Synthesis of Nitrogen-, Oxygen-, and Sulfur-Containing Derivatives of C_5–C_6 Alicyclic Olefins and Study of Their Bactericidal Activity

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Abstract. In this work, a series of new thiourea derivatives of methyl C_5–C_6 alicyclic olefins were synthesized via their condensation with formaldehyde and hydrohalic acids in the presence of a $ZnCl_2$ catalyst, followed by the reaction of the obtained [2-chloro(bromo)-2(5)-methylcyclopentyl(cyclohexyl)]methanols with thiourea. The reaction products were characterized by IR spectroscopy and ^1H and ^13C NMR spectroscopy, and their performance as antimicrobial additives for M-10 motor oil and the water-emulsion coolant Azerol-5 was evaluated. The results show that the thiourea derivatives exhibit enhanced antimicrobial activity in petroleum-based lubricating media, which is likely associated with their improved solubility. These findings demonstrate their potential applicability as multifunctional additives for industrial lubricants and cooling fluids.

Keywords: Polyfunctional Thiocarbamides, N-, O-, S-Containing Derivatives, Alicyclic Olefins, Antimicrobial Additives, Lubricant and Fuel Additives, Industrial Multifunctional Compounds.

1. Introduction

Polyfunctional N-, O-, and S-containing derivatives of C_5–C_{12} alicyclic hydrocarbons are distinguished by their remarkable combination of chemical versatility, structural complexity, and biological activity, which collectively make them highly valuable in both academic research and industrial applications. These compounds serve as versatile "building blocks" for the synthesis of a wide array of novel molecules, including synthetic analogues of naturally occurring biologically active substances, modern pharmaceutical agents, and specialty chemicals such as perfumery products and fine chemicals [1–3].

Organic compounds containing nitrogen, oxygen, and sulfur play a crucial role in modern chemical industries due to their distinctive chemical reactivity, diverse biological

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activities, and broad spectrum of practical applications across various sectors of the economy. Among these, ureas and thioureas have attracted considerable attention as versatile functional molecules, being extensively investigated for their antimicrobial properties, corrosion-inhibiting capabilities, and effectiveness as additives in lubricating oils and fuels [5,6]. The multifunctional nature of these compounds allows them to perform multiple roles simultaneously: they can act as coordinating ligands in complex formation, as surface-active agents in modifying interfacial properties, and as biocidal agents to inhibit the growth of microorganisms. This unique combination of chemical and biological functionality renders them highly valuable in both industrial formulations and the development of novel materials with tailored properties. Furthermore, ongoing research into their structural modifications continues to expand their applicability in pharmaceuticals, agrochemicals, and environmentally friendly industrial processes.

C_5–C_{12} alicyclic olefins, including methylcyclopentene and methylcyclohexene, are important petrochemical intermediates due to the presence of a reactive double bond within their cyclic structures, which allows for selective chemical transformations. Functionalization of these olefins with heteroatoms such as nitrogen, oxygen, and sulfur can produce polyfunctional derivatives with significantly enhanced physicochemical properties, improved stability, and diverse biological activities. While monofunctional derivatives of C_5–C_{12} alicyclic cycloolefins have been extensively studied, systematic investigations of polyfunctional derivatives incorporating N, O, and S atoms remain limited. The development of such multifunctional compounds is of particular interest because they can serve as versatile building blocks for the synthesis of bioactive molecules, industrial additives, and advanced functional materials. Their unique combination of structural complexity and chemical reactivity makes them promising candidates for applications ranging from pharmaceuticals and agrochemicals to lubricants and corrosion inhibitors, highlighting the need for further research in this area.

Their multifunctional nature not only allows for precise structural modifications but also imparts a spectrum of desirable properties, including enhanced solubility, stability, and reactivity under mild conditions.

