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N-ALKOXYMETHYL DERIVATIVES OF 2-AMINOTHIAZOLE AND THEIR PROTECTIVE PROPERTIES

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Abstract: Conditions for alkoxy methylation of 2-aminothiazole with semiformals obtained by the interaction of aliphatic alcohols with formaldehyde were worked out. Alkoxy methylation was performed by means of preliminary preparation of the semiformal of appropriate hydroxyl-containing compounds followed by interaction of semiformal with equimolar amount of 2-aminothiazole. The structure of the obtained compounds was acknowledged by means of IR and NMR ^1H spectroscopy. It was established that the reaction of the alkoxy methylation proceeds in the amino form of the starting 2-aminothiazole to form an appropriate monosubstituted N-alkoxymethyl derivative. As a result of microbiological tests, it was established that these compounds have high bactericidal properties against microorganisms which affect petroleum products and, at a concentration of 0.5%, completely protect both M-8 lubricating oil and diesel fuel from damage by bacteria even in terms of their forced infection. It found that at a concentration of 100 mg/l the obtained compounds protect the CT-3 steel from acid corrosion, moreover N-(isopropoxymethyl)thiazol-2-amine has the greatest protection effect.

Keywords: 2-aminothiazole, the tautomerism, imino form, amino form, the alkoxy methylation, semiformals, alkoxy methyl derivatives, antimicrobial activity, anticorrosion properties, oil products, microorganisms, biodamage.

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Introduction

As it is known that 2-aminothiazole is a reaction centers and can enter into chemical potentially tautomeric compound with several reactions in amino and imino forms [1]:

Studies of the effect of the type and position of the substituent on the conformational structure and amino-imine tautomerism, carried out in phases of gas, water and carbon tetrachloride showed that in these phases the amino form is more stable than the imino form and the amino tautomer is the predominant

species [2].

The presence of endocyclic sulfur and nitrogen atoms, as well as an amino group in 2-aminothiazole molecule, suggests the possibility of synthesizing numerous derivatives on its basis which could exhibit anticorrosive,

antioxidant, anti-wear properties, as well as potential antimicrobial activity.

It should be noted that 2-aminothiazole derivatives are widely used in medicine as antioxidants [3], chemotherapeutic agents [4], inhibitors of enzymes, including carboesterase [5] which are potentially powerful antidiabetic and antibacterial agents [6] demonstrating anti-tuberculosis activity [7] and exhibiting high antimicrobial properties [8-10]. Triazine derivatives containing 2-aminothiazole fragments as a substituent are recommended as

effective polyfunctional (namely anticorrosive, antiwear, and extreme pressure) additives to lubricating oils [11]. Anticorrosive and antimicrobial properties of 2-aminothiazole derivatives replaced in the position 4 by methyl, phenyl and naphthyl groups in watered jet fuel were studied [12, 13].

Object of these studies is to synthesize new derivatives of 2-aminothiazole and explore their protective (antimicrobial and anticorrosive) properties.

Experimental part

The presence of amine group with two active hydrogen atoms suggested the possibility of alkoxy methylation of this group.

Alkoxy methylation of 2-aminothiazole was carried out by preliminary preparation of

semiformal of corresponding alkanol. Paraform was used as a source of formaldehyde. Then a solution of an equimolar amount of 2-aminothiazole in ethanol was added to a semiformal cooled to 5 °C:

Synthesis of *N*-(ethoxymethyl)thiazol-2-amine

A three-necked reaction flask equipped with a mechanical stirrer, dropping funnel, thermometer, and reflux condenser was charged with 3.3g (0.1 mol) paraform, 4.6 g (0.1 mol) ethanol and ½ KOH granule. The reaction mixture was stirred at a temperature of 60°C until the paraform was completely depolymerized and semiformal formed, cooled to 5°C, and a solution of 5.0 g (0.05 mol) of 2-aminothiazole in 40 ml of ethanol was added dropwise. The mixture was stirred at 5°C for 2 hours and left at room temperature overnight. Then 50 ml of absolute benzene was added and

the reaction water was removed azeotropically with benzene in a Dean-Stark trap. After cooling, the reaction mixture was filtered. Benzene was distilled off on a water jet. The resulting crystalline product was recrystallized from boiling ethanol. There was received 3.8 g of substance (yield 48 %). The rest of alkoxy methyl derivatives were prepared in a similar manner.

