**[34] Obtained according to the general procedure, using N-Boc-imine **29g** (70 mg, 0.3 mmol), nitromethane (0.1 mL, 1.8 mmol) and thiourea **24** (15 mg, 0.015 mmol). The crude reaction mixture was purified by flash column chromatography (hexane/ethyl acetate: 8:1) to yield compound **30g** (81 mg, 0.27 mmol, 91%). Colorless solid. ^{1}H-NMR (500 MHz, $CHCl_3$) δ 1.45 (s, 9H, C$\underline{H}_3$), 3.81 (s, 3H, C$\underline{H}_3$), 4.68 (dd, *J* = 12.5 Hz, 5.5 Hz, 1H, C$\underline{H}$HN), 4.85 (m, 1H, CH$\underline{H}$N), 5.19 (m, 1H, C$\underline{H}$N), 5.32 (br s, 1H, N$\underline{H}$), 6.90 (m, 2H, $\underline{H}$ar), 7.23 (m, 2H, $\underline{H}$ar). HPLC (Chiralcel OD, hexane/*iso*-propanol = 90:10, 220 nm, 1 mL/min): t_R = 35.0 min (minor, *R*), 39.6 min (major, *S*). (er 97:3).

***tert*-Butyl (*S*)-1-(p-tolyl)-2-nitroethylcarbamate (30h).**[14] Obtained according to the general procedure, using N-Boc-imine **29h** (62 mg, 0.3 mmol), nitromethane (0.1 mL, 1.8 mmol) and thiourea **24** (15 mg, 0.015 mmol). The crude reaction mixture was purified by flash column chromatography (hexane/ethyl acetate: 8:1) to yield compound **30h** (81 mg, 0.29 mmol, 96%). Colorless solid. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.45 (s, 9H, C$\underline{H}_3$), 2.35 (s, 3H, C$\underline{H}_3$), 4.70 (m, 1H, C$\underline{H}$HN), 4.84 (m, 1H, CH$\underline{H}$N), 5.23 (m, 1H, C$\underline{H}$N), 5.34 (br s, 1H, N$\underline{H}$), 7.19 (s, 4H, $\underline{H}$ar). HPLC (Chiralcel OJ, hexane/*iso*-propanol = 90:10, 220 nm, 1.0 mL/min): t_R = 17.8 min (major, *S*), 23.3 min (minor, *R*). (er 95:5).

***tert*-Butyl (*S*)-1-(naphthalen-2-yl)-2-nitroethylcarbamate (30i).**[22] Obtained according to the general procedure, using N-Boc-imine **29i** (77 mg, 0.3 mmol),

nitromethane (0.1 mL, 1.8 mmol) and thiourea **24** (15 mg, 0.015 mmol). The crude reaction mixture was purified by flash column chromatography (hexane/ethyl acetate: 8:1) to yield compound **30i** (87 mg, 0.28 mmol, 91%). Colorless solid.[1]H-NMR (500 MHz, $CDCl_3$) δ 1.46 (s, 9H, C$\underline{H}_3$), 4.81 (dd, *J* = 12.5 Hz, 5.5 Hz, 1H, C$\underline{H}$HN), 4.95 (m, 1 H, CH$\underline{H}$N), 5.42 (m, 1H, C$\underline{H}$N), 5.56 (br s, 1H, N$\underline{H}$), 7.41 (dd, *J* = 8.5 Hz, 2.0 Hz, 1H, $\underline{H}$ar), 7.50-7.53 (m, 2H, $\underline{H}$ar), 7.78 (s, 1H, $\underline{H}$ar), 7.83-7.85 (m, 2H, $\underline{H}$ar), 7.88 (d, *J* = 8.5 Hz, 1H, $\underline{H}$ar). HPLC (Chiralpak AD-H, hexane/*iso*-propanol = 95:5, 254 nm, 1.0 mL/min): t_R = 21.2 min (major, *S*), 34.5min (minor, *R*). (er 94:6).

