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Organocatalytic Asymmetric Conjugate Addition of Nitroalkanes to α,β-Unsaturated Enones Using Novel Imidazoline Catalysts

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A new catalytic enantioselective conjugate addition of nitroalkanes to acyclic α,β-unsaturated enones catalyzed by novel organic catalysts has been developed. A series of chiral amines has been tested as catalysts for the addition of 2-nitropropane to benzylideneacetone, and it is found that a novel imidazoline catalyst, prepared from phenylalanine, can catalyze a highly enantioselective 1,4-addition reaction. The reaction of various acyclic and cyclic nitroalkanes was found to proceed well with enantioselectivities up to 86% ee, and enantiopure products can be obtained by recrystallization. The potential of the reaction is documented by the reaction of a series of substituted α,β-unsaturated enones with different nitroalkanes. Furthermore, the synthetic applicability of the reaction is demonstrated by the formation of optically active functionalized pyrrolines and pyrrolidines by reductive amination of the products. On the basis of the absolute configuration of the conjugate addition products, the mechanism for the reaction is discussed and a transition state proposed.

Introduction

The catalytic asymmetric conjugate addition—the Michael reaction—of stabilized carbanions to α,β-unsaturated enones is one of the fundamental C−C bond-forming reactions in organic chemistry.[1] This concept has over the years been developed for the reaction of several different stabilized carbanions with various types of α,β-unsaturated enones[1] and found use for the synthesis of many important molecules by further reaction of the Michael addition product.

For the Michael reaction of nitroalkanes[2] with α,β-unsaturated enones, the product of the 1,4-addition reaction is a very useful precursor to different complex organic molecules, such as aminocarbonyl, aminoalkanes, and pyrrolidines by reduction of the nitro functionality,[3] and to other functionalities that can be derived from the nitro group.[4]

Several attempts have been performed toward achieving asymmetric conjugate addition of nitroalkanes to α,β-unsaturated enones in the presence of chiral Lewis acids,[5] chiral rubidium prolinate, proline and proline derivatives,[6,7] and chiral phase-transfer catalysts,[8] but generally only low to moderate enantioselectivities have been obtained[6a,b] or the reaction has been limited to cyclic enones.[6c] The best results obtained so far have been by Bakó et al. using a sugar-derived crown ether for the addition of 2-nitropropane to chalcone in up to 89% ee[9] and by Shibasaki et al. using a lanthanum tris-binaphthoxide catalyst in the addition of nitromethane to chalcones in up to 97% ee;[5a] however, only nitromethane was utilized and up to 60 mol % of the chiral ligand was used.

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(8) For phase-transfer catalysts, see: (a) Annunziata, R.; Cinquini, M.; Colonna, S. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2422. (b) Colonna, S.; Hiemstra, H.; Wynberg, H. *J. Chem. Soc., Chem. Commun.* **1978**, 238. (c) Banfi, S.; Cinquini, M.; Colonna, S. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 1841.

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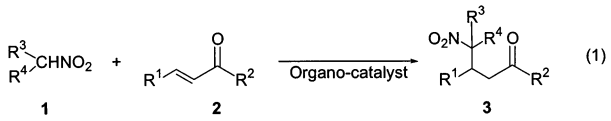
In this paper, we disclose the organocatalyzed[10] enantioselective conjugate addition of nitroalkanes to acyclic α,β-unsaturated enones using novel imidazoline catalysts. The reaction has been developed for various types of nitroalkanes **1** reacting with different acyclic α,β-unsaturated enones **2** (eq 1). The scope of the catalytic



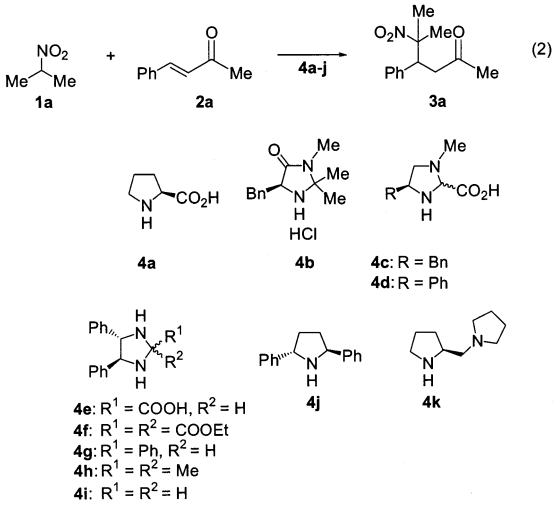
(1)

asymmetric conjugate addition will be presented by the reaction of acyclic and cyclic nitroalkanes, as well as functionalized nitroalkanes with various types of acyclic α,β-unsaturated enones. The applicability of the reaction will be demonstrated by the preparation of optically active functionalized pyrrolines and pyrrolidines. Furthermore, the mechanism for the reaction will be discussed.

Results and Discussion

The initial studies of the organocatalytic enantioselective addition of nitroalkanes to the α,β-unsaturated enones focused on the screening of different chiral amines as the catalyst for the reaction of 2-nitropropane **1a** with benzylideneacetone **2a** (eq 2). The results from these investigations are presented in Table 1.

In the absence of a base, 2-nitropropane **1a** did not react with benzylideneacetone **2a**. L-Proline turned out to be a poor catalyst in terms of enantioselectivity for the reaction (Table 1, entry 2), a result which is in accordance with the general observations from literature on proline-catalyzed Michael additions to acyclic enones.[6a,b] Surprisingly, the organocatalyst developed by MacMillan et al. (**4b**)[10k] gave no conversion for the Michael reaction of **1a** with **2a**, under the present reaction conditions, not even in the presence of Et_3N (Table 1, entry 3). However, catalyst **4c**, which can easily be prepared from phenylalanine by reaction with first thionyl chloride in MeOH and methylamine followed by reduction of the carbonyl functionality and ring closure with glyoxalic acid (Scheme 1), turned out to be an excellent catalyst for the reaction of **1a** with **2a**. The catalyst **4c** was obtained as a configurationally stable 2:1 mixture of diastereomers and used as such. Attempts to separate the diastereomers by chromatographic methods were not successful. In the presence of 20 mol % of **4c**, the Michael adduct **3a** was formed in high yield and with 79% ee (Table 1, entry 4). The reaction also proceeds well with 10 mol % of catalyst **4a** (Table 1, entry 5), as well as with 10 mol % of Et_3N as a base (Table 1, entry 6). However, it should be noted



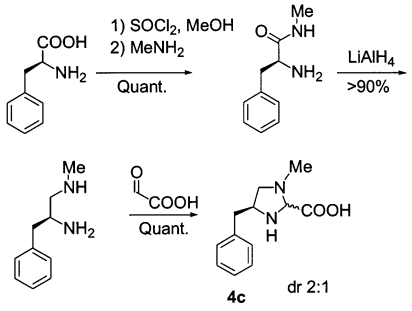
(2)

TABLE 1. Screening of Different Chiral Amines 4a–h as Catalysts for the Enantioselective Addition of 2-Nitropropane 1a to Benzylideneacetone 2a (eq 2)[a]

entry	catalyst (mol %)	Et_3N (mol %)	reaction time (h)	conversion[b] (%)	ee[c] (%)
1			24		
2	**4a** (10)	50	50	37	<5
3	**4b** (20)	20	60		
4	**4c** (20)		180	87	79
5	**4c** (10)		180	57	80
6	**4c** (10)	10	150	68	78
7	**4d** (10)		180	33	59
8	**4e** (20)		150	11	56
9	**4f** (20)	20	130	<5	
10	**4g** (20)		130	33	20
11	**4h** (20)		200	83	60
12	**4i** (20)		80	74	13
13	**4j** (20)		40	3	43
14	**4k** (20)		20	68	<5

[a] Reaction performed as neat reactions. [b] Determined by GC; the isolated yields are generally about 5% lower. [c] Determined by chiral GC using a Chirasil Dex-CB chiral stationary phase.

