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Polymer-Supported Enantioselective Bifunctional Catalysts for Nitro-Michael Addition of Ketones and Aldehydes

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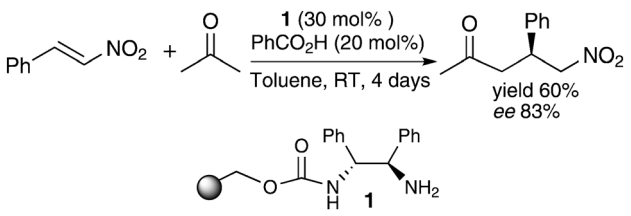
Abstract: Introduction of an L-amino acid as a spacer and a urea-forming moiety in a polymer-supported bifunctional urea–primary amine catalyst, based on (1*R*, 2*R*)-(+)-1,2-diphenylethylenediamine, significantly improves the catalyst's activity and stereoselectivity in the asymmetric addition of ketones and aldehydes to nitroolefins. Yields and enantioselectivities, unprecedented for immobilized catalysts, were obtained with such challenging donors as acetone, cyclopentanone, and α,α-disubstituted aldehydes, which usually perform inadequately in this reaction (particularly when a secondary-amine-based catalyst is used). Remarkably, though in the examined catalysts the D-amino acids as spacers were significantly inferior to the L isomers, for the chosen configuration of the diamine (match–mismatch pairs) the size of the side chain of the amino acid hardly influenced the enantioselectivity of the catalyst. These results, combined with the reactivity profile of the catalysts with substrates bearing two electron-withdrawing groups and the behavior of the catalysts' analogues based on tertiary (rather than primary) amine, suggest an enamine-involving addition mechanism and a particular ordered C–C bond-forming transition state as being responsible for the catalytic reactions with high enantioselectivity.

Keywords: asymmetric catalysis · bifunctional catalysis · immobilization · nitro-Michael addition · organocatalysis

Introduction

The revival of interest in enantioselective catalysis by small metal-free organic molecules (organocatalysts) has led to a reality wherein tens of new organocatalysts are designed and prepared each year. Although many new single-step and cascade organocatalyzed reactions are reported annually, some of the "textbook" organic processes are particularly suitable for testing new amine-based catalytic systems. Thus, the Michael addition of ketones and aldehydes to nitroolefins has emerged during the past 5 years into one of the "litmus test" reactions for new organocatalysts.[1,2] Among the numerous asymmetric carbon–carbon bond-forming reactions, this addition constitutes an important and powerful tool for the introduction of chirality and represents a convenient access to γ-nitro carbonyl compounds, useful intermediates en route to valuable building blocks.[3] Mostly, enantioselective nitro-Michael addition was explored with homogeneous catalytic systems, whereas only a few reports describing catalysts immobilized on insoluble supports have been published recently.[4] In the overwhelming majority of the reports, which deal with soluble as well as insoluble catalysts, the benchmark test reaction was that of cyclohexanone with β-nitrostyrene.[5] Outstanding yields and stereoselectivities are usually reported for this process, but changing the nucleophilic substrate from cyclohexanone to an acyclic ketone (e.g., acetone), sterically hindered ketone or aldehyde (e.g., isobutyraldehyde), or even to cyclopentanone frequently brings a dramatic decline in the catalyst performance.[4a–g,5b–d,6] Accordingly, we focused our study of supported organocatalysis of the nitro-Michael addition on the model reaction between acetone and β-nitrostyrene, and recently communicated our preliminary findings (Scheme 1) describing a polystyrene-supported bifunctional aminocarbamate catalyst **1**.[7]

Herein, we report the extension of these studies to other substrates, as well as elaboration of the catalyst design to a more active and stereoselective variant—an improvement that was achieved through the introduction of a second chiral center in a remote position.



Scheme 1. Nitro-Michael addition reaction promoted by catalyst **1**.

