Ferrocenylalkylation of 2-mercaptobenzoxazoles

E. Yu. Osipova,[a] A. S. Ivanova,[a] A. N. Rodionov,[a,b] A. A. Korlyukov,[a] D. E. Arkhipov,[a] and A. A. Simenel[a,c]*

[a]*A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 28 ul. Vavilova, 119991 Moscow, Russian Federation. Fax: +7 (499) 135 6549. E-mail: jdyotvet@yandex.ru*
[b]*State Environmental Agency "Mosekomonitoring", Build. 1, 2 Dal´niy per., 115419 Moscow, Russian Federation. Fax: +7 (495) 954 1525. E-mail: ecolaboratory@yandex.ru*
[c]*The National University of Science and Technology "MISiS", 2 Leninsky prosp., 119049 Moscow, Russian Federation. Fax: +7 (499) 236 2105*

Regioselectivity of the HBF_4-catalyzed ferrocenylalkylation of 2-mercaptobenzoxazole in two phase aqueous organic solvent mixture was studied. The reaction proceeds regioselectively at the heterocyclic nitrogen atom. Structures of the synthesized compounds were established by 2D NMR technique. Structure of 3-(1-ferrocenylbenzyl)benz[*d*]oxazol-2-thione was elucidated by X-ray diffraction.

Key words: ferrocene, 2-mercaptobenzoxazole, regioselectivity, ferrocenylalkylation.

Benzoxazole is an aromatic benzene-fused oxazole ring structure. Despite the fact that unsubstituted benzoxazole is of low practical value, its numerous derivatives found application in industry (*e.g.*, as optical brighteners for detergents[1]). Heterocyclic core of benzoxazole is an interesting starting ring system for the synthesis of biologically active substances. Aromaticity is a reason of the relative stability of benzoxazole, at the same time it has active sites for functionalization.[2] It should be emphasized that benzoxazole derivatives of both natural and synthetic origin possess a wide range of biological activity.[3] For instance, they show antibacterial,[4] anti-inflammatory,[5] cyclooxigenase-2 inhibitory,[6] antiviral,[7] anti-allergic,[8] antifungal,[9,10] and antihelmintic activities.[11] The benzoxazole moiety is a constitutive part of flunoxaprofen, a non-steroidal anti-inflammatory drug. Recent studies indicated that substituted benzoxazoles and related heterocycles combine low toxicity and high chemotherapeutic efficiency.[12] It was also found that 2-mercaptobenzoxazole is a promising candidate for biological[13] and medicinal applications.[14]

It is also known that introduction of the ferrocene fragment into different organic substances,[15—19] medicines,[20] and vitamins significantly decreases their toxicity. Moreover, *in vitro* and *in vivo* antitumor activities of ferrocene were extensively studied.[17,21—27] It has been found that ferrocenium salts exhibit not only antiproliferative activity[28,29] but also are capable of both inhibiting the DNA synthesis[30] and damaging the DNA molecule.[31] Ferrocene-containing heterocycles are effective against murine solid tumor[17,32] and human tumor cells.[17] Recently, a cytotoxic cooperative effect of cyclophosphamide, a known antitumor drug, and ferrocenylmethyl thymine against the Ca755 solid tumor model was demonstrated.[32] Therefore, the development of new efficient synthetic approaches towards ferrocene-containing heterocycles for the design of new low toxic antitumor agents is still an ongoing challenge to organic chemists.

Introduction of ferrocenylalkyl moiety into different structures can be achieved by ferrocenylalkylation;[33—41] however, regioselectivity of this reaction is still poorly studied. Earlier, we have described phase-transfer-catalyzed alkylation of unsymmetrically substituted heterocycles with ferrocenyl carbinols. It has been shown that the reaction is regioselective if the substituents exert different electronic effects.[42]

