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One-Pot Asymmetric Synthesis of γ-Nitroaldehydes from Aldehydes and Nitroalkanes through a Catalytic Tandem Reaction Using an Amino Acid Lithium Salt

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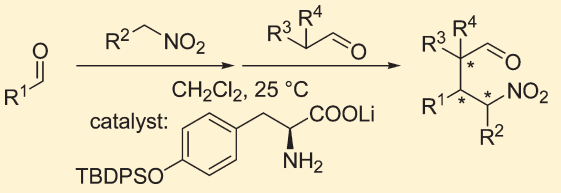
Supporting Information

ABSTRACT: One-pot asymmetric synthesis of γ-nitroaldehydes from aldehydes and nitroalkanes was achieved by a catalytic tandem reaction using a primary amino acid lithium salt, *O*-*tert*-butyldiphenylsilyl L-tyrosine lithium salt, as a catalyst. Various aryl, alkenyl, and alkyl aldehydes were converted into γ-nitroaldehydes via in situ generation of nitroalkenes.



To develop a cost-effective and an environmentally safe synthetic process, reduction of reaction steps is commonly attempted by employing a one-pot synthesis and/or a tandem reaction. The number of reports on one-pot synthesis or tandem reaction has been increasing due to the increasing interest in green chemistry.[1] In 2010, Fréchet's group achieved a one-pot synthesis of γ-nitroaldehydes from aldehydes and nitromethane using a two-mixed-catalyst system consisting of L-proline and an *O*-sily prolinol.[2] According to their report, L-proline works as a catalyst for the generation of a nitroalkene from an aldehyde and nitromethane. Then the *O*-silyl prolinol works as a catalyst for the Michael addition of the second aldehyde with the generated nitroalkene to produce a γ-nitroaldehyde. They confirmed that both catalysts, L-proline and the *O*-silyl prolinol, were necessary to achieve high yields and enantioselectivity of the product. By their method, several γ-nitroaldehydes were successfully synthesized; however, only water-soluble aldehydes, namely small aliphatic aldehydes, can be used as the first aldehyde to effectively generate a nitroalkene as a reaction intermediate.

We have recently reported that a primary amino acid lithium salt, especially L-phenylalanine lithium salt, is an effective catalyst for asymmetric Michael addition of aldehydes to nitroalkenes.[3] By using our reaction conditions, various aryl nitroalkenes were converted into γ-nitroaldehydes in good yields with high enantioselectivity.[4−6] On the other hand, nitroalkenes are commonly synthesized by dehydration of β-nitroalcohols, which can be prepared by Henry reaction (nitroaldol reaction) of aldehydes with nitroalkanes in a basic condition.[7] Dehydration of β-nitroalcohols can be accomplished by a transformation of the hydroxy group into a good leaving group or simply by heating in an acidic condition. In the case of using a primary aliphatic amine as a base for Henry reaction, it is known that a nitroalkene can be synthesized directly from an aldehyde and a nitroalkane via formation of a Schiff base.[8]

In this context, we planned to combine a nitroalkene synthesis with the asymmetric Michael addition of aldehydes to nitroalkenes by a catalytic tandem reaction using a primary amino acid lithium salt as a catalyst. That is, we designed a one-pot asymmetric synthesis of γ-nitroaldehydes from aldehydes and nitroalkanes as depicted in Scheme 1.

First, we examined the reaction of benzaldehyde (**1a**) with nitromethane (**2a**) in the presence of L-phenylalanine lithium salt (**4a**), which was the most effective catalyst in our previous works on asymmetric Michael addition of aldehydes to nitroalkenes (Scheme 2).[3] Various organic solvents were examined; however, the catalyst **4a** could not be dissolved in most of the solvents and only a trace amount of (*E*)-β-nitrostyrene (**3a**) was obtained along with a large amount of the starting material **1a**. The catalyst **4a** dissolved in a high-polarity solvent, DMSO; however, a Henry adduct, 2-nitro-1-phenylethanol (**5**), was generated as a major product and no generation of **3a** was detected by ^{1}H NMR of the crude product. To carry out the condensation reaction in CH_2Cl_2, which was the most effective solvent in our previous works on Michael addition reaction,[3] we next examined a lipophilic catalyst, *O*-*tert*-butyldiphenylsilyl L-tyrosine lithium salt (**4b**).[9] To our delight, the nitrostyrene **3a** was generated in 33% yield after the reaction was carried out for 24 h at 25 °C in CD_2Cl_2. The starting material **1a** (18%) and many minor byproducts were also observed by ^{1}H NMR analysis of the reaction mixture. Since treatment of the nitrostyrene **3a** and an equimolar amount of H_2O with the catalyst **4b** provided aldehyde **1a**, the condensation reaction of **1a** with **2a** is confirmed to be an equilibrium reaction.[2,8] To increase the yield of nitroalkenes **3**, an excess amount of nitroalkane **2** and/or a dehydrating reagent were employed for the condensation reaction (Table 1).

