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Faculty of Chemical
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NEW 1,2,3-TRIAZOLE-PYRIMIDINE/PYRROLO[2,3-*d*]PYRIMIDINE HYBRIDS: SYNTHESIS, CYTOSTATIC AND ANTIBACTERIAL EVALUATIONS

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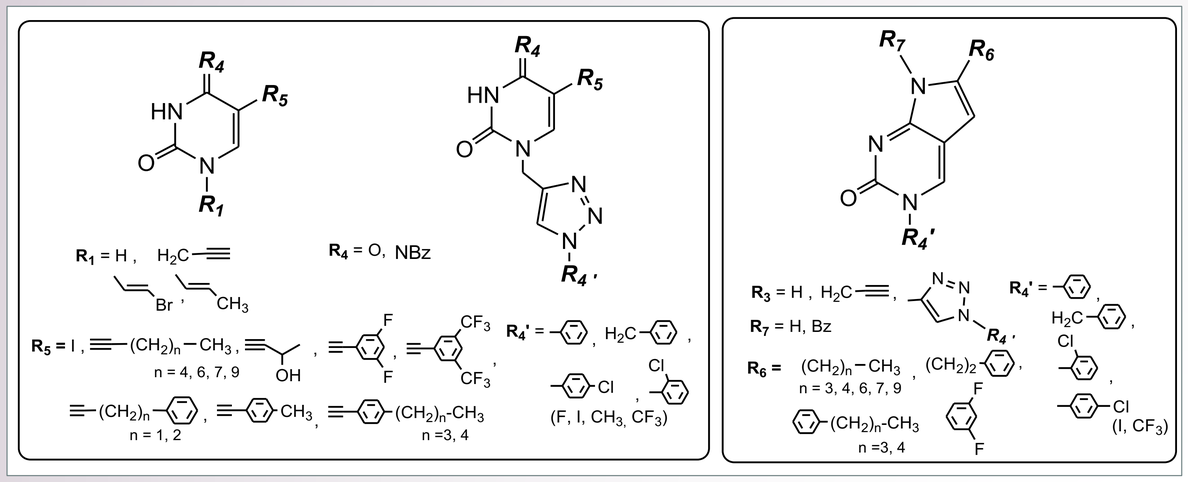
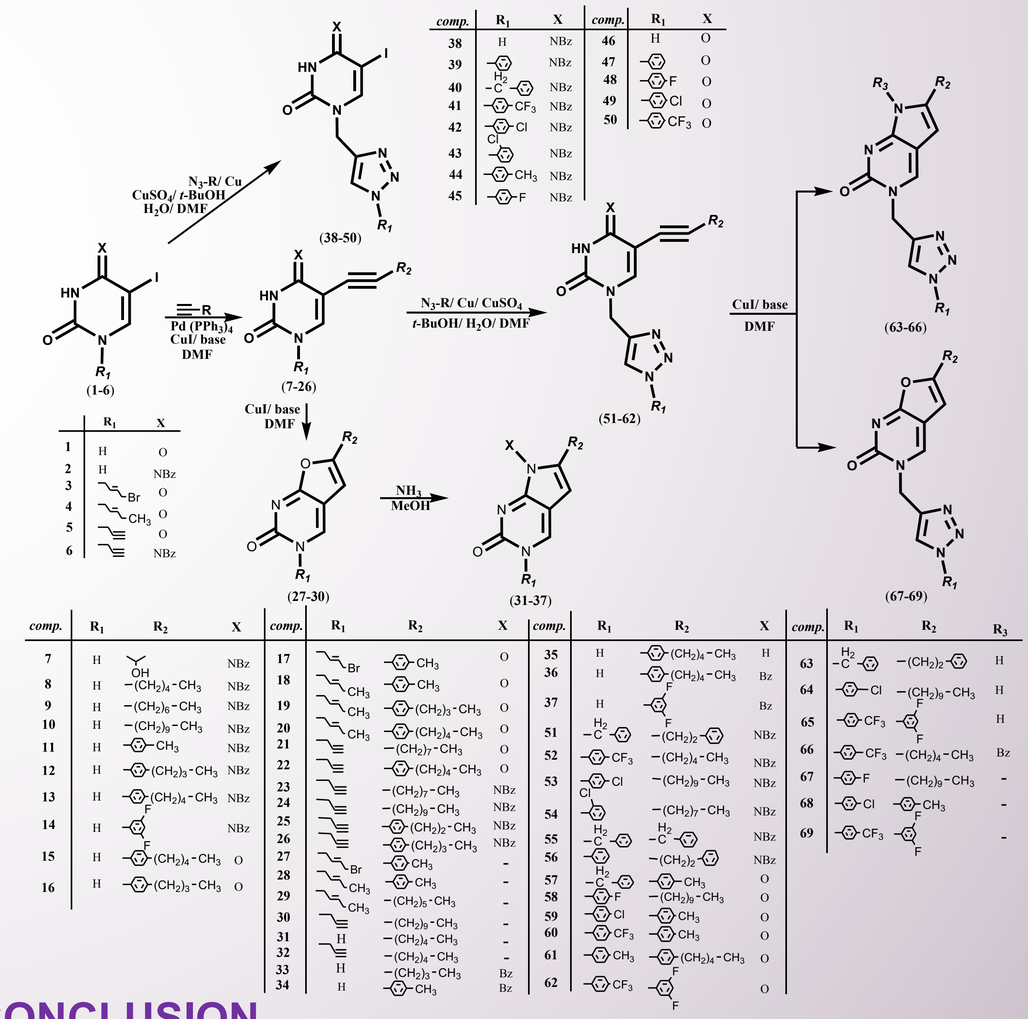
INTRODUCTION

