# Two New Dimeric Indole Alkaloids from *Tabernaemontana subglobosa* MERR. from Taiwan

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**The structures of two new bis-indole alkaloids, 19′(*R*)-hydroxyconodurine (11) and 19′(*R*)-hydroxyconoduramine (12), from the leaves of *Tabernaemontana subglobosa* MERR. (Apocynaceae), native to Taiwan, were determined by means of spectroscopic analysis and chemical reactions.**

**Keywords** *Tabernaemontana subglobosa*; bis-indole alkaloid; 19′(*R*)-hydroxyconodurine; 19′(*R*)-hydroxyconoduramine; fragmentation; [1,5]sigmatropic rearrangement

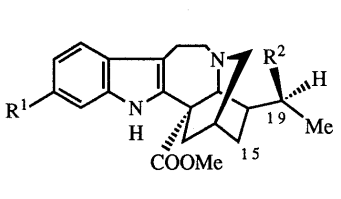
The genus *Tabernaemontana*, the largest group in the family Apocynaceae, is distributed over the whole tropical and subtropical zone of the world. Many species have been or are still used in traditional medicine.[1] Since the first isolation of a pure alkaloid from this genus in 1939, more than three hundred indole alkaloids have been found in *Tabernaemontana* plants.[2] Some of them have important pharmacological activities, such as antiparastic, hallucinogenic, and antimicrobial activities, *etc.*[1] *Tabernaemontana subglobosa* MERR. is native to Taiwan, but no chemical investigation has yet been reported. We collected roots and leaves of this plant in April 1989, and each part was extracted with hot methanol. The crude alkaloids obtained by the usual procedure (see the experimental section) were purified by the combination of $SiO_2$ and $Al_2O_3$ column chromatography. As shown in Table I, seven known alkaloids were isolated from the roots, and six known bases, as well as two new dimeric indole alkaloids, from the leaves. Interestingly, only three alkaloids were common constituents of these two parts, and the monomeric iboga-type indole alkaloids such as coronaridine (**1**), isovoacangine (**2**) and heyneanine (**3**) appeared only in the roots. We describe here the structure elucidation of two new alkaloids (**11** and **12**).

The first new alkaloid (**11**) was obtained as an amorphous powder, $[\alpha]_D^{12}$ −96.5 ($c$=1.0, $CHCl_3$). The ultraviolet (UV) spectrum (224, 285, 293 nm) and the mass spectral (MS) behavior[3] [720 ($M^+$, 18%), 702 (24), 522 (16), 509 (20), 194 (21), 180 (100), 136 (19), 134 (24), 122 (85)] suggested that the alkaloid is a derivative of conodurine (**8**),[4] which was simultaneously isolated from the leaves of this plant as a main alkaloidal component. The high-resolution mass spectrum of **11** displayed a molecular ion at $m/z$ 720.3874, corresponding to the formula $C_{43}H_{52}N_4O_6$. This contains one more oxygen than that of conodurine (**8**). Furthermore, the proton nuclear magnetic resonance ($^1$H-NMR) spectrum of **11** was very similar to that of **8** except that the alkaloid **11** had a hydroxyethyl group ($\delta$ 3.47, 1H, quintet-like, $J$=6.3 Hz, and $\delta$ 0.96, 3H, d, $J$=6.3 Hz) instead of the ethyl group of **8**. The carbon nuclear magnetic resonance ($^{13}$C-NMR) spectrum of **11** indicated the presence of sixteen aromatic carbons due to two indole nuclei, two ester groups, one ethylidene group, one *N*-methyl group, and twenty-one other aliphatic carbons. Unambiguous assignments of all the carbons and protons were obtained by using HH-correlation spectroscopy (COSY), CH-COSY and long-range coupling (COLOC)[5] spectra. The presence of a vobasinyl unit and an iboga unit in **11** was demonstrated by comparison of the $^{13}$C-NMR spectrum of **11** with that of conodurine (**8**)[4] (Table II). The signals of C-18′, 19′, and 20′ in **11** were observed at lower field by 9.2, 40.4 and 5.0 ppm, respectively, as compared with the corresponding signals of conodurine (**8**). This indicates that an additional hydroxy group exists at the C-19′ position in **11**. The stereochemistry at C-19′ could also be elucidated from the $^{13}$C-NMR data. Among the iboga-type monomeric indole alkaloids having a hydroxy group at C-19, the chemical shift of C-15 in heyneanine (**3**),[6] which possesses the 19(*S*) configuration, appears at $\delta$ 22.9, which is 6.7 ppm higher than that of C-19 isomer, *epi*-heyneanine (**13**) (Table III). That of C-21 in **13**, having 19(*R*) form, is shifted to upper field ($\delta$ 54.7, $\Delta$ 5.0 ppm) compared with that of the epimer **3**. This can be interpreted in terms of $\gamma$-steric interaction of the C-18 methyl group in the six-membered chair conformation (Fig. 2), which is fixed by the intramolecular hydrogen bonding between the $N_b$ lone-pair electrons and the C-19 hydroxy group.[6] In the new alkaloid (**11**), the signals of C-15′ and C-21′ appear