In addition to their utility in synthetic chemistry, these derivatives play an important role as intermediates or final products in the development of technologically significant materials. They function as effective additives that improve the quality, performance, and longevity of lubricating oils and fuels, while simultaneously exhibiting potent bactericidal and antiviral properties [4-5]. The integration of chemical functionality with biological efficacy underscores their potential as multifunctional industrial additives, capable of bridging the gap between chemical innovation, bioactivity, and practical technological application. These characteristics make them particularly promising candidates for the design of next-generation formulations with tailored physicochemical and biological properties, suitable for diverse industrial and biomedical applications.

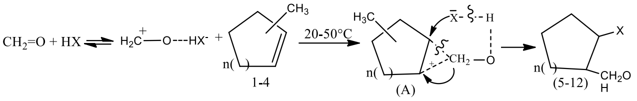
The aim of the present work is to obtain new polyfunctional compounds containing N-, O-, and S-functional groups with cyclopentane and cyclohexane fragments.

2. Experimental part

The structures of all synthesized compounds were confirmed by IR spectroscopy, ^1H and ^{13}C NMR spectroscopy, and elemental analysis. IR spectra were recorded on an Alpha FT-IR spectrometer in the range of 400–4000 cm^{-1} using KBr tablets. The ^1H and ^{13}C NMR spectra were obtained on a Bruker Biospin AG spectrometer operating at 300.18 MHz in $CdCl_3$. Elemental analysis was performed using a Tru Spec Micro analyzer (Leco Corporation, USA).

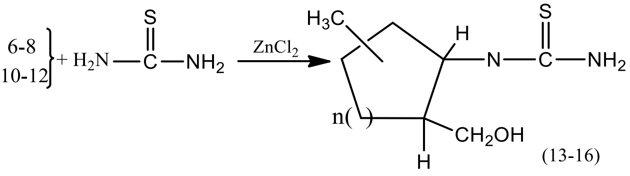
It was established that the condensation reactions of the isomers of methylcyclopentenes and methylcyclohexenes with a 40% aqueous formaldehyde solution and 36% HCl or 46% HBr acids lead to the formation of [2-chloro/bromo-2(5)-methylcyclopentyl/cyclohexyl]methanols (5–12) in a single step [6].

It should be noted that, in our case, the formation of CH_3–C_5–C_6 hydroxyhalogenides in the first stage of the condensation reactions of cycloolefins under catalytic conditions ($ZnCl_2$) proceeds analogously to the mechanism described by Krise S.S. [7]. At the beginning of the reaction, protonation of the most basic site of the formaldehyde molecule by the acid HX (X = Cl, Br) occurs, namely at the carbonyl oxygen atom, leading to the formation of a polar carbocation. The attack of this carbocation on the double bond of the cycloolefins (20–50°C) results in the formation of an active transition complex (A). Subsequently, electron density redistribution and bond cleavage within the complex take place, yielding the final products (5–12) according to Scheme 1.



Scheme 1. Where: n=1 (1,2); 1-CH_3 (5,6), 3-CH_3 (7,8), Cl (5,7), Br (6,8); n=2 (3,4); 1-CH_3 (9,10), 4-CH_3 (11,12), Cl (9,11), Br (10,12)

In the second stage, based on the synthesized [2-bromo-2(5)-methylcyclopentyl/cyclohexyl]methanols (6, 8, 10–12), their reaction with thiourea in a petroleum ether solution in the presence of anhydrous $ZnCl_2$ yielded N-, O-, S-containing derivatives: 1-(2-(hydroxymethyl)-1(3)-methylcyclopentyl) thioureas (13, 14) and 1-(2-(hydroxymethyl) -1(4)-methylcyclohexyl)thioureas (15, 16), according to Scheme 2.



Scheme 2. Where: n=1, 1-CH_3 (13), 3-CH_3 (14); n=2, 1-CH_3 (15), 4-CH_3 (16).

