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Coelenterazine derivatives as potential drugs for photodynamic therapy

Chaired by DR. ALFREDO BERZAL-HERRANZ;
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pharmaceuticals MDPI

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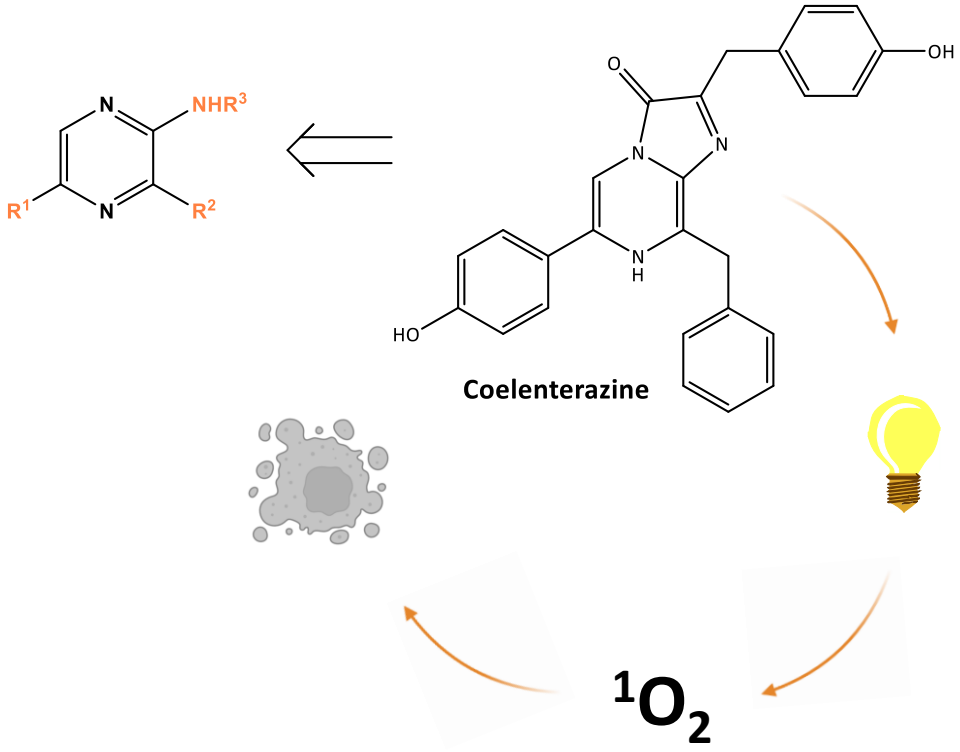
Graphical Abstract

Coelenterazine derivatives as potential drugs for photodynamic therapy



Abstract: Cancer is one of the main leading causes of death worldwide and its treatment is highly complex and known to cause serious side effects for patients. Photodynamic Therapy (PDT) has gained momentum as a promising alternative strategy to overcome or minimize these potential side effects observed in classical therapeutical approaches. This therapy is a minimally invasive treatment that combines a photosensitizer (PS), visible light, and molecular oxygen ($^3O_2$). When excited, the PS interacts with $^3O_2$ to generate reactive oxygen species (ROS), mainly as singlet oxygen which, in turn, induce cytotoxic effects in cancer cells. In a recent study led by our research group, coelenterazine (Clz) analogues have shown relevant cell-selective toxicity in different cancer cell lines (such as breast, liver, prostate, and neuroblastoma), without cytotoxic effects in the corresponding non-tumoral cells. Based on these results, this work aims to synthesize a new series of Clz-inspired PS derived from pyrazine scaffold, a common precursor in the synthesis of Clz and its structure-related analogues. Herein, we describe some methodological approaches for the synthesis of nine pyrazine-based precursors (with high chemical yields) and their chemical characterization, for the assembly of Clz analogues. Currently, these compounds are being studied for the assembly of new PS with potential application in PDT.

Keywords: Photodynamic Therapy (PDT); Cancer; Coelenterazine (Clz).

