Synthesis, crystal structure and cytotoxic activity of novel 5-methyl-4-thiopyrimidine derivatives.

Autorzy

Marcin Stolarczyk

Iwona Bryndal

Agnieszka Matera-Witkiewicz

Tadeusz Lis

Karolina Królewska-Golińska

Marcin Cieślak

Julia Kaźmierczak-Barańska

Jerzy Cieplik

Rok wydania

2018

Czasopismo

Acta Crystallographica Section C: Structural Chemistry

Numer woluminu

C74

Strony

1138-1145

DOI

10.1107/s2053229618012706

Kolekcja

Naukowa

Język

Angielski

Typ publikacji

Artykuł

Streszczenie

This article presents the synthesis of three new 4-thio-pyrimidine derivatives obtained from ethyl 4-methyl-2-phenyl-6-sulfanylpyrimidine-5-carboxylate as the starting material, namely, ethyl 4-[(4-chlorobenzyl)sulfanyl]-6-methyl-2-phenyl-pyrimidine-5-carboxylate, $C_{21}H_{19}ClN_2O_2S$, (**2**), {4-[(4-chloro-benzyl)sulfanyl]-6-methyl-2-phenylpyrimidin-5-yl}methanol, $C_{19}H_{17}ClN_2OS$, (**3**), and 4-[(4-chlorobenzyl)sulfanyl]-5,6-dimethyl-2-phenylpyrimidine, $C_{19}H_{17}ClN_2S$, (**4**), which vary in the substituent at the 5-position of the pyrimidine ring. The compounds were characterized by ^{1}H NMR, ^{13}C NMR, IR and mass spectroscopies, and also elemental analysis. The molecular structures were further studied by single-crystal X-ray diffraction. Compound (**2**) crystallizes in the space group *P* with one molecule in the asymmetric unit, whereas compounds (**3**) and (**4**) crystallize in the space group $P2_1/c$ with two and one molecule, respectively, in their asymmetric units. The conformation of each molecule is best defined by the dihedral angles formed between the pyrimidine ring and the planes of the two aryl substituents attached at the 2- and 4-positions. The only structural difference between the three compounds is the substituent at the 5-position of the pyrimidine ring, but they present significantly different features in the hydrogen-bond interactions. Compound (**2**) displays a one-dimensional chain formed by hydrogen bonds and the chains are further extended into a two-dimensional network. Molecules of (**3**) and (**4**) generate one-dimensional chains formed through inter-molecular interactions. The study examines the cytotoxicity of compounds (**3**) and (**4**) against Human umbilical vein endothelial cells (HUVEC) and HeLa, K562 and CFPAC cancer cell lines. The presence of the hydroxymethyl and methyl groups in (**3**) and (**4**), respectively, offers an interesting new insight into the structures and behaviour of these derivatives. Compound (**4**) was found to be nontoxic against CFPAC and HUVEC; however, it shows weak activity against the HeLa and K563 cell lines. The presence of a hydroxy group in (**3**) significantly increases its cytotoxicity towards both, *i.e.* the cancer (HeLa, K562 and CFPAC) and normal (HUVEC) cell lines.

Słowa kluczowe

4-thiopyrimidine derivatives, synthesis, crystal structure, cytotoxic activity

Adres publiczny

http://dx.doi.org/10.1107/s2053229618012706