the Ministry
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United Nations
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Junior Academy of Sciences
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SYNTHESIS OF IMIDAZO[2,1-*b*][1,3] THIAZINES AND DETERMINATION OF THEIR ANTI-INFLAMMATORY ACTIVITY

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National Center “Junior Academy of
Sciences of Ukraine” under the auspices of UNESCO

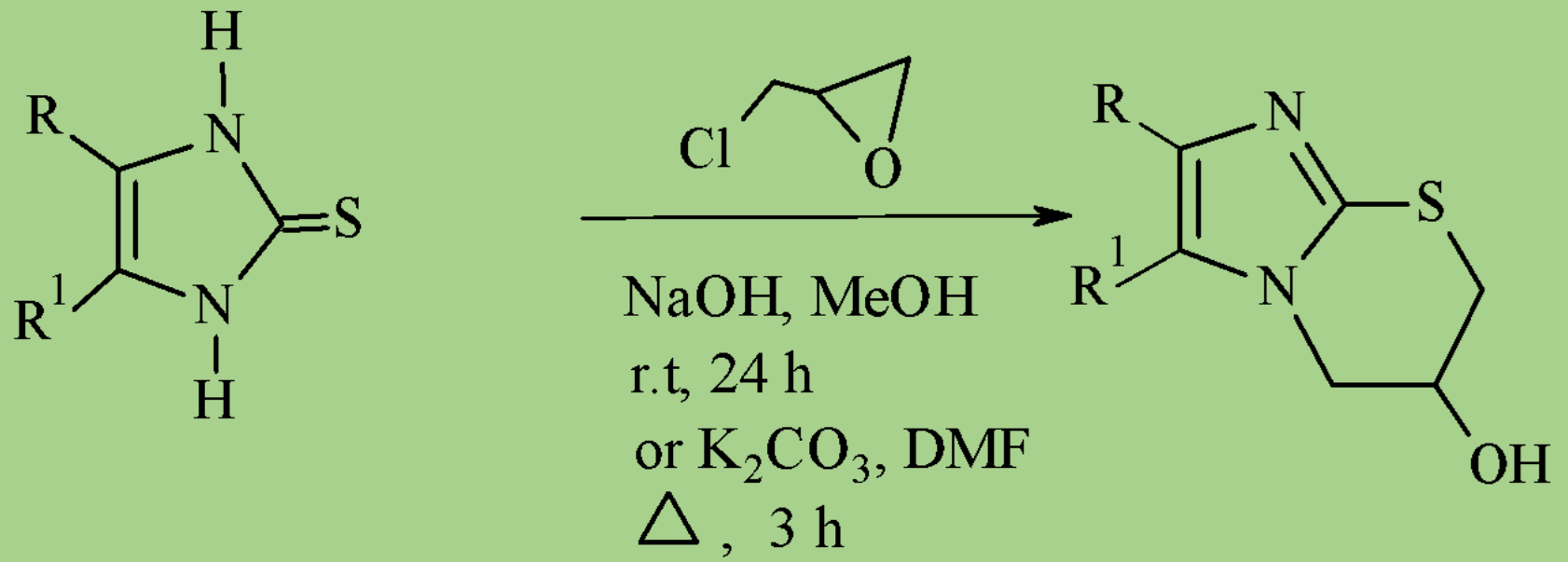
Project aim: to synthesize new functionalized derivatives of imidazo[2,1-*b*] thiazine.

Introduction

Since the 80s of the 20th century, the increased interest of scientists has focused on methods of synthesis and biological activity of imidazo[2,1-*b*]thiazine derivatives. Due to the fact that imidazothiazines exhibit various biological properties, namely antiviral, antitumor and others, this became a strong argument for the construction of new ones based on them.

