[Chem. Pharm. Bull. 25(7)1559—1565(1977)] UDC 547.759.04 : 546.271.04

Amino Acids and Peptides. XXVII.[1] A Novel Reductive Cleavage of N-C-N Bonds with Sodium Borohydride[2]

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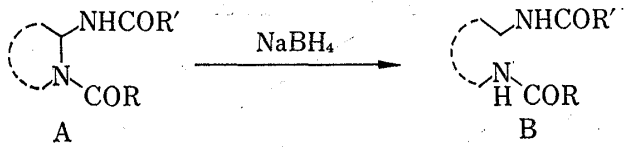
(Received October 12, 1976)

(3*S*)-*tert*-Butyl 2-benzyloxycarbonyl-1,2,3,4-tetrahydro-β-carboline-3-carbamate (III), prepared by the modified Curtius reaction of (3*S*)-2-benzyloxycarbonyl-1,2,3,4-tetrahydro-β-carboline-3-carboxylic acid (II) with diphenyl phosphorazidate (DPPA) and triethylamine in *tert*-butyl alcohol, afforded 2-ethyloxycarbonylaminomethyl-3-(2-*tert*-butyloxycarbonylamino)ethylindole (Va) by sodium borohydride reduction in ethanol, while reduction in 2-propanol gave the corresponding 2-propyl derivative (Vb) and the compound (VI) containing a novel diazocinoindole skeleton. The mechanism of the reductive cleavage was discussed. Tetrahydropyrrole analog (X) of III and 2-acetyl analog of III afforded the similar ring-cleavage products (XI and XV) by sodium borohydride reduction.

Keywords——modified Curtius reaction with diphenyl phosphorazidate; diazocinoindole skeleton; ring cleavage; ^{13}C-NMR spectra; tetrahydro-β-carbolines; sodium borohydride reduction

In relation to the biomimetic, chiral synthesis of Cinchona alkaloids, we have explored a reductive cleavage of N-C-N bonds with sodium borohydride, which allows the conversion of compounds of type A to their seco derivative B[4]:



(*S*)-1,2,3,4-Tetrahydro-β-carboline-3-carboxylic acid[5] (I) was treated with benzyloxycarbonyl chloride to give the Nb-benzyloxycarbonyl derivative (II), which was subjected to the modified Curtius reaction with diphenyl phosphorazidate (DPPA) in the presence of triethylamine in *tert*-butyl alcohol.[6] This ordinary procedure[6] resulted in the formation of the desired *tert*-butyl carbamate(III) in only 10% yield as well as the allophanate(IV) in 32% yield. This coincides with the known phenomenon in the modified Curtius reaction of N-benzyloxycarbonyl-L-proline with DPPA.[7] Although *tert*-butyl carbamate was found to be an efficient additive in the latter case,[7] addition of *tert*-butyl carbamate was not effective in the case of β-carboline derivative (II). However, the two-step procedure involving the treatment of II with DPPA in the presence of triethylamine in dimethylformamide and then the addition of *tert*-butyl alcohol to the resulting carboxylic acid azide raised the yield of III

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2) Presented in part at the 94th Annual Meeting of Pharmaceutical Society of Japan, Sendai, April 1974, Abstract II, p. 13.
3) Location: *7-3-1, Hongo, Bunkyo-ku, Tokyo, 113, Japan.*
4) A part of the work was preliminary communicated: S. Yamada, K. Murato, and T. Shioiri, *Tetrahedron Letters*, **1976**, 1605.
5) A. Brossi, A. Focella, and S. Teitel, *J. Med. Chem.*, **16**, 419 (1973).
6) T. Shioiri, K. Ninomiya, and S. Yamada, *J. Am. Chem. Soc.*, **94**, 6203 (1972); K. Ninomiya, T. Shioiri, and S. Yamada, *Tetrahedron*, **30**, 2151 (1974).
7) K. Murato, T. Shioiri, and S. Yamada, *Chem. Pharm. Bull.* (Tokyo), **23**, 1738 (1975).

