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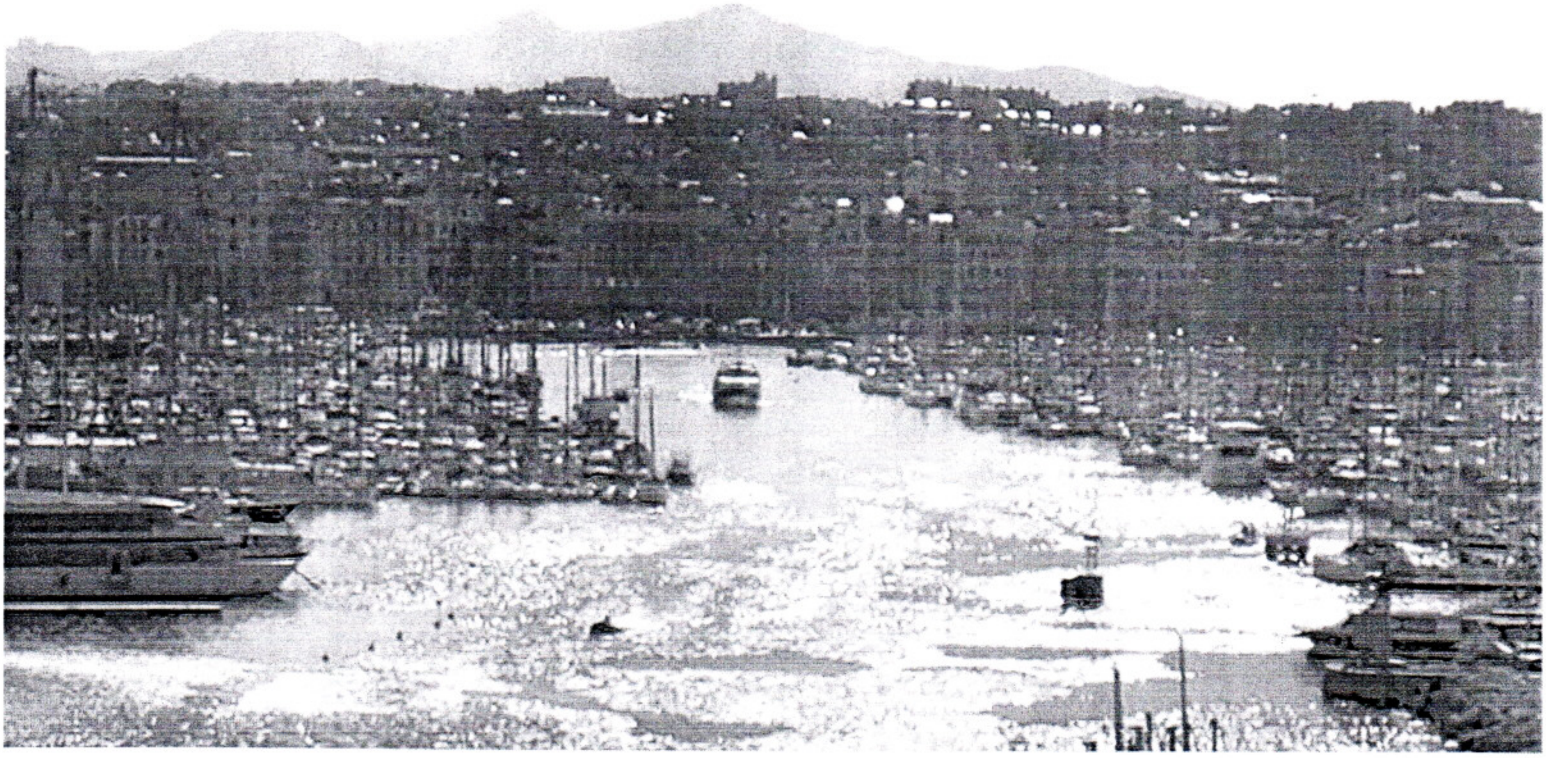