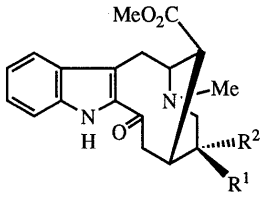
TABLE I. Alkaloids Isolated from *T. subglobosa* MERR.

| Alkaloid | Roots[a] (mg) | Leaves[b] (mg) |
|---|---|---|
| Coronaridine (**1**) | 122 | — |
| Isovoacangine (**2**) | 55 | — |
| Heyneanine (**3**) | 54 | — |
| Tabernaemontanine (**4**) | 965 | 89 |
| Dregamine (**5**) | 25 | 87 |
| Tabernaelegantine A (**6**) | 455 | 47 |
| Tabernaelegantine B (**7**) | 86 | — |
| Conodurine (**8**) | — | 256 |
| Conoduramine (**9**) | — | 52 |
| Tabernamine (**10**) | — | 82 |
| 19′(*R*)-Hydroxyconodurine (**11**) | — | 236 |
| 19′(*R*)-Hydroxyconoduramine (**12**) | — | 152 |

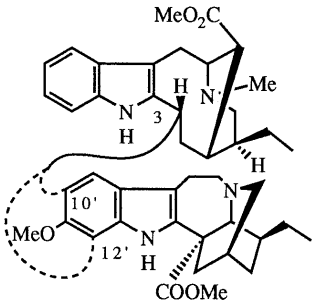
*a*) From 8 g of the crude base. *b*) From 3.9 g of the crude base.



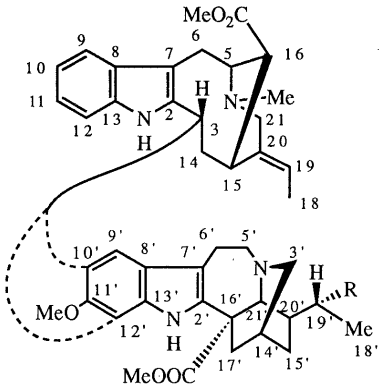
1: $R^1=R^2=H$ coronaridine
2: $R^1=OMe$, $R^2=H$ isovoacangine
3: $R^1=H$, $R^2=OH$ heyneanine



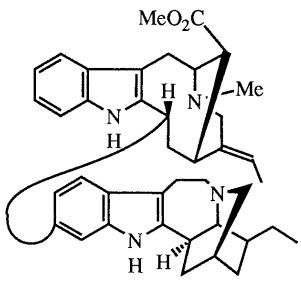
4: $R^1=Et$, $R^2=H$ tabernaemontanine
5: $R^1=H$, $R^2=Et$ dregamine



6: C3 is connected to C12'
tabernaelegantine A
7: C3 is connected to C10'
tabernaelegantine B



8: C3 is connected to C12', R=H
conodurine
9: C3 is connected to C10', R=H
conoduramine
11: C3 is connected to C12', R=OH
19'(*R*)-hydroxyconodurine
12: C3 is connected to C10', R=OH
19'(*R*)-hydroxyconoduramine



