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Synthesis and Antioxidant Activity of 2-Amino-5-R-1,3,4-Oxadiazoles with Hindered Phenol Fragments †

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Abstract: Compounds with hindered phenolic moiety are known to be effective inhibitors of oxidative processes in different materials; moreover, a number of phenols show a wide spectrum of biological activity. At the same time, five-membered heterocycles exhibit unique properties, including antioxidant activity. One of the ways to create new effective antioxidants with a set of useful properties is to combine hindered phenol and a heterocyclic fragment in one molecule. In this work, new 1-acyl-4-R-thiosemicarbazides were obtained during a reaction between 3-(4-hydroxy-3,5-di-tert-butylphenyl)propanoic acid hydrazide and a number of isothiocyanates. 2-Amino-5-R-1,3,4-oxadiazoles were prepared in good yields by heterocyclization of 1-acyl-4-R-thiosemicarbazides in presence of iodoxybenzoic acid and triethylamine. The antioxidant activity of 1,3,4-oxadiazoles was studied in vitro and was found to be higher than that of 4-methyl-2,6-di-tert-butylphenol.

Keywords: 2,6-di-tert-buthylphenol; heterocycles; antioxidant activity; IBX; hypervalent iodine

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1. Introduction

All organic substances undergo oxidative degradation under the influence of reactive oxygen species (ROS) such as hydroxyl $HO^{\bullet}$, superoxide $O_2^{\bullet}$, peroxide $ROO^{\bullet}$, alkoxyl $RO^{\bullet}$ and nitroxyl $NO^{\bullet}$ radicals [1]. ROS induce oxidative damage of cell membranes, lipids, proteins, and DNA repair system breakdown, which is connected with many degenerative diseases, such as cancer, atherosclerosis, and Alzheimer's disease [2–4]. Antioxidants aim to scavenge free radicals and inhibit oxidative stress processes through their ability to inhibit the chain process of free radical oxidation, that allows them toplay crucial roles in conserving intricate cellular functions [5]. A large number of natural antioxidants as well as synthetic ones have been found. Natural antioxidants include ones that are endogenous enzymatic (glutathione peroxidase, superoxide dismutase and catalase) [6], nonenzymatic (uric acid, lipoic acid, bilirubin, glutathione, metatonin) [7] and exogenous (carotenoids, vitamin E, A and C, natural flavonoids) [8]. Synthetic antioxidants are represented by a wide range of classes of organic compounds, such as amines [9], benzotriazole derivatives [10], alkylaminothiadiazoles [11] and others, but the most common structures in synthetic antioxidants are flavonoids [12,13], coumarins [14,15], and hindered phenols [16,17]. Despite the fact that the mechanism of oxidation, as well as the mechanism of action of antioxidants, has been studied for several decades, there is no universal approach to the creation of new antioxidants. The most rational way to obtain new antioxidants is to combine a fragment known for its antioxidant properties in a structure—for example, hindered phenol and structures with functional groups of various natures or heterocycles [18]. Thus, it was shown that chalcon derivatives with di-tert-butylphenol fragments are effective antioxidants [14]. Additionally, an increase in the antioxidant

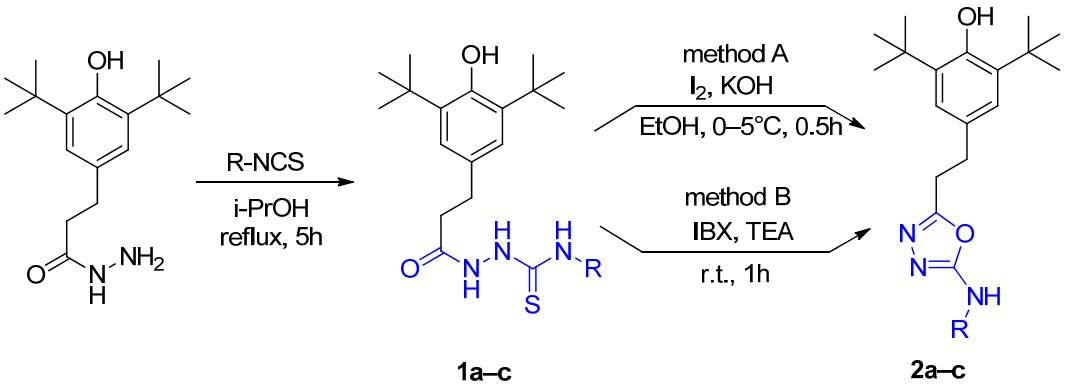
properties of phenols under some conditions was achieved by introducing a sulfur atom into the structure of an oxidation inhibitor [19,20]. Antioxidants containing heterocyclic fragments in their structures are of considerable interest [21,22]. Such compounds are able to act by several mechanisms at once: inhibition of free radical processes, decomposition of hydroperoxides, and chelating metals [23].