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to 22%.[8] The absolute configurations of III and IV were assigned (*S*)-form, based on the reasonable assumption that the modified Curtius reaction will proceed with retention of configuration as the ordinary Curtius rearrangement.[6,7]

Reduction of the *tert*-butyl carbamate(III) with a large excess of sodium borohydride in refluxing ethanol–dioxane (4: 1) smoothly proceeded to give the ring-cleavage product (Va) in 89% yield, but its nuclear magnetic resonance spectrum revealed that Nb-benzyloxycarbonyl function in III was replaced with ethoxycarbonyl one in the product (Va). Changing the reaction solvent from ethanol to 2-propanol again resulted in the formation of the 2-propyloxycarbonyl derivative (Vb) in 53% yield. In addition to Vb, another product was isolated in 8% yield in this case. The infrared spectrum of this by-product showed two NH absorptions at 3340 and 3210 cm^{-1} as well as two peaks at the CO stretching region. The nuclear magnetic resonance spectrum was quite similar to that of the carbamate (Vb) though neither 2-propyl nor benzyl proton was present. The elemental analysis as well as the accurate mass measurement of the molecular ion revealed its elemental composition to be $C_{17}H_{21}N_3O_3$. These results suggest that the structure of the second product may be represented by VI bearing a novel diazocinoindole skeleton as shown in Chart 1. Further evidence was obtained by the inspection of the natural abundance, proton-decoupled and single-frequency, off-resonance decoupled ^{13}C nuclear magnetic resonance spectra of VI, shown in Table I.

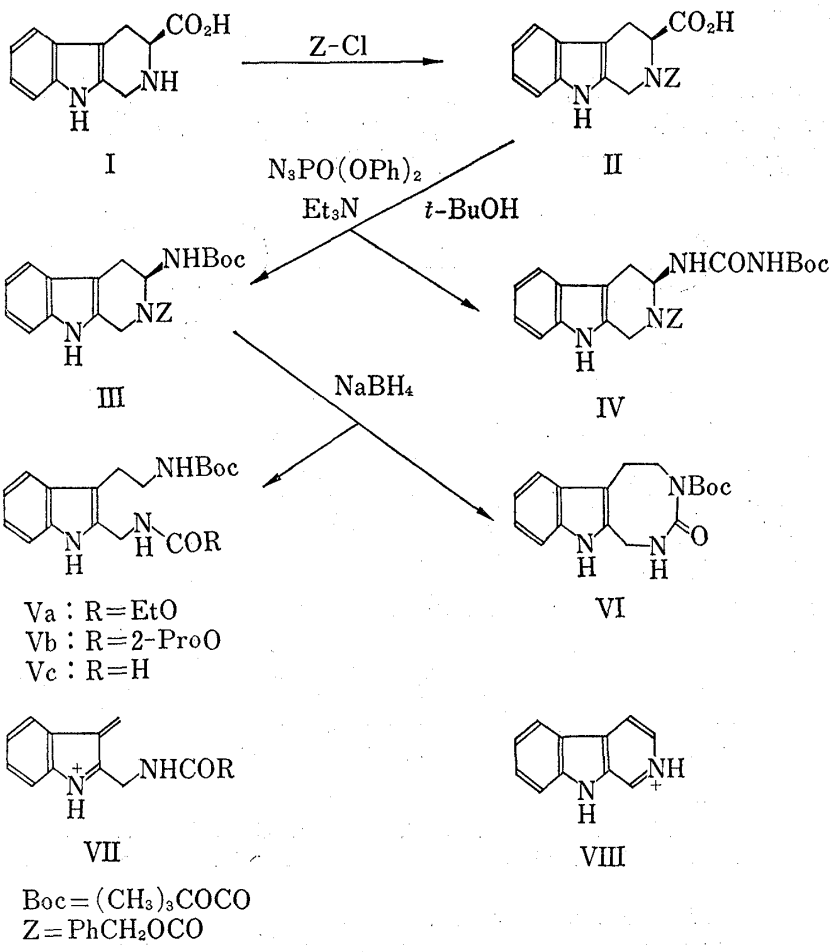

Chart 1

8) The two-step procedure is sometimes more efficient than the usual one,[6] more examples of which will be reported elsewhere.

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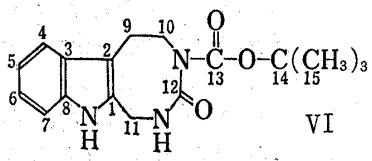
Table I. ^{13}C-NMR Chemical Shifts[a] of VI



VI

Position	ppm	Position	ppm
C-1	133.225	C- 8	133.675
C-2	107.679	C- 9	24.847
C-3	130.352	C-10 & 11	40.525
C-4	118.695	C-12 or 13	155.760
C-5	122.903	C-13 or 12	153.855
C-6	122.209	C-14	79.368
C-7	112.388	C-15	28.376

a) δ-Values in $CDCl_3$ with reference to internal TMS.