10: tabernamine

Fig. 1

at $\delta$ 28.3 and 53.5, respectively. These are reasonable values for 19(*R*) configuration. The connection position of the two indole units was demonstrated by spectroscopic analysis and chemical reactions, as follows. In the $^1$H-NMR spectrum of **11**, a set of four aromatic protons on an indole ring and a set of two aromatic *ortho*-coupling protons were observed. This is the connectivity-pattern as seen in conodurine (**8**), which has a carbon–carbon bond between C-3 and C-12′. In the COLOC spectrum, the C-3 proton had connectivities with C-2, 3, 14, 12′ and 13′, supporting the presence of a C3–C12′ bond. Büchi *et al.* reported the acid-catalyzed cleavage of the voacamine-type dimeric indole alkaloids[7] which had a bond between C-3 in the vobasinyl unit and C-11′ in the iboga unit. As a model experiment, conodurine (**8**) was treated with concentrated HCl in MeOH under reflux for 24 h to yield a monomeric indole alkaloid, isovoacangine (**2**), in 28% yield, a rearranged product (**9**) in 16% yield and the starting material (52%). The rearranged product was identical to conoduramine (**9**) on the basis of direct comparison with natural **9**. The monomeric compound (**2**) would be formed by initial protonation at the C-12′ position and subsequent fragmentation between C-3 and C-12′ as illustrated in Fig. 3. The rearranged compound would be generated from the common intermediate (**16**), followed by [1,5]sigmatropic rearrangement. Under the same reaction conditions, the new alkaloid (**11**) gave the monomeric alkaloids (**14**) in 14% yield and a small amount of rearranged compound (**12**), together with 80% recovery of the starting material. The UV and $^1$H- and $^{13}$C-NMR spectra indicated the presence of an 11-methoxy group in **14**. Since the original dimeric alkaloid (**11**) exhibited two *ortho*-coupled protons in the $^1$H-NMR spectrum, it became clear that vobasinyl unit is connected to the C-12 position in the iboga unit. The rearranged compound was identical to the second new alkaloid (**12**) (*vide infra*). From these data, the structure of the new alkaloid (**11**) was concluded to be 19′(*R*)-hydroxyconodurine.

The second new alkaloid (**12**), obtained as an amorphous powder, exhibited the same molecular formula as that of 19′-hydroxycondurine (**11**). The UV, $^1$H- and $^{13}$C-NMR spectra were very similar to those of **11**, except for a few changes. In the $^1$H-NMR spectrum, a set of four aromatic protons due to one indole nucleus and two additional singlet aromatic protons were observed, of which the latter were the clearly different from those of **11**. This signal pattern in the aromatic region can be seen in the known dimeric indole alkaloid, conoduramine (**9**),[4] which has a bond between the C-3 vobasinyl unit and the C-10 iboga unit. Actually, the $^{13}$C-NMR spectra of **12** and conoduramine (**9**)[4] were very similar except for the chemical shifts of some carbons around the C-19′ position

(Table II). The presence of a 19′-hydroxy group in the iboga unit and the 19′(*R*) configuration were clearly demonstrated by analyzing the $^1$H- and $^{13}$C-NMR spectral data, as in the case of the new alkaloid, 19′(*R*)-hydroxyconodurine (**11**). As described in connection with the structure elucidation of **11**, compound **12** was also obtained from **11** by acidic treatment. Therefore, the structure of the second new alkaloid (**12**) was concluded to be 19′(*R*)-hydroxyconoduramine.