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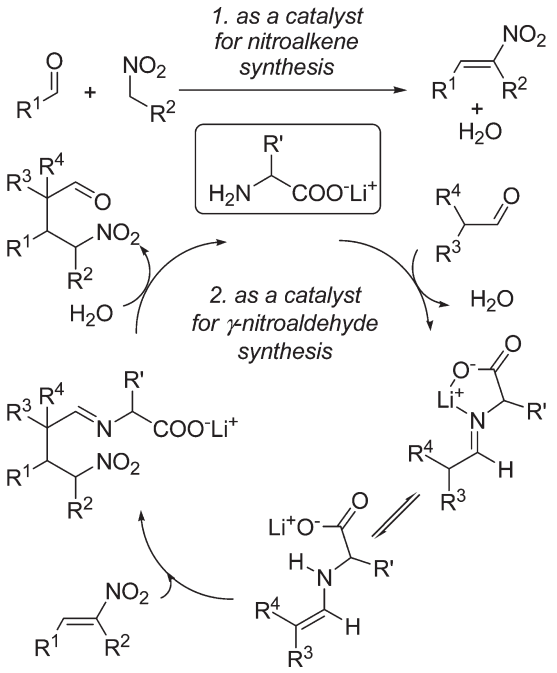
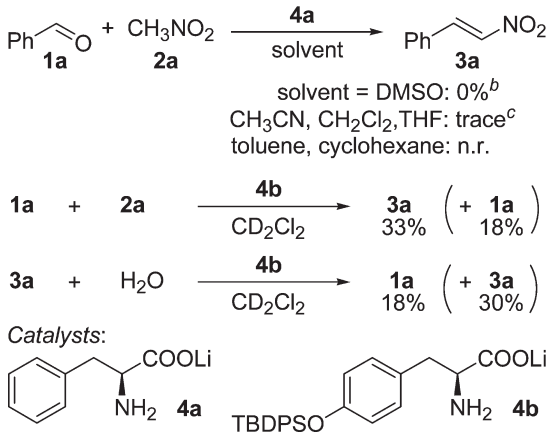
Scheme 1. One-Pot Asymmetric Synthesis of γ-Nitroaldehydes by a Catalytic Tandem Reaction



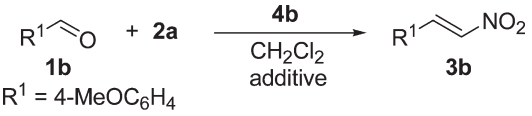
Scheme 2. First Approach to the Synthesis of Nitroalkenes 3[a]



[a] The reactions were carried out with **1a** (1 equiv), **2a** (1 equiv), and **4** (20 mol %) at 25 °C for 24 h. Yields of **1a** and **3a** were determined by ^{1}H NMR, using benzyl acetate as an internal standard. [b] 2-Nitro-1-phenylethanol (**5**) was a major product. [c] **1a** was recovered.

p-Anisaldehyde (**1b**) was employed as a substrate. First, the reaction of **1b** with an equimolar amount of **2a** was carried out with or without a dehydrating reagent. Without a dehydrating reagent, 70% of **1b** was consumed after seven days; however, nitroalkene **3b** was obtained in only 38% yield (Table 1, entry 1). It was found that the addition of a dehydrating reagent, $MgSO_4$, improved both the yield of **3b** and the mass balance of the reaction, although the addition of other dehydrating reagents, MS3A and Na_2SO_4, gave poor results (Table 1, entries 2−4). By using 5 equiv of **2a** to **1b**, the condensation reaction proceeded faster and the yield of **3b** was drastically increased (Table 1, entries 5−8). As a result of optimization of the amount of **2a**, no more improvement of the yield was achieved by using more than 5 equiv of **2a**. Since a gradual decomposition of **3b** was observed in longer reaction time, the most appropriate reaction time was

