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LETTERS TO THE EDITOR

Biomimetic Cyclization of *E*,*E*-Germacranolide (+)-Hanphilline

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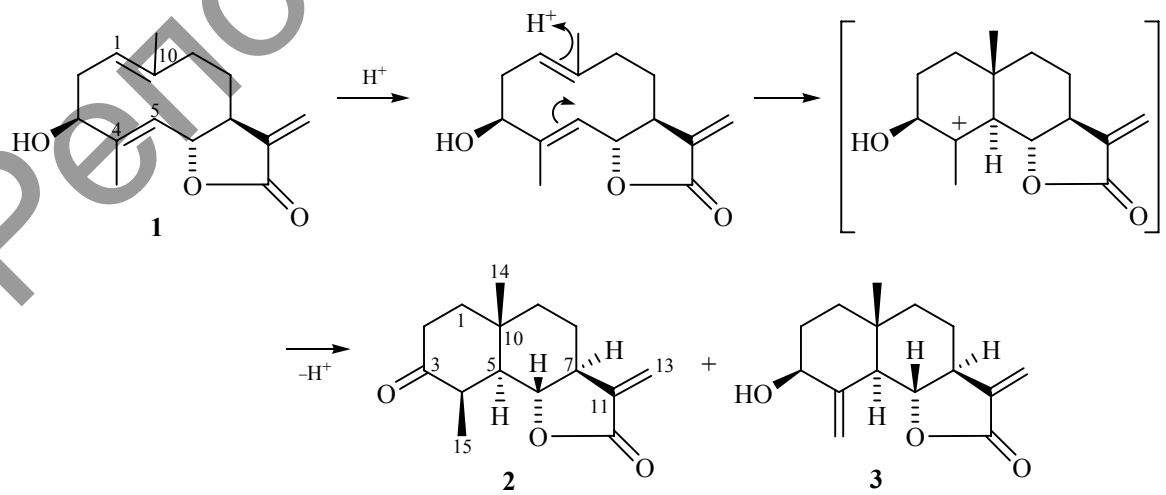
In continuation of our studies on biomimetic transformations of sesquiterpene γ-lactones of the germacranolide and guaian types [1, 2], we have performed stereoselective transannular cyclization of *E*,*E*-germacranolide hanphilline **1**, isolated from noble yarrow (*Achillea nobilis L.*), in the presence of cation exchange resin Amberlite IR-120 in dioxane. The reaction results in the formation of *trans*-fused 5α(H),10β(CH_3)-eudesmanolides **2** and **3** in 71 and 19% yield, respectively. The obtained compounds are the analogs of plant metabolites, *trans*-eudesmanolides epiartekalin and ridentin-β [3, 4] (Scheme 1).

Apparently, the acid-catalyzed carbocyclization of compound **1** proceeds via chemoselective protonation of the most electron-donor and sterically accessible $\Delta^{1.10}$-double bond of the compound with subsequent stereoselective nucleophilic attack of the $\Delta^{4.5}$-double bond leading via the intermediately formed tertiary cation to the *trans*-fused eudesmanolides **2** and **3**.

Synthesis of compounds 2 and 3. To the solution of 1.2 mmol of compound **1** in 20 mL of dioxane at room temperature 0.3 g of cation exchange resin Amberlite IR-120 was added. The reaction mixture was stirred at 40–50°C for 72 h, then poured into water and extracted with $CHCl_3$. The organic layer was washed with 10% $NaHCO_3$ solution (3 × 10 mL), water (3 × 10 mL), dried over $MgSO_4$, and evaporated. The residue (0.40 g) was chromatographed on a column paced with silica gel (eluent – hexane–ethyl acetate, 2 : 3 and 1 : 4).

Scheme 1.



(3a*S*,5a*S*,9*R*,9a*S*,9b*S*)-5a,9-Dimethyl-3-methylideneoctahydronaphtho[1,2-*b*]furan-2,8(3*H*,4*H*)-dione (2). Yield 71%, colorless crystals, mp 136–138°C, R_f 0.54 (hexane–ethyl acetate, 2 : 3), $[\alpha]_D^{18}$ 96° (c = 0.02, $CHCl_3$). IR spectrum, ν, cm^{-1}: 1760 (C=O), 1700 (C=O), 1650, 1640 (C=C). ^1H NMR spectrum($CDCl_3$), δ, ppm: 1.68 br.s (3H, CH_3C^4), 4.12 d.d (1H, HC^6, J_{HH} 10.0, 8.5 Hz), 1.43 s (3H, CH_3C^{10}), 5.52 d (1H, HC^{13}, J_{HH} 3.5 Hz), 6.26 d (1H, HC^{13}, J_{HH} 3.5 Hz). Mass spectrum, m/z (I_{rel}, %): 248 (32.4) $[M]^+$. Found, %: C 72.38; H 7.87. $C_{15}H_{20}O_3$. Calculated, %: C 72.58; H 8.06.

(3a*S*,5a*S*,9a*R*,9b*S*)-8-Hydroxy-5a-methyl-3,9-dimethylidenedecahydronaphtho[1,2-*b*]furan-2(3*H*)-one (3). Yield 19%, colorless crystals, mp 175–177°C, R_f 0.37 (hexane–ethyl acetate, 1 : 4), $[\alpha]_D^{18}$ = 106° (c = 0.02, $CHCl_3$). IR spectrum, ν, cm^{-1}: 3500 (OH), 1780 (C=O), 1655, 1640 (C=C). ^1H NMR spectrum, δ, ppm: 0.64 br.s (3H, CH_3C^{10}), 3.98 t (1H, HC^6, J_{HH} 11.0 Hz), 4.00 d.d (1H, HC^3, J_{HH} 10.0, 6.0 Hz), 4.95 br.s (1H, HC^{15}), 5.24 br.s (1H, HC^{15}), 5.39 d (1H, HC^{13}, J_{HH} 3.0 Hz), 6.06 d (1H, HC^{13}, J_{HH} 3.0 Hz). Mass spectrum, m/z (I_{rel}, %): 248 (44.7) $[M]^+$. Found, %: C 72.33; H 7.81. $C_{15}H_{20}O_3$. Calculated, %: C 72.58; H 8.06.

IR spectra were recorded on an Avatar-360 spectrometer in KBr pellets. ^1H NMR spectra were registered on a Jeol ECA-500 spectrometer (500.15 MHz) in $CDCl_3$. Mass spectra were obtained on an Agilent 7890A instrument. Specific rotation was determined on a Perkin-Elmer 141 polarimeter. Melting points were measured on a Boëtius heating block. Thin-layer chromatography was done on Sorbfil PTLC-AF-UV plates.

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