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SYNTHESIS OF NEW DERIVATIVES OF 2-ACYLISOTHIOCYANATE OF 1-NITRO-9,10-ANTHRAQUINONE WITH ANTIMICROBIAL ACTIVITY

Одержано нові ацильні похідні антрахінону взаємодією 1-нітро-2-ацилізотіоціанат-антрахінону-9,10 з гліцином, 2-амінобензойною кислотою, амінотіазолом, 2-меркаптобензтіазолом, *о*-фенілендіаміном, тіогліколевою кислотою та етиловим естером ціаноцтової кислоти. Виявлені нові похідні 1-нітро-2-ацилізотіоціанат-антрахінону-9,10 з антимікробною дією стосовно *Staphylococcus aureus* та *Candida tenuis*. Показано перспективні напрями досліджень синтезованих сполук на основі біологічного скринінгу *in silico*.

Ключові слова: антрахінон, гетероциклізація, мікробіологічний скринінг.

New acyl derivatives of anthraquinone by interaction of 1-nitro-2-acylisothiocyanate-anthracenedione-9,10 with glycine, 2-aminobenzoic acid, aminothiazole, 2-mercaptobenzthiazole, *o*-phenylenediamine, thioglycolic acid and ethyl cyanoacetate were obtained. New derivatives of 1-nitro-2-acylisothiocyanate-anthracenedione-9,10 with antimicrobial activity against *Staphylococcus aureus* and *Candida tenuis* were determined. Perspective research directions of synthesized compounds on the base on biological screening *in silico* were showed.

Key words: anthraquinone, heterocyclization, microbiological screening.

Introduction. Derivatives of 9,10-anthraquinone is one of the most important classes of organic compounds. Chemistry of anthraquinone and its derivatives have long stood out into an independent and large area of organic chemistry. Interest of anthraquinone and its derivatives due to ample opportunities for getting them as substances needed modern technology and medicine. The greatest part of 9,10-anthraquinone derivatives are used them as dyes, and with development of new areas of science and technology, they have found their application in color photography and electrophotography, laser technology, LCD and photochromic materials [1]. Among the various of anthraquinones are identified also biologically active compounds. Quite a large number of anthraquinone compounds are found in plants, microorganisms [2], among of them are natural antibiotics anthracyclines [3] and cidamicines [4]. In this regard, there is an increasing interest to anthraquinone derivatives as compounds prospective for multipurpose use which is an incentive for research to develop methods of synthesis of substituted anthraquinones. Recently, anthracene derivatives actively began to gain new application areas such as biologically active agents, analytical reagents [5–7], phosphors [8], the components of liquid crystal compositions, photo materials, chemical additives for polymeric materials and etc [1]. The possibility of obtaining derivatives of anthraquinone based on a large number of valuables in a practical of substances provides a close relationship of research in the chemistry of anthraquinone are most important area of synthetic organic chemistry - the targeted synthesis of new organic compounds with a given complex of chemical, physical and biological properties. Increasing the number of publications about the synthesis and application of anthraquinone derivatives shows continued interest to series of compounds like in our country and in the world. Actuality of research in chemistry of anthraquinone and its derivatives determined not only by tasks of synthetic organic chemistry, but also determined by tasks of the theoretical organic chemistry. From a theoretical point of view research of chemistry of anthraquinone and its

derivatives is important for understanding of reactivity, chemical transformations of organic molecules and the laws of organic reactions [9, 10].

As a result of electrophilic effects of two carbonyl groups the anthraquinone or its derivatives are not amenable to alkylation and acylation in the nucleus by the method of Friedel-Crafts. Introduction carboncontaining substituents with the formation of new C-C-bond between the substituent and anthraquinones nucleus yet been achieved only in narrow groups of similar structure compounds using techniques that do not have a general character. On the other hand, reactions of anthraquinones that occur with the formation of the carbon skeleton is lesser known today and can serve as a basis for improvement of consumer properties famous practically valuable substances (dyes, biologically active substances, photomaterials and etc.), and for obtaining new perspective intermediate of fine chemicals. The data that characterize relationship between the structure and reactivity of anthraquinone derivatives in these reactions are also have great interest as a scientific basis for planning the strategy and tactics of organic synthesis aimed at creating substances and materials of modern technology [9, 10].

