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Chiral ligand-controlled asymmetric conjugate amination of enoates with lithium mesitylmethyl(trimethylsilyl)amide

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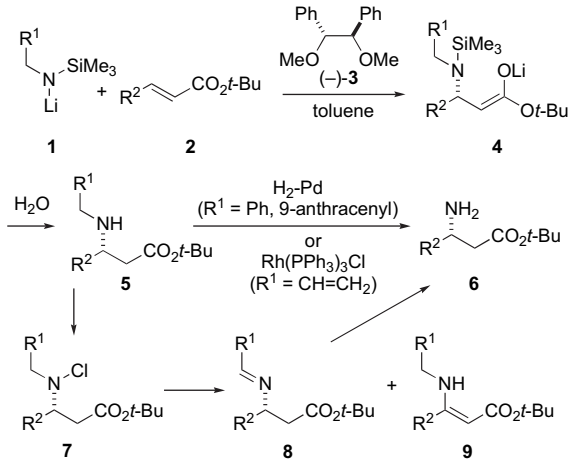
Abstract—Lithium mesitylmethyl(trimethylsilyl)amide behaved as a nice amination agent in a chiral ligand-controlled conjugate addition reaction of *tert*-butyl cinnamate to give the conjugate amination product with 99% ee in 90% yield. Other acyclic and cyclic enoates were also aminated in reasonably high enantioselectivity, while the deprotonation of abstractable proton of enoates caused yield loss of the conjugate amination products, due to the bulkiness and enriched basicity of the lithium amide. Although such steric bulkiness made hard the hydrogenolytic cleavage of a mesitylmethyl–N bond of the adducts, a new protocol comprising N-chlorination–regioselective dehydrochlorination–transoximation was developed for N-dearylmethylation, giving 3-aminoalkanoates in reasonably good yields.

1. Introduction

Chiral β-amino acids have been established to be the critical skeleton unit of biologically potent peptidic natural products,[1] medicinally important class of nonpeptidic β-lactams,[2] and pharmaceuticals.[3] Among several strategies for the synthesis of chiral β-amino acid derivatives,[4] the conjugate addition of nitrogen nucleophiles to α,β-unsaturated carboxylic acid derivatives is one of the most attractive and versatile methods as has been shown by the elegant reactions using chiral amine nucleophiles,[5,6] chiral enoates,[7] and chiral catalysts.[8] As part of our studies directed toward the development of asymmetric conjugate addition reactions of lithiated nucleophiles,[9] organocoppers,[10] and organoboranes,[11] we have been engaged in the asymmetric conjugate addition of nitrogen nucleophiles to enoates providing chiral β-amino acid equivalents.[12] Our methodology relies on the chiral ligand-mediated asymmetric conjugate addition[13] of lithiated arylmethyl(trimethylsilyl)amines **1** (R^1=Ar)[14] or allyl(trialkylsilyl)amines **1** (R^1=CH=CH_2)[15] to acyclic and cyclic enoates **2**, giving the corresponding β-alkylaminoalkanoates **5** in high enantioselectivity via protonation of enolates **4**, which were then converted to 3-aminoalkanoates **6** by hydrogenolysis of an arylmethylamino group or rhodium-catalyzed isomerization of an allylamino group into an imine followed by hydrolysis (Scheme 1). This two-step procedure to **6** from **2** seems very promising; however, hydrogenolysis and isomerization at the second step are not applicable to the substrates **5** bearing such sensitive functional groups. In our further studies toward the asymmetric conjugate amination of a bulky lithium amide, we developed another more general method for the removal of *N*-arylmethyl group of **5**, which comprised three successive steps, N-chlorination of **5** to **7**, regioselective dehydrochlorination to imines **8**, and finally transoximation to **6**. The problem to be solved is the regioselective dehydrochlorination of **7** to **8**, not to **9**.



Scheme 1. Asymmetric conjugate amination of **2** and subsequent conversion of **5** to 3-aminoalkanoates **6**.

2. Results and discussion

2.1. Steric tuning of arylmethyl(trimethylsilyl)amine

The chiral diether (−)-**3**[9]-controlled asymmetric conjugate addition reaction of a lithium amide **1a** (R^1=Ph) with

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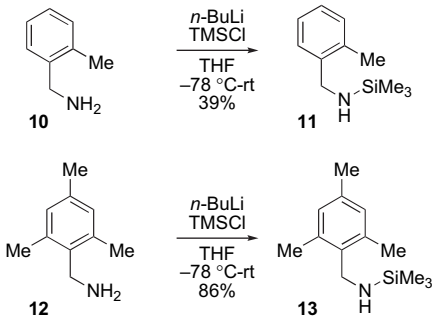
enoates **2** in the presence of trimethylsilylchloride (TMSCl) afforded **5** (R^1=Ph) with high enantioselectivity up to 99% ee (Scheme 1).[14a] However, the presence of TMSCl sometimes results in poorer chemical yield, and the reaction in the absence of TMSCl afforded **5** with poorer ee. TMSCl was added to the reaction for the conversion of the corresponding lithium enolate **4** to its TMS enol ether and consequently to avoid mixed aggregate formation with a lithium amide **1**,[12] which caused decreased enantioselectivity. Since the bulky R^1 group of **4** and **1** is another possibility in avoiding mixed aggregate formation due to the steric reason and such bulky lithium amide **1** may behave as a more powerful nucleophile due to the deaggregation,[16] we focused our study on the reaction of lithium amide **1** derived from bulkier amines **11** and **13** (Scheme 2).



Scheme 2. Trimethylsilylation of amines **10** and **12**.

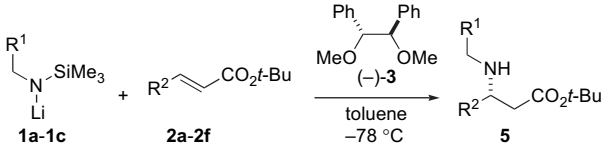
The reaction of **1b** (R^1=2-MeC_6H_4) bearing an *ortho*-methylphenyl group, prepared by the *n*-BuLi treatment of **11**, with *tert*-butyl cinnamate **2a** (R^2=Ph) in the presence of stoichiometric amount of (−)-**3** in toluene at −78 °C proceeded to completion within 0.5 h to give **5ba**[17] with 81% ee, disappointingly poorer ee by comparing with 93% ee of the reaction of lithium benzyl(TMS)amide **1a** (R^1=Ph) (Table 1, entries 1 and 2). However, it was very satisfactory to find that the reaction of **1c** (R^1=2,4,6-$Me_3C_6H_2$) bearing a mesityl group, prepared from **13**, gave **5ca** with 99% ee in 90% yield (entry 3). Prolonged reaction time, 2.5 h, indicated that the bulkiness of **1c** caused the loss of nucleophilic reactivity, and this bulkiness, in turn, helps to avoid the mixed aggregate formation of a resulting lithium enolate **4ca** with **1c**, giving excellently high enantioselectivity. It is also possible to speculate that the bulkiness of lithium amide **1c** itself prevents the self-aggregation of **1c**–**3** complex and exerts high stereoselectivity.