The obtained compounds are crystalline substances purified by recrystallization from boiling ethanol. Physico-chemical characteristics are given in Table 1.

Results and discussion

The structure of the synthesized compounds was established by IR and ¹H NMR spectroscopy data and their composition

determined by element analysis. In the ¹H NMR spectra of these substances the following signals were observed: a broadened singlet

which was characteristic for NH group in the range 2.47-2.86 m.d., and a singlet typical for NCH₂O group in the range 5.20-5.25 m.d. Note that ¹H NMR spectroscopic data are given in Table 1.

In the IR spectrum of these compounds there was an absorption band in the region of 3183-3211 cm⁻¹ typical for valence vibrations of NH group and there was no absorption band at

3400-3500 cm⁻¹ which was typical for valence vibrations of NH₂ group.

As shown by data of IR and ¹H NMR spectroscopy, the reaction of alkoxy methylation of 2-aminothiazole proceeds in the amino form with the formation of a monosubstituted N-alkoxymethyl derivative.

As an example, the spectra of some obtained compounds are given in Fig. 1, 2, 3.

Fig 1. ¹H-NMR spectra of N-(isopropoxymethyl)thiazol-2-amine

Fig 2. ¹³C-NMR spectra of N-(isopropoxymethyl)thiazol-2-amine

Fig 3. IR Spectrum of N-(methoxymethyl) thiazol-2-amine

Table 1. Physio-chemical characteristics of N-alkoxymethyl derivatives of 2-aminothiazole

№/ №	Compound	Melting point, °C	Yield, %	Content, %		¹ H NMR spectrum, δ, m.d.
				N, <i>found</i>	S, <i>found</i>	
				<i>calculated</i>	<i>calculated</i>	
1		126-127	35	<u>19.56</u> <u>19.44</u>	<u>22.61</u> <u>22.22</u>	3.24 (s. 3 H, OCH ₃), 2.47 – 2.77 (broadened singlet 1 H, NH), 5.20 (s. 2H, NCH ₂ O), 6.85-6.9 (d. 1H, NCH), 7.26-7.28 (d. 1H, SCH)
2		126-129	48	<u>18.01</u> <u>17.72</u>	<u>20.40</u> <u>20.25</u>	0.9-1.2 (t., 3 H, CH ₃), 2.4-2.8 (broadened singlet, 1 H, NH), 5.05 (broadened singlet, 2H, OCH ₂), 5.25 (s., 2H, NCH ₂ O), 6.69 (d., 1H, NH), 7.25-7.3 (d., 1H, SCH)
3		120-121	52	<u>16.50</u> <u>16.37</u>	<u>18.9</u> <u>18.71</u>	1.11-1.90 (t., 6 H, 2 CH ₃), 2.37-2.82 (broadened singlet, 1 H, NH), 5.10 (broadened singlet, 1 H, OCH), 5.29 (s., 2 H, NCH ₂ O), 6.68 (d., 1 H, NCH), 7.23-7.27 (d., 1H, SCH)
4		127-128	30	<u>16.41</u> <u>16.28</u>	<u>18.95</u> <u>18.60</u>	3.19 (s., 3H, OCH ₃), 2.86 (s., 1H, NH), 5.11 (t., 4H, OCH ₂ CH ₂ O), 5.20 (s., 2H, NCH ₂ O), 6.85-6.87 (broadened singlet. 1H, NCH=), 7.261-7.272 (d., 1H, SCH)

Table 2. Antimicrobial properties of N-alkoxymethyl derivatives of 2-aminothiazole

