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SYNTHESIS OF 1-METHOXYINDOLES AND RELATED ANALOGS OF PIMPRININE, (±)-CHELONIN A AND B, BASED ON 1-HYDROXY-INDOLE CHEMISTRY[1]

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Abstract – The total synthesis of pimprinine, (±)-chelonin A and B, and their analogs are achieved based on 1-hydroxyindole chemistry.

INTRODUCTION

In indole chemistry,[3] it is well known that any electronegative atom or group (L in Figure 1, **A**, $R^1 = H$) at the indolylmethyl position readily eliminates, following **a** route, leaving alkylideneindolenine intermediate (**B**), which is stabilized by the nitrogen of the indole nucleus by conjugation. The intermediate (**B**) can be trapped by various nucleophiles to afford product (**C**) or diindolylmethane derivatives. The reactivity has extensively applied for the synthetic use. Therefore indoles, having nitrogen or oxygen functional group at the indolylmethyl position, are generally unstable and not suitable building blocks for the synthesis except for the limited case as gramine.[3]

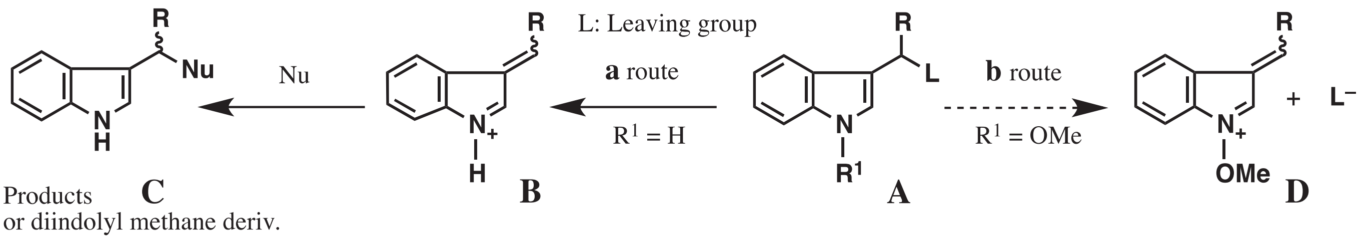


Figure 1

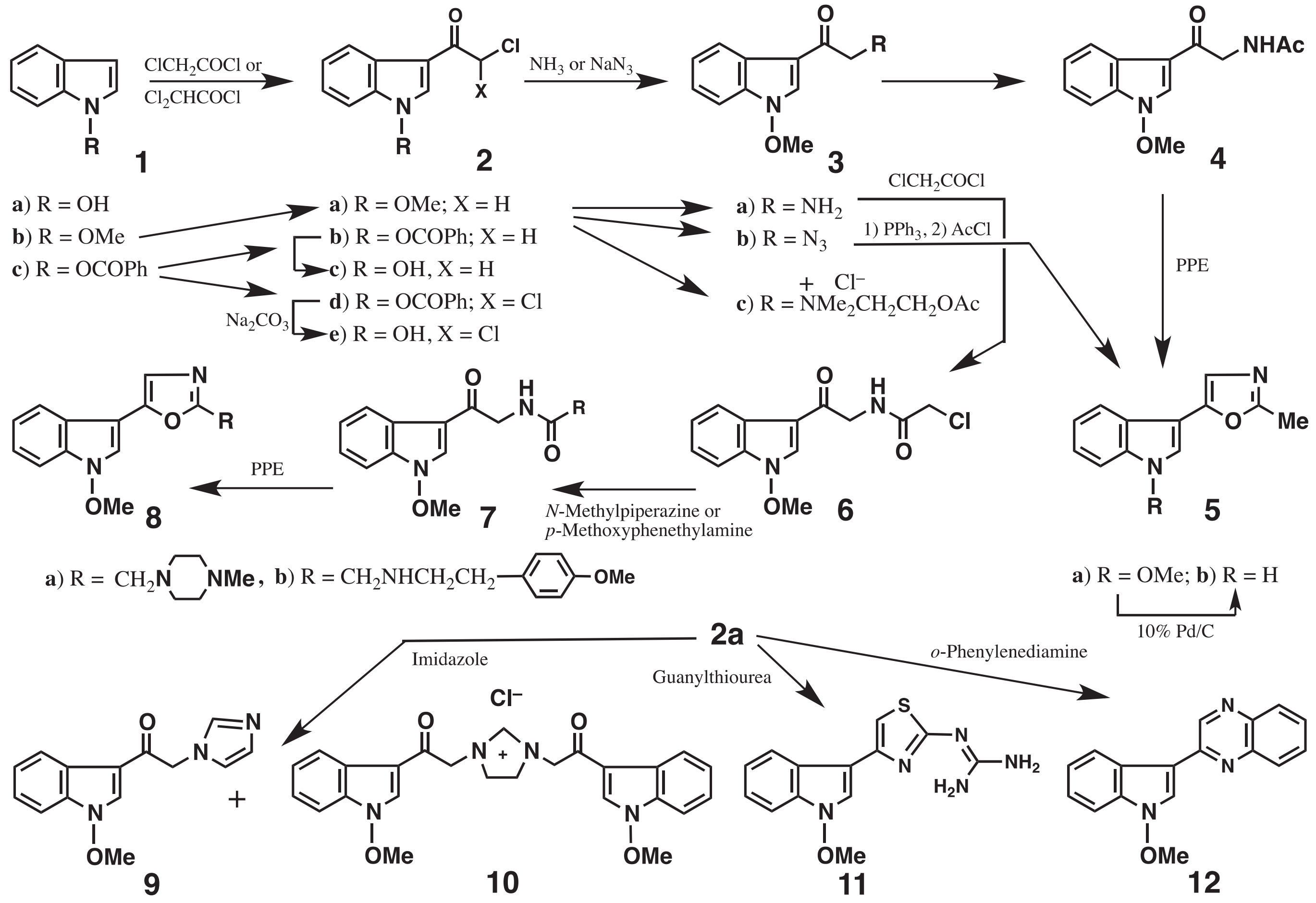
If we could put such electronegative group as OH and/or OMe group to the indole nitrogen, it decreases the nitrogen conjugation ability and destabilize the corresponding alkylideneindolenine intermediate (**D**), causing the **b** route reaction hardly to occur. It means that building blocks (**A**, R^1=OMe or OH) having nitrogen or oxygen functional group at the indolylmethyl position could be used for the synthesis.

As part of our synthetic study for various 1-methoxyindoles[4] and our original biologically active substances,[5] we examined the above expectation and found that it is true in the cases from **21** to **24**, **28**, from **34** to **40**. The results were successfully applied for such natural products synthesis as pimprinine,[6] (±)-chelonin A,[7] and various analogs, which are expected to be physiologically active substances. (±)-Chelonin B[7] was also synthesized by utilizing nucleophilic substitution reaction[8] in 1-hydroxyindole chemistry. This is the full report of the previous communications[9] with many new findings.

RESULTS AND DISCUSSION

I. Syntheses of 1-Methoxypimprinine, Various 1-Methoxyindoles Including Derivatives Having Electronegative Atoms at the Indolylmethyl Position

According to our synthetic method,[4,10] 1-hydroxy- (**1a**), 1-methoxy- (**1b**), and 1-benzoyloxyindoles (**1c**) are readily prepared from 2,3-dihydroindole (Scheme 1). Then, **1b** reacted with chloroacetyl chloride in refluxing benzene to afford 80% yield of 3-chloroacetyl-1-methoxyindole (**2a**). Similar reaction of **1c**

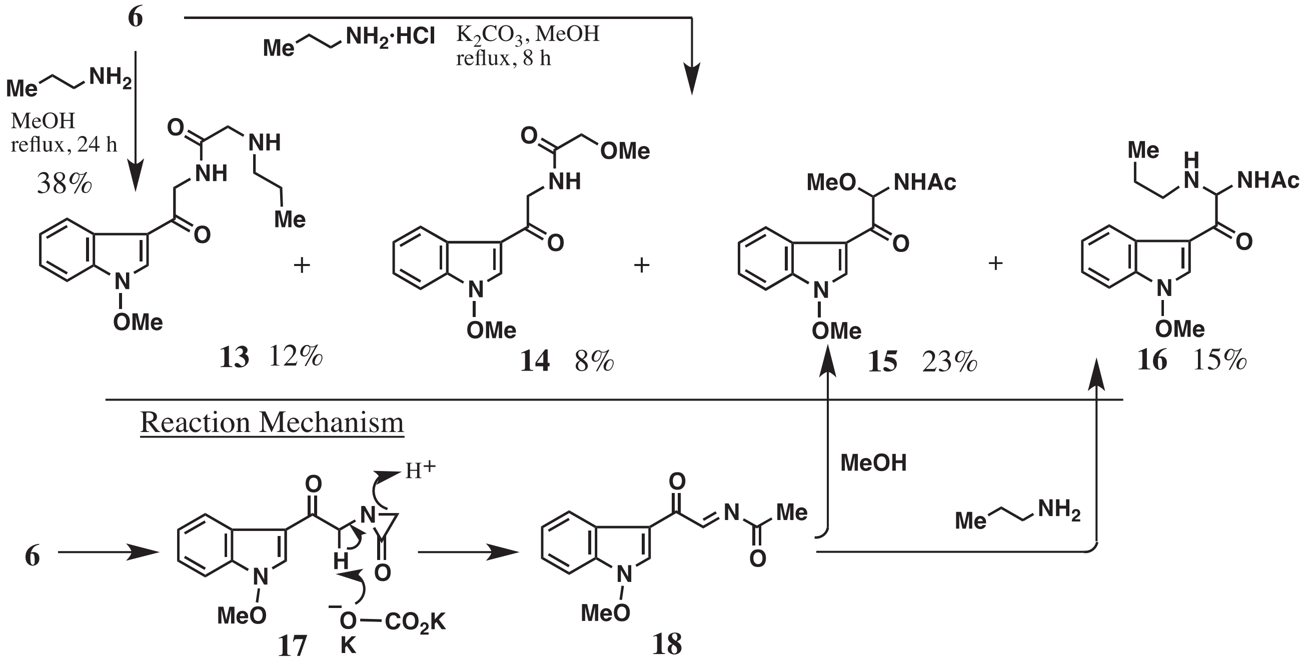


Scheme 1

with chloroacetyl chloride provided 1-benzoyloxy-3-chloroacetylindole (**2b**) in 18% yield. The reaction of **1c** with dichloroacetyl chloride gave 61% yield of 1-benzoyloxy-3-dichloroacetylindole (**2d**). Mild hydrolysis of **2b** and **2d** with Na_2CO_3 produced 1-hydroxy-3-chloroacetyl- (**2c**) and 1-hydroxy-3-dichloroacetylindole (**2e**) in 95% and 92% yields, respectively.

With these building blocks in hand, we next treated **2a** with aqueous ammonia in a sealed tube to yield 3-(2-aminoacetyl)-1-methoxyindole (**3a**) in 41% yield. The reaction of **2a** with NaN_3 in MeCN-H_2O afforded 3-(2-azidoacetyl)-1-methoxyindole (**3b**) in 90% yield. The reaction of **2a** with 2-dimethylaminoethyl acetate in refluxing benzene produced 94% yield of ammonium salt (**3c**), an analog of acetylcholine chloride.

Since the compound **3a** was found to be unstable and polymerize on standing, it was converted to a stable 3-(*N*-acetyl-2-aminoacetyl)-1-methoxyindole (**4**) in 44% overall yield by one-pot sequential procedure: 1) preparation of **3a**, 2) followed by the reaction with acetyl chloride in CH_2Cl_2 and Et_3N. Subsequent treatment of **4** with polyphosphate ester in refluxing $CHCl_3$ gave 78% yield of 1-methoxypimprinine (**5a**). The structure of **5a** was confirmed unequivocally by the fact that hydrogenolysis of **5a** over 10% Pd/C gave 99% yield of antibiotic pimprinine[6] (**5b**) which was identical with the sample prepared from 3-chloroacetylindole according to the same reaction sequences as described for **5a**. Directly from **3b**, **5a** was obtained in 31% yield by the treatment with PPh_3, followed by acetylation.

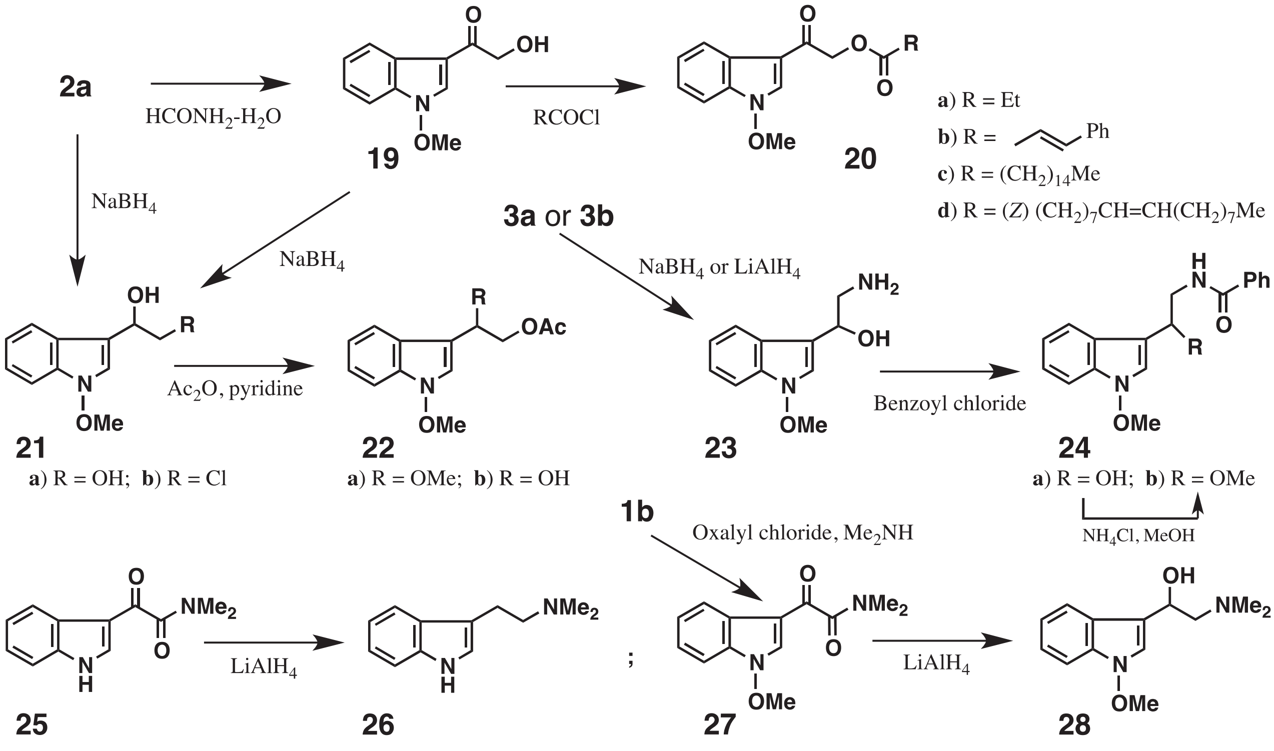


Scheme 2

Aiming at promising candidates for biologically active substances, we noticed that there are structural features among indole alkaloids in which two heterocycles are bonded through a single bond.[9] So, we next tried to prepare structurally similar compounds like pimprinine[6] (**5b**). First **3a** was led to 3-[2-(2-chloroacetylamino)acetyl]-1-methoxyindole (**6**) in 59% yield by the reaction with chloroacetyl chloride. Alternatively, **6** was obtained from **3b** in 17% yield by the treatment with PPh_3 and acetyl chloride. Subsequent reaction of **6** with *N*-methylpiperazine and 4-methoxyphenethylamine in the presence of base produced **7a** and **7b** in 98% and 54% yields, respectively.

Cyclization of **7a** and **7b** were successfully carried out by treatment with polyphosphate ester to afford oxazole derivatives 5-[(1-methoxyindol)-3-yl]-2-[(*N*-methylpiperazinyl)methyl]oxazole (**8a**) and 5-[(1-methoxyindol)-3-yl]-2-[(4-methoxyphenethylamino)methyl]oxazole (**8b**) in the respective yields of 75% and 59%. The reaction of **2a** with imidazole produced **9** and 1,3-bis[(1-methoxyindol-3-yl)carbonylmethyl]imidazolium chloride (**10**) in 84% and 10% yields, respectively. Furthermore, the reaction of **2a** with guanylthiourea afforded **11** in 70% yield. When *o*-phenylenediamine was reacted with **2a**, **12a** and demethoxy compound (**12b**) were produced in 48% and 35% yields, respectively. Thus, various pimprinine analogs were prepared.

When propylamine reacted with **6**, only normal product (**13**) was isolated in 38% yield (Scheme 2). Interestingly, propylamine hydrochloride was employed in the presence of K_2CO_3, unexpected products such as **15** and **16** were obtained in the respective yields of 23% and 15% in addition to the expected products, **13** and **14**, in 12% and 8% yields, respectively. Mechanism of the formation of **15** and **16** could



Scheme 3

be explained by the formation of the aziridinone intermediate (**17**) from **6**. Deprotonation and opening of the three membered ring generate imine compound (**18**). Subsequent addition of solvent MeOH or propylamine to the imine carbon produces **15** and **16**, respectively.

Chlorine atom of **2a** was readily substituted for hydroxy group by heating **2a** in a sealed tube with $HCONH_2$-H_2O at 110-115 °C to give **19** in 82% yield (Scheme 3). The reaction of **19** with propionyl chloride in pyridine produced 3-(2-propionyloxyacetyl)-1-methoxyindole (**20a**) in 96% yield.

Similar ester compounds such as 3-[2-(*E*)-cinnamoyloxyacetyl)- (**20b**), 3-(2-palmitoyloxyacetyl)- (**20c**), and 3-[2-(*Z*)-oleoyloxyacetyl]-1-methoxyindole (**20d**) were obtained from **19** in the respective yields of 89, 75, and 73%, by the reaction with the respective acid chlorides prepared from each (*E*)-cinnamic acid, palmitic acid, and (*Z*)-oleic acid.

