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Total Synthesis of (–)-Trypargine¹⁾

MASATO SHIMIZU, MASAYUKI ISHIKAWA,* YASUO KOMODA, and TERUMI NAKAJIMA*

*Institute for Medical and Dental Engineering, Tokyo Medical and Dental University,
2-3-10, Surugadai, Kanda, Chiyoda-ku, Tokyo, 101, Japan*

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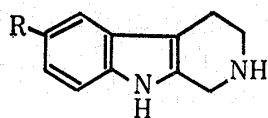
The total synthesis of (±)-trypargine (2) was accomplished to confirm the proposed structure, 1-(3'-guanidinopropyl)-1,2,3,4-tetrahydro-β-carboline. Optically active (–)-trypargine (2a) and its enantiomer (2b) were obtained by the optical resolution of the racemate. The stereochemistry at C-1 is discussed on the basis of the optical rotatory dispersion and circular dichroism curves.

Keywords—trypargine; total synthesis; tetrahydro-β-carboline; Pictet-Spengler reaction; 1,2,3,5,6,11b-hexahydro-3-oxo-11*H*-indolo[3,2-*g*]pyrrocoline; optical resolution; stereochemistry

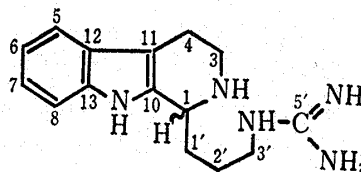
Recently, several tetrahydro-β-carbolines (1a–c)²⁾ were found in mammalian brain, urine, platelets and other tissues, and extensive studies by pharmacologists have indicated that these endogenously formed β-carbolines act relatively specifically on various aspects of serotonergic neurotransmitter functions.

(–)-Trypargine (2a), isolated from the skin of African frogs *Kassina senegalensis* by Akizawa *et al.*,¹⁾ is a new 1,2,3,4-tetrahydro-β-carboline derivative possessing a guanidino group. Though the biological activity of 2a has not been studied, this compound has biosynthetically and pharmacologically interesting structural features.

We wish to report in the present paper the total synthesis of (±)-trypargine (2) to confirm the proposed structure and also to obtain sufficient amounts for pharmacological tests, as well as studies on the stereochemistry of 2a by optical rotatory dispersion (ORD) and circular dichroism (CD) measurements. Both enantiomers 2a and 2b were obtained in optically pure form.



1a : R=H
1b : R=OH
1c : R=OCH₃



2a : (–)-trypargine : C(1)-αH
2b : (+)-trypargine : C(1)-βH

Chart 1

In our synthetic approach, β-cyanopropionaldehyde ethylene acetal (4b)³⁾ was chosen as an acyclic component corresponding to the nontryptophan-derived portion of trypargine (2), and the first objective in the synthesis was preparation of the compound (5) as a possible intermediate for 2.

The Pictet-Spengler reaction of tryptamine (3) with 4b prepared from bromoacetal (4a)⁴⁾ was carried out in 80% acetic acid (AcOH) at room temperature to afford an unstable compound, probably 5, as a main product, but this labile product was easily transformed into the tetracyclic compound (6) during purification, and many attempts to isolate it were unsuccessful. When the above Pictet-Spengler reaction was performed under reflux, 6 was obtained

in good yield. The structure of **6** was identified on the basis of spectral data, and by the transformation of **6** into 1,2,3,5,6,11b-hexahydro-3-oxo-11*H*-indolo[3,2-*g*]pyrrocoline (**7**),⁵⁾ whose structure had been proved unequivocally, by hydrolysis with hot methanolic NaOH.

