maytancarbutine (4) (32.2 mg, 66%) as a white crystalline solid: mp 159-162 °C; IR ($CDCl_3$) 3560, 3515, 3425, 2960, 1740, 1660 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 0.82 (s, 3 H, C-4 CH_3), 1.02 (d, J = 7 Hz, 3 H, C-4′ CH_3), 1.11 (d, J = 6 Hz, 3 H, C-6 CH_3), 1.12 (d, J = 7 Hz, 3 H, C-4′ CH_3), 1.13 (m, 1 H, C-8 H_β), 1.16 (m, 1 H, C-8 H_α), 1.37 (d, J = 6 Hz, 3 H, C-2′ CH_3), 1.43 (m, C-6 H), 1.63 (s, 3 H, C-14 CH_3), 2.17 (dd, $J_{2,2}$ = 14, $J_{2,3}$ = 3 Hz, C-2 H_β), 2.61 (dd, $J_{2,2}$ = 14, $J_{2,3}$ = 12 Hz, C-2 H_α), 2.78 (m, 1 H, C-4′ H), 2.83 (s, 0.5 H), and 2.88 (s, 2.5 H) (C-2′NCH_3), 3.05 (d, $J_{5,6}$ = 9 Hz, 1 H, C-5 H), 3.05 (d, $J_{15,15}$ = 13 Hz, 1 H, C-15 H), 3.10 (s, 1 H, C-9 OH), 3.18 (s, 3.0 H) (C-1 NCH_3), 3.29 (s, 3 H, C-10 OCH_3), 3.40 (dd, $J_{9,10}$ = 2, $J_{10,11}$ = 9 Hz, 1 H, C-10 H), 3.73 (d, $J_{15,15}$ = 13 Hz, 1 H, C-15 H), 3.85 (br d, $J_{8\alpha,9}$ = 10 $J_{9,10}$ < 2 Hz, 1 H, C-9 H), 3.98 (s, 3 H, C-20 OCH_3), 4.72 (dd, $J_{2,3}$ = 12, 3 Hz, C-3 H), 4.80 (m, 1 H, C-7 H), 4.90 (br s, 1 H, C-7 $OCONH_2$), 5.61 (q, J = 7 Hz, 1 H, C-2′ H), 5.81 (dd, $J_{10,11}$ = 9, $J_{11,12}$ = 15 Hz, 1 H, C-11 H), 6.32 (dd, $J_{11,12}$ = 15, $J_{12,13}$ = 11, 1 H, C-12 H), 6.87 (d, $J_{12,13}$ = 11 Hz, 1 H, C-13 H), 6.72, 6.82 (d, $J_{17,21}$ = 1.5 Hz, 2 H, C-17 H, C-21 H); FABMS, m/z 722 (M + H); high-resolution EIMS, m/z 678.3264 ($C_{35}H_{51}ClN_2O_9$ = 678.3283) [M^+ - 43 (HNCO)], 505.2155 ($C_{27}H_{36}ClNO_6$ = 505.2212) [M^+ - 156 (side chain)], 490.2107 ($C_{26}H_{33}ClNO_6$ = 490.1996) [505 - CH_3], 487.2163 ($C_{27}H_{34}ClNO_5$ = 487.2125) [505 - H_2O].

Anal. Calcd for $C_{36}H_{52}ClN_3O_{10}$: C, 59.83; H, 7.20; N, 5.82. Found: C, 58.37; H, 7.20; N, 5.43.

Maycarsine (6). Maysine (5) (19.2 mg, 0.0350 mmol) was subjected to the same reaction conditions and work-up procedures as maytanbutine (3) to give a yellow solid. PTLC of this material on silica gel 60 developed with 5% methanol in dichloromethane afforded maycarsine (6) (6.0 mg, 32%) as a white crystalline solid: mp 131-133 °C; IR (KBr) 3420, 2930, 1720, 1667, 1340, 1080 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.07 (s, 3 H, C-4 CH_3), 1.15 (d, J = 7 Hz, 3 H, C-6 CH_3), 1.23 (m, 1 H, C-8 H_β), 1.34 (m, 1 H, C-8 H_α), 1.60 (m, 1 H, C-6 H), 1.70 (s, 3 H, C-14 CH_3), 2.72 (d, $J_{5,6}$ = 10 Hz, 1 H, C-5 H), 3.08 (d, $J_{15,15}$ = 12 Hz, 1 H, C-15 H), 3.27 (s, 3 H, C-1 NCH_3), 3.29 (s, 3 H, C-10 OCH_3), 3.39 (dd, $J_{9,10}$ = 2, $J_{10,11}$ = 10 Hz, C-10 H), 3.47 (d, $J_{15,15}$ = 12 Hz, 1 H, C-15 H), 3.89 (br d, $J_{8\alpha,9}$ = 10 Hz, C-9 H), 3.99 (s, 3 H, C-20 OCH_3), 4.76 (br s, 2 H, C-7 $OCONH_2$), 4.86 (dd, $J_{6,7}$ = 11 Hz, $J_{7,8\beta}$ = 11 Hz, C-7 H), 5.72 (dd, $J_{10,11}$ = 10, $J_{11,12}$ = 15 Hz, 1 H, C-11 H), 5.75 (d, $J_{2,3}$ = 15 Hz, 1 H, C-2 H), 6.10 (d, $J_{12,13}$ = 11 Hz, 1 H, C-13 H), 6.30 (dd, $J_{11,12}$ = 15, $J_{12,13}$ = 11, 1 H, C-12 H), 6.43 (d, $J_{2,3}$ = 15 Hz, 1 H, C-3 H), 6.72, 6.81 (d, $J_{17,21}$ = 1.5 Hz, 2 H, C-17 H, C-21 H), 3.20-3.45 (1 H, C-9 OH); FABMS, m/z 549 (M^+ + H); high-resolution EIMS, m/z 505.2145 ($C_{27}H_{36}ClNO_6$ = 505.2242 [M^+ - HNCO].

