

SINTEZA, BOJADISARSKA SVOJSTVA I BIOLOŠKA AKTIVNOST NOVIH BENZOTIAZOLNIH AZO BOJILA

SYNTHESIS, DYEING PROPERTIES AND BIOLOGICAL ACTIVITY OF NEW BENZOTHIAZOLE AZO DYES

Magda Relić¹, Mario Herceg¹, Ana Sutlović¹, Mihajlo Banjanac², Vedrana Radovanović², Leentje Persoons³, Dirk Daelemans³, Livio Racané^{1*}

¹Sveučilište u Zagrebu Tekstilno-tehnološki fakultet, Prilaz baruna Filipovića 28a, 10000 Zagreb, Croatia.

²Pharmacology in vitro, Selvita Ltd. Prilaz baruna Filipovića 29, 10000 Zagreb, Croatia.

³KU Leuven, Department of Microbiology, Immunology and Transplantation, Rega Institute, 3000 Leuven, Belgium

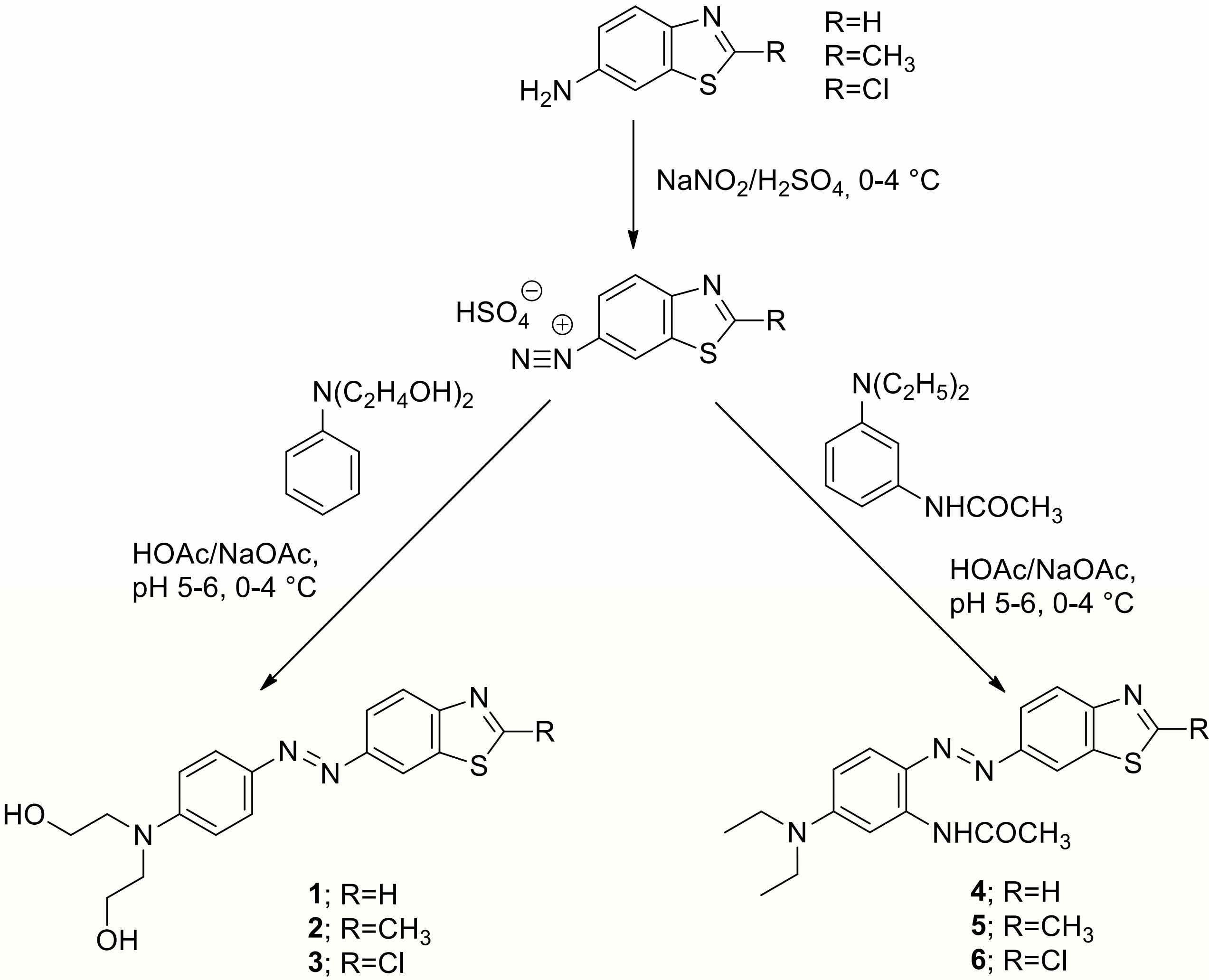
INTRODUCTION

Aromatic and heteroaromatic azo compounds represent the most numerous and diverse group of synthetic dyes, used not only as textile dyes, but also in many other different industry fields: for dyeing various substrates, biological-medical research, in the field of nonlinear optics and optical data storage. In a continuation of our previous research in the synthesis of benzothiazole azo dyes [1] and biological evaluation of 6-substituted benzothiazole derivatives [2] in this work we present synthesis, dyeing properties, antiproliferative and antimicrobial activity of 6-azo-substituted benzothiazole dyes.

RESULTS AND DISCUSSION

Synthesis

An efficient method for the synthesis of a small library of 6-azo-substituted benzothiazole molecules by diazotation reactions of three 6-amino-substituted benzothiazole derivatives and by copulation of the corresponding diazonium salts to two *N,N*-disubstituted aniline derivatives are presented in Scheme 1.