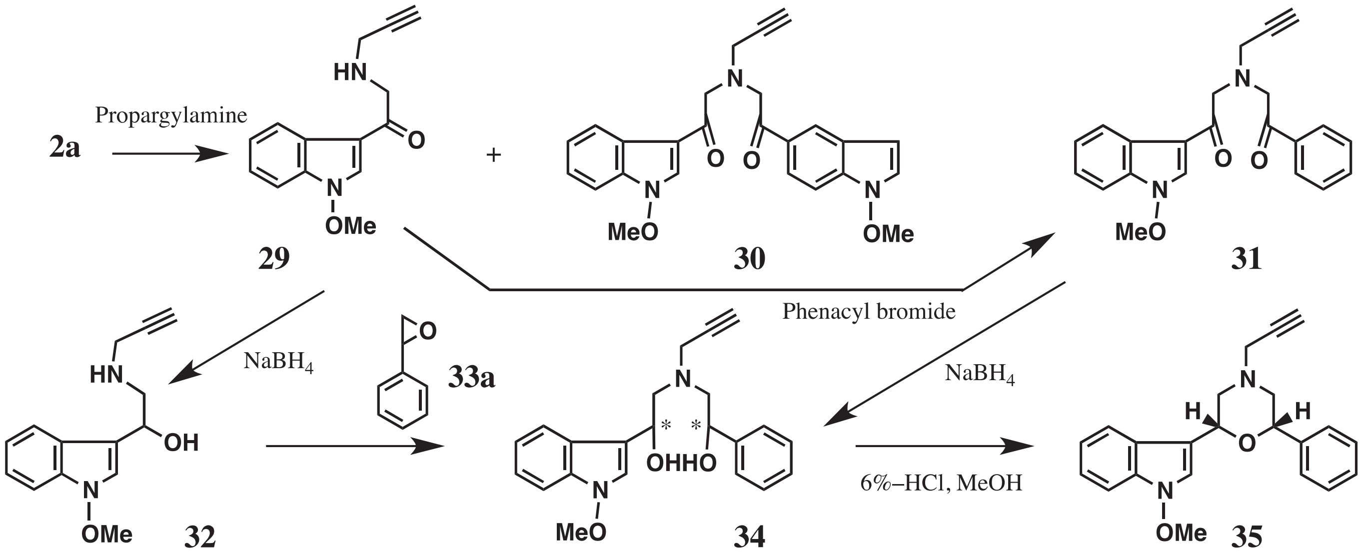
Reduction of **19** and **2a** with $NaBH_4$ in MeOH afforded 3-(1,2-dihydroxy)ethyl- (**21a**) and 3-(2-chloro-1-hydroxy)ethyl-1-methoxyindole (**21b**) as stable crystals in 93% and 92% yields, respectively. Subsequent acetylation of **21a** with Ac_2O-pyridine produced 3-(2-acetoxy-1-methoxyethyl)- (**22a**) and 3-(2-acetoxy-1-hydroxyethyl)-1-methoxyindole (**22b**) in 37 and 19% yields, respectively. As for the generation of **22a**, the hydroxy group originally at the indolylmethyl position is substituted by the methoxy group coming from the work-up solvent MeOH. Reduction of **3a** with $NaBH_4$ in MeOH and reduction of **3b** with $LiAlH_4$ in THF afforded the same product, 3-(2-amino-1-hydroxyethyl)-1-methoxyindole (**23**) in 72 and 48% yields, respectively. Further treatment of **23** with benzoyl chloride provided 65% yield of 3-(2-benzoylamino-1-hydroxyethyl-1-methoxyindole (**24a**). Treatment of **24a** with NH_4Cl in MeOH caused substitution of the hydroxy group at the indolylmethyl position for solvent to generate **24b** in 48% yield.

Interesting to note is the obvious difference in reduction reactivity of 3-(*N*,*N*-dimethyl)oxalylindole (**25**) and 3-(*N*,*N*-dimethyl)oxalyl-1-methoxyindole (**27**). Reduction of **25** with $LiAlH_4$ is well documented to give quantitative yield of *N*,*N*-dimethylaminoethylindole (**26**). On the other hand, the similar reduction of **27**, prepared from **1b**, produced 1-methoxy-3-(2-*N*,*N*-dimethyl-1-hydroxy)ethylindole (**28**) in 70% yield.

As stable compounds, isolations of products from **21** to **24**, and **28** clearly demonstrated that the expectation shown in Figure 1 is true and these compounds could be used as building blocks. Next, we applied these findings for the synthesis of (±)-chelonin A and related compounds.

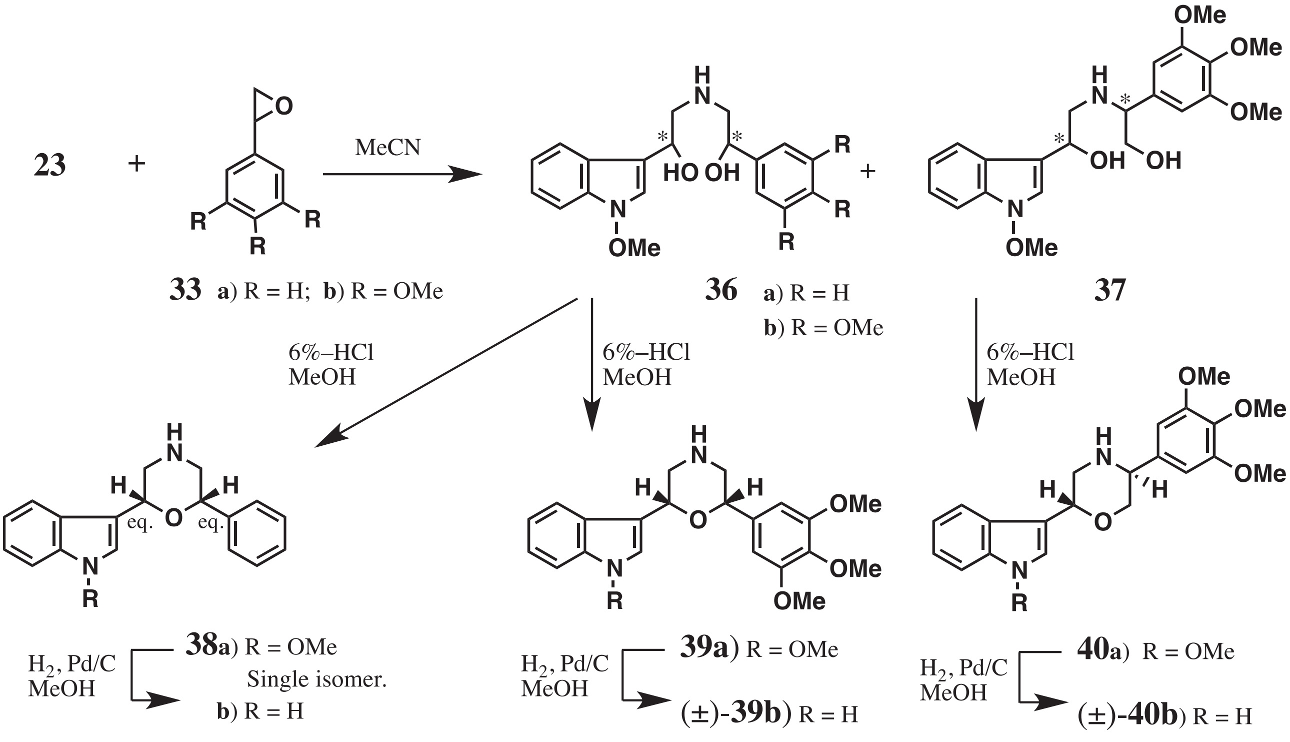
II. Synthesis of (±)-Chelonin A and Related Analogs

Chelonin A (**39b**, Scheme 5) was isolated from marine sponge *Chelonaplysilla* sp. and determined by Faulkner and co-workers.[7] They also reported its potent antimicrobial and anti-inflammatory activities.[7] So we believed that various chelonin analogs are promising candidates for obtaining new biologically active substances.



Scheme 4

First, we tried the synthesis of model compounds, 2,6-*cis*-2-(1-methoxyindol-3-yl)-6-phenyl-*N*-propargylmorpholine (**35**, Scheme 4). The compound **2a** reacted with propargylamine in refluxing MeOH to afford 1-methoxy-3-(2-propargylamino)acetylindole (**29**) and dimeric compound (**30**) in 60 and 14% yields, respectively.



Scheme 5

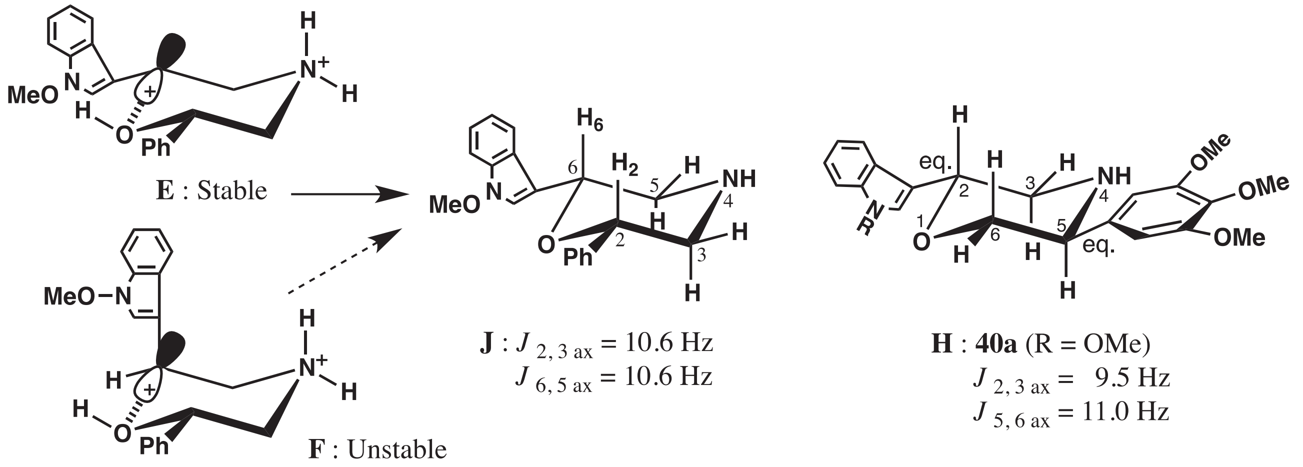
Reaction of **29** with phenacyl bromide in refluxing MeCN gave 1-methoxy-3-(2-*N*-phenacyl-propargylamino)acetylindole (**31**) in 35% yield. Reduction of **29** with $NaBH_4$ in MeOH provided **32** in

73% yield. Subsequent reaction of **32** with styrene oxide (**33a**) in refluxing MeCN afforded **34** in 58% yield as a 1:1 mixture of diastereomers. Alternatively, **34** was also obtained in 75% yield by the reduction of **31** with $NaBH_4$. Finally, the treatment of **34** with 6% aqueous HCl in MeOH formed morpholine ring and produced (±)-**35** in 70% yield.

We next tried the reaction of **23** with **33a** in refluxing MeCN to afford **36a** as a single product in 57% yield, then the treatment of **36a** with 6% aqueous HCl in MeOH produced **38a** in 74% yield (Scheme 5). Stereochemistry of (±)-**38a** was established by its ^{1}H -NMR spectrum which showed the presence of two sets of H_{axial}-H_{axial} coupling (J = 10.6 Hz). These facts clearly prove that phenyl and 1-methoxyindole-3-yl substituent are *cis* and equatorial. Catalytic hydrogenation of **38a** over 10% Pd/C at rt and 1 atm for 4 h produced (±)-**38b** in 51% yield.

Cyclisation mechanism of **36a** is shown in Scheme 6. Possible conformations of the intermediate of **36a** are **E** and **F**. In the case of **F**, indol-3-yl substituent is axial and phenyl group is equatorial, while **E** conformation has both substituents in the equatorial position. Therefore, **E** is more stable than **F** and cyclisation take place through **E** transition state to result in the formation of product **J** (**38b**).

Based on the successful production of model compounds, **35** and **38a**, synthesis of (±)-chelonin A was examined. Thus **23** reacted with 3,4,5-trimethoxystylene oxide (**33b**). In this case opening of epoxide ring occurred in two directions, producing regio-isomers **36b** and **37** in 19% and 21% yields, respectively.



Scheme 6

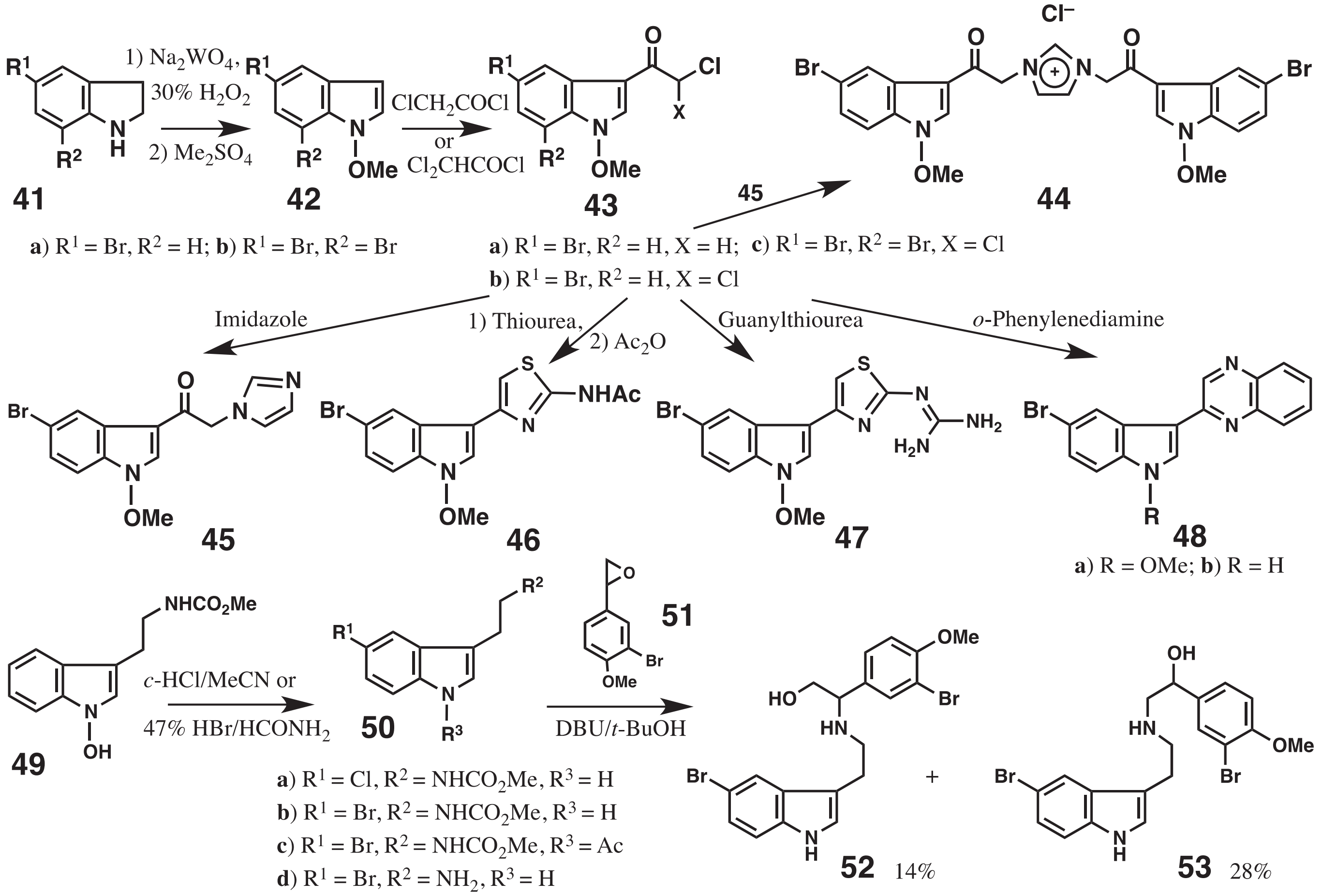
According to the similar cyclisation mechanism, treatments of **36b** and **37** with 6% HCl in MeOH at rt for 30 min smoothly produced the desired **39a** and **40a** in 89 and 81% yields, respectively. The ^{1}H -NMR spectrum of **39a** clearly proves that 3,4,5-trimethoxyphenyl and 1-methoxyindole-3-yl substituent are *cis* and equatorial. Catalytic hydrogenation of **39a** over 10% Pd/C at rt and 1 atm for 4 h produced (±)-**39b** in 60% yield, while the same hydrogenolysis of **40a** afforded (±)-**40b** in 57% yield. 3,4,5-Trimethoxyphenyl and indol-3-yl substituents of (±)-**40a** are proved to be *trans* and equatorial, based on its ^{1}H-NMR spectrum showing two sets of H_{axial}-H_{axial} coupling (J = 9.5 and 11.0 Hz) in the conformation **H** (Scheme 6).

Spectral data of natural product[7] (**39b**) are identical with those of (±)-**39b** and not with those of (±)-**40b**. Thus, the structure of chelonin A was alternatively proved by chemical synthesis.

III. Synthesis of Bromoindoles and (±)-Chelonin B

Many biologically active indole marine alkaloids have structural features in which indole nucleus having halogen substituent is involved. Therefore, we next examined halogen containing 1-methoxyindole building blocks.

First our synthetic method[4,10] for 1-methoxyindoles (**41a**) was applied to 5-bromo- (**41a**) and 5,7-dibromo-2,3-dihydroindoles (**41b**), resulting in the formations of the corresponding bromine containing 1-methoxyindoles, **42a** and **42b,** in 60% and 17% yields, respectively (Scheme 7).



Scheme 7

Subsequent reactions of **42a** with chloroacetyl chloride afforded **43a** in 48% yield. Further reactions of **42a** and **42b** with dichloroacetyl chloride afforded **43b** and **43c** in 90% and 35% yields, respectively. In the series of 5,7-dibromoindole compounds, the yields are poorer compared to the corresponding 5-bromoindoles, because due to the presence of sterically large 7-bromo substituent next to the 1-methoxy group, it was lost during reactions and work-up procedures. The reaction of **43a** with imidazole produced dimeric compound **44** and **45** in 54% and 89% yields, respectively, depending on the reaction conditions. Furthermore, the reaction of **43a** with thiourea, followed by the treatment with Ac_2O provided **46** in 77% yield. Guanylthiourea reacted with **43a** to afford **47** in 90% yield. When phenylenediamine was reacted with **43a**, **48a** and demethoxy compound (**48b**) were produced in 34% and 52% yields, respectively. Thus, various pimprinine analogs containing bromoindole nucleus were successfully prepared.

Finally, chelonin B[7] (**52**) was prepared by applying nucleophilic substitution reaction[8,9] of 1-hydroxyindole chemistry. The reaction with chloride and bromide with 1-hydroxy-*N*b-methoxycarbonyltryptamine (**49**) produced 5-chloro- (**50a**) and 5-bromo-*N*b-methoxycarbonyltryptamines (**50b**) in the respective yields of 61% and 39%, together with small amount of regio-isomers, 7-chloro- and 7-bromo-*N*b-methoxycarbonyltryptamines, respectively.