***tert*-Butyl (*S*)-1-(naphthalene-1-yl)-2-nitroethylcarbamate (30j).**[34] Obtained according to the general procedure, using N-Boc-imine **29j** (77 mg, 0.3 mmol), nitromethane (0.1 mL, 1.8 mmol) and thiourea **24** (15 mg, 0.015 mmol). The crude reaction mixture was purified by flash column chromatography (hexane/ethyl acetate: 8:1) to yield compound **30j** (88 mg, 0.28 mmol, 93%). Colorless solid. [1]H-NMR (500 MHz, $CDCl_3$): δ 1.45 (s, 9H, C$\underline{H}_3$), 4.91 (m, 2H, C$\underline{HH}$N), 5.31 (m, 1H, C$\underline{H}$N), 6.28 (br. s, 1H, N$\underline{H}$), 7.47 (m, 2H, $\underline{H}$Ar), 7.56 (t, *J* = 7.5 Hz, 1H, $\underline{H}$ar), 7.62 (t, *J* = 7.3 Hz, 1H, $\underline{H}$ar), 7.86 (dd, *J* = 5.7, 3.5 Hz, 1H, $\underline{H}$ar), 7.91 (d, *J* = 8.2 Hz, 1H, $\underline{H}$ar), 8.13 (d, *J* = 8.2 Hz, 1H, $\underline{H}$ar). HPLC (Chiralpak AD-H, hexane/*iso*-propanol = 90:10, 210 nm, 1.0 mL/min): t_R = 45.7 min (major, *S*), 58.5 min (minor, *R*). (er 96:4).

(*S*)-*tert*-Butyl 1-(furan-2-yl)-2-nitroethylcarbamate (30k).[34] Obtained according to the general procedure, using N-Boc-imine **29k** (59 mg, 0.3 mmol), nitromethane (0.1 mL, 1.8 mmol) and thiourea **24** (15 mg, 0.015 mmol).The crude reaction mixture was purified by flash column chromatography (hexane/ethyl acetate: 8:1) to yield compound **30k** (56 mg, 0.22 mmol, 73%). Colorless solid.[1]H-NMR (500 MHz, $CDCl_3$): δ 1.45 (s, 9H, C$\underline{H}_3$), 4.71-4.74 (dd, *J* = 12.9, 5.7 Hz, 1H, C$\underline{H}$HN), 4.85 (m, 1H, CH$\underline{H}$N), 5.29 (m, 1H, C$\underline{H}$N), 5.45 (br s, 1H, N$\underline{H}$), 6.30-6.34 (m, 2H, $\underline{H}$ar), 7.37

(s, 1H, Har). HPLC (Daicel Chiralpak AD-H, hexane/*iso*-propanol = 90:10, 220nm, 1.0 mL/min): t_R = 13.7min (major, *S*) 15.8 min (minor, *R*). (er 91:9).

***tert*-Butyldimethyl(2-nitroethoxy)silane (31c).** To a solution of the 2-nitroethanol (0.79 mL, 11 mmol) and imidazole (1.87 g, 27.5 mmol, 2.5 equiv) in DMF (15 mL) was added tert-butyldimethylsilyl chloride (1.98 g, 13.2 mmol, 1.2 equiv) and the mixture was stirred at room temperature overnight. The reaction was quenched with aqueous saturated NH_4Cl solution (25 mL) and decanted. The aqueous phase was extracted with ether (4 x 15 mL), the combined organic phases where washed with brine (4 x 15 mL), dried ($MgSO_4$) and the solvent was evaporated to yield an oil which was used without further purification. Yield (2.15 g, 10.5 mmol, 95%). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.05 (s, 6H, C$\underline{H}_3$), 0.85 (s, 9H, C$\underline{H}_3$), 4.13 (m, 2H, C$\underline{H}_2$), 4.44 (m, 2H, C$\underline{H}_2$). ^{13}C -NMR (126 MHz, $CDCl_3$) δ 3.6 (C$\underline{H}_3$), 25.6 (C$\underline{H}_3$), 25.7 (C$\underline{C}(CH_3)_3$), 59.5 (C$\underline{H}_2$O), 77.6 (C$\underline{H}_2$N). IR (ATR): 2953, 2934, 2858, 1554, 1468, 1373, 1259, 1116, 944, 830, 778 cm^{-1}. HRMS calcd. for $C_8H_{19}NO_3Si$ + H: 206.1207; found: 206.1202.

***tert*-Butyl [(1*R*, 2*S*)-2-nitro-1-phenylpropyl]carbamate (32aa).**[14] Obtained according to the general procedure, using N-Boc-imine **29a** (62 mg, 0.3 mmol), nitroethane (0.13 mL, 1.8 mmol) and thiourea **24** (15 mg, 0.015 mmol). The crude reaction mixture was purified by flash column chromatography (hexane/ethyl acetate: 15:1) to yield compound **32aa** as a mixture of *anti/syn* diastereomers (69 mg, 0.25 mmol, 84%). Colorless solid. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 1.44 (s, 9H, C$\underline{H}_3$), 1.54 (d, *J* = 7.0 Hz, 3H, C$\underline{H}_3$), 4.92 (br s, 1H, N$\underline{H}$), 5.11 (m, 0.2H, CH$\underline{H}$N), 5.19 (t, *J* = 7.5 Hz, 0.8H, CH$\underline{H}$N), 5.34 (br s, 0.8H, C$\underline{H}$HN), 5.58 (m, 0.2H, C$\underline{H}$HN), 7.22-7.27 (m, 2H, Har), 7.32-7.37 (m, 3H, Har). HPLC (Chiralpak IA, hexane/*iso*-propanol = 98:2, 220 nm, 1 mL/min): dr (*anti:syn*): 82:18; *major (anti)*: t_r (major) = 23.1 min, t_r

(minor) = 24.4 min, (er 92:8), t_r *minor (syn)*: t_r (major) = 36.0 min, t_r (minor) = 26.4 min. (er 83:17).