Despite a widely studied chemistry of 9,10-anthraquinone, many classes derivatives of anthraquinone are scarcely explored so seems actual to develop methods of synthesis of new, in this case, 2-acylalkylic and 2-acylheterocyclic compounds of 1-nitro-9,10-anthraquinone, study their chemical properties and identify among these compounds are useful for practical use.

Aim. Synthesis of new promising 2-acylalkylic and 2-acylheterocyclic derivatives of 1-nitro-9,10-anthraquinone and investigation of their antimicrobial activity.

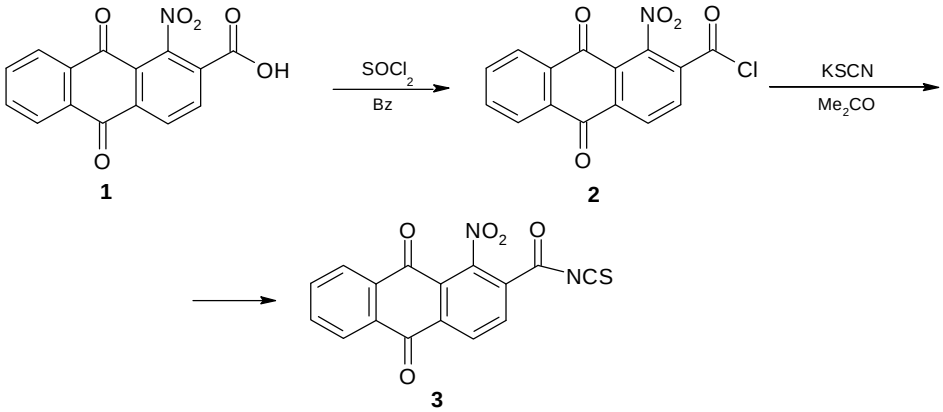
Scientific novelty of the obtained results. New derivatives of 1-nitro-9,10-anthraquinone with oxalidone, aminobenzimidazole, oxazine, quinasoline, benzothiazole, thiazole and dithiocarbamine acid fragment were obtained for the first time.

It was investigated that the interaction between glycine and acylthiocyanate in the presence of triethylamine formed thiourea derivative that followed by a cyclization with obtaining of acyloxalidone derivatives of 9,10-anthraquinone.

It was found that the interaction of acylisothiocyanate with o-phenylenediamine, in the presence of base, passes with elimination of hydrogen sulfide to form acylaminobenzimidazole.

