Hemolytic Polar Steroidal Constituents of the Starfish *Aphelasterias japonica*

Natalia V. Ivanchina,† Alla A. Kicha,† Anatoly I. Kalinovsky,† Pavel S. Dmitrenok,† Valentin A. Stonik,*,† Ricardo Riguera,‡ and Carlos Jiménez§

Pacific Institute of Bioorganic Chemistry of the Far East Branch of the Russian Academy of Science, Vladivostok-22, Russian Federation, Departamento de Quimica Organica and Instituto de Acuicultura, Universidad de Santiago de Compostela, Santiago de Compostela 15706, Spain, and Departamento de Quimica Fundamental e Industrial, Facultad de Ciencias, Universidad de La Coruna, La Coruna 15071, Spain

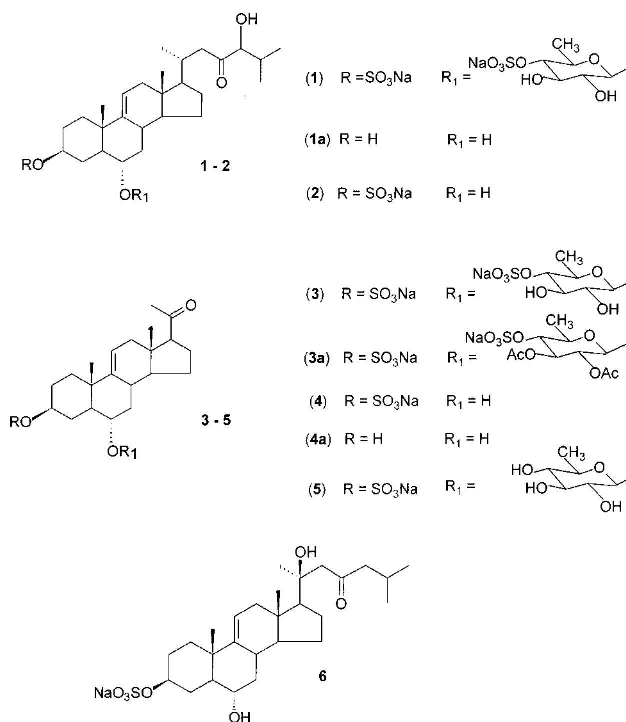
Received January 21, 2000

A reinvestigation of the polar steroid fraction from the starfish *Aphelasterias japonica*, collected near the Russian shore of the Sea of Japan, has afforded two new compounds, the disulfated quinovoside aphelasteroside C (**1**) and the monosulfated polyhydroxysteroid aphelaketotriol (**2**). Compounds **1** and **2** contain a unique 23-oxo-24-hydroxylated side chain that is unprecedented in marine steroids. The known compounds cheliferoside L1 (**3**), 3-*O*-sulfoasterone (**4**), forbeside E3 (**5**), and 3-*O*-sulfothornasterol A (**6**) were also isolated from this source. Compounds **1**−**3**, **5**, and **6** showed hemolytic activity to mouse erythrocytes.

Previous studies of the starfish *Aphelasterias japonica* Bell (order Forcipulatida, family Asteriidae) collected in Mutsu Bay, Aomore Prefecture, Japan, by Finamore et al. have yielded several new polar steroids.[1] Continuing our work on polyhydroxysteroids from the Far Eastern starfish [2,3] and their biological activities, we have analyzed the extracts of a population of *A. japonica* collected at Posyet Bay in the Sea of Japan. From the EtOH extracts of our collection of *A. japonica* we have obtained two new polar steroids, a disulfated quinovoside, designated as aphelasteroside C (**1**), and a monosulfated polyhydroxysteroid, named as aphelaketotriol (**2**), along with the known compounds cheliferoside L1 (**3**); 3-*O*-sulfoasterone (**4**), isolated as a natural product for the first time; forbeside E3 (**5**); and 3-*O*-sulfothornasterol A (**6**).