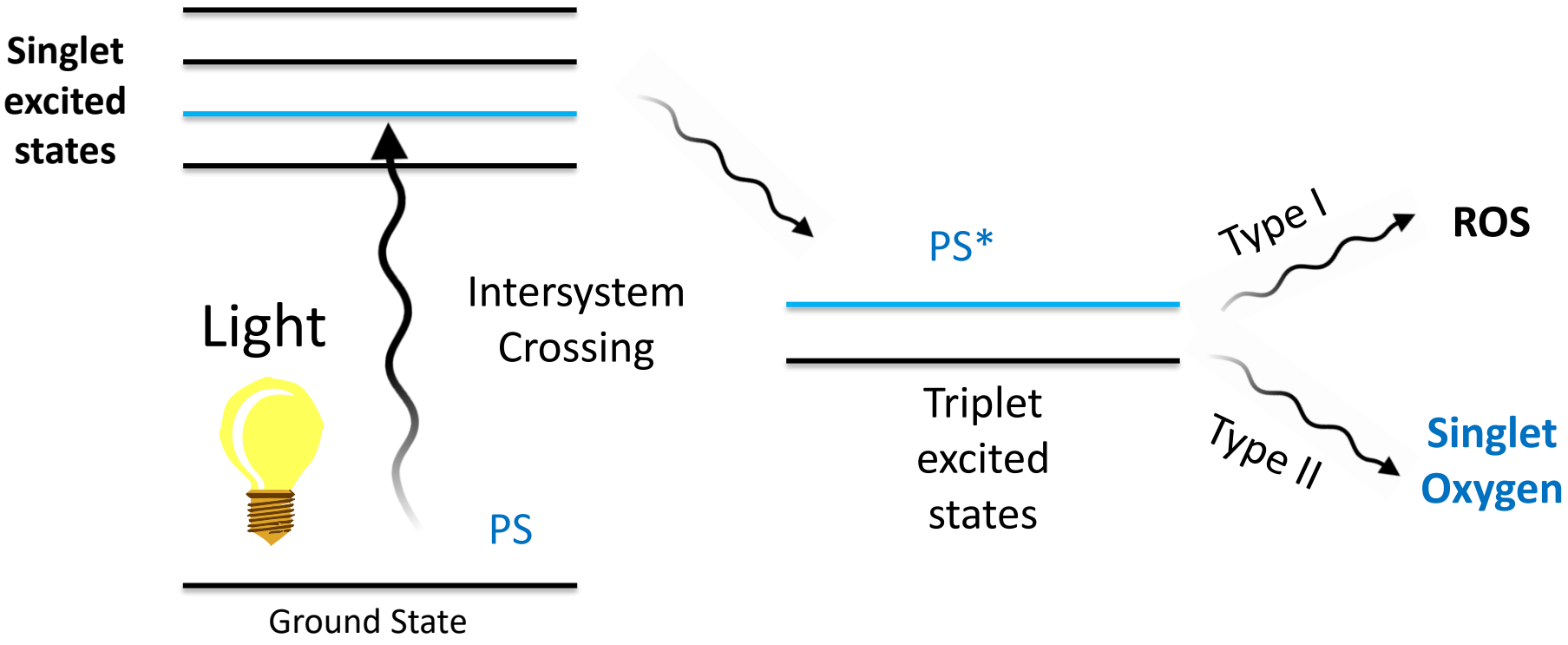
Introduction

Cancer is one of the main leading causes of death worldwide

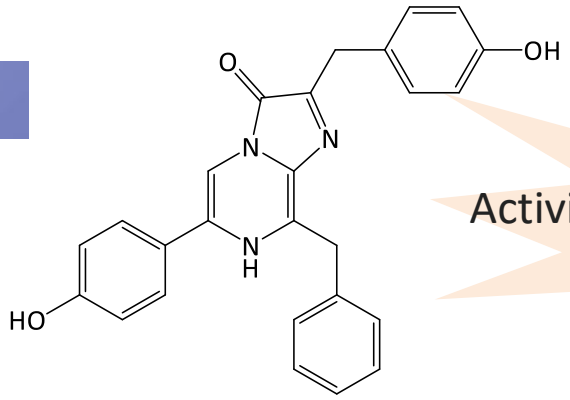
Conventional treatments are not efficient

