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SYNTHETIC STUDIES DIRECTED TOWARD ERGOT ALKALOIDS, (±)-6,7-SECOAGROCLAVINE, (±)-CHANOCLAVINE-I, (±)-CHANOCLAVINE-II, AND (±)-AGROCLAVINE-I, BY AN EFFICIENT AND COMMON SYNTHETIC ROUTE[1#]

Fumio Yamada, Yoshihiko Makita, and Masanori Somei*
Division of Pharmaceutical Sciences, Graduate School of Natural Science and Technology, Kanazawa University, Kakuma-machi, Kanazawa, 920-1192, Japan
Corresponding author: e-mail address: somei@p.kanazawa-u.ac.jp

Abstract – Novel three synthetic routes to (±)-6,7-secoagroclavine were developed from either methyl 3-(3-formylindol-4-yl)acrylate, indole-4-carbaldehyde, or 4-iodoindole-3-carbaldehyde. The total syntheses of (±)-chanoclavine-I, (±)-chanoclavine–II, and (±)-agroclavine-I were accomplished as well from the synthetic intermediates involved in the synthesis of (±)-6,7-secoagroclavine, culminating in establishing an efficient and common synthetic method for ergot alkaloids.

Ergot alkaloids (Scheme 1) are one of the attractive alkaloids due to both their multimodal biological activities and the possibility for the development of new medicinal drugs.[2] Their synthetic studies have been performed by many groups.[3−6] Nevertheless, an efficient total synthesis of ergot alkaloids has not been attained judged on our synthetic philosophy for evaluating the effectiveness.[7]

Our idea started from choosing 6,7-secoagroclavine (**1**, Scheme 1) as an important target, which was one of the ergot alkaloids isolated by D. C. Horwell's group.[3] Because once the synthetic route to **1** is established, the synthetic intermediates involved in the route would be derived by simple chemical modifications to the more complex ergot alkaloids, such as chanoclavine-I (**2**),[8] chanoclavine-II (**3**),[8] and agroclavine-I (**4**)[9] providing a common synthetic route to ergot alkaloids.

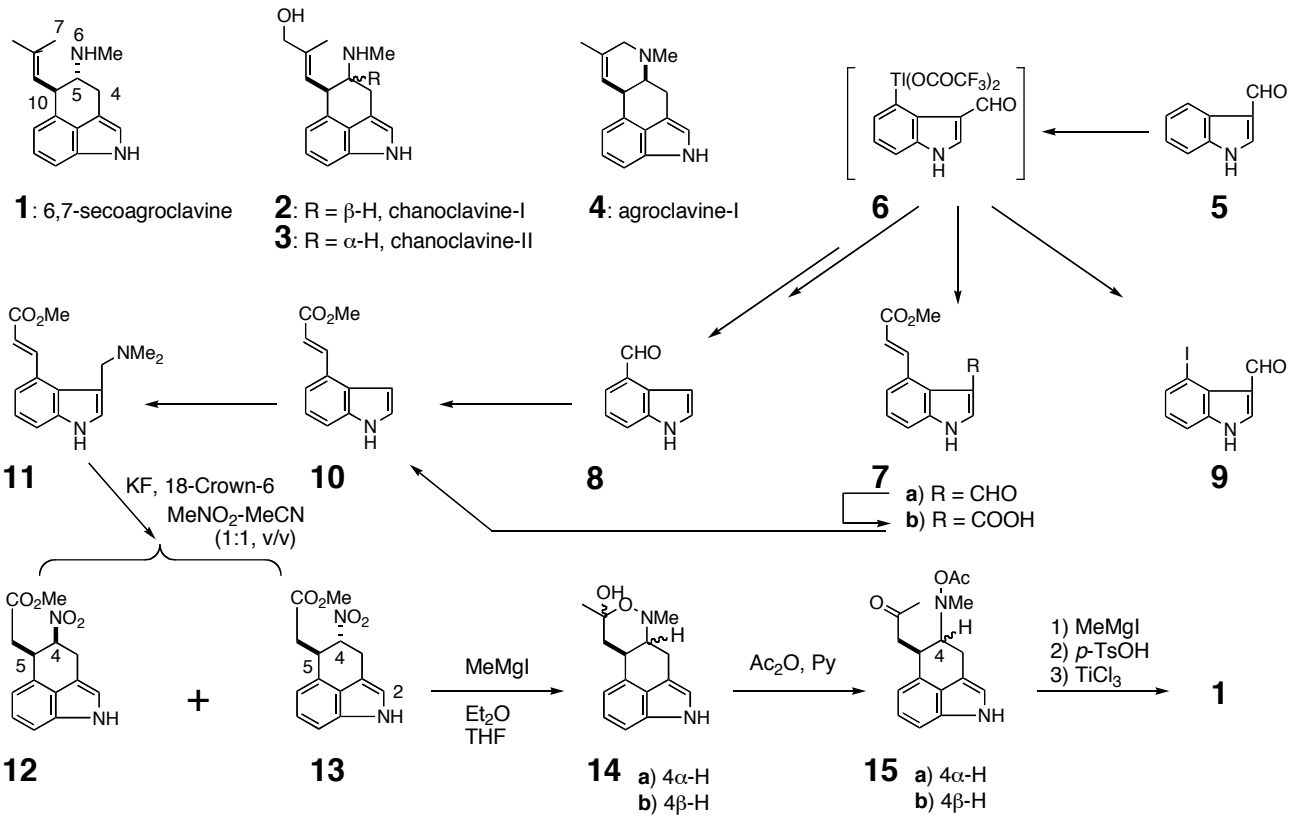
In order to meet our end, we have thus far created simple synthetic methods for various 4-substituted indoles from indole-3-carbaldehyde[10] (**5**) utilizing (3-formylindol-4-yl)thallium bis(trifluoroacetate) (**6**) as an intermediate (Scheme 1). The synthesis of methyl 3-(3-formylindol-4-yl)acrylate[11] (**7a**) was accom-

Dedicated to the 70th Birthday of Prof. Yoshito Kishi

plished by one pot procedure in 70% yield and indole-4-carbaldehyde (**8**) in five or six steps in 25—30% overall yield from **5**.[10] Preparation of 4-iodoindole-3-carbaldehyde[12] (**9**) was established as well by one pot procedure from **5** in 72% yield.

With these building blocks in hand, we succeeded in creating an efficient and common synthetic method for **1**, chanoclavine-I (**2**), chanoclavine-II (**3**), and agroclavine-I (**4**). Part of this work was published as preliminary communications.[13—18]

Scheme 1



A Ten-Step Synthetic Route to (±)-6,7-Secoagroclavine (1)

The oxidation of the formyl group of **7a** with $NaClO_2$ in *t*-BuOH-H_2O in the presence of NaH_2PO_4 and 2-methyl-2-butene[19] gave the corresponding carboxylic acid **7b** in 90% yield (Scheme 1). Decarboxylation of **7b** by heating in pyridine provided methyl 3-(indol-4-yl)acrylate (**10**)[20] in 91% yield. Compound **10** was also available by the following two alternative routes: 1) direct decarbonylation of **7a** with $(Ph_3P)_3RhCl$ in refluxing benzene in 32% yield, 2) Wittig reaction of **8** with $Ph_3P{=}CHCO_2Me$ in 99% yield. Subsequent Mannich reaction of **10** with Me_2NH and HCHO in AcOH afforded the corresponding gramine **11** in 95% yield. Treatment of **11** with $MeNO_2$ in refluxing MeCN in the presence of KF and 18-crown-6 gave the tricyclic compounds, 4,5-*cis*- (**12**) and 4,5-*trans*-5-methoxycarbonylmethyl-4-nitro-1,3,4,5-tetrahydrobenz[*cd*]indole (**13**), in 16 and 71% yields, respectively. Their stereochemistries were

determined by comparing their coupling constants between H-4 and H-5 (**12**: *J*=4.0 Hz, **13**: *J*=6.0 Hz) in addition to the fact that the *trans* isomer **13** was eventually derived to (±)-**1**.

In the next step, we needed a reductive methylation of the nitro group retaining the stereochemistry and the simultaneous transformation of the ester group to an isopropyl alcohol group. We conceived the idea that an excess amount of Grignard reagent could play dual role as a reducing reagent and a nucleophile, though nitroalkanes were rarely converted to *N*-substituted hydroxylamines with Grignard reagents.[21,22] In fact, the treatment of the *cis*-compound **12** with excess MeMgI in THF-Et_2O generated stereoselectively the hemiketal **14a** as a single product in 69% yield. The configuration of the hydroxy group in the hemiketal part is unknown. Subsequent treatment of **14a** with Ac_2O opened the hemiketal ring resulting in the formation of the *O*-acetyl compound **15a** in 93% yield. On the basis of these results, the *trans* isomer **13** was similarly treated with excess MeMgI in THF-Et_2O, followed by the acetylation without purification of the resulting methylhydroxylamine (**14b**), to afford the *O*-acetyl compound **15b** in 69% overall yield. Since we have already established the conversion of **15b** into (±)-6,7-secoagroclavine (**1**) in three steps,[14] the ten-step synthetic route of **1** was completed starting from indole-3-carbaldehyde (**5**). In this synthesis the originality rate (OR) is 27% because the following two steps, **5**→**7** and **13**→**14**, are our original findings.

An Eight-Step Synthetic Route to (±)-6,7-Secoagroclavine (1)

In order to raise the OR rate, we attempted to develop a shorter-step synthesis than the above ten-step one. Grignard reaction of **10** as a starting material with MeMgI in THF-Et_2O afforded the allyl alcohol **16** in 89% yield (Scheme 2). Subsequent Mannich reaction of **16** with Me_2NH and HCHO in AcOH gave many products and the desired gramine **17** was not obtained. However, dimethyl(methylene)ammonium chloride[23] reacted well with **16** in MeCN affording **17** in 70% yield. Our monoalkylation method with $MeNO_2$ in the presence of *n*-Bu_3P as a catalyst[24] was successfully applied to **17** resulting in the formation of nitroethyl compound **18** in 84% yield.