In continuation of our previous studies [24,25], in this work we combined in one structure a fragment of 2,6-di-tert-butylphenol and 2-alkyl/arylamino-1,3,4-oxadiazole and studied the antioxidant properties of the synthesized structures.

2. Results and Discussions

2.1. Synthesis

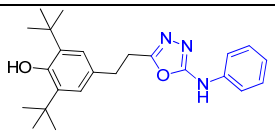
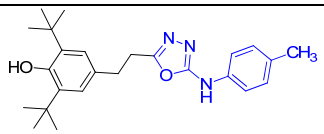
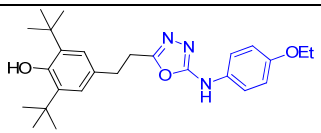
Preparation of the target compounds is outlined in Scheme 1. Initially, 1-acylthiosemicarbazides 1a–c were obtained by the reaction between 3-(4-hydroxy-3,5-di-tert-butylphenyl)propanoic acid hydrazide with a number of isothiocyanates. The reaction was carried out by boiling of the starting reagents in isopropanol for 5 h. The yields of thiosemicarbazides were 77–95%. The ^{1}H NMR spectra of the obtained compounds show peaks in the region of 9.5–10 ppm, corresponding to the protons of the NH-NH fragment.



Scheme 1. Scheme of preparation of oxadiazoles 2a–c.

In accordance with the convenient method of [26], the reaction was carried out in an alcoholic alkali solution with the presence of iodine at 0 °C. N-substituted 2-amino-1,3,4-oxadiazoles were obtained in 48–58% yield with a strong resinification of the reaction mixture, which made it difficult to isolate the products. It was also not possible to achieve complete conversion of the starting 1-acylthiosemicarbazides even by boiling of the reaction mixture. In this regard, the method of applied cyclization proposed by the author of [27] was applied: the reaction was carried out in chloroform in the presence of 2-iodoxybenzoic acid and triethylamine at room temperature. The yields of the target compounds increased to 74–80% (Table 1).

Table 1. The yields of oxadiazoles 2a–c.

Methods	2a	2b	2c
			
Method A	58%	56%	48%
Method B	74%	80%	75%

In the ^{1}H NMR spectra of compounds 2a–c, peaks corresponding to phenol fragment were observed: the singlet peak near 6.71 ppm is attributed to the O–H of the hindered

phenol; peaks at 7.42–7.54 ppm with the integration of two protons were assigned to the two symmetrical aromatic ring protons. In addition, singlet peaks in the range of 9.23–10.36 ppm, corresponding to the protons of the secondary amino group, were observed.

2.2. Antioxidant Properties

The antioxidant properties of the obtained 2a–c compounds were tested in a model reaction of oleic acid oxidation. The oxidation of oleic acid was investigated at 65 °C using a thermostated apparatus upon bubbling of air into a cell for the oxidation at a constant rate of 2–4 mL min^{-1}. The level of lipid peroxidation was estimated via the concentration of primary oxidation products, hydroperoxides (LOOH) and secondary carbonyl products, which form complexes with thiobarbituric acid (TBARS, thiobarbituric acid reactive species) [14]. Butylated hydroxytoluene was used as a standard. The results of antioxidation ability tests are shown in Figure 1.