It was observed that both the course of the reaction and the composition of the resulting products are strongly influenced by the molar ratio of the reactants and the reaction temperature. Specifically, increasing the molar number of compounds (6, 8, 10, 12) to two equivalents of thiourea, combined with raising the reaction temperature above 65 °C, favors the formation of bis-adducts, with yields in the range of 15–25%. This behavior can be attributed to the increased availability of thiourea molecules, which enhances the likelihood of sequential nucleophilic addition to the reactive intermediate species, as well as to the elevated temperature, which facilitates the kinetic and thermodynamic conditions necessary for multiple substitution events. Such observations highlight the critical role of precise control over stoichiometry and thermal parameters in steering the reaction toward the desired polyfunctional products. Under equimolar conditions, at reaction temperatures of 20–50 °C and durations of 3–5 hours, the reaction proceeds mainly toward the formation of mono-adducts: 65–74% for compounds (13, 14) and 67–78% for compounds (15, 16). In the IR spectra of products (13–16), absorption bands at 3447 and 3345 cm^{-1} correspond to the (OH) group, while those in the higher-frequency region at 1255, 1226, and 1195 cm^{-1} correspond to (C–N) vibrations, and the bands at 1160, 1138, 1091, and 1065 cm^{-1} correspond to (C=S) bonds.

In the ^{1}H NMR spectra of product

cts (5–12), a broad singlet at 3.62 ppm is observed, assigned to the protons of the OH groups. The protons of the CH_3 groups in compounds (5, 7, 9, 10) appear at 1.03 ppm as a singlet, while for compounds (6, 8, 11, 12) they also appear as singlets.

For thioureas (13–16), the CH_3 protons appear at 1.38 ppm as a singlet for compounds (13, 14) and at 1.01 ppm as a doublet for compounds (15, 16). The NH proton resonates as a broad singlet at 2.1 ppm, and the CH_3 protons of the cyclopentane and cyclohexane fragments appear as multiplets in the region of 1.27–1.87 ppm.

In the ^{13}C NMR spectrum of 1-(2-hydroxymethyl)-1(3)-methylcyclopentyl thioureas, characteristic signals are observed at δ (ppm): (13, 15) 182 (C=S); 61 (C^7), 50.8 (C^2), 43.4 (C^5), 26.5 (C^3), and 22 (C^6). For 1-(2-hydroxymethyl)-1(4)-methylcyclohexyl thioureas (14, 16), the characteristic signals are at δ (ppm): 183 (C^9=S), 65.6 (C1), 61 (C^8), 47.5 (C^2), 39.5 (C^6), 26.5 (C^4), 23 (C^3), and 22.3 (C^7).

The antimicrobial properties of compounds (13–16) were systematically evaluated in formulations of M-10 lubricating oil and the emulsion-type cutting fluid "Azerol-5" at concentrations ranging from 0.25% to 10%. A range of microbial test cultures was employed, including fungal species—Aspergillus niger, Candida tropicalis, Cladosporium resinae, and Penicillium chrysogenum—and bacterial species—Mycobacterium cacticola and Pseudomonas aeruginosa—following the procedures outlined in GOST 9.052–88 and 9.082–77. The microorganisms were incubated under controlled conditions at 28 ± 2 °C in a humidity-regulated thermostat maintaining 90–100% relative humidity, with fungi cultured for 5–7 days and bacteria for 2–3 days. Nutrient media were selected according to the type of microorganism: meat–peptone agar (MPA) for bacterial cultures and wort agar (WA) for fungal and mold cultures. This experimental setup ensured reproducible growth conditions, allowing for accurate assessment of the inhibitory effects of the thiocarbamide derivatives in both hydrocarbon and water-based media.

The synthesized polyfunctional thioureas (13–16) were tested as antimicrobial additives for M-10 motor oil and the emulsion-type lubricating and cooling fluid Azerol-5.

3. Results and discussion

The obtained test data indicate that certain representatives of this class of compounds exhibit pronounced protective activity at concentrations of 0.25–1.0%.

