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CHEMISTRY

Sesquiterpene Metylenelactones in a Palladium-Catalyzed Cross-Coupling Reaction

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Compounds containing an α-methylene-γ-lactone fragment, in particular sesquiterpene lactones, have attracted attention for the past 50 years owing to their diverse physiological activity, including antitumor properties [1]. The biological activity of sesquiterpene lactones are known to result from their behavior as alkylating agents. These compounds can form in vivo adducts with nucleophilic regions of biomolecules (like products of the Michael reaction with free sulfhydryl or amino groups) [2]. Eudesmane-type sesquiterpene lactones show antiproliferative activity in vitro in tumor cells MK-1, HeLa, and B16F10 [3]. The capability to inhibit the growth of human tumor cells (COLO-205, HT-29, HL-60, AGS) is explained by the initiation of apoptosis, which is considered to be associated with activation of a caspase cascade in these cells [4–6].

Antitumor drug Arglabin has been developed on the basis of one of sesquiterpene methylenelactones [7].

Sesquiterpene lactones isoalantolactone (**1**) and alantolactone (**2**), available metabolites of elecampane *Inula helenium L.* [8], have attracted our attention. In this report, we describe the modification of these lactones by introducing aromatic substituents via the Heck reaction. It should be noted that *exo* methylenelactones have not been involved in reactions with organometalic reagents until now.

We established for the first time that isoalantolactone **1** is a reactive alkene component in the palladium-catalyzed cross-coupling reaction with aryl halides (the Heck reaction [9]). The reaction of compound **1** with 4-iodoanisole, 4-iodoveratrole, or 2-iodothioanisole in DMF in the presence of catalytic amounts of palladium acetate and tris(*o*-tolyl)phosphine and triethylamine as a base (120°C, 8 h) leads to (*E*)-13-aryleudesm-11-en-8α,12-olides (**3**, **4**, **5**) in 79–85% yield. The products of double bond shift (**6**, **7**, **8**) also form in 9–17% yield (Scheme 1). The cross-coupling of alantolactone **2** with 4-iodoveratrole under noted conditions results in lower yield of aryl-substituted derivatives (**9**, **10**) (20 and 36%, respectively). Thus, the yield of the products of double bond shift in the reactions of alantolactone **2** (compound **10**) is considerably higher than that for isoalantolactone **1**. This fact can be explained by the tendency to form a system of conjugated double bonds.

The structure of lactones **3–10** was established on the basis of spectral data and elemental analysis. The (*E*) configuration of C-11,13 bond in arylidenelactones **3**–**5** and **9** follows from the presence in the ^{13}C NMR spectrum (monoresonance mode) of carbon–proton ^3J *cis* coupling constant between the olefin proton (H^{13}) and the carbonyl carbon of lactone ^3J = 6.9–7.5 Hz.

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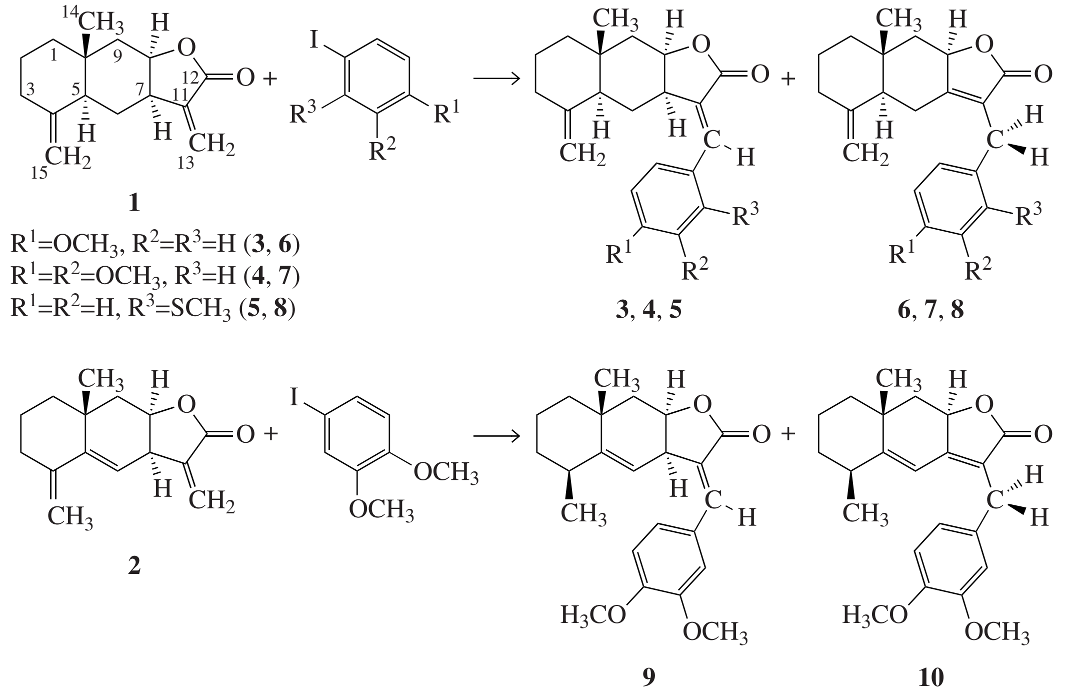
Scheme 1.



