# 1-(1-Pyrrolin-2-yl)-β-carbolines. Synthesis of Eudistomins H, I, and P[1)]

Tohru HINO,*[,a,b] Ziping LAI,[a] Hiroko SEKI,[b] Ritsuko HARA,[b] Tadao KURAMOCHI,[b] and Masako NAKAGAWA[a]

*Faculty of Pharmaceutical Sciences[a] and The Chemical Analytical Center,[b] Chiba University, Yayoi-cho, Chiba-shi 260, Japan.* *Received March 3, 1989*

**Three marine β-carboline alkaloids, eudistomin H, I, and P (5, 4, and 6), were synthesized. The Bischler–Napieralski reaction of *N*-(*N*-benzyloxycarbonylprolyl)tryptamine (11) gave the 3,4-dihydro-β-carboline (12), which was converted to eudistomin I (5) *via* 13 on deprotection and dehydrogenation. Compound 13 was obtained directly from *N*-(*N*-*tert*-butoxycarbonylprolyl)tryptamine (17) by means of the Bischler–Napieralski reaction with polyphosphoric ester–dichloroethane. The bromination of 5 with *N*-bromosuccinimide (NBS)–acetic acid gave eudistomin H (4). Bromination of the 5-methoxypyrrolo[2,3-*b*]indole (21) obtained from the 5-hydroxytryptamine (18) gave the 6-bromo derivative (22) which afforded 6-bromo-5-methoxytryptamine (25) on alkaline hydrolysis. The Bischler–Napieralski reaction of the 6-bromo-5-methoxy-*N*-prolyltryptamine (27) gave the 1-pyrrolinyl-3,4-dihydro-β-carboline (29). Dehydrogenation of 29 with NBS followed by demethylation with boron tribromide provided eudistomin P (6) *via* 30.**

**Keywords** eudistomin; 1-pyrrolin-2-yl-β-carboline; Bischler–Napieralsky reaction; bromination; dehydrogenation; dihydro-β-carboline; cyclic tautomer; prolyltryptamine

Eudistomins have been isolated from *Eudistoma olivaceum* and their structures were determined to be β-carboline derivatives by Rinehart and others.[2)] These eudistomins have antiviral and microbial activity. Eudistomins can be classified into four groups: 1) simple β-carbolines (**1**), 2) 1-(2-pyrrolyl)-β-carbolines (**2**), 3) 1-(1-pyrrolin-2-yl)-β-carbolines (**3**—**7**), and 4) tetrahydro-β-carbolines fused with an oxathiazepine ring (**8**). The last group has a unique ring system which has not been found in natural products before and has not been synthesized yet.[3)] Rinehart's group synthesized some eudistomins belonging to groups 2 and 3 from 1-cyano-β-carbolines to prove the structures.[2c)] Compounds **2**—**7**, (1-pyrrolyl)- and 1-(1-pyrrolinyl)-β-carbolines, are also new type of β-carbolines. We describe here the synthesis of eudistomin H (**4**), I (**5**), and P (**6**) from tryptamine and proline. To establish the synthetic route we chose eudistomin I (**5**), having no substituent at the benzene ring, as the first target.

The reaction of tryptamine (**9**) with *N*-benzyloxycarbonyl(Z)-L-prolyl chloride (**10**) gave the amide (**11**) in 74% yield. The Bischler–Napieralski reaction of the amide (**11**) with phosphorus oxychloride in benzene gave the 3,4-dihydro-β-carboline (**12**) in 70% yield. The dehydrogenation of **12** to the β-carboline was unsuccessful at this stage. However, deprotection of the Z-group[4)] by trimethyl silyl iodide gave the 1-pyrrolinyl-3,4-dihydro-β-carboline (**13**), mp 132.5—114 °C, in 48% yield. Oxidation of the pyrrolidine ring occurred simultaneously. The 1-pyrrolidinyl derivative (**14**) could not be isolated from the reaction mixture. Facile auto-oxidation of 1-pyrrolidinyl-3,4-dihydro-β-carboline (**14**) probably proceeded *via* the enamine (**15**).

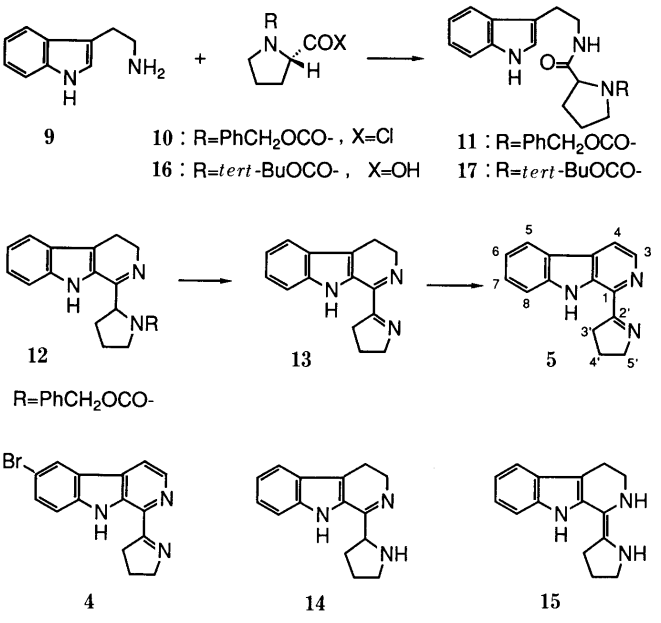


Chart 2

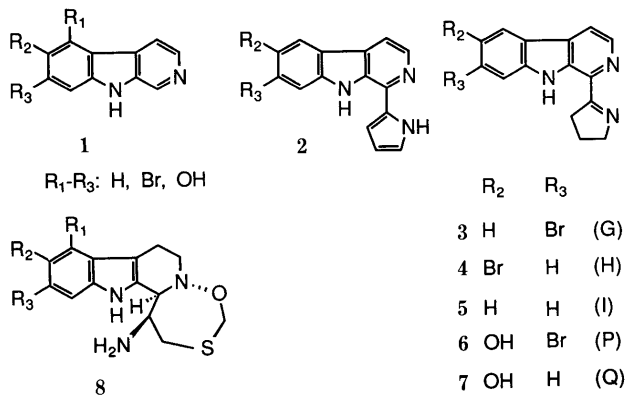


Chart 1

As the deprotection of Z group in **12** was not satisfactory, the *N*-protective group was replaced with a *tert*-butoxycarbonyl (BOC) group. Condensation of tryptamine with BOC-proline anhydride, prepared from *N*-BOC-proline (**16**)[5)] and dicyclohexylcarbodiimide (DCC) gave the amide (**17**), 142—144 °C, in 94% yield. Bischler–Napieralski reaction of **17** with polyphosphoric ester (PPE) in dichloroethane gave the 3,4-dihydro-β-carboline (**13**) in 74% yield directly. Deprotection and oxidation probably occurred during work-up. The structure of **13** was supported by the following spectral data and elemental analysis. The ultraviolet (UV) spectrum of **13** showed a 3,4-dihydro-β-carboline like chromophore ($\lambda_{max}$ 227, 250, 334, 387 sh nm). The proton nuclear magnetic resonance ($^1$H-NMR) spectrum of **13** showed signals peak at $\delta$ 2.00 ppm (2H) due to 4′-$H_2$, 2.96 ppm (4H) due to 4-$H_2$ and 3′-$H_2$, and 4.13 ppm (4H)

due to 3-$H_2$ and 5′-$H_2$. The mass spectrum (MS) of **13** showed a strong molecular ion peak at *m/z* 237.

