SYNTHESIS OF 1-MORPHOLINO- AND 1-PIPERIDINO-1-ALKOXYCARBONYLMETHYLTHIOCYCLOALKANES

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***Abstract**: The reactions of mercaptoacetic acid esters with enamines, specifically with 1-morpholino- and 1-piperidino-1-cycloalkenes, have been studied. It was established that the reactions proceed readily in the absence of a catalyst, yielding 1-morpholino- and 1-piperidino-1-alkoxycarbonylmethylthio-cycloalkanes. The composition and structure of the obtained aminosulfides were confirmed by IR and NMR (^1H and ^{13}C) spectroscopy, as well as by elemental analysis.*

***Keywords**: enamines, 1-morpholino-1-cycloalkenes, 1-piperidino-1-cycloalkenes, mercaptoacetic acid esters.*
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Introduction

The development of highly efficient ashless additives for lubricating oils is among the pressing challenges in modern petrochemistry. To address this issue, it is of primary importance to investigate the relationship between the structure, physicochemical properties, and performance efficiency of additives. Such studies would facilitate the establishment of theoretical foundations for the rational design of new compounds with predetermined properties. Among the various organic compounds studied as additives for lubricating oils, particular attention has been given to sulfides, both individually and in combination with other functional groups and atoms. It is well known that certain compounds containing sulfide sulfur and amine nitrogen exhibit high effectiveness as additives for lubricating oils [1–6]. However, only a limited number of studies have focused on the correlation between the structure and composition of these compounds and their performance efficiency [7–8]. Furthermore, it is crucial to investigate the functional properties of certain classes of organic compounds that have not yet been studied in this context.

It was previously established [9] that dialkylaminomethyl alkoxycarbonylmethyl sulfides, with the general formula $R_2NCH_2SCH_2COOR$ (where R is alkyl, morpholino-, piperidino-, or R_1-alkyl), exhibit high anticorrosive, antiwear, and antimicrobial properties. It has been shown that the esters of mercaptoacetic acid are effective additives for lubricating oils [10], moreover the ketosulfides obtained as a result of the reaction of mercaptoacetic acid esters with benzylacetone have proven to be effective inhibitors of metal corrosion [11].

We considered it of particular interest to synthesize and investigate the properties of 1-morpholino-1-alkoxycarbonylmethylthiocycloalkanes and 1-piperidino-1-alkoxycarbonylmethylthiocycloalkanes. These compounds are structurally distinguished by the absence of a methylene spacer between the nitrogen and sulfur atoms.

The synthesis was carried out by studying the reactions of thioglycolic acid esters with enamines, namely 1-morpholino- and 1-piperidino-1-cycloalkenes.

It is well established that enamines (α,β-unsaturated amines) lacking an N–H proton exhibit enhanced reactivity and are capable of participating in a wide range of synthetically valuable chemical transformations.

Enamines possess two reactive centers simultaneously — the nitrogen (N) and the carbon (C) atoms — which enable them to participate in addition and alkylation reactions.

The reactions of enamines with various electrophilic reagents have been extensively studied [12–18].

In these reactions, the electrophilic attack is directed not at the nitrogen atom, but rather at the β-carbon atom, since the partial carbonyl character of the α-carbon atom in the enamine facilitates the occurrence of α-alkylation and addition reactions.

It has previously been demonstrated that enamines undergo addition with thiophenols to form α-aminosulfides [19–20].

Experimental part

IR spectra were recorded on a UR-10 spectrophotometer in the range of 4000–400 cm^{-1}.

^1H and ^{13}C NMR spectra were obtained using a Bruker spectrometer operating at 300 MHz for ^1H and 75 MHz for ^{13}C, with DMSO-d_6 as the solvent.

The starting ester of thioglycolic acid was synthesized by the esterification of thioglycolic acid with isopropyl alcohol according to the procedure described in [23] and had the following characteristics: isopropyl ester of thioglycolic acid ($HSCH_2COOC_3H_7$-i), $T_b = 165–166$ °C, $d_4^{20} = 1.0408$, $n_D^{20} = 1.4509$.

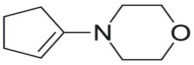
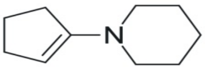
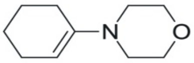
The following compounds were used as starting enamines: 1-morpholinocyclopent-1-ene, 1-morpholinocyclohex-1-ene, 1-piperidinocyclopent-1-ene, and 1-piperidinocyclohex-1-ene. These enamines were synthesized according to the procedure described in Ref. [24]. The physicochemical characteristics of the starting enamines are summarized in Table 1.