Other acyclic and cyclic enoates **2** were converted to the corresponding conjugate amination products **5** with satisfactorily high 93–96% ee, excepting **2c** that has a bulky isopropyl group at the reaction site (entries 4–8). However, the drawback of bulky **1c** became apparent by the moderate chemical yield, which was caused by the deprotonation of **2** bearing an abstractable proton, because of the stronger basicity of **1c**.

2.2. Unsuccessful hydrogenolysis of bulky arylmethyl group

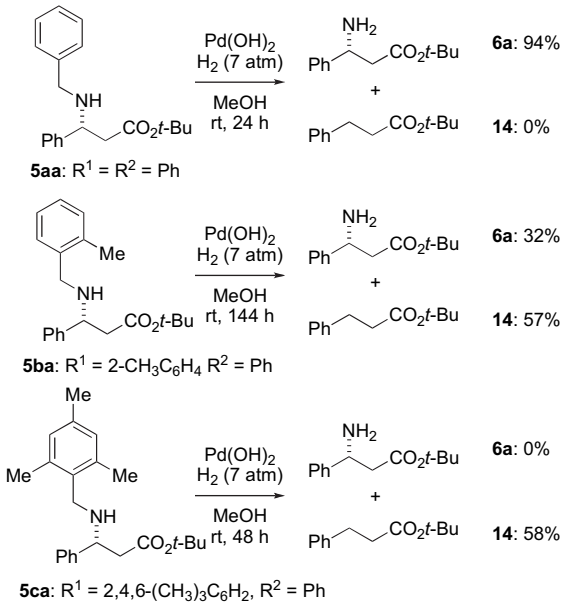
Another severe disaster came from the difficulty in the hydrogenolytic cleavage of a mesitylmethyl–N bond of **5** (Scheme 3). Hydrogenolysis of benzylamine adduct **5aa** with Perlman's catalyst in methanol under 7 atm hydrogen pressure successfully gave a debenzylation product **6a** in 94% yield without concomitant formation of phenylpropanoate **14** that arose from hydrogenolysis at the 3-position of **5aa**. *ortho*-Methylbenzyl group of **5ba** was hydrogenolyzed to give a mixture of **6a** in 32% yield and **14** in 57% yield. The mesitylmethyl group of **5ca** was extremely hard to be hydrogenolyzed to give **14** in 58% yield without formation of **6a**. The attempted N-demesitylmethylation of **5cb** (R^2=Me) was also totally unsuccessful, giving a complex mixture. A similar difficulty in the hydrogenolysis of substituted benzyl group has been also reported by Davies group.[19]

Table 1. Asymmetric conjugate amination of **2** with **1**[a]



Entry	1	R^1	2	R^2	Time (h)	5	Yield (%)	ee (%)[b]
1	**1a**	Ph	**2a**	Ph	0.7	**5aa**	92	93[c]
2	**1b**	2-Tol	**2a**	Ph	0.5	**5ba**	76	81
3	**1c**	Mes	**2a**	Ph	2.5	**5ca**	90	99
4	**1c**	Mes	**2b**	Me	0.1	**5cb**	62	93
5	**1c**	Mes	**2c**	*i*-Pr	15.0	**5cc**	61	75
6	**1c**	Mes	**2d**	*E*-Propenyl	12.0	**5cd**	26	94
7	**1c**	Mes	**2e**	1-Naph	2.0	**5ce**	52	96
8	**1c**	Mes	**2f**		1.5	*cis*-**5cf**	90	96

[a] Three equivalents of **1** were used.
[b] The ee was determined by chiral stationary phase HPLC. For entry 8, the ee was determined by ^{1}H NMR using (*S*)-(−)-1,1′-bi-2,2′-naphthol as a chiral shift reagent.[18]
[c] Quoted from Ref. 14a.

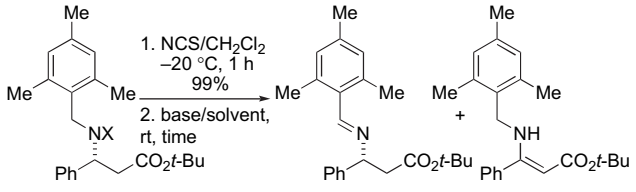


Scheme 3. Successful and unsuccessful hydrogenolysis of R^1CH_2 group.

2.3. Regioselective imine formation and transoximation for dearylmethylation

The problem in hydrogenolysis was circumvented by an oxidative imine formation from an amine **5ca**.[20] Chlorination of secondary amine of **5ca** with NCS in methylene chloride at −20 °C for 1 h gave an *N*-chlorinated product **15**, which was stable in silica gel chromatography, quantitatively (Table 2). Dehydrochlorination was then attempted by using a variety of bases. Treatment with KOH in ethanol[21] gave a mixture of desired imine and undesired enamine **8a** and **9a**, and **5ca** in a 32:20:48 ratio (Table 2, entry 1).

Table 2. Regioselective dehydrochlorination of **15** to imine **8a** and **9a** from **5ca**[a]

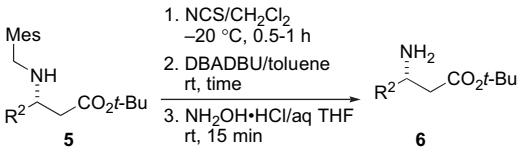


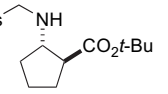
Entry	Base	Solvent	Time (h)	**8a** (%)	**9a** (%)	**5ca** (%)
1	KOH	EtOH	0.5	32	20	48
2	KO*t*-Bu	THF	0.5	0	0	0[b]
3	Et_3N	PhH	48	0	0	100
4	*i*-Pr_2NEt	PhH	144	0	0	100
5	Proton sponge	PhH	144	0	0	100
6	DABCO	PhH	96	48	38	14
7	$HN{=}C(NMe_2)_2$	PhH	17	29	71	0
8	DBN	PhH	12	62	38	0
9	DBU	PhH	17	79	21	0
10	DBADBU	PhH	84	85	15	0
11	DBADBU	PhMe	72	90	10	0

[a] Relative ratio determined by ^1H NMR of crude product.
[b] A complex mixture was obtained.

Potassium *tert*-butoxide,[22] triethylamine,[23] diisopropylethylamine,[23] and proton sponge as bases gave back **5ca** without formation of any imine and enamine (entries 2–5). Promising result was first obtained by treating with DABCO in benzene to give a 48:38:14 mixture (entry 6). Guanidine base gave a 29:71 mixture without recovery of **5ca** (entry 7). DBN and DBU[24] were found to give the desired **8a** as the major product in the mixture in a good recovery (entries 8 and 9). Much more improvement was obtained by using commercially available dibutylamino-DBU (DBADBU)[25] in benzene to give a 85:15 mixture of **8a** and **9a**, and the best result was obtained by the reaction in toluene at rt for 72 h to give a 90:10 mixture of **8a** and **9a** (entries 10 and 11). Further treatment of the mixture of imine and enamine with hydroxylamine hydrochloride[26] in aqueous THF at rt for 15 min gave **6a** without any racemization[27] in 81% three-step isolated yield from **5ca**, thus succeeding in the development of a generally applicable N-dearylmethylation protocol (Table 3, entry 1). (*E*)- and (*Z*)-Oximes of mesitylaldehyde were isolated in 73% combined yield, indicating transoximation of an imine. It is notable that DBADBU was recovered in 91% yield and was reusable.

