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Heterocycles. XIII.[1] Syntheses and Absolute Configurations of Chiral Benzo[*c*]phenanthridines

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Chiral benzo[*c*]phenanthridines have been synthesized. Aminolysis of the (−)-epoxyhydroxy lactone (**3**) with methylamine stereospecifically gives the (+)-trihydroxy lactam (**5**), from which the (+)-10b-hydroxychelidonine (**7**) and (+)-11-epichelidonine analogs (**10**) are derived. The absolute configurations of the compounds obtained are assigned on the basis of that of (−)-**3** and the results obtained from the subsequent stereo-controlled reactions. The absolute configurations of (+)-**7** and (+)-**10** are confirmed by Horeau's method.

Keywords——chiral benzo[*c*]phenanthridine; absolute configuration; circular dichroism; optical rotatory dispersion; proton magnetic resonance (contact shift)

Although many synthetic methods for benzo[*c*]phenanthridines have been presented, no approach to chiral ones has been attempted. We previously reported that the phase-transfer chiral epoxidation of the naphthoquinone (**1**) gave the (+)-naphthoquinone epoxide (**2**) (95%, 78% ee) which was recrystallized from ethanol to yield (+)-**2** (63%, 100% ee) and that reduction of (+)-**2** (100% ee) with sodium borohydride afforded the (−)-epoxyhydroxy lactone (**3**) (44%, 100% ee) having the 4b*S*, 10b*R*, 11*S*, 12*S* configuration.[2] On the other hand, in the course of our investigations on the benzo[*c*]phenanthridine alkaloids, it was found that (±)-**3** was a useful starting material for the synthesis of a benzo[*c*]phenanthridine framework.[3] Thus, the combination of these outcomes establishes a synthetic method for a chiral benzo[*c*]-phenanthridine, as has been preliminarily reported.[1] We now report in detail the stereospecific syntheses of chiral analogs of chelidonine from (−)-**3** together with the results of further investigations.

Treatment of (−)-**3** (84% ee)[4] with aqueous methylamine gave the (+)-trihydroxy lactam (**5**) (99%) which was reduced with lithium aluminum hydride/aluminum chloride to yield the (+)-trihydroxy amine (**6**) (99%). The infrared (IR) and proton magnetic resonance (^{1}H NMR) spectra of (+)-**6** showed Bohlmann bands (2775 and 2700 cm^{-1}), and a W-path coupling (2 Hz) between the 4b- and 11-protons and a coupling (3 Hz) between the 11- and 12-protons, respectively. Thus, the *cis* steroidal conformation having the 10b$_{ax}$-, 11$_{ax}$- and 12$_{eq}$-hydroxyl groups in the C ring can be assigned to the B/C ring fusion in (+)-**6**. Treatment of (±)-**3** with anhydrous ethanolic methylamine afforded (±)-**5** as a sole product.[3] This result proves that water does not take part in the opening of the oxirane ring. Since the structure of (+)-**5** should be similar to that of (+)-**6**, the stereo-controlled formation of (+)-**5** from (−)-**3** is thought to occur as follows. The dihydroxyepoxy amide (**4**), formed by the reaction of (−)-**3** with methylamine, recyclizes to form (+)-**5** by an S_N reaction of the amide group at the 1-position, accompanied by a concerted migration of the 1-hydroxyl group to the 2-position from the back side with respect to the oxirane ring in a *trans* ring opening mode. This is in accord with the finding that aminolysis of the (±)-4b-isomer of (−)-**3** with aqueous methylamine resulted in the formation of the (±)-1-isomer of **4**. Thus, on the basis of the configuration of (−)-**3**, the 4b*R*, 10b*S*, 11*S*, 12*S* configurations can be assigned to (+)-**5** and (+)-**6**.

Hydrogenolysis of (+)-**6** over palladium-carbon gave the (+)-10b-hydroxychelidonine analog (**7**) (78%). Its ^{1}H NMR spectrum showed two one-proton double doublets at δ 3.29

(J 17 and 4 Hz) and 2.93 (J 17 and 2 Hz) assignable to the 12-protons by comparison with the data for (+)-**6**, suggesting the 4b*R*, 10b*S*, 11*S* configuration for (+)-**7**. As expected from the structure having the *cis* steroidal B/C ring fusion, Bohlmann bands (2775 and 2700 cm^{-1}) and an intramolecular hydrogen-bonding (3225 cm^{-1}) between the 11-hydroxyl group and the nitrogen atom,[5] and a W-path coupling (2 Hz) between the 4b- and 11-protons were observed in the IR and ^1H NMR spectra of (+)-**7**, respectively.