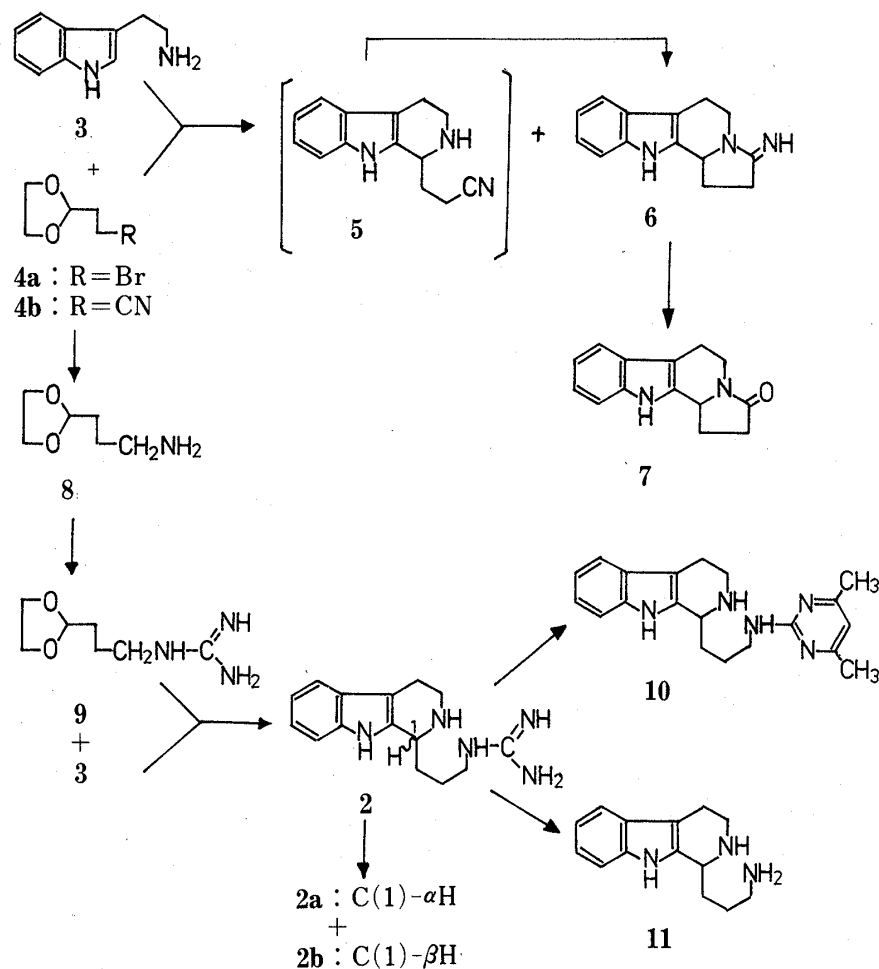


Chart 2

On the other hand, **4b** was subjected to reduction with LiAlH_4 to give the aminoacetal (**8**). Compound **8** was directly heated with *S*-methylisothiurea sulfate in water to afford guanidinoacetal sulfate (**9**). The condensation of **9** with **3** was carried out in 80% AcOH at 50°C, and provided the racemic tryptargine sulfate (**2**) in high yield. Since this sulfate has very low solubility in water and ordinary organic solvents used to take various spectral data and since natural tryptargine (**2a**) was isolated as a hydrochloride, the sulfate was converted into the corresponding hydrochloride, and the structure of the racemate (**2**) was established by elemental analysis, as well as measurement of ^{13}C -NMR spectra and other spectral data. Further evidence for the structure **2** was obtained by the preparation of volatile derivatives suitable for mass spectrometry; **10** was prepared from **2** on treatment with acetylacetone, and **11** was formed by hydrolysis of **2** with 50% aqueous hydrazine hydrate.

The synthetic ($\pm$)-tryptargine hydrochloride was identical with natural tryptargine hydrochloride in all respects except IR spectra (KBr). The disagreement in IR spectra indicated differences in crystalline form. As will be described later, this view was confirmed by the identity of the IR spectra of natural tryptargine hydrochloride and synthetic (–)-tryptargine hydrochloride obtained by the optical resolution of the racemate. Furthermore, **10** and **11** derived from the racemate were identical with those obtained from natural tryptargine, respectively. Thus, the structure of (–)-tryptargine (**2a**) was unambiguously established as (–)-1-(3'-guanidinopropyl)-1,2,3,4-tetrahydro- β -carboline.

Optically pure (–)-tryptargine (**2a**) and its dextrorotatory enantiomer (**2b**) were obtained by the optical resolution of the racemate using D-(+)-10-camphorsulfonic acid and D-(–)-tartaric acid, respectively.