Reduction of 7. The aromatic carbinolamide 3,4-dihydro-4-hydroxy-2*H*-1,3-benzoxazin-2-one (7) (228 mg, 1.38 mmol) was subjected to the same reaction conditions described for 3 with the exception that only 1.1 equiv of the $LiBH_4/Li(Et)_3BH$ mixture was used. After workup, a yellow oil, which crystallized upon standing, was obtained. The crystals obtained were washed with diethyl ether to afford 9. PTLC of the mother liquor on silica gel developed with 7% methanol in dichloromethane afforded 9 and 10 as white crystalline solids. Compound 9 (112 mg, 66%) was spectroscopically identical with authentic samples of *o*-hydroxybenzyl alcohol. Compound 10 was spectroscopically determined to be 3,4-dihydro-2*H*-1,3-benzoxazin-2-one (35 mg, 17%): mp 193 °C; IR (KBr) 3278, 3170, 1724, 1185, 735 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 4.54 (s, 2 H), 6.32 (br s, 1 H), 6.99-7.26 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 42.7 (t), 116.8 (d), 125.8 (d), 128.1 (d), 151.6 (s).

9-*O*-Methylmaytanbutine (8). Maytanbutine (3) (114.1 mg, 0.1585 mmol) was dissolved in 50 mL of freshly distilled absolute methanol. A few crystals of *p*-toluenesulfonic acid were added, and the reaction mixture was allowed to equilibrate for 84 h. Solvent was evaporated in vacuo to give a murky solution, which was diluted with dichloromethane. Visible water was removed and the organic solvent was dried (Na_2SO_4) and evaporated to a solid, which was applied to column of silica gel and eluted with 1:2 diethyl ether-dichloromethane to afford white crystalline 9-*O*-methylmaytanbutine (8) (102.7 mg, 88%): mp 158-160 °C; IR (KBr) 3450, 2950, 1730, 1665, 1075 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 0.81 (s, 3 H, C-4 CH_3), 1.05 (d, J = 7 Hz, 3 H, C-4′ CH_3), 1.13 (d, J = 7 Hz, 3 H, C-4′ CH_3), 1.28 (d, J = 6 Hz, 3 H, C-6 CH_3), 1.32 (d, J = 6 Hz, 3 H, C-2′ CH_3), 1.63 (s, 3 H, C-14 CH_3), 2.20 (dd, $J_{2,2}$ = 14, $J_{2,3}$ = 3 Hz, C-2 H_β), 2.65 (dd, $J_{2,2}$ = 14, $J_{2,3}$ = 12 Hz, C-2 H_α), 2.80 (m, 1 H, C-4′ H), 2.82 (s, 0.5 H), 2.88 (s, 2.0 H), and 2.97 (s, 0.5 H) (C-2′NCH_3), 3.18 (s, 3 H, C-1 NCH_3), 3.28, 3.40 (2 s, 3 H ea, C-9 OCH_3, C-10 OCH_3), 3.50 (d, $J_{10,11}$ = 9 Hz, 1 H, C-10 H), 3.68 (d, $J_{15,15}$ = 13 Hz, 1 H, C-15 H), 3.98 (s, 3 H, C-20 OCH_3), 4.26 (m, 1 H, C-7 H), 4.75 (dd, $J_{2,3}$ = 12,3 Hz, C-3 H), 5.53 (q, J = 7 Hz, 1 H, C-2′ H), 5.68 (dd, $J_{10,11}$ = 9, $J_{11,12}$ = 15 Hz, 1 H, C-11 H), 6.39 (s, 1 H, C-9 NH), 6.43 (dd, $J_{11,12}$ = 15, $J_{12,13}$ = 11, 1 H, C-12 H) 6.74 (d, $J_{12,13}$ = 11 Hz, 1 H, C-13 H), 6.66, 6.82 (2 d, $J_{17,21}$ = 1.5 Hz, 1 H ea, C-17 H, C-21 H), 0.82-2.00 (3 H, C-6 H, C-8 H_2), 3.00-3.20 (2 H, C-5 H, C-15 H).