The construction of the 1,3,4,5-tetrahydrobenz[*cd*]indole skeleton from **18** required a novel cyclization reaction.[25] Our working hypothesis to meet our end is the following. A base can form nitronate on the nitro ethyl side chain of **18**, while a Lewis acid can generate cation on the side chain at the 4-position, stabilized doubly by the allylic and benzylic systems. If a Lewis acid was added after the formation of the nitronate and if by chance the formation of the stable cation was faster than the disappearance of the nitronate, the desired cyclization would be realized. Hoping the existence of suitable combination, we examined various bases and acids and typical results are summarized in Table 1. As a result, the combination of zinc salt as a Lewis acid and Et_3N as a base was first found to be effective for our purpose. When **18** reacted with $ZnCl_2$ and Et_3N in refluxing $ClCH_2CH_2Cl$, 4,5-*trans*-5-(2-methyl-1-propen-1-yl)-4-nitro-1,3,4,5-tetrahydrobenz[*cd*]indole (**19**) was obtained in 41% yield together with 9% yield of diene **20**

(Entry 4). Finally, we succeeded in creating a convenient cyclization method using $NaBH_4$ as a base and aqueous HCl as an acid culminating in the formation of the desired **19** in 72% yield (Entry 7).[25] The stereochemistry of **19** was elucidated as shown by its ^{1}H-NMR spectrum showing the predicted coupling constant between H-4 and H-5 (J=9.5 Hz).

Scheme 2

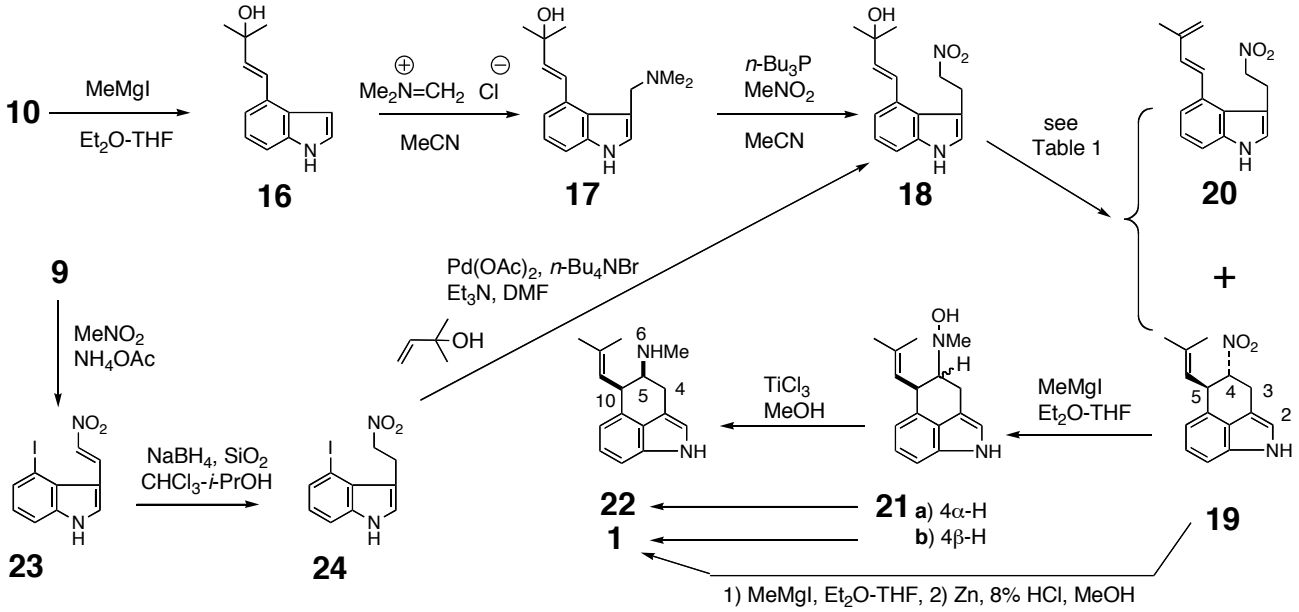


Table 1. Novel Intramolecular Cyclization of **18** with Base-Acid Catalyst

18 ⟶ **19** + **20**

Entry	Catalyst	Solvent	Yield (%) of **19**	Yield (%) of **20**	Yield (%) of **18**
1	$ZnCl_2/NEt_3$ (1.5:1)	THF	26	16	7
2	〃	$CHCl_3$	35	23	14
3	〃	DME	35	16	0
4	〃	$ClCH_2CH_2Cl$	41	9	4
5	$ZnBr_2/NEt_3$ (1.5:1)	〃	23	12	10
6	$Zn(OAc)_2/NEt_3$ (2:1)	〃	20	62	7
7	$NaBH_4/HCl$[ref.25]	MeOH-H_2O	72	0	3

We then applied our reductive methylation to the compound **19** using an excess amount of MeMgI. When the reaction was carried out at room temperature, epimerization at the 4-position occurred, and the 4,5-*cis*- **21a** and 4,5-*trans*-hydroxylamine **21b** were obtained in 19 and 20% yields, respectively. Subsequent reduction of **21a** and **21b** with $TiCl_3$[26] in MeOH in the presence of NH_4OAc gave (±)-5-*epi*-6,7-secoagroclavine (**22**) and (±)-6,7-secoagroclavine (**1**) in 44 and 27% yields, respectively. Based on the

results, the reductive methylation of **19** with MeMgI was carried out at 0°C expecting to minimize the epimerization. Without isolation of the hydroxylamines, the resulting reaction mixture was reduced with Zn-HCl instead of $TiCl_3$. As expected in one pot procedure, both the stereoselectivity and the yield were improved to give **1** and **22** in 66 and 9% yields, respectively. Thus, the eight-step synthetic route to **1** from **7** was established with OR rate of 55%, because the following four steps, **5**→**7**, **17**→**18**, **18**→**19**, and **19**→**1**, are our original findings.

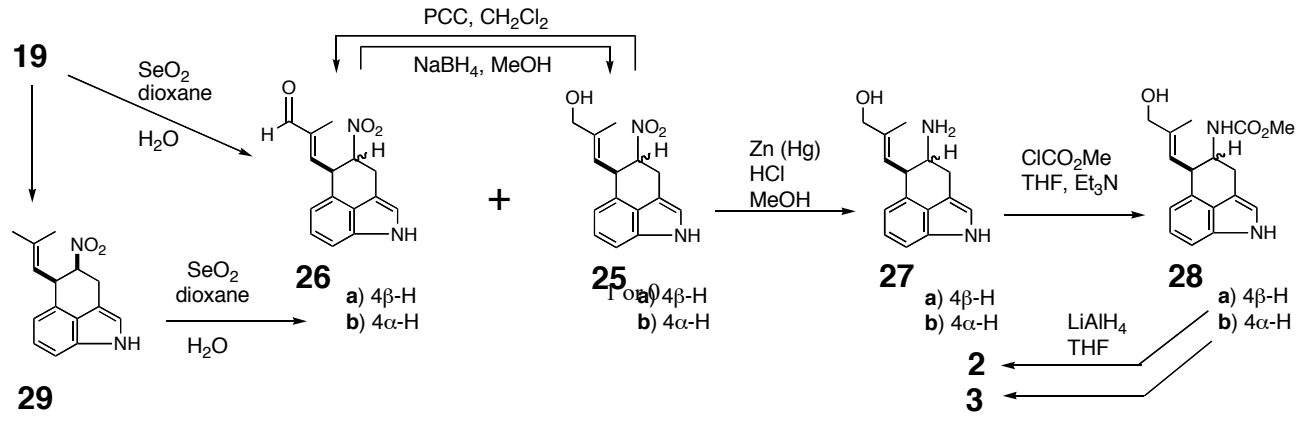
A Six-Step Synthetic Route to (±)-6,7-Secoagroclavine (1)

We were still not satisfied with the long steps in the above two synthetic routes. Therefore, further challenge was undertaken to develop a shorter-step and more practical synthetic route to **1** (Scheme 2). Aldol condensation reaction of 4-iodoindole-3-carbaldehyde (**9**) with $MeNO_2$ was performed in the presence of NH_4OAc to provide 4-iodo-3-(2-nitrovinyl)indole (**23**) in 96% yield. Reduction of **23** with $NaBH_4$ in *i*-PrOH and $CHCl_3$ in the presence of SiO_2[27] afforded 4-iodo-3-(2-ethyl)indole (**24**) in 84% yield. Improved procedure of Heck reaction in the presence of *n*-Bu_4NBr[14,28] with 2-methyl-3-buten-2-ol was successfully applied to **24** resulting in the formation of **18** in 84% yield. In the above second route, **18** had been converted to (±)-6,7-secoagroclavine (**1**) in two steps. Consequently, without using any protective groups,[29] we could create a six-step high regio- and stereo-selective synthesis of **1** from **7** with the OR rate of 57% because the following three steps, **5**→**9**, **18**→**19**, and **19**→**1**, are our original findings.

Total Syntheses of (±)-Chanoclavine-I (2) and (±)-Chanoclavine–II (3)

We expected that the oxidation of the methyl group on the side chain in (±)-6,7-secoagroclavine (**1**) would provide (±)-chanoclavine-I (**2**) and (±)-chanoclavine-II (**3**) (Scheme 3).

Scheme 3



According to the above idea, we first examined the oxidation of the methyl group of the side chain in the now readily available 4,5-*trans*-5-(2-methyl-1-propen-1-yl)-4-nitro-1,3,4,5-tetrahydrobenz[*cd*]indole (**19**) with SeO_2 in various solvents. Dioxane was finally found to be a solvent of choice producing the alcohol

25a and the aldehyde **26a** in 36 and 19% yields, respectively, together with a 32% yield of recovery. The structures of **25a** and **26a** were determined by spectral data and the following chemical conversions. Thus, oxidation of **25a** with PCC in CH_2Cl_2 afforded **26a** in 55% yield, while reduction of **26a** with $NaBH_4$ in MeOH gave **25a** in 93% yield.

Reduction of the alcohol **25a** with Zn (Hg) in refluxing methanolic HCl provided (±)-norchanoclavine-I (**27a**) as a single product in 98% yield retaining the configuration of the 4-position. Treatment of **27a** with $ClCO_2Me$ in THF afforded the carbamate **28a** in 92% yield. Subsequent reduction of **28a** with $LiAlH_4$ in refluxing THF achieved the total synthesis of (±)-chanoclavine-I (**2**) in 96% yield.[20,30−32]

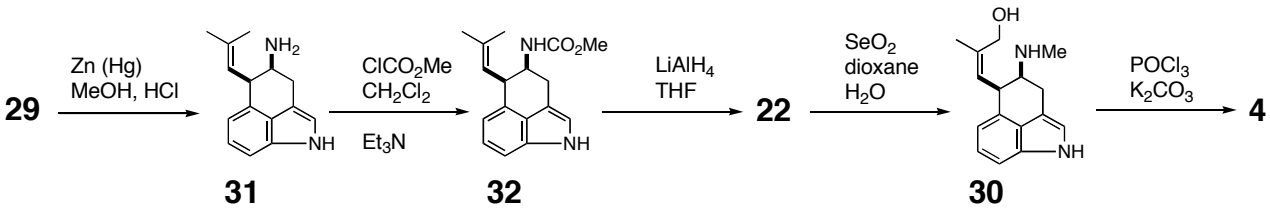
Both norchanoclavine-II (**27b**) and chanoclavine-II (**3**) have *cis*-configuration concerning the 4- and 5-positions. Aiming at the total synthesis of these alkaloids, we next examined the inversion of the stereochemistry at the 4-position in **19**. Treatment of **19** with excess NaOMe in refluxing MeOH and subsequent protonation afforded the desired *cis*-compound **29** in 85% yield. The *cis*-stereochemistry was proved by ^{1}H-NMR analysis of **29** observing the coupling constant (J=4.4 Hz) between H-4 and H-5.