(±)-Tryptargine sulfate (**2**) was passed through a column of SP Sephadex with 0.5 M HCO₂–NH₄ (pH 6.80) as an eluent, and the formate obtained was treated with D-(+)-10-camphorsulfonic acid in water affording the salt of the levorotatory enantiomer, mp 160–163°C, [α]_D –7.8° (MeOH). The formic acid salt of the levorotatory base recovered from the D-(+)-10-camphorsulfonate was applied to a column of Sephadex G-10, eluted with 0.02 M HCl, and converted into the corresponding synthetic (–)-tryptargine hydrochloride (**2a**), mp 210–213°C, [α]_D –37.3° (MeOH), whose melting point was undepressed on admixture with natural tryptargine hydrochloride; in addition, the IR (KBr) spectra, and the ORD and CD curves of both compounds were completely superimposable.

On the other hand, the first mother liquor of the (–)-tryptargine-D-(+)-10-camphorsulfonate was converted into the formate. Treatment of the above formate with D-(–)-tartaric acid in water afforded the corresponding tartrate of the dextrorotatory enantiomer, mp 198–200°C (dec.), [α]_D +9.9° (H₂O). The hydrochloride of the dextrorotatory enantiomer (**2b**), mp 204–207°C, [α]_D +37.2° (MeOH), was obtained in the same way as described above.

The ORD and CD spectra of **2a** are shown in Fig. 1 and Fig. 2, respectively.

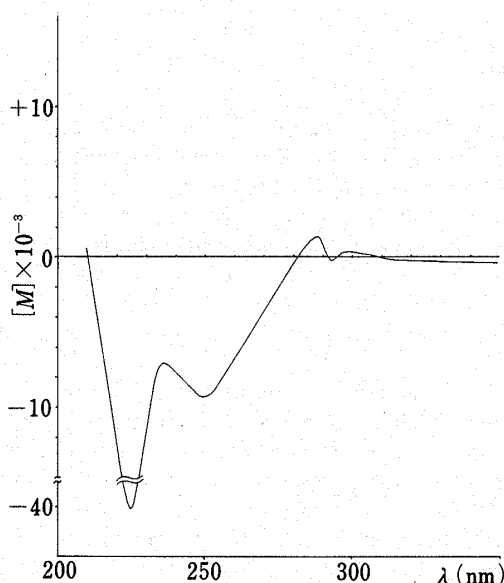


Fig. 1. ORD Curve of Synthetic (–)-Tryptargine (**2a**)

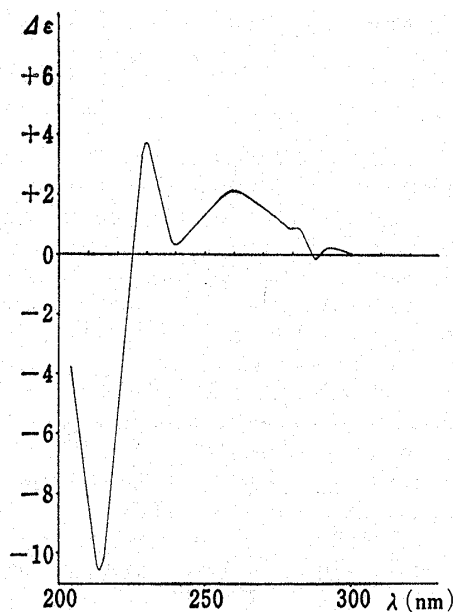


Fig. 2. CD Curve of Synthetic (–)-Tryptargine (**2a**)

It is known that the ORD curves can be used to determine the absolute configuration at C-3 of a variety of indole alkaloids. Klyne and co-workers⁶ found two Cotton effects, one at 295–280 nm, and the other at 275–250 nm. A positive Cotton effect in the 275–250 nm region is directly related to the absolute configuration at C-3 and corresponds to α -H configuration. Then, a third Cotton effect in the region of 250–200 nm was described by Trojáněk and co-workers.⁷ A deep trough at 227 nm reflects the α -H configuration at C-3, while a strong peak at 227 nm reflects the β -H configuration.