Treatment of (+)-**7** with mesyl chloride afforded the (+)-epoxy amine (**8**) (93%). Bohlmann bands (2775 and 2680 cm^{-1}) and a W-path coupling (2 Hz) between the 4b- and 11-protons were observed in the IR and ^1H NMR spectra of (+)-**8**, respectively, and are comp-

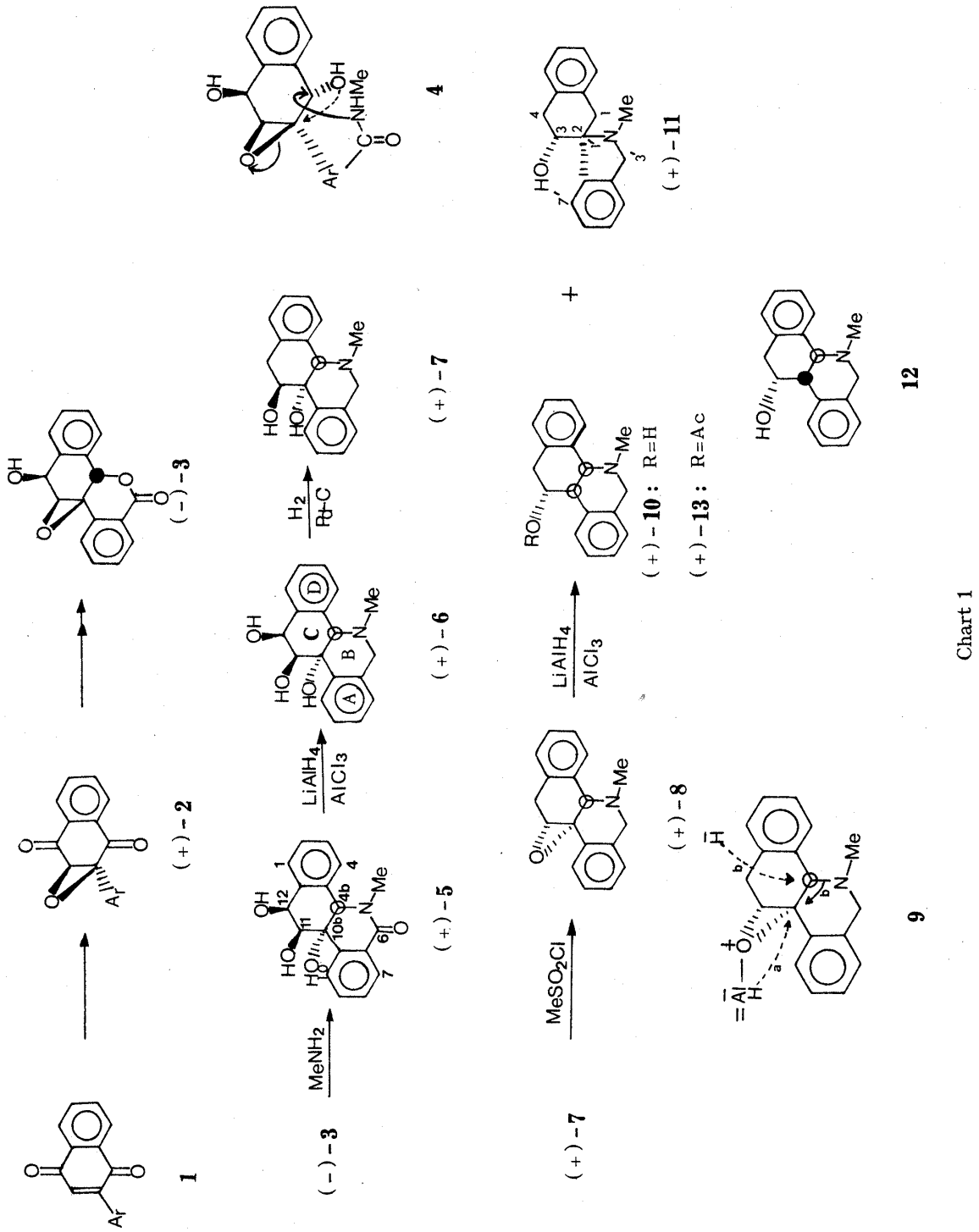
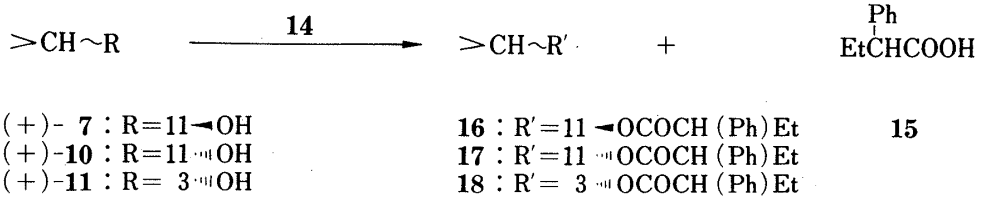


Chart 1

atible with the *cis* steroidal B/C ring fusion. Thus, it is clear that the oxirane ring is formed by the elimination of the 11-hydroxyl group, accompanied by the back side attack of the 10b-hydroxyl group. As a result, the 4b*R*, 10b*S*, 11*R* configuration can be assigned to (+)-**8**.