TABLE II. $^{13}$C-NMR Data for **8**, **11**, **9** and **12**

| Carbon | **8**[a] | **11**[b] | **9**[a] | **12**[b] |
|---|---|---|---|---|
| 2 | 136.1 | 136.5 | 135.3 | 137.9 |
| 3 | 35.2 | 34.9 | 37.0 | 37.0 |
| 5 | 59.7 | 59.2 | 59.8 | 59.5 |
| 6 | 19.5 | 18.9 | 19.4 | 18.8 |
| 7 | 109.1 | 108.6 | 109.8 | 109.5 |
| 8 | 129.6 | 128.9 | 130.0 | 129.5 |
| 9 | 118.0 | 117.8 | 117.4 | 117.1 |
| 10 | 119.4 | 118.2 | 118.7 | 117.5 |
| 11 | 122.1 | 121.1 | 121.3 | 120.4 |
| 12 | 109.8 | 109.8 | 109.8 | 109.8 |
| 13 | 136.8 | 136.2 | 135.8 | 136.1 |
| 14 | 33.8 | 34.2 | 36.6 | 37.0 |
| 15 | 33.6 | 33.2 | 33.6 | 33.4 |
| 16 | 47.3 | 46.5 | 47.1 | 46.6 |
| 18 | 12.3 | 11.8 | 12.2 | 11.8 |
| 19 | 118.7 | 117.0 | 118.4 | 116.4 |
| 20 | 137.7 | 138.3 | 138.0 | 139.0 |
| 21 | 53.0 | 51.7 | 52.5 | 51.9 |
| COOMe | 50.1 | 49.5 | 49.8 | 49.2 |
| COOMe | 171.8 | 170.4 | 171.6 | 170.3 |
| NMe | 42.5 | 42.0 | 42.4 | 42.1 |
| 2′ | 136.0 | 135.6 | 134.7 | 136.3 |
| 3′ | 51.2[c] | 51.1 | 51.5[c] | 52.5 |
| 5′ | 52.5[c] | 52.0 | 53.0[c] | 52.7 |
| 6′ | 22.1 | 21.3 | 22.1 | 21.4 |
| 7′ | 110.1 | 108.4 | 110.1 | 108.1 |
| 8′ | 124.5 | 124.0 | 122.5 | 121.6 |
| 9′ | 117.1 | 116.6 | 117.8 | 116.6 |
| 10′ | 105.1 | 105.7 | 127.3 | 126.7 |
| 11′ | 152.0 | 151.5 | 153.3 | 152.3 |
| 12′ | 114.5 | 115.1 | 92.7 | 93.1 |
| 13′ | 135.1 | 134.6 | 138.1 | 134.9 |
| 14′ | 27.1 | 26.3 | 27.3 | 26.5 |
| 15′ | 31.9 | 28.3 | 32.0 | 28.5 |
| 16′ | 54.6 | 53.6 | 55.0 | 54.0 |
| 17′ | 34.7 | 33.9 | 36.5 | 35.4 |
| 18′ | 11.6 | 20.8 | 11.6 | 21.0 |
| 19′ | 26.6 | 67.0 | 26.7 | 67.1 |
| 20′ | 38.9 | 43.9 | 39.1 | 43.7 |
| 21′ | 57.6 | 53.5 | 57.4 | 53.3 |
| COOMe′ | 52.3 | 52.2 | 52.4 | 52.3 |
| COOMe′ | 174.9 | 173.4 | 175.8 | 174.0 |
| ArOMe | 56.9 | 57.1 | 55.9 | 55.7 |

*a*) In $CDCl_3$. *b*) In DMSO-$d_6$. *c*) See reference 8.

## Experimental

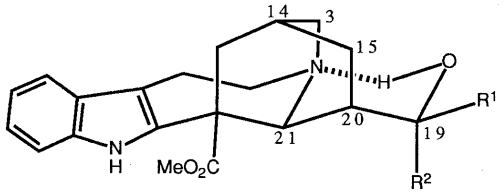
The instruments used in this study were as follows; UV spectra, Hitachi U3400 spectrophotometer; IR spectra, Hitachi 260 spectrophotometer; MS, Hitachi RMU-6E and RMU-7M spectrometers; $^1$H- and $^{13}$C-NMR spectra, JEOL GSX500 and JEOL JNM A500 instruments. Thin-layer chromatography was performed on Merck precoated Silica gel 60 $F_{254}$ plates. Column chromatography was carried out on Merck Silica gel 60 (230—400 mesh for flash chromatography) and a pre-packed column [silica gel, Kusano CPS-HS-221-05 for medium-pressure column chromatography (MPLC)]. Abbreviations used are: singlet (s), doublet (d), triplet (t), multiplet (m), shoulder (sh).