The ORD curve of **2a** in the region of 250–200 nm shows a deep trough at 225 nm, with a negative Cotton effect as a whole. Compound **2a** also exhibits a positive Cotton effect in the UV region above 250 nm. Moreover, the shape of the CD curves of **2a** closely resembles that of yohimban (**12a**) or allo-yohimban (**12b**)⁸ of known absolute configuration. The CD curve of pseudo-yohimban (**12c**) or 3-epi-allo-yohimban (**12b**) shows enantiomeric character

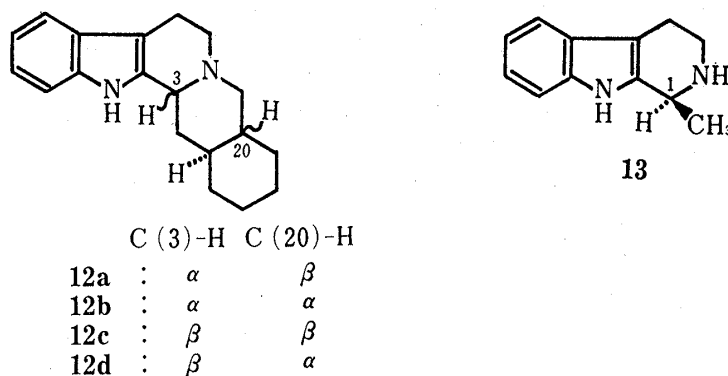


Chart 3

with respect to the curve of **2a**. The findings described above suggest that **2a** has the same stereochemistry as (1*S*)-(–)-1,2,3,4-tetrahydroharman (**13**).

Trypargine (**2a**) is an optically active metabolite derived from tryptophan, and it seems that **2a** is formed biosynthetically by the condensation of tryptophan with arginine, in contrast to the mevalonate-derived alkaloids of the yohimbine type.

Biological tests *in vivo* and *in vitro* of **2a** and the structure–activity relationship of **2a** and its congeners with **1a–c** are in progress.

Experimental

All melting points are uncorrected. Ultraviolet (UV) spectra were recorded on a Hitachi 323 recording spectrophotometer. Infrared (IR) spectra were recorded on a Hitachi 285 spectrophotometer. Mass spectra (MS) were taken by the electron impact ionization (EI-MS) and/or chemical ionization (CI-MS) methods on a JEOL JMS-D300 mass spectrometer. The proton magnetic resonance (¹H-NMR) spectra were recorded using a Hitachi R-600 NMR spectrometer. The carbon-13 magnetic resonance (¹³C-NMR) spectra were recorded using a JEOL FX-100 spectrometer. Chemical shifts for the ¹H- and ¹³C-NMR spectra are reported as δ values (parts per million) from tetramethylsilane as an internal standard. The ORD and CD curves were measured with a JASCO J-20 recording spectro-polarimeter and the optical rotations were measured with a JASCO DIP-140 polarimeter.

β -Cyanopropionaldehyde Ethylene Acetal (4b)—Sodium cyanide (14.70 g, 0.30 mol) and benzyltrimethylammonium chloride (5.57 g, 0.03 mol) were dissolved in 90 ml of water. β -Bromopropionaldehyde ethylene acetal⁴⁾ (**4a**, 42.25 g, 0.25 mol) was added to the stirred solution below 20°C, and the resulting emulsion was heated at 90°C for 4 h. The reaction mixture was diluted with 100 ml of water and extracted with ether (4 $\times$ 250 ml). The organic layer was washed with saturated sodium chloride solution, dried over anhydrous potassium carbonate, and concentrated. The residue was distilled to give **4b** (25.60 g, 80.6%), bp 89°C (5 mmHg) [lit.³⁾ bp 82°C (3 mmHg)]. IR $\nu_{\max}^{\text{Nujol}}$ cm^{−1}: 2250 (C $\equiv$ N). EI-MS *m/e* (%): 126 (*M*⁺−1, 31), 73 (100). CI-MS *m/e*: 128 (*M*⁺+1). ¹H-NMR (CDCl₃) δ : 2.25 (m, 4H), 3.93 (m, 4H), 4.97 (t, 1H, *J* = 3.7 Hz).