SCHEME 1. Synthesis of Catalyst 4c



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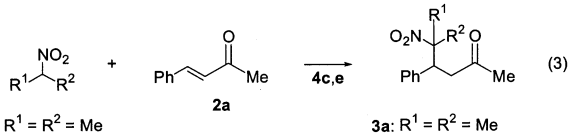
that an increase in the amount of base leads to a lower conversion, presumably due to salt formation with the catalyst. The phenyl analogue (**4d**) gave moderate conversion and enantioselectivity (Table 1, entry 7). We have also prepared a series of chiral organocatalysts based on optically active 1,2-diphenyl-1,2-diamine as the chiral backbone (**4e**−**i**), and of these, only catalysts **4h** and **4i** gave satisfactory conversion, and only the former catalyst provided a moderate enantioselectivity (entry 11). The C_2-symmetric catalyst **4j** and the chiral diamine **4k** turned out to be less effective catalysts for the addition of **1a** to **2a** (Table 1, entries 13 and 14). The simplicity of the nitroalkane Michael reaction should be emphasized: The bench-stable catalyst is added to a mixture of the nitroalkane and α,β-unsaturated enone under an aerobic atmosphere, taking no precautions to exclude water, and the mixture stirred for the time indicated. Addition of 5 or 10 equiv of water was not found to increase the reaction rate as observed by MacMillan et al.,[10j] but was found to produce identical results to reactions without added water both in terms of yield and enantioselectivity. After evaporation of the reaction mixture to remove excess nitroalkane, purification by flash chromatography yielded the pure product. It should also be noted that the reactions are very clean and that no byproducts are observed. Therefore, the reported yields are a consequence of the reaction time, as demonstrated by the addition of 2-nitropropane **1a** to benzylideneacetone **2a** (Table 2, entry 1), where the reaction has been allowed to go to completion. If the reaction between 2-nitropropane **1a** and benzylideneacetone **2a** proceeds at higher temperatures (50 °C) using 10 mol % of catalyst **4c**, the yield of **3a** was increased to 83%; however, the enantioselectivity was reduced to 59% ee. To demonstrate the preparative utility of the organocatalyzed reactions, a similar reaction was run on a kilogram scale using catalyst **4c** with recovery and reuse of the catalyst, without any observed decrease in catalytic activity or enantioselectivity.

A series of different nitroalkanes **1a**−**g** has been reacted with benzylideneacetone **1a** in the presence of **4c** or **4e** as the catalyst, as shown in eq 3 and Table 2.



(3)

1a: $R^1 = R^2 = Me$
1b: $R^1 = R^2 = H$
1c: $R^1 = H$, $R^2 = Me$
1d: $R^1 = R^2 = (CH_2)_4$
1e: $R^1 = R^2 = (CH_2)_5$
1f: $R^1 = H$, $R^2 = CO_2Et$
1g: $R^1 = H$, $R^2 = Ph$

3a: $R^1 = R^2 = Me$
3b: $R^1 = R^2 = H$
3c: $R^1 = H$, $R^2 = Me$
3d: $R^1 = R^2 = (CH_2)_4$
3e: $R^1 = R^2 = (CH_2)_5$
3f: $R^1 = H$, $R^2 = CO_2Et$
3g: $R^1 = H$, $R^2 = Ph$

The different nitroalkanes **1a**−**g** react well with benzylideneacetone **2a** in an enantioselective fashion, giving the Michael adducts **3a**−**g** in good yields and with very similar enantioselectivities for the various nitroalkanes studied. For all the acyclic nitroalkanes **1a**−**c** (Table 2, entries 1−3), the enantioselectivities of the Michael adducts **3a**−**c** are in the range 71−79% ee. The enantioselectivities of the Michael adducts can be improved by recrystallization to enantiopure products (99% ee), as shown for compound **3a**,**j**,**k** (Table 2, entry 1; Table 3, entries 4 and 5). Nitrocyclopentane **1d** and nitrocyclohexane **1e** also react well with **2a**, and **3d** and **3e** are formed with 77% ee and 71% ee, respectively (Table 2, entries 5 and 6). Nitroacetate **1f** gives a 1:1 mixture of diastereomers using both **4c** and **4e** as the catalysts and with up to 79% ee (Table 2, entries 7 and 8) (vide supra). The reaction of phenylnitromethane **1g** with **2a** is slightly more diastereoselective than **1f**, as a 2:1 mixture of diastereomers are obtained with up to 72% ee of one of the diastereomers (Table 2, entries 9 and 10); however, it should be noted that **3g** racemizes upon prolonged standing.

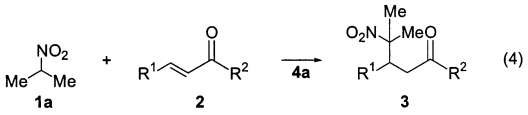
The results for the catalytic enantioselective conjugate addition of the nitroalkanes to benzylideneacetone show that both the yield and enantioselectivity of the reaction are very similar for the different nitroalkanes investigated, which demonstrates that the reaction is very

TABLE 2. Catalytic Enantioselective Addition of Nitroalkanes 1a−f to Benzylideneacetone 2a Catalyzed by 4c (20 mol %) and 4e (20 mol %) (eq 2)

entry	nitroalkane	catalyst	reaction time (h)	conversion[b] (%)	ee[c] (%)
1	**1a**	**4c**	240	**3a**, 100 (52)[d]	79 (99)[d]
2	**1b**	**4c**	150	**3b**, 52	73
3	**1c**	**4c**	130	**3c**, 80	71/73
4	**1d**	**4c**	100	**3d**, 100	77
5	**1e**	**4c**	275	**3e**, 64	71
6	**1f**	**4c**	110	**3f**, 89[e]	79[f]
7	**1f**	**4e**	110	**3f**, 70[e]	60[f]
8	**1g**	**4c**	170	**3g**, 71[g]	58/72
9	**1g**	**4e**	170	**3g**, 61[h]	58/63

[a] Reactions in entries 1−5 were performed under neat conditions, while reactions in entry 6−9 were performed in THF using 1.1 equiv of the nitroalkanes. [b] Determined by GC; the isolated yields are generally about 5% lower. [c] Determined by chiral stationary phase GC or HPLC. [d] Run on a 10 mmol scale; yield and ee after a single recrystallization in EtOH. [e] Diastereomeric ratio 1:1. [f] Measured after decarboxylation. [g] Diastereomeric ratio 2.2:1. [h] Diastereomeric ratio 1.7:1.

