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Oxidative bromination of tricyclic sesquiterpenoids (1*S*,3*S*,5*R*,6*S*,9*S*)-5-hydroxy-6,10,10-trimethyltricyclo[7.2.0.$0^{1,6}$]udecan-2-one and clovane-2β,9α-diol with the HBr—DMSO system

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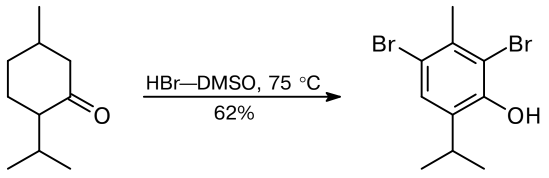
Oxidation of tricyclic sesquiterpenoids of the caryophyllene type with the HBr—DMSO system afforded α,β-unsaturated α-bromoketones. Since tricyclic derivatives, unlike simple alicyclic ketones, cannot undergo aromatization, all intermediate oxidation products can be isolated, which provide evidence that oxidation proceeds according to the following scheme: ketone→α-bromoketone→α,α-dibromoketone→α,β-unsaturated α-bromoketone.

Key words: hydrobromic acid, dimethyl sulfoxide, tricyclic sesquiterpenoids, caryophyllene, ketones, oxidation, bromination.

The HBr—DMSO system is known as a selective reagent used for oxidation of simplest alkenes, vicinal dibromides and diols, epoxides and ketones to form 1,2-diketones.**[1—3]** Oxidation of more structurally complex compounds with the HBr—DMSO system is sometimes accompanied by formation of products of bromination and deeper oxidation. For example, oxidation of dimedone under the action of the HBr—DMSO system afforded a mixture of 3,5-dibromo-2,6-dihydroxy-4,4-dimethylcyclohexa-2,5-dien-1-one (46%) and 3,5,5-tribromo-2-hydroxy-4,4-dimethylcyclopent-2-en-1-one (17%).**[4]** In the present study, we demonstrate the capabilities of this reagent in oxidation of a series of terpenic compounds whose oxidation products can subsequently be used in the synthesis of various bromo derivatives.

Oxidation of the simplest cyclic terpenic ketone, *viz*., menthone **1**, with the HBr—DMSO system gave rise to 2,4-dibromo-6-isopropyl-3-methylphenol (2,4-dibromothymol) (**2**) in 62% yield (Scheme 1). This reaction pathway is, apparently, typical of all cyclohexanone derivatives capable of undergoing aromatization.

Scheme 1



1 **2**

Under the action of the HBr—DMSO system, hydroxyketone **3** was initially converted into α-bromoketone **4**. Subsequent oxidation of compound **4** at higher temperature afforded successively α,α-dibromoketone **5**, α,β-unsaturated α-bromoketone **6**, and, finally, unsaturated bromodiketone **7**. Analysis of the spectral data (MS, IR, and 2D NMR) for compounds **4—7** demonstrated that their formation was not accompanied by the rearrangement of the carbon skeleton and only the substituted cyclohexanone fragment of the starting compound **3** underwent a change (Scheme 2). Monobromo derivative **4** was formed as the only stereoisomer with the *S* configuration of the C(3) atom, which corresponds to the attack of the Br^+ ion on intermediate enol of ketone **3** from the less hindered α-side. The configuration of the C(3) atom in compound **4** follows from analysis of the spin-spin coupling constants $^3J_{H-H}$. Judging from these constants, the twist conformation with the pseudoequatorial bromine atom and the pseudoequatorial hydroxyl group is the most favorable conformation of the six-membered ring in molecule **4**.

It is known that bromoketones are oxidized in DMSO to form bromo derivatives of 1,2-diketones,**[5]** whereas oxidation of substituted cyclic bromoketones in DMSO can afford either 1,2-diketones or unsaturated monobromoketones.**[6]** In our case, bromoketone **4** was not oxidized to 1,2-diketone under the action of the HBr—DMSO system; instead, it underwent the successive conversions α-bromoketone→α,α-dibromoketone→α,β-unsaturated α-bromoketone, which ended with oxidation of the OH group at the C(5) atom. When isolated in pure form, compounds **5** and **6** were readily

