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Polymer-Supported Organocatalysts: Asymmetric Reduction of Imines with Trichlorosilane Catalyzed by an Amino Acid-Derived Formamide Anchored to a Polymer†

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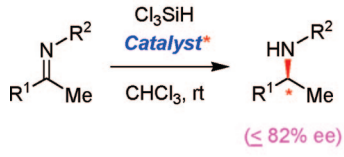

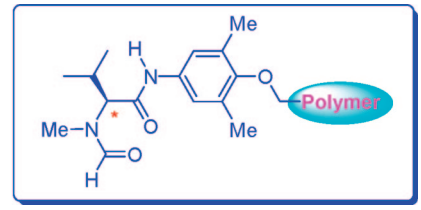

Asymmetric reduction of ketimines **1a**−**e** with trichlorosilane can be catalyzed by the *N*-methylvaline-derived Lewis basic formamide anchored to a polymeric support (**5a** and **5b**) with good enantioselectivity (≤82% ee) and low catalyst loading (typically 15 mol %) at room temperature. This protocol represents a considerable simplification of the isolation procedure and is particularly suitable for a parallel synthesis of chiral amines **2a**−**e**. The polymer-supported catalysts retain full activity after a multiple use.

Introduction

Asymmetric reduction of prochiral ketimines **1** represents an attractive route to chiral amines **2** (Scheme 1), which serve as valuable building blocks for pharmaceutical and other fine chemical industries. Catalytic hydrogenation, employing a variety of metals and chiral ligands, has evolved, over the years, into an established method[1–4] and is regarded as an advanced alternative to stoichiometric processes, such as hydride reduction, for which the enantioselective version[1] is less economical. Since both atoms of the H_2 molecule are transferred to the product, hydrogenation can serve as a prime example of atom economy. However, the potential leaching of the transition-metal catalyst requires special attention, since the allowed contamination of the product in pharmaceutical industry is at the ppm level. Iridium-catalyzed asymmetric hydrogenation[5] has now been generally accepted as the champion method for the synthesis of amines of high enantiopurity. However, aside from the leaching problems and the difficulties associated with the quantitative recovery of the catalyst, it is the need of high pressure that makes this method less attractive in view of the technical demands. This applies in particular to high-throughput parallel chemistry and scaling up.

Metal-free organocatalysis[6] has now emerged as a novel synthetic philosophy with the ambition to replace, whenever possible, the traditional transition metal catalysis. The past few years have witnessed the development of organocatalytic

† Dedicated to Dr. Vladimír Hanuš on the occasion of his 85 birthday.

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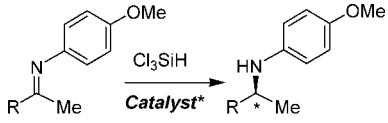
SCHEME 1. Asymmetric Reduction of Selected Ketimines



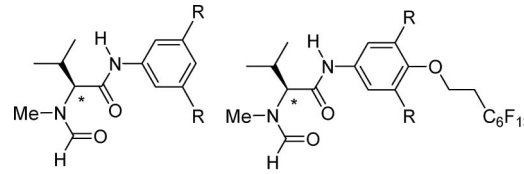
1a, R = Ph **2a**, R = Ph
1b, R = 2-Naphthyl **2b**, R = 2-Naphthyl
1c, R = 4-CF_3-C_6H_4 **2c**, R = 4-CF_3-C_6H_4
1d, R = 4-MeO-C_6H_4 **2d**, R = 4-MeO-C_6H_4
1e, R = 2,5-Me_2-3-furyl **2e**, R = 2,5-Me_2-3-furyl

reduction with Cl_3SiH,[7–10] Hantzsch ester,[11] and most recently, even with H_2 in the absence of a transition metal (though the latter one is yet awaiting its enantioselective version).[12]

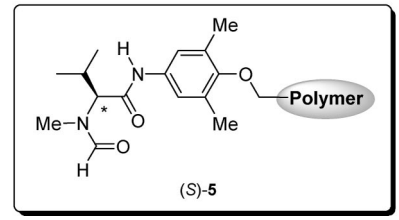
Matsumura, [9] Sun,[10] and we[7] have developed a series of chiral organocatalysts derived from α-amino acids to promote asymmetric reduction of prochiral imines[7,9,10] and ketones[8] with trichlorosilane (Scheme 1). This methodology is tolerant of various substitution patterns and the enantioselectivities regularly exceed 90% ee.

In general, most of the organocatalytic procedures developed to date require a rather high catalyst loading, with 20–30 mol % (or even more) of the catalyst being more the rule rather than an exception.[6] Organocatalysts are cheaper than their counterparts containing a precious transition metal coordinated to an expensive ligand, so that there is less economic pressure on the reduction of catalyst loading. Nevertheless, separation of copious quantities of an organocatalyst from the desired organic product is not a trivial task on a large scale and may also become a nuisance in high-throughput parallel chemistry.

CHART 1. Catalysts for the Asymmetric Reduction of Imines



(*S*)-**3a**, R = H (*S*)-**4a**, R = H
(*S*)-**3b**, R = Me (*S*)-**4b**, R = Me
(*S*)-**3c**, R = *i*-Pr (*S*)-**4c**, R = *i*-Pr
(*S*)-**3d**, R = *t*-Bu



Our amino acid derived formamide-type catalysts **3a**−**d** (Chart 1)[7] proved to be very efficient and, as a result, the loading was reduced to 1–5 mol % (Table 1, entries 1 and 2).[7,13] Nevertheless, even this considerably reduced amount still appears as a contaminant in the product that has to be separated. Recently, we have introduced a fluorous tag to the catalyst (**4a**−**c**),[7c] which simplified the separation to an ordinary filtration through a pad of fluorous silica gel that retained the catalyst, whereas the product was eluted. Subsequent change of the solvent resulted in elution of the catalyst that could be reused. The classical chromatography of the crude mixture after the workup was thus avoided. The introduction of the fluorous tag proved to have little effect on the catalytic activity (Table 1; compare entries 1 and 2 with 3).[7c] Herein, we describe a further simplification of the product isolation by attaching the catalyst to a solid support (**5**).[14]

Results and Discussion

As the next step toward developing a user-friendly methodology for the reduction of imines with Cl_3SiH, we resolved to anchor the catalyst to a polymer (**5**) by employing the ether link that proved suitable previously in the case of fluorous tag[7c] (Chart 2). While the previous reductions were all carried in a homogeneous solution (with toluene as an optimal solvent or in $CHCl_3$ or CH_2Cl_2),[7] the solid-supported catalysts operate in a heterogeneous system, which creates problems in its own right.[14] The choice of the type of polymer, to which the catalyst is to be anchored, is not trivial, and a number of factors have to be considered, including the swelling properties, the acces-

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TABLE 1. Reduction of Ketimine 1a with Trichlorosilane, Catalyzed by the Valine-Derived *N*-Methylformamides (*S*)-3b,d, (*S*)-4b, and (*S*)-5a−f[a]

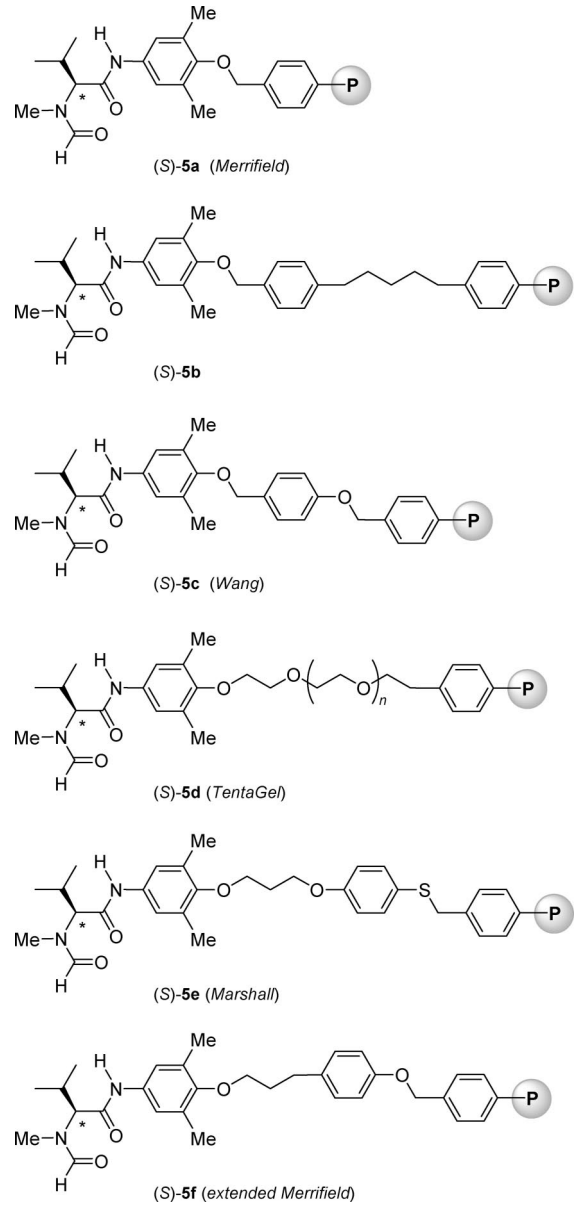
entry	catalyst (mol %)	solvent	run	yield[b] (%)	**2a**[c] % ee[d]
1	**3b** (10)	toluene	1	85	91[e]
2	**3d** (1)	toluene	1	92	93[e]
3	**4b** (10)	toluene	1	90	91[e]
4	**5a** (25)	toluene	1	84	63
5	**5a** (25)	$CHCl_3$	1	80	76
6	**5a** (25)	$CHCl_3$	2	81	82
7	**5a** (25)	$CHCl_3$	3	82	81
8	**5a** (25)	$CHCl_3$	4	80	82
9	**5a** (25)	$CHCl_3$	5	81	82
10	**5a** (25)	$CHCl_3$	6	78	81
11	**5b** (15)	$CHCl_3$	1	87	77
12	**5b** (15)	$CHCl_3$	2	84	82
13	**5b** (15)	$CHCl_3$	3	85	81
14	**5b** (15)	$CHCl_3$	4	83	81
15	**5b** (15)	$CHCl_3$	5	84	82
16	**5b** (15)	$CHCl_3$	6	83	81
17	**5b** (35)	$CHCl_3$	1	90	78
18	**5b** (35)	$CHCl_3$	2	92	81
19	**5c** (20)[f]	toluene	1	86	20
20	**5c** (20)[f]	$CHCl_3$	1	83	73
21	**5c** (20)[f]	$CHCl_3$	2	76	78
22	**5c** (20)[f]	$CHCl_3$	3	77	79
23	**5c** (20)[f]	$CHCl_3$	4	76	77
24	**5c** (20)[f]	$CHCl_3$	5	76	77
25	**5c** (20)[f]	$CHCl_3$	6	74	77
26	**5c** (40)[g]	$CHCl_3$	1	34	22
27	**5c** (40)[g]	$CHCl_3$	2	53	61
28	**5c** (40)[g]	$CHCl_3$	3	52	68
29	**5d** (15)[f]	toluene	1	74	73
30	**5d** (15)[f]	$CHCl_3$	2	68	77
31	**5d** (15)[f]	$CHCl_3$	3	69	76
32	**5d** (25)[g]	toluene	1	72	47
33	**5d** (25)[g]	toluene	2	69	47
34	**5d** (25)[g]	$CHCl_3$	3	72	63
35	**5e** (5)	toluene	1	72	30
36	**5e** (5)[h]	toluene	1	82	45
37	**5f** (30)	$CHCl_3$	1	71	51
38	**10** (10)	toluene	1	87	91
39	**10** (10)	$CHCl_3$	1	88	88
40	**11** (10)	toluene	1	94	86
41	**22** (10)	$CHCl_3$	1	81	86

