A Facile Synthesis of Optically Pure Amines by Reduction of *N*-Acyl-α-methoxyalkylamines Derived from α-Amino Acids Using Triethylsilane

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Optically pure amines were synthesized effectively by Lewis acid-catalyzed triethylsilane reduction of *N*-acyl-α-methoxyalkylamines which were readily obtained by anodic oxidation of *N*-acyl-α-amino acids. This method was also applied to the conversion of an *N*-acylpeptide into the corresponding optically pure amine derivative.

Keywords optically pure amine; triethylsilane; decarboxylation; α-amino acid; anodic oxidation; reduction; α-methoxyalkylamine

Optically active amines have recently attracted much attention as versatile building blocks[1] and chiral auxiliaries.[2] Decarboxylation of α-amino acids having an asymmetric center in the side chain such as isoleucine and threonine and of peptides is a most straightforward method for the preparation of optically active amines. However, difficulty is frequently encountered in the decarboxylation of α-amino acids and peptides, for which drastic conditions are usually required.[3,4] Recently, effective methods for the decarboxylation of α-amino acids and their derivatives have been reported based on the photochemical reductive decarboxylation of *N*-protected α-amino acid *N*-hydroxypyridine-2-thione esters[5] and thermal decarboxylation of α-amino acids in the presence of cyclohexenone.[6]

On the other hand, it is well known that anodic decarboxylation[7,8] is quite effective for the conversion of *N*-acyl-α-amino acids into the *N*-acyl-α-methoxyalkylamines. Thus, for the synthesis of optically pure amines we require the reductive removal of the methoxyl group from *N*-acetyl-α-methoxyalkylamines. Recently, Shono *et al.*[9] reported the successful preparation of 5-substituted *N*-acylpiperidine by the reduction of 5-substituted *N*-acyl-2-methoxypiperidine[10] using a large excess of $NaBH_4$. However, an effective method for the reductive cleavage of *N*-acyl-α-methoxyalkylamines has not yet been reported.

We herein wish to report a facile synthesis of optically pure amines by Lewis acid-catalyzed triethylsilane (Et_3SiH) reduction[11a,b] of *N*-acyl-α-methoxyalkylamines, which were obtained by anodic oxidation of *N*-acyl-α-amino acids. The extension of this method to the decarboxylation of a peptide is also described.

Anodic oxidation of *N*-acetyl-L-isoleucine (**1a**) in MeOH containing a catalytic amount of NaOMe at 10—15 °C at a constant current with graphite electrodes gave (2*R*)-*N*-acetyl-1-methoxy-2-methylbutylamine (**2a**) in 96% yield (Chart 1). In a similar way, the other *N*-acyl-α-amino acids **1b**—**e** were converted to the corresponding *N*-acyl-α-methoxyalkylamines **2b**—**e** in almost quantitative yields. In addition, anodic oxidation of the peptide **1f** resulted in the corresponding methoxylated compound **2f** in 86% yield.

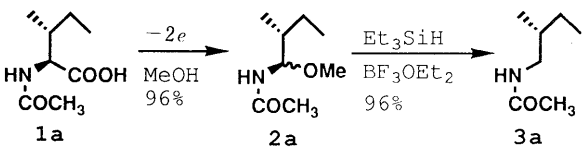


Chart 1

The results are shown in Table I. The electrolysis products **2a**—**f** were obtained as mixtures of two diastereomers,[12,13] and were used in the next step without further separation.

