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Unmodified Primary Amine Organocatalysts for Asymmetric Michael Reactions in Aqueous Media

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The organocatalytic asymmetric Michael addition of aldehydes to a nitro olefin in aqueous organic solvents catalysed by a broad range of simple primary amines and amino alcohols is reported. In particular, the use of (*S*,*S*)-diphenylethylenediamine, which is the chiral backbone of various organocatalysts, gave addition products in good yields and with good to high enantioselectivities (45–96 % *ee*). Remarkably high enantioselectivities were observed for the demanding conjugate addition of α,α-disubstituted aldehydes to nitrostyrene (96–98 % *ee*) in aqueous organic solvent mixtures.

Introduction

Of the various organocatalytic C–C bond-forming reactions,[1] organocatalytic asymmetric Michael additions play a significant role.[2] In particular, the conjugate addition reactions of nitroalkenes to carbonyl compounds result in the formation of γ-nitro carbonyl compounds, which are valuable building blocks in organic synthesis.[3]

Recently, research into the development of efficient organocatalytic reactions has also focussed on economic and ecological aspects.[4] Thus, additional efforts have been made to develop efficient organocatalysts for asymmetric reactions in water or in aqueous solvent mixtures.[5] The design of small-molecule organocatalysts with significant activity and selectivity within the principles of "green chemistry" is a crucial scientific challenge. Aqueous reactions promoted by small, commercially available catalysts are recognized as "green" processes because they have advantages from the points of view of environmental concerns, safety, and cost.[6]

A few examples of organocatalytic Michael reactions in aqueous media have recently been reported in the literature. In the very first example, Barbas et al. reported a highly enantioselective (up to 97% *ee*) direct Michael addition of aldehydes and ketones to nitro olefins catalysed by a proline-based diamine/TFA (trifluoroacetic acid) organocatalyst.[7] For this and most of the other reported cases, the organocatalysts were designed to be less water soluble, or even water insoluble, with a large hydrophobic group attached to the proline core.[8] Later, Headley and Ni developed two examples of water-soluble prolinol silyl ethers, which could be used to promote highly efficient asymmetric Michael addition reactions of aldehydes to nitro olefins.[9]

Interesting results were also obtained with primary amine catalysts, particularly a bifunctional sulfonamide–primary-amine catalyst developed from diaminocyclohexane,[10] and three different primary-thiourea-based catalysts based on diphenylethylenediamine.[11,12] In these cases, however, organic solvents were used; water was used in only a small amount (15–500 mol-%), although its presence resulted in significant improvements.

Interestingly, most of the previously published reports have described the use of complex organocatalysts, and the direct application of the primary amines used as the precursors of these complex organocatalysts was not exhaustively tested. For this reason, we propose that there is a need to study water-compatible organocatalysts, in particular readily available simple amines. In 2006, Chin demonstrated that the use of (*R*,*R*)-diphenylethylenediamine (10 mol-%) in THF resulted in the selective formation of (*R*)-warfarin from 4-hydroxycoumarin and *trans*-4-phenyl-3-buten-2-one (94% yield, ca. 80% *ee*).[13] In this case, however, dry organic solvents were used as the reaction medium. Nevertheless, this result encouraged us to undertake broader studies on the possible application of unmodified low-molecular-weight diamines as efficient and "greener" organocatalysts for the asymmetric Michael additions of nitroalkenes to aldehydes in aqueous solvents.[14]

Results and Discussion

We first tested a broad range of cheap and readily available unmodified amines as organocatalysts in the aqueous Michael reaction between nitrostyrene and 2-propanal

