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SYNTHETIC STUDIES OF MARINE ALKALOIDS HAPALINDOLES. Part 3. TOTAL SYNTHESIS OF (±)-HAPALINDOLES H and U

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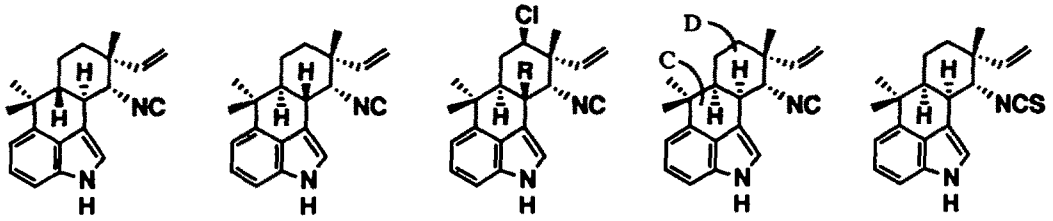
Abstract — A total synthesis of marine indole alkaloids (±)-hapalindoles H (1) and U (2) was achieved from the previously described compound 7 by way of 13, 21, and 26 for U (2), and 33 and 32 for H (1).

In Part 1 of this series,[1] we described a concise synthesis of antibacterial, antimycotic, and antialgal indole alkaloids, hapalindoles J (3) and M (4) obtained from a blue-green alga *Hapalosiphon fontinalis*.[2] These are representatives of about nine tetracyclic hapalindoles having structures of a C/D cis ring juncture. In addition to these, four tetracyclic indole alkaloids of C/D trans structures have been isolated and named hapalindoles G (5), H (1), U (2), and V (6). Here we report a synthesis of (±)-hapalindoles H and U.



1 Hapalindole H | 2 Hapalindole U | 5 R-H Hapalindole G, 6 R-OH Hapalindole V | 3 Hapalindole J | 4 Hapalindole M

The compound 7 obtained in Part 1 was brominated with *N*-bromosuccinimide in carbon tetrachloride in the presence of benzoyl peroxide. Then without separation, the resulting products were hydroxylated with silver nitrate in aqueous acetone to afford two mixtures of hydroxy epimers 8 and 9 in 33.5% and 31% yields, accompanied by the by-product[1] 10 in 4% yield (Chart 1). The unnecessary compound 9 was converted to 8 in 89% yield by treatment with 5% sulfuric acid in acetone and water (9:1) and used for further synthesis. Exact proof for the position of the hydroxy group in 8 was lacking at this stage. But the successful natural product synthesis starting from 8 showed that the oxidation site was at the 11 position. This also clarified the position of the ketone group in compound 11 in Part 1, obtained by selenium dioxide treatment of 7, since 8 was correlated with 11 by oxidation using Swern's method.[3]

Using our previous experience about the abnormal reaction with lithium aluminum hydride (LAH),[4] compound 8 was submitted to LAH reduction in the expectation that (i) the tetrasubstituted double bond in 8 would be reduced to give C/D cis derivatives 12 and 13, whose stereochemistry of the ring juncture is regulated by the configuration of the adjacent hydroxy group, and (ii) if the hydroxy group is oxidized to the ketone function, the neighboring

10 position could be epimerized to form the C/D trans ring juncture. The reduction compounds 12 and 13 were obtained in 49% and 15% yields, which corresponded roughly to the ratio of the hydroxy epimers of 8. This ratio was somewhat different in the compound 8 obtained by transformation from the isomer 9, and in this case 12 and 13 were produced in 34% and 20% yields. The hydroxyindole derivative 12 was very sensitive to most of oxidizing reagents except the Dess-Martin reagent.[5] Even with this mild reagent, a ketone compound 15 was obtained in an unsatisfactory yield of 49%, together with a by-product 14 and the recovery of 12 each in 17% yield. Furthermore compound 15 turned out to be unsuitable for the objective, since it gave the desired compound 16 in only 39% yield after prolonged refluxing in dichloromethane in the presence of triethylamine. Other compounds obtained were the enone derivative 14 and the recovery of 15 in 28% yield each.

To make the indole part tolerable to the oxidizing reagents, both 12 and 13 were converted to their *N*-tosylates by treatment with sodium hydride and tosyl chloride in a mixture of