Structural proof of **50b** was established as follows. Introduction of acetyl group onto the indole nitrogen of **50b** by the reaction with NaH/AcCl produced **50c** in 65% yield. Comparisons of ^{1}H-NMR spectra of **50b** and **50c** showed the C(7)-proton of **50b** at δ 7.31 (1H, d, J = 8.6 Hz) shifted to the down field to δ 8.25 (1H, d, J = 8.8 Hz). The coupling constant and the anisotropy effect by the introduced acetyl group clearly demonstrated that **50b** is a 5-substituted indole.

Hydrolysis of **50b** with 10% NaOH afforded 5-bromotryptamine (**50d**) in 88% yield. Subsequent reaction of **50d** with 2-bromo-3-methoxystyrene oxide (**51**) in the presence of DBU in *t*-BuOH produced (±)-Chelonin B (**52**) and its regio-isomer (**53**) in 14% and 28% yields, respectively.

In summary, we have developed a simple method for preparing biologically active indole compounds, such as pimprinine, (±)-chelonin A, B, and their analogs. Using the 1-hydroxy- and 1-methoxyindole building blocks reported thus far,[10] it will be possible to synthesize various natural products and promising biologically active substances.[5]

EXPERIMENTAL

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. Infrared (IR) spectra were determined with a Shimadzu IR-420 or Horiba FT-720 spectrophotometer, and proton nuclear magnetic resonance (^{1}H-NMR) spectra with a JEOL JNM-GSX 500 or FX100S spectrometer with tetramethylsilane as an internal standard. Mass spectra (MS) were recorded on a Hitachi M-80 or JEOL SX-102A spectrometer. Column chromatography was performed on silica gel (SiO_2, 100–200 mesh, from Kanto Chemical Co. Inc.) throughout the present study. Preparative thin-layer chromatography (p-TLC) was performed on Merck Kiesel-gel GF_{254} (Type 60) (SiO_2).

3-(2-Chloro)acetyl-1-methoxyindole (2a) from 1-Methoxyindole (1b) — A solution of chloroacetyl chloride (791.8 mg, 7.01 mmol) in dry benzene (1.0 mL) was added to a solution of **1b** (107.0 mg, 0.72

mmol) in dry benzene (2.0 mL) and refluxed for 9 h with stirring. Under ice cooling 8% aq. NaOH and H_2O were added. The whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was purified by column chromatography on SiO_2 with CH_2Cl_2–hexane (1:3–1:1, v/v) as an eluent to afford **2a** (130.7 mg, 80%). **2a**: mp 103.0–104.5 °C (pale brown prisms, recrystallized from CH_2Cl_2–hexane). IR (KBr): 1661, 1513 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 4.08 (3H, s), 4.37 (2H, s), 7.01–7.51 (3H, m), 7.84 (1H, s), 8.01–8.34 (1H, m). MS *m/z*: 225 and 223 (M^+). *Anal.* Calcd for $C_{11}H_{10}ClNO_2$: C, 59.07; H, 4.51; N, 6.26. Found: C, 59.10; H, 4.62; N, 6.21.

1-Benzoyloxy-3-(2-chloro)acetylindole (2b) from 1-Benzoyloxyindole (1c) — A solution of chloroacetyl chloride (514.4 mg, 4.55 mmol, 10 mol eq) in dry xylene (2.0 mL) was added to a solution of **1c** (108.0 mg, 0.45 mmol) in dry xylene (3.0 mL) and the mixture was refluxed for 7 h. After addition of ice and sat. aq. $NaHCO_3$ to the reaction mixture, the whole was extracted with CH_2Cl_2. The extract 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) to give **1c** (20.6 mg, 19%) and **2b** (25.5 mg, 18%). **2b**: mp 192.0–192.5 °C (colorless needles, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3090, 1765, 1670, 1235, 995, 705 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 4.54 (2H, s), 7.28–7.33 (1H, m), 7.34–7.40 (2H, m), 7.62 (2H, dddd, *J* = 7.7, 7.5, 2.0, 2.0 Hz), 7.78 (1H, dddd, *J* = 7.5, 7.5, 2.0, 2.0 Hz), 8.03 (1H, s), 8.25 (2H, dddd, *J* = 7.7, 2.0, 2.0, 2.0 Hz), 8.40–8.45 (1H, m). MS *m/z*: 315, 313 (M^+). *Anal.* Calcd for $C_{17}H_{12}ClNO_3$: C, 65.08; H, 3.86; N, 4.46. Found: C, 64.82; H, 3.92; N, 4.47.

3-(2-Chloro)acetyl-1-hydroxyindole (2c) from 2b — 20% Aq. Na_2CO_3 (5.0 mL) was added to a solution of **2b** (103.5 mg, 0.33 mmol) in MeOH (15.0 mL) and stirred at 50 °C for 15 min. Water and 6% HCl was added to make the reaction mixture to acidic (pH 1.0) and the whole was extracted with CH_2Cl_2. The extract 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 (98:2, v/v) to give **2c** (65.9 mg, 95%). **2c**: mp 155 °C (decomp., colorless prisms, recrystallized from MeOH). IR (KBr): 3200, 1629, 1507, 1394, 1329, 1282, 1194, 1060, 932, 794, 754,745, 700 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 8.33 (1H, s), 8.24 (1H, ddd, *J* = 7.9, 1.2, 0.8 Hz), 7.51 (1H, ddd, *J* = 8.2, 1.2, 0.8 Hz), 7.33 (1H, ddd, *J* = 8.2, 7.1, 1.2 Hz), 7.27 (1H, ddd, *J* = 7.9, 7.1, 1.2 Hz), 4.67 (2H, s). *Anal.* Calcd for $C_{10}H_8ClNO_2$: C, 57.30; H, 3.85; N, 6.68. Found: C, 57.44; H, 3.80; N, 6.64.

1-Benzoyloxy-3-(2,2-dichloro)acetylindole (2d) from 1-Benzoyloxyindole (1c) – A solution of dichloroacetyl chloride (1.29 g, 8.81 mmol, 20 mol eq) in dry benzene (2.0 mL) was added to a solution of **1c** (105.1 mg, 0.44 mmol) in dry benzene (2.0 mL) and the mixture was refluxed for 24 h with stirring. After addition of ice and sat. aq. $NaHCO_3$, the whole was extracted with CH_2Cl_2. The extract 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 (2:1, v/v) to give **2d** (93.6 mg, 61%). **2d**: mp 164.5–166.0 °C (colorless prisms, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3112, 1771, 1674, 1515, 1455, 1374, 1251, 1235, 993, 746, 722, 600 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 6.38 (1H, s), 7.31–7.33 (1H, m), 7.36–7.41 (2H, m), 7.60–7.64 (2H, m), 7.77–7.80 (1H, m), 8.25–8.28 (2H, m), 8.27 (1H, s), 8.43–8.45 (1H, m). MS m/z: 351, 349 and 347 (M^+), 264, 105. *Anal.* Calcd for $C_{17}H_{11}Cl_2NO_2$: C, 58.64; H, 3.18; N, 4.02. Found: C, 58.73; H, 3.13; N, 3.96.

3-(2,2-Dichloro)acetyl-1-hydroxyindole (2e) from 2d — 20% Aq. Na_2CO_3 (5.0 mL) was added to a solution of **2d** (28.7 mg, 0.082 mmol) in THF (10.0 mL) and the mixture was heated at 60 ℃ for 1 h with stirring. The reaction mixture was made acidic by addition of 6% HCl and the whole was extracted with CH_2Cl_2. The extract 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 *Rf* value of 0.32–0.15 with CH_2Cl_2–MeOH (95:5, v/v) afforded **2e** (18.6 mg, 92%). **2e**: mp 162.0–163.0 °C (colorless needles, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3124, 1632, 1531, 1501, 1488, 1373, 1323, 1263, 1215, 761, 720, 651 cm^{-1}. ^1H-NMR (CD_3OD) δ: 7.12 (1H, s), 7.31 (1H, ddd, J = 8.2, 7.1, 1.1 Hz), 7.36 (1H, ddd, J = 8.2, 7.1, 1.2 Hz), 7.54 (1H, ddd, J = 8.1, 1.1, 0.7 Hz), 8.26 (1H, ddd, J = 8.0, 1.2, 0.7 Hz), 8.46 (1H, s). MS *m/z*: 247, 245 and 243 (M^+), 160, 144. *Anal.* Calcd for $C_{10}H_7Cl_2NO_2$: C, 49.21; H, 2.89; N, 5.74. Found: C, 49.24; H, 2.81; N, 5.72.

3-(2-Aminoacetyl)-1-methoxyindole (3a) from 2a — A solution of **2a** (51.3 mg, 0.23 mmol) in MeOH (4.0 mL) and 28% aq. NH_3 (2.0 mL) were sealed in a tube and heated at 70 ℃ with stirring for 1 h. After cooling CH_2Cl_2 and 8% aq. NaOH were added. Organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil. Purification by column chromatography on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (100:20:2, v/v) afforded **3a** (19.1 mg, 41%). **3a**: colorless oil. IR (film): 3346, 1652, 1510 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 2.21 (2H, br s, NH_2), 3.92 (2H, br s.), 4.09 (3H, s), 6.82–7.60 (3H, m), 7.78 (1H, s), 7.99–8.42 (1H, m). MS *m/z*: 204 (M^+). High resolution MS *m/z*: Calcd for $C_{11}H_{12}N_2O_2$: 204.0898. Found: 204.0890.

3-(2-Azidoacetyl)-1-methoxyindole (3b) from 2a — A solution of NaN_3 (20.9 mg, 0.32 mmol) in H_2O (1.0 mL) was added to a solution of **2a** (49.0 mg, 0.22 mmol) in MeCN (2.0 mL) and stirred at reflux temperature for 3.5 h. After cooling H_2O was added and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v), and the extract was washed with brine, dried over Na_2SO_4. After evaporation of solvent the residue was purified by column chromatography with CH_2Cl_2–MeOH (95:5, v/v) to afford **3b** (45.4 mg, 90%). **3b**: mp 69.0–70.0 °C (colorless prisms, recrystallized from MeOH). IR (KBr): 3112, 2100, 1664, 1517, 1453, 1385, 1330, 1284, 1193, 1059, 939, 884, 757 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 4.19 (3H, s), 4.36

(2H, s), 7.34 (1H, td, *J* = 7.5, 1.3 Hz), 7.38 (1H, td, *J* = 7.5, 1.3 Hz), 7.49 (1H, ddd, *J* = 7.9, 1.2, 0.9 Hz), 7.96 (1H, s), 8.35 (1H, ddd, *J* = 7.9, 1.2, 0.9 Hz). MS *m/z*: 230 (M^+). *Anal.* Calcd for $C_{11}H_{10}N_4O_2$: C, 57.38; H, 4.38; N, 24.34. Found: C, 57.50; H, 4.32; N, 24.15.

***N*-(2-Acetoxy)ethyl-*N*-(1-methoxyindol-3-yl)carbonylmethyl-*N*,*N*-dimethylammonium Chloride (3c) from 2a — 9** (202.0 mg, 0.90 mmol) was added to a solution of 2-dimethylaminoethyl acetate (1.18 g, 9.02 mmol, 10 mol eq) in dry benzene (5.0 mL) and the mixture was heated at 76–82 °C for 24 h with stirring. After evaporation of the solvent under reduced pressure, benzene was added to the residue and precipitates were collected by filtration. Recrystallization from MeOH–CH_2Cl_2 afforded **3c** (302.1 mg, 94%). **3c**: mp 190.5–191.0 °C (decomp., colorless prisms, recrystallized from MeOH–CH_2Cl_2). IR (KBr): 3434, 3050, 3000, 1743, 1649, 1515, 1455, 1362, 1329, 1237, 950, 901, 737 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.78 (3H, s), 3.47 (6H, s), 4.12–4.14 (2H, m), 4.24 (3H, s), 4.56–4.58 (2H, m), 4.82–4.89 (2H, m), 7.34 (1H, ddd, *J* = 8.0, 7.1, 1.1 Hz), 7.41 (1H, ddd, *J* = 8.2, 7.1, 1.1 Hz), 7.59 (1H, dt, *J* = 8.2, 1.1 Hz), 8.30 (1H dt, *J* = 8.0, 1.1 Hz), 8.57 (1H, s). MS *m/z*: 244, 174. *Anal.* Calcd for $C_{17}H_{23}ClN_2O_4$: C, 57.54; H, 6.53; N, 7.89. Found: C, 57.31; H, 6.58; N, 7.80.

3-(2-Acetylamino)acetyl-1-methoxyindole (4) from 2a — A solution of **2a** (546.5 mg, 2.4 mmol) in MeOH (32.0 mL) and 28% aq. NH_3 (25.0 mL) were sealed in a tube and stirred at 70 °C for 1 h. After cooling 8% aq. NaOH was added to make the whole basic, and then extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4. After evaporation of solvent the residue was dissolved in a mixed solution of CH_2Cl_2 (20.0 mL) and Et_3N (5.0 mL). To the mixture a solution of AcCl (271.4 mg, 1.4 mol eq.) in CH_2Cl_2 (10.0 mL) was added and stirred at rt for 40 min. After addition of H_2O, the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v), and the extract was washed with brine, dried over Na_2SO_4. After evaporation of the solvent the residue was purified by column chromatography with CH_2Cl_2–Et_2O–MeOH (95:100:5, v/v) to afford **4** (262.2 mg, 44%). **4**: mp 149.0–150.5 °C (pale brown prisms, recrystallized from CH_2Cl_2). IR (KBr): 1656, 1640 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.06 (3H, s), 4.09 (3H, s), 4.53 (2H, d, *J* = 4.4 Hz), 6.63 (1H, br s), 7.00–7.53 (3H, m), 7.90 (1H, s), 8.00–8.33 (1H, m). MS *m/z*: 246 (M^+). *Anal.* Calcd for $C_{13}H_{14}N_2O_3 \cdot 1/2\ H_2O$: C, 61.16; H, 5.92; N, 10.98. Found: C, 61.23; H, 6.03; N, 10.96.

5-(1-Methoxyindol-3-yl)-2-methyloxazole (1-Methoxypimprinine, 5a) from 4 — A solution of **4** (40.0 mg, 0.16 mmol) in $CHCl_3$ (2.0 mL) was added to PPE (722.8 mg, 10 mol eq.) and refluxed for 4.5 h with stirring. After cooling 8% aq. NaOH was added to make the whole basic, and then extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4. After evaporation of solvent the residue was purified by column chromatography with CH_2Cl_2–Et_2O (1:1, v/v) to afford **5a** (28.9 mg, 78%). **5a**: mp 49.0–50.5 °C (colorless prisms, recrystallized from hexane). IR (KBr): 1637, 1578 cm^{-1}. ^{1}H-NMR (CCl_4) δ: 2.42 (3H, s), 4.00 (3H, s), 6.86 (1H, s), 6.78–7.27 (3H, m), 7.31 (1H, s), 7.48–7.75 (1H, m). High resolution MS *m/z*: Calcd for $C_{13}H_{12}N_2O_2$: 228.0897. Found: 228.0896.

5a from 3b — A solution of **3b** (50.8 mg, 0.22 mmol) in dry benzene (5.0 mL) was gradually added to a solution of PPh_3 (99.3 mg, 0.4 mmol) in dry benzene (5.0 mL). To the resultant solution, dry benzene solution (5.0 mL) of AcCl (19.0 mg, 0.24 mmol) was added at rt and stirred for 39 h. The precipitates were removed by filtration and washed with benzene. The combined benzene solution was washed with sat. aq. $NaHCO_3$, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil. Purification by column chromatography with CH_2Cl_2–MeOH (99:1, v/v) afforded **5a** (15.7 mg, 31%).

Pimprinine (5b) from 5a — 10% Pd/C (25.6 mg) was added to a solution of **5b** (20.0 mg, 0.08 mmol) in MeOH (4.0 mL) and the mixture was hydrogenated at rt and 1 atm for 1.5 h. After precipitates were filtered off, the filtrate was washed with MeOH. The combined filtrate and washings were evaporated under reduced pressure to leave an oil, which was subjected to p-TLC on SiO_2 with CH_2Cl_2–Et_2O (1:1, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.66–0.46 with CH_2Cl_2–MeOH (95:5, v/v) afforded **5b** (17.2 mg, 99%). **5b**: mp 211.0–212.5 °C (Lit.[6] mp 205 °C, colorless prisms, recrystallized from benzene). IR (KBr): 3115, 1638, 1588 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.49 (3H, s), 7.00 (1H, s), 7.05–7.31 (3H, m), 7.34 (1H, d, J = 2.5 Hz), 7.51–7.86 (1H, m), 8.47 (1H, br s, disappeared on addition of D_2O). MS *m/z*: 198 (M^+). *Anal.* Calcd for $C_{12}H_{10}N_2O$: C, 72.71; H, 5.09; N, 14.13. Found: C, 72.97; H, 5.09; N, 14.04.

3-[2-(2-Chloroacetamino)acetyl]-1-methoxyindole (6) from 3a — A solution of Et_3N (0.20 mL, 1.43 mmol) in CH_2Cl_2 (1.0 mL) was added to a solution of **3a** (66.1 mg, 0.32 mmol) and chloroacetyl chloride (72.9 mg, 0.65 mmol) in CH_2Cl_2 (2.0 mL) and the mixture was stirred at rt for 15 h. After addition of ice and H_2O, the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract 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 Et_2O–CH_2Cl_2–MeOH (1:9, v/v) as an eluent to give **6** (53.97 mg, 59%). **6**: mp 150.0–152.0 °C (yellow plates, recrystallized from MeOH). IR (KBr): 3250, 3111, 1685, 1671, 1641, 1549, 1515, 1396, 1196, 1058, 953, 742 cm^{-1}. ^{1}H-NMR (pyridine-d_5) δ: 4.01 (3H, s), 4.47 (2H, s), 4.95 (2H, d, J = 5.1 Hz), 7.35 (1H, t, J = 7.5 Hz), 7.38 (1H, t, J = 7.0 Hz), 7.55 (1H, d, J = 7.8 Hz), 8.69 (1H, d, J = 7.8 Hz), 8.71 (1H, s), 9.32 (1H, br s, D_2O exchange). MS *m/z*: 282 and 280 (M^+), 174. *Anal.* Calcd for $C_{13}H_{13}ClN_2O_3$: C, 55.62; H, 4.67; N, 9.98. Found: C, 55.47; H, 4.58; N, 9.83.

6 from 3b — A solution of chloroacetyl chloride (14.7 mg, 0.13 mmol, 1 mol eq. in dry benzene (3.0 mL) was added to a solution of Ph_3P (60.3 mg, 0.23 mmol, 1.7 mol eq) and **3b** (30.2 mg, 0.13 mmol) in dry benzene (6.0 mL) and the mixture was stirred at rt for 30 h. Precipitates were filtered off and washed with benzene. The washing and filtrate were combined and washed with brine and sat. aq. $NaHCO_3$, 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 (99:1, v/v) to give **2a** (6.9 mg, 24%) and **6** (6.2 mg, 17%).

