Synthesis of promising understudied heteroaromatic scaffolds for the drug discovery process

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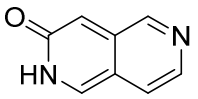
The chemical space is quite vast, it is estimated that there are more than 10^{62} compounds with molecular weight below 500 Da. However only a small fraction of this area is exploited for drug discovery, usually by high throughput screening (HTS) approaches. Inevitably, HTS libraries generally present a large number of non drug-like compounds which generates constantly false positive results. Therefore in the present work we had selected three heteroaromatic systems for study (2,6-naphthyridin-3(2H)-one **1**, 1,6-dihydro-5H-pyrazolo[3,4-c]pyridin-5-one **2**, 3,4-dihydropyrrolo[1,2-a]pyrazin-1(2H)-one **3**) to conduce a synthetic and computational study to provide new drug-like compounds and innovation to drug discovery libraries. We have developed three novel and efficient synthetic routes for the promising heterocyclic scaffolds **1**, **2** and **3**, which are still underexploited by medicinal chemistry. First, the unpublished heterocyclic **1** had a robust synthetic route described based on pyridine substitution methodologies. The heterocycle **2** was achieved through *N*-acyl-*N*-nitroso intermediate cyclization in a few steps and low cost synthetic route. Finally, the structure **3** was synthesized by substitution methods of pyrrole ring. In addition, we proposed the synthesis of **1**, **2** and **3** derivatives and also a computational analysis, in order to ascertain their use as building blocks and also their potential for drug discovery processes. The three heteroaromatic scaffolds showed interesting medicinal chemical properties related to their structure, thus their application for libraries development is a promising “innovation tool” to drug discovery processes.



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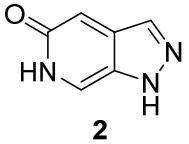

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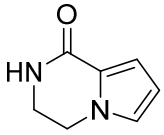

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