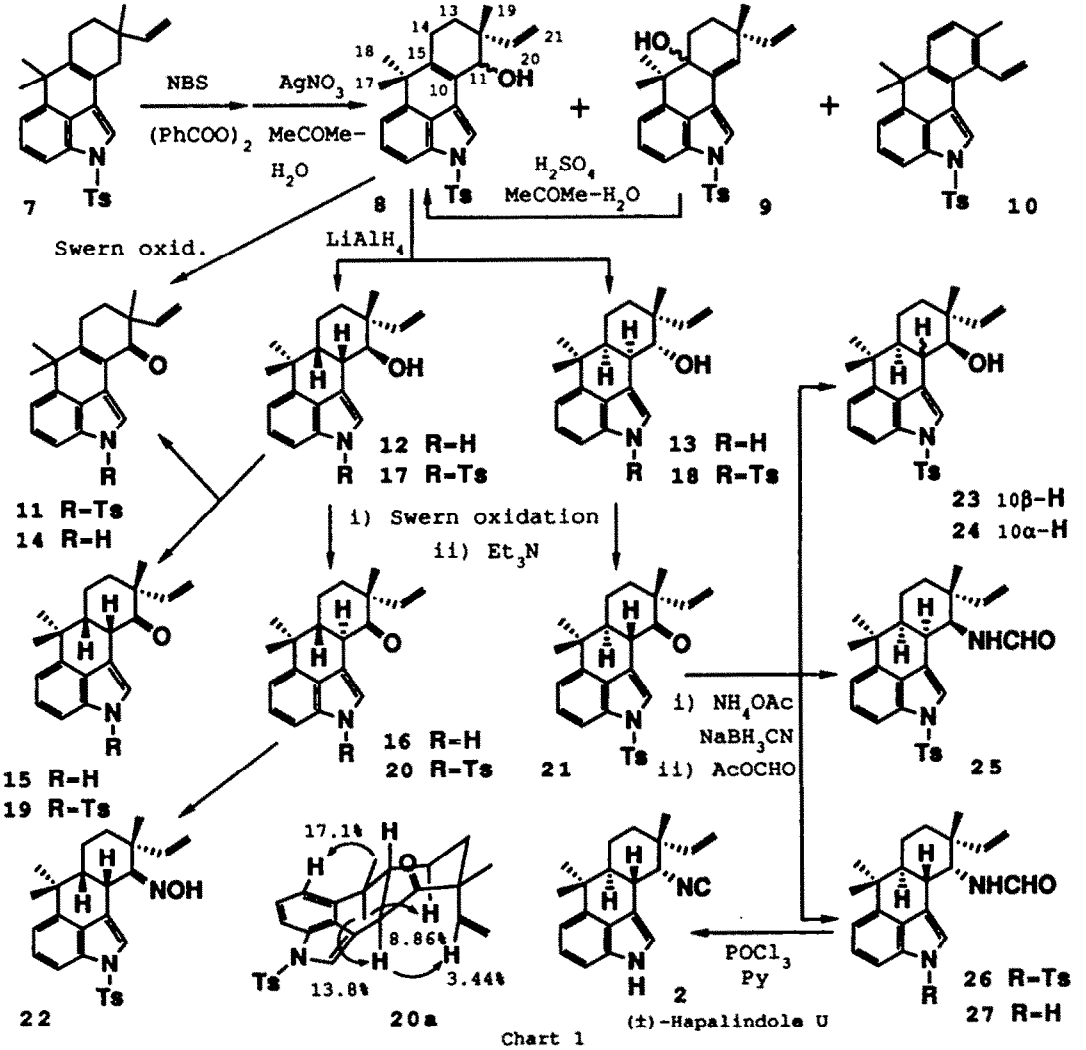


Chart 1

(±)-Hapalindole U

tetrahydrofuran and dimethylformamide (4:1) at -20°C for 2 h. Using this solvent system, formation of *N,O*-ditosylates was minimized to 8% yield in both cases, and **17** and **18** were obtained in 84% and 87% yields, respectively. Oxidation of **17** was tried using pyridinium chlorochromate[6] and the expected compound **19** was prepared in 68% yield. The Swern oxidation of **17** was superior to this and when the reaction mixture was further treated with triethylamine in refluxing dichloromethane, the ketone derivative **19** formed once was isomerized to a trans compound **20** in an overall yield of 78%. Stereostructure including the trans nature of the C/D ring juncture was established mostly by the nuclear Overhauser effect experiment shown in formula **20a**. The half height width of 15 Hz of the H-10 proton signal was characteristic of the trans compound, compared to that of 8.5 Hz in the corresponding cis compound **19**. Similarly the Swern oxidation of **18** afforded another trans compound **21** ($W_{1/2}$= 16 Hz of H-10) in 80% yield.

The next task, introduction of the nitrogen function at the 11 position, proved not to be straightforward. For example, the oxime formation from the ketone derivative **20** required prolonged refluxing in methanol, probably due to the steric hindrance around the ketone function. During this time, inversion of the C/D ring juncture took place and an oxime derivative **22** having the cis juncture ($J_{10,15}$=5 Hz) was obtained exclusively in 77% yield. The reductive amination of the ketone compound **21** was carried out by treatment with sodium cyanoborohydride in methanol in the presence of ammonium acetate.[7] The resulting mixture was separated after formylation with acetic formic anhydride and pyridine in dichloromethane. Two compounds, **23** and **26** having trans ring junctures and two compounds, **24** and **25** having cis ring junctures were isolated in 4%, 42%, 4%, and 16% yields, respectively, together with the recovery of the starting ketone derivative **21** in 6% yield. The structure of the major product **26** was assigned by the coupling constants of $J_{10,11}$=3 Hz and $J_{10,15}$=12 Hz, as well as the NOE experimental result that the 4.54% and 6.47% signal enhancements of the C-17 and C-19 methyl protons were observed when H-10 proton was irradiated in the proton NMR spectrum study. Structural assignment of the other three compounds **23**, **24**, and **25** was also made by analysis of their proton NMR spectra (see the Experimental part). Now that the stereochemical arrangement of all chiral centers in **26** was proved to be the same as that of hapalindole U (**2**), conversion of **26** to (±)-**2** was readily achieved by removal of the tosyl group with magnesium in methanol to give **27** in a quantitative yield. Then **27** was treated with phosphorus oxychloride in pyridine to complete the synthesis of (±)-hapalindole U (**2**) in 73% yield. Identity of this compound with the natural product was confirmed by comparison of the IR and proton NMR spectra.

The reductive amination of another ketone compound **20** furnished a complex mixture of products, which afforded five compounds **28**, **29**, **30**, **31**, and **32** in 11%, 15%, 29%, 22%, and 11% yields, respectively, after formylation (Chart 2). Alternatively the compounds **31** and **32** were obtained by chemical reduction of the formamide **33** using triethylsilane in trifluoroacetic acid[8] in 58% and 19% yields, accompanied by the formation of the compound **34** (identified as the tosylated compound from **35**[4] in 71% yield) in 2% yield and the recovery of **33** in 4.5% yield. The formamide **33** was prepared from **7** in four steps.[4] The stereostructures of **31** and **32** were studied by transformation into the isonitrile compounds **38** and (±)-**1** by way of **36** and **37** in overall 74% and 81% yields, respectively. The structure of **38** was unambiguously determined by the NOE analysis shown in formula **38a**, together with the complete assignment of all proton signals in the NMR spectrum. Compound **37** exhibited an interesting behavior in that two distinguishable compounds (**37A** and **37B**) were separated during the isolation process, but these were very unstable and on standing each rapidly afforded the same

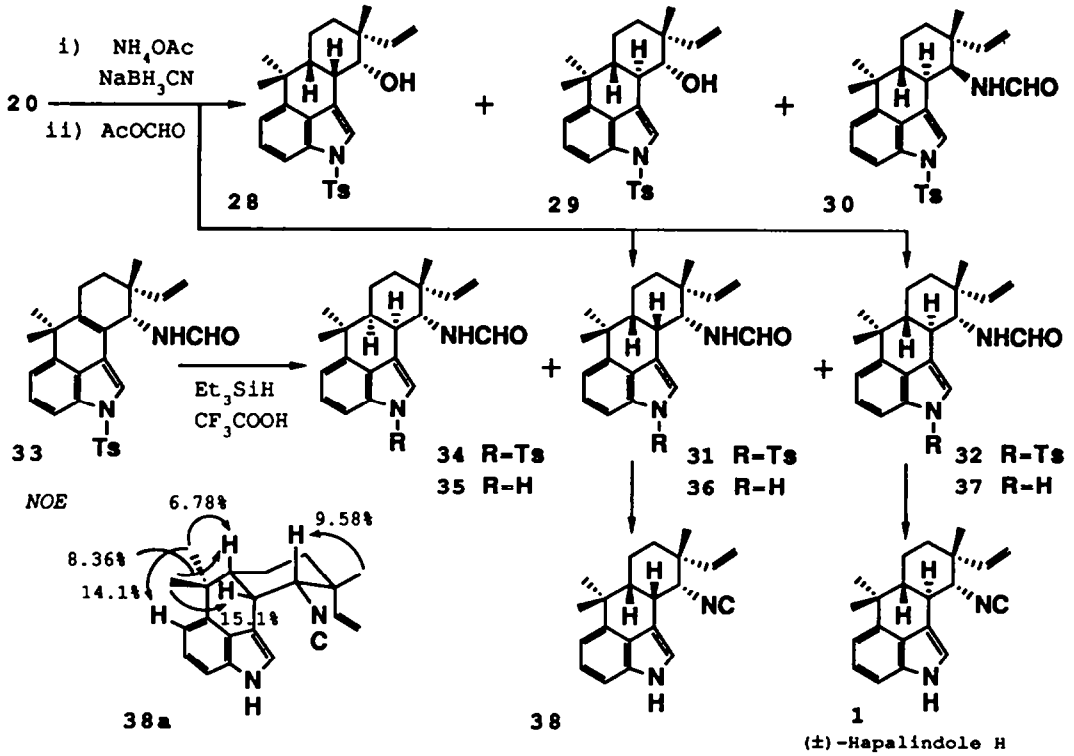


Chart 2

3:1 mixture of **37A** and **37B**. This phenomenon coincided nicely with the report that the formamide derivative obtained from hapalindole H showed two spots on the silica gel chromatogram, probably due to separation of two conformational isomers.[9] The isonitrile **1** obtained from **37** was identical with hapalindole H as indicated by their ^{1}H and ^{13}C NMR spectra. In summary (±)-hapalindoles H (**1**) and U (**2**) were synthesized from the readily available compound **7** in seven and ten steps respectively.