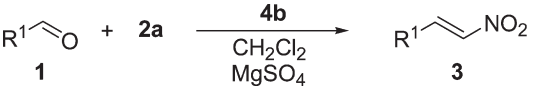
Table 1. Optimization of Reaction Conditions for the Synthesis of Nitroalkene 3b[a]



entry	**2a** (equiv)	additive	*t* (d)	conv (%)[b]	yield (%)[c]
1	1	none	7	70	38
2	1	$MgSO_4$	7	80	58
3	1	MS3A	7	79	19
4	1	Na_2SO_4	7	73	32
5	5	$MgSO_4$	0.5	97	76
6	5	$MgSO_4$	1	95	85
7	5	$MgSO_4$	2	98	80
8	5	$MgSO_4$	7	99	55

[a] The reactions were carried out with **1b** (0.5 mmol), **2a**, additive (MS3A (100 mg), $MgSO_4$ (0.5 mmol), or Na_2SO_4 (0.5 mmol)) and **4b** (0.1 mmol) in CH_2Cl_2 (1 mL) at 25 °C. [b] Determined by ^{1}H NMR analysis of the crude product. [c] Isolated yield based on **1b**.

Table 2. Synthesis of Nitroalkenes 3[a]



entry	R^1	*t* (h)	conv (%)[b]	yield (%)[c]
1	Ph, **1a**	48	96	81, **3a**
2	4-$MeOC_6H_4$, **1b**	24	95	85, **3b**
3	3-$MeOC_6H_4$, **1c**	60	93	82, **3c**
4	2-$MeOC_6H_4$, **1d**	24	100	92, **3d**
5	3,4-$(MeO)_2C_6H_3$, **1e**	48	90	84, **3e**
6	2,4-$(MeO)_2C_6H_3$, **1f**	6	100	96, **3f**
7	4-MeC_6H_4, **1g**	24	95	86, **3g**
8	4-BrC_6H_4, **1h**	60	91	80, **3h**
9	4-ClC_6H_4, **1i**	72	95	80, **3i**
10	4-FC_6H_4, **1j**	60	91	80, **3j**
11	thiophen-2-yl, **1k**	96	80	69, **3k**
12	(*E*)-PhCH=CH, **1l**	72	67	43, **3l**
13	cyclohexyl, **1m**	24	100	84,[d] **3m**
14	$PhCH_2CH_2$, **1n**	72	100	−,[d,e] **3n**
15	**1b**	96	88	81,[f] **3o**
16	acetophenone, **6**	24	0	0[g]

[a] Unless otherwise mentioned, the reactions were carried out with **1** (0.5 mmol), **2a** (2.5 mmol), $MgSO_4$ (0.5 mmol), and **4b** (0.1 mmol) in CH_2Cl_2 (1 mL) at 25 °C. [b] Determined by ^{1}H NMR analysis of the crude product. [c] Isolated yield based on **1**. [d] The reaction was carried out with 7.5 mmol of **2a**. [e] A complex mixture was obtained. [f] Nitroethane (**2b**) (2.5 mmol) was used instead of **2a**. [g] No reaction was observed when acetophenone (**6**) was used instead of **1**.

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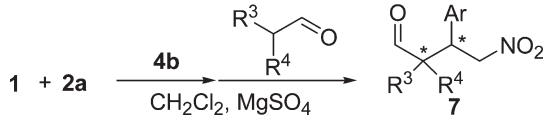
Table 3. One-Pot Asymmetric Synthesis of γ-Nitroaldehydes 7[a]



entry	1	R^3	R^4	yield (%)[b]	dr[c]	ee (%)[d]
1	**1a**	Me	Me	81, **7a**	—	96
2	**1b**	Me	Me	81, **7b**	—	96
3	**1c**	Me	Me	78, **7c**	—	95
4	**1d**	Me	Me	85, **7d**	—	93
5	**1g**	Me	Me	83, **7e**	—	96
6	**1h**	Me	Me	81, **7f**	—	96
7	**1i**	Me	Me	78, **7g**	—	96
8	**1j**	Me	Me	71, **7h**	—	96
9	**1a**	H	*iso*-Pr	40,[e] **7i**	6.7:1	90
10	**1a**	H	*n*-Pr	50,[f] **7j**	2.3:1	71
11	**1a**	H	$PhCH_2$	51,[g] **7k**	2.3:1	82

[a] The reactions were carried out for 72 h at 25 °C after addition of the second aldehyde (1 mmol). [b] Isolated yield based on **1**. [c] *Syn* product was obtained as a major diastereomer. The relative configuration was determined by ^{1}H NMR spectra. [d] Ee of the major diastereomer. Determined by chiral HPLC analysis. [e] **3a** was obtained in 50% yield. [f] **3a**: 35%. [g] **3a**: 43%.

determined to be 24 h. Hence, the best reaction conditions for the condensation reaction of **1b** with **2a** were determined as shown in entry 6, and **3b** was obtained in 85% yield.

