Supporting Information

First Asymmetric Total Synthesis of Us-7 and -8, Novel *D-seco* Corynanthe-Type Oxindole Alkaloids from *Uncaria attenuata*: Structure Revision of Us-7 and Determination of Absolute Stereochemistry

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Experimental procedures and copies of ^1H and ^{13}C NMR spectral data for compounds **13**, **14**, **17**, **18**, synthetic and natural Us-8 (**2**), **1**, and synthetic and natural Us-7 (**22**), as well as X-ray data (ORTEP and CIF) for compound **19**.

General UV: recorded in MeOH on a JASCO V-560 instrument. IR: recorded on a JASCO FT/IR-230 spectrophotometer. ^1H and ^{13}C NMR spectra: recorded on JEOL JNM A-400, JNM A-500, JNM ECP-400, or JNM ECP-600 spectrometers, *J* values are given in Hz. EI-MS: direct probe insertion at 70 eV recorded on a JEOL JMS GC-mate spectrometer. FAB-MS: recorded on a JEOL JMS-HX110 mass spectrometer. Optical Rotation: measured using a JASCO P-1020 polarimeter. CD: recorded on a JASCO J-720WI spectrometer. TLC: precoated Kieselgel 60 F₂₅₄ plates (Merck, 0.25 mm thick). Column Chromatography: Kieselgel 60 [Merck, 70-230 (for open chromatography) and 230-400 mesh (for flash chromatography)], medium pressure liquid column chromatography: silica gel prepacked column Kusano CPS-HS-221-05.

(*R*)-Butane-1,2-diol 1-^tbutyldimethylsilyl-2-tetrahydropyranyl ether

p-TsOH•H₂O (140 mg, 0.735 mmol) was added to a solution of **7** (15 g, 73.4 mmol) and dihydropyran (20 mL, 219 mmol) in dry dichloromethane (183 mL) and the mixture was stirred for 1 h at room temperature under argon atmosphere. To the reaction mixture, saturated aqueous NaHCO₃ solution was added and the whole mixture was extracted three times with chloroform. The combined extract was washed with brine, dried over MgSO₄, and

evaporated. The residual oil was chromatographed on silica gel (ethyl acetate/*n*-hexane = 1:20) to give 18.7 g (88%) of tetrahydropyranyl ethers as a colorless oil of the diastereomeric mixture: IR $\nu_{\max}$ (neat) cm^{-1} : 3583, 2929, 2856. ^1H NMR (400MHz, CDCl_3) δ 0.03 (6H, s, $-\text{Si}(\text{CH}_3)_2$), 0.04 (6H, s, $-\text{Si}(\text{CH}_3)_2$), 0.86~0.88 (18H, s, $-\text{Si}(\text{CH}_3)_3$ x2), 0.89 (3H, dd, $J_1=J_2=7.4$, $-\text{CH}_3$), 0.95 (3H, dd, $J_1=J_2=7.5$, $-\text{CH}_3$), 1.43~1.88 (16H, overlapped, $-\text{CH}_2-\text{CH}_3$ x2, $-\text{OCH}_2-\text{CH}_2-\text{CH}_2-$ x2, $-\text{CH}_2-\text{CH}_2-\text{CH}_2-$ x2, $-\text{OCH}-\text{CH}_2-\text{CH}_2-$ x2), 3.38~3.56 (4H, overlapped, $-\text{O}-\text{CH}_2-$, $-\text{O}-\text{CH}-$ x2), 3.64 (2H, m, $-\text{CH}_2-\text{OSi}-$), 3.76 (2H, m, $-\text{CH}_2-\text{OSi}-$), 3.92 (2H, m, $-\text{O}-\text{CH}_2-$), 4.65 (1H, dd, $J=4.6, 2.7$, $-\text{O}-\text{CH}-\text{O}-$), 4.83 (1H, dd, $J=2.8, 4.7$, $-\text{O}-\text{CH}-\text{O}-$). ^{13}C NMR (100MHz, CDCl_3) δ 5.42/5.48 ($-\text{Si}-\text{CH}_3$), 9.27/9.96 ($-\text{CH}_3$), 18.22/18.31 ($-\text{Si}-\text{C}(\text{CH}_3)_3$), 19.82/19.98, 25.10/25.80 ($-\text{Si}-\text{C}(\text{CH}_3)_3$), 25.46/25.54, 30.92/31.04, 62.49/62.78 ($-\text{O}-\text{CH}_2-$), 65.20/65.47 ($-\text{CH}_2-\text{OSi}-$), 78.30/78.92 ($-\text{O}-\text{CH}-$), 98.47/98.58 ($-\text{O}-\text{CH}-\text{O}-$). FABMS (KI in NBA) m/z : 288 ($[\text{M}+\text{H}]^+$), 327 ($[\text{M}+\text{K}]^+$). HR-FABMS (NBA): found 280.2145, calcd for $\text{C}_{15}\text{H}_{32}\text{O}_3\text{Si}$ $[\text{M}+\text{H}]^+$; 288.2120.

(*R*)-Butane-1,2-diol 2-tetrahydropyranyl ether

To a solution of silyl ethers (25 g, 86.7 mmol) in dry THF (170 mL) was added tetrabutylammonium fluoride (1.0 *M* solution in THF, 130 mL) and the mixture was stirred for 30 min at room temperature under argon atmosphere. After addition of water, the mixture was extracted three times with ethyl acetate. The combined extract was washed with brine, dried over MgSO_4 , and evaporated. The residual oil was chromatographed on silica gel (ethyl acetate/*n*-hexane = 1:9) to give 15.2 g (quant.) of primary alcohols as a colorless oil of a diastereomeric mixture. For the spectroscopic analysis, a portion of diastereomeric mixture was separated by SiO_2 column chromatography with the same solvent system as above. Fast eluted compound: $[\alpha]_D^{13} -36.5$ (*c* 1.02, CHCl_3). IR $\nu_{\max}$ (neat) cm^{-1} : 3436(OH), 2940, 2875. ^1H NMR (400MHz, CDCl_3) δ 0.92 (3H, dd, $J=7.5, 7.5$, $-\text{CH}_3$), 1.41~1.59 (6H, overlapped, $-\text{CH}_2\text{CH}_3$, $-\text{CH}_2-\text{CH}_2-\text{CH}_2-$), 1.81 (1H, m, $-\text{O}-\text{CH}-\text{CH}_2-$), 1.85 (1H, m, $-\text{O}-\text{CH}-\text{CH}_2-$), 3.46~3.56 (4H, overlap, $-\text{CH}_2-\text{OH}$, $-\text{O}-\text{CH}_2-$, $-\text{CH}_2-\text{OH}$), 3.88 (1H, dd, $J=9.4, 2.3$, $-\text{CH}_2-\text{OH}$), 4.00 (1H, m, $-\text{O}-\text{CH}-$), 4.46 (1H, dd, $J=7.1, 2.5$, $-\text{O}-\text{CH}-\text{O}-$). ^{13}C NMR (100MHz, CDCl_3) δ 10.10 ($-\text{CH}_3$), 21.24 ($-\text{CH}_2-\text{CH}_2-\text{CH}_2-$), 24.90 ($-\text{CH}_2-\text{CH}_2-\text{CH}_2-$), 25.02 ($-\text{CH}_2-\text{CH}_3$), 31.39 ($-\text{CH}_2-\text{CH}_2-\text{CH}-$), 65.04 ($-\text{O}-\text{CH}_2-$), 65.85 ($-\text{CH}_2-\text{OH}$), 84.87 ($-\text{O}-\text{CH}-$), 101.73 ($-\text{O}-\text{CH}-\text{O}-$). FABMS (NBA) m/z : 175 ($[\text{M}+\text{H}]^+$). HR-EIMS: found 174.1267, calcd for $\text{C}_9\text{H}_{18}\text{O}_3$ $[\text{M}]^+$; 174.1256. Slowly eluted compound: $[\alpha]_D^{14} +80.6$ (*c* 0.70, CHCl_3). IR $\nu_{\max}$ (neat) cm^{-1} : 3433 (OH), 2943. ^1H NMR (400MHz, CDCl_3) δ 0.90 (3H, dd, $J=7.6, 7.6$, $-\text{CH}_3$), 1.38~1.73 (6H, overlapped, $-\text{CH}_2\text{CH}_3$, $-\text{CH}_2-\text{CH}_2-\text{CH}_2-$), 1.77~1.82 (2H, m, $-\text{O}-\text{CH}-\text{CH}_2-$), 3.5 (3H, overlapped, $-\text{CH}_2-\text{OH}$, $-\text{O}-\text{CH}_2-$), 3.63 (1H, dd, $J=9.0, 3.5$, $-\text{CH}_2-\text{OH}$), 3.90 (1H, m, $-\text{O}-\text{CH}-$), 4.71 (1H, dd, $J=5.0, 2.5$, $-\text{O}-\text{CH}-\text{O}-$). ^{13}C NMR (100MHz, CDCl_3) δ 9.96 ($-\text{CH}_3$), 20.02 ($-\text{CH}_2-\text{CH}_2-\text{CH}_2-$), 24.45 ($-\text{CH}_2-\text{CH}_2-\text{CH}_2-$), 25.28 ($-\text{CH}_2-\text{CH}_3$), 31.04 ($-\text{CH}_2-\text{CH}_2-\text{CH}-$),

63.18 (-O-CH₂-), 63.60 (-CH₂-OH), 8.97 (-O-CH-), 101.66 (-O-CH-O-). FABMS (NBA) *m/z*: 175 ([M+H]⁺). HR-EIMS: found 174.1224, calcd for C₉H₁₈O₃ [M]⁺; 174.1256.