Reduction of 9-*O*-Methylmaytanbutine (8). 9-*O*-Methylmaytanbutine (8) (74.1 mg, 0.1011 mmol) was subjected to the same reaction conditions described for 3 with 11.0 equiv of the borohydride reagent. Workup followed by PTLC on silica gel 60 eluted with 5% methanol in dichloromethane afforded a major component which was found to be spectroscopically identical with the starting material (21.2 mg, 29%). A second major band (25.1 mg) was separated into two components by PTLC on alumina eluted with 2.5% methanol in dichloromethane. One component (9.0 mg) appeared to be 9-*O*-methylmaysine from its NMR spectrum: δ 0.83 (s, 3 H, C-4 CH_3), 1.28 (d, J = 5 Hz, 3 H, C-6 CH_3), 1.68 (s, 3 H, C-14 CH_3), 3.19 (s, 3 H, C-1 NCH_3), 3.28, 3.40 (2 s, 3 H ea, C-9 OCH_3, C-10 OCH_3), 3.98 (s, 3 H, C-20 OCH_3), 4.26 (m, 1 H, C-7 H), 5.54 (dd, $J_{10,11}$ = 9 Hz, $J_{11,12}$ = 10 Hz, C-11 H), 6.07-6.53 (m, 4 H, C-2 H, C-3 H, C-11 H, C-12 H), 6.81 (s, 1 H, C-9 NH), 6.94, 7.03 (2 d, 1 H ea, $J_{17,21}$ = 1.5 Hz, C-17 H, C-21 H). The other component (10.5 mg) decomposed in solution but did not show any resonances due to the C-3 ester in the NMR. The shifts of the C-7 H (δ 4.1), C-9 NH (δ 6.00), and C-9 OCH_3 (δ 3.34) indicated that the carbinol amide system was intact. No components were isolated that corresponded to maytancarbutine (4) or maycarsine (6).

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Electroorganic Chemistry. 113. Synthesis of (+)- and (-)-*N*-Methylpseudoconhydrine from L-Lysine Using Anodic Oxidation as the Key Reaction

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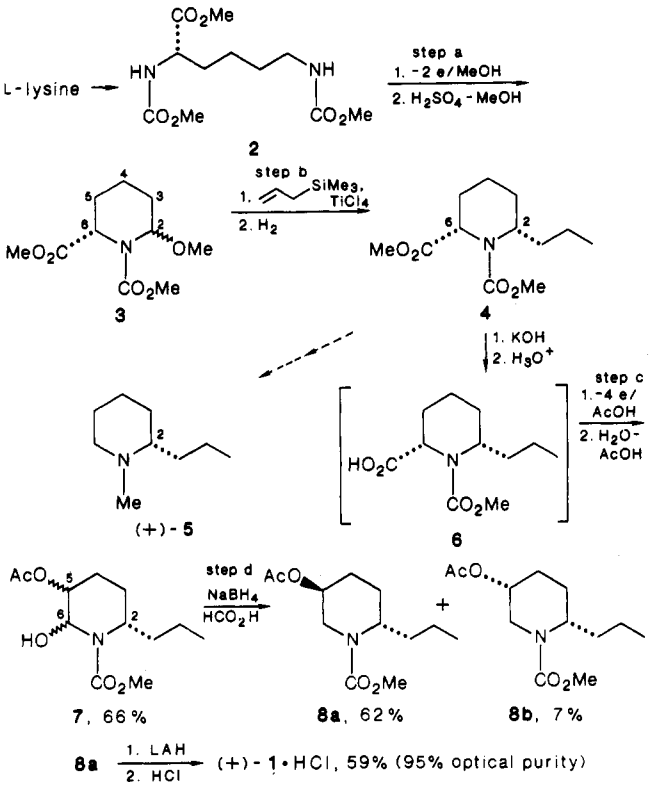
Synthesis of optically active piperidine alkaloids from L-lysine is particularly interesting since the piperidine skeleton found in some natural piperidine alkaloids has been known to be formed from L-lysine.[1]

As we have already reported, the anodic transformation of L-lysine to optically active pipecolinic acid is an excellent method of synthesis of piperidine skeleton from L-lysine.[2] Our previously reported enantioselective synthesis of (+)-*N*-methylconiine (5) from L-lysine was a typical example of applying this anodic transformation as the key reaction.[3,4] We report herein a first synthesis of optically

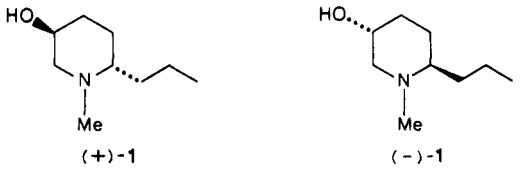
(1) Herbert, R. B. In *Rodd's Chemistry of Carbon Compounds*; Coffey, S., Ed.; Elsevier: Amsterdam, 1980; p 312.
(2) Shono, T.; Matsumura, Y.; Inoue, K. *J. Chem. Soc., Chem. Commun.* **1983**, 1169.

0022-3263/88/1953-4118$01.50/0

Scheme I



active (+)- and (−)-*N*-methylpseudoconhydrine, (+)- and (−)-**1**, from L-lysine using anodic oxidation as the key reaction.