EXPERIMENTAL

For the general description, refer to that in Part 1.[1]

2,6,7,8,9,10-Hexahydro-10ξ-hydroxy-6,6,9-trimethyl-2-*p*-toluenesulfonyl-9-vinylnaphth[1,2,3,-*cd*]indoles (8) and 2,6,6a,7,8,9-Hexahydro-6aξ-hydroxy-6,6,9-trimethyl-2-*p*-toluenesulfonyl-9-vinylnaphth[1,2,3-*cd*]indoles (9) — To a solution of **7** (402 mg) in CCl_4 (8 ml) were added NBS (179 mg) and benzoyl peroxide (51 mg) and the mixture was refluxed with stirring for 30 min. After the work-up as reported in Part 1, the residue (590 mg) was dissolved in acetone (5 ml) and to this was added a solution of $AgNO_3$ (317 mg) in H_2O (3 ml) at room temperature. After being stirred for 3 h, sat. $NaHCO_3$-H_2O was added and the whole was filtered through a celite bed. The celite was washed with CH_2Cl_2 and the organic layers were combined. Usual work-up and PTLC [hexane-EtOAc (12:1)] gave **8** (139.5 mg, 33.5%), **9** (129.5 mg, 31%), and a by-product **10**[1] (15 mg, 4%). **8**: Slightly yellow syrup. MS *m/z*: 447 (M^+). IR ($CHCl_3$) cm^{-1}: 1638. ^{1}H NMR ($CDCl_3$) of major and minor isomers δ: 1.13 and 1.06 (3H, s each), 1.39 (6H, s), 1.62 (1H, s, OH), 2.19-2.51 (2H, m, H-14), 2.29 (3H, s), 4.27 and 4.13 (1H, br s each, H-11), 4.87-5.29 (2H, m), 5.78 and 5.83-6.20 (1H, dd, J=18, 10.5 and m), 6.97-7.35 (4H, m), 7.41 and 7.37 (1H, s each, H-2), 7.51-7.87 (3H,

m). **9**: Slightly yellow syrup. MS *m/z*: 447 (M^+). IR ($CHCl_3$) cm^{-1}: 1635, 1628. ^1H NMR ($CDCl_3$) of major and minor isomers δ: 0.97 and 1.01 (3H, s each), 1.18 and 1.16 (3H, s each), 1.50 and 1.47 (3H, s each), 1.64 (1H, br s, OH), 2.30 (3H, s), 4.76-5.22 (2H, m), 5.73 and 5.89 (1H, dd each, J=17, 10.5 and J=17.5, 10.5), 6.06 and 6.13 (1H, s each, H-11), 6.97-7.44 (4H, m), 7.52 and 7.49 (1H, s each, H-2), 7.62-7.93 (3H, m).

Conversion of the Compound 9 to the Compound 8 — A solution of **9** (93 mg) in 5% H_2SO_4 in acetone-H_2O (9:1) (5 ml) was stirred at 0°C for 30 min and at room temperature for 3 h. Addition of sat. $NaHCO_3$-H_2O, extraction with CH_2Cl_2, usual work-up, and PTLC [hexane-CH_2Cl_2 (3:2)] afforded **8** (83 mg, 89%) as slightly yellow syrup.

Oxidation of the Compound 8 to the Compound 11 — To a cooled (-78°C) solution of 10% v/v $(COCl)_2/CH_2Cl_2$ (0.60 ml) in CH_2Cl_2 (2 ml) was added 10% v/v DMSO/CH_2Cl_2 (1.45 ml) under Ar atmosphere and the mixture was stirred for 5 min. A CH_2Cl_2 solution (3 ml) of **8** (122 mg) was added dropwise to this and the whole was stirred at -78 – -73°C for 30 min. After addition of Et_3N (0.57 ml), it was further stirred at -73°C for 10 min, and at -20°C for 30 min. Quenching with sat. $NaHCO_3$-H_2O, extraction with Et_2O, usual work-up, and PTLC [hexane-EtOAc (5:1)] gave **11**[1] (97 mg, 80%) as colorless prisms, mp 166-168°C (CH_2Cl_2-MeOH).

[6a*R-(6aβ,9α,10β,10aβ)]- and [6a*S**-(6aα,9α,10α,10aα)]-2,6,6a,7,8,9,10,10a-Octahydro-10-hydroxy-6,6,9-trimethyl-9-vinylnaphth[1,2,3-*cd*]indoles (12 and 13)** — (i) A solution of **8** (51 mg), obtained directly from **7**, in THF (5 ml) was stirred with $LiAlH_4$ (87 mg) at 0°C to room temperature for 15 h under Ar atmosphere. After the work-up as reported in Part 1, the residue was purified by PTLC [hexane-CH_2Cl_2 (3:5)] to yield **12** (13.5 mg, 40%) as a more polar isomer and **13** (5 mg, 15%) as a less polar isomer. **12**: Colorless prisms, mp 162-163°C (CH_2Cl_2-hexane). Anal. Calcd for $C_{20}H_{25}NO$: C, 81.31; H, 8.53; N, 4.74. Found: C, 81.13; H, 8.56; N, 4.81. MS *m/z*: 295 (M^+). IR (KBr) cm^{-1}: 1635. ^1H NMR ($CDCl_3$) δ: 1.10 (3H, s), 1.20 (3H, s), 1.45 (3H, s), 1.87 (1H, s, OH), 3.57 (1H, br dd, J=3.5, 3.5, H-10), 4.08 (1H, d, J=3.5, H-11), 4.55 (1H, dd, J=10.5, 1.5), 4.68 (1H, dd, J=17, 1.5), 5.66 (1H, dd, J=17, 10.5), 6.70 (1H, dd, J=1.5, 1.5, H-2), 6.76-7.03 (1H, m, H-5), 7.03-7.21 (2H, m, H-6 and H-7), 7.90 (1H, br s, NH). **13**: Colorless prisms, mp 192-193°C (CH_2Cl_2-hexane). Anal. Calcd for $C_{20}H_{25}NO$: C, 81.31; H, 8.53; N, 4.74. Found: C, 81.19; H, 8.49; N, 4.75. MS *m/z*: 295 (M^+). IR (KBr) cm^{-1}: 1640. ^1H NMR ($CDCl_3$) δ: 0.73 (3H, s), 1.17 (3H, s), 1.48 (3H, s), 1.92 (1H, s, OH), 3.59-3.78 (1H, m, $W_{1/2}$=9 Hz, H-10), 4.16 (1H, d, J=2.5, H-11), 5.05 (1H, dd, J=17, 1.5), 5.12 (1H, dd, J=11, 1.5), 5.91 (1H, dd, J=17, 11), 6.80 (1H, dd, J=2, 2, H-2), 6.80-7.00 (1H, m, H-5), 7.00-7.16 (2H, m, H-6 and H-7), 7.88 (1H, br s, NH). (ii) In the same way as above, **8** (49 mg), obtained from **9**, in THF (5 ml) was reduced with $LiAlH_4$ (83 mg) to afford **12** (11 mg, 34%) and **13** (6.5 mg, 20%).