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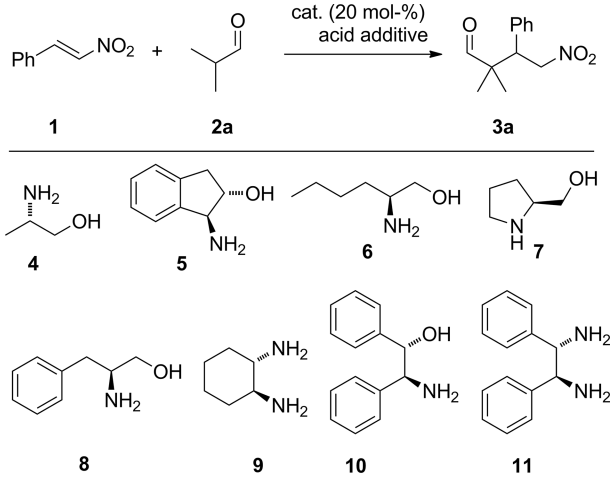
(Scheme 1). We turned our attention to this demanding aldehyde substrate as only a small number of reports have addressed α,α-disubstituted aldehydes as potential nucleophilic partners in combination with nitroalkenes.[7,12] The model reaction between nitrostyrene (**1**) and aldehyde **2** was initially carried out in a homogeneous DMF/water (9:1) solution in the presence of 20 mol-% of catalysts **4**–**11**. The screening results are shown in Table 1. The yield of Michael adduct **3a** was rather disappointing for most of the structures tested, reaching 50–60% for only two examples (Table 1, entries 2 and 3). For these amino alcohols, however, the observed enantioselectivity was poor. Only in the cases of amino alcohol **10** and diamine **11** did the enantioselectivity meet our expectations. In spite of the lower yields observed for these organocatalysts, we decided to use these amines for further optimization because of the observed higher stereoselectivity compared to the other examples. In particular, the use of readily available (*S*,*S*)-diphenylethylenediamine seemed exciting in terms of yield and enantioselectivity (91%). Diaminocyclohexane **9** (Table 1, entry 6) did not give promising results, unfortunately.



Scheme 1. Model Michael reaction of (*E*)-nitrostyrene and 2-methylpropanal promoted by primary amine-based organocatalysts.

Table 1. Initial catalyst screening.[a]

Entry	Catalyst	Yield [%][b]	*ee* [%][c]
1	**4**	20	22 (*R*)
2	**5**	62	16 (*S*)
3	**6**	57	20 (*S*)
4	**7**	45	48 (*R*)
5	**8**	36	11 (*S*)
6	**9**	22	30 (*R*)
7	**10**	28	93 (*S*)
8	**11**	42	91 (*S*)[d]

[a] The reaction was carried out using **1** (0.50 mmol), **2a** (1.00 mmol), catalyst **4**–**11** (20 mol-%), $PhCO_2H$ (20 mol-%) as additive, and DMF/H_2O (9:1) as solvent (1 mL) at room temp. for 5 d. [b] Isolated yield after silica gel chromatography. [c] *ee*'s were determined by HPLC analysis on a chiral phase (Daicel OD-H column). [d] 40 mol-% of $PhCO_2H$ was used.

It was reported[2,7] that the addition of a Brønsted acid to an amine-promoted Michael reaction can enhance the formation of the enamine, thereby improving the yield. Indeed, at the initial screening stage, we observed the best results when an acid additive was used. To explore this effect, diamine **11** was chosen for further evaluation, and was tested as a catalyst for the same reaction with and without acid additives. The results are summarized in Table 2. When benzoic acid was used, the reaction yield and the enantioselectivity both increased significantly (Table 2, entry 1 vs. 2). Some of the other Brønsted acids tested (acetic, formic, and salicylic acids) gave worse results. Interestingly, the use of stronger acids (HCl) resulted in a decrease of the reaction yield. The use of trifluoroacetic acid, which is usually beneficial for organocatalytic Michael addition reactions,[8a] resulted in the formation of only a trace of **3a** (Table 2, entry 6).

Table 2. Screening of acid additives.[a]

Entry	Additive	Yield [%][b]	*ee* [%][c]
1	–	14	84
2	$PhCO_2H$	42	91
3	AcOH	35	90
4	HCO_2H	21	92
5	HCl	20	93
6	CF_3CO_2H	<5	n.d.
7	Salicylic acid	22	98
8	3-Nitrophenol	22	76
9	PhOH	16	79

[a] The reaction was carried out using **1** (0.50 mmol), **2a** (1.00 mmol), (*S*,*S*)-catalyst **11** (20 mol-%), acid additive (40 mol-%), and DMF/H_2O (9:1) as solvent (1 mL) at room temp. for 3 d. [b] Isolated yield after silica gel chromatography. [c] *ee*'s were determined by HPLC analysis on a chiral phase (Daicel OD-H column).