**Extraction and Separation of the Alkaloidal Fraction** The plant material was collected at Lanyu, Taitung County, Taiwan, in April 1989. The dried powdered roots (4.2 kg) of the plant were extracted with hot MeOH three times. Concentration of the solution under reduced pressure gave a crude extract (339 g), a part of which (104 g) was dissolved in 3% HCl solution and washed with ethyl acetate (AcOEt). The aqueous layer was basified with concentrated ammonia water at 0 °C and extracted with $CHCl_3$. The organic layer was washed with brine, dried and evaporated to give the crude base (8.0 g, 0.062% from the dry roots). The same treatment of the dried powdered leaves (735 g) of the plant gave the crude base (3.9 g, 0.53% from the dried leaves). The crude base was roughly separated by column chromatography with a 30-fold amount of $SiO_2$, and then purified by the combination of $SiO_2$ flash column chromatography and $SiO_2$ MPLC. The obtained alkaloids and their yields are listed in Table I.

**Isolation of 19′(*R*)-Hydroxyconodurine (11)** The 3% MeOH/$CHCl_3$ eluate from the first $SiO_2$ column chromatography was subjected to $SiO_2$ flash column chromatography twice (5% isopropanol–$CHCl_3$ and then 2.5% isopropanol–$CHCl_3$) to give 236 mg of **11**. Colorless amorphous powder, $[\alpha]_D^{12}$ −96.5° ($c$=1.0, $CHCl_3$). UV $\lambda_{max}^{EtOH}$ nm: 224, 285, 293. IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 3450, 3370, 2940, 1720. $^1$H-NMR (500 MHz, DMSO-$d_6$) $\delta$: 10.44 (1H, s, NH), 7.61 (1H, d-like, $J$=7.4 Hz, 9-H), 7.43 (1H, s, NH′), 7.20 (1H, d, $J$=8.6 Hz, 9′-H), 7.06 (1H, d-like, $J$=7.4 Hz, 12-H), 7.00 (1H, t, $J$=7.4 Hz, 10-H), 6.99 (1H, t, $J$=7.4 Hz, 11-H), 6.85 (1H, d, $J$=8.6 Hz, 10′-H), 5.24 (1H, q, $J$=6.6 Hz, 19-H), 5.13 (1H, dd, $J$=13.2, 3.2 Hz, 3-H), 3.93 (3H, s, Ar-$OCH_3$), 3.89 (1H, td, $J$=9.0, 3.2 Hz, 5-H), 3.72 (1H, br s, 21′-H), 3.65 (3H, s, $CO_2CH_3$′), 3.63 (1H, m, 15-H), 3.49 (1H, d, $J$=12.9 Hz, 21-H), 3.47 (1H, quintet, $J$=6.3 Hz, 19′-H), 3.29 (2H, m, 6-$H_2$), 3.20 (1H, m, 5′-H), 2.85 (1H, d, $J$=12.9 Hz, 21-H), 2.84 (2H, m, 5′-H, 6′-H), 2.79 (1H, m, 6′-H), 2.60 (1H, t, $J$=3.2 Hz, 16-H), 2.56 (1H, m, 3′-H), 2.48 (3H, s, N–$CH_3$), 2.43 (3H, s, $CO_2CH_3$), 2.28 (1H, d, $J$=8.5 Hz, 3′-H), 1.74 (1H, ddd, $J$=15.1, 6.8, 3.4 Hz, 14-H), 1.64 (1H, d, $J$=13.6 Hz, 17′-H), 1.60 (3H, dd, $J$=6.6, 1.4 Hz, 18-$H_3$), 1.35

TABLE III. Selected $^{13}$C-NMR Data for **3**, **13**, **11** and **12**

| | Heyneanine (**3**) | *epi*-Heyneanine (**13**) | 19′-Hydroxy-conodurine (**11**) | 19′-Hydroxy-conoduramine (**12**) |
|---|---|---|---|---|
| C15 or 15′ ($\delta$) | 22.9 | 28.6 | 28.3 | 28.5 |
| C21 or 21′ ($\delta$) | 59.7 | 54.7 | 53.5 | 53.3 |
| Config. of C19 | (*S*) | (*R*) | (*R*) | (*R*) |




