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Synthesis and characterization of pyrazine-based precursors for the development of new photosensitizers

Chaired by **Dr. Alfredo Berzal-Herranz** and **Prof. Dr. Maria Emília Sousa**

pharmaceuticals MDPI

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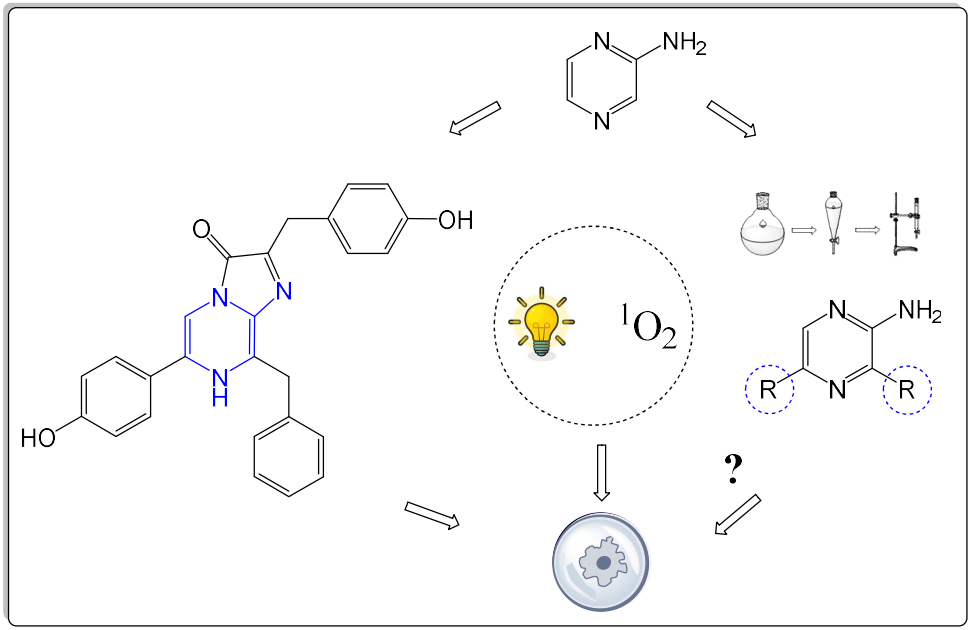


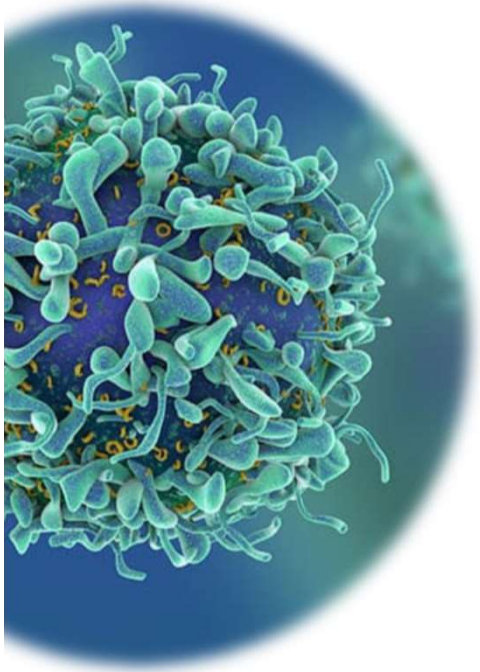
Abstract: Cancer belongs to a group of diseases involving abnormal cell growth with the potential to spread to other parts of the body, being currently the leading cause of death worldwide. Cancer therapy is still very challenging and most of the traditional treatments available are usually invasive and cause serious side effects to patients. In this context, photodynamic therapy (PDT) emerges as a good alternative for the treatment of cancer, since it offers great benefits, such as low invasiveness and highly selective.

This therapy combines a photosensitizer (PS), light of a specific wavelength, and molecular oxygen ($^3O_2$) to produce reactive oxygen species (ROS), mainly singlet oxygen ($^1O_2$) species. Recent studies have shown that Coelenterazine (Clz) and its analogues can be used in PDT exhibiting relevant toxicity to different cancer cells (e.g., breast, liver, prostate, and neuroblastoma) without appreciable harm toward healthy cells.

Synthetically, these compounds can be obtained from pyrazine units. To develop new photosensitizers for the application in the PDT, herein we present the synthesis of new pyrazine-based scaffolds to prepare novel PS. The different products were characterized by spectroscopy techniques.