Dehydrogenation of **13** with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) (3 eq) in benzene gave the desired aromatic β-carboline (eudistomin I (**5**)), mp 151—152 °C, in 90% yield. Similar dehydrogenation of **13** with *N*-bromosuccinimide (NBS) (1 eq) in methylene chloride gave **5** in 74% yield. In these reactions the fully aromatized 1-pyrrolyl derivative was not isolated. The spectral data of **5** were identical with those reported.[2b]

Rinehart's group reported that the bromination of β-carboline and 1-cyano-β-carboline with bromine in tetrahydrofuran gave the 6-bromo derivatives in good yields.[2c] We have also found that similar bromination of β-carboline with NBS in acetic acid gave the 6-bromo derivative, eudistomin N, in 68% yield. Therefore, bromination of eudistomin I (**5**) was examined. When **5** was treated with NBS (1 eq)–methylene chloride at room temperature, the 6-bromo-β-carboline (eudistomin H (**4**)), mp 148—150 °C, was obtained in 80% yield. Spectral data of the synthetic **4** were identical with those reported.[2b,c]

On the other hand, synthesis of eudistomin P (**6**) having a hydroxy group and a bromine atom at the benzene ring, has not been reported yet. For the synthesis of eudistomin P (**6**), 6-bromo-5-methoxytryptamine is required. We have synthesized this compound from a 5-hydroxytryptamine derivative utilizing its cyclic tautomer. 5-Hydroxy-$N_b$-methoxycarbonyltryptamine (**18**),[6] was dissolved in 85% phosphoric acid to form the cyclic tautomer[7] which was isolated as its diacetate **19**, mp 160—161 °C, in 72% yield after acetylation with acetic anhydride–pyridine. The UV spectrum showed an acetanilide-type chromophore ($\lambda_{max}$ 251, 283 nm). The NMR spectrum showed a doublet due to the $8_a$-proton at δ 6.24 ppm ($J$=6.6 Hz) and a multiplet due to the $3_a$-proton at δ 4.07 ppm. The hydrolysis of the acetoxy group in **19** with potassium carbonate–acetone–methanol gave the phenol (**20**), which gave the methoxy derivative (**21**), mp 143.5—144.5 °C, on methylation with methyl iodide. Without isolation of the phenol (**20**), the acetoxy derivative (**19**) gave **21** in 96% yield. The bromination of **21** with NBS–AcOH–dioxane at 0 °C gave the 6-bromo derivative (**22**), mp 191.5—193 °C, in 96% yield, and the 4-bromo derivative was not isolated. The position of the bromine atom in **22** was confirmed by the singlet signal due to the 7-proton at δ 8.31 ppm in its NMR spectrum.

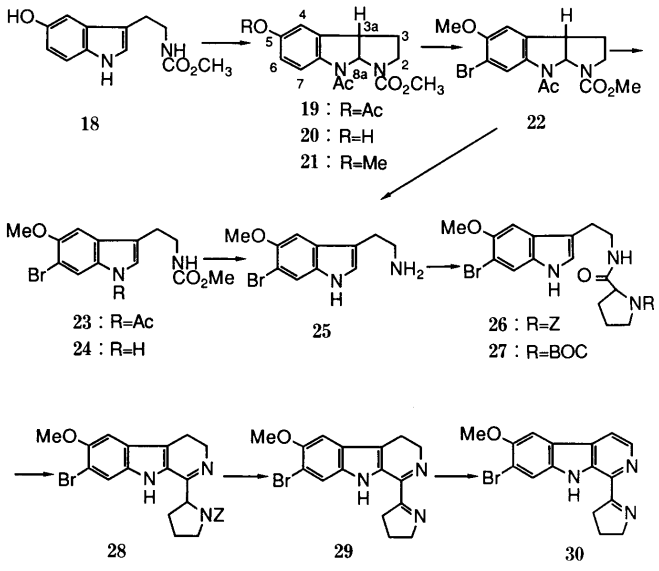


Chart 3

Ring opening of **22** with MeOH–HCl followed by the hydrolysis of the acetyl group with triethylamine–methanol gave the 6-bromo-5-methoxytryptamine (**24**), mp 147—148 °C, in 90% yield. Further hydrolysis of the carbamate group in **24** with KOH–aqueous ethanol provided the tryptamine (**25**), mp 143—144.5 °C, in 78% yield. The tryptamine (**25**) was also obtained directly by refluxing of **22** with KOH–aqueous ethanol in 62% yield. This is an example of ring opening of the cyclic tautomer by a base. Condensation of the substituted tryptamine (**25**) with Z-prolyl chloride (**10**) or BOC-proline (**16**) gave the amides **26** and **27** by a similar reaction to that described for tryptamine.

The Bishler–Napieralski reaction of **26** with phosphorus oxychloride in benzene gave the 3,4-dihydro-β-carboline (**28**) in 75% yield. Deprotection of the Z-group in **28** with trimethylsilyl iodide did not proceed. However, the Z-group of **28** could be cleaved by aluminum chloride in nitromethane to give the 3,4-dihydro-β-carboline (**29**), mp 165—167 °C, in 55% yield. The same compound (**29**) was obtained in 84% yield when **27** was refluxed in PPE–dichloroethane.[8]

The UV spectrum of **29** showed $\lambda_{max}$ 229 (33400), 355 (17300). The MS showed molecular ion peak at *m/z* 345 and 347. The NMR spectrum showed two singlets at δ 7.62 and 7.00 ppm due to the 5-proton and the 8-proton.