Photodynamic Therapy (PDT)

Introduction

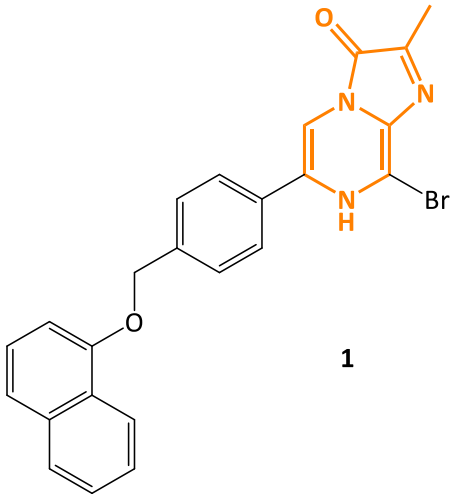


Introduction



Coelenterazine

Activity toward breast and prostate tumor cell lines



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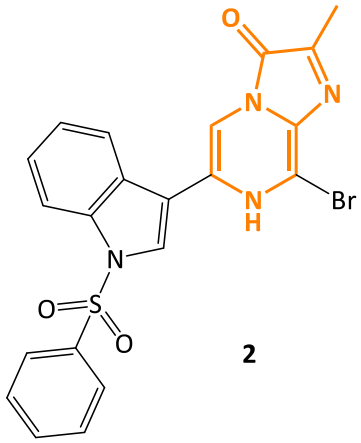

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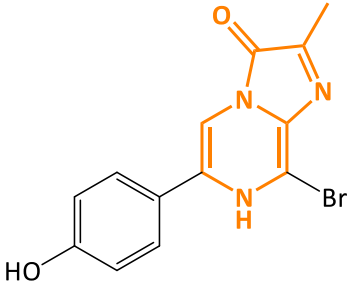
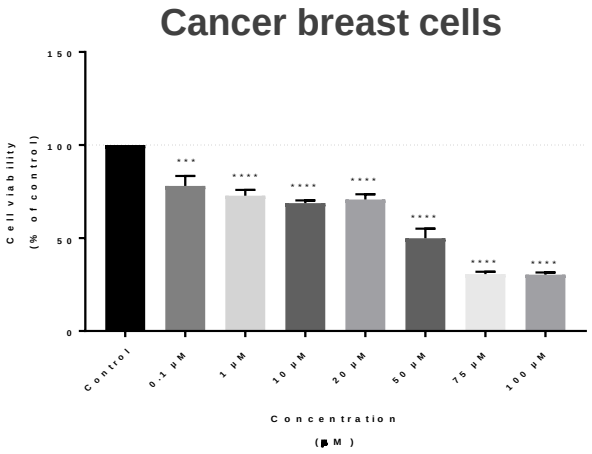


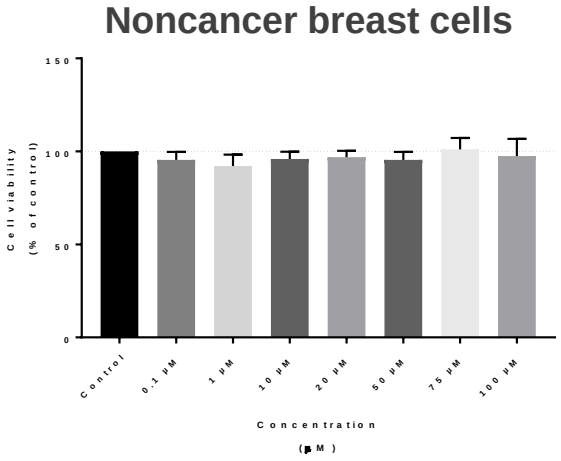
3

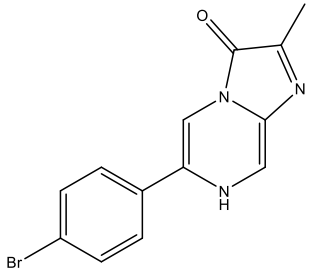
Biomolecules ***2019****, 9, 384.*

Introduction

In vitro selectivity evaluation in healthy breast cell line (MCF-10A)



