DOI: 10.1002/ejoc.200700058

Organocatalysis with Chiral Formamides: Asymmetric Allylation and Reduction of Imines

Christine Baudequin,[a] Devdutt Chaturvedi,[a] and Svetlana B. Tsogoeva*[a][‡]

Keywords: Chirality / Formamides / Organocatalysis / Allylation / Reduction

Simple aldimine, derived from *p*-nitrobenzaldehyde and 2-aminophenol, reacts with allyltrichlorosilane in the presence of chiral *N*-formylproline activator **5** and an L-proline additive to afford the corresponding homoallylic amine in good yield (84 %) and with moderate enantioselectivity (43 % *ee*). The role of the second formamide moiety in the activator is crucial to bring about the enhancement in the reaction rate and enantioselectivity, as C_2-chiral bisformamide **1** promotes for the same allylation reaction in higher yield (94 %) and enantioselectivity (83 % *ee*). Chiral monoformamide **5** (10 mol-%), with the assistance of HMPA as an additive, also catalyses the asymmetric reduction of ketimine **13** in the presence of trichlorosilane in good yield and enantioselectivity (75 %, 81 % *ee*).
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Introduction

The allylation of aldehydes and aldimines with allyltrichlorosilane is among the most useful C–C bond-forming reaction as it can provide valuable intermediates for the synthesis of bioactive natural products and pharmaceutically important compounds.[1]

Whereas a broad variety of chiral organocatalysts has been found to catalyse the enantioselective allylation of aldehydes,[2] as well as of *N*-acylhydrazones,[3] and fruitful results have been reported, enantioselective allylation of simple aldimines with allyltrichlorosilane was an unsolved task[4] until 2006.[5,6]

Quite recently, our group reported the first example of an organocatalytic enantioselective allylation of simple 2-aminophenol-derived aldimines utilising novel C_2-chiral bisformamide **1** (Figure 1) and an in situ generated L-proline-derived allylsilane reagent.[5] We proposed a plausible transition state model and, for simplicity, considered only one formamide group of the C_2-chiral bisformamide; we speculated that the second formamide moiety might coordinate in a similar manner to the silicon atom of the second molecule of the L-proline-derived allylsilane reagent.[5] To test this hypothesis and to elucidate the role of the second formamide moiety in reactivity and enantioselectivity, we decided to synthesise and use chiral monoformamides **2**–**6** (Figure 1) for the same allylation reactions. In this contribution, we also demonstrate the potential of these chiral formamides as organocatalysts for the reduction reaction of ketimines.

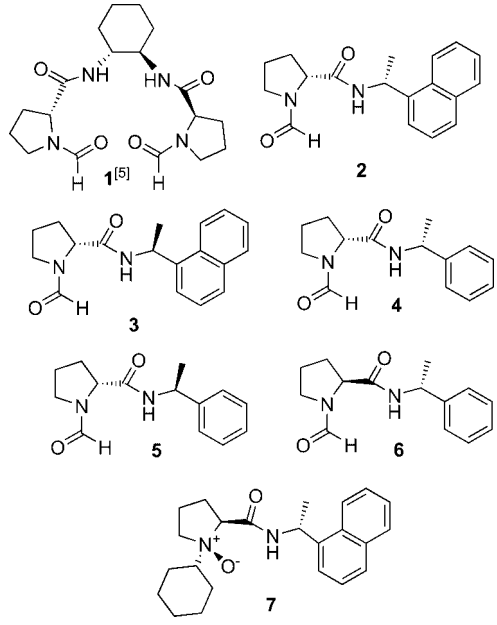

Figure 1. Structures of C_2-chiral bisformamide **1**, monoformamides **2**–**6** and proline-derived *N*-oxide **7**.

Results and Discussion

The syntheses of chiral formamide compounds **2**–**6** were accomplished by known methods[7] as summarised in Scheme 1. D- and L-proline were converted into their *N*-formyl derivatives by treatment with formic acid in the pres-

[a] Institut für Organische und Biomolekulare Chemie der Georg-August-Universität Göttingen,
Tammannstrasse 2, 37077 Göttingen, Germany
[‡] Present address: Institut für Organische Chemie der Friedrich-Alexander Universität Erlangen-Nürnberg,
Henkestrasse 42, 91054 Erlangen, Germany
Fax: +49-9131-85-26865
E-mail: tsogoeva@chemie.uni-erlangen.de

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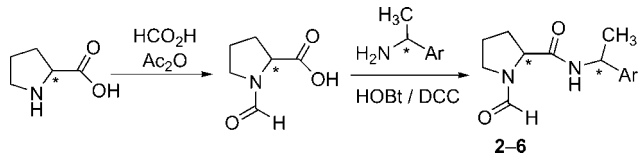
ence of acetic anhydride. The subsequent treatment of chiral *N*-formylprolines with (*R*)- or (*S*)-1-(1-naphthyl)ethylamine and (*R*)- or (*S*)-1-phenylethylamine in the presence of HOBt and DCC gave target chiral formamides **2**–**6** (Figure 1).



Scheme 1.