[6a*R-(6aβ,9α,10aβ)]-2,6,6a,7,8,9,10,10a-Octahydro-6,6,9-trimethyl-10-oxo-9-vinylnaphth[1,2,3-*cd*]indole (15) and the Compound 14** — To a cooled (0°C) solution of **12** (30 mg) in CH_2Cl_2 (3 ml) was added the Dess-Martin reagent[5] (151 mg) and the mixture was stirred at 0°C to room temperature for 50 min. Sat. $Na_2S_2O_3$-H_2O and sat. $NaHCO_3$-H_2O were added successively, and the whole was extracted with Et_2O. Usual work-up and PTLC [hexane-EtOAc (3:1)] afforded the recovery of **12** (5 mg, 17%) and a mixture of **14** and **15**. The latter was further separated by PTLC [hexane-CH_2Cl_2 (1:1)] to give **14** (5 mg, 17%) and **15** (14.5 mg, 49%). **14**: Slightly yellow powder. MS *m/z*: 291 (M^+). IR ($CHCl_3$) cm^{-1}: 1660. ^1H NMR ($CDCl_3$) δ: 1.27 (3H, s), 1.51 (6H, s), 1.71-2.15 (2H, m, H-13), 2.50-2.77 (2H, m, H-14), 4.94 (1H, d, J=17.5), 5.05 (1H, d, J=10.5), 5.96 (1H, dd, J=17.5, 10.5), 6.86-7.33 (3H, m), 7.75 (1H, d, J=1.5, H-2), 7.93 (1H, br s, NH). **15**: Colorless syrup. MS *m/z*: 293 (M^+). IR ($CHCl_3$) cm^{-1}: 1692, 1631. ^1H NMR ($CDCl_3$) δ: 1.17 (3H, s), 1.50 (3H, s), 2.13 (3H, s), 4.17 (1H, br d, J=4.5, H-10), 4.69 (1H, dd, J=10.5, 1), 4.84 (1H, dd, J=17.5, 1), 5.61 (1H, dd, J=17.5, 10.5), 6.53 (1H, dd, J=2, 2, H-2), 6.79-7.07 (1H, m, H-5), 7.07-7.21 (2H, m, H-6 and H-7), 7.97 (1H, br s, NH).

[6a*R-(6aβ,9α,10aα)]-2,6,6a,7,8,9,10,10a-Octahydro-6,6,9-trimethyl-10-oxo-9-vinylnaphth[1,2,3-*cd*]indole (16)** — A solution of **15** (9 mg) and Et_3N (0.3 ml) in CH_2Cl_2 (2.7 ml) was refluxed with stirring for 16 h. Evaporation to dryness and purification by PTLC

[hexane-CH_2Cl_2 (1:1)] gave **14** (2.5 mg, 28%) and **16** (3.5 mg, 39%) along with the recovery of **15** (2.5 mg, 28%). **16**: Colorless needles, mp 193-194°C (CH_2Cl_2-hexane). Anal. Calcd for $C_{20}H_{23}NO$: C, 81.87; H, 7.90; N, 4.78. Found: C, 81.68; H, 7.84; N, 4.81. MS *m/z*: 293 (M^+). IR (KBr) cm^{-1}: 1702, 1632. ^1H NMR ($CDCl_3$) δ: 1.15 (3H, s), 1.21 (3H, s), 1.49 (3H, s), 3.81-4.02 (1H, m, $W_{1/2}$=14 Hz, H-10), 5.11 (1H, d, J=17.5), 5.19 (1H, d, J=10.5), 6.06 (1H, dd, J=17.5, 10.5), 6.86-7.44 (3H, m), 7.44 (1H, dd, J=2, 2, H-2), 8.03 (1H, br s, NH).

[6a*R-(6aβ,9α,10β,10aβ)]-2,6,6a,7,8,9,10,10a-Octahydro-10-hydroxy-6,6,9-trimethyl-2-*p*-toluenesulfonyl-9-vinylnaphth[1,2,3-*cd*]indole (17)** — To a solution of **12** (35 mg) in THF (2 ml) and DMF (0.5 ml) was added 50% NaH in mineral oil (23 mg) at -20°C under Ar atmosphere and the mixture was stirred for 10 min. *p*-TsCl (28 mg) was added portionwise to this and the mixture was further stirred at -20°C for 2 h. Addition of sat. NH_4Cl-H_2O, extraction with Et_2O, usual work-up, and PTLC [hexane-EtOAc (7:1)] afforded **17** (45 mg, 84%) and *N,O*-ditosylate (5.5 mg, 8%). **17**: Colorless syrup. MS *m/z*: 449 (M^+). IR ($CHCl_3$) cm^{-1}: 1635. ^1H NMR ($CDCl_3$) δ: 1.04 (3H, s), 1.09 (3H, s), 1.38 (3H, s), 1.70-2.00 (1H, m, OH), 2.00 (1H, ddd, J=12, 4, 4, H-15), 2.31 (3H, s), 3.38-3.58 (1H, m, $W_{1/2}$=10 Hz, H-10), 4.10 (1H, d, J=2.5, H-11), 4.22 (1H, dd, J=10.5, 1), 4.56 (1H, dd, J=17.5, 1), 5.53 (1H, dd, J=17.5, 10.5), 6.99 (1H, d, J=7.5, H-5), 7.07 (1H, d, J=2, H-2), *ca.* 7.07-7.32 (1H, m, H-6), 7.15 and 7.74 (A_2B_2, J=8), 7.68 (1H, d, J=7.5, H-7). **Ditosylate of 12**: Colorless syrup. IR ($CHCl_3$) cm^{-1}: 1636. ^1H NMR ($CDCl_3$) δ: 0.82 (3H, s), 0.94 (3H, s), 1.35 (3H, s), 2.32 (3H, s), 2.36 (3H, s), 3.29-3.47 (1H, m, H-10), 4.19 (1H, d, J=10.5), 4.54 (1H, d, J=17), 5.00 (1H, d, J=2, H-11), 5.40 (1H, dd, J=17, 10.5).

[6a*S-(6aα,9α,10α,10aα)]-2,6,6a,7,8,9,10,10a-Octahydro-10-hydroxy-6,6,9-trimethyl-2-*p*-toluenesulfonyl-9-vinylnaphth[1,2,3-*cd*]indole (18)** — In the same manner as above, **13** (52 mg) was converted to **18** (69 mg, 87%) and *N,O*-ditosylate (9 mg, 8%) using 50% NaH (35 mg) and *p*-TsCl (41 mg). **18**: Colorless syrup. MS *m/z*: 449 (M^+). IR ($CHCl_3$) cm^{-1}: 1638. ^1H NMR ($CDCl_3$) δ: 0.60 (3H, s), 1.08 (3H, s), 1.41 (3H, s), 1.99 (1H, br s, OH), 2.24 (3H, s), 3.48-3.67 (1H, m, $W_{1/2}$=10 Hz, H-10), 4.11 (br s, H-11), 5.02 (1H, dd, J=17, 1.5), 5.11 (1H, dd, J=10.5, 1.5), 5.87 (1H, dd, J=17, 10.5), 6.94-7.34 (2H, m, H-5 and H-6), 7.10 and 7.71 (A_2B_2, J=8), 7.20 (1H, d, J=2, H-2), 7.60-7.81 (1H, m, H-7). **Ditosylate of 13**: Colorless syrup. IR ($CHCl_3$) cm^{-1}: 1641. ^1H NMR ($CDCl_3$) δ: 0.57 (3H, s), 0.85 (3H, s), 1.37 (3H, s), 2.29 (3H, s), 2.37 (3H, s), 3.45-3.66 (1H, m, H-10), 4.78 (1H, br d, J=10.5), 4.80 (1H, br d, J=18), 4.99 (1H, br s, H-11), 5.70 (1H, dd, J=18, 10.5).

