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Dirhodium(II)-Catalyzed C–H Amination Reaction of (*S*)-3-(*tert*-Butyldimethylsilyloxy)-2-methylpropyl Carbamate: A Facile Preparation of Optically Active Monoprotected 2-Amino-2-methyl-1,3-propanediol

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Dirhodium(II)-catalyzed C–H amination reaction of (*S*)-3-(*tert*-butyldimethylsilyloxy)-2-methylpropyl carbamate, which was easily prepared from methyl (*S*)-2-methyl-3-hydroxypropanoate, proceeded more smoothly than those of their 2-(methoxycarbonyl)propyl derivative to give the corresponding oxazolidinone in excellent yield. The resulting oxazolidinone was converted efficiently into both (*R*)-monoprotected and (*S*)-monoprotected 2-amino-2-methyl-1,3-propanediols.

Key words dirhodium(II); C–H amination; 3-silyloxy-2-methylpropyl carbamate; 2-amino-2-methyl-1,3-propanediol monoether; oxazolidinone

The direct amination of chiral substrates in a stereoselective manner is a simple and straightforward approach for the synthesis of optically active nitrogen-containing compounds. Metal catalyzed C–H amination[1—4] of carbamates and sulfonamides demonstrated by Du Bois' group and the other groups have become a powerful tool for this purpose in recent synthetic organic chemistry. In our recently reported stereoselective total synthesis of an immunomodulator (+)-conagenin,[5,6] we applied dirhodium(II)-catalyzed C–H amination reaction of carbamate (**2**) derived from optically active methyl 2-methyl-3-hydroxypropanoate (**1**) to prepare its α-methylserine moiety (**4**) (Chart 1). This method has proved to be a convenient procedure for synthesis of α-methylserine itself because of the short steps and ready availability of the starting material. Chiral α-methylserines have attracted much attention also as important synthetic intermediates of α-methyl-α-amino acids,[7—12] which are an important class of non-proteinogenic amino acids used to increase conformational restrictions in peptides and thereby change their biological activity and stability.[13] For intermediate synthesis of α-methyl-α-amino acids, however, the procedure is not satisfactory because of the only moderate yield of C–H amination reaction of carbamate (**2**). In this context and as a part of our studies on dirhodium(II)-catalyzed reactions,[14—23] we have been interested in the study and development of a more efficient route to α-methylserine derivatives using dirhodium(II)-catalyzed C–H amination reaction of carbamate.

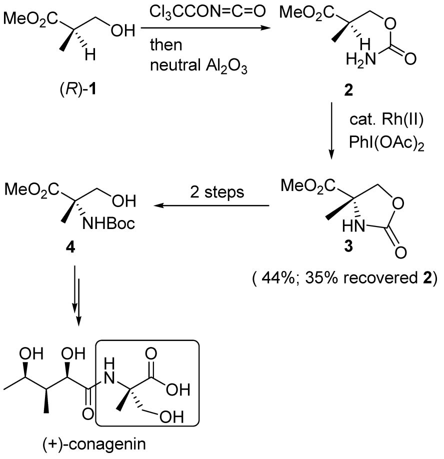

Chart 1

The unsatisfactory result in the reaction of **2** probably results from the low reactivity of C–H bond α to the electron-deficient ester group.[1,2,24] We anticipated that the C–H amination reaction can proceed more smoothly if carbamate has a protected hydroxymethyl group as an alternative to the ester group. The expected resultant oxazolidinone (**7**) should be converted easily into optically active monoprotected 2-amino-2-methyl-1,3-propanediol (**8**), which has proved to be a useful intermediate of α-methyl-α-amino acids.[25—28] Although dirhodium(II)-catalyzed C–H amination reaction of simple alkyl carbamates and carbamates derived from cycloalkanols bearing alkoxy groups[29—31] has been well investigated, little information is available concerning influences of protecting groups of hydroxy group in acyclic system. For those reasons, we examined dirhodium(II)-catalyzed C–H amination reaction of 3-hydroxy-2-methylpropyl carbamates having typical protecting groups (**6**) (Chart 2).

