

Synthesis, Structural and Conformational Study of Some Esters Derived from 3-Methyl-3-azabicyclo[3.2.1]octan-8 α -ol

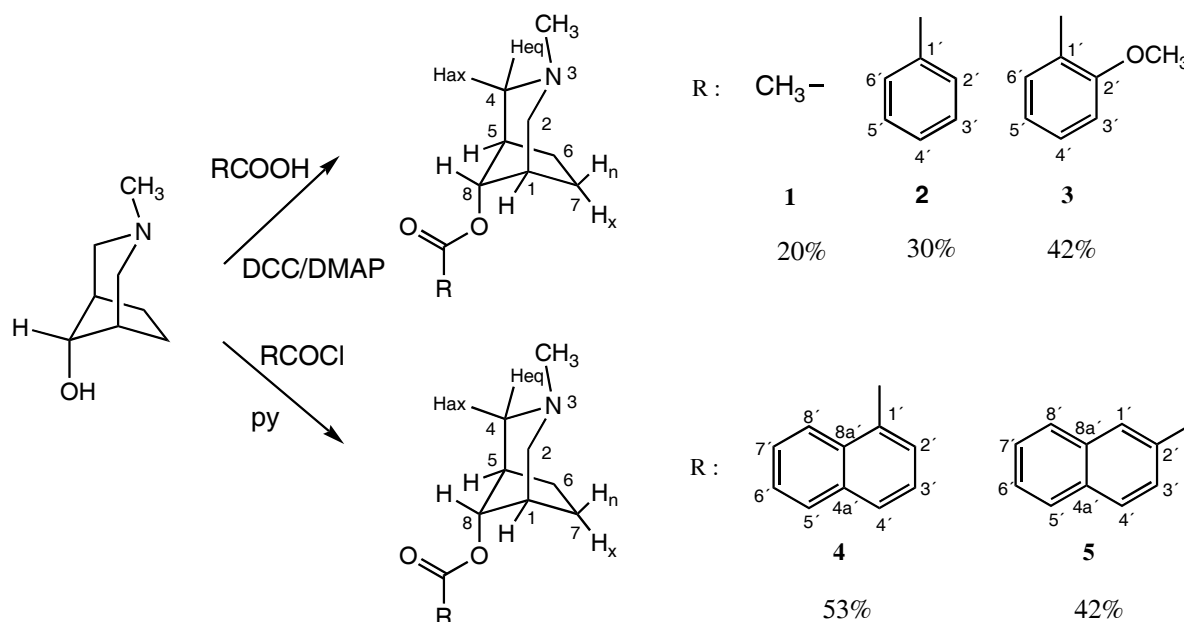
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As a part of a research program related to the synthesis and structural study of potential pharmacologically interesting compounds we have focused our attention on the preparation of some esters derived from 3-methyl-3-azabicyclo[3.2.1]octan-8 α -ol.



For compounds **1**, **2** and **3** higher yields have been obtained starting from the alcohol and the corresponding acid, whereas the reaction between the alcohol and the acyl chloride is the best method to obtain the compounds **4** and **5**.

A detailed study by ¹H and ¹³C NMR has been done to determine the preferred conformations in solution. The assignments of proton and carbon resonances have been made on the basis of the literature data for related systems and double resonance experiments for compound **2**.

The α esters (**1-5**) adopt in CDCl₃ solution a chair envelope conformation with the N-CH₃ group in equatorial position. ³JH₂(4)_{ec}-H₈ > ³JH₂(4)_{ax}-H₈; therefore, the piperidine ring adopts a non-flattened chair conformation. The shape of the signals corresponding to the aromatic protons accounts for a free rotation of the aciloxy group around the C-O bond.

Finally, although compounds **2** and **3** showed analgesics properties, they are much less active than the reference compound (morphine). Compound **2** shows higher potency than compound **3**; therefore, the introduction of the *o*-OCH₃ substituent in the aromatic ring produces a decreasing of the analgesic activity.