[a] The reaction was carried out on a 0.4 mmol scale with 2.0 equiv of Cl_3SiH at 25 °C for 16 h unless stated otherwise. [b] Isolated yield. [c] The absolute configuration was established from the optical rotation (measured in $CHCl_3$) by comparison with the literature data (see the Experimental Section) and by HPLC via comparison with an authentic sample; the resulting amines **2a** was found to be (*S*)-configured. [d] Determined by chiral HPLC. [e] Reference 7c. [f] Prepared by Williamson etherification. [g] Prepared by Mitsunobu reaction. [h] The polymer was acetylated with CH_3COCl prior to the reaction.

sibility of the catalyst surrounded by the mass of atoms of the polymeric chain, the compatibility of the polymer with the reaction conditions, etc. The nature and the length of the link between the polymer and the catalyst is another factor that has to be considered.[14] Of the plethora of commercially available resins compatible with the intended chemistry of anchoring the catalysts,[14] we have selected the series summarized in Chart 2, which included the most common Merrifield and Wang resin, TentaGel, etc.

In the synthesis of the catalyst carrying the fluorous tag,[7c] all of the chemistry involved was going to occur in a homogeneous solution, so that the tag could be introduced in an early stage of the synthesis.[7c] By contrast, in the present study, we resolved to construct the link between the catalyst and the polymer in the very last step in order to carry out most

CHART 2. L-Valine-Derived Formamide Anchored to Polymers with a Varying Spacer

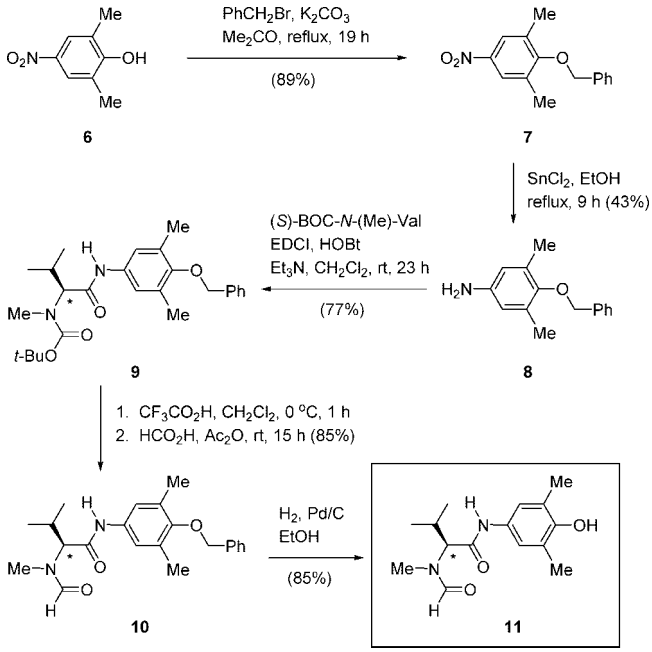


of the sequence in a homogeneous solution. Therefore, protection was required in the beginning.

In our previous work, an ether link was selected to connect the catalyst with the fluorous tag,[7c] and a similar strategy was employed in the present study. The ether link was constructed by using the catalyst precursor equipped with a free phenolic group (ArOH) and the alkylating agent R_fX. Optimization in our previous work led to the use of R_fOH as the alkylating agent under Mitsunobu conditions.[7c] An alternative that would require nucleophilic substitution at the aromatic ring of the catalyst with R_fOH serving as a nucleophile turned out to be much less efficient.[7c] This previous work thus set the scene for the present study.

Synthesis of the Catalytic Moiety Suitable for Immobilization. The phenolic derivative **11** (Scheme 2) was selected as a suitable catalyst precursor to be attached to the polymer. Its synthesis commenced with the protection of nitrophenol **6** by benzylation, and the resulting nitro ether **7**

SCHEME 2. Synthesis of the Catalyst with an Attachment Point



(89%)[15] was reduced with $SnCl_2$ under our standard conditions[7c] to afford the aniline derivative **8** (43%). Extension of the reaction time at the same temperature resulted in the formation of a significant amount of the debenzylated product, whereas at lower temperature the reaction did not proceed to completion. Acylation of the latter product with the BOC-protected *N*-methylvaline[7b] by using the carbodiimide method furnished amide **9** (77%), whose deprotection with trifluoroacetic acid, followed by formylation in one pot with a mixed anhydride generated from formic acid and acetic anhydride, gave rise to formamide **10** (85%). Finally, the protecting benzyl group was removed by catalytic hydrogenation to produce the desired phenol **11** (85%).

While phenol **11** could be used directly for the anchoring to some of the resins, as in the case of **5a**−**d**, others required further modification before the final attachment (**5e**,**f**). Thus, the chloropropyl ether **15** (Scheme 3) was prepared as a precursor of the catalyst anchored to the Marshall polymer (**5e**). Its synthesis differed from that of **11** in that the phenolic hydroxyl in **6** was first derivatized by alkylation with 3-chloropropan-1-ol under Mitsunobu conditions to afford ether **12** (79%), in which the chloropropyl group served both as a protection and as the final moiety to be used for the attachment. The rest of the synthesis followed the original scheme: the nitro derivative **12** was reduced with $SnCl_2$ and the resulting amine **13** (65%) was converted into amide **14** (86%) by the carbodiimide method. The one-pot deprotection with TFA and formylation with HCO_2H and Ac_2O afforded **15** (96%).

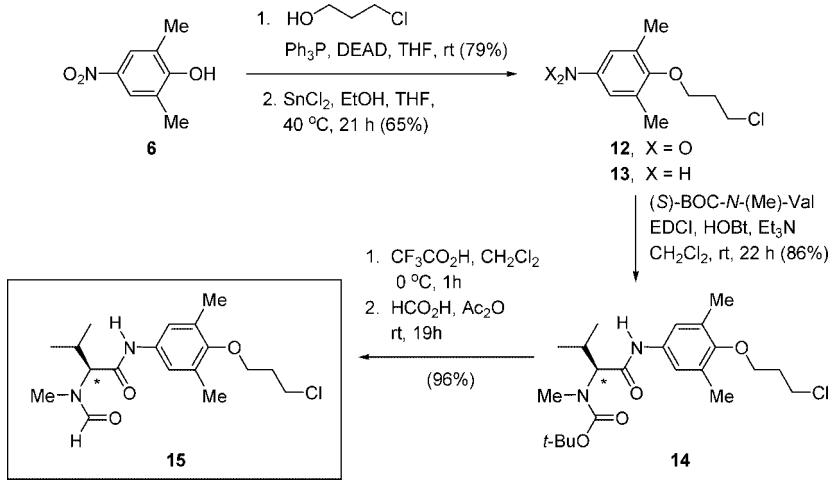
Synthesis of the extended polymer **5f** required the elongated phenol **23** as a precursor (Scheme 4). In its synthesis, alcohol **18** was selected as the electrophilic reagent to alkylate phenol **6**. Alcohol **18** itself was prepared in two steps from the phenolic acid **16**, involving protection of the hydroxyl by benzylation (BnBr, NaOH, EtOH; 56%),[16] followed by reduction of the resulting acid **17** with $LiAlH_4$ (95%).[17] Mitsunobu reaction was then employed to effect the alkylation of nitro phenol **6** with alcohol **18** and the resulting nitro derivative **19** (84%) was reduced with $SnCl_2$ to furnish amine **20** (51%). Acylation of the latter amine with the BOC-protected *N*-methylvaline[7b] provided amide **21** (76%), whose deprotection (TFA), followed by formylation (HCO_2H, Ac_2O), gave formamide **22** (87%). The final hydrogenation released phenol **23** (95%).

Anchoring the Catalyst to a Polymer. Immobilization of the catalyst in form of **5a**,**b** (Scheme 5) was effected by alkylation of the phenolic hydroxyl in **11** with polymeric benzyl chlorides **24** and **25**, respectively,[18] using the modified Williamson method (CsOH, DMF, 60 °C, 48 h), which afforded **5a** (0.75 mmol/g; 80%) and **5b** (0.53 mmol/g; 51%).[19,20] For the preparation of the derivatized Wang polymer **5c**, two approaches were investigated, namely the alkylation of phenol **11** with the bromo-Wang polymer **26** using the Williamson method (CsOH, DMF, 60 °C, 48 h; 0.71 mmol/g; 57%) and alkylation of **11** with alcohol **27** via Mitsunobu reaction (1.31 mmol/g; 64%). Similarly, this dual approach was utilized in the synthesis of the derivatized TentaGel polymer **5d**: the Williamson alkylation with bromide **28** (CsOH, DMF, 80 °C, 67 h) produced **5d** in 16% yield (0.21 mmol/g), whereas the Mitsunobu reaction with alcohol **29** was slightly more effective, affording **5d** in 39% yield (0.33 mmol/g). The reaction of the phenolic Marshall polymer **30** with the alkyl chloride **15** under Williamson conditions (CsI, CsOH, THF, 45 °C, 48 h) afforded **5e** (0.26 mmol/g; 20%). Finally, the extended Merrifield polymer **5f** was prepared by alkylation of phenol **23** with the benzylic chloride **24** under the Williamson conditions (0.69 mmol/g, 75%).

