

PREPARATION OF ISOINDOLE-CONDENSED HETEROCYCLES VIA RETRO DIELS-ALDER REACTIONS

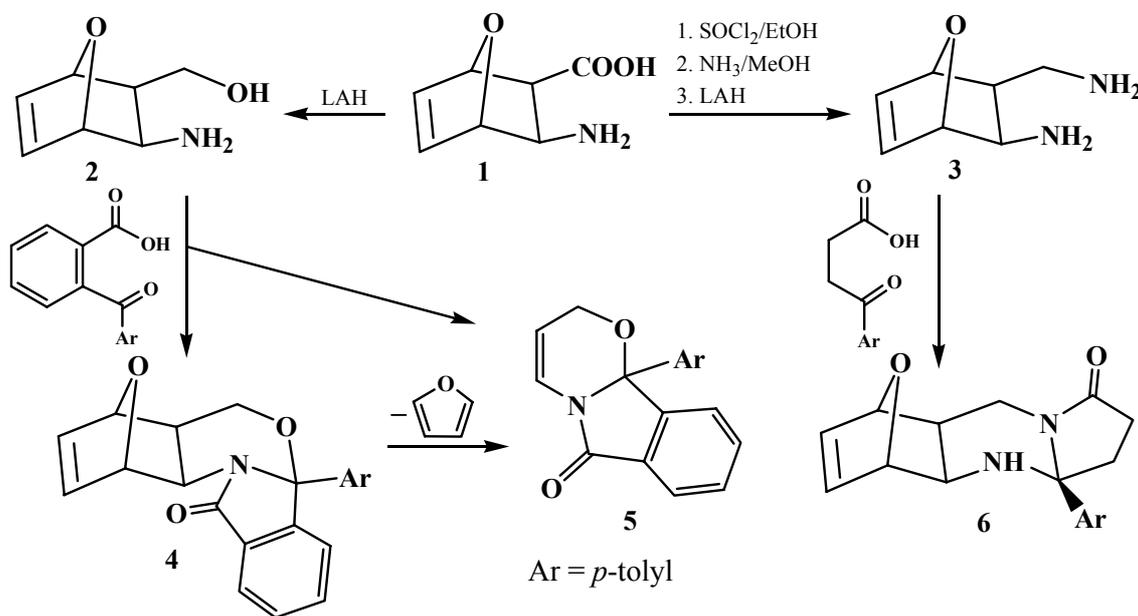
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In our earlier work, the cyclization of *diexo*- and *diendo*-3-aminobicyclo[2.2.1]heptane- and -hept-5-ene-2-carboxylic acids with oxocarboxylic acids resulted in pyrimidinediones, thioxypyrimidinones and 1,3-oxazines. On heating, cyclopentadiene (CP) was cleaved off and mono-, bi- and tricyclic heterocompounds were obtained [1].

As a continuation, furane has now been used as a diene which was expected to be removed more easily than CP. Its Diels-Alder adduct with maleic anhydride was transformed to aminoalcohol **2** by ammonolysis, which was followed Hofmann degradation and reduction of β -aminoacid **1**. Diamine **3** was synthesized by esterification of **1**, then ammonolysis and finally LAH-reduction of the carboxamide. Derivatives **2** and **3** were reacted with the oxocarboxylic acids **A** or **B** to obtain tetra-, penta- and heptacyclic compounds, e.g. **4-6**. On the basis of known compounds with similar structures, anorectic and HIV-1 reverse transcriptase inhibitor effects are expected [2].



Scheme

From **4**, furane was removed by heating, which resulted in 1,3-oxazinoisoindole **5** in good yield, in a basically new preparation. **6** did not undergo the retro Diels-Alder reaction. The structures of the new compounds were established by NMR spectroscopy.

[1] G. Stájer, F. Csende, F. Fülöp, *Curr. Org. Chem.* **2003**, *47*, 1

[2] A. Mertens, H. Zilch, B. König, *J. Med. Chem.* **1993**, *36*, 2526