Thus, in this work we accomplished for the first time the arylation of sesquiterpene methylenelactones via cross-coupling reaction catalyzed by palladium phosphine complexes.

EXPERIMENTAL

NMR spectra of the compounds as solutions in $CDCl_3$ were recorded on Bruker AV-300 (operating at 300.13 (^{1}H) and 75.47 MHz (^{13}C)), Bruker AM-400 (operating at 400.13 (^{1}H) and 100.78 MHz (^{13}C)), and Bruker DRX-500 (operating at 500.13 (^{1}H) and 125.76 MHz (^{13}C)) spectrometers. Signal assignment in NMR spectra was performed using different types of proton–proton and carbon–proton shift correlation spectroscopy (COSY, COLOC). Mass spectra, molecular weights, and elemental composition were measured with a Finnigan MAT-8200 high-resolution mass spectrometer at an ionizing voltage of 70 eV (injector temperature of 270–300°C). IR spectra were obtained on a Vector-22 spectrometer as KBr pellets. UV absorption spectra were recorded on a HP 8453 UV Vis spectrophotometer as solutions in ethanol or chloroform.

Reaction products were isolated by column chromatography on silica gel (Acros, 0.035–0.070 mm, pore size 6 nm) (elution with benzene–ethyl acetate, chloroform–ethanol).

Solvents used were freshly distilled, chemicals were of pure grade. Palladium(II) acetate was obtained according to the procedure in [10]. Lactones **1** and **2** were obtained by extraction of herbal raw material followed by isolation via morpholine adducts as described in [11].

The Heck reaction. General procedure. A two-necked glass ampoule was purged with argon. The ampoule was charged sequentially in an argon flow with 2.15 mmol (500 mg) of lactone **1** or **2**, 2.58 mmol of aryl iodide, 0.086 mmol (4 mol %) of palladium acetate, 0.34 mmol (16 mol %) of tris(*o*-tolyl)phosphine, 7 mL of DMF, 3.87 mmol of triethylamine, and molecular sieves 3 Å. The ampoule was sealed (small excess pressure of argon), and the reaction mixture was heated for 8–10 h at 120°C. After completion of the reaction, the ampoule was allowed to cool and opened, and the reaction mixture was poured into a Petri dish. The solid residue was dissolved in a minimal amount of chloroform and chromatographed on silica gel (chloroform–ethanol, 100 : 0 to 10 : 1 as an eluent). The following products were eluted sequentially: tris(*o*-tolyl)phosphine, the initial lactone, a mixture of the lactone with reaction product, and a mixture of two reaction products (chloroform as an eluent). Repeated chromatography and recrystallization from appropriate solvent was used to isolate pure arylation product.