Table 3. Chlorination of **5**, regioselective dehydrochlorination, and transoximation to 3-aminoalkanoates **6**



Entry	**5**	R^2	Time (h)	**6**	Yield (%)
1	**5ca**	Ph	72	(+)-(*S*)-**6a**	81
2	**5cb**	Me	72	(−)-(*S*)-**6b**	67[a]
3	**5cc**	*i*-Pr	48	**6c**	62
4	**5cd**	*E*-Propenyl	48	**6d**	71
5	**5ce**	1-Naph	72	**6e**	69
6	*trans*-**5cf**		48	(−)-(1*S*,2*S*)-**6f**	53

[a] The yield after conversion to Cbz-**6b** with the established absolute configuration.[28]

The established chlorination–regioselective dehydrochlorination with DBADBU–transoximation protocol was applicable to **5cb**–**5cf** giving 3-aminoalkanoates **6** in reasonably good yields (Table 3).

3. Conclusion

Lithium mesitylmethyl(trimethylsilyl)amide was developed as a new conjugate amination agent of enoates, giving the products in excellently high enantioselectivity, while bulkiness of the lithium amide decreased its nucleophilicity and enhanced basic character. For the N-dearylmethylation of the conjugate amination products, a new protocol, N-chlorination–regioselective dehydrochlorination–transoximation was successfully developed to give 3-aminoalkanoates in reasonably good yields.

4. Experimental

4.1. General

All melting points are uncorrected. IR spectra were expressed in cm^{-1}. ^1H and ^{13}C NMR spectra were taken in $CDCl_3$ at 500 and 125 MHz, respectively, unless otherwise noted. Chemical shift values are expressed in parts per million relative to internal TMS. *J* values are presented in hertz. Abbreviations are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad.

4.1.1. *N*-(2-Methylbenzyl)-*N*-trimethylsilylamine (11). The same procedure for **13** (vide infra) and distillation (106 °C/10 mmHg) gave **11** as a colorless oil in 39% yield. ^1H NMR (C_6D_6): 0.06 (9H, s), 0.28 (1H, br s), 2.15 (3H, s), 3.77 (2H, d, *J*=6.7), 7.03–7.12 (4H, m), 7.36 (1H, m). ^{13}C NMR (C_6D_6): −0.1, 18.7, 43.9, 126.2, 126.8, 127.6, 130.3, 135.6, 141.9. IR (neat): 3387, 1250. MS (EI) *m/z*: 193 (M^+), 120 (M^+-TMS). HRMS (EI) *m/z*: calcd for $C_{11}H_{19}NSi$: 193.1287. Found: 193.1296.

4.1.2. Mesitylmethylamine (12) hydrobromide.[29] To a solution of liquid NH_3 (135 g, 7.9 mol) in EtOH (220 mL) was added a solution of mesitylmethylbromide[30] (12.0 g, 56.4 mmol) in EtOH (120 mL) over 20 min at −78 °C. After stirring for 0.5 h under reflux, the mixture was concentrated. To the residue was added chloroform in which bismesitylmethylamine hydrobromide was dissolved and the mixture was filtrated. Recrystallization from water gave hydrobromide of **12** (6.64 g, 50% yield) as colorless needles of mp>270 °C. ^1H NMR (DMSO-d_6): 2.21 (3H, s), 2.34 (6H, s), 3.97 (2H, s), 6.89 (2H, s), 8.02 (3H, br s). ^{13}C NMR (DMSO-d_6): 19.4, 20.6, 36.2, 127.6, 129.0, 137.8, 138.1. IR (Nujol): 3550, 1570, 1460, 852. MS (EI) *m/z*: 149 (M^+-HBr). Anal. Calcd for $C_{10}H_{16}BrN\cdot 1/8H_2O$: C, 51.68; H, 7.05; N, 6.03. Found: C, 52.19; H, 7.01; N, 6.09.

4.1.3. Mesitylmethylamine (12).[31] The suspension of hydrobromide of **12** (21 g, 91 mmol) in 10% NaOH (100 mL) was extracted with ether. Organic layers were washed with brine and dried over sodium sulfate. Concentration and distillation (107 °C/10 mmHg) gave **12** (12.4 g, 91% yield) as a colorless oil. ^1H NMR (C_6D_6): 0.66 (2H, br s), 2.15 (3H, s), 2.20 (6H, s), 3.01 (2H, s), 6.76 (2H, s). ^{13}C NMR (C_6D_6): 19.2, 20.9, 40.2, 129.3, 135.8, 136.2, 137.0. IR (neat): 3368, 3294, 1612, 852. MS (EI) *m/z*: 149 (M^+), 132 (M^+-NH_2).

4.1.4. *N*-Mesitylmethyl-*N*-trimethylsilylamine (13). Under Ar atmosphere, to a solution of **12** (4.7 g, 31.5 mmol) in THF (30 mL) was added a 1.6 M hexane solution of *n*-BuLi (23.6 mL, 37.8 mmol) at −78 °C over 10 min. After 1 h stirring, TMSCl (5.3 mL, 37.8 mmol) was added over 3 min. The mixture was stirred for 2 h at −78 °C, and then stirred for additional 0.5 h at rt. After addition of benzene (10 mL), the mixture was stood for 10 min. The supernatant was concentrated and distilled (92 °C/1 mmHg) to give **13** as a colorless oil in 86% yield. ^1H NMR (C_6D_6): 0.07 (1H, br s), 0.09 (9H, s), 2.17 (3H, s), 2.30 (6H, s), 3.79 (2H, d, *J*=5.8), 6.79 (2H, s). ^{13}C NMR (C_6D_6): −0.2, 19.4, 21.0, 39.7, 129.3, 136.0, 136.4, 136.9. IR (neat): 3406, 1250. MS (EI) *m/z*: 221 (M^+), 149 (M^+-TMS). Anal. Calcd for $C_{13}H_{23}NSi$: C, 70.52; H, 10.47; N, 6.33. Found: C, 70.61; H, 10.70; N, 6.28.