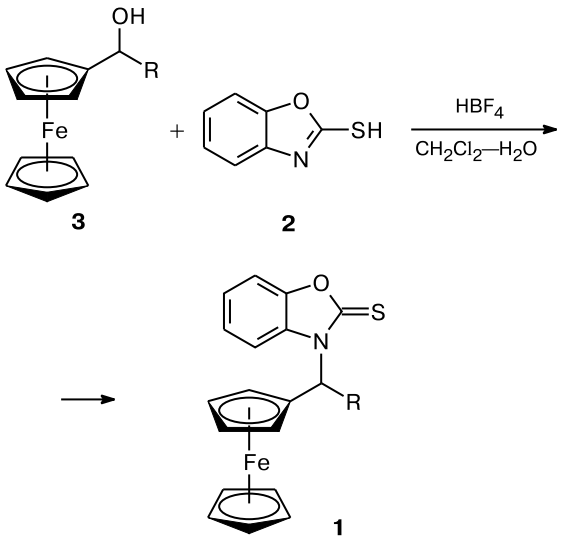
Results and Discussion

Ferrocenylalkylated thiobenzoxazoles **1a—e** were synthesized by the reaction of 2-mercaptobenzoxazole (**2**) with different ferrocenyl carbinols **3** in dichloromethane catalyzed by 48% tetrafluoroboric acid (Scheme 1). Reaction was carried out with equimolar amounts of ferrocenyl carbinol and 2-mercaptobenzoxazole at room tem-

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 12, pp. 2868—2872, December, 2016.
1066-5285/16/6512-2868

perature under vigorous stirring. The reaction products were purified by column chromatography, if necessary.

Scheme 1



1: R = H (**a**), Me (**b**), Et (**c**), Pr (**d**), Pr^i (**e**), Ph (**f**)

It is found that all reactions proceed regioselectively at the heterocyclic nitrogen atom. Structures of the reaction products were established by $^1H—^{13}C$ heteronuclear correlation experiments. Thus, HMBC NMR spectra of compounds **1** exhibit characteristic correlations of the bridging alkyl group protons of the ferrocenylalkyl moieties with the C atoms of the C=S group of oxazole fragment (at about δ 180) and with the C(9) atom (in the range of δ 129.8—131.5). This is evidence in support of the substitution at the benzoxazole ring nitrogen.

Structure of 3-(ferrocenylbenzyl)benz[*d*]oxazole-2-thione (**1f**) was examined by X-ray diffraction analysis (Fig. 1). The bond lengths and bond angles of compound **1f** are nearly the same as those found for substituted ferrocenes and benzoxazoles.

Regioselectivity of the substitution in 2-mercaptobenzoxazole agrees with our previous observations.[43] We have found[43] that acid-catalyzed ferrocenylalkylation of 2-mercaptobenzimidazole and 2-mercaptobenzothiazole occurred at the nitrogen atoms. Ferrocenylalkylation proceeds *via* thermodynamically stable α-ferrocenium carbocation, which is relatively hard Lewis acid efficiently reacting with somewhat harder basic center, in our case, with the benzoxazole nitrogen atom. Furthermore, quantum chemical calculations show that *N*-isomers **1**, **5**, and **7** are more thermodynamically stable than the corresponding *S*-isomers **4**, **6**, and **8** (Table 1).

Table 1 shows the differences between the energies of formation (Δ*G*) of *N*- and *S*-alkylation products for isolated and solvated (CH_2Cl_2) molecules **1** and **4—8**. For benzimidazole and benzoxazole derivatives, the Δ*G* values are generally higher than for benzothiazole derivatives with the exception of calculations for the isolated molecules **1b** and **1f**. Under solvation conditions, substitution at the nitrogen atom is always more favorable than substitution at the sulfur atom. Moreover, solvation results in an increase in the Δ*G* value between *N*- and *S*-isomers.

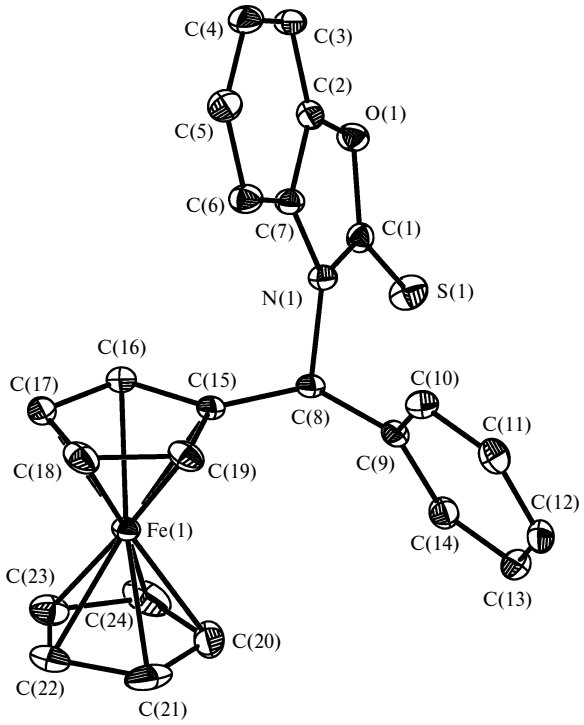


Fig. 1. Geometry of compound **1f**. The thermal displacement ellipsoids were drawn at 50% probability level.