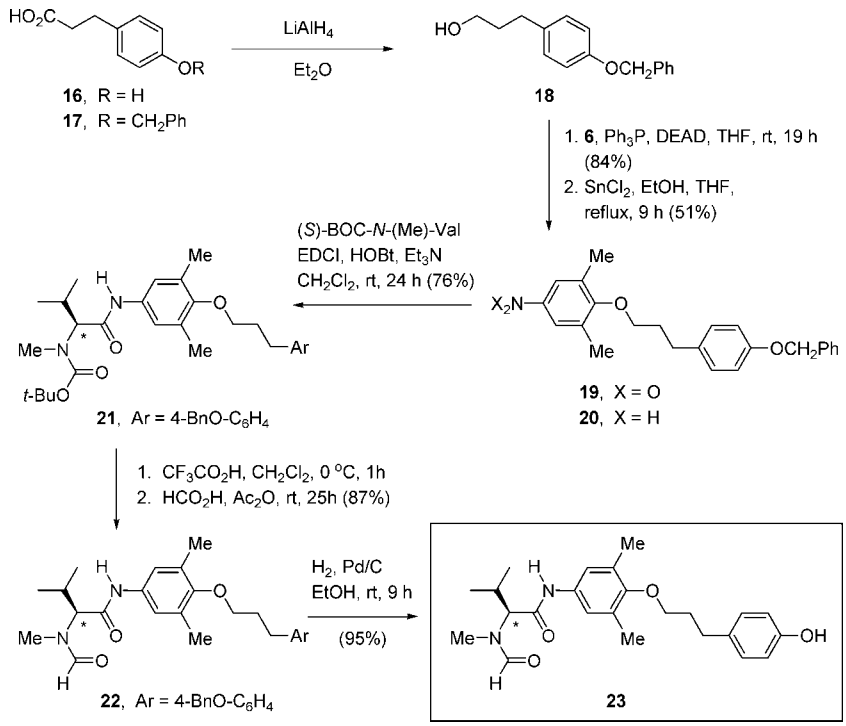
Asymmetric Reduction of Imines with Trichlorosilane Catalyzed by Solid-Supported Formamides. The activity of our immobilized catalysts in the reduction of imines was investigated by using the reaction conditions adopted from the homogeneous catalysis; catalyst **5a** was employed in the pilot reduction of imine **1a** (R = Ph). The reaction was carried out as follows: a small porous polypropylene reactor vessel (2.4 mL internal volume) with **5a** and imine **1a** was left in toluene for 30 min to ensure a proper swelling of the polymer, after which Cl_3SiH was added at 0 °C and the reduction was left to proceed at room temperature overnight. After separation from the mother liquor, the porous reactor vessel with the immobilized catalyst was washed with toluene to elute the rest of the product, followed by further washing with CH_2Cl_2, MeOH, and Et_2O to regenerate the immobilized catalyst. Aqueous workup of the toluene solution[7c] afforded pure amine **2a** (84% yield, 63% ee; Table 1, entry 4). Switching to chloroform as the solvent had a positive effect on the activity of **5a** (76% ee; entry 5).

(15) When THF was used as solvent, the yield dropped to 30%.
(16) Doherty, D. G. *J. Am. Chem. Soc.* **1955**, *77*, 4887.
(17) Henley-Smith, P.; Whiting, D. A.; Wood, A. F. *J. Chem. Soc., Perkin Trans. 1* **1980**, 614.
(18) The following resins were employed in this study: (a) Chloromethylpolystyrene (**24**) 1.23 mmol/g 75–150 μm (StratoSphere), obtained from Polymer Laboratories. (b) 5-[4-(Chloromethyl)phenyl]pentyl]styrene (**25**), polymer-bound 0.75–1.25 mmol/g 100–200 μm, obtained from Aldrich. (c) Bromomethylphenoxymethyl polystyrene (**26**) 1.40 mmol/g (StratoSphere) 150–300 μm, obtained from Polymer Laboratories. (d) 4-Hydroxymethylphenoxymethyl polystyrene (**27**) 1.70 mmol/g (StratoSphere) 150–300 μm, obtained from Polymer Laboratories. (e) TentaGel HL Br resin (**28**), 0.43 mmol/g, 110 μm, obtained from Rapp Polymere GmbH. (f) TentaGel HL OH resin (**29**) 0.43 mmol/g 110 μm, obtained from Rapp Polymere GmbH. (g) 4-Hydroxytiophenol resin (**30**), 1.58 mmol/g, 150–300 μm (StratoSphere), obtained from Polymer Laboratories.
(19) The yields were calculated by comparing the actual and theoretical increase of the mass of the product. The mmol/g content of the active catalyst anchored to a polymer was established by elemental analysis.

SCHEME 3



SCHEME 4



Repeated use of the regenerated catalyst **5a** has demonstrated retention of the activity (with chloroform as solvent; entries 6–10). Interestingly, the enantioselectivity turned out to be slightly higher in runs 2–6 than in the first cycle (82 vs 76% ee in the second vs first run; entries 6 and 5), which suggests that "conditioning" of the catalyst was required to attain its optimal performance.

Catalyst **5b** (∼15 mol %) exhibited similar reactivity and selectivity (entries 11–16) as its lower "homologue" **5a** with a shorter spacer. An attempt to improve the catalytic performance by increasing the catalyst load to 30 mol % was fruitless (entries 17 and 18).

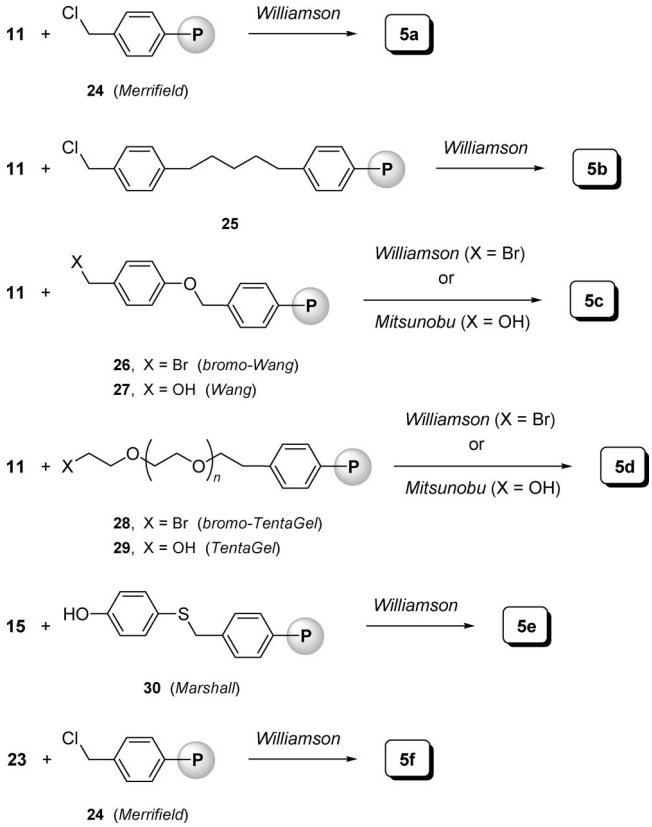
With the Wang resin **5c**, prepared by the Williamson reaction, a dramatic dependence on the solvent was observed. Thus, while the reduction of **1a** in toluene exhibited mere 20% ee (entry 19), the reaction in chloroform gave 73% ee (entry 20). The second run, as in the previous case, gave an improved result (78% ee; entry 21), and this remained practically constant in the next runs (entries 22–25). Interestingly, **5c** prepared by Mitsunobu reaction exhibited inferior results (entries 26–28). However, a considerable improvement was attained in the second and third run (entries 27 and 28), suggesting that the polymer was contaminated by impurities, which were partly removed during the first run.

The catalyst immobilized on TentaGel by Williamson etherification (**5d**) exhibited a similar level of activity as **5a** (compare entries 29–31 with 4–9), whereas the catalyst constructed via Mitsunobu reaction appeared to be slightly less active (entry 34) with significantly worse results attained in toluene (entries 32 and 33).

The catalyst anchored to the Marshall resin (**5e**) exhibited rather low selectivity and can be regarded as a failure (entry

(20) The reaction carried out at 45 °C gave **5a** in 62% yield, whereas at 80 °C the yield decreased to 31%. The use of THF or various mixtures of THF and DMF as solvent, gave inferior results.

SCHEME 5. Attaching the Catalyst to a Polymer[a]



[a] Williamson: CsOH, DMF, 60–80 °C, 48–67 h. Mitsunobu: Ph_3P, DEAD, THF, rt, 65–68 h.

35). Acetylation of any possible unfunctionalized phenolic groups on the polymer with acetyl chloride and using this product as a modified catalyst had only a marginal effect on the activity (entry 36).

Finally, catalyst **5f** also turned out to be rather inefficient, as it facilitated the reduction of **1a** with 51% ee (entry 37) even in chloroform.

Intermediates in the synthesis of the polymer-supported catalysts, namely **10**, **11**, and **22**, also proved to catalyze the reduction (entries 38–41), generally at the level attained with the original catalysts **3** (entries 1 and 2), i.e., by ~10% ee higher than those typical for the solid-supported catalysts **5**. Again, as with **3**, slightly better results were obtained when toluene was used as solvent (compare entries 38 and 39). These observations show that the modification within the core of the original catalysts **3** had little effect on its activity. Hence, the lower selectivity, characterizing the solid-supported catalysts, must originate from the polymeric framework and heterogeneous conditions.

The scope of the imine reduction with Cl_3SiH, catalyzed by **3a**−**d** and **4a**−**c** under homogeneous conditions (Scheme 1), is relatively broad and spans from a range of aromatic to heteroaromatic and some aliphatic substrates.[7] In order to verify if this is also the case with the solid-supported catalysts **5**, a brief screening was carried out with the aid of representative imines, including electron-rich and electron-poor aromatics and a heteroaromatic **1a**−**e** (Table 2). As shown above, our solid-supported catalysts retained their activity when reused. Therefore, this series (Table 2) was run with the same batch of catalyst **5b**. However, the previous experiments also demonstrated that the first run gave consistently poorer results than the subsequent

TABLE 2. Asymmetric Reduction of Imines 1a−e with Trichlorosilane Catalyzed by the Reused 5b (30 mol %) in $CHCl_3$[a]

run	imine	R^1	yield in %[b]	**2**[c] % ee[d]
2	**1a**	Ph	82	81[e]
3	**1b**	2-naphthyl	72	79
4	**1c**	4-$CF_3C_6H_4$	67	81
5	**1d**	4-$MeOC_6H_4$	62	77
6	**1e**	2,5-Me_2-3-furyl	67	78

[a] The reaction was carried out on a 0.4 mmol scale with 2.0 equiv of Cl_3SiH at 25 °C for 16 h unless stated otherwise. [b] Isolated yield. [c] The absolute configuration was established from the optical rotation (measured in $CHCl_3$) by comparison with the literature data (see the Experimental Section) and/or by HPLC via comparison with authentic samples. All amines **2a**−**e** were (*S*)-configured. [d] Determined by chiral HPLC. [e] See also Table 1, entry 18.

