

P11. Synthesis and antiproliferative activity of 4-(2,4-dimethylphenyl)thiosemicarbazide and its azomethine derivatives

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In order to develop novel antitumor medicines with improved clinical effectiveness, broadened spectrum of activity, and with reduced general toxicity 4-(2,4-dimethylphenyl)thiosemicarbazide and its five azomethine derivatives have been synthesised. The thiosemicarbazones **2-6** of 4-(2,4-dimethylphenyl)thiosemicarbazide **1** have been obtained by condensation of **1** with different aromatic carbonylic compounds: **2** 3-formylpyridine, **3** 4-formylpyridine, **4** 3-formylthiophene, **5** 2-formylquinoline, and **6** salicylaldehyde.

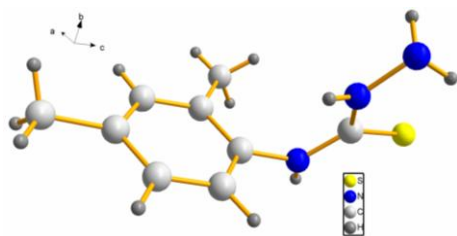
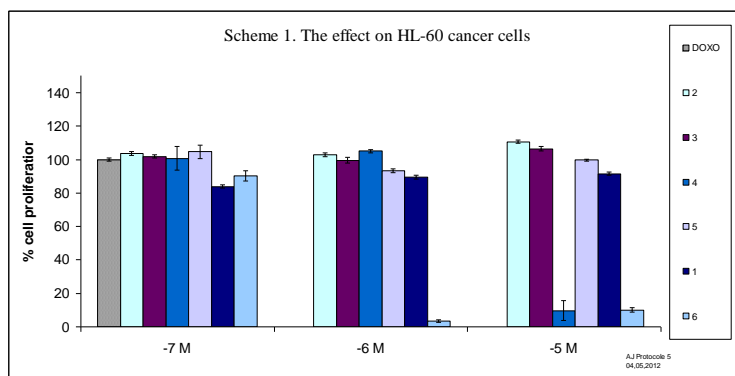


Fig. 1. Crystal structure of **1**

The composition and the structure of the synthesised substances have been determined by means of ¹H, ¹³C NMR spectroscopy and X-ray diffraction (Fig. 1). All substances have been tested as inhibitors of human leukaemia (HL-60) cells growth (Scheme 1).

Antileukaemia bioassays have shown that antiproliferative activity of the synthesised compounds is manifested mainly within the concentrations 10 μM and 1 μM, and increases in the following series: **2** ≤ **3** < **5** < **1** < **4** < **6**.

Therefore, the most active compounds **4** and **6** should be further studied as potential alternatives to traditional antileukaemia medicines. Also, from this study we have inferred that in order to obtain highly antiproliferative active azomethines from 4-(2,4-dimethylphenyl)thiosemicarbazide, it should be condensed with aromatic carbocyclic or heterocyclic aldehydes or ketones, which contain donor atoms (such as O or N) in the *ortho* position to the carbonyl group (e.g. salicylaldehyde, etc.).



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