1,2,3,5,6,11b-Hexahydro-3-imino-11*H*-indolo[3,2-*g*]pyrrocoline (6)—**4b** (0.95 g, 0.007 mol) was added to a solution of tryptamine hydrochloride (0.98 g, 0.005 mol) in 10 ml of 80% AcOH. The reaction mixture was heated at 120°C under O₂-free nitrogen for 4 h, then cooled and evaporated to dryness. The residue was dissolved in 50 ml of water, basified with concd. NH₄OH and extracted with chloroform (4 $\times$ 100 ml). The organic layer was dried over anhydrous sodium sulfate, and concentrated. Crystallization of the residue from MeOH–CH₂Cl₂ gave **6** (0.90 g, 80%). An analytical sample of **6** was prepared by repeated recrystallization from MeOH as pale brownish needles, mp 228–231°C (dec.). Anal. Calcd for C₁₄H₁₅N₃: C, 74.64; H, 6.71; N, 18.65. Found: C, 74.23; H, 6.80; N, 18.41. UV $\lambda_{\max}^{\text{MeOH}}$ nm (log ϵ): 221 (4.67), 273 (3.90), 278 (3.89), 289 (3.76). ¹H-NMR (CD₃OD+CDCl₃) δ : 4.52 (m, 1H), 4.94 (m, 1H) and 6.9–7.6 (m, 4H, arom.H). IR $\nu_{\max}^{\text{KBr}}$ cm^{−1}: 3300 (NH), 1620 (C=N). EI-MS *m/e* (%): 225 (*M*⁺, 100), 224 (33), 210 (20), 198 (10), 197 (6.7), 196 (6.7), 184 (10), 183 (10), 182 (15), 181 (15), 170 (6.7), 169 (18), 168 (15), 167 (16.7), 156 (11.2), 155 (11.2), 154 (11.2), 144 (8.3), 143 (11.7).

1,2,3,5,6,11b-Hexahydro-3-oxo-11*H*-indolo[3,2-*g*]pyrrocoline (7)—**6** (100 mg) was dissolved in 10 ml of MeOH–2*N* NaOH (1:1; v/v) and the reaction mixture was heated at 80°C for 3.5 h. After the removal of MeOH by evaporation, the residue was diluted with water (5 ml) and extracted with chloroform (3 $\times$ 30 ml). The organic layer was dried over anhydrous sodium sulfate and concentrated. The resulting yellow crystals (62 mg) were chromatographed on basic alumina (2 g, Merck) with benzene–chloroform (4:1; v/v) as an

eluent to give 42 mg of the lactam (7) as slightly yellow prisms. This product was recrystallized from MeOH as colorless prisms, mp 243–247°C (dec.). UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 224 (4.60), 274 (3.88), 280 (3.89), 290 (3.78). $^1\text{H-NMR}$ ($\text{CDCl}_3 + \text{CD}_3\text{OD}$) δ : 4.50 (m, 1H), 4.97 (m, 1H), 6.9–7.6 (m, 4H, arom.H). IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3270 (NH), 1665 (lactam). EI-MS m/e (%): 226 (M^+ , 100), 225 (90), 198 (7.3), 197 (7.3), 196 (2.4), 184 (3.6), 183 (7.3), 182 (12.2), 181 (2.4), 170 (12.2), 169 (29.3), 168 (19.5), 167 (7), 156 (9.7), 155 (4.9), 154 (7.3), 144 (4.9), 143 (7.3). The lactam (7) showed no mp depression on admixture with an authentic sample of 7, and its IR (KBr) spectrum was identical with that of the latter.

γ -Guanidinobutyraldehyde Ethylene Acetal (9)—Lithium aluminum hydride (5.07 g, 0.133 mol) was suspended in 300 ml of dry ether, and 4b (11.30 g, 0.089 mol) in 100 ml of dry ether was added to the stirred suspension at such a rate as to maintain a gentle reflux. The reaction mixture was refluxed for 22 h, then cooled. An aqueous solution saturated with sodium sulfate was added dropwise to decompose excess hydride, then the precipitate was removed by filtration and washed with ether. The organic layer was dried over anhydrous potassium carbonate, filtered and concentrated. Distillation of the residue afforded 8 (9.24 g, 79.2%), bp 65°C (5 mmHg). $^1\text{H-NMR}$ (CDCl_3) δ : 1.00 (s, 2H, disappeared on addition of D_2O), 1.63 (m, 4H), 2.71 (m, 2H), 3.84 (m, 4H), 4.81 (m, 1H).