We next examined the Lewis acid-catalyzed Et_3SiH reduction of the *N*-acyl-α-methoxyalkylamines obtained above. As a result, $BF_3 \cdot OEt_2$ was found to be a good catalyst for the reduction.[11a] Thus, the reduction of the methoxylated compound **2a** was carried out by use of Et_3SiH–$BF_3 \cdot OEt_2$ at 5 °C (method A), affording (2*R*)-*N*-acetyl-2-methylbutylamine (**3a**) in 96% yield (Chart 1). Under similar conditions, **2b** and **2f** were converted to **3b** and **3f** in 84% and 89% yields, respectively. In the reduction of **2c**, **2d**, and **2e** having acid-labile *tert*-butyldimethylsilyl (TBDMS) and *tert*-butoxycarbonyl(Boc) protecting groups, the reactions were carried out below −40 °C to give the desired products (method B). Trifluoroacetic acid (TFA)–Et_3SiH (method C)[11b,14] could also be employed for the reduction of **2b** and **2f** to afford **3b** and **3f**, respectively in satisfactory yields. However, in the case of **2c**, desilylation occurred together with the formation of the desired reduction product **3c**. These results are summarized in Table I.

The reduction of *N*-acyl-α-methoxyalkylamines described above presumably involves hydride transfer from silicon to the *N*-acyliminium ion and/or *N*-acylimine[15,16] which are formed under the Lewis acid-catalyzed conditions.

During the transformation, no epimerization took place at all at the asymmetric centers in the side chains; this was confirmed by the conversion of **3c** and **3e** into the known (2*R*)-(−)-hydroxypropylamine and (3*R*)-(−)-hydroxypyrrolidine, respectively.[6]

This method involving anodic oxidation and Et_3SiH reduction will provide a useful approach for the synthesis of optically pure amines from *N*-acyl-α-amino acids and peptides.

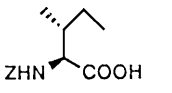
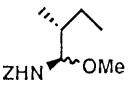
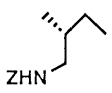
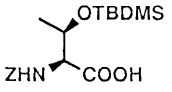
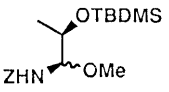
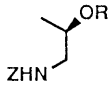
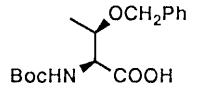
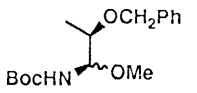
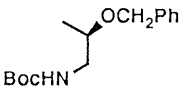
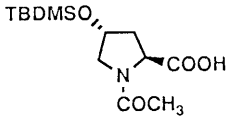
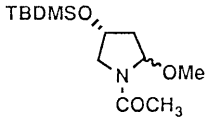
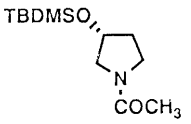
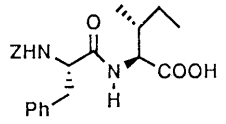
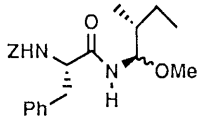
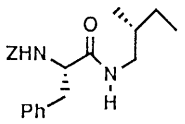
Experimental

All melting points are uncorrected. Infrared (IR) spectra were recorded on a Shimadzu IR-420 infrared spectrophotometer. ^{1}H-Nuclear magnetic resonance (^{1}H-NMR) spectra were taken at 200 MHz on a Bruker AC-200 spectrometer with tetramethylsilane (TMS) as an internal reference. Mass spectra (MS) were obtained with a Hitachi M-60 instrument. Optical rotations were measured by the use of a Perkin–Elmer model 243 polarimeter with a 1 cm^3 capacity (10 cm path length) quartz cell. The electrolyses were carried out by the use of a Hokuto Potentio-Galvanostat (10 A—100 V) coupled to Hokuto HA-108A coulomb meter.