4.1.5. (+)-*tert*-Butyl (*R*)-3-(mesitylmethylamino)-3-phenylpropanoate (5ca). Under Ar atmosphere, a 1.6 M hexane solution of *n*-BuLi (1.8 mL, 3.0 mmol) was added to a solution of an amine **13** (3.0 mmol) in toluene (8 mL) at −78 °C over 5 min. After stirring for 0.5 h, a solution of (−)-**3** (873 mg, 3.6 mmol) in toluene (6 mL) was added and the mixture was stirred for 0.5 h at −78 °C. A toluene solution of *tert*-butyl cinnamate **2a** (1.0 mmol) was added over 5 min and the mixture was stirred at −78 °C for 2.5 h, and then quenched with satd ammonium chloride (3 mL). After addition of 10% potassium carbonate (6 mL), the mixture was extracted with AcOEt. The organic layer was washed with brine and dried over sodium sulfate. Concentration and silica gel column chromatography (benzene/hexane/AcOEt=2/7/1) gave **5ca** (318 mg, 90% yield) as a colorless oil of $[\alpha]_D^{25}$+27.7 (*c* 1.26, $CHCl_3$) and recovered (−)-**3** (870 mg, quant yield); 99% ee (Daicel Chiralcel OD-H, hexane/2-PrOH=100/1, 0.5 mL/min, 254 nm, major 9.9 min and minor 12.5 min). ^1H NMR: 1.37 (9H, s), 1.61 (1H, br s), 2.23 (3H, s), 2.24 (6H, s), 2.51 (1H, dd, *J*=4.9, 15.6), 2.62 (1H, dd, *J*=9.2, 15.6), 3.45 and 3.53 (each 1H, d, *J*=11.3), 4.10 (1H, dd, *J*=4.9, 9.2), 6.80 (2H, s), 7.28 (1H, m), 7.33–7.36 (2H, m), 7.41–7.43 (2H, m). ^{13}C NMR: 19.3, 20.9, 28.0, 44.1, 45.9, 60.6, 80.6, 127.2, 127.4, 128.4, 128.8, 133.7, 136.4, 137.0, 143.1, 171.2. IR (neat): 3300, 1720. MS (EI) *m/z*: 353 (M^+), 296 (M^+-t-Bu). Anal. Calcd for $C_{23}H_{31}NO_2$: C, 78.15; H, 8.84; N, 3.96. Found: C, 77.99; H, 9.03; N, 4.02.

Recrystallization of recovered (−)-**3** from hexane gave pure (−)-**3** quantitatively and was reusable in an asymmetric reaction.

4.1.6. (+)-*tert*-Butyl (*R*)-3-(2-methylbenzylamino)-3-phenylpropanoate (5ba). Column chromatography (AcOEt/hexane=1/20) gave a white solid of mp 57–59 °C and $[\alpha]_D^{25}$ +23.6 (*c* 1.38, $CHCl_3$) in 76% yield; 81% ee (Daicel Chiralpak AD-H, hexane/2-PrOH=500/1, 1.0 mL/min, 254 nm, major 17.7 min and minor 19.7 min). ^1H NMR: 1.37 (9H, s), 1.61 (1H, br s), 2.25 (3H, s), 2.53 (1H, dd, *J*=5.2, 15.3), 2.64 (1H, dd, *J*=8.9, 15.3), 3.56 (2H, s), 4.10 (1H, dd, *J*=5.2, 8.9), 7.13–7.39 (9H, m). ^{13}C NMR: 18.8, 27.9, 44.3, 49.5, 59.9, 80.6, 125.9, 127.0, 127.3, 127.4, 128.5, 128.8, 130.3, 136.6, 138.3, 142.9, 171.2. IR (Nujol): 3321, 1713. MS (EI) *m/z*: 325 (M^+). Anal. Calcd for $C_{21}H_{27}NO_2$: C, 77.50; H, 8.36; N, 4.30. Found: C, 77.64; H, 8.48; N, 4.26.

4.1.7. (+)-*tert*-Butyl (*S*)-3-(mesitylmethylamino)butanoate (5cb). Column chromatography (hexane/AcOEt=10/1) gave a colorless oil of $[\alpha]_D^{25}$ +23.7 (*c* 0.99, $CHCl_3$) in 62% yield; 93% ee (Daicel Chiralpak AD, hexane/2-PrOH=100/1, 0.5 mL/min, 254 nm, major 9.3 min and minor 11.5 min). ^1H NMR: 1.17 (3H, d, *J*=6.4), 1.31 (1H, br s), 1.44 (9H, s), 2.24 (3H, s), 2.27 (1H, dd, *J*=5.5, 15.0), 2.35 (6H, s), 2.43 (1H, dd, *J*=7.3, 15.0), 3.17 (1H, ddq, *J*=5.5, 7.3, 6.4), 3.66 and 3.75 (each 1H, d, *J*=11.3), 6.83 (2H, s). ^{13}C NMR: 19.3, 20.4, 20.8, 28.0, 42.9, 45.1, 51.0, 80.3, 128.9, 133.8, 136.3, 136.8, 171.9. IR (neat): 3333, 1728, 1157. MS (EI) *m/z*: 291 (M^+), 234 (M^+-t-Bu).

Anal. Calcd for $C_{18}H_{29}NO_2$: C, 74.18; H, 10.03; N, 4.81. Found: C, 74.31; H, 9.91; N, 4.84.

4.1.8. (+)-*tert*-Butyl 3-(mesitylmethylamino)-4-methylpentanoate (5cc). Column chromatography (hexane/AcOEt=10/1) gave a colorless oil of $[\alpha]_D^{25}$ +27.0 (*c* 0.96, $CHCl_3$) in 61% yield; 75% ee (Daicel Chiralpak AD, hexane/2-PrOH=500/1, 0.3 mL/min, 254 nm, major 15.0 min and minor 16.6 min). ^{1}H NMR: 0.91 and 0.92 (each 3H, d, *J*=6.7), 1.42 (1H, br s), 1.43 (9H, s), 1.94 (1H, dqq, *J*=4.3, 6.7, 6.7), 2.24 (3H, s), 2.26 (1H, dd, *J*=8.3, 15.3), 2.35 (1H, dd, *J*=4.3, 15.3), 2.36 (6H, s), 2.90 (1H, ddd, *J*=4.3, 4.3, 8.3), 3.69 (2H, s), 6.83 (2H, s). ^{13}C NMR: 17.4, 18.8, 19.3, 20.8, 28.0, 30.1, 37.0, 45.9, 60.8, 80.2, 128.9, 134.1, 136.3, 137.1, 172.7. IR (neat): 3341, 1728, 1153. MS (EI) *m/z*: 319 (M^+), 276 (M^+-t-Bu). Anal. Calcd for $C_{20}H_{33}NO_2$: C, 75.19; H, 10.41; N, 4.38. Found: C, 75.31; H, 10.16; N, 4.31.

4.1.9. (−)-*tert*-Butyl 3-(mesitylmethylamino)-4-hexenoate (5cd). Column chromatography (benzene/AcOEt=10/1) gave a colorless oil of $[\alpha]_D^{25}$ −14.0 (*c* 1.04, $CHCl_3$) in 26% yield; 94% ee (Daicel Chiralpak AD+AS-H, hexane/2-PrOH=200/1, 0.5 mL/min, 254 nm, major 15.6 min and minor 17.3 min). ^{1}H NMR: 1.42 (9H, s), 1.43 (1H, br s), 1.72 (3H, dd, *J*=1.6, 6.4), 2.23 (3H, s), 2.328 (1H, dd, *J*=5.8, 15.3), 2.329 (6H, s), 2.42 (1H, dd, *J*=7.6, 15.3), 3.47 (1H, ddd, *J*=5.8, 7.6, 8.3), 3.53 and 3.71 (each 1H, d, *J*=11.3), 5.36 (1H, ddd, *J*=1.6, 8.3, 15.0), 5.68 (1H, qd, *J*=6.4, 15.0), 6.82 (2H, s). ^{13}C NMR: 17.6, 19.3, 20.8, 28.0, 42.2, 45.2, 58.4, 80.3, 127.3, 128.9, 132.8, 133.9, 136.3, 136.9, 171.4. IR (neat): 3333, 1728, 1157. MS (EI) *m/z*: 317 (M^+), 260 (M^+-t-Bu). Anal. Calcd for $C_{20}H_{31}NO_2$: C, 75.67; H, 9.84; N, 4.41. Found: C, 75.85; H, 9.63; N, 4.33.