3-{2-[2-(*N*-Methylpiperazinyl)acetamino]acetyl}-1-methoxyindole (7a) from 6 — A solution of *N*-methylpiperazine (290.8 mg, 2.90 mmol) in MeOH (5.0 mL) was added to a solution of **6** (157.3 mg, 0.56 mmol) in MeOH (20.0 mL) and the mixture was refluxed for 15 h with stirring. After addition of ice and H_2O, the whole was made alkaline with 8% NaOH and extracted with CH_2Cl_2. The extract 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_3 (46:2:0.2, v/v) to give **7a** (188.6 mg, 98%). **7a**: mp 141.0–143.0 °C (colorless prisms, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3370, 2789, 1672, 1657, 1502, 1391, 1331, 955, 922, 760 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.46 (3H, br s), 2.75 (8H, br s), 3.15 (2H, s), 4.19 (3H, s), 4.65 (2H, d, *J* = 4.8 Hz), 7.34 (1H, ddd, *J* = 7.5, 7.4, 1.2 Hz), 7.38 (1H, td, *J* = 7.5, 1.3 Hz), 7.50 (1H, dt, *J* = 8.3, 0.9 Hz), 8.04 (1H, s), 8.08 (1H, br t, *J* = 4.8 Hz, D_2O exchange), 8.32 (1H, dt, *J* = 8.1, 0.9 Hz). MS *m/z*: 344 (M^+). *Anal.* Calcd for $C_{18}H_{24}N_4O_3 \cdot 1/8H_2O$: C, 62.36; H, 7.05; N, 16.16. Found: C, 62.29; H, 6.99; N, 16.05.

3-{2-[2-(*p*-Methoxyphenethyl)amino]acetamino]acetyl}-1-methoxyindole (7b) from 6 — A solution of *p*-methoxyphenethylamine (301.4 mg, 1.99 mmol) in MeOH (5.0 mL) was added to a solution of **6** (108.9 mg, 0.38 mmol) in MeOH (15.0 mL) and the mixture was refluxed for 20 h with stirring. After addition of ice and H_2O, the whole was made alkaline with 8% NaOH and extracted with CH_2Cl_2. The extract 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 (97:3–95:5, v/v) to give **7b** (83.4 mg, 54%). **7b**: pale yellow oil. IR (film): 3327, 2938, 1653, 1515, 1454, 1387, 1331, 1249, 1179, 1032, 954, 743 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 2.76 (2H, t, *J* = 7.1 Hz), 2.85 (2H, dt, *J* = 7.1, 0.8 Hz), 3.35 (2H, s), 3.70 (3H, s), 4.20 (3H, s), 4.55 (2H, s), 6.82 (2H, d, *J* = 8.8 Hz), 7.15 (2H, d, *J* = 8.8 Hz), 7.28 (1H, ddd, *J* = 8.1, 7.2, 1.1 Hz), 7.35 (1H, ddd, *J* = 8.2, 7.2, 1.1 Hz), 7.54 (1H, dt, *J* = 8.1, 0.9 Hz), 8.27 (1H, dt, *J* = 7.9, 0.9 Hz), 8.51 (1H, s). High resolution MS *m/z*: Calcd for $C_{22}H_{25}N_3O_4$: 395.1844. Found: 395.1809.

5-(1-Methoxyindol-3-yl)-2-(4-methylpiperazin-1-yl)methyloxazole (8a) from 7a — PPE (1.0 mL) was added to a solution of **7a** (18.8 mg, 0.05 mmol) in $CHCl_3$ (2.0 mL) and the mixture was refluxed for 2.5 h with stirring. After addition of ice and H_2O, the whole was made alkaline with 8% NaOH and extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract 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_3 (46:2:0.2, v/v) as a developing solvent to give **8a** (13.4 mg, 75%). **8a**: colorless oil. IR (film): 2942, 2800, 1632, 1454, 1326, 1291, 1161, 1142, 1108, 1061, 1011, 953, 736 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 2.29 (3H, s), 2.54 (4H, br s), 2.69 (4H, br s), 3.81 (2H, s), 4.15 (3H, s), 7.22 (1H, ddd, *J* = 8.1, 7.1, 1.0 Hz), 7.29 (1H, s), 7.32 (1H, ddd, *J* = 8.1, 7.1, 0.9 Hz), 7.51 (1H, dt, *J* = 8.1, 0.8 Hz), 7.85 (1H, dt, *J* = 8.1, 0.9 Hz), 7.89 (1H, s). High resolution MS *m/z*: Calcd for $C_{18}H_{22}N_4O_2$: 326.1741. Found: 326.1743.

5-(1-Methoxyindol-3-yl)-2-(*p*-methoxyphenethylaminomethyl)oxazole (8b) from 7b — PPE (3.0 mL) was added to a solution of **7b** (64.3 mg, 0.16 mmol) in $CHCl_3$ (5.0 mL) and the mixture was refluxed for 3.5 h with stirring. After addition of ice and H_2O, the whole was made alkaline with 8% NaOH and extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract 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 (97:3, v/v) to give **8b** (36.4 mg, 59%). **8b**: pale yellow oil. IR (film): 2971, 2842, 1614, 1515, 1454, 1326, 1249, 1112, 1034, 737 cm^{-1}. ^1H-NMR (CD_3OD) δ: 2.77 (2H, t, *J* = 7.3 Hz), 2.88 (2H, dt, *J* = 7.4, 0.9 Hz), 3.73 (3H, s), 3.96 (2H, s), 4.15 (3H, s), 6.82 (2H, d, *J* = 8.8 Hz), 7.12 (2H, d, *J* = 8.8 Hz), 7.21 (1H, ddd, *J* = 8.1, 7.1, 1.0 Hz), 7.26 (1H, s), 7.32 (1H, ddd, *J* = 8.2, 7.2, 1.0 Hz), 7.50 (1H, dt, *J* = 8.2, 0.9 Hz), 7.82 (1H, dt, *J* = 8.1, 0.9 Hz), 7.83 (1H, s). High resolution MS *m/z*: Calcd for $C_{22}H_{23}N_3O_3$: 377.1738. Found: 377.1741.

3-[2-(Imidazol-1-yl)acetyl]-1-methoxyindole (9) and Bis(1-methoxyindol-3-carbonylmethyl)-imidazolium Chloride (10) from 2a — Imidazole (627.7 mg, 9.23 mmol) was added to a solution of **2a** (294.2 mg, 1.32 mmol) in MeOH (6.0 mL) solution and refluxed with stirring for 14 h. Water was added and the whole was extracted with $CHCl_3$–MeOH–28% NH_3 (100:20:5, v/v). The extract 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 (97:3, v/v) to give **9** (283.4 mg, 84%) and **10** (33.5 mg, 10%) in the order of elution. **9**: mp 134.0–136.0 °C (colorless prisms, recrystallized from EtOAc). IR (KBr): 3413, 3083, 2968, 2938, 1654, 1516, 1387, 1376, 1339, 1331, 1199, 1078, 957, 920, 816, 756, 745, 680, 660 cm^{-1}. ^1H-NMR (5% CD_3OD in $CDCl_3$) δ: 4.18 (3H, s), 5.19 (2H, s), 7.03 (1H, s), 7.16 (1H, s), 7.34 (1H, dd, *J* = 8.1, 1.3 Hz), 7.39 (1H, ddd, *J* = 8.1, 1.3, 1.3 Hz), 7.49 (1H, ddd, *J* = 8.1, 1.3, 1.3 Hz), 7.62 (1H, s), 7.72 (1H, s), 8.34 (1H, ddd, *J* = 8.1, 1.3, 1.3 Hz). MS *m/z*: 255 (M^+). *Anal.* Calcd for $C_{14}H_{13}N_3O_2$: C, 65.87; H, 5.13; N, 16.46. Found: C, 66.08; H, 5.10; N, 16.42. **10**: mp 243 °C (decomp., colorless powder, recrystallized from MeOH–acetone). IR (KBr): 3407, 3067, 1681, 1663, 1575, 1515, 1387, 1326, 1253, 1184, 1158, 1136, 1113, 1058, 948, 916, 725, 706, 628 cm^{-1}. ^1H-NMR (CD_3OD) δ: 4.27 (6H, s), 5.85 (4H, s), 7.60 (2H, ddd, *J* = 8.0, 1.1, 1.1 Hz), 7.72 (2H, d, *J* = 1.6 Hz), 7.32 (2H, ddd, *J* = 8.0, 7.3, 1.1 Hz), 7.41 (2H, ddd, *J* = 8.0, 7.3, 1.1 Hz), 8.25 (2H, ddd, *J* = 8.0, 1.1, 1.1 Hz), 8.68 (2H, s), 9.12 (1H, t, *J* = 1.6 Hz). *Anal.* Calcd for $C_{25}H_{23}ClN_4O_4$: C, 62.70; H, 4.84; N, 11.70. Found: C, 62.55; H, 5.01; N, 11.57.

2-Diaminomethyleneamino-4-(1-methoxyindol-3-yl)thiazole (11) from 2a — Guanylthiourea (51.1 mg, 0.43 mmol) was added to a solution of **2a** (31.7 mg, 0.14 mmol) in MeOH (2.0 mL) and refluxed with stirring for 3.5 h. Water and 8% aq. NaOH were added and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract 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_3 (46:3:0.3, v/v) to give **11** (28.5 mg, 70%). **11**: mp 132.5 °C (decomp., colorless prisms, recrystallized from MeOH–CH_2Cl_2). IR (KBr): 3395, 3045, 1660, 1599, 1560, 1548, 1376, 1232, 1150, 1065, 1019, 946, 732 cm^{-1}. ^1H-NMR (CD_3OD) δ: 4.13 (3H, s), 6.85 (1H, s), 7.16 (1H, ddd, J = 8.2, 7.2, 0.9 Hz), 7.26 (1H, ddd, J = 7.2, 0.9, 0.9 Hz), 7.46 (1H, ddd, J = 8.2, 0.9, 0.9 Hz), 7.82 (1H, s), 7.96 (1H, ddd, J = 8.2, 0.9, 0.9 Hz). MS *m/z*: 287 (M^+). *Anal*. Calcd for $C_{13}H_{13}N_5OS$: C, 54.34; H, 4.56; N, 24.37. Found: C, 54.42; H, 4.61; N, 24.09.

2-(1-Methoxyindol-3-yl)quinoxaline (12a) and 2-(Indol-3-yl)quinoxaline (12b) from 2a — *o*-Phenylenediamine (291.7 mg, 2.7 mmol) was added to a solution of **2a** (100.0 mg, 0.45 mmol) in benzene (2.0 mL) and refluxed for 7.5 h. After addition of water and sat. aq. $NaHCO_3$, the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was purified by column chromatography on SiO_2 with CH_2Cl_2–hexane (9:1, v/v) as an eluent to afford **12a** (64.6 mg, 48%) and **12b** (42.7 mg, 35%) in the order of elution. **12a**: mp 132.5–133.5 °C (yellow prisms, recrystallized from EtOAc–hexane). IR (KBr): 1555, 1450, 1373, 1199, 1125, 992, 954, 932, 812, 732 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 4.22 (3H, s), 7.35 (1H, dt, J = 1.3, 7.2 Hz), 7.39 (1H, dt, J = 1.3, 7.2 Hz), 7.52–7.56 (1H, m), 7.66 (1H, dd, J = 8.4, 1.5 Hz), 7.74 (1H, dd, J = 8.4, 1.5 Hz), 8.05 (1H, dd, J = 8.4, 1.5 Hz), 8.09 (1H, s), 8.13 (1H, dd, J = 8.4, 1.5 Hz), 8.75 (1H, dd, J = 7.2, 1.1 Hz), 9.20 (1H, s). MS *m/z*: 275 (M^+). *Anal*. Calcd for $C_{17}H_{13}N_3O$: C, 74.16; H, 4.76; N, 15.26. Found: C, 74.34; H, 4.67; N, 15.19. **12b**: mp 211.0–212.0 °C (orange prisms, recrystallized from EtOAc–hexane). IR (KBr): 1617, 1545, 1434, 1296, 1239, 1165, 1131, 945, 739 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 7.32–7.38 (2H, m), 7.45–7.50 (1H, m), 7.66 (1H, dd, J = 8.2, 1.3 Hz), 7.75 (1H, dd, J = 8.2, 1.3 Hz), 8.02 (1H, d, J = 2.9 Hz), 8.06 (1H, dd, J = 8.2, 1.3 Hz), 8.15 (1H, dd, J = 8.2, 1.3 Hz), 8.67 (1H, br s), 8.76–8.80 (1H, m), 9.25 (1H, s). MS *m/z*: 245 (M^+). *Anal*. Calcd for $C_{16}H_{11}N_3$: C, 78.35; H, 4.52; N, 17.13. Found: C, 78.53; H, 4.44; N, 17.02.

3-[2-(2-Propylaminoacetamino)acetyl]-1-methoxyindole (13) from 6 — A solution of propylamine (104.1 mg, 1.76 mmol) in MeOH (5.0 mL) was added to a solution of **6** (101.3 mg, 0.36 mmol) in MeOH (10.0 mL) and the mixture was refluxed for 24 h. After addition of sat. aq. $NaHCO_3$, the whole was extracted with CH_2Cl_2. The extract 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 Et_2O–$CHCl_3$ (1:14, v/v), $CHCl_3$–MeOH (97:3, v/v), and then $CHCl_3$–MeOH–28% NH_3 (46:2:0.2, v/v) to give **6** (2.9 mg, 3%) and **13** (41.2 mg, 38%) in the order of elution. **13**: pale yellow oil. IR (film): 3145, 3095, 2972, 2937, 2875, 1649, 1511, 1328, 1198, 956, 740 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 0.97 (3H, t, *J* = 7.3 Hz), 1.56 (2H, six, *J* = 7.3 Hz), 2.61 (2H, t, *J* = 7.3 Hz), 3.37 (2H, s), 4.21 (3H, s), 4.62 (2H, s), 7.28 (1H, ddd, *J* = 8.1, 7.1, 1.1 Hz), 7.35 (1H, ddd, *J* = 8.2, 7.1, 1.1 Hz), 7.54 (1H, dt, *J* = 8.2, 0.9 Hz), 8.26 (1H, dt, *J* = 8.0, 1.0 Hz), 8.52 (1H, s). High resolution MS *m/z*: Calcd for $C_{16}H_{21}N_3O_3$: 303.1582. Found: 303.1574.

3-[2-(*N*-2-Methoxyacetyl)aminoacetyl]- (14), 3-[2-(2-Acetoamino-2-methoxy)acetyl]- (15), and 3-(2-Acetoamino-2-propylamino)acetyl-1-methoxyindole (16) from 6 — K_2CO_3 (541.0 mg, 3.91 mmol) was added to a solution of **6** (199.0 mg, 0.70 mmol) and propylamine hydrochloride (339.6 mg, 3.55 mmol) in MeOH (30 mL) and the mixture was refluxed for 8 h with stirring. After addition of ice and H_2O, the whole was made alkaline with 8% NaOH and extracted with CH_2Cl_2. The extract 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 EtOAc–hexane (4:1, v/v) as an eluent to give **13** (26.4 mg, 12%), **14** (15.8 mg, 8%), **15** (45.8 mg, 23%) and **16** (33.3 mg, 15%). **14**: mp 122.0–124.0 ºC (colorless needles, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3386, 3086, 1679, 1644, 1516, 1393, 1207, 1114, 747 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.49 (3H, s), 4.00 (2H, s), 4.19 (3H, s), 4.66 (2H, d, *J* = 4.8 Hz), 7.34 (1H, td, *J* = 7.4, 1.4 Hz), 7.38 (1H, td, *J* = 7.9, 1.4 Hz), 7.49 (1H, d, *J* = 8.0 Hz), 7.60 (1H, br s), 8.03 (1H, s), 8.34 (1H, d, *J* = 7.6 Hz). MS *m/z*: 276 (M$^+$), 245. *Anal*. Calcd for $C_{14}H_{16}N_2O_4 \cdot 1/8H_2O$: C, 60.37; H, 5.88; N, 10.06. Found: C, 60.38; H, 5.77; N, 10.07. **15**: mp 155.0–158.0 ºC (colorless prisms, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3334, 3092, 2946, 1683, 1650, 1506, 1394, 1069, 739 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.15 (3H, s), 3.44 (3H, s), 4.20 (3H, s), 6.12 (1H, d, *J* = 8.2 Hz), 7.20 (1H, br d, *J* = 8.2 Hz), 7.35 (1H, td, *J* = 7.6, 1.4 Hz), 7.38 (1H, td, *J* = 7.8, 1.4 Hz), 7.49 (1H, d, *J* = 8.0 Hz), 8.21 (1H, s), 8.37 (1H, d, *J* = 8.2 Hz). MS *m/z*: 276 (M$^+$), 245. *Anal*. Calcd for $C_{14}H_{16}N_2O_4$: C, 60.86; H, 5.84; N, 10.14. Found: C, 60.61; H, 5.85; N, 10.06. **16**: mp 115.0–117.0 ºC (dec., pale orange prisms, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3154, 3092, 2965, 1670, 1652, 1510, 1364, 1200, 753 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 0.94 (3H, t, *J* = 7.4 Hz), 1.46–1.63 (2H, m), 2.00 (3H, s), 2.59 (1H, ddd, *J* = 11.4, 8.4, 6.0 Hz), 2.65 (1H, ddd, *J* = 11.4, 8.4, 6.4 Hz), 4.20 (3H, s), 5.83 (1H, s), 7.28 (1H, ddd, *J* = 8.0, 7.1, 0.9 Hz), 7.35 (1H, ddd, *J* = 8.2, 7.1, 1.1 Hz), 7.54 (1H, dt, *J* = 8.1, 0.9 Hz), 8.31 (1H, ddd, *J* = 8.0, 1.1, 0.7 Hz), 8.50 (1H, s). MS *m/z*: 303 (M$^+$), 174, 129. *Anal*. Calcd for $C_{16}H_{21}N_3O_3 \cdot 1/4H_2O$: C, 62.42; H, 7.04; N, 13.65. Found: C, 62.66; H, 6.97; N, 13.58.

