Pergamon

SCIENCE DIRECT®

Tetrahedron 59 (2003) 6393–6402

TETRAHEDRON

Stereocontrol in hydride addition to ketone-derived chiral *N*-acylhydrazones

Jun Qin and Gregory K. Friestad*

Department of Chemistry, University of Vermont, Cook Physical Sciences Building, Burlington, Vermont 05405 USA

Received 6 May 2003; revised 3 July 2003; accepted 10 July 2003

Abstract—Chiral *N*-acylhydrazones derived from various aldehydes and *N*-amino-4-benzyl-2-oxazolidinone have previously been shown to be effective for acyclic stereocontrol of intermolecular radical and allylsilane additions. Treatment of the propionaldehyde hydrazone with tributyltin hydride in the presence of boron trifluoride etherate led to rapid chemoselective reduction of the imine bond in high yield. Preparation of similar hydrazones from ketones led to *E*/*Z* isomer mixtures, usually in ratios of 4:1 or greater. Geometry of the C=N bond was assigned by steric compression shifts in ^{13}C NMR spectra. Reduction with tributyltin hydride and boron trifluoride etherate afforded diastereomer mixtures in ratios very similar to the original *E*/*Z* isomer ratios. The chiral auxiliary blocked the opposite face of the C=N bond relative to a related process using a chelated Lewis acid. A stereocontrol model involving monodentate interaction of the *N*-acylhydrazone and boron trifluoride is consistent with the observed stereochemical outcome.

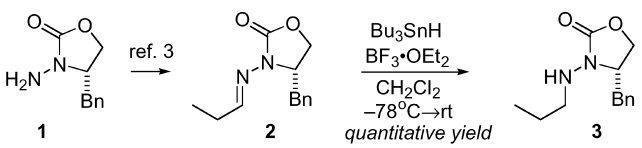
1. Introduction

Chiral amines are important substructures in biologically active materials of both natural and synthetic origin, and methods for their asymmetric synthesis are an important current objective. Asymmetric reduction of the C=N bond of ketone-derived imines is a convenient method for the synthesis of chiral amines, and a variety of chiral auxiliaries have been shown to be effective in this process.[1] Additionally, several excellent catalytic enantioselective approaches have been developed recently.[2] Often, high selectivity is limited to substrates derived from aryl alkyl ketones, where the two carbonyl substituents are easily distinguished. When both substituents of a ketimine have similar steric properties, low *E*/*Z* isomer ratios with respect to the C=N bond geometry and/or poor discrimination of enantiotopic faces of the imine can present difficult problems. Chiral auxiliaries offer a practical advantage under these circumstances, because in principle *E*/*Z* mixtures of the starting imine could be separated prior to use, or mixtures of diastereomeric products could be resolved before removal of the auxiliary.

We have previously described non-basic tin-mediated intermolecular radical addition reactions for construction of chiral α-branched amines using chiral *N*-acylhydrazone auxiliaries derived from *N*-amino-4-benzyl-2-oxazolidinone (**1**).[3] During the development of the radical addition reactions, we discovered that boron trifluoride etherate promoted an extremely rapid and quantitative reduction of chiral *N*-acylhydrazones by tributyltin hydride. Specifically, we found that in the presence of $BF_3{\cdot}OEt_2$, *N*-acylhydrazone **2** was reduced by Bu_3SnH to afford amine **3** in quantitative yield within 5 min (Scheme 1). Naito et al. recently reported quite similar BF_3-promoted racemic hydrostannation reactions involving achiral N-heteroatom-substituted aldimines and ketimines.[4]

In the context of the radical additions, hydridic behavior by the stannane reagent was undesirable. In that study, the reduction could be avoided by the use of $ZnCl_2$ or $InCl_3$ as Lewis acids, whereupon the chiral auxiliary afforded high stereoselectivity in the radical addition. A model involving Lewis acid chelation was invoked to explain the selectivity (Fig. 1).

Considered apart from the radical addition study, the reduction reaction raised some interesting questions which are summarized in Figure 1: could the chiral *N*-acylhydrazone stereocontrol element provide for stereoselective reduction of C=N bond of ketone *N*-acylhydrazones? Was



Scheme 1.

Keywords: asymmetric synthesis; amines; imines; chiral hydrazones; reduction; boron trifluoride; tributyltin hydride.
* Corresponding author. Tel.: +1-8026561042; fax: +1-8026568705; e-mail: gregory.friestad@uvm.edu

0040–4020/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/S0040-4020(03)01091-3

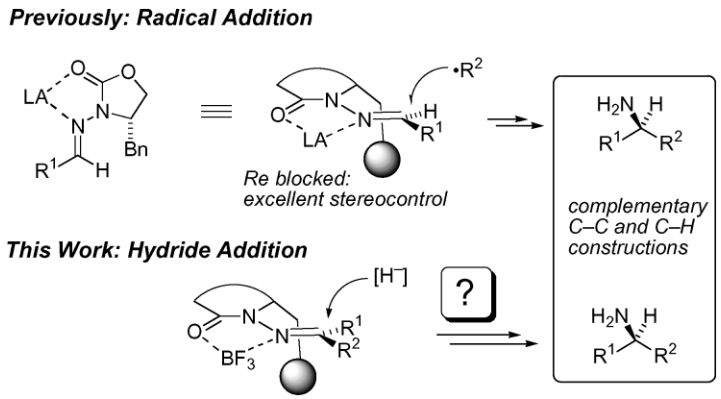
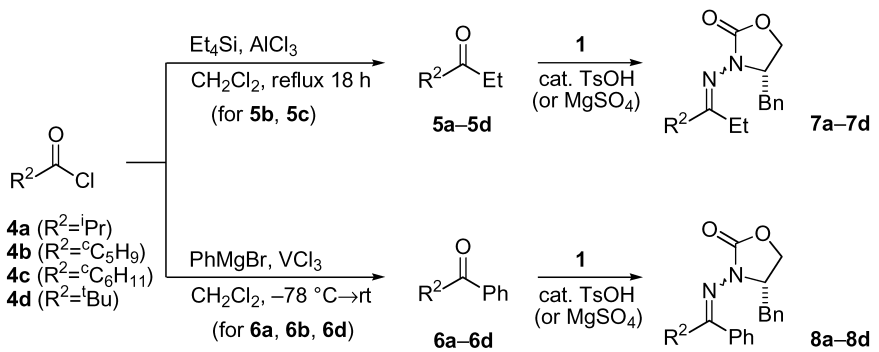


Figure 1. Complementary C–C or C–H bond constructions for chiral amine synthesis.



Scheme 2.

$BF_3{\cdot}OEt_2$ acting as a non-chelating or chelating Lewis acid in the reduction? Could the same stereocontrol model be applied to predict the outcome of the selectivity?

The very rapid reduction reaction of Scheme 1 seemed to offer some advantages in operational simplicity, along with potential for complementary chemoselectivity relative to asymmetric hydrogenation. Furthermore, hydride additions to ketone hydrazones could help lay a foundation for synthesis of quaternary carbon centers by analogous additions of carbon nucleophiles. For these reasons, and because of the synthetic value of alternative general approaches to asymmetric amine synthesis, we examined the sequence exemplified by Scheme 1 in greater detail in order to define its scope, examine the potential for stereoselectivity, and develop an understanding of the roles of the Lewis acid and chiral auxiliary. Here we present the full details of this study.

2. Results

2.1. Synthesis of ketone *N*-acylhydrazones

As a starting point for testing the configurational control in hydride additions of *N*-acylhydrazones such as that indicated in Scheme 1, prochiral ketimine substrates were required. It is now well-documented that *N*-aminooxazolidinones are reliably condensed with aldehydes to afford the corresponding *N*-acylhydrazones (i.e. hydrazides).[5–7] It was expected that various ketones would condense with *N*-amino-4-benzyl-2-oxazolidinone (**1**)[5] under standard conditions.

The choice of ketones was constrained by the desire to correlate the reductive amination products to known compounds which had previously been prepared in diastereomerically pure form by radical addition.[3] This required a series of ethyl ketones and phenyl ketones, some of which were commercially available. *tert*-Butyl ethyl ketone was prepared by oxidation of the corresponding alcohol (PCC, CH_2Cl_2). Others were prepared by direct coupling reactions with acyl chlorides **4a**–**4d** (Scheme 2). There are many methods available for direct coupling of carboxylic acid derivatives with organometallic reagents to afford ketones.[8] We found that, for preparation of the ethyl ketones, reaction of tetraethylsilane with the appropriate acid chloride[9] proved practical for ketones **5b** and **5c**. These

Table 1. Preparation of ketone hydrazones (Scheme 2)

Entry	R^1	R^2	Ketone (yield)	Hydrazone (yield)	*E*/*Z* ratio
1	Et	^{i}Pr	**5a**[a]	**7a** (84%)	77:23
2	Et	^{c}C$_5$H$_9$	**5b**[b]	**7b** (49%)	79:21
3	Et	^{c}C$_6$H$_{11}$	**5c**[b]	**7c** (64%)	85:15
4	Et	^{t}Bu	**5d**[b]	**7d** (67%)	>98:2
5	Ph	^{i}Pr	**6a** (72%[c])	**8a** (55%)	19:81
6	Ph	^{c}C$_5$H$_9$	**6b** (88%[c])	**8b** (59%)	26:74
7	Ph	^{c}C$_6$H$_{11}$	**6c**[a]	**8c** (55%)	13:87
8	Ph	^{t}Bu	**6d** (82%[c])	**8d** (73%)	<2:98

[a] Commercially available ketone was employed.
[b] Ketone was prepared and used directly without purification.
[c] Isolated yield of ketone based on **1**.

