Synthesis of Aza-Pterocarpan Analogues *via* 1,3 Intramolecular Dipolar Cycloadditions in *in situ* generated Iminoolefins

Julio C.F.Barcellos[1](PG)*, Ayres G. Dias[2](PQ), José M. Sansano[3](PQ), Carmen Nájera[3] (PQ), Paulo R. R. Costa[1](PQ)

**ju8liojpa@hotmail.com*

Keywords: 1,3 dipolar-cycloaddition, aza-pterocarpanes, imines in situ.

INTRODUCTION

As part of a program directed towards the discovery of new compounds with anticancer and antiparasitic action, we recently synthesized aza-pterocarpans such as **1** (Figure 1), through a aza-Heck palladium catalyzed reaction.[1] This substance showed significant activity against strains of cancer and Leshimania.[1]

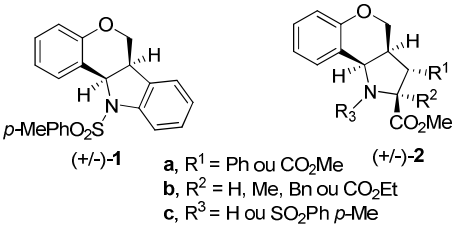
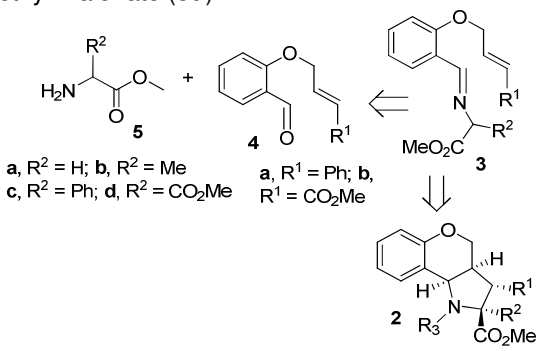


Figure 1. Aza-pterocarpan **1** and analogs (**2**).

Here, dipolar cycloaddition (1,3-DCI) of imines (**3**) were made. These intermediates were generate i*n situ* by reaction of salicylaldehydes (**4a**,**b**) with the amino acids glycine (**5a**), alanine and phenylalanine (**5b**,**c**) (used as racemates, we describe the synthesis of new derivatives of **1**, of type **2** (analogs of **1**) through intramolecular 1,3) and the amino diethyl malonate (**5d**).



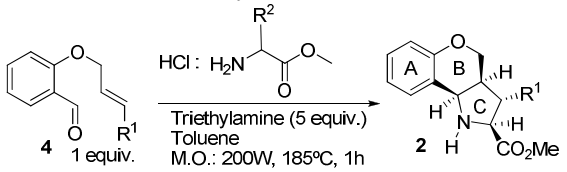
Scheme 1. Retro-analysis for the preparation of **2** through 1,3-dipolar cyclo-addition.

RESULTS AND DISCUSSION

Were performed in total, eight reactions in a microwave reactor (Table 1), at least in duplicate, using amino acids **5a**-**d** and acceptors **4a** (R_1=Ph) and **4b** (R_1=CO_2Me). Except for the entry 7, the major products presented fusion *cis* between the benzopiranic (B) and pirrolidinic (C) rings.[2] The major products in each reaction could be enriched after column chromatography. The structure of the major product of entry 1 was confirmed by X-ray of *N*-tosylated derivative **3** (Scheme 2).

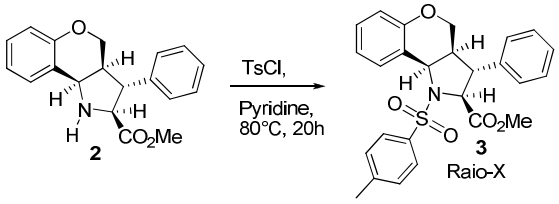
The structure of the other products (majors and minors) is being studied.

Table 1. Results obtained by 1,3-DCI of imines



Entry	R^1	R^2	(%) Major	(Major)/ (Others)	Reaction (%)
1	Ph	H	30	(65:35)	45
2	Ph	Me	67	(83:17)	77
3*	Ph	CO_2Et	75	(90:10)	83
4	Ph	Bn	54	(68:32)	79
5	CO_2Me	H	30	(60:40)	50
6	CO_2Me	Me	30	(60:40)	50
7*	CO_2Me	CO_2Et	25	(50:50)	50
8	CO_2Me	Bn	48	(70:30)	68

* Ethyl ester used in this case.



Scheme 2. Synthesis of **3.**

CONCLUSION

The microwave allowed the generation of imines *in situ*, eliminating a step for the formation of synthetic analogues of **1**. The prepared products are being evaluated as anticancer and antiparasitic.

ACKNOWLEDGEMENTS

CNPq, CAPES, FAPERJ.

REFERENCES

[1]Buarque, C.D. et al. *Bioorganic & Medicinal Chemistry* **2011**, *19*, 6885.
[2]Bashiardes G., et al. *Organic Letters*, **2003**, *25*, 4915.