Determination of the Absolute Stereochemistry of Cyclosmenospongine

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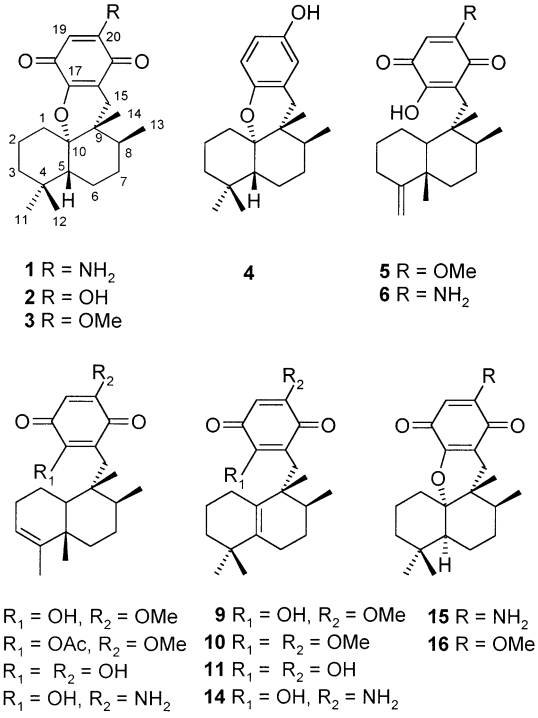
The absolute stereochemistry of the sponge metabolite cyclosmenospongine (**1**) was determined as 5*R*, 8*S*, 9*R*, 10*S* by chemical correlation. Substitution of the methoxyl group by an amino group in the cyclic product **3** of acid-catalyzed rearrangement of ilimaquinone (**5**) afforded cyclosmenospongine **1**. Cyclosmenospongine was also obtained by acid-catalyzed cyclization of smenospongine (**6**).

Cyclosmenospongine (**1**) was recently isolated from an Australian marine sponge *Spongia* sp.[1] The structure and relative stereochemistry of **1** were determined by spectroscopic analysis. Acid-catalyzed rearrangements of sesquiterpene quinones and hydroquinones have previously been successfully applied to define the absolute stereochemistry of sponge metabolites, for example, ilimaquinone (**5**),[2,3] isospongiaquinone (**7**),[2] arenarol,[4,5] and 5-*epi*-ilimaquinone.[5] A series of cyclic products have been formed during these acid-catalyzed rearrangements. Acid-catalyzed rearrangements of **5**[2] and arenarol[4] produced cyclic products **3** and **4**, respectively, whose absolute stereochemistries were defined as 5*R*, 8*S*, 9*R*, 10*S*. Since the skeleton of **1** was reminiscent of product **3**, we tried to prepare **3** from **5** and then to obtain an amino derivative by substitution of the methoxyl group in **3** with an amino group for determination of the absolute stereochemistry of **1**. Moreover, since acid-catalyzed rearrangement of smenospongine (**6**) has not been reported previously, we carried it out to see if **6** would readily form cyclic products. This paper describes the determination of the absolute stereochemistry of **1** by chemical correlation with products of acid-catalyzed rearrangements of ilimaquinone (**5**) and smenospongine (**6**).



Treatment of **5** with MeOH−HOAc−HCl (1:1:1) at room temperature for 15 min yielded a mixture of **7** and **9**, which was separated by crystallization from hexane. Compound **7** was identified by comparison of the $[\alpha]^{25}_{D}$, mp, and ^{1}H and ^{13}C NMR spectra with the reported data for isospongiaquinone (**7**).[6,7] Acetylation of **7** with acetic anhydride in pyridine gave the monoacetate **8**, identical in all respects with published data for the acetate of **7**.[6,7] To our knowledge it is the first report of the isolation of **7** as an intermediate product in this acid-catalyzed rearrangement of **5**. Compound **7** presumably arises via protonation at C-11 of **5** and loss of a C-3 proton to give a 3,4-double bond. Compound **9** was identified as a product of the boron trifluoride-catalyzed isomerization of **5** and 5-*epi*-ilimaquinone[8] by comparison of their ^{1}H NMR spectra. Methylation of **9** with CH_2N_2 yielded the dimethyl ether **10**, the spectral and physical data of which were identical with published values.[2]