Aldehyde (8)

Under argon atmosphere, a solution of dry DMSO (4.3 mL, 60.6 mmol) in dry dichloromethane (10 mL) was added dropwise to a solution of oxalyl dichloride (2.6 mL, 29.8 mmol) in dry dichloromethane (20 mL) at -78°C. After being stirred at the same temperature for 10 min, a solution of the primary alcohol (2.0 g, 11.5 mmol) in dry dichloromethane (10 mL) was added dropwise, and the mixture was stirred for 1 h at -78°C. Triethylamine (16.5 mL, 118 mmol) was added to the reaction mixture, which was stirred for 15 min at -78°C and then for 15 min at 0°C. The reaction mixture was poured onto the sat. aqueous ammonium chloride solution, which was extracted three times with chloroform. The combined extract was washed with brine, dried over MgSO₄, and evaporated. The residual oil was chromatographed on silica gel (ethyl acetate/*n*-hexane = 1:9) to give 1.51 g (76%) of **8** as a colorless oil of a diastereomeric mixture. IR $\nu_{\max}$ (neat) cm⁻¹: 3446, 2942, 2875, 1733 (C=O). ¹H NMR (400MHz, CDCl₃) δ 0.97 (3H, dd, *J*=7.5, 7.5, -CH₃), 1.03 (3H, dd, *J*=7.5, 7.5, -CH₃), 1.56~1.88 (16H, overlapped, -CH₃-CH₂- x2, -CH₂-CH₂-CH₂-CH₂-CH-O- x2), 3.45~3.54 (2H, overlapped, -O-CH₂-CH₂-), 3.86~3.94 (2H, overlapped, -O-CH₂-CH₂-), 3.74 (1H, ddd, *J*=5.7, 5.7, 2.6, -O-CH-), 4.10 (1H, ddd, *J*=7.2, 5.6, 1.7, -O-CH-), 4.58 (1H, dd, *J*=5.7, 2.6, -O-CH-O-), 4.71 (1H, dd, *J*=3.6, 3.6, -O-CH-O-), 9.64 (1H, s, O=CH-), 9.65 (1H, s, O=CH-). ¹³C NMR (100MHz, CDCl₃) δ 9.16/9.58 (-CH₃), 19.28/20.16 (-CH₂-CH₃), 19.28/20.16 (-CH₂-CH₂-CH₂-), 23.32/23.42 (-O-CH₂-CH₂-CH₂-), 30.55/30.66 (-CH₂-CH₂-CH-), 62.59/63.77 (-O-CH₂-CH₂-), 84.51/80.91 (-O-CH-), 97.69/100.72 (-O-CH-O-), 203.40/203.82 (O=CH-). FABMS (NBA) *m/z*: 173 ([M+H]⁺). HR-FABMS (NBA): found 173.1187, calcd for C₉H₁₇O₃ [M+H]⁺; 173.1178.

Z-Olefin (9)

A solution of 18-crown-6 (6.3 g, 23.9 mmol) and bis(2,2,2-trifluoroethyl)(methoxycarbonylmethyl)phosphonate (10 mL, 48.6 mmol) in dry THF (150 mL) was cooled to -78°C and treated with a solution of potassium bis(trimethylsilyl)amide in toluene (0.5 M solution, 100 mL) under argon atmosphere. A solution of **8** (8.3 g, 48.2 mmol) in dry THF (10 mL) was then added and the resulting mixture was stirred for 30 min at -78°C. Saturated ammonium chloride solution was added to the reaction mixture, that was extracted three times with ethyl acetate. The combined extract was washed with brine, dried over MgSO₄, and evaporated. The residual oil was chromatographed on silica gel (ethyl acetate/*n*-hexane = 1:9) to give 11.0 g (quant.) of **9** as a colorless oil of a diastereomeric mixture. IR $\nu_{\max}$ (neat) cm⁻¹: 3583, 2743, 1756. ¹H NMR (400MHz, CDCl₃) :

δ 0.95 (3H, dd, $J=7.5$, 7.5, $-\underline{\text{CH}}_3$), 0.99 (3H, dd, $J=7.5$, 7.5, $-\underline{\text{CH}}_3$), 1.50~1.84 (16H, overlapped, $\text{CH}_3-\underline{\text{CH}}_2-$ x2, $-\text{CH}_2-\underline{\text{CH}}_2-\underline{\text{CH}}_2-\underline{\text{CH}}_2-\text{CH}-\text{O}-$ x2), 3.46 (2H, m, $-\text{O}-\underline{\text{CH}}_2-\text{CH}_2-$), 3.71 (3H, s, $-\text{O}-\underline{\text{CH}}_3$), 3.72 (3H, s, $-\text{O}-\underline{\text{CH}}_3$), 3.88 (2H, m, $-\text{O}-\underline{\text{CH}}_2-\text{CH}_2-$), 4.58 (1H, dd, $J=4.1$, 3.2, $-\text{O}-\underline{\text{CH}}-\text{O}-$), 4.62 (1H, dd, $J=5.1$, 3.0, $-\text{O}-\underline{\text{CH}}-\text{O}-$), 5.11 (1H, m, $-\text{O}-\underline{\text{CH}}-$), 5.23 (1H, m, $-\text{O}-\underline{\text{CH}}-$), 5.75 (1H, dd, $J=11.9$, 1.5, $-\text{CH}=\underline{\text{CH}}-\text{CO}_2\text{CH}_3$), 5.88 (1H, dd, $J=11.9$, 1.1, $-\text{CH}=\underline{\text{CH}}-\text{CO}_2\text{CH}_3$), 6.08 (1H, dd, $J=11.7$, 8.6, $-\underline{\text{CH}}=\text{CH}-\text{CO}_2\text{CH}_3$), 6.32 (1H, dd, $J=11.7$, 8.2, $-\underline{\text{CH}}=\text{CH}-\text{CO}_2\text{CH}_3$). ^{13}C NMR (100MHz, CDCl_3): δ 9.57/9.86 ($-\underline{\text{CH}}_3$), 27.91/28.02 ($-\underline{\text{CH}}_2-\text{CH}_3$), 25.35/25.46 ($-\text{CH}_2-\underline{\text{CH}}_2-\text{CH}_2-$), 19.49/20.05 ($-\text{O}-\text{CH}_2-\underline{\text{CH}}_2-\text{CH}_2-$), 30.92/30.95 ($-\text{CH}_2-\underline{\text{CH}}_2-\text{CH}-$), 51.13/51.27 ($-\text{OCH}_3$), 62.30/63.14 ($-\text{O}-\underline{\text{CH}}_2-\text{CH}_2-$), 72.38/76.47 ($-\text{O}-\underline{\text{CH}}-$), 96.13/99.97 ($-\text{O}-\underline{\text{CH}}-\text{O}-$), 111.48/121.48 ($-\text{CH}=\underline{\text{CH}}-\text{CO}_2\text{CH}_3$), 150.63/152.56 ($-\text{CH}=\text{CH}-\underline{\text{CO}}_2\text{CH}_3$), 166.10/166.36 ($-\text{CO}_2\text{CH}_3$). EIMS m/z (%): 228 (M^+ , 2) 56 (100). HR-EIMS: found 228.1333, calcd for $\text{C}_{12}\text{H}_{20}\text{O}_4$ [M] $^+$; 228.1361.

(*R*)- γ -Butenolide (**10**)

A mixture of **9** (11.0 g, 48.2 mmol) and *p*-TsOH $\cdot\text{H}_2\text{O}$ (200 mg, 1.05 mmol) in methanol (180 mL) was stirred for 1.5 h at room temperature. Aqueous 5% NaHCO_3 was added to the reaction mixture, which was extracted three times with chloroform. The combined extract was washed with brine, dried over MgSO_4 , and concentrated carefully at room temperature due to the volatility of the compound. The crude product was chromatographed on silica gel (ethyl acetate/*n*-hexane = 1:4) to give 4.20 g (79%) of **10** as a colorless oil. $[\alpha]_{\text{D}}^{28}$ -89.4 (c 1.27, CHCl_3) (95% *ee* by chiral HPLC analysis; column: CHIRALCEL OB, detector: UV 220 nm, solvent: 10% *i*-propanol/*n*-hexane, flow rate: 0.5 ml/min, oven temperature: 30°C). IR ν_{max} (neat) cm^{-1} : 2975, 1754 ($\text{C}=\text{C}-\text{C}=\text{O}$). UV λ_{max} (MeOH) nm: 226.0, 238.0 (sh). ^1H NMR (400MHz, CDCl_3) δ 1.02 (3H, dd, $J=7.5$, 7.5, $-\underline{\text{CH}}_3$), 1.69~1.89 (2H, m, $-\underline{\text{CH}}_2\text{CH}_3$), 5.01 (1H, dddd, $J=6.1$, 6.1, 1.8, 1.8, $-\underline{\text{CH}}-\text{O}-$), 6.12 (1H, dd, $J=5.7$, 2.0, $-\text{CH}=\underline{\text{CH}}-\text{C}=\text{O}$), 7.45 (1H, dd, $J=5.8$, 1.5, $\text{O}=\text{C}-\text{C}=\underline{\text{CH}}-$). ^{13}C NMR (100MHz, CDCl_3) δ 8.99 ($-\underline{\text{CH}}_3$), 26.28 ($-\underline{\text{CH}}_2-\text{CH}_3$), 84.29 ($-\underline{\text{CH}}-\text{O}-$), 121.79 ($-\text{CH}=\underline{\text{CH}}-\text{C}=\text{O}$), 155.89 ($\text{O}=\text{C}-\text{C}=\underline{\text{CH}}-$), 173.12 ($\text{C}=\text{O}$). EIMS m/z (%): 112 (M^+ , 6), 56 (100).