TABLE 3. Catalytic Enantioselective Addition of 2-Nitropropane 1a to Different α,β-Unsaturated Enones 2a−i Catalyzed by 4c (20 mol %) (eq 4)[a]



(4)

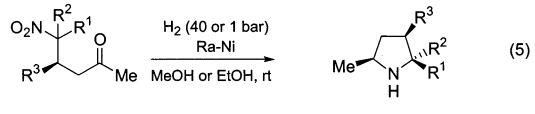
entry	α,β-unsatd enone	R^1	R^2	reaction time (h)	yield[b] (%)	ee[c] (%)
1	**2a**	Ph	Me	240	**3a**, 100 (52)[d]	79 (99)[d]
2	**2b**	Ph	Et	300	**3h**, 69	83
				130	**3h**, 33	86
3	**2c**	Ph	*i*-Pr	110	**3I**, <5	
4	**2d**	*p*-ClC_6H_4	Me	130	**3j**, 87	75 (94)[d]
5	**2e**	*p*-$NO_2C_6H_4$	Me	130	**3k,** 95	65 (98)[d]
6	**2f**	*p*-HOC_6H_4	Me	180	**3l**, 86	75
7	**2g**	2-thienyl	Me	200	**3m**, 87	73
8	**2h**	2-furyl[e]	Me	200	**3n**, 69	70
9	**2i**	2-pyridyl[e]	Me	80	**3o**, 60	52
10	**2j**	*n*-Bu	Me	150	**3p**, 50	73
11	**2k**	*i*-Pr	Me	160	**3q**, <10	73
12	**2l**	$-(CH_2)_3-$		130	**3r**, 84	49
13	**2m**	CO_2Me	Me	110	**3s**, 78	34

[a] Reaction conditions. [b] Determined by GC; the isolated yields are generally about 5% lower. [c] Determined by chiral stationary phase GC or HPLC. [d] After a single recrystallization. [e] Mixture of *E*-and *Z*-isomers.

tolerant to changes in the nitroalkane used. Therefore, 2-nitropropane **1a** was selected as the nitroalkane for the 1,4-addition to a series of different α,β-unsaturated enones in order to further expand the scope of the reaction, and the results are presented in Table 3.

It appears from the two first entries in Table 3 that an exchange of the methyl substituent in **2a** to an ethyl substituent in **2b** improves the enantioselectivity of the reaction, and the Michael adduct is formed with 83% ee. However, further increase of the steric bulk at R^2-position to an isopropyl substituent slows down the reaction and a very low conversion is observed (Table 3, entry 3). The Michael addition of 2-nitropropane **1a** to the other aromatic enones **2d**−**f** also proceeds well, and good enantioselectivities are obtained (entries 4−6). Furthermore, it is also demonstrated that the enantioselectivity of the products can be improved to be 94% ee and 98% ee for **3j** and **3k** by a single recrystallization (Table 3, entries 4 and 5). The heteroaromatic α,β-unsaturated enones **2g**−**i** also reacts well with **1a** in the presence of **4a** as the catalyst, and good enantioselectivities of the Michael adducts **3m**−**o** are obtained (Table 3, entries 7−9). The Michael addition of **2a** to the α,β-unsaturated enones substituted with an alkyl group is very dependent on the R^1-substituent: substrate **2j**, which has a butyl substituent as R^1, gives a moderate yield of **3p** having 73% ee (Table 3, entry 10), while **2k**, having an isopropyl substituent, gives less than 10% yield of **3q**, but with the same good enantioselectivity (Table 3, entry 11). The cyclic enone **2l** reacts also well with **1a**; however, the enantioselectivity of **3r** is moderate (Table 3, entry 12).

Product Modification. The Michael adducts obtained from the present catalytic enantioselective addition of nitroalkanes to the α,β-unsaturated enones opens up for a simple approach to optically active pyrrolidines by reductive amination (eq 5). Nitro ketones **3a** and **3m** were



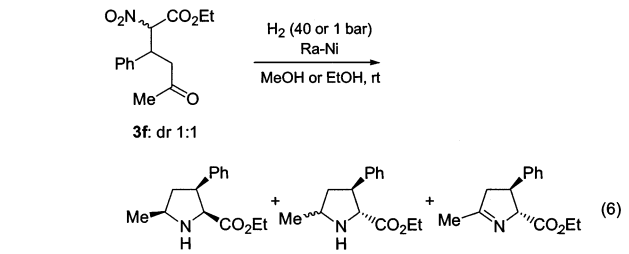
(5)

3a: $R^1 = R^2 = Me$, $R^3 = Ph$
3g: $R^1 = R^3 = Ph$, $R^2 = H$
3m: $R^1 = R^2 = Me$, $R^3 = 2$-thienyl

5a: $R^1 = R^2 = Me$, $R^3 = Ph$
5b: $R^1 = R^3 = Ph$, $R^2 = H$
5c: $R^1 = R^2 = Me$, $R^3 = n$-Bu

reduced by H_2/Ra−Ni in MeOH at 40 bar pressure to give a quantitative yield of the corresponding pyrrolidines **5a**,**c** with remarkable diastereoselectivity, as only a single diastereomer was obtained, with the enantiomeric excess obtained in the Michael addition step being maintained. For nitro ketone **3g**, containing a benzylic amine, much milder reduction conditions had to be employed, and the reduction was performed in EtOH at atmospheric pressure. Even then, under these mild conditions, the 2,3-trans-substituted diastereomer was unstable, and the only product obtained was the 2,3,5-cis-substituted pyrrolidine **5b** as a colorless solid. The structure of **5b** was confirmed by X-ray analysis (see Supporting Information).

The more functionalized Michael adduct **3f** was also subjected to the reductive amination conditions to yield optically active proline analogues **5d**,**e** or pyrroline **5f**, depending on the reaction conditions, as shown in eq 6. If the reductive amination was performed under forcing



(6)

conditions (MeOH, 40 bar), the two diastereomeric pyrrolidines **5d**,**e** were obtained in quantitative yield, but if the reduction was conducted at an atmospheric pressure, the main product obtained was the 2,3-*trans*-pyrroline **5f** and the 2,3,5-*cis*-pyrrolidine **5d** arising from the two diastereomers of nitro ketone **3f**.

Absolute Configuration and Mechanistic Aspects. The absolute configuration of the Michael adduct **3j** obtained from the reaction of 2-nitropropane **1a** with *p*-chlorobenzylideneacetone **2d** in the presence of catalyst **4c** has been assigned by X-ray analysis (see Supporting Information).

The configuration of the chiral center formed in the Michael addition reaction could be determined to have the (*S*)-configuration.

The observed stereochemistry of the product can be explained by formation of the catalyst−substrate iminium intermediate **6a** in which the benzyl group of the catalyst shields the *re*-face of the enone, leaving the *si*-face open for attack. Figure 1 shows the energy minimized (PM3)[16] structure of **6a**.

Obviously, there are several other possible conformations and isomers of the catalyst−substrate iminium intermediate (**6b**−**d**) than **6a** (Scheme 2). However, the catalyst−substrate iminium intermediates **6b**,**c** arising from the trans diastereomer of the catalyst are calculated to be considerably higher in energy (>3 kcal/mol) than **6a** and **6d**, due to steric interactions. The two catalyst−substrate iminium intermediates **6a** and **6d** obtained from the cis diastereomer of the catalyst are of similar energy, but conformation **6a** is slightly favored over **6d**. The favored intermediate **6a** can be due to either steric interactions between the methyl group of the ketone and the benzyl group, as proposed by MacMillan et al.,[10i] who have been using another phenylalanine-derived catalyst, or the possibility of a positive interaction (π-stacking) between the two π-systems. The latter argument is also in agreement with the fact that the catalyst made from D-phenylalanine produces the other enantiomer of the Michael addition product.

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(16) Performed using the protonated carboxylic acid and a positive charge on the nitrogen atom using the Chem3D program.

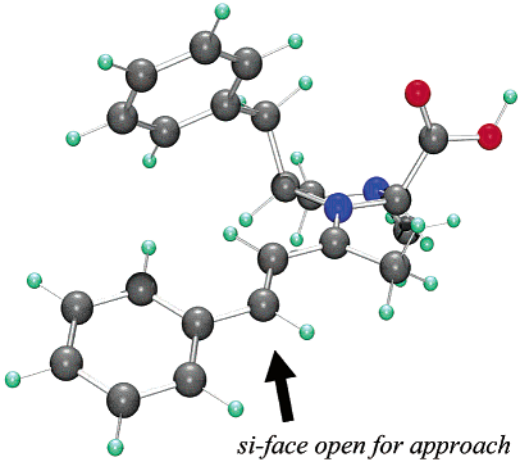
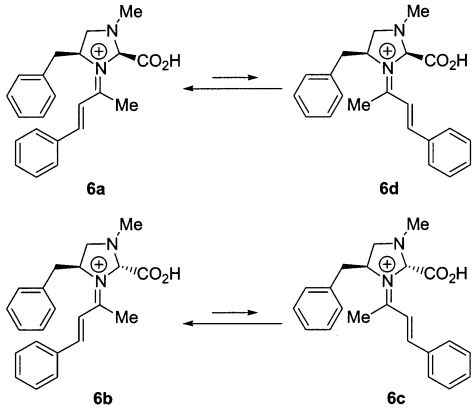


FIGURE 1. PM3-minimized structure of iminium ion **6a**.