Further studies revealed that the catalyst loading could not be decreased, but that the reaction time could be shortened from 5 to 3 d without influence on the reaction yield. These conditions were used for a screening of solvents to test the reaction efficiency. The results are collected in Table 3. Interestingly, in all cases (DMF, THF, MeOH,

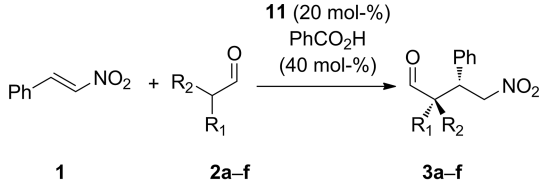
Table 3. Solvent screening.[a]

Entry	Solvent	Yield [%][b]	*ee* [%][c]
1	DMF	26	82
2	DMF/H_2O (9:1)	40	88
3	DMF/H_2O (1:1)	48	93
4	THF	30	97
5	THF/H_2O (9:1)	50	97
6	THF/H_2O (1:1)	52	96
7	MeOH	55	75
8	MeOH/H_2O (9:1)	58	88
9	MeOH/H_2O (1:1)	59	89
10	EtOH	54	76
11	EtOH/H_2O (9:1)	67	91
12	EtOH/H_2O (1:1)	65	90
13	EtOH/H_2O (1:1)	54	86[d]
14	H_2O	36	84
15	Neat	28	72

[a] The reaction was carried out using **1** (0.50 mmol), **2a** (1.00 mmol), (*S*,*S*)-catalyst **11** (20 mol-%), $PhCO_2H$ (40 mol-%) as additive, and solvent (1 mL) at room temp. for 3 d. [b] Isolated yield after silica gel chromatography. [c] *ee*'s were determined by HPLC analysis on a chiral phase (Daicel OD-H column). [d] The reaction was carried out using (*S*,*S*)-catalyst **11** (10 mol-%) and $PhCO_2H$ (20 mol-%).

EtOH), the presence of a large amount of water did not adversely affect the reaction yields or the enantioselectivity. On the contrary, the addition of water seems to be advantageous. Two aqueous solvent mixtures: THF/water (1:1) and EtOH/water (1:1) delivered the best results in terms of yields. By using a green chemistry protocol with pure water as the solvent, the reaction gave a good enantioselectivity but with a lower yield (Table 3, entry 14).

On the basis of the results summarized in Table 3, the reaction conditions of entries 6 and 12 were chosen to study the scope of the Michael reactions using a series of aldehydes **2a**–**2f**, and the results are summarized in Scheme 2. First, combinations of α,α-disubstituted aldehydes and nitrostyrene were surveyed to determine the efficiency of tested diamine catalyst **11**. To our delight, excellent enantioselectivity was maintained with aldehydes **2a**, **2b**, and **2c** in homogeneous THF/water and EtOH/water solutions. In all cases, the observed enantioselectivity for the formation of adducts **3a**–**3c** reached the same high level as was observed using the thiourea organocatalysts presented by Jacobsen[12] for similar substrates.



3a
53%, 96% *ee*
65%, 96% *ee*[a]

3b
50%, 97% *ee*

3c
54%, *dr* (2:1),
98% *ee*
63%, *dr* (2:1),
96% *ee*[a]

3d
48%, *dr* (2:1),
48% *ee*[a]

3e
53%, *dr* (2:1),
45% *ee*[a]

3f
70%, *dr* (2:1),
50% *ee*[a]

Scheme 2. Extension of the developed procedure to a wide range of substrates. Conditions: the reaction was carried out using **1** (0.50 mmol), **2a**–**2g** (1.00 mmol), (*S*,*S*)-catalyst **11** (20 mol-%), $PhCO_2H$ (40 mol-%) as additive, and THF/H_2O (1:1; 1 mL) as a solvent at room temp. for 2 d. Isolated yield after silica gel chromatography. *ee* and *dr* were determined by HPLC analysis on a chiral phase. [a] The reaction was carried out in EtOH/H_2O (1:1; 1 mL) as a solvent at room temp. for 3 d.

At the other extreme, only modest enantio- and diastereoselectivities were for observed for adducts **3d**–**3f** obtained from pentanal, decanal, and phenylethanal, respectively. The absolute stereochemistry of major product **3a** was determined to be (3*S*) by comparing its optical rotation with literature data.[7b,12]

These results confirm that chiral 1,2-diphenylethylenediamines could have broad applications as efficient organocatalysts for aqueous Michael reactions between α,α-disubstituted aldehydes and nitrostyrene. This particularly difficult reaction proceeds efficiently in the case of a diaminocyclohexane (DACH)-based thiourea organocatalyst,[11] but it seems reasonable to replace it by commercially available optically pure diphenylethylenediamine (DPEDA) **11**.