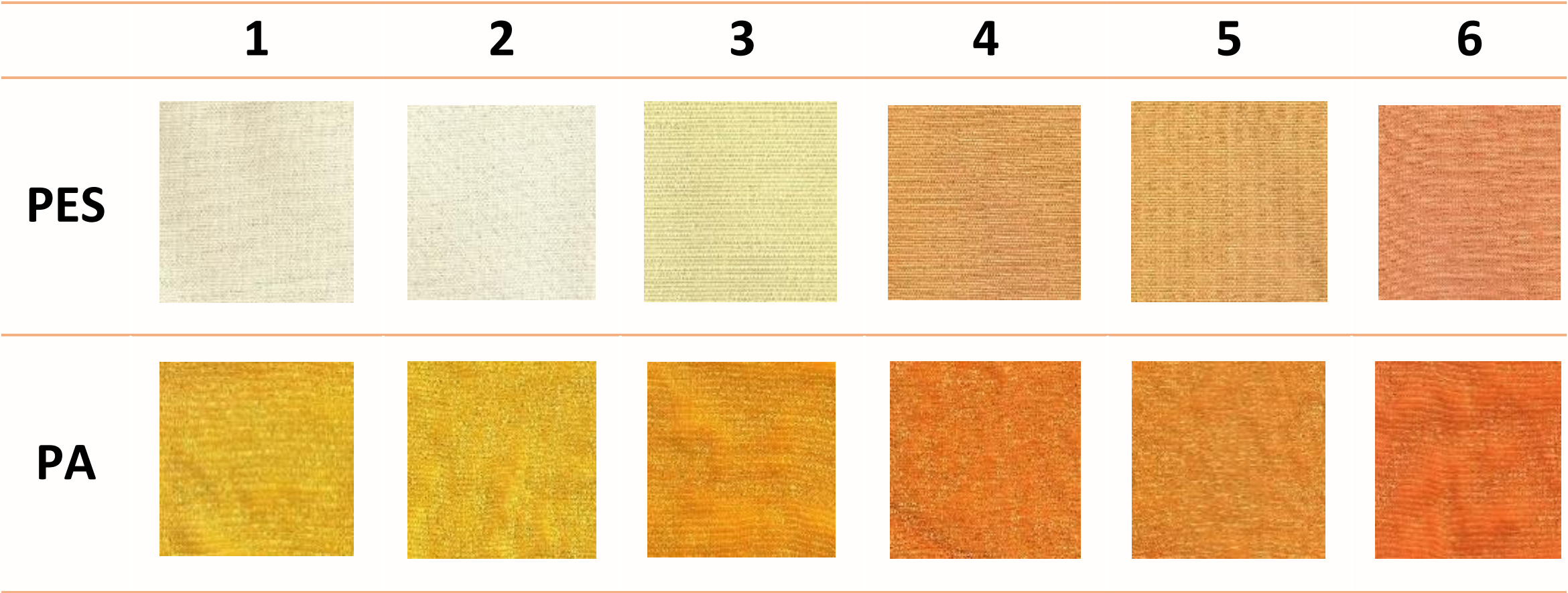


Scheme 1: Synthesis of benzothiazole azo-dyes 1-6

Dyeing properties

The obtained dyes have been tested as disperse dyes for polyester (PES) and polyamide (PA) textile material and the corresponding colour are showed in Figure 1. All six tested dyes have good application properties for dyeing PA textile materials, while dyes 4-6 proved to be good for PES.

Figure 1. Polyester (PES) and polyamide (PA) fabrics coloured with benzothiazole azo dyes 1-6



Biological activity

In order to determinate biological activity of presented new azo dyes *in vitro* anti-proliferative and antibacterial evaluations of azo dyes 1-6 were performed and the results are presented in Table 1. and 2. The anti-proliferative and antimicrobial activity strongly depends on the molecular structure of azo dyes. For azo dyes 4 and 5 the anti-proliferative activity in micromolar range of concentration was observed towards several tumor cell lines in contrast to azo dyes 2 and 3 which have no activity against tumor cell lines but showed activity against *S. aureus* and *E. coli* efflux.

Table 1. In vitro anti-proliferative activity of azo dyes

Compound	IC ₅₀ ^a (μM)							
	Capan-1	HCT-116	LN229	H460	DND-41	HL-60	K562	Z138