The same sequence of reactions in the synthesis of **2** was next applied to **29**. The oxidation with SeO_2 in dioxane-H_2O afforded the alcohol **25b** and the aldehyde **26b** in 31 and 4% yields, respectively, in addition to a 62% yield of recovery. Subsequent reduction of the alcohol **25b** with Zn (Hg) in refluxing methanolic HCl gave (±)-norchanoclavine-II (**27b**) in 95% yield. The carbamate **28b** was obtained in 98% yield by the treatment of **27b** with $ClCO_2Me$ in THF. Finally, the reduction of **28b** with $LiAlH_4$ in THF achieved the first total synthesis of (±)-chanoclavine-II (**3**) in 86% yield. ^{1}H-NMR spectrum of **3** was identical with that of the alkaloid reported in the literature.[8] Thus, the total syntheses of (±)-chanoclavine-I (**2**) and (±)-chanoclavine-II (**3**) are accomplished in nine and ten steps from **5** in 10 and 7% overall yields, respectively, and with the respective OR rates of 27 and 25%.

Total syntheses of (±)-Agroclavine-I (4)

Agroclavine-I (**4**) was isolated by Sakharovsky's group in 1984[9] and its total synthesis had been achieved by Kozikowski's[33] and Ninomiya's[34] groups in 1985. Wheeler also reported the formal synthesis of **4**.[35]

Scheme 4



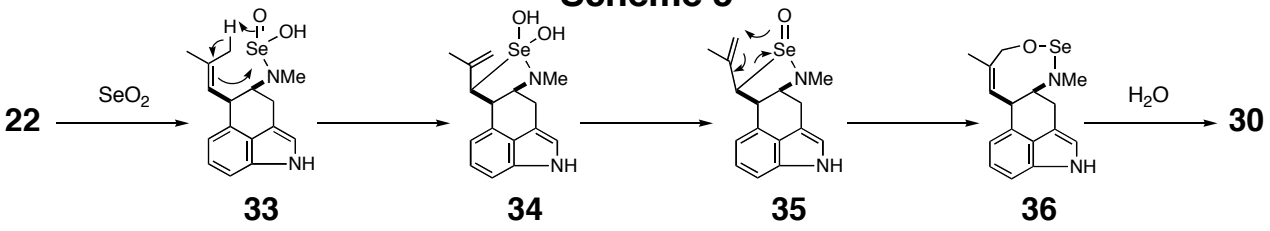
We considered that the synthesis of **4** would be readily achieved if we could create a regioselective oxidation method of the *Z*-methyl group of the isobutyl group at the 5-position of (±)-5-*epi*-6,7-

secoagroclavine (**22**). After elaborations, we found that SeO_2 in dioxane-H_2O was the reagent of choice resulting in the formation of the desired alcohol **30** in 34% yield (Scheme 4).

The mechanism of the above regioselective *Z*-methyl oxidation would be explained as shown in Scheme 5. Initial coordination of the methylamino-nitrogen (6-position of **22**) to SeO_2 forms a complex **33** placing SeO_2 to the close vicinity of the *Z*-methyl group. According to the ordinary oxidation mechanism of SeO_2,[36−38] **33** then transforms to **34**. Dehydration of **34** followed by [2,3] sigmatropic rearrangement generates **36** through **35**. Subsequent hydrolysis gives **30**.

The compound **22** is alternatively available from **29**. Thus, the reduction of **29** with Zn (Hg) in refluxing methanolic HCl gave the corresponding amine **31** in 98% yield. Then the carbamate **32** was prepared by the treatment with $ClCO_2Me$ in THF in a quantitative yield. Subsequent reduction of **32** with $LiAlH_4$ in THF provided **22** in 98% yield.

Scheme 5



Finally, treatment of **30** with $POCl_3$ in the presence of K_2CO_3[39] accomplished the total synthesis of **4** in 87% yield. Spectral data (^{1}H-NMR) of **4** was identical with that of the authentic (±)-agroclavine-I which was synthesized by Ninomiya's group.[34] Thus, the total synthesis of (±)-agroclavine-I (**4**) was accomplished in eleven steps from **5** in 9% overall yield. The OR rate is 41% because our original step, **22**→**30**, is added.

In conclusion, we succeeded in developing an efficient and common synthetic route for producing (±)-6,7-secoagroclavine[40,41] (**1**), (±)-chanoclavine-I (**2**), (±)-chanoclavine-II (**3**), and (±)-agroclavine-I (**4**) with high OR rates, respectively, without using any protective groups.[29]

ACKNOWLEDGMENTS

The authors are grateful to the late Dr. M. Natsume for a gift of (±)-6,7-secoagroclavine and (±)-chanoclavine-I and also to Professor I. Ninomiya for (±)-agroclavine-I. The authors wish to thank Professor H. G. Floss for offering the informations about (±)-norchanoclavine-II and (±)-chanoclavine-II and Dr. V. G. Sakharovsky as well for the information about (±)-agroclavine-I.

EXPERIMENTAL

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. IR

spectra were determined with a Shimadzu IR-420 spectrophotometer, and ^{1}H-NMR spectra with a JEOL JNM-PMX 60 or a JEOL JNM-FX100 spectrometer, with tetramethylsilane as an internal standard. MS were recorded on a JEOL 01SG or a HITACHI M-80 spectrometer. Preparative thin-layer chromatography (p-TLC) was performed on Merck Kiesel-gel GF_{254} (Type 60)(SiO_2). Column chromatography was performed on silica gel (SiO_2, 100—200 mesh, from Kanto Chemical Co. Inc.) throughout the present study. HPLC was conducted with a Kusano KPW-20 pump equipped with a Kusano KU-331 as a detector.

(*E*)-4-(2-Methoxycarbonylethen-1-yl)indole-3-carboxylic Acid (7b) from (*E*)-Methyl 3-(3-Formylindol-4-yl)acrylate (7a) — $NaClO_2$ (368.1 mg, 4.09 mmol) was added to a solution of **7a** (45.9 mg, 0.20 mmol) and NaH_2PO_4 (497.1 mg, 4.14 mmol) in a mixture of *t*-BuOH–2-methyl-2-butene–H_2O (2:2:1, v/v, 10 mL) and stirred at rt (19°C) for 19 h. After addition of CH_2Cl_2–MeOH (95:5, v/v), the whole was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave a solid, which was recrystallized from MeOH to give **7b** (32.1 mg) as colorless prisms. The mother liquor was subjected to p-TLC on SiO_2 with CH_2Cl_2–MeOH (9:1, v/v) as a developing solvent to give additional **7b** (12.3 mg). The total yield of **7b** was 44.4 mg (90%). **7b**: mp 232—233°C (decomp.). IR (KBr): 3200, 1669 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 3.84 (3H, s), 6.38 (1H, d, *J*=16 Hz), 7.23 (1H, t, *J*=7.8 Hz), 7.42—7.62 (2H, m), 8.10 (1H, s), 9.42 (1H, d, *J*=16 Hz). MS *m/z*: 245 (M^+). *Anal.* Calcd for $C_{13}H_{11}NO_4$: C, 63.67; H, 4.52; N, 5.71. Found: C, 63.51; H, 4.51; N, 5.91.

(*E*)-Methyl 3-(Indol-4-yl)acrylate (10) from 7b — A solution of **7b** (99.5 mg, 0.41 mmol) in pyridine (5 mL) was refluxed for 21 h with stirring. The solvent was evaporated under reduced pressure to leave a solid, which was subjected to p-TLC on SiO_2 with CH_2Cl_2 as a developing solvent. Extraction of the band having an *Rf* value of 0.62—0.38 with CH_2Cl_2–MeOH (95:5, v/v) gave **10** (74.2 mg, 91%). **10**: mp 129—130°C (lit.,[13] mp 125—126°C) (pale yellow prisms, recrystallized from AcOEt). IR (KBr): 3340, 1685 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 3.81 (3H, s), 6.58 (1H, d, *J*=16.1 Hz), 6.71 (1H, dd, *J*=3.2, 0.8 Hz), 7.09 (1H, t, *J*=7.7 Hz), 7.30 (1H, dd, *J*=7.7, 0.8 Hz), 7.34 (1H, d, *J*=3.2 Hz), 7.44 (1H, dt, *J*=7.7, 0.8 Hz), 8.04 (1H, d, *J*=16.1 Hz).

(*E*)-Methyl 3-(Indol-4-yl)acrylate (10) from 7a — $(Ph_3P)_3RhCl$ (422.9 mg, 0.46 mmol) was added to a solution of **9** (103.8 mg, 0.45 mmol) in benzene (20 mL) and the mixture was refluxed for 24 h with stirring under argon atmosphere. After evaporation of the solvent, CH_2Cl_2–MeOH (95:5, v/v) was added and insoluble precipitates were filtered off through SiO_2. The filtrate was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with CH_2Cl_2 to give **10** (29.1 mg, 32%).

(*E*)-Methyl 3-(Indol-4-yl)acrylate (10) from Indole-4-carbaldehyde (8) — A solution of **8** (293.7 mg, 2.03 mmol) and (methoxycarbonylmethylene)triphenylphosphorane (1172.4 mg, 3.51 mmol) in benzene

(25 mL) was refluxed for 4 h with stirring. The solvent was evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with CH_2Cl_2 to give **10** (403.4 mg, 99%).