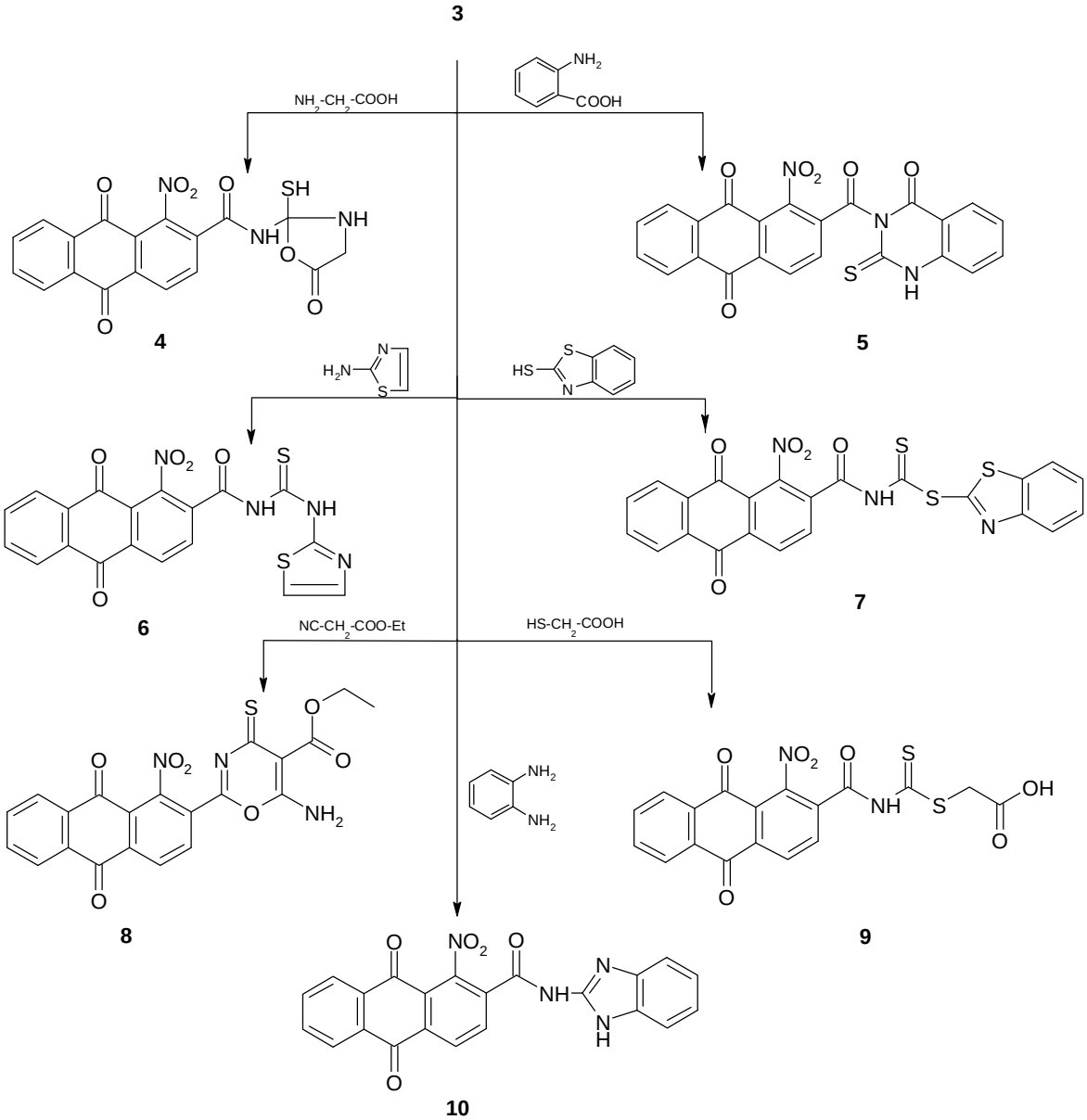
Formation of oxazine derivative occurs due to intramolecular cyclization.

Discussion of results. The starting compound for the synthesis of new derivatives of 9,10-anthraquinone was 1-nitro-9,10-dioxide-9,10-dyhydroanthracen-2-carboxylic acid (**1**) [11], which was treated with thionyl chloride in benzene in the presence of catalytic amounts of DMF. The reaction mixture was kept at reflux for 5 h., unlike methods [12] precipitate of 1-nitro-9,10-dioxo-9,10-dihydroanthracene-2-carbonyl chloride (2) was filtered, dried under vacuum and used for the following reactions (Scheme 1). The melting point of the product (2) meets the data in the literature [13].



Scheme 1. Obtain of 1-nitro-9,10-anthraquinone-2-carbonylisothiocyanate (3)

For new derivatives of acylisothiocyanate of 9,10-anthraquinone (4-10) held a one-step interaction of 1-nitro-9,10-anthraquinone-2-carbonyl chloride (2) with potassium thiocyanate in anhydrous acetone by boiling the reaction mixture for 2 h., followed by addition of the appropriate reagent - glycine, 2-aminobenzoic acid, aminothiazole, 2-mercaptobenzthiazole, o-phenylenediamine, thioglycolic acid and ethyl cyanoacetate (Scheme 2). Use of separately selected acylisothiocyanate are less convenient because there is a reduction target yield of the product by an average of 15 %.