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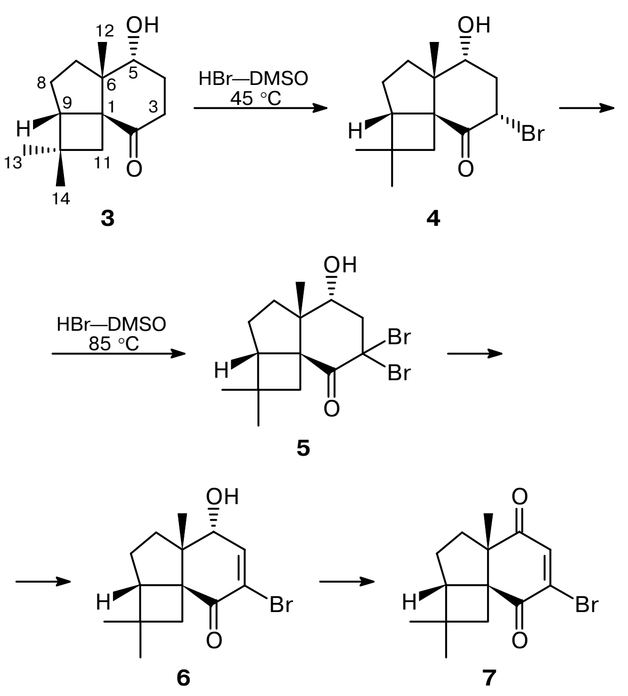
Scheme 2



converted into diketone **7** under the same conditions, which confirmed that these compounds are intermediates in the path **4**→**7**. In this case, the ratio of the oxidation rates of the products is such that either compound **4** or compound **7** can be obtained under particular conditions as the only product. Thus, oxidation of hydroxyketone **3** at 45 °C for 8 h afforded compound **4** in 95% yield, whereas oxidation of hydroxyketone **3** first at 45 °C for 8 h and then at 85 °C for 24 h gave rise to compound **7** in 85% yield.

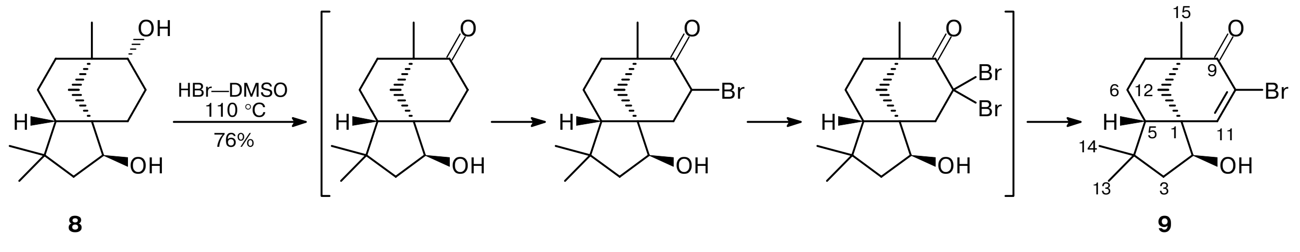
The ratio of the rates characterizing the individual stages of the oxidative conversions in the HBr—DMSO system depends substantially on the structure of the remaining portion of the molecule and is, apparently, associated primarily with the steric hindrances caused by molecular fragments, which are not involved in the reaction. It should be noted that not only ketones but also alcohols can undergo oxidative bromination. The latter are initially oxidized to the corresponding ketones; however, the reaction conditions should be more severe because oxidation of alcohols to ketones under the action of this system proceeds much more difficultly than the subsequent conversions of the resulting keto derivatives. Thus, oxidation of tricyclic derivative **8**, while afforded the final product **9** in good yield, required substantially more drastic conditions (110 °C). In the latter case, attempts to isolate intermediate products failed; however, the oxidation mechanism is, most likely, analogous to the mechanism of oxidation **3**→**6** (Scheme 3). The surprising thing is that only one of two hydroxyl groups of the starting diol **8** was involved in the reaction. Thus, the hydroxyl group in the six-membered ring was oxidized, whereas the hydroxyl group in the five-membered ring remained intact. It is noteworthy that in the latter case, no skeletal rearrangements were also observed in spite of the high temperature and the presence of the strong acid. The retention of the carbocyclic core of the molecule was confirmed by analysis of the 2D NMR spectra and the spin-spin coupling constants for compound **9**.