Allylation of Aldimines with Allyltrichlorosilane

The formamide derivatives were then examined for their ability to mediate the enantioselective allylation of simple aldimines derived from aldehydes and 2-aminophenols. As a first model, we studied the addition of allyltrichlorosilane to **8a**, which contains an electron-donating group on the aromatic ring, in the presence of the formamide derivatives at room temperature. The results obtained are summarised in Table 1 (Entries 1–7).

The use of **2** and **3** at 20 mol-% resulted in the formation of (*S*) product **9a** in low yields and moderate enantioselectivities (15%, 37%*ee* and 13%, 41%*ee* for Entries 1 and 3, respectively). Interestingly, formamides **2** and **3** in stoichiometric amounts showed approximately the same enantioselectivities (40 and 48%*ee*, respectively), but better yields (45 and 42%, respectively) than with 20 mol-% loading (Table 1, Entries 1, 3 vs. 2, 4).

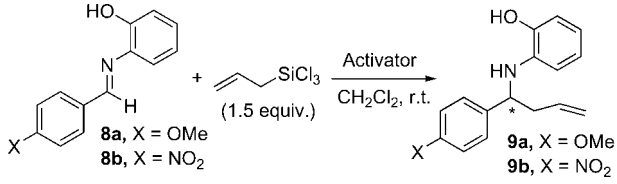
Similarly, moderate yields (48–52%) and enantioselectivities (47–57%*ee*) were observed with chiral formamides **4**–**6** under the same reaction conditions (Table 1, Entries 5–7). Notably, the (*S*) product was obtained with formamides **2**–**5**, which contained the *N*-formylproline moiety with the (*R*) configuration, independent of the absolute configuration of the arylethyl moiety [(*R*) or (*S*), respectively]. This shows that the absolute configuration of the product depends only on the configuration of the chiral centre in the proline moiety. Indeed, formamide **6**, which contains the *N*-formylproline unit in the (*S*) configuration, gave the (*R*) product (Table 1, Entry 7).

Chiral formamide **5** was found to be the best activator with respect to both the yield and the enantioselectivity (50%, 57%*ee*, Table 1, Entry 7) and was selected for further experiments with aldimine **8b** containing an electron-withdrawing group on the aromatic ring.

Whereas the yields are noticeably influenced by the loading of the formamide, the enantioselectivity appears to be rather insensitive to it (cf. Table 1, Entries 1, 3 vs. 2, 4). Furthermore, yields are slightly dependent on the substrate concentration and decrease when the concentration is increased from 0.05 to 0.5 and then up to 1.0 mol L^{-1} (cf. Table 1, Entry 8 vs. 9 vs. 10). Higher levels of asymmetric induction are observed at higher substrate concentrations (cf. Table 1, Entry 8 vs. 9 vs. 10).

The presence of electron-donating (**8a**) or electron-withdrawing (**8b**) groups on the aromatic ring of the aldimine

Table 1. Screening of chiral formamides **2**–**6** for asymmetric allylation of aldimines **8a** and **8b**.



Entry	X	Activator (equiv.)	*t* [h]	Concentration [mol L^{-1}]	Additive (equiv.)	Yield [%][a]	*ee* [%][b]	Configuration
1	OMe	**2** (0.2)	55	0.5	–	15	37	(*S*)
2	OMe	**2** (1)	72	0.5	–	45	40	(*S*)
3	OMe	**3** (0.2)	51	0.5	–	13	41	(*S*)
4	OMe	**3** (1)	72	0.5	–	42	48	(*S*)
5	OMe	**4** (1)	72	0.5	–	48	47	(*S*)
6	OMe	**5** (1)	72	0.5	–	50	57	(S)
7	OMe	**6** (1)	72	0.5	–	52	54	(*R*)
8	NO_2	**5** (1)	72	0.05	–	60	28	(*S*)
9	NO_2	**5** (1)	72	0.5	–	54	42	(*S*)
10	NO_2	**5** (1)	72	1	–	43	50	(*S*)
11	NO_2	**7** (1)	72	0.05	–	44	0	–
12[5]	NO_2	**1** (2)	48	0.5	–	93	54	(*S*)
13[5]	NO_2	**1** (2)	4	0.5	L-proline (2)	94	83	(*S*)
14	NO_2	**5** (1)	72	1	L-proline (1)	65	36	(*S*)
15	NO_2	**5** (2)	26	1	L-proline (2)	78	42	(*S*)
16	NO_2	**5** (2)	72	0.5	L-proline (2)	84	43	(*S*)
17	NO_2	**5** (1)	72	0.5	(+)-CSA (1)	50	36	(*S*)

[a] Yield of isolated product after column chromatography on SiO_2. [b] Enantioselectivities were determined by chiral HPLC analysis (Daicel Chiralpak AD) by comparison with an authentic racemic material.

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did not affect the yields significantly; however, the enantioselectivities were influenced and a higher enantiomeric excess was obtained with **8a** (cf. Table 1, Entry 6 vs. 9) at the same substrate concentration (0.5 mol L^{-1}).

Furthermore, we prepared a chiral proline-derived *N*-oxide **7** as an analogue of a known organocatalyst[2i] (identified as an effective catalyst for the reaction of allyltrichlorosilane with aldehydes[2i]) and employed it in the allylation reaction of aldimine **8b**. However, *N*-oxide **7** gave the product only in racemic form and in moderate yield (44%, Table 1, Entry 11).