The negative FABMS of **1** exhibits a pseudomolecular ion at *m*/*z* 759 [M − Na]$^-$, which is in agreement with the molecular formula $C_{33}H_{52}Na_2O_{14}S_2$, and peaks of ions with *m*/*z* 759 [M − Na]$^-$, 737 [M − 2Na + H]$^-$, and 657 [M − SO_3Na − Na + H]$^-$ indicated the presence of two sulfate groups. A fragment at *m*/*z* 511 [M − 269 + H]$^-$ showed the loss of a sulfated desoxyhexose unit ($C_6H_{10}O_7SNa$). The presence of sulfate groups was confirmed by the absorption bands at 1244 and 1220 cm^{-1} in the IR spectrum of **1**, which also displayed bands attributable to (OH) at 3429 cm^{-1}, (C=O) at 1706 cm^{-1}, and (C=C) at 1642 cm^{-1}. Extensive NMR analysis (^{1}H NMR, ^{13}C NMR, and DEPT) showed that **1** contained four quaternary carbons, eight methylenes, 15 methines, and six methyl groups. ^{1}H−^{1}H COSY and HMQC experiments allowed us to assign all the protons to the corresponding carbon atoms (Table 1). All these data indicated that compound **1** is a disulfated polyhydroxysteroid glycoside.

The proton and carbon resonances corresponding to the sugar part of the molecule showed the presence of a monosaccharide unit in **1**. This is clearly indicated by a signal for an anomeric carbon atom at δ 105.25 and an anomeric proton at δ 4.33 that resonates as a doublet with a coupling constant of J = 7.9 Hz, indicative of β-stereochemistry. A 4′-*O*-sulfo-β-quinovopyranose moiety was suggested as the monosaccharide residue by analysis of the ^{1}H−^{1}H COSY correlations and by acid hydrolysis of **1**. Hydrolysis of **1** gave D-quinovose (TLC, [α]$_D$) along with the desulfated aglycon **1a**, which showed in its negative FABMS a pseudomolecular anion peak at *m*/*z* 431 [M − H]$^-$.



Comparison of the ^{1}H and ^{13}C NMR spectral data (Table 1) of **1** with those of compound **3** (see Experimental Section) confirmed the presence in **1** of the suggested monosaccharide unit and indicated that both have the same steroid nuclei but with a different side chain. We have identified compound **3** as cheliferoside L1, isolated earlier by our group from the starfish *Lethasterias nanimensis chelifera*, the structure of which was determined by analysis of the NMR spectra of its diacetate and other derivatives.[4] In fact, acetylation of **3** afforded diacetate **3a**, having NMR spectra identical with spectra of diacetate cheliferoside L1.[4]

* To whom correspondence should be addressed. Tel.: 7 (4232) 312360. Fax: 7 (4232) 314050. E-mail: piboc@stl.ru.
† Pacific Institute of Bioorganic Chemistry.
‡ Universidad de Santiago de Compostela.
§ Universidad de La Coruna.

10.1021/np000030f CCC: $19.00 © 2000 American Chemical Society and American Society of Pharmacognosy
Published on Web 07/21/2000

Table 1. ^{1}H and ^{13}C NMR Data (CD_3OD) of Aphelasteroside C (**1**)[a]

DEPT	C	δ_C	δ_H
CH_2	1	36.86	1.75 m, 1.46 m
CH_2	2	29.60	2.13 m, 1.63 m
CH	3	79.67	4.20 m
CH_2	4	30.84	2.62 d (10.1), 1.31 m
CH	5	50.02	1.26 m
CH	6	80.69	3.57 td (10.5, 4.4)
CH_2	7	42.30	2.39 m, 0.96 m
CH	8	36.83	2.12 m
C	9	146.60	
C	10	39.21	
CH	11	117.72	5.34 d (5.35)
CH_2	12	42.89	2.16 m, 2.04 m
C	13	42.27	
CH	14	54.97	1.32 m
CH_2	15	26.27	1.77 m, 1.35 m
CH_2	16	29.49	1.90 m
CH	17	57.39	1.30 m
CH_3	18	11.94	0.67 s
CH_3	19	19.65	1.01 s
CH	20	33.06	2.08 m
CH_3	21	20.04	0.94 d (6,6)
CH_2	22	46.68	2.53 dd (17.3, 2.9), 2.39 dd (17.2,9.4)
C	23	214.70	
CH	24	82.24	3.91 d (3.6)
CH	25	32.27	2.09 m
CH_3	26	20.12	1.01 d (6.9)
CH_3	27	16.19	0.80 d (6.8)
	Quin(1→6)		
CH	1	105.25	4.33 d (7.9)
CH	2	75.61	3.27 dd (9.2, 7.9)
CH	3	76.55	3.61 t (9.2)
CH	4	83.00	3.89 t (9.1)
CH	5	71.18	3.47 m
CH_3	6	18.19	1.32 d (6.25)