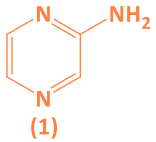
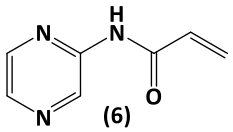
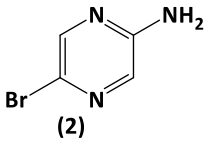
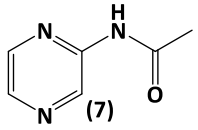
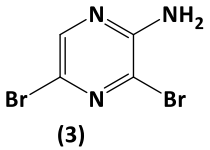
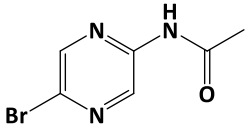
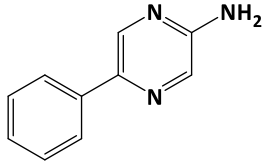
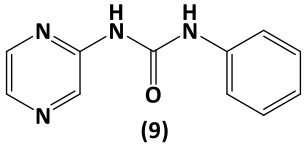
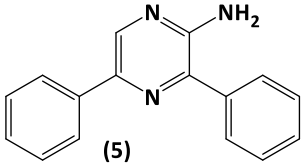
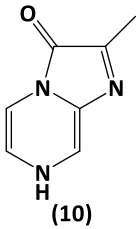




Selectivity to cancer cells

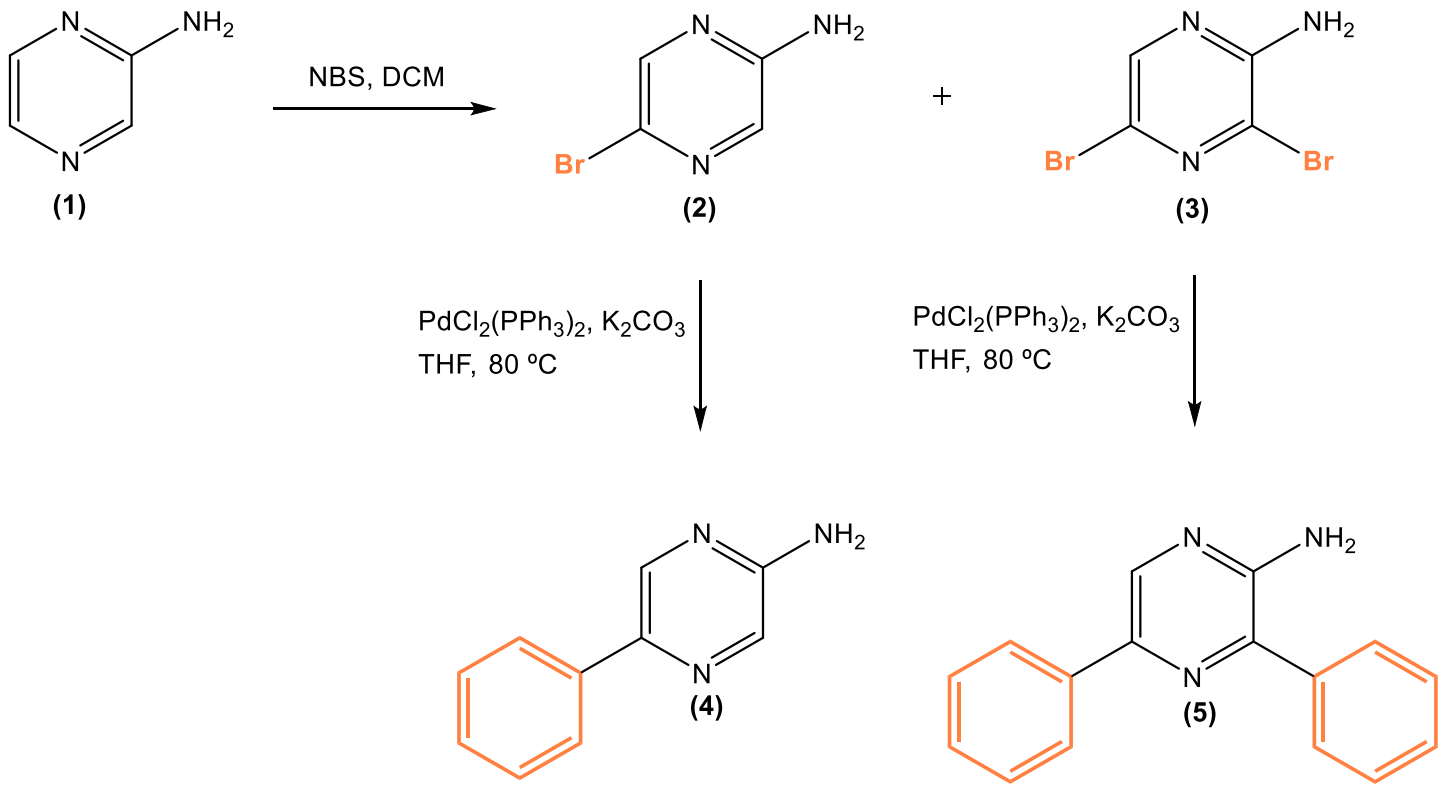
Eur. J. Med. Chem. **2019**, *183*, 116837.

