Chemical properties of marine terpenoids
1. Some reactions of (6*S*,10*R*)-10-bromo-3,11,11-trimethyl-7-methylidenespiro[5,5]undec-2-en-4-one, a sesquiterpenoid from the sea hare *Aplysia dactylomela*

*E. G. Lyakhova, S. N. Fedorov, L. K. Shubina, O. S. Radchenko, A. I. Kalinovsky, P. S. Dvitrenok, and V. A. Stonik**

Pacific Institute of Bioorganic Chemistry, Far-Eastern Branch of the Russian Academy of Sciences, 159 prosp. 100 let Vladivostoku, 690022 Vladivostok, Russian Federation. Fax: +7 (423 2) 31 4050. E-mail: stonik@piboc.dvo.ru

The structures of products obtained by reductive debromination and CF_3COOH- and KOH-induced transformations of natural chamigrane-type sesquiterpenoid (6*S*,10*R*)-10-bromo-3,11,11-trimethyl-7-methylidenespiro[5,5]undec-2-en-4-one (dactylone) isolated from the sea hare *Aplysia dactylomela* were analyzed. The absolute configurations of the reaction products were established by CD spectra taking into account the configuration of the starting dactylone.

Key words: chamigrane-type sesquiterpenoids, terpenoids, CD spectra, mass spectrometry, ^1H and ^{13}C NMR spectra, mollusc, Opisthobranchia, sea hare, *Aplysia dactylomela*.

Marine terpenoids represent an extensive group of secondary metabolites whose main producers are algae and marine invertebrates. Many of them have new skeleton systems, contain halogen atoms and/or isocyano-, nitro-, dichlorocarbonimide (—N=CCl_2), and other functional groups unusual for natural compounds.[1] Studies of terpenoids and other marine natural products are usually limited to their isolation, structure determination, study of the biological activities and, in some cases, synthesis. However, the chemical properties of most of these compounds remain absolutely unknown, although they may be of interest from both theoretical and practical standpoints. For example, recently we have demonstrated that a unique natural sesquiterpenoid aplydactone isolated from molluscs and containing two four-membered rings incorporated in a six-membered ring undergoes an unusual rearrangement on treatment with proton donors.[2] In addition, the routes of chemical transformations of natural compounds often coincide with biosynthetic transformations and, hence, data on the chemical properties of these compounds can contribute to the understanding of the biogenesis of related substances. Finally, study of the chemical properties of natural products promotes development of their syntheses and leads to the preparation of new biologically active substances.

Molluscs of the *Aplysia* genus feeding on red algae accumulate large amounts of halogenated sesquiterpenoids typical of these algae. Apparently, this is the way the soft-bodied molluscs protect themselves from predators. Some marine halogenated sesquiterpenoids exhibit bactericidal,[4] antifouling,[5] insecticidal,[6] and antitumor properties.[7]

When determining the absolute configuration of one of the newly isolated compounds of this series, we needed standard chamigrane derivatives with a known absolute configuration. To meet this demand, we converted the chamigrane sesquiterpenoid dactylone (**1**) from the mollusc *Aplysia dactylomela*, whose absolute configuration had been determined previously[8] by X-ray diffraction analysis, into derivative **2**. By examining the CD spectrum of the product and comparing the results obtained with the published data, we solved the problem of establishing the absolute configuration.[9]

In the present work, we considered this and some other reactions of dactylone **1** and studied the reaction products.

Results and Discussion

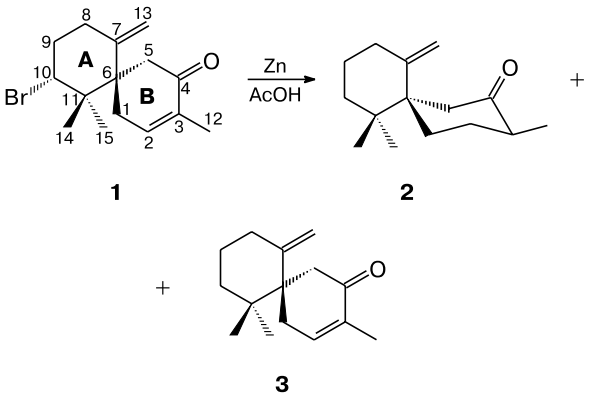
Reductive debromination of dactylone **1** was carried out using two procedures: treatment with Zn in AcOH and treatment with AIBN and Bu^n_3SnH in a benzene solution. The former reaction afforded new chamigrane sesquiterpenoids **2** and **3** and the latter afforded only compound **3** in almost quantitative yield (Scheme 1).