Various aryl, alkenyl, and alkyl aldehydes were then used as starting materials (Table 2). Study of the substituent effect on aryl aldehydes **1a**−**j** indicates that the condensation reaction with an electron-rich aryl aldehyde showed better reactivity than that with a relatively electron-poor aryl aldehyde (Table 2, entries 1−10). The reactivity can be explained by the stability of the Schiff base formed in situ from an aldehyde and catalyst **4b** as described in a previous report.[8] Sterically hindered substrates **1d** and **1f** were also converted into nitroalkenes **3d** and **3f**, respectively, in good yields (Table 2, entries 4 and 6). A heteroaryl aldehyde, thiophen-2-yl aldehyde (**1k**), and an alkenyl aldehyde, cinnamaldehyde (**1*l***), required longer reaction time than general aryl aldehydes **1a**−**j** and gave nitroalkenes **3k** and **3*l***, respectively, in lower yields (Table 2, entries 11 and 12). Alkyl aldehydes, cyclohexanecarboxaldehyde (**1m**) and hydrocinnamaldehyde (**1n**), were also subjected to the reaction; however, a large excess amount of **2a** was required to complete the reaction within a reasonable reaction time, and only a complex mixture was obtained from **1n** (Table 2, entries 13 and 14). It was found that the condensation reaction of **1b** with nitroethane (**2b**) also gave the corresponding (*E*)-nitroalkene **3o** stereoselectively in a good yield, while the reaction of acetophenone (**6**) with **2a** did not proceed at all (Table 2, entries 15 and 16). As for the stereochemistry of the nitroalkenes, no generation of a (*Z*)-isomer was observed in all cases.

Finally, we attempted one-pot asymmetric synthesis of γ-nitroaldehydes from aldehydes **1** and nitromethane **2a** through a catalytic tandem reaction using catalyst **4b** (Table 3). After the condensation reaction of **1** with **2a** was carried out under the conditions shown in Table 2, the second aldehyde was added to the resulting reaction mixture. When aldehyde **1a** was used as a starting material, to our

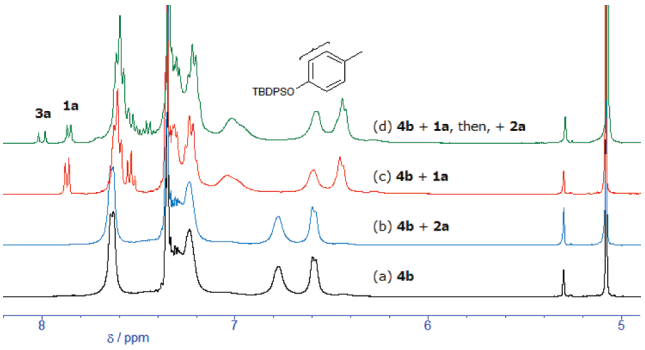
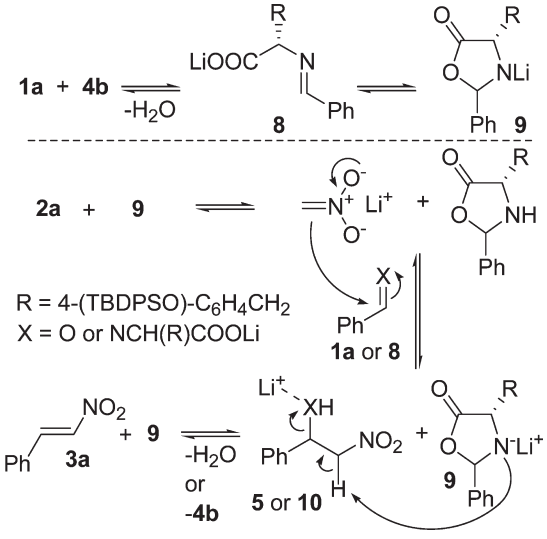


Figure 1. ^{1}H NMR studies on the condensation reaction of aldehyde **1a** with nitroalkane **2a** by catalyst **4b**. The reactions were carried out in CD_2Cl_2 (0.75 mL) at 25 °C and were analyzed by ^{1}H NMR (400 MHz). Benzyl acetate was added as an internal standard. Spectra: (a) **4b** only; (b) **4b** (0.1 mmol), **2a** (0.1 mmol), 10 min; (c) **4b** (0.1 mmol), **1a** (0.1 mmol), 10 min; (d) **4b** (0.1 mmol), **1a** (0.1 mmol), 10 min, then **2a** was added (0.1 mmol), 12 h.