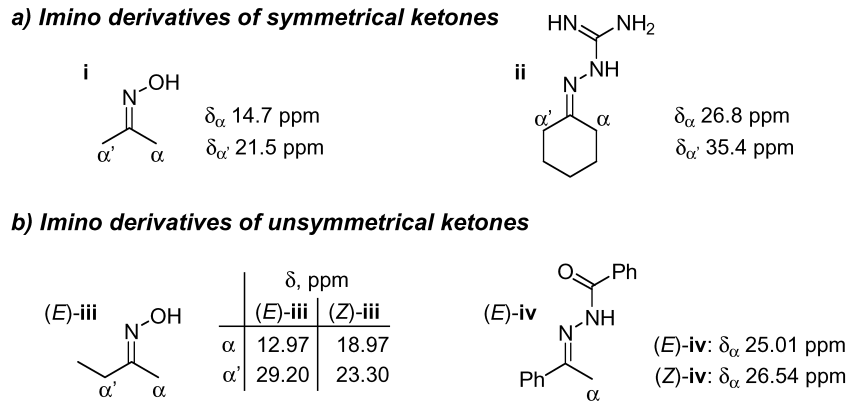


Figure 2. Ketimine steric compression shifts from literature sources (^{13}C NMR, $CDCl_3$).[11]

were used directly in the subsequent condensation reaction with **1**. On the other hand, an organovanadium-mediated method[10] proved convenient for the phenyl ketones. Reaction of phenylmagnesium bromide with vanadium(III) chloride at −78°C, followed by addition of the acyl chloride and warming to ambient temperature afforded ketones **6a**, **6b**, and **6d** in good yield.

Condensation of ketones **5** and **6** with *N*-aminooxazolidinone **1** in the presence of a catalytic amount of *p*-toluenesulfonic acid in refluxing toluene afforded ketone *N*-acylhydrazones **7** and **8** (Scheme 2, Table 1). Mixtures of *E*/*Z* isomers were obtained in the cases of **7a**–**c** and **8a**–**c**. Unfortunately, attempts to separate these isomers by flash chromatography were unsuccessful. Ketone *N*-acylhydrazones **7d** and **8d**, which have highly branched tertiary butyl (^{t}Bu) substituents, were formed as single isomers, presumably due to steric repulsion from the ^{t}Bu substituent.

2.2. Determination of *E*/*Z* isomer ratio by NMR analysis

Assignment of C=N bond geometry was achieved through comparison of ^{13}C NMR chemical shifts of the α-carbon of the *E* and *Z* isomers. Steric compression shifts are observed when a ketone is converted to ketone oxime or ketone hydrazone.[11] Steric compression shifts in ^{13}C NMR spectroscopy arise from steric perturbations of carbon nuclei, and have been utilized in the studies of diverse organic compounds.[12] Of relevance for this study is the ability of steric compression shifts to distinguish between carbons which have *cis* and *trans* relationships to the N-substituent of a C=N bond.

Four examples of steric compression shifts in assignment of C=N bond geometry are presented in Figure 2. First, the 2 equivalent methyl resonances in the ^{13}C NMR spectrum of acetone (30.7 ppm) become non-equivalent upon conversion to the oxime (**i**) (21.5 and 14.7 ppm). The *cis* α-carbon resonance is upfield from the *trans* α-carbon, and the difference of these chemical shifts (subtracting *cis* from *trans*), $\Delta\delta$=6.8 ppm, is the steric compression shift. A similar effect was also observed in the guanylhydrazone derived from cyclohexanone (**ii**), which exhibits a significant steric compression shift ($\Delta\delta$=8.6 ppm) for the α-carbon.[11c] For C=N bonds which have non-equivalent C-substituents, steric compression shift $\Delta\delta$ for each carbon may be obtained by comparison of *E* and *Z* isomers. In 2-butanone oxime (**iii**), *E*/*Z*=77:23, the steric compression shifts of C1 (α), C3 (α′) and C4 (β) are 6.0, 5.9 and 1.2 ppm, respectively.[11a,b] Finally, the effect has been used to assign the *E*/*Z* isomers of acetophenone *N*-benzoylhydrazone (**iv**); the methyl ^{13}C NMR chemical shifts for *E* and *Z* isomers are 25.01 and 26.54 ppm, respectively ($\Delta\delta$=1.53 ppm).[11d] In all these examples, the α-carbon with a *cis* relationship to the N-substituent is found upfield from the same α-carbon having a *trans* relationship to the N-substituent, usually by several ppm.

For ketone *N*-acylhydrazones obtained as mixtures of *E*/*Z* isomers, steric compression shifts ($\Delta\delta$) could be observed clearly for one or both of the α-carbons. The key data used for assignment of C=N bond geometries of the hydrazones are found in Table 2.

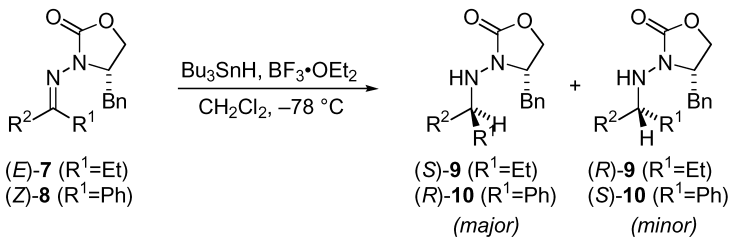
Upon assignment of structures **7a**–**7c** and **8a**–**8c** by ^{13}C chemical shifts according to the literature precedents noted above, the ^{1}H chemical shifts of the α-hydrogen within R^2 were also found to be reliable indicators of a *cis* or *trans* relationship of R^2 with the N-substituent on the C=N bond (i.e. the oxazolidinone). The *trans* methine (relative to the oxazolidinone) was found upfield of the *cis* methine in all compounds, with the differences in chemical shifts ranging from 0.45 to 0.84 ppm. Structures of hydrazones (*E*)-**7d** and (*Z*)-**8d** were assigned by analogy with the others, and also by consideration of the stereochemical outcome of the reduction reactions (vide infra).

Table 2. Key NMR data for (*E*)- and (*Z*)-hydrazones in $CDCl_3$ at 500 MHz (^{1}H) or 125 MHz (^{13}C)

Hydrazone	α-Carbon of R^2 (δ, ppm)			α-Hydrogen of R^2 (δ, ppm)	
	R^2-*trans*[a]	R^2-*cis*[a]	Δδ (ppm)	R^2-*trans*[a]	R^2-*cis*[a]
7a	34.2 (*E*)	30.9 (*Z*)	3.3	2.68[b] (*E*)	3.24 (*Z*)
7b	45.4 (*E*)	42.2 (*Z*)	3.2	2.85 (*E*)	3.30 (*Z*)
7c	44.3 (*E*)	41.9 (*Z*)	2.4	2.36[c] (*E*)	3.13 (*Z*)
8a	37.3 (*Z*)	31.3 (*E*)	6.0	2.99[b] (*Z*)	3.52 (*E*)
8b	48.5 (*Z*)	42.5 (*E*)	6.0	3.12 (*Z*)	3.54 (*E*)
8c	47.5 (*Z*)	42.9 (*E*)	4.6	2.62[c] (*Z*)	3.46 (*E*)

[a] The designations *trans* and *cis* refers to the relationship between R^2 and the N-substituent. Therefore (*E*)-**7a**–**7c** and (*Z*)-**8a**–**8c** are designated here as *trans*.
[b] cf. corresponding aldehyde hydrazone (*E*): δ 2.60.
[c] cf. corresponding aldehyde hydrazone (*E*): δ 2.34.

Table 3. Stereoselectivity and yield in reduction of *N*-acylhydrazones



N-Acylhydrazone (*E*/*Z* ratio)	Hydrazide (yield)	dr[a]
(*E*)-**7a** (77:23)	(*S*)-**9a** (89%)	80:20
(*E*)-**7b** (79:21)	(*S*)-**9b** (82%)	76:24
(*E*)-**7c** (85:15)	(*S*)-**9c** (76%)	85:15
(*E*)-**7d** (>98:2)	(*S*)-**9d** (94%)	89:11
(*Z*)-**8a** (19:81)	(*R*)-**10a** (92%)	19:81
(*Z*)-**8b** (26:74)	(*R*)-**10b** (78%)	26:74
(*Z*)-**8c** (13:87)	(*R*)-**10c** (94%)	18:82
(*Z*)-**8d** (<2:98)	(*R*)-**10d** (94%)	12:88

[a] Ratio of diastereomers *S*/*R* (configurations of new stereogenic center).

2.3. Reduction of ketone *N*-acylhydrazones by Bu_3SnH

With structural assignments in place, the stereochemical results of reduction reactions could give meaningful information regarding the hypothesis set forth in Figure 1. First, some variations to the conditions of Scheme 1 were explored. Changing reducing reagent from Bu_3SnH to less toxic Et_3SiH resulted in recovery of the unchanged starting material. Although reduction could be observed in some cases with other Lewis acids during the previous radical addition study, those reactions were not as reliable and smooth as the BF_3-mediated reduction. We employed the original conditions discovered for aldehyde hydrazones (Scheme 1) for the remainder of the study.

Ketone hydrazones were reduced to diastereomeric mixtures of *N*-acylhydrazines (i.e. hydrazides), and the diastereomer ratios were measured by ^1H NMR or HPLC (Table 3). In the presence of $BF_3{\cdot}OEt_2$ (1.5–2.0 equiv.) as Lewis acid, reductions of ketone *N*-acylhydrazones **7** and **8** by Bu_3SnH (1.5–2.5 equiv.) at −78°C afforded hydrazides **9** and **10** as diastereomer mixtures in good-to-excellent yield. In each case, the major isomer is that arising from addition of hydride from the α-face (as drawn in Table 3). Assignment of configuration rests on evidence from chemical correlation of **9a** to (*S*)-valinol and X-ray crystallography of the *N*-benzoyl derivative of **10d**, as described previously.[3]

When the reduction of **8a** was conducted with a substoichiometric amount (0.5 equiv.) of stannane, the diastereomer ratio of **10a** (38% yield, 74% yield based on stannane) was 17:83, with the same configuration (*R*) favored. Determination of the *E*/*Z* ratio of the remaining hydrazone was not possible due to complications by $BF_3{\cdot}OEt_2$-promoted hydrolysis during workup.

3. Discussion

The foregoing results show that both the chiral auxiliary and the configuration of the C=N bond participate to define the configuration of the newly formed stereocenter.