As demonstrated in our previous communication,[5] the reaction rate and the enantioselectivity could be significantly improved by combination of the chiral bisformamide activator with an L-proline additive (Table 1, Entry 12 vs. 13). Hence, we decided to examine this reaction by using monoformamide **5** with the L-proline additive. The reaction conditions (activator, substrate and additive concentration) were further varied to study and compare their effects on the allylation reaction of bis- and monoformamides (Table 1, Entries 12, 13 vs. 14–16).

Although the yield improved to 84% (Table 1, Entry 16), as expected,[5] by using L-proline (2 equiv.) as an additive in the presence of **5** (2 equiv.), no improvement in the enantioselectivity and reaction times (43%*ee*, 72 h) with monoformamide **5**, relative to those with C_2-chiral bisformamide **1** (83%*ee*, 4 h) was observed (Table 1, Entry 13 vs. 16).

Evidently, the second formamide group of **1**, as reported recently,[5] acts in a similar way to the first formamide moiety by coordination to a silicon atom of L-proline-derived allylsilane reagent and by steric hindrance, which provides higher reaction rates and enantioselectivities for the allylation reaction of aldimines (Table 1, Entry 13 vs. 16).

Exchange of the L-proline additive for (+)-CSA gave the (*S*) product in lower yield and enantioselectivity (Table 1, Entry 17).

To determine the absolute configuration of the allylated product, it was necessary to remove the *N*-hydroxyphenyl group. The Kobayashi group examined deprotection conditions and it was found that a 2-amino-*p*-cresol derivative gave better yields than 2-aminophenol-derived aldimine by using $PhI(OAc)_2$ for the deprotection.[4]

Aldimine **10** was also a suitable substrate for the asymmetric allylation reaction and gave compound **11** in 79% yield and 51%*ee* (Scheme 2). The absolute configuration of the allylated product was determined after converting **11** into useful homoallylamine **12**. Methylation of the phenolic OH group followed by deprotection using $PhI(OAc)_2$ gave allylated amine **12**.

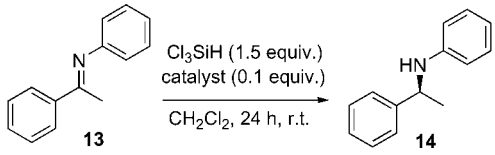
Comparison of the optical rotation value of 1-(4-nitrophenyl)-but-3-enylamine (**12**) with that of the literature data[8] allowed us to determine that the absolute configuration of the major enantiomer was (*R*). By a similar analogy, it was possible to determine that the absolute configuration of the allylated product that was obtained from aldimine **8** with formamides **2**–**5** was (*S*).

Reduction of Ketimine with Trichlorosilane

The asymmetric hydrogenation of imines represents one of the most important methods for the preparation of chiral amines;[9] nevertheless, this process is associated with metal-leaching and high pressure. Recently, some attention was turned to the development of chiral organocatalysts. In fact, several groups reported the use of chiral Lewis bases for the reduction of imines with trichlorosilane[10] and Brønsted acids for the transfer hydrogenation with Hantzch ester.[11] Also, chiral *N*-formylproline derivatives were reported as organocatalysts for the reduction of imines.[10a] We therefore decided to examine the catalytic efficiency of formamides **2**–**6** in the reduction reaction of ketimines in the presence of Cl_3SiH.

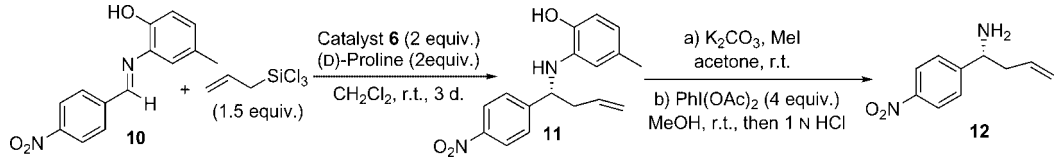
In the trial reduction reaction of imine **13** in CH_2Cl_2 at room temperature for 24 h, chiral formamide **5** (10 mol-%) afforded the highest *ee* value (64%*ee*, Table 2, Entry 5). The alternative catalyst, diastereomer **4**, promoted a significantly less-selective transformation to afford the product

Table 2. Screening of chiral catalysts **1**–**5** and **7** for the asymmetric reduction of ketimine **13**.



Entry	Catalyst	Yield[a] [%]	*ee* (*S*)[b] [%]
1	**1**	69[c]	33
2	**2**	48	20
3	**3**	53	44
4	**4**	48	19
5	**5**	47	64
6	**7**	34	0

[a] Yield of isolated product after column chromatography on SiO_2. [b] Enantioselectivities were determined by chiral HPLC analysis (Daicel Chiralpak OD) by comparison with an authentic racemic material. [c] Reaction was carried out for 70 h.



Scheme 2.