Methyl 3-ethylthio-3-oxopropanoate

To a solution of methyl malonyl chloride (6.0 mL, 55.9 mmol) in dry dichloromethane (18 mL) was added ethanethiol (6.6 mL, 89.1 mmol) dropwise at 0°C and the reaction mixture was stirred for 15 h at room temperature. After evaporation of the solvent, the crude residue was chromatographed on silica gel (ethyl acetate/*n*-hexane = 1:5) to give 9.10 g (quantitative) of thiol ester as a colorless oil. ^1H NMR (400MHz, CDCl_3) δ 1.28 (3H, dd, $J=7.7$, 7.7, $-\underline{\text{CH}}_3$), 2.95 (2H, ddd, $J=7.5$, 7.5, 7.5, $-\text{SCH}_2\text{CH}_3$), 3.59 (2H, s, $-\underline{\text{CH}}_2-$), 3.76 (3H, s, $-\text{OCH}_3$). ^{13}C NMR (100MHz, CDCl_3) δ 14.12 ($-\underline{\text{CH}}_3$), 20.96 ($-\text{SCH}_2\text{CH}_3$), 49.25 ($-\underline{\text{CH}}_2-$), 52.53 ($-\text{OCH}_3$),

166.45 (-S-C=O), 191.05 (O=C-OCH₃). EIMS m/z (%): 162 (M⁺, 16).

Conjugate addition of methyl 3-ethylthio-3-oxopropanoate to **10**

To a stirred suspension of *t*-BuOK (freshly sublimed before use, 25 mg, 0.223 mmol) in dry *t*-BuOH was added a solution of thiol ester (108 mg, 0.666 mmol) in dry *t*-BuOH (1 mL) at room temperature under argon atmosphere. After 10 min a solution of **10** (50 mg, 0.446 mmol) in dry *t*-BuOH (1 mL) was added dropwise and the reaction mixture was stirred for 3 h at room temperature. The reaction mixture was diluted with ethyl acetate and then washed with water. The water layer was back-extracted with chloroform. The chloroform extract was washed with brine and combined with the ethyl acetate layer, which was dried over MgSO₄, and evaporated. The residue was purified by pre-packed silica gel column chromatography (ethyl acetate/*n*-hexane = 1:3) to give 108 mg (88%) of **11** as a colorless oil. IR $\nu_{\max}$ (neat) cm⁻¹: 1779, 1745, 1679. UV $\lambda_{\max}$ (MeOH) nm: 237.0. ¹H NMR (400MHz, CDCl₃) δ 1.01 (3H, -CH₃), 1.28 (3H, -SCH₂CH₃), 1.64 (2H, -CH₂CH₃), 2.47 (1H, -CH₂-C=O), 2.80 (1H, -CH₂-C=O), 2.92~2.98 (3H, overlapped, -CH-, -SCH₂CH₃), 3.69 (1H, -CH-C=O), 3.77 (3H, -OCH₃), 4.27 (1H, -O-CH-). ¹³C NMR (100MHz, CDCl₃) (The spectrum exhibited a pair of the signals due to a diastereomeric mixture at the methine carbon of the malonate moiety) δ 9.36 (-CH₃), 14.14/14.16 (-S-CH₂CH₃), 24.19/24.16 (-CH₂CH₃), 27.89/28.70 (-CH-), 39.33/39.42 (-SCH₂CH₃), 31.88/32.52 (-CH₂-C=O), 52.95 (-OCH₃), 61.34/61.70 (-CH-C=O), 167.25/167.40 (-C=O), 192.89/192.93 (-CO₂CH₃). EIMS m/z (%): 274 (M⁺, 9), 56 (100). HR-FABMS: found 275.0973, calcd for C₁₂H₁₉O₅S [M+H]⁺; 275.0953.

Reduction of thiol ester (**11**)

To a stirred mixture of **11** (800 mg, 2.92 mmol) and 10% Pd on carbon (320 mg, 0.029 mmol) in acetone (7.5 mL) was added triethylsilane (1.4 mL, 8.77 mmol) at room temperature under argon atmosphere. Stirring was continued for 3 h at room temperature. The catalyst was filtered off using Celite and the filtrate was evaporated to give a crude residue, that was chromatographed on silica gel (ethyl acetate/*n*-hexane = 1:2 to 1:1) to give 630 mg (quantitative) of **12** as a colorless oil. IR $\nu_{\max}$ (neat) cm⁻¹: 1779, 1762, 1704, 1696, 1644. UV $\lambda_{\max}$ (MeOH) nm: 235.0. The NMR spectra exhibited that the product existed as a tautomeric mixture of keto/enol forms. ¹H NMR (400MHz, CDCl₃) δ 7.14 (1H, -C=CH-OH), 9.77 (1H, O=C-H), 11.68 (1H, -OH). ¹³C NMR (100MHz, CDCl₃) δ 103.00 (-C=CH-OH), 195.0 (O=C-H), 210.88 (-C=CH-OH). FABMS m/z (NBA): 215 ([M+H]⁺). HR-FABMS: found 215.0910, calcd for C₁₀H₁₅O₅ [M+H]⁺; 215.0920.

Lactone (**13**)

A diethyl ether solution of diazomethane was added dropwise to a stirred solution of **12**

(600 mg, 2.80 mmol) in ethanol (9.3 mL) at 0°C until the reaction mixture maintained a pale yellow color. The reaction mixture was concentrated carefully and the residue was chromatographed on silica gel (ethyl acetate/*n*-hexane = 1:2 to 1:1) to give 563 mg (88%) of **13** as a colorless oil. $[\alpha]_D^{28} = -4.27$ (*c* 1.55, CH₂Cl₂). IR $\nu_{\max}$ (neat) cm⁻¹: 1779, 1771, 1704, 1698, 1644. UV $\lambda_{\max}$ (MeOH) nm: 238.0. ¹H NMR (400MHz, CDCl₃) δ 0.98 (3H, dd, *J*=7.3, 7.3, -CH₃), 1.67 (2H, m, -CH₂CH₃), 2.58 (1H, dd, *J*=17.6, 9.8, -CH₂-C=O), 2.91 (1H, *J*=17.6, 9.8, -CH₂-C=O), 3.41 (1H, ddd, *J*=9.8, 9.8, 7.8, -CH-), 3.72 (3H, s, -OCH₃), 3.88 (3H, s, -OCH₃), 4.44 (1H, ddd, *J*=7.8, 5.4, 5.4, -CH-O-), 7.41 (1H, s, -C=CH-OCH₃). ¹³C NMR (100MHz, CDCl₃) δ 9.53 (-CH₃), 27.83 (-CH₂CH₃), 33.50 (-CH-), 36.37 (-CH₂-C=O), 51.05 (-OCH₃), 62.01 (-OCH₃), 84.98 (-CH-O-), 107.93 (-C=CH-OCH₃), 161.07 (-C=CH-OCH₃), 167.93 (-CO₂CH₃), 176.79 (-C=O). FABMS *m/z* (NBA): 229 ([M+H]⁺). HR-FABMS: found 229.1073, calcd for C₁₁H₁₇O₅ [M+H]⁺; 229.1076.