Scheme 3. Plausible Mechanism of the Condensation Reaction



delight, the addition of isobutyraldehyde as the second aldehyde successfully gave a γ-nitroaldehyde **7a** in 81% yield with 96% ee (Table 3, entry 1). Various other aryl aldehydes were also converted into the corresponding γ-nitroaldehydes **7b**−**h** in good yields with high enantioselectivity (Table 3, entries 2−8). The Michael addition of an α-unbranched aldehyde with nitroalkene **3a** generated in situ was very slow as expected,[3] although the corresponding γ-nitroaldehydes **7i**−**k** were obtained with moderate to high enantioselectivity (Table 3, entries 9−12).

We then performed NMR studies to understand the reaction mechanism of the condensation reaction of **1a** with **2a** using catalyst **4b** (Figure 1). According to the previous reports, the condensation reaction of an aldehyde with a nitroalkane using a primary aliphatic amine proceeds via formation of a Schiff base.[8] As can be seen from the results shown in Figure 1, catalyst **4b** immediately reacted with **1a** (Figure 1c), while no major change was observed by mixing **4b** with **2a** (Figure 1b). Probably, these

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results support the generation of a Schiff base in the initial step of the condensation reaction. Finally, it was confirmed that the addition of **2a** to the reaction mixture of **4b** and **1a** provides nitrostyrene **3a** (Figure 1d).

A plausible reaction mechanism of the condensation reaction of **1a** with **2a** by catalyst **4b** is depicted in Scheme 3. Initially, a Schiff base **8**, which can form an oxazolidinone **9**, is generated from **1a** and **4b**.[10] Then the oxazolidinone **9**, which is a stronger base than the Schiff base **8**, removes a proton from **2a** to give a nitronate, which attacks **1a** or **8** to produce β-nitroalcohol **5** or β-nitroamine **10**. Finally, the oxazolidinone **9** promotes dehydration or dehydroamination of **5** or **10** to provide nitroalkene **3a**.[11] The lithium cation of the catalyst will assist the dehydration or dehydroamination by its Lewis acidity[12] since the condensatoin reaction in DMSO, which can cause strong solvation of a lithium cation, gave only a β-nitroalcohol as shown in Scheme 2.

In conclusion, we found that a primary amino acid lithium salt, *O*-*tert*-butyldiphenylsilyl L-tyrosine lithium salt, is an effective catalyst for one-pot asymmetric synthesis of γ-nitroaldehydes from aldehydes and nitroalkanes. The catalyst played two different roles in the reaction: (1) a role as a catalyst for generation of a nitroalkene directly from an aldehyde and a nitroalkane and (2) a role as an organocatalyst for asymmetric Michael addition of an aldehyde to a nitroalkene to provide a γ-nitroaldehyde. By using the present method, various aryl, alkenyl, and alkyl aldehydes were converted into γ-nitroaldehydes in good yields with high enantioselectivity without isolation of nitroalkenes. The present method will also be useful for stereoselective synthesis of nitroalkenes under mild reaction conditions.

EXPERIMENTAL SECTION

Typical Procedure for the Synthesis of Nitroalkenes 3. In a 7 mL vial, *p*-anisaldehyde (**1b**) (68 mg, 0.5 mmol) and nitromethane (**2a**) (153 mg, 2.5 mmol) were successively added to a slurry of *O*-*tert*-butyldiphenylsilyl L-tyrosine lithium salt (**4b**) (42.5 mg, 0.1 mmol), $MgSO_4$ (60 mg, 0.5 mmol), and CH_2Cl_2 (1 mL) at 25 °C. After 24 h of stirring at 25 °C, sat. aq. NaCl (1.5 mL) was added to the vial and extracted with Et_2O (3 × 2 mL). The combined organic phase was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. (*E*)-1-(4-Methoxyphenyl)-2-nitroethene (**3b**) was isolated by column chromatography (silica gel, hexane/Et_2O) in 85% yield (76 mg) as a yellow solid. δ_H ($CDCl_3$) 3.88 (3H, s), 6.96 (2H, d, J = 8.8 Hz), 7.50−7.55 (3H, m), 7.99 (1H, d, J = 13.6 Hz).