3-(2-Hydroxy)acetyl-1-methoxyindole (19) from 2a — A solution of **2a** (1.004 g, 4.49 mmol) in $HCONH_2$-H_2O (10:1, v/v, 50 mL) was heated at 111–115 ºC with stirring for 3 h. After addition of 14% aq. NH_3, the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was column chromatographed on SiO_2 with CH_2Cl_2–MeOH (100:0–98:2, v/v) to afford **19** (753.2 mg, 82%). **19**: mp 119.5–120 ºC (pale brown prisms, recrystallized from EtOAc-hexane). IR (KBr): 3470, 3100, 1640, 1516, 1447, 1360, 1248, 1092, 950, 912, 745 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 4.20 (3H, s), 4.74 (2H, s), 7.34 (1H, dt, *J* = 1.5, 7.0 Hz), 7.38 (1H, dt, *J* = 1.5, 7.0 Hz), 7.50 (1H, br d, *J* = 7.0 Hz), 7.92 (1H, s), 8.24 (1H, br d, *J* = 7.0 Hz). High resolution MS *m/z*: Calcd for $C_{11}H_{11}NO_3$: 205.0738. Found: 205.0737.

3-(2-Propionyloxy)acetyl-1-methoxyindole (20a) from 19 — Propionyl chloride (0.05 mL, 0.57 mmol) was added to a solution of **19** (50.1 mmol, 0.24 mmol) in pyridine (2.0 mL) at 0 °C with stirring. Stirring was continued at rt for 1 h, and then ice and H_2O were added. The whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract 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 (99:1, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.61–0.31 with CH_2Cl_2–MeOH (95:5, v/v) afforded **20a** (61.4 mg, 96%). **20a**: pale yellow oil. IR (film): 3112, 2993, 2947, 1740, 1665, 1511, 1449, 1323, 1171, 954, 907, 743 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.23 (3H, t, *J* = 7.5 Hz), 2.54 (2H, q, *J* = 7.5 Hz), 4.18 (3H, s), 5.17 (2H, s), 7.32 (1H, td, *J* = 7.6, 1.3 Hz), 7.36 (1H, td, *J* = 7.6, 1.3 Hz), 7.48 (1H, ddd, *J* = 7.6, 1.3, 0.6 Hz), 7.98 (1H, s), 8.32 (1H, ddd, *J* = 7.6, 1.3, 0.6 Hz). High resolution MS *m/z*: Calcd for $C_{14}H_{15}NO_4$: 260.9168. Found: 261.1001.

3-(2-*trans*-Cinnamoyloxy)acetyl-1-methoxyindole (20b) from 19 — *trans*–Cinnamic acid (108.0 mg, 0.72 mmol) was added to a solution of $SOCl_2$ (261.2 mg, 2.19 mmol) in dry benzene (2.0 mL) and the mixture was heated at 70–73 °C for 3.5 h with stirring. To the residue obtained after evaporation of the solvent under reduced pressure, a solution of **19** (49.7 mg, 0.24 mmol) in pyridine (2.0 mL) was added and the mixture was stirred at rt for 1.5 h. After addition of ice and H_2O, the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract 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 0.65–0.45 with CH_2Cl_2–MeOH (95:5, v/v) afforded **20b** (72.6 mg, 89%). **20b**: mp 164.0–165.5 °C (colorless prisms, recrystallized from MeOH). IR (KBr): 3108, 1723, 1659, 1633, 1509, 1447, 1388, 1330, 1310, 1164, 954, 908, 761 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 4.19 (3H, s), 5.30 (2H, s), 6.62 (1H, d, *J* = 16.1 Hz), 7.33 (1H, td, *J* = 7.5, 1.1 Hz), 7.37 (1H, td, *J* = 7.5, 1.1 Hz), 7.39–7.42 (3H, m), 7.48 (1H, ddd, *J* = 7.5, 1.1, 0.9 Hz), 7.54–7.58 (2H, m), 7.83 (1H, d, *J* = 16.1 Hz), 8.02 (1H, s), 8.35 (1H, ddd, *J* = 7.5, 1.1, 0.9 Hz). MS *m/z*: 335 (M^+), 174. *Anal*. Calcd for $C_{20}H_{17}NO_4$: C, 71.63; H, 5.11; N, 4.18. Found: C, 71.58; H, 5.11; N, 4.09.

3-(2-Palmitoyloxy)acetyl-1-methoxyindole (20c) from 19 — Palmitic acid (750.9 mg, 2.93 mmol) was added to a solution of $SOCl_2$ (1.048 g, 8.80 mmol) in dry benzene (4.0 mL) and the mixture was heated at 71–77 °C for 3 h with stirring. To the residue obtained after evaporation of the solvent under reduced pressure, a solution of **19** (200.9 mg, 0.98 mmol) in pyridine (3.0 mL) was added and the mixture was stirred at rt for 3 h. After addition of ice and H_2O, the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract 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 (2:1, v/v) as an eluent to give **20c** (326.9 mg, 75%) and **19** (20.8 mg, 10%). **20c**: mp 57.5–58.5 ºC (colorless prisms, recrystallized from MeOH). IR (KBr): 3108, 2923, 2854, 1749, 1734, 1674, 1511, 1388, 1167, 949, 911, 766, 741 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, t, *J* = 7.0 Hz), 1.21–1.40 (24H, m), 1.71 (2H, f, *J* = 7.5 Hz), 2.50 (2H, t, *J* = 7.5 Hz), 4.18 (3H, s), 5.16 (2H, s), 7.32 (1H, td, *J* = 7.7, 1.1 Hz), 7.36 (1H, td, *J* = 7.7, 1.1 Hz), 7.47 (1H, ddd, *J* = 7.7, 1.1, 0.7 Hz), 7.98 (1H, s), 8.32 (1H, ddd, *J* = 7.7, 1.1, 0.7 Hz). MS *m/z*: 443 (M^+), 174. *Anal*. Calcd for $C_{27}H_{41}NO_4$: C, 73.10; H, 9.32; N, 3.16. Found: C, 73.00; H, 9.28; N, 3.14.

3-[2-(*Z*)-Oleyloxy]acetyl-1-methoxyindole (20d) from 19 — Oleic acid (207.7 mg, 0.75 mmol) was added to a solution of $SOCl_2$ (268.9 mg, 2.21 mmol) in dry benzene (2.0 mL) and the mixture was heated at 75–80 ºC for 2 h with stirring. To the residue obtained after evaporation of the solvent under reduced pressure, a solution of **19** (52.5 mg, 0.25 mmol) in pyridine (2.0 mL) was added and the mixture was stirred at 43–45 ºC for 16 h. After addition of ice and H_2O, the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract 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 as an eluent to give **20d** (87.9 mg, 73%). **20d**: pale yellow oil. IR (film): 2927, 2862, 1745, 1676, 1515, 1454, 1331, 1166, 955, 905, 739 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, t, *J* = 6.9 Hz), 1.33–1.41 (20H, m), 1.71 (2H, f, *J* = 7.4 Hz), 1.94–2.08 (4H, m), 2.50 (2H, t, *J* = 7.6 Hz), 4.18 (3H, s), 5.16 (2H, s), 5.30–5.40 (2H, m), 7.32 (1H, td, *J* = 7.9, 1.3 Hz), 7.36 (1H, td, *J* = 7.9, 1.3 Hz), 7.48 (1H, d, *J* = 7.9 Hz), 7.96 (1H, s), 8.32 (1H, d, *J* = 7.9 Hz). MS *m/z*: 469 (M^+), 206, 174. High resolution MS *m/z*: Calcd for $C_{29}H_{43}NO_4$: 469.3190. Found: 469.3183.

3-(1,2-Dihydroxyethyl)-1-methoxyindole (21a) from 19 — $NaBH_4$ (78.5 mg, 2.07 mmol) was added to a solution of **19** (422.3 mg, 2.06 mmol) in MeOH (60 mL) at rt and stirring was continued for 5 h. After evaporation of the solvent under reduced pressure, the residue was dissolved in CH_2Cl_2. The whole 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 **21a** (398.1 mg, 93%). **21a**: mp 100.0–102.0 ºC (colorless prisms, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3435, 3262, 1433, 1243, 1102, 1079, 1056, 1019, 953, 876, 738 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 3.78 (1H, dd, *J* = 11.3, 7.1 Hz), 3.81 (1H, dd, *J* = 11.3, 5.0 Hz), 4.06 (3H, s), 4.99 (1H, ddd, *J* = 7.1, 5.0, 0.7 Hz), 7.05 (1H, ddd, *J* = 8.1, 7.1, 0.9 Hz), 7.19 (1H, ddd, *J* = 8.1, 7.1, 0.9 Hz), 7.38 (1H, d, *J* = 0.7 Hz), 7.39 (1H, dt, *J* = 8.1, 0.9 Hz), 7.66 (1H, dt, *J* = 8.1, 0.9 Hz). MS *m/z*: 207 (M^+), 176. *Anal*. Calcd for $C_{11}H_{13}NO_3$: C, 63.75; H, 6.32; N, 6.76. Found: C, 63.53; H, 6.21; N, 6.64.

2-Chloro-1-(1-methoxyindol-3-yl)ethanol (21b) from 2a — $NaBH_4$ (10.0 mg, 0.26 mmol) was added to a solution of **2a** (19.7 mg, 0.09 mmol) in MeOH (3.0 mL) and the mixture was stirred at rt for 1.5 h. After addition of H_2O, the whole was extracted with CH_2Cl_2. The extract 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 (99:1, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.47–0.26 with CH_2Cl_2–MeOH (95:5, v/v) afforded **21b** (18.3 mg, 92%). **21b**: pale yellow oil. IR (film): 3385, 2946, 1451, 1352, 1323, 1227, 1098, 1063, 952, 758, 738, 667 cm^{-1}. ^1H-NMR (CD_3OD) δ: 3.82 (1H, dd, J = 11.2, 7.5 Hz), 3.86 (1H, dd, J = 11.2, 4.6 Hz), 4.07 (3H, s), 5.12 (1H, ddd, J = 7.5, 4.6, 0.7 Hz), 7.08 (1H, ddd, J = 8.1, 7.1, 0.9 Hz), 7.21 (1H, ddd, J = 8.2, 7.1, 0.9 Hz), 7.40 (1H, dt, J = 8.2, 0.9 Hz), 7.44 (1H, s), 7.66 (1H, dt, J = 8.1, 0.9 Hz). MS *m/z*: 227 and 225 (M^+), 176. High resolution MS *m/z*: Calcd for $C_{11}H_{12}ClNO_2$: 225.0556. Found: 225.0553.

3-(2-Acetoxy-1-methoxyethyl)- (22a) and 3-(2-Acetoxy-1-hydroxyethyl)-1-methoxyindole (22b) from 21a — Ac_2O (1.0 mL) was added to a solution of **21a** (31.4 mg, 0.15 mmol) in pyridine (2.0 mL) and stirring was continued at rt for 3.5 h. After evaporation of the solvent under reduced pressure, the residue was dissolved in 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 an oil, which was subjected to p-TLC on SiO_2 with EtOAc–hexane (1:2, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.55–0.42 with CH_2Cl_2–MeOH (95:5, v/v) afforded **22a** (14.9 mg, 37%). Extraction of the band having an *Rf* value of 0.24–0.15 with CH_2Cl_2–MeOH (95:5, v/v) afforded **22b** (7.2 mg, 19%). **22a**: pale yellow oil. IR (film): 2942, 1740, 1452, 1365, 1231, 1100, 1036, 952, 738 cm^{-1}. ^1H-NMR (CD_3OD) δ: 2.10 (3H, s), 3.34 (3H, s), 4.10 (3H, s), 4.37 (2H, d, J = 6.0 Hz), 4.75 (1H, t, J = 6.0 Hz), 7.13 (1H, ddd, J = 8.1, 7.1, 1.1 Hz), 7.27 (1H, ddd, J = 8.2, 7.1, 1.1 Hz), 7.27 (1H, s), 7.43 (1H, dt, J = 8.2, 1.1 Hz), 7.72 (1H, dt, J = 8.1, 1.1 Hz). MS *m/z*: 263 (M^+), 190. High resolution MS *m/z*: Calcd for $C_{14}H_{17}NO_4$: 263.1156. Found: 263.1167. **22b**: pale yellow oil. IR (film): 3429, 2937, 1739, 1453, 1374, 1228, 1036, 952, 739 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 2.12 (3H, s), 2.37 (1H, br s, D_2O exchange), 4.09 (3H, s), 4.35 (1H, dd, J = 11.5, 8.3 Hz), 4.45 (1H, dd, J = 11.5, 3.4 Hz), 5.28 (1H, dd, J = 8.3, 3.4 Hz), 7.14 (1H, ddd, J = 8.1, 7.1, 0.9 Hz), 7.27 (1H, ddd, J = 8.2, 7.1, 0.9 Hz), 7.32 (1H, s), 7.43 (1H, dt, J = 8.2, 0.9 Hz), 7.71 (1H, dt, J = 8.1, 0.9 Hz). MS *m/z*: 249 (M^+), 176. High resolution MS *m/z*: Calcd for $C_{13}H_{15}NO_4$: 249.1000. Found: 249.1005.

2-Amino-1-(1-methoxyindol-3-yl)ethanol (23) from 3a — $NaBH_4$ (18.9 mg, 0.49 mmol) was added to a solution of **3a** (49.9 mg, 0.24 mmol) and stirred at rt for 1 h. After addition of H_2O, the whole was extracted with CH_2Cl_2. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil. The residue was purified by column chromatography on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (46:5:0.5, v/v) to afford **23** (36.3 mg, 72%).

23 from 3b — $LiAlH_4$ (10.2 mg, 0.27 mmol) was added to a solution of **3b** (29.3 mg, 0.13 mmol) in dry THF (2.0 mL) and stirred at rt for 1 h. After addition of MeOH under ice cooling, 10% aqueous Rochelle salt was added. The whole was extracted with CH_2Cl_2–MeOH (95:5, v/v) and the extract was washed with brine, dried over Na_2SO_4. After evaporation of solvent the residue was purified by p-TLC with $CHCl_3$–MeOH–28% NH_3 (46:5:0.5, v/v) as a developing solvent to give **23** (12.6 mg, 48%). **23**: mp 124.5–126.0 ℃(colorless needles, recrystallized from CH_2Cl_2). IR (KBr): 3442, 3358, 3131, 2935, 1574, 1451, 1233, 1093, 1062, 1017, 941, 753, 745 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 2.97 (1H, dd, J = 13.1, 6.8 Hz), 3.00 (1H, dd, J = 13.1, 5.5 Hz), 4.07 (3H, s), 4.92 (1H, ddd, J = 6.8, 5.5, 0.7 Hz), 7.06 (1H, ddd, J = 8.1, 7.1, 1.0 Hz), 7.20 (1H, ddd, J = 8.0, 7.1, 1.0 Hz), 7.38 (1H, d, J = 0.4 Hz), 7.40 (1H, dt, J = 8.2, 0.9 Hz), 7.67 (1H, dt, J = 8.0, 0.9 Hz). High resolution MS *m/z*: Calcd for $C_{11}H_{14}N_2O_2$: 206.1054. Found: 206.1062. *Anal*. Calcd for $C_{11}H_{14}N_2O_2 \cdot 1/8H_2O$: C, 63.37; H, 6.89; N, 13.44. Found: C, 63.65; H, 6.86; N, 13.52.

2-Benzoylamino-1-(1-methoxyindol-3-yl)ethanol (24a) from 3b — $LiAlH_4$ (16.8 mg, 0.44 mmol) was added to a solution of **3b** (50.2 mg, 0.22 mmol) in dry THF (5.0 mL) and stirred at rt for 30 min. After addition of MeOH under ice cooling, 10% aq. Rochelle salt was added. The whole was extracted with EtOAc and the extract was washed with brine, dried over Na_2SO_4. After evaporation of solvent the residue was dissolved in dry THF (2.0 mL) and then a solution of benzoyl chloride (31.2 mg, 0.22 mmol) in dry THF (2.0 mL) and NEt_3 (0.15 mL, 1.0 mmol) was added and stirred at rt for 1 h. Water was added and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4. After evaporation of solvent the residue was purified by column chromatography with CH_2Cl_2–MeOH (99:1, v/v) to give **24a** (44.0 mg, 65%). **24a**: mp 100.0–103.0 °C (colorless prisms, recrystallized from CH_2Cl_2-hexane). IR (KBr): 3284, 1631, 1573, 1543, 1329, 1317, 1052, 738, 692 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 3.70 (1H, dd, J = 13.6, 7.9 Hz), 3.86 (1H, dd, J = 13.6, 4.8 Hz), 4.06 (3H, s), 5.22 (1H, ddd, J = 7.9, 4.8, 0.7 Hz), 7.06 (1H, ddd, J = 8.1, 7.1, 1.1 Hz), 7.20 (1H, ddd, J = 8.2, 7.1, 1.1 Hz), 7.40 (1H, dd, J = 8.2, 0.9 Hz), 7.43 (1H, s), 7.41–7.45 (2H, m), 7.51 (1H, ddt, J = 8.2, 6.8, 1.3 Hz), 7.76 (1H, dt, J = 8.1, 0.9 Hz), 7.78–7.81 (2H, m). MS *m/z*: 310 (M^+). *Anal*. Calcd for $C_{18}H_{18}N_2O_3$: C, 69.66; H, 5.85; N, 9.03. Found: C, 69.33; H, 5.77; N, 8.93.

[2-Benzoylamino-1-(1-methoxyindol-3-yl)]ethyl Methyl Ether (24b) from 24a — NH_4Cl (12.4 mg, 0.23 mmol) was added to a solution of **24a** (12.4 mg, 0.04 mmol) in MeOH (1.0 mL) and refluxed for 2 h with stirring. After cooling H_2O was added and the whole was extracted with CH_2Cl_2. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil. The residue was purified by p-TLC on SiO_2 with CH_2Cl_2–MeOH (98:2, v/v) to afford **24b** (6.2 mg, 48%). **24b**: colorless oil. IR (film): 3332, 2943, 1639, 1630, 1317, 1102, 955, 738, 707 cm^{-1}. ^{1}H-NMR (pyridine-d_5) δ: 3.30 (3H, s), 3.92 (3H, s), 4.12 (1H, ddd, J = 13.5, 7.9, 5.5 Hz), 4.21 (1H, dt, J = 13.5, 5.8 Hz), 5.08

(1H, dd, *J* = 7.9, 4.9 Hz), 7.19 (1H, dd, *J* = 7.9, 7.0 Hz), 7.32 (1H, dd, *J* = 8.0, 7.3 Hz), 7.39–7.47 (3H, m), 7.52 (1H, dd, *J* = 8.2 and 0.6 Hz), 7.58 (1H, s), 8.03 (1H, dd, *J* = 8.0, 0.6 Hz), 8.26 (2H, d, *J* = 7.5 Hz), 9.31 (1H, br t, *J* = 5.5 Hz, D_2O exchange). High resolution MS *m/z*: Calcd for $C_{19}H_{20}N_2O_3$: 324.1473. Found: 324.1485.