Dehydrogenation of **29** with NBS (1.4 eq) in $CH_2Cl_2$ at room temperature smoothly gave the β-carboline (**30**), mp 197—199 °C, in 70% yield. Dehydrogenation with Pd/C-*p*-cymene or DDQ (3 eq) in benzene gave less satisfactory results. Demethylation of **30** with boron tribromide in methylene chloride did not proceed at room temperature. However, eudistomin P (**6**) was obtained in 64% yield when **30** was refluxed in methylene chloride with an excess of boron tribromide. Spectral data (NMR, infrared (IR), UV) of the synthetic sample were identical with those of the natural product, although the melting point of the synthetic sample (mp 193—195 °C) was higher than the reported melting point, 128—130 °C, for the natural product.[2b] Recently synthesis of a similar β-carboline alkaloid, eudistomidin-A has been reported by Murakami and coworkers.[9]

## Experimental

All melting points were measured with a Yamato MP-1 or a Yanagimoto micro melting point apparatus and are uncorrected. UV spectra were measured with a Hitachi 323 or 340 spectro photometer, and IR spectra with a Hitachi 260-10 or 295 spectro photometer. MS were obtained with a Hitachi M-60 or RMU-7M. NMR spectra were measured in $CDCl_3$ solution by a JEOL FX-270 or GX-270 spectrometer with tetramethylsilane as the internal standard. Kiesel gel 60 (70—230 mesh, Merck) or Silica gel BW-820 MH (Fuji-Davison) was used for silica gel column chromatography. Aluminiumoxyd 90 standardisiert (Aktivitatsstufe II—III, Merck) was used for alumina column chromatography.

**$N_b$-(*N*-Z-Prolyl)tryptamine (11)** *N*-Z-Prolyl chloride (**10**) (prepared from Z-proline (3.10 g, 12.5 mmol) and thionyl chloride (1.8 ml)) and NaOH solution (0.5 g in $H_2O$ (20 ml)) were added simultaneously to a solution of tryptamine **9** (500 mg, 3.12 mmol) in $CH_2Cl_2$ (20 ml) during 5 min under ice-cooling. The mixture was stirred for 1 h under ice-cooling and diluted with $CH_2Cl_2$ (100 ml). The organic layer was washed with 10% HCl, saturated $NaHCO_3$, and saturated NaCl solution, and then dried. Evaporation of the solvent gave a residue, which was chromatographed on

a silica gel column (15 g, AcOEt–hexane (1 : 1)) to give the amide (**11**, 900 mg, 74%) as a yellow caramel. UV $\lambda_{max}^{EtOH}$ nm: 223, 285, 292. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3300 (NH), 1700 (CO). $^1$H-NMR $\delta$: 7.92 (1H, br s, indole NH), 6.85—7.56 (10H, m, arom. H), 5.08 (2H, s, $-CH_2Ph$), 4.10 (1H, m, 2′-H), 3.53 (2H, m, $-CH_2-NHCO$ or 5′-$H_2$), 3.37 (2H, m, 5′-$H_2$ or $-CH_2-NHCO$), 2.92 (2H, m, Ind-$CH_2$), 2.21 (2H, m, 3′-H), 1.83 (2H, m, 4′-H). MS *m/z* (%): 391 ($M^+$, 8), 143 (100). Exact MS Calcd for $C_{22}H_{25}N_3O_3$: 391.1897. Found: 391.1886. The same amide (**11**) was obtained in 73% yield from tryptamine and Z-proline with DCC in $CH_2Cl_2$.

**$N_b$-(*N*-BOC-Prolyl)tryptamine (17)** DCC (1.03 g, 5.1 mmol) was added to a solution of *N*-BOC-L-proline[5] (2.00 g, 9.3 mmol) in $CH_2Cl_2$ (30 ml) under ice-cooling. The mixture was stirred for 2 h under ice-cooling and separated precipitates were removed by filtration. Tryptamine **9** (0.72 g, 4.5 mmol) and $Et_3N$ (0.70 ml, 1 eq) were added to the solution and the mixture was stirred for 2 h at room temperature. The mixture was diluted with $CH_2Cl_2$ and washed with 10% aqueous citric acid solution, saturated $NaHCO_3$ and saturated NaCl solutions, and then dried. Evaporation of the solvent gave the amide (**15**, 1.52 g, 94%), which was recrystallized from AcOEt–hexane to give colorless prisms, mp 142—144 °C. UV $\lambda_{max}^{EtOH}$ nm ($\varepsilon$): 225 (37600), 285 (8100), 293 (7300). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3300 (NH), 1660 (C=O). $^1$H-NMR $\delta$: 8.18 (1H, br s, indole NH, exchangeable), 7.6—7.1 (4H, m, arom. H), 7.03 (1H, d, $J$=2.14 Hz, 2-H), 6.80 (1/2 H, br, amide NH), 6.12 (1/2 H, br, amide NH), 3.59 (2H, m, 5′-$H_2$ or $-CH_2-NHCO$), 3.30 (2H, m, $-CH_2-NHCO$ or 5′-$H_2$), 2.96 (2H, m, Ind-$CH_2$–), 2.10 (2H, m, 3′-H), 1.81 (2H, m, 4′-H), 1.39 (9H, s, 3 × $CH_3$). MS *m/z* (%): 357 ($M^+$, 8), 143 (100). *Anal.* Calcd for $C_{20}H_{27}N_3O_3$: C, 67.20; H, 7.61; N, 11.76. Found: C, 66.95; H, 7.52; N, 11.62.

**1-(2-Pyrrolinyl)-3,4-dihydro-β-carboline (13)** i) From **11** *via* **12**: A mixture of the amide (**11**, 150 mg, 0.38 mmol) in benzene (15 ml) and $POCl_3$ (1 ml) was refluxed for 1 h. The mixture was evaporated *in vacuo* to leave a residue, which was dissolved in $CH_2Cl_2$ and this solution was poured into 20% NaOH solution under cooling. The aqueous layer was extracted with $CH_2Cl_2$ and the combined $CH_2Cl_2$ solution was washed with saturated NaCl solution and dried. Evaporation of the solvent gave a residue, which was chromatographed on an alumina column (10 g, $CH_2Cl_2$–acetone (5 : 1)) to give **12** (100 mg, 70%) as a yellow powder. UV $\lambda_{max}^{EtOH}$ nm: 240 sh, 318; $\lambda_{max}^{EtOH-HCl}$ nm: 252, 358. MS *m/z* (%): 373 ($M^+$, 39). Exact MS Calcd for $C_{23}H_{23}N_3O_2$: 373.1792. Found 373.1781.

