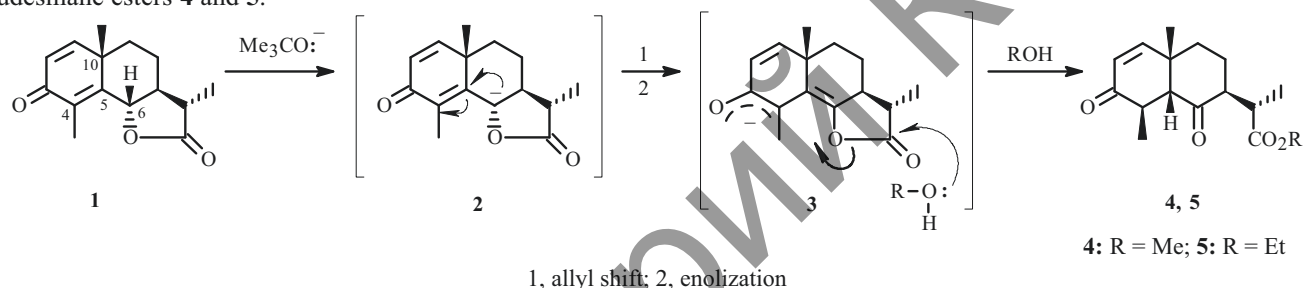


STEREOSELECTIVE SYNTHESIS OF *cis*-EUDESMANE ESTERS BASED ON (–)- α -SANTONIN

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In continuation of research on the chemistry of natural eudesmane and germacrane sesquiterpene γ -lactones [1–4], we studied intramolecular cross-couplings of the eudesmanolide (–)- α -santonin (**1**) with the base Me_3COK –DMSO– Me_3COH . Reaction of **1** with the base followed by reaction with MeOH and EtOH formed stereoselectively *cis*-condensed-10 β (CH₃),5 β (H),4 β (CH₃)-6-keto-eudesmane esters **4** and **5** in 70 and 76% yields, respectively.

Compound **1** under the reaction conditions initially formed anion **2** and initiated subsequent steps of intramolecular electrophilic rearrangements to give enolate-ion **3**, which then underwent nucleophilic attack by alcohol to afford *cis*-condensed eudesmane esters **4** and **5**.



IR spectra were recorded in KBr pellets on an Avatar-360 spectrometer. PMR spectra were taken in CDCl_3 on a JEOL ECA-500 instrument (operating frequency 500.15 MHz). Mass spectra were measured on an Agilent 7890A instrument. Specific rotation was determined on a PerkinElmer 141 polarimeter. Melting points were measured on a Boetius compact apparatus. TLC used Sorbfil PTSKh-AF-UF plates.

Synthesis of Eudesmane Esters 4 and 5. A solution of *t*-BuOK in Me_3COH and DMSO [prepared from metallic K (0.03 g), alcohol (1 mL), and DMSO, 1.5 mL] at room temperature under Ar was treated with **1** (0.2 g, 0.8 mmol), stirred at room temperature for 7 min, treated with MeOH or EtOH (0.15 mL), and stored for another 40 min. The alcohol was distilled off *in vacuo*. The residue was dissolved in EtOAc, washed with H_2O (3 \times 10 mL), and dried over MgSO_4 . The solvent was evaporated *in vacuo*. The residue (0.3 g) was chromatographed over a column of silica gel (eluent hexane–EtOAc, 4:1).

Methyl 2-[(2*S*,4*aR*,8*R*,8*aRa*)-1,7-Dioxo-1,2,3,4,4*a*,7,8,8*a*-octahydronaphthalen-2-yl]propanoate [Methyl-10 β (CH₃),5 β (H),4 β (CH₃)-6-ketoeudesmane Ester] (4**). Yield 0.39 g (70%), colorless oily compound, R_f 0.67 (hexane–EtOAc, 3:2), $[\alpha]_D^{20} -106^\circ$ (*c* 0.05; CHCl_3). IR spectrum (ν , cm^{-1}): 1730 (C=O), 1710 (C=O), 1630 (C=C). ^1H NMR spectrum (500 MHz, CDCl_3 , δ , ppm, J/Hz): 5.94 (1H, d, J = 10.0, H-1), 6.58 (1H, d, J = 10.0, H-2), 1.26 (3H, d, J = 6.0, CH₃-13), 1.06 (3H, s, CH₃-14), 1.05 (3H, d, J = 6.6, CH₃-15), 4.10 (3H, s, CH₃-16). Mass spectrum (EI, 70 eV), m/z (I_{rel} , %): 278 (M^+ , 40.4).**

Ethyl 2-[(2*S*,4*aR*,8*R*,8*aRa*)-1,7-Dioxo-1,2,3,4,4*a*,7,8,8*a*-octahydronaphthalen-2-yl]propanoate [Ethyl-10 β (CH₃),5 β (H),4 β (CH₃)-6-ketoeudesmane Ester] (5**). Yield 0.44 g (76%), colorless crystals, mp 94–96°C, R_f 0.65 (hexane–EtOAc, 3:2), $[\alpha]_D^{18} -90^\circ$ (*c* 0.05; CHCl_3). IR spectrum (ν , cm^{-1}): 1732 (C=O), 1710 (C=O), 1630 (C=C). ^1H NMR spectrum (500 MHz, CDCl_3 , δ , ppm, J/Hz): 5.94 (1H, d, J = 10.0, H-1), 6.58 (1H, d, J = 10.0, H-2), 1.18 (3H, d, J = 7.1, CH₃-13), 1.06 (3H, s, CH₃-14), 1.05 (3H, d, J = 6.6, CH₃-15), 4.20 (2H, m, H-16), 1.27 (3H, t, J = 7.2, CH₃-17). Mass spectrum (EI, 70 eV), m/z (I_{rel} , %): 292 (M^+ , 41).**

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Репозиторий Қарғу