SCHEME 2. Possible Catalyst−Substrate Iminium Intermediates, 6a−d



In summary, we have developed a new organocatalytic enantioselective Michael addition of nitroalkanes to α,β-unsaturated enones using a new imidazoline catalyst, easily prepared from phenylalanine. The Michael addition of both acyclic and cyclic nitroalkanes to a variety of different α,β-unsaturated enones proceeds in high yields and with up to 86% ee, and enantiopure products are obtained by recrystallization. The optically active nitro ketones formed undergo a reductive amination, and functionalized pyrrolines and pyrrolidines are obtained with very high diastereomeric excess and the enantiomeric excess is maintained. To account for the absolute configuration of the Michael addition adduct, a catalyst−substrate iminium intermediate in which the benzyl group of the catalyst (**4c**) shields the *re*-face of the α,β-unsaturated enone leaving the *si*-face available for approach has been proposed.

Experimental Section

General Methods. The ^{1}H NMR and ^{13}C NMR were recorded at 400 and 100 MHz, respectively. The chemical shifts are reported in ppm downfield to TMS ($\delta = 0$) for ^{1}H NMR and relative to the to the central $CDCl_3$ resonance ($\delta = 77.0$). Flash chromatography (FC) was carried out using silica gel 60 (230−400 mesh). The enantiomeric excess (ee) of the products were determined by chiral stationary phase GC or HPLC, as indicated in the respective entries.

Materials. All solvents and commercially available chemicals were used as received. 1-Phenylpent-1-en-3-one **2b**,[11] 4-methyl-1-phenylpent-1-en-3-one **2c**,[12] phenylnitromethane **1g**,[13] 4-pyridin-2-ylbut-3-en-2-one **2i,**[14] and 2,5-diphenylpyrrolidine **4j**[15] were prepared according to literature procedures.

General Procedure for the Catalytic Asymmetric Michael Addition to α,β-Unsaturated Enones. In an ordinary test tube equipped with a magnetic stirring bar, 0.5 mmol of the enone was added to 1.0 mL of the nitroalkane, and then the catalyst (0.1 mmol) was added, the tube closed with a rubber stopper, and the reaction mixture stirred at ambient temperature for the time indicated in table. The crude reaction mixture was purified by FC on silica gel after evaporation of the nitroalkane.

5-Methyl-5-nitro-4-phenylhexan-2-one (3a) was purified by FC using Et_2O/pentane and isolated as a colorless oil. Enantiomers were separated by GC using a Chirasil Dex-CB chiral stationary phase. A single recrystalization in EtOH increased the enantioselectivity to 99% ee: $[\alpha^{rt}_D] = -34.1°$ (*c* = 1.0 g/100 mL, EtOH, 99% ee); ^{1}H NMR ($CDCl_3$) δ 1.47 (s, 3H), 1.55 (s, 3H), 2.03 (s, 3H), 2.71 (dd, J = 16.8, 3.6 Hz, 1H), 3.09 (dd, J = 16.8, 10.8 Hz, 1H), 3.92 (dd, J = 10.8, 3.6 Hz, 1H), 7.16−7.21 (m, 2H), 7.24−7.33 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 22.3, 25.8, 30.3, 44.0, 48.8, 91.0, 127.9, 128.5, 129.1, 137.5, 205.2; HRMS *m*/*z* 258.1109 (M + Na^+), calcd for $C_{13}H_{17}O_3NNa^+$ 258.1106.

5-Nitro-4-phenylpentan-2-one (3b) was purified by FC using Et_2O/pentane and isolated as a colorless solid. Enantiomers were separated by GC using an Chiraldex G-TA chiral stationary phase: ^{1}H NMR ($CDCl_3$) δ 2.12 (s, 3H), 2.92 (d, J = 6.8 Hz, 2H), 4.01 (q, J = 6.8 Hz, 1H), 4.60 (dd, J = 7.6, 12.4 Hz, 1H), 4.69 (dd, J = 6.8, 12.4 Hz, 1H), 7.20−7.34 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 30.3, 38.9, 46.0, 79.4, 127.3, 127.5, 129.0, 138.7, 205.4; HRMS *m*/*z* 230.0785 (M + Na^+), calcd for $C_{11}H_{13}O_3NNa^+$ 230.0793.

5-Nitro-4-phenylhexan-2-one (3c). Diastereomers were separated by FC using Et_2O/pentane and isolated as colorless oils. Enantiomers were separated by GC using a Chirasil Dex-CB chiral stationary phase. Diastereomer A: ^{1}H NMR ($CDCl_3$) δ 1.32 (d, J = 6.8 Hz, 3H), 2.00 (s, 3H), 2.73 (dd, J = 4.0, 17.2 Hz, 1H), 2.99 (dd, J = 9.6, 17.2 Hz, 1H), 3.70 (td, J = 10.0, 4.0 Hz, 1H), 4.76 (dq, J = 10.4, 6.8 Hz, 1H), 7.17−7.20 (m, 2H), 7.25−7.35 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 17.7, 30.4, 45.2, 46.2, 87.0, 127.8, 128.1, 129.0, 138.2, 205.0; HRMS *m*/*z* 244.0951 (M + Na^+), calcd for $C_{12}H_{15}O_3NNa^+$ 244.0950. Diastereomer B: ^{1}H NMR ($CDCl_3$) δ 1.48 (d, J = 6.4 Hz), 2.12 (s, 3H), 2.89 (dd, J = 7.6, 17.6 Hz, 1H), 3.05 (dd, J = 6.4, 17.6 Hz, 1H), 3.72 (q, J = 6.8 Hz, 1H), 4.87 (quintet, J = 6.4 Hz, 1H), 7.11−7.15 (m. 2H), 7.25−7.33 (m. 3H); ^{13}C NMR ($CDCl_3$) δ 16.7, 30.5, 44.4, 44.6, 85.8, 127.8, 128.1, 128.7, 137.8, 205.9; HRMS *m*/*z* 244.0953 (M + Na^+), calcd for $C_{12}H_{15}O_3NNa^+$ 244.0950.

4-(1-Nitrocyclopentyl)-4-phenylbutan-2-one (3d) was purified by FC using Et_2O/pentane and isolated as a colorless oil. Enantiomers were separated by HPLC using a Chiralpak AS chiral stationary phase in hexane/2-propanol 90/10: ^{1}H NMR ($CDCl_3$) δ 1.51−1.68 (m, 4H), 1.75−1.84 (m, 2H), 2.01 (s, 3H), 2.41−2.57 (m, 2H), 2.90 (dd, J = 17.2, 3.6 Hz, 1H), 3.11 (dd, J = 17.2, 10.0 Hz, 1H), 3.84 (dd, J = 10.0, 3.6 Hz, 1H), 7.08−7.14 (m, 2H), 7.22−7.29 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 22.9, 23.0, 30.4, 33.9, 36.3, 45.0, 47.2, 103.8, 127.7, 128.4, 128.6, 138.2, 205.6; HRMS *m*/*z* 284.1263 (M + Na^+), calcd for $C_{15}H_{19}O_3NNa^+$ 284.1263.