[a] *J* (Hz) values are shown in parentheses. Assignments from 500 MHz $^{1}H-^{1}H$ COSY and HMQC data.

We have compared the ^{13}C NMR spectral data of the side chains of **1** and some known cholestane derivatives such as the 5α-cholestane-1β,3β,5,6β-tetraol with the side chain having no functional groups from the soft coral *Sarcophyton glaucum*,[5] the steroid glycoside santiagoside with a 23-oxo group in the side chain from the starfish *Neosmilaster georgianus*,[6] and the (24*S*)-5α-cholestane-3β,4β,6β,8,15β,-24-hexaol with a 24-hydroxy group from the starfish *Henricia derjugini.*[7] On the basis of calculations of the joint effects of 23-oxo and 24-hydroxy groups on carbon chemical shifts of side chain carbons, we suggest that **1** has both 23-oxo and 24-hydroxy groups.

The assignment of the structure of the side chain of the aglycon part of **1** was based on the following information. The spin system $Me_2CH-CHOH-$ was indicated by the two doublets in its ^{1}H NMR spectrum at δ_H 1.01 (δ_C 20.12) and 0.80 (δ_C 16.19) corresponding to CH_3-26 and CH_3-27. These were coupled to H-25 at δ_H 2.09 (δ_C 32.27), which was, in turn, coupled to an oxygenated methine H-24 at δ_H 3.91 (δ_C 82.24) in the $^{1}H-^{1}H$ COSY. CH_3-21 resonates as a doublet at δ_H 0.94 (δ_C 20.04) coupled to the methine H-20 at δ_H 2.08 (δ_C 33.06), and H-20 coupled to the CH_2-22 at δ_H 2.53 and 2.39 (δ_C 46.68). The remaining signal of the side chain is a quaternary carbon at δ_C 214.7, which was assigned to a ketone group. All these data confirmed the presence of 23-oxo and 24-hydroxy groups in the side chain of **1**.

This oxygenated substitution in the side chain has no precedent in the field of marine steroids. Therefore, the structure of aphelasteroside C (**1**) was established as the 3,4′-sodium disulfate of 6-*O*-[β-D-quinovopyranosyl]-3β,6α,-24-trihydroxy-5α-cholest-9(11)-en-23-one.

Compound **2** showed a pseudomolecular anion peak at *m*/*z* 511 [M − Na]$^-$ in the negative FABMS. The ^{1}H NMR spectrum of **2** is practically identical to that of the aglycon part of **1** (except that the signal of H-6 resonates at δ 3.52 rather than at δ 3.57), indicating that they consist of the same framework. Spin-decoupling experiments confirmed the structure of the side chain of **2**: irradiation of CH_3-26 (δ 1.01) and CH_3-27 (δ 0.79) produced the collapse of the multiplet at δ 2.09 due to H-25, while doublets for H-24, CH_3-26, and CH_3-27 became singlets at the homodecoupling of H-25.

Furthermore, the ^{1}H NMR spectrum of **2** is practically identical to that of **1a**, except that the signal of H-3 now resonates at δ 4.21 instead of δ 3.50. It is in good agreement with the α-effect of sulfation in that position. Thus, compound **2** is the genuine aglycon of **1**, and its structure was established as the 3-sodium sulfate of 3β,6α,24-trihydroxy-5α-cholest-9(11)-en-23-one.