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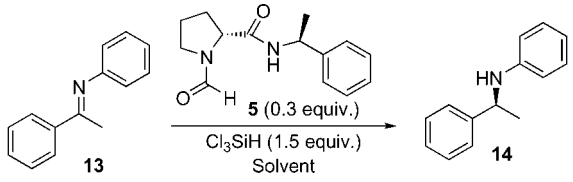
with the same absolute configuration (19%*ee*, Table 2, Entry 4). Replacement of the phenyl group with a naphthyl moiety (catalyst **5** vs. **3**, Figure 1) led to a reduction in the enantioselectivity of the imine from 64 to 44%*ee* (Table 2, Entry 5 vs. 3). As in the case of the allylation reaction, chiral *N*-oxide **7** gave no induction, and the amine was obtained in a racemic form (Table 2, Entry 6).

We then studied the solvent effects on the chemical yield and enantioselectivity. Some results, with the use of 30 mol-% of selected catalyst **5**, are shown in Table 3. Reactions performed in chloroform, toluene and 1,2-dichloroethane showed a small difference in terms of enantioselectivity, compared to the results obtained in CH_2Cl_2.

Table 3. Optimisation of reaction conditions with selected catalyst **5**.



Entry	Additive (equiv.)	Solvent	*T* [°C]	*t* [h]	Yield [%][a]	*ee* (*S*) [%][b]
1	–	CH_2Cl_2	r.t.	24	52	67
2	–	$CHCl_3$	r.t.	24	38	61
3	–	Toluene	r.t.	24	66	58
4	–	$ClCH_2CH_2Cl$	r.t.	24	58	64
5	HMPA (0.3)	CH_2Cl_2	r.t.	24	64	74
6	*p*-nitrobenzoic acid (0.3)	CH_2Cl_2	r.t.	24	63	62
7	HMPA (0.3)	CH_2Cl_2	–20	72	75	81

[a] Yield of isolated product after column chromatography on SiO_2. [b] Enantioselectivities were determined by chiral HPLC analysis (Daicel Chiralpak OD) in comparison with authentic racemic material.

Finally, we examined two additives, HMPA and *p*-nitrobenzoic acid (Table 3, Entries 5–7). The most effective of these was found to be HMPA, which provided in combination with formamide **5** the best yield and enantioselectivity at –20 °C (75%, 81%*ee*, Table 3, Entry 7).

Conclusions

Chiral monoformamide **5** in combination with L-proline as an additive was shown to promote the enantioselective allylation of simple aldimines with allyltrichlorosilane with up to 84% yield and 43%*ee* within 72 h. The study presented undoubtedly suggests the importance of the second formamide moiety for higher rates and stereoselectivities in the allylation reaction, as C_2-chiral bisformamide **1** promotes the same reaction with higher yield (94%) and enantioselectivity (83%*ee*) within 4 h.

The use of chiral formamides **1**–**6** in the reduction of ketimine **13** and in the presence of trichlorosilane was also demonstrated. The reaction gave good results (75%, 81%*ee*) with monoformamide **5** in the presence of an HMPA additive.

Further development of new formamide-derived chiral bifunctional organocatalysts and new applications in catalysis are currently underway in our laboratory.

Experimental Section

General: All solvents were purified by standard procedures and distilled prior to use. Reagents obtained from commercial sources were used without further purification. TLC chromatography was performed on precoated aluminium silica gel SIL G/UV_{254} plates (Marcherey, Nagel & Co.) or silica gel 60-F_{254} precoated glass plates (Merck). ^1H NMR spectra were recorded with a Varian Unity 300 spectrometer. ESI mass spectra were recorded with a LCQ Finnigan spectrometer. High-resolution mass spectra were measured with a Bruker APEX IV 7T FT-ICR instrument. A Perkin–Elmer 241 polarimeter was used for optical rotation measurements.

***N*-Formyl-D-proline:** D-Proline (3 g, 26.05 mmol) was dissolved in 85% formic acid (55 mL) and cooled to 0 °C. Acetic anhydride (18 mL) was added, and the reaction mixture was stirred at room temperature for 2 h. Ice cold water (21 mL) was then added, and the solvent was removed under reduced pressure. The residual pale yellow oil was dissolved in methanol, and the solvent was removed under reduced pressure to give the product as a white solid in 91% yield (3.4 g). $[\alpha]_D^{20}$ = +121.5 (*c* = 1.2, EtOH). ^1H NMR (300 MHz, $CDCl_3$): δ = 11.32 (s, 1 H, COOH), 8.26 and 8.22 (2 × s, 1 H, CHO), 4.45–4.39 (m, 1 H), 3.68–3.47 (m, 2 H), 2.30–1.95 (m, 4 H) ppm. MS (ESI+): *m*/*z* = 143.9 $[M + H]^+$, 166.0 $[M + Na]^+$, 308.8 $[2M + Na]^+$.

***N*-Formyl-L-proline:** This compound was prepared from L-proline by the same procedure as described above as to give the product as a white solid in 93%. $[\alpha]_D^{20}$ = –118.4 (*c* = 0.8, EtOH). ^1H NMR (300 MHz, $CDCl_3$): δ = 8.81 (s, 1 H, COOH), 8.29 and 8.26 (2 × s, 1 H, CHO), 4.51–4.41 (m, 1 H), 3.67–3.51 (m, 2 H), 2.29–2.20 (m, 2 H), 2.08–1.87 (m, 2 H) ppm. MS (ESI+): *m*/*z* = 144.0 $[M + H]^+$, 166.0 $[M + Na]^+$, 308.8 $[2M + Na]^+$.