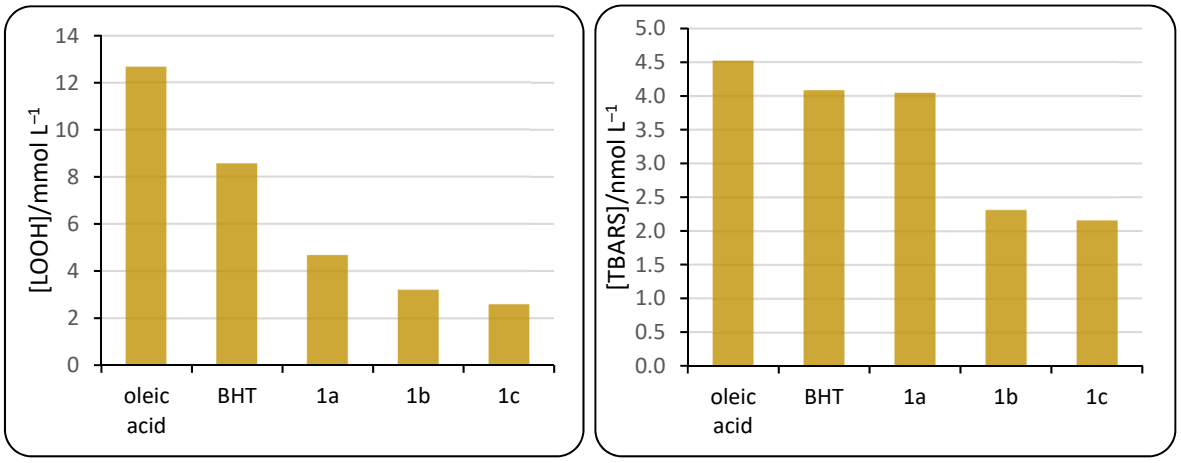


Figure 1. Antioxidant properties of prepared compounds.

In the presence of compounds 2a–c, the concentrations of both hydroperoxides and secondary oxidation products decreases. All compounds have a significant effect on the concentration of hydroperoxides, according to this parameter, the activity of the synthesized substances significantly exceeds activity of BHT. In the presence of 2c and 2c, the concentration of TBARS also significantly decreases; compound 2a exhibits an efficiency comparable to that of BHT.

3. Materials and Methods

3.1. General Information

NMR ^{1}H and ^{13}C spectra of solutions in DMSO-d_6 were recorded on a Bruker AM-300 spectrometer. All experiments were performed according to the standard methods of Bruker. Chemical shifts were reported relative to Me_4Si. The values of SSCCs are given in Hz. The mass spectra were recorded on an MS-30 Kratos device (Eu, 70 eV). A peak of the molecular ion M^+ was observed for all synthesized compounds. The melting points of the obtained compounds were determined in an open capillary. Elemental analysis was carried out using an Elemental analyzer Vario micro cube. The course of reactions and purity of the compounds obtained was monitored by TLC on silica gel plates in a 10:1 toluene-ethanol solvent system.

3.2. Synthesis and Analytical Data of Preparated Compounds

3.2.1. Synthesis of Compounds 1a–c

A mixture of 20 mmol of hydrazide and 20 mmol of isothiocyanate in 70 mL of propanol-2 was stirred and refluxed for 5 h. The reaction mixture was cooled to room

temperature; the formed precipitate was filtered off and recrystallized using a suitable solvent.

1-[2-(4-hydroxy-3,5-di-tert-butylphenyl)ethyl]-4-phenylthiosemicarbazide **1a**: Yield—85%. M.p = 165–167 °C (ethanol:water—70:30). ^{1}H NMR (DMSO-d_6, δ, ppm): 1.36 s (18H, t-Bu), 2.34–2.62 m (4H, CH_2CH_2), 6.68 s (1H, HO), 7.05 s (2H, Har), 7.15–7.44 m (5H, Har), 9.56 br.c. (2H, NH), 10.02 s (1H, NH). MS: (M^+) *m/z* 427. Calculated, %: C—67.41; H—7.78; N—9.83; S—7.50; found, %: C—67.26; H—7.98; N—9.68; S—7.35.

1-[2-(4-hydroxy-3,5-di-tert-butylphenyl)ethyl]-4-(4-methylphenyl)thiosemicarbazide **1b**: Yield—77%. Mp = 203–204 °C (isopropanol:water—1:1). ^{1}H NMR (DMSO-d6, δ, ppm): 1.35 s (18H, t-Bu), 2.31 s (3H, CH_3), 2.44 t (J = 7.3, 2H, CH_2), 2.75 t (J = 7.2, 2H, CH_2), 6.71 s (1H, OH), 6.97 s (2H, Nar), 7.14 d (2H, Nar), 7.30 d (2H, Nar), 9.48 br.s (2H, NH), 9.86 s (1H, NH). MS: (M^+), *m/z* 444. Calculated, %: C—67.99; H—7.99; N—9.51; S—7.26; found, %: C—67.81; H—7.85; N—9.68; S—7.36.