***N*,*N*-Dimethyl-1-methoxyindol-3-oxalic Amide (27) from 1b —** Oxalyl chloride (958.1 mg, 7.6 mmol) in dry THF (5.0 mL) was added to a solution of 1-methoxyindole (111.3 mg, 0.75 mmol) in dry THF (5.0 mL) and stirred at rt for 1.5 h, then 50% aq. Me_2NH (5.0 mL) was added and stirred for 4 h. Water was added and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was column chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (100:10:5, v/v) to afford **27** (39.3 mg, 21%). **27**: pale yellow oil. IR (film): 3500, 3099, 2950, 1641 (broad), 1514, 1502, 1451, 1364, 1208, 1053, 962, 745 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.08 (3H, s), 3.10 (3H, s), 4.18 (3H, s), 7.35 (1H, td, *J* = 1.0, 8.0 Hz), 7.38 (1H, td, *J* = 1.0, 8.0 Hz), 7.48 (1H, dm, *J* = 8.0 Hz), 8.07 (1H, s), 8.6 (1H, dm, *J* = 8.0 Hz). High resolution MS *m/z*: Calcd for $C_{13}H_{14}N_2O_3$: 246.1002. Found: 246.0999.

1-(1-Methoxyindol-3-yl)-2-(*N*,*N*-dimethylamino)ethanol (28) from 27 — $LiAlH_4$ (191.3 mg, 5.0 mmol) was added to a solution of **27** (378.7 mg, 1.53 mmol) in dry THF (6.0 mL) and refluxed with stirring for 15 min. Water and aq. Rochelle salt were added. The whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was column chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (100:10:5, v/v) to afford **28** (252.3 mg, 70%). **28**: mp 85.0–86.0 °C (colorless needles, recrystallized from EtOAc–hexane). IR (KBr): 3121, 2950, 1449, 1222, 1058, 955, 757 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.40 (6H, s), 2.53 (1H, dd, *J* = 12.3, 3.3 Hz), 2.78 (1H, dd, *J* = 12.3, 11.0 Hz), 4.07 (3H, s), 5.40 (1H, dd, *J* = 11.0, 3.3 Hz), 4.55 (1H, br s, OH), 7.11 (1H, dt, *J* = 1.0, 8.0 Hz), 7.24 (1H, dt, *J* = 1.0, 8.0 Hz), 7.28 (1H, br s), 7.41 (1H, dt, *J* = 8.0, 1.0 Hz), 7.67 (1H, dt, *J* = 8.0, 1.0 Hz). MS *m/z*: 234 (M^+). *Anal.* Calcd for $C_{13}H_{18}N_2O_2$: C, 66.64; H, 7.74; N, 11.96. Found: C, 66.54; H, 7.66; N, 11.93.

3-[2-(*N*-Propargyl)amino]acetyl-1-methoxyindole (29) and *N*,*N*-Bis(1-methoxyindol-3-carbonylmethyl)propargylamine (30) from 2a — Propargylamine (128 mg, 10 eq.) was added to a solution of **2a** (49.9 mg, 0.22 mmol) in MeOH (3.5 mL) and refluxed for 1.8 h with stirring. After evaporation of the solvent, water and 4% aq. NaOH were added. The whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was column chromatographed on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (100:1:0.1, v/v) to afford **29** (32.4 mg, 60%) and **30** (13.5 mg, 14%). **29**: mp 76.0–77.0 °C (colorless prisms, recrystallized from EtOAc–hexane). IR (KBr): 3260, 2110, 1660, 1508, 1370, 1325, 1190, 965, 758 cm^{-1}. ^{1}H-NMR ($CDCl_3$)

δ: 2.24 (1H, t, *J* = 2.5 Hz), 3.60 (2H, d, *J* = 2.5 Hz), 4.09 (2H, s), 4.18 (3H, s), 7.32 (1H, dt, *J* = 7.5, 1.3 Hz), 7.36 (1H, dt, *J* = 7.5, 1.3 Hz), 7.47 (1H, br d, *J* = 7.5 Hz), 8.01 (1H, s), 8.33 (1H, br d, *J* = 7.5 Hz). *Anal*. Calcd for $C_{14}H_{14}N_2O_2$: C, 69.40; H, 5.83; N, 11.56. Found: C, 69.25; H, 5.82; N, 11.42. **30**: 173.0–174.0 °C (colorless prisms, recrystallized from EtOAc–hexane). IR (KBr): 3420, 2120, 1655, 1626, 1310, 1180, 958, 750 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.36 (1H, t, *J* = 2.4 Hz), 3.79 (2H, s), 4.06 (4H, s), 4.16 (6H, s), 7.29–7.35 (4H, m), 7.46 (2H, br d, *J* = 6.7 Hz), 8.40 (2H, br d, *J* = 6.7 Hz), 8.55 (2H, s). High resolution MS *m/z*: Calcd for $C_{25}H_{23}N_3O_4$: 429.1686. Found: 429.1675. *Anal*. Calcd for $C_{25}H_{23}N_3O_4$: C, 69.91; H, 5.40; N, 9.79. Found: C, 69.57; H, 5.48; N, 9.62.

***N*-(1-Methoxyindol-3-carbonylmethyl)-*N*-(phenacyl)propargylamine (31) from 29 —** Phenacyl bromide (262.5 mg, 1.32 mmol) was added to a solution of **29** (30.4 mg, 0.13 mmol) in MeCN (3.0 mL) and stirred at reflux for 2 h. After evaporation of solvent, water was added, then the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was purified by p-TLC on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (100:10:1, v/v) to afford **31** (16.0 mg, 35%). **31**: colorless oil. IR (film): 3280, 3100, 2940, 2110, 1688, 1638, 1517, 1488, 1365, 1320, 1217, 955, 741 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.36 (1H, t, *J* = 2.4 Hz), 3.79 (2H, s), 4.06 (2H, s), 4.16 (3H, s), 4.35 (2H, s), 7.29–7.35 (2H, m), 7.46 (3H, t, *J* = 7.9 Hz), 7.58 (1H, t, *J* = 7.5 Hz), 8.00 (2H, dd, *J* = 8.6, 1.3 Hz), 8.39 (1H, dd, *J* = 7.0, 1.3 Hz), 8.76 (1H, s). High resolution MS *m/z*: Calcd for $C_{22}H_{20}N_2O_3$: 360.1473. Found: 360.1478.

1-(1-Methoxyindol-3-yl)-2-(propargylamino)ethanol (32) from 29 — $NaBH_4$ (16.4 mg, 0.43 mmol) was added to a solution of **29** (50.2 mg, 0.20 mmol) and stirred at rt for 1 h. After addition of H_2O, the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was purified by p-TLC on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (100:10:1, v/v) to afford **32** (37.0 mg, 73%). **32:** mp 95.0–96.0 °C (colorless prisms, recrystallized from CH_2Cl_2-hexane). IR (KBr): 3414, 3280, 3040, 2920, 2810, 2140, 1466, 1448, 1344, 1124, 1104, 1066, 1040 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.23 (1H, t, *J* = 2.5 Hz), 3.07 (1H, dd, *J* = 12.1, 8.6 Hz), 3.17 (1H, dd, *J* = 12.1, 3.9 Hz), 3.51 (2H, d, *J* = 2.4 Hz), 4.07 (3H, s), 5.08 (1H, ddd, *J* = 8.6, 3.9, 0.7 Hz), 7.12 (1H, td, *J* = 7.5, 0.9 Hz), 7.25 (1H, td, *J* = 7.5, 0.9 Hz), 7.30 (1H, s), 7.42 (1H, d, *J* = 8.1Hz), 7.61 (1H, d, *J* = 8.1 Hz). MS *m/z*: 244 (M^+). *Anal*. Calcd for $C_{14}H_{16}N_2O_2 \cdot 1/4H_2O$: C, 67.58; H, 6.68; N, 11.26. Found: C, 67.84; H, 6.44; N, 11.21.

3,4,5-Trimethoxystyrene Oxide (33b) from 3,4,5-Trimethoxybenzaldehyde — Under Ar atmosphere, a solution of trimethylsulfoxonium iodide (8.633 g, 39.2 mmol) in dry THF (30.0 mL) was added to 60% NaH (1.32 g, 33.0 mmol, washed with dry benzene two times) with stirring and the mixture was refluxed for 6 h. To the reaction mixture at 55 °C, a solution of 3,4,5-trimethoxybenzaldehyde (5.886 g, 30.0

mmol) in dry THF (30.0 mL) was added dropwise within 1.5 h with stirring. After additional stirring for 4 h at 55 ºC, H_2O was added and the whole was extracted with CH_2Cl_2. The extract 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 EtOAc–hexane (1:3, v/v) to give **33b** (pale yellow oil, 4.228 g, 57%). Although this sample includes EtOAc and CH_2Cl_2 as impurities (85% pure by ^{1}H-NMR estimation), it was used immediately to the next reaction without further purification.

***N*-[2-Hydroxy-2-(1-methoxyindol-3-yl)]ethyl-*N*-[(2-hydroxy-2-phenyl)ethyl]propargylamine (34) from 31 —** $NaBH_4$ (51.2 mg, 1.35 mmol) was added to a solution of **31** (21.2 mg, 0.05 mmol) in MeOH (2.0 mL) and stirred at rt for 1 h. After addition of H_2O, the whole was extracted with EtOAc. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was purified by column chromatography on SiO_2 with EtOAc–hexane (1:1, v/v) to give **34** (16.2 mg, 75%). **34**: colorless oil. IR (KBr): 3390, 3330, 3060, 2940, 2850, 2140, 1493, 1452, 1320, 1123, 1101, 1064 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.26 (1H, dd, J = 6.3, 2.3 Hz), 2.82 (1H, dd, J = 13.4, 9.8 Hz), 2.99–3.23 (3H, m), 3.64–3.83 (2H, m), 4.07 (3H, d, J = 1.8 Hz), 4.88 (1H, ddd, J = 28.9, 9.8, 3.3 Hz), 5.19 (1H, ddd, J = 20.6, 9.8, 3.3 Hz), 7.12 (1H, t, J = 7.5 Hz), 7.24–7.27 (3H, m), 7.32 (1H, d, J = 3.3 Hz), 7.34–7.40 (3H, m), 7.42 (1H, dd, J = 8.0, 0.9 Hz), 7.80 (1H, dd, J = 8.0, 0.9 Hz). High resolution MS *m/z*: Calcd for $C_{22}H_{24}N_2O_3$: 364.1787. Found: 364.1782.

34 from 32 — Styrene oxide (269.3 mg, 2.24 mmol) was added to a solution of **32** (50.1 mg, 0.21 mmol) in MeCN (5.0 mL) and refluxed for 2 h with stirring. After addition of H_2O, the whole was extracted with EtOAc. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was purified by column chromatography on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (100:5:0.5, v/v) to give **34** (43.4 mg, 58%).

(±)-2,6-*cis*-2-(1-Methoxyindol-3-yl)-6-phenyl-4-propargylmorpholine (35) from 34 — Aq. 6% HCl (4.0 mL) was added to a solution of **34** (40.2 mg, 0.11 mmol) in MeOH (4.0 mL) and stirred at rt for 20 min. After addition of H_2O, the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was purified by column chromatography on SiO_2 with EtOAc–hexane to afford **35** (26.6 mg, 70%). **35**: colorless oil. IR (KBr): 3295, 3080, 2950, 2820, 2120, 1455, 1322, 1305, 1220, 1082, 1050 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.27 (1H, s), 2.46 (1H, t, J = 10.7 Hz), 2.69 (1H, t, J = 10.7 Hz), 3.06 (1H, d, J = 11.5 Hz), 3.12 (1H, d, J = 11.5 Hz), 3.43 (2H, d, J = 1.2 Hz), 4.08 (3H, s), 4.89 (1H, d, J = 9.7 Hz), 5.15 (1H, d, J = 9.7 Hz), 7.14 (1H, td, J = 7.0, 0.9 Hz), 7.23–7.30 (3H, m), 7.33–7.37 (3H, m), 7.42 (1H, d, J = 8.1 Hz), 7.46 (1H, dd, J = 8.1, 1.5 Hz), 7.77 (1H, d, J = 8.1 Hz). High resolution MS *m/z*: Calcd for $C_{22}H_{22}N_2O_2$: 346.1679. Found: 346.1676.

***N*-[2-Hydroxy-2-(1-methoxyindol-3-yl)ethy)]-*N*-[(2-hydroxy-2-phenyl)ethyl]amine (36a) from 23 —** A solution of styrene oxide (**33a**, 1.497 g, 12.46 mmol) in MeCN (4.0 mL) was added to a solution of **23** (128.7 mg, 0.62 mmol) in MeCN (4.0 mL) and the mixture was refluxed for 24 h with stirring. After addition of sat. aq. $NaHCO_3$, the whole was extracted with EtOAc. The extract 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_3 (46:2:0.2, v/v) to give **36a** (115.8 mg, 57%) and **23** (6.1 mg, 5%) in the order of elution. **36a**: colorless oil, mixture of diastereomers. IR (film): 3296, 3050, 2934, 1452, 1062, 951, 737, 699 cm^{-1}. ^1H-NMR (CD_3OD) δ: 2.84–3.20 (4H, m), 4.056 and 4.059 (3H, s), 4.81 (1H, dd, *J* = 8.3, 4.6 Hz), 5.09–5.13 (1H, m), 7.070 and 7.072 (1H, ddd, *J* = 8.3, 7.3, 0.9 Hz), 7.20 and 7.21 (1H, ddd, *J* = 8.3, 7.3, 1.0 Hz), 7.23–7.27 (1H, m), 7.29–7.37 (4H, m), 7.39 (1H, s), 7.39 and 7.40 (1H, dt, *J* = 8.2 and 0.9 Hz), 7.683 and 7.689 (1H, dt, *J* = 7.9, 0.9 Hz). Chemical ionization MS *m/z*: 327 (M^++1), 309.

***N*-[2-Hydroxy-2-(1-methoxyindol-3-yl)ethyl]-*N*-[(2-hydroxy-3,4,5-trimethoxyphenyl)ethyl]amine (36b) and *N*-[2-Hydroxy-2-(1-methoxyindol-3-yl)ethyl]-*N*-[1-hydroxymethyl-1-(3,4,5-trimethoxyphenyl)]amine (37) from 23 —** A solution of **33b** (85% content, 1.585 g, 6.42 mmol) in MeCN (6.0 mL) was added to a solution of **23** (131.9 mg, 0.64 mmol) in MeCN (4.0 mL) and the mixture was refluxed for 24 h with stirring. After addition of sat. aq. $NaHCO_3$, the whole was extracted with EtOAc. The extract 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 (from 100:0 to 50:50, v/v) to give **23** (4.9 mg, 4%), **36b** (50.5 mg, 19%), and **37** (56.3 mg, 21%). **36b**: colorless oil, mixture of diastereomers. IR (film): 3342, 2938, 2838, 1593, 1505, 1454, 1419, 1328, 1231, 1123, 1006, 740 cm^{-1}. ^1H-NMR (CD_3OD) δ: 2.80–2.91 (2H, m), 2.99–3.13 (2H, m), 3.724 (6/3H, s), 3.728 (3/3H, s), 3.810 (12/3H, s), 3.814 (6/3H, s), 4.048 (6/3H, s), 4.054 (3/3H, s), 4.71–4.74 (1H, m), 5.08–5.10 (1H, m), 6.66 (2H, s), 7.061 and 7.063 (1H, ddd, *J* = 8.1, 7.1, 0.9 Hz), 7.201 and 7.203 (1H, ddd, *J* = 8.1, 7.1, 0.9 Hz), 7.37 and 7.38 (1H, s), 7.38 and 7.39 (1H, dt, *J* = 8.2, 0.9 Hz), 7.675 and 7.679 (1H, dt, *J* = 8.1, 0.9 Hz). Chemical ionization MS *m/z*: 417 (M^++1), 399, 210. **37**: colorless oil, mixture of diastereomers. IR (film): 3342, 2938, 2842, 1594, 1507, 1456, 1422, 1328, 1234, 1124, 1006, 737 cm^{-1}. ^1H-NMR (CD_3OD) δ: 2.84–2.93 (2H, m), 3.56 (3/7H, dd, *J* = 10.8, 8.6 Hz), 3.57 (4/7H, dd, *J* = 11.0, 8.2 Hz), 3.65 (4/7H, dd, *J* = 10.8, 4.8 Hz), 3.66 (3/7H, dd, *J* = 10.8, 4.6 Hz), 3.73 (12/7H, s), 3.74 (3/7H, dd, *J* = 8.6, 4.6 Hz), 3.75 (9/7H, s), 3.78 (24/7H, s), 3.79 (18/7H, s) 3.83 (4/7H, dd, *J* = 8.2, 4.8 Hz), 4.040 (12/7H, s), 4.044 (9/7H, s), 5.03 (4/7H, ddd, *J* = 7.4, 5.5, 0.6 Hz), 5.11 (3/7H, ddd, *J* = 7.0, 5.5, 0.6 Hz), 6.65 (8/7H, s), 6.68 (6/7H, s), 7.00 (3/7H, ddd, *J* = 8.1, 7.1, 1.1 Hz), 7.01 (4/7H, ddd, *J* = 8.1, 7.1, 1.1 Hz), 7.18 (1H, ddd, *J* = 8.2, 7.1, 1.1 Hz), 7.34 and 7.37 (1H, s), 7.37 (1H, d, *J* = 7.5 Hz), 7.50 (3/7H, dt, *J* = 8.1, 0.9 Hz), 7.53 (4/7H, dt, *J* = 8.1, 0.9 Hz). Chemical ionization MS *m/z*: 417 (M^++1), 399, 211.

(±)-2,6-*cis*-2-(1-Methoxyindol-3-yl)-6-phenylmorpholine (38a) from 36a — 6% HCl (5.0 mL) was added to a solution of **36a** (115.8 mg, 0.35 mmol) in MeOH (5.0 mL) and the mixture was stirred at rt for 1 h. After addition of sat. aq. $NaHCO_3$, the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract 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) as an eluent to give **38a** (80.9 mg, 74%). **38a**: colorless hard oil. IR (film): 3297, 3054, 2935, 2831, 1454, 1333, 1229, 1062, 954, 738, 698 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 2.77 (1H, dd, *J* = 12.9, 10.6 Hz), 3.04 (1H, dd, *J* = 12.9, 10.6 Hz), 3.08 (1H, ddd, *J* = 12.9, 2.4, 1.0 Hz), 3.13 (1H, ddd, *J* = 12.9, 2.8, 1.0 Hz), 4.07 (3H, s), 4.75 (1H, dd, *J* = 10.6, 2.4 Hz), 4.99 (1H, ddd, *J* = 10.6, 2.8, 0.7 Hz), 7.09 (1H, ddd, *J* = 8.1, 7.1, 1.0 Hz), 7.21 (1H, ddd, *J* = 8.2, 7.1, 1.1 Hz), 7.25–7.29 (1H, m), 7.32–7.36 (2H, m), 7.40 (1H, dt, *J* = 8.1, 0.9 Hz), 7.42–7.44 (2H, m), 7.46 (1H, s), 7.75 (1H, dt, *J* = 8.1, 0.9 Hz). High resolution MS *m/z*: Calcd for $C_{19}H_{20}N_2O_2$: 308.1524. Found: 308.1526.

