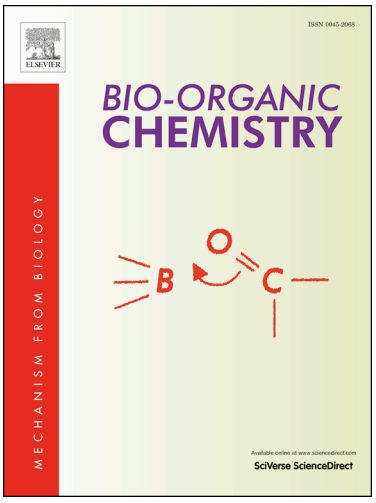

Design, Synthesis and Docking Study of Pyridine and Thieno[2,3-b] pyridine Derivatives as Anticancer PIM-1 Kinase inhibitors

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Abstract

A series of pyridine and thieno[2,3-*b*]pyridine derivatives have been designed and synthesized as anticancer PIM-1 kinase inhibitors. Thirty-seven compounds were selected by NCI to be tested initially at a single dose (10 µM) in the full NCI 60 cell line panel. Compound **5b** showed potent anticancer activity and was tested twice in the five-dose assay which confirmed its potent antitumor activity (GI_{50} values 0.302 to 3.57 µM) against all tested tumor cell lines except six cell lines where they showed moderate sensitivity. This compound was sent to NCI biological evaluation committee and still under consideration for further testing. In addition, the most active anticancer compounds in each series, **5b**, **8d**, **10c**, **13h**, and **15e**, were evaluated for their PIM-1 kinase inhibitory activity. Compound **8d** was the most potent one with IC_{50} = 0.019 µM followed by **5b**, **15e**, **10c** and **13h** with IC_{50} values 0.044, 0.083, 0.128 and 0.479 µM respectively. Moreover, docking study of the most active compounds inPIM-1 kinase active site was consistent with the *in vitro* activity.

Keywords:
Pyridine
Thieno[2,3-*b*]pyridine
PIM-1 Kinase inhibitors
Anticancer

1. Introduction