Heterocyclization of 2-Arylidencyclohexan-1,3-dione: Synthesis of thiophene, thiazole and isoxazole derivatives with potential antitumor activities

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ABSTRACT

The reaction of cyclohexan-1,3-dione with benzaldhyde, 4-chlorobenzaldhyde and 4-methoxy benzaldhyde in ethanol in the presence of catalytic amount of piperidine afforded 2-Arylidencyclohexan-1,3-dione. The latter compounds reacted with elemental sulfer and either of malonanitrile or ethyl cyanoacetate in 1,4-dioxan in the presence of triethylamine to give tetrahydrobenzo[*b*]thiophen-5-one derivatives**.** The latter compounds were used for the synthesis of thiophene, thiazole and isoxazale derivatives through their reactions with different chemical reagents. The analytical and spectral data of newly synthesized compounds were consistent with their respective structures.The anti-proliferative activities of the newly synthesized compounds were evaluated against the six cancer cell lines A549, HT-29, MKN-45, U87MG, SMMC-7721 and H460. The most potent compounds toward the cancer cell lines were seven compounds, were further investigated towards the five tyrosine kinases c-kit, FIT-3, VEGFR-2, EGFR and PDGFR. Three compounds were selected for testing of their inhibition for the Pim-1 kinase due to their anti-proliferation activities against the cancer cell lines and their high activities against the tyrosine kinases.

KEY WORDS

Cyclohexan-1,3-dione, Thiophene, Thiazole, Isoxazale, Anti-proliferative activity, Tyrosine kinases, Pim-1 kinase.