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

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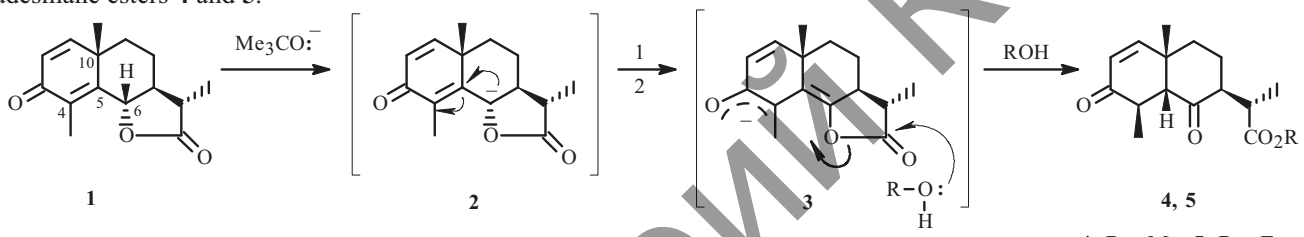
In continuation of research on the chemistry of natural eudesmane and germacrane sesquiterpene γ-lactones [1–4], we studied intramolecular cross-couplings of the eudesmanolide (–)-α-santonin (**1**) with the base Me_3COK–DMSO–Me_3COH. Reaction of **1** with the base followed by reaction with MeOH and EtOH formed stereoselectively *cis*-condensed-10β(CH_3),5β(H),4β(CH_3)-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**.



1, allyl shift; 2, enolization

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 × 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*,4a*R*,8*R*,8a*R*a)-1,7-Dioxo-1,2,3,4,4a,7,8,8a-octahydronaphthalen-2-yl]propanoate [Methyl-10β(CH_3),5β(H),4β(CH_3)-6-ketoeudesmane Ester] (4). Yield 0.39 g (70%), colorless oily compound, R_f 0.67 (hexane–EtOAc, 3:2), $[\alpha]_D^{20}$ –106° (*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, CH_3-13), 1.06 (3H, s, CH_3-14), 1.05 (3H, d, J = 6.6, CH_3-15), 4.10 (3H, s, CH_3-16). Mass spectrum (EI, 70 eV), *m/z* (I_{rel}, %): 278 (M^+, 40.4).

Ethyl 2-[(2*S*,4a*R*,8*R*,8a*R*a)-1,7-Dioxo-1,2,3,4,4a,7,8,8a-octahydronaphthalen-2-yl]propanoate [Ethyl-10β(CH_3),5β(H),4β(CH_3)-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° (*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, CH_3-13), 1.06 (3H, s, CH_3-14), 1.05 (3H, d, J = 6.6, CH_3-15), 4.20 (2H, m, H-16), 1.27 (3H, t, J = 7.2, CH_3-17). Mass spectrum (EI, 70 eV), *m/z* (I_{rel}, %): 292 (M^+, 41).

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