Conclusions

We have shown that chiral (*S*,*S*)-diphenylethylenediamine (**11**) can efficiently promote the highly enantioselective Michael addition of aldehydes to nitro olefins in aqueous organic solvents. This cheap and commercially available chiral primary amine, which is the chiral backbone of various organocatalysts, gives the addition products in good yields and with good to high enantioselectivities (45–96% *ee*). It is noteworthy that high enantioselectivities were observed for the more demanding conjugate addition of α,α-disubstituted aldehydes to nitrostyrene (96–98% *ee*) in THF/water or EtOH/water solvents. These remarkably enantioselective examples of the application of unmodified amines represents a promising foundation for further screening, not only for laboratory-scale work, but also for industrial applications of small and readily available catalysts without any modification of their structures.

Experimental Section

General Remarks: Unless otherwise stated, all reagents were purchased from commercial sources and used as received. Infrared (IR) spectra were recorded with a Fourier-transform infrared (FTIR) spectrometer. ^1H NMR spectra were measured at 400 MHz in $CDCl_3$. Data are reported as follows: chemical shifts in parts per million (ppm), calibrated using the residual solvent as an internal standard, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, m = multiplet, br = broad), coupling constants (in Hz), integration. ^{13}C NMR spectra were measured at 100 MHz with complete proton decoupling. Chemical shifts are reported in ppm, calibrated using the residual solvent as an internal standard. High-resolution mass spectra (HRMS) were measured with an electron ionization (EI) mass spectrometer. Optical rotations were measured with a digital polarimeter at room temperature. Reactions were monitored using TLC on silica [aluminium-backed plates (0.2 mm)]. All reagents and solvents were purified and dried according to common methods. All organic solutions were dried with anhydrous magnesium sulfate. Reaction products were purified by flash chromatography using silica gel 60 (240–400 mesh). HPLC analysis was carried out with an HPLC system equipped with chiral stationary-phase columns.

General Procedure for the Organocatalytic Michael Reaction of Aldehydes with Nitro Olefins: β-Nitrostyrene (**1**; 75.0 mg, 0.5 mmol), (*S*,*S*)-1,2-diphenylethylene-1,2-diamine (**11**; 0.1 mmol, 20 mol-%), and the carboxylic acid (0.2 mmol, 40 mol-%) were dissolved in an appropriate solvent, and aldehyde **2a**–**2f** (1.0 mmol) was added. The mixture was stirred at room temperature for 2 or 3 d, depending on the solvent. The organic solvent was then removed. The mixture was partitioned between EtOAc and water, and then the

crude product was purified by column chromatography on silica gel (hexane/ethyl acetate) to give the pure product. The enantiomeric excess of the products was determined by HPLC using a chiral stationary phase.

2,2-Dimethyl-4-nitro-3-phenylbutanal (3a):[12] The compound was isolated as a colourless to pale yellow liquid. The enantiomeric excess was determined by HPLC analysis of the purified product with a Daicel OD-H column [hexane/*i*PrOH (4:1), 1.0 mL min^{-1}, λ = 220 nm]: t_R = 13.7 min (minor), t_R = 20.2 min (major). Data for sample with *ee* = 90% (*S*): $[\alpha]_D^{26}$ = –4.7 (*c* = 1.1, $CHCl_3$) [ref.[7b] $[\alpha]_D^{26}$ = –4.9 (*c* = 1.0, $CHCl_3$), *ee* = 98% (*S*)]. IR (film, CH_2Cl_2): $\tilde{\nu}$ = 2962, 2919, 2849, 1724, 1553, 1378, 881, 704 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.53 (s, 1 H), 7.35–7.27 (m, 3 H), 7.20–7.18 (m, 2 H), 4.85 (dd, $J_{H,H}$ = 13.1, 11.2 Hz, 1 H), 4.69 (dd, $J_{H,H}$ = 13.1, 4.2 Hz, 1 H), 3.78 (dd, $J_{H,H}$ = 11.2, 4.2 Hz, 1 H), 1.13 (s, 3 H), 1.01 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 204.2, 135.4, 129.1, 128.7, 128.1, 76.3, 48.5, 48.2, 21.7, 18.9 ppm. MS (EI): *m*/*z* (%) = 221 (0.5) $[M]^+$, 145 (25), 131 (11), 117 (12), 104 (100), 91 (60), 77 (16), 72 (22), 43 (23). HRMS (EI): calcd. for $C_{12}H_{15}NO_3$ $[M]^+$ 221.1052; found 221.1048.