№	Compound	Oil product	Concentration, %	Diameter of inhibition zone in the growth of microorganisms, cm	
				bacteria	fungi
1		Diesel fuel Lubricating oil M-8	0.5	1.6-1.5	+
			0.5	2.2-2.0	+
2		Lubricating oil M-8	0.5	2.2-2.1	+
3		Diesel fuel Lubricating oil M-8	0.5	1.7-1.5	+
			0.5	2.0-2.0	+
4		Diesel fuel Lubricating oil M-8	0.5	1.6-1.5	+
			0.5	2.0-2.0	+
5	Diesel fuel without biocide			++	++
6	Lubricating oil M-8 without biocide			++	++

+ - growth of microorganisms.

Microbiological activity against microorganisms affecting oil products (lubricating oil M-8 and diesel fuel) was investigated of a unified system of protection against corrosion and aging in accordance with GOST 9.082-77 "Oils and Lubricants. Methods of laboratory tests for resistance to bacteria", GOST 9.052-88 "Oils and Lubricants. Methods of laboratory tests for resistance to mold fungi", GOST 9.023-74 «Petroleum fuels. Method of laboratory tests for biostability of fuels protected by antimicrobial additives". Tests results are presented in Table 2.

Test results show that N-alkoxymethyl derivatives of 2-aminothiazole have good bactericidal properties. However, they are completely ineffective against mold fungi. Perhaps this is due to the poor solubility of these substances in petroleum products.

The presence of thiazole and alkoxyethylamine groups in the synthesized compounds suggests that they have potential anticorrosive properties. These properties were studied in respect of steel Cr-3 according to GOST 9.502-82 in an aggressive medium created by 0.1 N aqueous solutions of HCl and H₂SO₄.

200 ml of 0.1 N solution of acid was poured in a beaker, and the required amount of the test substance dissolved in 3 ml of ethanol was added thereto. Two coupons (40x20x0.5) Cr-3 steel were immersed in this solution so that they did not touch each other. Three hours after, the metal coupons were rinsed under running water and dried. The thin plaque on them was cleaned with rubber, the coupons were rinsed with hexane, dried with acetone and weighed to the nearest 0.0001g.

Corrosion rate was determined by the formula:

$$\rho = \frac{m_1 - m_2}{S \cdot \tau}$$

m_1 - coupon weight before testing, g.

m_2 - coupon weight after testing, g.

S - coupon area, m^2 .

τ - test time, hours.

Degree of corrosion protection was determined by the formula:

$$Z = \frac{\rho_0 - \rho}{\rho_0} \cdot 100 \%$$

ρ_0 - corrosion rate without inhibitor, $g/m^2 \cdot \text{hour}$

ρ - corrosion rate with inhibitor, $g/m^2 \cdot \text{hour}$

The test results are presented in Table 3.

Table 3. Test results of inhibiting properties

№	Inhibitor	Concentration, mg/l	0.1 N HCl		0.1 N H ₂ SO ₄	
			Corrosion rate ρ , $g/m^2 \cdot \text{hour}$	Protective effect Z, %	Corrosion rate ρ , $g/m^2 \cdot \text{hour}$	Protective effect Z, %
1	Medium: 0.1 N acid solution without inhibitor + 3 ml EtOH		3.6		5.4	
2		100	1.04	71		
3		-<<-	0.40	88		
4		-<<-	0.35	90	0.41	92
5		-<<-	0.55	85		

Test results are indicative that synthesized 2-alkoxymethyl derivatives of 2-aminothiazole possess anticorrosive properties. Their protective effect is 71-90 % at a concentration of 100 mg/l in acidic medium created by 0.1 N

solution of HCl. The sample 4 has protective effect of 90 % in 0.1 N solution of HCl, and it exhibits practically the same protective effect of 92 % in 0.1 N solution of H₂SO₄.