Starting Materials Compounds **1a**—**e** were obtained from the corresponding α-amino acids by the usual methods.[17]

A Typical Electrolysis Procedure A solution of **1a** (20 mmol) in MeOH

TABLE I. Anodic Oxidation of **1b—f** and Et_3SiH Reduction of **2b—f**

N-Acyl-α-amino acid	*N*-Acyl-α-methoxyalkylamine	Yield (%)	*N*-Acylamine	Method[a]	Yield (%)
 **1b**[b]	 **2b**	98	 **3b**	A C	84 75
 **1c**[b]	 **2c**	96	 **3c** (R = TBDMS) **3c'** (R = H)	B C	88 42 (**3c**) 51 (**3c'**)
 **1d**[b]	 **2d**	98	 **3d**	B	98
 **1e**	 **2e**	97	 **3e**	B	96
 **1f**	 **2f**	86	 **3f**	A C	89 87

a) Method A, Et_3SiH–$BF_3 \cdot OEt_2$ at 5 °C; method B, Et_3SiH–$BF_3 \cdot OEt_2$ at −40 °C; method C, Et_3SiH–TFA at room temperature. *b*) Z = benzyloxycarbonyl; Boc = *tert*-butoxycarbonyl; TBDMS = *tert*-butyldimethylsilyl.

(30 ml) containing NaOMe (1 mmol) was electrolyzed at 5—10 °C using a 6.4 cm^2 of graphite anode–graphite cathode system in a non-divided cell. The electrolysis current was maintained at 0.6 A during the electrolysis. After the theoretical amount of electricity had passed, the electrolyzed solution was evaporated to dryness *in vacuo*. The residue was dissolved in EtOAc. The solution was washed with saturated aqueous $NaHCO_3$ solution and brine, dried ($MgSO_4$) and evaporated to dryness *in vacuo* to afford compound **2a**.

(2*R*)-*N*-Acetyl-1-methoxy-2-methylbutylamine (2a) mp 36—37 °C. IR (Nujol): 3300 (NH), 1660 (CO) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.91 (t, 3H, J = 6.0 Hz, C_4-H), 0.93 (d, 3H, J = 5.5 Hz, CH_3), 1.03—1.29 (m, 1H, C_3-H), 1.41—1.73 (m, 2H, C_2-H, C_3-H), 2.10 (s, 3H, $COCH_3$), 3.32 (s, 3H, OCH_3), 4.90—5.00 (m, 1H, C_1-H), 6.05 (br 1H, NH). MS *m/z*: 128 ($M^+ - CH_3O$). *Anal.* Calcd for $C_8H_{17}NO_2$: C, 60.34; H, 10.76; N, 8.80. Found: C, 60.46; H, 11.10; N, 8.69.

(2*R*)-*N*-Benzyloxycarbonyl-1-methoxy-2-methylbutylamine (2b) Colorless syrup. IR (film); 3320 (NH), 1705 (CO), 1520 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (d, 3H, J = 6.8 Hz, CH_3), 0.90 (t, 3H, J = 6.6 Hz, C_4-H), 1.00—1.30 (m, 1H, C_3-H), 1.40—1.75 (m, 2H, C_3-H, C_2-H), 3.34 (s, 3H, OCH_3), 4.65—4.82 (m, 1H, C_1-H), 4.99 (br, 1H, NH), 5.13 (s, 2H, $PhC\underline{H}_2O$), 7.34 (s, 5H, Ar-H). MS *m/z*: 219 ($M^+ - CH_3OH$). *Anal.* Calcd for $C_{14}H_{21}NO_3$: C, 66.91; H, 8.42; N, 5.57. Found: C 66.72; H, 8.51; N, 5.45.

(2*R*)-*N*-Benzyloxycarbonyl-1-methoxy-2-(*tert*-butyldimethylsilyloxy)-propylamine (2c) Colorless syrup. IR (film): 3460 (NH), 3350, (NH), 1730 (CO), 1720 (CO), 1500 cm^1. ^{1}H-NMR ($CDCl_3$) δ: −0.06—0.05 (m, 6H, $SiCH_3$), 0.81—0.84 (m, 9H, *tert*-Bu), 1.04, 1.11 (each d, 3H, J = 6.4 Hz, C_3-H), 3.29, 3.33 (each s, 3H, OCH_3), 3.80—3.95 (m, 1H, C_2-H), 4.61, 4.71 (each dd, 1H, J = 1.8, 9.9 Hz, C_1-H), 5.09 (s, 2H, $PhC\underline{H}_2O$), 5.42 (d, 1H, J = 9.9 Hz, NH), 7.25—7.36 (m, 5H, Ar-H). MS *m/z*: 321 ($M^+ - CH_3OH$). *Anal.* Calcd for $C_{18}H_{31}NO_4Si$: C, 61.15; H, 8.84; N, 3.96; Si, 7.94. Found: C, 60.98; H, 9.27; N, 3.96; Si, 8.05.