Trimethylsilyl iodide (0.09 ml) was added to a solution of **12** (100 mg, 0.27 mmol) in $CHCl_3$ (5 ml) under an argon atmosphere. The mixture was stirred for 15 min at room temperature. MeOH (1 ml) was then added and the whole was stirred for 5 min at room temperature and evaporated *in vacuo*. The residue was dissolved in $CH_2Cl_2$ and this solution was washed with 20% NaOH and saturated NaCl solution, and then dried. Evaporation of the solvent gave a residue, which was chromatographed on a silica gel column (5 g, AcOEt–hexane (2 : 1)) to give the dihydro-β-carboline **13** (31 mg, 48%). Recrystallizations from AcOEt–hexane gave yellow prisms, mp 132.5—134 °C. UV $\lambda_{max}^{EtOH}$ nm ($\varepsilon$): 227 (31300), 250 (12200), 334 (11400), 387 (5500). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3350 (NH), 1580 (C=N). $^1$H-NMR $\delta$: 10.35 (1H, br, indole NH, exchangeable), 7.6—7.1 (4H, m, arom. H), 4.13 (4H, m, 3-$H_2$, 5′-$H_2$), 2.96 (4H, m, 4-$H_2$, 3′-$H_2$), 2.00 (2H, m, 4′-$H_2$). MS *m/z* (%): 237 ($M^+$, 84), 236 ($M^+ - 1$,100). *Anal.* Calcd for $C_{15}H_{15}N_3$: C, 75.92; H, 6.37; N, 17.70. Found: C, 75.64; H, 6.44; N, 17.65.

ii) From **17**: PPE (24.60 g) was added to a solution of **17** (330 mg, 0.88 mmol) in dichloroethane (20 ml) under an $N_2$ atmosphere. The mixture was refluxed for 50 min and evaporated *in vacuo*. The residue was poured into $H_2O$ (20 ml) and the mixture was stirred for 3 h at room temperature to decompose PPE, then basified (pH 9—10) with 20% KOH and extracted with benzene. The extract was washed with saturated NaCl solution and dried. Evaporation of the solvent *in vacuo* gave a residue, which was purified through a silica gel column to give **13** (163 mg, 74%). This sample was identical with the specimen obtained above (thin-layer chromatography (TLC), mp, IR).

**1-(1-Pyrrolin-2-yl)-β-carboline (Eudistomin I) (5)** i) DDQ (540 mg, 2.38 mmol) was added to a solution of **13** (200 mg, 0.84 mmol) in benzene (40 ml) under an $N_2$ atmosphere. The mixture was stirred overnight at room temperature and poured into $H_2O$ (20 ml). The aqueous layer was extracted with $CH_2Cl_2$, and the combined organic layer was washed with saturated NaCl solution and dried. Evaporation of the solvent *in vacuo* gave a residue, which was chromatographed on a silica gel column (20 g, AcOEt–hexane (1 : 1)) to give the β-carboline **5** (180 mg, 90%) as a yellow powder. Recrystallizations from AcOEt gave colorless prisms, mp 151—152 °C (reported mp 153—155 °C[2c]). UV $\lambda_{max}^{EtOH}$ nm ($\varepsilon$): 220 (38600), 242 (16000), 261 (15000), 283 (18800), 302 (10300), 370 (9800). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3330 (NH), 1600. $^1$H-NMR $\delta$: 10.83 (1H, br, indole NH, exchangeable), 8.50 (1H, d, $J$=5.5 Hz, 3-H), 8.00 (1H, d, $J$=5.1 Hz, 4-H), 8.15 (1H, d, $J$=8.1 Hz, 5-H), 7.55 (1H, m, 8-H), 7.53 (1H, m, 7-H), 7.29 (1H, m, 6-H), 4.27 (2H, m, 5′-$H_2$), 3.32 (2H, m, 3′-$H_2$), 2.08 (2H, m, 4′-$H_2$). MS *m/z* (%): 235 ($M^+$, 100). *Anal.* Calcd for $C_{15}H_{13}N_3$: C, 76.57; H, 5.57; N, 17.86. Found: C, 76.50; H, 5.67; N, 17.76.

ii) NBS (236 mg, 1.05 eq) was added to a solution of **13** (310 mg, 1.27 mmol) in $CH_2Cl_2$ (30 ml) under an $N_2$ atmosphere. The mixture was stirred for 70 min at room temperature and diluted with $CH_2Cl_2$. Work-up as above gave the β-carboline (**5**, 220 mg, 74%).

**Bromination of β-Carboline (1, $R^1$–$R^3$=H)** NBS (130 mg, 0.73 mmol) was added to a solution of β-carboline (100 mg, 0.60 mmol), which was prepared by the dehydrogenation of 3,4-dihydro-β-carboline[8] with Pd/C, in AcOH (4 ml) and the mixture was stirred for 2 h at room temperature. The solvent was evaporated off *in vacuo* and the residue was dissolved in $CH_2Cl_2$. The solution was washed with saturated $NaHCO_3$ and NaCl solutions, and dried. The solvent was evaporated off to leave a residue, which was chromatographed on a silica gel column (20 g, AcOEt–hexane (1 : 1)→AcOEt) to give 6-bromo-β-carboline (**1**, $R^1$, $R^3$=H, $R^2$=Br, eudistomin N, 100 mg, 68%), mp 277—278 °C (reported mp 265—268 °C[2i]). Its spectral data (NMR and UV) were identical with those reported.[2i]

**6-Bromo-1-(1-pyrrolin-2-yl)-β-carboline (Eudistomin H) (4)** NBS (63 mg, 1.1 eq) was added to a solution of **5** (75 mg, 0.32 mmol) in $CH_2Cl_2$ under an $N_2$ atmosphere. The mixture was stirred for 45 min at room temperature and for a further 45 min after the addition of further NBS (20 mg). The mixture was diluted with $CH_2Cl_2$ and washed with saturated $NaHCO_3$ and saturated NaCl solutions, and then dried. Evaporation of the solvent gave a residue, which was chromatographed on a silica gel column (20 g, $CH_2Cl_2$–acetone (10 : 1)) to give eudistomin H (**4**) (80 mg, 80%) as a yellow powder. Repeated recrystallizations from AcOEt gave pale yellow crystals, mp 148—150 °C (reported mp 140—142 °C[2c]). UV $\lambda_{max}^{EtOH}$ nm ($\varepsilon$): 226 (43800), 244 (20700), 290 (21800), 375 (9200). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3340, 1600. $^1$H-NMR $\delta$: 10.94 (1H, br, indole NH, exchangeable), 8.48 (1H, d, $J$=5.19 Hz, 3-H), 8.29 (1H, d, $J$=1.84 Hz, 5-H), 7.96 (1H, d, $J$=5.19 Hz, 4-H), 7.65 (1H, dd, $J$=8.55, 1.84 Hz, 7-H), 7.49 (1H, d, $J$=8.55 Hz, 8-H), 4.25 (2H, m, 5′-H), 3.27 (2H, m, 3′-H), 2.07 (2H, m, 4′-H). MS *m/z* (%): 315 ($M^+$+2, 97), 313 ($M^+$, 100).

