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Synthesis of triazolyl derivatives based on thiazolo[3,2-*a*]pyrimidine propargyl ethers

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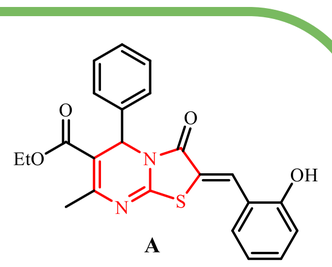
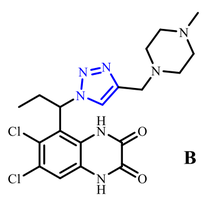
ABSTRACT

This work is devoted to the synthesis of triazolyl derivatives based on propargyl ethers of thiazolo[3,2-*a*]pyrimidine series by [3+2]-cycloaddition and the study of their structure in solution and crystalline phase. The influence of the solvent on the self-assembly of triazolyl derivatives in the crystalline phase was studied. The formation of homochiral chains or racemic dimers was found to be possible under different conditions.

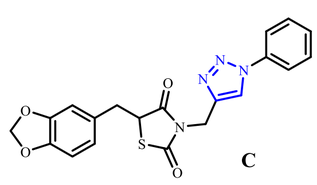
2-Arylmethylidenthiazolo[3,2-*a*]pyrimidine derivatives exhibit high biological and pharmacological activity, making them promising molecules with significant potential as antitumor agents. For example, compound **A** was observed to exhibit enhanced cytotoxic activity and selectivity towards M-Hela and HuTu 80 cancer cell lines in comparison to the comparator drug *Sorafenib*.



A



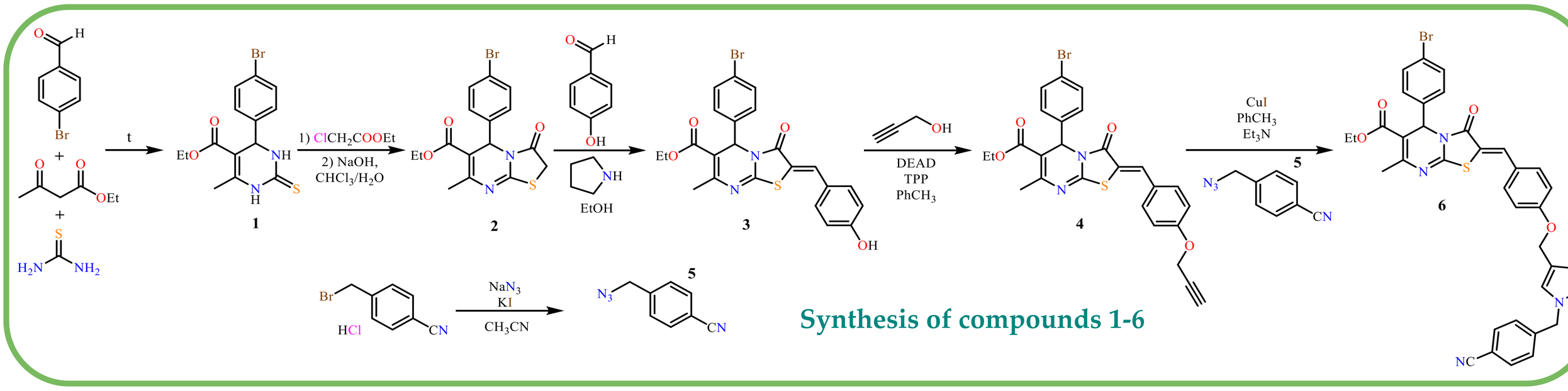
B



C

Additionally, heterocyclic compounds based on 1,2,3-triazole demonstrated notable efficacy in the creation of synthetic frameworks with pronounced anti-HIV, anti-cancer, and antibacterial activity. Compound **B** was identified as an NMDA receptor antagonist, while compound **C** displayed antitumor activity.

In this context, it is worthwhile to examine the structure and biological properties of compounds that contain both a thiazolo[3,2-*a*]pyrimidine and a 1,2,3-triazole fragment.



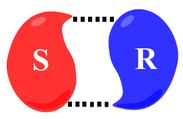
Synthesis of compounds 1-6

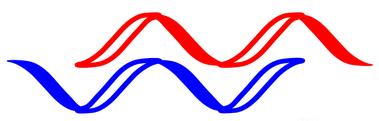
Effect of the solvent used in crystallization

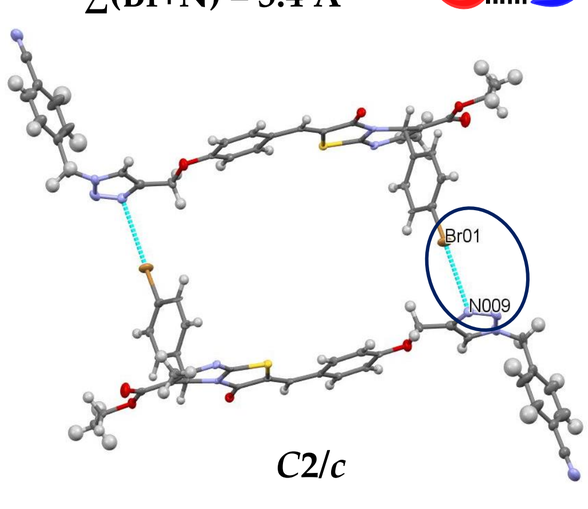
s: MeOH/EtOAc

s: DMF/MeOH

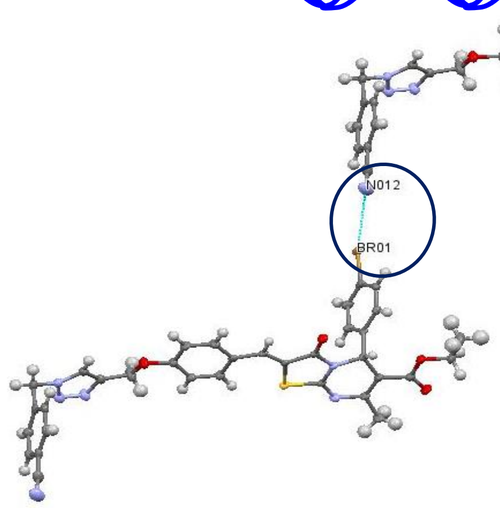
$d_{Br1 \ldots N9}$ = 3.272 Å
∑(Br+N) = 3.4 Å