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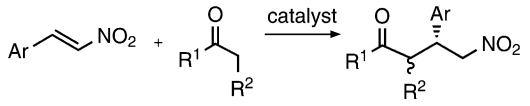
Results and Discussion

We recently reported that the bifunctional catalyst **1** incorporating a carbamate and primary amine functions, synthesized on a solid support by using a chiral diphenylethylenediamine building block, promotes the reaction of acetone and nitroolefins (Scheme 1) with appreciable enantioselectivity, unmatched by heterogeneous catalysts known at that time (Table 1, entries 1–3).[7]

Table 1. Asymmetric nitro-Michael addition of ketones to nitroolefins.[a]



Entry	Catalyst	Ar	R^1, R^2	Additive	Yield [%][b]	d.r. (*syn*/*anti*)[c]	*ee* [%][d]
1	**1**	Ph	CH_3, H	$PhCO_2H$	60	–	83
2	**1**	2-furanyl	CH_3, H	$PhCO_2H$	30	–	92[e]
3	**1**	2,4-$Cl_2C_6H_3$	CH_3, H	$PhCO_2H$	73	–	82
4	**1**	Ph	-$(CH_2)_4$-	$PhCO_2H$	52	1.2:1	73, 93
5	**1**	Ph	-$(CH_2)_3$-	$PhCO_2H$	82	4:1	97, 62[e]
6	**1**	Ph	CH_3, H	(*S*)-2-phenyl-propionic acid	52	–	81
7	**1**	Ph	CH_3, H	(*R*)-2-phenyl-propionic acid	61	–	80
8	**2**	Ph	CH_3, H	$PhCO_2H$	99	–	91
9[f]	**2**	Ph	CH_3, H	$PhCO_2H$	99	–	91
10[f]	**2**	Ph	CH_3, H	–	89	–	91
11	**2**	2-furanyl	CH_3, H	$PhCO_2H$	99	–	97[e]
12	**2**	Ph	-$(CH_2)_4$-	$PhCO_2H$	82	2.6:1	86, 92
13	**2**	Ph	-$(CH_2)_3$-	$PhCO_2H$	99	4:1	96, 88[e]

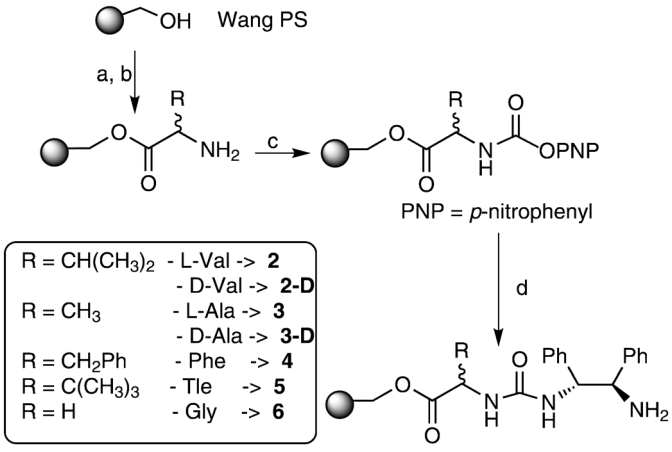
[a] Reaction conditions: nitroolefin (0.25 mmol), ketone (1.25 mmol), additive (0.05 mmol),catalyst (0.075 mmol), solvent (2 mL); 4 days, RT. [b] Determined by NMR spectroscopy. [c] Diastereomeric ratio. [d] Enantiomeric excess (*ee*) was determined by HPLC with a Chiralcel OJ column. [e] *ee* value was determined by HPLC with a Chiralpak AD column. [f] Reaction time 2 days.

This enantioselectivity was, however, still inferior to that of the best homogeneous systems.[8] Moreover, only a moderate yield could be reached with this catalytic system, even with prolonged reaction times and with benzoic acid as a co-catalyst. By using the same catalytic systems cyclic ketones could be added to nitroolefins (Table 1, entries 4 and 5), but again with moderate to good yields (although one of the diastereomers in this case was formed with a very high enantioselectivity). Surprisingly, the results obtained with cyclopentanone were notably better than those with cyclohexanone, although frequently the opposite tendency is observed.[4e–g,5b,c,6b–h,9]

Seeking to improve the reaction outcome, we tried to substitute the achiral benzoic acid by a chiral carboxylic acid co-catalyst (Table 1, entries 6 and 7). Although a minor mismatch effect on the activity was observed for the (*S*)-2-phenylpropionic acid, the enantioselectivity with both isomers of the catalyst was practically unchanged.