(2*R*)-*N*-*tert*-Butyloxycaronyl-1-methoxy-2-benzyloxypropylamine (2d) Colorless syrup. IR (film): 3450 (NH), 3320, 1725 (CO), 1500 cm^{-1}, ^{1}H-NMR ($CDCl_3$) δ: 1.14, 1.23 (each d, 3H, J = 6.5 Hz, C_3-H), 1.44, 1.46 (each s, 9H, *tert*-Bu), 3.37, 3.38 (each s, 3H, OCH_3), 3.49—3.62, 3.65—3.82 (each m, 1H, C_2-H), 4.40—4.85 (m, 3H, C_1-H, OCH_2), 5.20, 5.35 (each br, 1H, NH), 7.25—7.35 (m, 5H, Ar-H). MS *m/z*: 263 ($M^+ - CH_3OH$). *Anal.* Calcd for $C_{16}H_{25}NO_4$: C, 65.06; H, 8.53; N, 4.74. Found: C, 64.81; H, 8.35; N, 4.41.

(4*R*)-1-Acetyl-2-methoxy-4-(*tert*-butyldimethylsilyloxy)-pyrrolidine (2e) Colorless syrup. IR (film): 3450 (NH), 1665 (CO), 1415 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.07 (s, 6H, $SiCH_3$), 0.88 (s, 9H, *tert*-Bu), 1.75—2.10, 2.15—2.39 (each m, 2H, C_3-H), 2.07, 2.13, 2.14 (each s, 3H, $COCH_3$), 3.27, 3.29, 3.37, 3.40 (each s, 3H, OCH_3), 3.10—3.55, 3.65—3.95 (each m, 2H, C_5-H), 4.30—4.50, 4.50—4.75 (each m, 1H, C_4-H), 5.00—5.45 (m, 1H, C_2-H). MS *m/z*: 242 ($M^+ - CH_3O$). *Anal.* Calcd for $C_{13}H_{27}NO_3Si$: C, 57.10; H, 9.95; N, 5.12; Si, 10.27. Found: C, 56.84; H, 9.75; N, 4.78; Si, 9.82.

***N*-Benzyloxycarbonyl-L-phenylalanine *N*-(1-Methoxy-2(*R*)-methyl)butyl Aimde (2f)** mp 138—139 °C (MeOH). IR (Nujol): 3300 (NH), 1690 (CO), 1660 (CO), 1540 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.66 (d, 3H, J = 6.8 Hz, CH_3), 0.80—0.90 (m, 3H, $CH_2C\underline{H}_3$), 0.85—1.60 (m, 3H, $C\underline{H}C\underline{H}_2$), 3.11 (s, 3H, OCH_3), 2.90—3.10 (m, 2H, $C\underline{H}_2$ph), 4.45 (q, 1H, J = 7.0 Hz, $NHC\underline{H}CO$), 4.80—5.00 (m, 1H, $NHC\underline{H}O$), 5.05, 5.13 (ABq, 2H, J = 12.3 Hz, $PhC\underline{H}_2O$), 5.43 (m, 1H, NH), 5.90—6.10 (m, 1H, NH), 7.00—7.35 (m, 5H, Ar-H), 7.33 (s, 5H, Ar-H). MS *m/z*: 366 ($M^+ - CH_3OH$). *Anal.* Calcd for $C_{23}H_{30}N_2O_4$: C, 69.32; H, 7.59; N, 7.03. Found: C, 69.42; H, 7.70; N, 7.01.