Reduction of (+)-**8** with lithium aluminum hydride/aluminum chloride in 1,2-dimethoxyethane gave the (+)-11-epichelidonine analog (**10**) (27%) and (+)-isoindoline (**11**) (45%). The IR spectrum of (+)-**10** showed Bohlmann bands (2770 and 2675 cm^{-1}), and the ^1H NMR spectrum exhibited a coupling (3 Hz) between the 4b- and 10b-protons and a coupling (9 Hz) between the 10b- and 11-protons. These spectral properties are compatible with the *cis* steroidal B/C ring fusion. Furthermore, couplings (9 and 6 Hz) observed between the 11- and 12-protons in the ^1H NMR spectrum indicate the 11-hydroxyl group to be oriented equatorially. Thus, the structure with the 4b*S*, 10b*R*, 11*R* configuration like that of 11-epichelidonine, which is formed by reduction at the 10b-position in a *cis* ring opening mode (a-path)[6] as shown in the oxirane-alane complex (**9**), is assigned to (+)-**10**. The structure of (+)-**11** with the 2*S*, 3*R* configuration shown in Chart 1 is in accord with the ^1H NMR data observed (see "Experimental"). The formation of (+)-**11** is thought to arise *via* a concerted migration of the nitrogen atom to the 10b-position from the back side with respect to the oxirane ring, followed by reduction at the 4b-position in **9** (b-path).[6] It was already reported that reduction of (±)-**8** with the same reagents in tetrahydrofuran gave the (±)-4b-epichelidonine analog (**12**) (44%) and (±)-**11** (9%).[3] This result is in marked contrast to that obtained above in the reduction of (+)-**8**. Reduction of (±)-**8** in 1,2-dimethoxyethane afforded (±)-**10** (25%) and (±)-**11** (34%). The ratio of the compounds isolated is also similar to that obtained from (+)-**8**.

Acetylation of (+)-**10** with acetic anhydride/pyridine gave the (+)-acetate (**13**) (62%) (IR: 1735 cm^{-1} for OAc).



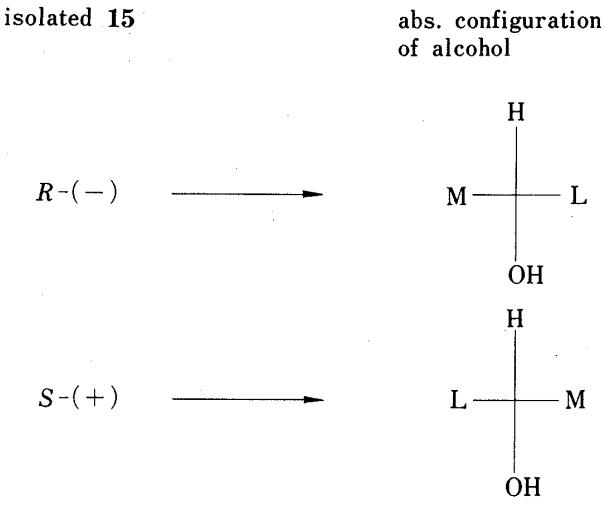


Chart 2

Horeau found a novel method to determine the absolute configurations of secondary alcohols, *i.e.* (1) esterification of a chiral alcohol with (±)-2-phenylbutanoic anhydride (**14**), (2) hydrolysis of excess **14** at the end of the reaction and (3) determination of the rotatory power of 2-phenylbutanoic acid (**15**) thus isolated. The relationship, in general, between the configuration of the alcohol and the sign of **15** is as shown in Chart 2.[2,7] In applications of this method, *R*-(−)-**15**, *S*-(+)-**15** and *S*-(+)-**15** were obtained from (+)-**7**, (+)-**10** and (+)-**11**, respectively. These results lead to the 11*S*, the 11*R*, and the 3*R* configurations for (+)-**7**, (+)-**10** and (+)-**11**, respectively, which are in accord with those assigned to the corresponding positions in these compounds on the basis of the configuration of (−)-**3** and the results obtained from the subsequent stereo-controlled reactions.

The optical purities of (+)-**8**, (+)-**11** and (+)-**13** were estimated to be 80, 81 and 81% ee's, respectively, by ^{1}H NMR spectroscopy in the presence of tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorato]europium(III) [Eu(hfc)$_3$] (see Figs. 1, 2 and 3).

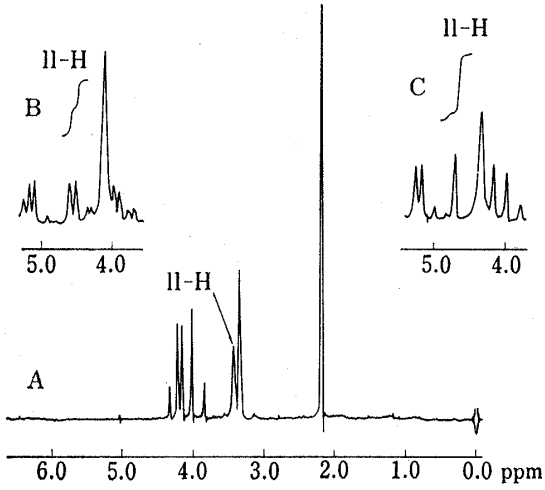


Fig. 1. ^{1}H NMR Spectra of **8** taken on a Varian EM-390 Spectrometer

A, normal spectrum (in part) of (±)-**8** (35 mg, 1.3×10^{-4} mol) in $CDCl_3$ (0.3 ml) at 90 MHz; B, 90 MHz spectrum of (±)-**8** (43 mg, 1.6×10^{-4} mol) in $CDCl_3$ (0.3 ml) containing Eu(hfc)$_3$ (67 mg); C, 90 MHz spectrum of (+)-**8** (80% ee) (43 mg, 1.6×10^{-4} mol) in $CDCl_3$ (0.3 ml) containing Eu(hfc)$_3$ (52 mg).