2,2-Diethyl-4-nitro-3-phenylbutanal (3b): The compound was isolated as a colourless oil. The enantiomeric excess was determined by HPLC analysis of the purified product with a Daicel OD-H column [hexane/*i*PrOH (97:3), 0.5 mL min^{-1}, λ = 220 nm]: t_R = 32.1 min (minor), t_R = 34.6 min (major). Data for sample with *ee* = 94% (*S*): $[\alpha]_D^{24}$ = +7.7 (*c* = 1.0, $CHCl_3$). IR (film, CH_2Cl_2): $\tilde{\nu}$ = 2969, 2942, 2882, 1719, 1556, 1455, 1379, 704 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.58 (s, 1 H), 7.40–7.27 (m, 3 H), 7.15–7.12 (m, 2 H), 4.88–4.78 (m, 2 H), 3.70 (dd, $J_{H,H}$ = 9.8, 5.8 Hz, 1 H), 1.79–1.49 (m, 4 H), 0.92 (t, $J_{H,H}$ = 7.5 Hz, 3 H), 0.89 (t, $J_{H,H}$ = 7.5 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 207.6, 135.6, 129.1, 128.7, 128.1, 76.9, 53.3, 48.1, 23.5, 22.7, 7.9, 7.5 ppm. MS (EI): *m*/*z* (%) = 249 (3) $[M]^+$, 173 (20), 150 (15), 131 (33), 117 (26), 104 (100), 100 (80), 91 (73), 85 (13), 77 (20), 71 (26), 57 (30), 43 (52). HRMS (EI): calcd. for $C_{14}H_{19}NO_3$ $[M]^+$ 249.1365; found 249.1374.

2-Methyl-2-(2-nitro-1-phenylethyl)pentanal (3c):[7b] The compound was isolated as a colourless oil. The enantiomeric excess was determined by HPLC analysis of the purified product with a Daicel OJ-H column [hexane/*i*PrOH (9:1), 0.8 mL min^{-1}, λ = 254 nm]: t_R = 29.4 min (major, *syn*), t_R = 32.7 min (minor, *anti*), t_R = 38.3 min (major, *anti*) and t_R = 46.7 min (minor, *syn*). IR (film, CH_2Cl_2): $\tilde{\nu}$ = 2963, 2935, 2873, 1723, 1555, 1456, 1379, 751, 705 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.54 (s, 0.8 H), 9.52 (s, 0.2 H), 7.37–7.27 (m, 3 H), 7.22–7.15 (m, 2 H), 4.90–4.71 (m, 1 H), 4.63 (dd, $J_{H,H}$ = 13.0, 3.9 Hz, 1 H), 3.80–3.75 (m, 1 H), 1.56–1.41 (m, 1 H), 1.29–1.16 (m, 3 H), 1.11 (s, 2.4 H), 1.10 (s, 0.6 H), 0.92–0.82 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 205.3, 135.4, 129.2, 128.7, 128.1, 77.2, 51.6, 47.7, 37.6, 17.0, 15.9, 14.5 ppm. MS (EI): *m*/*z* (%) = 249 (0.4) $[M]^+$, 203 (7), 173 (11), 159 (13), 150 (14), 131 (34), 104 (100), 100 (74), 91 (69), 77 (13), 71 (32), 43 (38). HRMS (EI): calcd. for $C_{14}H_{19}NO_3$ $[M]^+$ 249.1365; found 249.1369.

2-(2-Nitro-1-phenylethyl)pentanal (3d):[15] The compound was isolated as a pale yellow oil. The enantiomeric excess was determined by HPLC analysis of the purified product with a Daicel OD-H column [hexane/*i*PrOH (9:1), 0.8 mL min^{-1}, λ = 208 nm]: t_R = 23.4 min (major, *syn*), t_R = 25.5 min (major, *anti*), t_R = 28.3 min (minor, *syn*) and t_R = 38.9 min (minor, *anti*). IR (film, CH_2Cl_2): $\tilde{\nu}$ = 2961, 2933, 2873, 1721, 1554, 1380, 702 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.71 (d, $J_{H,H}$ = 2.8 Hz, 0.6 H), 9.48 (d, $J_{H,H}$ = 3.0 Hz, 0.4 H), 7.37–7.28 (m, 3 H), 7.21–7.12 (m, 2 H), 4.83–4.62 (m, 2 H), 3.81–3.75 (m, 1 H), 2.74–2.60 (m, 1 H), 1.75–1.11 (m, 4 H), 0.93 (t, $J_{H,H}$ = 7.3 Hz, 1.2 H), 0.81 (t, $J_{H,H}$ = 7.1 Hz, 1.8 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 203.3, 203.1, 136.8, 136.2, 129.1, 129.1, 128.2, 128.2, 128.1, 128.0, 78.4, 77.9, 53.8, 53.3, 44.5, 43.2, 29.6, 29.5, 20.3, 19.8, 13.9, 13.9 ppm. MS (EI): *m*/*z* (%) = 235 (2) $[M]^+$, 145 (77), 131 (15), 117 (49), 104 (86), 91 (100), 78 (26), 55 (21), 41 (27). HRMS (EI): calcd. for $C_{13}H_{17}NO_3$ $[M]^+$ 235.1208; found 235.1208.