TABLE 3. Reduction of Imine 1a with Trichlorosilane Catalyzed by Resins 24–30 [a]

entry	resin[b] (mol %)	run	solvent	conversion[c] (%)
1	**24**(40)	1	$CHCl_3$	15
2	**24**(40)	2	$CHCl_3$	10
3	**24**(40)	3	toluene	40
4	**25**(30)	1	$CHCl_3$	6
5	**26**(40)	1	toluene	70
6	**27**(40)	1	$CHCl_3$	7
7	**28**(30)	1	$CHCl_3$	9
8	**29**(30)	1	$CHCl_3$	9
9	**30**(35)	1	toluene	85

[a] The reaction was carried out on a 0.4 mmol scale with 2.0 equiv of Cl_3SiH at 25 °C for 16 h. [b] The mol % loading of the resin relates to the mmol/g content of the active group in the resin (ref 19). [c] Established by ^1H NMR spectroscopy of the isolated crude mixture of the starting material and product.

runs. Therefore, we first "conditioned" the catalyst with **1a** in run 1; Table 2 shows runs 2–6 with the "conditioned" catalyst. As expected, little variation of the yield and enantioselectivity was observed for **1a**–**e** (77–81% ee), which is consistent with the results obtained for homogeneous solution.

The Effect of the Solid Support and the Solvent on the Reactivity and Selectivity. The solid-supported catalysts **5**consistently exhibited lower enantioselectivity (by ca. 10% ee) than their soluble counterparts **3** and **4** (compare, e.g., entries 1 in Tables 1 and 2), suggesting that either the polymeric backbone affects the catalyst selectivity in an adverse way or that the background, nonenantioselective reaction is faster in the heterogeneous system than in a homogeneous solution. To shed light on this issue, control experiments with resins **24**–**30** (i.e., those lacking the catalytic formamide moiety) were carried out (Table 3). It turned out, indeed, that the free resins did catalyze the reaction, though at a considerably lower rate. In toluene (Table 3, entries 3, 5, and 9), this background reaction proved to be faster than in chloroform (entries 1, 2, 4, 6–8), which can account for the inferior enantioselectivities obtained in toluene (vide supra). Hence, it can be concluded that the lower enantioselectivities observed for the heterogeneous systems originate from the enhanced rate of the nonenantioselective, background reaction, catalyzed by the polymeric backbone. Furthermore, comparison of the catalytic activity of the Merrifield resin **24** in chloroform in the first and second run (entries 1 and 2) could explain the changes observed between the first

(21) Dichloromethane behaved in a similar way as chloroform, exhibiting only slightly lower enantioselectivities. On the other hand, solvents such as THF or MeCN proved to be unsuitable for homogeneous solutions and were, therefore, excluded from this study.

and second run, i.e., the chemical background of the "conditioning" (vide supra). In the case of the reaction performed in toluene, the Merrifield resin exhibited a relatively high catalytic activity even after the "conditioning" (entry 3), which shows that this solvent is not suitable for the heterogeneous reduction.[21]

The actual mechanism of the "conditioning" is intriguing. With the polymers originally containing hydroxy groups prior to anchoring the catalyst (**27**, **29**, and **30**), it can be speculated that some of these groups remained unreacted and could then interfere in the first run of the catalytic reduction. Their exposition to the excess Cl_3SiH would then lead to their "capping" or 'disabling' for the second run, which would result in an improved asymmetric induction. However, this mechanism would not apply to the benzyl chloride type resins (**24**–**26** and **28**), indicating that the mechanism must be different. Interestingly, after the first run with the supported catalyst **5a** and decomposition of the excess Cl_3SiH, followed by rigorous drying of the recovered catalyst, we noticed an increase of its weight by about 25%, which was not repeated after the following runs. The latter increase apparently stems from the formation of a small amount of a gel by decomposition of Cl_3SiH during the workup. This gel, being itself an oligomer, could not be removed from the polymer and its presence is apparently associated with the improved enantioselectivity in the $n + 1$ runs. However, the chemical basis of its action remains obscure. The infrared spectra of the catalyst **5a**, taken before and after the first run, exhibit characteristic differences: thus, two strong additional vibrations could be detected in the spectrum of the regenerated catalyst, namely at 841 cm^{-1} (Si−O) and 2253 cm^{-1} (Si−H), which is consistent with the mass increase.

Conclusions

In conclusion, an effective methodology for asymmetric reductions of imines **1a**−**e** with trichlorosilane, promoted by organocatalysts immobilized on a solid support (**5**), has been developed. The methodology simplifies the recovery of the catalyst while enabling the preparation of chiral amines in good chemical yields and with good enantioselection, regardless of the substitution pattern in the substrate. The catalysts can be reused at least 5 times without any loss of activity, which demonstrates their suitability for multiple and parallel use. The highest level of catalytic activity and enantioselectivity (≤82% ee) was attained with the catalysts directly attached to the polymer (**5a**) or via a suitable spacer (**5b**). A strong influence of the solvents on the catalytic performance was observed; the best results were obtained for chloroform, whereas toluene proved to be much less suitable. Further improvements of these polymer-supported catalysts are underway and will be reported in due course.

Experimental Section

Merrifield Resin-Supported Catalyst 5a. Cesium hydroxide monohydrate (57 mg, 0.34 mmol) was added to a reaction tube with a solution of phenol **11** (90 mg, 0.32 mmol) in DMF (3 mL), followed by shaking at 60 °C for 30 min. A small porous polypropylene reactor vessel (2.4 mL internal volume and 74 μm pore size) with chloromethylpolystyrene **24** [1.23 mmol/g (130 mg, 0.16 mmol)] was placed into the reaction tube, and the shaking was continued at 60 °C for 48 h. The porous reactor vessel was then removed from the organic solution and successively washed with DMF (2 × 25 mL) and then alternately with MeOH and CH_2Cl_2 (4 × 25 mL of each solvent) and ether (25 mL). Vacuum drying afforded a brownish solid (160 mg, 80%): IR (KBr) ν 3444, 2919, 1942, 1869, 1802, 1661, 1602, 1541, 1491, 1450 cm^{-1}. Anal. Found: C, 84.77; H, 7.15; N, 2.11. This corresponds to 0.75 mmol/g loading.

Modified Merrifield Resin-Supported Catalyst 5b. Cesium hydroxide monohydrate (57 mg, 0.34 mmol) was added to a reaction tube with a solution of phenol **11** (90 mg, 0.32 mmol) in DMF (3 mL), followed by shaking at 60 °C for 30 min. A small porous polypropylene reactor vessel (2.4 mL internal volume and 74 μm pore size) with [5-[4-(chloromethyl)phenyl]pentyl]styrene, polymer-bound **25** [0.75–1.25 mmol/g (130 mg, 0.097–0.16 mmol)] was placed into the reaction tube, and the shaking was continued at 60 °C for 48 h. The porous reactor vessel was then removed from the organic solution and successively washed with MeOH (2 × 25 mL), a 1:1 mixture of MeOH and H_2O (2 × 25 mL), a 1:1 mixture of THF and H_2O (2 × 25 mL), and then alternately with MeOH and CH_2Cl_2 (4 × 25 mL of each solvent), and ether (25 mL). Vacuum drying afforded a brownish solid (142 mg, 51%): IR (KBr) ν 3317, 2916, 1942, 1871, 1803, 1694, 1600, 1547, 1490, 1449, 1372 cm^{-1}. Anal. Found: C, 85.08; H, 7.76; N, 1.49; this corresponds to 0.53 mmol/g loading.

Wang Resin-Supported Catalyst 5c. Method A. Cesium hydroxide monohydrate (57 mg, 0.34 mmol) was added to a reaction tube with a solution of phenol **11** (90 mg, 0.32 mmol) in DMF (3 mL), followed by shaking at 60 °C for 30 min. A small porous polypropylene reactor vessel (2.4 mL internal volume and 74 μm pore size) with bromomethylphenoxymethyl polystyrene **26** [1.40 mmol/g (114 mg, 0.16 mmol)] was placed into the reaction tube, and shaking was continued at 60 °C for 48 h. The porous reactor vessel was then removed from the organic solution and successively washed with MeOH (2 × 25 mL), a 1:1 mixture of MeOH and H_2O (25 mL), a 1:1 mixture of THF and H_2O (25 mL), and then alternately with MeOH and CH_2Cl_2 (4 × 25 mL of each solvent) and ether (25 mL). Vacuum drying afforded a brownish solid (130 mg, 57%): IR (KBr) ν 3431, 3024, 2920, 1943, 1877, 1805, 1725, 1674, 1602, 1550, 1512, 1451 cm^{-1}. Anal. Found: C, 82.30; H, 7.55; N, 1.98; this corresponds to 0.71 mmol/g loading.

Method B. Diethyl azodicarboxylate (80 μL, 0.51 mmol) was added to a reaction tube containing a small porous poypropylene reactor vessel (2.4 mL internal volume and 74 μm pore size) with hydroxymethylphenoxymethyl polystyrene **27** [1.70 mmol/g (100 mg, 0.17 mmol)], phenol **11** (142 mg, 0.51 mmol), and triphenylphosphine (134 mg, 0.51 mmol) in THF (3 mL) at 0 °C. The mixture was shaken at 25 °C for 65 h, and the porous reactor vessel was then removed from the organic solution and washed alternately with MeOH and THF (4 × 25 mL of each solvent), then CH_2Cl_2 (3 × 25 mL), and ether (25 mL). Vacuum drying afforded a white solid (128 mg, 64%): IR (KBr) ν 3315, 3061, 2337, 1944, 1876, 1799, 1600, 1512, 1493, 1454 cm^{-1}. Anal. Found: C, 79.10; H, 7.25; N, 3.68; this corresponds to 1.31 mmol/g loading.