(*E*)-Methyl 3-(3-Dimethylaminomethylindol-4-yl)acrylate (11) from 10 — A solution of **10** (392.1 mg, 1.95 mmol) in AcOH (1 mL) was added to a solution of 50% Me_2NH (193.3mg, 2.15 mmol) and 37% HCHO (162.8 mg, 2.01 mmol) in AcOH (2 mL), and the mixture was stirred at rt for 7.5 h. The resulting solution was made basic by adding 5% NaOH and extracted with CH_2Cl_2–MeOH (95:5, v/v). The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_4OH (46:5:0.5, v/v) to give **11** (476.1 mg, 95 %) as pale yellow oil. **11**: IR (film): 3320, 1705 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.27 (6H, s), 3.50 (2H, s), 3.74 (3H, s), 6.31 (1H, d, *J*=16.0 Hz), 6.18—7.36 (4H, m), 8.31 (1H, br s), 8.73 (1H, d, *J*=16.0 Hz). High-resolution MS *m/z*: Calcd for $C_{15}H_{18}N_2O_2$: 258.1366. Found: 258.1363.

4,5-*cis*- (12) and 4,5-*trans*-5-Methoxycarbonylmethyl-4-nitro-1,3,4,5-tetrahydrobenz[*cd*]indole (13) from 11 — KF (26.7 mg, 0.46 mmol) was added to a solution of **11** (72.1 mg, 0.28 mmol) and 18-crown-6 (26.5 mg, 0.10 mmol) in MeCN–$MeNO_2$ (1:1, v/v, 25 mL) and the mixture was refluxed for 37.5 h with stirring. The solvent was evaporated under reduced pressure to leave an oil, which was subjected to p-TLC on SiO_2 (developed three times with ether–hexane as a developing solvent). Extraction of the band having an *Rf* value of 0.41—0.33 with CH_2Cl_2–MeOH (95:5, v/v) gave **12** (12.2 mg, 16%) as a colorless oil. **12**: IR (film): 3400, 1730, 1541, 1364 cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 2.64 (2H, d, *J*=6.8 Hz), 3.44 (2H, d, *J*=7.2 Hz), 3.61 (3H, s), 4.29 (1H, dt, *J*=6.8, 4.0 Hz), 5.01 (1H, dt, *J*=7.2, 4.0 Hz), 6.65—7.26 (4H, m), 7.93 (1H, br s). High-resolution MS *m/z*: Calcd for $C_{14}H_{14}N_2O_4$: 274.0952. Found: 274.0951. Extraction of the band having an *Rf* value of 0.33—0.17 with CH_2Cl_2–MeOH (95:5, v/v) gave **13** (54.7 mg, 71%) as colorless oil. **13**: IR (film): 3410, 1730, 1541, 1361 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.68 (2H, d, *J*=6.0 Hz), 3.27 (1H, dd, *J*=15.5, 4.8 Hz), 3.64 (3H, s), 3.68 (1H, dd, *J*=15.5, 6.0 Hz), 4.26 (1H, q, *J*=6.0 Hz), 5.07 (1H, dt, *J*=6.0, 4.8 Hz), 6.61—7.17 (4H, m), 7.94 (1H, br s). High-resolution MS *m/z*: Calcd for $C_{14}H_{14}N_2O_4$: 274.0952. Found: 274.0955.

5,10-*cis*-6,8-Dimethyl-7-oxaergolin-8-ol (14a) from 12 — An ether solution of MeMgI was prepared with Mg ribbon (237.2 mg, 9.76 mmol) and MeI (1407.7 mg, 9.92 mmol) in anhydrous Et_2O (20 mL) under argon atmosphere. To the resulting solution was added a solution of **12** (82.8 mg, 0.30 mmol) in anhydrous THF (5 mL) and the mixture was stirred at rt for 1 h under argon atmosphere. After cooling to 0°C, 20% NH_4Cl was added and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with CH_2Cl_2–MeOH (95:5, v/v) to give **14a** (53.5 mg, 69%). **14a**: mp 185—187°C (decomp., colorless prisms, recrystallized from AcOEt). IR (KBr): 3330, 3260, 1607 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.37 (3H, s), 1.63 (1H, dd, *J*=13.6, 12.6 Hz), 1.93 (1H, dd, *J*=13.6, 5.3

Hz), 2.78 (3H, s), 2.97—3.78 (4H, m), 4.74 (1H, br s), 6.70—6.96 (2H, m), 6.96—7.28 (2H, m), 7.93 (1H, br s). MS *m/z*: 258 (M^+). *Anal.* Calcd for $C_{15}H_{18}N_2O_2$: C, 69.74; H, 7.02; N, 10.85. Found: C, 69.67; H, 7.10; N, 10.62.

4,5-*cis*-5-Acetonyl-4-(*N*-acetoxy-*N*-methyl)amino1,3,4,5-tetrahydrobenz[*cd*]indole (15a) from 14a — A solution of **14a** (26.5 mg, 0.10 mmol) in pyridine (2 mL) and Ac_2O (1 mL) was stirred at rt for 6.5 h. The solvent was evaporated under reduced pressure to leave an oil, which was subjected to p-TLC on SiO_2 with CH_2Cl_2–MeOH (95:5, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.33—0.49 with CH_2Cl_2–MeOH (95:5, v/v) gave **15a** (27.8 mg, 93%) as a colorless oil. **15a**: IR (film): 3310, 1747, 1703, 1617 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.00 (3H, s), 2.09 (3H, s), 2.40 (1H, dd, *J*=17.6, 9.8 Hz), 2.50—3.38 (4H, m), 2.89 (3H, s), 3.98 (1H, dt, *J*=9.8, 3.3 Hz), 6.76—7.22 (4H, m), 7.96 (1H, br s). High-resolution MS *m/z*: Calcd for $C_{17}H_{20}N_2O_3$: 300.1473. Found: 300.1476.

4,5-*trans*-5-Acetonyl-4-(*N*-acetoxy-*N*-methyl)amino-1,3,4,5-tetrahydrobenz[*cd*]indole (15b) from 13 — An ether solution of MeMgI was prepared with Mg ribbon (637.4 mg, 26.2 mmol) and MeI (3516.7 mg, 24.8 mmol) in anhydrous Et_2O (30 mL) under argon atmosphere. To the resulting solution was added a solution of **13** (221.4 mg, 0.81 mmol) in anhydrous THF (20 mL) and the mixture was stirred at rt for 1 h under argon atmosphere. After cooling to 0°C, 20% NH_4Cl was added and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was dissolved in pyridine (2 mL) and Ac_2O (1 mL). The resulting solution was stirred at rt for 2 h. The solvent was evaporated under reduced pressure to leave an oil, which was subjected to p-TLC on SiO_2 with CH_2Cl_2–MeOH (95:5, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.33—0.57 with CH_2Cl_2–MeOH (95:5, v/v) gave **15b** (164.7 mg, 69%). **15b**: mp 137.5—139.5°C (lit.,[13] mp 136.5—137.5°C) (colorless prisms, recrystallized from MeOH). IR (KBr): 3300, 1721, 1704 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.88 (3H, s), 2.28 (3H, s), 2.71—3.51 (5H, m), 2.83 (3H, s), 3.63—3.91 (1H, m), 6.59—6.75 (1H, m), 6.85 (1H, br s), 6.95—7.19 (2H, m), 7.95 (1H, br s).

(*E*)-1-(Indol-4-yl)-3-methyl-1-buten-3-ol (16) from 10 — An ether solution of MeMgI was prepared with Mg ribbon (373.7 mg, 15.4 mmol) and MeI (0.9 mL, 14.6 mmol) in anhydrous Et_2O (5 mL) under argon atmosphere. To the resulting solution was added a solution of **10** (96.4 mg, 0.48 mmol) in anhydrous THF (20 mL) and the mixture was stirred at rt for 2 h under argon atmosphere. After cooling to 0°C, brine was added and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was subjected to p-TLC on Al_2O_3 with CH_2Cl_2 as a developing solvent. Extraction of the band having an *Rf* value of 0.47—0.78 with CH_2Cl_2–MeOH (95:5, v/v) gave **16** (85.4 mg, 89%). **16**: mp 98—99°C (colorless prisms, recrystallized from benzene). IR (KBr): 3530, 3240 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.45

(6H, s), 6.47 (1H, d, *J*=16.1 Hz), 6.65 (1H, dd, *J*=3.2, 0.8 Hz), 6.92—7.34 (3H, m), 6.95 (1H, d, *J*=16.1 Hz), 7.23 (1H, d, *J*=3.2 Hz). MS *m/z*: 201 (M^+). *Anal.* Calcd for $C_{13}H_{15}NO$: C, 77.58; H, 7.51; N, 6.96. Found: C, 77.71; H, 7.68; N, 6.69.

(*E*)-1-(3-Dimethylaminomethylindol-4-yl)-3-methyl-1-buten-3-ol (17) from 16 — *N*,*N*-Dimethyl(methylene)ammonium chloride (233.9 mg, 2.50 mmol) was added to a solution of **16** (412.8 mg, 2.05 mmol) in anhydrous MeCN (4 mL) and the mixture was stirred at rt for 10 min. After addition of 10% NaOH, the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on Al_2O_3 with CH_2Cl_2 to give **17** (372.7 mg, 70%). **17**: mp 132—134°C (colorless needles, recrystallized from benzene). IR (KBr): 3570, 3140 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.44 (6H, s), 2.16 (1H, br s, disappeared on addition of D_2O), 2.23 (6H, s), 3.52 (2H, s), 6.20 (1H, d, *J*=16.0 Hz), 6.87—7.28 (4H, m), 7.60 (1H, d, *J*=16.0 Hz), 8.10 (1H, br s, disappeared on addition of D_2O). MS *m/z*: 258 (M^+). *Anal.* Calcd for $C_{16}H_{22}N_2O$: C, 74.38; H, 8.58; N, 10.84. Found: C, 74.65; H, 8.63; N, 10.62.

(*E*)-1-[3-(2-Nitroethyl)indol-4-yl]-3-methyl-1-buten-3-ol (18) from 17 — *n*-Bu_3P[24] (54.2 mg, 0.27 mmol) was added to a solution of **17** (148.6 mg, 0.58 mmol) in $MeNO_2$ (3 mL) and MeCN (3 mL), and the mixture was refluxed for 2 h with stirring under argon atmosphere. The solvent was evaporated under reduced pressure to leave an oil, which was subjected to p-TLC on SiO_2 with CH_2Cl_2–MeOH (97:3, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.23—0.41 with CH_2Cl_2–MeOH (95:5, v/v) gave **18** (132.2 mg, 84%). **18**: mp 106—107°C (pale yellow prisms, recrystallized from MeOH). IR (KBr): 3450, 3310, 3230, 1562, 1537, 1382, 1370, 1344 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.45 (6H, s), 1.91 (1H, br s, disappeared on addition of D_2O), 3.51 (2H, t, *J*=7.5 Hz), 4.55 (2H, t, *J*=7.5 Hz), 6.16 (1H, d, *J*=15.2 Hz), 6.74—7.24 (4H, m), 7.16 (1H, d, *J*=15.2 Hz), 8.06 (1H, br s, disappeared on addition of D_2O). MS *m/z*: 274 (M^+). *Anal.* Calcd for $C_{15}H_{18}N_2O_3$: C, 65.67; H, 6.61; N, 10.24. Found: C, 65.83; H, 6.75; N, 10.09.