**5-Acetoxy-8-acetyl-1-methoxycarbonyl-1,2,3,3a,8,8a-hexahydropyrrolo-[2,3-*b*]indole (19)** A mixture of the hydroxytryptamine **18**[7] (4.00 g, 14 mmol) and 85% $H_3PO_4$ (30 ml) was stirred for 17 min at room temperature. The clear solution was poured into aqueous alkaline solution ($K_2CO_3$ (120 g), and KOH (40 g) in $H_2O$ (500 ml)) under ice-cooling. The mixture was extracted with $CH_2Cl_2$ and the extracts were washed with saturated NaCl solution and dried. The solvent was evaporated off to leave a residue (3.9 g), which was dissolved in pyridine (50 ml) and $Ac_2O$ (10 ml). The mixture was stirred overnight at room temperature and evaporated *in vacuo*. The residue was extracted with $CH_2Cl_2$ and the extract was washed with $H_2O$, 5% HCl, saturated NaCl and $NaHCO_3$ solutions, and then dried. The solvent was evaporated off to leave a residue, which was recrystallized from AcOEt–hexane to give the acetyl cyclic tautomer **19** (3.52 g). From the mother liquor, a further crop of **19** (380 mg, total 3.90 g, 72%) and 5-acetoxytryptamine (150 mg) were obtained. Recrystallization of **19** from AcOEt–hexane gave colorless prisms, mp 160—161 °C. UV $\lambda_{max}^{EtOH}$ nm ($\varepsilon$): 251 (16300), 283 (4700). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1760, 1705, 1660 (CO). $^1$H-NMR (500 MHz, 50 °C) $\delta$: 8.04 (1H, d, $J$=8.33 Hz, 7-H), 6.92 (2H, m, 4 and 6-H), 6.24 (1H, d, $J$=6.62 Hz, $8_a$-H), 4.05 (1H, t, $J$=6.63 Hz, $3_a$-H), 3.83 (1H, m, 2-$H_a$), 3.73 (3H, s, $OCH_3$), 2.93 (1H, m, 2-$H_b$), 2.54 (3H, s, $COCH_3$), 2.26 (3H, s, $COCH_3$), 2.13 (2H, m, 3-$H_2$), MS *m/z* (%): 318 ($M^+$, 20), 234 (100). *Anal.* Calcd for $C_{16}H_{18}N_2O_5$: C, 60.37; H, 5.70; N, 8.80. Found: C, 60.40; H, 5.73; N, 8.74. Recrystallization of 5-acetoxytryptamine from AcOEt–hexane gave colorless prisms, mp 125—126 °C. UV $\lambda_{max}^{EtOH}$ nm ($\varepsilon$): 228 (31500), 288 (7700). $^1$H-NMR $\delta$: 8.21 (1H, s, indole NH), 7.29 (1H, d, $J$=9 Hz, 7-H), 7.26 (1H, d, $J$=2.3 Hz, 4-H), 6.98 (1H, s, 2-H), 6.88 (1H, dd, $J$=8.9, 2.3 Hz, 6-H), 4.75 (1H, br, NH), 3.66 (3H, s, $OCH_3$), 3.48 (2H, m, $-CH_2N$), 2.90 (2H, m, Ind-$CH_2$), 2.32 (3H, s, $COCH_3$). *Anal.* Calcd for $C_{14}H_{16}N_2O_4$: C, 60.84; H, 5.84; N, 10.14. Found: C, 60.84; H, 5.85; N, 10.08.

**8-Acetyl-5-hydroxy-1-methoxycarbonyl-1,2,3,3a,8,8a-hexahydropyrrolo-[2,3-*b*]indole (20)** A mixture of **19** (750 mg, 2.35 mmol), MeOH (5 ml), acetone (35 ml), and $K_2CO_3$ (3.0 g, 21.7 mmol) was stirred for 12 h at room temperature. The mixture was filtered and evaporated to leave a residue, which was chromatographed on a silica gel column (25 g, AcOEt–hexane (3 : 2)) to give **20** (570 mg, 88%) as a colorless powder. Recrystallization from AcOEt–hexane gave colorless prisms, mp 220—222 °C. UV $\lambda_{max}^{EtOH}$ nm ($\varepsilon$): 255 (15000), 298 (5100). $^1$H-NMR (500 MHz), $\delta$: 7.88 (1H, d, $J$=

6.6 Hz, 7-H), 6.67 (2H, m, 6-H, 4-H), 6.20 (1H, d, $J$=6.4 Hz, $8_a$-H), 4.88 (1H, s, OH, exchangeable), 4.00 (1H, m, $3_a$-H), 3.81 (1H, m, 2-$H_a$), 3.72 (3H, s, $OCH_3$), 2.90 (1H, m, 2-$H_b$), 2.51 (3H, s, $COCH_3$), 2.11 (2H, m, 3-$H_2$). MS $m/z$ (%): 276 ($M^+$, 29), 234 (100). *Anal.* Calcd for $C_{14}H_{16}N_2O_4$: C, 60.86; H, 5.84; N, 10.14. Found: C, 60.59; H, 5.91; N, 10.03.

**8-Acetyl-5-methoxy-1-methoxycarbonyl-1,2,3,3a,8,8a-hexahydropyrrolo-[2,3-*b*]indole (21)** i) From **20**: A mixture of **20** (60 mg, 0.21 mmol), acetone 10 ml), $K_2CO_3$ (120 mg), and $CH_3I$ (3 ml, excess) was refluxed for 2 d. The mixture was filtered and the solvent was evaporated off to leave a residue, which was chromatographed on a silica gel column (10 g, AcOEt–hexane (3:1)) to give **21** (36 mg, 60%). Recrystallization from AcOEt–hexane gave colorless prisms, mp 143.5—144.5 °C. UV $\lambda_{max}^{EtOH}$ nm ($\varepsilon$): 254 (16000), 295 (7400). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1705, 1660 (CO). $^1$H-NMR (55 °C), $\delta$: 7.94 (1H, d, $J$=8.9 Hz, 7-H), 6.76 (1H, dd, $J$=8.9, 2.6 Hz, 6-H), 6.73 (1H, d, $J$=2.9 Hz, 4-H), 6.21 (1H, d, $J$=6.6 Hz, $8_a$-H), 4.02 (1H, m, $3_a$-H), 3.83 (1H, m, 2-$H_a$), 3.78 (3H, s, $OCH_3$), 3.72 (3H, s, $OCH_3$), 2.92 (1H, m, 2-$H_b$), 2.51 (3H, s, $COCH_3$), 2.14 (2H, m, 3-$H_2$). MS $m/z$ (%): 290 ($M^+$, 38), 248 (100). *Anal.* Calcd for $C_{14}H_{18}N_2O_4$: C, 62.04; H, 6.25; N, 9.65. Found: C, 61.83; H, 6.24; N, 9.52.

ii) From **19**: A mixture of **19** (1.15 g, 3.6 mmol), MeOH (8 ml), acetone (16 ml) and $K_2CO_3$ (6.0 g) was stirred overnight at room temperature. The solvent was evaporated off to leave a residue. Acetone (24 ml) and $CH_3I$ (12 ml) were added to the residue and the whole was refluxed for 6 h. The mixture was filtered and the solvent was evaporated off to leave a residue, which was purified by silica gel column chromatography to give **21** (1.00 g, 96%).