Synthesis of 1-morpholino-1-isopropoxycarbonylmethylthiocyclohexane (IV)

To a solution of 13.4 g (0.1 mol) of isopropyl ester of thioglycolic acid in dry benzene, maintained at −5 to 0 °C with vigorous stirring, 16.7 g (0.1 mol) of 1-morpholino-1-cyclohexene was gradually added (the reaction is exothermic). After the addition was complete, the reaction mixture was stirred at 40–50 °C for 5 hours. Following the removal of benzene by distillation, the product was purified by vacuum distillation. Yield: 23.63 g (78.5%).

Other 1-morpholino- and 1-piperidino-isopropoxycarbonylmethylthiocycloalkanes (compounds I, II, and III) were synthesized in a similar manner. The characteristics of these compounds are presented in Table 2.

Table 1. Physicochemical characteristics of enamines

№	Compound	Yield, %	B.p., °C (P, mmHg)	d_4^{20}	n_D^{20}
1.	 1-morpholinocyclopentene-1	82	92-93 (1.5)	1.0281	1.5121
2.	 1-piperidinocyclopentene-1	48.3	89-90 (1.5)	0.9476	1.4807
3.	 1-morpholinocyclohexene-1	60.1	95-97 (1)	1.0217	1.5132

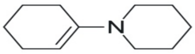
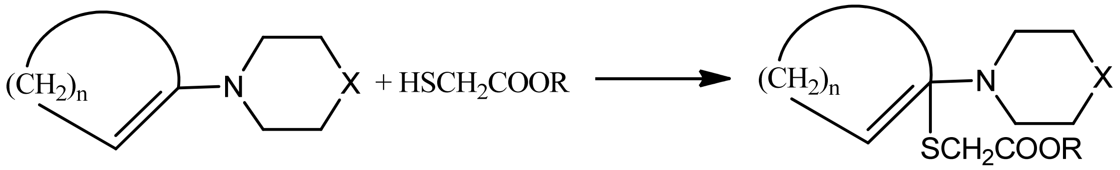
4.	 1-piperidinocyclohexene-1	72.4	96-98 (1)	0.9515	1.5004

Table 2. Characteristics of 1-morpholino(piperidino)-1-alkoxycarbonylmethylthiocycloalkanes (I-IV)

Compound	Yield, %	T_b., °C (P, mmHg)	d_4^{20}	n_D^{20}	Found, %				Formula	Calculated %			
					C	H	N	S		C	H	N	S
I	69.5	88-90 (0.5)	0.8196	1.4952	62.99	9.60	4.72	11.42	$C_{15}H_{27}O_2SN$	63.16	9.47	4.91	11.23
II	75.2	90-92 (0.5)	0.8531	1.4685	58.80	8.43	5.01	11.37	$C_{14}H_{25}O_3SN$	58.54	8.71	4.88	11.15
III	70.8	94-96 (0.5)	0.8303	1.4801	63.98	10.01	4.38	10.93	$C_{16}H_{29}O_2SN$	64.21	9.70	4.68	10.70
IV	78.5	182- 184	-	-	59.65	9.35	4.36	10.90	$C_{15}H_{27}O_3SN$	59.80	8.97	4.65	10.63

Results and Discussion

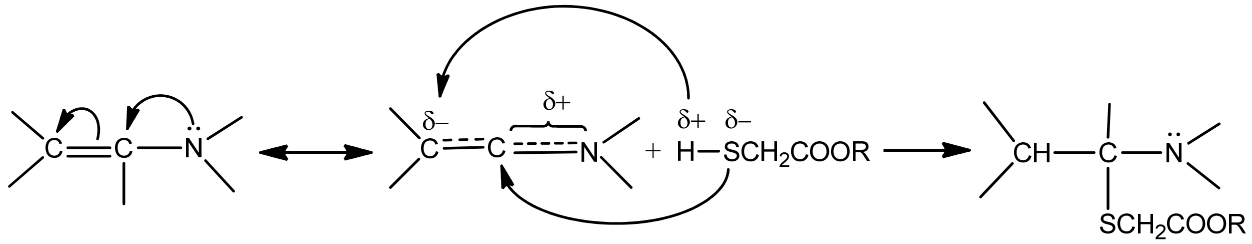
It was found that esters of thioglycolic acid readily undergo reactions with 1-morpholino- and 1-piperidino-1-cycloalkenes in the absence of a catalyst, leading to the formation of 1-morpholino- and 1-piperidino-1-alkoxycarbonylmethylthiocycloalkanes, respectively:



I - IV

n=3, X=CH_2, R= C_3H_{7-i} (I); n=3, X=O, R= C_3H_{7-i} (II)
n=4, X= CH_2, R=i-C_3H_7 (III); n=4, X=O, R= C_3H_{7-i} (IV)

In an enamine, the non-bonding electron pair of the nitrogen atom interacts with the π-bond of the C=C double bond through p–π conjugation. As a result of the positive mesomeric effect of nitrogen, the β-carbon atom becomes electron-rich, while the α-carbon atom may acquire a partial positive charge. This distribution of electron density within the conjugated system leads to the nucleophilic addition of (S–CH_2COOR) to the carbon atom at the α-position relative to nitrogen.



The structures of the synthesized compounds were confirmed by IR and NMR spectroscopy [21–22].

In the IR spectra of compounds I–IV (Fig. 1), absorption bands were observed in the range of 764–665 cm^{-1}, corresponding to the stretching vibrations of the C–S bond, as well as bands at

1732–1728 cm^{-1} and 1106–1104 cm^{-1}, indicating the presence of carbonyl (C=O) and C–N groups, respectively [21].

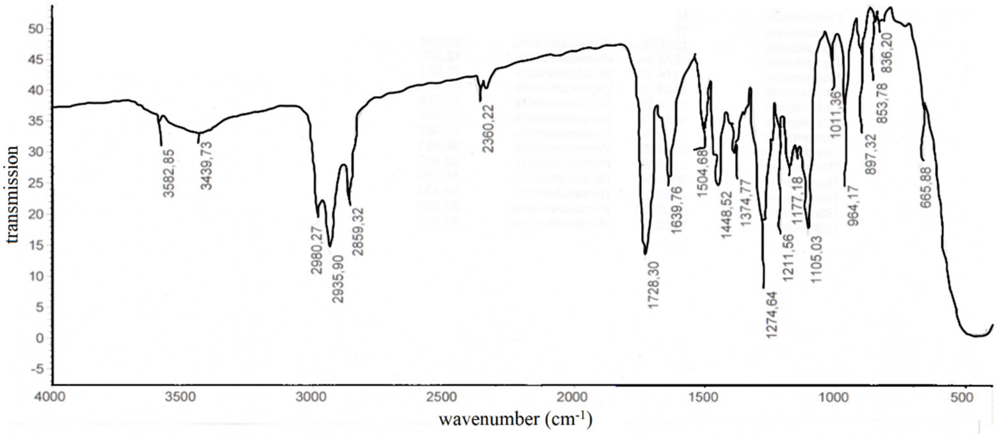


Fig.1. Infrared spectrum of 1-piperidino-1-propoxycarbonylmethylthiocyclohexane

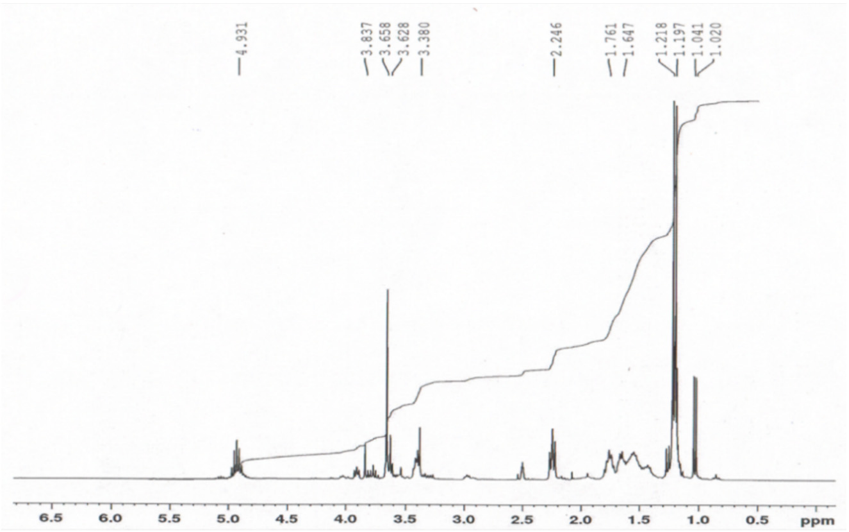


Fig.2. ^{1}H NMR spectrum of 1-piperidino-1-propoxycarbonylmethylthiocyclohexane

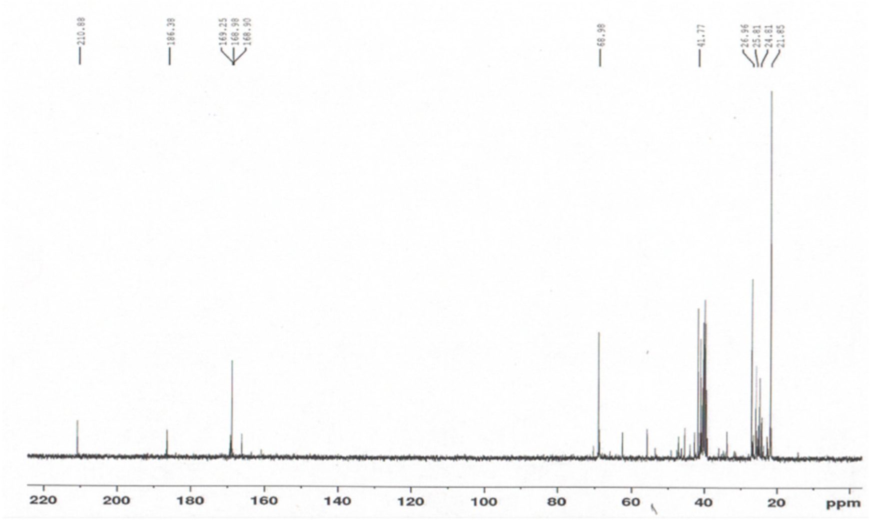


Fig. 3. ^{13}C NMR spectrum of 1-piperidino-1-propoxycarbonylmethylthiocyclohexane

The absence of an absorption band at 2600–2550 cm^{-1} indicates the involvement of the –SH group of mercaptoacetic acid ester in the addition reaction.