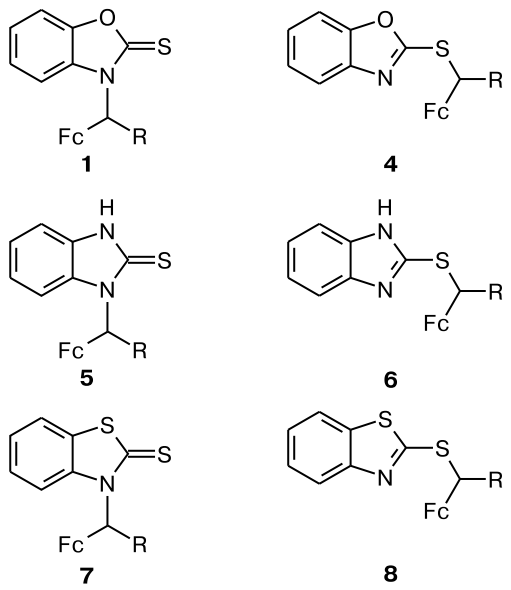


Table 1. ΔG values for isolated and solvated molecules of ferrocenylated heterocyclic compounds **1**, and **4—8**

Possible isomers	R	ΔG/kcal mol^{-1}	
		Gas	Solution (CH_2Cl_2)
1, 4	H	5.1	7.4
	Me	1.6	4.3
	Et	–1.1	2.3
	Pr^i	3.8	6.5
	Ph	0.6	2.9
5, 6	H	9.3	10.3
	Me	9.9	10.6
	Et	9.8	11.0
	Pr^i	8.7	9.4
	Ph	8.1	8.6
7, 8	H	3.9	4.8
	Me	4.0	5.1
	Et	3.6	4.8
	Pr^i	2.7	3.9
	Ph	1.8	2.6

Experimental

Solvents were dried following the standard procedures and distilled under argon prior to use. EI mass spectra were taken on a FINNIGAN POLARIS Q spectrometer at 70 eV and the temperature of the ion chamber 250 °C. ^{1}H and ^{13}C NMR spectra were obtained on a Bruker Advance 400 spectrometer (at 400 and 100 MHz, respectively) in $CDCl_3$ at 30 °C. The chemical shifts are given in the δ scale relative to the residual solvent signal. All signals in the NMR spectra were attributed using gradient HSQC and HMBC heteronuclear correlation techniques. Melting points were determined with a Stuart SMP30 apparatus (Bibby Scientific). Commercially available 2-mercaptobenzoxazole (Acros Organics) was used as purchased. Ferrocenylmethanol (**3a**) was synthesized from trimethylferrocenylmethylammonium iodide by the known procedure.[44] Ferrocenyl carbinols **3b—e** were accessed from ferrocene by the Friedel—Crafts acylation with the corresponding acid chlorides and subsequent reduction with lithium aluminum hydride in diethyl ether or THF.[45]

Quantum chemical calculations were performed with a Gaussian09 program package. Full geometry optimization of the isolated molecules were done with PBE0 exchange-correlation functional and 6-311G(d,p) basis set followed by oscillator vibrational frequency calculations. Effects of non-specific solvation from CH_2Cl_2 was accounted for by the PCM model.

Synthesis of ferrocenylalkyl-2-mercaptobenzoxazoles (general procedure). A 48% aqueous solution of tetrafluoroboric acid (0.21 mL, 1.2 mmol) was added to a suspension of ferrocenyl carbinol (1 mmol) and 2-mercaptobenzoxazole (1 mmol) in dichloromethane (1 mL) under vigorous stirring. The stirring was continued for 5—15 mL. Then water (10 mL) and diethyl ether (10 mL) were added to the reaction mixture. The resulting mixture was washed with water (2×20 mL), the organic layer was separated and dried with Na_2SO_4. The solvent was removed under water pump vacuum.