[6a*R-(6aβ,9α,10aβ)]-2,6,6a,7,8,9,10,10a-Octahydro-6,6,9-trimethyl-10-oxo-2-*p*-toluenesulfonyl-9-vinylnaphth[1,2,3-*cd*]indole (19)** — To a CH_2Cl_2 solution (2.5 ml) of **17** (17 mg) was added PCC (82 mg) and the mixture was stirred at room temperature for 40 min. After quenching with sat. $NaHCO_3$-H_2O, the whole was filtered through a celite bed. The celite was washed with Et_2O and the combined organic layers was worked up as usual. Purification of the residue by PTLC [hexane-EtOAc (8:1)] gave **19** (11.5 mg, 68%) as colorless syrup. MS *m/z*: 447 (M^+). IR ($CHCl_3$) cm^{-1}: 1696, 1635. ^1H NMR ($CDCl_3$) δ: 1.09 (3H, s), 1.18 (3H, s), 1.44 (3H, s), 2.31 (3H, s), 3.97-4.13 (1H, m, H-10), 4.57 (1H, dd, J=10.5, 1), 4.83 (1H, dd, J=17, 1), 5.51 (1H, dd, J=17, 10.5), 6.90 (1H, d, J=2, H-2), 7.02 (1H, d, J=7.5, H-5), 7.15 and 7.70 (A_2B_2, J=8.5), 7.22 (1H, dd, J=7.5, 7.5, H-6), 7.68 (1H, d, J=7.5, H-7).

[6a*R-(6aβ,9α,10aα)]-2,6,6a,7,8,9,10,10a-Octahydro-6,6,9-trimethyl-10-oxo-2-*p*-toluenesulfonyl-9-vinylnaphth[1,2,3-*cd*]indole (20)** — To a solution of 10% v/v $(COCl)_2/CH_2Cl_2$ (0.34 ml) in CH_2Cl_2 (1 ml) was added 10% v/v DMSO/CH_2Cl_2 (0.83 ml) at -75°C and the mixture was stirred for 3 min under Ar atmosphere. A CH_2Cl_2 solution (3 ml) of **17** (44 mg) was added dropwise to this and stirring was continued at -75 – -67°C for 20 min. After addition of Et_3N (0.27 ml), the mixture was stirred at -67°C for 5 min, and at -20°C for 30 min. Addition of sat. $NaHCO_3$-H_2O, extraction with Et_2O, usual work-up, and PTLC [hexane-EtOAc (9:1)] afforded colorless syrup. A solution of this and Et_3N (0.3 ml) in CH_2Cl_2 (2.7 ml) was refluxed with stirring for 3 h. Evaporation to dryness and purification by PTLC [hexane-CH_2Cl_2 (3:2)] gave **20** (34 mg, 78%) as colorless prisms, mp 205-206°C (CH_2Cl_2-hexane). Anal. Calcd for $C_{27}H_{29}NO_3S$: C, 72.45; H, 6.53; N, 3.13. Found: C, 72.50; H, 6.56; N, 3.07. MS *m/z*: 447

(M^+). IR (KBr) cm^{-1}: 1710, 1632. ^1H NMR ($CDCl_3$, 400 MHz) δ: 1.10 (3H, s, H-18), 1.23 (3H, s, H-19), 1.44 (3H, s, H-17), 1.59-1.71 (1H, m), 1.85-2.01 (3H, m), 2.19 (1H, ddd, J=13.5, 2.5, 2.5, H-13e), 2.33 (3H, s), 3.77-3.85 (1H, m, H-10), 5.13 (1H, d, J=17.5), 5.25 (1H, d, J=10.5), 6.02 (1H, dd, J=17.5, 10.5), 7.12 (1H, d, J=7.5, H-5), 7.22 and 7.84 (A_2B_2, J=8.5), 7.25 (1H, dd, J=8, 7.5, H-6), 7.75 (1H, d, J=8, H-7), 7.82 (1H, d, J=2, H-2).

[6a*S-(6aα,9α,10aβ)]-2,6,6a,7,8,9,10,10a-Octahydro-6,6,9-trimethyl-10-oxo-2-*p*-toluenesulfonyl-9-vinylnaphth[1,2,3-*cd*]indole (21)** — By the same proce-dure as above, **18** (70 mg) was converted to **21** (56 mg, 80%), colorless prisms, mp 218-219°C (CH_2Cl_2-hexane). Anal. Calcd for $C_{27}H_{29}NO_3S$: C, 72.45; H, 6.53; N, 3.13. Found: C, 72.35; H, 6.54; N, 3.09. MS *m/z*: 447 (M^+). IR (KBr) cm^{-1}: 1708, 1640. ^1H NMR ($CDCl_3$) δ: 1.12 (3H, s), 1.40 (3H, s), 1.42 (3H, s), 1.70-2.14 (5H, m), 2.27 (3H, s), 3.62-3.92 (1H, m, H-10), 5.02 (1H, dd, J=17.5, 1), 5.12 (1H, dd, J=11, 1), 6.19 (1H, dd, J=17.5, 11), 7.00-7.33 (4H, m), 7.65-7.89 (3H, m), 7.80 (1H, d, J=2, H-2).

[6a*R-(6aβ,9α,10aβ)]-2,6,6a,7,8,9,10,10a-Octahydro-10-hydroxyimino-6,6,9-trimethyl-2-*p*-toluenesulfonyl-9-vinylnaphth[1,2,3-*cd*]indole (22)** —A mixture of **20** (10 mg), $HONH_2$·HCl (32 mg) and NaOAc (37 mg) in MeOH (3 ml) was refluxed with stirring for 13.5 h. After cooling in an ice bath, sat. $NaHCO_3$-H_2O was added and the mixture was extracted with CH_2Cl_2. Usual work-up and PTLC [hexane-EtOAc (5:1)] gave **22** (8 mg, 77%) as colorless syrup. MS *m/z*: 462 (M^+). IR ($CHCl_3$) cm^{-1}: 1632. ^1H NMR ($CDCl_3$) δ: 1.19 (3H, s), 1.27 (3H, s), 1.44 (3H, s), 2.31 (3H, s), 4.39 (1H, d, J=10.5), 4.73 (1H, d, J=17), 5.06-5.21 (1H, m, H-10, changed to d, J=5 on irradiation at H-2), 5.55 (1H, dd, J=17, 10.5), 6.94-7.34 (3H, m, H-2, H-5 and H-6), 7.16 and 7.73 (A_2B_2, J=8), 7.68 (1H, d, J=7.5, H-7), 8.78 (1H, br s, OH).