TentaGel Resin-Supported Catalyst 5d. Method A. Cesium hydroxide monohydrate (57 mg, 0.34 mmol) was added to a reaction tube with a solution of phenol **11** (90 mg, 0.32 mmol) in DMF (3 mL), followed by shaking at 80 °C for 30 min. A small porous polypropylene reactor vessel (2.4 mL internal volume and 74 μm pore size) with TentaGel HL Br resin **28** [0.43 mmol/g (300 mg, 0.13 mmol)] was placed into the reaction tube, and the shaking was continued at 80 °C for 67 h. The porous reactor vessel was then removed from the organic solution and successively washed with MeOH (2 × 25 mL), a 1:1 mixture of MeOH and H_2O (2 × 25 mL), a 1:1 mixture of THF and H_2O (2 × 25 mL), and then alternately with MeOH and CH_2Cl_2 (4 × 25 mL of each solvent) and ether (25 mL). Vacuum drying afforded a brownish solid (304 mg, 16%): IR (KBr) ν 3448, 2917, 2870, 1664, 1602, 1492, 1453, 1106 cm^{-1}. Anal. Found: C, 67.67; H, 8.56; N, 0.59; this corresponds to 0.21 mmol/g loading.

Method B. Diethyl azodicarboxylate (55 μL, 0.35 mmol) was added to a reaction tube containing a small porous polypropylene reactor vessel (2.4 mL internal volume and 74 μm pore size) with

TentaGel HL OH resin **29** [0.43 mmol/g (300 mg, 0.129 mmol)], phenol **11** (90 mg, 0.32 mmol), and triphenylphosphine (92 mg, 0.35 mmol) in THF (3.5 mL) at 0 °C. The mixture was shaken at 25 °C for 68 h, and the porous reactor vessel was then removed from the organic solution and washed with THF (2 × 25 mL), then alternately with MeOH and CH_2Cl_2 (4 × 25 mL of each solvent) and ether (25 mL). Vacuum drying afforded a white solid (314 mg, 39%): IR (KBr) ν 3509, 2869, 1948, 1733, 1695, 1601, 1492, 1453, 1349 cm^{-1}. Anal. Found: C, 67.69; H, 8.56; N, 0.93; this corresponds to 0.33 mmol/g loading.

Marshall Resin-Supported Catalyst 5e. A solution of formamide **15** (90 mg, 0.25 mmol) in THF (3 mL) was added dropwise to a reaction tube containing a small porous polypropylene reactor vessel (2.4 mL internal volume and 74 μm pore size) with 4-hydroxytiophenol resin **30** [1.58 mmol/g (80 mg, 0.13 mmol)], cesium hydroxide monohydrate (27 mg, 0.16 mmol), and cesium iodide (44 mg, 0.17 mmol), and the mixture was shaken at 45 °C for 48 h. The porous reactor vessel was then removed from the organic solution and successively washed with THF (20 mL), a 1:1 mixture of THF and water (2 × 20 mL), a 1:1 mixture of THF and 1 M HCl (2 × 20 mL), and alternately with MeOH and CH_2Cl_2 (4 × 25 mL of each solvent) and ether (25 mL). Vacuum drying afforded a brownish solid (88 mg, 20%): IR (KBr) ν 3429, 2920, 1944, 1873, 1804, 1655, 1599, 1580, 1491, 1451 cm^{-1}. Anal. Found: C, 77.67; H, 6.67; N, 0.72; this corresponds to 0.26 mmol/g loading.

Merrifield Resin-Supported Catalysts with a Long Spacer 5f. Cesium hydroxide monohydrate (57 mg, 0.34 mmol) was added to a reaction tube with a solution phenol **23** (132 mg, 0.32 mmol) in DMF (3 mL), followed by shaking at 60 °C for 30 min. A small porous polypropylene reactor vessel (2.4 mL internal volume and 74 μm pore size) with chloromethylpolystyrene **24** [1.23 mmol/g (130 mg, 0.16 mmol)] was placed into the reaction tube and shaking was continued at 60 °C for 65 h. The porous reactor vessel was then removed from the organic solution and successively washed with MeOH (2 × 25 mL), a 1:1 mixture of MeOH and H_2O (25 mL), a 1:1 mixture of THF and H_2O (25 mL), and then alternately with MeOH and CH_2Cl_2 (4 × 25 mL of each solvent) and ether (25 mL). Vacuum drying afforded a brownish solid (177 mg, 75%): IR (KBr) ν 3318, 2915, 1942, 1872, 1803, 1694, 1599, 1546, 1489, 1448, 1374 cm^{-1}. Anal. Found: C, 84.20; H, 7.46; N, 1.93; this corresponds to 0.69 mmol/g loading.

4-Benzyloxy-3,5-dimethylnitrobenzene 7. Benzyl bromide (3.56 mL, 29.99 mmol) and K_2CO_3 (5.00 g, 36.20 mmol) were consecutively added to a stirred solution of 2,6-dimethyl-4-nitrophenol **6** (2.00 g, 11.96 mmol) in dry acetone (50 mL), and the mixture was refluxed for 19 h. The mixture was then evaporated, the residue was partitioned between ether (80 mL) and water (40 mL), and the organic phase was additionally washed with a 1 M aqueous solution of NaOH (40 mL). The organic solution was dried over $MgSO_4$ and evaporated to afford the crude product (6.05 g), which was purified by chromatography on a column of silica gel (50 g) with a mixture of petroleum ether and CH_2Cl_2 (5:1) to remove benzyl bromide. Continued elution with a mixture of CH_2Cl_2 and petroleum ether (2:1) afforded **7** (2.74 g, 89%) as a white solid: mp 68–69 °C; R_f = 0.25 (petroleum ether−CH_2Cl_2, 5:1); ^{1}H NMR (400 Hz, $CDCl_3$) δ 2.24 (s, 6H), 4.88 (s, 2H), 7.36–7.47 (m, 5H), 7.94 (s, 2H); ^{13}C NMR δ 16.7 (CH_3), 74.4 (CH_2), 124.3 (CH), 127.9 (CH), 128.5 (CH), 128.7 (CH), 132.7 (C), 136.5 (C), 143.6 (C), 161.1 (C); MS (EI) *m*/*z* 257 ($M^{\cdot+}$, 4), 91 (100), 89 (5), 65 (27), 39 (9); HRMS (EI) 257.1053 ($C_{15}H_{15}NO_3$ requires 257.1052).

4-Benzyloxy-3,5-dimethylaniline 8. Tin(II) chloride dihydrate (3.16 g, 14 mmol) was added to a solution of nitro ether **7** (900 mg, 3.5 mmol) in ethanol (20 mL), and the mixture was refluxed for 9 h. The mixture was then cooled, a saturated aqueous solution of $NaHCO_3$ (50 mL) was added to reach pH 10, and the product was extracted with ether (3 × 150 mL). The organic phase was dried over $MgSO_4$ and evaporated, and the residue (820 mg) was purified by chromatography on a column of silica gel (30 g) with CH_2Cl_2 to afford contaminated **8** (530 mg) as a red oil. The oil was dissolved in Et_2O (20 mL), followed by the addition of 1 M hydrochloric acid (10 mL). The white solid amine salt thus formed was isolated by filtration and washed with Et_2O to remove impurities and then dissolved in a mixture of Et_2O (20 mL), water (10 mL), and saturated $NaHCO_3$ (10 mL) and stirred for 10 min. The organic phase was separated, dried over $MgSO_4$, and evaporated to afford pure **8** (340 mg, 43%) as a yellowish oil: R_f = 0.25 (CH_2Cl_2−petroleum ether 2:1); ^{1}H NMR (400 Hz, $CDCl_3$) δ 2.24 (s, 6H), 4.75 (s, 2H), 6.44 (s, 2H), 7.32–7.49 (m, 5H); ^{13}C NMR δ 16.4 (CH_3), 74.3 (CH_2), 115.9 (CH), 127.8 (CH), 127.8 (CH), 128. Five (CH), 131.8 (C), 137.9 (C), 141.1 (C), 148.9 (C); MS (EI) *m*/*z* (%) 227 ($M^{\cdot+}$, 19), 136 (100), 108 (18), 91 (28); HRMS (EI) 227.1311 ($C_{15}H_{17}NO$ requires 227.1310).

Amide (*S*)-(−)-9. Triethylamine (0.32 mL, 2.30 mmol) was added to a solution of (*S*)-BOC-*N*-methylvaline (390 mg, 1.69 mmol) in dry CH_2Cl_2 (8 mL) at 0 °C. To the resulting clear solution were successively added a solution of aniline **8** (340 mg, 1.50 mmol) in CH_2Cl_2 (3 mL), 1-hydroxybenzotriazole (HOBt; 230 mg, 1.70 mmol), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI; 330 mg, 1.72 mmol). The reaction mixture was stirred at 0 °C for 1 h and then at room temperature for 23 h. The mixture was then diluted with ethyl acetate (70 mL) and washed successively with water (30 mL), cold 0.5 M HCl (2 × 30 mL), saturated $NaHCO_3$ (2 × 30 mL), and brine (30 mL) and dried over $MgSO_4$ and evaporated. The residue (680 mg) was purified by chromatography on a column of silica gel (50 g) with a mixture of petroleum ether and ethyl acetate (8:1) to afford pure amide (*S*)-(−)-**9** (510 mg, 77%) as a white solid: mp 132–134 °C; R_f = 0.50 (petroleum ether−AcOEt, 6:1); $[\alpha]_D$ –81.6 (*c* 0.5, EtOH); ^{1}H NMR (400 Hz, $CDCl_3$) δ 0.91 (d, J = 6.5 Hz, 3H), 1.02 (d, J = 6.5 Hz, 3H), 1.49 (s, 9H), 2.28 (s, 6H), 2.32–2.41 (m, 1H), 2.83 (s, 3H), 4.10 (d, J = 10.7 Hz, 1H), 4.76 (s, 2H), 7.20 (s, 2H), 7.33–7.49 (m, 5H), 8.07 (br s, 0.78H); ^{13}C NMR δ 16.5 (CH_3), 18.6 (CH_3), 19.9 (CH_3), 25.9 (CH), 28.4 (CH_3), 30.4 (CH_3), 66.0 (CH), 74.2 (CH_2), 80.6 (C), 120.2 (CH), 127.8 (CH), 128.0 (CH), 128.5 (CH), 131.6 (C), 133.7 (C), 137.5 (C), 152.2 (C), 157.4 (CO), 168.6 (CO); MS (EI) *m*/*z* 440 ($M^{\cdot+}$, 22), 214 (36), 158 (95), 136 (100), 91 (54), 57 (49); HRMS (EI) 440.2674 ($C_{26}H_{36}N_2O_4$ requires 440.2675).