Amide (14)

A solution of trimethylaluminum (1.0 *M* solution in hexane, 0.84 mL, 0.84 mmol) was added dropwise to a solution of **9** (119 mg, 0.52 mmol) and tryptamine (134 mg, 0.84 mmol) in dry dichloromethane (183 mL) and the mixture was stirred for 5.5 h at room temperature under argon atmosphere. After addition of saturated aqueous ammonium chloride solution, the reaction mixture was extracted three times with chloroform. The combined extract was dried over MgSO₄ and evaporated. The residue was chromatographed on silica gel (ethyl acetate/*n*-hexane = 1:1) to give 172 mg (85%) of **14** as a colorless amorphous powder. $[\alpha]_D^{30} = -10.9^\circ$ (*c* 1.01, CH₂Cl₂). IR $\nu_{\max}$ (neat) cm⁻¹: 3478, 1656. UV $\lambda_{\max}$ (MeOH) nm: 223.0, 246.5 (sh), 291.0. ¹H NMR (400MHz, CDCl₃) δ 0.92 (3H, dd, *J*=7.3, 7.3, H-18), 1.33 (1H, m, H-19), 1.49 (1H, m, H-19), 2.41 (1H, dd, *J*=15.0, 7.7, H-14), 2.73 (1H, dd, *J*=15.1, 6.4, H-14), 2.92 (2H, dd, *J*=6.8, 6.8, H-6), 3.25 (1H, ddd, *J*=6.9, 6.9, 6.9, H-15), 3.55 (2H, ddd, *J*=6.0, 6.0, 6.0, H-5), 3.64 (3H, s, H-23), 3.72 (3H, s, H-24), 3.72 (1H, overlapped, H-20), 5.79 (1H, br-dd, H-4), 7.01 (1H, s, H-2), 7.10 (1H, dd, *J*=7.4, 7.4, H-10), 7.19 (1H, *J*=7.6, 7.6, H-11), 7.26 (1H, s, H-17), 7.37 (1H, d, *J*=8.3, H-12), 7.59 (1H, d, *J*=7.8, H-9), 8.11 (1H, br-s, H-1). ¹³C NMR (100MHz, CDCl₃) δ 9.97 (C-18), 25.23 (C-6), 25.32 (C-19), 36.94 (C-14), 38.07 (C-15), 39.60 (C-5), 51.34 (C-23), 61.61 (C-24), 74.99 (C-20), 111.25 (C-16), 111.46 (C-12), 112.86 (C-7), 118.64 (C-9), 119.34 (C-10), 122.05 (C-11), 122.13 (C-2), 127.28 (C-8), 136.41 (C-13), 160.38 (C-17), 168.93 (C-22), 173.21 (-N_b-C=O). FABMS (NBA) *m/z*: 389 ([M+H]⁺). HR-FABMS (NBA+PEG): found 389.2084, calcd for C₂₁H₂₉O₅N₂ [M+H]⁺; 389.2077.

Carbonate (15)

To a stirred solution of **14** (1.32 g, 3.40 mmol) and dibenzyl dicarbonate (5.20 g, 18.2 mmol)

in dry THF (130 mL) was added CeCl_3 (0.40 g, 1.62 mmol) at room temperature and the mixture was heated for 1 h at 60°C under argon atmosphere. After cooling, the reaction mixture was filtered through the filter paper and the filtrate was evaporated to give a crude residue, that was chromatographed on silica gel (ethyl acetate/*n*-hexane = 2:1) to give 1.51 g (85%) of **15** as a colorless amorphous powder. IR ν_{max} (CHCl_3) cm^{-1} : 3479, 3009, 1738, 1699, 1663. UV λ_{max} (MeOH) nm: 223.0, 282.5. ^1H NMR (400MHz, CDCl_3) δ 0.84 (3H, dd, $J=7.3$, 7.3, H-18), 1.45 (1H, m, H-19), 1.63 (1H, m, H-19), 2.46 (1H, dd, $J=14.6$, 5.1, H-14), 2.61 (1H, dd, $J=14.6$, 10.4, H-14), 2.89 (2H, dd, $J=7.0$, 7.0, H-6), 3.42~3.56 (3H, overlapped, H-5, 15), 3.63 (3H, s, H-23), 3.65 (3H, s, H-24), 4.99 (1H, ddd, $J=8.8$, 8.8, 3.8, H-20), 5.13 (2H, s, OCH_2Ph), 5.64 (1H, br-s, H-4), 7.01 (1H, d, $J=2.2$, H-2), 7.11 (1H, dd, $J=7.3$, 7.3, H-10), 7.19 (1H, dd, $J=6.8$, 6.8, H-11), 7.30~7.40 (6H, overlapped, H-12, OCH_2Ph), 7.58 (1H, d, $J=7.7$, H-9), 8.00 (1H, br-s, H-1). ^{13}C NMR (100MHz, CDCl_3) δ 9.01 (C-18), 25.12 (C-6), 25.23 (C-19), 36.39 (C-14), 36.69 (C-15), 39.40 (C-5), 51.32 (C-23), 61.71 (C-24), 69.38 (OCH_2Ph), 80.85 (C-20), 108.48 (C-16), 111.21 (C-12), 112.75 (C-7), 118.59 (C-9), 119.24 (C-10), 121.96 (C-2)*, 122.07 (C-11)*, 127.23 (C-8), 128.11, 128.37, 128.51, 135.40 (OCH_2Ph), 136.37 (C-13), 155.17 ($\text{OCO}_2\text{CH}_2\text{Ph}$), 161.31 (C-17), 168.07 (C-22), 171.49 (C-4) (*interchangeable). EIMS m/z (%): 522 (M^+ , 4), 143 (100). HR-FABMS (NBA+PEG): found 523.2399, calcd for $\text{C}_{29}\text{H}_{35}\text{O}_7\text{N}_2$ [$\text{M}+\text{H}$] $^+$; 523.2444.

Bischler-Napieralski reaction of **15**

To a stirred solution of **15** (338 mg, 0.647 mmol) in dry benzene (15 mL) was added phosphorus oxychloride (0.18 mL, 1.93 mmol) at room temperature and the mixture was heated by refluxing for 1.5 h under argon atmosphere. After cooling, the reaction mixture was concentrated under reduced pressure to give 391 mg of crude imine **16**, which was subjected to the next reaction without purification.

*N*_b-formyl-tetrahydro- β -carbolines (**17**, **18**)

To a stirred solution of crude imine **16** (391 mg) in methanol (15 mL) was added sodium borohydride (36.7 mg, 0.97 mmol) at 0°C and the mixture was stirred for 1 h at the same temperature under argon atmosphere. Saturated aqueous NaHCO_3 was added to the reaction mixture, which was then extracted thoroughly with 5% methanol-chloroform. The combined extract was dried over MgSO_4 and concentrated to give a residue, that was purified by pre-packed silica gel column chromatography (2–10% methanol/chloroform gradient) to give 92.6 mg (rapidly eluted compound) and 206.7 mg (slowly eluted compound) of amines, which were directly subjected to the next formylation, respectively. The fast eluted amine was dissolved in dry dichloromethane (4 mL) and a solution of freshly prepared pentafluorophenyl formate (90 mg, 0.423 mmol) in dichloromethane (1 mL) was added at room temperature under argon atmosphere. Stirring was continued for 1 h.

Saturated aqueous NaHCO_3 was added to the reaction mixture, which was then extracted three times with chloroform. The combined extract was washed with brine, dried over MgSO_4 , and concentrated to give a residue, that was purified by pre-packed silica gel column chromatography (ethyl acetate/*n*-hexane = 1:1 to ethyl acetate gradient) to give 71.3 mg (21% overall yield from **15**) of **17** as a colorless amorphous powder. IR ν_{max} (CHCl_3) cm^{-1} : 3018, 2941, 1735, 1665, 1635. UV λ_{max} (MeOH) nm: 225.0, 290.0. In the NMR spectra, some signals appeared as a pair of peaks due to a mixture of rotation isomers of *N*-formyl function. ^1H NMR (400MHz, CDCl_3) δ 0.87 (dd, $J=7.3$, 7.3, H-18), 0.89 (dd, $J=7.5$, 7.5, H-18), 1.48 (m, H-19), 1.63~1.75 (overlapped, H-14, 19), 2.01 (ddd, $J=14.6$, 10.4, 4.4, H-14), 2.06 (m, H-14), 2.52 (ddd, $J=14.5$, 11.9, 2.9, H-14), 2.71 (dd, $J=15.4$, 4.4, H-6), 2.80 (m, H-6), 2.97 (ddd, $J=11.7$, 11.7, 4.8, H-5), 3.22 (ddd, $J=12.1$, 8.1, 4.6, H-15), 3.29 (m, H-15), 3.52 (m, H-5), 3.74 (m, H-5), 3.71/ 3.75 (each s, H-23), 3.78/ 3.85 (each s, H-24), 4.48 (br-d, $J=8.4$, H-3), 4.67 (dd, $J=12.6$, 4.9, H-5), 4.91 (m, H-20), 5.10 (d, $J=12.1$)/5.13 (d, $J=12.1$)/5.14 (d, $J=12.1$)/5.17 (d, $J=12.1$, OCH_2Ph), 5.44 (dd, $J=9.5$, 4.2, H-3), 7.10 (m, H-10), 7.18 (m, H-11), 7.24~7.37 (overlapped, H-12, OCH_2Ph), 7.44 (br-d, $J=7.9$)/7.47 (d, $J=7.9$, H-9), 7.49/ 7.53 (each s, H-17), 8.03 (s, H-21), 8.16 (br-s, H-1, 21), 8.47 (br-s, H-1). ^{13}C NMR (150MHz, CDCl_3) δ 9.50/9.87 (C-18), 21.04/22.93 (C-6), 24.59/25.02 (C-19), 33.51/33.76 (C-14), 34.98/40.79 (C-5), 36.03/36.15 (C-15), 45.96/52.33 (C-3), 51.41/51.65 (C-23), 61.87/62.23 (C-24), 69.56/69.63 (OCH_2Ph), 81.40/82.17 (C-20), 106.88/108.65 (C-7), 107.67 (C-16), 111.10/111.18 (C-12), 117.94/118.31 (C-9), 119.49/119.72 (C-10), 121.89/122.20 (C-11), 126.65/126.72 (C-8), 128.29/128.34/128.49/128.51/128.59/135.44/135.54 (C- OCH_2Ph), 133.15/133.69 (C-2), 136.14/136.17 (C-13), 154.45/155.27 ($\text{OCO}_2\text{CH}_2\text{Ph}$), 161.94/162.08 (C-21), 162.60/163.05 (C-17), 168.12/168.68 (C-22). EIMS m/z (%) : 534 (M^+ , 24), 199 (100). HR-FABMS (NBA+PEG): found 535.2401, calcd for $\text{C}_{30}\text{H}_{35}\text{O}_7\text{N}_2$ [$\text{M}+\text{H}$] $^+$; 535.2444. CD (c 0.194 mmol/L, MeOH, 23°C) λ_{nm} ($\Delta\epsilon$): 202 (0), 214 (−14.7), 229 (0), 239 (+7.5), 274 (0), 289 (−0.7), 300 (0). The slowly eluted amine was formylated by the same procedure as described above (160 mg of pentafluorophenyl formate was used) and the product was purified by pre-packed silica gel column chromatography (ethyl acetate/*n*-hexane = 3:1) to give 145.9 mg (43% overall yield from **15**) of **18** as a colorless amorphous powder. IR ν_{max} (CHCl_3) cm^{-1} : 3319, 3009, 1736, 1667. UV λ_{max} (MeOH) nm: 223.0, 290.0. In the NMR spectra, some signals appeared as a pair of peaks due to a mixture of rotation isomers of *N*-formyl function. ^1H NMR (400MHz, CDCl_3) δ 0.84 (3H, dd, $J=7.5$, 7.5, H-18), 1.50 (1H, m, H-19), 1.68 (1H, m, H-19), 2.00 (1H, ddd, $J=12.1$, 12.1, 4.0, H-14), 2.28 (1H, ddd, $J=12.6$, 12.6, 2.7, H-14), 2.82 (2H, m, H-6), 3.28 (1H, ddd, $J=13.2$, 9.9, 4.2, H-15), 3.49 (1H, m, H-5), 3.76 (1H, m, H-5), 3.81 (3H, s, H-23), 3.93 (3H, s, H-24), 5.07 (1H, ddd, $J=9.9$, 7.9, 3.3, H-20), 5.11 (2H, s, OCH_2Ph), 5.25 (1H, br-dd, $J=11.4$, 2.6, H-3), 7.08 (1H, ddd, $J=7.0$, 7.0, 0.9, H-10), 7.17 (1H, ddd, $J=8.2$, 8.2, 1.3, H-11), 7.28~7.42 (5H, overlapped, CH_2Ph), 7.44