(3a*R*,4a*S*,8a*R*,9a*R*,*E*)-3-(4-Methoxybenzylidene)-8a-methyl-5-methylenedecahydronaphtho[2,3-*b*]furan-2(3*H*)-one (3). Yield 85%, mp 199–201°C (from ethyl acetate), $[\alpha]_{589}$ + 561 (*c* 1.445, $CHCl_3$). IR (ν, cm^{-1}): 787, 908, 1001, 1032, 1073, 1089, 1169, 1186, 1201, 1225, 1247, 1281, 1299, 1334, 1368, 1417, 1440, 1518, 1586, 1649, 1689, 1709, 1745 (C=O). UV (chloroform, λ_{max}, nm (log ε)): 241 (3.66), 314

(4.40). ^{1}H NMR (CDCl$_3$, δ, ppm, *J*, Hz): 0.86 (s, 3H, 14-H$_3$), 1.26 (m, 1H, 1-H), 1.39 (ddd, 1H, 6-H, *J* = 13.9, 12.6, 12.2), 1.47–1.68 (m, 4H, 1,2,2,9-H), 1.90–2.06 (m, 3H, 3,5,6-H), 2.24 (dd, 1H, 9-H, *J* = 13.3, 1.2), 2.34 (ddd, 1H, 3-H, *J* = 13.4, 1.8, 1.5), 3.40 (ddd, 1H, 7-H, *J* = 11.7, 5.6, 5.3), 3.83 (s, 3H, OCH$_3$), 4.41 (br s, 1H, 15-H), 4.48 (dd, 1H, 8-H, *J* = 4.7, 3.5), 4.75 (br s, 1H, 15-H), 6.93 (d, 2H, 3',5'-H, *J* = 8.8), 7.37 (s, 1H, 13-H), 7.48 (d, 2H, 2',6'-H, *J* = 8.8). ^{13}C NMR (δ, ppm): 17.66 (q, C-14), 22.72 (t, C-2), 24.54 (t, C-6), 34.50 (s, C-10), 36.85 (t, C-3), 39.46 (d, C-7), 41.38 (t, C-9), 42.19 (t, C-1), 46.37 (d, C-5), 55.32 (q, OCH$_3$), 76.84 (d, C-8), 106.67 (t, C-15), 114.48 (d, C-3',5'), 126.84 (s, C-1'), 129.67 (s, C-11), 131.45 (d, C-2',6'), 134.72 (d, C-13), 149.13 (s, C-4), 168.80 (s, C-4'), 172.77 (s, C-12).

For C$_{22}$H$_{26}$O$_3$ anal. calcd. (%): C, 78.07; H, 7.74. Found (%): C, 78.01; H, 7.95.

(3a*R*,4a*S*,8a*R*,9a*R*,*E*)-3-(4-Dimethoxybenzylidene)-8a-methyl-5-methylenedecahydronaphtho[2,3-*b*]furan-2(3*H*)-one (4). Yield 81%, mp 160–162°C (from ethanol), [α]$_{589}$ +534 (*c* 1.047, CHCl$_3$). IR (ν, cm^{-1}): 808, 890, 1001, 1033, 1139, 1172, 1214, 1248, 1272, 1327, 1337, 1464, 1520, 1594, 1651, 1743 (C=O). UV (chloroform, λ$_{\max}$, nm (logε)): 246 (4.13), 326 (4.32). ^{1}H NMR (CDCl$_3$, δ, ppm, *J*, Hz): 0.81 (s, 3H, 14-H3), 1.22 (m, 1H, 1-H), 1.34 (ddd, 1H, 6-H, *J* = 13.0, 12.8, 12.6), 1.45–1.58 (m, 4H, 1,2,2,9-H), 1.87 (d, 1H, 5-H, *J* = 12.9), 1.91–2.04 (m, 2H, 3,6-H), 2.19 (d, 1H, 9-H, *J* = 15.5), 2.28 (d, 1H, 3-H, *J* = 13.2), 3.37 (ddd, 1H, 7-H, *J* = 11.4, 5.6, 5.5), 3.82 (s, 3H, OCH$_3$), 3.85 (s, 3H, OCH$_3$), 4.36 (br s, 1H, 15-H), 4.44 (dd, 1H, 8-H, *J* = 4.1, 3.6), 4.70 (br s, 1H, 15-H), 6.86 (d, 1H, 5'-H, J = 8.5), 6.97 (s, 1H, 2'-H), 7.12 (d, 1H, 6'-H, *J* = 7.0), 7.30 (s, 1H, 13-H). ^{13}C NMR (δ, ppm): 17.47 (q, C-14), 22.53 (t, C-2), 24.56 (t, C-6), 34.34 (s, C-10), 36.68 (t, C-3), 39.40 (d, C-7), 41.21 (t, C-9), 42.02 (t, C-1), 46.20 (d, C-5), 55.76 (q, two OCH$_3$), 76.66 (d, C-8), 106.48 (t, C-15), 111.22 (d, C-6'), 112.72 (d, C-2'), 122.92 (d, C-5'), 126.97 (s, C-1'), 129.93 (s, C-11), 134.84 (d, C-13), 148.88 (s, C-4,3'), 150.37 (s, C-4'), 172.44 (s, C-12).