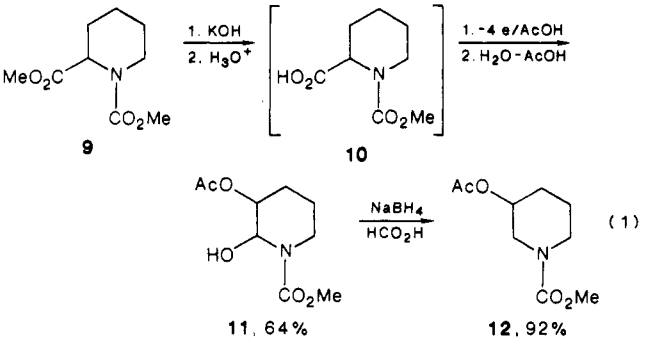


(+)-*N*-Methylpseudoconhydrine, (+)-**1**, is an alkaloid yielded from South African *Conium* species and possesses a structure of (2*S*,5*S*)-5-hydroxy-1-methyl-2-propylpiperidine.[5] Although some methods have been exploited for the diastereoselective construction of 5-hydroxy-2-propylpiperidines,[6] no studies on the synthesis of optically active ones have been carried out so far except a synthesis of (+)-pseudoconhydrine from D-glucosamine.[7]

Synthesis of (+)-*N*-Methylpseudoconhydrine [(+)-1]. Our methodology for synthesis of (+)-**1** is shown in Scheme I in which (1) a chiral piperidine *N*,*O*-acetal **3** is prepared from L-lysine derivative **2** (step a), (2) a propyl group is diastereoselectively introduced to the 2-position of **3** under the influence of the methoxycarbonyl group on the chiral 6-position (step b), (3) an acetoxyl group is introduced to the 5-position of **4** under the influence of the propyl group on the chiral 2-position (step c), and (4) the 6-hydroxyl group of **7** is eliminated to afford **8** (step d). Of these steps, anodic oxidations are utilized in steps (a) and (c).

The synthesis of **4** from L-lysine has been described in our previous report,[3] in which the 2-methoxyl group of **3** was substituted by an allyl group and the product was hydrogenated and decarboxylated to give finally **5**. Since the stereochemistry at the 2-position of the resulting **5** was *S* and its optical purity was more than 96%, **4** is expected to be an excellent precursor for the synthesis of (+)-**1** provided that both elimination of a methoxycarbonyl group at the 6-position of **4** and stereoselective introduction of a hydroxyl group into the 5-position are achievable.

Using compound **9** as a model, we have examined the effectiveness of the anodic oxidation as the key method and found that it worked nicely. Namely, hydrolysis of **9** and subsequent anodic oxidation of **10** in acetic acid gave **11**, which was easily reduced to **12** in 59% overall yield (eq 1).



(1)

Compound **7**, a key intermediate for the synthesis of (+)-**1**, was obtained from **4** in 71% yield by similar procedures. The hydroxyl group of **7** was easily removed by reducing **7** with $NaBH_4$ and a stereoisomeric mixture of **8a** and **8b** was obtained in 69% yield. The stereochemistry of the 5-acetoxyl group of **7** was unknown, but the stereochemistry of **8** was found to mainly be trans (9:1). After each stereoisomer was separated by column chromatography, the reduction of main isomer **8a** with LAH followed by treatment with HCl gave (+)-**1**·HCl in 95% optical purity.[5]

The anodic oxidation of **6** to **7** (or **10** to **11**) probably proceeded through the intermediary formation of **13**, **14**, and **15** (eq 2). Anodic decarboxylation of α-amino acid derivatives has been known[8] and anodic diacetoxylation of 1-(methoxycarbonyl)-1,2,3,4-tetrahydropyridines has already been reported by us.[9]

Synthesis of (−)-*N*-Methylpseudoconhydrine [(−)-1]. Unnatural type alkaloid (−)-**1** has the structure of (2*R*,5*R*)-5-hydroxy-1-methyl-2-propylpiperidine. Hence, the key intermediate **4** was not utilizable for the synthesis of (−)-**1** since the stereochemistry at the 2-position of **4** was *S*.

Scheme II shows a route for the synthesis of (−)-**1** from L-lysine. Anodic oxidation of **3** in acetic acid gave **16** in which the stereochemistry is unknown.[9,10] Then, treat-

(3) Shono, T.; Matsumura, Y.; Tsubata, K.; Uchida, K. *J. Org. Chem.* **1986**, *51*, 2590.

(4) Synthesis of (+)-sedamine from L-lysine by the similar procedure; see: Irie, K.; Aoe, K.; Tanaka, T.; Saito, S. *J. Chem. Soc., Chem. Commun.* **1985**, 633.