1-[2-(4-Hydroxy-3,5-di-tert-butylphenyl) ethyl]-4-(3-ethoxyphenyl)thiosemicarbazide **1c**: Yield—80%. Mp = 165–167 °C (ethanol:water—1:1). ^{1}H NMR (DMSO-d6, δ, ppm): 1.35 s (18H, t-Bu), 2.31 t (3H, CH_3), 2.45 t (2H, CH_2), 2.75 t (2H, CH_2), 3.99 m (2H, CH_2), 6.71 s (1H, OH), 6.89 d (2H, Nar.), 6.97 s (2H, Nar), 7.24 d (2H, Nar), 9.45 br.s (2H, NH), 9.88 s (1H, NH). MS: (M^+) *m/z* 471. Calculated, %: C—66.21; H—7.91; N—8.91; S—6.80; found, %: C—66.02; H—7.91; N—8.91; S—6.80.

3.2.2. Synthesis of Compounds 2a–c

Method A: To a suspension of 14 mmol of 1-acylthiosemicarbazide in ethanol, 0.7 mL of 4N NaOH solution was added. The reaction mixture was cooled and I_2 in an aqueous solution of KI was added dropwise at the temperature of 0–5 °C until a nonfading color of iodine appeard. The reaction mixture was heated to boiling point, then cooled and poured into 200 mL of ice water; the precipitate was filtered off and the product was crystallized using a suitable solvent.

Method B: To 113 mmol of 1-acylthiosemicarbazide in chloroform, 113 mmol of triethylamine and 23 mmol of iodoxybenzoic acid (IBX) were added. The reaction mixture was stirred at room temperature for 2.5 h. A solution of K_2CO_3 was added to the reaction mixture, the target substance was extracted from the aqueous layer with chloroform, and then the resulting extracts were dried over calcined Na_2SO_4. The solvent was evaporated, threated with cold water and the product was filtered off and crystallized using a suitable solvent.

2-N-(phenyl)amino-5-[2-(4-hydroxy-3,5-di-tert-butylphenyl) ethyl]-1,3,4-oxadiazole **2a**: Yield—58% (Method A), 74% (Method B), Mp. = 186–188 °C, (ethanol:water—5:1). ^{1}H NMR (DMSO-d6, δ, ppm): 10.36 s (1H, NH), 7.54 d (J = 8.2 Hz, 2H, Har), 7.34 t (J = 7.6 Hz, 1H, Har), 6.91 s (2H, Har), 6.76 s (1H, OH), 3.01 t (J = 7.0 Hz, 2H, CH_2-CH_2), 2.90 t (J = 7.3 Hz, 2H, CH_2-CH_2), 1.35 s (18H, t-Bu). MS: (M^+) *m/z* 393. Calculated, %: C—73.25; H—7.94; N—10.68; found, %: C—73.11; H—8.13; N—10.52.

2-N-(4-methylphenyl)amino-5-[2-(4-hydroxy-3,5-di-tert-butylphenyl) ethyl]-1,3,4-oxadiazole **2b**: Yield—56% (Method A), 80% (Method B), Mp. = 172–174 °C, (ethanol:water—3:1). ^{1}H NMR (DMSO-d_6, δ, ppm): 10.23 s (1H. NH), 7.42 (d, J = 8.1 Hz, 2H, Har), 7.14 (d, J = 8.2 Hz, 2H, Nar), 6.91 s (2H, Har), 6.76 s (1H, OH), 2.89 (t, J = 7.0, 2H, CH_2-CH_2), 2.99 t (J = 6.8, 2H, CH_2-CH_2), 1.35 s (18H, t-Bu). MS: (M^+) *m/z* 437. Calculated, %: C—73.68; H—8.16; N—10.31; found, %: C—73.79; H—8.33; N—10.15.