For C$_{23}$H$_{28}$O$_4$ anal. calcd. (%): C, 74.97; H, 7.66. Found (%): C, 74.90; H, 7.92.

(3a*R*,4a*S*,8a*R*,9a*R*,*E*)-3-(2-Methylthiobenzylidene)-8a-methyl-5-methylenedecahydronaphtho[2,3-*b*]furan-2(3*H*)-one (5). Yield 79%, mp 95–98°C, [α]$_{589}$ + 355 (*c* 1.126, CHCl$_3$). IR (ν, cm^{-1}): 748, 759, 898, 1103, 1171, 1218, 1440, 1647, 1746 (C=O). UV (chloroform, λ$_{\max}$, nm (logε)): 257 (4.16), 283 (3.98), 338 (3.46). ^{1}H NMR (CDCl$_3$, δ, ppm, *J*, Hz): 0.83 (s, 3H, 14-H3), 1.21 (ddd, 1H, H^1, *J* = 12.7, 12.3, 5.8), 1.44 (ddd, 1H, 6-H, *J* = 13.4, 12.6, 12.3), 1.48–1.57 (m, 4H, 1,2,2,9-H), 1.80 (ddd, 1H, 6-H, *J* = 14.0, 6.7, 2.4), 1.83 (br d, 1H, 5-H, *J* = 14.0), 1.97 (ddd, 1H, 3-H, *J* = 12.6, 12.0, 6.2), 2.18 (br d, 1H, 9-H, *J* = 15.5), 2.29 (br d, 1H, 3-H, *J* = 13.0), 2.43 (s, 3H, SCH$_3$), 3.22 (ddd, 1H, 7-H, *J* = 11.8, 6.0, 5.3), 4.39 (br d, 1H, 15-H), 4.46 (dd, 1H, 8-H, *J* = 4.6, 4.5), 4.73 (br s, 1H, 15-H), 7.15 (br dd, 1H, 4'-H, *J* = 7.5, 7.0), 7.27 (br d, 1H, 6'-H, *J* = 7.8), 7.31 (br dd, 1H, 5'-H, *J* = 8.0, 6.9), 7.39 (br d, 1H, 3'-H, *J* = 7.6), 7.76 (s, 1H, 13-H). ^{13}C NMR (δ, ppm): 16.15 (q, SCH$_3$), 17.66 (q, C-14), 22.64 (t, C-2), 25.73 (t, C-6), 34.33 (s, C-10), 36.74 (t, C-3), 39.10 (d, C-7), 41.24 (t, C-9), 42.05 (t, C-1), 46.27 (d, C-5), 77.03 (d, C-8), 106.54 (t, C-15), 125.11 (d, C-5'), 126.49 (d, C-6'), 127.88 (d, C-3'), 129.63 (d, C-4'), 132.08 (d, C-13), 133.12 (s, C-1'), 134.53 (s, C-11), 139.67 (s, C-2'), 149.04 (s, C-4), 171.69 (s, C-12).