[6a*S-(6aα,9α,10α,10aβ)]-10-Formamido-2,6,6a,7,8,9,10,10a-octahydro-6,6,9-trimethyl-2-*p*-toluenesulfonyl-9-vinylnaphth[1,2,3-*cd*]indole (26) and the Compounds 23, 24, and 25** — To a solution of **21** (26 mg) in MeOH (4 ml) and THF (1 ml) were added NH_4OAc (180 mg) and 95% $NaBH_3CN$ (78 mg) and the mixture was stirred at room temperature for 5.5 days under Ar atmosphere. Sat. $NaHCO_3$-H_2O was added and the mixture was extracted with CH_2Cl_2. Usual work-up gave a residue (33 mg), which was dissolved in CH_2Cl_2 (1.5 ml) containing pyridine (0.4 ml) and the solution was cooled to -20°C. A CH_2Cl_2 solution (0.5 ml) of acetic formic anhydride (0.2 ml) was added and the mixture was stirred at -20°C to room temperature for 5 h. After quenching with sat. $NaHCO_3$-H_2O, the mixture was extracted with Et_2O. Usual work-up and PTLC [hexane-CH_2Cl_2 (1:3)] afforded the recovery of crude **21**, **23** (1 mg, 4%), **24** (1 mg, 4%), **26** (11.5 mg, 42%), and the crude **25** in the order of increasing polarity. The crude **21** and **25** were further purified by PTLC using hexane-EtOAc (9:1) and hexane-EtOAc (3:1), respectively, to give **21** (1.5 mg, 6%) and **25** (4.5 mg, 16%). **23**: Colorless syrup. MS *m/z*: 449 (M^+). ^1H NMR ($CDCl_3$) δ: 1.04 (3H, s), 1.11 (3H, s), 1.38 (3H, s), 1.92 (1H, d, J=3, OH), 2.30 (3H, s), 2.82 (1H, dd, J=10, 10, H-10), 3.47 (1H, dd, J=10, 3, H-11, changed to d, J=10 with D_2O), 5.16 (1H, d, J=17.5), 5.16 (1H, d, J=10.5), 5.76 (1H, dd, J=17.5, 10.5), 7.01-7.34 (4H, m), 7.61-7.86 (4H, m). **24**: Colorless syrup. MS *m/z*: 449 (M^+). ^1H NMR ($CDCl_3$) δ: 1.10 (3H, s), 1.23 (3H, s), 1.39 (3H, s), 2.01 (1H, s, OH), 2.30 (3H, s), 3.68-3.87 (2H, m, H-10 and H-11), 5.07 (1H, d, J=17.5), 5.12 (1H, d, J=10.5), 5.75 (1H, dd, J=17.5, 10.5), 6.94-7.33 (4H, m), 7.58 (1H, s, H-2), 7.71 (1H, d, J=8, H-7), 7.75 ($\underline{A}_2B_2$, J=8.5). **25**: Colorless syrup. MS *m/z*: 476 (M^+). IR ($CHCl_3$) cm^{-1}: 1683. ^1H NMR ($CDCl_3$) δ: 0.72 (3H, s), 1.07 (3H, s), 1.40 (3H, s), 2.28 (3H, s), 3.92-4.12 (1H, m, $W_{1/2}$=11 Hz, H-10), 4.17 (1H, dd, J=7, 5, H-11), 4.93 (1H, dd, J=16.5, 1), 4.98 (1H, dd, J=10.5, 1), 5.67 (1H, dd, J=16.5, 10.5), 6.17 (1H, br d, J=7, NHCHO), 6.90-7.34 (4H, m), 7.37 (1H, d, J=2, H-2), 7.67 (1H, d, J=7.5, H-7), 7.70 ($\underline{A}_2B_2$, J=8), 8.32 (1H, s, CHO). **26**: Colorless needles, mp 280.5-281.5°C (CH_2Cl_2-hexane). Anal. Calcd for $C_{28}H_{32}N_2O_3S$: C, 70.56; H, 6.77; N, 5.88. Found: C, 70.52; H, 6.83; N, 5.86. MS *m/z*: 476 (M^+). IR (KBr) cm^{-1}: 1692, 1640. ^1H NMR ($CDCl_3$, 400 MHz) of major and minor rotamers δ: 1.07 (3H, s, H-17), 1.28 (3H, s, H-19), 1.37 (1H, ddd, J=12, 12, 3.5, H-15), 1.43 (3H, s, H-18), 1.49-1.76 (3H, m), 1.89-1.97 (1H, m), 2.32 (3H, s), 3.29 (ddd, J=12, 3, 2) and ca. 3.29-3.35 (m) (1H, H-10), 4.72 and 3.82 (1H, dd each, J=11, 3, H-11), 4.96 and 5.06 (1H, d each, J=17.5), 5.01 and 5.14 (1H, d each, J=10.5), 5.27 (d, J=11) and 5.36 (dd, J=11, 11) (1H, NHCHO),

5.94 and 5.82 (1H, dd each, J=17.5, 10.5), 7.13 (1H, d, J=8, H-5), 7.20 ($\underline{A}_2B_2$, J=8.5), *ca.* 7.20-7.29 (1H, m, H-6), 7.32 and 7.10 (1H, d each, J=2, H-2), 7.77 and 7.66 (1H, d each, J=8, H-7), 7.82 and 7.70 ($A_2\underline{B}_2$, J=8.5), *ca.* 7.82-7.84 (m) and 8.08 (d, J=11) (1H, CHO).

[6a*S-(6aα,9α,10α,10aβ)]-10-Formamido-2,6,6a,7,8,9,10,10a-octahydro-6,6,9-trimethyl-9-vinylnaphth[1,2,3-*cd*]indole (27)** — To a solution of **26** (10 mg) in MeOH (3 ml) was added Mg (36 mg) and the mixture was stirred at room temperature for 9 h. Addition of sat. NH_4Cl-H_2O, extraction with CH_2Cl_2, usual work-up, and PTLC [hexane-EtOAc (3:2)] gave **27** (7 mg, 100%) as colorless amorphous compound. MS *m/z*: 322 (M^+). IR ($CHCl_3$) cm^{-1}: 1679. ^1H NMR ($CDCl_3$) δ: 1.13 (3H, s), 1.30 (3H, s), 1.47 (3H, s), 3.39 (1H, br d, J=10.5, H-10), 4.71 (1H, dd, J=11, 4, H-11), 4.91 (1H, dd, J=17.5, 1.5), 4.95 (1H, dd, J=11, 1.5), 5.42 (1H, br d, J=11, NHCHO), 5.77-6.13 (1H, m), 6.86-6.94 (1H, m, H-2), *ca.* 6.86-7.19 (3H, m), 7.85 (1H, s, CHO), 8.04 (1H, br s, indole NH).