Treatment of **5** with the same acid mixture under gentle reflux for 2 h at 40 °C, as was described,[2] quantitatively yielded a single product, **11**, but not **3**, as was expected. The same result was obtained by treatment of **5** with MeOH−HOAc−HCl at room temperature for 10 days. Spectroscopic analysis of **11** confirmed the presence of a tetrasubstituted double bond and a geminal dimethyl moiety. Methylation of **11** with CH_2N_2 yielded the dimethyl ether **10**. Thus **11** was the demethylated precursor to the cyclized products.

Treatment of **5** with the same acid mixture under reflux for 1 h at 80 °C gave a five-component mixture of **2**, **3**, **7**, **9**, and **12**. The main component of the mixture was **12**. ^{1}H and ^{13}C NMR spectra and a molecular peak at 344 *m*/*z* in the EIMS of **12** showed that it was the demethylated analogue of **7**. A compound with the same structure was previously described as a metabolite of the marine sponge *Dysidea cinerea*[9] and as a product of dehydration of chiatoquinone with *p*-TsOH.[10,11] Spectroscopic and physical data of compounds **2** and **3** were identical with published values.[2,6] Since ^{13}C NMR data for **2** and **3**, previously reported,[2,6] were unassigned, spectra for **2** were assigned from DEPT, HMQC, and HMBC experiments.

Reaction of **3** with NH_3 in aqueous EtOH yielded **1**, whose optical rotation and other spectral data were coincident with those for natural cyclosmenospongine (**1**). Consequently, the absolute configuration of **1** can be assigned as 5*R*, 8*S*, 9*R*, 10*S*.

Treatment of an authentic sample of smenospongine (**6**) with MeOH−HOAc−HCl (1:1:1) at room temperature for 15 min gave a 1:1.5 mixture of **13** and **14**. Attempts to

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Table 1. ^{13}C NMR Data for **1**, **2**, **15**, and **16** ($CDCl_3$, 75 MHz)

	δ_C			
C	**1**	**2**	**15**	**16**[a]
1	29.1	29.8	28.9	28.9
2	17.8	17.9	18.2	18.3
3	40.9	41.7	33.2	33.4
4	33.2	33.5	33.6	33.7
5	45.7	45.8	45.0	45.1
6	22.0	22.0	22.6	22.5
7	30.1	30.3	27.5	27.7
8	32.3	32.4	39.1	39.0
9	37.6	37.3	38.2	37.9
10	88.6	87.5	89.9	87.8
11	22.4	22.2	29.7	29.7
12	32.4	32.5	31.9	31.9
13	16.3	16.7	17.2	17.1
14	17.1	17.0	19.8	20.1
15	26.7	26.4	30.6	30.7
16	113.3	112.8	113.0	115.3
17	153.6	154.8	152.6	151.1
18	180.5	182.2	180.9	181.5
19	98.1	104.8	97.8	104.7
20	152.3	155.3	152.6	159.5
21	177.6	181.5	177.6	181.5

[a] ^{13}C NMR data reported by Bourguet-Kondracki et al.[14]

separate **13** from **14** were unsuccessful; thus we performed the spectral analysis on the mixture. The ^1H and ^{13}C NMR spectra contained two sets of signals. A set of signals for the minor component **13** in the ^1H NMR spectrum indicated the presence of an olefinic proton (δ 5.12) and a methyl group (δ 1.54) connected with a double bond. The remaining terpenoid part of this set of signals was similar to those of **7** and **12**. Indeed one set of terpenoid carbon signals in the ^{13}C NMR spectrum was characteristic of a *trans*-4,9-friedodrim-3-ene skeleton[7] and was similar to those of **7**. A set of signals for the major component **14** revealed the presence of a tetrasubstituted double bond (δ 131.9, 135.3) and a geminal dimethyl moiety and was similar to signals of a terpenoid moiety of **11**. The ^1H and ^{13}C NMR spectra of the quinonoid parts of the two compounds were similar to those of **6**.[12,13] Prolonged treatment of the mixture of **13** and **14** with MeOH−HOAc−HCl (1:1:1) under reflux for 2 h at 80 °C gave an inseparable mixture of degradated products.