(2H, overlapped, H-9, 12), 7.51/7.59 (1H, s, H-17), 8.06/8.16 (1H, s, H-21), 9.87 (1H, br-s, H-1). ^{13}C NMR (150MHz, CDCl_3) δ 9.12 (C-18), 22.54 (C-6), 25.76 (C-19), 33.75 (C-14), 38.19 (C-15), 41.59 (C-5), 46.49 (C-3), 52.37 (C-23), 62.65 (C-24), 69.40 (OCH_2Ph), 80.52 (C-20), 106.41 (C-7), 107 (C-16), 111.53 (C-12), 117.86 (C-9), 119.21 (C-10), 21.68 (C-11), 126.43 (C-8), 128.09, 128.40, 128.57, 135.56 (OCH_2Ph), 132.85 (C-2), 135.56 (OCH_2Ph), 136.25 (C-13), 155.36 ($\text{CO}_2\text{CH}_2\text{Ph}$), 160.87 (C-21), 162.84 (C-17), 170 (C-22). EIMS m/z (%): 534 (M^+ , 21), 505 (5), 199 (100). HR-FABMS (NBA+PEG): found 535.2453, calcd for $\text{C}_{30}\text{H}_{35}\text{O}_7\text{N}_2$ [$\text{M}+\text{H}$] $^+$; 535.2444. CD (c 0.175 mmol/L, MeOH, 23°C) λ_{nm} ($\Delta\epsilon$): 201 (−10.2), 209 (0), 219 (+10.7), 232 (0), 252 (−1.1), 287 (−0.5), 300 (0).

***O*-Acetyl derivative (19)**

A solution of **17** (6.0 mg, 0.0112 mmol) in ethanol (2 mL) was hydrogenated in the presence of 10% Pd on carbon (3.0 mg) for 30 min at room temperature. The catalyst was filtered off, and the filtrate was evaporated to give a residue, which was treated with acetic anhydride (3.0 μl) and dimethylaminopyridine (2.0 mg) in dry dichloromethane (1 mL) for 4.5 h at room temperature. Saturated aqueous ammonium chloride was added to the reaction mixture, which was then extracted three times with 5% methanol-chloroform. The combined extract was washed with brine, dried over MgSO_4 , and concentrated to give a residue, that was purified by pre-packed silica gel column chromatography (1% methanol-chloroform) to give 4.7 mg (95% overall yield from **17**) of **19** as a colorless prisms, m.p. 231–233°C (from methanol). IR ν_{max} (neat) cm^{-1} : 3283, 2941, 1732, 1698, 1652. UV λ_{max} (MeOH) nm: 225.0, 288.0. In the NMR spectra, some signals appeared as a pair of peaks due to a mixture of rotation isomers of *N*-formyl function. ^1H NMR (400MHz, CDCl_3) δ 0.83 (dd, $J=7.3$, 7.3, H-18)/0.87 (dd, $J=7.6$, 7.6, H-18), 1.44 (m)/1.62 (m)/1.71 (m, H-19), 2.00 (ddd, $J=14.6$, 10.7, 4.3, H-14), 2.01 (s)/2.05 (s, COCH_3), 2.47 (m)/2.51 (ddd, $J=14.3$, 11.9, 2.4, H-14), 2.75 (dd, $J=15.6$, 4.3)/2.85 (m, H-6), 3.03 (br-ddd, $J=12.5$, 11.9, 4.9, H-5), 3.16 (ddd, $J=11.9$, 7.6, 4.3)/3.26 (ddd, $J=10.7$, 6.1, 6.1, H-15), 3.57 (m, H-5), 3.73/3.78 (s, H-23), 3.80 (m, H-5), 3.86/3.92 (s, H-24), 4.49 (d, $J=9.5$, H-3), 4.72 (dd, $J=13.1$, 5.2, H-5), 5.03 (ddd, $J=10.1$, 7.0, 3.4)/5.08 (ddd, $J=7.9$, 7.9, 3.7, H-20), 5.46 (1H, dd, $J=8.5$, 4.9, H-3), 7.08 (ddd, $J=8.2$, 8.2, 1.2)/7.10 (ddd, $J=7.9$, 7.9, 1.2, H-10), 7.16 (ddd, $J=6.7$, 6.7, 1.2)/7.17 (ddd, $J=7.0$, 7.0, 1.1, H-11), 7.34 (d, $J=7.9$)/7.36 (d, $J=7.9$, H-12), 7.43 (d, $J=7.6$)/7.46 (d, $J=7.6$, H-9), 7.48/7.54 (each s, H-17), 8.06/8.17 (each s, H-21), 8.21/8.68 (each br-s, H-1). ^{13}C NMR (125MHz, CDCl_3) δ 9.41/9.90 (C-18), 20.98/22.83 (C-6), 21.05/21.17 (COCH_3), 24.27/24.95 (C19), 33.31/33.89 (C-14), 34.87/40.79 (C-5), 35.81/36.02 (C-15), 46.13/52.26 (C-3), 51.37/51.54 (C-23), 61.80/62.12 (C-24), 106.68/108.46 (C-7), 108.00/108.19 (C-16), 111.02/111.14 (C-12), 117.80/118.19 (C-9), 119.34/119.62 (C-10), 121.78/122.11 (C-11), 126.44/126.55 (C-8), 133.09/133.55 (C-2), 136.07 (C-13), 161.73/162.07 (C-21), 162.30/162.59 (C-17),

168.07/168.79 (C-22), 170.80/171.37 (COCH_3). EIMS m/z (%): 442 (M^+ , 43), 413 (10), 199 (100). HR-FABMS (NBA/PEG): found 442.2118, calcd for $\text{C}_{24}\text{H}_{30}\text{N}_2\text{O}_6$ [$\text{M}+\text{H}$] $^+$; 442.2104. CD (c 0.226 mmol/L, MeOH, 22°C) λ_{nm} ($\Delta\epsilon$): 210 (–5.0), 213 (–4.5), 216 (–4.8), 224 (0), 233 (+4.0), 290 (0).

X-ray crystallographic analysis of **19**: All measurements were made on a Rigaku/MS C Mercury CCD diffractometer with graphite monochromated Mo-K α radiation ($\lambda=0.71069$ Å). Crystal data; orthorhombic, $\text{C}_{24}\text{H}_{30}\text{N}_2\text{O}_6$ (Mw: 442.51), space group $\text{P2}_1\text{2}_1\text{2}$ with $a=7.943(2)$ Å, $b=14.737(4)$ Å, $c=20.804(5)$ Å, $V=2435(1)$ Å 3 , $Z=4$, and $D_{\text{calc}}=1.207$ g/cm 3 . The structure was solved by direct methods (SIR97) and expanded using Fourier techniques (DIRDIF94). The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. The final cycle of full-matrix least-squares refinement was based on 2890 reflections ($I>0.00\sigma$ (I), $2\theta<57.21^\circ$) and 291 variable parameters and converged with unweighted and weighted agreement factors of $R=0.073$ and $R_w=0.051$.