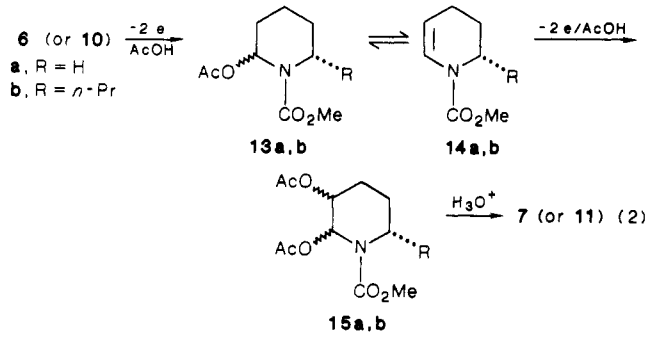
(5) Pure (+)-**1**·HCl: mp 157 °C; $[\alpha]^{25}_D$ +25° (MeOH). See: Roberts, M. F.; Brown, R. T. *Phytochemistry* **1981**, *20*, 447.

(6) For a mixture of the trans form and the cis form, see: (a) Gruber, W.; Schlogl, K. *Monatsch. Chem.* **1949**, *80*, 499. (b) Marion, L.; Cockburn, W. F. *J. Am. Chem. Soc.* **1949**, *71*, 3402. (c) Sorm, F.; Sicher, J. *Collect. Czech. Chem. Commun.* **1949**, *14*, 331. For the trans form, see: (d) Brown, E.; Lavoue, J.; Dhal, R. *Tetrahedron* **1973**, *29*, 455. (e) Harding, K. E.; Burks, S. R. *J. Org. Chem.* **1984**, *49*, 40. For the cis form, see: (f) Renger, B.; Kalinowski, H.-O.; Seebach, D. *Chem. Ber.* **1977**, *110*, 1866. For each of the trans form and the cis form, see: (f) Shono, T.; Matsumura, Y.; Onomura, O.; Kanazawa, T.; Habuka, M. *Chem. Lett.* **1984**, 1101.

(7) Tadano, K.; Iimura, Y.; Suami, T. *J. Carbohydr. Chem.* **1985**, *4*, 129.

(8) For examples, see: (a) Horikawa, H.; Iwasaki, T.; Matsumoto, K.; Miyoshi, M. *Tetrahedron Lett.* **1976**, 191. (b) Horikawa, H.; Iwasaki, T.; Matsumoto, K.; Miyoshi, M. *J. Org. Chem.* **1977**, *42*, 2419. (c) Renand, P.; Seebach, D. *Helv. Chim. Acta* **1986**, *69*, 1704.

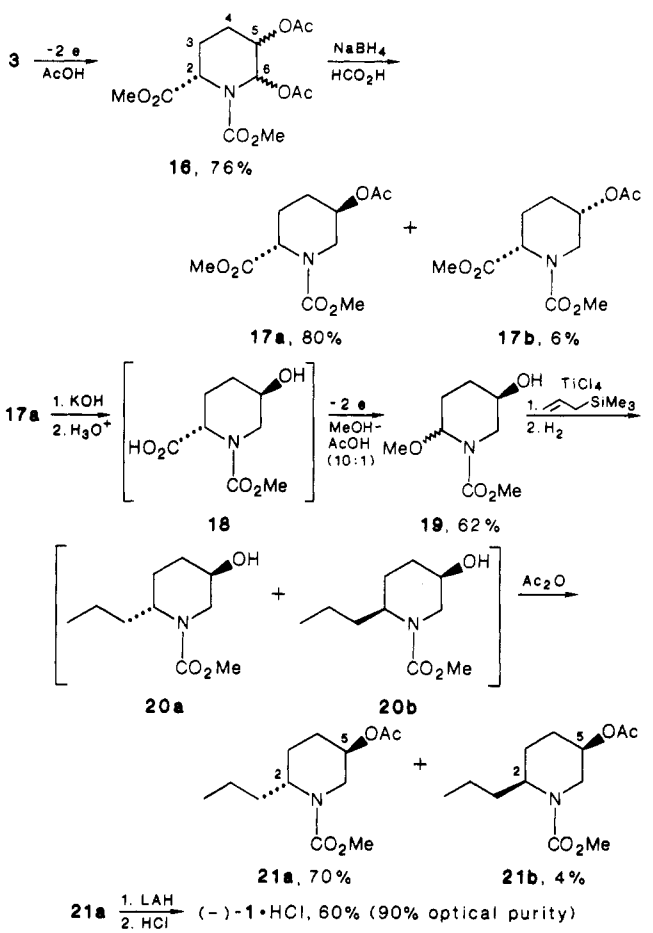
(9) Shono, T.; Matsumura, Y.; Onomura, O.; Ogaki, M.; Kanazawa, T. *J. Org. Chem.* **1987**, *52*, 536.



ment of **16** with $NaBH_4$ under acidic conditions gave trans isomer **17a** (80% yield) together with a small amount of cis isomer **17b** (6% yield). The ratio of **17a** and **17b** (93:7) was measured by separation with column chromatography. The stereochemistry at the 5-position of the main product **17a** was *R*, which was determined at the final stage. Alkaline hydrolysis of **17a** followed by anodic decarboxylation in a mixed solvent of methanol and acetic acid gave **19** (62% yield),[11] which was then treated with allyltrimethylsilane in the presence of $TiCl_4$ and hydrogenated successively to give a mixture of **20a** and **20b**. It was then acetylated and each isomer was separated by column chromatography. The main product, 2*R*,5*R* isomer **21a** (69% yield), was reduced with LAH to give (−)-**1**, which was identified as its HCl salt, (−)-**1**·HCl (90% optical purity).[5] The stereochemistry of the minor isomer **21b** (5% yield) was 2*S*,5*R*.