The structures of **2** and **3** were established by comparing their NMR and CD spectra with the spectra of the starting dactylone **1**. The data from mass spectrometry corresponded to the proposed molecular structures. The

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 4, pp. 970—974, April, 2003.

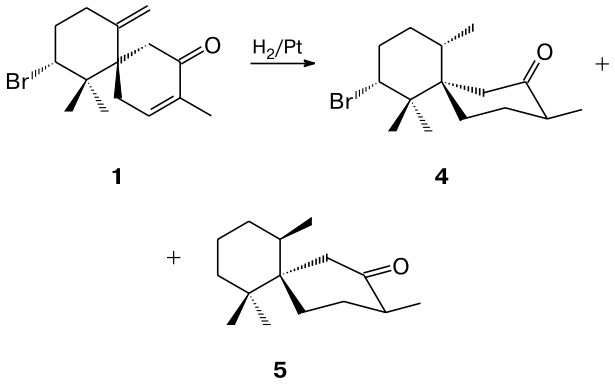
1066-5285/03/5204-1022 $25.00

Scheme 1



1 **2** **3**

Scheme 2



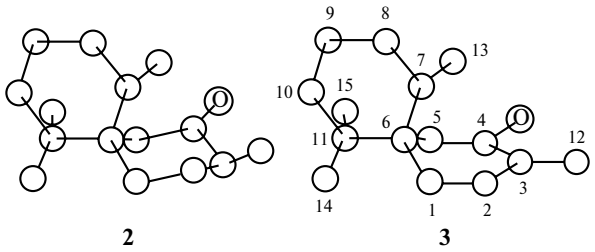
1 **4** **5**

preferred conformation of ring **B** in compound **2** is a chair with an equatorial methyl group ($J_{5eq,1eq}$ = 3.3 Hz, $J_{5ax,3ax}$ = 1.4 Hz) (full assignment of the signals for this compound was carried out using the COSY-45 and HMQC NMR spectroscopy for solutions in C_6D_6). Indeed, the former of the two spin-spin coupling constants corresponds to the *W* constant, while the latter is typical of coupling of axial protons located in the α-positions relative to the carbonyl group.[10] The CD spectrum of compound **2** showed a negative Cotton effect $[\theta]_{288} = -29.3 \cdot 10^4$. For other conformations of ring **B**, either one of the above-mentioned constants would not be observed or a positive Cotton effect would be present in the CD spectrum.

Terpenoid **3** differs from the starting **1** only in the absence of the Br atom at C(10). In view of the foregoing, together with the fact that the configuration of the spiro atom was not changed during the reaction and using the octant rule, we established the absolute configurations for terpenoids **2** and **3** on the basis of CD spectra (Fig. 1).

Thus, we obtained two standard substances with established absolute configurations and showed that treatment with zinc in acetic acid can induce both dehalogenation and reduction of the conjugated double bond in dactylone **1**.

Hydrogenation of dactylone **1** over the Adams catalyst gave rise to other two new chamigrane sesquiterpenoids **4** and **5** (Scheme 2).



2 **3**

Fig. 1. Structures of molecules **2** and **3**.

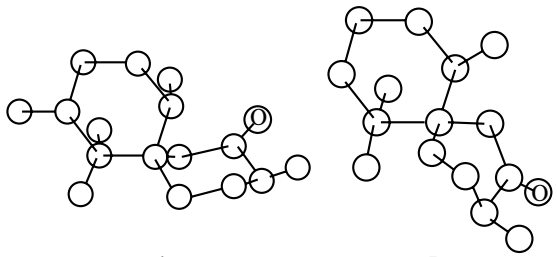
The structures of these compounds were also determined by comparing their NMR, mass, and CD spectra with the spectra of the starting terpenoid **1**.

The conformation of ring **B** in compound **4** was identified as a chair, because a spin-spin coupling constant $J_{5eq,1eq}$ equal to 2 Hz was observed and the methyl group at the C(3) atom was equatorial (cross-peaks in the COSY-45 spectrum between $H_{ax}C(3)$ and $H_{ax}C(5)$ with J = 1.2 Hz). The C(7)—CH_3 group is axial because a NOE signal is recorded for this group with irradiation of $H_{eq}C(5)$. The equatorial arrangement of $CH_3(12)$ and $CH_3(13)$ in molecule **5** was inferred from the spin-spin coupling constants $J_{2ax,3}$ = 12.2 Hz; $J_{2eq,3}$ = 5.2 Hz; $J_{8ax,7}$ = 10.7 Hz; and $J_{8eq,7}$ = 4.6 Hz.