4,5-*trans*-5-(2-Methyl-1-propen-1-yl)-4-nitro-1,3,4,5-tetrahydrobenz[*cd*]indole (19) and (*E*)-4-(3-methyl-1,3-butadien-1-yl)-3-(2-nitroethyl)indole (20) from 18 — [Entry 1] — A solution of **18** (50.8 mg, 0.19 mmol), $ZnCl_2$ (379.0 mg, 2.78 mmol), and Et_3N (181.6 mg, 1.79 mmol) in THF (4 mL) was refluxed for 4 h with stirring. MeOH was added to the resulting solution. After evaporation of the solvent, CH_2Cl_2–MeOH (95:5, v/v) was added and insoluble precipitates were filtered off through SiO_2. The filtrate was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was subjected to p-TLC on SiO_2 with Et_2O–hexane (1:1, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.44—0.51 with CH_2Cl_2–MeOH (95:5, v/v) gave **19** (12.4 mg, 26%). **19**: mp 164—165°C (pale yellow prisms, recrystallized from MeOH). IR (KBr): 3420, 1540, 1342 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.78 (3H, d, *J*=1.4 Hz), 1.84 (3H, d, *J*=1.4 Hz), 3.51 (2H, dd, *J*=7.1, 1.0 Hz), 4.51 (1H, t,

J=9.5 Hz), 4.75 (1H, dt, *J*=9.5, 7.1 Hz), 5.14 (1H, br d, *J*=9.5 Hz), 6.70—6.85 (1H, m), 6.90 (1H, dt, *J*=2.0, 1.0 Hz), 6.98—7.26 (2H, m), 7.98 (1H, br s). MS *m/z*: 256 (M^+). *Anal.* Calcd for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.93. Found: C, 70.06; H, 6.15; N, 11.08. Extraction of the band having an *Rf* value of 0.28—0.44 with CH_2Cl_2–MeOH (95:5, v/v) gave **20** (7.6 mg, 16%) as an unstable colorless oil. **20**: IR (film): 3410, 1546, 1380 cm^{-1}. ^{1}H-NMR (20% CD_3OD in $CDCl_3$) δ: 2.00 (3H, d, *J*=0.8 Hz), 3.54 (2H, t, *J*=7.0 Hz), 4.55 (2H, t, *J*=7.0 Hz), 5.01 (2H, br s), 6.48—7.48 (6H, m). High-resolution MS *m/z*: Calcd for $C_{15}H_{16}N_2O_2$: 256.1211. Found: 256.1211. Extraction of the band having an *Rf* value of 0.13—0.24 with CH_2Cl_2–MeOH (95:5, v/v) gave **18** (3.3 mg, 7%).

[Entry 2] — A solution of **18** (32.0 mg, 0.12 mmol), $ZnCl_2$ (245.4 mg, 1.80 mmol), and Et_3N (116.7 mg, 1.15 mmol) in $CHCl_3$ (4 mL) was refluxed for 2 h with stirring. After the same work-up and separation as described in entry 1, **19** (10.5 mg, 35%), **20** (7.0 mg, 23%), and **18** (4.5 mg, 14%) were obtained.

[Entry 3] — A solution of **18** (31.4 mg, 0.12 mmol), $ZnCl_2$ (243.4 mg, 1.79 mmol), and Et_3N (117.0 mg, 1.15 mmol) in dimethoxyethane (4 mL) was refluxed for 2 h with stirring. After the same work-up and separation as described in entry 1, **19** (10.3 mg, 35%) and **20** (4.8 mg, 16%) were obtained.

[Entry 4] — A solution of **18** (31.6 mg, 0.12 mmol), $ZnCl_2$ (240.8 mg, 1.77 mmol), and Et_3N (119.6 mg, 1.18 mmol) in 1,2-dichloroethane (4 mL) was refluxed for 2 h with stirring. After the same work-up and separation as described in entry 1, **19** (12.0 mg, 41%), **20** (2.5 mg, 9%), and **18** (1.2 mg, 4%) were obtained.

[Entry 5] — A solution of **18** (29.8 mg, 0.11 mmol), $ZnBr_2$ (377.6 mg, 1.68 mmol), and Et_3N (118.7 mg, 1.17 mmol) in 1,2-dichloroethane (4 mL) was refluxed for 45 min with stirring. After the same work-up and separation as described in entry 1, **19** (6.4 mg, 23%), **20** (3.3 mg, 12%), and **18** (3.0 mg, 10%) were obtained.

[Entry 6] — A solution of **18** (30.0 mg, 0.11 mmol), $Zn(OAc)_2$ (362.1 mg, 1.97 mmol), and Et_3N (108.4 mg, 1.07 mmol) in 1,2-dichloroethane (4 mL) was refluxed for 47 h with stirring. After the same work-up and separation as described in entry 1, **19** (5.5 mg, 20%), **20** (17.4 mg, 62%), and **18** (2.2 mg, 7%) were obtained.

[Entry 7] — See reference 25.

4,5-*cis*- (21a) and 4,5-*trans*-4-(*N*-Hydroxy-*N*-methyl)amino-5-(2-methyl-1-propen-1-yl)-1,3,4,5-tetrahydrobenz[*cd*]indole (21b) from 19 — An ether solution of MeMgI was prepared with Mg ribbon (0.36 g, 15.0 mmol) and MeI (1.92 g, 13.5 mmol) in anhydrous Et_2O (8 mL) under argon atmosphere. To the resulting solution was added a solution of **19** (76.3 mg, 0.30 mmol) in anhydrous THF (4 mL) and the mixture was stirred at rt for 0.5 h under argon atmosphere. After cooling to 0°C, 20% NH_4Cl was added and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was subjected to p-TLC

on SiO_2 with $CHCl_3$–MeOH–28% NH_4OH (46:5:0.5, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.54—0.66 with $CHCl_3$–MeOH–28% NH_4OH (46:5:0.5, v/v) gave **21a** (14.5 mg, 19%) as a colorless oil. **21a**: IR (KBr): 3400, 1619 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.67 (3H, d, *J*=1.5 Hz), 1.93 (3H, d, *J*=1.5 Hz), 2.75—3.49 (3H, m), 2.77 (3H, s), 4.28 (1H, dd, *J*=10.0, 2.0 Hz), 5.01 (1H, br s, disappeared on addition of D_2O), 5.30 (1H, br d, *J*=10.0 Hz), 6.64—7.27 (4H, m), 7.82 (1H, br s, disappeared on addition of D_2O). High-resolution MS *m/z*: Calcd for $C_{16}H_{20}N_2O$: 256.1575. Found: 256.1614. Extraction of the band having an *Rf* value of 0.47—0.54 with $CHCl_3$–MeOH–28% NH_4OH (46:5:0.5, v/v) gave **21b** (15.3 mg, 20%). **21b**: mp 147—149°C (decomp., colorless prisms, recrystallized from benzene). IR (KBr): 3400, 3310, 1603 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.82 (6H, d, *J*=1.5 Hz), 2.68 (3H, s), 2.86—3.40 (3H, m), 3.90—4.24 (1H, m), 4.94 (1H, br s), 5.19 (1H, br d, *J*=9.5 Hz), 6.59—6.79 (1H, m), 6.83 (1H, br s), 6.96—7.20 (2H, m), 7.83 (1H, br s). High-resolution MS *m/z*: Calcd for $C_{16}H_{20}N_2O$: 256.1575. Found: 256.1616.

(±)-5-*epi*-6,7-Secoagroclavine (22) from 21a — A $TiCl_3$ solution (16%, 0.2 mL, 0.31 mmol) was added to a solution of **21a** (14.5 mg, 0.06 mmol) and NH_4OAc (100.7 mg, 1.31 mmol) in MeOH (2 mL) and the mixture was stirred at rt for 7 min. The resulting solution was made basic with 8% NaOH and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was subjected to p-TLC on Al_2O_3 with Et_2O–AcOEt–CH_2Cl_2 (5:2:8, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.31—0.41 with CH_2Cl_2–MeOH (95:5, v/v) gave **22** (6.0 mg, 44%). **22**: mp 177—178°C (colorless prisms, recrystallized from MeOH–H_2O). IR (KBr): 3140, 3090, 3050, 2860, 1661, 1616, 1603, 1437, 1092 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.57 (1H, s, disappeared on addition of D_2O), 1.73 (3H, d, *J*=1.2 Hz), 1.89 (3H, d, *J*=1.2 Hz), 2.51 (3H, s), 2.77 (1H, ddd, *J*=15.4, 10.3, 1.5 Hz), 2.93—3.22 (2H, m), 4.14 (1H, dd, *J*=10.3, 3.7 Hz), 5.21 (1H, br d, *J*=10.3 Hz), 6.69—6.87 (1H, m), 6.81 (1H, br s), 6.91—7.15 (2H, m), 8.01 (1H, br s, disappeared on addition of D_2O). MS *m/z*: 240 (M^+). *Anal.* Calcd for $C_{16}H_{20}N_2$: C, 79.95; H, 8.39; N, 11.66. Found: C, 79.99; H, 8.51; N, 11.60.

(±)-6,7-Secoagroclavine (1) from 21b — A $TiCl_3$ solution (16%, 0.2 mL, 0.31 mmol) was added to a solution of **21b** (12.6 mg, 0.05 mmol) and NH_4OAc (96.6 mg, 1.29 mmol) in MeOH (2 mL) and the mixture was stirred at rt for 7 min. After the same work-up and separation as described above, **1** (3.2 mg, 27%) was obtained. **1**: mp 202—203°C (lit.,[3] mp 202—205°C) (colorless prisms, recrystallized from MeOH). IR (KBr): 3300, 3150, 2950, 2900, 1609, 1440, 1350, 1340, 1329, 1140, 1091, 1030 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.58 (1H, s), 1.84 (3H, d, *J*=1.5 Hz), 1.88 (3H, d, *J*=1.5 Hz), 2.51 (3H, s), 2.51—3.05 (2H, m), 3.05—3.44 (1H, m), 3.86 (br dd, *J*=10.0, 8.0 Hz and d, *J*=10.0 Hz, total 1H), 5.13 (1H, br d, *J*=10.0 Hz), 6.72 (1H, ddd, *J*=5.0, 3.0, 1.0 Hz), 6.90 (1H, d, *J*=1.0 Hz), 6.98—7.27 (2H, m), 7.95 (1H, br s). MS *m/z*: 240 (M^+).

