ISSN 1070-3632, Russian Journal of General Chemistry, 2020, Vol. 90, No. 11, pp. 2038–2042. © Pleiades Publishing, Ltd., 2020.
Russian Text © The Author(s), 2020, published in Zhurnal Obshchei Khimii, 2020, Vol. 90, No. 11, pp. 1654–1660.

Synthesis of Isonicotinic and Salicylic Acids Derivatives from (–)-α-Pinene and (+)-Δ^3-Carene

Yu. V. Myasoedova[a], E. R. Nurieva[a],*, L. R. Garifullina[a], and G. Yu. Ishmuratov[a]

[a] *Ufa Institute of Chemistry, Ufa Federal Research Center of the Russian Academy of Sciences, Ufa, 450054 Russia*
**e-mail: eva_lala@bk.ru*

Received June 18, 2020; revised June 18, 2020; accepted July 1, 2020

Abstract—Optically active cyclobutanediyl- and cyclopropanediylbisalkylidene dihydrazides of isonicotinic and salicylic acids were synthesized when the peroxide products of ozonolysis of (–)-α-pinene and (+)-Δ^3-carene were reduced with isonicotinic and salicylic acid hydrazides in methanol, methylene chloride or tetrahydrofuran. Using QSAR models, high antituberculosis activity in combination with low values of acute toxicity and minimal inhibitory concentration was predicted for the obtained compounds.

Keywords: (–)-α-pinene, (+)-Δ^3-carene, ozonolysis, isonicotinic and salicylic acid hydrazides, diacylhydrazones, ketoesters, ketoacids

DOI: 10.1134/S1070363220110031

The synthesis of hybrid molecules containing fragments of natural compounds and pharmacophoric groups opens the way to a wide range of new compounds with potential biological activity [1, 2]. Hydrazide and hydrazone groups are present in many biologically active compounds exhibiting antibacterial, anti-tuberculosis, antifungal, antitumor, anti-inflammatory, anticonvulsant, antiviral, and antiprotozoal activity [3, 4].

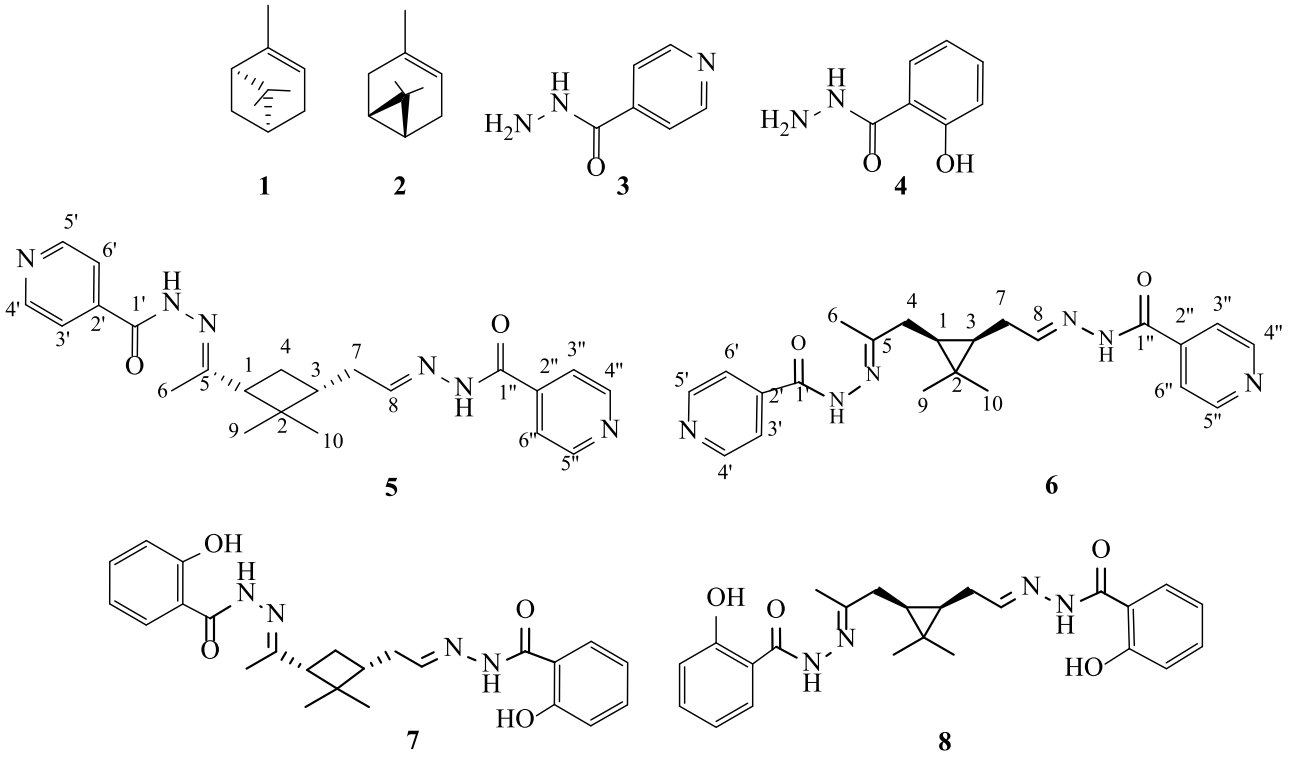
In continuation of studies on the synthesis of new compounds, in whose molecules monoterpene fragments are combined with acylhydrazone groups [5–7], we carried out ozonolysis of (–)-α-pinene **1** and (+)-Δ^3-carene **2** with the participation of isonicotinic (**3**) and salicylic (**4**) acids hydrazides. Derivatives of the latter are known for their wide application in the treatment of tuberculosis [8]. As a result, optically active acylhydrazones **5**–**8** were obtained (Scheme 1).