Repetition of the reduction experiments on III without alcoholic solvent afforded VI and the formyl derivative (Vc) in 16 and 40% yields, respectively. Interestingly, no reaction occurred when aqueous tetrahydrofuran was used as solvent. The 2,3-seco carbon skeleton of the reduction products (Va—c) was verified by their mass spectra showing base or strong peaks VII but no peak of β-carboline(VIII).

A probable mechanism of the novel reductive cleavage will be depicted in Chart 2. Fragmentation followed by hydride attack or direct hydride attack at C-3 will give the isocyanate(IX) which undergoes nucleophilic attack with hydroxylic solvents or hydride (attack a) to give V, while intramolecular cyclization (attack b) will give VI.

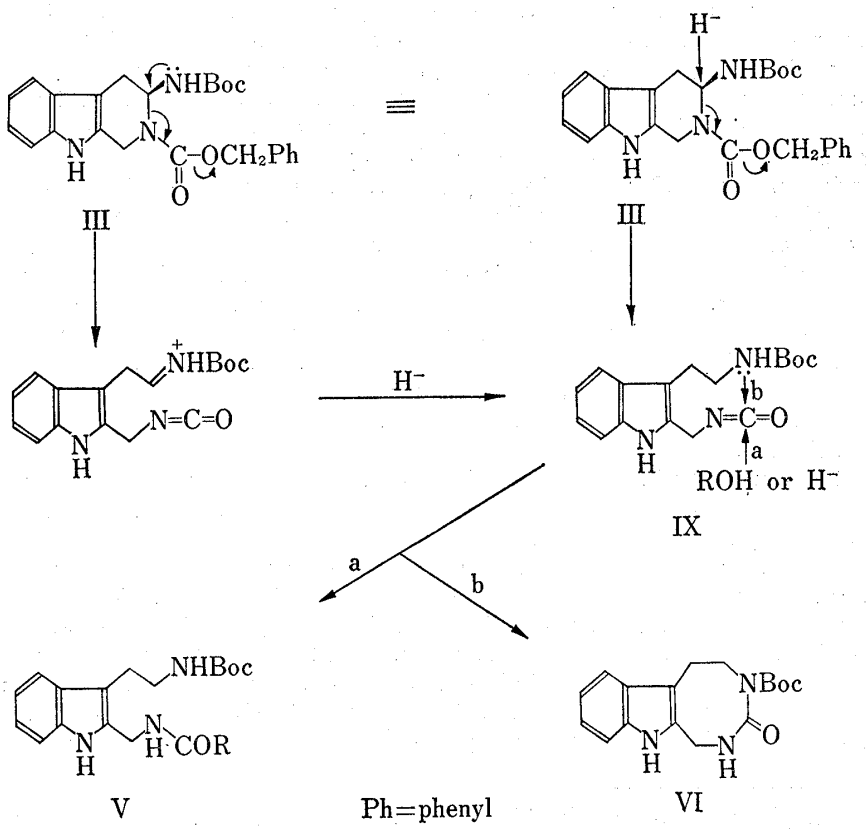


Chart 2

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Reduction of *rac-tert*-butyl 1-benzyloxycarbonyl-pyrrolidine-2-carbamate[7] (X) with sodium borohydride in refluxing ethanol also yielded ring-cleavage products (XIa and XIb) in 40 and 20% yields, respectively.[9] Borohydride reduction of X in diglyme, however, gave the formyl derivative (XII) as the only identified product.

Finally the acetyl analog of the β-carboline(XIV), obatined by the modified Curtius reaction with DPPA, was subjected to reduction with sodium borohydride in refluxing ethanol-dioxane (3: 1) to give the expected ring-cleavage product (XV) in 90% yield.