The CD spectrum of compound **4** exhibited a negative Cotton effect $[\theta]_{285} = -41.1 \cdot 10^2$, while the spectrum of **5** displayed a positive effect $[\theta]_{285} = +50.5 \cdot 10^2$. With allowance for the positive Cotton effect, two conformations of the oxygen-containing ring, *viz.*, a chair and a boat, can be proposed for the oxygen-containing ring in compound **5**. According to COSY-45 experiments, the proton at C(3) and the protons at C(5) in compound **5** occupy *trans*-diaxial positions: $J_{3,5}$ = 1.0 Hz and the diequatorial coupling constant for the protons at C(5) and C(1) is absent. On irradiation of the protons of the $CH_3(14)$ equatorial group, a NOE is observed for the proton at C(3) and no NOE is observed for $C(12)H_3$. Only the boat conformation of the oxygen-containing ring in terpenoid **5** is consistent with the results of these experiments. Apparently, transition of ring **B** into the boat conformation is driven by the resulting decrease in the steric strain between the $C(13)H_3$ group and the carbonyl group. By using the octant rule, we determined the absolute configurations for terpenoids **4** and **5** on the basis of CD spectroscopic data (Fig. 2).

Thus, catalytic hydrogenation of dactylone **1** involves reduction of both the conjugated and nonconjugated double bonds and is accompanied by dehalogenation.

Treatment of dactylone **1** with a solution of CF_3COOH in MeOH for 7 days at ~20 °C resulted in the migration of



4 **5**

Fig. 2. Structures of molecules **4** and **5**.

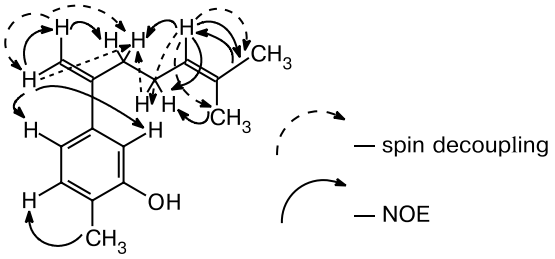


Fig. 3. Some spin-decoupling NOE correlations for terpenoid **7**.

the exocyclic double bond to an endocyclic position. The only reaction product, (6*S*,10*R*)-10-bromo-3,7,11,11-tetramethylspiro[5,5]undeca-2,7-dien-4-one (**6**), was obtained in 82% yield (Scheme 3). A similar migration has been found previously[11] for the cytotoxic sesquiterpenoid $\Delta^{9,15}$-africanene isolated from soft-bodied corals. The structure of sesquiterpenoid **6** was established relying on NMR spectroscopy and mass spectrometry.

It is assumed that marine chamigrane sesquiterpenoids are biosynthesized by cyclization of bisabolane precursors.[1] We found that the reverse transformation of halogenated chamigranes into sesquiterpenoids of the bisabolane type readily proceeds in a nearly quantitative yield when chamigranes react with an alkali. Thus on treatment with KOH in MeOH for 24 h at ~20 °C, dactylone **1** or its α-isomer **6** rearrange with opening of the bromo-containing ring giving rise to bisabolane-type derivatives **7** and **8**, respectively. Analogous transformations of chamigrane precursors might take place in living organisms.

The mass spectrum of sesquiterpenoid **7** exhibited a molecular ion peak at *m/z* 216, which corresponds to the molecular formula $C_{15}H_{20}O$. The UV spectrum showed the presence of absorption maxima at λ = 246 and 285 nm typical of a styrene chromophore. These data, together with the results of ^{1}H and ^{13}C NMR studies including the NOE and spin decoupling experiments, definitely led to structure **7** (Fig. 3).

In the ^{1}H NMR spectrum of compound **8**, unlike the spectrum of terpenoid **7**, additional signals were found for the protons of the exocyclic double bond and for the protons of the Me group at the double bond. The spectrum showed the presence of only allylic methylene group in molecule **8**. The mass and UV spectra were also in line with the proposed structural formula of **8**.