Compound 2: A solution of DCC (2.16 g, 10 mmol) in DMF (10 mL) at 0 °C was added dropwise to a mixture of *N*-formyl-D-proline (1 g, 6.98 mmol), anhydrous $CuCl_2$ (1.41 g, 10 mmol) and HOBt (1.6 g, 10 mmol) in dry DMF (20 mL), and the reaction mixture was stirred for 30 min. (*R*)-1-(1-naphthyl)ethylamine (2.24 g, 13 mmol) was added and the stirring was continued for 24 h (0 °C, room temp.). The reaction mixture was diluted with EtOAc (50 mL) and washed with cold 0.1 N HCl, saturated $NaHCO_3$ and brine. The organic layer was dried with anhydrous sodium sulfate, and the solvent was removed under reduced pressure. The crude material was purified by column chromatography on silica gel (hexane/EtOAc) to give pure amide **2** as a white solid in 35% yield (0.7 g). $[\alpha]_D^{20}$ = +123.0 (*c* = 0.7, EtOH). ^1H NMR (300 MHz, $CDCl_3$, *cis* and *trans* forms): δ = 8.31 (s, 1 H, CHO), 8.09–8.06 and 8.01–7.98 (m, 1 H), 7.87–7.74 (m, 2 H), 7.54–7.41 (m, 4 H), 7.38 and 6.19 (2 × d, *J* = 8.7 and 8.6 Hz, 1 H, NH), 5.91 and 5.84 (2 × quintet, *J* = 6.9 and 7.0 Hz, 1 H), 4.42 and 4.30 (2 × dd, *J* = 8.3 and 4.1 Hz; *J* = 8.1 and 3.3 Hz, 1 H), 3.58 (m, 2 H), 2.51–2.40 (m, 1 H), 2.21–2.01 (m, 1 H), 1.97–1.79 (m, 2 H), 1.64 and 1.59 (2 × d, *J* = 6.3 and 6.9 Hz, 3 H, Me) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$, major isomer): δ = 169.22, 162.17, 138.68, 133.84, 130.79, 128.75, 127.98, 126.25, 125.63, 125.35, 123.16, 122.42, 57.87, 46.91, 45.03, 27.04, 24.18, 21.30 ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$, minor isomer): δ = 170.17, 162.05, 137.44, 133.89, 130.94, 128.87, 128.55, 126.54, 125.91, 125.12, 122.96, 122.60, 60.67, 44.82, 44.31,

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30.36, 22.85, 20.53 ppm. IR (KBr): ṽ = 3297, 3257, 3106, 3070, 2978, 2933, 2878, 1666, 1597, 1571, 1552, 1508, 1448, 1416, 1383, 1336, 1310, 1286, 1250, 1197, 1116, 978, 921, 805, 781, 448 cm^{-1}. MS (ESI+): *m/z* = 319.2 $[M + Na]^+$, 614.9 $[2M + Na]^+$. $C_{18}H_{20}N_2O_2$ (296.36): calcd. C 72.95, H 6.80, N 9.45; found C 73.12, H 7.06, N 9.24.

Compound 3: This compound was prepared from *N*-formyl-D-proline and (*S*)-1-(1-naphthyl)ethylamine in a manner analogous to **2** and was obtained as a white solid. $[\alpha]_D^{20}$ = +155.0 (*c* = 0.5, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$, *cis* and *trans* forms): δ = 8.19 and 8.14(2 × s, 1 H, CHO), 8.02–7.94 (m, 1 H), 7.86–7.70 (m, 2 H), 7.54–7.38 (m, 4 H), 6.35 (d, *J* = 8.4 Hz, 1 H, NH), 5.90 and 5.80 (2 × quintet, *J* = 7.5 and 7.2 Hz, 1 H), 4.54 and 4.30 (2 × dd, *J* = 6.9 and 3.6 Hz; *J* = 8.1 and 3.3 Hz, 1 H), 3.52–3.31 (m, 2 H), 2.55–2.43 and 2.22–2.04 (m, 1 H), 2.02–1.71 (m, 3 H), 1.64 and 1.60 (2 × d, *J* = 6.9 Hz, 3 H, Me) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$, major isomer): δ = 169.11, 162.27, 138.81, 133.81, 130.73, 128.74, 127.91, 126.10, 125.60, 125.34, 123.13, 122.28, 57.90, 46.74, 45.15, 26.90, 24.02, 21.57 ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$, minor isomer): δ = 170.15, 162.17, 137.28, 133.89, 130.98, 128.90, 128.64, 126.53, 125.93, 125.15, 122.94, 122.70, 60.89, 44.72, 44.17, 30.34, 22.65, 20.21 ppm. IR (KBr): ṽ = 3288, 3051, 2976, 2875, 1657, 1535, 1448, 1379, 1238, 1182, 1043, 802, 779, 443 cm^{-1}. MS (ESI+): *m/z* = 319.2 $[M + Na]^+$, 614.9 $[2M + Na]^+$. $C_{18}H_{20}N_2O_2$ (296.36): calcd. C 72.95, H 6.80, N 9.45; found C 72.80, H 6.52, N 9.22.

