Multi-gram synthesis of 7-nitroquinoxalin-2-amine.

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Abstract

We describe a facile and multi-gram methodology to obtain 7-nitroquinoxalin-2-amine in a five-step procedure in good yields without further purification such as crystalization or chromatography column.

Introduction

So far, synthesis of 7-nitroquinoxalin-2-amine was described once in literature by Wolf and co-workers in 1949.[1] Wolf's methodology uses 4-nitro-*o*-phenylendiamine as starting material and it is not regioselective.

We describe a methodology that would be affordable in an academic and/or commercial way by a five-step synthetic pathway through simple synthetic procedures in multi-gram scale (up to 10 grams of starting material).

Results and discussion

Our procedure uses *o*-phenylenediamine as starting material to prepare initially quinoxalin-2-ol in good yields and different scales (0.3g - 10g).[2] Next, 7-nitro-quinoxalin-2-ol was obtained by a regioselective methodology using fuming nitric acid and glacial acetic acid at room temperature.[3] Using phosphoryl chloride under reflux we prepared the corresponding aryl chloride.[4] Use of benzylamines was proposed to act as amino group carrier using 1.1 eq of amine and 3 eq of TEA in ethanol under reflux.[5] Then, in a second step amino group deprotection was done using TFA on 50ºC for 24 hours and final compound was obtained in high yields and purity as an orange solid.[6] **(Figure 1)**

7-nitroquinoxalin-2-amine is an orange powder (mp>300ºC), insoluble in common organic solvents as dicloromethane, chloroform, ethyl acetate, methanol, ethanol and acetonitrile.

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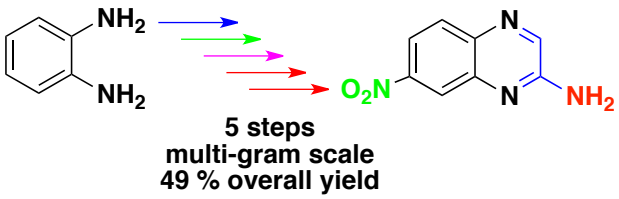

Figure 1. Representation of methodology employed to obtain target-molecule, 7-nitroquinoxalin-2-amine.

Conclusions

We obtained 7-nitroquinoxalin-2-amine in 49% global yield through a five step linear synthetic route and its chemical characterization is also reported.

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