The hydride additions appear to be quite stereospecific; the diastereomeric ratios of products were similar to the *E*/*Z* isomer ratios of the hydrazones, in some cases identical. For example, reduction of **7c** as 85:15 *E*/*Z* mixture afforded hydrazine **9c** with a diastereomer ratio (*S*/*R*) 85:15. This suggests a stereospecific process in which both *E* and *Z* isomers are reduced with good stereocontrol. The stereospecificity is not complete, however: The reductions of hydrazones **7d** and **8d**, employed as single isomers, gave 89:11 and 88:12 diastereomeric ratios, respectively. These latter two examples have lower stereospecificity compared to the complementary radical addition to aldehyde *N*-acylhydrazones (generally dr>13:1) favoring the diastereomeric products.[3]

In considering possible binding modes for the Lewis acid with the *N*-acylhydrazones, the question of chelation versus non-chelation demanded some attention. There has been some interesting discussion in the literature regarding the proposed bidentate binding to boron trifluoride. Widely used as a Lewis acid in organic synthesis,[13] $BF_3{\cdot}OEt_2$ is generally presumed to involve the formation of tetracoordinate complexes LBF_3 with binding of the ligand L at a single Lewis basic atom.[14] Although bidentate binding of BF_2^+ is well-known,[15] few examples of pentacoordinate complexes of the general formula L_2BX_3 have been postulated, and chelate structures are rarely invoked with boron trifluoride.[16] On the other hand, chelation should be an important consideration with the combination $BF_3{\cdot}OEt_2$/Bu_3SnH in view of the very interesting studies on the reactions of $B(C_6F_5)_3$ with stannanes[16d] and silanes[17] which have implicated hydride or allyl transfer from tin (or silicon) to boron, leaving Bu_3Sn^+ available to serve as a chelating Lewis acid.

The diastereoface selectivity observed in these hydride additions to ketone *N*-acylhydrazones is opposite that of radical[3] or allylsilane[6] additions using Zn(II) or In(III) salts as Lewis acids. The latter give product configurations

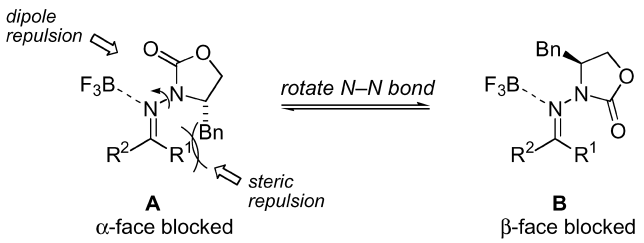


Figure 3.

consistent with chelated Lewis acids and addition from the face opposite the benzyl group of the oxazolidinone (Fig. 1). In contrast, if the same N–N bond dihedral angle (**A**, Fig. 3) is assumed in these reductions, the hydride addition would be required to preferentially take place from the face proximal to the benzyl group, a prospect which seems unlikely.

A non-chelated model of the hydrazone geometry can be invoked in the present case which is consistent with the outcome of the reduction reaction, and which may explain its stereochemical difference from the radical[3] and allylsilane[6] additions. It is important to note that Lewis acid activation of C=N bonds was necessary, since no reaction was observed without $BF_3{\cdot}OEt_2$. A tetracoordinate BF_3 complex with boron bound only to the imino nitrogen would lack rotational restriction of the N–N bond. Steric repulsions between R^1/R^2 and the benzyl stereocontrol element would be expected to destabilize conformer **A** (Fig. 3), in which the benzyl group blocks the α-face. Furthermore, the interactions of B–F and C=O bond dipoles would be expected to further disfavor **A**. The alternative conformer **B** appears more favorable; this places the benzyl stereocontrol element on the β-face of the C=N bond relative to **A**. Hydride addition on the more exposed α-face of **B**, opposite the benzyl substituent of the auxiliary, is consistent with all the observed results.

The key difference between this proposed model and the radical addition model is that with a non-chelating Lewis acid, a different N–N bond rotamer is preferred. Further support for this model is offered by the lower stereoselectivity in comparison to the radical additions; this is consistent with conformer **B** because the stereocontrol element is farther away from the C=N carbon in the non-chelated N–N bond rotamer.

Finally, it is worth noting that rate of reduction appears to be independent of the C=N bond geometry. In the control experiment with substoichiometric stannane, where the reduction of **15a** was incomplete, the ratio of the products (17:83) was almost the same as in the reaction with complete conversion (19:81). Unfortunately, the hydrolytic instability of the hydrazone in the presence of boron trifluoride prevented the complementary analysis of the *E*/*Z* ratio of the recovered starting material. Nevertheless, the result of this competition experiment implies that both *E* and *Z* isomers were reduced at nearly the same rate.

Interconversion of C=N bond isomers under the reaction conditions has not been rigorously ruled out. Thus, a conceivable alternative hypothesis involves rapid equilibration of C=N bond isomers having differential rates of reduction.[18] Evidence of relevance to this issue may be seen in the close correlations of initial *E*/*Z* ratio with product diastereomer ratios across several different examples. This evidence makes the equilibration hypothesis highly unlikely, since it would require a scenario where all examples of Table 3 have the concentrations of equilibrating hydrazone·BF_3 isomers balanced with the reduction rates in such a way as to give product ratios which are coincidentally similar to that of the hydrazone *E*/*Z* ratio. Such a remarkable coincidence can be considered even more unlikely in light of the experiment with substoichiometric stannane, where it is reasonable to assume that the precise balance might be altered by the different stannane concentration.[19] In fact, an almost identical ratio is obtained regardless of the concentration of stannane. Various literature precedents also seem to indicate that *N*-acylhydrazone isomers may not be prone to equilibration under these conditions: (1) it has been suggested previously that C=N bond isomerization of *N*-acylhydrazones may be slower than Rh-mediated reduction;[11d] (2) complexation of *E*/*Z* isomeric mixtures of imines with $B(C_6F_5)_3$ preserves the C=N geometry at −40°C (i.e. higher temperature than that employed in this study), and excess $B(C_6F_5)_3$ inhibits isomerization even at higher temperatures;[20] (3) Interconversion of imine C=N isomers occurs only to a small extent at 65°C during hydrogenation in the presence of a titanocene catalyst, even over 2–3 days.[21] These precedents argue against C=N isomer equilibration of *N*-acylhydrazones during the reductions by $BF_3{\cdot}OEt_2/Bu_3SnH$, especially considering the low temperatures employed in the present study.

4. Conclusion

Clean and efficient reduction of ketone *N*-acylhydrazones by $BF_3{\cdot}OEt_2/Bu_3SnH$ gave hydrazine products in good yield and good stereospecificity. A non-chelating stereocontrol model is proposed to be involved in the reactions, wherein BF_3 activates the C=N bond toward hydride addition by the stannane, although an intervening hydride exchange has not been excluded. The products of the overall reductive amination process were obtained with complementary, albeit lower, stereoselectivity compared to their preparation by radical addition to aldehyde *N*-acylhydrazones. For synthetic applications, the possibility of resolving the diastereomers before removal of the auxiliary is a distinct advantage. In conjunction with known methods for N–N bond cleavage,[22] reduction of chiral *N*-acylhydrazones offers a complementary alternative to other reductive amination methods.

5. Experimental

5.1. Materials and methods

Reactions employed oven- or flame-dried glassware under nitrogen unless otherwise noted. Tetrahydrofuran (THF) and toluene were distilled from sodium/benzophenone ketyl under argon. Benzene, triethylamine and CH_2Cl_2 were distilled from CaH_2 under argon or nitrogen. Nitrogen was

passed successively through columns of anhydrous $CaSO_4$ and R3-11 catalyst (Schweizer-Hall, South Plainfield, NJ) for removal of water and oxygen, respectively. All other materials were used as received from Aldrich or purified by standard procedures. Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates with UV indicator. Flash chromatography columns were packed with 230–400 mesh silica gel as slurry in the initial elution solvent. Gradient flash chromatography was conducted by adsorption of product mixtures on silica gel, packing over a short pad of clean silica gel as a slurry in hexane, and eluting with a continuous gradient from hexane to the indicated solvent. Radial chromatography refers to centrifugally accelerated thin-layer chromatography performed using a Chromatotron (Harrison Research, Palo Alto CA) with precast rotors supplied by Analtech (Newark, DE). Melting points were determined on a Meltemp apparatus and are uncorrected. Proton and carbon NMR data were obtained with a Bruker ARX 500 spectrometer. Infrared spectra were recorded with a Perkin–Elmer 2000 FT-IR spectrophotometer. Optical rotations were determined using a Rudolph Research Autopol IV polarimeter. Low resolution mass spectra were obtained with a Finnegan 4610 quadrupole spectrometer or a Hewlett Packard 5988 GCMS. Combustion analyses were performed by Atlantic Microlab (Norcross, GA) or Robertson Laboratories (Madison, NJ). Diastereomer ratios were determined by integration of ^{1}H NMR spectra, or by HPLC using a Varian HPLC system equipped with dual ProStar 210 pumps and a ProStar 320 single-wavelength UV detector.

5.1.1. Isobutyrophenone (6a). According to the known method,[10] a suspension of VCl_3 (1.57 g, 10 mmol) in CH_2Cl_2 (20 mL) was added phenylmagnesium bromide (3.3 mL, 3.0 M in diethyl ether, 11 mmol) dropwise at −78°C. After 20 min, isobutyryl chloride (1.05 mL, 10 mmol) was added, and the mixture was allowed to warm slowly to ambient temperature. After ca. 16 h, concentration and gradient flash chromatography (20:1 to 7:1 hexane/EtOAc) afforded **6a** (1.2 g, 82% yield).

5.1.2. Cyclopentyl phenyl ketone (6b). By the procedure described for **6a**, from cyclopentanecarbonyl chloride (1.22 mL, 10 mmol) was obtained **6b** (1.25 g, 72% yield).

5.1.3. 2,2-Dimethyl-1-phenyl-1-propanone (6d). By the procedure described for **6a**, from 2,2-dimethylpropionyl chloride (1.23 mL, 10 mmol) was obtained **6d** (1.4 g, 88% yield).