The starting carbamates (**6a**—**d**) were easily prepared using the usual protocol[6] from known alcohols (**5a**—**d**),[32—34] which were all obtainable from (*S*)-**1**. The results of dirhodium(II)-catalyzed C–H amination reactions of **6a**—**d** are summarized in Table 1. Thus, according to our reported prodcedure,[6] treatment of **6a** with 10 mol% of dirhodium(II)

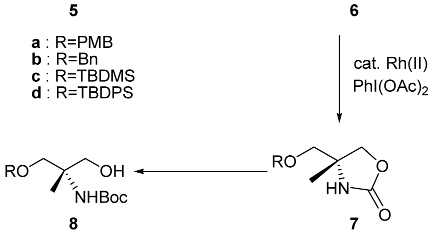

Chart 2

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Table 1. Dirhodium(II)-Catalyzed C–H Amination of Carbamates (**6**)[a]

Entry	**6**	Rh(II)	Solvent	Yield of **7** (%)	Recovery of **6** (%)	Yield based on comsumed **6** (%)
1	**a**	$Rh_2(OAc)_4$	CH_2Cl_2	28	22	36
2	**b**	$Rh_2(OAc)_4$	CH_2Cl_2	32	26	43
3	**c**	$Rh_2(OAc)_4$	CH_2Cl_2	63	31	91
4	**d**	$Rh_2(OAc)_4$	CH_2Cl_2	24	57	56
5[b]	**c**	$Rh_2(OAc)_4$	CH_2Cl_2	59	16	70
6	**c**	$Rh_2(OAc)_4$	$CHCl_3$	20	20	25
7	**c**	$Rh_2(OAc)_4$	$(CH_2Cl)_2$	35	0	35
8	**c**	$Rh_2(oct)_4$	CH_2Cl_2	54	30	77
9	**c**	$Rh_2(tpa)_4$	CH_2Cl_2	57	22	73
10	**c**	$Rh_2(esp)_2$	CH_2Cl_2	67	2	69

a) The reaction was carried out using 10 mol% of Rh(II) catalyst, 4.2 eq of $PhI(OAc)_2$, and 6.9 eq of MgO under reflux for 17 h. *b*) The reaction was heated for 40 h.

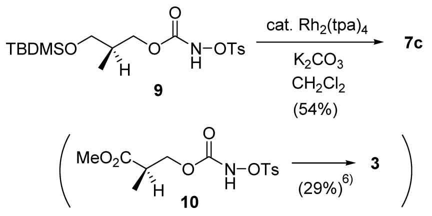

Chart 3

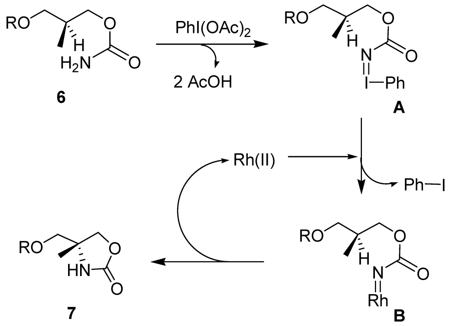

Chart 4

tetraacetate, 4.2 eq of phenyliodine(III) diacetate, and 6.9 eq of magnesium oxide in dichloromethane under reflux for 17 h gave the corresponding C–H amination product **7a** in 28% yield along with 22% of recovered **6a** and a complicated mixture (entry 1). A similar reaction of **6b** gave **7b** in 32% yield with 26% of **6b** (entry 2). However, reaction of TBDMS ether (**6c**) afforded 63% of **7c** along with 31% of **6c** (91% yield based on the consumed **6c**, entry 3). Reaction of TBDPS ether (**6d**) proceeded slowly to provide **7d** in 24% yield (entry 4). Because the TBDMS group is the most suitable protecting group among the examined groups, we next sought to optimize the reaction conditions. Unfortunately, we observed no better result than that shown in entry 3, although the starting **6c** was not completely consumed. Consequently, longer reaction time was ineffective (entry 5). Reactions at higher temperatures decreased the yield of **7c** and recovery of **6c** (entries 6, 7). Slightly lower yields were obtained in the reactions using dirhodium(II) tetraoctanoate [$Rh_2(oct)_4$] and dirhodium(II) tetrakis(triphenylacetate) [$Rh_2(tpa)_4$] (entries 8, 9). When **6c** was reacted with dirhodium(II) bis($\alpha,\alpha,\alpha',\alpha'$-tetramethyl-1,3-benzenedipropanoate) [$Rh_2(esp)_2$],[35] which gave the best result in the reaction of ester **2**,[6] **7c** was obtained in the highest yield (67%). However, recovery of the starting **6c** was only 2%; therefore, the yield based on the consumed **6c** was calculated as 69% (entry 10).

Alternatively, we examined the C–H amination of tosyloxycarbamate (**9**), which was prepared from **5c** according to Lebel's procedure[36] (Chart 3). The C–H amination reaction proceeded more smoothly than that of ester derivative (**10**)[6] when **9** was treated with $Rh_2(tpa)_4$ in the presence of potassium carbonate in dichloromethane at room temperature to give oxazolidinone (**7c**) in 54% yield (29% for **10**). In this reaction, the starting **9** was consumed completely.