The negative FABMS of **4** exhibited a pseudomolecular anion peak at *m*/*z* 411 [M − Na]$^-$. The ^{1}H NMR spectral data of **4** are practically identical to those of 3-*O*-sulfoasterone, obtained by partial acid hydrolysis of asterosaponin A from the starfish *Asterias amurensis*.[8] Nevertheless, the chemical shift of H-3 (δ 4.13) in **4** differs from that reported in 3-*O*-sulfoasterone (δ 4.20), but this could be due to the existence of different cations in the sample. Solvolysis of **4** in dioxane/pyridine afforded the desulfated derivative **4a**, which is identical (^{1}H NMR, TLC) to known asterone.[9] This is the first time that 3-*O*-sulfoasterone (**4**) has been reported as a natural product.

Spectral data (^{1}H NMR, MS, and optical rotation) of compound **5** matched those reported by Findlay et al.[10] for forbeside E3 from the starfish *Asterias forbesi*, while the data for compound **6** were identical with those reported by Finamore et al.[1] for 3-*O*-sulfothornasterol A from the starfish *A. japonica*. The structure of compound **6** was confirmed by direct comparison (^{1}H NMR, TLC) with an authentic sample obtained from the starfish *L. nanimensis chelifera.*[4]

When tested for hemolytic activity using 0.2% suspensions of mouse erythrocytes, we found compounds **1**−**3**, **5**, and **6** to be active, with ED_{50} values of 1.9×10^{-4} M, 4.0×10^{-5} M, 1.75×10^{-4} M, 3.3×10^{-4} M, and 1.1×10^{-4} M, respectively. 3-*O*-Sulfoasterone (**4**) was not active in doses below 5×10^{-4} M.

Aphelasteroside C (**1**) and aphelaketotriol (**2**) contain a unique 23-oxo-24-hydroxylated side chain structure without any precedent in marine steroid compounds. We observe that compounds **1**−**6** share with asterosaponins the 3β,6α-diol moiety, the 9(11)-double bond, and a sulfate group at C-3. However, they differ in the sugar part attached to C-6, which in asterosaponins consists of a long chain of five or six sugar units, while in **1**, **3**, and **5** only one sugar residue is present.

Of all the compounds isolated in this study, only compound **6** was previously found by Finamore et al.[1] in their study of a Japanese population of *A. japonica*. We may assume that the steroid composition of these starfish either depends on ecological factors, for instance on diet and season, or these Japanese and Russian populations differ from each other taxonomically. Finally, the starfish *A. japonica* is the third species, along with *L. nanimensis chelifera*[4] and *A. forbesi*,[10] in which new versions of asterosaponins with shortened carbohydrate chain have been found.

Experimental Section

General Experimental Procedures. Optical rotations were determined on a Perkin-Elmer 141 polarimeter. ^{1}H and ^{13}C NMR spectra of compounds **2**–**6** were recorded on a Bruker WM-250 spectrometer at 250 and 62.9 MHz, respectively, while ^{1}H and ^{13}C NMR spectra of compound **1** were obtained on a Bruker AMX 500 spectrometer at 500 and 125.77 MHz, respectively, with tetramethylsilane as an internal standard. Negative FABMS spectra of compounds **1a** and **2**–**6** were recorded on an LKB-2091 mass spectrometer, the FABMS spectrum of compound **1** was obtained on an Autospec-M mass spectrometer using glycerol/thioglycerol (1:1) as a matrix. HPLC separations were conducted on a column with Silasorb C_{18} (13 μ, 250 × 9.4 mm) using a DuPont 8800 chromatograph equipped with a differential refractometer. The IR spectrum of **1** was taken on a Bruker "Vector 22" spectrophotometer. Determination of sodium was performed using an atomic absorption spectrometer (Nippon Jarrel Ash AA-780).

Low-pressure column liquid chromatography was performed using Si gel L (40/100 μm, Chemapol, Praha, Czech Republic), Florisil (100–200 mesh, Koch-Light Laboratories Ltd., U.K.), Amberlite XAD-2 (20–80 mesh), and Sephadex LH-20 (Sigma, Chemical Co). Si gel plates 4.5 × 6.0 cm, (5–17 μ, Sorbfil, Russia) were used for thin-layer chromatography.