Keywords: Cancer; photodynamic therapy (PDT); photosensitizers (PS); pyrazine; reactive oxygen species (ROS); singlet oxygen ($^1O_2$) species.

Introduction

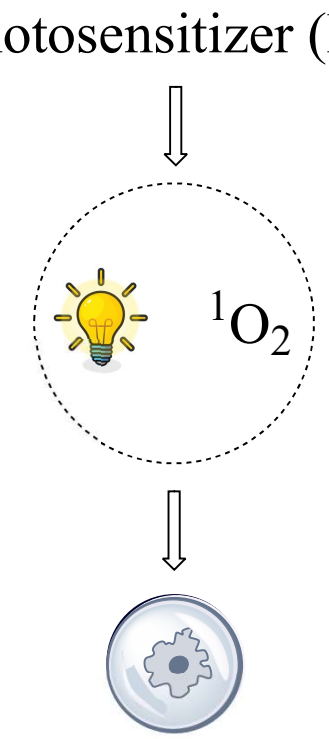


Challenge:

Cancer is the leading cause of death worldwide, and statistics show that in 2020 there were around 10 million deaths caused by these diseases.

Treatments:

- Surgery
- Chemotherapy
- Radiotherapy
- **Photodynamic therapy (PDT)**



[1] S. Wang, Y. Liu, Y. Feng, J. Zhang, J. Swinnen, Y. Li, Y. Ni. Cancers 11 (2019) E1782.
[2] C.M. Magalhães, J.C.G. Esteves da Silva, L. Pinto da Silva. ChemPhysChem 17 (2016) 2286.
[3] K.A.D.F. Castro, J.A. Prandini, J.C. Biazzotto, J.P.C. Tomé, R.S. da Silva, L.M.O. Lourenço. Front. Chem. 10 (2022) 825716.

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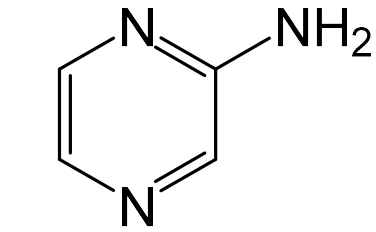
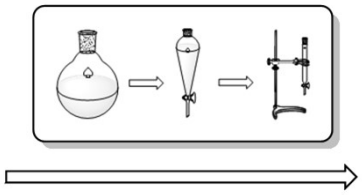
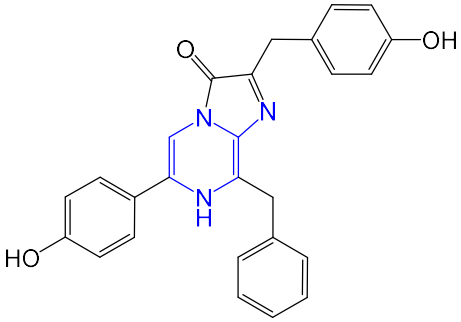