	Pancreatic Adenocarcinoma	Colorectal Carcinoma	Glioblastoma	Lung Carcinoma	Acute Lymphoblastic Leukemia	Acute Myeloid Leukemia	Chronic Myeloid Leukemia	non-Hodgkin Lymphoma
1	36.9	50.5	51.3	21.9	>100	90.5	92.0	79.1
2	>100	>100	>100	>100	>100	78.9	>100	72.4
3	18.2	>100	>100	>100	79.0	42.3	>100	52.4
4	2.2	2.7	3.4	6.2	>100	2.9	>100	>100
5	2.0	3.9	3.5	10.7	>100	>100	>100	>100
6	37.2	66.5	75.2	93.6	>100	88.8	>100	88.7
Etoposide	0.03	3.4	3.7	6.1	1.0	0.8	4.0	0.7
Nocodazole	0.02	0.04	0.4	0.5	0.7	0.04	0.04	0.04

^aCompound concentration required to inhibit tumor cell proliferation by 50%; standard deviation was omitted for clarity

Table 2. Antibacterial activity of azo dyes

Compound	MICs ^a (μg/mL)			
	<i>S. aureus</i> ATCC 29213	<i>E. coli</i> ATCC 25922	<i>E. coli</i> efflux del	<i>S. pneumoniae</i> ATCC 49619
1	>64	>64	>64	>64
2	32	>64	16	>64
3	64	>64	8	>64
4	>64	>64	>64	>64
5	>64	>64	>64	>64
6	>64	>64	>64	>64
Ampicillin	0.5	2	2	<0.125
Ceftazidime	8	<0.125	0.25	0.5
Ciprofloxacin	0.125	<0.125	<0.125	0.5
Meropenem	<0.125	<0.125	<0.125	<0.125

^aminimal inhibitory concentrations

References

[1] Racané, L., Mihalić, Z., Cerić, H., Popović, J., Tralić-Kulenović, V. *Dyes and Pigments*, 96, **2013**, 672–678. [2] Racané, L., Ptiček, L., Fajdetic, G., Tralić-Kulenović, V., Klobučar, M., Kraljević Pavelić, S., Perić, M., Paljetak, H. Č., Verbanac, D., Starčević, K. *Bioorganic Chemistry*, 95, **2020**, 103537.