Synthesis and biological properties of chosen symmetrical amides and thioamides of terephthalic acid

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Introduction

Modern Organic Chemistry is a research area which connects not only the synthesis of new chemical compounds with interesting properties, but also the design and prediction of attractive structures and properties. The new compounds are widely used in various industries such as pharmaceutical, electronics, chemical and others.

Diamides of terephthalic acid obtained in the reactions with amino acids possess interesting properties. Functionalization using bioactive compounds is attractive in terms of synthesis, as in this way it is possible to get new active analogs.

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Experimental methods

The aim of this study was the synthesis of new diamide and dithioamide derivatives of terephtalic acid and testing for biological activity.

Synthesis of diamides of terephthalic acid consisted in reactions of aminoacids with terephthalic acid chloride[1)]. Synthesis of dithioamide derivatives consisted in thionation[2)].

Table 1. Antifungal activity

	MIC (IC_{80}) (μM/L)			
	clogP	***C. albicans* CCM 8261**	***C. krusei* CCM 8271**	***C. parapsilosis* CCM 8260**
1a	–0.15 ± 0.52	> 128	> 128	> 128
2a	3.83 ± 0.67	> 128	> 128	> 128
3a	1.61 ± 0.53	> 128	> 128	> 128
1b	1.66 ± 0.66	**64**	**64**	**64**
2b	6.00 ± 0.66	> 128	> 128	> 128
3b	3.42 ± 0.66	> 128	> 128	> 128

Table 2. Antibacterial activity

	MIC (IC_{80}) (μM/L)					
	clogP	***S. aureus* MRSA SA 630**	***S. aureus* MRSA SA 3032**	***S. aureus* MRSA Sa**	***S. aureus* SA 63718 ATCC 29213**	***Escheric hia coli***
1a	–0.15 ± 0.52	> 256	> 256	> 256	> 256	> 256
2a	3.83 ± 0.67	> 256	> 256	> 256	> 256	> 256
3a	1.61 ± 0.53	> 256	> 256	> 256	> 256	> 256
1b	1.66 ± 0.66	**256**	**64**	**64**	**64**	> 256
2b	6.00 ± 0.66	> 256	**256**	**128**	> 256	> 256
3b	3.42 ± 0.66	**256**	**128**	**128**	**128**	> 256

The compounds were tested for their antibacterial[3)], antifungal[4)] and antimycobacterial[3)] activities.

Results and discussion

The chemical structure of the received compounds, oxygen (1a-3a) and sulphur (1b-3b) analogs, was confirmed using ^{1}H spectra and ^{13}C NMR, and mass spectrometry.

Setting a MIC (Minimal Inhibitory Concentration) parameter defined antifungal properties (Table 1). For the tests, three pathogenic species of the fungi species Candida (*C. albicans, C. fragile, C. parapsolosis*) were used.

Table 3. Antimycobacterial activity

	MIC (IC_{80}) (μM/L)			
	clogP	***M. smegmatis*** **ATCC 700084**	***M. marinum*** **CAMP 5644**	***M. kansasii*** **DSM 44162**
1a	–0.15 ± 0.52	> 256	> 256	**256**
2a	3.83 ± 0.67	> 256	> 256	> 256
3a	1.61 ± 0.53	> 256	> 256	> 256
1b	1.66 ± 0.66	**256**	> 256	**128**
2b	6.00 ± 0.66	> 256	> 256	> 256
3b	3.42 ± 0.66	> 256	> 256	**256**

The next stage of research was to determine the antimicrobial properties (Table 2). For this purpose the strains of Gram-positive bacteria *S. aureus* (Sa ATCC 29213), methicillin-resistant *S. aureus* (MRSA 63718, SA 630, SA 3202) and Gram-negative *E. coli* were used.

The final stage of biological research was to test the activity of bacteria species mycobacterium (Table 3). The tests were carried out using different incubation time, i.e. 3 to 21 days for the corresponding strain of bacteria.

Conclusions

The tests of biological properties of new derivatives show an increase in activity for the thioamides in relation to their oxygen counterparts. However, none of the analogs tested showed high biological activity.

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Conflicts of interest: none.

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