Conclusion

Conditions of three-component condensation of 2-aminothiazole, paraform and aliphatic alcohols were worked out, and a number of 2-alkoxymethyl derivatives of 2-aminothiazole synthesized. Their structure was proved out by the data of IR and NMR ^1H spectroscopy. It was established that

synthesized compounds in the composition of petroleum products at a concentration of 0.5 % exhibited high bactericidal properties. And they successfully protect ST-3 steel against acid corrosion caused by 0.1 N solutions of HCl and H_2SO_4 .

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2- AMINOTIAZOLUN N- ALKOKSIMETİL TÖRƏMƏLƏRİ VƏ ONLARIN MÜHAFİZƏEDİCİ XASSƏLƏRİ

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Alifatik spirtlərin formaldehidlə qarşılıqlı təsiri nəticəsində alınan poluformalların 2-aminotiazolla aminometilləşmə reaksiyası işlənib hazırlanmışdır. Alkosimetilləşmə əvvəlcədən müvafiq hidrosilsaxlayan birləşmələrin poluformalının alınması, sonra isə onun 2-aminotiazolun ekvimolyar miqdarı ilə təsiri nəticəsində aparılmışdır. Alınmış birləşmələrin quruluşu İQ- və NMR ^1H – spektroskopiya üsulu ilə təyin etmişdir. Müəyyən olunmuşdur ki, alkoksimetilləşmə ilkin 2-aminotiazolun amino-formasında gedir və uyğun monoəvəzölünmüş 2-alkoksimetil törəməsinin alınması ilə nəticələnir. Mikrobioloji sınaqlar nəticəsində təyin edilmişdir ki, bu birləşmələr neft məhsullarını zədələyən mikroorqanizmlərə qarşı yüksək bakterisid xassəyə malikdirlər və 0.5 % qatılıqda M-8 sürtkü yağı, eyni zamanda dizel yanacağını bakteriyalardan zədələnməyindən qoruyur, hətta onu məcburən zədələyəndə. Müəyyən edilmişdir ki, alınmış birləşmələr 100 mq/l qatılığında Ст-3 poladı turş mühitdə korroziyadan qoruyurlar və N-(izopropoksimetil)tiazol-2-amin ən yüksək qoruyucu effektə malikdir.

Açar sözlər: 2-aminotiazol, tautomeriya, amino-forma, imino-forma, alkoksimetilləşmə, poluformallar, alkoksimetil törəmələri, neft məhsulları, korroziya, mikroorqanizmlər, biozədələmə.

N-АЛКОКСИМЕТИЛЬНЫЕ ПРОИЗВОДНЫЕ 2-АМИНОТИАЗОЛА И ИХ ЗАЩИТНЫЕ СВОЙСТВА

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Разработаны условия реакции алкоксиметилирования 2-аминотиазола полуформальями, получаемыми взаимодействием алифатических спиртов с формальдегидом. Алкоксиметилирование проводили путем предварительного получения полуформалья соответствующего гидроксилсодержащего соединения с последующим его взаимодействием с эквимольным количеством 2-аминотиазола. Строение полученных соединений подтверждено методами ИК-, ЯМР ^1H -спектроскопии. Установлено, что реакция алкоксиметилирования протекает в amino-форме исходного 2-аминотиазола с образованием соответствующего монозамещенного N-алкоксиметильного производного. В результате

микробиологических испытаний установлено, что эти соединения обладают высокими бактерицидными свойствами в отношении микроорганизмов, поражающих нефтепродукты и при концентрации 0.5 % полностью защищают как смазочное масло М-8, так и дизельное топливо от поражения бактериями даже в условиях их принудительного заражения. Обнаружено, что полученные соединения при концентрации 100 мг/л обеспечивают защиту стали СТ-3 от кислотной коррозии, причем наибольшим защитным эффектом обладает N-(изопропоксиметил)тиазол-2-амин.

Ключевые слова: 2-аминотиазол, таутомерия, amino-форма, имино-форма, алкоксиметилирование, полуформали, алкоксиметильные производные, антимикробная активность, антикоррозионные свойства, нефтепродукты, микроорганизмы, биоповреждение.