Our preliminary study implied that the introduction of a short linear spacer between the polymer core and the catalytic unit improves the reactivity of the catalyst, with only a minor impairment of its stereoselectivity. Inspired by the ability of peptides and peptidomimetics to promote enantioselective catalysis,[10] as well as by the structure of some of the highly selective homogeneous thiourea catalysts for the nitro-Michael addition developed by Tsogoeva et al. and Jacobsen et al.,[8a–c,11] we decided to introduce an amino acid spacer between the catalyst and the Wang linker of the support, thus transposing an aminocarbamate catalyst into an amino-urea catalyst (Scheme 2). Through this design, we hoped to achieve a cooperative enhancement of the stereoselectivity. Remarkably, the incorporation of L-valine, as described in Scheme 2, led to catalyst **2** which displayed an enhanced activity and stereoselectivity in the reaction of ketones with nitroolefins. Thus, the enantiomeric excess (*ee*) in the reactions of acetone reached 91–97%, with a concurrent sharp increase in the reaction yield (Table 1, compare entries 1 and 2 with 8 and 11, respectively). With benzoic acid as a co-catalyst, the time required for the quantitative addition of acetone to nitrostyrene could be reduced to 48 h, whereas without acid a slightly lower yield was obtained (Table 1, entries 9 and 10). For cyclic ketones, the yields were also substantially improved, and for the adducts derived from cyclopentanone, the *ee* value of the minor isomer was notably improved, whereas the high *ee* value of the major isomer was preserved (Table 1, compare entries 4 and 5 with 12 and 13, respectively). Notably, the NMR analysis of the crude filtrates of the reaction mixture demonstrated that the presence of the benzoic acid additive did not lead to any detectable cleavage of the catalyst **2** from the Wang support during the course of the reaction.

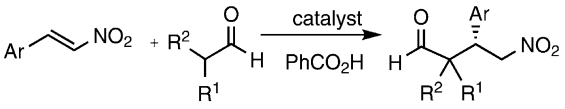
The catalysts **1** and **2** were also tested in the nitro-Michael addition of aldehydes and nitroole-



Scheme 2. Synthesis of amino acid-linked catalysts. Reagents and conditions: a) Fmoc-D/L-AA-OH, DIC, DMAP, DMF, RT, 6 h; b) piperidine/DMF (2:8), RT, 2–3 min; c) *p*-nitrophenylchloroformate, DIPEA, THF, RT, 2 h; d) (1*R*,2*R*)-(+)-1,2-diphenylethylenediamine, DMF, 50 °C, 24 h. Fmoc = 9-fluorenylmethoxycarbonyl, AA = amino acid, DIC = diisopropylcarbodiimide, DMAP = 4-dimethylaminopyridine, DIPEA = *N*,*N*-diisopropylethylamine.

fins (Table 2).[12] The reaction exhibited a very good chemoselectivity, producing the conjugate addition product only, without formation of the homoaldol or other byproducts in any substantial amount. In the reactions of the α-branched

Table 2. Asymmetric nitro-Michael addition of aldehydes to nitroolefins.[a]



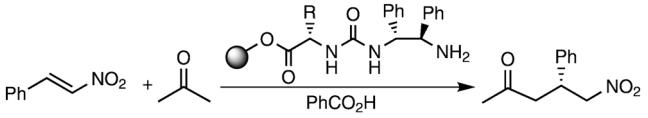
Entry	Catalyst	Ar	R^1, R^2	Yield [%][b]	d.r. (*syn*/*anti*)	*ee* [%][c]
1	**1**	Ph	Me, Me	60	–	99
2	**2**	Ph	Me, Me	70	–	99
3	**1**	2-furanyl	Me, Me	84	–	99
4	**2**	2-furanyl	Me, Me	93	–	99
5	**1**	Ph	$(CH_2)_5$	12	–	12[d]
6	**2**	Ph	$(CH_2)_5$	42	–	55[d]
7	**1**	2-furanyl	$(CH_2)_5$	32	–	99[d]
8	**2**	2-furanyl	$(CH_2)_5$	57	–	99[d]
9	**1**	Ph	$(CH_3)_2CH$, H	20	3:1	82[d,f]
10	**2**	Ph	$(CH_3)_2CH$, H	23	99:1	81[d,f]
11	**1**	Ph	Me, H	47	2:1	40[e,f]
12	**2**	Ph	Me, H	71	2:1	38[e,f]