2-N-(4-ethoxyphenyl)amino-5-[2-(4-hydroxy-3,5-di-tert-butylphenyl)ethyl]-1,3,4-oxadiazole **2c**: Yield—48% (Method A), 75% (Method B), Mp. = 179–181 °C, (ethanol:water—3:1). ^{1}H NMR (DMSO-d_6, δ, ppm): 9.33 s 1H, NH, 7.42 (s 2H, Har), 6.90 s (2H, Har), 6.51 s (1H, OH), 3.97, br. s (2H, CH_2), 2.8–3.07 m (2H, CH_2-CH_2), 1.35 br s (18H, t-Bu). MS: (M^+) *m/z* 438. Calculated, %: C—71.37; H—8.06; N—9.60; found, %: C—71.25; H—8.18; N—9.80.

3.2. Antioxidant Properties of Preparated Compounds

Determination of the concentration of LOOH in oleic acid**.**

The studied compounds (1 mmol L^{-1}) were added to oleic acid and thermostated at 65 °C for 6 h. 0.5 mL of oleic acid, 9 mL of glacial acetic acid, 6 mL of chloroform, and 0.5 mL of a saturated freshly prepared KI solution were poured into a flask. The flask was shaken for 2 min, then 50 mL of distilled water and 0.5 mL of 1% starch solution were poured into it. Thereafter, they were immediately titrated with 0.01 N $Na_2S_2O_3$ solution. The LOOH concentration was calculated according to the following formula:

$$[LOOH] = [(V - V_0) \bullet 0.001269K \bullet 100]/m$$

V is the volume of 0.01 N $Na_2S_2O_3$ solution, consumed during the titration of working sample, mL; V_0 is the volume of 0.01 N $Na_2S_2O_3$ solution, consumed during the titration of control sample, mL; K is the conversion factor to the exactly 0.01 N $Na_2S_2O_3$ solution; m is the mass of studied oleic acid; 0.001269 is the amount of I_2 expressed in g, equivalent to 1 mL of 0.01 N $Na_2S_2O_3$ solution. The [LOOH] content equal to 1% corresponds to 78.7 mM of active O_2 per 1 L of lipids (mmol L^{-1}).

Determination of the concentration of TBARS in oleic acid**.**

The studied compounds (1 mmol L^{-1}) were added to oleic acid and thermostated at 65 °C for 6 h. After cooling, samples (0.01 mL) of oleic acid were taken from the thermostat and put into a test tube. A mixture of phosphate buffer (0.8 mL), distilled water (1.2 mL), and freshly prepared thiobarbituric acid solution (0.8%, 1 mL) were added; the tube was heated for 10 min in a boiling water bath, and after cooling the absorption of the samples was measured in comparison with that of control at λ = 532 nm. The concentration of carbonyl compounds was calculated according to the formula:

$$[TBARS] = (E \bullet 3)/0.156 \quad (1)$$

[TBARS] is the content of carbonyl compounds, nmol L^{-1}; E is the absorbance of a sample relative to the control (mixture without oleic acid); 3 is the sample volume, mL; and 0.156 is the extinction of malondialdehyde (1 nmol) dissolved in 1 mL at λ = 532 nm [14].

4. Conclusions

In this study, the synthesis and antioxidant activity of three 2,6-di-tert-buthylphenol derivatives linked to 2-amino-5-R-1,3,4-oxadiazoles are described. Carrying out the cyclization of 1-acylthiosemicarbazides by the action of iodoxybenzoic acid made it possible to increase the yields of the target compounds in comparison with the previously mentioned convenient method. All investigated substances exhibited antioxidant capacity superior or comparable to that of BHT. 2-N-(4-ethoxyphenyl)amino-5-[2-(4-hydroxy-3,5-di-tert-butylphenyl)ethyl]-1,3,4-oxadiazole 2c possesses the best antioxidant properties among the studied oxadiazoles.

Author Contributions: O.V.P.—conception, performing chemical synthesis and purification, spectroscopy experiments, writing manuscript. S.V.V.—analyzing spectroscopy data, writing manuscript. N.V.A.—antioxidant activity experiments, analyzing data, writing manuscript. V.N.K.—conception, supervision, writing manuscript. All authors have read and agreed to the published version of the manuscript.