Scheme 2. Synthesis of new acyl derivatives of 9,10-anthraquinone

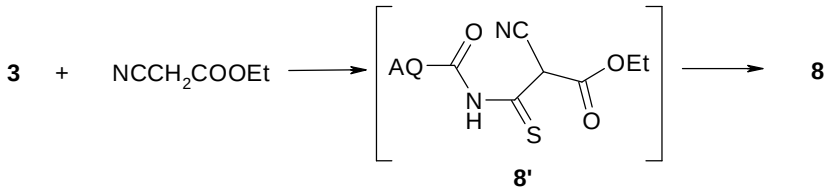
Glycine at interacting with acylisothiocyanate **(3)** in the presence of triethylamine formed thiourea derivative, which cyclization in N-(2-mercapto-5-oxooxazolidin-2-yl)-1-nitro-9,10-dioxo-9,10-dihydroanthracene-2-carboxamide **(4),** for which in the IR spectrum are the specific absorption band formed of oxalidone fragment: NH-group at 3370, 3178 cm^{-1}, SH-group at 2063 cm^{-1} and C = O at 1740 cm^{-1} in oxalidone fragment and at 1645 cm-1 in the acyl fragment. In the ^{1}H NMR spectrum there are signals of oxalidone fragment ~ - two singlet at 5.21 and 10.64 ppm, which correspond to SH-and NH-groups. Mass spectrum of oxalidone **(4)** shows a molecular ion peak [M +1] with mass 414.

Interaction of 2-aminobenzoic acid with 1-nitro-9,10-anthraquinone-2-carbonylisothiocyanate **(3)** led to the formation of 1-nitro-2-(4-oxo-2-thioxo-1,2,3,4-tetrahydroquinazoline-3-carbonyl)anthracene-9,10-dione **(5)**. IR spectrum of quinazoline derivative **(5)** is the characteristic band at 1706 cm^{-1} and 1649 cm^{-1} for C = O groups of acylic fragment at 1337 cm^{-1}, which correspond to fluctuations of C = S-group and characteristic peaks of quinazolines ring at 1630-1620, 1580-1570 and 1515-1480 cm^{-1}.

Addition of acylisothiocyanate to S-nucleophiles - 2-mercaptobenzothiazole and thioglycolic acid in the presence of a base was to produce 2-acyldithiobenzamine derivatives - benzo[d]thiazol-2-yl(9,10-dioxo-9,10-dihydroanthracene-2-carbonyl)carbamodithioate **(7)** and 2-(((1-nitro-9,10-dioxo-9,10-dihydroanthracene-2-carbonyl)carbamothioyl)thio)acetic acid **(9)**. Acylbenzothiazoles fragment **(7)** in the IR spectrum is characterized by absorption bands in the region 3370-3170 (NH-and OH-), 1710 and 1610 (C = O) and at 1320 cm^{-1} (C = S). Chromatography-mass spectrum of compound **(9)** shows the molecular peak [M +1] with mass 389 (61%).

1-Nitro-9,10-dioxo-N-(thiazol-2-ylcarbamothioyl)-9,10-dihydroanthracene-2-carboxamide **(6)** was obtained by nucleophilic addition of aminothiazole to the anthraquinone with formation of zwitter ion followed by protons transfer stage.

1-Nitro-9,10-dioxo-9,10-dihydroanthracene-2-carbonyl isothiocyanate **(3)** reacted with ethyl cyanoacetate in the presence of triethylamine to give ethyl 6-amino-2-(1-nitro-9,10-dioxo-9,10-dihydroanthracen-2-yl)-4-thioxo-4H-1,3-oxazine-5-carboxylate **(8)**. Formation of oxazine occurs through uninsulated thioamides, which undergoes intramolecular cyclization (Scheme 3).