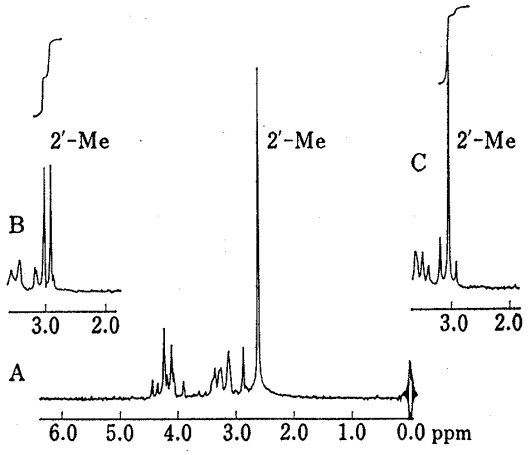


Fig. 2. ^{1}H NMR Spectra of **11** taken on a Hitachi R-24B Spectrometer

A, normal spectrum (in part) of (±)-**11** (10 mg, 3.8×10^{-5} mol) in $CDCl_3$ (0.2 ml) at 60 MHz; B, 60 MHz spectrum of (±)-**11** (10 mg, 3.8×10^{-5} mol) in $CDCl_3$ (0.2 ml) containing Eu(hfc)$_3$ (4.7 mg): C, 60 MHz spectrum of (+)-**11** (81% ee) (27 mg, 1.0×10^{-4} mol) in $CDCl_3$ (0.2 ml) containing Eu(hfc)$_3$ (5.4 mg).

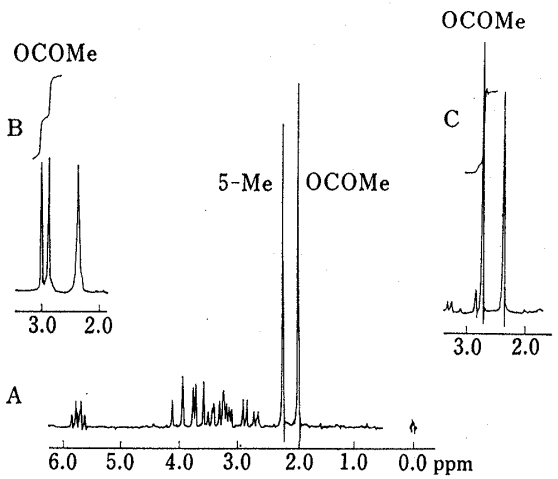


Fig. 3. ^{1}H NMR Specta of **13** taken on a Varian EM-390 Spectrometer

A, normal spectrum (in part) of (±)-**13** (24 mg, 7.8×10^{-5} mol) in $CDCl_3$ (0.2 ml) at 90 MHz; B, 90 MHz spectrum of (±)-**13** (4.9 mg, 1.6×10^{-5} mol) in $CDCl_3$ (0.2 ml) containing Eu(hfc)$_3$ (4.9 mg); C, 90 MHz spectrum of (+)-**13** (81% ee) (24 mg, 7.8×10^{-5} mol) in $CDCl_3$ (0.2 ml) containing Eu(hfc)$_3$ (13 mg).

Experimental

Melting points were determined on a micro hot-stage apparatus and are uncorrected. Optical rotations were taken on a JASCO DPI-181 polarimeter. Spectral data were recorded on the following spectrometers: IR, JASCO IR-G and JASCO DS-701G (hydrogen-bondings); UV, Hitachi EPS-2U; circular dichroism (CD) and optical rotatory dispersion (ORD), JASCO J-20; ^{1}H NMR, Varian EM-390 (90 MHz); mass (MS), JEOL

JMS-01S. Signal assignments in the ^{1}H NMR spectra were made by comparison with the data for related compounds. Preparative thin-layer chromatographies (prep. TLC) were performed on silica gel plates. Crystalline compounds were used for subsequent reactions without recrystalization.

(+)-4b*R*,10b*S*,11*S*,12*S*)-4b,5,6,10b,11,12-Hexahydro-10b,11,12-trihydroxy-5-methyl-6-oxobenzo[*c*]-phenanthridine (5)——A solution of (−)-**3** (178 mg) in 40% aqueous methylamine (8 ml) was stirred at room temperature for 1 h. Concentration of the reaction mixture *in vacuo*, followed by dilution with water, gave (+)-**5** (195 mg, 99%) as light yellow prisms of mp 289—293°C. Optical rotation $[\alpha]^{17.5}$ (nm): +83.3° (589), +88.9° (577), +103.7° (546), +237.0° (435), +518.5° (365) (c=0.108, dioxane). IR ν_{max}^{KBr} cm^{-1}: 3375, 3210 (OH), 1638 (NC=O). UV $\lambda_{max}^{methanol}$ nm (ε): 254 (shoulder) (5794), 234 (shoulder) (9304). CD ($c=1.02\times10^{-3}$, dioxane) $[\theta]^{20}$ (nm): 0 (304), +21518 (272.5) (positive maximum), +21212 (271) (negative maximum), +25638 (265.5) (positive maximum), +25333 (263.5) (negative maximum), +29301 (254) (positive maximum), 0 (240), −53107 (221) (negative maximum). ORD ($c=1.00\times10^{-3}$, dioxane) $[\phi]^{22}$ (nm): +8686 (300), +13542 (284) (peak), 0 (265), −52924 (238) (trough), 0 (222). ^{1}H NMR (dimethyl sulfoxide-d_6) δ: 8.30 (1H, dd, J 8 and 2 Hz, 7-H), 7.78 (1H, dd, J 8 and 2 Hz, 4- or 10-H), 7.52—7.07 (6H, m, aromatic H's), 5.84 (1H, d, J 4 Hz, 11-OH),[8] 5.79 (1H, s, 10b-OH),[8] 5.69 (1H, d, J 7 Hz, 12-OH),[8] 4.66 (1H, s, 4b-H), 4.58 (1H, dd, J 8 and 7 Hz, 12-H), 4.02 (1H, dd, J 8 and 4 Hz, 11-H), 3.40 (3H, s, 5-Me). On addition of D_2O, the following signals changed: δ 4.58 (12-H) dd→d, J 8 Hz; δ 4.02 (11-H) dd→d, J 8 Hz. MS Calcd for $C_{18}H_{17}NO_4-H_2O$: M−H_2O, 293.105. Found m/e: $(M-H_2O)^+$, 293.107.