Preparation of oxindole 20a from 17 by oxidation with lead tetraacetate

To a stirred solution of **17** (48.6 mg, 0.091 mmol) in dry dichloromethane (5 mL) was added lead tetraacetate (189 mg, 72% purity, 0.307 mmol) at 0°C and the mixture was stirred for 2 h at room temperature under argon atmosphere. Saturated aqueous NaHCO_3 was added to the reaction mixture, which was then extracted thoroughly with 5% methanol-chloroform. The combined extract was washed with brine, dried over MgSO_4 and concentrated to give a residue, that was subjected to the next reaction. A solution of the crude material in methanol (1 mL) was added to a pre-refluxed solution (methanol:water = 2:1, 9 mL) containing one drop of acetic acid, and the mixture was heated by refluxing for 15 min under argon atmosphere. After cooling, the reaction mixture was neutralized with ammonium water, and then extracted thoroughly with 5% methanol-chloroform. The combined extract was washed with brine, dried over MgSO_4 , and concentrated to give a residue, that was purified by pre-packed silica gel column chromatography (ethyl acetate/ n -hexane = 1:1 to ethyl acetate gradient) to give 24.4 mg (49%) of **20a** as a colorless amorphous powder. IR ν_{max} (CHCl_3) cm^{-1} : 1728, 1651, 1623. UV λ_{max} (MeOH) nm: 208.5, 243.0. ^1H NMR (500MHz, CDCl_3) δ 0.80 (3H, dd, $J=7.3$, 7.3, H-18), 1.38 (1H, m, H-19), 1.57 (2H, overlapped, H-14, 19), 1.90 (1H, br-dd, $J=12.2$, 12.2, H-14), 2.03 (1H, ddd, $J=13.1$, 8.9, 4.3, H-6), 2.32 (1H, m, H-6), 3.12 (1H, ddd, $J=12.2$, 8.8, 3.7, H-15), 3.59 (3H, s, H-23), 3.64 (1H, m, H-5), 3.73 (3H, s, H-24), 3.76 (1H, m, H-3), 3.95 (1H, ddd, $J=13.4$, 8.2, 4.6, H-5), 4.85 (1H, m, H-20), 5.06 (1H, d, $J=12.2$, OCH_2Ph), 5.10 (1H, d, $J=12.2$, OCH_2Ph), 6.89 (1H, d, $J=7.6$, H-12), 6.96 (1H, d, $J=7.6$, H-9), 6.98 (1H, t, $J=7.6$, H-10), 7.22 (1H, m, H-11), 7.31~7.39 (5H, overlapped, CH_2Ph), 7.38 (1H, s, H-17), 8.04 (1H, br-s, H-1), 8.25 (1H, s, H-22). ^{13}C NMR (125MHz, CDCl_3) δ 8.92 (C-18), 25.11 (C-19), 30.05 (C-14), 33.07 (C-6), 37.00 (C-15), 42.21

(C-5), 51.38 (C-23), 56.49 (C-7), 61.89 (C-3, 24), 69.27 (OCH₂Ph), 80.91 (C-20), 107.30 (C-16), 110.00 (C-12), 122.60 (C-10), 124.76 (C-9), 128.08, 128.42, 128.58, 128.84, 135.54 (C-8, 11, CH₂Ph), 140.41 (C-13), 155.13 (CO₂CH₂Ph), 161.67 (C-21), 162.07 (C-17), 167 (C-22), 178.61 (C-2). EIMS *m/z* (%): 550 (M⁺, 5), 522 (11), 91 (100). HR-FABMS (NBA/PEG): found 551.2444, calcd for C₃₀H₃₅N₂O₈ [M+H]⁺; 551.2393. CD (*c* 0.176 mmol/L, MeOH, 23°C) λ_{nm} (Δε): 213 (−18.1), 220 (0), 233 (+22.0), 246 (0), 257 (−11.1), 288 (−2.7), 306 (−0.3).

Preparation of oxindoles **20a** and **20b** by oxidation with *t*-BuOCl

To a stirred mixture of **17** (32.8 mg, 0.0614 mmol) and triethylamine (12.3 μl, 0.0882 mmol) in dry dichloromethane (1.5 mL) cooled to −30°C was added a solution of *t*-BuOCl (13.4 mg, 0.124 mmol) in dry dichloromethane (0.1 mL) and the mixture was stirred for 20 min at the same temperature. The volatile material was removed under reduced pressure at −30°C and the residue was immediately subjected to the next reaction. A solution of the crude material in methanol (1 mL) was added to a pre-refluxed solution (methanol:water = 2:1, 1.5 mL) containing one drop of acetic acid, and the mixture was heated by refluxing for 15 min under argon atmosphere. After cooling, the reaction mixture was neutralized with ammonium water, and then extracted thoroughly with 5% methanol-chloroform. The combined extract was washed with brine, dried over MgSO₄, and concentrated to give a residue, that was purified by pre-packed silica gel column chromatography (ethyl acetate/*n*-hexane = 1:1 to ethyl acetate gradient) to give 6.6 mg (20%) of **20b** and 22.8 mg (68%) of **20a** as a colorless amorphous powder, respectively. Compound **20a** was identical with the product obtained by the above reaction by comparison of the spectroscopic data. Compound **20b**: IR ν_{max} (CHCl₃) cm^{−1}: 1732, 1654. UV λ_{max} (MeOH) nm: 209, 244. ¹H NMR (400MHz, CDCl₃, VT 50°C) δ 0.79 (3H, dd, *J*=7.5, 7.5, H-18), 1.34 (1H, dddd, *J*=7.3, 7.3, 7.3, 7.3, H-19), 1.60 (1H, m, H-19), 1.93 (1H, ddd, *J*=13.7, 9.9, 3.8, H-14), 2.07 (1H, m, H-6), 2.19 (1H, ddd, *J*=14.5, 11.5, 2.7, H-14), 2.44 (1H, m, H-6), 3.07 (1H, ddd, *J*=7.5, 7.5, 3.5, H-15), 3.54 (3H, s, H-23), 3.65 (m, H-3), 3.65 (3H, s, H-24), 3.72 (1H, m, H-5), 3.98 (1H, m, H-5), 4.89 (1H, ddd, *J*=7.5, 7.5, 3.5, H-20), 5.14 (1H, d, *J*=12.3, OCH₂Ph), 5.18 (1H, d, *J*=12.3, OCH₂Ph), 6.85 (1H, d, *J*=7.7, H-12), 6.93 (1H, d, *J*=6.8, H-9), 7.00 (1H, ddd, *J*=7.5, 7.5, 0.9, H-10), 7.21 (1H, ddd, *J*=7.7, 7.7, 1.3, H-11), 7.27 (1H, s, H-17), 7.23~7.40 (5H, overlapped, CH₂Ph), 7.55 (1H, br-s, H-1), 8.21/8.31 (1H, s, H-21). ¹³C NMR (150MHz, CDCl₃) δ 8.94 (C-18), 25.07 (C-19), 29.76 (C-14), 33.51 (C-6), 36.91 (C-15), 41.75 (C-5), 51.29 (C-23), 55.86 (C-7), 61.80 (C-24), 63.99 (C-3), 69.41 (OCH₂Ph), 81.16 (C-20), 108.34 (C-16), 109.60 (C-12), 122.87 (C-9)*, 122.92 (C-10)*, 128.15, 128.34, 128.52, 128.60, 135.82 (C-11, OCH₂Ph), 132.21 (C-8), 140.10 (C-13), 155.24 (OCO₂CH₂Ph), 161.41 (C-21), 161.53 (C-17), 167.64 (C-22), 177.12 (C-2) (*interchangeable). EI-MS *m/z* (%) : 550 (M⁺, 13), 522 (27), 91 (100). HR-FABMS (NBA/PEG): found 551.2391, calcd for C₃₀H₃₅N₂O₈ [M+H]⁺; 551.2393. CD (*c* 0.224 mmol/L,

MeOH, 23°C) λ_{nm} ($\Delta\epsilon$): 202 (0), 210 (+5.0), 216 (0), 234 (−6.0), 237 (−4.5), 255 (−9.4), 273 (0), 292 (+1.7), 309 (0).