Direct Synthesis of 1 from 19 — An ether solution of MeMgI was prepared with Mg ribbon (1113.3 mg, 45.8 mmol) and MeI (2.5 mL, 40.2 mmol) in anhydrous Et_2O (20 mL) under argon atmosphere. To the resulting solution was added a solution of **19** (499.1 mg, 1.95 mmol) in anhydrous THF (20 mL) and the mixture was stirred at rt for 1 h under argon atmosphere. After cooling to 0°C, 20% NH_4Cl was added and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was dissolved in MeOH (80 mL). The resulting solution was added to a suspension of Zn (3998.7 mg, 61.2 mmol) in 6% HCl (25 mL) and the mixture was refluxed for 12 h with stirring. Unreacted Zn was filtered off. The filtrate was concentrated and made basic with 8% NaOH, and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave a solid, which was recrystallized from MeOH to give **1** (207 mg) as colorless prisms. The mother liquor was subjected to HPLC [column, CPS-223L-1 (*i.d.* 22x100 mm); solvent, AcOEt–Et_2O–Et_3N (100:10:1, v/v); flow rate, 1.0 mL/min; detection, UV 303 nm]. **22** (40.4 mg, 9%) and additional **1** (102.7 mg) were obtained in the order of elution. The total yield of **1** was 309.9 mg (66%).

(*E*)-4-Iodo-3-(2-nitrovinyl)indole (23) from 4-Iodo-3-indolecarbaldehyde (9) — NH_4OAc (108.5 mg, 1.41 mmol) was added to a solution of **9** (103.1 mg, 0.38 mmol) in $MeNO_2$ (5 mL) and the mixture was refluxed for 1 h with stirring. After evaporation of the solvent, brine was added and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave a solid, which was recrystallized from AcOEt to give **23** (114.7 mg, 96%). **23**: mp 255—265°C (decomp., orange needles, recrystallized from MeOH–$CHCl_3$). IR (KBr): 3230, 1597, 1478 cm^{-1}. ^{1}H-NMR (pyridine-d_5) δ: 6.83 (1H, dd, *J*=8.0, 7.2 Hz), 7.42 (1H, dd, *J*=8.0, 1.0 Hz), 7.67 (1H, dd, *J*=7.2, 1.0 Hz), 7.75 (1H, s), 8.07 (1H, d, *J*=13.2 Hz), 9.65 (1H, d, *J*=13.2 Hz). MS *m/z*: 314 (M^+). *Anal.* Calcd for $C_{10}H_7N_2O_2I$: C, 38.24; H, 2.25; N, 8.92. Found: C, 38.34; H, 2.20; N, 8.69.

4-Iodo-3-(2-nitroethyl)indole (24) from 23 — $NaBH_4$ (45.8 mg, 1.28 mmol) was added to a suspension of **23** (95.2 mg, 0.30 mmol) and SiO_2 (1213.8 mg) in $CHCl_3$ (10 mL) and *i*-PrOH (2 mL), and the mixture was stirred at rt for 1 h. The resulting solution was made acidic by adding 1% HCl and extracted with CH_2Cl_2–MeOH (95:5, v/v). The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was subjected to p-TLC on SiO_2 with CH_2Cl_2–MeOH (95:5, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.69—0.85 with CH_2Cl_2–MeOH (95:5, v/v) gave **24** (80.5 mg, 84%). **24**: mp 97—98°C (yellow prisms, recrystallized from MeOH–H_2O). IR (KBr): 3320, 1604, 1539 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.63 (2H, t, *J*=6.8 Hz), 4.67 (2H, t, *J*=6.8 Hz), 6.74 (1H, dd, *J*=8.0, 7.2 Hz), 6.96 (1H, d, *J*=2.5 Hz), 7.21 (1H, dd, *J*=8.0, 1.2 Hz), 7.47 (1H, dd, *J*=7.2, 1.2 Hz), 8.04 (1H, br s). MS *m/z*: 316 (M^+). *Anal.* Calcd for $C_{10}H_9N_2O_2I$: C, 38.00; H, 2.87; N, 8.86. Found: C, 37.75; H, 2.64; N, 8.90.

(*E*)-4,5-*trans*-5-(2-Formyl-1-propen-1-yl)- (26a) and (*E*)-4,5-*trans*-5-(2-Hydroxymethyl-1-propen-1-yl)-4-nitro-1,3,4,5-tetrahydrobenz[*cd*]indole (25a) from 19 — SeO_2 (143.8 mg, 1.30 mmol) was added to a solution of **19** (57.2 mg, 0.22 mmol) in 1,4-dioxane (8 mL) and H_2O (2 mL), and the mixture was refluxed for 12 h with stirring. After evaporation of the solvent, brine was added and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was subjected to p-TLC on SiO_2 with CH_2Cl_2–MeOH (98:2, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.64—0.72 with CH_2Cl_2–MeOH (95:5, v/v) gave **19** (18.3 mg, 32%). Extraction of the band having an *Rf* value of 0.53—0.64 with CH_2Cl_2–MeOH (95:5, v/v) gave **26a** (11.5 mg, 19%). **26a**: mp 186—188°C (decomp., colorless prisms, recrystallized from MeOH). IR (KBr): 3400, 1677, 1542, 1341 cm^{-1}. ^{1}H-NMR (10% CD_3OD in $CDCl_3$) δ: 1.95 (3H, d, *J*=1.5 Hz), 3.47—3.75 (2H, m), 4.75—5.10 (2H, m), 6.48 (1H, br d, *J*=8.3 Hz), 6.65 (1H, d, *J*=6.8 Hz), 7.03 (1H, br s), 7.14 (1H, dd, *J*=8.3, 6.8 Hz), 7.30 (1H, d, *J*=8.3 Hz), 9.51 (1H, s). MS *m/z*: 270 (M^+). *Anal.* Calcd for $C_{15}H_{14}N_2O_3$: C, 66.65; H, 5.22; N, 10.37. Found: C, 66.76; H, 5.20; N, 10.54. Extraction of the band having an *Rf* value of 0.16—0.23 with CH_2Cl_2–MeOH (95:5, v/v) gave **25a** (21.6 mg, 36%). **25a**: mp 156—156.5°C (colorless prisms, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3520, 3250, 1540, 1345 cm^{-1}. ^{1}H-NMR (10% CD_3OD in $CDCl_3$) δ: 1.81 (3H, d, *J*=1.5 Hz), 3.53 (2H, d, *J*=7.4 Hz), 4.09 (2H, s), 4.60 (1H, dd, *J*=9.7, 9.5 Hz), 4.81 (1H, dt, *J*=9.7, 7.4 Hz), 5.48 (1H, dq, *J*=9.5, 1.5 Hz), 6.76 (1H, d, *J*=6.8 Hz), 6.96 (1H, br s), 7.00—7.34 (2H, m), 9.16 (1H, br s). MS *m/z*: 272 (M^+). *Anal.* Calcd for $C_{15}H_{16}N_2O_3$: C, 66.16; H, 5.92; N, 10.29. Found: C, 65.97; H, 5.86; N, 10.04.

Oxidation of 25a with PCC to 26a — A solution of **25a** (55.8 mg, 0.21 mmol) in CH_2Cl_2 (10 mL) was added to a solution of PCC (67.9 mg, 0.32 mmol) in CH_2Cl_2 (5 mL) and the mixture was stirred at rt for 1.5 h. *i*-PrOH (0.1 mL) was added and the resulting solution was stirred at rt for 0.5 h. After addition of CH_2Cl_2–MeOH (95:5, v/v), insoluble precipitates were filtered off through SiO_2. The filtrate was evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with CH_2Cl_2 to give **26a** (30.5 mg, 55%).

Reduction of 26a with $NaBH_4$ to 25a — $NaBH_4$ (4.3 mg, 0.11 mmol) was added to a solution of **26a** (24.1 mg, 0.09 mmol) in MeOH (10 mL) and the mixture was stirred at rt for 0.5 h. The resulting solution was made acidic by adding 3% HCl and the whole was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was subjected to p-TLC on SiO_2 with CH_2Cl_2–MeOH (98:2, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.20—0.32 with CH_2Cl_2–MeOH (95:5, v/v) gave **25a** (22.6 mg, 93%).

(±)-Norchanoclavine-I (27a) from 25a — A solution of **25a** (50.8 mg, 0.19 mmol) in MeOH (12 mL) and 6% HCl (4 mL) was added to Zn(Hg), prepared from Zn powder (353.0 mg, 5.40 mmol) and $HgCl_2$

(54.2 mg, 0.20 mmol) in 6% HCl (4 mL), and the mixture was refluxed for 2 h with stirring. Unreacted Zn(Hg) was filtered off and the filtrate was evaporated under reduced pressure. The residue was made basic by adding 8% NaOH and the whole was extracted with CH_2Cl_2. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave a solid, which was recrystallized from MeOH–CH_2Cl_2 to give **27a** (44.5 mg, 98%) as colorless prisms. **27a**: mp 184—185°C. IR (KBr): 3230, 3050—3150 cm^{-1}. ^{1}H-NMR (pyridine-d_5) δ: 2.03 (3H, d, *J*=1.2 Hz), 2.95 (1H, dd, *J*=15.4, 10.3 Hz), 3.18—3.50 (2H, m), 4.00 (1H, dd, *J*=9.8, 6.5 Hz), 4.45 (2H, s), 5.85 (1H, br d, *J*=9.8 Hz), 6.98 (1H, d, *J*=6.6 Hz), 7.06—7.48 (3H, m), 11.50 (1H, br s). MS *m/z*: 242 (M^+). *Anal.* Calcd for $C_{15}H_{18}N_2O\cdot 1/8H_2O$: C, 73.66; H, 7.52; N, 11.46. Found: C, 73.67; H, 7.51; N, 11.42.