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References

1. Yang, B.; Chen, Y.; Shi, J. Reactive oxygen species (ROS)-based nanomedicine. *Chem. Rev.* **2019**, *119*, 4881–4985, doi:10.1021/acs.chemrev.8b00626.
2. Gandhi, S.; Abramov, A.Y. Mechanism of oxidative stress in neurodegeneration. *Oxidative Med. Cell. Longev.* **2012**, *2012*, doi:10.1201/9781420026559.
3. Mezeiova, E.; Spilovska, K.; Nepovimova, E.; Gorecki, L.; Soukup, O.; Dolezal, R.; Malinak, D.; Janockova, J.; Jun, D.; Kuca, K. Profiling donepezil template into multipotent hybrids with antioxidant properties. *J. Enzym. Inhib. Med. Chem.* **2018**, *33*, 583–606, doi:10.1080/14756366.2018.1443326.
4. Hanikoglu, A.; Ozben, H.; Hanikoglu, F.; Ozben, T. Hybrid compounds & oxidative stress induced apoptosis in cancer therapy. *Curr. Med. Chem.* **2020**, *27*, 2118–2132, doi:10.2174/0929867325666180719145819.
5. Neha, K.; Haider, M.R.; Pathak, A.; Yar, M.S. Medicinal prospects of antioxidants: A review. *Eur. J. Med. Chem.* **2019**, *178*, 687–704, doi:10.1016/j.ejmech.2019.06.010.
6. Aguilar, T.A.F.; Navarro, B.C.H.; Perez, J.A.M. Endogenous antioxidants: A review of their role in oxidative stress. *Master Regul. Oxidative Stress-Transcr. Factor Nrf2* **2016**, 1–20, doi:10.5772/65715.
7. Mirończuk-Chodakowska, I.; Witkowska, A.M.; Zujko, M.E. Endogenous non-enzymatic antioxidants in the human body. *Adv. Med. Sci.* **2018**, *63*, 68–78, doi:10.1016/j.advms.2017.05.005.
8. Kocyigit, A.; Selek, Ş. Exogenous Antioxidants are Double-edged Swords. *Bezmialem Sci.* **2016**, *2*, 70–75, doi:10.14235/bs.2016.704.
9. Dhahad, H.A.; Fayad, M.A. Role of different antioxidants additions to renewable fuels on NOX emissions reduction and smoke number in direct injection diesel engine. *Fuel* **2020**, *279*, 118384, doi:10.1016/j.fuel.2020.118384.
10. El-Ashry, E.S.; El-Rafey, M.; El-Nagdi, M.; Abou-Elnaga, H.; Bakry, W.; Boghdady, Y. Synthesis of benzotriazole derivatives as antioxidants for industrial lubricating oils. *Lubr. Sci.* **2006**, *18*, 109–118, doi:10.1002/ls.10.
11. Cressier, D.; Prouillac, C.; Hernandez, P.; Amourette, C.; Diserbo, M.; Lion, C.; Rima, G. Synthesis, antioxidant properties and radioprotective effects of new benzothiazoles and thiadiazoles. *Bioorgan. Med. Chem.* **2009**, *17*, 5275–5284, doi:10.1016/j.bmc.2009.05.039.
12. Vavříková, E.; Křen, V.; Jezova-Kalachova, L.; Biler, M.; Chantemargue, B.; Pyszkova, M.; Riva, S.; Kuzma, M.; Valentová, K.; Ulrichova, J. Novel flavonolignan hybrid antioxidants: From enzymatic preparation to molecular rationalization. *Eur. J. Med. Chem.* **2017**, *127*, 263–274, doi:10.1016/j.ejmech.2016.12.051.
13. Williams, R.J.; Spencer, J.P.; Rice-Evans, C. Flavonoids: Antioxidants or signalling molecules? *Free Radic. Biol. Med.* **2004**, *36*, 838–849, doi:10.1016/j.freeradbiomed.2004.01.001.
14. Osipova, V.; Polovinkina, M.; Telekova, L.; Velikorodov, A.; Stepkina, N.; Berberova, N. Synthesis and antioxidant activity of new hydroxy derivatives of chalcones. *Russ. Chem. Bull.* **2020**, *69*, 504–509, doi:10.1007/s11172-020-2790-y.