Formamide (*S*)-(−)-10. Trifluoroacetic acid (18.5 mL) was added dropwise to a solution of the BOC derivative **9** (1.62 g, 4.40 mmol) in CH_2Cl_2 (30 mL) at 0 °C and stirring continued at the same temperature for 1 h. The acid was removed under reduced pressure, and the residue was coevaporated with toluene (2 × 20 mL) to afford a TFA salt of the deprotected amine as a brownish oil, which was used in the following step without further purification. The crude amine salt was dissolved in formic acid (20.7 mL), and the resulting solution was cooled to 0 °C. Acetic anhydride (15.4 mL) was then added dropwise and the mixture was allowed to stir at room temperature for 15 h. The volatiles were then evaporated and the residue (1.58 g) was purified by chromatography on a column of silica gel (75 g) with a mixture of CH_2Cl_2 and MeOH (99:1) to afford formamide (*S*)-(−)-**10** (1.15 g; 85%) as a light orange solid: mp 123–124 °C; R_f = 0.62 and 0.37 (two spots; CH_2Cl_2−MeOH, 49:1); $[\alpha]_D$ –153.40 (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 Hz, $CDCl_3$, a mixture of rotamers in ca. 4:1 ratio; the signals for the minor rotamer are marked with an *) δ 0.92 (d, J = 6.5 Hz, 3H), 1.05 (d, J = 6.5 Hz, 3H), 2.27 (s, 6H), 2.41–2.54 (m, 1H), 2.98 (s, 0.59H*), 3.00 (s, 2.36H), 3.68 (d, J = 10.95, 0.16H*), 4.37 (d, J = 11.0, 0.86H), 4.76 (s, 2H) 7.21 (s, 1.86 H), 7.24 (s, 0.13 H*), 7.32–7.47 (m, 5H), 8.01 (s, br. 0.85H), 8.15 (s, 0.91H), 8.50 (s, 0.16H); ^{13}C NMR δ 16.5 (CH_3), 18.6 (CH_3), 19.6 (CH_3), 25.2 (CH), 31.6 (CH_3), 63.2 (CH), 74.2 (CH_2), 120.4 (CH), 127.8 (CH), 128.0 (CH), 128.5 (CH) 131.7 (C), 133.2 (C), 137.5 (C), 152. Five (C), 164.0 (CO), 167.0 (CO); IR (KBr) ν 3459, 3317, 3069, 2965, 1658, 1613, 1551, 1482, 1411, 1211 cm^{-1}; MS (EI) *m*/*z* 368 ($M^{\cdot+}$, 9), 277 (17), 164 (12), 142 (91), 114 (100), 91 (75) 86 (23), 55 (13), 42 (11); HRMS (EI) 368.2103 ($C_{22}H_{28}N_2O_3$ requires 368.2100).

Formamide (*S*)-(−)-11. A mixture of the benzyl derivative **10** (280 mg, 0.76 mmol) and 10% palladium on activated charcoal (80 mg, 10 mol%) in absolute ethanol (14 mL) was stirred under a hydrogen atmosphere for 9 h. The mixture was then filtered through Celite, and the solvent was evaporated. The residue (220 mg) was purified by chromatography on a column of silica gel (30 g) with a mixture of CH_2Cl_2 and MeOH (49:1) to afford (*S*)-(−)-**11** (180 mg, 85%) as an enamel: R_f = 0.37 and 0.25 (two spots; CH_2Cl_2−MeOH, 49:1); $[\alpha]_D$ –141.30 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 Hz, $CDCl_3$, a mixture of rotamers in ca. 4:1 ratio; the signals for the minor rotamer are marked with an *) δ 0.91 (d, J = 6.5 Hz, 3H), 1.04 (d, J = 6.5 Hz, 3H), 2.18 (s, 6H), 2.39–2.50 (m, 1H), 2.92 (s, 0.60H*), 3.00 (s, 2.35H), 3.51 (d, J = 10.5 Hz, 0.19H*), 4.40 (d, J = 11.2, 0.78H), 5.18 (s, 0.77H), 5.25 (s, 0.20H), 7.07 (s, 0.36 H*), 7.10 (s, 1.59H), 8.10 (s, br. 0.81H), 8.13 (s, 0.89H), 8.21 (s, 0.23H); ^{13}C NMR δ 16.1 (CH_3), 18.5 (CH_3), 19.5 (CH_3), 25.3 (CH), 31.6 (CH_3), 62.9 (CH), 120.7 (CH), 123.8 (C), 129.8 (C), 149.3 (C), 163.9 (CHO), 167.0 (CO); IR (KBr) ν 3433, 3086, 3069, 2965, 1655, 1557, 1490, 1469, 1410, 1210 cm^{-1}; MS (EI) *m*/*z* 278 ($M^{\bullet+}$, 39), 137 (66), 114 (100), 86 (38) 55 (19), 42 (19); HRMS (EI) 278.1632 ($C_{15}H_{22}N_2O_3$ requires 278.1630).

4-(3′-Chloro-1′-propyloxy)-3,5-dimethylnitrobenzene 12. Triphenylphosphine (980 mg, 3.74 mmol), 3-chloropropanol (0.31 mL, 3.70 mmol), and 97% diethyl azodicarboxylate (0.59 mL, 3.73 mmol) were added consecutively to a stirred solution of 2,6-dimethyl-4-nitrophenol **6** (500 mg, 2.99 mmol) in THF (7 mL) at 0 °C. The resulting mixture was stirred at 25 °C for 21 h, and the solvent was then evaporated to afford the crude product (2.04 g), which was purified by chromatography on a column of silica gel (40 g) with a mixture of petroleum ether and CH_2Cl_2 (4:1) to give **12** (580 mg, 79%) as a white solid: mp 53–55 °C; R_f = 0.42 (petroleum ether−CH_2Cl_2, 5:1); ^{1}H NMR (400 Hz, $CDCl_3$) δ 2.27 (pent, 2H, J = 5.9 Hz), 2.36 (s, 6H), 3.84 (t, 2H, J = 6.2 Hz), 3.97 (t, J = 5.8 Hz, 2H), 7.92 (s, 2H); ^{13}C NMR δ 16.5 (CH_3) 33.0 (CH_2), 41.2 (CH_2), 68.3 (CH_2), 124.3 (CH), 132.4 (CH), 143.6 (C), 160.9 (C); MS (CI) *m*/*z* (%) 243 ($M^{\cdot+}$, 37), 167 (86), 137 (77), 121 (15), 91 (54), 82 (100), 47 (59); HRMS (EI) 243.0658 ($C_{11}H_{14}ClNO_3$ requires 243.0662).

4-(3′-Chloro-1′-propyloxy)-3,5-dimethylaniline 13. Tin(II) chloride dihydrate (4.30 g, 19.04 mmol) was added to a solution of the nitro ether **12** (1.16 g, 4.76 mmol) in a 1:1 mixture of THF and EtOH (24 mL), and the resulting solution was stirred at 40 °C for 23 h. The mixture was then cooled, and a saturated aqueous solution of $NaHCO_3$ (70 mL) was added to reach pH 10. The product was extracted with ether (3 × 200 mL) and the organic phase was dried over $MgSO_4$ and evaporated. The residue (1.15 g) was purified by chromatography on a column of silica gel (50 g) with CH_2Cl_2 to afford aniline **13** (660 mg, 65%) as a brownish solid: mp 62–63 °C; R_f = 0.40 (CH_2Cl_2); ^{1}H NMR (400 Hz, $CDCl_3$) δ 2.20–2.23 (m, 8H), 3.54 (s, br, 1.94 H), 3.83 (t, J = 6.4 Hz, 2H), 3.84 (t, J = 5.8 Hz, 2H), 6.38 (s, 2H); ^{13}C NMR δ 16.2 (CH_3) 33.3 (CH_2), 41.8 (CH_2) 68.3 (CH_2), 115.5 (CH), 131.7 (C), 141.5 (C), 148.4 (C); MS (CI) *m*/*z* 213 ($M^{\bullet+}$, 45), 136 (100), 120 (9), 108 (52), 93 (38), 91 (19), 41 (52); HRMS (EI) 213.0916 ($C_{11}H_{16}CION$ requires 213.0920).

Amide (*S*)-(−)-14. Triethylamine (0.16 mL, 1.15 mmol) was added to a solution of (*S*)-BOC-*N*-methylvaline (210 mg, 0.91 mmol) and aniline **13** (180 mg 0.84 mmol) in dry CH_2Cl_2 (6 mL) at 0 °C. To the resulting clear solution were consecutively added 1-hydroxybenzotriazole (HOBt; 160 mg, 1.18 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI; 210 mg, 1.09 mmol). The reaction mixture was stirred at 0 °C for 1 h and then at room temperature for 22 h. The mixture was then diluted with ethyl acetate (35 mL), washed successively with water (20 mL), cold 0.5 M HCl (2 × 20 mL), saturated $NaHCO_3$ (2 × 20 mL), and brine (20 mL), dried over $MgSO_4$, and evaporated. The residue (430 mg) was purified by chromatography on a column of silica gel (40 g) with a mixture of petroleum ether and ethyl acetate (8:1) to afford pure amide (*S*)-(−)-**14** (310 mg, 86%) as a yellowish oil: R_f = 0.27 (petroleum ether−ethyl acetate, 8:1); $[\alpha]_D$ –81.6 (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 Hz, $CDCl_3$) δ 0.90 (d, J = 6.5 Hz, 3H), 1.00 (d, J = 6.5 Hz, 3H), 1.48 (s, 9H), 2.22 (pent, J = 6.0 Hz, 2H) partly overlapped with 2.25 (s, 6H), 2.31–2.41 (m, 1H), 2.82 (s, 3H), 3.83 (t, J = 6.3 Hz, 3H), 3.85 (t, J = 5.7 Hz, 2H), 4.09 (d, J = 11.1 Hz, 1H), 7.18 (s, 2H), 8.08 (s, 0.87 H); ^{13}C NMR δ 16.3 (CH_3), 18.6 (CH_3), 19.8 (CH_3), 25.9 (CH), 28.4 (CH_3), 30.4 (CH_3), 33.2 (CH_2), 41.6 (CH_2), 65.9 (CH), 68.1 (CH_2), 80.6 (C), 120.2 (CH), 131.4 (C), 133.6 (C), 151.9 (C), 157.4 (CO), 168.6 (CO); MS (CI) *m*/*z* 426 ($M^{\bullet+}$, 25), 213 (75), 136 (79), 130 (100), 82 (92), 57 (95); HRMS (EI) 426.2291 ($C_{22}H_{35}ClN_2O_4$ requires 426.2285).