Aminopyrazine

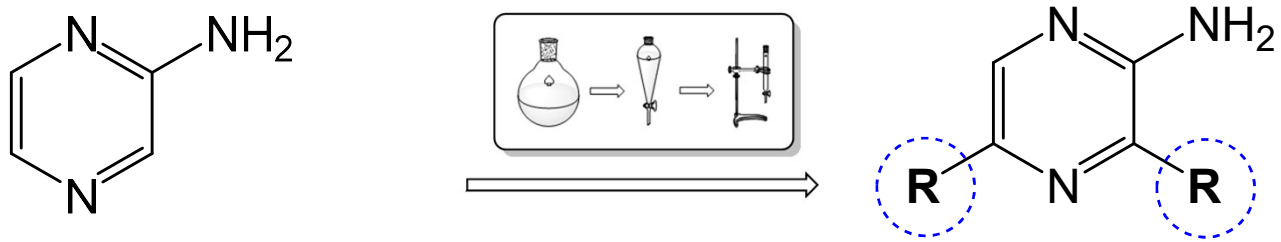




Clz

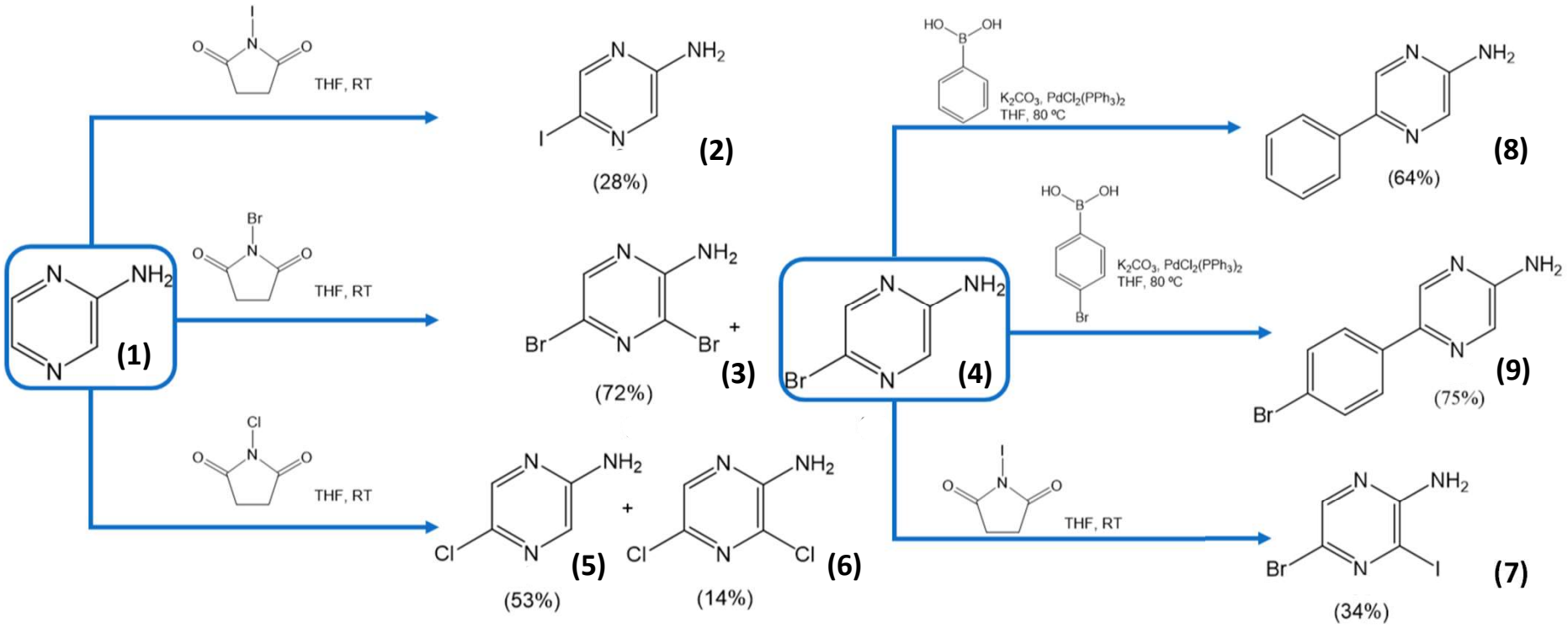
[4] L.P. Silva, C.M. Magalhães, A.N. Montenegro, P.J.O. Ferreira, D. Duarte, J.E. Rodríguez-Borges, N. Vale, J.C.G.E. Silva. Biomolecules 9 (2019) 384.

Introduction



R: H, Br, Cl, I, Ph, 4-Br-Ph

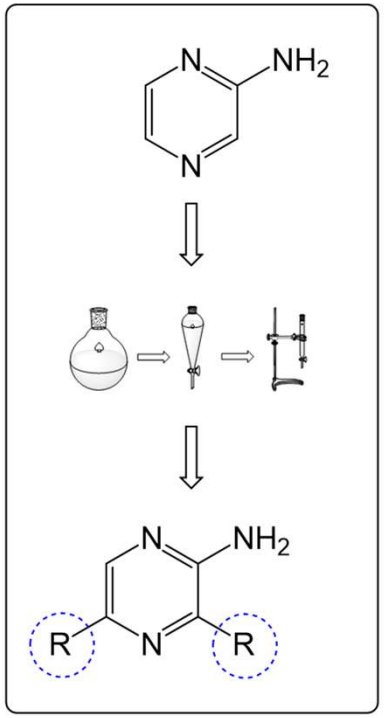
Results and discussion



The products **2**-**7** were obtained through halogenation reactions. From product **4**, it was possible to synthesize **8** and **9** through the Suzuki coupling. The work-up was performed by conventional methodologies in organic chemistry. The obtained products were characterized by ^{1}H and ^{13}C NMR spectroscopies.

Conclusions

- ✓ Synthesis
- ✓ Reaction optimization
- ✓ Chemical characterization



Next steps

- ❑ Physical-chemical studies
- ❑ Biological tests

Acknowledgments

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