Treatment of **6** with *p*-TsOH in dry benzene at reflux for 30 min yielded a multicomponent mixture from which only products **1** and **15** in a ratio of 1:1.4 could be separated in pure form. One product was identical with cyclosmenospongine (**1**) isolated from a marine sponge *Spongia* sp.[1] The molecular formula $C_{21}H_{29}NO_3$ of **15** was the same as that of **1**. Close similarity between the ^1H and ^{13}C NMR data for **15** and those for **1** suggested that **15** was a stereoisomer of **1**. Moreover, the isomer **15** showed an optical rotation opposite of **1**. The relative stereochemistry of **15** was established on the basis of the following NOE correlations. Irradiation of the Me-13 protons enhances the resonance observed for Hβ-1. Irradiation of the Me-12 protons enhances the resonance observed for H-5, while irradiation of the Me-11 protons enhances the resonance observed for H-5 and Hβ-2. Irradiation of Hα-15 enhances the resonances observed for Hβ-15, Hβ-7, H-5, and H-8. Irradiation of Hβ-15 enhances the resonances observed for Hα-15, H-8, and Me-14 protons.

Comparison of the ^{13}C NMR data for **15** with that of smenoqualone (**16**)[14] indicated that **15** and **16** have the same sesquiterpenoid skeleton and relative stereochemistry (Table 1). Thus product **15** is 5-*epi*-cyclosmenospongine, and its absolute configuration is 5*S*, 8*S*, 9*R*, 10*S*.

When we compared the ^{13}C NMR data (Table 1) for compounds with the *trans*-fused (**1** and **2**) and with the *cis*-fused decalin system (**15** and **16**), we noted that the significant differences were in the chemical shifts of C-3, C-8, and C-11. Thus the chemical shifts of C-3, C-8, and C-11 may be the best guides to the stereochemistry at C-5 in sesquiterpenes bearing the same rearranged drimane skeleton with an oxygen atom at C-10.

Experimental Section

General Experimental Procedures. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker AVANCE DPX-300 MHz NMR spectrometer. Chemical shifts were referenced to TMS ($\delta = 0.0$ ppm). HMBC spectra were optimized for 10 Hz coupling. EIMS were measured on a LKB-9000S mass spectrometer at 70 eV. IR spectra were recorded on a Bruker Vector-22 FT-IR spectrometer. UV spectra were recorded on a Specord M-40 spectrophotometer. Optical rotations were recorded on a Perkin-Elmer 141 polarimeter. Silufol plates coated with silica gel F_{254} (Kavalier, Czech Republic) were used for TLC, Sephadex LH-20 (Pharmacia Fine Chemicals) was used for column chromatography, and Si gel ICN (63-100, 60 Å, ICN Biomedicals, Germany) was used for vacuum flash chromatography. All solvents were distilled prior to use. Concentration of HCl was 34%. Melting points (uncorrected) were determined on a Boetius apparatus.

Acid Rearrangement of 5 (First Procedure). Ilimaquinone (**5**) was isolated by us previously.[1,15] A mixture of **5** (11 mg) and MeOH−HOAc−HCl (1:1:1) (1 mL) was stirred at room temperature for 15 min. The solvent was evaporated under reduced pressure, and the residue was partitioned between water (5 mL) and $CHCl_3$ (3 × 5 mL). The combined organic extracts were washed with water (2 × 3 mL) and dried over Na_2SO_4. Evaporation of the solvent gave 10.5 mg of a 4:1 mixture of **7** and **9**. Crystallization of this mixture from hexane gave **9** (1.5 mg). Slow solvent evaporation from a mother liquor gave **7** (6 mg).

Isospongiaquinone (7): orange needles (hexane); mp 94−96 °C; $[\alpha]^{25}_D$ +64.4° (*c* 0.6, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ) 213 (3.96), 289 (4.12) nm; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.48 (1H, s), 5.85 (1H, s), 5.13 (1H, br s), 3.86 (3H, s), 2.62, 2.48 (each 1H, d, J = 13.6 Hz), 1.53 (3H, s), 1.01 (3H, s), 0.97 (3H, d, J = 7 Hz), 0.84 (3H, s); EIMS *m*/*z* 358 (12) [M^+], 191 (40).