(*E*)-4,5-*trans*-5-(2-Hydroxymethyl-1-propen-1-yl)-4-methoxycarbonylamino-1,3,4,5-tetrahydrobenz[*cd*]indole (28a) from 27a — $ClCO_2Me$ (0.07 mL, 0.88 mmol) was added to a solution of **27a** (51.0 mg, 0.21 mmol) and Et_3N (0.15 mL, 1.08 mmol) in THF (3 mL), and the mixture was stirred at rt for 1 h. Brine was added and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was subjected to p-TLC on SiO_2 with $CHCl_3$–MeOH–28% NH_4OH (46:5:0.5, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.35—0.53 with CH_2Cl_2–MeOH (95:5, v/v) gave **28a** (58.4 mg, 92%) as a colorless oil. **28a**: IR (KBr): 3380, 1690 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.63 (1H, s), 1.92 (3H, d, *J*=1.4 Hz), 2.84 (1H, dd, *J*=15.7, 5.4Hz), 3.25 (1H, ddd, *J*=15.7, 3.9, 1.2 Hz), 3.62 (3H, s), 3.85—4.37 (2H, m), 4.03 (2H, s), 4.75 (1H, br d, *J*=8.0 Hz), 5.38 (1H, dq, *J*=9.2, 1.4 Hz), 6.80 (1H, dd, *J*=5.9, 2.0 Hz), 6.90 (1H, s), 7.02—7.28 (2H, m), 8.02 (1H, br s). High-resolution MS *m/z*: Calcd for $C_{17}H_{20}N_2O_3$: 300.1472. Found: 300.1464.

(±)-Chanoclavine-I (2) from 28a — $LiAlH_4$ (542.8 mg, 14.3 mmol) was added to a solution of **28a** (353.2 mg, 1.18 mmol) in anhydrous THF (15 mL) and the mixture was refluxed for 1 h with stirring. To the resulting solution, MeOH was added at 0°C to decompose excess $LiAlH_4$. After addition of 20% potassium sodium tartrate, the whole was extracted with CH_2Cl_2. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave a solid, which was recrystallized from MeOH–H_2O to give **2** (288.2 mg, 96%) as colorless prisms. **2**: mp 194—195°C (lit.,[20] mp 185—186°C). IR (KBr): 3230, 1600, 1435, 1034, 743 cm^{-1}. ^{1}H-NMR (pyridine-d_5) δ: 2.02 (3H, d, *J*=1.5 Hz), 2.40 (3H, s), 2.70—3.15 (2H, m), 3.41 (1H, dd, *J*=18.8, 8.3 Hz), 4.03—4.29 (1H, m), 4.41 (2H, s), 5.85 (1H, dq, *J*=10.0, 1.5 Hz), 6.42 (1H, br s, disappeared on addition of D_2O), 6.97 (1H, d, *J*=6.6 Hz), 7.06—7.47 (3H, m), 11.49 (1H, br s). MS *m/z*: 256 (M^+). *Anal.* Calcd for $C_{16}H_{20}N_2O$: C, 74.96; H, 7.86; N, 10.93. Found: C, 74.91; H, 7.99; N, 10.96.

(*E*)-4,5-*cis*-5-(2-Methyl-1-propen-1-yl)-4-nitro-1,3,4,5-tetrahydrobenz[*cd*]indole (29) from 19 — NaOMe (3757.9 mg, 69.6 mmol) was added to a solution of **19** (3015.8 mg, 11.8 mmol) in anhydrous

MeOH (300 mL) and the mixture was refluxed for 5 h with stirring. After evaporation of the solvent, the residue was made acidic (pH 4) by adding 10% AcOH and the whole was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was column-chromatographed on SiO_2 with CH_2Cl_2–hexane (1:1, v/v) and recrystallized from MeOH to give **29** (2035.1 mg) as colorless prisms. The mother liquor was a mixture of **19** and **29** in the ratio of 1:2.3 by ^{1}H-NMR analysis. Therefore, the yields of **19** and **29** were 8 and 85%, respectively. **29**: mp 147—148°C. IR (KBr): 3380, 1526, 1378 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.67 (3H, d, *J*=1.2 Hz), 1.83 (3H, d, *J*=1.2 Hz), 3.33 (1H, dd, *J*=15.4, 5.3 Hz), 3.59 (1H, ddd, *J*=15.4, 10.0, 1.5 Hz), 4.73 (1H, dd, *J*=10.3, 4.4 Hz), 4.96 (1H, ddd, *J*=10.0, 5.3, 4.4 Hz), 5.13 (1H, br d, *J*=10.3 Hz), 6.75—6.98 (1H, m), 6.92 (1H, br s), 7.00—7.25 (2H, m), 7.98 (1H, br s). MS *m/z*: 256 (M^+). *Anal.* Calcd for $C_{15}H_{16}N_2O_2 \cdot 1/6H_2O$: C, 69.48; H, 6.35; N, 10.93. Found: C, 69.38; H, 6.14; N, 10.89.

(*E*)-4,5-*cis*-5-(2-Formyl-1-propen-1-yl)- (26b) and (*E*)-4,5-*cis*-5-(2-Hydroxymethyl-1-propen-1-yl)-4-nitro-1,3,4,5-tetrahydrobenz[*cd*]indole (25b) from 29 — SeO_2 (89.4 mg, 0.81 mmol) was added to a solution of **29** (57.2 mg, 0.22 mmol) in 1,4-dioxane–H_2O (4:1, v/v, 8 mL) and the mixture was refluxed for 4 h with stirring. After evaporation of the solvent, brine was added and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was subjected to p-TLC on SiO_2 with CH_2Cl_2 as a developing solvent. Extraction of the band having an *Rf* value of 0.76—0.86 with CH_2Cl_2–MeOH (95:5, v/v) gave **29** (30.3 mg, 62%). Extraction of the band having an *Rf* value of 0.36—0.46 with CH_2Cl_2–MeOH (95:5, v/v) gave **26b** (2.0 mg, 4%) as a colorless oil. **26b**: IR (KBr): 3400, 1676, 1636, 1544, 1362 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.96 (3H, d, *J*=1.5 Hz), 3.32—3.84 (2H, m), 4.89—5.21 (2H, m), 6.41 (1H, br d, *J*=10.2 Hz), 6.83 (1H, dd, *J*=6.2, 1.5 Hz), 7.01 (1H, br s), 7.12 (1H, dd, *J*=8.2, 6.2 Hz), 7.25 (1H, dd, *J*=8.2, 1.5 Hz), 8.15 (1H, br s), 9.51 (1H, s). High-resolution MS *m/z*: Calcd for $C_{15}H_{14}N_2O_3$: 270.1003. Found: 270.1008. Extraction of the band having an *Rf* value of 0.11—0.20 with CH_2Cl_2–MeOH (95:5, v/v) gave **25b** (16.0 mg, 31%). **25b**: mp 134—135°C (colorless prisms, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3490, 3240, 1532, 1366 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.56 (1H, s), 1.86 (3H, d, *J*=1.5 Hz), 3.36 (2H, dd, *J*=15.5, 5.5 Hz), 3.61 (1H, ddd, J=15.5, 10.0, 1.5 Hz), 3.92 (2H, s), 4.81 (1H, dd, *J*=10.4, 4.4 Hz), 5.01 (1H, ddd, *J*=10.0, 5.5, 4.4 Hz), 5.43 (1H, br d, *J*=10.4 Hz), 6.83 (1H, dd, *J*=5.8, 2.4 Hz), 6.94 (1H, br s), 7.00—7.27 (2H, m), 8.03 (1H, br s). MS *m/z*: 272 (M^+). *Anal.* Calcd for $C_{15}H_{16}N_2O_3$: C, 66.16; H, 5.92; N, 10.29. Found: C, 66.05; H, 5.91; N, 10.08.

(±)-Norchanoclavine-II (27b) from 25b — A solution of **25b** (52.3 mg, 0.19 mmol) in MeOH (12 mL) and 6% HCl (4 mL) was added to Zn(Hg), prepared from Zn powder (358.6 mg, 5.49 mmol) and $HgCl_2$ (53.4 mg, 0.20 mmol) in 6% HCl (4 mL), and the mixture was refluxed for 1.5 h with stirring. Unreacted Zn(Hg) was filtered off and the filtrate was evaporated under reduced pressure. The residue was made

basic by adding 8% NaOH and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave a solid, which was recrystallized from AcOEt to give **27b** (39.4 mg) as colorless prisms. The mother liquor was subjected to p-TLC on SiO_2 with $CHCl_3$–MeOH–28% NH_4OH (46:5:0.5, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.24—0.32 with $CHCl_3$–MeOH–28% NH_4OH (46:5:0.5, v/v) gave additional **27b** (4.6 mg). The total yield of **27b** was 44.0 mg (95%). **27b**: mp 208—210°C (decomp.). IR (KBr): 3360, 3150 cm^{-1}. ^{1}H-NMR (pyridine-d_5) δ: 2.06 (3H, d, *J*=1.0 Hz), 2.98 (1H, dd, *J*=15.3, 7.3 Hz), 3.19 (1H, dd, *J*=15.3, 3.9 Hz), 3.50—3.77 (1H, m), 4.28 (1H, dd, *J*=9.8, 3.9 Hz), 4.34 (2H, s), 6.05 (1H, br d, *J*=9.8 Hz), 7.01 (1H, d, *J*=6.8 Hz), 7.09—7.46 (3H, m), 11.55 (1H, br s). MS *m/z*: 242 (M^+). *Anal*. Calcd for $C_{15}H_{18}N_2O \cdot 1/8H_2O$: C, 73.66; H, 7.52; N, 11.46. Found: C, 73.88; H, 7.49; N, 11.33.

(*E*)-4,5-*cis*-5-(2-Hydroxymethyl-1-propen-1-yl)-4-methoxycarbonylamino-1,3,4,5-tetrahydrobenz[*cd*]indole (28b) from 27b — A solution of $ClCO_2Me$ (16.9 mg, 0.18 mmol) in THF (0.5 mL) was added to a solution of **27b** (10.1 mg, 0.04 mmol) and Et_3N (0.03 mL, 0.22 mmol) in THF (1 mL), and the mixture was stirred at rt for 0.5 h. H_2O was added and the whole was extracted with CH_2Cl_2. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was subjected to p-TLC on SiO_2 with CH_2Cl_2–MeOH (95:5, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.47—0.55 with CH_2Cl_2–MeOH (95:5, v/v) gave **28b** (12.3 mg, 98%) as a colorless oil. **28b**: IR (KBr): 3350, 1695 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.86 (3H, d, *J*=1.2 Hz), 2.91 (1H, dd, *J*=15.5, 6.3 Hz), 3.14 (1H, dd, *J*=15.5, 4.5 Hz), 3.60 (3H, s), 4.07 (2H, s), 4.14 (1H, dd, *J*=9.8, 3.7 Hz), 4.20—4.57 (1H, m), 4.89 (1H, br d, *J*=9.5 Hz), 5.56 (1H, br d, *J*=9.8 Hz), 6.64—6.96 (2H, m), 6.96—7.31 (2H, m), 8.07 (1H, br s). High-resolution MS *m/z*: Calcd for $C_{17}H_{20}N_2O_3$: 300.1472. Found: 300.1521.