*C*2/*c*

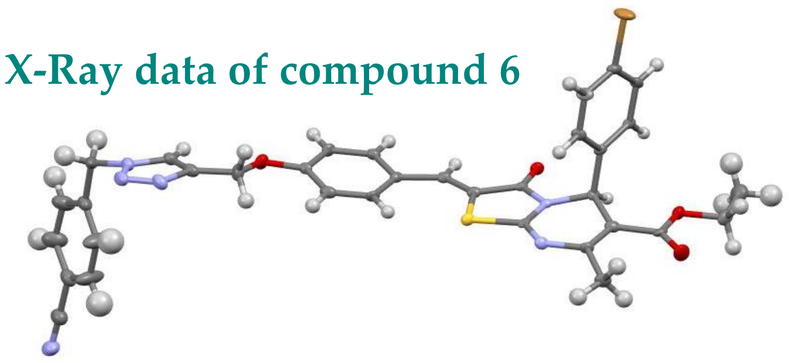


$d_{Br1 \ldots N12}$ = 3.322 Å
∑(Br+N) = 3.4 Å

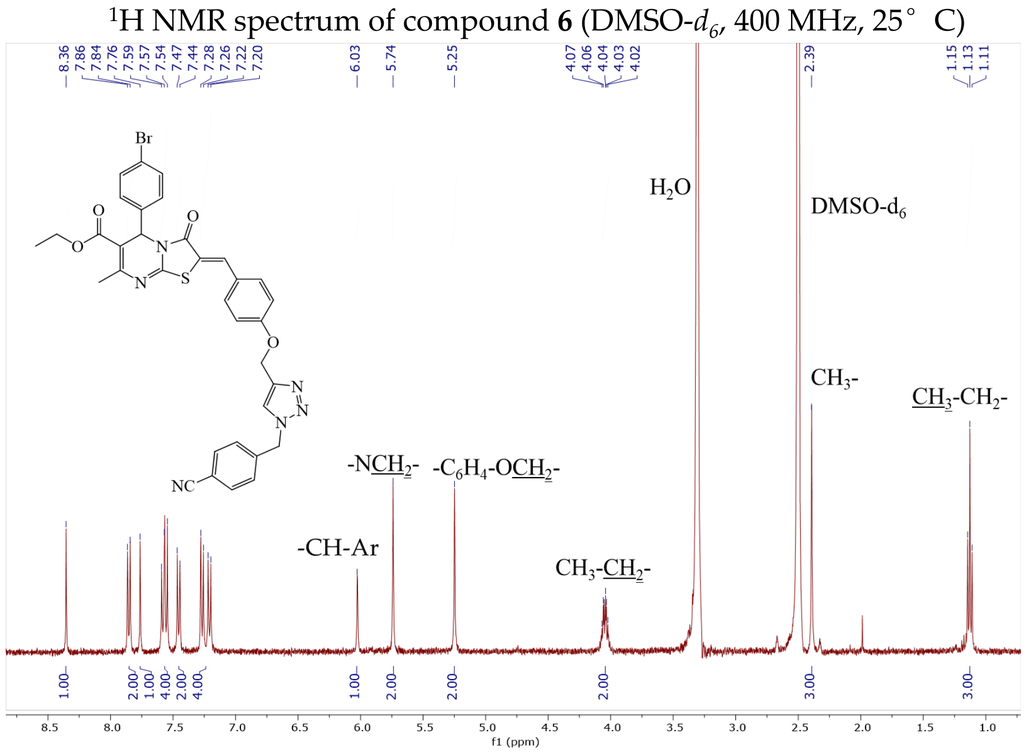
*P*2/*c*

ORTEP-view of supramolecular dimers resulting from intermolecular halogen bonding in crystals. The ellipsoids are presented with 50% probability and the H-atoms are omitted for clarity. Halogen bonding is presented by blue dotted lines.

X-Ray data of compound 6



^{1}H NMR spectrum of compound **6** (DMSO-d_6, 400 MHz, 25° C)



Conclusions

- In this work ethyl (*Z*)-5-(4-bromophenyl)-2-(4-((1-(4-cyanobenzyl)-1*H*-1,2,3-triazol-4-yl)methoxy)benzylidene)-7-methyl-3-oxo-2,3-dihydro-5*H*-thiazolo[3,2-*a*]pyrimidine-6-carboxylate was first obtained. The structure of the obtained compounds was confirmed by a complex of physicochemical methods of analysis.
- Two crystalline samples of the newly synthesized derivative were obtained using different solvent systems. The formation of homochiral chains in the crystalline phase is explained by the formation of a halogen bond between the bro-mine atom and the nitrogen atom of the nitrile group. In addition, the formation of the racemic dimer is associated with the formation of a halogen bond between the bromine at-om and the nitrogen atom of the triazolyl fragment.

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