In conclusion, the anodic methos, namely, both anodic decarboxylation of pipecolinic acid derivatives and anodic 2,3-diacetoxylation of 1-(methoxycarbonyl)piperidines have been shown to be highly effective in the synthesis of optically active piperidine alkaloids from L-lysine.

Scheme II



Experimental Section

^1H NMR spectra were measured on a Varian Associates EM-360 or EM-390 spectrometer with chemical shifts given in parts per million (δ) downfield from tetramethylsilane as an internal standard. IR spectra were recorded on a Hitachi 260-10 spectrometer. Elemental analyses were determined by the Center for Instrumental Analysis of Kyoto University. Optical rotations were measured with a Perkin-Elmer 241 polarimeter. Mass spectra were recorded on a JEOL IMS-DS300 mass spectrometer. Melting points are uncorrected.

Anodic oxidation was carried out with a DC power supply (GP 050-2) of Takasago Seisakusho, Ltd. A glass beaker (50 mL) equipped with a carbon-rod anode and cathode (8-mm diameter) was used as an electrolysis cell.

Preparation of 5-Acetoxy-6-hydroxy-1-(methoxycarbonyl)-2-propylpiperidine (7). A solution of **4**[3] (1.868 g, 7.69 mmol) and 85% KOH (2.5 g, 38.4 mmol) in a mixed solvent of methanol (10 mL) and water (10 mL) was stirred at 0 °C and gradually warmed to room temperature. After the mixture was stirred for 10 h, the solvent was evaporated to remove methanol. The residual aqueous layer was acidified with concentrated HCl and the organic portion was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layer was dried over $MgSO_4$, and the solvent was removed to give crude carboxylic acid **6** (1.874 g),[3] which was used without purification.

Into an electrolysis cell described above was added a solution of crude **6** (1.874 g) and AcOK (3 g, 26.3 mmol) in acetic acid (50 mL). After 13 F/mol of electricity was passed at a constant current of 0.2 A (2.9 h, terminal voltage ca. 30 V) through the solution cooled with water, water (100 mL) was added to the reaction mixture and the mixture stirred for 3 h. The organic portion was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layer was dried over $MgSO_4$ and the solvent was removed in vacuo. The residue was chromatographed on silica gel (AcOEt–hexane = 1:4) to afford **7** (1.412 g, 5.45 mmol) in 71% yield. Spectroscopic data of **7** were consistent with those of known racemic sample.[9]

Reduction of 7. Into a solution of **7** (0.698 g, 2.7 mmol) in formic acid (10 mL) was added, in portions, 90% $NaBH_4$ (0.46 g, 10.9 mmol). After 1 h, water (30 mL) was poured into the reaction mixture and the organic portion was extracted with CH_2Cl_2 (3 × 30 mL). After the extract was dried over $MgSO_4$ and the solvent was removed in vacuo, the residue was chromatographed on silica gel (AcOEt–hexane = 1:4) to afford (2*S*,5*S*)-5-acetoxy-1-(methoxycarbonyl)-2-propylpiperidine (**8a**) and 2*S*,5*R* isomer **8b** in 62% (0.406 g, 1.67 mmol) and 7% (0.046 g, 0.19 mmol) yields, respectively.

8a (polar isomer): IR (neat) 2950, 2860, 1736, 1695, 1444, 1368, 1230, 1158, 1020, 958, 840, 770 cm^{-1}; NMR ($CDCl_3$) δ 0.93 (t, *J* = 7 Hz, 3 H), 1.26–1.81 (m, 8 H), 2.03 (s, 3 H), 2.97 (dd, *J* = 15 and 2 Hz, 1 H), 3.68 (s, 3 H), 4.18 (d, *J* = 14 Hz, 1 H), 4.32 (br s, 1 H), 4.84 (br s, 1 H). Anal. Calcd for $C_{12}H_{21}NO_4$: C, 59.24; H, 8.70; N, 5.76. Found: C, 59.14; H, 8.87; N, 5.64.

8b (less polar isomer): IR (neat) 2952, 2865, 1736, 1698, 1442, 1362, 1235, 1160, 1092, 1039, 768 cm^{-1}; NMR ($CDCl_3$) δ 0.93 (t, *J* = 7 Hz, 3 H), 1.21–1.94 (m, 8 H), 2.05 (s, 3 H), 2.69 (dd, *J* = 13 and 11 Hz, 1 H), 3.69 (s, 3 H), 4.16–4.35 (m, 2 H), 4.64 (m, 1 H). Anal. Calcd for $C_{12}H_{21}NO_4$: C, 59.24; H, 8.70; N, 5.76. Found: C, 58.99; H, 8.41; N, 5.63.

