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# An eco-friendly approach to the synthesis of 3-(phenylsulfonyl) chromenes

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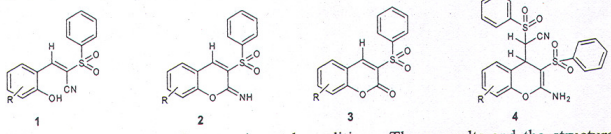
Compounds incorporating the chromene scaffold are present in a diversity of biologically active molecules.[1] Structural modifications of this core unit led to new drug candidates including molecules used for the treatment of psychiatric and neurological disorders, a research area of recent interest for our research group.
Considering that the substituent in position 3of the chromene ring is a crucial element for biological activity, the incorporation of a good leaving group in this position was expected to allow the preparation of different 3-substituted chromene derivatives. The phenylsulfonyl substituent was selected for that purpose and the aim of the present work was the synthesis of 3-phenylsulfonyl-2*H*-chromenes.Only few reports on the synthesis of this type of compounds are referred in the literature, and the experimental procedures always involve non-aqueoussolvents.[2,3]
In order to generate chromene derivatives with a good leaving group on the C-3 position, the phenylsulfonyl substituent wasincluded in that position by combining salicylaldehyde and phenylsulfonylacetonitrile, in aqueous media.



1 2 3 4

Compounds **1-4** were generated, depending on the experimental conditions. These results and the structural characterization of the products will be presented and discussed.

***References***
[1] M. F Proença, M. Costa, Tetrahedron, 66 (2010) 4542-4550.
[2] A. El-Shafei,, A. A. Fadda, I. I. Abdel-Gawad, E. H. E., Youssif, Synthetic Communications 39: 16 (2009) 2954 -2972
[3] A. A. Fadda, Hala M. Refat, M. E. A. Zaki, Molecules, 5 (2000) 701-709.



# Synthesis of 1,3-diarylureas from different(thieno[3,2-*b*]pyridin-7-ylthio)anilines

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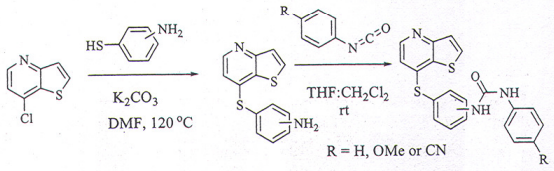
Recently some thieno[3,2-*c*]pyridine 1,3-diarylurea derivatives were prepared as VEGFR-2 (Vascular endothelium growth Factor Receptor-2) tyrosine kinase domain inhibitors. This receptor is related with tumor vascularisation (angiogenesis) and metastasis [1].
Here in we present the synthesis of new 1,3-diarylurea derivatives of several (thieno[3,2-*b*]pyridin-7-ylthio)anilines. The latter were obtained by regioselective nucleophilic substitution of the 7-chlorothieno[3,2-*b*]pyridine with different aminothiophenols and the 1,3-diarylureas were then formed by reaction of the amino groups with arylisocyanates (Scheme).




**Scheme**-Synthesis of 1,3-diarylureas from different (thieno[3,2-*b*]pyridin-7-ylthio)anilines

The 1,3-diarylureas synthesized will be studied as VEGFR-2 tyrosine kinase inhibitors either by virtual screening or enzymatic inhibition assays. The best compounds will be also studied in cell lines that express this receptor.

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***References***
[1] Heyman, H.R. *et al.Bioorg. Med. Chem. Lett.* 17 (2007) 1246-1249.