Compound 4: This compound was prepared from *N*-formyl-D-proline and (*R*)-phenylethylamine by the same procedure as described above for **2** to give **4** as a white solid in 88% yield. $[\alpha]_D^{20}$ = +194.5 (*c* = 1, EtOH). ^1H NMR (300 MHz, $CDCl_3$, *cis* and *trans* forms): δ = 8.31 and 8.22(2 × s, 1 H, CHO), 7.41 and 6.18 (2 × d, *J* = 6.6 Hz, 1 H, NH), 7.38–7.19 (m, 5 H), 5.11 and 5.00 (2 × quintets, *J* = 7.5 and 7.1 Hz, 1 H), 4.46 and 4.32 (2 × dd, *J* = 8.1 and 3.9 Hz, 1 H), 3.62–3.46 (m, 2 H), 2.52–2.41 and 2.23–2.17 (m, 1 H), 2.08–1.76 (m, 3 H), 1.47 and 1.42 (2 × d, *J* = 6.3 and 7.2 Hz, 3 H, Me) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$, major isomer): δ = 169.32, 162.15, 143.30, 128.45, 127.01, 125.90, 57.78, 49.02, 46.85, 27.00, 24.04, 22.09 ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$, minor isomer): δ = 170.40, 162.07, 142.62, 128.54, 127.30, 126.00, 60.61, 48.63, 44.25, 30.27, 22.78, 21.31 ppm. IR (KBr): ṽ = 3296, 3065, 2969, 2946, 2925, 2889, 2870, 2783, 2657, 2600, 2468, 2339, 2166, 2048, 1963, 1897, 1882, 1823, 1602, 1493, 1474, 1463, 1353, 1305, 1284, 1268, 1210, 1145, 1134, 1099, 1091, 1075, 1030, 1014, 976, 954, 923, 912, 900, 874, 842, 736, 648 cm^{-1}. MS (ESI+): *m/z* = 247.0 $[M + H]^+$, 269.1 $[M + Na]^+$, 514.8 $[2M + Na]^+$. HRMS (ESI): calcd. for $C_{14}H_{18}N_2O_2$ $[M + H]^+$ 247.14410; found 247.14405. $C_{14}H_{18}N_2O_2$ (246.30): calcd. C 68.27, H 7.37, N 11.37; found C 68.11, H 7.52, N 11.18.

Compound 5: This compound was prepared from *N*-formyl-D-proline and (*S*)-phenylethylamine by the same procedure as described above for **2** to give **5** as a white solid in 93% yield. $[\alpha]_D^{20}$ = +89.8 (*c* = 1, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$, *cis* and *trans* forms): δ = 8.21 and 8.18(2 × s, 1 H, CHO), 7.46 and 6.76 (2 × d, *J* = 7.2 and 7.5 Hz, 1 H, NH), 7.29–7.17 (m, 5 H), 5.09 and 4.99 (2 × quintets, *J* = 7.5 and 7.1 Hz, 1 H), 4.48 and 4.29 (2 × dd, *J* = 7.7 and 4.1 Hz; *J* = 7.7 and 3.8 Hz, 1 H), 3.52–3.39 (m, 2 H), 2.46–2.40 and 2.15–2.07 (m, 1 H), 1.97–1.72 (m, 3 H), 1.43 and 1.41 (2 × d, *J* = 7.2 and 6.6 Hz, 3 H, Me) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$, major isomer): δ = 169.20, 162.21, 143.36, 128.44, 126.92, 125.73, 57.79, 49.02, 46.81, 26.82, 24.01, 22.55 ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$, minor isomer): δ = 170.40, 162.10, 142.75, 128.60, 127.33, 125.84, 60.69, 48.74, 44.22, 30.31, 22.76, 21.45 ppm. IR (KBr): ṽ = 3290, 3062, 2968, 2927, 2916, 2893, 2866, 2851, 2782, 2656, 2599, 2350, 2167, 1961, 1896, 1823, 1681, 1574, 1495, 1448, 1424, 1385, 1353, 1306, 1284, 1270, 1242, 1230, 1182, 1144, 1101, 1090, 1077, 1024, 1017, 974, 956, 924, 900, 874, 841, 802, 761, 749, 738, 700, 628, 611, 544, 525, 480, 428 cm^{-1}. MS (ESI+): *m/z* = 269.2 $[M + Na]^+$, 514.8 $[2M + Na]^+$. $C_{14}H_{18}N_2O_2$ (246.30): calcd. C 68.27, H 7.37, N 11.37; found C 68.16, H 7.45, N 11.30.