3-(Ferrocenylmethyl)benz[*d*]oxazole-2-thione (1a). Yield 72%. Yellow powder. M.p. 166.8—167.2 °C. Found (%): C, 61.97; H, 4.32; N, 4.04; Fe, 15.96. Calculated (%): C, 61.91; H, 4.33; N, 4.01; Fe, 15.99. R_f 0.6 (petroleum ether—ethyl acetate, 3 : 1). MS, *m/z* (I_{rel}(%)): 349 $[M]^+$ (100). ^{1}H NMR, δ: 4.18 (s, 2 H, C_5H_4); 4.27 (s, 5 H, C_5H_5); 4.48 (s, 2 H, C_5H_4); 5.21 (s, 2 H, CH_2); 7.15 (d, 1 H, Het, J = 7.6 Hz); 7.22—7.31 (m, 2 H, Het); 7.32 (d, 1 H, Het, J = 7.6 Hz). ^{13}C NMR, δ: 45.66 (CH_2), 68.74 (C_5H_4), 68.96 (C_5H_5), 69.69 (C_5H_4), 80.29 (*ipso*-C_5H_4), 109.81 (Het), 110.34 (Het), 124.17 (Het), 124.75 (Het), 131.51 (Het), 147.05 (Het), 180.06 (C=S).

3-(1-Ferrocenylethyl)benz[*d*]oxazole-2-thione (1b). Yield 65%. Orange oil. R_f 0.6 (petroleum ether—ethyl acetate, 3 : 1). MS, *m/z* (I_{rel}(%)): 364 $[M]^+$ (80). ^{1}H NMR, δ: 1.86 (d, 3 H, CH_3, J = 7.0 Hz); 4.20 (s, 1 H, C_5H_4); 4.27 (m, 6 H, C_5H_4); 4.31 (s, 1 H, C_5H_4); 4.52 (s, 1 H, C_5H_4); 6.37 (q, 1 H, CH, J = 7.1 Hz); 6.92 (d, 1 H, Het, J = 8.0 Hz); 7.06 (t, 1 H, Het, J = 7.8 Hz); 7.15 (t, 1 H, Het, J = 7.8 Hz); 7.31 (d, 1 H, Het, J = 8.0 Hz). ^{13}C NMR, δ: 16.29 (CH_3), 54.30 (CH), 66.78 (C_5H_4), 67.78 (C_5H_4), 69.17 (C_5H_4), 69.29 (C_5H_5), 69.43 (C_5H_4), 84.89 (*ipso*-C_5H_4), 110.27 (Het), 111.42 (Het), 123.78 (Het), 124.37 (Het), 129.81 (Het), 147.14 (Het), 179.48 (C=S).

3-(1-Ferrocenylpropyl)benz[*d*]oxazole-2-thione (1c). Yield 70%. Orange powder. M.p. 117.2—118.8 °C. Found (%): C, 61.70; H, 5.10; N, 3.74; Fe, 14.84. Calculated (%): C, 61.67; H, 5.05; N, 3.71; Fe, 14.80. R_f 0.6 (petroleum ether—ethyl acetate, 3 : 1). MS, *m/z* (I_{rel}(%)): 378 (100). ^{1}H NMR, δ: 1.04 (t, 3 H, CH_3, J = 7.4 Hz); 2.35 (m, 1 H, CH_2); 2.43 (m, 1 H, CH_2); 4.15 (s, 1 H, C_5H_4); 4.22 (s, 1 H, C_5H_4); 4.26 (s, 5 H, C_5H_5); 4.29 (s, 1 H, C_5H_4); 4.47 (s, 1 H, C_5H_4); 6.28 (m, 1 H, CH); 7.01 (d, 1 H, Het, J = 8.0 Hz); 7.07 (t, 1 H, Het, J = 7.8 Hz); 7.15 (t, 1 H, Het, J = = 7.8 Hz); 7.30 (d, 1 H, Het, J = 8.0 Hz). ^{13}C NMR, δ: 11.07 (CH_3), 24.56 (CH_2), 59.88 (CH), 66.63 (C_5H_4), 67.67 (C_5H_4), 68.70 (C_5H_4), 68.88 (C_5H_4), 69.29 (C_5H_5), 85.06 (*ipso*-C_5H_4), 110.32 (Het), 111.28 (Het), 123.83 (Het), 124.37 (Het), 129.79 (Het), 147.03 (Het), 180.84 (C=S).