N-substituted pyrimidine and pyrrolo[2,3-*d*]pyrimidine derivatives have a great role in modern medicine and have shown rather marked antitumor and antimicrobial activities.[1] In addition, 1,2,3-triazole moiety is an attractive connecting unit and a pharmacophore present in molecules which show diverse biological activities.[2,3] Considering the above mentioned biological activities, we efficiently synthesized the novel 1,2,3-triazole-pyrimidine/pyrrolo[2,3-*d*]pyrimidine hybrids.



CHEMISTRY

N-1 substituted and C-5 alkynylated N^4-benzoylcytosine and uracil derivatives were synthesized by *N*-alkylation reaction of pyrimidine bases and subsequent Pd-catalysed Sonogashira cross-coupling reaction with corresponding acetylenes. *N*-1 triazolyl derivatives were afforded via "click" reaction, while C-6 substituted pyrrolo[2,3-*d*]pyrimidine derivatives were prepared by base promoted in situ *N*-heteroannulation of C-5 alkynylated derivatives.



comp.	R1	X	comp.	R1	X
38	H	NBz	46	H	O
39		NBz	47		O
40		NBz	48	F	O
41	CF3	NBz	49	Cl	O
42	Cl	NBz	50	CF3	O
43		NBz			
44	CH3	NBz			
45	F	NBz			

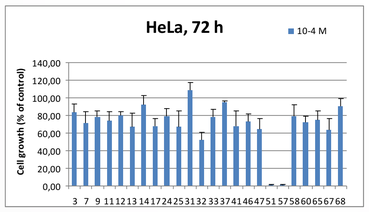
	R1	X
1	H	O
2	H	NBz
3	Br	O
4	CH3	O
5		O
6		NBz

