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P023

Synthesis of Novel 1-Aryl-3-[2-,3- or 4-(thieno[3,2-*b*]pyridin-7-ylthio)phenyl]ureas and Evaluation as VEGFR2 Tyrosine Kinase Inhibitors

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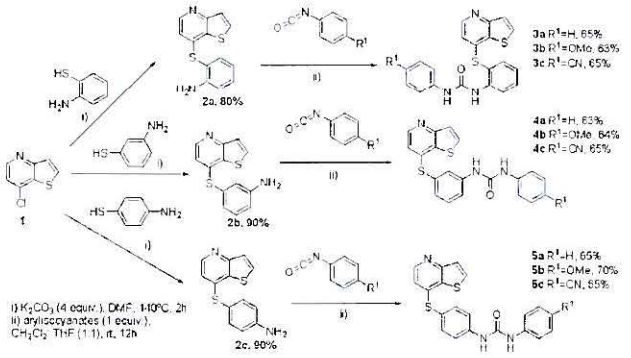

Vascular endothelial growth factor receptor 2 (VEGFR2) tyrosine kinase is involved in cancer and in angiogenesis.[1] Herein, we report the synthesis of novel 1-aryl-3-[2-, 3- or 4-(thieno[3,2-*b*]pyridin-7-ylthio) phenyl]ureas as VEGFR2 inhibitors by promoting the regioselective attack of the thiol group of the 4-aminothiophenol in the chlorine nucleophilic displacement on 7-chlorothieno[3,2-*b*]pyridine **1**, obtaining the aminated compounds **2a–c**. These were reacted with arylisocyanates to give the corresponding 1,3-diarylureas **3a–c**, **4a–c** and **5a–c** (see scheme).

1-Aryl-3-[3-(thieno[3,2-*b*]pyridin-7-ylthio)phenyl]ureas **4a–c** with the arylurea in the *meta* position relative to the thioether showed the lowest IC_{50} values (0.4–0.9 μM) in enzymatic assays using VEGFR2 tyrosine kinase domain, and the binding mode for these compounds was predicted by docking simulations.

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