3-(1-Ferrocenylbutyl)benz[*d*]oxazole-2-thione (1d). Yield 75%. Orange powder. M.p. 116—118 °C. Found (%): C, 64.49; H, 5.44; N, 3.56; Fe, 14.31. Calculated (%): C, 64.46; H, 5.40; N, 3.50; Fe, 14.27. R_f 0.8 (petroleum ether—ethyl acetate, 3 : 1). MS, *m/z* (I_{rel}(%)): 391 (100). ^{1}H NMR, δ: 1.05 (t, 3 H, CH_3, J = = 7.3 Hz); 1.33 (m, 2 H, CH_2); 1.53 (m, 2 H, CH_2); 4.15 (s, 1 H, C_5H_4); 4.22 (s, 1 H, C_5H_4); 4.26 (s, 5 H, C_5H_5); 4.30 (s, 1 H, C_5H_4); 4.46 (s, 1 H, C_5H_4); 6.34 (s, 1 H, CH); 7.04 (d, 1 H, C_6H_5, J = 7.7 Hz); 7.10 (t, 1 H, C_6H_5, J = 7.6 Hz); 7.17 (t, 1 H, C_6H_5, J = 7.7 Hz); 7.32 (d, 1 H, C_6H_5, J = 7.9 Hz). ^{13}C NMR, δ: 14.07 (CH_3), 19.47 (CH_2), 33.28 (CH_2), 58.06 (CH), 66.65 (C_5H_4), 67.65 (C_5H_4), 68.71 (C_5H_4), 68.90 (C_5H_4), 69.27 (C_5H_4), 85.26 (*ipso*-C_5H_4), 110.30 (Het), 111.29 (Het), 123.80 (Het), 124.36 (Het), 129.81 (Het), 147.05 (Het), 180.66 (C=S).

3-(1-Ferrocenyl-2-methylpropyl)benz[*d*]oxazole-2-thione (1e). Yield 60%. Yellow powder. M.p. 146—148 °C. Found (%): C, 64.40; H, 5.40; N, 3.56; Fe, 14.35. Calculated (%): C, 64.46; H, 5.41; N, 3.58; Fe, 14.27. R_f 0.6 (petroleum ether—ethyl acetate, 3 : 1). MS, *m/z* (I_{rel}(%)): 391 $[M]^+$ (55). ^{1}H NMR, δ: 0.88 (d, 3 H, J = 6.6 Hz); 1.36 (d, 3 H, J = 6.6 Hz); 2.61 (m, 1 H, CH); 4.13 (m, 6 H, Fc); 4.15 (s, 1 H, C_5H_4); 4.23 (s, 1 H, C_5H_4); 4.43 (s, 1 H, C_5H_4); 5.92 (d, 1 H, J = 10.5 Hz); 7.07 (d, 1 H, J = 7.7 Hz); 7.15 (t, 1 H, J = 7.7 Hz); 7.21 (t, 1 H, J = 7.7 Hz); 7.36 (d, 1 H, J = = 7.7 Hz). ^{13}C NMR, δ: 20.03 (CH_3), 21.89 (CH_3), 31.49 (CH_2), 64.39 (CH), 67.26 (C_5H_4), 67.41 (C_5H_4), 68.47 (C_5H_4), 68.74 (C_5H_4), 69.28 (C_5H_4), 86.04 (*ipso*-C_5H_4), 110.38 (Het), 111.69 (Het), 123.96 (Het), 124.40 (Het), 130.40 (Het), 146.82 (Het), 180.83 (C=S).