15. Pojero, F.; Poma, P.; Spanò, V.; Montalbano, A.; Barraja, P.; Notarbartolo, M. Targeting multiple myeloma with natural polyphenols. *Eur. J. Med. Chem.* **2019**, *180*, 465–485, doi:10.1016/j.ejmech.2019.07.041.
16. Koshelev, V.; Kelarev, V.; Belov, N. Effect of azoles and sym-triazines with hindered phenol fragments on protective properties of turbine oils. *Chem. Technol. Fuels Oils* **1995**, *31*, doi:10.1007/bf00727660.
17. Latyuk, V.; Kelarev, V.; Koshelev, V.; Korenev, K. Sulfides of the sym—Triazine Series as Oil—Soluble Corrosion Inhibitors. *Chem. Technol. Fuels Oils* **2002**, *38*, 312–315, doi:10.1023/A:1021282614918.
18. Zhang, H.-Y. Structure-activity relationships and rational design strategies for radical-scavenging antioxidants. *Curr. Comput. Aided Drug Des.* **2005**, *1*, 257–273, doi:10.2174/1573409054367691.
19. Perevozkina, M. Synergism of sulfur-containing phenol (SO-4) with mexidol, α-tocopherol, and phospholipids. *Pharm. Chem. J.* **2006**, *40*, 441–447, doi:10.1007/s11094-006-0148-x.
20. Liu, P.; Zhu, L.; Fang, Y.; Zhang, H.; Chen, D.; He, T.; Chen, M.; Xu, K. Catalytic Thioalkylation of Phenols Based on Mannich-Type Phenol. *Synth. Commun.* **2007**, *37*, 2609–2613, doi:10.1080/00397910701462971.
21. Ivanović, N.; Jovanović, L.; Marković, Z.; Marković, V.; Joksović, M.D.; Milenković, D.; Djurdjević, P.T.; Ćirić, A.; Joksović, L. Potent 1, 2, 4-Triazole-3-thione Radical Scavengers Derived from Phenolic Acids: Synthesis, Electrochemistry, and Theoretical Study. *ChemistrySelect* **2016**, *1*, 3870–3878, doi:10.1002/slct.201600738.
22. Dvornikova, I.; Buravlev, E.; Fedorova, I.; Shevchenko, O.; Chukicheva, I.Y.; Kutchin, A. Synthesis and antioxidant properties of benzimidazole derivatives with isobornylphenol fragments. *Russ. Chem. Bull.* **2019**, *68*, 1000–1005, doi:10.1007/s11172-019-2510-7.
23. Yehye, W.A.; Abdul Rahman, N.; Saad, O.; Ariffin, A.; Abd Hamid, S.B.; Alhadi, A.A.; Kadir, F.A.; Yaeghoobi, M.; Matlob, A.A. Rational design and synthesis of new, high efficiency, multipotent Schiff base-1, 2, 4-triazole antioxidants bearing butylated hydroxytoluene moieties. *Molecules* **2016**, *21*, 847, doi:10.3390/molecules21070847.
24. Koshelev, V.N.; Primerova, O.V.; Vorobyev, S.V.; Ivanova, L.V. Synthesis, Redox Properties and Antibacterial Activity of Hindered Phenols Linked to Heterocycles. *Molecules* **2020**, *25*, 2370, doi:10.3390/molecules25102370.
25. Vorobyev, S.V.; Primerova, O.V.; Ivanova, L.V.; Ryabov, V.D.; Koshelev, V.N. Facile synthesis of phenolic derivatives, containig lactamomethyl substituents. *Izvestiya Vysshikh Uchebnykh Zavedenii Khimiya Khimicheskaya Tekhnologiya* **2019**, *62*, 40–48, doi:10.6060/ivkkt.20196210.5930.

26. Karakhanov, R.; Kelarev, V.; Koshelev, V.; Morozova, G.; Dibi, A. Synthesis and properties of furan derivatives. 4. Synthesis of 2, 5-disubstituted 1, 3, 4-oxadiazoles containing furan fragments. *Chem. Heterocycl. Compd.* **1995**, *31*, 208–218, doi:10.1007/bf01169682.
27. Prabhu, G.; Sureshbabu, V. Hypervalent iodine (V) mediated mild and convenient synthesis of substituted 2-amino-1, 3, 4-oxadiazoles. Tetrahedron Lett. 2012, 53, 4232–4234, doi:10.1016/j.tetlet.2012.05.154.