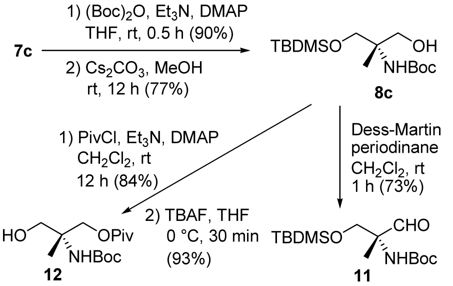

Chart 5

A possible reaction mechanism for C–H amination of **6** is shown in Chart 4.[2] Carbamate (**6**) is first oxidized with $PhI(OAc)_2$ to form iodonium ylide (**A**), which is transformed to rhodium nitrenoid (**B**) with elimination of iodobenzene. The nitrogen atom is inserted stereospecifically to the methine C–H bond with release of Rh(II) species, which can be reused to form **B**, to give oxazolidinone (**7**). The electron-donating silyloxymethyl group in **6c** would enhance the reactivity of C–H bond at its α-position against the electrophilic rhodium nitrenoid, on the other hand, the electron-deficient ester group of **2** would decrease the reactivity of α C–H bond.[1,2,24] In the reactions of PMB and benzyl ethers (**6a**, **b**), oxidations of PMB and benzyl groups by $PhI(OAc)_2$[37—40] might occur as side reactions to produce complex mixtures and to give low yields of oxazolidinones (**7a**, **b**). The bulky TBDPS group might decrease the reactivity of C–H group by steric hindrance to cause low yield.

Application to the preparation of the optically active monoprotected 2-amino-2-methyl-1,3-propanediol was investigated (Chart 5). The NH group of oxazolidinone (**7c**) was protected with *tert*-butoxycarbonyl (Boc) group in 90%

yield, followed by oxazolidinone ring opening by treatment with cesium carbonate in methanol[41] to give optically active (*S*)-2-(Boc)amino-2-methyl-3-TBDMSoxypropanol (**8c**) in 77% yield. Dess–Martin oxidation of **8c** proceeded smoothly to provide the corresponding aldehyde (**11**) in 73% yield. On the other hand, **8c** was acylated with pivaloyl chloride and desilylated to afford the known (*R*)-2-(Boc)amino-2-methyl-3-pivaloyloxypropanol (**12**),[42] $[\alpha]_D^{28}$ −8.71°(c=1.26, $CHCl_3$) {lit.[42] $[\alpha]_D^{25}$ −8.6° (c=0.90, $CHCl_3$)}. Optical purity of **12** was determined to be 92.4% ee by chiral HPLC analysis using Daicel Chiralpak OF (hexane/^{i}PrOH, 70/30, 0.4 ml/min). This result reveals that the dirhodium(II)-catalyzed C–H amination of **6c** proceeded with retention of the configuration.[1,6]

In summary, we showed that dirhodium(II)-catalyzed C–H amination reaction of 3-(TBDMSoxy)-2-methylpropyl carbamate (**6c**) proceeded more smoothly than those of ester derivative (**2**) to give the corresponding oxazolidinone (**7c**) in excellent yield. The resulting oxazolidinone was converted efficiently into the optically active monoprotected 2-amino-2-methyl-1,3-propanediols (**8c**, **12**).

Experimental

Melting points are uncorrected. IR spectra were recorded using JASCO FT/IR-460 Plus spectrophotometer. ^{1}H-NMR spectra were determined with Varian Gemini 300 (300 MHz) and JEOL JNM-FX270 (270 MHz) spectrometers, tetramethylsilane as an internal standard. ^{13}C-NMR spectra were determined with Varian Gemini 300 (75 MHz) and JEOL JNM-FX270 (67.5 MHz) spectrometers. All ^{13}C-NMR spectra were determined with complete proton decoupling. High resolution MS were determined with JEOL JMS-GCmate and JEOL JMS-AX505HAD instruments. Optical rotations were measured with JASCO DIP-1000 polarimeter. Column chromatography was performed on Silica Gel 60 PF_{254} (Nacalai Tesque) under pressure. Methyl (*S*)-3-hydroxy-2-methylpropanoate [(*S*)-**1**] was provided by Mitsubishi Rayon Co., Ltd. The known alcohols (**5a**,[32] **5b**,[33] **5c**,[34] **5d**[34]) were prepared from (*S*)-**1** according to the reported procedures.

General Procedure for the Preparation of Carbamates (6a—d) Trichloroacetyl isocyanate (1.1—1.2 eq) was added to a solution of alcohol (**5**) (1.0 eq) in dichloromethane at room temperature under a nitrogen atmosphere and the mixture was stirred for 1 h. Then a mixture was passed through a short neutral Al_2O_3 column with ethyl acetate and the mixture was concentrated. The residue was chromatographed on silica gel to give pure **6**. The following compounds were thus obtained.