Spectroscopic data of **3a**−**d**, **3f**−**h**, **3j**, and **3k** are in agreement with that of samples purchased from commercial suppliers. Spectroscopic data of **3e**,[13a] **3i**,[13b] **3*l***,[13c] **3m**,[13d] and **3o**[13e] are in agreement with the published data.

Typical Procedure for the One-Pot Asymmetric Synthesis of γ-Nitroaldehydes 7. In a 7 mL vial, benzaldehyde (**1a**) (53 mg, 0.5 mmol) and **2a** (153 mg, 2.5 mmol) were successively added to a slurry of **4b** (42.5 mg, 0.1 mmol), $MgSO_4$ (60 mg, 0.5 mmol), and CH_2Cl_2 (1 mL) at 25 °C. After 48 h of stirring at 25 °C, isobutyraldehyde (72 mg, 1 mmol) was added to the resulting reaction mixture. After a further 72 h of stirring, the same workup was performed as mentioned above. (*S*)-2,2-Dimethyl-4-nitro-3-phenylbutanal (**7a**)[3] was isolated by column chromatography (silica gel, hexane/Et_2O) in 81% yield (89.5 mg) as a yellow oil. The enantioselectivity was determined by HPLC analysis (96% ee). δ_H ($CDCl_3$) 1.01 (3H, s), 1.14 (3H, s), 3.79 (1H, dd, J = 4.2, 11.3 Hz), 4.69 (1H, dd, J = 4.2, 13.1 Hz), 4.86 (1H, dd, J = 11.3, 13.1 Hz), 7.20−7.21 (2H, m), 7.30−7.36 (3H, m), 9.53 (1H, s).

Spectroscopic data of **7a**−**b**,[3] **7c**−**e**,[5l,ad] **7f**,[3] **7g**,[5l,ad] and **7h**−**k**[3] are in agreement with the published data.,

ASSOCIATED CONTENT

Supporting Information. Experimental details of Scheme 2 and Figure 1, ^{1}H NMR spectra of **3e**, **3i**, **3*l*,m**, **3o**, and **7a**−**k**, and HPLC analysis of **7a**−**k**. This material is available free of charge via the Internet at http://pubs.acs.org.

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REFERENCES

(1) The number of reports related to "green chemistry" or "one-pot and tandem" was analyzed by SciFinder Scholar.

(2) Scroggins, S. T.; Chi, Y.; Fréchet, J. M. J. *Angew. Chem., Int. Ed.* **2010**, *49*, 2393.

(3) (a) Yoshida, M.; Sato, A.; Hara, S. *Org. Biomol. Chem.* **2010**, *8*, 3031. (b) Sato, A.; Yoshida, M.; Hara, S. *Chem. Commun.* **2008**, 6242.

(4) Reviews on asymmetric Michael addition of aldehydes to nitroalkenes: (a) Berner, O. M.; Tedeschi, L.; Enders, D. *Eur. J. Org. Chem.* **2002**, 1877. (b) Tsogoeva, S. B. *Eur. J. Org. Chem.* **2007**, 1701. (c) Almaşi, D.; Alonso, D. A.; Nájera, C. *Tetrahedron: Asymmetry* **2007**, *18*, 299.