Scheme 3. Obtain of ethyl 6-amino-2-(1-nitro-9,10-dioxo-9,10-dihydroanthracen-2-yl) -4-thioxo-4H-1,3-oxazine-5-carboxylate (8)

The structure of the synthesized compounds confirmed by IR, ^{1}H NMR and elemental analysis. Monitoring the progress of the reaction was performed by TLC.

For new 2-acyl derivatives of 1-nitro-9,10-anthraquinone was carried out biological screening *in silico* using software PASS C & T (Prediction of Activity Spectra for Substances) [14, 15], that predicted by the structural formula of the chemical substance 565 kinds of biological activity, including main and side pharmacological effects, mechanisms of action, mutagenicity, carcinogenicity, teratogenicity and embryotoxicity.

Application of PASS C & T is comfortable and useful, because is to identify new effects and mechanisms of action for old compounds; finding the most likely new leaders with the appropriate spectrum of activity among the compounds with research and commercial databases; identifying the most promising compounds for large-scale screening of most existing samples, identify areas of screening, which most important for the individual compounds. Biological activity described in the PASS system by qualitative way (presence / absence), which is explained by including the necessity to use information from different sources in the formation of training samples [14,15]. Result of prediction represented as a list of activities with the approach of P_a and P_i, built in order of reducing dependence $(P_a-P_i)>0$. Pa is an estimate of the probability of a compound to be active and inactive, respectively, for each type of activity spectrum of biological effects.

Data of prediction of biological activity of 2-acylisothiocyanate-1-nitro-9,10-anthraquinone derivatives obtained online [16] and presented in Table. 1.

Table 1

Predicted biological activity
of derivatives of 2-acylisothiocyanate-1-nitro-9,10-anthraquinone if P_a> 0.2 %

Compound / Biological action	4	5	6	7	8	9	10
Treatment of liver diseases					0,906	0,571	
Inhibitor of superoxide dismutase	0,529			0,443	0,323	0,865	0,371
Inhibitor of aldehydeoxidase				0,766		0,304	
Treatment of diarrhea	0,447					0,722	0,563
Treatment of cerebral ischemic disease		0,323		0,632			
Anticancer effect	0,562	0,556	0,521	0,596	0,541	0,505	0,581
Inhibitor of transcription factor STAT3	0,344		0,56	0,469			0,524
Anthelmintic (Nematodes)				0,596		0,592	0,557
Treatment of allergic dermatitis	0,546		0,417			0,377	0,318
Carcinogenic properties	0,258	0,218			0,211	0,243	
Anticancer effect (breast cancer)		0,523		0,538		0,561	
Treatment of hepatitis		0,501		0,431		0,557	0,455
Violation of the endocrine system		0,508		0,304		0,372	
Inhibition of alcohol dehydrogenase				0,492			
Optic neuritis	0,415	0,345		0,519		0,514	0,435
Radiosensitizing property	0,484						0,474
Mutagenic property	0,221					0,269	0,287
Inhibitor of tioredoksyne		0,418		0,487			0,368
Anthelmintic action						0,576	0,575
Insecticidal action						0,577	0,576
Causes gastrointestinal bleeding	0,465	0,324				0,313	
Antihelicobacter pylori		0,556					
Optic neuropathy	0,418	0,335		0,477		0,47	0,396
Reproductive dysfunction	0,351	0,345					0,311
Antitumor effects (cancer of the pancreas)		0,512	0,503				0,578
Hyperthermic effect							0,337
Antifungal action	0,509					0,547	
Antyshystomal action		0,345				0,333	0,323
Antiprotozoal action	0,341		0,322				0,312
Antiviral action			0,327				
Cytostatic effect					0,388	0,335	
Antimycobacterial action	0,354		0,376		0,351		

The results of predicted screening indicate the promising of research of synthesized compounds for anticancer, anthelmintic and hepatoprotective action.