- trypanocidal
- antiviral
- antifungal
- antituberculosis
- antiparasitic

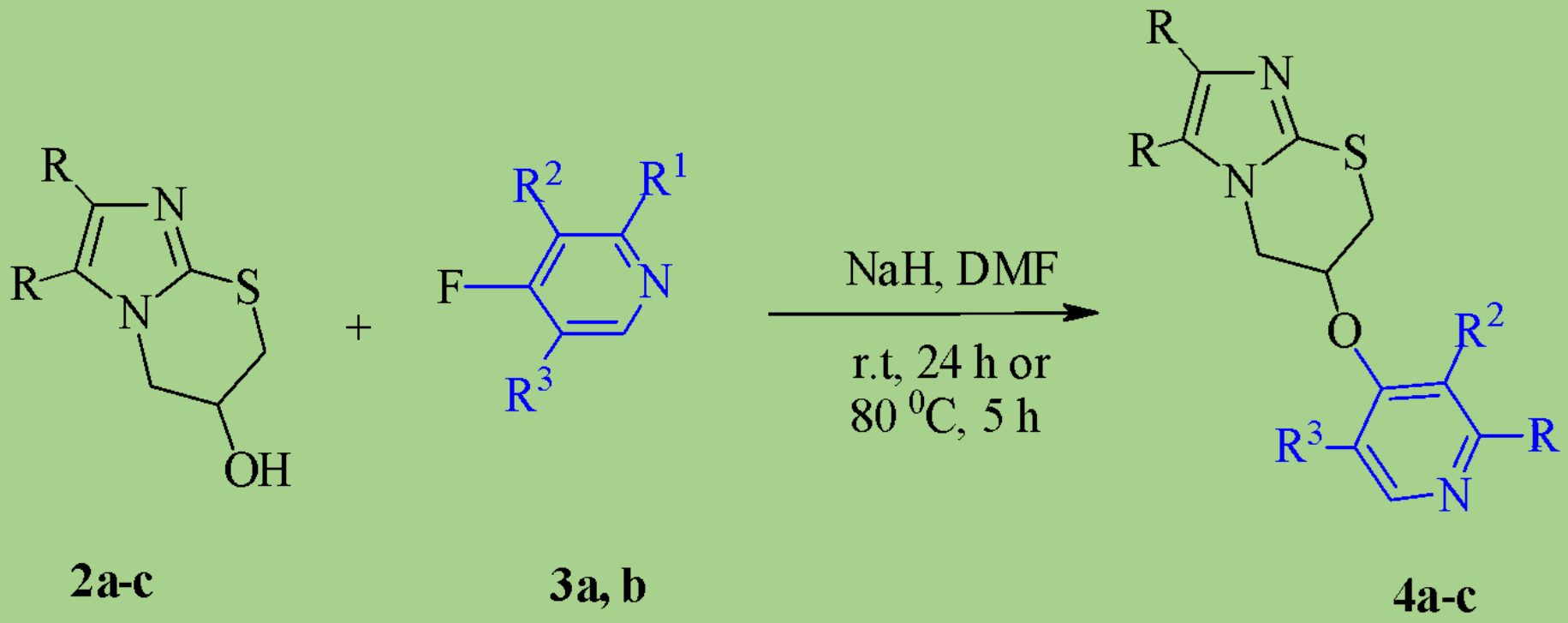
Synthesis of 3-hydroxy(benzo)imidazo[2,1-*b*][1,3]thiazines