Preparation of oxindoles **21a and **21b** from **18** by oxidation with lead tetraacetate**

To a stirred solution of **18** (76.8 mg, 0.128 mmol) in dry dichloromethane (6 mL) was added lead tetraacetate (157 mg, 72% purity 0.255 mmol) at 0°C and the mixture was stirred for 1.5 h at room temperature under argon atmosphere. Saturated aqueous NaHCO₃ was added to the reaction mixture, which was then extracted thoroughly with 5% methanol-chloroform. The combined extract was washed with brine, dried over MgSO₄ and concentrated to give a residue, that was subjected to the next reaction. A solution of the crude material in methanol (1 mL) was added to a pre-refluxed solution (methanol:water = 2:1, 9 mL) containing one drop of acetic acid, and the mixture was heated by refluxing for 15 min under argon atmosphere. After cooling, the reaction mixture was neutralized with ammonium water, and then extracted thoroughly with 5% methanol-chloroform. The combined extract was washed with brine, dried over MgSO₄, and concentrated to give a residue, that was purified by pre-packed silica gel column chromatography (ethyl acetate/*n*-hexane = 1:1 to ethyl acetate gradient) to give 48.2 mg (69%) of **21b** and 3.2 mg (5%) of **21a** as a colorless amorphous powder, respectively. Compound **21b**: IR ν_{max} (CHCl₃) cm^{−1}: 1731, 1654. UV λ_{max} (MeOH) nm: 209.0, 244.0. In the ¹H-NMR spectrum, some signals appeared as a pair of peaks due to a mixture of rotation isomers of *N*-formyl function. ¹H NMR (500MHz, CDCl₃, VT 50°C) δ 0.59 (dd, *J*=7.3, 7.3)/0.80 (dd, *J*=7.3, 7.3, H-18), 1.22 (2H, m, H-19), 1.63 (1H, m, H-14), 2.00 (1H, m, H-6), 2.34 (1H, m, H-6), 2.54 (1H, m, H-15), 3.59 (1H, m, H-5), 3.68 (3H, s, H-23), 3.71 (3H, s, H-24), 3.99 (2H, overlap, H-3, 5), 4.60 (1H, m, H-20), 5.02 (1H, d, *J*=12.2, OCH₂Ph), 5.11 (1H, d, *J*=12.2, OCH₂Ph), 6.86 (d, *J*=7.6)/6.90 (d, *J*=7.6, H-12), 6.98 (1H, dd, *J*=7.3, 7.3, H-10), 7.06 (1H, d, *J*=7.6, H-9), 7.22 (1H, dd, *J*=7.9, 7.9, H-11), 7.33 (1H, s, H-17), 7.31~7.38 (5H, overlapped, CH₂Ph), 7.54/7.58 (1H, br-s, H-1), 8.24/8.26 (1H, s, H-21). ¹³C NMR (125MHz, CDCl₃, VT 50) δ 9.27 (C-18), 24.80 (C-19), 29.55 (C-14), 35.18 (C-6), 36.73 (C-15), 43.04 (C-5), 51.45 (C-23), 56.57 (C-7), 61.91 (C-3)*, 62.01 (C-24)*, 69.30 (OCH₂Ph), 81.63 (C-20), 107.97 (C-16), 110.19 (C-12), 122.72 (C-10), 124.85 (C-9), 128.06, 128.29, 128.48, 128.57, 128.75, 129.11, 135.76 (C-8, 11, CH₂Ph), 140.52 (C-13), 155.13 (OCO₂CH₂Ph), 161.27 (C-17), 161.48 (C-21), 167.89 (C-22), 177.99 (C-2) (*interchangeable). EIMS *m/z* (%): 550 (M⁺, 5), 522 (13), 91 (100). HR-FABMS (NBA/PEG): found 551.2397, calcd for C₃₀H₃₅N₂O₈ [M+H]⁺; 551.2393. CD (*c* 0.200 mmol/L, MeOH, 23°C) λ_{nm} ($\Delta\epsilon$): 209 (−1.8), 237 (−7.2), 246 (0), 258 (+10.0), 280 (+2.0), 306 (0). Compound **21a**: IR ν_{max} (CHCl₃) cm^{−1}: 1731, 1659. UV λ_{max} (MeOH) nm: 208.5, 243.5. In the ¹H-NMR spectrum, some signals appeared as a pair of peaks due to a mixture of rotation isomers of *N*-formyl function. ¹H NMR (500MHz, CDCl₃, VT 50°C) δ 0.72 (dd, *J*=7.3, 7.3)/0.77 (dd, *J*=7.3, 7.3, H-18), 1.38 (1H, m, H-19), 1.53 (1H, m, H-19), 2.07 (1H, m, H-6),

2.30 (2H, m, H-14), 2.43 (1H, m, H-6), 2.70 (1H, m, H-15), 3.56 (3H, s, H-23), 3.62 (3H, s, H-24), 3.68 (1H, m, H-5), 3.82 (1H, dd, $J=7.3$, 7.3, H-3), 3.95 (1H, m, H-5), 4.81 (1H, ddd, $J=7.9$, 7.9, 4.0, H-20), 5.10 (1H, d, $J=12.2$, OCH₂Ph), 5.15 (1H, d, $J=12.2$, OCH₂Ph), 6.79 (1H, d, $J=7.9$, H-12), 6.96 (1H, d, $J=7.6$, H-9), 6.98 (1H, t, $J=7.6$, H-10), 7.18 (1H, m, H-11), 7.23 (1H, s, H-17), 7.31~7.45 (5H, overlapped, CH₂Ph), 8.20/8.26 (1H, s, H-21). ¹³C NMR (125MHz, CDCl₃, VT 50°C) δ 9.28 (C-18), 24.77 (C-19), 31.02 (C-14), 34.70 (C-6), 36.80 (C-15), 41.85 (C-5), 51.32 (C-23), 55.49 (C-7), 61.76 (C-24), 64.31 (C-3), 69.38 (OCH₂Ph), 81.89 (C-20), 108.78 (C-16), 109.61 (C-12), 122.82 (C-10)*, 122.85 (C-9)*, 128.22, 128.31, 128.42, 128.56, 128.61, 132.43, 135.82 (C-8, 11, CH₂Ph), 139.77 (C-13), 155.12 (OCO₂CH₂Ph), 160.88 (C-17), 161.23 (C-21), 167.58 (C-22), 177.11 (C-2) (*interchangeable). EIMS m/z (%): 550 (M⁺, 16), 522 (23), 91 (100). HR-FABMS (NBA/PEG): found 551.2393, calcd for C₃₀H₃₅N₂O₈ [M+H]⁺; 551.2393. CD (c 0.170 mmol/L, MeOH, 23°C) λ_{nm} ($\Delta\epsilon$): 220 (+3.1), 235 (0), 257 (+8.2), 280 (0), 291 (−0.9), 308 (0).

Preparation of Us-8 (2)

A solution of **20a** (14.4 mg, 0.0262 mmol) in ethanol (2 mL) was hydrogenated in the presence of 10% Pd on carbon (4.0 mg) for 5 h at room temperature. The catalyst was filtered off, and the filtrate was evaporated to give a residue, that was treated with Dess-Martin periodinane (12.7 mg, 0.029 mmol) in dry dichloromethane (2 mL) for 20 min at room temperature. Aqueous sodium sulfite was added to the reaction mixture, which was then extracted three times with 5% methanol-chloroform. The combined extract was washed with brine, dried over MgSO₄, and concentrated to give a residue, that was purified by pre-packed silica gel column chromatography (2% methanol-chloroform) to give 8.8 mg (88% overall yield from **20a**) of **2** as a colorless amorphous powder. The following spectroscopic data were completely identical with those of natural Us-8. IR ν_{max} (CHCl₃) cm^{−1}: 1717, 1654. UV λ_{max} (MeOH) nm : 207.5, 244.5. ¹H NMR (500MHz, CDCl₃) δ 0.97 (dd, $J=7.3$, 7.3, H-18), 1.65 (1H, ddd, $J=14.9$, 8.2, 4.9, H-14), 2.18 (1H, ddd, $J=12.7$, 8.4, 4.2, H-6), 2.23 (dq, $J=14.4$, 7.3, H-19), 2.29 (dq, $J=14.4$, 7.3, H-19), 2.36 (1H, m, H-6), 2.44 (1H, m, H-14), 3.48 (1H, dd, $J=8.4$, 5.9, H-15), 3.59 (3H, s, H-23), 3.67 (1H, m, H-5), 3.79 (3H, s, H-24), 3.89 (1H, dd, $J=8.6$, 4.7, H-3), 3.99 (1H, ddd, $J=12.3$, 9.5, 4.4, H-5), 6.91 (1H, d, $J=7.7$, H-12), 7.04 (1H, dd, $J=7.7$, 7.7, H-10), 7.15 (1H, d, $J=7.7$, H-9), 7.25 (1H, dd, $J=7.7$, 7.7, H-11), 7.39 (1H, s, H-17), 7.81 (1H, br-s, H-1), 8.32 (1H, s, H-21). ¹³C NMR (150MHz, CDCl₃) δ 7.97 (C-18), 29.26 (C-14), 33.04 (C-19), 33.77 (C-6), 42.23 (C-5), 44.84 (C-15), 51.55 (C-23), 56.29 (C-7), 61.65 (C-3), 62.11 (C-24), 107.83 (C-16), 110.08 (C-12), 122.74 (C-10), 124.96 (C-9), 128.63 (C-11), 128.66 (C-8), 140.47 (C-13), 161.42 (C-17), 161.80 (C-21), 167.11 (C-22), 178.84 (C-2), 208.29 (C-20). EIMS m/z (%): 414 (M⁺, 36), 382 (53), 187 (100). HR-FABMS (NBA/PEG): found 415.1862, calcd for C₂₂H₂₇N₂O₆ [M+H]⁺; 415.1869. CD (c 0.242 mmol/L, MeOH, 23°C) λ_{nm} ($\Delta\epsilon$): 209 (0), 215 (−2.2), 218 (0), 236 (+9.2), 255 (0), 287 (−8.2).