When creating new drugs, an important role is assigned to the search for compounds that have low toxicity along with high biological activity. For example, isonicotinic acid hydrazide **3** is included in almost all schemes for the prevention and treatment of tuberculosis, but it is toxic [9], therefore, it remains relevant to reduce the general toxicity by introducing its fragment into various structures. In order to predict the properties of synthesized molecules, it is convenient to use mathematical models that quantitatively describe the relationship between the structure of organic compounds and biological activity and toxicity. We used the QSAR (Quantitative Structure-Activity Relationship) method of analysis, one of the advantages of which is the identification of various types of toxicity along with biological activity, including acute one (LD_{50}) [10].

The QSAR analysis was performed using the OCHEM version of the expert system. Using training and test samples, the quantitative probability of anti-tuberculosis activity (Consensus Anti-TB activity_Model_5 [11]), the probable minimum inhibitory concentration (M3 T2 Consensus Anti-TB activity MIC [12]) were calculated, as well as the probable acute toxicity after oral administration to mice (LD_{50} mouse oral ASNN [10]) for both starting hydrazides **3** and **4** and their derivatives **5**–**8** (Table 1).

Calculations have shown a significant increase (up to 91%) in anti-tuberculosis activity in isoniazid derivatives **5** and **6**, as well as a high probability (63–74%) of the appearance of activity in salicylhydrazide derivatives **7** and **8**. A sharp decrease in the probable minimum inhibitory concentration (MIC) in compounds **5**–**8** we associate, firstly, with the presence of C=N groups, and secondly, with an increase in the number of pharmacologically active fragments in the molecule. The probable acute toxicity of compounds **5**–**8** is reduced by 1.5–4 times in comparison with the initial hydrazides **3** and **4**.

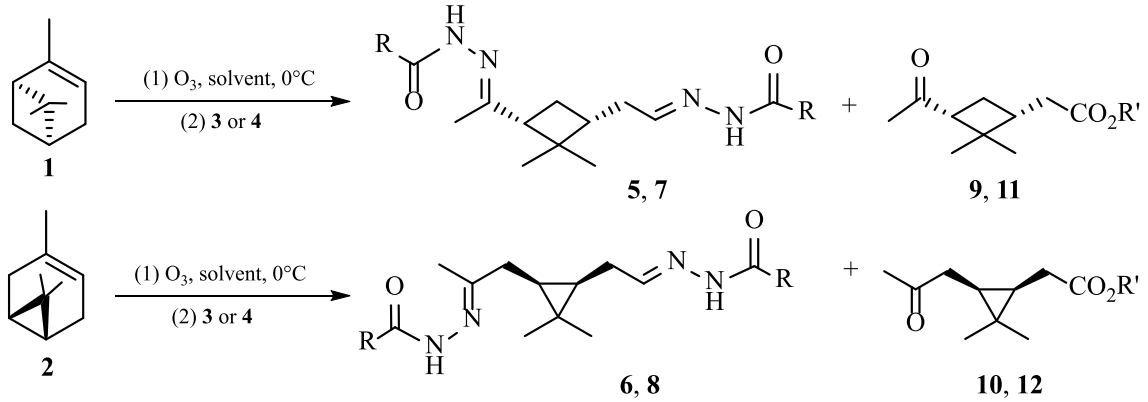
Scheme 1.



The general procedure for the synthesis of compounds **5**–**8** consisted in the ozonolysis of monoterpenes **1** or **2** in proton-donor (MeOH) or aprotic (DCM, THF) solvents at 0°C, followed by treatment of the resulting peroxide ozonolysis products with an excess (3 equiv.) of hydrazides **3** or **4** and maintaining the reaction mixture at room temperature until the disappearance of peroxides. There are two possible directions of the reaction (Scheme 2): the formation of diacylhydrazones **5**–**8** or keto acids/ketoesters **9**–**12** (the mechanisms of these reactions have been described in detail in [7]).