3-Acetoxy-1-(methoxycarbonyl)piperidine (12) was prepared according to a similar procedure described above with use of **10** and **11**[9] from **9**[2] in 59% overall yield: IR (neat) 2960, 2875, 1741, 1452, 1238, 1049, 776 cm^{-1}; NMR (CCl_4) δ 1.33–2.13 (m, 4 H), 1.98 (s, 3 H), 3.21–3.55 (m, 4 H), 3.60 (s, 3 H), 4.56–4.67 (m, 1 H). Anal. Calcd for $C_9H_{15}NO_4$: C, 53.72; H, 7.51; N, 6.96.

(10) In contrast with the 6-acetoxyl group of **15**, the 6-acetoxyl group of **16** was not hydrolyzed during workup.

(11) The yield of **19** was 32% in a case using only methanol as a solvent. Improvement of yields by adding acetic acid into the reaction systems has also been observed in anodic α-methoxylation of aliphatic ethers.[12]

(12) Shono, T.; Matsumura, Y.; Onomura, O.; Yamada, Y. *Synthesis* **1987**, 1099.

Found: C, 53.64; H, 7.63; N, 6.94.

(+)-*N*-Methylpseudoconhydrine Hydrochloride [(+)-1·HCl]. To a stirred suspension of LAH (0.078 g, 2.05 mmol) in dry ether (10 mL) was added dropwise a solution of **8a** (0.29 g, 1.19 mmol) in dry ether (10 mL). The mixture was refluxed for 2 h and then cooled to room temperature. Usual workup followed by treatment with HCl gas gave a crude solid (0.245 g). After the solid was washed with AcOEt, (+)-**1**·HCl was crystallized from methanol–acetone (1:9) at −20 °C in 95% optical purity[5] (0.137 g, 0.7 mmol, 59% yield): mp 169–170 °C; $[\alpha]^{25}_D$ +23.8° (*c* 0.7, MeOH). The free base: liquid; MS, *m/e* 157 (M^+), 128, 115, 114 (base), 96; IR ($CHCl_3$) 3602, 2965, 2945, 2875, 2800, 1467, 1382, 1098, 1060, 1008, 968, 888 cm^{-1}; NMR ($CDCl_3$) δ 0.90 (t, J = 7 Hz, 3 H), 1.00–2.33 (m, 11 H), 2.24 (s, 3 H), 2.95 (ddd, J = 10, 4, and 2 Hz, 1 H), 3.35–3.93 (m, 1 H).

Anodic oxidation of 3[2] in acetic acid was carried out according to a procedure similar to the anodic oxidation of **6** described above. 2,3-Diacetoxy-1,2-bis(methoxycarbonyl)piperidine (**16**)[9] was obtained in 76% yield (8 F/mol).

Reduction of 16. Into a solution of **16** (1.828 g, 5.77 mmol) in formic acid (20 mL) was added, in portions, 90% $NaBH_4$ (1.21 g, 28.9 mmol). After stirring at room temperature for 1 h, the solution was worked up by a similar method described above to give *trans*-5-acetoxy-1,2-bis(methoxycarbonyl)piperidine (**17a**) and cis isomer **17b** in 80% (1.200 g, 4.63 mmol) and 6% (0.096 g, 0.37 mmol) yields, respectively.

17a (polar isomer): IR (neat) 2965, 1740, 1710, 1452, 1374, 1236, 1158, 1124, 1024 cm^{-1}; NMR (CCl_4) δ 1.38–2.21 (m, 4 H), 2.04 (s, 3 H), 3.11–3.41 (m, 1 H), 3.75 (s, 3 H), 3.79 (s, 3 H), 3.96–4.37 (m, 1 H), 4.92 (br s, 2 H). Anal. Calcd for $C_{11}H_{17}NO_6$: C, 50.96; H, 6.61; N, 5.40. Found: C, 51.18; H, 6.75; N, 5.30.

17b (less polar isomer): IR (neat) 2965, 1740, 1710, 1450, 1370, 1242, 1232, 1162, 1048 cm^{-1}; NMR (CCl_4) δ 1.40–2.30 (m, 4 H), 1.98 (s, 3 H), 2.57–3.00 (m, 1 H), 3.71 (s, 3 H), 3.77 (s, 3 H), 3.95–4.33 (m, 1 H), 4.47–4.97 (m, 2 H); MS, *m/e* 258 (M^+ − H), 230, 200, 140 (base). Anal. Calcd for $C_{11}H_{17}NO_6$: C, 50.96; H, 6.61; N, 5.40. Found: C, 51.25; H, 6.66; N, 5.26.

