Synthesis and *In Vitro* Anticancer Evaluation of Symmetrically Bridged 1,3-thiazine Derivatives

Abstract

A series of *bis*-1,3-thiazine derivatives **3a–o** were synthesized from the condensation reactions of symmetric dialdehydes **1a–c** possessing aliphatic ether spacer units with 3-substituted-amino-2-cyano-3-mercaptoacrylamides **2a–e**. The chemical structures of the products were fully characterized by using different spectroscopic techniques, such as ^{1}H NMR, ^{13}C NMR, IR, electron impact mass spectrometry, and elemental analysis. Compounds **3a**, **3f**, and **3k** underwent ring opening followed by recyclization and alkylation in basic medium to afford *bis*-pyrimidinones **4a–c** and **5a–c**. The anticancer potential of the new *bis*-1,3-thiazines was assessed *in vitro* against six different human cell lines, including lung A549, colon HCT116, breast MCF-7, prostate PC3, liver HepG2, and normal melanocyte HFB4. The results revealed a potent activity of compounds **3e** and **3k** against breast and liver cancer cell lines in comparison with the reference drug doxorubicin with no noticeable toxicity on normal cells.