4.1.10. (+)-*tert*-Butyl 3-(mesitylmethylamino)-3-(1-naphthyl)propanoate (5ce). Column chromatography (hexane/AcOEt=20/1) gave a colorless amorphous solid of $[\alpha]_D^{25}$ +47.0 (*c* 1.05, $CHCl_3$) in 52% yield; 96% ee (Daicel Chiralcel OD-H, hexane/2-PrOH=200/1, 1.0 mL/min, 254 nm, major 9.7 min and minor 19.9 min). ^{1}H NMR: 1.38 (9H, s), 1.81 (1H, br s), 2.24 (3H, s), 2.27 (6H, s), 2.70 (2H, d, *J*=6.4), 3.59 (2H, s), 5.02 (1H, t, *J*=6.4), 6.82 (2H, s), 7.48–7.55 (3H, m), 7.79–7.81 (2H, m), 7.88 (1H, m), 8.36 (1H, m). ^{13}C NMR: 19.3, 20.8, 28.0, 43.5, 46.1, 80.7, 123.2, 123.9, 125.47, 125.53, 126.0, 127.7, 128.9, 129.0, 131.4, 133.7, 134.1, 136.5, 137.2, 138.6, 171.6. IR (neat): 3337, 1724, 1150. MS (EI) *m/z*: 403 (M^+), 346 (M^+-t-Bu). Anal. Calcd for $C_{27}H_{33}NO_2$: C, 80.36; H, 8.24; N, 3.47. Found: C, 80.26; H, 8.28; N, 3.44.

4.1.11. (+)-*tert*-Butyl (1*R*,2*S*)-2-(mesitylmethylamino)-cyclopentanecarboxylate (*cis*-5cf). Column chromatography (toluene/AcOEt=30/1–10/1) gave a colorless oil of $[\alpha]_D^{25}$ +3.9 (*c* 0.98, $CHCl_3$) in 90% yield; 96% ee (^{1}H NMR (C_6D_6) using (*S*)-(−)-1,1′-bi-2,2′-naphthol as a chiral shift reagent,[18] judged by the integral areas of the peaks of the C2 protons (the major peak at 2.70 ppm and the minor peak at 2.64 ppm)). ^{1}H NMR: 1.37 (1H, br s), 1.40 (9H, s), 1.59 (1H, m), 1.72–1.88 (4H, m), 1.97 (1H, m), 2.24 (3H, s), 2.34 (6H, s), 2.79 (1H, m), 3.32 (1H, m), 3.68 and 3.71 (each 1H, d, *J*=11.6), 6.81 (2H, s). ^{13}C NMR: 19.4, 20.8, 22.0, 27.0, 28.1, 31.5, 46.2, 49.1, 62.3, 80.0, 128.8, 134.1, 136.2, 136.9, 173.8. IR (neat): 3341, 1720, 1150. MS (EI) *m/z*: 317 (M^+), 260 (M^+-t-Bu). Anal. Calcd for $C_{20}H_{31}NO_2$: C, 75.67; H, 9.84; N, 4.41. Found: C, 75.91; H, 9.81; N, 4.27.

4.1.12. (+)-*tert*-Butyl (1*S*,2*S*)-2-(mesitylmethylamino)-cyclopentanecarboxylate (*trans*-5cf). A colorless oil of $[\alpha]_D^{25}$ +73.4 (*c* 1.15, $CHCl_3$) in 3% yield; 95% ee (^{1}H NMR (C_6D_6) using (*S*)-(−)-1,1′-bi-2,2′-naphthol as a chiral shift reagent, judged by the integral areas of the peaks of the C2 protons (the major peak at 2.50 ppm and the minor peak at 2.43 ppm)). ^{1}H NMR: 1.44 (9H, s), 1.40–1.52 (2H, m), 1.66–1.75 (2H, m), 1.85 (1H, m), 1.96 (1H, m), 2.05 (1H, m), 2.24 (3H, s), 2.36 (6H, s), 2.50 (1H, m), 3.32 (1H, m), 3.70 (2H, s), 6.84 (2H, s). ^{13}C NMR: 19.3, 20.8, 23.5, 28.0, 28.7, 33.2, 46.4, 51.9, 64.1, 80.1, 129.0, 133.8, 136.5, 136.8, 175.3. IR (neat): 3325, 1724, 1150. MS (EI) *m/z*: 317 (M^+), 260 (M^+-t-Bu). HRMS (EI) *m/z*: calcd for $C_{20}H_{31}NO_2$: 317.2355. Found: 317.2359.

4.1.13. Epimerization of *cis*-5cf to *trans*-5cf.[32] To a solution of *tert*-butanol (1.03 mL, 10.9 mmol) in THF (25 mL) was added a 0.5 M toluene solution of potassium bis(trimethylsilyl)amide (12.5 mL, 6.2 mmol) at 0 °C over 5 min. After stirring for 15 min, *cis*-**5cf** (500 mg, 1.6 mmol) in toluene (5 mL) was added and the mixture was stirred for 15 min at rt. The mixture was quenched with satd ammonium chloride (10 mL). After addition of 10% potassium carbonate (25 mL), the mixture was extracted with AcOEt. The organic layers were washed with brine and dried over sodium sulfate. Concentration and column chromatography (acetone/hexane=1/30) gave *trans*-**5cf** (387 mg, 77% yield) and *cis*-**5cf** (21 mg, 4% yield).

4.1.14. (−)-*tert*-Butyl (*R*)-3-(*N*-chloro-*N*-mesitylmethylamino)-3-phenylpropanoate (15). To a solution of **5ca** (0.62 mmol) in methylene chloride (13 mL) was added NCS (249 mg, 1.87 mmol) at −20 °C. The mixture was stirred for 14 h at −20 °C and then washed with brine and dried over sodium sulfate. Concentration and column chromatography (AcOEt/hexane=1/20) gave **15** (238 mg, 99% yield) as a pale yellow oil of $[\alpha]_D^{25}$ −10.4 (*c* 0.91, $CHCl_3$). ^{1}H NMR: 1.31 (9H, s), 2.24 (3H, s), 2.25 (6H, s), 2.87 (1H, dd, *J*=8.3, 15.3), 3.27 (1H, dd, *J*=6.5, 15.3), 3.89 and 3.95 (each 1H, d, *J*=13.5), 4.53 (1H, dd, *J*=6.5, 8.3), 6.81 (2H, s), 7.33–7.39 (3H, m), 7.43–7.44 (2H, m). ^{13}C NMR: 20.1, 20.9, 27.8, 39.7, 57.9, 70.6, 80.8, 128.2, 128.3, 129.06, 129.10, 130.5, 137.2, 138.0, 138.3, 170.5. IR (neat): 1732, 1150. MS (FAB) *m/z*: 388 (M^++H). Anal. Calcd for $C_{23}H_{30}ClNO_2$: C, 71.21; H, 7.79; N, 3.61. Found: C, 71.03; H, 8.00; N, 3.38.