To summarize, oxidation of the tricyclic sesquiterpenoid derivatives under study afford products, which do not undergo aromatization because of the presence of quaternary carbon atoms in the six-membered ring of compound **3**. Because of this, the oxidation process can be followed step by step and all intermediates can be isolated, which provides proof of the scheme of the multistage oxidation process involving ketones. Analogous oxidative conversions involving the corresponding secondary alcohols can also be performed; however, attempts to isolate intermediates failed because alcohols are oxidized to ketones under more severe conditions, and only the final product in the oxidative chain can be obtained.

Experimental

Thin-layer chromatography was carried out on Silufol® plates with a SILPEARL silica gel layer fixed on an aluminum foil (Czech Republic). The components were visualized by spraying the plates with concentrated H_2SO_4 followed by heating to 100—150 °C. Column chromatography was performed on KSK silica gel (Russia; the particle size was 0.10—0.20 mm), which was dried in air and activated by heating at 140 °C for 5 h. The IR spectra were recorded on a Specord M-80 spectrophotometer for solutions in $CHCl_3$ (*c* 1%). The UV spectra were measured on a Specord UV VIS spectrophotometer for solutions in 95% EtOH. The optical rotation was measured on a Polamat A polarimeter at the wavelength of 578 nm for solutions in $CHCl_3$. The melting points were determined on a Kofler stage. Microanalyses were carried out on Hewlett Packard 185 and Carlo Erba 1106 analyzers. The mass spectra

Scheme 3



were obtained on a Finnigan MAT-8200 mass spectrometer (EI, 70 eV). The NMR spectra were recorded on a Bruker AM-400 spectrometer (400.13 MHz for ^{1}H and 100.61 MHz for ^{13}C) at room temperature (23—25 °C), unless otherwise stated, using the signals of the solvent as the internal standard (δ_C = 76.900 and δ_H = 7.240 for $CDCl_3$, δ_C = 128.000 and δ_H = 7.150 for C_6D_6, δ_C = 123.500 and δ_H = 7.190 for C_5D_5N). The assignment of the signals was made using the ^{13}C NMR spectra, which were recorded with *J* modulation (proton-noise-decoupled spectra, the opposite phases for the signals of the atoms with the odd and even numbers of the attached protons, tuning to the constant *J* = 135 Hz), and based on the 2D spectra, *viz.*, 1) homonuclear ^{1}H—^{1}H correlation, 2) heteronuclear ^{13}C—^{1}H correlation at the direct spin-spin coupling constants (*J* = 135 Hz), and 3) heteronuclear ^{13}C—^{1}H correlation at the long-range spin-spin coupling constants (*J* = 10 Hz).

(−)-Caryophyllene ($[\alpha]^{20}$ −9 in pure form; > 97% according to GLC; prepared by rectification of the hydrocarbon fraction of a clove oil) was converted into 4β,5α-epoxide (caryophyllene epoxide), which was oxidized with $KMnO_4$ to the 4,5-epoxy-8-oxo-13-nor derivative (kobusone). Cyclization of the latter in an alkaline medium afforded keto alcohol **3**.[7] Clovane-2β,9α-diol **8** was prepared by acid isomerization of caryophyllene epoxide as described previously.[8]

(1*S*,5*R*,6*S*,9*S*)-5-Hydroxy-6,10,10-trimethyltricyclo[7.2.0.0^{1,6}]undecan-2-one (3). ^{1}H NMR (C_6D_6—CCl_4, 1 : 4 v/v), δ: 0.73 (s, 3 H, H(12)); 0.83 (s, 3 H, H(13)); 0.97 (s, 3 H, H(14)); 1.27 (d, 1 H, H_a(11), *J* = 12.1 Hz); 1.31 (br.s, 1 H, OH); 1.51 (ddd, 1 H, H_b(7), *J* = 12.6, 12.6, and 7.5 Hz); 1.67 (dddd, 1 H, H_b(4), *J* = 14.0, 12.7, 11.4, and 4.2 Hz); 1.69 (dd, 1 H, H_b(8), *J* = 14.0 and 7.5 Hz); 1.76 (dddd, 1 H, H_a(4), *J* = 12.7, 5.6, 4.3, and 3.0 Hz); 1.87 (dddd, H_a(8), *J* = 14.0, 12.4, 8.6, and 7.5 Hz); 1.99 (dd, 1 H, H_a(7), *J* = 12.6 and 5.8 Hz); 2.15 (dd, 1 H, H(9), *J* = 7.5 and 3.1 Hz); 2.18 (ddd, 1 H, H_a(3), *J* = 14.1, 4.2, and 3.0 Hz); 2.29 (ddd, 1 H, H_b(3), *J* = 14.1, 14.0, and 5.6 Hz); 2.49 (dd, 1 H, H_b(11), *J* = 12.1 and 3.0 Hz); 3.60 (dd, 1 H, H(5), *J* = 11.7 and 4.3 Hz). ^{13}C NMR, δ: 12.18 (C(12)); 24.95 (C(13)); 25.50 (C(9)); 30.18 (C(14)); 30.80 (C(4)); 31.45 (C(10)); 33.60 (C(11)); 36.31 (C(3)); 37.74 (C(7)); 53.26 (C(6)); 54.94 (C(9)); 58.25 (C(1)); 70.27 (C(5)); 209.42 (C(2)).