**3**: $R^1$=Me, $R^2$=H heyneanine
**13**: $R^1$=H, $R^2$=Me *epi*-heyneanine

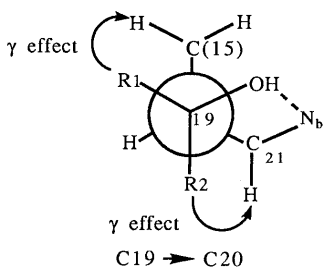



Fig. 2

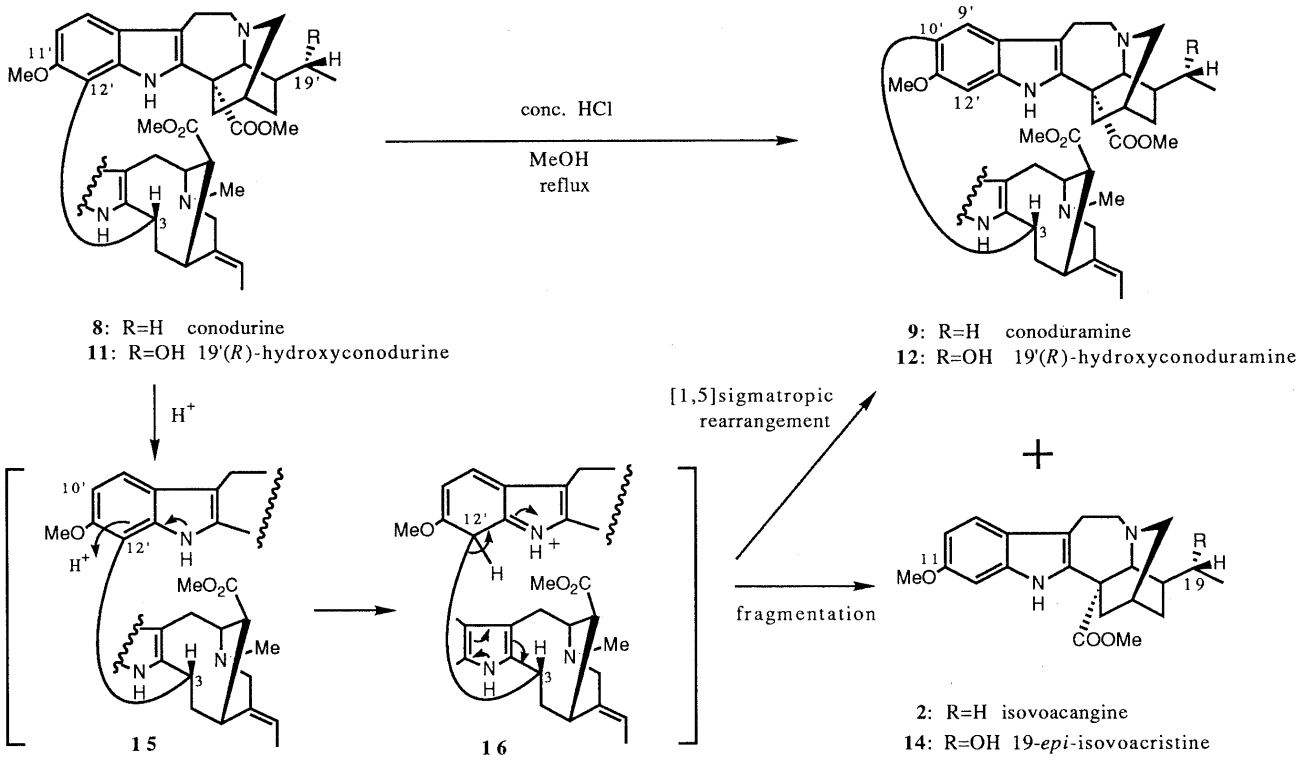



Fig. 3

(1H, brs, 14'-H), 1.28 (1H, brt, $J$=11.8 Hz, 15'-H), 0.96 (3H, d, $J$=6.3 Hz, 18'-$H_3$), 0.94 (1H, m, 20'-H), 0.84 (1H, dd, $J$=11.8, 7.0 Hz, 15'-H), 0.41 (1H, brd, $J$=13.6 Hz, 17'-H). $^{13}$C-NMR (Table II). MS $m/z$ (%): 720 ($M^+$, 18), 702 (24), 522 (16), 509 (20), 507 (21), 194 (21), 180 (100), 136 (19), 134 (24), 122 (85). High-resolution MS Calcd for $C_{43}H_{52}N_4O_6$: 720.3883. Found: 720.3874.