Formamide (*S*)-(−)-15. Trifluoroacetic acid (3.5 mL) was added dropwise to a solution of the BOC derivative **14** (300 mg, 0.70 mmol) in CH_2Cl_2 (6 mL) at 0 °C, and stirring was continued at the same temperature for 1 h. The acid was removed under reduced pressure, and the residue was coevaporated with toluene (2 × 10 mL) to afford a TFA salt of the deprotected amine as a brownish oil, which was used in the following step without further purification. The crude amine salt was dissolved in formic acid (4 mL), and the resulting solution was cooled to 0 °C. Acetic anhydride (3 mL) was then added dropwise and the mixture was allowed to stir at room temperature for 19 h. The volatiles were then evaporated, and the residue (290 mg) was purified by chromatography on a column of silica gel (40 g) with a mixture of CH_2Cl_2 and MeOH (70:1) to afford formamide (*S*)-(−)-**15** (230 mg; 96%) as a white solid: mp 117–119 °C; R_f = 0.50 and 0.42 (two spots; CH_2Cl_2−MeOH, 49:1); $[\alpha]_D$ –154.20 (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 Hz, $CDCl_3$ a mixture of rotamers in ca. 4:1 ratio; the signals for the minor rotamer are marked with an *) δ 0.91 (d, J = 6.5 Hz, 3H), 1.04 (d, J = 6.5 Hz, 3H), 2.21 (pent, J = 6.0 Hz, 2H) partly overlapped with 2.24 (s, 6H), 2.40–2.52 (m, 1H), 2.98 (s, 0.6 H*), 2.99 (s, 2.42 H), 3.74 (d, J = 10.6 Hz, 0.18H*), 3.82 (t, J = 6.3 Hz, 2H), 3.85 (t, J = 5.7 Hz, 2H), 4.37 (d, J = 11.3 Hz, 0.83H) 7.18 (s, 1.69H), 8.05 (s, br, 0.74 H), 8.14 (s, 0.86 H), 8.57 (s, 0.29 H); ^{13}C NMR δ 16.3 (CH_3), 18.5 (CH_3), 19.5 (CH_3), 25.2 (CH), 31.6 (CH_3), 33.2 (CH_2), 41.6 (CH_2), 63.1 (CH), 68.2 (CH_2), 120.4 (CH), 131.5 (C), 133.2 (C), 162.2 (C), 164.0 (CO), 167.0 (CO); IR (KBr) ν 3285, 3215, 3148, 3081, 2965, 2875, 1658, 1613, 1555, 1485, 1411, 1215 cm^{-1}; MS (EI) *m*/*z* 354 ($M^{\bullet+}$, 54), 213 (96), 166 (15), 142 (82), 114 (100), 86 (52), 55 (28), 41 (28); HRMS (EI) 354.1715 ($C_{18}H_{27}ClN_2O_3$ requires 354.1710).

4-[3′-(4″-Benzyloxyphenyl-1″-propyl)oxy]-3,5-dimethylnitrobenzene 19. Triphenylphosphine (4.31 g, 16.42 mmol), alcohol **18** (3.98 g, 16.42 mmol), and diethyl azodicarboxylate (2.58 mL, 16.42 mmol) were added successively to a stirred solution of 2,6-dimethyl-4-nitrophenol **6** (2.22 g, 13.28 mmol) in THF (30 mL) at 0 °C, and the resulting mixture was stirred at 25 °C for 19 h. The solvent was evaporated, and the residue was purified by chromatography on a column of silica gel (100 g) with a mixture of petroleum ether and dichloromethane (3:2) to afford a slightly contaminated product as a brownish solid. The solid was washed with ether (2 × 15 mL) to give pure ether **19** (4.36 g, 84%) as a yellowish solid: mp 97–99 °C; R_f = 0.3 (petroleum ether−CH_2Cl_2, 3:2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.09–2.17 (m, 2H), 2.33 (s, 6H), 2.81 (t, J = 7.7 Hz, 2H), 3.84 (t, J = 6.4 Hz, 2H), 5.06 (s, 2H), 6.93 (d, J = 8.6 Hz, 2H), 7.15 (d, J = 8.6 Hz, 2H), 7.33–7.45 (m, 5H), 7.91 (s, 2H); ^{13}C NMR δ 16.7 (CH_3), 31.3 (CH_2), 32.1 (CH_2), 70.1 (CH_2), 71.9 (CH_2), 114.9 (CH), 124.2 (CH), 127.4 (CH), 127.9 (CH), 128.6 (CH), 129.3 (CH), 132.3 (C), 133.5 (C), 137.1 (C), 143.4 (C), 157.2 (C), 161.6 (C); MS (EI) *m*/*z* 391 ($M^{\bullet+}$, 82), 285 (8), 256 (9), 225 (5), 197 (7), 167 (6), 133 (8), 91 (100), 86 (100), 47 (93); HRMS (EI) 391.1781 ($C_{24}H_{25}NO_4$ requires 391.1784).

4-[3′-(4″-Benzyloxyphenyl-1″-propyl)oxy]-3,5-dimethylaniline 20. Tin(II) chloride dihydrate (4.82 g, 21.36 mmol) was added to a solution of nitro ether **19** (2.00 g, 5.11 mmol) in a 1:1 mixture of ethanol and THF (30 mL), and the mixture was refluxed for 9 h. The mixture was then cooled, and a saturated aqueous solution of $NaHCO_3$ (75 mL) was added to reach pH 10. The product was

extracted with ethyl acetate (3 × 125 mL), and the organic phase was dried over $MgSO_4$. The solvent was evaporated, and the residue (2.60 g) was purified by chromatography on a column of silica gel (70 g) with CH_2Cl_2 to afford aniline **20** (950 mg, 51%) as a reddish solid: mp 53–55 °C; R_f = 0.20 (CH_2Cl_2);^{1}H NMR (400 MHz, $CDCl_3$) δ 2.03–2.10 (m, 2H), 2.20 (s, 6H), 2.78 (t, J = 7.8 Hz, 2H), 3.72 (t, J = 6.4 Hz, 2H), 5.05 (s, 2H), 6.47 (s, 2H), 6.92 (d, J = 8.6 Hz, 2H), 7.16 (d, J = 8.6 Hz, 2H), 7.31–7.45 (m, 5H); ^{13}C NMR δ 16.3 (CH_3), 31.6 (CH_2), 32.2 (CH_2), 70.0 (CH_2), 71.8 (CH_2), 114.7 (CH), 116.5 (CH), 127.5 (CH), 127.9 (CH), 128.5 (CH), 129.3 (CH), 131.8 (C), 134.2 (C), 137.1 (C), 139.2 (C), 149.8 (C), 157.0 (C); MS (EI) m/z 361 ($M^{\bullet+}$, 55), 136 (69), 91 (100), 84 (19), 65 (13); HRMS (EI) 361.2044 ($C_{24}H_{27}NO_2$ requires 361.2042).

Amide (*S*)-(−)-21. Triethylamine (0.85 mL, 6.12 mmol) was added to a solution of (*S*)-BOC-*N*-methylvaline (850 mg, 3.68 mmol) in dry CH_2Cl_2 (25 mL) at 0 °C. To the resulting clear solution were consecutively added aniline **20** (950 mg, 2.63 mmol), 1-hydroxybenzotriazole (HOBt; 630 mg, 4.66 mmol), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI; 780 mg, 4.07 mmol), and the reaction mixture was stirred at 0 °C for 1 h and then at room temperature for 24 h. The mixture was then diluted with ethyl acetate (150 mL) and washed successively with water (75 mL), cold 0.5 M HCl (2 × 75 mL), saturated $NaHCO_3$ (2 × 75 mL), and brine (75 mL), dried over $MgSO_4$, and evaporated. The residue (1.92 g) was purified by chromatography on a column of silica gel (100 g) with a mixture of petroleum ether and ethyl acetate (8:1) to afford pure amide (*S*)-(−)-**21** (1.15 g, 76%) as an orange oil: R_f = 0.42 (petroleum ether−AcOEt, 6:1); $[\alpha]_D$ –70.4 (c 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (d, J = 6.6 Hz, 3H), 1.01 (d, J = 6.5 Hz, 3H), 1.49 (s, 9H), 2.04–2.11 (m, 2H), 2.24 (s, 6H), 2.32–2.41 (m, 1H), 2.79 (t, J = 7.7 Hz, 2H), 2.83 (s, 3H), 3.73 (t, J = 6.4 Hz, 2H), 4.09 (d, J = 11.0 Hz, 1H), 5.05 (s, 2H), 6.92 (d, J = 8.6 Hz, 2H), 7.15 (d, J = 8.6 Hz, 2H) partly overlapped with 7.16 (s, 2H), 7.30–7.45 (m, 5H), 8.05 (br s, 0.84H); ^{13}C NMR δ 16.4 (CH_3), 18.6 (CH_3), 19.9 (CH_3), 25.9 (CH), 28.4 (CH_3), 30.5 (CH_3), 31.5 (CH_2), 32.2 (CH_2), 66.0 (CH), 70.1 (CH_2), 71.7 (CH_2), 80.6 (C), 114.8 (CH), 120.1 (CH), 127.5 (CH), 127.9 (CH), 128.5 (CH), 129.3 (CH), 131.5 (C), 133.4 (C), 134.1 (C) 137.2 (C), 152.5 (C) 157.1 (C), 157.4 (CO), 168.6 (CO); MS (EI) m/z 574 ($M^{\bullet+}$, 26), 361 (53), 130 (54), 91 (100), 86 (69), 57 (44); HRMS (EI) 574.3404 ($C_{35}H_{46}N_2O_5$ requires 574.3407).