4.1.15. (+)-*tert*-Butyl (*S*)-3-(*N*-chloro-*N*-mesitylmethylamino)butanoate from 5cb. Column chromatography (AcOEt/hexane=1/10) gave a pale yellow oil of $[\alpha]_D^{25}$ +18.6 (*c* 1.03, $CHCl_3$) in quantitative yield. ^{1}H NMR: 1.29 (3H, d, *J*=6.2), 1.43 (9H, s), 2.26 (3H, s), 2.360 (1H, dd, *J*=7.4, 15.3), 2.361 (6H, s), 2.74 (1H, dd, *J*=6.2, 15.3), 3.55 (1H, ddq, *J*=6.2, 7.4, 6.2), 4.03 and 4.15 (each 1H, d, *J*=13.5), 6.84 (2H, s). ^{13}C NMR: 15.4, 20.0, 20.9, 28.0, 40.3, 57.8, 60.3, 80.5, 129.1, 130.6, 137.3, 138.2, 171.2. IR (neat): 1732, 1157. MS (FAB) *m/z*: 326 (M^++H). Anal.

Calcd for $C_{18}H_{28}ClNO_2$: C, 66.34; H, 8.66; N, 4.30. Found: C, 66.55; H, 8.61; N, 4.13.

4.1.16. (+)-*tert*-Butyl 3-(*N*-chloro-*N*-mesitylmethylamino)-4-methylpentanoate from 5cc. Column chromatography (AcOEt/hexane=1/10) gave a colorless oil of $[\alpha]_D^{25}$ +32.7 (*c* 1.11, $CHCl_3$) in 89% yield. ^1H NMR: 0.93 and 1.00 (each 3H, d, *J*=6.8), 1.47 (9H, s), 1.91 (1H, m), 2.26 (3H, s), 2.37 (6H, s), 2.45 (1H, dd, *J*=6.1, 16.8), 2.90 (1H, dd, *J*=3.7, 16.8), 3.06 (1H, m), 3.94 and 4.20 (each 1H, d, *J*=13.4), 6.85 (2H, s). ^{13}C NMR: 19.4, 20.1, 20.4, 20.9, 28.0, 32.6, 35.2, 58.4, 70.8, 80.7, 129.1, 130.6, 137.3, 138.3, 172.5. IR (neat): 1728, 1157. MS (FAB) *m/z*: 353 (M^++H). Anal. Calcd for $C_{20}H_{32}ClNO_2$: C, 67.87; H, 9.11; N, 3.96. Found: C, 67.89; H, 8.95; N, 3.96.

4.1.17. (−)-*tert*-Butyl 3-(*N*-chloro-*N*-mesitylmethylamino)hex-4-enoate from 5cd. Column chromatography (AcOEt/hexane=1/10) gave a colorless oil of $[\alpha]_D^{25}$ −27.1 (*c* 1.03, $CHCl_3$) in 94% yield. ^1H NMR: 1.42 (9H, s), 1.79 (3H, d, *J*=5.8), 2.25 (3H, s), 2.34 (6H, s), 2.49 (1H, dd, *J*=7.6, 15.0), 2.80 (1H, dd, *J*=6.4, 15.0), 3.86 (1H, ddd, *J*=6.4, 7.6, 8.0), 3.88 and 4.16 (each 1H, d, *J*=13.4), 5.69 (1H, dd, *J*=8.0, 15.3), 5.77 (1H, dq, *J*=15.3, 5.8), 6.83 (2H, s). ^{13}C NMR: 17.9, 20.1, 20.9, 28.0, 40.2, 58.0, 67.9, 80.5, 127.4, 129.1, 130.6, 131.2, 137.2, 138.3, 170.6. IR (neat): 1732, 1157. MS (FAB) *m/z*: 352 (M^++H). Anal. Calcd for $C_{20}H_{30}ClNO_2$: C, 68.26; H, 8.59; N, 3.98. Found: C, 68.20; H, 8.67; N, 3.93.

4.1.18. (−)-*tert*-Butyl 3-(*N*-chloro-*N*-mesitylmethylamino)-3-(1-naphthyl)propanoate from 5ce. Column chromatography (AcOEt/hexane=1/10) gave a colorless amorphous solid of $[\alpha]_D^{25}$ −19.1 (*c* 1.45, $CHCl_3$) in 89% yield. ^1H NMR: 1.18 (9H, s), 2.12 (6H, s), 2.22 (3H, s), 3.17 (1H, dd, *J*=9.2, 15.3), 3.49 (1H, dd, *J*=5.5, 15.3), 3.98 and 4.03 (each 1H, d, *J*=13.1), 5.43 (1H, dd, *J*=5.5, 9.2), 6.77 (2H, s), 7.46–7.50 (3H, m), 7.69 (1H, m), 7.82–7.86 (2H, m), 8.14 (1H, m). ^{13}C NMR: 20.0, 20.8, 27.6, 37.9, 56.8, 80.8, 123.9, 124.8, 125.5, 125.6, 128.2, 128.7, 128.98, 129.04, 130.4, 132.3, 133.9, 134.8, 137.3, 138.3, 170.4. IR (neat): 1728, 1146. MS (FAB) *m/z*: 438 (M^++H). Anal. Calcd for $C_{27}H_{32}ClNO_2$: C, 74.04; H, 7.36; N, 3.20. Found: C, 73.80; H, 7.14; N, 3.21.

4.1.19. (−)-*tert*-Butyl (1*R*,2*S*)-2-(*N*-chloro-*N*-mesitylmethylamino)cyclopentane-1-carboxylate from *cis*-5cf. Column chromatography (AcOEt/hexane=1/10) gave a pale yellow oil of $[\alpha]_D^{25}$ −47.0 (*c* 0.89, $CHCl_3$) in 85% yield. ^1H NMR: 1.43 (9H, s), 1.73 (1H, m), 1.85 (1H, m), 1.96–2.13 (3H, m), 2.19 (1H, m), 2.26 (3H, s), 2.38 (6H, s), 3.09 (1H, m), 3.58 (1H, m), 4.02 and 4.13 (each 1H, d, *J*=12.8), 6.83 (2H, s). ^{13}C NMR: 20.3, 20.9, 22.9, 27.3, 28.0, 29.3, 49.4, 60.1, 76.6, 80.0, 129.0, 130.8, 137.2, 138.3, 173.5. IR (neat): 1724, 1150. MS (FAB) *m/z*: 352 (M^++H). Anal. Calcd for $C_{20}H_{30}ClNO_2$: C, 68.26; H, 8.59; N, 3.98. Found: C, 68.00; H, 8.44; N, 3.84.