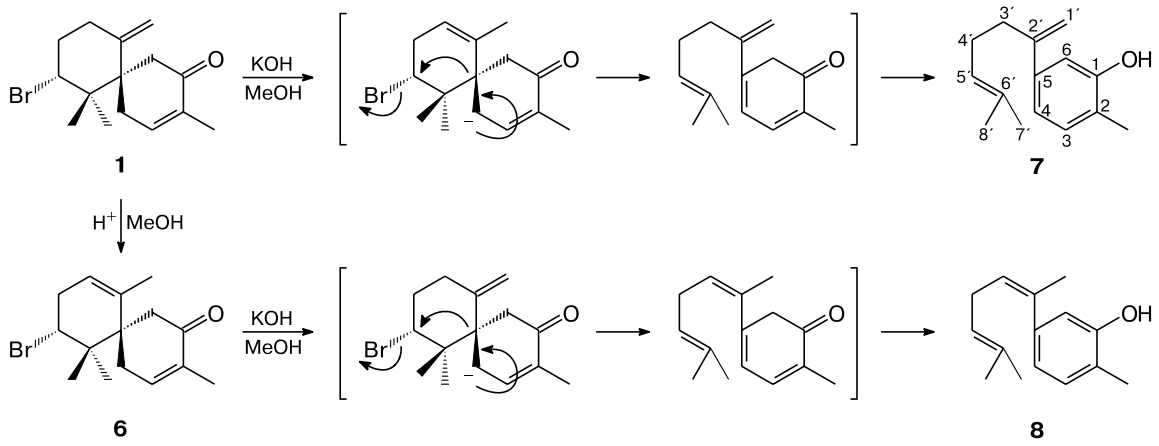
Sesquiterpenoids with a carbon skeleton similar to that in compounds **7** and **8** have been isolated previously[12,13] from a number of gorgonians and sponges.

Thus, we studied the transformations of the natural sesquiterpenoid **1**, synthesized a number of compounds, studied their CD and NMR properties, and determined the absolute configurations, which would promote determination of the structures and absolute configurations of new marine terpenoid derivatives.

Experimental

^{1}H and ^{13}C NMR spectra were recorded on Bruker WM-250 and Bruker DPX-300 spectrometers in $CDCl_3$ with Me_4Si as the internal standard. Optical rotation was measured on a Perkin—Elmer 141 polarimeter. HPLC was carried out on a Du Pont Model 8800 chromatograph (with refractometer as the detector) using an Altex Ultrasphere-Si column (5 μm, 250×4.6 mm). GC/MS analysis was done on a Hewlett Packard HP 6890 GC System instrument with a mass selective de-

Scheme 3



1 **7** **6** **8**

tector 5973 (a HP-5MS column, 5% phenylmethylsiloxane (30.0 m × 250 μm × 0.25 μm)). GC/MS conditions were as follows: injector temperature 210 °C, split ratio 15/1, temperature mode 150 °C→(3 °C)→230 °C (15 min); detector temperature 230 °C. An AMD-604S high-resolution mass spectrometer was used to determine the molecular masses and the elemental composition. CD spectra were recorded on a JASCO J-500 A spectropolarimeter. UV spectra were measured on a Specord M-40 spectrophotometer. Thin layer chromatography was performed on glass plates (4.6×6.0 cm) with a fixed silica gel layer. Melting points were determined on a Boetius hot stage. GLC analyses were carried out on a Perkin—Elmer Sigma 2000 chromatograph with a flame ionization detector and a CBP-5 capillary column (50 m) using helium as the carrier gas. GLC conditions: injector temperature 210 °C, temperature mode 150 °C→(3 °C)→230 °C (15 min); detector temperature 230 °C. Commercial Bu^n_3SnH and AIBN (Aldrich) were used. The activated zinc and the platinum catalyst for reduction were prepared by known procedures.[14,15] The starting dactylone **1** was isolated by a previously described[8] method from extracts from the sea hare *Aplysia dactylomela*. The ^1H and ^{13}C NMR spectra of this compound were reported previously.

(6*S*,10*R*)-10-Bromo-3,11,11-trimethyl-7-methylidenespiro[5,5]undec-2-en-4-one (dactylone) (1), $[\alpha]_D^{20}$ −145 (*c* 0.1, MeOH), m.p. 134—135 °C.[8] ^1H NMR, δ: 0.99 (s, 3 H, C(14)H_3); 1.19 (s, 3 H, C(15)H_3); 1.73 (d, 3 H, C(12)H_3, J = 1.8 Hz); 2.11 (m, 1 H, H´C(9)); 2.17 (m, 1 H, HC(8)); 2.26 (m, 1 H, HC(9)); 2.37 (m, 1 H, H´C (8)); 2.57 (d, 1 H, HC(5), J = 16.5 Hz); 2.65 (m, 2 H, H_2C(1)); 2.74 (br.d, 1 H, HC(5), J = 16.5 Hz); 4.52 (dd, 1 H, HC(10), J = 4.5 Hz, J = 12.5 Hz); 4.61 (s, 1 H, HC(13)); 4.98 (br.d, 1 H, HC(13), J = 1.5 Hz); 6.50 (m, 1 H, HC(2)). ^{13}C NMR, δ: 15.3 (C(12)); 17.7 (C(15)); 25.1 (C(14)); 30.0 (C(8)); 33.7 (C(1)); 35.5 (C(9)); 43.2 (C(11)); 44.2 (C(5)); 51.4 (C(6)); 63.0 (C(10)); 114.0 (C(13)); 135.5 (C(3)); 140.7 (C(2)); 146.1 (C(7)); 198.8 (C(4)).

