Preparation of 5-Deoxypterocarpens by α-Arylation of Tetralones with *o*-Bromo-methoxyarenes Followed by BBr_3 Mediated Cyclization

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INTRODUCTION

Pterocarpens are members of the family of isoflavonoids, natural products that are produced in response to microbial infections.
It was reported that pterocarpens (**1**) and 5-deoxy-analogues (**2**), bind to estrogenic receptors (ERs) as strong as the natural ligand 17β-estradiol (Fig. 1).[1] These compounds were claimed to be useful for the treatment of cancer and other hormone-dependent diseases.

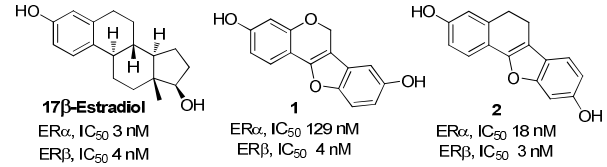
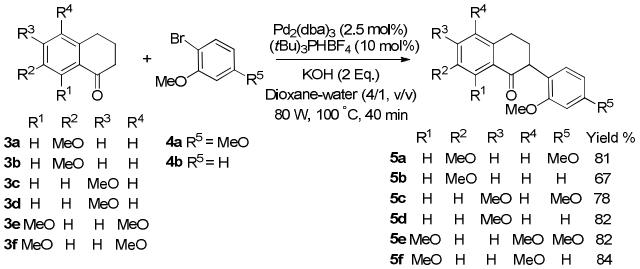


Figure 1 - Binding affinity to ER of Estradiol, Pterocarpen (1) and 5-Deoxy-analogue (2)

Some strategies for the preparation of deoxy-pterocarpens are described in literature, but they are labourious and low yielding.We envisaged that the most straightforward and green approach to prepare these compounds would be the direct α-arylation of tetralones[2] with *o*-halogen *O*-protected phenols, followed by desprotection and cyclization.

RESULTS AND DISCUSSION

The synthesis of desoxypterocarpens was started with the α-arylation of tetralones **3** with bromoarenes **4**, catalyzed by $Pd_2(dba)_3$, under microwave irradiation (Scheme 1).



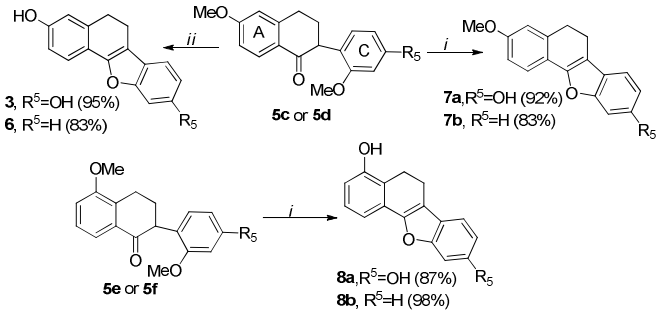
	R1	R2	R3	R4
3a	H	MeO	H	H
3b	H	MeO	H	H
3c	H	H	MeO	H
3d	H	H	MeO	H
3e	MeO	H	H	MeO
3f	MeO	H	H	MeO

4a R^5 = MeO
4b R^5 = H

	R1	R2	R3	R4	R5	Yield %
5a	H	MeO	H	H	MeO	81
5b	H	MeO	H	H	H	67
5c	H	H	MeO	H	MeO	78
5d	H	H	MeO	H	H	82
5e	MeO	H	H	MeO	MeO	82
5f	MeO	H	H	MeO	H	84

Scheme 1-Preparation of α-aryl-tetralones

Under these conditions the α-aryltetralones **5** were obtained from good to high yields.
The next step was the conversion of **5** into the 5-deoxypterocarperns through the one-pot demethylation-cyclization catalyzed by BBr_3 (Scheme 2). The products were obtained in high yields, without needing any process of purification. In the case of **5c-d** the demethylation was chemoselective, and methoxy derivatives **7a-b** were obtained only by keeping the reaction at 0 °C.



Scheme 2- Preparation of 5-Deoxypterocarpens. ***Conditions: i) BBr_3 (15 Eq.), CH_2Cl_2, 0 °C , 1,5h; ii) BBr_3 (15 Eq.), CH_2Cl_2, 0 °C, 1,5h, then rt, 2h.***

CONCLUSION

5-deoxypterocarpens were prepared in high yields through a two step synthesis: the α-arylation reaction of tetralones with *o*-bromoarenes, both commercially available, followed by the demethylation and cyclization catalyzed by BBr_3.
Other α-aryltetralones are being converted into the corresponding deoxypterocarpens. These compounds are under pharmacological evaluation.

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