**8-Acetyl-6-bromo-5-methoxy-1-methoxycarbonyl-1,2,3,3a,8,8a-hexa-hydropyrrolo[2,3-*b*]indole (22)** NBS (344 mg, 1.1 eq) was added to a solution of **21** (510 mg, 1.76 mmol) in AcOH (5 ml) and dioxane (2.5 ml) under ice-cooling. The mixture was stirred for 1.5 h under ice-cooling and for 1 h at room temperature. The mixture was evaporated *in vacuo* (30—40 °C, bath temperature) to leave a residue, which was dissolved in $CH_2Cl_2$ (200 ml). The $CH_2Cl_2$ solution was washed with saturated $NaHCO_3$ and saturated NaCl solution, and then dried. The solvent was evaporated off to leave a residue, which was recrystallized from AcOEt to give **22** (620 mg, 96%) as pale yellow prisms. Recrystallization from AcOEt–hexane gave colorless prisms, mp 191.5—193 °C. UV $\lambda_{max}^{EtOH}$ nm ($\varepsilon$): 210 (22700), 256 (13600), 304 (4600). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1700, 1660 (CO). $^1$H-NMR $\delta$: 8.31 (1H, s, 7-H), 6.74 (1H, s, 4-H), 6.23 (1H, d, $J$=6.7 Hz, $8_a$-H), 4.03 (1H, dd, $J$=6.4, 7.0 Hz, $3_a$-H), 3.84 (3H, s, $OCH_3$), 3.83 (1H, m, 2-$H_a$), 3.72 (3H, s, $CO_2CH_3$), 2.94 (1H, m, 2-$H_b$), 2.52 (3H, s, $COCH_3$), 2.20 (2H, m, 3-$H_2$). MS $m/z$ (%): 370 ($M^+$+2, 27), 368 ($M^+$, 26), 328 (100), 326 (99). *Anal.* Calcd for $C_{15}H_{17}BrN_2O_4$: C, 48.78; H, 4.64; N, 7.59. Found: C, 48.73; H, 4.60; N, 7.71. When AcOH and dioxane in the above reaction mixture were evaporated off *in vacuo* (40 °C bath temperature), **23** was obtained in 79% yield. Recrystallization of **23** from AcOEt gave colorless prisms, mp 174—175.5 °C. UV $\lambda_{max}^{EtOH}$ nm ($\varepsilon$): 258 (21400), 284 (14000), 305 (10200), 317 (9400). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3400 (NH), 1700 (CO). $^1$H-NMR $\delta$: 8.67 (1H, s, 7-H), 7.23 (1H, s, 4-H), 6.99 (1H, s, 2-H), 4.81 (1H, s, NH, exchangeable), 3.95 (3H, s, $OCH_3$), 3.68 (3H, s, $OCH_3$), 3.51 (2H, m, C$\underline{H}_2$NH), 2.89 (2H, t, $J$=6.7 Hz, Ind-$CH_2$), 2.58 (3H, s, $COCH_3$). MS $m/z$ (%): 370 ($M^+$+2, 31), 368 ($M^+$, 31), 238 (100), 236 (98). *Anal.* Calcd for $C_{15}H_{17}BrN_2O_4$: C, 48.78; H, 4.64; N, 7.59. Found: C, 48.56; H, 4.62; N, 7.61.

**6-Bromo-5-methoxy-$N_b$-methoxycarbonyltryptamine (24)** The 6-bromo derivative **22** (610 mg, 1.65 mmol) was dissolved in MeOH (30 ml) saturated with HCl gas, and the mixture was stirred for 12 h at room temperature. The mixture was evaporated *in vacuo* to leave a residue, which was found to be **23** by TLC comparison. The residue was dissolved in $Et_3N$ (10 ml) and MeOH (20 ml) and the mixture was stirred for 14 h at room temperature then refluxed for 4 h. The mixture was evaporated *in vacuo* and extracted with $CH_2Cl_2$. The $CH_2Cl_2$ solution was washed with 5% HCl, saturated $NaHCO_3$, and saturated NaCl solution, and then dried. The solvent was evaporated off to leave a residue, which was chromatographed on a silica gel column (15 g, AcOEt–hexane (2:1)) to give **24** (460 mg, 85%). Recrystallization from AcOEt–hexane gave pale yellow prisms, mp 147—148 °C. UV $\lambda_{max}^{EtOH}$ nm ($\varepsilon$): 228 (31400), 294 (10300), 306 (9900), 317 (6600). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3400 (NH), 1700 (CO).$^1$H-NMR $\delta$: 7.97 (1H, br s, indole NH, exchangeable), 7.56 (1H, s, 7-H), 7.05 (1H, s, 4-H), 7.00 (1H, d, $J$=2.3 Hz, 2-H), 4.75 (1H, br, amide NH, exchangeable), 3.93 (3H, s, $OCH_3$), 3.67 (3H, s, $OCH_3$), 3.48 (2H, m, C$\underline{H}_2$NH), 2.92 (2H, t, $J$=6.6 Hz, Ind-$CH_2$). MS $m/z$ (%): 328 ($M^+$+2, 34), 326 ($M^+$, 34), 240, 238 (100). *Anal.* Calcd for $C_{13}H_{15}BrN_2O_4$: C, 47.70; H, 4.62; N, 8.56. Found: C, 47.80; H, 4.61; N, 8.66.

**6-Bromo-5-methoxytryptamine (25)** A solution of the carbamate **24** (100 mg, 0.3 mmol) in KOH (2.40 g)–EtOH (8 ml)–$H_2O$ (8 ml) was refluxed for 4 h. The EtOH was evaporated off and the mixture was extracted with $CH_2Cl_2$. The extract was washed with saturated $NaHCO_3$ and saturated NaCl solution, and then dried. Evaporation of the solvent gave **25** (64 mg, 78%) as a yellow powder. Repeated recrystallization from AcOEt–hexane gave pale yellow prisms, mp 143—144.5 °C. UV $\lambda_{max}^{EtOH}$ nm ($\varepsilon$): 228 (29700), 294 (9300). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3300 (NH). $^1$H-NMR $\delta$: 8.00 (1H, br s, indole NH, exchangeable), 7.56 (1H, s, 7-H), 7.07 (1H, s, 4-H), 7.02 (1H, d, $J$=2.1 Hz, 2-H), 3.93 (3H, s, $OCH_3$), 3.03 (2H, t, $J$=6.7 Hz, $CH_2NH$), 2.87 (2H, t, $J$=6.7 Hz, Ind-$CH_2$), 1.39 (2H, s, $NH_2$, exchangeable). MS $m/z$ (%): 270 ($M^+$+2, 31), 268 ($M^+$, 32), 240 (100), 238 (94). *Anal.* Calcd for $C_{11}H_{13}BrN_2O$: C, 49.06; H, 4.87; N, 10.41. Found: C, 48.94; H, 4.92; N, 10.31.