Acetylation of 7. Acetylation of **7** (4 mg) was performed at room temperature during 24 h, using a 1:1 mixture of Ac_2O and pyridine (1 mL). After evaporation of excess of reactant the residue was dissolved in $CHCl_3$ (5 mL) and washed with water (2 × 5 mL). The organic layer was dried over Na_2SO_4 and evaporated to give the monoacetate **8** (4 mg).

Isospongiaquinone acetate (8): yellow amorphous solid; $[\alpha]^{25}_D$ +80° (*c* 0.13, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 5.80 (1H, s), 5.12 (1H, br s), 3.80 (3H, s), 2.52, 2.48 (each 1H, d, J = 12 Hz), 2.34 (3H, s), 1.53 (3H, s), 1.01 (3H, s), 0.90 (3H, d, J = 7 Hz), 0.84 (3H, s); EIMS *m*/*z* 400 (6) [M^+], 358 (8), 191 (66), 168 (62).

Compound 9: yellow needles (hexane); mp 193−194 °C; $[\alpha]^{25}_D$ +11° (*c* 0.09, $CHCl_3$); ^1H NMR data identical with previously reported values.[6]

Methylation of 9. Treatment of **9** with an ethereal solution of CH_2N_2 quantitatively yielded **10**, which exhibited $[\alpha]^{25}_D$, ^1H NMR, ^{13}C NMR, and EIMS identical with published values.[2] Methylation of compounds **2** and **11** was performed using the same method.

Acid Rearrangement of 5 (Second Procedure). A mixture of **5** (43 mg) and MeOH−HOAc−HCl (1:1:1) (4 mL) was stirred at room temperature for 10 days. The solvent was evaporated under reduced pressure, and the residue was partitioned between water (15 mL) and $CHCl_3$ (3 × 20 mL). The combined organic extracts were washed with water (2 × 5 mL) and dried over Na_2SO_4. Evaporation of the solvent gave **11** in a quantitative yield.

Compound 11: orange needles ($CHCl_3$); mp 204−205 °C; $[\alpha]^{25}_D$ +9.5° (*c* 0.11, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ) 205 (4.05),

291 (3.94) nm; IR ($CHCl_3$) ν_{max} 3343, 3312, 1637, 1611, 1328, 1186 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.75 (2H, br), 6.02 (1H, s), 2.69, 2.56 (each 1H, d, J = 13 Hz), 0.99 (3H, s), 0.96 (3H, s), 0.85 (3H, s), 0.79 (3H, d, J = 7 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 15.6 (C*H*$_3$), 20.2 (C*H*$_2$), 21.1 (C*H*$_2$), 22.2 (C*H*$_3$), 26.2 (C*H*$_2$), 26.7 (C*H*$_2$), 28.2 (C*H*$_3$), 29.0 (C*H*$_3$), 32.8 (C*H*$_2$), 34.5 (C*H*), 35.2 (C), 40.1 (C*H*$_2$), 43.0 (C), 102.3 (C*H*), 115.8 (C), 131.5 (C), 135.6 (C) (signals of carbon atoms of a quinoid ring connected with oxygen atoms were not observed); EIMS *m*/*z* 345 (7.2) $[M + 1]^+$, 344 (6.3) $[M^+]$, 191 (100), 153 (10); *anal.* C 73.21%, H 8.23%, calcd for $C_{21}H_{28}O_4$, C 73.23%, H 8.19%.

Acid Rearrangement of 5 (Third Procedure). A mixture of **5** (141 mg) and MeOH−HOAc−HCl (1:1:1) (20 mL) was agitated under reflux at 80 °C for 1 h. The solvent was evaporated under reduced pressure, and the residue was partitioned between water (50 mL) and $CHCl_3$ (3 × 50 mL). The combined organic extracts were dried over Na_2SO_4. Evaporation of the solvent gave 140 mg of a mixture of **2**, **3**, **7**, **9**, and **12**. Chromatography of the mixture on a Sephadex LH-20 column in $CHCl_3$ gave four fractions. The first fraction yielded **3** (6 mg, 4.2%). The second fraction contained a 1:1 mixture of **7** and **9**, which was separated by crystallization from hexane to obtain **7** (15 mg, 10.6%) and **9** (15 mg, 10.6%). The third fraction yielded **2** (16 mg, 11.3%). Evaporation of the fourth fraction gave **12** (88 mg, 62.4%).