Typical Procedures for Et_3SiH Reduction Method A: A solution of **2a** (2 mmol) and Et_3SiH (2.4 mmol) in dry CH_2Cl_2 (3 ml) was treated with BF_3OEt_2 (2.4 mmol) at 5 °C. After being stirred at 5 °C for 2 h, the reaction mixture was diluted with $CHCl_3$. The solution was washed with saturated aqueous $NaHCO_3$ solution and brine. The organic layer was dried ($MgSO_4$) and concentrated to dryness *in vacuo*, and the resulting syrup was subjected to silica gel chromatography ($CHCl_3$–acetone, 5 : 1) to afford compound **3a**.

Method B: A solution of **2c** (2 mmol) and Et_3SiH (4 mmol) in dry CH_2Cl_2 (3 ml) was treated with BF_3OEt_2 (4 mmol) at −40 °C. The temperature of the solution was maintained at −40 °C until the starting material disappeared on thin layer chromatography (TLC) (1—2 h). The reaction mixture was diluted with $CHCl_3$. The solution was washed with saturated aqueous $NaHCO_3$ solution and brine. The organic layer was dried ($MgSO_4$) and evaporated to dryness *in vacuo*. Purification of the

residue by silica gel chromatography (*n*-hexane–EtOAc, 10:1) gave compound **3c**.

Method C: A solution of **2b** (2 mmol) and Et_3SiH (2.4 mmol) in dry CH_2Cl_2 (3 ml) was treated with TFA (6 mmol) at 5°C. The reaction mixture was stirred at room temperature for 2 h, then quenched by addition of saturated aqueous $NaHCO_3$ solution. The mixture was extracted with $CHCl_3$. The organic layer was separated, dried ($MgSO_4$) and then evaporated to dryness *in vacuo* to give a syrup, which was purified by silica gel chromatography (*n*-hexane–EtOAc, 10:1) to afford compound **3b**.

(2*R*)-*N*-Acetyl-2-methylbutylamine (3a) This compound was prepared by method A. Colorless syrup, $[\alpha]_D^{22.5}$ +5.23° (c=1.11, $CHCl_3$). IR (film): 3300 (NH), 1655 (CO) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.87—0.94 (m, 6H, C_4-H, CH_3), 1.04—1.26 (m, 1H, C_3-H), 1.30—1.67 (m, 2H, C_2-H, C_3-H), 1.99 (s, 3H, $COCH_3$), 2.99—3.26 (m, 2H, C_1-H), 5.61 (br, 1H, NH). MS *m/z*: 129 (M^+). *Anal.* Calcd for $C_7H_{15}NO$: C, 65.07; H, 11.70; N, 10.84. Found: C, 64.92; H, 12.08; N, 10.61.

(2*R*)-*N*-Benzyloxycarbonyl-2-methylbutylamine (3b) This compound was obtained by both method A and method C. Colorless syrup, $[\alpha]_D^{25.5}$ +4.07° (c=1.13, $CHCl_3$). IR (film): 3330 (NH), 1710 (CO), 1540 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.89 (d, 3H, J=6.6 Hz, CH_3), 0.90 (t, 3H, J=7.2 Hz, C_4-H), 1.00—1.63 (m, 3H, C_2-H, C_3-H), 2.90–3.23 (m, 2H, C_1-H), 4.77 (br, 1H, NH), 5.10 (s, 2H, $PhC\underline{H}_2O$), 7.33 (s, 5H, Ar-H). MS *m/z*. 221 (M^+). *Anal.* Calcd for $C_{13}H_{19}NO_2$: C, 70.56; H, 8.65; N, 6.33. Found: C, 70.41; H, 9.07; N, 6.36.