(+)-(4b*R*,10b*S*,11*S*,12*S*)-4b,5,6,10b,11,12-Hexahydro-10b,11,12-trihydroxy-5-methylbenzo[*c*]phenanthridine (6)——$LiAlH_4$ (102 mg) and $AlCl_3$ (100 mg) were added to a solution of (+)-**5** (52.0 mg) in anhydrous 1,2-dimethoxyethane (40 ml), and the mixture was refluxed under nitrogen for 1.5 h. After addition of water (0.6 ml), 10% aqueous NaOH (0.6 ml) and then water (1.8 ml), the reaction mixture was filtered and concentrated *in vacuo*, then extracted with ethyl acetate. Work-up gave light brown crystals (52.1 mg) which were purified by prep. TLC (chloroform/methanol=18/1, v/v) to yield (+)-**6** (49.4 mg, 99%), Rf 0.50, as colorless prisms of mp 193—195°C. Optical rotation $[\alpha]^{20}$ (nm): +102.9° (589), +104.8° (577), +131.4° (546), +240.0° (435), +411.4° (365) (c=0.105, dioxane). IR $\nu_{max}^{chloroform}$ cm^{-1}: 3580, 3370 (OH), 2775, 2700 (Bohlmann bands). UV $\lambda_{max}^{methanol}$ nm (ε): 356 (49), 259 (670). CD ($c=1.08\times10^{-3}$, dioxane) $[\theta]^{21.5}$ (nm): 0 (300), −991 (270.5) (negative maximum), −661 (267.5) (positive maximum), −950 (264.5) (negative maximum), −385 (255) (positive maximum), −440 (254) (negative maximum), −193 (251) (positive maximum), −262 (248) (negative maximum), 0 (246). ORD ($c=1.25\times10^{-3}$, dioxane) $[\phi]^{22}$ (nm): +3211 (300), +9039 (250), +21408 (230) +29139 (220) (peak). ^{1}H NMR (dimethyl sulfoxide-d_6) δ: 7.78 (1H, dd, J 8 and 2 Hz, 10-H), 7.67—7.10 (7H, m, aromatic H's), 6.84 (1H, br s, W_H 10 Hz, 11-OH),[8] 5.58 (1H, s, 10b-OH),[8] 5.09 (1H, d, J 8 Hz, 12-OH),[8] 4.63 (1H, dd, J 8 and 3 Hz, 12-H), 4.02 (1H, d, J 16 Hz, 6-H), 3.81 (1H, br s, W_H 9 Hz, 11-H), 3.68 (1H, d, J 2 Hz, 4b-H), 3.65 (1H, d, J 16 Hz, 6-H), 2.15 (3H, s, 5-Me). On addition of D_2O, the following signals changed: δ 4.63 (12-H) dd→d, J 3 Hz; δ 3.81 (11-H) br s→d, J 3 Hz. MS Calcd for $C_{18}H_{19}NO_3$: M, 297.136. Found m/e: M^+, 297.137.

(+)-(4b*R*,10b*S*,11*S*)-4b,5,6,10b,11,12-Hexahydro-10b,11-dihydroxy-5-methylbenzo[*c*]phenanthridine (7)——A solution of (+)-**6** (175 mg) and 70% $HClO_4$ (1 ml) in 10% HCl (30 ml) was shaken with hydrogen over 10% Pd-C (152 mg) and PdO (131 mg) at 70°C under a pressure of 5 atm for 66 h. The reaction mixture was filtered and washed with chloroform/methanol (1/1, v/v) (300 ml). The combined filtrates were concentrated *in vacuo*, and made alkaline with 10% aqueous NaOH, then extracted with chloroform. Work-up gave light brown crystals (163 mg) which were purified by prep. TLC (chloroform/ethyl acetate=10/1, v/v) to yield (+)-**7** (130 mg, 78%) as colorless crystals of mp 186—192°C, Rf 0.35. Optical rotation $[\alpha]^{19}$ (nm): +125.2° (589), +135.7° (577), +153.0° (546), +271.3° (435), +448.7° (365) (c=0.115, chloroform). IR $\nu_{max}^{chloroform}$ cm^{-1}: 3600, 3380 (OH), 2775, 2700 (Bohlmann bands); hydrogen-bondings, 3599 (ε=65.4) (OH···π), 3225 cm^{-1} (ε=39.8) (OH···N) ($c=8.89\times10^{-4}$ mol/l, tetrachloromethane). UV $\lambda_{max}^{methanol}$ nm (ε): 310 (shoulder) (34), 271 (59), 262 (71), 256 (shoulder) (60). CD ($c=1.15\times10^{-3}$, dioxane) $[\theta]^{22.5}$ (nm): 0 (291), −43 (285.5) (negative maximum), −41 (283.5) (positive maximum), −702 (272) (negative maximum), −379 (267) (positive maximum), −506 (264.5) (negative maximum), −56 (260) (positive maximum), −66 (259) (negative maximum), 0 (257), +14434 (230). ORD ($c=1.15\times10^{-3}$, dioxane) $[\phi]^{22.5}$ (nm): +3058 (300), +10153 (250), +26911 (224.5) (peak), 0 (219). ^{1}H NMR (dimethyl sulfoxide-d_6) δ: 7.71 (1H, dd, J 8 and 2 Hz, 10-H), 7.44—7.07 (7H, m, aromatic H's), 7.00 (1H, s, 11-OH),[8] 5.37 (1H, s, 10b-OH),[8] 4.01 (1H, d, J 16 Hz, 6-H), 3.90 (1H, m, 11-H), 3.68 (1H, d, J 16 Hz, 6-H), 3.60 (1H, d, J 2 Hz, 4b-H), 3.29 (1H, dd, J 17 and 4 Hz, 12-H), 2.93 (1H, dd, J 17 and 2 Hz, 12-H), 2.13 (3H, s, 5-Me). MS Calcd for $C_{18}H_{19}NO_2$: M, 281.142. Found m/e: M^+, 281.140.