S-Methylisothiurea sulfate (5.57 g, 0.04 mol) in 70 ml of water was added to 5.90 g (0.045 mol) of 8. The reaction mixture was heated at 50°C for 2 h and then refluxed for 5 h. The solvent was removed *in vacuo*, and the residue was crystallized from MeOH to give 9 (7.50 g, 75%) as colorless needles. An analytical sample of 9 was prepared by repeated recrystallization from MeOH, mp 196–199°C. Anal. Calcd for $\text{C}_7\text{H}_{15}\text{N}_3\text{O}_2 \cdot 1/2\text{H}_2\text{SO}_4$: C, 37.83; H, 7.26; N, 18.91. Found: C, 37.84; H, 7.18; N, 18.96. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 1675, 1645. $^1\text{H-NMR}$ (D_2O) δ : 1.74 (m, 4H), 3.28 (m, 2H), 4.03 (m, 4H).

($\pm$)-Trypargine (2)—Compound 9 (1.42 g, 0.0064 mol) was added to a stirred solution of tryptamine hydrochloride (1.17 g, 0.006 mol) in 80% AcOH (40 ml). The reaction mixture was heated at 50°C under O_2 -free nitrogen for 3 d. The white precipitates were separated, washed with water and EtOH, and dried to afford 1.23 g of ($\pm$)-trypargine (2) as the sulfate. The filtrate was concentrated *in vacuo*. The residue was crystallized from water–MeOH to give 0.28 g of 2 as the sulfate. The total yield of the sulfate was 78.5%. Recrystallization from water afforded colorless needles, mp 254–257°C (dec.). This sulfate was transformed into the corresponding hydrochloride as described later (methods I and II). An analytical sample of the hydrochloride 2 was prepared by repeated recrystallization from MeOH–ether as pale yellow prisms, mp 202–206°C. Anal. Calcd for $\text{C}_{15}\text{H}_{21}\text{N}_5 \cdot 2\text{HCl}$: C, 52.33; H, 6.73; N, 20.34. Found: C, 52.09; H, 6.68; N, 20.42. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 222 (4.54), 272 (3.88), 279 (3.87), 289 (3.74). IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 1675, 1640, 1615. $^{13}\text{C-NMR}$ ($\text{CD}_3\text{OD} + \text{CDCl}_3$) δ : C(1), 54.2; C(3), 42.8; C(4), 19.6; C(5), 118.9; C(6), 120.4; C(7), 123.4; C(8), 112.3; C(10), 129.4; C(11), 107.2; C(12), 127.0; C(13), 138.0; C(1'), 30.3; C(2'), 25.4; C(3'), 41.8; C(5'), 158.3. ($\pm$)-Trypargine hydrochloride was identical with natural trypargine hydrochloride in all respects except for the IR spectrum and mp.

Pyrimidyl Derivative (10) of ($\pm$)-Trypargine—($\pm$)-Trypargine sulfate (2, 130 mg) was suspended in water (1.2 ml), EtOH (2.4 ml), triethylamine (1.2 ml) and acetylacetone (2.4 ml). The reaction mixture was heated at 95°C under nitrogen for 4 h, and acidified to pH 4.0 with AcOH. This solution was heated at 100°C for 10 min, cooled, and extracted with ether (3 $\times$ 15 ml) to remove excess acetylacetone and its condensation dimer. The aqueous layer was basified with concd. NH_4OH and extracted with chloroform (3 $\times$ 30 ml). The chloroform layer was dried over anhydrous sodium sulfate and concentrated to give 10 (99.4 mg) as pale yellow crystals. Recrystallization from MeOH afforded colorless prisms, mp 176.5–178.5°C. EI-MS m/e (%): 335 (M^+ , 42.5), 211 (4), 199 (4), 184 (10), 171 (100), 156 (4), 154 (4), 144 (8.8), 136 (12.5), 123 (12.5). CI-MS m/e : 336 ($\text{M}^+ + 1$). UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 225 (4.62), 239 (sh, 4.06), 276 (sh, 3.95), 282 (3.99), 289 (3.96). $^1\text{H-NMR}$ (CDCl_3) δ : 2.29 (s, 6H, arom.2 $\times$ CH_3), 4.09 (m, 1H, C(1)–H), 5.23 (m, 4H, disappeared on addition of D_2O), 6.31 (s, 1H, arom.H), 7.0–7.6 (m, 4H, arom.H), 8.43 (s, 1H, indole NH, disappeared on addition of D_2O). Anal. Calcd for $\text{C}_{20}\text{H}_{25}\text{N}_5$: C, 71.61; H, 7.51; N, 20.88. Found: C, 71.59; H, 7.48; N, 21.03. IR (CHCl_3) and mass spectra of 10 were identical with those of 10 derived from natural trypargine (2a).

