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SHORT COMMUNICATIONS

Reactions of (–)-Estafiatin with Acidic Reagents

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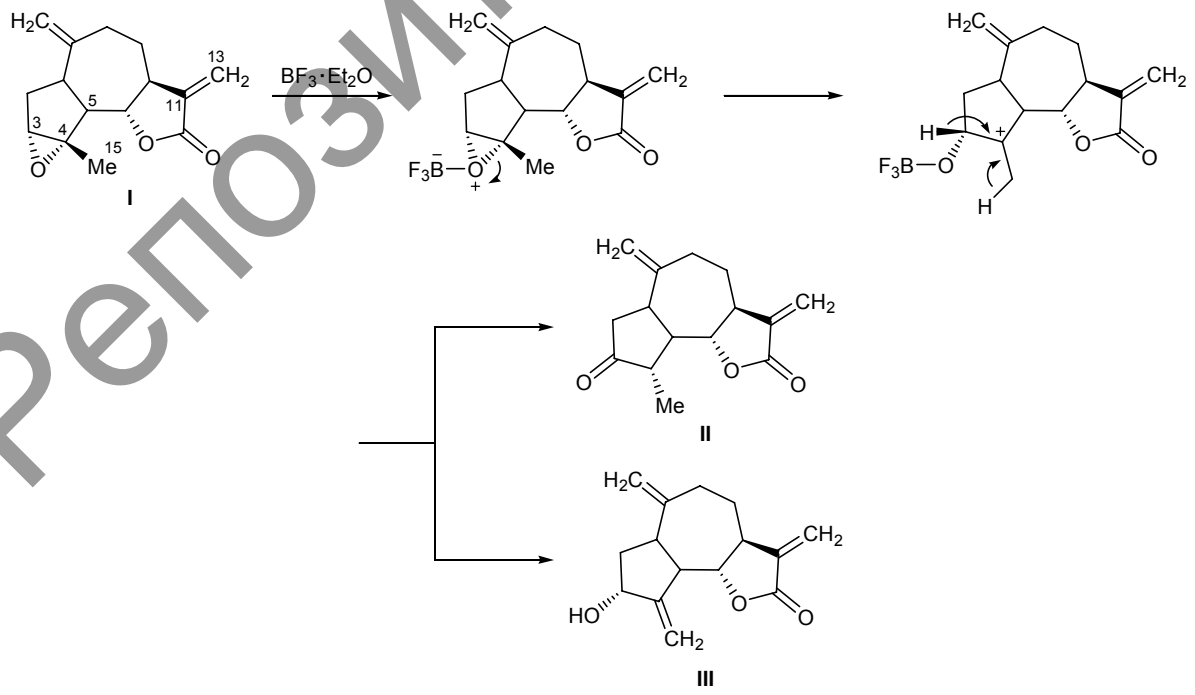
In continuation of our studies in the field of mono- and bicyclic sesquiterpene γ-lactones [1–3], we examined reactions of guaianolide (–)-estafiatin (**I**) isolated from noble yarrow (*Achillea nobilis L.*) with such acidic reagents as boron trifluoride–diethyl ether complex and magnesium bromide. The reaction of **I** with $BF_3 \cdot Et_2O$ in THF at room temperature afforded a mixture of ketone **II** and allylic alcohol **III** in 56 and 40% yield, respectively. Compounds **II** and **III** were isolated previously from plant sources and are known as guaianolides, estafiatone and isozaluzanin C, which exhibit pronounced antitumor activity [4, 5].

A probable mechanism of the formation of compounds **II** and **III** is shown below. Obviously, opening of the oxirane ring with formation of tertiary carbocation is followed by stereoselective 1,2-hydride shift leading to ketone **II** with the inversed configuration of C^4, while regioselective elimination of proton from C^{15} yields allylic alcohol **III**.

We also found that the reaction direction is largely determined by the reaction medium. When the reaction of estafiatin (**I**) with $BF_3 \cdot Et_2O$ was carried out in methylene chloride or chloroform at room temperature, the only product was ketone **II** (yield 98–99%).

Estafiatone (II) and isozaluzanin C (III). Boron trifluoride–diethyl ether complex, 0.3 ml, was added at room temperature to a solution of 0.50 g (2 mmol) of compound **I** in 5 ml of anhydrous tetrahydrofuran. The mixture was stirred for 30 min at room temperature, the solvent was distilled off under reduced pressure,



the residue was dissolved in 20 ml of chloroform, and the solution was washed with water (3×10 ml), dried over $MgSO_4$, and evaporated. According to the TLC data, the residue, 0.54 g, was a mixture of two compounds with R_f 0.72 and 0.60; the products were separated by column chromatography on silica gel using hexane–ethyl acetate (3:2 and 2:3) as eluent.

Compound **II**. Yield 0.28 g (56%), R_f 0.72 (diethyl ether), colorless crystals, mp 140–142°C, $[\alpha]_D^{19}$ = +126° (c = 0.05, $CHCl_3$). IR spectrum, ν, cm^{-1}: 1780 (C=O), 1745 (C=O), 1680, 1655 (C=C). ^1H NMR spectrum, δ, ppm: 1.22 d (3H, 4-CH_3, J_{HH} = 6.0 Hz), 3.95 t (1H, 6-H, J_{HH} = 8.5 Hz), 5.52 d and 6.22 d (1H each, 13-H, J_{HH} = 3.0 Hz), 4.62 br.s and 4.92 br.s (1H each, 14-H). Found, %: C 72.97; H 7.21. $C_{15}H_{18}O_3$. Calculated, %: C 73.17; H 7.31.

Compound **III**. Yield 0.20 g (40%), R_f 0.60 (hexane–diethyl ether, 2:3), colorless crystals, mp 142–144°C (from Et_2O). IR spectrum, ν, cm^{-1}: 3500 (OH), 1780 (C=O), 1680, 1655 (C=C). ^1H NMR spectrum, δ, ppm: 4.68 t (1H, 3-H, J_{HH} = 8.0 Hz), 3.98 t (1H, 6-H, J_{HH} = 9.0 Hz), 5.48 d and 6.21 d (1H each, 13-H, J_{HH} = 3.5 Hz), 4.78 br.s and 4.92 br.s (1H each, 14-H), 5.35 br.s and 5.48 br.s (1H each, 15-H). Found, %: C 72.97; H 7.21. $C_{15}H_{18}O_3$. Calculated, %: C 73.17; H 7.31.

The IR spectra were recorded in KBr on a Bruker Avatar-360 spectrometer. The ^1H NMR spectra were obtained on a Bruker WP-300 SY instrument (300.13 MHz) from solutions in $CDCl_3$ using tetramethylsilane as internal reference.

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