Preparation of 5-Hydroxy-2-methoxy-1-(methoxycarbonyl)piperidine (19). Carboxylic acid **18** was obtained as a white solid by hydrolysis of **17a** (1.988 g, 7.68 mmol) carried out as described above (1.56 g). Into an electrolysis cell as described above was added a solution of the crude **18** (1.56 g) and AcOK (2 g, 20 mmol) in methanol (20 mL) and acetic acid (2 mL). After 5 F/mol of electricity was passed at a constant current of 0.2 A (5.1 h, terminal voltage ca. 10 V) through the solution cooled with water, water (20 mL) was poured into the resulting reaction mixture. The organic portion was extracted with CH_2Cl_2 (3 × 20 mL) and the combined organic layer was dried over $MgSO_4$. The solvent was removed in vacuo to give a residue, which was chromatographed on silica gel (AcOEt–hexane = 1:2) to afford **19** (0.900 g, 4.76 mmol) in 62% yield: IR (neat) 3450, 2948, 1695, 1260, 1155, 1070, 1001 cm^{-1}; NMR (CCl_4) δ 1.30–2.06 (m, 4 H), 2.30–4.20 (m, 4 H), 3.14 (s, 3 H), 3.62 (s, 3 H), 5.10 (br s, 1 H); MS, *m/e* 172 (M^+ − OH), 157 (M^+ − MeOH), 140, 114 (base); exact mass calcd *m/e* 157.0739 (M^+ − MeOH), found 157.0722 (M^+ − MeOH). Anal. Calcd for $C_8H_{15}NO_4$: C, 50.78; H, 7.99; N, 7.40. Found: C, 51.05; H, 8.13; N, 7.10.

(2*R*,5*R*)- and (2*S*,5*R*)-Acetoxy-2-propyl-1-(methoxycarbonyl)piperidine (21a and 21b). To a stirred solution of $TiCl_4$ (0.42 mL, 3.83 mmol) in CH_2Cl_2 (7 mL) was added dropwise a solution of **19** (0.723 g, 3.83 mmol) and allyltrimethylsilane (0.91 mL, 5.75 mmol) in CH_2Cl_2 (17 mL) at −70 °C under an atmosphere of nitrogen. The mixture was gradually warmed to room temperature. Water (25 mL) was added to the solution and the organic portion was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layer was dried over $MgSO_4$ and the solvent was removed. A mixture of the residue and a catalytic amount of PtO_2 in acetic acid (10 mL) was stirred overnight at room temperature under an atmosphere of hydrogen (1 atm). After the catalyst and solvent were removed, the residue was dissolved in a mixed solvent of acetic anhydride (1.08 mL, 11.5 mmol) and pyridine (0.93 mL, 11.5 mmol). After the solution was stirred for 2 h, dilute HCl (20 mL) was added into the reaction mixture. The organic portion was extracted with CH_2Cl_2 (3 × 30 mL) and the combined organic layer was dried over $MgSO_4$. After the solvent was removed in vacuo, the residue was chromatographed on silica gel (AcOEt–hexane = 1:4) to afford 2*R*,5*R* isomer **21a** and 2*S*,5*R* isomer **21b** in 69% (0.635 g, 2.64 mmol) and 5% (0.050 g, 0.21 mmol) yields, respectively. Their spectroscopic data were consistent with those of **8a**,**b**.

(−)-*N*-Methylpseudoconhydrine Hydrochloride [(−)-1·HCl]. Treatment of **21a** with LAH in a way similar to the synthesis of (+)-**1** from **8a** gave (−)-**1** in more than 70% yield. IR, NMR, and MS spectrum of (−)-**1** were consistent with those of (+)-**1**. The optical purity of synthesized (−)-**1** was determined as its HCl salt (60% yield from **21a**, 90% optical purity):[5] mp 157–158 °C; $[\alpha]^{25}_D$ −22.6° (*c* 1.0, MeOH).

A Novel Reaction of Benzoyl Chlorides in Dimethyl Sulfoxide

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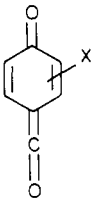
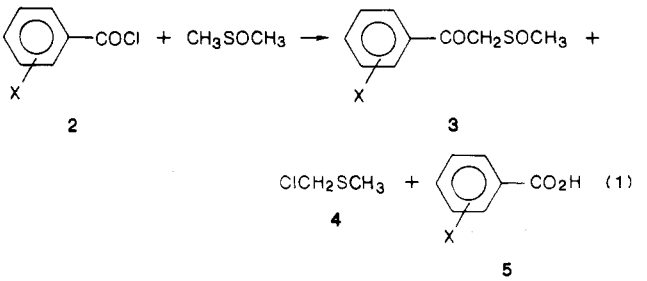
Previous research from this laboratory has shown that acyl-group transfer from substituted aryl 4-hydroxybenzoates to water or other acceptors takes place through either the "usual" $B_{Ac}2$ mechanism[1] or an unprecedented E1cB mechanism involving *p*-oxo ketenes **1** as reactive intermediates.[2]



1

We are currently attempting to generate and characterize compounds **1** in nonaqueous solvents from substituted 4-hydroxybenzoyl chlorides in the presence of bases, and in the course of this work we have discovered a novel reaction between benzoyl chlorides and dimethyl sulfoxide (DMSO).

Careful addition of 3,5-di-*tert*-butyl-4-hydroxybenzoyl chloride (**2a**) to excess DMSO at room temperature afforded not only the expected chloromethyl methyl sulfide **4** and the carboxylic acid **5a**,[3-5] but also a significant amount of the β-keto sulfoxide **3a** (eq 1 and Table I, entry



2 **3**

4 **5** (1)

1). Formation of a deeply red compound was noticed as well, whose spectroscopic and elemental analysis data were consistent with those reported in the literature[6] for

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