**Isolation of 19'(*R*)-Hydroxyconoduramine (12)** The 3% MeOH–$CHCl_3$ eluate from the first $SiO_2$ column chromatography was successively subjected to $SiO_2$ flash column chromatography (acetone: *n*-hexane=2:1—MeOH) and then $SiO_2$ flash column chromatography (*n*-hexane:$CHCl_3$:$Et_3N$=4:5:1) to give 152 mg of **12**. Colorless amorphous powder, $[\alpha]_D^{12}$ −78.5° ($c$=1.0, $CHCl_3$). UV $\lambda_{max}^{EtOH}$ nm: 227, 288, 295. IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 3450, 2940, 1720. $^1$H-NMR (500 MHz, DMSO-$d_6$) $\delta$: 10.11 (1H, s, NH'), 10.05 (1H, s, NH), 7.49 (1H, d, $J$=6.9 Hz, 9-H), 7.05 (1H, d, $J$=6.9 Hz, 12-H), 6.92 (2H, m, 10-H, 11-H), 6.81 (1H, s, 12'-H), 6.60 (1H, s, 9'-H), 5.21 (1H, q, $J$=6.6 Hz, 19-H), 4.95 (1H, brd, $J$=11.7 Hz, 3-H), 3.89 (3H, s, Ar-$OCH_3$), 3.81 (1H, td, $J$=9.3, 2.9 Hz, 5-H), 3.78 (1H, brs, 21'-H), 3.68 (1H, d, $J$=13.4 Hz, 21-H), 3.54 (3H, s, $CO_2CH_3$'), 3.53 (1H, m, 19'-H), 3.51 (1H, m, 15-H), 3.41 (1H, brt, $J$=11.0 Hz, 6-H), 3.14 (2H, m, 6-H, 5'-H), 2.79 (1H, d, $J$=13.4 Hz, 21-H), 2.74 (1H, m, 5'-H), 2.51 (1H, brs, 16-H), 2.45 (3H, s, N-$CH_3$), 2.33 (3H, s, $CO_2CH_3$), 1.79 (1H, brs, 14'-H), 1.72 (1H, d, $J$=13.2 Hz, 17'-H), 1.59 (3H, d, $J$=5.8 Hz, 18-$H_3$), 1.49 (1H, brt, $J$=12.0 Hz, 15'-H), 1.14 (1H, m, 20'-H), 0.99 (3H, d, $J$=5.7 Hz, 18'-H). $^{13}$C-NMR (Table II). MS $m/z$ (%): 720 ($M^+$, 1), 702 (13), 658 (24), 613 (53), 225 (49), 194 (60), 180 (53), 136 (100), 122 (71). High-resolution MS Calcd for $C_{43}H_{52}N_4O_6$: 720.3883. Found: 720.3865.

**Acid Treatment of Conodurine (8)** A mixture of **8** (25 mg) and concentrated HCl (0.7 ml) in MeOH (7.0 ml) was refluxed under argon for 24 h. The reaction mixture was diluted with chilled water, basified with $Na_2CO_3$ solution, and then extracted with $CHCl_3$. The organic layer was washed with brine, dried over $MgSO_4$, and evaporated. The residue was purified by MPLC using 3% MeOH–$CHCl_3$ to afford 2 mg (16%) of isovoacangine (**2**), 7 mg (28%) of conoduramine (**9**), and 12.5 mg (50%) of the starting material. The products **2** and **9** were identical with the corresponding natural compounds, on the basis of their chromatographic behavior, and UV, MS and NMR conparisons.