In the ^{1}H NMR spectrum of 1-piperidino-1-propoxycarbonylmethylthiocyclohexane (IV) (Fig. 2), the observation of a doublet corresponding to six hydrogen atoms of two methyl groups at 1.20 ppm, a multiplet corresponding to sixteen hydrogen atoms in the region of 1.41–1.76 ppm, four hydrogen atoms corresponding to two methylene groups adjacent to the nitrogen atom in the region of 2.24 ppm, a singlet corresponding to two hydrogen atoms of a methylene group at 3.38 ppm, and a multiplet of the isopropyl fragment at 4.93 ppm, as well as the corresponding carbon signals observed in the ^{13}C NMR spectrum, confirm the structure of the compound (Fig. 3). ^{13}C NMR spectrum of compound (IV) (DMSO-d$_6$, δ, ppm): 21.8 (CH_3), 24.5 (CH_2), 25.75 (CH_2), 25.8 (CH_2), 26.9 (CH_2), 38.9 (CH_2), 41.7 (CH_2), 54.7 (CH_2), 55.3 (CH), 62.1 (C), 169.3 (CO).

Based on the experimental results (Table 2), it was determined that while the yield of the obtained aminosulfides depends on the nature of the amine fragment, the size of the cycloalkene ring has almost no effect on the yield.

Conclusion

The nucleophilic addition reaction of alkyl esters of mercaptoacetic acid to 1-morpholino- and 1-piperidino-1-cycloalkenes has been investigated, and an efficient method for obtaining 1-morpholino- and 1-piperidino-1-alkoxycarbonylmethylthiocycloalkanes has been proposed. It was established that the reaction proceeds in the absence of a catalyst and affords the corresponding aminosulfides in 69.5–78.5% yields. The compositions of the synthesized compounds were confirmed by elemental analysis, and their structures were verified using IR and NMR (1H and 13C) spectroscopy.

In contrast to the previously studied aminosulfides, the synthesized 1-morpholino- and 1-piperidino-1-alkoxycarbonylmethylthiocycloalkanes are of interest for investigation as lubricant additives, since they lack a methylene group between the nitrogen and sulfur atoms. Therefore, further studies in this direction are planned at the next stage.

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