Results and Discussion

	Yield (%)			Yield (%)
 (1)		 (6)		25
 (2)	70	 (7)		40
 (3)	72	 (8)		52
 (4)	64	 (9)		95
 (5)	58	 (10)		43

All compounds were characterized by NMR (^{1}H, ^{13}C, and DEPT-135)

Results and Discussion



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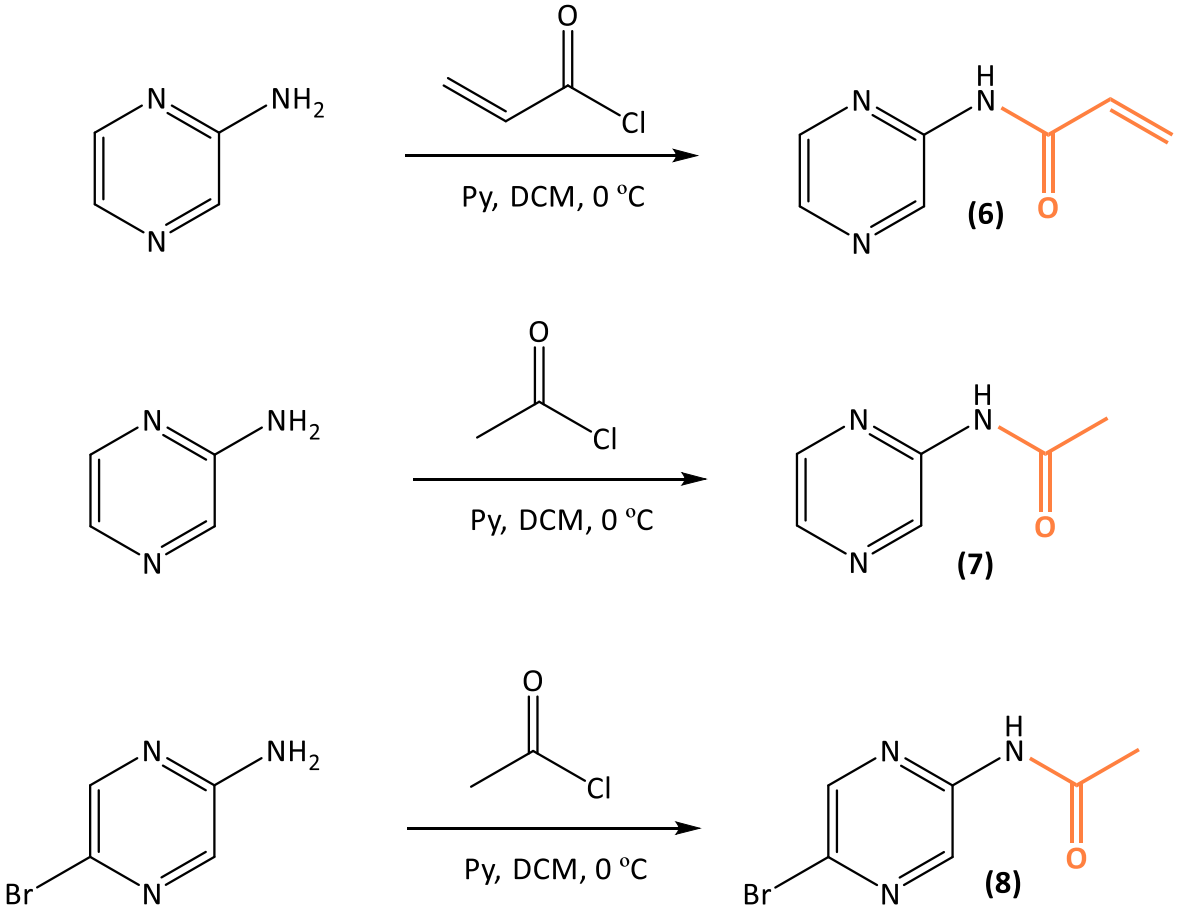
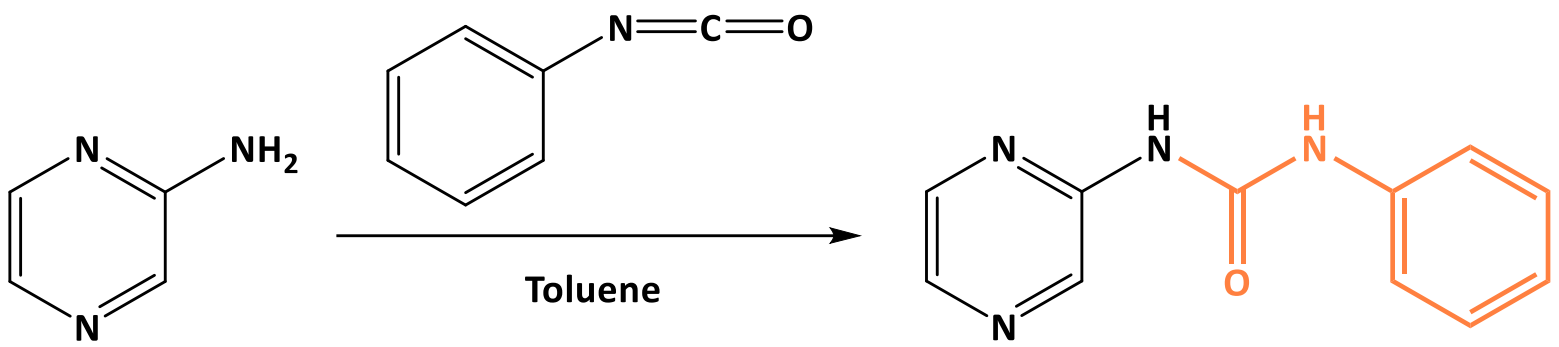
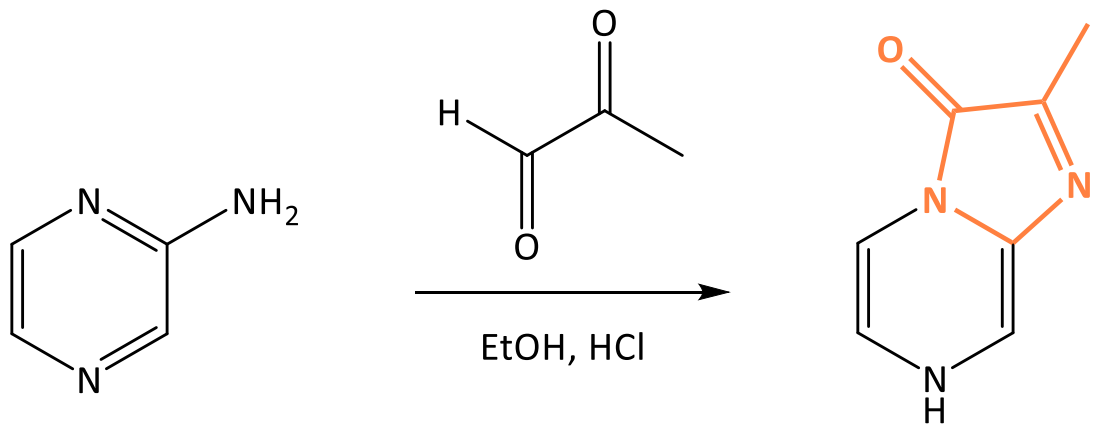