Experimental biological screening was carried out at the Department of Technology Biologically Active Substances, Pharmacy and Biotechnology of Lviv Polytechnic National University. Preliminary antimicrobial activity was studied by the deffusion method [17]. To establish the exact effective concentrations of synthesized compounds were carried out by experimental research *in vitro* by method of “serial dilution” [17] (minimum

bactericidal concentration (MBCC), the minimum bacteriostatic concentration (MBSC), the minimum fungicidal concentration (MFCC), fungiostatic minimum concentration (MFSC)). In the experiments used the following test strains: bacteria Escherichia coli, Staphylococcus aureus, Mycobacterium luteum and fungi Candida tenuis, Aspergillus niger. Activity of synthesized compounds was compared (control C) with antibacterial drug like Vancomycin and antifungal - Nystatin.

Some of the compounds showed moderate antimicrobial activity. However, there were determined substances with pronounced activity (Table 2, 3).

Table 2

Antimicrobial activity of 2-acylisothiocyanate-1-nitro-9,10-anthraquinone by diffusion method

№	№ compounds	Concentration, %	Diameter of growth inhibition zone microorganisms, mm				
			E. coli	S. aureus	M. luteum	C. tenuis	A. niger
1.	**4**	0,5	0	14.0	12.0	11.0	0
		0,1	0	8.0	0	0	0
2.	**5**	0,5	0	21,4	13,4	15.0	0
		0,1	0	14.4	7.0	9.0	0
3.	**6**	0,5	0	25.4	10.6	14.0	0
		0,1	0	12.4	0	8.0	0
4.	**7**	0,5	0	13.4	16.7	20.0	15.0
		0,1	0	7.0	0	18.0	10.0
5.	**8**	0,5	0	15.7	15.0	19.0	0
		0,1	0	10.0	0	13.0	0
6.	**9**	0,5	0	16.0	15.0	21.0	10.0
		0,1	0	10.0	0	15.0	0
7.	**10**	0,5	0	15.7	16.4	15.0	0
		0,1	0	0	0	12.0	0
8.	C	0,1	14.0	15.0	18.0	19.0	20.0

Table 3

Antimicrobial activity of 2-acylisothiocyanate-1-nitro-9,10-anthraquinone by "serial dilutions" method

№	№ compound	Strain cultures							
		Staphylococcus aureus		Mycobacterium luteum		Candida tenuis		Aspergillus niger	
		MBCC, μg / ml	MBSC, μg / ml	MBCC, μg / ml	MBSC, μg / ml	MFCC, μg / ml	MFSC, μg / ml	MFCC, μg / ml	MFSC, μg / ml
1.	4	+	+	15.6	31.2	31.2	62.5	+	+
2.	5	+	+	15.6	31.2	15.6	31.2	+	+
3.	6	62.5	250.0	15.6	31.2	15.6	31.2	+	+
4.	7	15.6	125.0	7.8	31.2	15.6	31.2	3.9	125.0
5.	8	250.0	*	7.8	31.2	31.2	62.5	31.2	*
6.	9	15.6	*	31.2	125.0	31.2	*	31.2	*
7.	10	125.0	*	15.6	31.2	15.6	31.2	+	+

* – in evalueted concentrations the indexes of biocidic effect not found

+ – growth of microorganism

Experimental part. 1-Nitro-9,10-anthraquinone-2-carbonylchloride (2). To 10 g (0.035 mmol) of 1-nitro-9,10-anthraquinone-2-carboxylic acid **(1)** in 200 ml of dry benzene at room temperature was added 9 ml thionyl chloride and a catalytic amount of DMF. The reaction mixture was maintained at reflux 5 h., cooled, the precipitate filtered. Yield 9.73 g (91%).