Debromination of dactylone 1. ***A.*** Terpenoid **1** (108 mg, 0.36 mmol) was treated with activated Zn (545 mg, 8.38 mmol) in a mixture of 6.5 mL of MeOH and 4.0 mL of AcOH at 100 °C for 2 h. Excess AcOH was neutralized with $NaHCO_3$. The precipitate was extracted with $CHCl_3$. The reaction products **2** and **3** were separated by HPLC in a petroleum ether—EtOAc (25 : 1) system to give compound **2** (14 mg, 17.7%) and compound **3** (17.2 mg, 23.4%).

B. Terpenoid **1** (30 mg, 0.1 mmol) was refluxed in benzene with Bu^n_3SnH (60 mg, 0.21 mmol) and AIBN (2 mg, 0.01 mmol). The resulting terpenoid **3** (18 mg, 82%) was purified by HPLC as described above.

(3*S*,6*S*)-3,11,11-Trimethyl-7-methylidenespiro[5,5]undecan-4-one (2), $[\alpha]_D^{20}$ −13 (*c* 0.1, EtOH), m.p. 93—95 °C (from MeOH). ^1H NMR, δ: 0.83 (s, 3 H, C(15)H_3); 0.97 (s, 3 H, C(14)H_3); 1.0 (d, C(12)H_3, J = 7.0 Hz); 2.30 (dd, 1 H, HC(1), J = 16.0 Hz, J = 1.0 Hz); 2.59 (dd, 1 H, HC(1), J = 16.0 Hz, J = 3.5 Hz); 4.58 (s, 1 H, HC(13)); 4.94 (s, 1 H, HC (13)). ^{13}C NMR, δ: 14.6 (C(12)); 23.2 (C(15)); 23.6 (C(9)); 25.0 (C(14)); 28.1 (C(1)); 29.7 (C(2)); 32.8 (C(8)); 36.8 (C(10)); 37.7 (C(11)); 44.9 (C(3)); 45.7 (C(5)); 51.4 (C(6)); 113.6 (C(13)); 150.7 (C(7)); 214.1 (C(4)). High-resolution MS, m/z: 220.1834 $[M]^+$. $C_{15}H_{24}O$. Calculated: M 220.1827. MS (EI, 70 eV), m/z (I_{rel} (%)): 220 $[M]^+$ (100), 200 (19), 177 (12), 164 (18), 151 (52), 138 (15), 123 (24), 109 (37), 95 (29), 82 (51), 69 (56), 55 (32), 41 (54). CD (EtOH): $[\theta]_{288} = -29.3 \cdot 10^4$, $[\theta]_{205} = +29.3 \cdot 10^4$.

(6*S*)-3,11,11-Trimethyl-7-methylidenespiro[5,5]undec-2-en-4-one (3), $[\alpha]_D^{20}$ −38 (*c* 0.1, EtOH), m.p. 47—48 °C (from MeOH). ^1H NMR, δ: 0.92 (s, 6 H, C(14)H_3, C(15)H_3); 1.72 (q, 3 H, C(12)H_3, J = 2.5 Hz); 2.51 (d, 1 H, HC(5), J = 16.0 Hz); 2.56 (m, 2 H, CH_2(1)); 2.76 (d, 1 H, HC(5), J = 16.0 Hz); 4.45 (d, 1 H, HC(13), J = 0.8 Hz); 4.90 (s, 1 H, HC(13)); 6.59 (m, 1 H, HC(2)). ^{13}C NMR, δ: 15.4 (C(12)); 23.5 (C(10)); 24.2 (C(14)); 24.5 (C(15)); 30.4 (C(1)); 32.3 (C(9)); 36.4 (C(8)); 37.7 (C(11)); 43.4 (C(5)); 50.2 (C(6)); 112.6 (C(13)); 134.8 (C(3)); 143.0 (C(2)); 148.3 (C(7)); 200.2 (C(4)). High-resolution MS, m/z: 218.1686 $[M]^+$. $C_{15}H_{22}O$. Calculated: M 218.1672. MS (EI, 70 eV), m/z (I_{rel} (%)): 218 $[M]^+$ (48), 203 $[M - CH_3]^+$ (16), 190 (25), 176 (25), 175 (28), 162 (50), 148 (60), 134 (65), 121 (60), 109 (85), 91 (48), 82 (45), 69 (83), 55 (53), 41 (100). CD (EtOH): $[\theta]_{218} = -23.5 \cdot 10^6$, $[\theta]_{249} = +15.3 \cdot 10^6$.