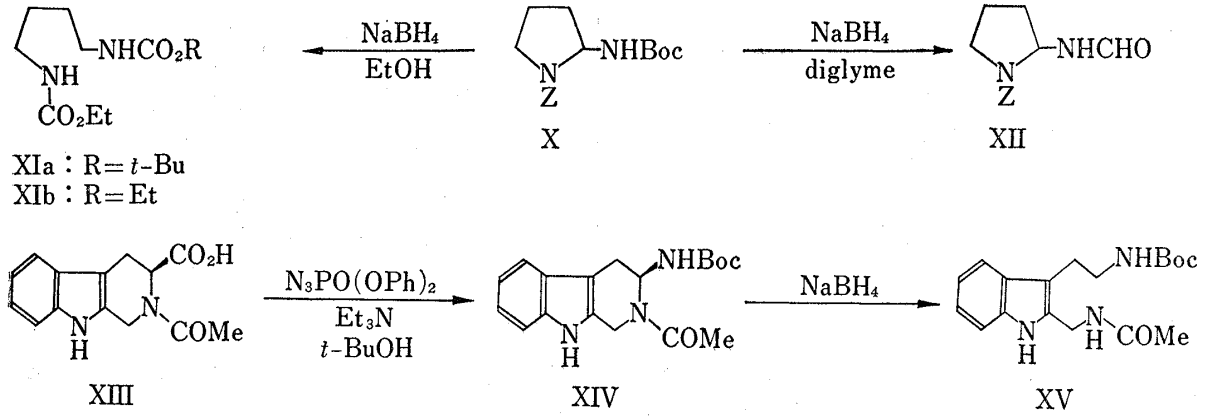

Chart 3

Extension of the novel reductive process to the biomimetic synthesis of Cinchona alkaloids is now under way.[4]

Experimental

Unless otherwise stated melting points were measured on a hot stage apparatus and uncorrected; infrared (IR) spectra were measured in nujol mulls; ^{1}H-nuclear magnetic resonance (^{1}H–NMR) spectra (60 or 100 MHz) were measured in $CDCl_3$, and chemical shifts (δ) are given in ppm relative to internal tetramethylsilane; mass spectra were measured at 70 eV. Silica gel (Wakogel C-200) was used for column chromatography. The organic solutions were dried over magnesium sulfate before vacuum evaporation. PLC refers to preparative thick-layer chromatography on Merck Kieselgel GF_{254} plates.

(3*S*)-2-Benzyloxycarbonyl-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid (II)——To a solution of (3*S*)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic acid (I)[5] (5.4 g, 25 mmol) in 2 N sodium hydroxide (15 ml, 30 mmol) were alternately added benzyloxycarbonyl chloride (5.1 g, 30 mmol) and 10% aqueous sodium carbonate (21 ml) with vigorous stirring and ice-cooling. After the addition, the mixture was stirred at room temperature for 18 hr, washed with ethyl acetate (100 ml), acidified with 5% aqueous hydrochloric acid, and extracted with ethyl acetate. The organic extracts were washed with water, dried, and evaporated to give a yellow foam, which was treated with methanol to furnish II (7.9 g, 90%) as a colorless powder. Recrystallization from methanol gave colorless prisms, mp 177—179° (decomp.), $[\alpha]_D^{20}$ +59° (c=1.0, chloroform), IR ν_{max} cm^{-1}: 3440, 1720, 1640, 1620. *Anal.* Calcd. for $C_{20}H_{18}N_2O_4$: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.48; H, 5.14; N, 8.00.

Modified Curtius Reaction of the Acid (II) with DPPA——(i) One-step Procedure: A mixture of the acid (II), (1.75 g, 5 mmol), DPPA (1.51 g, 5.5 mmol), and triethylamine (0.56 g, 5.5 mmol) in *tert*-butyl alcohol (30 ml) was gently refluxed for 18 hr. The evaporated residue was dissolved in ethyl acetate (75 ml), and successively washed with 10% aqueous sodium carbonate (25 ml×3), water (25 ml), 5% aqueous citric acid (30 ml×2), water (25 ml), and saturated aqueous sodium chloride (25 ml). The solution was evaporated, and the residue was chromatographed over silica gel using methylene chloride–diethyl ether (10: 1).

The first fraction to be eluted was the carbamate (III) (0.20 g, 10%) as colorless needles (recrystallized from diethyl ether–hexane), mp 193—194°, $[\alpha]_D^{26}$ +67° (c=0.54, chloroform); IR ν_{max} cm^{-1}: 3360, 3290, 1700, 1685, 1500; NMR 1.40 (9H, singlet, $(CH_3)_3C$), 2.94 (2H, broad, 4-CH_2), 4.24 and 4.92 (2H, AB type, J=15 Hz, 1-CH_2) 5.23 (3H, broad singlet, CH_2 of Z group and NH of Boc group), 6.40 (1H, multiplet, 3-CH), 6.95—

9) In this case, benzyl alcohol was obtained in 74% yield in addition to the recovery of the starting material (X) in 5% yield.

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7.55 (9H, multiplet, indole and benzene H), 8.63 (1H, singlet, NH of indole); Mass Spectrum *m/e*: 421 (M^+), 304, 169 (VIII). *Anal.* Calcd. for $C_{24}H_{27}N_3O_4$: C, 68.39; H, 6.46; N, 9.97. Found: C, 68.30; H, 6.45; N, 9.74.