2-(2-Nitro-1-phenylethyl)decanal (3e): The compound was isolated as a pale oil. The enantiomeric excess was determined by HPLC analysis of the purified product with a Daicel OD-H column [hexane/*i*PrOH (4:1), 0.2 mL min^{-1}, λ = 254 nm]: t_R = 47.5 min (major, *syn*), t_R = 50.5 min (major, *anti*), t_R = 58.9 min (minor, *syn*) and t_R = 79.7 min (minor, *anti*). IR (film, CH_2Cl_2): $\tilde{\nu}$ = 2953, 2926, 2855, 1724, 1555, 1455, 1379, 701 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.71 (d, $J_{H,H}$ = 2.8 Hz, 0.6 H), 9.48 (d, $J_{H,H}$ = 3.0 Hz, 0.4 H), 7.38–7.27 (m, 3 H), 7.17 (dd, $J_{H,H}$ = 8.1, 1.2 Hz, 2 H), 4.86–4.59 (*m*, 2 H), 3.84–3.73 (m, 1 H), 2.74–2.57 (m, 1 H), 1.74–1.42 (m, 2 H), 1.35–1.07 (m, 12 H), 0.87 (dt, $J_{H,H}$ = 8.5, 6.9 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 203.3, 203.2, 136.8, 136.3, 129.1, 129.1, 128.2, 128.2, 128.1, 128.0, 78.4, 77.9, 53.9, 53.5, 44.5, 43.2, 31.8, 31.7, 29.5, 29.4, 29.2, 29.1, 29.1, 29.0, 27.5, 27.3, 27.0, 26.4, 22.6, 22.6, 14.0, 14.0 ppm. MS (EI): *m*/*z* (%) = 305 (2) $[M]^+$, 258 (8), 162 (27), 145 (95), 131 (41), 117 (57), 104 (100), 91 (93), 78 (18), 69 (23), 55 (34), 41 (43). HRMS (EI): calcd. for $C_{18}H_{27}NO_3$ $[M]^+$ 305.1991; found 305.1982.

4-Nitro-2,3-diphenylbutanal (3f):[15,16] The compound was isolated as a white solid. The enantiomeric excess was determined by HPLC analysis of the purified product with a Daicel OD-H column [hexane/*i*PrOH (98:2), 0.8 mL min^{-1}, λ = 208 nm]: t_R = 27.3 min (major, *anti*), t_R = 30.3 min (minor, *syn*), t_R = 33.9 min (major, *syn*) and t_R = 36.5 min (minor, *anti*). IR (KBr): $\tilde{\nu}$ = 3406 (br), 3026, 2861, 1712, 1546, 1382, 758, 702, 559 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.56 (d, $J_{H,H}$ = 2.1 Hz, 1 H), 7.46–7.25 (m, 10 H), 4.49 (dd, $J_{H,H}$ = 12.8, 10.2 Hz, 1 H), 4.40 (dd, $J_{H,H}$ = 12.8, 4.4 Hz, 1 H), 4.30 (dt, $J_{H,H}$ = 10.2, 4.4 Hz, 1 H), 4.07 (dd, $J_{H,H}$ = 10.2, 2.1 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.7, 137.0, 132.4, 129.8, 129.4, 129.1, 128.9, 128.2, 128.1, 78.4, 61.7, 44.4 ppm. MS (EI): *m*/*z* (%) = 269 (13) $[M]^+$, 193 (23), 178 (15), 120 (100), 115 (30), 104 (97), 91 (86), 78 (17), 65 (16). HRMS (EI): calcd. for $C_{16}H_{15}NO_3$ $[M]^+$ 269.1052; found 269.1054.

Supporting Information (see footnote on the first page of this article): ^{1}H and ^{13}C NMR spectra of reaction products.

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