(±)-Chanoclavine-II (3) from 28b — $LiAlH_4$ (379.8 mg, 10.0 mmol) was added to a solution of **28b** (95.2 mg, 0.32 mmol) in anhydrous THF (6 mL) and the mixture was refluxed for 1 h with stirring. To the resulting solution, MeOH was added at 0°C to decompose excess $LiAlH_4$. After addition of 20% potassium sodium tartrate, the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was subjected to p-TLC on SiO_2 with $CHCl_3$–MeOH–28% NH_4OH (46:5:0.5, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.18—0.32 with $CHCl_3$–MeOH–28% NH_4OH (46:5:0.5, v/v) gave **3** (69.5 mg, 86%). **3**: mp 153.5—154°C (colorless prisms, recrystallized from acetone). IR (KBr): 3220, 1617, 1604, 1440, 1335, 1068, 746 cm^{-1}. ^{1}H-NMR (pyridine-d_5) δ: 2.12 (3H, d, *J*=1.2 Hz), 2.47 (3H, s), 2.96 (1H, dd, *J*=15.0, 9.5 Hz), 3.06—3.39 (2H, m), 4.29 (2H, s), 4.44 (1H, dd, *J*=10.2, 3.5 Hz), 6.03 (1H, d, *J*=10.2 Hz), 6.26 (1H, br s, disappeared on addition of D_2O), 7.04 (1H, d, *J*=6.5 Hz), 7.11—7.34 (2H, m), 7.40 (1H, dd, *J*=8.0, 1.2 Hz), 11.53 (1H, br s, disappeared on addition of D_2O). MS *m/z*: 256

(M^+). *Anal.* Calcd for $C_{16}H_{20}N_2O$: C, 74.96; H, 7.86; N, 10.93. Found: C, 74.73; H, 7.90; N, 10.80.

(*Z*)-4,5-*cis*-5-(2-Hydroxymethyl-1-propen-1-yl)-4-methylamino-1,3,4,5-tetrahydrobenz[*cd*]indole (30) from 22 — SeO_2 (16.5 mg, 0.15 mmol) was added to a solution of **22** (30.5 mg, 0.13 mmol) and Et_3N (84.3 mg, 0.83 mmol) in 1,4-dioxane (3 mL), and the mixture was heated at 90°C for 4 h with stirring. The resulting solution was made basic by adding 8% NaOH and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was subjected to p-TLC on SiO_2 with $CHCl_3$–MeOH–28% NH_4OH (46:5:0.5, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.33—0.43 with $CHCl_3$–MeOH–28% NH_4OH (46:5:0.5, v/v) gave **22** (14.0 mg, 46%). Extraction of the band having an *Rf* value of 0.24—0.33 with $CHCl_3$–MeOH–28% NH_4OH (46:5:0.5, v/v) gave **30** (11.0 mg, 34%). **30**: mp 179—182°C (decomp., colorless prisms, recrystallized from acetone). IR (KBr): 3190, 1620, 1470, 1438, 1101, 1038, 1011, 745 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.79 (3H, d, *J*=1.2 Hz), 2.39—3.39 (3H, m), 2.55 (3H, s), 2.87 (2H, br s), 3.83 (1H, d, *J*=12.0 Hz), 4.21 (1H, dd, *J*=10.5, 4.2 Hz), 4.55 (1H, dd, *J*=12.0, 1.0 Hz), 5.19 (1H, br d, *J*=10.5 Hz), 6.75 (1H, dd, *J*=5.4, 2.4 Hz), 6.84 (1H, br s), 7.06 (1H, dd, *J*=8.1, 5.4 Hz), 7.15 (1H, dd, *J*=8.1, 2.4 Hz), 7.98 (1H, br s). MS *m/z*: 256 (M^+). *Anal.* Calcd for $C_{16}H_{20}N_2O$: C, 74.96; H, 7.86; N, 10.93. Found: C, 74.95; H, 7.90; N, 10.95.

(±)-Agroclavine-I (4) from 30 — A solution of $POCl_3$ (134.5 mg, 0.88 mmol) in CH_3CN (0.5 mL) was added to a suspension of **30** (7.4 mg, 0.03 mmol) and K_2CO_3 (55.5 mg, 0.40 mmol) in CH_3CN (1 mL) at 0°C, and the mixture was stirred at 0°C for 1 h and at rt for an additional 3 h. After cooling to 0°C, the resulting solution was made basic by adding 8% NaOH and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was subjected to p-TLC on SiO_2 with $CHCl_3$–MeOH–28% NH_4OH (46:5:0.5, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.45—0.55 with $CHCl_3$–MeOH–28% NH_4OH (46:5:0.5, v/v) gave **4** (6.0 mg, 87%). **4**: mp 157—158°C (colorless prisms, recrystallized from acetone). IR (KBr): 3400, 3100, 2860, 1618, 1607, 1444 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.63 (3H, br s), 2.56 (3H, s), 2.78 (1H, ddd, *J*=15.0, 10.0, 1.5 Hz), 2.98 (1H, dd, *J*=15.0, 4.5 Hz), 3.07 (2H, br s), 3.24—3.49 (1H, m,), 3.78—4.08 (1H, m), 5.48 (1H, br s), 6.74—6.98 (1H, m), 6.79 (1H, br s), 6.98—7.18 (2H, m), 7.87 (1H, br s). High-resolution MS *m/z*: Calcd for $C_{16}H_{18}N_2$: 238.1468. Found: 238.1467.

4,5-*cis*-5-(2-Methyl-1-propen-1-yl)-4-amino-1,3,4,5-tetrahydrobenz[*cd*]indole (31) from 29 — A solution of **29** (129.6 mg, 0.51 mmol) in MeOH (30 mL) and 6% HCl (10 mL) was added to Zn (Hg), prepared from Zn powder (997.8 mg, 15.3 mmol) and $HgCl_2$ (154.2 mg, 0.57 mmol) in 6% HCl (10 mL), and the mixture was refluxed for 4 h with stirring. Unreacted Zn (Hg) was filtered off and the filtrate was evaporated under reduced pressure. The residue was made basic by adding 8% NaOH and the whole was

extracted with CH_2Cl_2–MeOH (95:5, v/v). The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave a solid, which was subjected to p-TLC on SiO_2 with $CHCl_3$–MeOH–28% NH_4OH (46:5:0.5, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.33—0.60 with $CHCl_3$–MeOH–28% NH_4OH (46:5:0.5, v/v) gave **31** (112.0 mg, 98%). **31**: mp 113—114°C (colorless prisms, recrystallized from AcOEt–hexane). IR (KBr): 3130, 3080, 3030, 2980, 2920, 2870, 1598, 1572 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.69 (2H, s), 1.81 (3H, d, *J*=1.2 Hz), 1.85 (3H, d, *J*=1.2 Hz), 2.81 (1H, ddd, *J*=15.2, 7.3, 1.0 Hz), 3.05 (1H, ddd, *J*=15.2, 4.4, 1.0 Hz), 3.44 (1H, ddd, *J*=7.3, 4.4, 3.5 Hz), 3.98 (1H, dd, *J*=10.0, 3.5 Hz), 5.27 (1H, br d, *J*=10.0 Hz), 6.70—6.91 (1H, m), 6.83 (1H, br s), 6.97—7.19 (2H, m), 8.03 (1H, br s). MS *m/z*: 226 (M^+). *Anal.* Calcd for $C_{15}H_{18}N_2$: C, 79.60; H, 8.02; N, 12.38. Found: C, 79.37; H, 8.27; N, 12.35.

4,5-*cis*-5-(2-Methyl-1-propen-1-yl)-4-methoxycarbonylamino-1,3,4,5-tetrahydrobenz[*cd*]indole (32) from 31 — A solution of $ClCO_2Me$ (0.065 mL, 0.89 mmol) in CH_2Cl_2 (1 mL) was added to a solution of **31** (104.3 mg, 0.46 mmol) in Et_3N (0.20 mL, 1.43 mmol) and CH_2Cl_2 (4 mL), and the mixture was stirred at rt for 1 h. Saturated $NaHCO_3$ was added and the whole was extracted with CH_2Cl_2. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was subjected to p-TLC on SiO_2 with CH_2Cl_2–MeOH (97:3, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.36—0.66 with CH_2Cl_2–MeOH (95:5, v/v) gave **32** (130.9 mg, 100%). **32**: mp 139—141°C (colorless needles, recrystallized from MeOH–H_2O). IR (KBr): 3320, 1669 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.79 (3H, d, *J*=2.0 Hz), 1.81 (3H, d, *J*=1.5 Hz), 2.87 (1H, dd, *J*=15.5, 7.0 Hz), 3.11 (1H, dd, *J*=15.5, 4.2 Hz), 3.61 (3H, s), 4.05 (1H, dd, *J*=9.8, 3.7 Hz), 4.30 (1H, dddd, *J*=9.5, 7.0, 4.2, 3.7 Hz), 4.75 (1H, br d, *J*=9.5 Hz), 5.21 (1H, br d, *J*=9.8 Hz), 6.68—6.92 (1H, m), 6.85 (1H, br s), 6.96—7.25 (2H, m), 7.93 (1H, br s). MS *m/z*: 284 (M^+). *Anal.* Calcd for $C_{17}H_{20}N_2O_2$: C, 71.80; H, 7.09; N, 9.85. Found: C, 71.90; H, 7.05; N, 9.82.

(±)-5-*epi*-6,7-Secoagroclavine (22) from 32 — $LiAlH_4$ (1962.7 mg, 51.7 mmol) was added to a solution of **32** (927.2 mg, 3.26 mmol) in anhydrous THF (30 mL) at 0°C and the mixture was refluxed for 3 h with stirring. To the resulting solution, MeOH was added at 0°C to decompose excess $LiAlH_4$. After addition of 20% potassium sodium tartrate, the whole was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave a solid, which was recrystallized from MeOH–H_2O to give **22** (706.5 mg) as colorless prisms. The mother liquor was subjected to p-TLC on SiO_2 with $CHCl_3$–MeOH–28% NH_4OH (46:5:0.5, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.03—0.43 with $CHCl_3$–MeOH–28% NH_4OH (46:5:0.5, v/v) gave additional **22** (63.4 mg). The total yield of **22** was 769.9 mg (98%).

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$$\mathrm{OR} = 100 \times \frac{\text{The Number of Newly Developed Steps} + \begin{cases} 1 \text{ (by a New Route)} \\ 0 \text{ (by a Known Route)} \end{cases}}{\text{Total Number of Synthetic Steps} + 1}$$