(±)-Hapalindole U (2) — To a cooled (-20°C) solution of **27** (6.5 mg) in pyridine (0.4 ml) was added $POCl_3$ (11 μl) under Ar atmosphere and the mixture was stirred at the same temperature for 40 min. Addition of sat. $NaHCO_3$-H_2O, extraction with 10% MeOH-CH_2Cl_2, usual work-up, and PTLC [hexane-EtOAc (4:1)] afforded (±)-hapalindole U (**2**) (4.5 mg, 73%) as colorless needles, mp 240-242°C (CH_2Cl_2-hexane). Anal. Calcd for $C_{21}H_{24}N_2$: C, 82.85; H, 7.95; N, 9.20. Found: C, 82.74; H, 7.94; N, 9.01. MS *m/z*: 304 (M^+). IR (KBr) cm^{-1}: 2145, 1640. IR ($CHCl_3$) cm^{-1}: 2145, 1638. ^1H NMR ($CDCl_3$, 400 MHz) δ: 1.15 (3H, s, H-17), 1.28 (3H, s, H-19), 1.50 (3H, s, H-18), 1.56-1.71 (2H, m, H-13a and H-14a), 1.91-2.05 (2H, m, H-13e and H-14e), 1.92 (1H, ddd, J=11.5, 11.5, 3.5, H-15), 3.24-3.32 (1H, m, H-10), 4.10 (1H, br d, J=1.5, H-11), 5.17 (1H, dd, J=17.5, 1), 5.19 (1H, dd, J=11, 1), 6.05 (1H, dd, J=17.5, 11), 6.91 (1H, dd, J=2, 2, H-2), 7.01-7.06 (1H, m, H-5), 7.15-7.20 (2H, m, H-6 and H-7), 8.01 (1H, br s, NH).

[6a*R-(6aβ,9α,10α,10aα)]-10-Formamido-2,6,6a,7,8,9,10,10a-octahydro-6,6,9-trimethyl-2-*p*-toluenesulfonyl-9-vinylnaphth[1,2,3-*cd*]indole (32) and the Compounds 28, 29, 30, and 31** — In the same manner as above, **20** (13 mg) in MeOH (4 ml) and THF (1 ml) was stirred with NH_4OAc (180 mg) and 95% $NaBH_3CN$ (78 mg) at room temperature for 6 days under Ar atmosphere. After the work-up as before, followed by the formylation with AcOCHO (0.2 ml) in CH_2Cl_2 (2 ml) and pyridine (0.4 ml), the resulting residue was separated by PTLC (CH_2Cl_2) to give a less polar alcohol **29** (2 mg, 15%) and a more polar alcohol **28** (1.5 mg, 11%) as well as a mixture of other products. The mixture was further separated by PTLC [hexane-EtOAc (2:1)] to yield **31** (3 mg, 22%), **30** (4 mg, 29%), and **32** (1.5 mg, 11%) in the order of decreasing polarity. **28**: Colorless syrup. MS *m/z*: 449 (M^+). ^1H NMR ($CDCl_3$) δ: 1.09 (6H, s), 1.40 (3H, s), 2.01 (1H, br s, OH), 2.31 (3H, s), 3.60-3.79 (1H, m, $W_{1/2}$=12 Hz, H-10), 3.79 (1H, br d, J=6, H-11), 4.45 (1H, d, J=11), 4.68 (1H, d, J=17.5), 5.72 (1H, dd, J=17.5, 11), 6.92-7.34 (4H, m), 7.42 (1H, s, H-2), 7.69 (1H, d, J=7, H-7), 7.76 ($\underline{A}_2B_2$, J=8). **29**: Colorless syrup. MS *m/z*: 449 (M^+). ^1H NMR ($CDCl_3$) δ: 1.02 (3H, s), 1.17 (3H, s), 1.37 (3H, s), 1.50 (1H, s, OH), 2.30 (3H, s), 2.67 (1H, br dd, J=12, 10.5, H-10), 3.38 (1H, dd, J=10.5, 9, H-11, changed to d, J=10.5 with D_2O), 5.20 (1H, dd, J=17, 1.5), 5.29 (1H, dd, J=11.5, 1.5), 6.23 (1H, dd, J=17, 11.5), 7.00-7.35 (4H, m), 7.63-7.89 (4H, m). **30**: Colorless syrup. MS *m/z*: 476 (M^+). IR ($CHCl_3$) cm^{-1}: 1689. ^1H NMR ($CDCl_3$) δ: 0.96 (3H, s), 1.01 (3H, s), 1.37 (3H, s), 2.30 (3H, s), 3.17 (1H, br d, J=11, H-10), 4.77 (1H, dd, J=10.5, 3, H-11), *ca.* 5.07-5.40 (1H, m, NHCHO), 5.18 (1H, d, J=10.5), 5.18 (1H, d, J=18), 5.94 (1H, dd, J=18, 10.5), 6.98-7.34 (5H, m), 7.74 (1H, d, J=7.5, H-7), 7.78 ($\underline{A}_2B_2$, J=8), 7.93 (1H, s, CHO). **31**: Colorless syrup. MS *m/z*: 476 (M^+). IR ($CHCl_3$) cm^{-1}: 1681. ^1H NMR ($CDCl_3$) δ: 1.06 (3H, s), 1.09 (3H, s), 1.42 (3H, s), 2.33 (3H, s), 3.90 (1H, br dd, J=5, 5, H-10), 4.18 (1H, dd, J=8, 5, H-11), 4.84 (1H, dd, J=10.5, 1.5), 4.95 (1H, dd, J=17.5, 1.5), 5.65 (1H, dd, J=17.5, 10.5), 6.12 (1H, br d, J=8, NHCHO), 7.03 (1H, d, J=7.5, H-5), 7.12-7.38 (4H, m), 7.70 (1H, d, J=7.5, H-7), 7.75 ($\underline{A}_2B_2$, J=8.5), 8.42 (1H, s, CHO). **32**: Colorless syrup. MS *m/z*: 476 (M^+). IR ($CHCl_3$) cm^{-1}: 1692. ^1H NMR ($CDCl_3$) of major and minor rotamers δ: 0.94 and 0.99 (3H, s each), 1.08 (3H, s), 1.34 and 1.40 (3H, s each), 2.24 and 2.29 (3H, s each), *ca.* 2.58-3.04 (1H, m, H-10), 4.13 (dd, J=11, 11) and 3.11 (dd, J=10.5, 10.5) (1H, H-11), 5.20 (1H, br d, J=18), 5.33 (1H, br d, J=11), *ca.* 5.70-6.17 (1H, m, NHCHO), 6.24 (1H, dd, J=18, 11), 6.98-7.42 (5H, m), 7.60-7.89

(3H, m), 8.55 and 8.06 (1H, br s and d, J=12, CHO).

Reduction of the Compound 33 with Et_3SiH — A solution of **33** (133 mg) in CF_3COOH (2 ml) containing Et_3SiH (0.90 ml) was stirred at room temperature for 14 h. It was evaporated to dryness, sat. $NaHCO_3$-H_2O was added to the residue, and the mixture was extracted with CH_2Cl_2. Usual work-up and PTLC [benzene-EtOAc (5:2)] gave **32** (25 mg, 19%), recovery of the crude **33**, the crude **31**, and **34** (2.5 mg, 2%) in the order of increasing polarity. The pure **31** (78 mg, 58%) and **33** (6 mg, 4.5%) were obtained by PTLC using 0.05% MeOH-CH_2Cl_2 and CH_2Cl_2 respectively. **34**: Colorless syrup. MS *m/z*: 476 (M^+). IR ($CHCl_3$) cm^{-1}: 1682. ^1H NMR ($CDCl_3$) of two rotamers δ: 0.71 (3H, s), 1.04 (3H, s), 1.42 (3H, s), 2.28 (3H, s), 3.45-3.66 (1H, m, H-10), 4.58 (1H, br d, J=8, H-11), 4.87 (1H, d, J=17.5), 4.96 (1H, d, J=11), *ca.* 5.74-6.08 (1H, m, NHCHO), 5.86 (1H, dd, J=17.5, 11), 6.92-7.43 (5H, m), 7.61-7.84 (1H, m, H-7), 7.72 (A_2B_2, J=8.5), 8.01 (minor) and 8.15 (major) (1H, br s and s, CHO).