Table 2. Main crystallographic data and refinement parameters for compound **1f**

Parameters	Values
Molecular formula	$C_{24}H_{19}FeNOS$
Molecular weight	425.31
T/K	120
Space group	*Cc*
Z	4
a/Å	16.6720(11)
b/Å	10.4091(7)
c/Å	13.0438(7)
b/deg	122.445(2)
V/Å^3	1910.3(2)
d_{calc}/g cm^{-3}	1.479
μ/cm^{-1}	9.13
F(000)	880
2 θ_{max}/deg	52
Number of measured reflections	12940
Number of independent reflections	5838
Number reflections with $I > 2\sigma(I)$	5468
Number of refined parameters	253
R_1	0.0291
wR_2	0.0630
GOOF	0.986
Residual electron density (ρ_{max}/ρ_{min})/e Å^{-3}	0.384/−0.205

3-(1-Ferrocenylbenzyl)benz[*d*]oxazole-2-thione (1f). Yield 59%. Orange powder. M.p. 146—148 °C. Found (%): C, 67.80; H, 4.58; N, 3.33; Fe, 13.15. Calculated (%): C, 67.77; H, 4.50; N, 3.29; Fe, 13.13. R_f 0.6 (petroleum ether—ethyl acetate, 3 : 1). MS, m/z (I_{rel}(%)): 425 $[M]^+$ (29). ^{1}H NMR, δ: 4.20 (s, 2 H, C_5H_4); 4.25 (s, 5 H, C_5H_5); 4.27 (s, 1 H, C_5H_4); 4.29 (s, 1 H, C_5H_4); 6.71 (d, 1 H, CH, J = 7.9 Hz); 7.03 (t, 1 H, Het, J = 7.9 Hz); 7.17 (t, 1 H, Het, J = 8.1 Hz); 7.37 (m, 7 H, CH). ^{13}C NMR, δ: 61.96 (CH), 68.10 (C_5H_4), 68.42 (C_5H_4), 69.04(C_5H_4), 69.46 (C_5H_5), 69.81 (C_5H_4), 84.68 (*ipso*-C_5H_4), 110.30 (Het), 112.50 (Het), 123.85 (Het), 124.34 (Het), 128.08 (C_6H_5), 128.27 (*ipso*-C_6H_5), 128.54 (C_6H_5), 130.90 (Het), 137.31 (C_6H_5), 147.05 (Het), 180.41 (C=S).

X-ray diffraction analysis of compound 1f. Crystals of 3-(ferrocenylbenzyl)benz[*d*]oxazole-2-thione (**1f**) were grown by slow diffusion form a solution in deuterated chloroform at ~22 °C. X-ray analysis was carried out with a Bruker APEX II diffractometer (Mo-Kα irradiation, graphite monochromator, ω scan mode). The structure was solved by direct methods and refined anisotropically by full-matrix least squares against F^2_{hkl}. The atoms were positioned geometrically and refined with constraints on the C—H bond lengths and equivalent thermal parameters $U_{eq}(H) = 1.2U_{eq}(C)$. Main crystallographic data and refined parameters are summarized in Table 2. All calculations were performed with SHELXT,[46] SHELXL,[47] and OLEX2 program packages.[48] Crystal structure of compound **1** was deposited with a Cambridge Crystallographic Data Center (CCDC 1493347).

This work was financially supported by the Russian Foundation for Basic Research (Project No. 16-33-60163 mol_a_dk). A. A. Korlyukov is grateful for the Russian Science Foundation for the financial support (Project No. 14-13-00884; quantum chemical calculations).