Compound 6: This compound was prepared from *N*-formyl-L-proline and (*R*)-phenylethylamine by the same procedure as described above for **2** to give **6** as a white solid in 85% yield. $[\alpha]_D^{20}$ = –100.2 (*c* = 1, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$, *cis* and *trans* forms): δ = 8.29 and 8.26(2 × s, 1 H, CHO), 7.45 and 6.15 (2 × d, *J* = 7.2 and 8.7 Hz, 1 H, NH), 7.36–7.16 (m, 5 H), 5.12 and 5.02 (2 × quintets, *J* = 7.2 Hz, 1 H), 4.53 and 4.35 (2 × dd, *J* = 6.9 and 4.2 Hz and *J* = 7.5 and 3.9 Hz, 1 H), 3.61–3.38 (m, 2 H), 2.53–2.47 and 2.20–2.12 (m, 1 H), 2.06–1.76 (m, 3 H), 1.48 and 1.45 (2 × d, *J* = 7.2 Hz, 3 H, Me) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$, major isomer): δ = 169.21, 162.09, 143.30, 128.34, 126.82, 125.66, 57.69, 48.88, 46.71, 26.90, 23.92, 22.41 ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$, minor isomer): δ = 170.38, 161.95, 142.83, 128.45, 127.15, 125.79, 60.51, 48.63, 44.10, 30.23, 22.69, 21.39 ppm. IR (KBr): ṽ = 3293, 3061, 2978, 2969, 2927, 2885, 2866, 1681, 1638, 1547, 1496, 1463, 1448, 1424, 1386, 1306, 1270, 1230, 1182, 1143, 1100, 1098, 1017, 974, 924, 900, 875, 841, 801, 760, 738, 699, 627, 611, 545, 525, 480, 426 cm^{-1}. MS (ESI+): *m/z* = 247.0 $[M + H]^+$, 269.1 $[M + Na]^+$, 514.8 $[2M + Na]^+$. $C_{14}H_{18}N_2O_2$ (246.30): calcd. C 68.27, H 7.37, N 11.37; found C 67.94, H 7.65, N 11.15.

Compound 7: This compound was prepared from (*R*)-1-(1-naphthyl)ethylamine and L-proline by the same procedures as described in the literature for its derivative.[2i] The crude material was purified by flash chromatography on silica gel (CH_2Cl_2/MeOH, 95:5) to give pure **7** as a white solid (478 mg, 70% yield). $[\alpha]_D^{20}$ = –34.0 (*c* = 1.152, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ = 11.79 (d, *J* = 9.0 Hz, 1 H, NH), 8.07 (d, *J* = 7.8 Hz, 1 H), 7.81 (d, *J* = 8.4 Hz, 1 H), 7.71 (d, *J* = 8.4 Hz, 1 H), 7.50 (d, *J* = 7.2 Hz, 1 H), 7.49–7.46 (m, 1 H), 7.44–7.39 (m, 2 H), 5.89 (quintet, *J* = 7.2 Hz, 1 H), 3.65 (br. s, 1 H), 3.37–3.33 (m, 1 H), 3.22–3.17 (m, 1 H), 3.11 (m, 1 H), 2.36–2.23 (m, 4 H), 2.11–2.09 (m, 1 H), 1.91–1.88 (m, 2 H), 1.84–1.79 (m, 1 H), 1.68–1.59 (m, 3 H), 1.61 (d, *J* = 7.2 Hz, 3 H), 1.31–1.23 (m, 2 H), 1.18–1.11 (m, 1 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 167.92, 139.12, 133.82, 130.74, 128.71, 127.65, 126.00, 125.45, 125.43, 123.27, 122.54, 76.23, 72.59, 66.51, 44.22, 28.39, 27.61, 27.48, 25.38, 25.26, 24.97, 21.66, 20.06 ppm. MS (ESI+): *m/z* = 367.3 $[M + H]^+$, 389.3 $[M + Na]^+$, 733.1 $[2M + H]^+$, 755.2 $[2M + Na]^+$. HRMS (ESI): calcd. for $C_{23}H_{30}N_2O_2$ $[M + H]^+$ 367.23800; found 367.23798. $C_{23}H_{30}N_2O_2$ (366.50): calcd. C 75.37, H 8.25, N 7.64; found C 75.67, H 8.08, N 7.40.

General Procedure for the Allylation of Aldimines with Allyltrichlorosilane in the Presence of a Chiral Formamide: Allyltrichlorosilane (0.33 mmol, 1.5 equiv.) was added dropwise to a solution of aldimine (0.22 mmol) and formamide (0.22 mmol, 1 equiv.) in dry CH_2Cl_2 (0.44 mL). After stirring at room temperature for 72 h, triethylamine (0.15 mL) in methanol (0.8 mL) was added to quench the reaction. The mixture was diluted with CH_2Cl_2 and water. The organic layer was separated, dried with anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (CH_2Cl_2) to give the pure product.

9a: ^1H NMR (300 MHz, $CDCl_3$): δ = 7.27 (d, *J* = 8.9 Hz, 2 H), 6.85 (d, *J* = 8.9 Hz, 2 H), 6.69–6.67 (m, 2 H), 6.58–6.53 (m, 1 H), 6.41 (d, *J* = 7.2 Hz, 1 H), 5.84–5.70 (m, 1 H), 5.21–5.10 (m, 2 H), 4.32 (t, *J* = 6.5 Hz, 1 H), 3.77 (s, 3 H), 2.59–2.53 (m, 2 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 158.38, 143.65, 135.96, 135.50,

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134.69, 127.41, 121.36, 118.09, 117.64, 114.09, 113.88, 113.69, 57.15, 55.20, 43.14 ppm. The enantiomeric excess of the product was determined by chiral HPLC analysis (Daicel Chiralpak AD) by comparison with an authentic racemic material: *n*-hexane/2-propanol = 90:10, flow rate 1 mL min^{-1}, λ = 254 nm: t_R = 10.74 min, t_R = 16.43 min.