$[\alpha]_D^{24} -122$ (*c* 0.05, CHCl₃) (natural Us-8, $[\alpha]_D^{24} -110$ (*c* 0.08, CHCl₃)).

Preparation of **1** (Reported Us-7)

A solution of **21a** (5.3 mg, 0.0096 mmol) in ethanol (2 mL) was hydrogenated in the presence of 10% Pd on carbon (3.0 mg) for 30 min at room temperature. The catalyst was filtered off, and the filtrate was evaporated to give a residue, which was treated with Dess-Martin periodinane (5.1 mg, 0.0117 mmol) in dry dichloromethane (1 mL) for 10 min at room temperature. Aqueous sodium sulfite was added to the reaction mixture, which was then extracted three times with 5% methanol-chloroform. The combined extract was washed with brine, dried over MgSO₄, and concentrated to give a residue, that was purified by pre-packed silica gel column chromatography (2% methanol-chloroform) to give 2.3 mg (56% overall yield from **21a**) of **1** as a colorless amorphous powder. IR $\nu_{\max}$ (CHCl₃) cm⁻¹: 1715, 1659. UV $\lambda_{\max}$ (MeOH) nm : 205.5, 245.5. In the ¹H-NMR spectrum, some signals appeared as a pair of peaks due to a mixture of rotation isomers of *N*-formyl function. ¹H NMR (600MHz, CDCl₃) δ 0.96/0.97 (each dd, *J*=7.4, 7.4, H-18), 1.74 (1H, ddd, *J*=14.6, 9.1, 5.2, H-14), 2.12 (1H, ddd, *J*=12.6, 9.1, 3.8, H-6), 2.25 (1H, m, H-19), 2.37 (1H, m, H-19), 2.62~2.68 (2H, overlapped, H-6, 14), 3.48 (1H, m, H-15), 3.62 (m, H-5), 3.62/3.66 (3H, each s, H-23), 3.67/3.76 (3H, each s, H-24), 4.00 (1H, m, H-5), 4.05 (1H, dd, *J*=9.1, 5.8, H-3), 6.86 (d, *J*=7.7)/6.89 (d, *J*=7.7, H-12), 6.90 (d, *J*=7.4)/7.05 (d, *J*=6.9, H-9), 7.00 (1H, ddd, *J*=7.7, 7.7, 0.8, H-10), 7.21 (ddd, *J*=7.7, 7.7, 1.4)/7.23 (ddd, *J*=7.7, 7.7, 1.1, H-11), 7.33/7.38 (1H, each s, H-17), 7.50/7.55 (1H, each br-s, H-1), 8.07/8.38 (1H, each s, H-21). ¹³C NMR (150MHz, CDCl₃) δ 8.18 (C-18), 30.70 (C-14), 33.26 (C-6), 33.36 (C-19), 41.07 (C-5), 44.56 (C-15), 51.54 (C-23), 54.80 (C-7), 62.09 (C-24), 64.07 (C-3), 109.35 (C-12), 109.66 (C-16), 122.74 (C-9), 123.26 (C-10), 128.55 (C-11), 133.88 (C-8), 139.12 (C-13), 160.61 (C-17), 161.23 (C-21), 167.35 (C-22), 176.63 (C-2), 209.68 (C-20). FABMS (NBA): 415 [M+1]⁺. HR-FABMS (NBA/PEG): found 415.1865, calcd for C₂₂H₂₇N₂O₆ [M+H]⁺; 415.1869. CD (*c* 0.254 mmol/L, MeOH, 23°C) λ_{nm} ($\Delta\epsilon$): 205 (0), 216 (+23.5), 236 (+1.1), 252 (+4.9), 263 (0), 285 (-8.2), 317 (-0.3).

Preparation of **22** (Revised Us-7)

A solution of **20b** (5.8 mg, 0.0105 mmol) in ethanol (2 mL) was hydrogenated in the presence of 10% Pd on carbon (3.0 mg) for 20 min at room temperature. The catalyst was filtered off, and the filtrate was evaporated to give a residue, which was treated with Dess-Martin periodinane (5.6 mg, 0.0126 mmol) in dry dichloromethane (1 mL) for 10 min at room temperature. Aqueous sodium sulfite was added to the reaction mixture, which was then extracted three times with 5% methanol-chloroform. The combined extract was washed with brine, dried over MgSO₄, and concentrated to give a residue, that was purified by

pre-packed silica gel column chromatography (2% methanol-chloroform) to give 3.7 mg (84% overall yield from **20b**) of **22** as a colorless amorphous powder. The following spectroscopic data were completely identical with those of natural Us-7. IR $\nu_{\max}$ (CHCl₃) cm⁻¹: 1716, 1655. UV $\lambda_{\max}$ (MeOH) nm : 209.5, 245.5. ¹H NMR (500MHz, CDCl₃) δ 0.84 (3H, dd, *J*=7.0, 7.0, H-18), 1.84 (1H, dq, *J*=17.4, 7.0, H-19), 1.93 (1H, ddd, *J*=13.4, 6.7, 6.7, H-14), 2.11~2.23 (2H, overlapped, H-6, 19), 2.44 (1H, ddd, *J*=12.8, 8.2, 4.6, H-6), 2.62 (1H, ddd, *J*=14.6, 7.3, 7.3, H-14), 3.26 (1H, dd, *J*=7.0, 7.0, H-15), 3.62 (3H, s, H-23), 3.79 (3H, s, H-24), 3.81 (1H, m, H-5), 3.98 (1H, ddd, *J*=12.5, 8.9, 4.3, H-5), 4.02 (1H, dd, *J*=7.0, 7.0, H-3), 6.93 (1H, d, *J*=7.6, H-12) 7.01 (1H, d, *J*=7.6, H-9), 7.03 (1H, t, *J*=7.6, H-10), 7.25 (1H, ddd, *J*=7.6, 7.6, 1.5, H-11), 7.35 (1H, s, H-17), 7.99 (1H, br-s, H-1), 8.37 (1H, s, H-21). ¹³C NMR (150MHz, CDCl₃) δ 7.88 (C-18), 30.00 (C-14), 32.88 (C-19), 34.28 (C-6), 42.16 (C-5), 44.68 (C-15), 51.60 (C-23), 55.61 (C-7), 62.08 (C-24), 62.66 (C-3), 108.57 (C-16), 109.90 (C-12), 122.78 (C-10)*, 122.89 (C-9)*, 128.64 (C-11), 131.50 (C-8), 140.09 (C-13), 160.96 (C-17), 161.34 (C-21), 167.27 (C-22), 177.61 (C-2), 208.44 (C-20) (* interchangeable). EIMS *m/z* (%): 414 (M⁺, 27), 382 (32), 187 (100). HR-FABMS (NBA/PEG): found 415.1865, calcd for C₂₂H₂₇N₂O₆ [M+H]⁺; 415.1869. CD (*c* 0.338 mmol/L, MeOH, 23°C) λ_{nm} ($\Delta\epsilon$): 208 (0), 212 (−3.6), 218 (−4.5), 247 (0), 239 (+2.4), 247 (0), 281 (−8.7), 324 (0). $[\alpha]_D^{23}$ −101 (*c* 0.08, CHCl₃) (natural Us-7, $[\alpha]_D^{23}$ −96 (*c* 0.05, CHCl₃)).

19

Synthetic Us-8 IWARA\FUJIWARA-SYN-US8\SKFUJIWARA-SYN-US8.a1s

D:\NMR-Data\Fujiwara\DUS\SK-natural-US-8:
Natural US-8

Synthetic Us-8

Us-8 (2)

OBNUC : 13C
 OBFQ : 125.65 MHz
 OBSE : 127782.65 Hz
 IRNUC : 1H
 IRFQ : 500.00 MHz
 IRSE : 162410.00 Hz
 IRATN : 511
 IRAPW : 50.0 usec
 IRBP1 : 30
 IRBP2 : 5
 IRPNS : 0
 ADBIT : 16
 CTEMP : -204.8 C
 CSPED : 14 Hz
 SLVNT : CDCL3
 RESOL : 0.46 Hz
 BF : 3.00 Hz
 T1 : 0.00 %
 T2 : 0.00 %
 T3 : 90.00 %
 T4 : 100.00 %
 REFL : 77.00 ppm
 XE : 26023.80 Hz
 XS : -1159.53 Hz
 operator

D:\NMR-Data\Fujiwara\DUS\61-70\SKFUJIWARA-DUS63-6.NMR;1
 Synthetic Us-7

D:\NMR-Data\Fujiwara\“V’R”\SKFUJIWARA-US7-2.NMR;1
 Natural US-7

D:\NMR-Data\Fujiwara\[-]-INNMR\SKFUJIWARA-DUS 63-6BCM.a1s
 Synthetic Us-7 BCM

D:\NMR-Data\Fujiwara\[-]-INNMR\SKFUJIWARA-US7-BCM.a1s
 Natural US-7 BCM