(1*S*,2*S*,5*S*,8*R*,9*R*)-4,4,8-Trimethyltricyclo[6.3.1.0^{1,5}]dodecane-2,9-diol (clovane-2β,9α-diol) (8). ^{1}H NMR (Py-d_5, +30 °C), δ: 0.91 (s, 3 H, H(14)); 1.03 (d, 3 H, H_a(12), *J* = 11.9 Hz, $W_{1/2}$ = 6 Hz); 1.11 (s, 3 H, H(13)); 1.195 (s, 3 H, H(15)); 1.200 (m, H(7a)); 1.35 (m, 1 H, H_a(7)); 1.38—1.45 (m, 2 H, H(6) and H_a(11)); 1.57 (dd, 1 H, H(5), *J* = 11.4 and 5.2 Hz); 1.87 (d, 2 H, H(3), *J* = 7.6 Hz); 1.92 (ddd, 1 H, H_a(10), *J* = 14.3, 4.8, and 2.4 Hz); 2.12 (dddd, 1 H, H_b(10), *J* = 14.3, 13.4, 4.8, and 3.2 Hz); 2.17 (d, 1 H, H_b(12), *J* = 11.9 Hz); 2.47 (ddd, 1 H, H_b(11), *J* = 13.3, 13.3, and 4.8 Hz); 3.56 (dd, 1 H, H(9), *J* = 3.2 and 2.4 Hz); 4.12 (t, 1 H, H(2), *J* = 7.6 Hz); 5.56 (br.s, 2 H, OH). ^{13}C NMR, δ: 21.33 (C(6)); 25.76 (C(14)); 27.26 (C(10)); 27.84 (C(11)); 29.45 (C(15)); 31.78 (C(13)); 33.77 (C(7)); 35.38 (C(8)); 36.52 (C(12)); 37.32 (C(4)); 45.24 (C(1)); 48.43 (C(3)); 51.15 (C(5)); 74.60 (C(9)); 80.41 (C(2)).

2,4-Dibromo-6-isopropyl-3-methylphenol (2). Menthone (**1**) (332 mg, 2.16 mmol, Aldrich) was added to a solution of 47% aqueous HBr (1 mL) in DMSO (10 mL) and the resulting mixture was heated at 75 °C for 22 h. After cooling to ~20 °C, the mixture was diluted with water (200 mL) and the reaction products were extracted with Et_2O (2×50 mL). The combined organic extracts were washed successively with water (3×50 mL) and a saturated aqueous solution of NaCl (50 mL) and then dried with $MgSO_4$. The solvent was distilled off *in vacuo* and the resulting product was chromatographed (hexane—benzene, 3 : 1 v/v). 2,4-Dibromo-6-isopropyl-3-methylphenol (**2**)[9] was obtained as a yellow oil in a yield of 0.413 g (62%). IR ($CHCl_3$), ν/cm^{-1}: 3501 (O—H). ^{13}C NMR ($CDCl_3$), δ: 22.27 (Ar—$\underline{C}H_3$); 26.86 (2 C, CH_3); 28.01 (Ar—$\underline{C}$H); 114.00 and 115.03 (C(2) and C(4)); 129.2 (C(5)); 134.9 (C(6)); 148.8 (C(1)). MS, *m/z* (I_{rel} (%)): 306/308/310 $[M]^+$ (31), 293 $[M - 15]^+$ (100), 212/214 $[M - Br - Me]^+$ (38), 133 $[C_9H_9O]^+$ (8), 115 $[C_9H_7]^+$ (10). Found (%): C, 39.0; H, 3.8. $C_{10}H_{12}Br_2O$. Calculated (%): C, 38.99; H, 3.93.