(±)-2,6-*cis*-2-(Indol-3-yl)-6-phenylmorpholine (38b) from 38a — 10% Pd/C (29.7 mg) was added to a solution of **38a** (29.6 mg, 0.09 mmol) in MeOH (10.0 mL) and the mixture was hydrogenated at rt and 1 atm for 4 h. After precipitates were filtered off, the filtrate was washed with MeOH. The combined filtrate and washings were evaporated under reduced pressure to leave an oil, which was subjected to p-TLC on SiO_2 with $CHCl_3$–MeOH–28% NH_3 (46:5:0.5, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.88–0.56 with CH_2Cl_2–MeOH (95:5, v/v) afforded **38a** (2.3 mg, 8%). Extraction of the band having an *Rf* value of 0.42–0.25 with CH_2Cl_2–MeOH (95:5, v/v) afforded **38b** (13.5 mg, 51%). **38b**: colorless hard oil. IR (KBr): 3396, 3292, 3049, 2911, 2842, 1451, 1259, 1083, 1058, 801, 741, 697 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 2.81 (1H, dd, *J* = 12.8, 10.8 Hz), 3.12 (1H, ddd, *J* = 12.8, 2.8, 0.6 Hz), 3.14 (1H, dd, *J* = 12.8, 9.2 Hz), 3.17 (1H, ddd, *J* = 12.8, 4.0, 0.7 Hz), 4.79 (1H, dd, *J* = 10.8, 2.5 Hz), 5.05 (1H, ddd, *J* = 9.2, 4.3, 0.6 Hz), 7.04 (1H, ddd, *J* = 8.1, 7.0, 1.1 Hz), 7.11 (1H, ddd, *J* = 8.1, 7.0, 1.1 Hz), 7.28 (1H, s), 7.25–7.29 (1H, m), 7.32–7.36 (2H, m), 7.36 (1H, dt, *J* = 8.1, 0.9 Hz), 7.43–7.46 (2H, m), 7.75 (1H, dt, *J* = 7.9, 1.0 Hz). High resolution MS *m/z*: Calcd for $C_{18}H_{18}N_2O$: 278.1418. Found: 278.1422.

2,6-*cis*-2-(1-Methoxyindol-3-yl)-6-(3,4,5-trimethoxyphenyl)morpholine (39a) from 36b — 6% HCl (2.5 mL) was added to a solution of **36b** (55.8 mg, 0.13 mmol) in MeOH (2.5 mL) and the mixture was stirred at rt for 30 min. After addition of sat. aq. $NaHCO_3$, the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract 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 (97:3, v/v) to give **39a** (47.6 mg, 89%). **39a**: colorless oil. IR (film): 2946, 2850, 1593, 1507, 1454, 1418, 1329, 1234, 1123, 1100, 1006, 738 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 2.76 (1H, dd, *J* = 12.8, 10.6 Hz), 3.07 (1H, dd, *J* = 12.8, 10.6 Hz), 3.09 (1H, ddd, *J* = 12.8, 2.6, 0.8 Hz), 3.13 (1H, ddd, *J* = 12.8, 2.8, 0.7 Hz), 3.74 (3H, s), 3.83 (6H, s), 4.08 (3H, s), 4.71 (1H, dd, *J* = 10.6, 2.6 Hz), 4.99 (1H, ddd, *J* = 10.6, 2.9, 0.6 Hz), 6.75 (2H, s), 7.08 (1H, ddd, *J* = 8.1, 7.1, 1.0 Hz), 7.22 (1H, ddd, *J* = 8.2, 7.1, 1.0 Hz), 7.42 (1H, dt, *J* = 8.2, 0.9 Hz), 7.47 (1H, s), 7.80 (1H, dt, *J* = 8.0, 0.9 Hz). High resolution MS *m/z*: Calcd for $C_{22}H_{26}N_2O_5$: 398.1840. Found: 398.1837.

(±)-Chelonin A ((±)-39b) from 39a — 10% Pd/C (45.6 mg) was added to a solution of **39a** (46.2 mg, 0.11 mmol) in MeOH (30.0 mL) and the mixture was hydrogenated at rt and 1 atm for 4 h. After precipitates were filtered off, the filtrate was washed with MeOH. The combined filtrate and washings were 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 (±)-**39b** (25.5 mg, 60%). (±)-**39b**: mp 161.0–162.0 °C (colorless prisms, recrystallized from EtOAc–hexane). UV (MeOH) λ max nm: 287, 276, 270, 206. IR (KBr): 3373, 1592, 1508, 1458, 1421, 1332, 1227, 1122, 1089, 997, 748 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 2.80 (1H, dd, *J* = 13.0, 10.6 Hz), 3.14 (1H, dd, *J* = 13.0, 2.6 Hz), 3.18 (2H, dd, *J* = 13.4, 7.0 Hz), 3.73 (3H, s), 3.82 (6H, s), 4.74 (1H, dd, *J* = 10.6, 2.4 Hz), 5.04 (1H, t, *J* = 6.6 Hz), 6.76 (2H, s), 7.03 (1H, ddd, *J* = 8.0, 7.0, 1.0 Hz), 7.11 (1H, ddd, *J* = 8.1, 7.0, 1.1 Hz), 7.28 (1H, s), 7.36 (1H, dt, *J* = 8.2, 0.9 Hz), 7.79 (1H, dt, *J* = 8.1, 0.9 Hz). ^{13}C-NMR (CD_3OD) δ: 51.0, 52.7, 56.6, 61.1, 75.0, 79.9, 104.4, 112.5, 115.1, 120.0, 120.3, 122.7, 123.3, 127.3, 137.6, 138.2, 138.5, 154.4. MS *m/z*: 368 (M^+), 194, 143. *Anal*. Calcd for $C_{21}H_{24}N_2O_4$: C, 68.46; H, 6.57; N, 7.60. Found: C, 68.17; H, 6.59; N, 7.49. [lit.,[7] (+)-**39b**: mp 182 °C (white crystals, recrystallized from MeOH). UV (MeOH) λ max nm (log ε): 288 (5100), 278 (6400), 272 (6300), 213 (37100). IR ($CHCl_3$): 3480, 1595, 1510, 1505, 1465, 1455, 1420, 1335, 1130, 1095 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 2.74 (dd, 1H, *J* = 12.8, 10.6 Hz), 3.08 (1H, dd, 1H, *J* = 12.8, 2.4 Hz), 3.11 (2H, br d, *J* = 6.8 Hz), 3.73 (3H, s), 3.82 (6H, s), 4.70 (1H, dd, *J* = 10.6, 2.4 Hz), 5.00 (1H, br t, *J* = 6.8 Hz), 6.74 (2H, s), 7.01 (1H, ddd, *J* = 6.9, 6.9, 1.2 Hz), 7.10 (1H, ddd, *J* = 7.0, 6.9, 1.0 Hz), 7.25 (1H, s), 7.35 (1H, dd, *J* = 7.0, 1.2 Hz), 7.77 (1H, dd, *J* = 6.9, 1.0 Hz). 50 MHz ^{13}C-NMR (CD_3OD) δ: 51.1 (t), 52.8 (t), 56.5 (q), 61.1 (q), 75.1 (d), 80.0 (d), 104.4 (d), 112.6 (d), 115.3 (s), 120.1 (d), 120.5 (d), 122.7 (d), 123.3 (d), 127.3 (s), 137.8 (s), 138.1 (s), 138.4 (s), 154.4 (s). High resolution MS *m/z*: Calcd for $C_{21}H_{24}N_2O_4$: 368.1736. Found: 368.1713.

2,5-*trans*-2-(1-Methoxyindol-3-yl)-5-(3,4,5-trimethoxyphenyl)morpholine (40a) from 37 — 6% HCl (3.0 mL) was added to a solution of **37** (71.1 mg, 0.17 mmol) in MeOH (3.0 mL) and the mixture was stirred at rt for 30 min. After addition of sat. aq. $NaHCO_3$, the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract 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 (98:2, v/v) to give **40a** (55.1 mg, 81%). **40a**: mp 124.0–126.0 °C (colorless prisms, recrystallized from EtOAc–hexane). UV (MeOH) λ max nm: 296, 286, 271, 205. IR (KBr): 3423, 3308, 2946, 2842, 1590, 1508, 1453, 1424, 1338, 1226, 1128, 1081, 1004, 740 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 3.23 (1H, dd, *J* = 12.5, 9.5 Hz), 3.27 (1H, dd, *J* = 12.5, 3.5 Hz), 3.66–3.72 (1H, m, D_2O addition, change to dd, *J* = 12.3, 11.0 Hz), 3.75 (3H, s), 3.88 (6H, s), 3.97–4.02 (2H, m, D_2O addition, change to 1H, dd, *J* = 11.0, 3.1 Hz and 1H, dd, *J* = 12.3, 3.1 Hz), 4.08 (3H, s), 4.90 (1H, dd, *J* = 9.5, 3.5 Hz), 6.79 (2H, s), 7.09 (1H, ddd, *J* = 8.1, 7.1, 1.0 Hz), 7.22 (1H, ddd, *J* = 8.2, 7.1, 0.9 Hz), 7.42 (1H, dt, *J* = 8.2, 0.9 Hz), 7.45 (1H, s), 7.72 (1H, dt, *J* = 8.1, 0.9 Hz). MS *m/z*: 398 (M$^+$), 367, 194, 173. *Anal*. Calcd for $C_{22}H_{26}N_2O_5$: C, 66.32; H, 6.58; N, 7.03. Found: C, 66.29; H, 6.58; N, 6.99.

(±)-2,5-*trans*-2-(Indol-3-yl)-5-(3,4,5-trimethoxyphenyl)morpholine ((±)-40b) from 40a — 10% Pd/C (49.2 mg) was added to a solution of **40a** (48.5 mg, 0.12 mmol) in MeOH (30.0 mL) and the mixture was hydrogenated at rt and 1 atm for 3 h. After precipitates were filtered off, the filtrate was washed with MeOH. The combined filtrate and washings were evaporated under reduced pressure to leave an oil, which was column chromatographed on SiO_2 with CH_2Cl_2–MeOH (98:2, v/v) to give (±)-**40b** (25.4 mg, 57%). (±)-**40b**: mp 105.0–107.0 °C (white crystals, recrystallized from EtOAc–hexane). UV (MeOH) λ max nm: 288, 277, 270, 207. IR (KBr): 3389, 2939, 2843, 1591, 1505, 1457, 1419, 1334, 1227, 1121, 1001, 743 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 3.26 (1H, dd, *J* = 12.5, 2.9 Hz), 3.32 (1H, dd, *J* = 12.5, 10.3 Hz), 3.71 (1H, dd, *J* = 11.7, 11.2 Hz), 3.75 (3H, s), 3.88 (6H, s), 3.98–4.03 (2H, m), 4.94 (1H, dd, *J* = 10.3, 2.9 Hz), 6.80 (2H, s), 7.04 (1H, ddd, *J* = 7.9, 7.0, 1.0 Hz), 7.11 (1H, ddd, *J* = 8.2, 7.1, 1.1 Hz), 7.27 (1H, s), 7.36 (1H, dt, *J* = 8.1, 1.0 Hz), 7.71 (1H, dt, *J* = 7.8, 1.0 Hz). MS *m/z*: 368 (M$^+$), 194, 143. *Anal*. Calcd for $C_{21}H_{24}N_2O_4$: C, 68.46; H, 6.57; N, 7.60. Found: C, 68.25; H, 6.61; N, 7.45

5-Bromo-1-methoxyindole (42a) from 5-Bromo-2,3-dihydroindole (41a) — A solution of $Na_2WO_4 \cdot 2H_2O$ (1.69g, 0.2 eq.) in H_2O (25.0 mL) was added to a solution of **41a** (5.012 g, 25.3 mmol) in MeOH (250.0 mL) and then 30% aq. H_2O_2 (8.62 g, 10 eq.) was added with stirring at rt. Stirring was continued for 30 min and then K_2CO_3 (14.06 g, 4.0 eq.) and Me_2SO_4 (6.40 g, 2.0 eq.) were added. After stirring at rt for 1.5 h, water was added. The whole was extracted with CH_2Cl_2. The extract 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 (1:2, v/v) to give **42a** (3.424 g, 60%). **42a**: colorless oil. IR (film): 2910, 1562, 1452, 1077, 1039, 890, 790, 704, 589 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 4.04 (3H, s), 6.27 (1H, dd, *J* = 3.5, 0.7 Hz), 7.22 (1H, d, *J* = 3.5Hz), 7.28 (1H, ddd, *J* = 8.6, 0.7, 0.7 Hz), 7.30 (1H, dd, *J* = 8.6, 1.7 Hz), 7.70 (1H, dd, *J* = 1.7, 0.7 Hz). High resolution MS *m/z*: Calcd for C_9H_8BrNO: 226.9769, 224.9789. Found: 226.9723, 224.9776.

5,7-Dibromo-1-methoxyindole (42b) from 5,7-Dibromo-2,3-dihydroindole (41b) — A solution of

$Na_2WO_4 \cdot 2H_2O$ (23.6 mg, 0.2 eq.) in H_2O (1.0 mL) was added to a solution of **41b** (98.6 mg, 0.36 mmol) in MeOH (8.0 mL) and then 30% aq. H_2O_2 (121.9 mg, 10 eq.) was added with stirring at rt. Stirring was continued for 30 min and then K_2CO_3 (14.06 g, 4.0 eq.) and Me_2SO_4 (6.40 g, 2.0 eq.) were added. After stirring at rt for 2 h, water was added. The whole was extracted with CH_2Cl_2. The extract 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) to give **42b** 16.6 mg, 17%). **42b**: colorless oil. IR (film): 2929, 1549, 1452, 1401, 1329, 1302, 1253, 1186, 1091, 1039, 960, 930, 838, 734, 705, 631, 578 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 4.10 (3H, s), 6.31 (1H, d, $J = 3.5$ Hz), 7.28 (1H, d, $J = 3.5$ Hz), 7.51 (1H, d, $J = 1.7$ Hz), 7.64 (1H, d, $J = 1.7$ Hz). High resolution MS *m/z*: Calcd for $C_9H_7Br_2NO$: 302.8895. Found: 302.8890.

5-Bromo-3-(2-chloroacetyl)-1-methoxyindole (43a) from 42a — A solution of chloroacetyl chloride (2.563 g, 22.7 mmol) in dry benzene (5.0 mL) was added to a solution of **42a** (509.4 mg, 2.25 mmol) in dry benzene (10.0 mL) and the mixture was refluxed for 20 h. After cooling, water and 8% aq. NaOH were added and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract 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 (2:1, v/v) to give **43a** (331.9 mg, 48%). **43a**: mp 124.0–124.5 °C (colorless needles, recrystallized from MeOH). IR (KBr): 3090, 3000, 2930, 1857, 1759, 1667, 1562, 1510, 1450, 1391, 1361, 1193, 1136, 1057, 959, 782, 693 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 4.19 (3H, s), 4.45 (2H, s), 7.35 (1H, d, $J = 8.8$ Hz), 7.46 (1H, dd, $J = 8.8$, 1.8 Hz), 8.01 (1H, s), 8.52 (1H, d, $J = 1.8$ Hz). MS *m/z*: 305, 303, 301 (M^+). *Anal.* Calcd for $C_{11}H_9BrClNO_2$: C, 43.67; H, 3.00; N, 4.63. Found: C, 43.73; H, 3.20; N, 4.57

5-Bromo-3-dichloroacetyl-1-methoxyindole (43b) from 42a — Dichloroacetyl chloride (794.6 mg, 5.39 mmol) in dry benzene (1.0 mL) was added to a solution of **42a** (119.0 mg, 0.53 mmol) in dry benzene (2.0 mL) and refluxed with stirring for 13 h. Water and 8% aq. NaOH were added and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was purified by column chromatography on SiO_2 with CH_2Cl_2–hexane (1:1, v/v) to give **43b** (159.0 mg, 90%). **43b**: mp 157.0–157.5 °C (colorless prisms, recrystallized from MeOH). IR (KBr): 3130, 1668, 1523, 1465, 1377, 1048, 953, 790, 699 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 4.21 (3H, s), 6.28 (1H, s), 7.37 (1H, dd, $J = 8.6$, 0.5 Hz), 7.48 (1H, dd, $J = 8.6$, 1.8 Hz), 8.28 (1H, s), 8.55 (1H, dd, $J = 1.8$, 0.5 Hz). *Anal.* Calcd for $C_{11}H_8BrCl_2NO_2$: C, 39.20; H, 2.39; N, 4.16. Found: C, 39.18; H, 2.52; N, 4.07.

5,7-Dibromo-3-dichloroacetyl-1-methoxyindole (43c) from 42b — Dichloroacetyl chloride (152.5 mg, 1.03 mmol) in dry benzene (1.0 mL) was added to a solution of **42b** (29.4 mg, 0.09 mmol) in dry benzene

(1.0 mL) and refluxed with stirring for 16 h. Water and 8% aq. NaOH were added and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was purified by column chromatography on SiO_2 with CH_2Cl_2–hexane (1:2, v/v) to give **43c** (13.9 mg, 35%). **43c**: mp 164.0–166.0 °C (colorless plates, recrystallized from benzene–hexane). IR (KBr): 3423, 3123, 3008, 1651, 1603, 1551, 1515, 1449, 1431, 1405, 1368, 1345, 1326, 1285, 1191, 1150, 1081, 1061, 982, 947, 846, 788, 763, 668, 479 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 4.23 (3H, s), 6.26 (1H, s), 7.67 (1H, d, J = 1.8 Hz), 8.32 (1H, s), 8.55 (1H, d, J = 1.8 Hz). *Anal.* Calcd for $C_{11}H_7Br_2Cl_2NO_2$: C, 31.77; H, 1.70; N, 3.37. Found: C, 31.84; H, 1.64; N, 3.31.