References

1. E. Smulders, E. Sung, *Laundry Detergents*, *2. Ingredients and Products*, 2012, **20**, 393.
2. E. Şener, I. Yalçin, E. Sungur, *Quant. Struct.-Act. Relat.*, 1991, **10**, 223.
3. L. P. Singh, V. Chawla, P. Chawla, S. K. Saraf, *Pharma Chem.*, 2010, **2**, No. 4, 206.
4. Y. K. Liu, D. J. Lou, J. Q. Qian, Z. Y. Xu, *J. Zhejiang Univ. Sci.*, 2009, **10**, No. 6, 472.
5. A. Srinivas, J. Vidyasagar, M. Sarangapani, Design, *J. Chem. Pharm. Res.*, 2010, **2**, № 1, 319.
6. A. Srinivas, J. Vidyasagar, K. Swathi, M. Sarangapani, *J. Chem. Pharm. Res.*, 2010, **2**, 213.
7. N. Siddiqui, M. Sarafroz, M. M. Alam, W. Ahsan, *Acta Pol. Pharm. — Drug Res.*, 2008, **65**, No. 4, 44.
8. J. R. Boot, W. J. F. Sweatman, B. A. Cox, K. Stone, W. Dawson, *Int. Arch. Allergy Immunol.*, 1982, **67**, 340.
9. S. T. Patil, P. A. Bhatt, *Pharm. Sin.*, 2010, **1**, No. 2, 105.
10. Z. A. Kaplancikli, G. T. Ztouni, G. Revial, K. Guven, *Arch. Pharm. Res.*, 2004, **27**, 1081.
11. R. V. Satyendra, K. A. Vishnumurthy, H. M. Vagdevi, B. L. Dhananjaya, A. Shruthi, *Med. Chem. Res.*, 2015, **24**, 1342.
12. S. Ampati, R. Jukanti, V. Sagar, R. Ganta, S. Manda, *Chem. Sin.*, 2010, **1**, No. 3, 157.
13. S. K. Srivastava, A. Jain, S. D. Srivastava, *J. Indian. Chem. Soc.*, 2006, **83**, 1118.
14. C. Safak, R. Simsek, K. Erol, K. Vural, *Pharmazie*, 1996, **51**, No. 3, 180.
15. P. Meunier, I. Quattara, B. Gautheron, J. Tirouflet, D. Camboli, J. Besanson, F. Boulay, *Eur. J. Med. Chem.*, 1991, **26**, 351.
16. L. V. Popova (Snegur), V. N. Babin, Yu. A. Belousov, Yu. S. Nekrasov, A. E. Snegireva, N. P. Borodina, G. M. Shaposhnikova, O. B. Bychenko, P. M. Raevskii, N. B. Morozova, A. I. Ilyina, K. G. Shitkov, *Appl. Organomet. Chem.*, 1993, **7**, 85.
17. L. V. Snegur, A. A. Simenel, Yu. S. Nekrasov, E. A. Morozova, Z. A. Starikova, S. M. Peregudova, Yu. V. Kuzmenko, V. N. Babin, L. A. Ostrovskaya, N. V. Bluchterova, M. M. Fomina, *J. Organomet. Chem.*, 2004, **689**, 2473.
18. L. V. Snegur, Yu. S. Nekrasov, N. S. Sergeeva, Zh. V. Zhilina, V. V. Gumenyuk, Z. A. Starikova, A. A. Simenel, N. B. Morozova, I. K. Sviridova, V. N. Babin, *Appl. Organomet. Chem.*, 2008, **22**, 139.
19. A. A. Simenel, S. V. Samarina, L. V. Snegur, Z. A. Starikova, L. A. Ostrovskaya, N. V. Bluchterova, M. M. Fomina, *Appl. Organomet. Chem.*, 2008, **22**, 276.
20. G. N. Yashchenko, A. A. Shashmurina, G. M. Anoshina, L. A. Gorelova, N. G. Evstigneeva, L. V. Alekseeva, L. B. Radina, *Pharm. Chem. J.* (*Engl. Transl.*), 1978, **12**, 1317 [*Khim.-Farm. Zh.*, 1978, **12**, No. 10, 68].
21. D. A. Oparin, V. D. Makhaev, V. D. Vilrchevskaya, T. I. Zimatkina, Zh. V. Motylevich, S. M. Zimatkin, S. V. Zabrodskaya, A. I. Krylova, Yu. Yu. Gorelikova, *Pharm. Chem. J.* (*Engl. Transl.*), 1996, **30**, 79 [*Khim.-Farm. Zh.*, 1996, **30**, No. 2, 1].
22. P. Köpf-Maier, H. Köpf, *Chem. Rev.*, 1987, **87**, 1137.
23. P. Köpf-Maier, *Eur. J. Clinic. Pharm.*, 1994, **47**, 1.