Amino Derivative (11) of ($\pm$)-Trypargine—($\pm$)-Trypargine sulfate (2, 224 mg) was suspended in 10 ml of hydrazine hydrate–water (1:1; v/v), and the reaction mixture was heated at 75°C for 0.5 h, then at 95°C for 1 h. The solution was cooled and evaporated to dryness *in vacuo*. The residue was diluted with water, basified with concd. NH_4OH , and extracted with chloroform (4 $\times$ 30 ml). The organic layer was dried over anhydrous sodium sulfate and concentrated. The residue was treated with dil. HCl to give 153 mg of crude hydrochloride, which was recrystallized from EtOH–MeOH–ether to yield the pure hydrochloride as pale yellow needles, mp 245–247°C (dec.). EI-MS m/e (%): 229 (M^+ , 41.2), 211 (20.6), 199 (10.3), 184 (14.7), 171 (100), 156 (11.8), 154 (8.8), 144 (14.7), 130 (14.7), 115 (7.4). CI-MS m/e : 230 ($\text{M}^+ + 1$). UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 221.5 (4.53), 272 (3.87), 279 (3.85), 289 (3.73). $^{13}\text{C-NMR}$ (CD_3OD) δ : C(1), 54.2; C(3), 42.9; C(4), 19.4; C(5), 119.2; C(6), 120.6; C(7), 123.6; C(8), 112.4; C(10), 129.5; C(11), 107.6; C(12), 127.6; C(13), 138.3; C(1'), 30.3; C(2'), 24.4; C(3'), 40.3. Anal. Calcd for $\text{C}_{14}\text{H}_{19}\text{N}_3 \cdot 2\text{HCl} \cdot 1/5\text{H}_2\text{O}$: C, 54.89; H, 7.05; N, 13.74. Found: C, 54.93; H, 6.89; N, 13.75. IR (CHCl_3) and mass spectra of 11 were identical with those of 11 prepared from natural trypargine (2a).

Conversion of Trypargine into the Formate and the Hydrochloride; General Procedure—Method I: ($\pm$)-Trypargine sulfate (1.0 g) was dissolved in water (about 10–20 ml) and passed through a column of SP

Sephadex C-25 (1.6 × 25 cm, H⁺ form), on which free tryptargine was strongly adsorbed. After being washed with water (2 × column volume), the column was eluted with 0.5 M HCO₂NH₄ (pH 6.80), and the fractions containing tryptargine formate were collected and lyophilized.

Method II: A solution of the above formate (500 mg) in water (1–2 ml) was applied to a column of Sephadex G-10 (1.6 × 88 cm), and the column was eluted with 0.02 M HCl. The fractions containing tryptargine hydrochloride were combined and concentrated *in vacuo*, and the residue was dried.