1a-c **2a-c (89-93%)**

1,2 **a** R=H, **b** R=R^1=Ph, **c** RR^1=(CH=CH)$_2$

Synthesis of 6-[(pyridin-2-yl)oxy]-6,7-dihydro-5H-imidazo[2,1-*b*][1,3]thiazines



2a-c

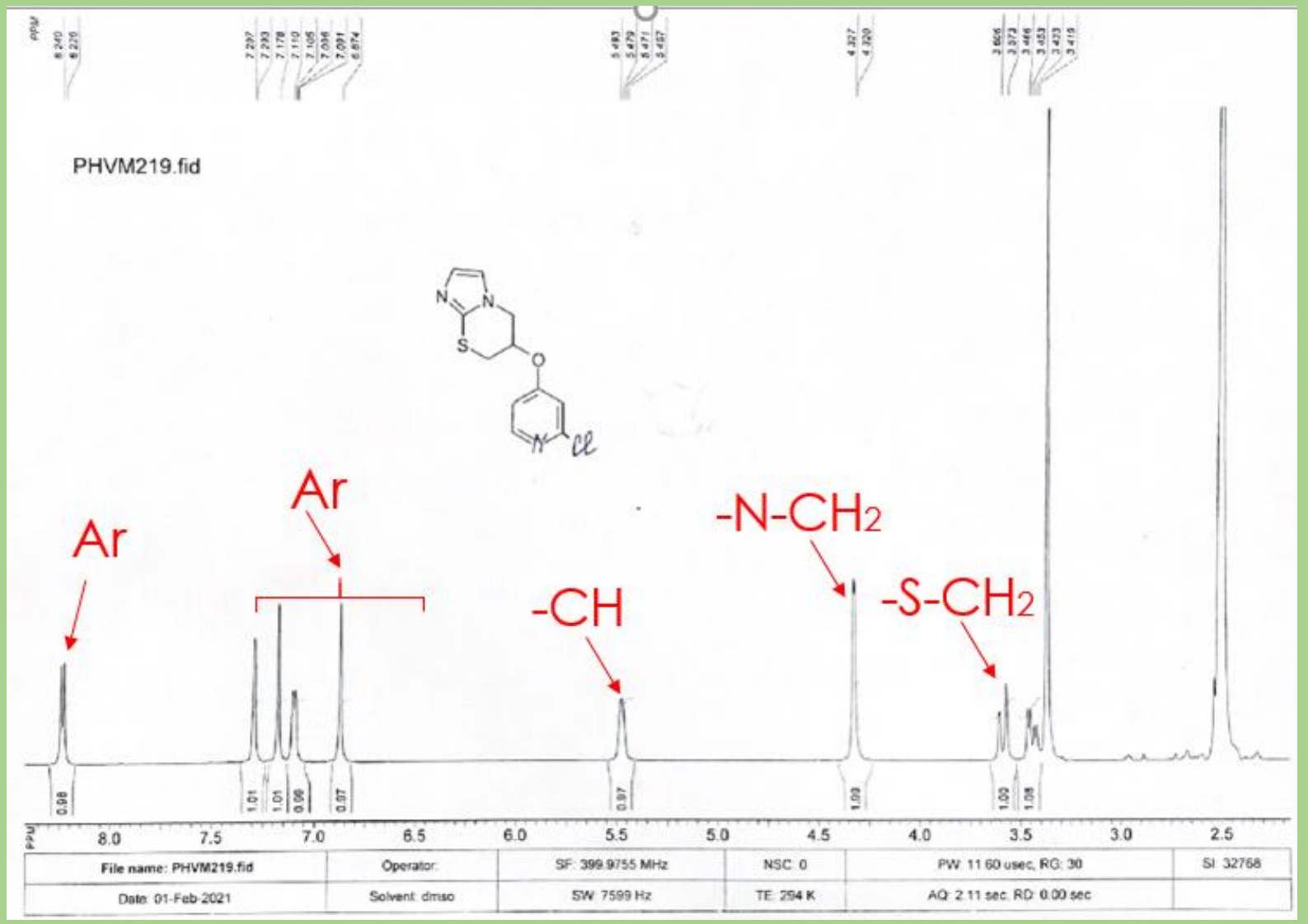
3a, b

4a-c

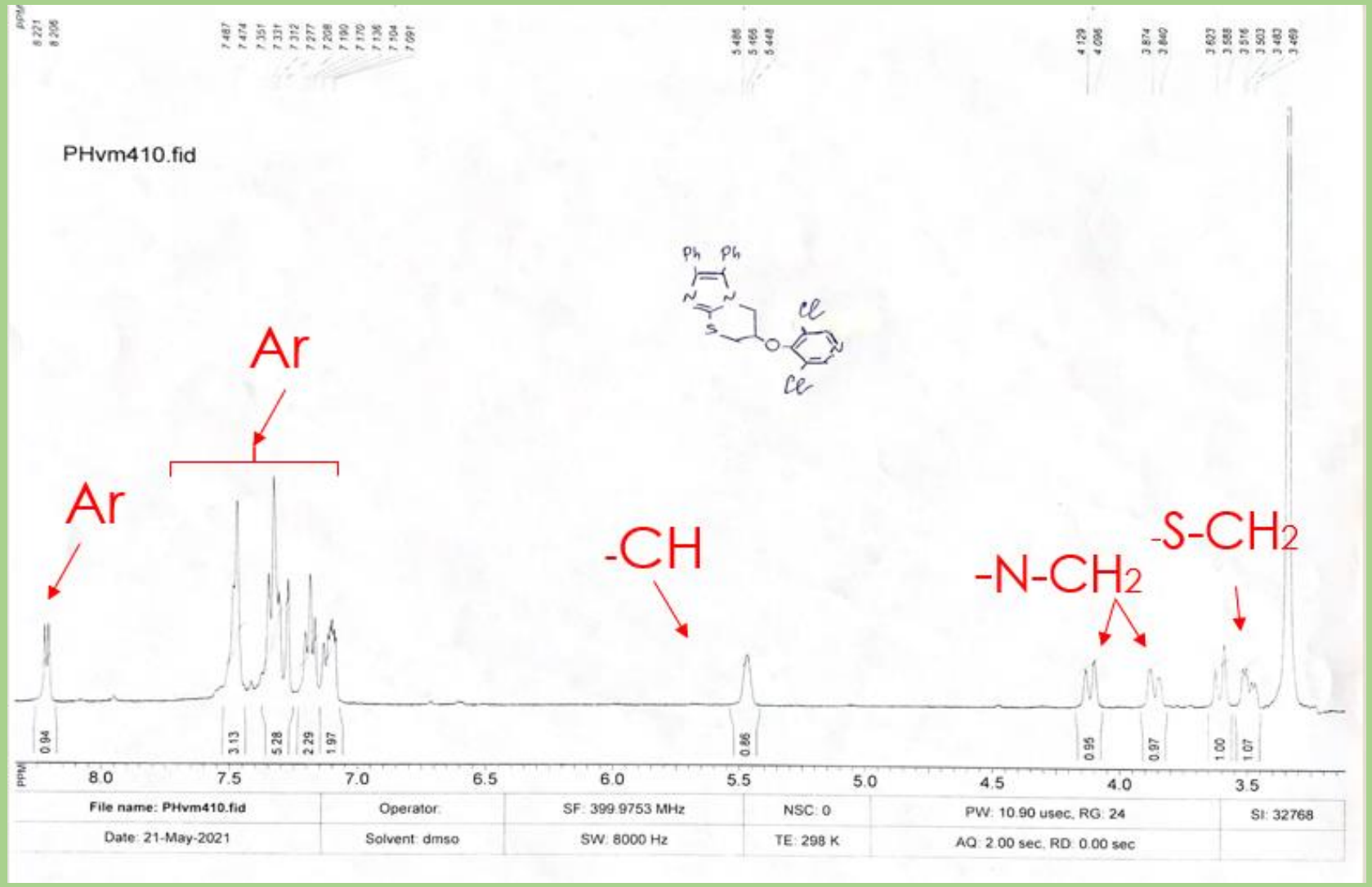
2 a R=H;
b R=Ph;
c RR=(CH=CH)$_2$

3 a R^1=Cl, R^2=R^3=H;
b R^1=H, R^2=R^3=Cl

^{1}H NMR of 6-[(2-chloropyridin-4-yl)oxy]-6,7-dihydro-5H-imidazo[2,1-*b*][1,3]thiazine

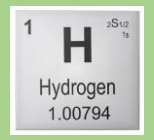


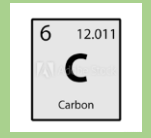
^{1}H NMR of 6-[(3,5-Dichloropyridin-4-yl)oxy]-2,3-diphenyl-6,7-dihydro-5H-imidazo[2,1-*b*][1,3]thiazine

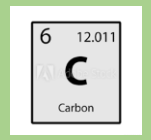


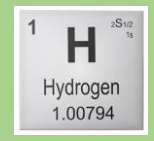
Elemental analysis of compound synthesis

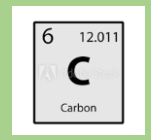
Compounds	Found, %	Anal. Calcd. %	M.p.°C
4a	C 49.10; H 3.80; N 15.77	C 49.35; H 3.76; N 15.69	124-125
4b	C 60.61; H 3.73; N 15.79	C 60.80; H 3.77; N 15.61.	108-110
4c	C 56.47; H 3.77; N 13.36.	C 56.69; H 3.81; N 13.22.	177-178