The second fraction to be eluted was the allophanate (IV) (0.75 g, 32%) as colorless needles (recrystallized from methanol), mp 189.5—192° (dec.), $[\alpha]_D^{19}$ −24° (c=0.1, methanol); IR ν_{max} cm^{-1}: 3385, 3305, 3220, 1715, 1700, 1630, 1550, 1540; NMR 1.30 (9H, singlet, $(CH_3)_3C$), 3.00 (2H, broad, 4-CH_2), 4.30 and 4.95 (2H, AB type, J=16 Hz, 1-CH_2), 5.16 (2H, singlet, CH_2 of Z group), 6.66 (1H, multiplet, 3-CH), 6.90—7.50 (9H, multiplet, indole and benzene H), 7.58 (1H, singlet, N<u>H</u>-Boc), 8.36 (1H, doublet, J=8 Hz, CHN<u>H</u>CO), 8.49 (1H, singlet, NH of indole); Mass Spectrum *m/e*: 464 (M^+), 304, 169 (VIII). *Anal.* Calcd. for $C_{25}H_{28}N_4O_5$: C, 64.65; H, 6.08; N, 12.07. Found: C, 64.64; H, 6.08; N, 12.06.

(ii) Two-step Procedure: To a stirred mixture of the acid (II) (350 mg, 1 mmol) and triethylamine (110 mg, 1.1 mmol) in dimethylformamide (1.5 ml) was added DPPA (303 mg, 1.1 mmol) in dimethylformamide (0.5 ml) at 0°. The mixture was stirred at 0° for 4 hr and poured into methylene chloride-ice water. After separation of the methylene chloride layer, the aqueous layer was extracted with methylene chloride. The combined methylene chloride extracts (50 ml) were washed with water, dried, and evaporated below 15°. *tert*-Butyl alcohol (12 ml) was added to the residue, and the mixture was gently refluxed overnight. After evaporation followed by addition of ethyl acetate (40 ml), the solution was washed with water (20 ml × 3), dried, and evaporated to give a brown foam. Purification was made by a silica gel column chromatography using methylene chloride-diethyl ether (20: 1) to give the carbamate (III) (91 mg, 22%) identified with the sample obtained in (i).

No efforts were made to isolate the allophanate (IV) in this case.

Sodium Borohydride Reduction of the Carbamate (III)——(i) In Ethanol-dioxane: To a stirred solution of the carbamate (III) (210 mg, 0.5 mmol) in ethanol (8 ml)–dioxane (2 ml) was added sodium borohydride (190 mg, 5 mmol), and the mixture was refluxed for 4 hr. After the addition of more sodium borohydride (190 mg, 5 mmol), the mixture was refluxed for 10 hr, poured into ice-water, and extracted with diethyl ether. The ethereal extracts were washed with water, dried, and evaporated. The residue was purified on a PLC plate (diethyl ether–hexane (5:2)) to give the ring-cleavage product (Va) (0.16 g, 89%) as a colorless solid. Recrystallization from diethyl ether–hexane gave colorless needles, mp 148—148.5°; IR ν_{max} cm^{-1}: 3320, 1700—1680, 1550, 1530; NMR 1.16 (3H, triplet, J=7 Hz, C<u>H</u>$_3$CH$_2$), 1.36 (9H, singlet, $(CH_3)_3C$), 2.83 (2H, triplet, J=7 Hz, C<u>H</u>$_2$CH$_2$N), 3.26 (2H, multiplet, CH$_2$C<u>H</u>$_2$N), 4.05 (2H, quartet, J=7 Hz, C<u>H</u>$_2$CH$_3$), 4.28 (2H, doublet, J=6 Hz, CH$_2$N), 4.72 (1H, broad, NH), 5.73 (1H, broad, NH), 6.90—7.50 (4H, multiplet, indole H), 8.90 (1H, singlet, NH of indole); Mass Spectrum *m/e*: 361 (M^+), 305, 231 (VII, base). *Anal.* Calcd. for $C_{19}H_{27}N_3O_4$: C, 63.14; H, 7.53; N, 11.63. Found: C, 63.03; H, 7.63; N, 11.61.