5.2. Preparation of *N*-acylhydrazones, general procedure A

To a solution of (*S*)-3-amino-4-phenylmethyl-2-oxazolidinone **1**[5] in CH_2Cl_2, toluene or benzene (0.2 M) was added $TsOH{\cdot}H_2O$ (cat.) and ketone (5–10 equiv.) at ambient temperature or reflux temperature of the solvent (if necessary to complete the reaction). When the reaction was complete (TLC) the mixture was concentrated and purified by gradient flash chromatography (hexane to 1:1 hexane/EtOAc) to afford the hydrazone.

5.2.1. 2-Methyl-3-pentanone *N*-acylhydrazone 7a. From **1** (100 mg, 0.52 mmol) and 2-methyl-3-pentanone (0.13 mL, 1.04 mmol) by General Procedure A was obtained **7a** (120 mg, 0.44 mmol, 84% yield, *E*:*Z*=3.4:1 by ^{1}H NMR analysis) as colorless oil. IR (film) 3029, 2935, 2970, 1764, 1631, 1454, 1393, 1354, 1214, 1103, 1067, 1036, 756, 699 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$), *E* isomer δ 7.30 (dd, *J*=7.5, 7.5 Hz, 2H), 7.24 (dd, *J*=7.2, 7.2 Hz, 1H), 7.15 (dd, *J*=7.5, 7.5 Hz, 2H), 4.34–4.20 (m, 2H), 4.02 (dd, *J*=8.3, 8.3 Hz, 1H), 3.16–3.05 (m, 1H), 2.77–2.64 (m, 2H), 2.54–2.44 (m, 1H), 2.41–2.31 (m, 1H), 1.22–1.10 (m, 9H); *Z* isomer δ 7.35–7.10 (m, 5H), 4.34–4.20(m, 2H), 4.06–3.99 (m, 1H), 3.24 (m, apparent sextet, *J*=6.8 Hz, 1H), 3.16–3.05 (m, 1H), 2.77–2.64 (m, 1H), 2.41–2.31 (m, 2H), 1.22–1.10 (m, 6H), 1.06 (d, *J*=7.2 Hz, 3H) (multiplicity for some resonances could not be determined due to overlap with *E* isomer); ^{13}C NMR (125 MHz, $CDCl_3$), *E* isomer δ 184.9, 154.7, 135.8, 129.0, 128.7, 127.0, 66.6, 60.9, 38.4, 34.2, 24.5, 20.7, 20.1, 10.6; *Z* isomer δ 185.3, 155.2, 129.0, 66.8, 38.6, 30.9, 24.0, 19.7, 19.2, 11.1 (some resonances were not reported due to overlap with *E* isomer); MS (CI) *m*/*z* (relative intensity) 275 ([M+H]$^+$, 100%). Anal. calcd for $C_{21}H_{24}N_2O_2$: C, 70.04; H, 8.08; N, 10.21. Found: C, 69.91; H, 8.20; N, 10.23.

5.2.2. 1-Cyclopentyl-1-propanone *N*-acylhydrazone 7b. 1-Cyclopentyl-1-propanone was prepared according to the known method[9] from cyclopentanecarbonyl chloride (1.22 mL, 10 mmol) and tetraethylsilane (1.88 mL, 10 mmol), and $AlCl_3$ (1.33 g, 10 mmol). To a solution of the unpurified 1-cyclopentyl-1-propanone in CH_2Cl_2 (30 mL) was added **1** (150 mg, 0.780 mmol) and $MgSO_4$ (2 g), and the mixture was stirred at ambient temperature for 2 days. Concentration and flash chromatography (3:1 hexanes/ethyl acetate) afforded **7b** (116 mg, 0.387 mmol, 49% yield, *E*:*Z*=3.8:1, ^{1}H NMR analysis) as colorless oil. IR (film) 3063, 3028, 2955, 1759, 1627, 1497, 1454, 1394, 1212, 1072, 1028, 755, 699 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$), *E* isomer δ 7.38–7.22 (m, 3H), 7.15 (d, *J*=7.2 Hz, 2H), 4.35–4.22 (m, 2H), 4.03 (dd, *J*=7.9 Hz, 1H), 3.11 (dd, *J*=13.9, 4.15 Hz, 1H), 2.85 (m, apparent quartet, *J*=7.91 Hz, 1H), 2.73 (dd, *J*=13.9, 9.1 Hz, 1H), 2.53–2.32 (m, 2H), 1.98–1.52 (m, 8H), 1.14 (dd, *J*=7.5, 7.5 Hz, 3H); *Z* isomer δ 7.37–7.11 (m, 5H), 4.36–4.22 (m, 2H), 4.07–3.99 (m, 1H), 3.28 (m, apparent quartet, 9.0 Hz, 1H), 3.15–3.06 (m, 1H), 2.77–2.68 (m, 1H), 2.43–2.30 (m, 2H), 2.08–1.98 (m, 1H), 1.97–1.41 (m, 6H), 1.52–1.42 (m, 1H), 1.19–1.11 (m, 3H) (multiplicity for some resonances could not be determined due to overlap with *E* isomer); ^{13}C NMR (125 MHz, $CDCl_3$), *E* isomer δ 183.5, 154.8, 135.8, 129.0, 128.7, 126.9, 66.6, 60.9, 45.4, 38.4, 30.8, 30.2, 25.5, 25.3 (2C), 10.7; *Z* isomer δ 184.3, 155.2, 135.8, 66.6, 42.2, 38.5, 30.3, 25.9, 25.2, 11.6 (some resonances were not reported due to overlap with *E* isomer); MS (CI) *m*/*z* (relative intensity) 301 ([M+H]$^+$, 100%). Anal. calcd for $C_{18}H_{24}N_2O_2$: C, 71.97; H, 8.05; N, 9.33. Found: C, 71.81; H, 8.05; N, 9.20.

5.2.3. 1-Cyclohexyl-1-propanone *N*-acylhydrazone 7c. 1-Cyclohexyl-1-propanone was prepared according to the known method[9] from cyclohexanecarbonyl chloride (1.34 mL, 10 mmol) and tetraethylsilane (1.88 mL, 10 mmol), and $AlCl_3$ (1.33 g, 10 mmol). To a solution of the unpurified 1-cyclohexyl-1-propanone in CH_2Cl_2

(30 mL) was added **1** (190 mg, 0.989 mmol) and $MgSO_4$ (2 g), and the mixture was stirred at ambient temperature for 2 days. Concentration and flash chromatography (3:1 hexanes/ethyl acetate) afforded **7c** (200 mg, 0.637 mmol, 64% yield, *E*:*Z*=5.6:1, ^{1}H NMR analysis) as a colorless oil. IR (film) 3028, 2930, 2853, 1764, 1628, 1498, 1451, 1394, 1353, 1211, 1075, 1030, 754, 700 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$), *E* isomer δ 7.35–7.27 (m, 2H), 7.27–7.22 (m, 1H), 7.20–7.11 (m, 2H), 4.35–4.20 (m, 2H), 4.03 (dd, *J*=8.7, 8.7 Hz, 1H), 3.11 (dd, *J*=13.6, 4.1 Hz, 1H), 2.72 (dd, *J*=13.6, 8.7 Hz, 1H), 2.51–2.42 (m, 1H), 2.41–2.30 (m, 2H), 2.00–1.78 (m, 10H), 1.12 (dd, *J*=7.5 Hz, 3H); *Z* isomer δ 7.37–7.09 (m, 5H), 4.35–4.22 (m, 2H), 4.05 (dd, *J*=8.7, 8.7 Hz, 1H), 3.15–3.11 (m, 1H), 2.95–2.85 (m, 1H), 2.69 (dd, *J*=13.9, 9.1 Hz, 1H), 2.42–2.32 (m, 2H), 2.00–1.18 (m, 10H), 1.15 (dd, *J*=7.2, 7.2 Hz, 3H) (multiplicity for some resonances could not be determined due to overlap with *E* isomer); ^{13}C NMR (125 MHz, $CDCl_3$), *E* isomer δ 184.5, 154.7, 135.8, 129.0, 128.7, 127.0, 66.6, 60.9, 44.3, 38.4, 31.1, 30.5, 26.2, 26.1, 26.0, 24.7, 10.6; *Z* isomer δ 184.6, 155.2, 66.7, 41.9, 38.6, 29.8, 29.1, 26.0, 25.9, 25.5, 11.1 (some resonances were not reported due to overlap with *E* isomer); MS (CI) *m*/*z* (relative intensity) 315 ([M+H]$^+$, 100%). Anal. calcd for $C_{19}H_{26}N_2O_2$: C, 72.58; H, 8.33; N, 8.91. Found: C, 72.88; H, 8.43; N, 8.83.

5.2.4. 2,2-Dimethyl-3-pentanone *N*-acylhydrazone 7d. From **1** (70 mg, 0.37 mmol) and 2,2-dimethyl-3-pentanone (208 mg, 1.82 mmol) by General Procedure A was obtained **7d** (70 mg, 0.24 mmol, 67% yield, *E*:*Z* >98:2, ^{1}H NMR analysis) as a colorless oil. $[\alpha]_D^{24}=-47.5°$ (*c* 2.5, $CHCl_3$). IR (film) 3029, 2970, 1763, 1625, 1455, 1394, 1352, 1201, 1171, 1081, 1042, 756, 703 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (dd, *J*=7.2, 7.2 Hz, 2H), 7.25 (d, *J*=7.5 Hz, 1H), 7.20 (d, *J*=7.2 Hz, 2H), 4.31–4.21 (m, 2H), 4.09–4.01 (m, 1H), 3.14 (dd, *J*=13.6, 4.2 Hz, 1H), 2.73 (dd, *J*=13.6, 8.3 Hz, 1H), 2.59–2.49 (m, 1H), 2.45–2.35 (m, 1H), 1.20 (s, 9H), 1.13 (dd, *J*=7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 187.1, 154.6, 136.0, 128.9, 128.7, 127.0, 66.8, 61.3, 39.9, 38.4, 28.0, 22.3, 11.4; MS (CI) *m*/*z* (relative intensity) 289 ([M+H]$^+$, 100%). Anal. calcd for $C_{17}H_{24}N_2O_2$: C, 70.80; H, 8.39; N, 9.71. Found: C, 70.81; H, 8.54; N, 9.56.