4-(1-Nitrocyclohexyl)-4-phenylbutan-2-one (3e) was purified by preparative TLC using 10% Et_2O/CH_2Cl_2 and isolated as a colorless oil. Enantiomers were separated by HPLC using a Chiralpak AS chiral stationary phase in hexane/2-propanol 90/10: ^{1}H NMR ($CDCl_3$) δ 1.04−1.69 (m, 8H), 2.02 (s, 3H), 2.32 (br dd, J = 2.4, 14.4 Hz, 1HH), 2.52 (br dd, J = 2.4, 14.4 Hz, 1H), 2.92 (dd, J = 4.4, 17.6 Hz, 1H), 3.02 (dd, J = 9.6, 17.6 Hz, 1H), 3.64 (dd, J = 4.4, 9.6 Hz, 1H), 7.11 (dd, J = 1.6, 7.6 Hz, 2H), 7.25−7.29 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 22.0, 22.2, 24.4, 30.5, 31.3, 33.7, 43.6, 49.6, 94.1, 127.8, 128.4, 129.1, 137.8, 205.6; HRMS *m*/*z* 298.1416 (M + Na^+), calcd for $C_{16}H_{21}O_3NNa^+$ 298.1419.

2-Nitro-5-oxo-3-phenylhexanoic Acid Ethyl Ester (3f) was purified as a 1:1 diastereomeric mixture by FC using Et_2O/pentane and isolated as a colorless oil. Enantiomeric excess was determined as for compound **3b** after decarboxylation ($EtOH/H_2O$, Et_3N, 50 °C overnight): ^1H NMR ($CDCl_3$, mixture of diastereomers) δ 1.06 (t, J = 6.8 Hz, 3H), 1.29 (t, J = 7.6 Hz, 3H), 2.06 (s, 3H), 2.03 (s, 3H), 2.92−3.14 (m, 4H, CH_2 for both diastereomers), 4.05 (q, J = 7.2 Hz, 1H), 4.07 (q, J = 6.8 Hz, 1H), 4.22−4.30 (m, 4H, CH_2 for both diastereomers), 5.40 (d, J = 8.8 Hz, 1H), 5.47 (d, J = 9.6 Hz, 1H), 7.23−7.31 (m, 10H); ^{13}C NMR ($CDCl_3$, mixture of diastereomers) δ 13.4, 13.6, 30.0, 30.1, 41.1, 41.4, 45.0, 45.2, 62.7, 63.1, 91.1, 127.8, 127.9, 128.2, 128.7, 128.8, 136.7, 137.7, 163.1, 163.4, 204.7; HRMS m/z 302.1004 (M + Na^+), calcd for $C_{14}H_{17}O_5NNa^+$ 302.1004.

5-Nitro-4,5-diphenylpentan-2-one (3g) was purified by FC using Et_2O/pentane, and the diastereomers were isolated as colorless solids. Enantiomers were separated by HPLC using a Chiralcel OB stationary phase in ethanol/hexane 50/50 for the major diastereomer and a Chiralpak AS chiral stationary phase in hexane/2-propanol 50/50 for the minor diastereomer: ^1H NMR ($CDCl_3$, minor diastereomer) δ 1.71 (s, 3H), 2.28 (dd, J = 3.6, 17.2 Hz, 1H), 2.61 (dd, J = 10.0, 17.2 Hz, 1H), 4.25 (dt, J = 3.6, 12.4 Hz, 1H), 5.69 (d, J = 12.0 Hz, 1H), 7.11−7.28 (m, 5H), 7.32−7.35 (m, 3H), 7.50−7.53 (m, 2H); ^{13}C NMR ($CDCl_3$, minor diastereomer) δ 30.6, 44.6, 45.7, 95.5, 127.8, 128.2, 128.3, 128.4, 128.7, 128.9, 132.6, 138.6, 205.1; ^1H NMR ($CDCl_3$, major diastereomer) δ 2.01 (s, 3H), 2.78 (dd, J = 3.2, 17.2 Hz, 1H), 3.11 (dd, J = 10.4, 17.2 Hz, 1H), 4.32 (dt, J = 3.2, 11.2 Hz, 1H), 5.69 (d, J = 11.2 Hz, 1H), 7.04−7.14 (m, 5H), 7.20−7.24 (m, 3H), 7.31−7.34 (m, 2H); ^{13}C NMR ($CDCl_3$, major diastereomer) δ 30.6, 44.5, 46.5, 95.1, 127.4, 128.2, 128.3, 128.6, 128.7, 129.6, 132.5, 137.4, 205.0; HRMS m/z 306.1111 (M + Na^+), calcd for $C_{17}H_{17}O_3NNa^+$ 306.1106.

6-Methyl-6-nitro-5-phenylheptan-3-one (3h) was purified by FC using Et_2O/pentane and isolated as a colorless oil. Enantiomers were separated by GC using a Chirasil Dex-CB chiral stationary phase: ^1H NMR ($CDCl_3$) δ 0.90 (t, J = 7.2 Hz, 3H), 1.48 (s, 3H), 1.55 (s, 3H), 2.22 (dq, J = 18.0, 7.6 Hz, 1H), 2.37 (dq, J = 18.0, 7.6 Hz, 1H), 2.67 (dd, J = 3.6, 16.8 Hz, 1H), 3.07 (dd, J = 10.8, 16.8 Hz, 1H), 3.94 (dd, J = 3.6, 10.8 Hz, 1H), 7.16−7.19 (m, 2H), 7.23−7.31 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 7.5, 22.4, 25.9, 36.4, 42.8, 48.8, 91.0, 127.8, 128.5, 129.1, 137.7, 207.8; HRMS m/z 272.1263 (M + Na^+), calcd for $C_{14}H_{19}O_3NNa^+$ 272.1263.

2,6-Dimethyl-6-nitro-5-phenylheptan-3-one (3i) was purified by FC using Et_2O/pentane and isolated as a colorless solid: ^1H NMR ($CDCl_3$) δ 0.90 (d, J = 6.8 Hz, 3H), 0.98 (d, J = 6.8 Hz, 3H), 1.49 (s, 3H), 1.56 (s, 3H), 2.48 (septet, J = 6.8 Hz, 1H), 2.71 (dd, J = 3.2, 17.2 Hz, 1H), 3.14 (dd, J = 10.4, 17.2 Hz, 1H), 3.94 (dd, J = 3.2, 10.4 Hz, 1H), 7.16−7.19 (m, 2H), 7.24−7.29 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 17.8, 17.9, 18.5, 22.6, 26.0, 41.0, 48.7, 91.0, 127.7, 128.4, 129.2, 137.9, 211.0; HRMS m/z 286.1416 (M + Na^+), calcd for $C_{15}H_{21}O_3NNa^+$ 286.1419.

4-(4-Chlorophenyl)-5-methyl-5-nitrohexan-2-one (3j) was purified by FC using Et_2O/pentane and isolated as a colorless oil. Enantiomers were separated by GC using an Chiraldex G-TA chiral stationary phase. A single recrystallization in EtOH increased the enantioselectivity to 94% ee: $[\alpha^{rt}_D] = -38.0°$ (c = 1.0 g/100 mL, EtOH, 94% ee). For details on the X-ray analysis, see the Supporting Information. ^1H NMR ($CDCl_3$) δ 1.47 (s, 3H), 1.53 (s, 3H), 2.04 (s, 3H), 2.73 (dd, J = 3.2, 17.2 Hz, 1H), 3.03 (dd, J = 10.8, 17.2 Hz, 1H), 3.89 (dd, J = 3.2, 10.8 Hz, 1H), 7.12 (d, J = 8.4 Hz, 2 H), 7.28 (d, J = 8.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 22.5, 25.4, 30.3, 43.8, 48.1, 90.7, 128.7, 130.3, 133.7, 136.1, 204.8; HRMS m/z 292.0719 (M + Na^+), calcd for $C_{13}H_{16}O_3NClNa^+$ 292.0716.