P2-207

Cyclization of monoanilides of arylidene malonic acid

Agnese Stikute, Inese Mierina, Mara Jure

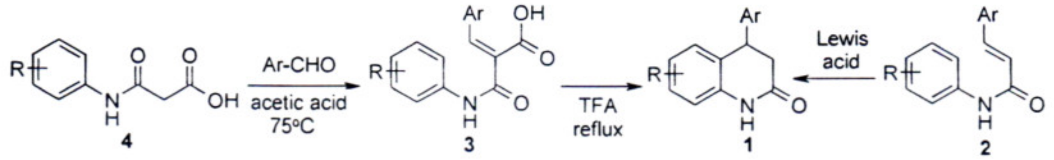
Riga Technical University, Faculty of Material Science and Applied Chemistry, Azenes Str. 14/24, Riga, Latvia, LV 1048

Email: inesem@ktf.rtu.lv - **web page**: http://www.rtu.lv/en/

Compounds containing 3,4-dihydro-1*H*-quinolin-2-one moiety have been studied as potential atypical antipsychotic, antiproliferative and anticonvulsant agents, inhibitors of p38 MAP kinase and blood coagulant factor Xa, as well as antidepressants. 3,4-Dihydro-1*H*-quinolin-2-ones containing hydroxyl group in benzene ring are starting compounds for synthesis of phosphodiesterase inhibitor *Cilostazol* and atypical antipsychotic and antidepressant *Aripiprazole*.

4-Aryl-3,4-dihydro-1*H*-quinolin-2-ones **1** often are synthesized by cyclization of corresponding cinnamoyl anilines **2**. The reaction can be catalyzed by different Lewis acids; unfortunately, in case of $AlCl_3$[1] elimination of aryl group from 4-position of compound **1** may occur. The best choice for the cyclization of cinnamoyl anilines **2** is trifluoroacetic,[2] triflic[3] or polyphosphoric acid.[4]

The most convenient way for synthesis of cinnamoyl anilines **2** is decarboxylation of corresponding arylidene malonic acids **3**. We decided to combine 2 steps – decarboxylation and cyclization – in one pot. We synthesized a range of arylidene malonic acids **3** from malonic acid monoanilides **4** and aromatic aldehydes by Knoevenagel condensation; this reaction was realized by heating in glacial acetic acid at 75°C for 7-40 h. In case of increased reaction temperature decarboxylation of compound **4** was the main reaction, leading to corresponding acetanilide. Treatment of the arylidene malonic acids **3** with trifluoroacetic acid under reflux for 8 h gave 4-aryl-3,4-dihydro-1*H*-quinolin-2-ones **1**. Further we managed to combine all 3 above mentioned steps in one pot and obtained quinolinones **1** without isolation of the intermediates **3**: heating of malonic acid monoanilides **4** with corresponding aromatic aldehyde in trifluoroacetic acid under reflux in most of the cases provided quinolin-2-ones **1** as the only product (the mixture of cyclic compound **1** and cinnamoyl anilide **2** was obtained, when *p*-dialkylaminobenzaldehyde was used). The average duration of the one-pot process was 10-30 h. Antiradical activity of compounds **1** and **2** has been detected; some of them demonstrate antioxidant properties.



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[1] K. M. Johnston, R. M. Luker, G. H. Williams, *J. Chem. Soc. Perkin Transaction. 1* **1972**, 13, 1648-1652.

[2] K. Li, L. N. Foresee, J. A. Tunge, *J. Org. Chem.* **2005**, *70*, 2881-2883.

[3] L. Yu. Safina, G. A. Selivanova, K. Yu. Koltunov, V. D. Shteingarts, *Tetrahedron Lett.* **2009**, *50*, 5245-5247.

[4] (a) R. T. Conley, W. N. Knopka, *J. Org. Chem.* **1964**, *29*, 496-497. (b) K. M. Johnston, *J. Het. Chem.* **1969**, *6*, 847-848.