Bis(5-bromo-1-methoxyindol-3-carbonylmethyl)imidazolium Chloride (44) from 43a — 43a (32.3 mg, 0.10 mmol) was added to a solution of **45** (23.7 mg, 0.07 mmol) in MeOH (5.0 mL) and refluxed with stirring for 34 h. After evaporation of solvent the residue was column chromatographed on SiO_2 with CH_2Cl_2–MeOH (4:1, v/v) to give **44** (24.4 mg, 54%). **44**: mp 203.0–204.5 °C (colorless prisms, recrystallized from MeOH). IR (KBr): 3395, 3085, 3028, 1661, 1513, 1370, 1339, 1142, 1058 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 4.24 (6H, s), 5.90 (4H, s), 7.57 (2H, dd, J = 8.0, 1.8 Hz), 7.68 (2H, dd, J = 8.6, 0.5 Hz), 7.81 (2H, d, J = 1.4 Hz), 8.32 (2H, dd, J = 1.8, 0.5 Hz), 9.10 (2H, s), 9.17 (1H, t, J = 1.4 Hz). *Anal.* Calcd for $C_{25}H_{21}Br_2ClN_4O_4$: C, 47.16; H, 3.32; N, 8.80. Found: C, 47.12; H, 3.48; N, 8.74.

5-Bromo-3-[2-(imidazol-1-yl)acetyl]-1-methoxyindole (45) from 43a — Imidazole (676.2 mg, 9.93 mmol) was added to a solution of **43a** (298.3 mg, 0.97 mmol) in MeOH (6.0 mL) and refluxed with stirring for 5 h. Water was added and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to give crystalline solid, which was purified by column chromatography on SiO_2 with CH_2Cl_2–MeOH (95:5, v/v) to give **45** (292.9 mg, 89%). **45**: mp 184.5–186.5 °C (colorless needles, recrystallized from EtOAc). IR (KBr): 3128, 2967, 1660, 1512, 1339, 1190, 960 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 4.16 (3H, s), 5.17 (2H, s), 7.03 (1H, s), 7.17 (1H, s), 7.35 (1H, d, J = 8.6 Hz), 7.47 (1H, ddd, J = 8.6, 1.6, 0.7 Hz), 7.62 (1H, s), 7.64 (1H, s), 8.53 (1H, d, J = 1.6 Hz). *Anal.* Calcd for $C_{14}H_{12}BrN_3O_2$: C, 50.32; H, 3.62; N, 12.57. Found: C, 50.50; H, 3.58; N, 12.45.

2-Acetamino-4-(5-bromo-1-methoxyindol-3-yl)thiazole (46) from 43a — Thiourea (110.1 mg, 1.45 mmol) was added to a solution of **43a** (272.6 mg, 0.90 mmol) in MeOH (6.0 mL) and refluxed with stirring for 1.5 h. Water and 8% aq. NaOH were added and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave the residue. To the residue was added Ac_2O (5.0 mL) and stirred at rt for 18 h. Then water was added and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to give crystalline solid.

Recrystallization from MeOH afforded **46** (254.2 mg, 77%). **46**: mp 180.0–181.0 °C (colorless prisms, recrystallized from MeOH). IR (KBr): 3190, 3095, 3017, 1643, 1572, 1550, 1298, 1229, 789 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.09 (3H, s), 4.12 (3H, s), 7.00 (1H, s), 7.35 (1H, dd, *J* = 8.6, 0.4 Hz), 7.39 (1H, dd, *J* = 8.6, 1.8 Hz), 7.67 (1H, s), 8.19 (1H, d, *J* = 1.8 Hz), 9.85 (1H, br s). *Anal.* Calcd for $C_{14}H_{12}BrN_3O_2S$: C, 45.91; H, 3.30; N, 11.47. Found: C, 45.99; H, 3.21; N, 11.42.

2-Diaminomethyleneamino-4-(5-bromo-1-methoxyindol-3-yl)thiazole (47) from 43a — Guanylthiourea (38.4 mg, 2 eq.) was added to a solution of **43a** (49.0 mg, 0.16 mmol) in MeOH 2.0 mL) and refluxed with stirring for 3 h. Water and 8% aq. NaOH were added and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract 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_3 (50:5:0.5, v/v) to give **47** (53.2 mg, 90%). **47**: mp 145.5–146.5 °C (pale brown prisms, recrystallized from MeOH). IR (KBr): 3410, 3109, 1639, 1610, 1539, 1450, 1438, 1248 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 4.13 (3H, s), 6.83 (1H, s), 7.35 (1H, dd, *J* = 8.6, 1.6 Hz), 7.39 (1H, dd, *J* = 8.6, 0.4 Hz), 7.87 (1H, s), 8.11 (1H, dd, *J* = 1.6, 0.4 Hz). *Anal.* Calcd for $C_{13}H_{12}BrN_5OS$: C, 42.63; H, 3.30; N, 19.12. Found: C, 42.75; H, 3.26; N, 18.92.

2-(5-Bromo-1-methoxyindol-3-yl)quinoxaline (48a) and 2-(5-Bromoindol-3-yl)quinoxaline (48b) from 43a — *o*-Phenylenediamine (54.7 mg, 3 eq.) was added to a solution of **43a** (50.0 mg, 0.17 mmol) in benzene (2.0 mL) and refluxed with stirring for 4 h. Water and sat. aq. $NaHCO_3$ were added and the whole was extracted with CH_2Cl_2–MeOH (9:1, v/v). The extract 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 EtOAc to give **48a** (20.0 mg, 34%) and **48b** (30.4 mg, 52%) in the order of elution. **48a**: mp 182.0–183.0 °C (yellow needles, recrystallized from MeOH). IR (KBr): 3075, 1553, 1449, 1373, 993, 792, 760 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 4.22 (3H, s), 7.41 (1H, dd, *J* = 8.6, 0.6 Hz), 7.48 (1H, dd, *J* = 8.6, 1.8 Hz), 7.68 (1H, ddd, *J* = 8.5, 6.9, 1.5 Hz), 7.77 (1H, ddd, *J* = 8.5, 6.9, 1.5 Hz), 8.06 (1H, dd, *J* = 8.5, 1.5 Hz), 8.07 (1H, s), 8.17 (1H, dd, *J* = 8.5, 1.5 Hz), 8.96 (1H, dd, *J* = 1.8, 0.6 Hz), 9.14 (1H, s). *Anal.* Calcd for $C_{17}H_{12}BrN_3O$: C, 57.65; H, 3.41; N, 11.86. Found: C, 57.68; H, 3.28; N, 11.73. **48b**: mp 245.0–246.0 °C (colorless plates, recrystallized from MeOH). IR (KBr): 3155, 3095, 2948, 1548. 1438, 1167 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 7.35 (1H, dd, *J* = 8.5, 1.5 Hz), 7.39 (1H, dd, *J* = 8.5, 0.5 Hz), 7.68 (1H, ddd, *J* = 8.4, 6.9, 1.4 Hz), 7.78 (1H, ddd, *J* = 8.4, 6.9, 1.4 Hz), 7.97 (1H, dd, *J* = 8.4, 1.4 Hz), 8.08 (1H, ddd, *J* = 8.4, 1.4, 0.5 Hz), 8.30 (1H, s), 8.93 (1H, dd, *J* = 1.5, 0.5 Hz), 9.25 (1H, s). *Anal.* Calcd for $C_{16}H_{10}BrN_3$: C, 59.27; H, 3.11; N, 12.96. Found: C, 59.27; H, 3.22; N, 12.95.

5-Chloro- (50a) and 7-Chloro-*N*b-methoxycarbonyltryptamine from 49 — *c*-HCl (1.0 mL) was added to a solution of **49** (53.2 mg, 0.22 mmol) in MeCN (2.0 mL) and stirred at 80 °C for 1 h. Sat. aq. $NaHCO_3$

was added and then the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was purified by column chromatography on SiO_2 with EtOAc–hexane (1:2, v/v) to give 7-chloro-*N*b-methoxycarbonyltryptamine (2.7 mg, 5%) and **50b** (34.8 mg, 61%) in the order of elution. **50a**: colorless oil. IR (film): 3320, 2930, 1701, 1524, 1460, 1259, 1096, 794 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.79 (2H, t, J = 7.4 Hz), 3.22 (2H, dt, J = 7.4, 5.9 Hz), 3.53 (3H, s), 7.05 (1H, dd. J = 8.6, 2.0 Hz), 7.19 (1H, br t, J = 5.9 Hz), 7.22 (1H, d, J = 2.4 Hz), 7.35 (1H, d, J = 8.6 Hz), 7.54 (1H, d, J = 2.0 Hz). High resolution MS *m/z*: Calcd for $C_{12}H_{13}ClN_2O_2$: 254.0636, 252.0666. Found: 254.0636, 252.0656. **7-Chloro-*N*b-methoxycarbonyltryptamine**: colorless oil. IR (film): 3420, 3320, 2930, 1704, 1521, 1259, 782 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.82 (2H, t, J = 7.3 Hz), 3.25 (2H, dt, J = 7.3, 5.7 Hz), 3.52 (3H, s), 7.00 (1H, t. J = 7.7 Hz), 7.15 (1H, d, J = 7.7 Hz), 7.20 (1H, br t, J = 5.7 Hz), 7.22 (1H, d, J = 2.4 Hz), 7.51 (1H, d, J = 7.7 Hz). High resolution MS *m/z*: Calcd for $C_{12}H_{13}ClN_2O_2$: 254.0636, 252.0666. Found: 254.0656, 252.0647.

5-Bromo- (50b) and 7-Bromo-*N*b-methoxycarbonyltryptamine from 49 — 47% HBr (3.0 mL) was added to a solution of **49** (31.5 mg, 0.14 mmol) in $HCONH_2$ (3.0 mL) and stirred at 80 °C for 10 min. Sat. aq. $NaHCO_3$ was added and then the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave an oil, which was purified by column chromatography on SiO_2 with EtOAc–hexane (1:2, v/v) to give 7-bromo-*N*b-methoxycarbonyltryptamine (2.4 mg, 6%) and **50b** (15.6 mg, 39%) in the order of elution. **50b**: colorless oil. IR (film): 3290, 2920, 1703, 1540, 1452, 1262, 1025 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.79 (2H, t, J = 7.2 Hz), 3.22 (2H, dt, J = 7.2, 5.7 Hz), 3.53 (3H, s), 7.16 (1H, dd. J = 8.6, 2.0 Hz), 7.19 (1H, br t, J = 5.7 Hz), 7.21 (1H, d, J = 2.0 Hz), 7.31 (1H, d, J = 8.6 Hz), 7.68 (1H, d, J = 1.5 Hz). High resolution MS *m/z*: Calcd for $C_{12}H_{13}BrN_2O_2$: 298.0140, 296.0161. Found: 298.0138, 296.0178. **7-Bromo-*N*b-methoxycarbonyltryptamine**: mp 68.0–69.5 °C (colorless prisms, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3420, 3320, 2950, 1703, 1523, 1260, 1085, 1046 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.82 (2H, t, J = 7.3 Hz), 3.25 (2H, dt, J = 7.3, 5.7 Hz), 3.52 (3H, s), 6.94 (1H, t. J = 7.7 Hz), 7.20 (1H, br t. J = 5.7 Hz), 7.21 (1H, d, J = 2.4 Hz), 7.29 (1H, t, J = 7.7 Hz), 7.54 (1H, d, J = 7.7 Hz). MS *m/z*: 298, 296 (M^+). *Anal*. Calcd for $C_{12}H_{13}BrN_2O_2$: C, 48.51; H, 4.41; N, 9.43. Found: C, 48.59; H, 4.42; N, 9.31.

1-Acetyl-5-bromo-*N*b-methoxycarbonyltryptamine (50c) from 50b — A solution of **50b** (28.5 mg, 0.09 mmol) in dry DMF (3.0 mL) was added to 60% NaH (9.5 mg, 0.19 mmol) and stirred at 0 °C for 5 min. Then a solution of AcCl (24.3 mg, 0.28 mmol) in dry DMF (2.0 mL) was added and stirred at rt for 3 h. Water and sat. aq. $NaHCO_3$ were added and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v).

The extract 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_3 (100:1:0.1, v/v) to give **50c** (21.1 mg, 65%). **50c**: mp 131.0–132.0 ºC (colorless prisms, recrystallized from CH_2Cl_2-hexane). IR (KBr): 3420, 1726, 1701, 1539, 1446, 1390, 1263, 1243, 1056 cm^{-1}. ^1H-NMR (DMSO-d_6) δ: 2.61 (3H, s), 2.80 (2H, t, J = 6.9 Hz), 3.29 (2H, dt, J = 6.9, 5.7 Hz), 3.53 (3H, s), 7.27 (1H, br t, J = 5.7 Hz), 7.47 (1H, dd, J = 8.8, 1.9 Hz), 7.73 (1H, s), 7.81 (1H, d, J = 1.9 Hz), 8.25 (1H, d, J = 8.8 Hz). MS *m/z*: 340, 338 (M^+). *Anal.* Calcd for $C_{14}H_{15}BrN_2O_3 \cdot 1/8H_2O$: C, 49.25; H, 4.43; N, 8.20. Found: C, 49.21; H, 4.44; N, 8.14.

5-Bromotryptamine (50d) from 50b — Aq. 8% NaOH (7.0 mL) was added to a solution of **50b** (132.4 mg, 0.44 mmol) in MeOH (7.0 mL) and refluxed with stirring for 7 h. Water was added and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract 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_3 (100:20:2, v/v) to give **50d** (94.0 mg, 88%). **50d**: colorless oil. IR (film): 3130, 2940, 2870, 1582, 1564, 1459, 1094, 880, 792 cm^{-1}. ^1H-NMR (DMSO-d_6) δ: 2.72–2.82 (4H, m), 7.16 (1H, dd, J = 8.4, 1.9 Hz), 7.20 (1H, d, J = 8.4 Hz), 7.30 (1H, d, J = 8.4 Hz), 7.69 (1H, d, J = 1.9 Hz). High resolution MS *m/z*: Calcd for $C_{10}H_{11}BrN_2$: 240.0086, 238.0104. Found: 240.0092, 238.0104.

***N*-5-Bromo-{[1-(3-bromo-4-methoxyphenyl)-2-hydroxy]ethyl}tryptamine (52) and *N*-5-Bromo-{2-hydroxy-[2-(3-bromo-4-methoxy)phenyl]ethyl}tryptamine (53) from 50d —** A solution of DBU (8.9 mg, 0.06 mmol) in *t*-BuOH (1.0 mL) was added to a solution of **50d** (74.1 mg, 0.31 mmol) in *t*-BuOH (5.0 mL) and refluxed with stirring for 9 h. Water was added and the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract 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_3 (100:20:2, v/v) to give **52** (20.8 mg, 14%), **53** (40.3 mg, 28%), and **50d** (unreacted starting material, 28.4 mg, 38%) in the order of elution. **52**: mp 98.5–100.0 ºC (colorless prisms, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3400, 3280, 2950, 2860, 1603, 1500, 1462, 1282, 1260, 1056, 1020, 880, 796, 736 cm^{-1}. ^1H-NMR (DMSO-d_6) δ: 2.55–2.66 (2H, m), 2.72–2.83 (2H, m), 3.31 (1H, t, J = 9.0 Hz), 3.41 (1H, dd, J = 10.2, 5.1 Hz), 3.66 (1H, dd, J = 7.7, 4.5 Hz), 3.81 (3H, s), 4.82 (1H, br s), 7.02 (1H, d, J = 8.4 Hz), 7.14 (1H, dd, J = 8.4, 2.0 Hz), 7.16 (1H, d, J = 2.2 Hz), 7.28 (2H, d, J = 9.0 Hz), 7.50 (1H, d, J = 2.0 Hz), 7.57 (1H, d, J = 2.0 Hz). MS *m/z*: 470, 468, 466 (M^+). *Anal.* Calcd for $C_{19}H_{20}Br_2N_2O_2 \cdot 1/8H_2O$: C, 48.51; H, 4.34; N, 5.96. Found: C, 48.28; H, 4.30; N, 5.92. **53 (chelonin B)**: mp 172.0–173.0 ºC (colorless prisms, recrystallized from EtOAc–hexane). IR (KBr): 3230, 1605, 1500, 1460, 1402, 1282, 1260, 1048 cm^{-1}. ^1H-NMR (DMSO-d_6) δ: 2.63–2.71 (2H, m), 2.78–2.84 (4H, m), 3.82 (3H, s), 4.58 (1H, dd, J = 7.3, 5.1 Hz), 5.32 (1H, br s), 7.02 (1H, d, J = 8.6 Hz), 7.16 (1H, dd, J = 8.6, 2.0 Hz), 7.19 (1H, d, J

= 2.2 Hz), 7.26 (1H, dd, *J* = 8.6, 2.2 Hz), 7.31 (1H, d, *J* = 8.6 Hz), 7.51 (1H, d, *J* = 2.0 Hz), 7.69 (1H, d, *J* = 2.0 Hz), 11.00 (1H, br s). ^{13}C-NMR (DMSO-d_6) δ: 25.2, 49.7, 56.0, 57.2, 70.4, 110.0, 110.7, 112.0, 112.4, 113.2, 120.6, 123.1, 124.2, 126.3, 129.1, 130.2, 134.8, 138.3, 154.0. MS *m/z*: 470, 468, 466 (M^+). *Anal*. Calcd for $C_{19}H_{20}Br_2N_2O_2 \cdot 1/4H_2O$: C, 48.28; H, 4.37; N, 5.93. Found: C, 48.15; H, 4.24; N, 5.95. [Lit.[7] (+)-**53**: white gum. IR (KBr): 3470, 3330, 1605, 1500, 1460, 1445, 1420, 1285, 1260, 1055 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.63 (2H, br d, *J* = 5.9 Hz), 2.79 (4H, br s), 3.81 (3H, s), 4.55 (1H, br t, *J* = 5.9 Hz), 5.25 (1H, br s), 6.98 (1H, d, *J* = 8.4 Hz), 7.13 (1H, dd, *J* = 8.5, 1.6 Hz), 7.14 (1H, br s), 7.23 (1H, dd, *J* = 8.4, 1.7 Hz), 7.28 (1H, d, *J* = 8.5 Hz), 7.48 (1H, d, *J* = 1.7 Hz), 7.66 (1H, d, *J* = 1.6 Hz), 11.04 (1H, br s). ^{13}C-NMR (DMSO-d_6) δ: 24.7, 49.4, 56.1, 56.7, 69.9, 110.2, 110.9, 112.0, 112.1, 113.3, 120.6, 123.2, 124.4, 126.4, 129.1, 130.3, 134.9, 137.9 154.2. High resolution MS *m/z*: Calcd for $C_{19}H_{20}Br_2N_2O_2$: 465.9893. Found: 465.9891.]

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