(1*S*,3*S*,5*R*,6*S*,9*S*)-3-Bromo-5-hydroxy-6,10,10-trimethyltricyclo[7.2.0.0^{1,6}]undecan-2-one (4). Keto alcohol **3** (0.220 g, 1.00 mmol) was added to a solution of 40% aqueous HBr (0.5 mL) in DMSO (5 mL). The resulting mixture was heated at 45 °C for 8 h, cooled to ~20 °C, diluted with water (100 mL), and extracted with Et_2O (2×50 mL). The combined organic extracts were washed successively with water (3×50 mL) and a saturated aqueous solution of NaCl (50 mL) and then dried with $MgSO_4$. The solvent was distilled off *in vacuo* and the solid residue was crystallized from C_6H_6. Bromoketone **4** was isolated as white crystals in a yield of 0.285 g (95%), m.p. 167—169 °C (from benzene), $[\alpha]^{22}$ ±0 (*c* 6.00, $CHCl_3$). IR ($CHCl_3$), ν/cm^{-1}: 3616 (O—H), 1712 (C=O). ^{1}H NMR ($CDCl_3$), δ: 0.85 (s, 3 H, H(12)); 0.87 (s, 3 H, H(13)); 0.97 (s, 3 H, H(14)); 1.48 (d, 1 H, H_a(11), *J* = 12.4 Hz); 1.66 (ddd, 1 H, H_a(7), *J* = 13.0, 12.7, and 7.5 Hz); 1.82 (dd, 1 H, H_a(8), *J* = 14.8 and 7.5 Hz); 1.75 (br.s, OH); 1.98 (dddd, 1 H, H_b(8), *J* = 14.8, 13.0, 8.6, and 7.5 Hz); 2.05 (dd, 1 H, H_b(7), *J* = 12.7 and 7.5 Hz); 2.26 (ddd, 1 H, H_a(4), *J* = 13.9, 12.5, and 12.0 Hz); 2.31 (dd, 1 H, H(9), *J* = 8.6 and 3.1 Hz); 2.58 (dd, 1 H, H_b(11), *J* = 12.4 and 3.1 Hz); 2.59 (ddd, 1 H, H_b(4), *J* = 12.5, 5.5, and 4.0 Hz); 3.92 (dd, 1 H, H(5), *J* = 12.0 and 4.0 Hz); 4.78 (dd, 1 H, H(3), *J* = 13.9 and 5.5 Hz). ^{13}C NMR, δ: 11.52 (C(12)); 24.29 (C(13)); 25.08 (C(9)); 29.78 (C(14)); 31.50 (C(10)); 34.53 (C(11)); 37.28 (C(7)); 42.43 (C(4)); 50.36 (C(3)); 53.78 (C(6)); 55.13 (C(9)); 57.41 (C(1)); 69.74 (C(5)); 202.25 (C(2)). High-resolution MS. Found: *m/z* = 300.07174 $[M]^+$. $C_{14}H_{21}BrO_2$. Calculated: M = 300.07253. MS, *m/z* (I_{rel} (%)): 302/300 $[M]^+$ (3/3), 247/245 (43/43), 221 (100), 203 (30), 175 (9), 166 (10), 165 (59), 163 (38), 161 (14), 147 (30), 137 (25), 135 (12), 123 (18), 121 (30), 119 (24), 109 (30), 107 (20), 105 (18), 95 (16), 93 (22), 85 (43), 81 (20), 79 (26), 77 (19), 69 (20), 67 (18), 57 (13), 56 (33), 55 (32), 53 (14), 43 (19), 41 (50), 39 (13).