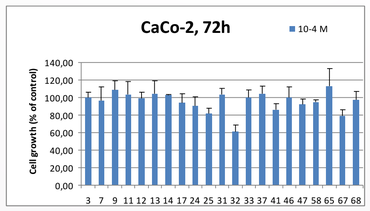
comp.	R1	R2	X
7	H	OH	NBz
8	H	-(CH2)4-CH3	NBz
9	H	-(CH2)6-CH3	NBz
10	H	-(CH2)9-CH3	NBz
11	H	-CH3	NBz
12	H	-(CH2)3-CH3	NBz
13	H	-(CH2)4-CH3	NBz
14	H	F	NBz
15	H	-(CH2)4-CH3	O
16	H	-(CH2)3-CH3	O
17	Br	-CH3	O
18	CH3	-CH3	O
19	CH3	-(CH2)3-CH3	O
20	CH3	-(CH2)4-CH3	O
21		-(CH2)7-CH3	O
22		-(CH2)4-CH3	O
23		-(CH2)7-CH3	NBz
24		-(CH2)9-CH3	NBz
25		-(CH2)2-CH3	NBz
26		-(CH2)3-CH3	NBz
27		-CH3	-
28	Br	-CH3	-
29	CH3	-(CH2)5-CH3	-
30	CH3	-(CH2)9-CH3	-
31		-(CH2)4-CH3	-
32	H	-(CH2)4-CH3	-
33		-(CH2)3-CH3	Bz
34	H	-CH3	Bz
35	H	-(CH2)4-CH3	H
36	H	-(CH2)4-CH3	Bz
37	H	F	Bz
51	H2C	-(CH2)2-	NBz
52	CF3	-(CH2)4-CH3	NBz
53	Cl	-(CH2)9-CH3	NBz
54	Cl	-(CH2)7-CH3	NBz
55	H2C	H2C	NBz
56		-(CH2)2-	NBz
57	H2C	CH3	O
58	F	-(CH2)9-CH3	O
59	Cl	CH3	O
60	CF3	CH3	O
61	CH3	-(CH2)4-CH3	O
62	CF3	F	O

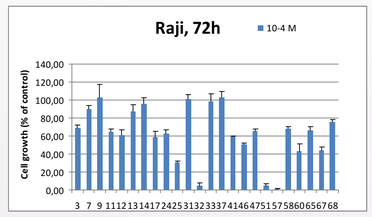
comp.	R1	R2	R3
63	H2C	-(CH2)2-	H
64	Cl	-(CH2)9-CH3	H
65	CF3	F	H
66	CF3	-(CH2)4-CH3	Bz
67	F	-(CH2)9-CH3	-
68	Cl	CH3	-
69	CF3	F	-

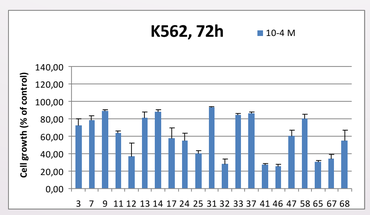
CYTOSTATIC AND ANTIBACTERIAL EVALUATIONS

The novel compounds were evaluated against HeLa, CaCo-2, Raji and K562 tumor and normal MDCK I cell lines, as well as against a panel of gram negative and gram positive bacterial strains. Triazole derivative **46** inhbits the growth of K562 cells to 75 % and about 50 % of Raji cells. Compound **32** inhibits Raji cell growth almost completely, while inhibitory properties on K562 and HeLa cells is weaker. In addition, cytosine derivative **25** inhibits the growth of K562 and Raji cells more than 54 %, but has no effect on HeLa tumor cells. Furopyrimidine derivative **67** has shown the most prominent cytostatic effects on K562 and Raji cells at about 55 % inhibition of cell growth. HeLa and Raji cell lines have shown stronger resistance to compounds **41** and **66** in comparison to K562 cells. C-5 alkynylated *N*-1-triazolyluracil derivative **60** inhibits 50 % of Raji cell growth as well as less than 35 % on HeLa cell growth. *p*-chlorophenyl-1,2,3-triazolyl-5-iodouracil derivative (**49**) showed the best antibacterial activity against *Enterococcus faecalis* cell lines.









CONCLUSION

Compounds with the most prominent antitumor activities will serve as leading molecules for synthetic structure modification in aim to develop more selective and more active antitumor compounds.

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