(5) Asymmetric Michael addition of aldehydes to nitroalkenes with a secondary amine catalyst: (a) Zhu, S.; Yu, S.; Wang, Y.; Ma, D. *Angew. Chem., Int. Ed.* **2010**, *49*, 4656. (b) Enders, D.; Kruell, R.; Bettray, W. *Synthesis* **2010**, 567. (c) Kelleher, F.; Kelly, S.; Watts, J.; McKee, V. *Tetrahedron* **2010**, *66*, 3525. (d) Hu, F.; Guo, C.-S.; Xie, J.; Zhu, H.-L.; Huang, Z.-Z. *Chem. Lett.* **2010**, *39*, 412. (e) Bai, J.-F.; Xu, X.-Y.; Huang, Q.-C.; Peng, L.; Wang, L.-X. *Tetrahedron Lett.* **2010**, *51*, 2803. (f) Lu, D.; Gong, Y.; Wang, W. *Adv. Synth. Catal.* **2010**, *352*, 644. (g) Wang, B. G.; Ma, B. C.; Wang, Q.; Wang, W. *Adv. Synth. Catal.* **2010**, *352*, 2923. (h) Demir, A. S.; Eymur, S. *Tetrahedron: Asymmetry* **2010**, *21*, 112. (i) Wiesner, M.; Neuburger, M.; Wennemers, H. *Chem.—Eur. J.* **2009**, *15*, 10103. (j) Lombardo, M.; Chiarucci, M.; Quintavalla, A.; Trombini, C. *Adv. Synth. Catal.* **2009**, *351*, 2801. (k) Luo, R.-S.; Weng, J.; Ai, H.-B.; Lu, G.; Chan, A. S. C. *Adv. Synth. Catal.* **2009**, *351*, 2449. (l) Chang, C.; Li, S.-H.; Reddy, R. J.; Chen, K. *Adv. Synth. Catal.* **2009**, *351*, 1273. (m) Laars, M.; Ausmees, K.; Uudsemaa, M.; Tamm, T.; Kanger, T.; Lopp, M. *J. Org. Chem.* **2009**, *74*, 3772. (n) Zhang, X.-J.; Liu, S.-P.; Li, X.-M.; Yan, M.; Chan, A. S. C. *Chem. Commun.* **2009**, 833. (o) Guo, L.; Chi, Y.; Almeida, A. M.; Guzei, I. A.; Parker, B. K.; Gellman, S. H. *J. Am. Chem. Soc.* **2009**, *131*, 16018. (p) Wiesner, M.; Revell, J. D.; Tonazzi, S.; Wennemers, H. *J. Am. Chem. Soc.* **2008**, *130*, 5610. (q) Chi, Y.; Guo, L.; Kopf, N. A.; Gellman, S. H. *J. Am. Chem. Soc.* **2008**, *130*, 5608. (r) Wiesner, M.; Revell, J. D.; Wennemers, H. *Angew. Chem., Int. Ed.* **2008**, *47*, 1871. (s) García-García, P.; Ladépêche, A.; Halder, R.; List, B. *Angew. Chem. Int., Ed.* **2008**, *47*, 4719. (t) Hayashi, Y.; Ito, T.; Ohkubo, M.; Ishikawa, H. *Angew. Chem., Int. Ed.* **2008**, *47*, 4722. (u) Wu, L.-Y.; Yan, Z.-Y.; Xie, Y.-X.; Niu, Y.-N.; Liang, Y.-M. *Tetrahedron: Asymmetry* **2007**, *18*, 2086. (v) Barros, M. T.; Phillips, A. M. F. *Eur. J. Org. Chem.* **2007**, 178. (w) Mase, N.; Watanabe, K.; Yoda, H.; Takabe, K.; Tanaka, F.; Barbas, C. F., III. *J. Am. Chem. Soc.* **2006**, *128*, 4966. (x) Palomo, C.; Vera, S.; Mielgo, A.; Gómez-Bengoa, E. *Angew. Chem., Int. Ed.* **2006**, *45*, 4984. (y) Wang, J.; Li, H.; Lou, B.; Zu, L.; Guo, H.; Wang, W. *Chem.*

—*Eur. J.* **2006**, *12*, 4321. (z) Luo, S.; Mi, X.; Zhang, L.; Liu, S.; Xu, H.; Cheng, J.-P. *Angew. Chem., Int. Ed.* **2006**, *45*, 3093. (aa) Mossé, S.; Laars, M.; Kriis, K.; Kanger, T.; Alexakis, A. *Org. Lett.* **2006**, *8*, 2559. (ab) Ishii, T.; Fujioka, S.; Sekiguchi, Y.; Kotsuki, H. *J. Am. Chem. Soc.* **2004**, *126*, 9558. (ac) Alexakis, A.; Andrey, O. *Org. Lett.* **2002**, *4*, 3611. (ad) Ting, Y.-F.; Chang, C.; Reddy, R. J.; Magar, D. R.; Chen, K. *Chem.—Eur. J.* **2010**, *16*, 7030.

(6) Asymmetric Michael addition of aldehydes to nitroalkenes with a primary amine catalyst: (a) He, T.; Gu, Q.; Wu, X.-Y. *Tetrahedron* **2010**, *66*, 3195. (b) Zhang, X.-J.; Liu, S.-P.; Lao, J.-H.; Du, G.-J.; Yan, M.; Chan, A. S. C. *Tetrahedron: Asymmetry* **2009**, *20*, 1451. (c) Lalonde, M. P.; Chen, Y.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2006**, *45*, 6366. (d) McCooey, S. H.; Connon, S. J. *Org. Lett.* **2007**, *9*, 599. (e) Xu, Y.; Zou, W.; Sundén, H.; Ibrahem, I.; Córdova, A. *Adv. Synth. Catal.* **2006**, *348*, 418.