By a similar procedure **23** (1.50 g) was converted to **25** (920 mg, 84%). Furthermore the same product (**25**) was obtained from **22** in 62% yield by similar treatment.

**6-Bromo-5-methoxy-$N_b$-(*N*-Z-Prolyl)tryptamine (26)** *N*-Z-L-Prolyl chloride (prepared from Z-proline (2.30 g, 3 eq)) in $CH_2Cl_2$ (15 ml) and NaOH (0.31 g, 2.7 eq) in $H_2O$ (10 ml) were added simultaneously to a solution of **25** (780 mg, 2.9 mmol) in $CH_2Cl_2$ (20 ml) under ice-cooling. The mixture was stirred for 25 min under ice-cooling. Work-up as in the case of unsubstituted tryptamine gave **26** (1.14 g, 78%) as a yellow amorphous powder. UV $\lambda_{max}^{EtOH}$ nm: 227, 292, 303, 315 sh. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3300 (NH), 1690 (CO). $^1$H-NMR $\delta$: 7.88 (1H, br s, indole NH, exchangeable), 7.52 (1H, s, 7-H), 7.36 (5H, s, arom. H for Z-group), 7.03 (1H, s, 4-H), 6.93 (1H, d, $J$=2.4 Hz, 2-H), 5.09 (2H, s, C$\underline{H}_2$-Ph), 4.31 (1H, m, 2′-H), 3.92 (3H, s, $OCH_3$), 3.73 (2H, m, C$\underline{H}_2$NH), 3.49 (2H, m, 5′-$H_2$), 2.82 (2H, m, Ind-$CH_2$), 2.15 (1H, m, 3′-$H_a$), 2.02 (1H, m, 3′-$H_b$), 1.86 (2H, m, 4′-$H_2$). MS $m/z$ (%): 501 ($M^+$+2, 11), 499 ($M^+$, 11), 393, 391 (M−$OCH_2Ph$, 8), 253 (97), 251 (100).

**6-Bromo-5-methoxy-$N_b$-(1-BOC-Prolyl)tryptamine (27)** By a procedure similar to that in the case of tryptamine, the reaction of **25** (1.30 g, 4.83 mmol) and BOC-proline (2.15 g, 9.98 mmol) with DCC gave **27** (2.01 g, 89%), mp 197—199 °C (AcOEt), as colorless prisms. UV $\lambda_{max}^{EtOH}$ nm ($\varepsilon$): 228 (32800), 294 (11100). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3600 (NH), 1660 (CO). $^1$H-NMR $\delta$: 8.10 (1H, br s, indole NH, exchangeable), 7.56 (1H, s, 7-H), 7.06 (1H, s, 4-H), 7.01 (1H, d, $J$=1.7 Hz, 2-H), 6.14 (1H, br, amide NH, exchangeable), 4.23 (1H, m, 2′-H), 3.94 (3H, s, $OCH_3$), 3.58 (2H, m, C$\underline{H}_2$NH), 3.33 (2H, m, 5′-$H_2$), 2.92 (2H, m, Ind-$CH_2$), 2.20 (2H, m, 3′-$H_2$), 1.84 (2H, m, 4′-$H_2$), 1.40 (9H, s, 3×$CH_3$). MS $m/z$ (%): 467 ($M^+$+2, 9), 465 ($M^+$, 9), 253 (100), 251 (97). *Anal.* Calcd for $C_{21}H_{28}BrN_3O_4$: C, 54.08; H, 6.05; N, 9.01. Found: C, 54.00; H, 5.99; N, 9.02.

**6-Bromo-5-methoxy-1-(*N*-Z-Prolyl)-3,4-dihydro-β-carboline (28)** Phosphorus oxychloride (2.0 ml) was added to a solution of the amide (**26**) (1.06 g, 2.12 mmol) in benzene (20 ml) and the mixture was refluxed for 10 min. Evaporation of the solvent gave a residue which was dissolved in $CH_2Cl_2$ and ice-water. The aqueous layer was extracted with $CH_2Cl_2$, and the combined extract was washed with saturated NaCl solution and dried. Evaporation of the solvent gave a residue, which was purified through an alumina column (30 g, $CH_2Cl_2$–acetone (5:1)) to give the dihydro-β-carboline (**28**, 760 mg, 75%) as a yellow powder. UV $\lambda_{max}^{EtOH}$ nm: 214, 335; $\lambda_{max}^{EtOH-HCl}$ nm: 210, 379. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3250 (NH), 1690 (CO). MS $m/z$ (%): 483 ($M^+$+2, 28), 481 ($M^+$, 40), 375, 373 ($M^+$−$OCH_2Ph$, 25), 91 (100). Its NMR spectrum showed complicated signals due to the presence of rotamers.

**6-Bromo-5-methoxy-1-(1-pyrrolin-2-yl)-3,4-dihydro-β-carboline (29)** i) From **28**: Aluminum chloride (40 mg, 4 eq) and anisole (0.05 ml, 6 eq) in $CH_3NO_2$ (1 ml) were added to a solution of **28** (40 mg, 0.08 mmol) in $CH_3NO_2$ (1 ml). The mixture was stirred for 3 h at room temperature, and for a further 3 h after the addition of $AlCl_3$ (40 mg). The mixture was diluted with benzene after decomposition of $AlCl_3$ by $H_2O$ (1 ml). The mixture was washed with saturated $NaHCO_3$ and saturated NaCl solution, and then dried. Evaporation of the solvent gave a residue, which was purified through a silica gel column (5 g, AcOEt–hexane (3:1)) to give **29** (16 mg, 55%) as a yellow powder. Recrystallization from AcOEt–hexane gave yellow prisms, mp 165—167 °C. UV $\lambda_{max}^{EtOH}$ nm ($\varepsilon$): 229 (33400), 355 (17300). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3360 (NH), 1600 (C=N). $^1$H-NMR $\delta$: 10.29 (1H, br s, indole NH, exchangeable), 7.62 (1H, s, 8-H), 7.00 (1H, s, 5-H), 4.10 (4H, m, 3-$H_2$, 5′-$H_2$), 3.93 (3H, s, $OCH_3$), 2.90 (4H, m, 4-$H_2$, 3′-$H_2$), 2.05 (2H, m, 4′-$H_2$). MS $m/z$ (%): 347 ($M^+$+2, 88), 345 ($M^+$, 100). *Anal.* Calcd for $C_{16}H_{16}BrN_2O$: C, 55.51; H, 4.66; N, 12.14. Found: C, 55.53; H, 4.66; N, 12.23.

ii) From **27**: The amide **27** (1.00 g, 2.15 mmol) was treated with PPE (70.00 g)–dichloroethane (20 ml) as in the case of **17** to give **29** (0.62 g, 84%) as a yellow powder. Recrystallization from AcOEt gave pale yellow prisms, mp 165—167 °C; this product was identical with the above

specimen (IR, NMR).