5.2.5. Isobutyrophenone *N*-acylhydrazone 8a. From **1** (150 mg, 0.780 mmol) and isobutyrophenone (1.15 g, 7.80 mmol) by General Procedure A was obtained **8a** (136 mg, 0.422 mmol, 54% yield, *Z*:*E*=4.3:1, ^{1}H NMR analysis) as a colorless oil. IR (film) 3061, 3028, 2931, 2969, 2873, 1765, 1604, 1443, 1392, 1351, 1213, 1029, 701 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$), *Z* isomer δ 7.45–7.21 (m, 8H), 7.10 (d, *J*=7.2 Hz, 2H), 4.00–3.92 (m, 1H), 4.01 (dd, *J*=7.9, 7.9 Hz, 1H), 3.84 (dd, *J*=7.9, 6.4 Hz, 1H), 3.10 (dd, *J*=13.6, 4.1 Hz, 1H), 2.99 (m, apparent septet, *J*=6.8 Hz, 1H), 2.58 (dd, *J*=13.6, 9.0 Hz, 1H), 1.20 (dd, *J*=8.7, 7.2 Hz, 6H); *E* isomer δ 7.46–7.06 (m, 10H), 4.48–4.39 (m 1H), 4.30 (dd, *J*=7.5, 7.5 Hz, 1H), 4.10 (dd, *J*=8.7, 8.7 Hz, 1H), 3.52 (m, apparent septet, *J*=6.8 Hz, 1H), 3.22 (dd, *J*=13.6, 4.9 Hz, 1H), 2.79 (dd, *J*=13.6, 9.4 Hz, 1H), 1.25 (d, *J*=6.8 Hz, 3H), 1.15 (d, *J*=7.2 Hz, 3H) (multiplicity for some resonances could not be determined due to overlap with *Z* isomer); ^{13}C NMR (125 MHz, $CDCl_3$), *Z* isomer δ 180.4, 155.1, 136.7, 135.7, 129.0, 128.8, 128.7, 128.1, 127.1, 126.7, 66.0, 59.8, 37.4, 37.4, 20.4, 20.1; *E* isomer δ 67.0, 61.2, 39.0, 31.3, 20.2, 19.6 (some resonances were not reported due to overlap with *Z* isomer); MS (CI) *m*/*z* (relative intensity) 323 ([M+H]$^+$, 100%). Anal. calcd for $C_{20}H_{22}N_2O_2$: C, 74.51; H, 6.88; N, 8.69. Found: C, 74.68; H, 6.90; N, 8.62.

5.2.6. Cyclopentyl phenyl ketone *N*-acylhydrazone 8b. From **1** (70 mg, 0.365 mmol) and cyclopentyl phenyl ketone (190 mg, 1.09 mmol) by General Procedure A was obtained **8b** (78 mg, 0.224 mmol, 59% yield, *Z*:*E*=2.9:1, ^{1}H NMR analysis) as a colorless oil. IR (film) 3027, 2955, 2869, 1764, 1603, 1454, 1392, 1213, 1086, 1029, 699 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6), *Z* isomer δ 7.38–7.34 (m, 2H), 7.29–7.00 (m, 6H), 6.80 (d, *J*=6.8 Hz, 2H), 3.85–3.75 (m, 1H), 3.38 (dd, *J*=8.7, 7.5 Hz, 1H), 3.26 (dd, *J*=8.7, 8.7 Hz, 1H), 3.01 (dddd, apparent quintet, *J*=7.9 Hz, 1H), 2.95 (dd, *J*=13.2, 4.9 Hz, 1H), 2.33 (dd, *J*=13.2, 9.4 Hz, 1H), 2.10–1.40 (m, 8H); *E* isomer δ 7.54–7.50 (m, 2H), 7.41–7.00 (m, 6H), 6.85 (d, *J*=7.9 Hz, 2H), 4.08–4.00 (m, 1H), 3.65–3.53 (m, 2H), 2.91 (dd, *J*=4.5, 3.6 Hz, 1H), 2.50 (dd, *J*=13.9, 8.7 Hz, 1H), 2.43–2.33 (m, 1H), 2.10–1.40 (m, 8H) (multiplicity for some resonances could not be determined due to overlap with *Z* isomer); ^{13}C NMR (125 MHz, $CDCl_3$), *Z* isomer δ 178.8, 155.1, 137.4, 135.7, 129.0, 128.8, 128.6, 128.1, 127.0, 126.5, 66.0, 59.8, 48.5, 37.5, 30.7, 30.3, 25.1 (2C); *E* isomer δ 181.7, 155.0, 136.8, 135.6, 129.1, 128.6, 127.9, 66.9, 61.2, 42.5, 38.8, 30.6, 30.5, 25.6, 25.6 (some resonances were not reported due to overlap with *Z* isomer); ^{13}C NMR (125 MHz, C_6D_6), *Z* isomer δ 179.2, 155.0, 138.6, 136.4, 129.5, 129.2, 128.8, 127.1, 127.0, 65.9, 60.6, 48.9, 38.3, 30.9, 30.8, 25.4 (2C) (one resonance was overlap with solvent peaks); *E* isomer δ 179.7, 155.1, 137.8, 136.3, 66.3, 61.4, 42.9, 38.8, 26.02, 25.95 (some resonances were not reported due to overlap with *Z* isomer); MS (CI) *m*/*z* (relative intensity) 349 ([M+H]$^+$, 100%). Anal. calcd for $C_{22}H_{24}N_2O_2$: C, 75.83; H, 6.94; N, 8.04. Found: C, 75.67; H, 6.74; N, 7.68.

5.2.7. Cyclohexyl phenyl ketone *N*-acylhydrazone 8c. From **1** (120 mg, 0.625 mmol) and cyclohexyl phenyl ketone (235 mg, 1.25 mmol) by General Procedure A was obtained **8c** (125 mg, 0.345 mmol, 55% yield, *Z*:*E*=6.5:1, ^{1}H NMR analysis) as a colorless oil. IR (film) 3061, 3028, 2929, 2853, 1764, 1621, 1496, 1444, 1392, 1213, 1086, 1029, 755, 699 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6), *Z* isomer δ 7.34 (d, *J*=8.3 Hz, 2H), 7.27–7.01 (m, 6H), 6.83 (d, *J*=6.8 Hz, 2H), 3.86–3.76 (m, 1H), 3.39 (dd, *J*=8.3, 8.3 Hz, 1H), 3.28 (dd, *J*=8.3, 8.3 Hz, 1H), 2.95 (dd, *J*=13.9, 4.5 Hz, 1H), 2.62 (m, *J*=11.3, 3.4 Hz, 1H), 2.36 (dd, *J*=13.6, 9.4 Hz, 1H), 2.08–1.99 (m, 1H), 1.97–1.88 (m, 1H), 1.78–1.65 (m, 2H), 1.62–1.52 (m, 2H), 1.25–1.08 (m, 3H), 0.32 (s, 1H); *E* isomer δ 7.50–7.44 (m, 2H), 7.42–6.75 (m, 8H), 4.11–4.00 (m, 1H), 3.64–3.53 (m, 2H), 3.49–3.42 (m, 1H), 3.00–2.91 (m, 1H), 2.52 (dd, *J*=13.6, 9.0 Hz, 1H), 2.47–2.42 (m, 1H), 1.88–1.83 (m, 1H), 1.82–0.90 (m, 8H) (multiplicity for some resonances could not be determined due to overlap with *Z* isomer); ^{13}C NMR (125 MHz, C_6D_6), *Z* isomer δ 179.8, 154.7, 137.7, 136.1, 128.9, 128.5, 128.2, 126.9, 126.7, 65.6, 60.2, 47.0, 37.8, 30.6, 30.5, 26.1, 26.0 (2C) (one resonance was overlap with solvent peaks); *E* isomer δ 180.3, 154.9, 138.0, 136.0, 129.1, 128.3, 66.1, 61.2, 42.7, 38.5, 30.2, 29.6, 26.2, 25.8 (some resonances

were not reported due to overlap with *Z* isomer); MS (CI) *m/z* (relative intensity) 363 ([M+H]$^+$, 100%). Anal. calcd for $C_{23}H_{26}N_2O_2$: C, 76.21; H, 7.23; N, 7.73. Found: C, 75.93; H, 7.24; N, 7.56.

5.2.8. 2,2-Dimethyl-1-phenyl-1-propanone *N*-acylhydrazone 8d. From **1** (95 mg, 0.49 mmol) and 2,2-dimethyl-1-phenyl-1-propanone (160 mg, 1.0 mmol) by General Procedure A was obtained **8d** (120 mg, 0.36 mmol, 73% yield, *Z*:*E* > 98:2, ^{1}H NMR analysis) as a colorless oil. $[\alpha]_D^{23}=-132.5°$ (*c* 2.0, $CHCl_3$). IR (film) 3062, 3029, 2931, 2972, 2868, 1765, 1617, 1442, 1394, 1359, 1214, 1200, 1077, 1030, 753, 702 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41–7.10 (m, 10H), 3.88–3.78 (m, 1H), 3.33 (dd, *J*=8.3, 8.3 Hz, 1H), 3.15 (dd, *J*=8.7, 8.7 Hz, 1H), 2.91 (dd, *J*=13.6, 4.52 Hz, 1H), 2.30 (dd, *J*=13.6, 9.42 Hz, 1H), 1.25 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 185.2, 154.8, 136.2, 135.8, 128.9, 128.8, 128.0, 127.4, 127.1, 127.0, 66.2, 60.1, 39.6, 37.8, 28.5; ^{13}C NMR (125 MHz, C_6D_6) δ 184.8, 154.6, 136.7, 136.2, 128.8, 128.5, 127.2, 126.7, 65.7, 60.4, 39.3, 38.2, 28.3; MS (CI) *m/z* (relative intensity) 337 ([M+H]$^+$, 100%). Anal. calcd for $C_{21}H_{24}N_2O_2$: C, 74.97; H, 7.19; N, 8.33. Found: C, 74.79; H, 7.20; N, 8.30.