(*S*)-3-(*p*-Methoxybenzyloxy)-2-methylpropyl Carbamate (6a) According to the general procedure, **5a**[32] (99 mg, 0.47 mmol) was treated with trichloroacetyl isocyanate (107 mg, 0.55 mmol) in dichloromethane (5 ml) and crude material was chromatographed on silica gel (30% EtOAc in hexane) to give **6a** (111 mg, 94%) as colorless crystals, mp 47—49 °C (EtOAc–hexane). $[\alpha]_D^{28}$ +2.19°(c=0.97, $CHCl_3$). IR (KBr) cm^{-1}: 3411, 1688, 1612, 1513. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 0.96 (3H, d, J=6.6 Hz), 2.10 (1H, octet, J=6.4 Hz), 3.31 (1H, dd, J=9.2, 5.9 Hz), 3.37 (1H, dd, J=9.2, 6.6 Hz), 3.80 (3H, s), 3.98 (1H, dd, J=10.5, 6.3 Hz), 4.07 (1H, dd, J=10.6, 5.9 Hz), 4.42 (2H, s), 4.78 (2H, br s), 6.86 (2H, d, J=8.6 Hz), 7.25 (2H, d, J=8.6 Hz). ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ: 14.0, 33.6, 55.2, 67.2, 71.8, 72.7, 113.7 (2), 129.1 (2), 130.5, 157.1, 159.1. *Anal.* Calcd for $C_{13}H_{19}NO_4$: C, 61.64; H, 7.56; N, 5.53. Found: C, 61.73; H, 7.67; N, 5.57.

(*S*)-3-Benzyloxy-2-methylpropyl Carbamate (6b) According to the general procedure, **5b**[33] (769 mg, 4.26 mmol) was treated with trichloroacetyl isocyanate (963 mg, 5.12 mmol) in dichloromethane (25 ml) and crude material was chromatographed on silica gel (40% EtOAc in hexane) to give **6b** (952 mg, quant) as colorless crystals, mp 39—41 °C (EtOAc–hexane). $[\alpha]_D^{28}$ +3.37° (c=1.17, $CHCl_3$). IR (KBr) cm^{-1}: 3350, 1715, 1602, 1455. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 0.98 (3H, d, J=6.6 Hz), 2.13 (1H, octet, J=6.5 Hz), 3.36 (1H, dd, J=9.2, 5.9 Hz), 3.41 (1H, dd, J=9.2, 6.6 Hz), 4.00 (1H, dd, J=10.6, 6.3 Hz), 4.09 (1H, dd, J=10.6, 6.3 Hz), 4.50 (2H, s), 4.65 (2H, br s), 7.22—7.40 (5H, m). ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ: 14.0, 33.6, 67.2, 72.2, 73.1, 127.5 (3), 128.3 (2), 138.5, 157.0. *Anal.* Calcd for $C_{12}H_{17}NO_3$: C, 64.55; H, 7.67; N, 6.27. Found: C, 64.36; H, 7.75; N, 6.16.

(*R*)-3-(*tert*-Butyldimethylsilyloxy)-2-methylpropyl Carbamate (6c) According to the general procedure, **5c**[34] (491 mg, 2.4 mmol) was treated with trichloroacetyl isocyanate (542 mg, 2.88 mmol) in dichloromethane (20 ml) and crude material was chromatographed on silica gel (40% EtOAc in hexane) to give **6c** (593 mg, quant) as a colorless oil. $[\alpha]_D^{28}$ +4.03° (c=0.99, $CHCl_3$). IR (neat) cm^{-1}: 3352, 1715, 1603, 1472, 1408. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 0.04 (6H, s), 0.89 (9H, s), 0.93 (3H, d, J=6.9 Hz), 1.96 (1H, octet, J=6.4 Hz), 3.52 (2H, d, J=5.9 Hz), 3.97 (1H, dd, J=10.6, 6.3 Hz), 4.05 (1H, dd, J=10.6, 6.3 Hz), 4.64 (2H, br s). ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ: −5.5 (2), 13.6, 18.3, 25.9 (3), 35.6, 64.7, 67.0, 157.1. HR-MS m/z: 190.08899 (Calcd for $C_7H_{16}NO_3Si$ ($M^+ - {}^t$Bu): 190.08995).