(2*R*)-*N*-Benzyloxycarbonyl-2-(*tert*-butyldimethylsilyloxy)propylamine (3c) This compound was prepared by both method B and method C. Colorless syrup, $[\alpha]_D^{25.5}$ −22.1° (c=1.26, $CHCl_3$). IR (film): 3470 (NH), 3350 (NH), 1730 (CO), 1710 (CO) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.01 (s, 6H, $SiCH_3$), 0.85 (s, 9H, *tert*-Bu), 1.07 (d, 3H, J=6.2 Hz, C_3-H), 2.91—3.05 (m, 1H, C_1-H), 3.18—3.31 (m, 1H, C_1-H), 3.83—3.92 (m, 1H, C_2-H), 4.96 (br, 1H, NH), 5.06 (s, 2H, $PhC\underline{H}_2O$), 7.21—7.34 (m, 5H, Ar-H). MS *m/z*: 323 (M^+). *Anal.* Calcd for $C_{17}H_{29}NO_3Si$: C, 63.12; H, 9.04; N, 4.33; Si, 8.68. Found: C, 62.88; H, 8.90; N, 4.10; Si, 8.32.

(2*R*)-*N*-Benzyloxycarbonyl-2-hydroxypropylamine (3c′) This compound was formed as a by-product in the reduction of **3c** using method C. Colorless syrup, $[\alpha]_D^{25.5}$ −20.3° (c=1.19, $CHCl_3$). IR (film): 3350 (NH), 2910 (OH), 1700 (CO) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.18 (d, 3H, J=6.3 Hz, CH_3), 2.04 (br, 1H, OH), 2.98—3.12 (m, 1H, C_1-H), 3.28—3.40 (m, 1H, C_1-H), 3.91 (m, 1H, C_2-H), 5.11 (s, 2H, $PhC\underline{H}_2O$), 5.21 (br, 1H, NH), 7.26—7.37 (m, 5H, Ar-H). MS *m/z*: 209 (M^+). *Anal.* Calcd for $C_{11}H_{15}NO_3$: C, 63.14; H, 7.23; N, 6.69. Found: C, 62.83; H, 7.25; N, 6.49.

(2*R*)-*N*-*tert*-Butyloxycarbonyl-2-benzyloxypropylamine (3d) This compound was prepared by method B. Colorless syrup, $[\alpha]_D^{26}$ −37.9° (c=1.22, $CHCl_3$). IR (film): 3450 (NH), 3350, 1720 (CO), 1500 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.19 (d, 3H, J=6.2 Hz, C_3-H), 1.44 (s, 9H, *tert*-Bu), 3.00—3.13 (m, 1H, C_1-H), 3.20—3.40 (m, 1H, C_1-H), 3.58—3.66 (m, 1H, C_2-H), 4.45, 4.61 (ABq, 2H, J=11.7 Hz, $PhC\underline{H}_2O$), 4.86 (br, 1H, NH), 7.26—7.36 (m, 5H, Ar-H). MS *m/z*: 264 (M^+). *Anal.* Calcd for $C_{15}H_{23}NO_3$: C, 67.90: H, 8.74; N, 5.28. Found: C, 67.71; H, 8.65; N, 5.06.

(3*R*)-*N*-Acetyl-3-(*tert*-butyldimethylsilyloxy)propylamine (3e) This compound was prepared by method B. Colorless syrup, $[\alpha]_D^{24.5}$ −23.4° (c=1.22, $CHCl_3$); IR (film): 3350 (NH), 1650 (CO) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.01 (s, 6H, $SiCH_3$), 0.80 (s, 9H, *tert*-Bu), 1.60—2.10 (m, 2H, C_4-H), 1.95, 1.98 (each s, 3H, CH_3), 3.10—3.80 (m, 4H, C_2-H, C_5-H), 4.25—4.58 (m, 1H, C_3-H). MS *m/z*: 228 ($M^+ - CH_3$). *Anal.* Calcd for $C_{12}H_{25}NO_2Si$: C, 59.21; H, 10.35; N, 5.75; Si, 11.54. Found: C, 58.85; H, 10.38; N, 5.80; Si, 11.18.