[a] Reaction conditions: nitroolefins (0.25 mmol), aldehyde (0.5 mmol), $PhCO_2H$ (0.05 mmol), catalyst (0.075 mmol), solvent (2 mL); 4 days, RT. [b] Determined by NMR spectroscopy. [c] *ee* value was determined by HPLC with a Chiralcel OD column. [d] *ee* value was determined by HPLC with a Chiralpak AD column. [e] *ee* was determined by HPLC with a Chiralcel OJ column. [f] *ee* value for major diastereomer.

isobutyraldehyde and cyclohexylcarboxaldehyde the yields were notably better for catalyst **2**, and in most cases near-perfect enantioselectivity was demonstrated. In the case of cyclohexylcarboxaldehyde and β-nitrostyrene, the surprisingly low enantioselectivity reached by catalyst **1** was markedly improved for catalyst **2**. Replacement of catalyst **1** by **2** also led to a slight yield and substantial diastereoselectivity improvement in the reaction of the β-branched isovaleraldehyde, while the enantioselectivity was preserved. Improvement in yield along with the preservation of diastereo- and enantioselectivity was also observed for the comparison of **2** and **1** in the reaction of a linear propionaldehyde. Notably, it seems that, in aldehydes, substitution at the α position does not lead, by itself, to a reduced reactivity in the reaction, whereas substitution at the β-carbon atoms has a strong inhibiting effect on the reaction.

We prepared a series of analogues of catalyst **2** to assess the importance of the second chiral center in the molecule and the influence of the adjacent substituents (the side chain of the amino acid). Remarkably, in the reaction of nitrostyrene with acetone all L-amino acid-based catalysts exhibited similar enantioselectivity (ca. 90% *ee*, Table 3, entries 1–4), whereas only a moderate influence of the steric size of the amino acid side chain on the yield is notable. Thus, the yield achieved under the indicated conditions increases from 87% for **3** based on L-Ala to >99% for **5** based on L-Tle. The inversion of the stereochemistry at the

Table 3. Influence of the side chains of different amino acids on the asymmetric nitro-Michael addition of acetone to *trans*-β-nitrostyrene.[a]



Entry	Catalyst	R	Yield [%][c]	*ee* [%][d]
1	**3**	CH_3	87	89
2	**4**	CH_2Ph	92	91
3	**2**	$CH(CH_3)_2$	99	91
4	**5**	$C(CH_3)_3$	99	89
5	**3**-D[b]	CH_3	37	80[e]
6	**2**-D[b]	$CH(CH_3)_2$	62	77[e]
7	**6**	H	89	86

[a] Reaction conditions: nitroolefins (0.25 mmol), acetone (1.25 mmol), $PhCO_2H$ (0.05 mmol), catalyst (0.075 mmol), solvent (2 mL); 4 days, RT. [b] Isomer D of the amino acid. [c] Determined by NMR spectroscopy. [d] *ee* value was determined by HPLC with a Chiralcel OJ column. [e] The opposite enantiomer is predominantly formed.

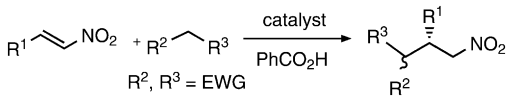
amino acid chiral center led, however, to catalysts with reduced enantioselectivity and significantly reduced yield (Table 3, entries 5 and 6). The catalyst **6** based on Gly still exhibits a reasonable yield and only a slightly reduced selectivity. In all cases, the configuration of the favored stereoisomer of the adduct was dictated by the chiral centers of the diamine component, rather than by that of the amino acid.

The intriguing dependence of the catalyst selectivity on the configuration of the α-carbon of the amino acid, but not on the steric size of its side chain, must be a consequence of the reaction mechanism and particularly the transition state. A number of experiments conducted in our group, though less impressive than the aforementioned reactions in terms of enantioselectivity, may shed light on the mechanism of the addition of ketones and aldehydes to nitroolefins with our catalytic systems.

Thus, pronucleophiles stabilized by two electron-withdrawing functionalities can be divided into two groups, based on their reactivity towards nitroolefins promoted by **1** or **2** (Table 4). Substrates including the ketone group (i.e., acetylacetone and acetoacetates; Table 4, entries 1–4) react with moderate to excellent yields, while exhibiting appreciable enantioselectivity.[13] On the other hand, pronucleophiles lacking the ketone (i.e., malonates; Table 4, entries 5 and 6) exhibited low reactivity toward nitroolefins when our catalytic systems were applied, and formed racemic or almost racemic products.