Oxidation of keto alcohol 3. Keto alcohol **3** (0.103 g, 0.46 mmol) was added to a solution of 40% aqueous HBr (0.25 mL) in DMSO (2.5 mL). The resulting mixture was heated successively at 45 °C for 8 h (according to TLC, compound **4** was formed in quantitative yield) and at 85 °C for 12 h. Then the reaction mixture was treated as in the case of formation of bromoketone **4** (see above) and the resulting product (0.150 g) was chromatographed with a EtOAc—hexane mixture. Unsaturated bromodiketone **7** (0.050 g, 36% yield), dibromoketone **5** (0.044 g, 25% yield), and unsaturated bromoketo alcohol **6** (0.032 g, 23% yield) were successively eluted.

(1*S*,6*S*,9*S*)-3-Bromo-6,10,10-trimethyltricyclo[7.2.0.0^{1,6}]undec-3-ene-2,5-dione (7). Yellowish crystals, m.p. 106—107 °C (from benzene), $[\alpha]^{22}$ −329 (*c* 1.00, $CHCl_3$). IR ($CHCl_3$), ν/cm^{-1}: 1723 and 1699 (C=O), 1597 (C=C). UV (EtOH), λ_{max}/nm (lg ε): 277 (3.7). ^{1}H NMR ($CDCl_3$), δ: 0.90 (s, 3 H, H(13)); 0.98 (s, 3 H, H(14)); 1.15 (s, 3 H, H(12)); 1.52 (d, 1 H, H_a(11), *J* = 13.0 Hz); 1.66 (dddd, 1 H, H_a(8), *J* = 14.5, 13.5, 8.5, and 7.0 Hz); 1.80 (dd, 1 H, H_b(8), *J* = 14.5 and 7.0 Hz); 1.91 (dd, 1 H, H_a(7), *J* = 13.0 and 7.0 Hz); 2.00 (ddd, 1 H, H_b(7), *J* = 13.5, 13.0, and 7.0 Hz); 2.45 (dd, 1 H, H(9), *J* = 8.5 and 2.5 Hz); 2.58 (dd, 1 H, H_b(11), *J* = 13.0 and 2.5 Hz); 7.30 (s, 1 H, H(4)). ^{13}C NMR, δ: 19.24 (C(12)); 23.94 (C(13)); 26.07 (C(9)); 30.31 (C(14)); 30.54 (C(10)); 32.01 (C(11)); 41.03 (C(7));

53.54 (C(9)); 53.97 (C(6)); 59.64 (C(1)); 122.78 (C(3)); 160.97 (C(4)); 178.98 (C(5)); 193.72 (C(2)). High-resolution MS. Found: m/z 296.03940 $[M]^+$. $C_{14}H_{17}BrO_2$. Calculated: M = 296.04124. MS, m/z (I_{rel} (%)): 298/296 $[M]^+$ (13/13), 243/245 (9/9), 242/240 (60/60), 217 (92), 215 (11), 189 (20), 175 (18), 161 (22), 149 (100), 147 (13), 134 (15), 133 (65), 121 (17), 119 (9), 107 (32), 105 (32), 93 (38), 91 (22), 79 (24), 77 (29), 69 (20), 67 (13), 65 (17), 55 (35), 53 (19), 43 (10), 41 (55).