5.3. Reduction of *N*-acylhydrazones, general procedure B

In a solution of the *N*-acylhydrazone in CH_2Cl_2 (ca. 0.1 M) was added $BF_3{\cdot}OEt_2$ (1.5–2 equiv.) at −78°C and stirred for 15 min. Then Bu_3SnH (1.5–2.5 equiv.) was added and the reaction mixture was allowed to warm up to room temperature. Stannanes were removed by dilution with EtOAc, stirring overnight with excess KF, and filtration through a short pad of silica gel. Concentration and gradient flash chromatography (hexane to 3:1 hexane/EtOAc) afforded *N*-acylhydrazine **3** and *N*-acylhydrazines **9a**–**9d** and **10a**–**10d** as mixtures of diastereomers. Diastereomer ratios were determined by HPLC (**9**) or a combination of GCMS and ^{1}H NMR (**10**). Major isomers of *N*-acylhydrazines **10** were separated from the diastereomeric mixtures by radial chromatography for full characterization, but *N*-acylhydrazines **9** required characterization within the diastereomeric mixture. Characterization data for the minor diastereomers (obtained through a different method) have been reported previously.[3]

5.3.1. (*S*)-3-(1′-Propylamino)-4-phenylmethyl-2-oxazolidinone (3). Reduction of aldehyde *N*-acylhydrazone **2**[3] (71 mg, 0.31 mmol) by General Procedure B gave **3** (73 mg, 0.31 mmol, 100% yield) as a colorless oil; $[\alpha]_D^{23}=+42.6°$ (*c* 0.15, $CHCl_3$). IR (film) 3293, 3028, 2961, 1757, 1604, 1497, 1402, 1093 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (dddd, *J*=7.0, 7.0, 1.1, 1.1 Hz, 2H), 7.24 (dddd, *J*=7.3, 7.3, 1.2, 1.2 Hz, 1H), 7.15 (ddd, *J*=6.8, 1.4, 1.4 Hz, 2H), 4.13 (dd, *J*=8.6, 7.7 Hz, 1H), 4.02–3.97 (m, 2H), 3.96–3.90 (m, 1H), 3.30 (dd, *J*=13.6, 3.7 Hz, 1H), 3.00–2.93 (m, 1H), 2.91–2.85 (m, 1H), 2.64 (dd, *J*=13.5, 9.7 Hz, 1H), 1.53 (m, apparent sextet, *J*=7.3 Hz, 2H), 0.97 (dd, *J*=7.4, 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.4, 135.9, 129.0, 128.9, 127.0, 66.2, 58.9, 52.7, 37.7, 21.3, 11.4; MS (CI) *m/z* (relative intensity) 235 ([M+H]$^+$, 100%). Anal. calcd for $C_{13}H_{18}N_2O_2$: C, 66.64; H, 7.74; N, 11.96. Found: C, 66.39; H, 7.72; N, 11.75.

5.3.2. (4*S*,3′*S*)-3-(2′-Methyl-3′-pentylamino)-4-phenylmethyl-2-oxazolidinone [(*S*,*S*)-9a]. Reduction of **7a** by General Procedure B (39 mg, 0.142 mmol) gave diastereomeric mixture **9a** (35 mg, 0.127 mmol, 89% yield, (*S*,*S*):(*S*,*R*)=4.0:1) as a colorless oil. (*S*,*S*)-**9a**: HPLC retention time 11.8 min, Si C8 MICROSORB-MV™ 100 Å column, gradient elution (hexane to ^{i}PrOH/hexane 1:9, 0–20 min); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (dd, *J*=7.1, 7.1 Hz, 2H), 7.25 (dd, *J*=7.4, 7.4 Hz, 1H), 7.16 (dd, *J*=7.1, 1.4 Hz, 2H), 4.13 (dd, *J*=8.2, 8.2 Hz, 1H), 4.05–4.00 (m, 2H), 3.92–3.87 (m, 1H), 3.36 (dd, *J*=13.4, 3.5 Hz, 1H), 2.82–2.77 (m, 1H), 2.61 (dd, *J*=13.4, 10.1 Hz, 1H), 1.93–1.83 (m, 1H), 1.54–1.46 (m, 1H), 1.39–1.31 (m, 1H), 1.04 (dd, *J*=7.5, 7.5 Hz, 3H), 0.99 (d, *J*=6.9 Hz, 3H), 0.94 (d, *J*=6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.4, 136.1, 129.1, 128.9, 127.0, 66.2, 65.5, 59.7, 36.8, 28.6, 20.8, 18.5, 16.9, 10.9. Diastereomer mixture **9a**: IR (film) 3304, 3028, 2961, 2874, 1758, 1604, 1498, 1454, 1397, 1238, 1089, 1029, 743, 702 cm^{-1}; MS (CI) *m/z* (relative intensity) 277 ([M+H]$^+$, 100%), 193(58%). Anal. calcd for $C_{16}H_{24}N_2O_2$: C, 69.53; H, 8.75; N, 10.14. Found: C, 69.52; H, 8.78; N, 9.98.

5.3.3. (4*S*,1′*S*)-3-(1′-Cyclopentyl-1′-propylamino)-4-phenylmethyl-2-oxazolidinone [(*S*,*S*)-9b]. Reduction of **7b** by General Procedure B (57 mg, 0.19 mmol) gave diastereomeric mixture **9b** (47 mg, 0.156 mmol, 82% yield, (*S*,*S*):(*S*,*R*)=3.1:1) as a colorless oil. (*S*,*S*)-**9b**: HPLC retention time 10.2 min, Chiralcel OD 250×0.46 mm (L×I.D.) column, ^{i}PrOH/hexane 1:9; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (dd, *J*=7.2, 7.2 Hz, 2H), 7.26 (dd, *J*=7.2, 7.2 Hz, 1H), 7.16 (d, *J*=7.1 Hz, 2H), 4.12 (dd, *J*=8.7, 8.7 Hz, 1H), 4.04–4.00 (m, 2H), 3.93–3.88 (m, 1H), 3.34 (dd, *J*=13.4, 3.6 Hz, 1H), 2.86 (m, apparent quintet, *J*=4.6 Hz, 1H), 2.62 (dd, *J*=13.4, 10.0 Hz, 1H), 1.99 (m, apparent sextet, *J*=7.9 Hz, 1H), 1.86–1.80 (br m, 1H), 1.79–1.72 (br m, 1H), 1.69–1.44 (br m, 6H), 1.37–1.24 (br m, 2H), 1.00 (dd, *J*=7.4, 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.7, 136.1, 129.1, 128.9, 127.1, 65.9, 64.1, 59.0, 41.2, 37.0, 29.3, 29.1, 25.6 (2C), 23.0, 9.3. Diastereomer mixture **9b**: IR (film) 3299, 3062, 3027, 2954, 2868, 1759, 1604, 1497, 1454, 1397, 1362, 1237, 1089, 1029, 912, 744, 702 cm^{-1}; MS (CI) *m/z* (relative intensity) 303 ([M+H]$^+$, 84%), 193 (100%). Anal. calcd for $C_{18}H_{26}N_2O_2$: C, 71.47; H, 8.67; N, 9.26. Found: C, 71.73; H, 8.67; N, 9.17.

5.3.4. (4*S*,1′*S*)-3-(1′-Cyclohexyl-1′-propylamino)-4-phenylmethyl-2-oxazolidinone [(*S*,*S*)-9c]. Reduction of **7c** by General Procedure B (92 mg, 0.290 mmol) gave diastereomeric mixture **9c** (70 mg, 0.222 mmol, 76% yield, (*S*,*S*):(*S*,*R*)=5.6:1) as a colorless oil. (*S*,*S*)-**9c**: HPLC retention time 9.1 min, Chiralcel OD 250×0.46 mm (L×I.D.) column, ^{i}PrOH/hexane 1:9; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (m, 2H), 7.26–7.23 (m, 1H), 7.15 (m, 2H), 4.13 (m, apparent quartet, *J*=8.6 Hz, 1H), 4.03 (dd, *J*=8.9, 4.4 Hz, 1H), 3.99 (d, *J*=4.1 Hz, 1H), 3.90–3.84 (m, 1H), 3.35 (dd, *J*=13.2, 3.2 Hz, 1H), 2.78–2.71 (m,1H), 2.60 (dd, *J*=13.4, 9.8 Hz, 1H), 1.85–1.78 (m, 3H), 1.72–1.64 (m, 2H), 1.56–1.44 (m, 2H), 1.42–1.32 (m, 1H), 1.28–1.06 (m, 5H), 1.02 (dd, *J*=7.4, 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.4, 136.2, 129.1, 128.9, 127.0, 65.8, 65.6, 59.7, 39.5, 36.9, 29.2, 27.9, 26.8, 26.7 (2C), 21.5, 10.9. Diastereomer mixture **9c**: IR (film) 3303, 3063, 3027,

2926, 2852, 1759, 1604, 1497, 1452, 1398, 1363, 1238, 1198, 1088, 1029, 958, 743, 702 cm^{-1}; MS (CI) *m/z* (relative intensity) 317 ($[M+H]^+$, 100%), 193 (39%). Anal. calcd for $C_{19}H_{28}N_2O_2$: C, 72.12; H, 8.92; N, 8.85. Found: C, 72.27; H, 9.00; N, 8.82.