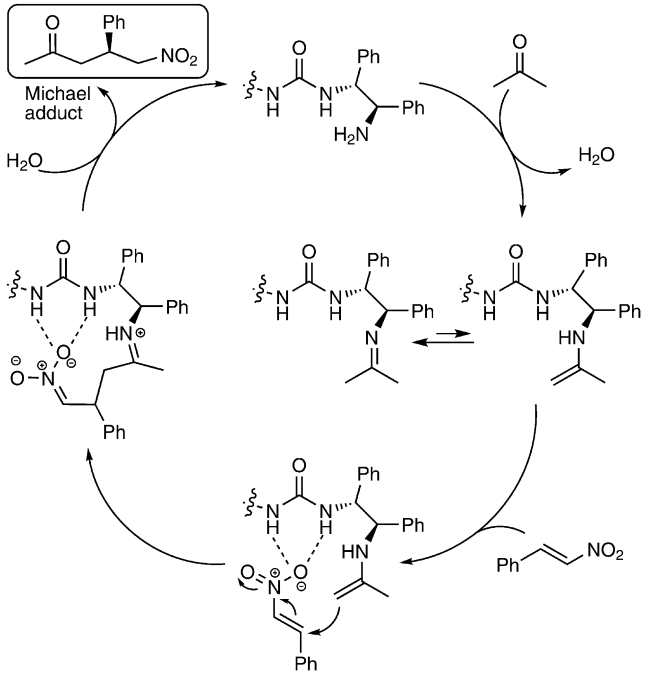
Our results, in combination with a vast array of data found in the literature, provide a number of insights into the design of organocatalysts for different variants of the nitro-Michael addition and into the mechanism of the catalysis. The substantial activity of the catalysts with ketone- or aldehyde-containing nucleophiles, versus the low efficiency of catalysis and lack of enantioselectivity with such substrates as dimethyl malonate, point to the enamine-involving mechanism of activation of the nucleophile in the case of the former substrates (Scheme 3). In the case of the malonate and similar highly activated pronucleophiles, the deprotona-

Table 4. Asymmetric nitro-Michael addition of nucleophiles with two electron-withdrawing groups to nitroolefins.[a]

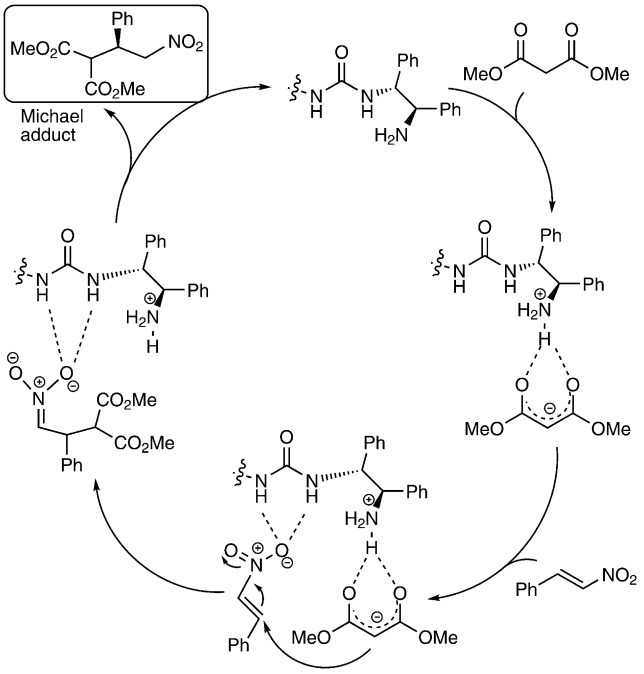


Entry	Catalyst	R^1	R^2, R^3	Yield [%][b]	d.r.	*ee* [%][c]
1	**2**	Ph	CH_3CO, CH_3CO	25	–	63[e]
2[d]	**2**	Ph	CH_3CO, CH_3CO	79	–	47[e]
3	**2**	Ph	CH_3CO, CO_2CH_3	99	1:1	nd
4	**2**	Ph	CH_3CO, $CO_2C_2H_5$	99	1:1.2	nd
5	**1**	Ph	CO_2CH_3, CO_2CH_3	15	–	rac
6	**2**	Ph	CO_2CH_3, CO_2CH_3	14	–	27

[a] Reaction conditions: nitroolefins (0.25 mmol), nucleophile (1.25 mmol), $PhCO_2H$ (0.05 mmol), catalyst (30 mol%), solvent (2 mL); 4 days, RT. [b] Determined by NMR spectroscopy. [c] *ee* value was determined by HPLC with a Chiralcel OJ column. [d] Reaction temperature 75°C. [e] *ee* value was determined by HPLC with a Chiralpak AD column. nd = not determined.