General method for preparation of derivatives of 2-acylisothiocyanate-1-nitro-9,10-anthraquinone (4-10). To 2 g (0.007 mol) of 1-nitro-9,10-anthraquinone-2-carbonyl chloride **(2)** in 50 mL of acetone by heating added 0.75 g (0.007 mmol) of potassium thiocyanate, kept 2 h. Then added 0.007 mole of the appropriate amine / thiol / CH-acid and 1 ml of triethylamine. The reaction mixture was boiled 6 h., cooled, the precipitate filtered, washed with a small amount of acetone, then with water and dried.

N-(2-Mercapto-5-oxooxazolidin-2-yl)-1-nitro-9,10-dioxo-9,10-dihydroanthracene-2-carboxamide (4). Yield 0.86 g (60%). Mp = 252 ° C, $C_{18}H_{11}N_3O_7S$. Calculated,%: C 52.30, H 2.68; N 10.17; S 7.76. Found,%: C 52.05, H 2.91; N 10.35; S 7.61.

1-Nitro-2-(4-oxo-2-thioxo-1,2,3,4-tetrahydroquinazoline-3-carbonyl)anthracene-9,10-dione (5). Yield 1.136 g (63%). Mp = 242 ° C, $C_{23}H_{11}N_3O_6S$. Calculated,%: C 60.39, H 2.42; N 9.19; S 7.01. Found,%: C 60.51, H 2.47; N 9.22; S 7.22.

1-Nitro-9,10-dioxo-N-(thiazol-2-ylcarbamothioyl)-9,10-dihydroanthracene-2-carboxamide (6). Yield 0.84 g (60%). Mp = 230 ° C, $C_{19}H_{10}N_4OS_2$. Calculated,%: C 52.05, H 2.30; N 12.78; S 14.63. Found,%: C 52.20, H 2.27; N 17.73; S 14.68.

Benzo[d]thiazol-2-yl(9,10-dioxo-9,10-dihydroanthracene-2-carbonyl)carbamodithioate (7). Yield 1.2 g (82.7%). Mp = 224 ° C, $C_{23}H_{12}N_2O_3S_3$. Calculated,%: C 59.98, H 2.63; N 6.08; S 20.89. Found,%: C 60.07, H 2.70; N 6.11; S 20.80.

Ethyl 6-amino-2-(1-nitro-9,10-dioxo-9,10-dihydroanthracen-2-yl)-4-thioxo-4H-1,3-oxazine-5-carboxylate (8). Yield 35%, Mp = 228 ° C, $C_{21}H_{13}N_3O_7S$. Calculated,%: C 55.88, H 2.90; N 9.31; S 7.10. Found,%: C 55.96, H 2.99; N 9.24; S 7.14.

2-(((1-nitro-9,10-dioxo-9,10-dihydroanthracene-2-carbonyl)carbamothioyl)thio)acetic acid (10). Yield 42%. Mp = 214 ° C, $C_{18}H_{10}N_2O_7S_2$. Calculated,%: C 50.23, H 2.34; N 6.51; S 14.90. Found,%: C 50.28, H 2.38; N 6.58; S 14.88.

N-(1H-benzo[d]imidazol-2-yl)-1-nitro-9,10-dioxo-9,10-dihydroanthracene-2-carboxamide (10). Yield 0.94 g (65%). Mp = 270 ° C, $C_{22}H_{12}N_4O_5$. Calculated,%: C 64.08, H 2.93; N 13.59. Found,%: C 64.12, H 2.95; N 13.71.

Data of ^{1}H NMR and IR spectroscopy of the compounds obtained are given in Table 4.