(*R*)-3-(*tert*-Butyldiphenylsilyloxy)-2-methylpropyl Carbamate (6d) According to the general procedure, **5d**[34] (447 mg, 1.36 mmol) was treated with trichloroacetyl isocyanate (307 mg, 1.63 mmol) in dichloromethane (14 ml) and crude material was chromatographed on silica gel (30% EtOAc in hexane) to give **6d** (506 mg, quant) as a colorless oil. $[\alpha]_D^{28}$ −1.28° (c=0.70, $CHCl_3$). IR (neat) cm^{-1}: 3456, 3342, 1717. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 0.96 (3H, d, J=6.9 Hz), 1.05 (9H, s), 2.02 (1H, octet, J=6.3 Hz), 3.58 (2H, d, J=5.3 Hz), 4.04 (1H, dd, J=10.6, 6.3 Hz), 4.11 (1H, dd, J=10.6, 6.6 Hz), 4.66 (2H, br s), 7.32—7.45 (6H, m), 7.60—7.72 (4H, m). ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ: 13.6, 19.3, 26.8 (3), 35.5, 65.2, 66.8, 127.6 (4), 129.6 (2), 133.7 (2), 135.6 (4), 157.1. HR-MS m/z: 314.12079 (Calcd for $C_{17}H_{20}NO_3Si$ ($M^+ - {}^t$Bu): 314.12125).

Dirhodium(II)-Catalyzed C–H Amination of Compound 6a. General Procedure A suspension of **6a** (51 mg, 0.20 mmol), $PhI(OAc)_2$ (273 mg, 0.84 mmol), MgO (57 mg, 1.38 mmol), and $Rh_2(OAc)_4$ (9 mg, 0.02 mmol) in dichloromethane (1.5 ml) was refluxed for 17 h. After the mixture was cooled to room temperature, it was passed through a short Celite pad and the filtrate was concentrated. The residue was chromatographed on silica gel (30% EtOAc in hexane) to give **7a** (14 mg, 28%) and recovered **6a** (11 mg, 22%). (*R*)-4-(*p*-Methoxybenzyloxymethyl)-4-methyloxazolidin-2-one (**7a**) was obtained as a colorless oil. $[\alpha]_D^{26}$ +14.3° (c=1.04, $CHCl_3$). IR (neat) cm^{-1}: 3282, 1754, 1612, 1514. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.34 (3H, s), 3.33 (2H, s), 3.80 (3H, s), 4.00 (1H, d, J=8.5 Hz), 4.23 (1H, d, J=8.5 Hz), 4.47 (2H, s), 5.96 (1H, br s), 6.88 (2H, d, J=8.8 Hz), 7.22 (2H, d, J=8.8 Hz). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 23.2, 55.3, 57.7, 73.1, 73.4, 74.6, 113.8 (2), 129.2 (2), 129.4, 159.0, 159.2. HR-MS m/z: 251.11318 (Calcd for $C_{13}H_{17}NO_4$ (M^+): 251.11576).

Dirhodium(II)-Catalyzed C–H Amination of 6b Following to the general procedure, **6b** (100 mg, 0.45 mmol) was treated with $PhI(OAc)_2$ (606 mg, 1.88 mmol), MgO (125 mg, 3.09 mmol), and $Rh_2(OAc)_4$ (20 mg, 0.044 mmol) in refluxing dichloromethane (3.5 ml) and crude material was chromatographed on silica gel (40% EtOAc in hexane) to give **7b** (32 mg, 32%) and recovered **6b** (26 mg, 26%). (*R*)-4-Benzyloxymethyl-4-methyloxazolidin-2-one (**7b**) was obtained as a colorless oil. $[\alpha]_D^{26}$ +13.5° (c=0.93, $CHCl_3$). IR (neat) cm^{-1}: 3277, 1753. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 1.37 (3H, s), 3.37 (2H, s), 4.01 (1H, d, J=8.9 Hz), 4.24 (1H, d, J=8.6 Hz), 4.55 (2H, s), 5.76 (1H, br s), 7.24—7.41 (5H, m). ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ: 23.1, 57.7, 73.3, 73.5, 75.0, 127.6 (2), 127.9, 128.5 (2), 137.4, 159.0. HR-MS m/z: 221.10376 (Calcd for $C_{12}H_{15}NO_3$ (M^+): 221.10520).

Dirhodium(II)-Catalyzed C–H Amination of 6c Following to the general procedure, **6c** (51 mg, 0.21 mmol) was treated with $PhI(OAc)_2$ (279 mg, 0.86 mmol), MgO (58 mg, 1.42 mmol), and $Rh_2(OAc)_4$ (9 mg, 0.021 mmol) in refluxing dichloromethane (1.6 ml) and crude material was chromatographed on silica gel (10% EtOAc in hexane) to give **7c** (32 mg, 63%) and recovered **6c** (16 mg, 31%). (*S*)-4-(*tert*-Butyldimethylsilyloxymethyl)-4-methyloxazolidin-2-one (**7c**) was obtained as colorless crystals, mp 75—78 °C. $[\alpha]_D^{28}$ +11.4° (c=1.04, $CHCl_3$). IR (KBr) cm^{-1}: 3347, 1720. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 0.08 (6H, s), 0.91 (9H, s), 1.34 (3H, s), 3.51 (2H, s), 4.01 (1H, d, J=8.6 Hz), 4.27 (1H, d, J=8.2 Hz), 5.95 (1H, br s). ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ: −5.6 (2), 18.1, 22.5, 25.7 (3), 58.6, 68.4, 73.0, 159.3. *Anal.* Calcd for $C_{11}H_{23}NO_3Si$: C, 53.84; H, 9.45; N, 5.71. Found: C, 53.73; H, 9.35; N, 5.68.