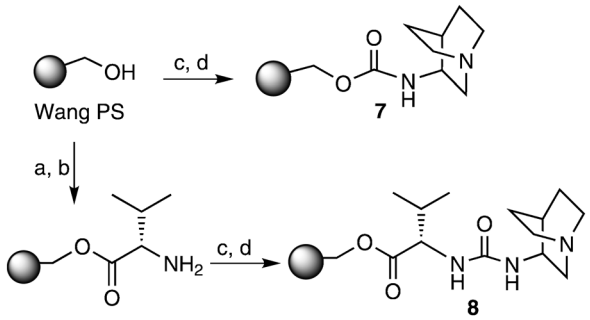


Scheme 3. Enamine-based mechanism.



Scheme 4. Deprotonation-based mechanism.

amine (Scheme 5). These new catalysts **7** and **8** promoted the nitro-Michael addition of dimethyl malonate to nitro-



Scheme 5. Synthesis of urea–tertiary amine catalysts. Reagents and conditions: a) Fmoc-Val-OH, DIC, DMAP, DMF, RT, 6 h; b) piperidine/DMF (2:8), RT, 2–3 min; c) *p*-nitrophenylchloroformate, DIPEA, THF, RT, 2 h; d) (*S*)-(−)-3-aminoquinuclidine·2HCl, DIPEA, DMF, 50°C, 24 h.

tion-based mechanism may be active (Scheme 4), but it must be inefficient due to the relatively low basicity of the primary amine. The somewhat reduced *ee* value in the case of diketones and ketoesters, as compared to simple ketones, may originate from both mechanistic pathways being active, whereas the deprotonation-based mechanism acts as a "non-selective bypass".

The above explanation is further strengthened by the experimental results that we obtained with the analogues of catalysts **1** and **2** that incorporate tertiary rather than primary amine. These catalysts were prepared by a synthesis similar to that of **1** and **2**, but using the chiral building block of 3-aminoquinuclidine rather than 1,2-diphenylethylenedi-

styrene with the lack of any enantioselectivity, but with yields that are substantially higher than those achieved with **1** or **2** (presumably because the tertiary quinuclidine amine is much more basic than the primary amine in **1** or **2**). Although similarly designed catalysts (thiourea-based as well as urea-based) reported by Takemoto et al. performed the addition of malonates and β-ketoesters to nitroolefins with high enantioselectivity,[14] presumably through a deprotonation-involving mechanism, this did not happen with our polymer-supported catalysts.

Since the enamine-based mechanism of the addition of ketones seems highly likely in the case of catalyst **2** and related catalysts incorporating other L-amino acids, we consid-

er the transition state depicted in Figure 1 as "responsible" for the lack of influence of the steric size of the amino acid side chain on the enantioselectivity of the reaction (at least

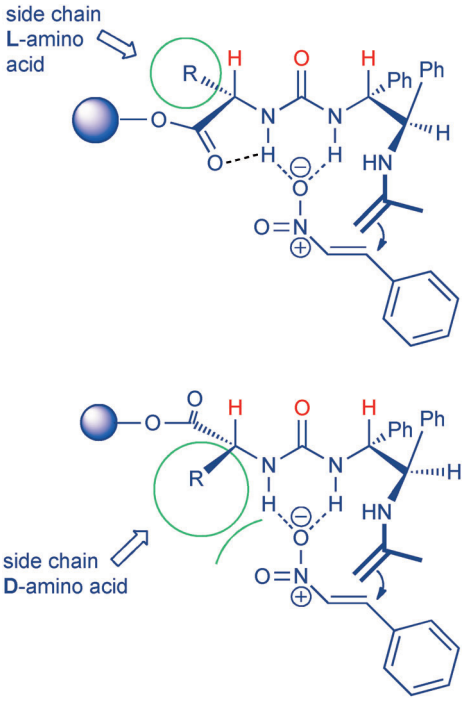


Figure 1. Proposed transition state and the influence of the configuration of the α-carbon atom of the amino acid component of the catalyst. Atoms marked in red are aligned in a coplanar manner with the carbonyl group to reduce the allylic strain.