Animal Material. Specimens of *A. japonica* were collected at depths of 3–10 m in Posyet Bay, the Sea of Japan, in August 1996. Species identification was carried out by Dr. Y. M. Yakovlev (Institute of Marine Biology of the Russian Academy of Science, Vladivostok, Russia). A voucher specimen [no. P-12–08(96)] is on deposit at the marine specimen collection of the Pacific Institute of Bioorganic Chemistry, Vladivostok, Russia.

Extraction and Isolation. The fresh animals (9.1 kg) were chopped and extracted twice with EtOH. The combined extracts were evaporated, and the residue was dissolved in H_2O (3 L). The H_2O-soluble fraction was passed, in portions of 500 mL, through an Amberlite XAD-2 column (6 × 20 cm), and each portion was eluted with distilled H_2O until a negative chloride ion reaction was obtained, followed by elution with MeOH. The combined MeOH eluate was evaporated to give a brownish material (27.39 g) that was chromatographed on a Sephadex LH-20 column (3 × 50 cm) with MeOH/H_2O (2:1). Two subfractions containing mixtures of polyhydroxylated steroids were purified by chromatography on a Si gel column (6 × 20 cm) using $CHCl_3$/EtOH (8:1 → 1:2), and each subfraction was chromatographed on Florisil columns (2 × 15 cm) using the system $CHCl_3$/EtOH (7:1 → 2:1). Fractions were analyzed by TLC on Si gel using the eluent $CHCl_3$/MeOH/H_2O (30:15:2) and detected by spraying with H_2SO_4.

HPLC of the remaining fractions on a Silasorb C_{18} column (13 μ, 250 × 9.4 mm, 3 mL/min) with MeOH/H_2O (55:45) yielded **1** (39 mg, R_f 0.36), **2** (6 mg, R_f 0.79), **3** (3 mg, R_f 0.33), **4** (3 mg, R_f 0.77), **5** (3 mg, R_f 0.6), and **6** (65 mg, R_f 0.78).

Aphelasteroside C (1): amorphous powder; $[\alpha]_D$ +15.4° (*c* 1.7, MeOH); ^{1}H and ^{13}C NMR data, see Table 1; IR (KBr) 3429 cm^{-1} (OH), 1706 cm^{-1} (C=O), 1642 cm^{-1} (C=C), 1244 and 1220 cm^{-1} (OSO_3); FABMS(–) *m/z* $[M - Na]^-$ 759 (100%), $[M - 2Na + H]^-$ 737 (12%), $[M - SO_3Na - Na + H]^-$ 657 (84%), $[759 - C_6H_{10}O_7SNa + H]^-$ 511 (16%).

Acid Hydrolysis of 1. A solution of glycoside **1** (6 mg) in aqueous 2 N CF_3COOH (3 mL) was heated at 100 °C for 2 h and then extracted with $CHCl_3$. The chloroform-soluble materials were chromatographed on a Si gel column (1.5 × 3 cm) using hexane/EtOAc (10:1 → 2:1) to give the desulfated aglycon **1a** (1.5 mg). The aqueous layer was neutralized by the addition of Dowex (HCO_3^-) resin, the resin was filtered off, and quinovose was identified in the filtrate by TLC on Si gel in BuOH/EtOH/H_2O (4:1:2). The quinovose was assigned D-configuration by the observed optical rotation $[\alpha]_D$ +24.6° (*c* 0.5, H_2O).

Compound 1a: ^{1}H NMR (CD_3OD) δ 0.63 (3H, s, H_3-18), 0.79 (3H, d, J = 7.0 Hz, H_3-27), 0.94 (3H, d, J = 6.9 Hz, H_3-21), 0.98 (3H, s, H_3-19), 1.01 (3H, d, J = 7.0 Hz, H_3-26), 3.50 (1H, m, H-3), 3.52 (1H, m, C-6), 3.91 (1H, d, J = 4.0 Hz, H-24), 5.35 (1H, d, J = 5.5 Hz, H-11); FABMS(–) *m/z* $[M - H]^-$ 431 (100%).