Dirhodium(II)-Catalyzed C–H Amination of 6d Following to the general procedure, **6d** (70 mg, 0.19 mmol) was treated with $PhI(OAc)_2$ (254 mg, 0.79 mmol), MgO (52 mg, 1.3 mmol), and $Rh_2(OAc)_4$ (8 mg, 0.019 mmol) in refluxing dichloromethane (1.4 ml) and crude material was chromatographed on silica gel (10% EtOAc in hexane) to give **7d** (17 mg, 24%) and recovered **6d** (40 mg, 57%). (*S*)-4-(*tert*-Butyldiphenylsilyloxymethyl)-4-methyloxazolidin-2-one (**7d**) was obtained as colorless crystals, mp 103—105 °C. $[\alpha]_D^{29}$ +6.74° (c=0.68, $CHCl_3$). IR (KBr) cm^{-1}: 3855, 1725. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 1.06 (9H, s), 1.33 (3H, s), 3.32 (1H, d, J=10.3 Hz), 3.71 (1H, d, J=10.3 Hz), 4.01 (1H, d, J=8.6 Hz), 4.26 (1H, d, J=8.6 Hz), 5.27 (1H, br s), 7.36—7.50 (6H, m), 7.60—7.70 (4H, m). ^{13}C-NMR (67.5 MHz, $CDCl_3$) δ:

19.2, 22.8, 26.8 (3), 58.7, 69.0, 73.0, 127.9 (4), 130.02, 130.05, 132.5 (2), 135.52 (2), 135.59 (2), 158.8. HR-MS *m*/*z*: 312.10686 (Calcd for $C_{17}H_{18}NO_3Si$ ($M^+-{}^tBu$): 312.10560).

(*R*)-3-(*tert*-Butyldimethylsilyloxy)-2-methylpropyl *p*-Toluenesulfonyloxycarbamate (9) According to the reported procedures,[36] **5c** (240 mg, 1.17 mmol) was slowly added to a solution of 1,1′-carbonyldiimidazole (285 mg, 1.76 mmol) in THF (11 ml) and the resulting mixture was stirred at room temperature for 2 h. The mixture was diluted with EtOAc. The solution was washed with saturated aqueous NH_4Cl, water, and brine, dried ($MgSO_4$) and concentrated. The product was dissolved in pyridine (6 ml), hydroxylamine hydrochloride (245 mg, 3.52 mmol) was added and the resulting mixture was stirred at room temperature for 4 h. Most of the pyridine was removed under reduced pressure and the residue was dissolved in EtOAc. The mixture was washed with 10% aqueous HCl, saturated aqueous $NaHCO_3$, water, and brine, dried ($MgSO_4$) and concentrated. The residue was chromatographed on silica gel (15% EtOAc in hexane) to give *N*-hydroxycarbamate (222 mg, 72%) as a colorless oil, which was used in the next step without further purification. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.04 (6H, s), 0.89 (9H, s), 0.92 (3H, d, *J*=6.9 Hz), 1.65 (1H, br s), 1.92—2.05 (1H, m), 3.49 (1H, dd, *J*=9.9, 6.0 Hz), 3.53 (1H, dd, *J*=9.9, 5.5 Hz), 4.07 (1H, dd, *J*=10.4, 6.0 Hz), 4.16 (1H, dd, *J*=10.4, 6.3 Hz), 6.35 (1H, br s). *p*-Toluenesulfonyl chloride (370 mg, 1.94 mmol) was added to a solution of *N*-hydroxycarbamate (465 mg, 1.76 mmol) in Et_2O (18 ml) at 0 °C. Triethylamine (232 mg, 2.29 mmol) was then added slowly and the resulting white suspension was stirred at room temperature for 12 h. The mixture was diluted with Et_2O. The solution was washed with water, and brine, dried ($MgSO_4$) and concentrated. The residue was chromatographed on silica gel (20% EtOAc in hexane) to give **9** (313 mg, 43%) as a colorless oil. $[\alpha]_D^{26}$ +4.39° (*c*=1.14, $CHCl_3$). IR (neat) cm^{-1}: 3278, 1742, 1598, 1471. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.01 (6H, s), 0.81 (3H, d, *J*=6.9 Hz), 0.86 (9H, s), 1.84 (1H, octet, *J*=6.3 Hz), 2.44 (3H, s), 3.39 (1H, dd, *J*=9.9, 6.3 Hz), 3.45 (1H, dd, *J*=10.2, 5.2 Hz), 3.93 (1H, dd, *J*=10.4, 6.0 Hz), 4.03 (1H, dd, *J*=10.4, 6.0 Hz), 7.34 (2H, d, *J*=8.0 Hz), 7.86 (2H, d, *J*=8.2 Hz), 8.11 (1H, br d, *J*=4.4 Hz). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: −5.4 (2), 13.3, 18.3, 21.8, 25.9 (3), 35.3, 64.1, 68.8, 129.3 (2), 129.6 (2), 130.2, 145.9, 155.6. HR-MS *m*/*z*: 418.17675 (Calcd for $C_{18}H_{32}NO_6SSi$ (M^++H): 418.17196).

