ONE-POT SYNTHESIS OF 2-AMINOBENZO[b]THIOPHENES AND CYTOTOXIC EFFECT OF THEM AGAINST K562 AND HELA TUMOR CELL LINES

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Benzo[b]thiophene and its derivatives have a special place among chalcogen-containing heterocycles, since the compounds containing this fragment have a surprisingly wide range of biological activity. Benzo[b]thiophene derivatives possess a wide spectrum of activities, among them substances with anticancer, antidiabetic, antituberculosis, antimalarial, and antifungal activities are known. It should be mentioned that 2-aminobenzo[b]thiophenes have been successfully used to create the selective estrogen receptor modulator (SERM) raloxifene and its analogs. Inhibitors of acetyl-CoA carboxylase and tubulin polymerization were also synthesized on the basis of benzo [b] thiophene.

A row of 2-substituted benzo[b]thiophenes were synthesised according to developed by us protocol, including one pot copper(I/II) catalysed reaction of 4-aryl-1,2,3-thiadiazoles with amines in the presence of potassium carbonate in the DMF medium, and tested for their potential antiproliferative activity against two cancer cell lines. Among them 1-(benzo[b]thiophen-2-yl)-2-ethylpiperidine was the most promising compound against both K562 and HeLa cell lines tested. The obtained experimental data indicate the expediency of searching for pharmacologically active substances among 2-aminobenzo[b]thiophene derivatives [1].

$R^1 = \text{H}$, $\text{Hal} = \text{Br}$, $\text{NR}^2\text{R}^3 = \text{pyrrolidin-1-yl}$ (**a**); $R^1 = \text{H}$, $\text{Hal} = \text{Br}$, $\text{NR}^2\text{R}^3 = 2\text{-ethylpiperidin-1-yl}$ (**b**); $R^1 = \text{H}$, $\text{Hal} = \text{Br}$, $\text{NR}^2\text{R}^3 = \text{morpholin-4-yl}$ (**c**); $R^1 = \text{MeO}$, $\text{Hal} = \text{Br}$, $\text{NR}^2\text{R}^3 = \text{morpholin-4-yl}$ (**d**); $R^1 = \text{NO}_2$, $\text{Hal} = \text{Cl}$, $\text{NR}^2\text{R}^3 = \text{morpholin-4-yl}$ (**e**).

Reaction conditions: for (**a-d**) $\text{HN R}^2\text{R}^3$, K_2CO_3 , CuI (20 mol %), DMF, Ar, 4-8 h, 80°C, for (**d**): morpholine, DMF, Ar, 12 h, 80°C.

References

- [1] E. A. Popova, A. A. Kornev, S. V. Shmakov, G. D. Nepochaty, O. A. Kotyunina, M. L. Petrov, V. M. Boitsov and A. V. Stepanov, Russian Journal of General Chemistry. 2020, Vol. 90, No. 11, pp. 2214–2218.