(7) Various methods for the synthesis of nitroalkenes have been reported. Selected papers are listed below: (a) Kuster, G. J. T.; Steeghs, R. H. J.; Scheeren, H. W. *Eur. J. Org. Chem.* **2001**, 553. (b) Mahmood, S. Y.; Lallemand, M.-C.; Sader-Bakaouni, L.; Charton, O.; Vérité, P.; Dufat, H.; Tillequin, F. *Tetrahedron* **2004**, *60*, 5105. (c) Dockendorff, C.; Sahli, S.; Olsen, M.; Milhau, L.; Lautens, M. *J. Am. Chem. Soc.* **2005**, *127*, 15028. (d) Duursma, A.; Minnaard, A. J.; Feringa, B. L. *Tetrahedron* **2002**, *58*, 5773. (e) Lucet, D.; Sabelle, S.; Kostelitz, O.; Gall, T. L.; Mioskowski, C. *Eur. J. Org. Chem.* **1999**, 553. (f) Pathak, R.; Shaw, A. K.; Bhaduri, A. P.; Chandrasekhar, K. V. G.; Srivastava, A.; Srivastava, K. K.; Chaturvedi, V.; Srivastava, R.; Srivastava, B. S.; Arorac, S.; Sinhac, S. *Bioorg. Med. Chem.* **2002**, *10*, 1695.

(8) (a) Jones, G. *Organic Reactions*; John Wiley & Sons, Inc.: New York, 1967; Vol. 15, Chapter 2. (b) Robertson, D. N. *J. Org. Chem.* **1960**, *25*, 49. (c) Worrall, D. E. *J. Am. Chem. Soc.* **1934**, *56*, 1556.

(9) (a) Yoshida, M.; Ohno, Y.; Hara, S. *Tetrahedron Lett.* **2010**, *51*, 5134. (b) Yoshida, M.; Narita, M.; Hara, S. *Tetrahedron Lett.* **2009**, *50*, 7297. (c) Teo, Y.-C.; Lau, J.-J.; Wu, M.-C. *Tetrahedron: Asymmetry* **2008**, *19*, 186. (d) Teo, Y.-C.; Chua, G.-L. *Tetrahedron Lett.* **2008**, *49*, 4235. (e) Wu, X.; Jiang, Z.; Shen, H.-M.; Lu, Y. *Adv. Synth. Catal.* **2007**, *349*, 812. (f) Cheng, L.; Wu, X.; Lu, Y. *Org. Biomol. Chem.* **2007**, *5*, 1018. (g) Aratake, S.; Itoh, T.; Okano, T.; Nagae, N.; Sumiya, T.; Shoji, M.; Hayashi, Y. *Chem.—Eur. J.* **2007**, *13*, 10246. (h) Itagaki, N.; Kimura, M.; Sugahara, T.; Iwabuchi, Y. *Org. Lett.* **2005**, *7*, 4185.

(10) Abell, A. D.; Oldham, M. D. *Bioorg. Med. Chem. Lett.* **1999**, 497.

(11) Generation of the nitroalkene **3a** was monitored by ^{1}H NMR after the addition of **2a** or **5** to the mixture of **4b** and **1a**. See the Supporting Information.

(12) (a) Yamamoto, H., Ed. *Lewis Acids in Organic Synthesis*; Wiley-VCH: Weinheim, Germany, 2000. (b) Yamaguchi, M.; Yokota, N.; Minami, T. *J. Chem. Soc., Chem. Commun.* **1991**, 1088. (c) Yamaguchi, M.; Shiraishi, T.; Hirama, M. *J. Org. Chem.* **1996**, *61*, 3520. (d) Yamaguchi, M.; Shiraishi, T.; Hirama, M. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1176.

(13) (a) Sawant, D.; Kumar, R.; Maulik, P. R.; Kundu, B. *Org. Lett.* **2006**, *8*, 1525. (b) Andrey, O.; Alexakis, A.; Bernardinelli, G. *Org. Lett.* **2003**, *5*, 2559. (c) Dockendorff, C.; Sahli, S.; Olsen, M.; Milhau, L.; Lautens, M. *J. Am. Chem. Soc.* **2005**, *127*, 15028. (d) Duursma, A.; Minnaard, A. J.; Feringa, B. L. *Tetrahedron* **2002**, *58*, 5773. (e) Yan, S.; Gao, Y.; Xing, R.; Shen, Y.; Liu, Y.; Wu, P.; Wu, H. *Tetrahedron* **2008**, *64*, 6294.