Optical Resolution of (±)-Tryptargine—Synthetic (–)-Tryptargine (2a): (±)-Tryptargine sulfate was converted into the corresponding diformate by method I (column size: 1.6 × 25 cm). ¹H-NMR (CD₃OD) δ: 4.60 (m, 1H, C(1)–H), 6.99–7.44 (m, 4H, arom.H), 8.55 (s, 2H, 2 × CCO₂H). ¹³C NMR (CD₃OD) δ: C(1), 54.1; C(3), 42.7; C(4), 19.6; C(5), 119.0; C(6), 120.4; C(7), 123.3; C(8), 112.4; C(10), 130.4; C(11), 107.5; C(12), 127.5; C(13), 138.3; C(1'), 30.6; C(2'), 25.6; C(3'), 41.9; C(5'), 158.9; HCO₂H, 170.4. D-(+)-10-Camphorsulfonic acid (710 mg, 0.0028 mol), [α]_D²⁵ +36.6° (c=1.00, MeOH) was added to a solution of the formate (818 mg, 0.0023 mol) in water (5 ml). The solution was then lyophilized, and the residue was dissolved in MeOH-acetonitrile. The solution was seeded with (–)-tryptargine-D-(+)-10-camphorsulfonate. The colorless prisms (396 mg) that separated were recrystallized three times from MeOH-acetonitrile to give the D-(+)-10-camphorsulfonate of the levorotatory enantiomer (201 mg) as colorless prisms, mp 160–163°C. [α]_D²⁵ –7.8° (c=1.03, MeOH). The formate of the levorotatory base (131 mg) which was obtained by method I (column size: 0.5 × 25 cm) was converted into the corresponding hydrochloride by method II (column size: 0.9 × 57 cm). Recrystallization twice from MeOH-ether afforded 104 mg of synthetic (–)-tryptargine hydrochloride (2a) as colorless needles, mp 211–213°C, [α]_D²⁵ –37.3° (c=1.00, MeOH) [natural tryptargine hydrochloride: mp 210–213°C, [α]_D²⁵ –34.2° (c=1.02, MeOH)]. UV λ_{max}^{MeOH} nm (log ε): 222 (4.53), 272 (3.87), 280 (3.86), 289 (3.74). Anal. Calcd for C₁₅H₂₁N₅·2HCl·1/4H₂O: C, 51.65; H, 6.79; N, 20.08. Found: C, 51.60; H, 6.63; N, 20.07. The IR (KBr) spectrum was identical with that of natural tryptargine hydrochloride (2a). ORD (c=0.01, MeOH) [M]_D²⁵ (nm): –147 (589); –324 (360, trough); 0 (310); +413 (298, peak); 0 (294); –259 (293, trough); 0 (291); +1550 (288, peak); 0 (281); –9300 (250, trough); –6900 (235, peak); –40700 (225, trough); 0 (210). CD (c=0.01, MeOH) Δε_D²⁵ (nm): 0 (300); +0.14 (295); +0.21 (292); 0 (289); –0.19 (287); 0 (286); +0.84 (282); +0.81 (280); +2.14 (260); +0.28 (240); +3.73 (230); 0 (225); –10.55 (215); –4.83 (205).

Synthetic (+)-Tryptargine (2b): The first mother liquor (984 mg) of the (–)-tryptargine-D-(+)-10-camphorsulfonate was converted into the formate using method I (column size: 0.9 × 56 cm). Treatment of the resulting formate (427 mg, 0.0012 mol) with D-(–)-tartaric acid (212 mg, 0.0014 mol), [α]_D²⁵ –14.0° (c=1.00, H₂O), in water (4 ml) provided the corresponding D-(–)-tartrate after lyophilization. Crystallization from water and then recrystallization from water-EtOH gave the D-(–)-tartrate of the dextrorotatory enantiomer (145 mg) as colorless needles, mp 198–200°C (dec.). [α]_D²⁵ +9.92° (c=0.50, H₂O). The hydrochloride of the dextrorotatory enantiomer was prepared as described above. Recrystallization from MeOH-ether gave 79 mg of synthetic (+)-tryptargine hydrochloride (2b) as colorless needles, mp 204–207°C. [α]_D²⁵ +37.2° (c=0.54, MeOH). The IR (KBr) spectrum was virtually identical with that of 2a. ORD (c=0.01, MeOH) [M]_D²⁵ (nm): +134 (589); +302 (360, peak); 0 (311); –350 (300, trough); 0 (292); +350 (291, peak); 0 (289); –2400 (286, trough); 0 (279); +9500 (250, peak); +9400 (235, trough); +33000 (225, peak); 0 (210). CD (c=0.01, MeOH) Δε_D²⁵ (nm): 0 (300); –0.11 (295); –0.16 (292); 0 (289); +0.16 (287); 0 (286); –0.68 (282); –0.63 (280); –2.13 (260); 0 (238); –4.24 (230); 0 (225); +11.06 (215); +5.91 (205).

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