(ii) In 2-Propanol-dioxane: A mixture of the carbamate (III) (170 mg, 0.4 mmol) and sodium borohydride (190 mg, 5 mmol) in 2-propanol (8 ml)-dioxane (2 ml) was gently refluxed with stirring for 5 hr. The mixture was poured into ice-water, and extracted with diethyl ether. The extracts were washed with water, dried, and evaporated. The residue was fractionated on a PLC plate (diethyl ether–hexane (2: 1)). The upper fraction was the ring-cleavage product (Vb) (80 mg, 53%), which was recrystallized from diethyl ether–hexane to give colorless plates, mp 99—100°; IR ν_{max} cm^{-1}: 3410, 3350, 1705, 1535, 1515; NMR 1.20 (6H, doublet, J=6 Hz, $(C\underline{H}_3)_2$CH), 1.40 (9H, singlet, $(CH_3)_3C$), 2.95 (2H, triplet, J=7 Hz, C<u>H</u>$_2$CH$_2$N), 3.30 (2H, multiplet, CH$_2$C<u>H</u>$_2$N), 4.36 (2H, doublet, J=7 Hz, CH$_2$N), 4.5—5.0 (2H, multiplet, NH and CH), 5.75 (1H, broad, NH), 6.95—7.60 (4H, multiplet, indole H), 9.10 (1H, singlet, NH of indole); Mass Spectrum *m/e* 375 (M^+), 245 (VII), 159. *Anal.* Calcd. for $C_{20}H_{29}N_3O_4$: C, 63.97; H, 7.79; N, 11.19. Found: C, 64.26; H, 7.96; N, 11.02.

The lower fraction was the diazocinoindole (VI) (10 mg, 8%), which was identified with the sample obtained below (iii) by spectral and chromatographic comparisons.

(iii) In Diglyme: A mixture of the carbamate (III) (170 mg, 0.4 mmol) and sodium borohydride (150 mg, 4 mmol) in diglyme (5 ml) was stirred at 85° for 5 hr. After cool, acetone (1 ml) was added. The mixture was stirred for 10 min, poured into ice-water, and extracted with diethyl ether. The extracts were washed with water, dried, and evaporated. The residue was fractionated on a PLC plate (diethyl ether–hexane (3: 1)). The upper fraction was the diazocinoindole (VI) (20 mg, 16%), which was recrystallized from diethyl ether–hexane to give colorless needles, mp 172°; IR ν_{max}^{KBr} cm^{-1}: 3340, 3210, 1736, 1688, 1458, 740; NMR 1.42 (9H, singlet, $(CH_3)_3C$), 2.86 (2H, triplet, J=6 Hz, C<u>H</u>$_2$CH$_2$N), 3.41 (2H, quartet, J=6 Hz, CH$_2$C<u>H</u>$_2$N), 4.46 (2H, singlet, CH$_2$N), 6.63 (1H, broad singlet, NHCO), 7.00—7.52 (4H, multiplet, indole H), 7.89 (1H, singlet, NH of indole); Mass Spectrum *m/e*: 315 (M^+), 259, 185. *Anal.* Calcd. for $C_{17}H_{21}N_3O_3$: C, 64.74; H, 6.71; N, 13.33. Found: C, 65.02; H, 6.84; N, 13.14. Molecular weight Calcd.: 315.15839. Found: 315.15520 (by mass measurement).

The lower fraction was the ring-cleavage product (Vc) (50 mg, 40%), which was recrystallized from diethyl ether–hexane to give colorless plates, mp 106—108°; IR ν_{max} cm^{-1}: 3350, 1695, 1650, 1540; NMR 1.38 (9H, singlet, $(CH_3)_3C$), 2.86 (2H, triplet, J=6 Hz, C<u>H</u>$_2$CH$_2$N), 3.30 (2H, multiplet, CH$_2$C<u>H</u>$_2$N), 4.43 (2H, doublet, J=6 Hz, CH$_2$N), 4.89 (1H, broad, NH), 6.80—7.52 (5H, multiplet, indole H and NH), 8.06 (1H, singlet, CHO), 9.12 (1H, singlet, NH of indole); Mass Spectrum *m/e*: 317 (M^+), 261, 187 (VII). *Anal.* Calcd. for $C_{17}H_{23}N_3O_3$: C, 64.33; H, 7.30; N, 13.24. Found: C, 64.17; H, 7.37; N, 12.98.

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Sodium Borohydride Reduction of *tert*-Butyl 1-Benzyloxycarbonylpyrrolidine-2-carbamate (X)——(i) In Ethanol: A mixture of the carbamate[7] (X) (160 mg, 0.5 mmol) and sodium borohydride (190 mg, 5 mmol) in ethanol (5 ml) was refluxed for 23 hr. After the addition of more sodium borohydride (190 mg, 5 mmol) in ethanol (2 ml), the mixture was refluxed for 7 hr, poured into water (100 ml), and extracted with diethyl ether (25 ml×5). The ethereal extracts were washed with water, dried, and evaporated. The residue was fractionated by a column chromatography using diethyl ether–hexane (9: 5). The first fraction to be eluted was benzyl alcohol (40 mg, 74%) indentified with the authentic sample.