in the tested case of acetone addition). The conformation of the catalyst–substrates complex is based on the minimization of the allylic strain of the amide bonds,[15] thus placing the hydrogen atoms marked in red coplanar with the urea carbonyl group. The presumed double hydrogen-bond activation of the nitroolefin through a single oxygen atom of the nitro group was proposed and supported by calculations of Tsogoeva et al.[8a] When the nitroolefin approaches the enamine with its other face, a less favorable alignment of the hydrogen bonds must result in the substantially lower activation of the electrophile and slower reaction; hence, it is the source of the enantioselectivity. Inversion at the amino acid chiral center of the catalyst puts the side chain in the proximity of the nitro group, possibly forcing the nitroolefin out of the most favorable hydrogen-bond alignment, and consequently lowering the degree of its activation, the reaction rate toward the dominant enantiomer of the product and, as a result, the yield and the enantioselectivity.

The results of our study are aligned with the trends and conclusions that one is able to deduce from a careful survey of the outcome observed for various catalytic systems in the nitro-Michael addition of aldehydes and ketones. According to the recent analyses in the literature,[1–2,16] the majority of catalytic systems for this reaction are derived from secondary amines, primarily pyrrolidine (e.g., proline and prolinol derivatives). Along with the excellent results (in terms of yield, and diastereo- and enantioselectivity) that many of these systems exhibited in the addition of six-membered cyclic ketones or linear aldehydes to nitroolefins,[17–19] the outcome in the case of five-membered cyclic ketones, acyclic ketones, and α-branched sterically hindered aldehydes was less impressive.[20–24]

On the other hand, the catalytic systems based on primary amines, though significantly less abundant and explored, induce outstanding reactivity and enantioselectivity in the case of the sterically hindered aldehyde addition to nitroolefins.[11,12e,25] Moreover, the only systems capable of inducing higher than 90% *ee* in the acetone addition to nitroolefins are those few based on primary amines.[8b–e,26] The use of primary amine-derived catalysts in the reaction of cyclopentanone with nitroolefins, though entirely unexplored,[27] can lead to a very good catalytic outcome, as revealed by our results.

Moreover, the results of our current study demonstrate that the differences between the catalytic systems based on secondary versus primary amines are even more pronounced and significant in heterogeneous catalysis of the nitro-Michael reaction. Thus, although for the reaction of nitrostyrene with a "classical" cyclohexanone substrate the previously reported polystyrene- and silica-supported secondary amine-based catalysts outperform our systems,[4b–i] for the reaction of this nitroolefin with acetone, cyclopentanone or isobutyraldehyde the catalyst **2**, which is based on a primary amine, provided outstanding yields and enantioselectivities. These parameters are remarkably better for our catalysts than for all systems immobilized on insoluble supports that have previously been reported.

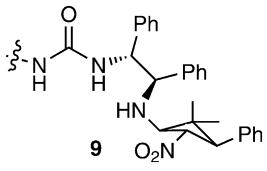
In our preliminary report, we showed that in the case of acetone addition to β-nitrostyrene the catalyst can be recycled a number of times without a significant decrease in the reaction yield and with perfect reproducibility of the *ee* value.[7] In parallel experiments carried out with isobutyraldehyde and nitrostyrene (Table 5), the excellent enantioselectivity is, once again, preserved, but the activity of the catalyst diminishes steeply. Despite the fact that we are presently unable to prove this, it appears likely that some irreversible side reaction of the catalyst with aldehyde, or aldehyde and nitrostyrene, causes this outcome.

Table 5. Attempted recycling of catalyst **1** in the asymmetric nitro-Michael addition of isobutyraldehyde to *trans*-β-nitrostyrene.[a]

Cycle	Yield [%][b]	*ee* [%][c]
1	63	99
2	30	99
3	15	99

[a] Reaction conditions: *trans*-β-nitrostyrene (0.25 mmol), acetone (1.25 mmol), $PhCO_2H$ (0.05 mmol), catalyst (0.075 mmol), toluene (2 mL); 4 days, RT. [b] Determined by NMR spectroscopy. [c] *ee* value was determined by HPLC with a Chiralpak OJ column.