Dirhodium(II)-Catalyzed C–H Amination of 9 According to the reported procedures,[36] a white suspension of **9** (91 mg, 0.22 mmol), potassium carbonate (90 mg, 0.65 mmol), and $Rh_2(tpa)_4$ (18 mg, 0.012 mmol) in dichloromethane (2 ml) was stirred at room temperature for 5 h. The mixture was filtered through a celite pad and the filtrate was concentrated. The residue was chromatographed on silica gel (30% EtOAc in hexane) to give **7c** (29 mg, 54%), whose spectroscopic data were identical with those of the sample prepared from **6c**.

3-*tert*-Butyl (*S*)-4-(*tert*-Butyldimethylsilyloxymethyl)-4-methyl-2-oxooxazolidine-3-carboxylate A mixture of **7c** (125 mg, 0.51 mmol), $(Boc)_2O$ (223 mg, 1.02 mmol), triethylamine (181 mg, 1.78 mmol), and DMAP (13 mg, 0.1 mmol) in THF (5 ml) was stirred at room temperature under a nitrogen atmosphere for 30 min. The mixture was diluted with Et_2O. The solution was washed with saturated aqueous NH_4Cl, water, and brine, dried ($MgSO_4$) and concentrated. The residue was chromatographed on silica gel (10% EtOAc in hexane) to give the titled compound (158 mg, 90%) as a colorless oil. $[\alpha]_D^{28}$ −17.5° (*c*=0.96, $CHCl_3$). IR (neat) cm^{-1}: 1817, 1790, 1725. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.05 (3H, s), 0.06 (3H, s), 0.88 (9H, s), 1.45 (3H, s), 1.55 (9H, s), 3.50 (1H, d, *J*=10.2 Hz), 3.86 (1H, d, *J*=8.2 Hz), 4.02 (1H, d, *J*=10.2 Hz), 4.31 (1H, d, *J*=8.2 Hz). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: −5.5, −5.4, 18.1, 20.9, 25.7 (3), 28.1 (3), 62.4, 65.6, 70.9, 83.6, 149.5, 152.7. HR-MS *m*/*z*: 345.19706 (Calcd for $C_{16}H_{31}NO_5Si$ (M^+): 345.19715).

(*S*)-2-(*tert*-Butoxycarbonylamino)-3-(*tert*-butyldimethylsilyloxy)-2-methylpropanol (8c) A mixture of 3-*tert*-butyl (*S*)-4-(*tert*-butyldimethylsilyloxymethyl)-4-methyl-2-oxooxazolidine-3-carboxylate (28 mg, 0.081 mmol) and Cs_2CO_3 (40 mg, 0.12 mmol) in MeOH (0.8 ml) was stirred at room temperature for 12 h. The mixture was diluted with Et_2O. The solution was washed with saturated aqueous NH_4Cl, water, and brine, dried ($MgSO_4$) and concentrated. The residue was chromatographed on silica gel (30% EtOAc in hexane) to give **8c** (20 mg, 77%) as a colorless oil. $[\alpha]_D^{27}$ −4.97° (*c*=1.74, $CHCl_3$). IR (neat) cm^{-1}: 3600—3300, 1719, 1697. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.08 (6H, s), 0.90 (9H, s), 1.18 (3H, s), 1.44 (9H, s), 3.55 (1H, dd, *J*=11.5, 8.5 Hz), 3.61 (1H, d, *J*=9.9 Hz), 3.70 (1H, dd, *J*=11.5, 4.4 Hz), 3.77 (1H, d, *J*=9.9 Hz), 4.04 (1H, br s), 5.14 (1H, br s). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: −5.45, −5.40, 18.3, 19.6, 25.9 (3), 28.5 (3), 56.6, 67.7, 69.2, 79.5, 155.7. HR-MS *m*/*z*: 320.22583 (Calcd for $C_{15}H_{34}NO_4Si$ (M^++H): 320.22571).