***N*-Benzyloxycarbonyl-L-phenylalanine *N*-(2(*R*)-Methylbutyl)amide (3f)** Both method A and method C were applied to obtain this compound. mp 133—134 °C (MeOH), $[\alpha]_D^{25.5}$ +5.49° (c=1.02, $CHCl_3$). IR (Nujol): 3300 (NH), 1690 (CO), 1655 (CO); 1530 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.72 (d, 3H, J=6.7 Hz, $CHC\underline{H}_3$), 0.81 (3H, t, J=7.3 Hz, $CH_2C\underline{H}_3$), 0.85—1.50 (m, 3H, $C\underline{H}C\underline{H}_2CH_3$), 2.85—3.18 (m, 4H, $C\underline{H}_2Ph$, $NHC\underline{H}_2$-), 4.29—4.41 (m, 1H, $NHC\underline{H}CO$), 5.08 (s, 2H, $PhC\underline{H}_2O$), 5.45 (br, 1H, NH), 5.70 (br, 1H, NH), 7.17—7.37 (m, 10H, Ar-H). MS *m/z*: 366 ($M^+ - H_2$). *Anal.* Calcd for $C_{22}H_{28}N_2O_3$: C, 71.71; H, 7.66; N, 7.60. Found: C, 71.46; H, 7.75; N, 7.48.

Conversion of 3c to 2(*R*)-(−)-Hydroxypropylamine Hydrochloride Compound **3c** (835 mg, 2.68 mmol) was dissolved in MeOH (30 ml) and the solution was subjected to hydrogenolysis over 10% Pd-C (0.1 g) at atmospheric pressure. After a theoretical amount of hydrogen had been absorbed, the catalyst was filtered off and the filtrate was evaporated to dryness *in vacuo*. The resulting syrup was dissolved in 22% HCl in MeOH (1 ml) and the solvent was removed under reduced pressure. The resulting crystals were triturated with ether to give colorless needles (190 mg, 63%), mp 111—113 °C (lit.[6] 113 °C), $[\alpha]_D^{25.5}$ −32.5° (c=2.74, H_2O) (lit.[6] $[\alpha]_D^{20}$ −32.4° (c=1.46, H_2O)). IR (film): 3350 (NH), 2850, 1960, 1600 cm^{-1}. ^{1}H-NMR (D_2O) δ: 1.24 (d, 3H, J=6.4 Hz, CH_3), 2.88 (dd, 1H, J=9.0, 13.1 Hz, C_1-H), 3.10 (dd, 1H, J=3.4, 13.1 Hz, C_1-H), 3.95—4.12 (m, 1H, C_2-H). MS *m/z*: 76 (M^+).

Conversion of 3e to (3*R*)-(−)-Hydroxypyrrolidine Hydrochloride A mixture of compound **3e** (1.26 g, 5.18 mmol) and 6 N HCl (5 ml) was refluxed for 6 h. After cooling, the reaction mixture was diluted with H_2O (5 ml), and the solution was washed with EtOAc. The aqueous layer was concentrated to dryness *in vacuo*. The crystalline residue was triturated with ether to give pale brown needles (550 mg, 85%). An analytical sample was prepared by recrystallization from EtOH–ether (1:1), mp 107—108 °C (lit.[6] 109 °C), $[\alpha]_D^{26}$ −9.20° (c=1.74, MeOH) (lit.[6] $[\alpha]_D^{20}$ −7.60° (c=3.45, MeOH)). IR (Nujol): 3400 (NH), 1620, 1450 cm^{-1}. ^{1}H-NMR (D_2O) δ: 2.02—2.25 (m, 2H, C_4-H), 3.26—3.55 (m, 4H, C_2-H, C_5-H), 4.61—4.68 (m, 1H, C_3-H). MS *m/z*: 87 (M^+).

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