Hydrogenation of dactylone 1. The Adams catalyst (0.5 mg) was added to a solution of terpenoid **1** (113 mg, 0.38 mmol) in 2 mL of EtOH and the mixture was stirred under H_2 for 15 h at ~20 °C. The catalyst was filtered off, the solvent was evaporated, and the hydrogenation products **4** and **5** were separated by HPLC in a petroleum ether—EtOAc (25 : 1) system to give 14.7 mg (17.5%) of compound **4** and 14.5 mg (17.2%) of compound **5**.

(3*S*,6*S*,7*S*,10*R*)-10-Bromo-3,7,11,11-tetramethylspiro[5,5]undecan-4-one (4), $[\alpha]_D^{20}$ −4 (*c* 0.1, EtOH). ^1H NMR, δ: 1.01 (d, 3 H, C(12)H_3, J = 6.7 Hz); 1.12 (s, 3 H, C(14)H_3); 1.13 (s, 3 H, C(15)H_3); 1.15 (d, 3 H, C(13)H_3, J = 6.7 Hz); 4.48 (dd, 1 H, HC(10), J = 4.5 Hz, J = 13.0 Hz). ^{13}C NMR, δ: 14.5 (C(12)); 16.9 (C(13)); 20.3 (C(15)); 26.5 (C(14)); 29.0 (C(1)); 29.2 (C(8)); 30.3 (C(9)); 31.1 (C(7)); 31.2 (C(2)); 43.0 (C(11)); 44.2 (C(3)); 46.7 (C(5)); 48.5 (C(6)); 66.4 (C(10)); 210.6 (C(4)). High-resolution MS, m/z: 221.1911 $[M - Br]^+$. For the $C_{15}H_{25}O$ ion, calculated: $[M - Br]^+$ 221.1905. MS (EI, 70 eV), m/z (I_{rel} (%)): 302/300 $[M]^+$ (1), 259 (1), 221 (74), 203 (40), 192 (1), 175 (2), 163 (9), 149 (16), 135 (13), 125 (16), 109 (37), 95 (32), 81 (30), 69 (100), 55 (36), 41 (34). CD (EtOH): $[\theta]_{285} = -41.1 \cdot 10^2$.

(3*R*,6*S*,7*R*)-3,7,11,11-Tetramethylspiro[5,5]undecan-4-one (5), $[\alpha]_D^{20}$ +80 (*c* 0.1, EtOH). ^1H NMR, δ: 0.76 (s, 3 H, C(14)H_3); 0.91 (s, 3 H, C(15)H_3); 0.96 (d, 3 H, C(12)H_3, J = 7.0 Hz); 1.09 (d, 3 H, C(13)H_3, J = 7.0 Hz); 2.23 (d, 1 H, HC(5), J = 15.7 Hz); 2.35 (d, 1 H, HC(5), J = 15.7 Hz, J = 1.0 Hz). ^{13}C NMR, δ: 16.6 (C(12)); 17.1 (C(13)); 21.7 (C(9)); 22.5 (C(15)); 26.6 (C(14)); 30.4* (C(1)); 30.5 (C(8)); 30.7* (C(2)); 36.7 (C(10)); 38.3 (C(11)); 38.5 (C(7)); 40.2 (C(5)); 43.7 (C(6)); 43.9 (C(3)); 218.4 (C(4)). High-resolution MS, m/z: 222.1998 $[M]^+$. $C_{15}H_{26}O$. Calculated: M 222.1983. MS (EI, 70 eV), m/z (I_{rel} (%)): 222 $[M]^+$ (48), 207 (4), 189 (2), 179 (4), 165 (7), 151 (78), 138 (63), 123 (11), 111 (100), 95 (26), 81 (30), 69 (33), 55 (41). CD (EtOH): $[\theta]_{285} = +50.5 \cdot 10^2$.