5-Methyl-5-nitro-4-(4-nitrophenyl)hexan-2-one (3k) was purified by FC using Et_2O/pentane and isolated as a colorless oil. Enantiomers were separated by HPLC using a Chiralpak AD chiral stationary phase in hexane/2-propanol 90/10. A single recrystalization in hexane/2-propanol increased the enantioselectivity to 98% ee: $[\alpha^{rt}_D] = -56.4°$ (c = 1.0 g/100 mL, EtOH, 98% ee); ^1H NMR ($CDCl_3$) δ 1.50 (s, 3H), 1.55 (s, 3H), 2.06 (s, 3H), 2.85 (dd, J = 3.2, 17.6 Hz, 1H), 3.11 (dd, J = 10.4, 17.6 Hz, 1H), 4.01 (dd, J = 3.2, 10.4 Hz, 1H), 7.36 (d, J = 8.8 Hz, 2 H), 8.14 (d, J = 8.8 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 23.1, 25.1, 30.2, 43.7, 48.2, 90.3, 123.5, 130.0, 145.5, 147.3, 204.2; HRMS m/z 303.0952 (M + Na^+), calcd for $C_{13}H_{16}O_5N_2Na^+$ 303.0957.

4-(4-Hydroxyphenyl)-5-methyl-5-nitrohexan-2-one (3l) was purified by FC using Et_2O/CH_2Cl_2 and isolated as a colorless solid. Enantiomers were separated by HPLC using a Chiralpak AD chiral stationary phase in hexane/2-propanol 90/10: ^1H NMR ($CDCl_3$) δ 1.47 (s, 3H), 1.53 (s, 3H), 2.04 (s, 3H), 2.67 (dd, J = 3.2, 16.4 Hz, 1H), 3.04 (dd, J = 10.8, 16.4 Hz, 1H), 3.84 (dd, J = 3.2, 10.8 Hz, 1H), 5.57 (br s, 1H), 6.68 (d, J = 8.4 Hz, 2 H), 7.02 (d, J = 8.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$ + CD_3OD) δ 22.0, 25.3, 30.0, 43.9, 48.1, 91.3, 115.1, 127.9, 130.0, 156.3, 206.7; HRMS m/z 254.1053 (M + Na^+), calcd for $C_{13}H_{17}O_4NNa^+$ 254.1055.

5-Methyl-5-nitro-4-thiophen-2-ylhexan-2-one (3m) was purified by FC using Et_2O/pentane and isolated as a colorless oil. Enantiomers were separated by GC using a Chirasil Dex-CB chiral stationary phase after reductive amination to 2,2,5-trimethyl-3-(tetrahydrothiophen-2-yl)pyrrolidine **5c** and TFA protection of the amine (TFAA, CH_2Cl_2, 60 °C, 30 min): ^1H NMR δ 1.53 (s, 3H), 1.62 (s, 3H), 2.06 (s, 3H), 2.65 (dd, J = 3.2, 16.4 Hz, 1H), 3.01 (dd, J = 10.8, 16.8 Hz, 1H), 4.30 (dd, J = 3.2, 10.8 Hz, 1H), 6.90−6.95 (m, 2H), 7.20 (dd, J = 1.2, 5.2 Hz, 1H); ^{13}C NMR δ 22.4, 25.5, 30.3, 44.2, 45.5, 90.9, 124.8, 126.8, 127.4, 140.1, 204.4.

4-Furan-2-yl-5-methyl-5-nitrohexan-2-one (3n) was purified by FC using Et_2O/pentane and isolated as a colorless oil. Enantiomers were separated by GC using an Chiraldex G-TA chiral stationary phase: ^1H NMR δ 1.49 (s, 3H), 1.56 (s, 3H), 2.07 (s, 3H), 2.52 (dd, J = 3.2, 17.2 Hz, 1H), 3.07 (dd, J = 10.8, 17.2 Hz, 1H), 4.10 (dd, J = 3.2, 10.8 Hz, 1H), 6.17 (d, J = 3.6 Hz, 1H), 6.29 (dd, J = 1.6, 3.2 Hz, 1H), 7.31 (m, 1H); ^{13}C NMR δ 22.3, 25.7, 30.0, 42.0, 42.4, 90.4, 109.1, 110.4, 142.1, 151.1, 204.6; HRMS m/z 248.0898 (M + Na^+), calcd for $C_{11}H_{15}O_4NNa^+$ 248.0899.

5-Methyl-5-nitro-4-pyridin-2-ylhexan-2-one (3o) was purified by FC using Et_2O/pentane and isolated as a colorless oil. Enantiomers were separated by HPLC using a Chiralcel OJ chiral stationary phase in hexane/2-propanol 92/8; ^1H NMR ($CDCl_3$) δ 1.43 (s, 3H), 1.62 (s, 3H), 2.03 (s, 3H), 2.56 (dd, J = 2.8, 17.6 Hz, 1H), 3.58 (dd, J = 10.8, 17.6 Hz, 1H), 4.07 (dd, J = 2.8, 10.8 Hz, 1H), 7.14 (dd, J = 5.2, 8.0 Hz, 1H), 7.25 (d, J = 7.2 Hz, 1H), 7.59 (dt, J = 1.6, 8.0 Hz, 1H), 8.48 (d, J = 5.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 22.5, 25.2, 30.2, 43.0, 49.3, 91.1, 122.5, 126.2, 136.3, 148.9, 157.5, 205.8; HRMS m/z 237.1241 (M + Na^+), calcd for $C_{12}H_{17}O_3N_2Na^+$ 237.1239.

4-(1-Methyl-1-nitroethyl)octan-2-one (3p) was purified by FC using Et_2O/pentane and isolated as a colorless oil. Enantiomers were separated by GC using a Chirasil Dex-CB chiral stationary phase: ^1H NMR ($CDCl_3$) δ 0.86 (t, J = 6.8 Hz, 3H), 1.03−1.44 (m, 6H), 1.51 (s, 3H), 1.52 (s, 3H), 2.17 (s, 3H), 2.34 (dd, J = 6.0, 18.4 Hz, 1H), 2.52 (dd, J = 4.4, 18.4 Hz, 1H), 2.75 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 13.6, 22.5, 23.4, 23.5, 29.7, 30.7, 41.0, 44.7, 91.5, 205.9; HRMS m/z 238.1420 (M + Na^+), calcd for $C_{11}H_{21}O_3NNa^+$ 238.1419.

4-Isopropyl-5-methyl-5-nitrohexan-2-one (3q) was purified by FC using Et_2O/pentane and isolated as a colorless oil. Enantiomers were separated by GC using a Chirasil Dex-CB chiral stationary phase: ^1H NMR ($CDCl_3$) δ 0.75 (d, J = 7.2 Hz, 3H), 0.87 (d, J = 7.2 Hz, 3H), 1.51 (s, 6H), 1.87 (d septet, J = 2.4, 6.8 Hz, 1H), 2.18 (s, 3H), 2.39−2.57 (m, 2H), 2.76 (dt, J = 2.4, 6.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 17.6, 23.8, 24.5, 24.8, 27.4, 29.8, 39.8, 45.9, 91.4, 206.6; HRMS m/z 224.1258 (M + Na^+), calcd for $C_{10}H_{19}O_3NNa^+$ 224.1258.