Aphelaketotriol (2): amorphous powder; $[\alpha]_D$ +12.8° (*c* 0.2, MeOH); ^{1}H NMR (CD_3OD) δ 0.67 (3H, s, H_3-18), 0.79 (3H, d, J = 6.9 Hz, H_3-27), 0.94 (3H, d, J = 6.8 Hz, H_3-21), 0.99 (3H, s, H_3-19), 1.01 (3H, d, J = 7.0 Hz, H_3-26), 2.09 (1H, m, H-25; identified by spin-decoupling experiments), 3.52 (1H, td, J = 10.3, 4.0 Hz, H-6), 3.91 (1H, d, J = 4.0 Hz, H-24), 4.21 (1H, m, H-3), 5.35 (1H, d, J = 5.5 Hz, H-11); FABMS(–) *m/z* $[M - Na]^-$ 511 (49%), $[M - Na - 2H]^-$ 509 (24%), $[M - Na - H_2O]^-$ 493 (26%), $[M - SO_3Na - 108]^-$ 323 (100%), $[M - SO_3Na - 122]^-$ 309 (49%).

Cheliferoside L1 (3): amorphous powder; $[\alpha]_D$ +21.9° (*c* 0.23, MeOH); ^{1}H NMR (CD_3OD) δ (aglycon) 0.54 (3H, s, H_3-18), 1.00 (3H, s, H_3-19), 2.13 (3H, s, H_3-21), 3.57 (1H, m, C-6), 4.19 (1H, m, C-3), 5.41 (1H, m, H-11); δ (sugar) 1.33 (3H, d, J = 6.0 Hz, H-6′), 3.27 (1H, m, H-2′), 3.47 (1H, m, H-5′), 3.61 (1H, t, J = 9.0 Hz, H-3′), 3.81 (1H, t, J = 9.1 Hz, C-4′), 4.33 (1H, d, J = 7.8 Hz, H-1′); ^{13}C NMR (C_5D_5N/D_2O, 5:1) δ (aglycon) 35.8 (C-1), 28.9 (C-2), 78.5 (C-3), 30.3 (C-4), 48.7 (C-5), 79.4 (C-6), 41.1 (C-7), 35.6 (C-8), 145.8 (C-9), 38.3 (C-10), 116.0 (C-11), 40.5 (C-12), 42.7 (C-13), 53.6 (C-14), 23.3 (C-15), 25.4 (C-16), 63.4 (C-17), 13.1 (C-18), 19.2 (C-19), 211.1 (C-20), 31.1 (C-21); δ (sugar) 104.4 (C-1′), 74.9 (C-2′), 76.0 (C-3′), 82.2 (C-4′), 70.6 (C-5′), 18.3 (C-6′); FABMS(–) *m/z* $[M - Na]^-$ 659 (75%), $[M - SO_3Na - Na + H]^-$ 557 (100%), $[M - Na - 148]^-$ 511 (69%), $[M - C_6H_{10}O_7SNa - Na + H]^-$ 411 (56%).

Acetylation of 3. Compound **3** (14 mg) was treated with 3 mL of Ac_2O/pyridine mixture (1:1) at room temperature for 16 h. The reaction solution was evaporated under reduced pressure and the residue chromatographed on a Si gel column (3 × 10 cm) eluting with $CHCl_3$/EtOH (3:2) to give the diacetate **3a** (8.0 mg). ^{1}H and ^{13}C NMR data of **3a** were identical with those reported by Kicha et al.[4]

3-*O*-Sulfoasterone (4): amorphous powder; $[\alpha]_D$ +34.5° (*c* 0.32, MeOH); ^{1}H NMR (CD_3OD) δ 0.55 (3H, s, H_3-18), 0.98 (3H, s, H_3-19), 2.13 (3H, s, H_3-21), 3.53 (1H, td, J = 11.0, 4.0 Hz, H-6), 4.13 (1H, m, H-3), 5.42 (1H, m, H-11); FABMS(–) *m/z* $[M - Na]^-$ 411 (100%).