9b: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.16 (d, J = 8.6 Hz, 2 H), 7.52 (d, J = 8.6 Hz, 2 H), 6.71–6.53 (m, 3 H), 6.20 (d, J = 7.8 Hz, 1 H), 5.81–5.67 (m, 1 H), 5.23–5.15 (m, 2 H), 4.48–4.44 (m, 1 H), 2.67–2.52 (m, 2 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 151.54, 146.96, 143.18, 135.33, 133.33, 127.25, 123.88, 121.39, 119.19, 117.88, 114.28, 112.71, 57.10, 42.68 ppm. The enantiomeric excess of the product was determined by chiral HPLC analysis (Daicel Chiralpak AD) by comparison with an authentic racemic material: *n*-hexane/2-propanol = 90:10, flow rate 1 mL min^{-1}, λ = 254 nm: t_R = 18.00 min, t_R = 27.12 min.

Compound 11: This compound was prepared by the same procedures as described in the literature for a similar compound[4] by using chiral formamide **6** as an activator. The crude product was purified by flash chromatography on silica gel (CH_2Cl_2) to give pure enantioenriched homoallylic amine **11** as a white solid in 79% yield and 51%*ee* (*R*). $[\alpha]_D^{20}$ = +39.1 (c = 0.672, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.17 (d, J = 8.4 Hz, 2 H), 7.53 (d, J = 8.4 Hz, 2 H), 6.58 (d, J = 7.2 Hz, 1 H), 6.35 (d, J = 7.2 Hz, 1 H), 6.01 (s, 1 H), 5.80–5.66 (m, 1 H), 5.22–5.14 (m, 2 H), 4.77 (br. s, 1 H), 4.55 (br. s, 1 H), 4.45 (m, 1 H), 2.64–2.50 (m, 2 H), 2.05 (s, 3 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 151.61, 147.09, 140.93, 135.23, 133.41, 130.96, 127.23, 123.92, 119.19, 118.04, 114.14, 113.54, 57.08, 42.83, 21.02 ppm. The enantiomeric excess of the product was determined by chiral HPLC analysis (Daicel Chiralpak AD) by comparison with an authentic racemic material: *n*-hexane/2-propanol = 90:10, flow rate 1 mL min^{-1}, λ = 254 nm: t_R = 22.37 min, t_R = 25.49 min.

(1*R*)-1-(4-Nitrophenyl)but-3-en-1-amine (12): This compound was prepared from **11** by the same procedures as described in the literature.[4] $[\alpha]_D^{20}$ = +4.3 (c = 0.463, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.17 (d, J = 8.7 Hz, 2 H), 7.51 (d, J = 8.7 Hz, 2 H), 5.76–5.62 (m, 1 H), 5.13–5.07 (m, 2 H), 4.12 (dd, J = 8.0 and 5.3 Hz, 1 H), 2.49–2.28 (m, 2 H), 1.79 (br. s, 2 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 153.24, 146.95, 134.20, 127.24, 123.63, 118.62, 54.82, 44.02 ppm.

General Procedure for the Reduction of Imine with Trichlorosilane: Trichlorosilane (29 μL, 0.29 mmol) was added dropwise to a stirred solution of imine **13** (37.33 mg, 0.19 mmol), chiral formamide (0.1 or 0.3 equiv.) and additive (0.3 equiv.) in anhydrous solvent (1 mL) at 0 °C (or at –20 °C). The reaction mixture was stirred 10 min at 0 °C and then at room temperature under an argon atmosphere for 24 h. The reaction was quenched with a saturated solution of $NaHCO_3$, and the product was extracted with CH_2Cl_2. The organic layer was dried with Na_2SO_4 and filtered, and the solvent was evaporated. The residue was purified by column chromatography on silica gel (CH_2Cl_2) to afford desired product **14**. The yields and enantioselectivities are given in Tables 2 and 3. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.29 (m, 4 H), 7.26–7.20 (m, 1 H), 7.13–7.07 (m, 2 H), 6.68–6.63 (m, 1 H), 6.55–6.51 (m, 2 H), 4.49 (q, J = 6.9 Hz, 1 H), 1.52 (d, J = 6.9 Hz, 3 H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 147.14, 145.12, 129.07, 128.60, 126.84, 125.81, 117.23, 113.28, 53.45, 24.99 ppm. The enantiomeric excess of the product was determined by chiral HPLC analysis (Daicel Chiralpak OD) by comparison with an authentic racemic material: *n*-hexane/2-propanol = 94:6, flow rate 0.5 mL min^{-1}, λ = 254 or 210 nm: t_R = 15.66 min, t_R = 19.20 min.

Acknowledgments

The authors gratefully acknowledge the Deutsche Forschungsgemeinschaft (Schwerpunktprogramm 1179 "Organokatalyse") for generous financial support.

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Received: January 23, 2007
Published Online: April 18, 2007

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