Compound 2: ^1H NMR ($CDCl_3$, 300 MHz) δ 7.37 (1H, s, O*H*), 5.90 (1H, s, H-19), 2.55, 2.02 (each 1H, d, J = 18.5 Hz, C*H*$_2$-15), 1.72 (1H, m, Hα-1), 1.62 (1H, m, Hα-2), 1.62 (1H, m, Hα-6), 1.52 (1H, m, Hα-7), 1.49 (1H, m, Hα-3), 1.46 (1H, m, H-5), 1.43 (1H, m, H-8), 1.42 (1H, m, Hβ-1), 1.39 (1H, m, Hβ-7), 1.36 (1H, m, Hβ-2), 1.19 (1H, m, Hβ-6), 1.16 (3H, s, C*H*$_3$-11), 0.97 (3H, s, C*H*$_3$-14), 0.93 (3H, s, C*H*$_3$-12), 0.78 (3H, d, J = 7 Hz, C*H*$_3$-13); ^{13}C NMR, see Table 1; HMBC-correlation C*H*$_3$-11/C-3, C-4, C-5, C-12; C*H*$_3$-12/C-3, C-4, C-5, C-11; C*H*$_3$-13/C-7, C-8, C-9; C*H*$_3$-14/C-8, C-9, C-10, C-15; Hα-15/C-9, C-10, C-16, C-17; Hβ-15/C-8, C-9, C-14, C-16, C-17; H-19/C-18, C-20.

Compound 12: orange needles ($CHCl_3$); mp 180−181 °C; $[\alpha]^{25}_D$ +64.1° (*c* 0.12, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ) 205 (4.09), 290.5 (4.09) nm; IR ($CHCl_3$) ν_{max} 3340, 3310, 1638, 1609, 1350 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.88 (2H, br), 6.02 (1H, s), 5.13 (1H, br s), 2.63, 2.46 (each 1H, d, J = 21 Hz), 1.54 (3H, s), 0.97 (3H, d, J = 6.4 Hz), 0.85 (3H, s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 17.4 (*C*H$_3$), 17.8 (*C*H$_3$), 18.3 (*C*H$_2$), 20.0 (*C*H$_2$), 20.3 (*C*H$_3$), 27.1 (*C*H$_2$), 28.0 (*C*H$_2$), 32.6 (*C*H$_3$), 36.0 (*C*H$_2$), 37.9 (*C*H), 38.6 (C), 43.1 (C), 47.8 (*C*H), 102.1 (*C*H), 115.1 (C), 120.8 (*C*H), 144.2 (C) (signals of carbon atoms of a quinoid ring connected with oxygen atoms were not observed); EIMS *m*/*z* 345 (2) $[M + 1]^+$, 344 (7.3) $[M^+]$, 191 (69), 153 (10); *anal.* C 73.27%, H 8.18%, calcd for $C_{21}H_{28}O_4$, C 73.23%, H 8.19%.

Synthesis of 1 from 3. A mixture of **3** (13.5 mg), pyridine (0.1 mL), and 25% aqueous NH_3 (0.1 mL) in 50% aqueous EtOH (20 mL) was stirred at room temperature for 24 h. After evaporation to dryness, residue was purified on a Sephadex LH-20 column in $CHCl_3$−EtOH (1:1) to afford **1** (6 mg, 44%).

Compound 1: wine-colored oil, $[\alpha]^{25}_D$ −18° (*c* 0.1, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 5.65 (2H, br, N*H*$_2$), 5.54 (1H, s, H-19), 2.57, 2.06 (each 1H, d, J = 19 Hz, C*H*$_2$-15), 1.02 (3H, s, C*H*$_3$-11), 0.98 (3H, s, C*H*$_3$-12), 0.97 (3H, s, C*H*$_3$-14), 0.78 (3H, d, J = 6.5 Hz, C*H*$_3$-13); ^{13}C NMR, see Table 1.