The second fraction was the starting material (X) (8 mg, 5%).

The third fraction to be eluted was the *tert*-butyl ethyl carbamate (XIa) (42 mg, 40%) as colorless needles (recrystallized from diethyl ether–hexane), mp 108—109°; IR ν_{max} cm^{-1}: 3340, 1685, 1540; NMR 1.22 (3H, triplet, J=7 Hz, C$\underline{H}_3$CH$_2$), 1.44 (9H, singlet, (CH$_3$)$_3$C), 1.50—1.70 (4H, multiplet, CH$_2$CH$_2$), 3.05—3.40 (4H, multiplet, 2×CH$_2$N), 4.17 (2H, quartet, J=7 Hz, C$\underline{H}_2$CH$_3$), 4.80—5.50 (2H, broad, 2×NH). *Anal.* Calcd. for $C_{12}H_{24}N_2O_4$: C, 55.36; H, 9.29; N, 10.76. Found: C, 55.11; H, 9.40; N, 11.00.

The fourth fraction to be eluted was the diethyl carbamate (XIb) (23 mg, 20%) as colorless needles (recrystallized from diethyl ether–hexane), mp 88—89°; IR ν_{max} cm^{-1}: 3330, 1685, 1540; NMR 1.21 (6H, triplet, J=7 Hz, 2×CH$_3$), 1.52 (4H, multiplet, 2×CH$_2$), 3.10 (4H, multiplet, 2×CH$_2$N), 4.10 (4H, quartet, J=7 Hz, 2×C$\underline{H}_2$CH$_3$), 5.20 (2H, broad, 2×NH). *Anal.* Calcd. for $C_{10}H_{20}N_2O_4$: C, 51.70; H, 8.68; N, 12.06. Found: C, 51.98; H, 8.65; N, 11.94.

(ii) In Diglyme: A mixture of the carbamate[7] (X) (160 mg, 0.5 mmol) and sodium borohydride (190 mg, 5 mmol) in diglyme (2 ml) was stirred at 55—60° for 24 hr. After ice-cooling, acetone (1 ml) was added, the mixture was stirred for 10 min, and poured into water (10 ml). After extraction with diethyl ether (15 ml×6), the extracts were washed with water, dried, and evaporated. The residue was purified on a silica gel column using methylene chloride and diethyl ether (4: 1) to give the formyl derivative (XII) as a colorless semisolid, which crystallized on standing with acetone. Recrystallization from methylene chloride–hexane afforded colorless plates, mp 91—91.5°; IR ν_{max} cm^{-1}: 3190, 3080, 1710, 1685, 765, 725; NMR 1.85—2.20 (4H, multiplet, CH$_2$CH$_2$), 3.40—3.60 (2H, multiplet, CH$_2$N), 5.12 (2H, singlet, CO$_2$CH$_2$), 5.20 (1H, multiplet, CH), 7.30 (5H, singlet, benzene H), 7.48 (1H, broad, NH), 8.01 (1H, singlet, CHO); Mass Spectrum *m/e*: 248 (M$^+$), 203, 113. *Anal.* Calcd. for $C_{13}H_{16}N_2O_3$: C, 62.89; H, 6.50; N, 11.28. Found: C, 62.61; H, 6.63; N, 11.22.

(3*S*)-2-Acetyl-1,2,3,4-tetrahydro-β-carboline-3-carboxylic Acid (XIII)——To a solution of (3*S*)-1,2,3,4-tetrahydro-β-carboline-3-carboxylic acid (I)[5] (2.16 g, 10 mmol) in 2 N sodium hydroxide (8 ml, 16 mmol)–water (40 ml) were alternately added acetic anhydride (1.33 g, 13 mmol) and sodium carbonate (1.59 g, 15 mmol) in water (20 ml) with vigorous stirring and ice-cooling. The mixture was stirred at room temperature for 4 hr, washed with ethyl acetate, acidified with concentrated aqueous hydrochloric acid, and extracted with ethyl acetate. The organic extracts were washed with water, dried, and evaporated to give a pale yellow solid, which was recrystallized from methanol to furnish XIII (1.80 g, 70%) as colorless crystals, mp 211—215° (decomp.), $[\alpha]_D^{20}$ +145° (c=1.0, methanol), IR ν_{max} cm^{-1}: 3340, 1745, 1585. *Anal.* Calcd. for $C_{14}H_{14}N_2O_3$: C, 65.10; H, 5.46; N, 10.85. Found: C, 64.90; H, 5.48; N, 10.55.