**7-Bromo-6-methoxy-1-(1-pyrrolin-2-yl)-β-carboline (30)** NBS (205 mg, 1.4 eq) was added to a solution of **29** (285 mg, 0.82 mmol) in $CH_2Cl_2$ (30 ml) under an $N_2$ atmosphere. The mixture was stirred for 30 min at room temperature and diluted with $CH_2Cl_2$. This mixture was washed with saturated $NaHCO_3$ and saturated NaCl solution, and then dried. Evaporation of the solvent gave a residue, which was chromatographed on a silica gel column (20 g, AcOEt–hexane (1 : 1)) to give **30** (200 mg, 71%) as a yellow powder. Recrystallizations from AcOEt gave yellow prisms, mp 197—199 °C. UV $\lambda_{max}^{EtOH}$ nm (ε): 252 (20000), 301 (19900), 318 (19500), 379 (8800). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3330 (NH), 1600. $^1$H-NMR δ: 10.74 (1H, br s, indole NH, exchangeable), 8.48 (1H, d, $J$=5.2 Hz, 3-H), 7.93 (1H, d, $J$=5.2 Hz, 4-H), 7.79 (1H, s, 8-H), 7.58 (1H, s, 5-H), 4.25 (2H, m, 5′-$H_2$), 4.02 (3H, s, $OCH_3$), 3.31 (2H, m, 3′-$H_2$), 2.08 (2H, m, 4′-$H_2$). MS $m/z$ (%): 345 ($M^+$+2, 98), 343 ($M^+$, 100). *Anal.* Calcd for $C_{16}H_{14}BrN_2O$: C, 55.83; H, 4.10; N, 12.21. Found: C, 55.72; H, 4.14; N, 12.32.

Dehydrogenation of **29** (100 mg, 0.29 mmol) with DDQ (196 mg, 3 eq) in benzene gave **30** (30 mg, 30%).

**Eudistomin P (6)** $BBr_3$ (1.5 ml) in $CH_2Cl_2$ (30 ml) was added to a solution of **30** (300 mg, 0.87 mmol) in $CH_2Cl_2$ (5 ml) under a $N_2$ atmosphere. The mixture was refluxed for 5 h, then stirred for 4 h after the addition of $H_2O$. The aqueous layer was extracted with $CHCl_3$ and the combined organic layer was washed with saturated NaCl solution and dried. Evaporation of the solvent gave a residue, which was chromatographed on a silica gel column (50 g, AcOEt–hexane (2 : 3)) to give eudistomin P (**6**) (183 mg, 64%). Recrystallizations from AcOEt–hexane gave yellow prisms, mp 193—195 °C (reported mp 128—130 °C[2b]). UV $\lambda_{max}^{EtOH}$ nm: 220, 255, 305, 325, 385. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3330, 1600. $^1$H-NMR ($CD_2Cl_2$) δ: 10.75 (1H, br s, indole NH, exchangeable), 8.43 (1H, d, $J$=5.2 Hz, 3-H), 7.93 (1H, d, $J$=5.2 Hz, 4-H), 7.75 (1H, s, 8-H), 5.7 (1H, br, OH, exchangeable), 4.24 (2H, m, 5′-$H_2$), 3.26 (2H, m, 3′-$H_2$), 2.06 (2H, m, 4′-H). MS $m/z$ (%): 331 ($M^+$+2, 96), 329 ($M^+$, 100). Exact MS Calcd for $C_{15}H_{12}{}^{79}BrN_3O$: 329.0161. Found: 329.0184. Calcd for $C_{15}H_{12}{}^{81}BrN_3O$: 331.0144. Found: 331.0168.

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**References**

1) A part of this work was presented at the Annual Meeting of the Pharmaceutical Society of Japan, April 1987, Kyoto, Abstracts p. 177.
2) *a*) K. L. Rinehart Jr., J. Kobayashi, G. C. Harbour, R. G. Hughes, S. A. Mizsak, and T. A. Scahiel, *J. Am. Chem. Soc.*, **106**, 1524 (1984); *b*) J. Kobayashi, G. C. Harbour, J. Gilmore, and K. L. Rinehart Jr., *ibid.*, **106**, 1526 (1984); *c*) K. L. Rinehart Jr., J. Kobayashi, G. C. Harbour, J. Gilmore, M. Mascal, R. G. Holt, L. S. Shield, and F. Lafargue, *ibid.*, **109**, 3378 (1987); *d*) J. Kobayashi, H. Nakamura, Y. Ohizumi, and Y. Hirata, *Tetrahedron Lett.*, **27**, 1191 (1986); *e*) K. F. Kinzer and J. H. Cardellina II, *ibid.*, **28**, 925 (1987).
3) M. Nakagawa, Jin-Jun Liu, K. Ogata, and T. Hino, *Tetrahedron Lett.*, **27**, 6087 (1986); *idem*, *J. Chem. Soc., Chem. Commun.*, **1988**, 463.
4) R. S. Lott, V. S. Chauhan, and C. H. Otammer, *J. Chem. Soc., Chem. Comm.*, **1979**, 495.
5) M. Itoh, D. Hagiwara, and T. Kamiya, *Bull. Chem. Soc. Jpn.*, **50**, 718 (1977).
6) M. Taniguchi, T. Anjiki, M. Nakagawa, and T. Hino, *Chem. Pharm. Bull.*, **32**, 2544 (1984).
7) T. Hino and M. Taniguchi, *J. Am. Chem. Soc.*, **100**, 5564 (1978); M. Taniguchi and T. Hino, *Tetrahedron*, **37**, 1487 (1981).
8) Y. Kanaoka, E. Sato, and Y. Ban, *Chem. Pharm. Bull.*, **15**, 101 (1967).
9) Y. Murakami, H. Takahashi, Y. Nakazawa, M. Koshimizu, T. Watanabe, and Y. Yokoyama, *Tetrahedron Lett.*, **30**, 2099 (1989).