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Synthesis of Glucose Spiropiperazinone Derivatives

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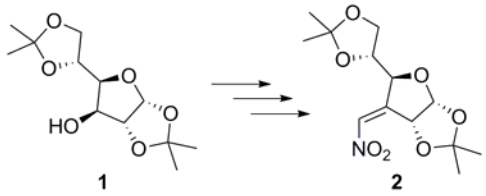
Piperazinone derivatives are noticeable peptidometics [1]; therefore, they can replace peptides, such as RGD [2] and Leu-enkephalin [3] in different biological processes. Some piperazinone derivatives are anticoagulants [4], others act like neurotransmitters.

Herein, we report an approach for the synthesis of novel piperazinone ring containing spiro-derivatives of glucose. Diacetone-α-D-glucose (DAG) **1** was used as an inexpensive and easily available starting material. 3-Deoxy-3-*C*-nitromethylene DAG derivative **2** was obtained through a three-step synthesis (Scheme 1) [5].



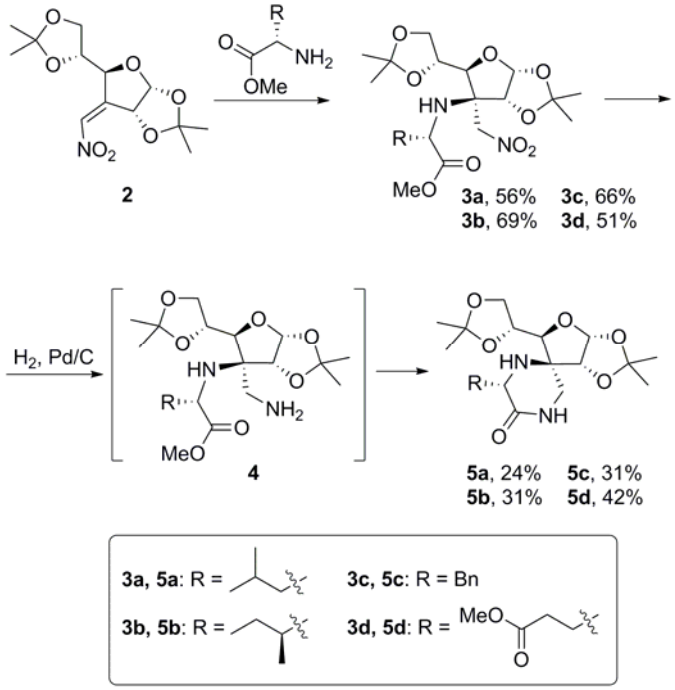
Scheme 1. Synthesis of the intermediate **2**

Alcohol **1** was oxidized by NaOCl in the presence of TEMPO [6], followed by nitromethane addition to the ketone (Henry reaction) and Moffatt dehydration [7].

Aza-Michael addition of L-amino acid esters to compound **2** was used to obtain products **3** (Scheme 2).

Adducts **3a-d** were formed as (3*S*)-stereoisomers due to steric hindrance of 1,2-isopropylidene group [5]. Catalytic reduction of nitro group led to spiropiperazinones **5a-d**. As expected, aminomethyl derivatives **4** produced in the reduction process could not be isolated and served as active intermediates.

Optimisation of the experimental conditions is in progress and will be discussed.



Scheme 2. Synthesis of spiropiperazinones **5**

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