5.3.5. (4*S*,3′*S*)-3-(2′,2′-Dimethyl-3′-pentylamino)-4-phenylmethyl-2-oxazolidinone [(*S*,*S*)-9d]. Reduction of **7d** by General Procedure B (55 mg, 0.191 mmol) gave diastereomeric mixture **9d** (52 mg, 0.179 mmol, 94% yield, (*S*,*S*):(*S*,*R*)=7.8:1) as a colorless oil. (*S*,*S*)-**9d**: HPLC retention time 8.3 min, Chiralcel OD 250×0.46 mm (L×I.D.) column, ^{i}PrOH/hexane 1:9; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (dd *J*=7.6, 7.6 Hz, 2H), 7.25 (dd, *J*=7.3, 7.3 Hz, 1H), 7.16 (d, *J*=6.9 Hz, 2H), 4.15–4.02 (m, 2H), 3.96–3.91 (m, 2H), 3.35 (dd, *J*=13.4, 3.3 Hz, 1H), 2.60 (dd, *J*=13.5, 10.0 Hz, 1H), 2.54–2.51 (m, 1H), 1.75–1.67 (m, 1H), 1.46–1.37 (m, 1H), 1.09 (dd, *J*=7.6, 7.6 Hz, 3H), 0.99 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.4, 136.1, 129.1, 128.9, 127.0, 70.1, 65.2, 58.6, 36.1, 34.5, 27.0, 23.4, 13.4. Diastereomer mixture **9d**: IR (film) 3308, 3063, 3028, 2959, 2873, 1758, 1604, 1498, 1478, 1394, 1237, 1216, 930, 745, 702 cm^{-1}; MS (CI) *m/z* (relative intensity) 291 ($[M+H]^+$, 77%), 193 (100%). Anal. calcd for $C_{17}H_{26}N_2O_2$: C, 70.31; H, 9.02; N, 9.65. Found: C, 70.38; H, 9.00; N, 9.62.

5.3.6. (4*S*,1′*R*)-3-(2′-Methyl-1′-phenyl-1′-propylamino)-4-phenylmethyl-2-oxazolidinone [(*S*,*R*)-10a]. Reduction of **8a** by General Procedure B (13 mg, 0.040 mmol) gave diastereomeric mixture **10a** (12 mg, 0.037 mmol, 92% yield, (*S*,*R*):(*S*,*S*)=4.2:1). Radial chromatography afforded (*S*,*R*)-**10a** as a colorless solid. (*S*,*R*)-**10a**: GCMS retention time 6.9 min, 15 m×0.25 mm×0.25 μ (L×I.D.×F.T.) 5%-phenyl-95%-dimethylsiloxane column, Helium; mp 110–112°C; $[\alpha]_D^{26}$=+32.0° (*c* 0.45, $CHCl_3$). IR (film) 3311, 3289, 3084, 3062, 2959, 2869, 1778, 1603, 1491, 1453, 1388, 1292, 1029, 948, 762, 742, 703 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35–7.20 (m, 8H), 7.04 (d, *J*=7.4 Hz, 2H), 4.38 (d, *J*=1.9 Hz, 1H), 3.98 (dd, *J*=8.0, 8.0 Hz, 1H), 3.93 (dd, *J*=6.7, 2.4 Hz, 1H), 3.87–3.80 (m, 2H), 3.01 (dd, *J*=13.9, 3.5 Hz, 1H), 2.12–2.01 (m, 2H), 1.00 (d, *J*=6.6 Hz, 3H), 0.79 (d, *J*=6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.7, 139.7, 136.1, 129.0, 128.9 (2C), 127.9, 127.6, 127.0, 69.6, 66.3, 59.0, 37.4, 31.2, 19.9, 18.4; MS (CI) *m/z* (relative intensity) 325 ($[M+H]^+$, 15%), 193 (100%). Anal. calcd for $C_{20}H_{24}N_2O_2$: C, 74.04; H, 7.46; N, 8.63. Found: C, 73.75; H, 7.48; N, 8.38.

5.3.7. (4*S*,1′*R*)-3-(1′-Cyclopentyl-1′-phenylmethylamino)-4-phenylmethyl-2-oxazolidinone [(*S*,*R*)-10b]. Reduction of **8b** by General Procedure B (27 mg, 0.077 mmol) gave diastereomeric mixture **10b** (21 mg, 0.060 mmol, 78% yield, (*S*,*R*):(*S*,*S*)=2.9:1). Radial chromatography gave (*S*,*R*)-**10b** as a colorless solid. (*S*,*R*)-**10b**: GCMS retention time 5.9 min, 15 m×0.25 mm×0.25 μ (L×I.D.×F.T.) 5%-phenyl-95%-dimethylsiloxane column, Helium; mp 105–107°C; $[\alpha]_D^{26}$=+50.1° (*c* 0.3, $CHCl_3$). IR (film) 3290, 3061, 3028, 2953, 2867, 1758, 1603, 1496, 1398, 1219, 1086, 956, 913, 761, 744, 701 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (ddd, *J*=6.9, 1.5, 1.5 Hz, 2H), 7.29 (dddd, *J*=7.1, 7.1, 1.5, 1.5 Hz, 2H), 7.23 (dddd, *J*=7.4, 7.4, 1.5, 1.5 Hz, 3H), 7.18 (dddd, *J*=7.2, 7.2, 1.4, 1.4 Hz, 1H), 6.95 (ddd, *J*=6.9, 1.4, 1.4 Hz, 2H), 4.44 (d, *J*=2.2 Hz, 1H), 3.92–3.90 (m, 2H), 3.75–3.70 (m, 2H), 2.77 (dd, *J*=13.6, 3.1 Hz, 1H), 2.24 (m, apparent sextet, *J*=9.3 Hz, 1H), 2.02–1.94 (m, 1H), 1.74–1.66 (m, 2H), 1.64–1.49 (m, 3H), 1.47–1.40 (m, 1H), 1.39–1.31 (m, 1H), 1.09–1.01 (m 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.4, 141.7, 136.2, 129.0, 128.8, 128.7, 128.1, 127.7, 126.9, 69.4, 66.8, 59.1, 43.9, 37.6, 30.6, 30.3, 25.7, 24.9; MS (CI) *m/z* (relative intensity) 351 ($[M+H]^+$, 37%), 350 (M, 46%), 193 (100%); HRMS (FAB^+) calcd for $C_{22}H_{26}N_2O_2Li$: 357.2154. Found: 357.2119.

5.3.8. (4*S*,1′*R*)-3-(1′-Cyclohexyl-1′-phenylmethylamino)-4-phenylmethyl-2-oxazolidinone [(*S*,*R*)-10c]. Reduction of **8c** by General Procedure B (20 mg, 0.055 mmol) gave diastereomeric mixture **10c** (19 mg, 0.052 mmol, 94% yield, (*S*,*R*):(*S*,*S*)=4.7:1). Radial chromatography gave (*S*,*R*)-**10c** as a colorless solid. (*S*,*R*)-**10c**: GCMS retention time 10.1 min, 15 m×0.25 mm×0.25 μ (L×I.D.×F.T.) 5%-phenyl-95%-dimethylsiloxane column, Helium; mp 103–104°C; $[\alpha]_D^{26}$=+26.9° (*c* 0.95, $CHCl_3$). IR (film) 3503, 3321, 3062, 2928, 1767, 1603, 1496, 1453, 1367, 1214, 1029, 954, 841, 755, 701 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33–7.21 (m, 8H), 7.05 (d, *J*=7.1 Hz, 2H), 4.43 (d, *J*=2.6 Hz, 1H), 3.99–3.95 (m, 2H), 3.86–3.81 (m, 2H), 3.01 (dd, *J*=13.9, 3.8 Hz, 1H), 2.10–2.04 (m, 1H), 1.93 (d, *J*=12.7 Hz, 1H), 1.78 (d, *J*=13.3 Hz, 1H), 1.75–1.62 (m, 3H), 1.56 (d, *J*=11.0 Hz, 1H), 1.32–1.23 (m, 1H), 1.20–1.00 (m, 3H), 0.89–0.80 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.7, 140.1, 136.2, 128.9 (2C), 128.8, 127.9, 127.6, 127.0, 68.9, 66.3, 58.9, 41.3, 37.5, 30.5, 28.9, 26.4, 26.2, 26.1; MS (CI) *m/z* (relative intensity) 365 ($[M+H]^+$, 18%), 193 (100%). Anal. calcd for $C_{23}H_{28}N_2O_2$: C, 75.79; H, 7.74; N, 7.69. Found: C, 75.63; H, 7.87; N, 7.66.

5.3.9. (4*S*,1′*R*)-3-(2′,2′-Dimethyl-1′-phenyl-1′-propylamino)-4-phenylmethyl-2-oxazolidinone [(*S*,*R*)-10d]. Reduction of **8d** by General Procedure B (20 mg, 0.060 mmol) gave diastereomeric mixture **10d** (19 mg, 0.057 mmol, 94% yield, (*S*,*R*):(*S*,*S*)=7.4:1). Radial chromatography gave (*S*,*R*)-**10d** as a colorless solid. (*S*,*R*)-**10d**: GCMS retention time 6.7 min, 15 m×0.25 mm×0.25 μ (L×I.D.×F.T.) 5%-phenyl-95%-dimethylsiloxane column, Helium; mp 129–131°C; $[\alpha]_D^{26}$=+61.3° (*c* 0.5, $CHCl_3$). IR (film) 3325, 3062, 3025, 2972, 2957, 1760, 1492, 1478, 1399, 1296, 1204, 1101, 962, 876, 742, 702 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (d, *J*=6.8 Hz, 2H), 7.29 (dd, *J*=6.9, 6.9 Hz, 4H), 7.26–7.22 (m, 2H), 7.08 (d, *J*=7.4 Hz, 2H), 4.45 (d, *J*=3.6 Hz, 1H), 3.88–3.78 (m, 4H), 3.05 (dd, *J*=13.3, 3.3 Hz, 1H), 2.19 (dd, *J*=13.6, 8.8 Hz, 1H), 0.97 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.5, 139.4, 136.2, 129.6, 128.9 (2C), 127.5 (2C), 127.0, 72.5, 66.2, 57.5, 37.8, 34.4, 27.2; MS (CI) *m/z* (relative intensity) 339 ($[M+H]^+$, 19%), 193 (100%). Anal. calcd for $C_{21}H_{26}N_2O_2$: C, 74.52; H, 7.74; N, 8.28. Found: C, 74.35; H, 7.87; N, 8.32.