For C$_{22}$H$_{26}$O$_2$S anal. calcd. (%): C, 74.54; H, 7.39; S, 9.05. Found (%): C, 74.42; H, 7.35; S, 9.02.

(4a*S*,8a*R*,9a*R*)-3-(4-Methoxybenzyl)-8a-methyl-5-methylene-4a,5,6,7,8,8a,9,9a-octahydronaphtho[2,3-*b*]furan-2(4*H*)-one (6). Yield 9%, mp 136–139°C (from ethyl acetate), [α]$_{589}$ +125 (*c* 0.733, CHCl$_3$). IR (ν, cm^{-1}): 895, 1017, 1045, 1055, 1177, 1247, 1512, 1678, 1746 (C=O). ^{1}H NMR (CDCl$_3$, δ, ppm, *J*, Hz): 0.86 (s, 3H, 14-H$_3$), 1.12 (dd, 1H, 9-H, *J* = 12.2, 11.7), 1.29 (ddd, 1H, 1-H, *J* = 13.7, 13.2, 4.9), 1.54–1.62 (m, 3H, 1,2,2-H), 1.70 (br d, 1H, 5-H, *J* = 10.8), 1.94 (ddd, 1H, 3-H, *J* = 12.7, 12.7, 5.4), 2.26–2.36 (m, 3H, 3,6,9-H), 2.74 (dd, 1H, 6-H, *J* = 13.7, 3.9), 3.48 (d, 1H, 13-H, *J* = 14.7), 3.55 (d, 1H, 13-H, *J* = 14.7), 3.75 (s, 3H, OCH$_3$), 4.54 (br s, 1H, 15-H), 4.81 (m, 1H, 8-H), 4.84 (br s, 1H, 15-H), 6.79 (ddd, 2H, 3',5'-H, *J* = 8.3, 2.9, 2.2), 7.13 (ddd, 2H, 2',6'-H, *J* = 8.3, 3.2, 2.2). ^{13}C NMR (δ, ppm): 16.01 (q, C-14), 21.87 (t, C-2), 25.33 (t, C-6), 27.98 (t, C-13), 35.82 (t, C-3), 36.48 (s, C-10), 40.33 (t, C-1), 47.14 (t, C-9), 49.58 (d, C-5), 54.81 (q, OCH$_3$), 77.47 (d, C-8), 106.53 (t, C-15), 113.58 (d, C-3',5'), 123.51 (s, C-1'), 128.96 (d, C-2',6'), 130.04 (s, C-11), 147.88 (s, C-4), 157.77 (s, C-4'), 162.94 (s, C-7), 173.66 (s, C-12). MS (*m*/*z* (I_{rel}, %)): 340 (3), 339 (24), 338 (100), 293 (74), 215 (30), 171 (19), 123 (20), 121 (51).

For C$_{22}$H$_{26}$O$_3$ calcd.: M = 338.1876. Found: *m*/*z* 338.1872 [M]$^+$.

(4a*S*,8a*R*,9a*R*)-3-(3,4-Dimethoxybenzyl)-8a-methyl-5-methylene-4a,5,6,7,8,8a,9,9a-octahydronaphtho[2,3-*b*]furan-2(4*H*)-one (7). Yield 13%. Oily matter. ^{1}H NMR (CDCl$_3$, δ, ppm, *J*, Hz): 0.87 (s, 3H, 14-H$_3$), 1.12 (dd, 1H, 9-H, *J* = 11.8, 11.8), 1.29 (ddd, 1H, 1-H, *J* = 13.3, 13.3, 5.3), 1.55–1.64 (m, 3H, 1,2,2-H), 1.80 (dddd, 1H, 5-H, *J* = 12.5, 3.3, 1.7, 1.3), 1.93 (ddd, 1H, 3-H, *J* = 12.8, 12.8, 5.8), 2.28 (m, 1H, 6-H), 2.30 (dd, 1H, 9-H, *J* = 12.3, 6.4), 2.36 (dddd, 1H, 3-H, *J* = 13.4, 3.8, 2.2, 1.8), 2.77 (dd, 1H, 6-H, *J* = 13.8, 3.8), 3.50 (d, 1H, 13-H, *J* = 15.5), 3.56 (d, 1H, 13-H, *J* = 14.8), 3.83 (s, 3H, OCH$_3$), 3.84 (s, 3H, OCH$_3$), 4.55 (dd, 1H, 15-H,