2-(1-Methyl-1-nitroethyl)-4-oxopentanoic acid methyl ester (3s) was purified by FC using Et_2O/pentane and isolated

as a colorless solid. Enantiomers were separated by GC using a Chirasil Dex-CB chiral stationary phase: ^{1}H NMR ($CDCl_3$) δ 1.58 (s, 3H), 1.61 (s, 3H), 2.16 (s, 3H), 2.40 (dd, J = 2.8, 18.0 Hz, 1H), 3.04 (dd, J = 11.2, 18.0 Hz, 1H), 3.67 (dd, J = 2.8, 11.2 Hz, 1H), 3.71 (s, 3H): ^{13}C NMR ($CDCl_3$) δ 22.9, 25.6, 29.8, 41.4, 48.2, 52.5, 88.2, 171.4, 205.0; HRMS m/z 240.0844 (M + Na^+), calcd for $C_9H_{15}O_5NNa^+$ 240.0848.

Procedure for the Synthesis 4-Benzyl- and 4-Phenyl-1-methylimidazolidine-2-carboxylic Acid (4c,d). Synthesized According to Scheme 1. (*S*)-Phenylalanine-*N*-methylamide was prepared by the method of Macmillan et al.[10j] in quantitative yield followed by reduction of the amide by $LiAlH_4$ in refluxing THF for 12 h or until all starting material was consumed (TLC). After quenching with a minimal amount of H_2O, filtration, and extraction with CH_2Cl_2, N^1-methyl-3-phenylpropane-1,2-diamine was obtained as a colorless oil in 92% yield. If necessary, the N^1-methyl-3-phenylpropane-1,2-diamine could be further purified by distillation (bp 120 °C, 0.4 mbar). Condensation with an equimolar amount of glyoxylic acid monohydrate was performed in CH_2Cl_2 at ambient temperature for 15 h, after which the solvent was evaporated to give 4-benzyl-1-methylimidazolidine-2-carboxylic acid (**4c**) as a slightly hygroscopic colorless solid that could be stored for months after drying under vacuum. The 1-methyl-4-phenylimidazolidine-2-carboxylic acid (**4d**) was prepared similarly.

4-Benzyl-1-methylimidazolidine-2-carboxylic acid (4c) was isolated as a colorless solid in a 2:1 mixture of diastereomers: ^{1}H NMR ($CDCl_3$, major diastereomer) δ 2.52−2.93 (m, 2H), 2.89 (s, 3H), 3.21 (dd, J = 5.8, 13.4 Hz, 1H), 3.41−3.48 (m, 1H), 3.74 (quintet, J = 6.8 Hz, 1H), 4.19 (s, 1H), 7.20−7.31 (m, 5H); ^{13}C NMR ($CDCl_3$, major diastereomer) δ 38.4, 40.6, 58.1, 58.8, 85.6, 126.9, 128.8, 128.7, 137.4, 168.8; ^{1}H NMR ($CDCl_3$, minor diastereomer) δ 2.52−2.93 (m, 2H), 2.84 (s, 2H), 3.01 (dd, J = 6.3, 13.4 Hz, 1H), 3.64−3.71 (m, 1H), 4.01 (quintet, J = 6.7 Hz, 1H), 4.12 (s 1H), 7.20−7.31 (m, 5H); ^{13}C NMR ($CDCl_3$, minor diastereomer) δ 39.3, 40.3, 57.3, 58.9, 82.3, 126.8, 128.6, 129.2, 137.3, 169.4; HRMS m/z 243.1100 (M + Na^+), calcd for $C_{12}H_{16}O_2N_2Na^+$ 243.1109.

1-Methyl-4-phenylimidazolidine-2-carboxylic acid (4d) was isolated as a colorless solid in a 1.5:1 mixture of diastereomers; ^{1}H NMR ($CDCl_3$, major diastereomer) δ 2.78−2.83 (dd, J = 7.6, 11.2 Hz, 2H), 2.93 (s, 3H), 4.27 (s, 1H), 4.90 (t, J = 7.6 Hz, 1H), 7.24−7.50 (m, 5H); ^{13}C NMR ($CDCl_3$, major diastereomer) δ 38.8, 58.6, 61.1, 83.1, 126.1, 127.3, 128.6, 136.5, 169.5; ^{1}H NMR ($CDCl_3$, minor diastereomer) δ_2.99 (s, 3H), 3.20 (dd, J = 7.2, 11.2 Hz, 2H), 4.39 (s, 1H), 4.61 (t, J = 7.6 Hz, 1H), 7.24−7.50 (m, 5H); ^{13}C NMR ($CDCl_3$, minor diastereomer) δ 40.6, 59.4, 59.8, 83.8, 126.4, 127.2, 128.4, 140.0, 169.4; HRMS m/z 229.0952 (M + Na^+), calcd for $C_{12}H_{16}O_2N_2Na^+$ 229.0953.

General Procedure for the Synthesis of (4*R*,5*R*)-Diphenylimidazolidine Catalysts (4*e*−*i*). To a solution of (*R*,*R*)-diphenylethanediamine in CH_2Cl_2 was added an equimolar amount of glyoxylic acid monohydrate **4e**, or diethyl ketomalonate **4f**, or benzaldehyde **4g**, or 2 equiv of acetone **4h**, or paraformaldehyde **4i**, and the reaction mixture was stirred at ambient temperature for 15 h. The solvent was removed by rotary evaporation to yield the catalyst as a colorless solid, which was further dried under vacuum.

4,5-Diphenylimidazolidine-2-carboxylic acid (4e) was isolated as a colorless solid. ^{1}H NMR ($(CD_3)_2CO$) δ 4.01 (d, J = 9.0 Hz, 1H), 4.30 (d, J = 9.0 Hz, 1H), 5.29 (s, 1H), 7.09 (m, 3H), 7.21−7.28 (m, 10H); ^{13}C NMR ($(CD_3)_2SO$) δ 68.1, 69.2, 74.6, 127.5, 127.7, 127.9, 128.4, 128.5, 137.9, 138.5, 171.4.

4,5-Diphenylimidazolidine-2,2-dicarboxylic acid diethyl ester (4f) was isolated as a colorless solid: ^{1}H NMR ($CDCl_3$) δ 1.39 (t, J = 7.2 Hz, 6H), 4.39 (q, J = 7.2 Hz, 4H), 4.67 (s, 1H), 4.69 (s, 1H), 7.00−7.26 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 13.9, 59.9, 62.8, 64.7, 84.1, 127.4, 127.8, 127.9, 128.0, 128.2, 128.3, 137.2, 137.6, 166.9, 170.2.

2,4,5-Triphenylimidazolidine (4g) was isolated as a colorless solid: ^{1}H NMR ($CDCl_3$) δ 2.35 (br s, 2H), 4.36 (s, 2H), 5.50 (s, 1H), 7.18−7.46 (m, 13H), 7.72 (d, J = 7.6 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 69.5, 71.4, 76.8, 126.6, 126.8, 126.9, 127.1, 127.6, 127.7, 127.8, 128.0, 128.1, 128.3, 128.4, 128.5, 140.7, 142.4; HRMS m/z 302.1703 (M + H^+), calcd for $C_{21}H_{21}N_2^+$ 302.1705.

2,2-Dimethyl-4,5-diphenylimidazolidine (4h) was isolated as a colorless solid: ^{1}H NMR ($CDCl_3$) δ 1.54 (s, 6H), 1.79 (br s, 2H), 4.10 (s, 1H), 4.25 (s, 1H), 7.25−7.28 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 30.3, 61.6, 70.0, 75.6, 126.6, 126.7, 126.8, 127.1, 127.9, 128.1, 140.4, 143.2; HRMS m/z 275.1491 (M + Na^+), calcd for $C_{17}H_{20}N_2Na^+$ 275.1524.