Acknowledgements

We thank NIGMS (RO1 GM67187-01) and NSF Vermont EPSCoR (Graduate Research Fellowship to J. Q.) for generous support.

References

1. Review: (a) Martens, J. *Methods of Organic Chemistry (Houben-Weyl)*; Helmchen, G., Ed.; Thieme: New York, 1995; Vol. E21d, pp 4199–4238. For recent examples using various chiral auxiliaries, see: (b) *N*-sulfinylimines: Kochi, T.; Tang, T. P.; Ellman, J. A. *J. Am. Chem. Soc.* **2002**, *124*, 6518–6519. 1-arylethylamines: (c) Cayuela, E. M.; Xiao, L.; Sturm, T.; Manzano, B. R.; Jalon, F. A.; Weissensteiner, W. *Tetrahedron: Asymmetry* **2000**, *11*, 861–869. (d) Roland, S.; Mangeney, P. *Eur. J. Org. Chem.* **2000**, 611–616. phenylglycinol: (e) Stalker, R. A.; Munsch, T. E.; Tran, J. D.; Nie, X. P.; Warmuth, R.; Beatty, A.; Aakeroy, C. B. *Tetrahedron* **2002**, *58*, 4837–4849.
2. Reviews: (a) Spindler, F.; Blaser, H.-U. *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Berlin, 1999; Vol. 1, p 248. (b) Kobayashi, S.; Ishitani, H. *Chem. Rev.* **1999**, *99*, 1069–1094. (c) Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; Wiley: New York, 1994. Selected recent examples: (d) Mao, J. M.; Baker, D. C. *Org. Lett.* **1999**, *1*, 841–843. (e) Hansen, M. C.; Buchwald, S. L. *Org. Lett.* **2000**, *2*, 713–715. (f) Abe, H.; Amii, H.; Unemaya, K. *Org. Lett.* **2001**, *3*, 313–315. (g) Xiao, D.; Zhang, X. *Angew. Chem. Int. Ed.* **2001**, *40*, 3425–3428. (h) Takei, I.; Nishibayashi, Y.; Ishii, Y.; Mizobe, Y.; Uemura, S.; Hidai, M. *Chem. Commun.* **2001**, 2360–2361. (i) Xie, Y. N.; Mi, A. Q.; Jiang, Y. Z.; Liu, H. *Synth. Commun.* **2001**, *31*, 2767–2771. (j) Blaser, H.-U. *Adv. Synth. Catal.* **2002**, *344*, 17–31. (k) Chen, Y. C.; Wu, T. F.; Deng, J. G.; Liu, H.; Cui, X.; Zhu, J.; Jiang, Y. Z.; Choi, M. C. K.; Chan, A. S. C. *J. Org. Chem.* **2002**, *67*, 5301–5306. (l) Jiang, X. B.; Minnaard, A. J.; Hessen, B.; Feringa, B. L.; Duchateau, A. L. L.; Andrien, J. G. O.; Boogers, J. A. F.; de Vries, J. G. *Org. Lett.* **2003**, *5*, 1503–1506.
3. Friestad, G. K.; Qin, J. *J. Am. Chem. Soc.* **2000**, *122*, 8329–8330.
4. (a) Ueda, M.; Miyabe, H.; Namba, M.; Nakabayashi, T.; Naito, T. *Tetrahedron Lett.* **2002**, *43*, 4369–4371. For related reactions, see: (b) Apodaca, R.; Xiao, W. *Org. Lett.* **2001**, *3*, 1745–1748. (c) Blackwell, J. M.; Sonmor, E. R.; Scoccitti, T.; Piers, W. E. *Org. Lett.* **2000**, *2*, 3921–3923. (d) Suwa, T.; Shibata, I.; Nishino, K.; Baba, A. *Org. Lett.* **1999**, *1*, 1579–1581.
5. Synthesis of oxazolidinone-derived *N*-acylhydrazones: Shen, Y.; Friestad, G. K. *J. Org. Chem.* **2002**, *67*, 6236–6239.
6. Friestad, G. K.; Ding, H. *Angew. Chem. Int. Ed.* **2001**, *40*, 4491–4493.
7. Friestad, G. K.; Qin, J. *J. Am. Chem. Soc.* **2001**, *123*, 9922–9923.
8. Dieter, R. K. *Tetrahedron* **1999**, *55*, 4177–4236.
9. Olah, G. A.; Ho, T.-L.; Prakash, G. K. S.; Gupta, B. *Synthesis* **1977**, 677–678.
10. Hirao, T.; Misu, D.; Yao, K.; Agawa, T. *Tetrahedron Lett.* **1986**, *27*, 929–932.
11. (a) Levy, G. C.; Nelson, G. L. *J. Am. Chem. Soc.* **1972**, *94*, 4897–4901. (b) Hawkes, G. E.; Herwig, K.; Roberts, J. D. *J. Org. Chem.* **1974**, *39*, 1017–1028. (c) Györgydeák, Z.; Holzer, W. *Heterocycles* **1998**, *48*, 1395–1406. (d) Burk, M. J.; Martinez, J. P.; Feaster, J. E.; Cosford, N. *Tetrahedron* **1994**, *50*, 4399–4428.
12. (a) Grant, D. M.; Cheney, B. V. *J. Am. Chem. Soc.* **1967**, *89*, 5315. (b) Dalling, D. K.; Grant, D. M. *J. Am. Chem. Soc.* **1967**, *89*, 6612. (c) Grutzner, J. B.; Jautelat, M.; Dence, J. B.; Smith, R. A.; Roberts, J. D. *J. Am. Chem. Soc.* **1970**, *92*, 7107.
13. (a) Bednarski, M. D.; Lyssikatos, J. P. *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 2, p 661. (b) Yamaguchi, M. *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 1, p 325.
14. (a) Santelli, M.; Pons, J.-M. *Lewis Acids and Selectivity in Organic Synthesis*; CRC: Boca Raton, 1995. (b) Guryanova, E. N.; Goldshtein, I. P.; Romm, I. P. *Donor–Acceptor Bond*; Wiley: New York, 1975. (c) Reetz, M. T. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 556.
15. (a) For some examples of BF_2^+ chelates formed from $BF_3{\cdot}OEt_2$, see: Plazuk, D.; Klys, A.; Zakrzewski, J.; Rybarczyk-Pirek, A.; Olszak, T. A. *Organometallics* **2001**, *20*, 4448–4450. (b) Borle, F.; Fehr, F.; Nesvadba, P.; Gossauer, A. *Photochem. Photobiol.* **1997**, *65*, 949–956. (c) Five-membered BF_2^+ chelates form more readily than six-membered: Hartman, J. S.; Shoemaker, J. A. W. *Can. J. Chem.* **2001**, *79*, 426–436.
16. Ground-state pentacoordinate boron intermediates have generated some controversy. (a) Maruyama, K.; Ishihara, Y.; Yamamoto, Y. *Tetrahedron Lett.* **1981**, *22*, 4235–4238. (b) Reetz, M. T.; Kesseler, K.; Jung, A. *Tetrahedron Lett.* **1984**, *25*, 729–732. (c) Lee, D. Y.; Martin, J. C. *J. Am. Chem. Soc.* **1984**, *106*, 5745–5746. (d) Ooi, T.; Uraguchi, D.; Kagoshima, N.; Maruoka, K. *J. Am. Chem. Soc.* **1998**, *120*, 5327–5328. (e) Maruoka, K.; Ooi, T. *Chem. Eur. J.* **1999**, *5*, 829–833. (f) Blackwell, J. M.; Piers, W. E.; Parvez, M. *Org. Lett.* **2000**, *2*, 695–698. (g) Blackwell, J. M.; Piers, W. E.; McDonald, R. *J. Am. Chem. Soc.* **2002**, *124*, 1295–1306. (h) Aubrecht, K. B.; Winemiller, M. D.; Collum, D. B. *J. Am. Chem. Soc.* **2000**, *122*, 11084–11089. (i) Cardillo, G.; Gentilucci, L.; Gianotti, M.; Tolomelli, A. *Org. Lett.* **2001**, *3*, 1165–1167. (j) Marshall, J. A.; Gill, K. *J. Organomet. Chem.* **2001**, *624*, 294–299.
17. (a) Gevorgyan, V.; Rubin, M.; Benson, S.; Liu, J.-X.; Yamamoto, Y. *J. Org. Chem.* **2000**, *65*, 6179–6186. (b) Blackwell, J. M.; Morrison, D. J.; Piers, W. E. *Tetrahedron* **2002**, *58*, 8247–8254. (c) Parks, D. J.; Blackwell, J. M.; Piers, W. E. *J. Org. Chem.* **2000**, *65*, 3090–3098, See also Ref. 4c.
18. Enhancement of the diastereomer or enantiomer ratio versus the initial *E*/*Z* ratio has been previously observed in reductions of imines. (a) Borg, G.; Cogan, D. A.; Ellman, J. A. *Tetrahedron Lett.* **1999**, *40*, 6709–6712. (b) Verdaguer, X.; Lange, U. E. W.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **1998**, *37*, 1103–1107.
19. The effect of stannane concentration on the rate of reduction has not been determined.
20. Blackwell, J. M.; Piers, W. E.; Parvez, M.; McDonald, R. *Organometallics* **2002**, *21*, 1400–1407.
21. Willoughby, C. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 8952–8965.
22. For numerous examples, see footnotes 21–28 within Ref. 22a. (a) Friestad, G. K. *Tetrahedron* **2001**, *57*, 5461–5496. See also: (b) Ghelfi, F.; Parsons, A. F. *J. Org. Chem.* **2000**, *65*, 6249–6253. (c) Luna, A. P.; Ceschi, M.-A.; Bonin, M.; Micouin, L.; Husson, H.-P.; Gougeon, S.; Estenne-Bouhtou, G.; Marabout, B.; Sevrin, M.; George, P. *J. Org. Chem.* **2002**, *67*, 3522–3524. (d) Chandrasekhar, S.; Reddy, C. C.; Rao, R. J. *Synlett* **2001**, 1561–1562.