(+)-(4b*R*,10b*S*,11*R*)-10b,11-Epoxy-4b,5,6,10b,11,12-hexahydro-5-methylbenzo[*c*]phenanthridine (8)——A solution of mesyl chloride (74 mg) in anhydrous pyridine (1 ml) was added to a solution of (+)-**7** (101 mg) in anhydrous pyridine (2 ml), and the mixture was stirred with cooling for 1 h and then stirred at room temperature for 4 h. After addition of water (30 ml), the reaction mixture was extracted with ethyl acetate. Work-up gave a green oil (116 mg) which was purified by prep. TLC (benzene/ethyl acetate=3/1, v/v) to yield (+)-**8** (88 mg, 93%) as a light green oil, Rf 0.45. Optical rotation $[\alpha]^{23}$ (nm): +193.0° (589), +210.0° (577), +286.0° (546), +417.3° (435), +680.5° (365) (c=0.147, chloroform). IR $\nu_{max}^{chloroform}$ cm^{-1}: 2775, 2680 (Bohlmann bands). UV $\lambda_{max}^{methanol}$ nm (ε): 496 (29), 364 (shoulder) (153), 345 (194), 310 (452), 297

(455), 257 (1899). CD ($c=2.20\times10^{-3}$, dioxane) $[\theta]^{25}$: 0 (339), +48 (314) (positive maximum), 0 (302), −53 (289) (negative maximum), 0 (281), +10 (279.5) (positive maximum), 0 (278.5), −239 (274) (negative maximum), 0 (269.5), +2334 (249) (positive maximum), +957 (235.5) (negative maximum). ^{1}H NMR (deuteriochloroform) δ: 7.39—7.06 (8H, m, aromatic H's), 4.27, 3.99 (1H each, d, J 16 Hz, 6-H_2), 4.27 (1H, d, J 2 Hz, 4b-H), 3.47 (1H, m, 11-H), 3.38 (2H, br s, W_H 4 Hz, 12-H_2), 2.20 (3H, s, 5-Me). MS Calcd for $C_{18}H_{17}NO$: M, 263.131. Found m/e: M$^+$, 263.133.

(+)-(4b*S*,10b*R*,11*R*)-4b,5,6,10b,11,12-Hexahydro-11-hydroxy-5-methylbenzo[*c*]phenanthridine (10) and (+)-(2*S*,3*R*)-1,2,3,4-Tetrahydro-3-hydroxynaphthalene-2-spiro-1′-2′-methylisoindoline (11)——$LiAlH_4$ (21 mg) and $AlCl_3$ (10 mg) were added to a solution of (+)-**8** (45.3 mg) in anhydrous 1,2-dimethoxyethane (7 ml), and the mixture was refluxed under nitrogen for 15 min. After addition of 2% aqueous KOH (3 drops), the reaction mixture was filtered, and the precipitate was washed with ethyl acetate. Work-up of the combined filtrates gave an oil (37.9 mg) which was purified by prep. TLC (benzene/ethyl acetate=20/9, v/v) to yield (+)-**10** (12.1 mg, 27%), Rf 0.42, and (+)-**11** (20.4 mg, 45%), Rf 0.25.