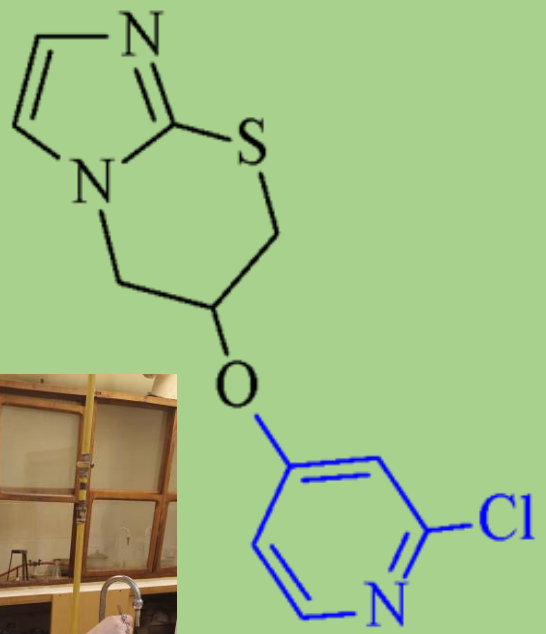




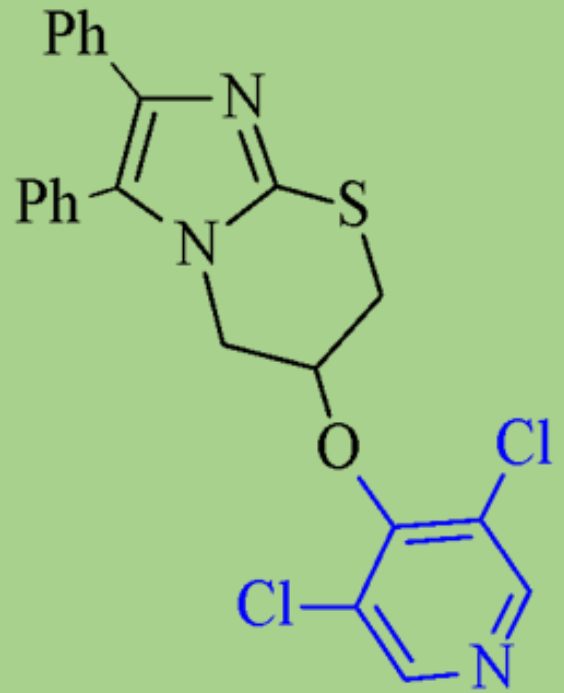




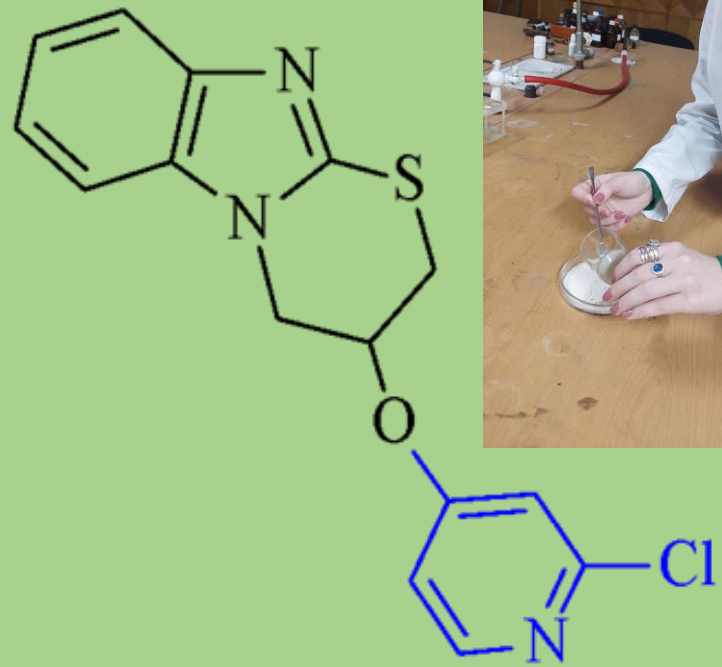
Determination of anti-inflammatory activity



4a



4b



4c

Volume of paw edema (%) and percentage of inhibition inflammation (%)

Compounds/Reference drug, Doses	Rat hind limb volume increase, 4 hours, %	Inflammation inhibition, %
Carrageenin	122.9±10.8	-
4a	71.8±8.1	41.6
4b	99.1±10.8	19.4
4c	75.1±8.3	38.9
Diclofenac sodium	65.9±5.3	46.3

Prediction of acute toxicity

Parameters/Groups	Animals with ulcers	Ulcer degree, points
Intact control	0	0±0.00
4a	0	0±0.00
4c	0	0±0.00
Diclofenac sodium	6	1.6±0.2

Conclusions

1. The reaction of nucleophilic substitution of 3-hydroxy-3,4-dihydro-2H-(benzo)imidazo [2,1-*b*][1,3]thiazines with substituted halopyridines synthesized a series of (pyridin-4-yl)oxy(benzo)imidazo[2,1-*b*][1,3]thiazines was synthesized with yields of 63-72%.

2. The composition and structure of the obtained 6-arylidene derivatives of imidazo[2,1-*b*]thiazine were reliably confirmed by complex physicochemical analysis. In particular, the data of NMR ^{1}H-, ^{13}C- and chromatography-mass spectrometry, as well as the data of elemental analysis.

3. Studies on anti-inflammatory activity have shown that imidazo[2,1-*b*]thiazine derivatives have a sufficiently high anti-inflammatory effect at low toxicometric parameters *in vivo*.

4. It was established that all compounds synthesized for the first time are non-toxic, when administered intraperitoneally.

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