4,5-Diphenylimidazolidine (4i) was isolated as a colorless solid after purification by FC on silica using 2-propanol/CH_2Cl_2: ^{1}H NMR ($CDCl_3$) δ 2.80−3.30 (br, 2H), 4.25 (s, 2H), 4.32 (s, 2H), 7.20−7.33 (m, 10H); ^{13}C NMR ($CDCl_3$ + CD_3OD) δ 60.5, 64.1, 69.0, 126.6, 126.7, 127.7, 127.8, 128.2, 128.5, 137.9, 139.0.

General Procedure for the Reductive Amination of Nitro Ketones. To a suspension of Raney-nickel in MeOH or EtOH in an appropriate vessel was added nitro ketone and H_2 at the indicated pressure, and the reaction mixture was stirred at ambient temperature overnight (12−16 h). After reaction the Raney-nickel catalyst was filtered off using a fine filter (0.45 μm), to give quantitative yields of the analytically pure pyrrolidine.

3,5-*cis*-2,2,5-Trimethyl-3-phenylpyrrolidine (5a). After reductive amination, the Raney-nickel catalyst was filtered off to yield **5a** as an analytically pure compound. The diastereomeric ratio was determined by GC. Enantiomers were separated by GC using a Chirasil Dex-CB chiral stationary phase: ^{1}H NMR ($CDCl_3$) δ 0.73 (s, 3H), 1.24 (s, 3H), 1.26 (d, J = 6.4 Hz, 3H), 1.84 (dt, J = 9.6, 12.0 Hz, 1H), 2.21 (quintet, J = 6.4 Hz), 3.03 (dd, J = 6.4, 12.0 Hz, 1H), 3.36 (dq, J = 16.4, 5.6 Hz, 1H), 7.18−7.22 (m, 3H), 7.26−7.30 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 22.1, 27.1, 30.1, 40.6, 51.7, 56.6, 61.6, 126.2, 127.9, 128.2, 141.3; HRMS m/z 190.1592 (M + H^+), calcd for $C_{13}H_{20}N^+$ 190.1596.

2,3,5-*cis*-5-Methyl-2,3-diphenylpyrrolidine (5b). After reductive amination, the Raney-nickel catalyst was filtered off to yield **5b** as an analytically pure compound. The diastereomeric ratio was determined by GC. Enantiomers were separated by GC using a Chirasil Dex-CB chiral stationary phase. For details on the X-ray analysis, see the Supporting Information: ^{1}H NMR ($CDCl_3$) δ 1.43 (d, J = 6.4 Hz, 3H), 1.79 (dt, J = 12.4, 9.0 Hz, 1H), 1.94 (br, 1H), 2.36 (ddd, J = 6.8, 8.0, 12.4 Hz, 1H), 3.51 (ddq, J = 6.4, 12.4, 9.2 Hz, 1H), 3.65 (q, J = 8.4 Hz, 1H), 4.57 (d, J = 8.0 Hz, 1H), 6.90−6.93 (m, 2H), 6.97−7.05 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 21.1, 40.2, 50.8, 53.5, 67.2, 125.6, 126.1, 127.3, 127.4, 127.5, 128.7, 142.0, 142.3; HRMS m/z 238.1588 (M + H^+), calcd for $C_{17}H_{20}N^+$ 238.1596.

3-Butyl-2,2,5-trimethylpyrrolidine (5c). After reductive amination, the Raney-nickel catalyst was filtered off to yield **5c** as an analytically pure compound. The diastereomeric ratio was determined by GC. Enantiomers were separated by GC using a Chirasil Dex-CB chiral stationary phase after TFA protection of the amine (TFAA, CH_2Cl_2, 60 °C, 30 min): ^{1}H NMR ($CDCl_3$) δ 0.85−0.89 (m, 3H), 1.12−1.61 (m, 8H), 1.37 (s, 3H), 1.52 (d, J = 3.2 Hz, 3H), 1.55 (s, 3H), 1.91−2.01 (m, 1H), 2.28−2.37 (m, 1H), 3.84 (ddq, J = 7.2, 14.4, 10.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.9, 19.8, 21.1, 22.7, 25.7, 28.5, 30.4, 37.9, 48.5, 52.7, 66.0.

2,3,5-*cis*-5-Methyl-3-phenylpyrrolidine-2-carboxylic acid ethyl ester (5d) was separated from **5e** by FC on silica gel using MeOH/CH_2Cl_2. The diastereomeric ratio was determined by GC. Enantiomers were separated by GC using a Chirasil Dex-CB chiral stationary phase: ^{1}H NMR ($CDCl_3$) δ 0.73 (t, J = 7.2 Hz, 3H), 1.37 (d, J = 6.4 Hz, 3H), 1.37 (q, J = 10.4 Hz, 1H), 2.00−2.18 (br, 1H), 2.21−2.27 (m, 1H), 3.27 (septet, J = 5.2 Hz, 1H), 3.49 (dq, J = 10.4, 7.2 Hz, 1H), 3.64−3.74 (m, 2H), 4.03 (d, J = 10.0 Hz, 1H), 7.16−7.27 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 13.4, 20.0, 41.2, 50.0, 54.0, 60.4, 66.1, 126.7, 127.9,

128.0, 140.5, 173.2; HRMS *m/z* 256.1313 ($M + Na^+$), calcd for $C_{14}H_{19}NO_2Na^+$ 256.1313.

2,3-*trans*-5-Methyl-3-phenylpyrrolidine-2-carboxylic acid ethyl ester (5e) was separated from **5d** by FC on silica gel using $MeOH/CH_2Cl_2$. The diastereomeric ratio was determined by GC. Enantiomers were separated by GC using a Chirasil Dex-CB chiral stationary phase: ^1H NMR ($CDCl_3$, major diastereomer) δ 1.18 (t, $J = 6.8$ Hz, 3H), 1.25 (d, $J = 6.4$ Hz, 3H), 1.62 (dt, $J = 11.6$, 10.8 Hz, 1H), 2.29−2.35 (m, 1H), 3.36 (dt, $J = 10.8$, 7.6 Hz, 1H), 3.47 (septet, $J = 6.0$ Hz, 1H), 3.84 (d, $J = 7.6$ Hz, 1H), 4.05−4.23 (m, 2H), 7.30−7.33 (m, 5H); ^{13}C NMR ($CDCl_3$, major diastereomer) δ 14.1, 21.1, 44.0, 50.7, 54.5, 60.9, 67.1, 126.6, 127.3, 128.5, 142.9, 175.2; HRMS *m/z* 256.1313 ($M + Na^+$), calcd for $C_{14}H_{19}NO_2Na^+$ 256.1314.

***trans*-5-Methyl-3-phenyl-3,4-dihydro-2*H*-pyrrole-2-carboxylic acid ethyl ester (5f)** was separated from **5e**,**f** by FC on silica gel using $MeOH/CH_2Cl_2$. Enantiomers were separated by GC using a Chirasil Dex-CB chiral stationary phase: ^1H NMR ($CDCl_3$) δ 1.25 (t, $J = 7.6$ Hz, 3H), 2.14 (d, $J = 2.0$ Hz, 3H), 2.70 (dd, $J = 6.8$, 17.2 Hz, 1H), 3.15 (ddd, $J = 2.0$, 10.0, 17.2 Hz, 1H), 3.73 (dt, $J = 10.0$, 6.8 Hz, 1H), 4.15−4.23 (m, 2H), 4.65−4.68 (m, 1H), 7.16−7.31 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 14.1, 19.7, 46.6, 48.3, 61.1, 82.2, 126.7, 126.9, 128.7, 143.0, 172.3, 177.3; HRMS *m/z* 254.1154 ($M + Na^+$), calcd for $C_{14}H_{17}NO_2Na^+$ 254.1157.

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Supporting Information Available: Complete X-ray data for compounds **3j** and **5b**. This material is available free of charge via the Internet at http.//pubs.acs.org.

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