Modified Curtius Reaction of the Acid (XIII) with DPPA——(i) One-step Procedure: A mixture of the acid (XIII) (258 mg, 1 mmol), DPPA (303 mg, 1.1 mmol), and triethylamine (111 mg, 1.1 mmol) in *tert*-butyl alcohol (10 ml) was stirred at reflux for 24 hr. The evaporated residue was dissolved in ethyl acetate (30 ml), and successively washed with 10% aqueous sodium carbonate (10 ml×3), water (10 ml), 5% aqueous citric acid (10 ml×3), water (10 ml), saturated aqueous sodium chloride (10 ml). The solution was evaporated, and the residue was purified on a PLC plate (ethyl acetate–hexane (4: 1)) to give the carbamate (XIV) (16 mg, 5%) as a colorless crystalline powder (Rf 0.2), mp 193—195° (decomp.), $[\alpha]_D^{20}$ +42.5° (c=0.31, methanol); IR ν_{max} cm^{-1}: 3260, 1720, 1620, 1525; NMR in CD$_3$OD 1.34 (9H, singlet, (CH$_3$)$_3$C), 2.42 (3H, singlet, CH$_3$CO), 3.28 (2H, broad, 4-CH$_2$), 4.04 and 5.29 (2H, AB type, J=16 Hz, CH$_2$N), 6.16 (1H, multiplet, 3-CH), 6.92—7.44 (4H, multiplet, indole H). Mass Spectrum *m/e* 329, 273, 229. *Anal.* Calcd. for $C_{18}H_{23}N_2O_3$: C, 65.65; H, 7.04; N, 12.76. Found: C, 65.91; H, 7.10; N, 12.66.

(ii) Two-step Procedure: To a stirred mixture of the acid (XIII) (258 mg, 1 mmol) and triethylamine (111 mg, 1.1 mmol) in dimethylformamide (1.5 ml) was added DPPA (303 mg, 1.1 mmol) in dimethylformamide (0.5 ml) at 0°. The mixture was stirred at 0° for 4 hr, and poured into methylene chloride-ice water. After separation of the methylene chloride layer followed by extraction of the aqueous layer with methylene chloride, the combined extracts (50 ml) were washed with water, dried, and evaporated below 15°. *tert*-Butyl alcohol (12 ml) was added to the evaporated residue, and the mixture was gently refluxed overnight. After evaporation, ethyl acetate (40 ml) was added, and the solution was washed with water (20 ml×3) and dried. The evaporated residue was purified by a column chromatography using methylene chloride–diethyl ether (3: 1) to give the carbamate (XIV) (71 mg, 22%), identified with the sample obtained in (i).

Sodium Borohydride Reduction of the Carbamate (XIV)——A mixture of the carbamate (XIV) (82 mg, 0.25 mmol) and sodium borohydride (95 mg, 2.5 mmol) in ethanol (6 ml)-dioxane (2 ml) was refluxed for 20 hr. After the addition of more sodium borohydride (95 mg, 2.5 mmol), the mixture was refluxed for 8 hr, poured into ice-water, and extracted with diethyl ether. The ethereal extracts were washed with water and dried. The residue was purified on a PLC plate using ethyl acetate–hexane (4: 1) to give the ring-cleavage

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product (XV) (74 mg, 90%) as colorless needles (recrystallized from methylene chloride–hexane), mp 176.5—177.5°; IR ν_{max} cm^{-1}: 3300, 1700, 1640, 1550; NMR 1.38 (9H, singlet, $(CH_3)_3C$), 1.98 (3H, singlet, CH_3CO), 2.87 (2H, triplet, $J=6$ Hz, $C\underline{H}_2CH_2N$), 3.30 (2H, multiplet, $CH_2C\underline{H}_2N$), 4.39 (2H, doublet, $J=5$ Hz, CH_2N), 4.65 (1H, broad, NH), 6.80 (1H, broad, NH), 6.96—7.52 (4H, multiplet, indole H), 9.06 (1H, singlet, NH of indole); Mass Spectrum *m/e*: 331 (M^+), 275, 201 (VII, base). *Anal.* Calcd. for $C_{18}H_{25}N_3O_3$: C, 65.23; H, 7.60; N, 12.68. Found: C, 65.20; H, 7.62; N, 12.58.

Acknowledgement We wish to thank Dr. M. Matsuo of Tokyo Metropolitan Institute of Gerontology for ^{13}C-NMR spectra and Mr. K. Ozawa of Teijin Co., Ltd. for high resolution mass spectra.

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