J = 3.0, 1.2), 4.84 (dd, 1H, 8-H, J = 11.5, 6.3), 4.85 (dd, 1H, 15-H, J = 2.8, 1.4), 6.73 (dd, 1H, 6'-H, J = 8.2, 2.0), 6.76 (d, 1H, 5'-H, J = 8.2), 6.81 (d, 1H, 2'-H, J = 2.0). ^{13}C NMR (δ, ppm): 16.35 (q, C-14), 22.18 (t, C-2), 25.70 (t, C-6), 28.77 (t, C-13), 36.14 (t, C-10), 36.83 (s, C-3), 40.68 (t, C-1), 47.55 (t, C-9), 49.97 (d, C-5), 55.72 (q, two OCH_3), 77.82 (d, C-8), 106.89 (t, C-15), 111.15 (d, C-6'), 111.67 (d, C-2'), 120.04 (d, C-5'), 123.76 (s, C-1'), 130.97 (s, C-11), 147.53 (s, C-3'), 148.17 (s, C-4), 148.99 (s, C-4'), 163.41 (s, C-7), 174.05 (s, C-12).

For $C_{23}H_{28}O_4$ anal. calcd. (%): C, 74.97; H, 7.66. Found (%): C, 74.90; H, 7.92.

(4a*S*,8a*R*,9a*R*)-3-(2-Methylthiobenzyl)-8a-methyl-5-methylene-4a,5,6,7,8,8a,9,9a-octahydronaphtho[2,3-*b*]furan-2(4*H*)-one (8). Yield 17%, mp 112–113°C (from ethanol). IR (ν, cm^{-1}): 755, 906, 1015, 1058, 1099, 1128, 1223, 1265, 1584, 1543, 1680, 1748 (C=O). UV (ethanol, λ_{max}, nm (logε)): 210 (4.07), 251 (3.15), 292 (1.36). ^{1}H NMR ($CDCl_3$, δ, ppm, J, Hz): 0.85 (s, 3H, 14-H_3), 1.16 (dd, 1H, 9-H, J = 11.8, 11.8), 1.30 (m, 1H, 1-H), 1.53–1.61 (m, 3H, 1,2,2-H), 1.79 (br d, 1H, 5-H, J = 11.1), 1.91 (ddd, 1H, 3-H, J = 13.0, 13.0, 5.8), 2.18 (dd, 1H, 3-H, J = 13.7, 13.1), 2.28–2.34 (m, 2H, 6,9-H), 2.44 (s, 3H, SCH_3), 2.67 (dd, 1H, 6-H, J = 14.0, 3.5), 3.66 (d, 1H, 13-H, J = 15.8), 3.71 (d, 1H, 13-H, J = 16.0), 4.44 (d, 1H, 15-H, J = 1.3), 4.78 (d, 1H, 15-H, J = 1.3), 4.85 (dd, 1H, 8-H, J = 11.3, 6.3), 7.09 (m, 1H, 4'-H), 7.18–7.23 (m, 3H, 3',5',6'-H). ^{13}C NMR (δ, ppm): 15.97 (q, C-14), 16.37 (q, SCH_3), 22.20 (t, C-2), 25.76 (t, C-6), 27.41 (t, C-13), 36.13 (t, C-3), 36.67 (s, C-10), 40.70 (t, C-1), 47.57 (t, C-9), 49.83 (d, C-5), 77.89 (d, C-8), 106.76 (t, C-15), 121.91 (s, C-1'), 125.01 (d, C-3'), 125.77 (d, C-5'), 127.24 (d, C-6'), 129.27 (d, C-4'), 135.70 (s, C-11), 137.16 (s, C-2'), 148.15 (s, C-4), 164.42 (s, C-7), 173.91 (s, C-12). MS (m/z (I_{rel}, %)): 356 (8), 355 (25), 354 (100), 339 (14), 307 (40), 293 (21), 137 (50), 121 (51). For $C_{22}H_{26}O_2S$ calcd.: M = 354.1648. Found: m/z 354.1647 $[M]^+$.

