

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.

Table 1. Antifungal activity

	clogP	MIC (IC ₅₀) (µM/L)		
		<i>C. albicans</i> CCM 8261	<i>C. krusei</i> CCM 8271	<i>C. parapsilosis</i> 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

	clogP	MIC (IC ₅₀) (µM/L)				
		<i>S. aureus</i> MRSA SA 630	<i>S. aureus</i> MRSA SA 3032	<i>S. aureus</i> MRSA Sa	<i>S. aureus</i> SA 63718 ATCC 29213	<i>Escherichia coli</i>
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

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.

Experimental methods

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

Synthesis of diamides of terephthalic acid consisted in reactions of aminoacids with terephthalic acid chloride¹⁾. Synthesis of dithioamide derivatives consisted in thionation²⁾.

The compounds were tested for their antibacterial³⁾, antifungal⁴⁾ and antimycobacterial³⁾ activities.

Results and discussion

The chemical structure of the received compounds, oxygen (1a-3a) and sulphur (1b-3b) analogs, was confirmed using ¹H spectra and ¹³C 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

	clogP	MIC (IC ₅₀) (µM/L)		
		<i>M. smegmatis</i> ATCC 700084	<i>M. marinum</i> CAMP 5644	<i>M. kansasii</i> 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.

References

1. Yu S-L., Doub X-Q., Qua D-H., Feng Ch-L. C2-symmetric benzene-based organogels: A rationally designed LMOG and its application in marine oil spill. *J. Mol. Liq.*, 2014; 190, 94–98.
2. Polshettiwar V., Kaushik M. P. A new, efficient and simple method for the thionation of ketones to thioketones using P4S10/Al2O3. *Tetrahedron Lett.* 2004; 45, 6255–6257.
3. Pauk K., Zadrazilova I., Imramovsky A., Vinsova J., Pokorna M., Masarikova M., Cizek A., Jampilek J. New derivatives of salicylamides: Preparation and antimicrobial activity against various bacterial species. *Bioorg. Med. Chem.* 2013; 21, 6574–6581.
4. Adlard P. A., Cherny R. A., Finkelstein D. I., Gautier E., Robb E., Cortes M., Volitakis I., Liu X., Smith J. P., Perez K., Laughton K., Li Q-X., Charman S. A., Nicolazzo J. A., Wilkins S., Deleva K., Lynch T., Kok G., Ritchie C. W., Tanzi R. E., Cappai R., Masters C. L., Barnham K. J., Bush A. I. Rapid Restoration of Cognition in Alzheimer's Transgenic Mice with 8-Hydroxy Quinoline Analogs Is Associated with Decreased Interstitial AB, *Neuron* 2008; 59, 43–55.