Acid Rearrangement of 6 (First Procedure). Smenospongine (**6**) was isolated by us previously.[1,15] Treatment of **6** (41 mg) with a mixture of MeOH−HOAc−HCl (1:1:1) (5 mL) was performed using the first procedure of rearrangement of **5**. A mixture of rearranged products was chromatographed on a Sephadex LH-20 column in $CHCl_3$ to obtain a wine-colored fraction containing an inseparable 1:1.5 mixture of **13** and **14** (27.8 mg, 67.8%).

Mixture of 13 and 14: ^1H NMR ($CDCl_3$, 300 MHz) δ 8.12 (2H, br), 5.67 (1H, s), 5.12 (1H, br s), 2.58, 2.43 (each 1H, d, J = 13.9 Hz), 1.54 (3H, s), 1.00 (3H, s), 0.96 (3H, d, J = 6 Hz), 0.85 (3H, s) (assigned to **13**), 8.10 (2H, br), 5.64 (1H, s), 2.66, 2.51 (each 1H, d, J = 13.2 Hz), 0.99 (3H, s), 0.96 (3H, s), 0.83 (3H, s), 0.79 (3H, d, J = 6.8 Hz) (assigned to **14**); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 17.8 (*C*H$_3$), 18.2 (*C*H$_3$), 18.3 (*C*H$_2$), 18.7 (*C*H$_2$), 20.5 (*C*H$_2$), 20.6 (*C*H$_3$), 27.8 (*C*H$_2$), 28.5 (*C*H$_2$), 32.8 (*C*H$_3$), 36.5 (*C*H$_2$), 38.2 (*C*H), 38.9 (C), 43.2 (C), 48.1 (*C*H), 96.2 (*C*H), 115.4 (C), 121.3 (*C*H), 144.6 (C), 151.2 (C), 156.5 (C), 180.1 (C), 183.7 (C) (assigned to **13**), 15.9 (*C*H$_3$), 20.4 (*C*H$_2$), 21.3 (*C*H$_2$), 22.4 (*C*H$_3$), 26.4 (*C*H$_2$), 27.5 (*C*H$_2$), 28.5 (*C*H$_3$), 29.4 (*C*H$_3$), 32.8 (*C*H$_2$), 34.7 (*C*H), 35.0 (C), 40.4 (*C*H$_2$), 43.0 (C), 96.1 (*C*H), 114.9 (C), 131.9 (C), 135.3 (C), 150.8 (C), 156.0 (C), 180.5 (C), 183.5 (C) (assigned to **14**); EIMS *m*/*z* 343 (3), 191 (97), 153 (100).

Acid Rearrangement of 6 (Fourth Procedure). A mixture of **6** (59.4 mg, 0.17 mmol) with *p*-TsOH (149 mg, 0.85 mmol) in dry benzene (20 mL) was refluxed for 30 min. Excess *p*-TsOH was filtered off, and the benzene solution was washed with water (3 × 20 mL), dried over Na_2SO_4, and evaporated. The residue was subjected to flash chromatography over Si gel using a step gradient of acetone in hexane to obtain three fractions. Fraction 1 eluted with acetone−hexane (1:7) contained an inseparable mixture of **13** and **14** and a mixture of degradated products, which was not investigated. Fraction 2 eluted with acetone−hexane (2:7) contained a mixture of **1** and **15**, which was separated on Silufol plates in $CHCl_3$−hexane (9:1) to obtain **1** (7.9 mg, 13%) and **15 (**8 mg). Fraction 3 eluted with acetone−hexane (3:7) gave an additional 2.9 mg of **15** (total yield 18.5%). Compound **1** was identical in all respects with cyclosmenospongine.[1]