(3a*R*,8a*R*,9a*R*,*E*)-3-(3,4-Dimethoxybenzylidene)-5,8a-dimethyl-3,3a,6,7,8,8a,9,9a-octahydronaphtho[2,3-*b*]furan-2(5*H*)-one (9). Yield 20%. Oily matter. IR (ν, cm^{-1}): 759, 1024, 1140, 1182, 1232, 1250, 1275, 1331, 1420, 1464, 1516, 1597, 1645, 1745 (C=O). UV (λ_{max}, nm (logε)): 240 (4.05), 328 (4.19). ^{1}H NMR ($CDCl_3$, δ, ppm, J, Hz): 1.04 (d, 3H, 15-H_3, J = 7.6), 1.14 (ddd, 1H, 1-H, J = 13.5, 13.2, 3.5), 1.25 (s, 3H, 14-H_3), 1.38–1.60 (m, 5H, 1,2,3,3,9-H), 1.82 (m, 1H, 2-H), 2.13 (dd, 1H, 9-H, J = 14.7, 2.9), 2.40 (ddd, 1H, 3-H, J = 7.9, 4.4, 3.0), 3.90 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 4.07 (ddd, 1H, 7-H, J = 6.5, 2.5, 1.8), 4.79 (ddd, 1H, 8-H, J = 6.4, 3.0, 2.6), 5.39 (d, 1H, 6-H, J = 3.5), 6.91 (d, 1H, 5'-H, J = 8.5), 7.09 (d, 1H, 2'-H, J = 2.0), 7.21 (dd, 1H, 6'-H, J = 8.2, 2.0), 7.39 (d, 1H, 13-H, J = 1.8). ^{13}C NMR (δ, ppm): 16.76 (t, C-2), 22.37 (q, C-15), 28.54 (q, C-14), 32.80 (s, C-10), 32.83 (t, C-3), 38.03 (d, C-4), 38.87 (d, C-7), 41.96 (t, C-1), 42.44 (t, C-9), 55.95 (q, OCH_3), 76.17 (d, C-8), 111.33 (d, C-5'), 112.76 (d, C-2'), 114.53 (d, C-6), 123.71 (d, C-6'), 127.11 (s, C-11), 128.23 (s, C-1'), 135.81 (d, C-13), 149.13 (s, C-4'), 150.30 (s, C-5), 150.60 (s, C-3'), 172.38 (s, C-12). MS (m/z (I_{rel}, %)): 370 (5), 369 (28), 368 (100), 337 (21), 323 (42), 307 (35), 305 (43), 241 (18), 165 (20), 152 (25), 151 (69), 138 (20), 105 (21).

For $C_{23}H_{28}O_4$ calcd.: M = 368.1982. Found: m/z 368.1978 $[M]^+$.