***tert*-Butyl [(1*R*, 2*S*)-2-nitro-1-phenylbutyl]carbamate (32ab).**[14] Obtained according to the general procedure, using N-Boc-imine **29a** (62 mg, 0.3 mmol), 1-nitropropane (0.16 mL, 1.8 mmol) and thiourea **24** (15 mg, 0.015 mmol). The crude reaction mixture was purified by flash column chromatography (hexane/ethyl acetate: 15:1) to yield compound **32ab** as a mixture of *anti/syn* diastereomers (68 mg, 0.23 mmol, 77%). Colorless solid. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.98 (t, J = 7.0 Hz, 3H, C<u>H</u>$_3$), 1.42 (s, 9H, C<u>H</u>$_3$), 1.85-1.90 (m, 1H, C<u>H</u>H), 2.04 (m, 1H, CH<u>H</u>), 4.73 (br s, 1H, N<u>H</u>), 5.13 (m, 2H, C<u>HH</u>N), 7.22 (m, 2H, <u>H</u>Ar), 7.34 (m, 3H, <u>H</u>Ar). HPLC (Chiralpak AD-H, hexane/iso-propanol = 95:5, 220 nm, 1 mL/min): dr (*anti:syn*): 78/22; *major (anti*): t_r (major) = 13.9 min, t_r (minor) 15.5 min. (er 96:4), *minor (syn*): t_r (major) = 11.9 min, t_r (minor) = 17.3 min (er 72:28).

(1*S*,2*R*)-3-(*tert*-Butyldimethylsilyloxy)-2-nitro-1-phenylpropyl carbamic acid t-butyl ester (32ac).[14] Obtained according to the general procedure, using N-Boc-imine **29a** (62 mg, 0.3 mmol), *tert*-Butyldimethyl(2-nitroethoxy)silane (**31c**) (0.37g, 1.8 mmol) and thiourea **24** (15 mg, 0.015 mmol).The crude reaction mixture was purified by flash column chromatography (n-pentane/ CH_2Cl_2: 2:1) to yield compound **32ac** as a mixture of *anti/syn* diastereomers (91 mg, 0.22 mmol, 74%). Colorless oil.^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.05 (s, 3H, C<u>H</u>$_3$), 0.07 (s, 3H, C<u>H</u>$_3$), 0.89 (s, 9H, C<u>H</u>$_3$), 1.40 (s, 9H, C<u>H</u>$_3$), 3.99 (dd, *J* = 5.9 Hz, 11.9 Hz, 1H, CH<u>H</u>OTBDMS), 4.12-4.15 (dd, *J* = 3.2 Hz, 11.9 Hz, 1H, C<u>H</u>HOTBDMS), 4.73 (m, 1H, C<u>H</u>N), 5.43 (m, 1H, C<u>H</u>NO_2), 5.81 (br s, 1H, N<u>H</u>), 7.28-7.35 (m, 5H, <u>H</u>ar). HPLC [Chiralpak AD-H, hexane/*iso*-propanol = 98:2, λ 220 nm, 1 mL/min]: dr (*anti:syn*): 56/44 ; *major (anti)*: t_r (major)

18.3 min, t_r (minor) 41.5 min; *minor* (er 88:12); *(syn)*: t_r (major) 31.7 min, t_r (minor) 21.1 min (er 87:13).