Table 1. Antimicrobial activity of compounds in M-10 motor oil and Azerol-5 cutting fluid at concentrations of 0.25–1.0%.

Compounds	**Concentration, %**	**Diameter of the microorganism inhibition zone**			
		M-10 oil		**Lubricating-cooling emulsion**	
		Bacterial mix. Meat–Peptone Agar)	***Mixture of fungi (Wort Agar)***	***Bacterial mixture. (Meat–Peptone Agar)***	***Mix. of fungi (Wort Agar)***
13	1 0,5 0.25	1.3-1.4 + + + +	1.7–1.9 1.3-1.5 1.1-1.3	1.5–1.3 1.3–1.3 + +	1.8–2.0 1.6–1.8 1.4-1.4
14	1 0,5 0.25	2.3-2.5 2.1-2.3 1.7-1.9	1.9–2.1 1.4-1.7 1.3-1.5	2.7–2.5 2.3-2.5 1.9-2.1	1.6–1.8 1.9–2.1 1.7-1.9
15	1 0,5 0.25	2.6-2.8 2.4-2.6 2.2-2.4	1.5-1.7 + + + +	1.7–2.1 1.5-1.9 1.3–1.3	1.6–1.8 1.5-1.7 1.2-1.2
16	1 0,5 0.25	2.5-2.7 2.3-2.5 2.1-2.1	1.3-1.3 1.2-1.7 + +	1.7–15 1.3-1.3 + +	1.5–1.7 1.3-1.6 1.2-1.2
Sodium pentachlorophenate	1 0.5	1.1-1.3 0.8-1.2	1.5–1.5 0.9-1.2		
M-10 (Without additives.)		+ +	+ +		
Azerol-5 cutting fluid				+ +	+ +

As can be seen from the presented data, the amino-thiocarbamide derivatives containing methylcyclopentene and methylcyclohexene fragments exhibit significantly higher antimicrobial activity when incorporated into the cutting fluid (Azerol-5) compared to their performance in lubricating oils (M-10). This enhanced activity is likely attributable to the superior solubility of these compounds in the aqueous emulsion medium of the cutting fluid, which facilitates better interaction with microbial cells. In contrast, their limited solubility in the hydrocarbon-based oil matrix may reduce their bioavailability and, consequently, their antimicrobial efficiency. These observations suggest that the choice of carrier medium plays a crucial role in the effectiveness of polyfunctional thiocarbamide derivatives as antimicrobial additives, highlighting the importance of optimizing both chemical structure and formulation for industrial applications.

4. Conclusion

A novel series of polyfunctional N-, O-, and S-containing thiocarbamides derived from C_5–C_6 alicyclic olefins has been successfully synthesized. The reactions proceeded efficiently under mild conditions, allowing for the isolation of stable products with well-characterized and confirmed functional groups. Structural verification using IR and NMR spectroscopy, along with elemental analysis, confirmed the integrity of the synthesized compounds and the presence of the targeted functional moieties.

Antimicrobial evaluations demonstrated that these thiocarbamide derivatives exhibit pronounced activity, particularly in water-emulsified cutting fluids, highlighting the importance of solubility and medium compatibility for biocidal effectiveness. Compared to hydrocarbon-based lubricating oils, the enhanced solubility in aqueous media allows for better interaction with microbial cells, resulting in superior antimicrobial performance.

These findings underscore the potential of such compounds as multifunctional additives in various industrial chemical applications, including lubricants, cooling fluids, and potentially other formulations requiring biocidal and stabilizing properties. Future studies will focus on a comprehensive investigation of their anticorrosion and antioxidant capabilities, as well as the optimization of formulations for enhanced performance across diverse industrial environments. Additionally, exploring structure–activity relationships may provide insights for the design of next-generation multifunctional additives with improved efficacy and broader applicability.

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