Solvolysis of 4. A solution of compound **5** (1.5 mg) in 2 mL of dioxane/pyridine (1:1) was heated at 100 °C for 2 h. The reaction mixture was evaporated under reduced pressure and chromatographed on a Si gel column (1.5 × 3 cm) using $CHCl_3$/EtOH (6:1) as eluent to give the derivative **4a**, which was found to be identical (^{1}H NMR, TLC) with known asterone.[9]

Forbeside E3 (5): amorphous powder; $[\alpha]_D$ +20.9° (*c* 0.33, MeOH); ^{1}H NMR data were identical with those reported by Findlay et al.[10] for forbeside E3; FABMS(–) *m/z* $[M - H]^-$ 579 (13%), $[M - Na]^-$ 557 (100%).

3-*O*-Sulfothornasterol A (6): amorphous powder; $[\alpha]_D$ +1.2° (*c* 0.41, MeOH); ^{1}H NMR data were identical with those reported by Kicha et al.[4] (C_5D_5N) and Finamore et al.[1] (CD_3OD); FABMS(–) *m/z* $[M - Na]^-$ 511 (82%), $[M - Na - C_6H_{12}O]^-$ 411 (100%).

Bioassay. Hemolytic activity was determined as previously reported.[11]

Acknowledgment. We are grateful to Dr. I. A. Gorshkova (Laboratory of Marine Natural Products Chemistry, Pacific Institute of Bioorganic Chemistry) for help with hemolytic assays. We also thank Dr. V. P. Glasunov (Laboratory of Structural and Analytic Methods, Pacific Institute of Bioorganic Chemistry) for performing IR spectroscopy. R.R. and C.J. acknowledge financial support from Plan Nacional I+D (1FD97-2157 and MAR99-0287) and Xunta de Galicia (PPGIDT99BIO20901 and XUGA-10301A97). The research described in this publication was made possible in part by Grant 99-04-58854 from the Russian Foundation of Basic Research.

References and Notes

(1) Finamore, E.; Zollo, F.; Minale, L.; Yasumoto, T. *J. Nat. Prod.* **1992**, *55*, 767−772.
(2) Kicha, A. A.; Kalinovsky, A. I.; Stonik, V. A. *Izv. Akad. Nauk., Ser. Khim.* **1997**, 190−195.
(3) Kicha, A. A.; Kalinovsky, A. I.; Ivanchina, N. V.; Stonik, V. A. *J. Nat. Prod.* **1999**, *62*, 279−282.
(4) Kicha, A. A.; Kalinovsky, A. I.; Stonik V. A. *Khim. Prir. Soedin.* **1991**, *4*, 520−523.
(5) Kobayashi, M.; Hayashi, T.; Hayashi, K.; Tanabe, M.; Nakagawa, T.; Mitsuhashi, H. *Chem. Pharm. Bull.* **1983**, *31*(*6*), 1848−1855.
(6) Vazquez, M. J.; Quinoa, E.; Riguera R.; San Martin, A.; Darias, J. *Tetrahedron* **1992**, *48*, 6739−6746.
(7) Kicha, A. A.; Kalinovsky, A. I.; Gorbach, N. V.; Stonik, V. A. *Khim. Prir. Soedin.* **1993**, *9*, 249−253.
(8) Ikegami, S.; Kamiya, Y.; Tamura, S. *Tetrahedron* **1973**, *29*, 1807−1810.
(9) Kicha, A. A.; Kalinovsky, A. I.; Stonik, V. A. *Khim. Prir. Soedin.* **1992**, *1*, 145−146.
(10) Findlay, J. A.; He, Z.-Q. *J. Nat. Prod.* **1990**, *53*, 710−712.
(11) Gorshkov, B. A.; Kapustina, I. I.; Kicha, A. A.; Aminin, D. L.; Gorshkova, I. A. *Comp. Biochem. Physiol., C* **1998**, *120*, 235−239.

NP000030F