The (+)-11-Epichelidonine Analog (**10**): A colorless oil. Optical rotation $[\alpha]^{25.5}$ (nm): +48.0° (589), +56.0° (577), +68.0° (546), +96.0° (435), +116.0° (365) ($c=0.050$, chloroform). IR $\nu_{max}^{chloroform}$ cm^{-1}: 3590 (OH), 2770, 2675 (Bohlmann bands). UV $\lambda_{max}^{methanol}$ nm (ε): 271 (408), 264 (481), 258 (shoulder) (421). CD ($c=1.05\times10^{-3}$, dioxane) $[\theta]^{26}$ (nm): 0 (300), −1186 (266.5) (negative maximum), −717 (251) (positive maximum), −4972 (228) (negative maximum), 0 (219). ^{1}H NMR (deuteriochloroform) δ: 7.37—7.01 (8H, m, aromatic H's), 4.56 (1H, dt, J 6 and 9 Hz, 11-H), 4.03 (1H, d, J 16 Hz, 6-H), 3.67 (1H, d, J 3 Hz, 4b-H), 3.57 (1H, d, J 16 Hz, 6-H), 3.35 (1H, dd, J 17 and 6 Hz, 12-H), 2.91 (1H, dd, J 9 and 3 Hz, 10b-H), 2.81 (1H, dd, J 17 and 9 Hz, 12-H), 2.28 (1H, s, 11-OH),[8] 2.20 (3H, s, 5-Me). Decoupling: δ 4.56 (11-H)→δ 3.35 (dd→d, J 17 Hz, 12-H), 2.91 (dd→d, J 3 Hz, 10b-H), 2.81 (dd→d, J 17 Hz, 12-H); δ 3.67 (4b-H)→δ 2.91 (dd→d, J 9 Hz, 10b-H). MS Calcd for $C_{18}H_{19}NO$: M, 265.147. Found m/e: M$^+$, 265.146.

The (+)-Isoindoline (**11**): Colorless needles of mp 184.5—185.5°C (from benzene/hexane). Optical rotation $[\alpha]^{26.5}$ (nm): +148.1° (589), +166.9° (577), +191.3° (546), +343.1° (435), +603.8° (365) ($c=0.106$, chloroform). IR $\nu_{max}^{chloroform}$ cm^{-1}: 3570, 3410 (OH). UV $\lambda_{max}^{methanol}$ nm (ε): 271 (1184), 264 (1356), 258 (shoulder) (1110). CD ($c=9.50\times10^{-4}$, dioxane) $[\theta]^{31}$ (nm): 0 (294), +2639 (265) (positive maximum), +2067 (252) (negative maximum), +2109 (246.5) (positive maximum), +824 (231) (negative maximum). ORD ($c=1.00\times10^{-3}$, dioxane) $[\phi]^{30}$ (nm): +1765 (300), +3595 (274) (peak), +2189 (260) (trough), +7297 (230). ^{1}H NMR (deuteriochloroform) δ: 7.28—6.93 (7H, m, aromatic H's), 6.76 (1H, d, J 7 Hz, 7′-H), 4.31 (1H, d, J 13 Hz, 3′-H), 4.21 (1H, dd, J 11 and 6 Hz, 3-H), 4.05 (1H, d, J 13 Hz, 3′-H), 3.37 (1H, dd, J 17 and 6 Hz, 4-H), 3.23 (1H, d, J 17 Hz, 1-H), 3.10 (1H, dd, J 17 and 11 Hz, 4-H), 2.79 (1H, d, J 17 Hz, 1-H), 2.60 (4H, s, 3-OH[8] and 2′-Me). MS Calcd for $C_{18}H_{19}NO$: M, 265.147. Found m/e: M$^+$, 265.147.

(+)-(4b*S*,10b*R*,11*R*)-11-Acetoxy-4b,5,6,10b,11,12-hexahydro-5-methylbenzo[*c*]phenanthridine (13)——A solution of (+)-**10** (38.9 mg) and acetic anhydride (0.3 ml) in anhydrous pyridine (0.6 ml) was stirred at room temperature for 2 h. Work-up of the reaction mixture gave an oil which was purified by prep. TLC (benzene/ethyl acetate=4/1, v/v) to yield (+)-**13** (28.1 mg, 62%), Rf 0.40, as a colorless oil. Optical rotation $[\alpha]^{25.5}$ (nm): +6.4° (589), +10.7° (577), +12.9° (546), +15.0° (465), +8.6° (365) ($c=0.093$, chloroform). IR $\nu_{max}^{chloroform}$ cm^{-1}: 2750, 2675 (Bohlmann bands), 1735 (OC=O). UV $\lambda_{max}^{methanol}$ nm (ε): 364 (952), 312 (897), 270 (641), 262 (shoulder) (104). CD ($c=1.05\times10^{-3}$, dioxane) $[\theta]^{25}$ (nm): 0 (291), −2459 (266) (negative maximum), −1976 (253) (positive maximum), −9368 (230). ORD ($c=1.05\times10^{-3}$, dioxane) $[\phi]^{25}$ (nm): 0 (294.5), −878 (273.5) (trough), 0 (269), +834 (230). ^{1}H NMR (deuteriochloroform) δ: 7.42—6.98 (8H, m, aromatic H's), 5.74 (1H, dt, J 7 and 6 Hz, 11-H), 4.02 (1H, d, J 16 Hz, 6-H), 3.75 (1H, d, J 3 Hz, 4b-H), 3.52 (1H, d, J 16 Hz, 6-H), 3.36 (1H, dd, J 16 and 6 Hz, 12-H), 3.17 (1H, dd, J 7 and 3 Hz, 10b-H), 2.81 (1H, dd, J 16 and 6 Hz, 12-H), 2.23 (3H, s, 5-Me), 1.97 (3H, s, 11-OAc). MS Calcd for $C_{20}H_{21}NO_2$: M, 307.157. Found m/e: M$^+$, 307.159.