Results and Discussion



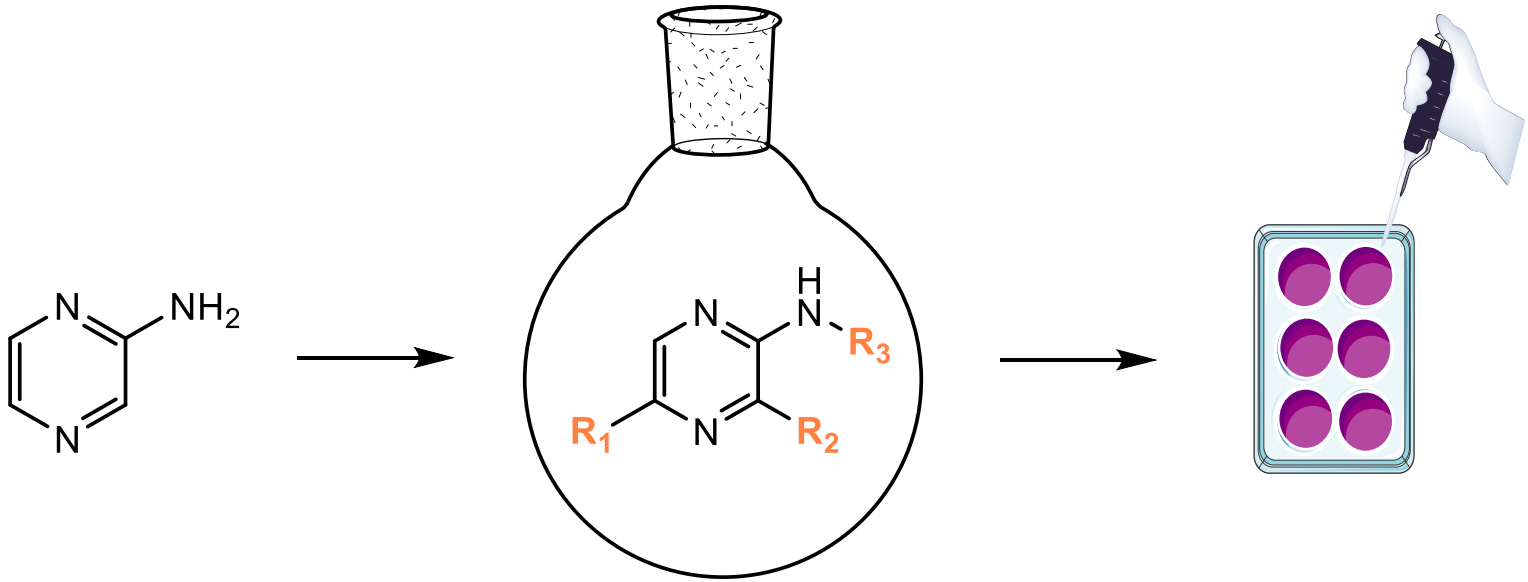
(9)

Results and Discussion



(10)

Conclusions



Acknowledgments

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