***tert*-Butyl (1*S*,2*R*)-2-nitro-1,2-diphenylethyl)carbamate (32ad).** Obtained according to the general procedure, using N-Boc-imine **29a** (62 mg, 0.3 mmol), phenylnitromethane (0.213 mL, 1.8 mmol) and thiourea **24** (15 mg, 0.015 mmol). The crude reaction mixture was purified by flash column chromatography (hexane/ethyl acetate: 15:1) to yield compound **32ad** as a mixture of *anti/syn* diastereomers (81 mg, 0.24 mmol, 79%). Colorless solid. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.26 (s, 9H, C<u>H</u>$_3$), 4.77 (s, 1H, N<u>H</u>), 5.69 (br s, 1H, C<u>H</u>N), 5.78 (br s, 1H, C<u>H</u>N), 7.35-7.59 (m, 9H, <u>H</u>ar). ^{13}C- NMR (126 MHz, $CDCl_3$) δ 27.4 (<u>C</u>H$_3$), 56.1 (<u>C</u>HNO$_2$), 78.6 (<u>C</u>(CH$_3$)$_3$), 94.1 (<u>C</u>HN), 127.7, 128.3, 128.7, 128.8, 130.1 (CHar), 132.7 (<u>C</u>ar), 138.9 (Car), 154.5 (<u>C</u>O). IR (ATR)**:** 3390, 2978, 2924, 2849, 1684, 1545, 1521, 1456, 1367, 1288, 1253, 1010, 891, 856, 792, 757, 742, 697, 588, 539 cm^{-1}**.** HRMS calcd. for $C_{19}H_{22}N_2O_4$ + Na: 365.1472; found: 365.1475. HPLC (Chiralpak AD-H, hexane/iso-propanol = 95:5, 210 nm, 1 mL/min): dr (*anti:syn*): 91:9; *major (anti*): t_r (major) = 52.7 min, t_r (minor) 59.3 min (er 71:29), *minor (syn*): t_r (major) = 37.1 min, t_r (minor) = 81.4 min (er 66:35). Recrystallization from toluene provided **32ad** as a colorless solid of dr 97:3 and er 65:35. $[\alpha]_D^{23}$ = +11.5 (c = 1.0, $CHCl_3$).

***tert*-Butyl (1*S*,2*R*)-1-(4-chlorophenyl)-2-nitro-2-phenylethylcarbamate (32cd).**[17b]

Obtained according to the general procedure, using N-Boc-imine **29c** (62 mg, 0.3 mmol), phenylnitromethane (0.213 g, 1.8 mmol) and thiourea **24** (15 mg, 0.015 mmol). The crude reaction mixture was purified by flash column chromatography (hexane/ethyl acetate: 15:1) to yield compound **32cd** as a mixture of *anti/syn* diastereomers (91 mg, 0.25 mmol, 84%). Colorless solid. $[\alpha]_D^{23}$ = +4.0 (c = 1, $CHCl_3$). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.26 (s, 9H, C<u>H</u>$_3$), 4.86 (br s, 1H, N<u>H</u>), 5.62

(br s, 1H, CHN), 5.76 (br s, 1H, $CHNO_2$), 7.28-7.55 (m, 9H, Har). HPLC (Chiralpak IA, hexane/iso-propanol = 97:3, 230 nm, 1 mL/min): dr (*anti:syn*): 96:4; *major (anti*): t_r (major) = 44.5 min, t_r (minor) 33.0 min (er 66:34), *minor (syn*): t_r (major) = 86.5 min, t_r (minor) = 37.8 min (er 72:28).

***tert*-Butyl ((2-nitroethoxy)(phenyl)methyl)carbamate (33).** Obtained according to the general procedure, using N-Boc-imine **29a** (62 mg, 0.3 mmol), 2-nitroethanol (0.13 mL, 1.8 mmol) and thiourea **24** (15 mg, 0.015 mmol). The crude reaction mixture was purified by flash column chromatography (hexane/ethyl acetate: 4:1) to yield compound **33** as a racemate (78 mg, 0.26 mmol, 88%). Colorless oil. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.49 (s, 9H, CH_3), 4.22 (dd, J = 55.9, 5.9 Hz, 2H, CHHO), 4.61 (d, J = 2.7 Hz, 2H, CHHN), 5.20 (d, J = 10Hz, 1H, NH), 6.00 (d, J = 9.9 Hz, 1H, CHN), 7.36 (m, 5H, HAr). ^{13}C- NMR (126 MHz, $CDCl_3$) δ 28.3 (CH_3), 63.5 (CH_2N), 75.0 (CH_2O), 80.6 ($C(CH_3)_3$), 82.3 (CHO), 125.8 (Car, 2C), 128.6 (Car, 2C), 138.48 (Car), 155.34 (C=O). IR (ATR): 3343, 3060, 2982, 2937, 1693, 1553, 1513, 1362, 1247, 1167, 1101, 1021, 876, 695 cm^{-1}. HRMS calcd. for $C_{14}H_{20}N_2O_5$ + Na: 319.1264; found: 319.1266. HPLC (Chiralpak AD-H, hexano/isopropanol 95:5, 1mL/min, λ= 210 nm) t_R = 15.8 min (mayor, *S*), 19.8 min (minor, *R*) (er 50:50).

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Electronic Supplementary Information Available: Experimental procedure for the synthesis of supported catalysts, copies of ^{1}H-NMR and ^{13}C-NMR spectra for all new compounds and copies of the HPLC chromatograms are available as supplementary information.

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