(1*S*,5*R*,6*S*,9*S*)-3,3-Dibromo-5-hydroxy-6,10,10-trimethyltricyclo[7.2.0.0^{1,6}]undecan-2-one (5). White crystals, m.p. 54—56 °C (from hexane), $[\alpha]^{22}$ −137 (c 2.10, $CHCl_3$). IR ($CHCl_3$), ν/cm^{-1}: 3616 (O—H), 1707 (C=O). ^{1}H NMR ($CDCl_3$), δ: 0.85 (s, 3 H, H(12)); 0.88 (s, 3 H, H(13)); 1.11 (s, 3 H, H(14)); 1.56 (d, 1 H, H_a(11), J = 12.5 Hz); 1.63 (ddd, 1 H, H_b(7), J = 13.5, 13.0, and 7.0 Hz); 1.75 (dd, 1 H, H_b(8), J = 14.5 and 7.5 Hz); 2.03 (dddd, 1 H, H_a(8), J = 14.5, 13.0, 8.5, and 7.0 Hz); 2.05 (br.s, OH); 2.11 (dd, 1 H, H_a(7), J = 13.0 and 7.0 Hz); 2.56 (dd, 1 H, H_b(11), J = 12.5 and 3.0 Hz); 2.89 (dd, 1 H, H(9), J = 8.5 and 3.0 Hz); 2.90 (dd, 1 H, H_a(4), J = 14.5 and 11.5 Hz); 3.03 (dd, 1 H, H_b(4), J = 14.5 and 4.0 Hz); 4.20 (dd, 1 H, H(5), J = 11.5 and 4.0 Hz). ^{13}C NMR, δ: 12.28 (C(12)); 24.28 (C(13)); 24.71 (C(9)); 29.63 (C(14)); 31.20 (C(10)); 35.45 (C(11)); 37.15 (C(7)); 51.40 (C(4)); 52.00 (C(6)); 55.60 (C(1)); 60.70 (C(9)); 64.48 (C(3)); 67.37 (C(5)); 197.63 (C(2)). High-resolution MS. Found: m/z 377.98237 $[M]^+$. $C_{14}H_{20}Br_2O_2$. Calculated: M = 377.98310. MS, m/z (I_{rel} (%)): 382/380/378 $[M]^+$ (2.5/5/2.5), 327/325/323 (10/21/10), 301/299 (64/64), 283/281 (26/26), 259/257 (11/11), 245/243 (20/20), 220 (11), 219 (29), 217/215 (16/16), 201 (21), 191 (16), 177 (11), 173 (14), 165 (38), 164 (23), 163 (39), 159 (17), 149 (12), 147 (13), 146 (11), 145 (12), 138 (18), 137 (15), 136 (10), 135 (12), 131 (13), 125 (28), 123 (20), 121 (26), 119 (16), 117 (14), 109 (30), 107 (44), 105 (20), 95 (22), 93 (38), 91 (34), 83 (22), 81 (12), 79 (47), 69 (43), 67 (28), 65 (16), 57 (19), 56 (52), 55 (67), 53 (26), 43 (53), 41 (100), 39 (23), 29 (20), 27 (25).

(1*S*,5*R*,6*S*,9*S*)-3-Bromo-5-hydroxy-6,10,10-trimethyltricyclo[7.2.0.0^{1,6}]undec-3-en-2-one (6). White crystals, m.p. 117—119 °C (from a mixture of hexane and benzene, 1 : 1 v/v), $[\alpha]^{22}$ −174 (c 0.90, $CHCl_3$). IR ($CHCl_3$), ν/cm^{-1}: 3615 (O—H), 1676 (C=O), 1613 (C=C). UV (EtOH), λ_{max}/nm (lg ε): 259 (3.7), 337 (2.0). ^{1}H NMR ($CDCl_3$), δ: 0.89 (s, 3 H, H(13)); 0.93 (s, 3 H, H(12)); 1.20 (s, 3 H, H(14)); 1.55 (d, 1 H, H_a(11), J = 13.0 Hz); 1.63 (ddd, 1 H, H_b(7), J = 13.0, 13.0, and 7.5 Hz); 1.73—1.86 (m, 1 H, H_a(8)); 1.73—1.86 (m, 1 H, H_b(8)); 2.02 (dd, 1 H, H_a(7), J = 13.0 and 6.5 Hz); 2.35 (dd, 1 H, H_b(11), J = 13.0 and 3.0 Hz); 2.36 (m, 1 H, H(9)); 2.9 (br.s, OH); 4.47 (d, 1 H, H(5), J = 2.0 Hz); 7.22 (d, 1 H, H(4), J = 2.0 Hz). ^{13}C NMR, δ: 12.28 (C(12)); 24.53 (C(13)); 25.97 (C(9)); 28.66 (C(14)); 30.42 (C(10)); 36.10 (C(7)); 36.69 (C(11)); 53.49 (C(9)); 53.74 (C(6)); 55.72 (C(1)); 70.31 (C(5)); 121.54 (C(3)); 152.48 (C(4)); 193.60 (C(2)). Found: m/z 298.05629 $[M]^+$. $C_{14}H_{19}BrO_2$. Calculated: M = 298.05689. MS, m/z (I_{rel} (%)): 300/298 $[M]^+$ (36/36), 245/243 (43/43), 244/242 (30/30), 220/218 (12/12), 219 (78), 217 (13), 216 (18), 214 (11), 213 (45), 204 (19), 203 (12), 202 (10), 201 (30), 191 (13), 175 (9), 173 (11), 165 (10), 162 (38), 161 (14), 159 (13), 147 (15), 146 (27), 137 (12), 136 (24), 134 (49), 133 (38), 131 (12), 119 (16), 117 (14), 115 (11), 109 (22), 107 (37), 105 (20), 95 (12), 93 (34), 91 (42), 83 (26), 81 (24), 79 (47), 77 (40), 69 (29), 67 (22), 65 (19), 56 (33), 55 (71), 53 (34), 43 (39), 41 (100), 29 (21), 27 (29).