Formamide (*S*)-(−)-22. Trifluoroacetic acid (10.1 mL) was added dropwise to a solution of the BOC derivative **21** (1.15 g, 2.00 mmol) in CH_2Cl_2 (17 mL) at 0 °C and stirring continued at the same temperature for 1 h. The acid was removed under reduced pressure, and the residue was coevaporated with toluene (2 × 20 mL) to afford a TFA salt of the deprotected amine as a brownish oil, which was used in the following step without further purification. The crude amine salt was dissolved in formic acid (12.1 mL), and the resulting solution was cooled to 0 °C. Acetic anhydride (9 mL) was then added dropwise, and the mixture was allowed to stir at room temperature for 25 h. The volatiles were then evaporated, and the residue was coevaporated with toluene (2 × 10 mL). The latter residue (940 mg) was purified by chromatography on a column of silica gel (100 g) with a mixture of CH_2Cl_2 and MeOH (90:1) to afford formamide (*S*)-(−)-**22** (870 mg; 87%) as a colorless oil: R_f = (2 spots 0.70 and 0.50) (CH_2Cl_2−MeOH, 49:1); $[\alpha]_D$ –95.20 (c 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, a mixture of rotamers in ca. 4:1 ratio; the signals for the minor rotamer are marked by an *) δ 0.91 (d, J = 6.6 Hz, 3H), 1.05 (d, J = 6.5 Hz, 3H), 2.04–2.11 (m, 2H), 2.23 (s, 6H), 2.39–2.52 (m, 1H), 2.78 (t, J = 7.7 Hz, 2H), 2.93 (s, 0.41H*), 2.99 (s, 2.55H), 3.49 (d, J = 10.3 Hz, 0.11H*), 3.73 (t, J = 6.4 Hz, 2H), 4.38 (d, J = 11.2 Hz, 0.83H), 5.05 (s, 2H), 6.92 (d, J = 8.6 Hz, 2H), 7.15 (d, J = 8.6 Hz, 2H), 7.17 (s, 2H), 7.30–7.45 (m, 5H), 7.76 (s, 0.12H*), 8.02 (br s, 0.83H), 8.14 (s, 0.86H), 8.24 (s, 0.13H*); ^{13}C NMR δ 16.4 (CH_3), 18.5 (CH_3), 19.5 (CH_3), 25.2 (CH), 31.5 (CH_2), 31.6 (CH_3), 32.2 (CH_2), 63.1 (CH), 70.1 (CH_2), 71.7 (CH_2), 114.8 (CH), 120.3 (CH), 127.4 (CH), 127.9 (CH), 128.5 (CH), 129.3 (CH), 131.5 (C), 133.0 (C), 134.1 (C) 137.2 (C), 152.8 (C) 157.1 (C), 163.9 (CHO), 167.0 (CO); IR (KBr) ν 3448, 2925, 1655, 1552, 1509, 1484, 1215 cm^{-1}; MS (EI) m/z 502 ($M^{\bullet+}$, 18), 361 (25), 276 (10), 233 (100), 231 (40), 121 (47), 78 (92), 44 (55); HRMS (EI) 502.2831 ($C_{31}H_{38}N_2O_4$ requires 502.2832).

Formamide (*S*)-(−)-23. A mixture of the benzyl derivative **22** (870 mg, 1.73 mmol) and a 10% palladium on activated charcoal (180 mg, 10 mol%) in absolute ethanol (40 mL) was stirred under a hydrogen atmosphere for 8 h. Ethanol (300 mL) was then added, and the mixture was filtered through Celite and evaporated. The residue (720 mg) was purified by chromatography on a column of silica gel (70 g) with a mixture of CH_2Cl_2 and MeOH (49:1) to afford (*S*)-(−)-**23** (670 mg, 95%) as an enamel: R_f = 0.37 and 0.25 (two spots, CH_2Cl_2−MeOH, 49:1); $[\alpha]_D$ –140.60 (c 0.5, $CHCl_3$); ^{1}H NMR (400 Hz, $CDCl_3$, a mixture of rotamers in ca. 4:1 ratio; the signals for the minor rotamer are marked with an *) δ 0.90 (d, J = 6.6 Hz, 3H), 1.02 (d, J = 6.5 Hz, 3H), 2.02–2.09 (m, 2H), 2.21 (s, 6H), 2.40–2.50 (m, 1H), 2.75 (t, J = 7.7 Hz, 2H), 2.94 (s, 0.43H*), 3.02 (s, 2.60H), 3.51 (d, J = 10.4 Hz, 0.14H*), 3.71 (t, J = 6.4 Hz, 2H), 4.37 (d, J = 11.2 Hz, 0.86H), 6.37 (br s, 0.96H), 6.79 (d, J = 8.5 Hz, 2H), 7.07 (d, J = 8.5 Hz, 2H), 7.14 (s, 0.14H*), 7.16 (s, 1.69H), 8.03 (br s, 0.12H*), 8.14 (s, 0.93H), 8.19 (s, 0.78H), 8.25 (s, 0.13H*); ^{13}C NMR δ 16.4 (CH_3), 18.5 (CH_3), 19.4 (CH_3), 25.4 (CH), 31.4 (CH_2), 31.7 (CH_3), 32.2 (CH_2), 63.1 (CH), 71.7 (CH_2), 115.3 (CH), 120.5 (CH), 129.4 (CH), 131.5 (C), 132.8 (C), 133.5 (C), 152.8 (C) 154.0 (C), 164.1 (CHO), 167.0 (CO); IR (KBr) ν 3396, 2960, 2871, 1654, 1549, 1517, 1480, 1218 cm^{-1}; MS (CI) m/z 413 ($[MH]^{\bullet+}$, 40), 412(68), 271 (27), 143 (90), 115 (100), 88 (28); HRMS (CI) 413.2436 ($C_{24}H_{33}N_2O_4$ $[MH]^{\bullet+}$ requires 413.2440).

General Procedure for the Asymmetric Reduction of 1a−e, Catalyzed by 5a−f or 24–30. The imine **1** (100 mg, 4.44 mmol) was added to a reaction tube containing a small porous polypropylene reactor vessel (2.4 mL internal volume and 74 μm pore size) with an immobilized catalyst or resin (for the number of mmol, see Tables 1 and 3) in a solvent (4 mL), and the tube was shaken at room temperature for 30 min. Trichlorosilane (100 μL) was added at 0 °C, followed by overnight shaking at room temperature. The porous reactor vessel was separated from the mother liquor and washed with chloroform (2 × 30 mL). Combined organic solutions were quenched with a saturated aqueous solution of $NaHCO_3$ (25 mL), the layers were separated, and the aqueous layer was additionally extracted with chloroform (60 mL). Combined chloroform solutions were dried over $MgSO_4$, and the solvent was evaporated to give a crude product, which was purified by chromatography on a column of silica gel (15 g) to afford pure amines **2**. The results are summarized in the Tables 1 and 3.

Regeneration of Immobilized Catalysts. After separation from the mother liquor and washing with chloroform, the porous reactor vessel with immobilized catalyst was alternately washed with methanol and CH_2Cl_2 (4 × 25 mL of each solvent) and ether (25 mL). An overnight drying under vacuum afforded the regenerated catalyst, which was used for the next transformation without further purification.

Amine (*S*)-(−)-2a. Purified by column chromatography on silica gel with a hexane−ethyl acetate mixture (10:1, R_f = 0.3): $[\alpha]_D$ –4.0 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.50 (d, J = 6.7 Hz, 3H), 3.70 (s, 3H), 3.79 (br s, 1H), 4.42 (q, J = 6.7 Hz, 1H), 6.46–6.50 (m, 2H), 6.68–6.72 (m, 2H), 7.20–7.25 (m, 1H), 7.30–7.38 (m, 4H) in agreement with data for an authentic sample;[7] chiral HPLC (Chiracel OD-H, hexane/2-propanol 99:1, 0.9 mL/min) showed 81% ee (t_R = 21.6 min, t_S = 24.4 min).

Amine (*S*)-(−)-2b. Purified by column chromatography on silica gel with a hexane-ethyl acetate mixture (10:1): $[\alpha]_D$ −23.2 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.58 (d, J = 6.7 Hz, 3H), 3.68 (s, 3H), 3.90 (br s, 1H), 4.57 (q, J = 6.7 Hz, 1H), 6.50–6.54 (m, 2H), 6.66–6.70 (m, 2H), 7.41–7.52 (m, 3H), 7.79–7.83 (m, 4H) in agreement with literature data;[11a–c] chiral HPLC (Chiracel OD-H, hexane/2-propanol 99:1, 0.9 mL/min) showed 79% ee (t_R = 27.4 min, t_S = 33.4 min).

Amine (*S*)-(+)-2c. Purified by column chromatography on silica gel with a petroleum ether−ethyl acetate mixture (9:1): $[\alpha]_D$ +6.5 (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 1.51 (d, $J = 6.7$ Hz, 3H), 3.70 (s, 3H), 3.83 (br s, 1H), 4.46 (q, $J = 6.7$ Hz, 1H), 6.41–6.45 (m, 2H), 6.67–6.71 (m, 2H), 7.48 (d, $J = 8.2$ Hz, 2H), 7.57 (d, $J = 8.2$ Hz, 2H) in agreement with literature data;[11a–c] chiral HPLC (Chiracel OD-H, hexane/2-propanol 95:5, 0.9 mL/min) showed 81% ee ($t_R = 15.7$ min, $t_S = 21.8$ min).

Amine (*S*)-(−)-2d. Purified by column chromatography on silica gel with a petroleum ether−ethyl acetate mixture (9:1): $[\alpha]_D$ −16.1 (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 1.47 (d, $J = 6.7$ Hz, 3H), 3.70 (s, 3H), 3.78 (s, 3H), 4.37 (q, $J = 6.7$ Hz, 1H), 6.46–6.70 (m, 2H), 6.67–6.71 (m, 2H), 6.84–6.87 (m, 2H), 7.25–7.29 (m, 2H) in agreement with literature data;[11a–c] chiral HPLC (Chiracel OD-H, hexane/2-propanol 98:2, 0.6 mL/min) showed 77% ee ($t_R = 28.8$ min, $t_S = 33.9$ min).

Amine (*S*)-(−)-2e. Purified by column chromatography on silica gel with a petroleum ether−ethyl acetate mixture (10:1): $[\alpha]_D$ –4.5 (*c*, 2, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 1.42 (d, $J = 6.7$, 3H), 2.21 (br s, 3H), 2.25 (br s, 3H), 3.36 (br s, 1H), 3.74 (s, 3H), 4.29 (q, $J = 6.6$ Hz, 1H), 5.88 (br s, 1H), 6.53–6.57 (m, 2H), 6.73–6.77 (m, 2H); ^{13}C NMR δ 11.9 (CH_3), 13.6 (CH_3), 23.2 (CH_3), 46.4 (CH), 55.8 (CH_3), 104.6 (CH), 114.8 (2 × CH), 114.9 (2 × CH), 123.6 (C), 141.8 (C), 144.9 (C), 149.7 (C), 152.1 (C); IR ν 3398, 2964, 2921, 1583, 1511, 1450, 1234 cm^{-1}; MS (EI) *m*/*z* 245 ($M^{\bullet+}$, 25), 123 (100), 86 (35), 84 (54), 83 (25), 51 (24), 49 (77), 43 (35); HRMS (EI) 245.1414 ($C_{15}H_{19}NO_2$ requires 245.1416); HPLC analysis (Chiralpak IB, hexane−propan-2-ol (99:1), 0.75 mL/min,) showed 79% ee ($t_{minor} = 12.782$ min, $t_{major} = 14.546$ min).

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Supporting Information Available: General experimental methods and ^1H and ^{13}C NMR spectra for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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