(6*S*,10*R*)-10-Bromo-3,7,11,11-tetramethylspiro[5,5]undeca-2,7-dien-4-one (6). Trifluoroacetic acid (50 mg, 0.44 mmol) was added to a solution of terpenoid **1** (100 mg, 0.34 mmol) in 2 mL of MeOH and the mixture was left for 7 days at ~20 °C. Then the reaction mixture was diluted threefold with water and extracted 3 times with equal volumes of Et_2O. The extracts were combined, neutralized with a 5% solution of $NaHCO_3$, dried

* The assignment of signals is ambiguous.

with Na_2SO_4, and concentrated to dryness. Product **6** was purified by HPLC in a petroleum ether—EtOAc (25 : 1) mixture. The yield of compound **6** was 90 mg (80%). Compound **6**, $[\alpha]_D^{20}$ −105 (*c* 0.1, EtOH). ^{1}H NMR, δ: 1.00 (s, 3 H, C(14)H_3); 1.15 (s, 3 H, C(15)H_3); 1.63 (q, 3 H, C(13)H_3, *J* = 1.6 Hz); 1.78 (q, 3 H, C(12)H_3, *J* = 1.8 Hz); 2.33 (dq, 1 H, HC(1), *J* = 19.8 Hz, *J* = 1.9 Hz); 2.58 (m, 2 H, H_2C(9)); 2.62 (s, 2 H, H_2C(5)); 2.77 (dm, 1 H, HC(1), *J* = 19.7 Hz); 4.51 (dd, 1 H, HC(10), *J* = 6.9 Hz, *J* = 10.4 Hz); 5.18 (m, 1 H, HC(8)); 6.64 (m, 1 H, HC(2)). ^{13}C NMR, δ: 15.6 (C(12)); 17.2 (C(14)); 22.6 (C(13)); 26.3 (C(15)); 34.0 (C(1)); 36.0 (C(9)); 42.0 (C(11)); 42.5 (C(5)); 48.3 (C(6)); 60.6 (C(10)); 121.4 (C(8)); 134.6 (C(3)); 140.5 (C(7)); 143.9 (C(2)); 199.6 (C(4)). High-resolution MS, *m/z*: 298.0741 $[M]^+$. $C_{15}H_{21}O^{81}Br$. Calculated: M 298.0756. MS (EI, 70 eV), *m/z* (I_{rel} (%)): 298/296 $[M]^+$ (38), 283/281 (3), 256/254 (5), 217 (58), 175/173 (61), 109 (100), 105 (100).

Dehydrobromination of dactylone 1 and its isomer 6. Potassium hydroxide (50 mg, 0.09 mmol) was added to a solution of terpenoid **1** or **6** (50 mg, 0.17 mmol) in 3 mL of MeOH and the mixture was kept for 24 h at ~20 °C. Then the reaction mixture was diluted threefold with water and extracted 3 times with equal volumes of $CHCl_3$. The extracts were combined and concentrated. Product **7** or **8** was purified by HPLC in a petroleum ether—EtOAc system (25 : 1), the yields were 70 or 72%, respectively.

2-Methyl-5-(6′-methylhepta-1′,5′-dien-2′-yl)phenol (7). ^{1}H NMR, δ: 1.55 (br.s, 3 H, C(7′)H_3); 1.68 (br.d, 3 H, C(8′)H_3, *J* = 1.2 Hz); 2.13 (m, 2 H, H_2C(4′)); 2.24 (s, 3 H, MeC(2)); 2.45 (m, 2 H, H_2C(3′)); 5.00 (q, 1 H, HC(1′), *J* = 1.2 Hz); 5.14 (tm, 1 H, HC(5′), *J* = 7.0 Hz); 5.24 (d, 1 H, HC(1′), *J* = 1.8 Hz); 6.83 (d, 1 H, HC(6), *J* = 1.8 Hz); 6.90 (dd, 1 H, HC(4), *J* = 1.8 Hz, *J* = 7.7 Hz); 7.06 (d, 1 H, HC(3), *J* = 7.6 Hz). ^{13}C NMR, δ: 15.7 (MeC(2)); 17.9 (C(7′)); 25.8 (C(8′)); 27.3 (C(4′)); 35.7 (C(3′)); 111.7 (C(1′)); 113.0 (C(6)); 118.8 (C(4)); 122.8 (C(2)); 124.1 (C(5′)); 130.8 (C(3)); 131.8 (C(6′)); 141.0 (C(5)); 148.0 (C(2′)); 153.7 (C(1)). High-resolution MS, *m/z*: 216.1507 $[M]^+$. $C_{15}H_{20}O$. Calculated: M 216.1514. MS (EI, 70 eV), *m/z* (I_{rel} (%)): 216 $[M]^+$ (56), 201 (2), 174 (14), 173 (100), 158 (7), 145 (10), 131 (7), 115 (5), 91 (6), 77 (10), 69 (33). UV, λ/nm (ε/L mol^{-1} cm^{-1}): 246 ($1.0 \cdot 10^4$); 285 ($4.3 \cdot 10^3$).