Oxidation of dibromoketone 5. Dibromoketone **5** (0.01 g) was added to a solution of 40% aqueous HBr (0.1 mL) in DMSO (1 mL) and the resulting mixture was heated at 85 °C. After 4 h, spots of the starting compound and compounds **6** and **7** were detected by TLC. After 12 h, only a spot of compound **7** was observed.

Oxidation of bromoketo alcohol 6. Unsaturated bromoketo alcohol **6** (0.01 g) was added to a solution of 40% aqueous HBr (0.1 mL) in DMSO (1 mL) and the resulting mixture was heated at 85 °C for 12 h after which only a spot of compound **7** was detected by TLC.

(1*S*,2*S*,5*S*,8*R*)-10-Bromo-2-hydroxy-4,4,8-trimethyl-9-oxotricyclo[6.3.1.0^{1,5}]dodec-10-ene or (1*R*,2*S*,5*S*,8*R*)-10-bromo-2β-hydroxy-10-cloven-9-one (9). Clovane-2β,9α-diol (**8**) (0.970 g, 4.10 mmol) was added to a solution of 40% aqueous HBr (2.5 mL) in DMSO (40 mL) and the resulting mixture was heated at 110 °C for 16 h. The reaction product (1.10 g) was purified by column chromatography (EtOAc—hexane, 15 : 85 v/v) and hydroxybromoketone **9** was obtained as colorless needle-like crystals in a yield of 0.972 g (76%), m.p. 160—162 °C (from a mixture of hexane and benzene, 1 : 1 v/v), $[\alpha]^{22}$ −27.9 (c 4.30, $CHCl_3$). IR ($CHCl_3$), ν/cm^{-1}: 3627 and 3588 (O—H), 1685 (C=O), 1591 (C=C). UV (EtOH), λ_{max}/nm (lg ε): 264 (3.76). ^{1}H NMR (Py-d_5, +30 °C), δ: 1.05 (s, 3 H, H(14)); 1.14 (s, 3 H, H(15)); 1.17 (s, 3 H, H(13)); 1.38 (m, 1 H, H_a(7)); 1.46—1.62 (m, 3 H, H_b(7) and 2 H(6)); 1.53 (dd, 1 H_a(12), J = 12.9 and 2.0 Hz); 1.79 (ddd, 1 H, H_b(12), J = 12.9, 1.3, and 1.3 Hz); 1.89 (dd, 1 H, H_a(3), J = 13.9 and 2.2 Hz); 1.91 (m, 1 H, H(5)); 2.04 (dd, 1 H, H_b(3), J = 13.9 and 5.0 Hz); 4.06 (dd, 1 H, H(2), J = 5.0 and 2.2 Hz); 8.18 (d, 1 H, H(11), J = 2.0 Hz). ^{13}C NMR, δ: 18.66 (C(6)); 26.02 (C(15)); 28.44 (C(14)); 33.87 (C(13)); 34.15 (C(7)); 39.62 (C(4)); 40.29 (C(12)); 43.98 (C(8)); 45.12 (C(5)); 49.59 (C(3)); 53.82 (C(1)); 76.85 (C(2)); 122.87 (C(10)); 156.78 (C(11)); 197.00 (C(9)). High-resolution MS. Found: m/z 312.07253 $[M]^+$. $C_{15}H_{21}BrO_2$. Calculated: M = 312.07253. MS, m/z (I_{rel} (%): 314/312 $[M]^+$ (1/1), 296/294 (10/10), 281/279 (15/15), 233 (100), 235 (5), 215 (51), 187(18), 161(42), 159(24), 145(12), 137(55), 131(12), 121 (44), 119 (13), 107 (15), 105 (24), 95 (14), 91 (23), 79 (14), 77 (16), 69 (16), 55 (24), 53 (11), 43 (12), 41 (33), 39 (11), 29 (12).

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