(8a*R*,9a*R*)-3-(3,4-Dimethoxybenzyl)-5,8a-dimethyl-6,7,8,8a,9,9a-hexahydronaphtho[2,3-*b*]furan-2(5*H*)-one (10). Yield 36%. Oily matter. [$[\alpha]_{589}$ –123 (c 0.780, $CHCl_3$). IR (ν, cm^{-1}): 732, 756, 1029, 1059, 1107, 1140, 1237, 1262, 1341, 1419, 1464, 1515, 1590, 1658, 1746 (C=O). UV (λ_{max}, nm (logε)): 234 (4.00), 280 (4.19). ^{1}H NMR ($CDCl_3$, δ, ppm, J, Hz): 1.15 (d, 3H, 15-H_3, J = 6.3), 1.27 (m, 1H, 1-H), 1.29 (s, 3H, 4-H_3), 1.41–1.45 (m, 2H, 2,9-H), 1.56–1.61 (m, 3H, 1,3,3-H), 1.81 (ddddd, 1H, 2-H, J = 13.7, 13.3, 13.2, 3.9, 3.4), 2.04 (dd, 1H, 9-H, J = 11.7, 4.9), 2.57 (ddd, 1H, 4-H, J = 12.7, 7.3, 5.8), 3.47 (d, 1H, 13-H, J = 14.7), 3.55 (d, 1H, 13-H, J = 15.1), 3.79 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 4.95 (dd, 1H, 8-H, J = 13.2, 4.9), 6.09 (s, 1H, 6-H), 6.72 (dd, 1H, 6'-H, J = 8.1, 1.7), 6.73 (d, 1H, 5'-H, J = 8.1), 6.79 (d, 1H, 2'-H, J = 1.4). ^{13}C NMR (δ, ppm): 16.40 (t, C-2), 22.18 (q, C-15), 26.01 (q, C-14), 28.96 (t, C-13), 32.46 (t, C-3), 38.04 (s, C-10), 38.18 (d, C-4), 41.77 (t, C-1), 46.67 (t, C-9), 55.72 (q, OCH_3), 75.95 (d, C-8), 111.15 (d, C-5'), 111.93 (d, C-2'), 113.97 (d, C-6), 119.60 (s, C-11), 120.29 (d, C-6'), 130.98 (s, C-1'), 147.50 (s, C-3'), 148.82 (s, C-4'), 157.70 (s, C-7), 162.25 (s, C-5), 174.76 (s, C-12). MS (m/z (I_{rel}, %)): 370 (4), 369 (27), 368 (100), 323 (73), 324 (19), 246 (30), 215 (18), 201 (21), 171 (12), 151 (38).

For $C_{23}H_{28}O_4$ calcd.: M = 368.1982. Found: m/z 368.1985 $[M]^+$.

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REFERENCES

1. Zhang, S., Wong, Y.K., Ong, C.N., and Shen, H.M., *Curr. Med. Chem. Anticancer Agents*, 2005, vol. 5, pp. 239–249.
2. Schmidt, T.J., Lyss, G., Pahl, H.L., and Merfort, I., *Bioorg. Med. Chem.*, 1999, vol. 7, pp. 2849–2855.

3. Konishi, T., Shimada, Y., Nagao, T., Okabe, H., and Konoshimq, T., *Biolog. Pharm. Bull.*, 2002, vol. 25, p. 1370.
4. Bai, N., Lai, C.-S., He, K., Zhou, Z., Zhang, L., Quan, Z., Zhu, N., Zheng, Q.Y., Pan, M.-H., and Ho, S.-T., *J. Nat. Prod.*, 2006, vol. 69, pp. 531–535.
5. Bang, M.-H., Han, M.-W., Song, M.-C., Cho, J.-G., Chung, H.G., Jeong, T.-S., Lee, K.-T., Choi, M.-S., Kim, S.Y., and Baek, N.-I., *Chem. Pharm. Bull.*, 2008, vol. 56, p. 1168.
6. Triana, J., Eiroa, J.L., Ortega, J.J., Leon, F., Brouard, I., Torres, F., Quintana, J., Estevez, F., and Bermejo, J., *J. Nat. Prod.*, 2008, vol. 71, pp. 2015–2020.
7. Adekenov, S.M., *Ros. Bioterapevt. Zh.*, 2005, vol. 2, pp. 7–14.
8. Milman, I.A., *Khim. Prir. Soedin.*, 1990, vol. 3, pp. 307–320.
9. Larhed, M. and Hallberg, A., in *Handbook of Organopalladium Chemistry for Organic Synthesis,* New York: Wiley, 2002.
10. Shul'pin, G.B., *Organicheskie reaktsii, kataliziruemye kompleksami metallov* (Organic Reactions Catalyzed by Metal Complexes), Moscow: Nauka, 1988.
11. Srivastava, S.C., Mehra, M.M., Trivedi, G.K., and Bhattacharyy, S.C., *Indian J. Chem.*, 1971, vol. 9, pp. 512–514.