2-Methyl-5-(6′-methylhepta-2′,5′-dien-2′-yl)phenol (8). ^{1}H NMR, δ: 1.53 (br.s, 3 H, C(7′)H_3); 1.68 (br.d, 3 H, C(8′)H_3, *J* = 1.2 Hz); 1.99 (q, 3 H, H_3C(1′), *J* = 1.4 Hz); 2.24 (s, 3 H, MeC(2)); 2.67 (m, 2 H, H_2C(4′)); 5.10 (tm, 1 H, HC(5′), *J* = 7.0 Hz); 5.38 (tm, 1 H, HC(3′), *J* = 8.0 Hz); 6.62 (d, 1 H, HC(6), *J* = 1.7 Hz); 6.69 (dd, 1 H, HC(4), *J* = 1.7 Hz, *J* = 8.2 Hz); 7.07 (d, 1 H, HC(3), *J* = 8.4 Hz). ^{13}C NMR, δ: 15.5 (MeC(2)); 17.8 (C(7′)); 25.5 (C(1′)); 25.8 (Me—C(6′)); 28.4 (C(4′)); 114.6 (C(6)); 120.5 (C(4)); 121.9 (C(2)); 123.2 (C(5′)); 126.1 (C(3′)); 130.7 (C(3)); 131.8 (C(6′)); 135.6 (C(2′)); 141.3 (C(5)); 153.5 (C(1)). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 216 $[M]^+$ (44), 201 (29), 186 (13), 173 (100), 159 (40), 145 (38), 131 (13), 121 (18), 115 (19), 91 (20), 77 (18). UV, λ/nm (ε/L mol^{-1} cm^{-1}): 250 ($3.0 \cdot 10^3$); 283 ($1.4 \cdot 10^3$).

This work was financially supported by the Russian Foundation for Basic Research (Projects No. 99-04-48854 and No. 00-15-97806) and the government of the Primorski Krai (RFBR regional grant No. 01-03-96903).

References

1. G. B. Elyakov and V. A. Stonik, *Terpenoidy morskikh organizmov* [*Terpenoids of Marine Organisms*], Nauka, Moscow, 1986, 271 pp. (in Russian).
2. S. N. Fedorov, O. S. Radchenko, L. K. Shubina, A. I. Kalinovsky, A. V. Gerasimenko, D. Y. Popov, and V. A. Stonik, *J. Am. Chem. Soc.*, 2001, **123**, 504.
3. D. J. Faulkner, *Nat. Prod. Rep.*, 1995, **12**, 223.
4. D. J. Faulkner, *Nat. Prod. Rep.*, 1996, **13**, 75.
5. G. M. Konig and A. D. Wright, *J. Nat. Prod.*, 1997, **60**, 967.
6. K. A. El Sayed, D. C. Dunbar, T. L. Perry, S. P. Wilkins, and M. T. Hamman, *J. Agric Food Chem.*, 1997, **45**, 2735.
7. E. G. Juagdun, R. Kalidindi, and P. J. Scheuer, *Tetrahedron*, 1997, **53**, 521.
8. S. N. Fedorov, M. V. Reshetnyak, A. P. Shchedrin, S. G. Il′in, Yu. T. Struchkov, V. A. Stonik, and G. B. Elyakov, *Dokl. Akad. Nauk SSSR*, 1989, **305**, 877 [*Dokl. Chem.*, 1989 (Engl. Transl.)].
9. S. N. Fedorov, L. K. Shubina, A. I. Kalinovsky, E. G. Lyakhova, and V. A. Stonik, *Tetrahedron Lett.*, 2000, **41**, 1979.
10. B. Lacoume, *Bull. Soc. Chim. Fr.*, 1967, 3496.
11. N. S. Reddy, T. V. Goud, and Y. Venkateswarlu, *J. Chem. Res. S*, 2000, **9**, 438.
12. F. J. McEnroe and W. Fenicial, *Tetrahedron*, 1978, **34**, 1661.
13. C. Y. Chen, Y. C. Shen, Y. J. Chen, J. H. Sheu, and C. Y. Duh, *J. Nat. Prod.*, 1999, **62**, 573.
14. L. Fieser and M. Fieser, *Reagents for Organic Synthesis*, New York, 1967, **1**, 1276.
15. *Organic Synthesis*, Ed. H. Gilman, Quins College, Flushing, New York, 1944.

Received November 13, 2001;
in revised form December 6, 2002