4.1.20. (+)-*tert*-Butyl (1*S*,2*S*)-2-(*N*-chloro-*N*-mesitylmethylamino)cyclopentane-1-carboxylate from *trans*-5cf. Column chromatography (AcOEt/hexane=1/20) gave a colorless oil of $[\alpha]_D^{25}$ +87.0 (*c* 1.00, $CHCl_3$) in 95% yield. ^1H NMR: 1.42 (9H, s), 1.70–1.80 (3H, m), 1.95–2.05 (3H, m), 2.26 (3H, s), 2.37 (6H, s), 2.97 (1H, m), 3.89 (1H, m), 4.08 (2H, s), 6.84 (2H, s). ^{13}C NMR: 20.1, 20.9, 24.9, 27.9, 29.1, 30.6, 48.8, 59.6, 74.0, 80.3, 129.1, 130.7, 137.3, 138.1, 175.2. IR (neat): 1724, 1150. MS (FAB) *m/z*: 352 (M^++H). Anal. Calcd for $C_{20}H_{30}ClNO_2$: C, 68.26; H, 8.59; N, 3.98. Found: C, 68.38; H, 8.81; N, 4.07.

4.1.21. (−)-*tert*-Butyl (*R*)-3-(*N*-benzyl-*N*-chloroamino)-3-phenylpropanoate from 5aa. Column chromatography (AcOEt/hexane=1/10) gave a colorless oil of $[\alpha]_D^{25}$ −10.4 (*c* 1.02, $CHCl_3$) in 97% yield. ^1H NMR: 1.32 (9H, s), 2.84 (1H, dd, *J*=8.6, 15.3), 3.26 (1H, dd, *J*=6.5, 15.3), 3.87 and 3.93 (each 1H, d, *J*=13.7), 4.53 (1H, dd, *J*=6.5, 8.6), 7.26–7.43 (10H, m). ^{13}C NMR: 27.8, 40.4, 64.3, 70.1, 80.7, 127.7, 128.3, 128.36, 128.43, 128.9, 129.0, 137.4, 137.7, 170.3. IR (neat): 1728, 1150. MS (FAB) *m/z*: 346 (M^++H). Anal. Calcd for $C_{20}H_{24}ClNO_2$: C, 69.45; H, 6.99; N, 4.05. Found: C, 69.30; H, 7.07; N, 4.02.

4.1.22. *tert*-Butyl (*Z*)-3-(*N*-mesitylmethylamino)cinnamate (9a) (Table 2, entry 9). Column chromatography (Et_2O/hexane=1/10) of the dehydrochlorination products with DBU gave **9a** as colorless plates of mp 106–107 °C in 18% yield. ^1H NMR: 1.43 (9H, s), 2.227 (6H, s), 2.235 (3H, s), 4.11 (2H, d, *J*=4.6), 4.52 (1H, s), 6.81 (2H, s), 7.41–7.45 (5H, m), 8.14 (1H, br s). ^{13}C NMR: 19.5, 20.8, 28.5, 43.3, 78.2, 87.4, 127.8, 128.4, 129.1, 129.2, 131.7, 136.9, 137.0, 137.1, 163.8, 170.0. IR (KBr): 3290, 1639, 1593, 1570, 1150. MS (EI) *m/z*: 351 (M^+), 294 (M^+−*t*-Bu). Anal. Calcd for $C_{23}H_{29}NO_2$: C, 78.59; H, 8.32; N, 3.99. Found: C, 78.64; H, 8.44; N, 3.96. Stereochemistry was determined to be (*Z*) by NOE (6.4%) between a vinyl α-proton (4.52 ppm) and the *ortho* protons of phenyl group (7.42 ppm).

4.1.23. (+)-*tert*-Butyl (*R*)-3-amino-3-phenylpropanoate (6a).[28] To a solution of **15** (122 mg, 0.31 mmol) in toluene (5 mL) was added a solution of 6-(dibutylamino)-1,8-diazabicyclo[5.4.0]undec-7-ene (DBADBU) (958 mg, 3.4 mmol) in toluene (3 mL) under Ar at rt. The mixture was stirred for 72 h at rt. The mixture was washed with 1 N HCl and brine, and dried over sodium sulfate. Concentration gave an imine as a pale yellow oil. DBADBU was recovered by extraction with chloroform from acidic water layer after alkalization with 10% NaOH. Organic layers were washed with brine and dried over sodium sulfate. Concentration and distillation gave DBADBU (872 mg, 91% yield).

Hydroxylamine hydrochloride (77 mg, 1.1 mmol) was added to a solution of the above imine in a 1:1 mixture of THF and water (1 mL). After 15 min stirring at rt, 10% HCl was added. The whole was extracted with AcOEt to remove oximes (vide infra). The aqueous layer was treated with potassium carbonate to be pH 10 and then extracted with ether. The organic layer was dried over potassium carbonate. Concentration and column chromatography (AcOEt/hexane=1/2) gave **6a** (56 mg, 82% yield) as a colorless oil of $[\alpha]_D^{20}$ +20.0 (*c* 0.71, $CHCl_3$); 99% ee (Daicel Chiralcel OD-H, hexane/2-PrOH/Et_2NH=100/10/0.1, 0.5 mL/min, 254 nm, major 11.8 min and minor 14.4 min). ^1H NMR: 1.42 (9H, s), 1.69 (2H, br s), 2.58 (2H, d, *J*=6.7), 4.37 (1H, t, *J*=6.7), 7.24–7.37 (5H, m). ^{13}C NMR: 28.0, 45.3, 52.8, 80.7, 126.3, 127.3, 128.6, 144.8, 171.4. IR (neat): 3379, 1724, 1150. MS (EI) *m/z*: 221 (M^+), 164 (M^+−*t*-Bu).

Column chromatography (Et_2O/hexane=1/10) of organic layers above including oximes gave (*E*)- and (*Z*)-mesitaldehyde oximes in 51% (26 mg) and 22% (11 mg) yields, respectively. (*E*)-oxime: colorless prisms of mp 126–127 °C.[33] ^1H NMR: 2.29 (3H, s), 2.38 (6H, s), 6.89 (2H, s), 8.00 (1H, br s), 8.42 (1H, s). ^{13}C NMR: 21.01, 21.04, 126.4, 129.4, 137.6, 138.9, 150.0. IR (Nujol): 3252, 1609. MS (EI) *m/z*: 163 (M^+), 146 (M^+-OH). (*Z*)-oxime: colorless needles of mp 178–179 °C.[33] ^1H NMR: 2.25 (6H, s), 2.29 (3H, s), 6.89 (2H, s), 7.62 (1H, s), 8.17 (1H, br s). ^{13}C NMR: 19.7, 21.0, 128.1, 135.7, 138.7, 149.0. IR (Nujol): 3209, 1612. MS (EI) *m/z*: 163 (M^+), 146 (M^+-OH).