24. V. N. Babin, P. M. Raevskii, K. G. Shitkov, L. V. Snegur, Yu. S. Nekrasov, *Mendeleev Chem. J.*, 1995, **39**, 17.
25. D. R. van Staveren, N. Metzler-Nolte, *Chem. Rev.*, 2004, **104**, 5931.
26. E. W. Neuse, *J. Inorg. Organomet. Polym. Materials*, 2005, **15**.
27. U. Schatzschneider, N. Metzler-Nolte, *Angew. Chem., Int. Ed.*, 2006, **45**, 1504.
28. G. Jaouen, S. Top, A. Vessières, G. Leclercq, M. J. McGlinchey, *Curr. Med. Chem.*, 2004, **11**, 2505.
29. A. Vessières, S. Top, W. Beck, E. Hillard, G. Jaouen, *Dalton Trans.*, 2006, 529.
30. G. Tabbi, C. Cassino, G. Cavigiolio, D. Colangelo, A. Ghiglia, I. Viano, D. Osella, *J. Med. Chem.*, 2002, **45**, 5786.
31. H. Tamura, M. Miwa, *Chem. Lett.*, 1997, 1177.
32. A. A. Simenel, E. A. Morozova, L. V. Snegur, S. I. Zykova, V. V. Kachala, L. A. Ostrovskaya, N. V. Bluchterova, M. M. Fomina, *Appl. Organomet. Chem.*, 2009, **23**, 219.
33. V. I. Boev, L. V. Snegur, V. N. Babin, Yu. S. Nekrasov, *Russ. Chem. Rev.*, 1997, **66**, 613.
34. I. Yu. Shirokobokov, A. V. Sachivko, V. P. Tverdokhlebov, V. A. Ostrovskii, I. V. Tsrlinskii, G. I. Koldobskii, *Zh. Org. Khim.*, 1986, **22**, 1763 [*J. Org. Chem. USSR* (*Engl. Transl.*), 1986, **22**].
35. L. V. Snegur (Popova), V. N. Babin, Yu. A. Belousov, Yu. S. Nekrasov, A. E. Snegireva, N. P. Borodina, G. M. Shaposhnikova, O. B. Bychenko, P. M. Raevskii, N. B. Morozova, A. I. Ilyina, K. G. Shitkov, *Appl. Organomet. Chem.*, 1993, **7**, 85.
36. L. V. Snegur, A. A. Simenel, Yu. S. Nekrasov, E. A. Morozova, Z. A. Starikova, S. M. Peregudova, Yu. V. Kuzmenko, V. N. Babin, L. A. Ostrovskaya, N. V. Bluchterova, M. M. Fomina, *J. Organomet. Chem.*, 2004, **689**, 2473.
37. L. V. Snegur, Yu. S. Nekrasov, N. S. Sergeeva, Zh. V. Zhilina, V. V. Gumenyuk, Z. A. Starikova, A. A. Simenel, N. B. Morozova, I. K. Sviridova, V. N. Babin, *Appl. Organomet. Chem.*, 2008, **22**, 139.
38. *Ferrocenes. Homogeneous Catalysis*, *Organic Synthesis. Materials Science*, Eds A. Togni, T. Hayashi, VCH, Weinheim, Germany, 1995.
39. E. G. Perevalova, M. D. Reshetova, K. I. Grandberg, *Metody elementoorganicheskoi khimii. Ferrotsen* [*Methods in Organoelement Chemistry. Ferrocene*], Nauka, Moscow, 1983, 544 pp. (in Russian).
40. B. W. Rockett, G. Marr, *J. Organomet. Chem.*, 1991, **416**, 327.
41. M. I. Rybinskaya, *Bull. Russ. Acad. Sci., Div. Chem. Sci.* (*Engl. Transl.*), 1992, **41**, 850 [*Izv. Akad. Nauk, Ser. Khim.*, 1992, 1083].
42. E. Yu. Osipova, A. A. Simenel, A. N. Rodionov, V. V. Kachala, *Zh. Org. Khim.* [*Russ. J. Org. Chem.*], 2012, **48**, 1449 (in Russian).
43. A. N. Rodionov, K. Ya. Zherebker, L. V. Snegur, A. A. Korlyukov, D. E. Arhipov, A. S. Peregudov, M. M. Ilyin, M. M. Ilyin, Jr., O. M. Nikitin, N. B. Morozova, A. A.Simenel, *J. Organomet. Chem*, 2015, **783**, 83.
44. K. Lindsay, C. R. Hauser, *J. Org. Chem.*, 1957, **22**, 355.
45. F. S. Arimoto, A. S. Haven, *J. Am. Chem. Soc.*, 1955, **77**, 6295.
46. G. M. Sheldrick, *Acta Crystallogr., Sect. A*, 2015, **71**, 3—8.
47. G. M. Sheldrick, *Acta Crystallogr., Sect. C*, 2015, **71**, 3—8.
48. O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard, H. Puschmann, *J. Appl. Crystallogr.*, 2009, **42**, 339—341.

Received August 16, 2016;
in revised form October 4, 2016