



Synthesis and reactivity of pyrazolo-pyridone ring, an understudied heteroaromatic scaffold

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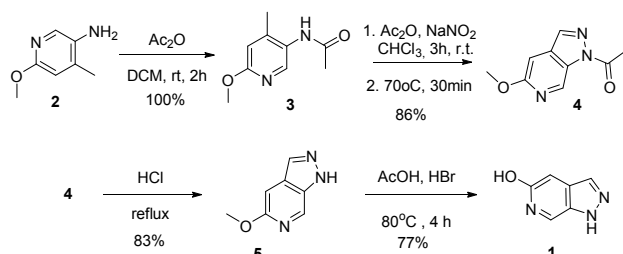
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INTRODUCTION

The chemical structural space of all possible compounds is vast, with more than 10^{62} compounds¹ with molecular weights below 500 Da. Heteroaromatic rings are common in bioactive molecules and both medicinal and agro chemists have exploited these scaffolds to provide high value materials, for example Glivec, an anti cancer drug, and Exjade to treat iron overload. However, only a small fraction of the heteroaromatic space is currently exploited for drug discovery, and has established synthetic routes to access them, supporting a scenario in which is shown the disclosure of new heterocyclic skeletons follows a rate of 5-10 per year. The main scope of this work is to study the synthesis of underexplored heterocyclic scaffold, based on a recent computational study², which listed interesting yet under represented heterocyclic skeletons with drug discovery potential.

RESULTS AND DISCUSSION

The selected scaffold is a pyrazolo-pyridone **1**, it is a 6,5 fused ring system with mixed electronic characteristics. The synthesis of the target heterocycles had been achieved by an N-acyl-N-nitroso rearrangement approach (Scheme 1).³



Scheme 1. Synthesis of the pyrazolo-pyridinone ring system through the cyclisation of a N-acyl-N-nitroso intermediate.

Once a suitable synthetic methodologies have been found, the core's reactivity had been studied under a range of synthetically useful transformations (Scheme 2).

Minisci chemistry	7%
Palladium mediated C-H activation	24%
Iridium borylation	no results
Nitration	46%
Halogenation	34%
Mitsunobu Reaction	7%
Suzuki Reaction	12%
Heck Reaction	no results

Scheme 2. Exploratory studies about the reactivity of pyrazolo-pyridine rings.

CONCLUSION

The selected heteroaromatic ring represents a promising scaffold to obtain libraries, based on its reaction capacity in several positions, revealing its versatility. However, further studies are needed to improve conditions and yields.

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