4.1.24. (−)-*tert*-Butyl (*S*)-*N*-(benzyloxycarbonyl)-3-aminobutanoate (Cbz-6b).[28] To a solution of a crude imine in a 1:1 mixture of THF and water, hydroxylamine hydrochloride was added. After the mixture was stirred for 20 min at rt, sodium bicarbonate and CbzCl were added. After stirring for 16 h, to the mixture was added satd ammonium chloride and satd sodium bicarbonate (5 mL). The mixture was extracted with AcOEt, and organic layers were washed with brine and then dried over sodium sulfate. Concentration and column chromatography (Et_2O/hexane=1/15, then acetone/hexane=1/10) gave Cbz-**6b** (67% yield) as a colorless oil of $[\alpha]_D^{20}$ −11.0 (*c* 1.05, CH_2Cl_2). ^1H NMR: 1.23 (3H, d, *J*=6.8), 1.44 (9H, s), 2.42 (2H, d, *J*=5.8), 4.08 (1H, qt, *J*=6.8, 5.8), 5.09 (2H, s), 5.26 (1H, br s), 7.29–7.36 (5H, m). ^{13}C NMR: 20.2, 27.9, 41.6, 44.1, 66.3, 80.9, 128.0, 128.4, 136.6, 155.5, 170.7. IR (neat): 1724. MS (EI) *m/z*: 293 (M^+), 237 (M^+-t-Bu).

4.1.25. (+)-*tert*-Butyl 3-amino-4-methylpentanoate (6c). Column chromatography (AcOEt/MeOH=10/1) gave **6c** as a colorless oil of $[\alpha]_D^{25}$ +19.1 (*c* 0.68, $CHCl_3$) in 72% yield. ^1H NMR: 0.91 and 0.92 (each 3H, d, *J*=6.7), 1.46 (9H, s), 1.50 (2H, br s), 1.62 (1H, dqq, *J*=4.5, 6.7, 6.7), 2.15 (1H, dd, *J*=9.8, 15.3), 2.38 (1H, dd, *J*=3.7, 15.3), 2.98 (1H, ddd, *J*=3.7, 4.5, 9.8). ^{13}C NMR: 17.7, 18.7, 28.1, 33.3, 40.9, 53.6, 80.4, 172.6. IR (neat): 3387, 1728, 1153. MS (FAB) *m/z*: 188 (M^++H). HRMS (FAB) *m/z*: calcd for $C_{10}H_{21}NO_2$+H: 188.1651. Found: 188.1659.

4.1.26. (−)-*tert*-Butyl 3-amino-4-hexenoate (6d). Column chromatography (AcOEt/MeOH=10/1) gave **6d** as a colorless oil of $[\alpha]_{405}^{25}$ −13.8 (*c* 0.93, MeOH) in 76% yield. ^1H NMR: 1.45 (9H, s), 1.61 (2H, br s), 1.67 (3H, d, *J*=6.4), 2.30 (1H, dd, *J*=8.3, 15.3), 2.37 (1H, dd, *J*=4.9, 15.3), 3.70 (1H, ddd, *J*=4.9, 7.1, 8.3), 5.44 (1H, dd, *J*=7.1, 15.3), 5.61 (1H, dq, *J*=15.3, 6.4). ^{13}C NMR: 17.6, 28.1, 43.8, 50.6, 80.5, 125.3, 134.4, 171.5. IR (neat): 3375, 1728, 1153. MS (EI) *m/z*: 185 (M^+), 128 (M^+-t-Bu). HRMS (EI) *m/z*: calcd for $C_{10}H_{19}NO_2$: 185.1416. Found: 185.1420.

4.1.27. (+)-*tert*-Butyl 3-amino-3-(1-naphthyl)propanoate (6e). Column chromatography (AcOEt/hexane=1/1) gave **6e** as a colorless solid of mp 74–75 °C and $[\alpha]_D^{25}$ +41.3 (*c* 1.09, $CHCl_3$) in 78% yield. ^1H NMR: 1.45 (9H, s), 1.81 (2H, br s), 2.65 (1H, dd, *J*=9.8, 15.9), 2.81 (1H, dd, *J*=3.4, 15.9), 5.24 (1H, dd, *J*=3.4, 9.8), 7.46–7.67 (3H, m), 7.67 (1H, m), 7.77 (1H, m), 7.88 (1H, m), 8.17 (1H, m). ^{13}C NMR: 28.1, 44.6, 48.0, 80.9, 122.7, 122.8, 125.6, 126.2, 127.8, 129.0, 130.6, 133.9, 140.4, 171.7. IR (KBr): 3248, 3167, 1728, 1161. MS (EI) *m/z*: 271 (M^+), 214 (M^+-t-Bu). Anal. Calcd for $C_{17}H_{21}NO_2$: C, 75.25; H, 7.80; N, 5.16. Found: C, 74.99; H, 7.70; N, 5.19.

4.1.28. (−)-*tert*-Butyl (1*R*,2*S*)-2-aminocyclopentane-1-carboxylate (*cis*-6f)[32] from *cis*-5cf. Column chromatography (AcOEt/hexane=1/2) gave *cis*-**6f** as a colorless oil of $[\alpha]_D^{25}$ −1.7 (*c* 0.35, $CHCl_3$) in 12% yield. ^1H NMR: 1.47 (9H, s), 1.50–2.00 (8H, m), 2.70 (1H, m), 3.57 (1H, br s). ^{13}C NMR: 22.3, 26.2, 28.2, 34.8, 51.1, 54.9, 80.3, 173.7. IR (neat): 3383, 1724, 1366, 1153. MS (EI) *m/z*: 185 (M^+).

4.1.29. (+)-*tert*-Butyl (1*S*,2*S*)-2-aminocyclopentane-1-carboxylate (*trans*-6f) from *trans*-5cf. Column chromatography (Et_2O/MeOH=5/1) gave *trans*-**6f** as a colorless oil of $[\alpha]_D^{20}$ +50.8 (*c* 1.15, $CHCl_3$) in 56% yield. ^1H NMR: 1.30–2.05 (8H, m), 1.46 (9H, s), 2.32 (1H, m), 3.39 (1H, m). ^{13}C NMR: 22.5, 28.0, 28.1, 35.1, 54.6, 57.0, 80.2, 174.7. IR (neat): 3368, 1720, 1153. MS (EI) *m/z*: 185 (M^+), 169 (M^+-NH_2), 128 (M^+-t-Bu). HRMS (EI) *m/z*: calcd for $C_{10}H_{19}NO_2$: 185.1416. Found: 185.1407.

4.1.30. Determination of the absolute configuration of *trans*-6f by conversion to (+)-(1*S*,2*S*)-2-aminocyclopentanecarboxylic acid.[32] A solution of *trans*-**6f** (21.6 mg, 0.11 mmol) in trifluoroacetic acid (0.5 mL) was stirred at rt for 12 h. Concentration gave a pale yellow oil. After addition of MeOH (0.5 mL) and 4.7 N HCl in ether (0.5 mL), the mixture was concentrated to give a solid, which was recrystallized from a mixture of EtOH and AcOEt to give (1*S*,2*S*)-2-aminocyclopentanecarboxylic acid (7.2 mg, 40% yield) as colorless needles of mp 146–147 °C and $[\alpha]_D^{25}$ +67.2 (*c* 0.61, H_2O). ^1H NMR (D_2O): 1.73–1.89 (4H, m), 2.18–2.22 (2H, m), 3.00 (1H, m), 3.76 (3H, s), 3.91 (1H, m). ^{13}C NMR (D_2O): 23.6, 29.4, 31.4, 49.2, 55.0, 176.8. IR (KBr): 3445, 2955, 1728. MS (EI) *m/z*: 128 (M^+-HCl), 112 ($M^+-HCl-NH_2$).

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