The irreversible formation of a cyclobutane side product **9** following the C–C bond-forming step of the catalysis, as was suggested by Jacobsen et al., can be one plausible explanation for the catalyst deactivation in this type of catalytic reaction.[11] However, the recently demonstrated reversibility of such cyclobutane formation under the reaction conditions and, consequently, its postulated role as the resting state of the catalyst in the amine-catalyzed nitro-Michael addition suggests that other modes of catalyst deactivation may also be possible.[28]



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To the best of our knowledge, effective recycling of a supported catalyst in the addition of an aldehyde to nitroolefin still remains a challenge. Most catalysts rapidly lose activity upon recycling or require regenerating treatment between the cycles.[4a] Only the peptide catalyst, recently reported by Wennemers et al., could be reused numerous times without loss of activity.[29]

Conclusion

We have prepared, for the first time, polymer-supported bifunctional catalysts incorporating a primary amine, for the enantioselective nitro-Michael addition of aldehydes and ketones. Introduction of simple L-α-amino acid spacers in the structures of the "first-generation" catalyst that we preliminarily communicated led to a substantially more active and stereoselective catalytic system. The profiles of reactivity and selectivity, which the new catalysts exhibit in the nitro-Michael reaction of various ketones and aldehydes, emphasized the differences between the primary and secondary amine-based catalysts.

Experimental Section

General procedure for the preparation of amino-urea catalysts: *p*-Nitrophenyl chloroformate (10 equiv per amino unit), DIPEA (20 equiv per amino unit), and a catalytic amount of pyridine (0.1 equiv) were added to a suspension of amine-terminated resin (1 equiv) in THF (10 mL per 1 g resin). The suspension was stirred at room temperature for 2 h. The resin was washed with water, THF/water, THF, and dichloromethane, and then dried under vacuum. The resin was stirred in DMF (10 mL per 1 g resin) and the appropriate chiral diamine (7 equiv per carbonate unit) was added. The suspension was heated to 50 °C overnight. The resin was washed with DMF/water, DMF, THF/water, THF, and dichloromethane, and then dried under vacuum.

Catalyst 2: Starting materials: Wang-Val-NH_2 resin (0.97 mmol g^{-1}, preloaded Fmoc-Val on Wang resin (ChemImpex), subjected to deprotection) and (1*R*, 2*R*)-(+)-1,2-diphenylethylenediamine. Yield >99%, loading 0.78 mmol g^{-1}. Following trifluoroacetic acid (TFA)-induced cleavage: ^{1}H NMR (400 MHz, $CDCl_3$/TFA 1:1): δ = 7.55 (br s, 3H), 7.35–7.37 (m, 4H), 7.25–7.34 (m, 4H), 7.15–7.17 (m, 4H), 5.43 (d, J = 11.2 Hz, 1H), 4.81–4.82 (m, 1H), 4.37 (m, 1H), 2.29–2.31 (m, 1H), 0.98 ppm (d, J = 7.1 Hz, 6H); partial ^{13}C NMR (100 MHz, $CDCl_3$/TFA 1:1): δ = 135.7, 132.4, 131.1, 130.2, 129.9, 129.6, 127.8,127.4, 62.7, 59.8, 59.6, 31.3, 18.8, 17.2 ppm.

General procedure for the catalytic asymmetric nitro-Michael addition: The appropriate Michael donor (0.5 mmol for aldehydes or 1.25 mmol for other donors) and benzoic acid (0.025 mmol) were added to a mixture of catalyst (0.075 mmol of the catalytic unit) and nitroolefin (0.25 mmol) in toluene (2 mL). The suspension was stirred at room temperature for 4 days. After the reaction, the mixture was filtered and the catalyst was washed with AcOEt (3×10 mL) and dried for reuse. The organic layer was evaporated and the residue was analyzed by ^{1}H NMR spectroscopy, and then purified by flash column chromatography on silica gel (hexane/AcOEt) to afford the Michael adduct. The *ee* value of the product was determined by chiral HPLC analysis with Chiralcel OJ, Chiralcel OD, or Chiralpak AD columns. The majority of the products are known and were characterized by comparison of their NMR spectra to the corresponding data in the literature.[8c,9c,17b,20f,21e,24g–i,30] Characterization of new compounds is provided in the Supporting Information.

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