(+)-(4b*S,10b*R**,11*R**)-4b,5,6,10b,11,12-Hexahydro-11-hydroxy-5-methylbenzo[*c*]phenanthridine (10) and (±)-(2*S**,3*R**)-1,2,3,4-Tetrahydro-3-hydroxynaphthalene-2-spiro-1′-2′-methylisoindoline (11)**——$LiAlH_4$ (50 mg) and $AlCl_3$ (25 mg) were added to a solution of (±)-**8**[3] (40.0 mg) in anhydrous 1,2-dimethoxyethane (12 ml), and the mixture was refluxed under nitrogen for 4 h. Work-up of the reaction mixture gave (±)-**10** (10.0 mg, 25%) as a colorless oil and (±)-**11**[3] (13.6 mg, 34%) as colorless pillars of mp 157—158°C (from ethanol). The IR and ^{1}H NMR spectra of (±)-**10** were superimposable on those of (+)-**10**. MS of (±)-**10** Calcd for $C_{18}H_{19}NO$: M, 265.147. Found m/e: M$^+$, 265.146.

(±)-(4b*S,10b*R**,11*R**)-11-Acetoxy-4b,5,6,10b,11,12-hexahydro-5-methylbenzo[*c*]phenanthridine (13)**——The (±)-acetate (**13**) was prepared in 65% yield as a colorless oil by the procedure described for (+)-**13**. The IR and ^{1}H NMR spectra were superimposable on those of (+)-**13**. MS Calcd for $C_{20}H_{21}NO_2$: M, 307.157. Found m/e: M$^+$, 307.154.

Reaction of (+)-7 with (±)-14——A solution of (±)-**14** (215 mg) in anhydrous pyridine (1.9 ml) was added to a solution of (+)-**7** (100 mg) in anhydrous pyridine (1 ml), and the mixture was stirred at room temperature for 17 h. Water (0.5 ml) was added to hydrolyze excess **14**, and the mixture was stirred at room temperature for 45 min. Neutralization in the presence of benzene (5 ml) and phenolphthalein (1 mg) required 10.3 ml of 0.1 N NaOH (factor=1.001): the esterification yield was therefore 100%. The reaction mixture was diluted with water, and the aqueous phase was extracted with benzene. Work-up of the com-

bined benzene extracts gave an oil (187 mg) which was purified by prep. TLC (benzene/ethyl acetate=5/1, v/v) to yield the ester (**16**) (136 mg, 90%), *Rf* 0.75, as a colorless oil. IR $\nu_{max}^{chloroform}$ cm^{-1}: 3570 (OH), 2770, 2675 (Bohlmann bands), 1730 (OC=O). MS Calcd for $C_{28}H_{29}NO_3$: M, 427.215. Found *m/e*: M^+, 427.214. The aqueous phase was acidified with 10% HCl, and then extracted with benzene. Work-up gave **15** (167 mg, 99%) as a colorless oil with $[\alpha]_{589}^{23}$ −0.305° (*c*=11.13, benzene), corresponding to an optical yield of 0.92%. The spectral data for isolated **15** were in accord with those for an authentic sample.

Reaction of (+)-10 with (±)-14——A solution of (±)-**14** (136 mg) in anhydrous pyridine (1.6 ml) was added to a solution of (+)-**10** (58.0 mg) in anhydrous pyridine (0.5 ml), and the mixture was stirred at room temperature for 23 h. After hydrolysis of excess **14** with water (0.5 ml), it was found that 6.55 ml of 0.1 N NaOH (factor=1.001) was required for neutralization (esterification yield, 100%). Work-up of the reaction mixture afforded the ester (**17**) (65 mg, 72%), *Rf* 0.65, as a colorless oil. IR $\nu_{max}^{chloroform}$ cm^{-1}: 2760, 2680 (Bohlmann bands), 1729 (OC=O). MS Calcd for $C_{28}H_{29}NO_2$: M, 411.220. Found *m/e*: M^+, 411.217. In addition, **15** (102 mg, 94%) was obtained as a colorless oil with $[\alpha]_{589}^{27}$ +8.235° (*c*=6.80, benzene), corresponding to an optical yield of 26.2%.

Reaction of (+)-11 with (±)-14——A solution of (±)-**14** (118 mg) in anhydrous pyridine (0.9 ml) was added to a solution of (+)-**11** (50.0 mg) in anhydrous pyridine (0.5 ml), and the mixture was stirred at 70°C for 24 h. After hydrolysis of excess **14** with water (0.5 ml), it was found that 5.95 ml of 0.1 N NaOH (factor=1.001) was required for neutralization (esterification yield, 88%). Work-up of the reaction mixture afforded the ester (**18**) (61.4 mg, 79%), *Rf* 0.60, as a colorless oil. IR $\nu_{max}^{chloroform}$ cm^{-1}: 1728 (OC=O). MS Calcd for $C_{28}H_{29}NO_2$: 411.220. Found *m/e*: M^+, 411.220. In addition, **15** (95 mg) was quantitatively obtained as a colorless oil with $[\alpha]_{589}^{27}$ +0.322° (*c*=6.21, benzene) corresponding to an optical yield of 1.21%, and (+)-**11** (5.9 mg, 11%) was recovered.

References and Notes

1) Part XII: Y. Harigaya, S. Takamatsu, H. Yamaguchi, and M. Onda, *Heterocycles*, **17**, 83 (1982).
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4) The enantiomeric excess (ee) was determined from the ^1H NMR spectrum in the presence of $Eu(hfc)_3$, and a distinct difference in the 11-proton signal was observed.
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8) On addition of deuterium oxide, this signal disappeared.