(*R*)-2-(*tert*-Butoxycarbonylamino)-3-(*tert*-butyldimethylsilyloxy)-2-methylpropanal (11) A mixture of **8c** (30 mg, 0.094 mmol) and Dess–Martin periodinane (68 mg, 0.16 mmol) in CH_2Cl_2 (1 ml) was stirred at room temperature for 1 h. The mixturewas diluted with Et_2O, the whole was washed with saturated aqueous $Na_2S_2O_3$, saturated aqueous $NaHCO_3$, and brine, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel (30% EtOAc in hexane) to give **11** (22 mg, 73%) as a colorless oil. $[\alpha]_D^{27}$ +16.0° (*c*=1.27, $CHCl_3$). IR (neat) cm^{-1}: 3370, 1737, 1715. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.043 (3H, s), 0.048 (3H, s), 0.88 (9H, s), 1.34 (3H, s), 1.45 (9H, s), 3.80 (2H, br s), 5.30 (1H, br s), 9.48 (1H, s). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: −5.47, −5.44, 17.2, 18.3, 25.8 (3), 28.4 (3), 63.6, 64.5, 80.0, 154.8, 200.5. HR-MS *m*/*z*: 317.20019 (Calcd for $C_{15}H_{31}NO_4Si$ (M^+): 317.20224).

(*S*)-2-*tert*-Butoxycarbonylamino-3-(*tert*-butyldimethylsilyloxy)-2-methylpropyl 2,2-Dimethylpropanoate A mixture of **8c** (65 mg, 0.20 mmol), pivaloyl chloride (37 mg, 0.3 mmol), triethylamine (31 mg, 0.3 mmol), and DMAP (13 mg, 0.1 mmol) in CH_2Cl_2 (2 ml) was stirred at room temperature for 12 h. The mixture was diluted with EtOAc, the whole was washed with saturated aqueous Na_2CO_3, water, and brine, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel (5% EtOAc in hexane) to give the titled compound (69 mg, 84%) as a colorless oil. $[\alpha]_D^{27}$ +1.95° (*c*=1.18, $CHCl_3$). IR (neat) cm^{-1}: 3381, 1727, 1496. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.05 (6H, s), 0.89 (9H, s), 1.21 (9H, s), 1.31 (3H, s), 1.43 (9H, s), 3.54 (1H, d, *J*=9.6 Hz), 3.62 (1H, d, *J*=9.6 Hz), 4.10 (1H, d, *J*=10.7 Hz), 4.22 (1H, d, *J*=10.7 Hz), 4.77 (1H, s). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: −5.4 (2), 18.3, 19.1, 25.9 (3), 27.3 (3), 28.5 (3), 38.9, 55.6, 65.2, 65.6, 79.2, 154.5, 177.8. HR-MS *m*/*z*: 404.28450 (Calcd for $C_{20}H_{42}NO_5Si$ (M^++H): 404.28322).

(*R*)-2-*tert*-Butoxycarbonylamino-3-hydroxy-2-methylpropyl 2,2-Dimethylpropanoate (12) A ether solution of tetrabutylammonium fluoride (1.0 mol/l, 0.1 ml, 0.1 mmol) was added to a solution of (*S*)-2-*tert*-butoxycarbonylamino-3-(*tert*-butyldimethylsilyloxy)-2-methylpropyl 2,2-dimethylpropanoate (30 mg, 0.074 mmol) in THF (1 ml) under a nitrogen atmosphere at 0 °C and the resulting mixture was stirred at the same temperature for 30 min. The mixture was diluted with EtOAc. The solution was washed with saturated aqueous NH_4Cl, water, and brine, dried ($MgSO_4$) and concentrated. The residue was chromatographed on silica gel (25% EtOAc in hexane) to **12** (20 mg, 93%) as colorless crystals, mp: 108—109 °C (lit.[42] mp 106—107 °C). $[\alpha]_D^{28}$ −8.71° (*c*=1.26, $CHCl_3$) {lit.[42] $[\alpha]_D^{25}$ −8.6° (*c*=0.90, $CHCl_3$)}. IR (KBr) cm^{-1}: 3273, 1728, 1681. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.22 (9H, s), 1.26 (3H, s), 1.43 (9H, s), 3.55 (1H, dd, *J*=11.9, 7.1 Hz), 3.61 (1H, dd, *J*=11.9, 6.6 Hz), 3.90 (1H, br s), 4.20 (1H, d, *J*=11.1 Hz), 4.25 (1H, d, *J*=11.1 Hz), 4.86 (1H, br s). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 20.2, 27.2 (3), 28.4 (3), 39.0, 56.4, 65.7, 67.1, 80.0, 155.5, 178.5. HPLC (Daicel Chiralpak OF (0.46×25 cm); hexane/^{i}PrOH, 70/30; flow rate 0.4 ml/min; UV 220 nm): (*S*)-**12**: t_R 10.30 min (3.8%); (*R*)-**12**, t_R 11.83 min (96.2%).

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