**Acid Treatment of 19'(*R*)-Hydroxyconodurine (11)** Compound **11** (30 mg) was treated as described above, by using concentrated HCl (0.75 ml) in MeOH (7.5 ml). The residue obtained by usual work-up purified by MPLC using 3% MeOH–$CHCl_3$ to afford 2 mg (14%) of 19-*epi*-isovoacristine (**14**), 0.5 mg of 19'(*R*)-hydroxyconoduramine (**12**), and 24 mg (80%) of the starting material. The rearranged product **12** was identical with the natural compound on the basis of a comparison of their chromatographic behavior and NMR spectra. **14**: amorphous powder. UV $\lambda_{max}^{EtOH}$ nm: 226, 278 (sh), 296. $^1$H-NMR (500 MHz, $CDCl_3$) $\delta$: 7.66 (1H, brs, NH), 7.33 (1H, d, $J$=9.2 Hz, 9-H), 6.76 (2H, 10-H, 12-H), 4.06 (1H, s, 21-H), 3.99 (1H, qd, $J$=6.4, 2.4 Hz, 19-H), 3.83 (3H, s, Ar-$OCH_3$), 3.73 (3H, s, $CO_2CH_3$), 3.41 (1H, m, 5-H), 3.13 (2H, m, 5-H, 6-H), 3.04 (1H, m, 6-H), 2.99 (1H, m, 3-H), 2.82 (1H, brd, $J$=8.3 Hz, 3-H), 2.56 (1H, ddd, $J$=13.6, 2.0, 2.0 Hz, 17-H), 2.02 (1H, m, 14-H), 1.96 (1H, ddd, $J$=13.6, 4.4, 2.7 Hz, 17-H), 1.85 (1H, dddd, $J$=12.7, 7.6, 2.2, 2.2 Hz, 20-H), 1.77 (1H, dddd, $J$=10.5, 10.5, 4.3, 1.8 Hz, 15-H), 1.40 (1H, ddd, $J$=10.5, 7.6, 2.3 Hz, 15-H), 1.28 (3H, d, $J$=6.4 Hz, 18-$H_3$). $^{13}$C-NMR (125 MHz, $CDCl_3$) $\delta$: 136.2 (C-2), 51.9 (C-3), 50.4 (C-5), 22.3 (C-6), 109.7 (C-7), 123.0 (C-8), 119.2 (C-9), 109.3 (C-10), 156.8 (C-11), 94.2 (C-12), 134.3 (C-13), 27.0 (C-14), 28.7 (C-15), 53.9 (C-16), 36.7 (C-17), 22.7 (C-18), 70.9 (C-19), 40.1 (C-20), 54.4 (C-21), 175.1 (CO), 52.7 (COOMe), 55.7 (Ar-OMe). MS $m/z$ (%): 384 ($M^+$, 12), 366 (100), 339 (13), 244 (25), 224 (16), 212 (16), 184 (22), 152 (27), 134 (14), 122 (21). High-resolution MS Calcd for $C_{22}H_{28}N_2O_4$: 384.2049. Found: 384.2052.

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**References and Notes**

1) T. A. van Beek, M. A. J. T. van Gessel, "Alkaloids: Chemical and Biological Perspectives," Vol. VI, ed. by S. W. Pelletier, John Wiley and Sons, New York, 1988.
2) I. W. Southon, J. Buckingham, "Dictionary of Alkaloids," Chapman and Hall, London, 1989.
3) M. Hesse, "Indolealkaloide," ed. by H. Budzikiewicz, Verlag Chemie, Weinheim, p. 229, 1974.
4) *a*) D. G. I. Kingston, B. T. Li, F. Ionescu, *J. Pharm. Sci.*, **66**, 1135 (1977); *b*) T. A. van Beek, F. L. C. Kuijlaars, P. H. A. M. Thomassen, R. Verpoorte, A. B. Svendsen, *Phytochemistry*, **23**, 1171 (1984); *c*) T. A. van Beek, R. Verpoorte, A. B. Svendsen, R. Fokkens, *J. Nat. Prod.*, **48**, 400 (1985).
5) H. Kessler, C. Griesinger, J. Zarbock, H. R. Looshi, *J. Magn.*

*Reson.*, **67**, 331 (1984).
6) a) M. De Bellefon, M. M. Debray, L. Le Men-Olivier, J. Le Men, *Phytochemistry*, **14**, 1649 (1975); *b*) E. Wenkert, D. W. Cochran, H. E. Gottlieb, E. W. Hagaman, R. B. Filho, F. J. A. Matos, M. I. L. M. Madruga, *Helv. Chim. Acta*, **59**, 2437 (1976).
7) G. Büchi, R. E. Manning, S. A. Monti, *J. Am. Chem. Soc.*, **86**, 4631 (1964).
8) The literature[4] assignments of the resonances of C-3′ and C-5′ in **8** and **9**, respectively, were revised on the basis of CH-COSY spectra.