Compound 15: wine-colored oil, $[\alpha]^{25}_D$ +17° (*c* 0.21, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ) 211 (2.91), 313 (2.73) nm; IR (CCl_4) ν_{max} 3479, 3415, 1669, 1638, 1598, 1244 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 5.52 (1H, s, H-19), 5.38 (2H, br, N*H*$_2$), 2.87, 1.97 (each 1H, d, J = 18 Hz, C*H*$_2$-15), 2.03 (1H, m, Hβ-7), 1.88 (2H, m, C*H*$_2$-1), 1.86 (1H, m, Hα-2), 1.80 (1H, m, H-8), 1.78 (1H, m, Hα-6), 1.63 (1H, m, Hβ-2), 1.55 (1H, m, H-5), 1.52 (1H, m, Hβ-6), 1.47 (1H, td, J = 4; 13.5 Hz, Hα-3), 1.37 (1H, m, Hα-7), 1.27 (1H, m, Hβ-3), 1.09 (3H, d, J = 7.5 Hz, C*H*$_3$-13), 1.03 (3H, s, C*H*$_3$-12), 0.88 (6H, s, C*H*$_3$-11, 14); ^{13}C NMR, see Table 1; HMBC-correlations C*H*$_3$-11/C-3, C-4, C-5, C-12; C*H*$_3$-12/C-3, C-4, C-5, C-11; C*H*$_3$-13/C-7, C-8, C-9; C*H*$_3$-14/C-8, C-9, C-10, C-15; Hα-15/C-9, C-14, C-16, C-17; Hβ-15/C-9, C-10, C-14, C-16, C-17; H-19/C-18, C-20; H-8/C-6, C-9, C-13; EIMS *m*/*z* 343 (30) $[M^+]$, 191 (100), 153 (33); *anal.* C 73.43%, H 8.50%, N 4.04%, calcd for $C_{21}H_{29}NO_3$, C 73.47%, H 8.45%, N 4.08%.

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References and Notes

(1) Utkina, N. K.; Denisenko, V. A.; Scholokova, O. V.; Virovaya, M. V.; Prokof'eva, N. G. *Tetrahedron Lett.* **2003**, *44*, 101−102.
(2) Capon, R. J. *J. Nat. Prod.* **1990**, *53*, 753−756.
(3) Capon, R. J.; MacLeod, J. K. *J. Org. Chem.* **1987**, *52*, 5059−5060.
(4) Lakshmi, V.; Gunasekera, S. P.; Schmitz, F. J.; Ji, X.; van der Helm, D. *J. Org. Chem.* **1990**, *55*, 4709−4711.
(5) Urban, S.; Capon, R. J. *Aust. J. Chem.* **1994**, *47*, 1023−1029.
(6) Kazlauskas, R.; Murphy, P. T.; Warren, R. G.; Wells, R. J.; Blount, J. F. *Aust. J. Chem.* **1978**, *31*, 2685−2697.
(7) Salmoun, M.; Devijver, C.; Daloze, D.; Braekman, J. C.; Gomez, R.; de Kluijver, M.; Van Soest, R. W. M. *J. Nat. Prod.* **2000**, *63*, 452−456.
(8) Carte, B.; Rose, C. E.; Faulkner, D. J. *J. Org. Chem.* **1985**, *50*, 2785−2787.
(9) Hirsch, S.; Rudi, A.; Kashman, Y. *J. Nat. Prod.* **1991**, *54*, 92−97.
(10) Rebachuk, N. M.; Denisenko, V. A.; Fedoreyev, S. A. *Khim. Prirod. Soed.* **1987**, 793−796.
(11) Il'in, S. G.; Schedrin, A. P.; Rebachuk, N. M.; Fedoreyev, S. A.; Struchkov, Y. T. *Khim. Prirod. Soed.* **1991**, 467−471.
(12) Kondracki, M.-L.; Guyot, M. *Tetrahedron Lett.* **1987**, *28*, 5815−5818.
(13) Kondracki, M.-L.; Guyot, M. *Tetrahedron* **1989**, *45*, 1995−2004.
(14) Bourguet-Kondracki, M.-L.; Martin, M.-T.; Guyot, M. *Tetrahedron Lett.* **1992**, *33*, 8079−8080.
(15) Utkina, N. K.; Veselova, M. V. *Khim. Prirod. Soed.* **1990**, 47−51.

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