Tosylation of the Compound 35 — To a solution of **35**[4] (23 mg) in THF (2 ml) and DMF (0.5 ml) was added 50% NaH (14 mg) at -20°C and it was stirred for 10 min. *p*-TsCl (27 mg) was added to this and the mixture was further stirred at -20°C for 1.5 h. Quenching with sat. NH_4Cl-H_2O, extraction with Et_2O, usual work-up, and PTLC [hexane-EtOAc (1:1)] gave **34** (24 mg, 71%) as colorless syrup.

[6a*R-(6aβ,9α,10α,10aβ)]-10-Formamido-2,6,6a,7,8,9,10,10a-octahydro-6,6,9-trimethyl-9-vinylnaphth[1,2,3-*cd*]indole (36)** — In the same manner as preparing **27** from **26**, **31** (11 mg) in MeOH (2 ml) was stirred with Mg (29 mg) for 17 h. PTLC [hexane-EtOAc (1:1)] gave **36** (7 mg, 94 %) as colorless syrup. MS *m/z*: 322 (M^+). IR ($CHCl_3$) cm^{-1}: 1680, 1632. ^1H NMR ($CDCl_3$) of two rotamers δ: 1.07 (3H, s), 1.17 (3H, s), 1.48 (3H, s), 4.00 (1H, br dd, J=5, 5, H-10), 4.24 (1H, dd, J=9, 5, H-11), 4.89 (1H, dd, J=10.5, 1.5), 4.94 (1H, dd, J=18, 1.5), 5.78 (1H, dd, J=18, 10.5), 6.02 (1H, br d, J=9, NHCHO), 6.74-6.87 (1H, m, H-2), 6.83-7.21 (3H, m), 8.03 (1H, br s, indole NH), 8.29 (minor) and 8.40 (major) (1H, s each, CHO).

[6a*R-(6aβ,9α,10α,10aα)]-10-Formamido-2,6,6a,7,8,9,10,10a-octahydro-6,6,9-trimethyl-9-vinylnaphth[1,2,3-*cd*]indole (37)** — In the same way as above, **32** (25 mg) in MeOH (5 ml) was converted with Mg (101 mg) to **37** (16 mg, 95%) after PTLC (3% MeOH-CH_2Cl_2) purification. **37**: Colorless syrup. MS *m/z*: 322 (M^+). IR ($CHCl_3$) cm^{-1}: 1680. ^1H NMR ($CDCl_3$) of major and minor rotamers δ: 1.04 and 1.00 (3H, s each), 1.04 (3H, s), 1.43 and 1,38 (3H, s each), *ca.* 2.58-3.03 (1H, m, H-10), 4.04 and 3.03 (1H, dd, each, J=11, 11, H-11), 5.14 (1H, br d, J=17), 5.24 (1H, br d, J=11), 5.88 (br d, J=11) and *ca.* 6.08-6.47 (m) (1H, NHCHO), 6.16 and 6.20 (1H, dd each, J=17, 11), 6.64-6.81 (1H, m, H-2), 6.86-7.20 (3H, m), 8.16-8.58 (1H, m, indole NH), 8.31 and 8.01 (1H, br s and d, J=12, CHO).

[6a*R-(6aβ,9α,10α,10aβ)]-2,6,6a,7,8,9,10,10a-Octahydro-10-isocyano-6,6,9-trimethyl-9-vinylnaphth[1,2,3-*cd*]indole (38)** — A solution of **36** (8 mg) in pyridine (0.5 ml) was stirred with $POCl_3$ (14 μl) at -20°C for 40 min under Ar atmosphere. The same work-up as for (±)-**2** afforded **38** (6 mg, 79%) as colorless syrup after PTLC [hexane-EtOAc (4:1)] purification. HRMS Calcd for $C_{21}H_{24}N_2$: 304.194. Found: 304.194. IR ($CHCl_3$) cm^{-1}: 2140, 1637. ^1H NMR ($CDCl_3$, 400 MHz) δ: 1.05 (1H, dddd, J=14, 14, 12.5, 3.5, H-14a), 1.21 (3H, s, H-17), 1.22 (3H, s, H-19), 1.29 (1H, ddd, J=14, 14, 3.5, H-13a), 1.48 (3H, s, H-18), 1.51 (1H, ddddd, J=14, 3.5, 3.5, 3.5, 1.5, H-14e), 1.67 (1H, ddd, J=12.5, 3.5, 3.5, H-15), 1.77 (1H, br ddd, J=14, 3.5, 3.5, H-13e), 3.83 (1H, ddd, J=5, 2, 2, H-11), 3.98-4.04 (1H, m, H-10), 4.77 (1H, dd, J=10.5, 1), 4.86 (1H, dd, J=17.5, 1), 5.80 (1H, dd, J=17.5, 10.5), 6.92 (1H, dd, J=7, 1, H-5), 7.14 (1H, dd, J=7.5, 7, H-6), 7.18 (1H, dd, J=7.5, 1, H-7), 7.39 (1H, dd, J=2, 2, H-2), 8.00 (1H, br s, NH).

(±)-Hapalindole H (1) — A pyridine solution (0.5 ml) of **37** (15 mg) and $POCl_3$ (26 μl) was stirred at -20°C for 1 h under Ar atmosphere. The same work-up as above and PTLC [hexane-EtOAc (4:1)] afforded (±)-hapalindole H (**1**) (12 mg, 85%) as colorless prisms, mp 192-193°C (CH_2Cl_2-hexane). Anal. Calcd for $C_{21}H_{24}N_2$: C, 82.85; H, 7.95; N, 9.20. Found: C, 82.71; H, 8.03; N, 9.02. MS *m/z*: 304 (M^+). IR (KBr) cm^{-1}: 2150, 1635. IR ($CHCl_3$) cm^{-1}: 2145, 1640. ^1H NMR ($CDCl_3$, 400 MHz) δ: 1.10 (3H, s, H-18), 1.27 (3H, s, H-19), 1.38 (1H, ddd, J=13.5, 13.5, 3.5, H-13a), 1.45 (3H, s, H-17), 1.51 (1H, ddd, J=12, 11, 3.5, H-15), 1.65 (1H, dddd, J=13.5,

13, 12, 3.5, H-14a), 1.79 (1H, dddd, J=13, 3.5, 3.5, 3.5, H-14e), 2.06 (1H, ddd, J=13.5, 3.5, 3.5, H-13e), 3.16 (1H, br ddd, J=11, 11, 1.5, H-10), 3.51 (1H, br d, J=11, H-11), 5.29 (1H, d, J=17.5), 5.35 (1H, d, J=11), 6.28 (1H, dd, J=17.5, 11), 6.99-7.05 (1H, m, H-5), 7.15-7.21 (2H, m, H-6 and H-7), 7.63 (1H, dd, J=2, 1.5, H-2), 8.02 (1H, br s, NH). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 20.85, 24.53, 24.80, 27.36, 36.24, 36.33, 37.32, 40.56, 49.84, 67.94, 108.08, 112.66, 113.33, 115.90, 118.38, 122.73, 124.98, 133.33, 138.55, 140.71, 157.76.

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