Table 4

Spectral data of acyl derivatives of 1-nitro-9,10-anthraquinone

№	^{1}H NMR, ppm	IR, cm^{-1}
4	4.13-4.24 (2H, dd, *J* = 15.6, CH_2); 5.21 (1H, s, SH); 6.18 (1H, s, NH); 7.93-8.01 (2H, m, CH_{ar}); 8.11-8.24 (3H, m, CH_{ar}); 8.49 (d, 1H, *J*=8.45 Hz, CH_{ar}); 10.64 (1H, s, NH)	3370, 3178 (NH), 2063 (SH), 1740, 1682, 1645 (C=O)
5	7.54-7.68 (3H, m, CH_{ar}); 7.87-7.99 (3H, m, CH_{ar}); 8.23-8.32 (2H, m, CH_{ar}); 8.43 (d, 1H, *J*=8.45 Hz, CH_{ar}); 8.33 (d, 1H, *J*=8.45 Hz, CH_{ar}); 10.71(1H, s, NH)	1706, 1686, 1660, 1649 (C=O), 1337 (C=S), 1630-1620, 1580-1570 i 1515-1480 (quazolines ring)
6	7.68 (d, 1H, *J*=4.16 Hz, CH); 7.88-7.98 (2H, m, CH_{ar}); 8.05 (d, 1H, *J*=4.16 Hz, CH); 8.21-8.30 (2H, m, CH_{ar}); 8.48, 8.50 (2d, each 1H, *J*=8.45 Hz, CH); 10.45(1H, s, NH); 10.68 (1H, br. s, NH)	3364, 3171 (NH), 1722, 1683, 1645 (C=O), 1332 (C=S)
7	7.08-7.17(2H, m, CH_{ar}); 7.77-8.07 (3H, m, CH_{ar}); 8.21-8.31 (3H, m, CH_{ar}); 8.46, 8.48 (2d, each 1H, *J*=8.45 Hz, CH); 10.72 (1H, br. s, NH)	3360 (NH), 1731, 1685, 1623 (C=O), 1333 (C=S)
8	1.29 (3H, t, ^2J=2.88 Hz, ^3J=7.1Hz, CH_3); 4.26 (2H, q, ^2J=-10.79 Hz, ^3J=7.1Hz, CH_2); 7.81 (2H, br. s, NH_2); 7.86-7.96 (2H, m, CH_{ar}); 8.23-8.33 (2H, m, CH_{ar}); 8.61 (d, 1H, *J*=8.45 Hz, CH_{ar}); 9.15 (d, 1H, *J*=8.45 Hz, CH_{ar})	3570-3500 (NH_2); 1723, 1648, 1665 (C=O); 1331 (C=S)
9	4.25 (2H, d, *J*=15 Hz, CH_2); 7.85-7.97 (2H, m, CH_{ar}); 8.20-8.31 (2H, m, CH_{ar}); 8.41-8.49 (2H, m, CH_{ar}); 10.65 (1H, br. s, NH); 11.41 (1H, br. s, OH)	3360 (NH), 3000-2500 (COOH), 1723, 1670, 1659 (C=O); 1335 (C=S)
10	7.11-7.17 (2H, m, CH); 7.36-7.40 (2H, m, CH); 7.83-7.99 (2H, m, CH_{ar}); 8.23-8.33 (2H, m, CH_{ar}); 8.45, 8.64 (2d, each 1H, *J*=8.45 Hz, CH); 10.21, 10.67 (2H, s, 2NH)	3372, 3168 (NH), 1707, 1685, 1642 (C=O)

Conclusions. As a result of the work proposed preparative methods for the synthesis of new 2-acyl derivatives of 1-nitro-9,10-anthraquinone. It was found that the interaction between 1-nitro-9,10-anthraquinone-2-carbonylisothiocyanates with glycine formed thiourea derivative which cyclization in oxalidone acyl derivative of 9,10-anthraquinone; with o-phenylenediamine we can passes elimination of hydrogen sulfide to form acylaminobenzimidazole; and obtaining of ethyl 6-amino-2-(1-nitro-9,10-dioxo-9,10-dihydroanthracen-2-yl)-4-thioxo-4H-1,3-oxazine-5-carboxylate passes through intramolecular cyclization. Based on the computer screening showed promising directions for further experimental research in a order of synthesized compounds. Experimental screening for antimicrobial action discovered compounds with antibacterial and antifungal action againts to *Staphylococcus aureus* and *Candida tenuis.*

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