Ozonolysis of monoterpenes **1** or **2** in MeOH followed by treatment of peroxide compounds with an excess of isonicotinic acid hydrazide **3** leads to the formation of diacylhydrazones **5** and **6** in 87 and 63% yields, respectively [6]. The minor formation (up to 10%) of methyl esters **9** and **10** was recorded. When the peroxides **3** in aprotic solvents (THF, DCM), a significant decrease in the yields of hydrazones **5** and **6** and the predominant formation of keto acids **11** and **12** is observed.

Scheme 2.



R = C_6H_4N (**5**, **6**); *o*-HOC_6H_4 (**7**, **8**); R' = Me (**9**, **10**), H (**11**, **12**).

Table 1. Results of calculations of the activity and toxicity of compounds **3–8** using the QSAR prediction procedure

Parameter	Compounds					
	3	**4**	**5**	**7**	**6**	**8**
Quantitative probability of anti-tuberculosis activity[a]	+ (54.0%)	– (55.0%)	+ (91.0%)	+ (63.0%)	+ (91.0%)	+ (74.0%)
Probable minimum inhibitory concentration[b]	21.7 mg/kg	9.6 mg/kg	0.256 mg/kg	1.74 mg/kg	0.129 mg/kg	0.871 mg/kg
Probable acute toxicity (LD_{50})[c]	585 mg/kg	258 mg/kg	1070 mg/kg	776 mg/kg	849 mg/kg	1020 mg/kg

[a] Consensus Anti-TB activity_Model_5 [11].
[b] M3_T2_Consensus Anti-TB activity MIC, 271938 [12].
[c] When administered orally to mice (per day) (LD_{50} mouse oral ASNN [10]).

Table 2. Yields of ozonolysis products of (–)-α-pinene **1** and (+)-Δ^3-carene **2** in the presence of hydrazides **3** and **4** depending on the solvent used

Solvent	Terpene	Product, %	
		with hydrazide **3**	with hydrazide **4**
MeOH	**1**	**5** (71%), **9** (10%)	**7** (53%), **9** (5%)
	2	**6** (69%), **10** (10%)	**8** (52%), **10** (15%)
CH_2Cl_2	**1**	**5** (24%), **11** (47%)	**7** (70%), **11** (16%)
	2	**6** (20%), **12** (52%)	**8** (61%), **12** (17%)
THF	**1**	**5** (17%), **11** (47%)	**7** (67%), **11** (14%)
	2	**6** (21%), **12** (67%)	**8** (56%), **12** (19%)

The opposite situation is observed when using salicylic acid hydrazide **4**. Hydrazones **7** and **8** are formed in higher yields when the reaction is carried out in methylene chloride (Table 2), which is probably due to the higher reducing ability of salicylic acid hydrazide **4** in comparison with isoniazid **3**.

In conclusion, using QSAR models, high anti-tuberculosis activity was predicted in combination with low values of acute toxicity and minimum inhibitory concentration of diacylhydrazones obtained by ozonolysis of (–)-α-pinene and (+)-Δ^3-carene in the presence of isonicotinic or salicylic acid hydrazides in one-pot procedure.

EXPERIMENTAL

IR spectra were recorded on an IR Prestige-21 Shimadzu instrument from a thin layer. NMR spectra were recorded on a Bruker Avance III 500 spectrometer [operating frequencies 500.13 (^{1}H), 125.76 MHz (^{13}C)] from $CDCl_3$, internal standard – TMS. GLC was performed on a Chrom-5 instrument [column length 1.2 m, stationary phase – silicone SE-30 (5%) on a Chromaton N-AW-DMCS support (0.16–0.20 mm), operating temperature 50–300°C], the carrier gas is helium. Optical rotation was measured on a PerkinElmer 241-MC polarimeter. Mass spectra were recorded on an LCMS-2010 EV (Shimadzu) gas chromatography-mass spectrometer (sample injection with a syringe, eluent—acetonitrile–water, 95:5, flow rate—0.1 mL/min) in the mode of registration of positive and negative ions. TLC control was performed on Sorbfil silicagel (Russia). For column chromatography, SiO_2 (70–230 mesh) from Lancaster (Great Britain) was used.

We used (–)-α-pinene (97%, Acros Organics) and (+)-Δ^3-carene (97%). Elemental analysis data for all compounds were in agreement with the calculated data. Ozonator productivity is 40 mmol O_3/h.

The QSAR analysis was performed using the online version of the OCHEM expert system (https://ochem.eu) and the Consensus Anti-TB activity_Model_5 model (training sample accuracy 79%±2.0, test sample accuracy 81%±3.0), M3 T2 Consensus Anti-TB activity (training sample accuracy 78%±2.0, test sample accuracy 76%±4.0), LD_{50} mouse oral ASNN (training sample accuracy 72%±2.0, test sample accuracy 74%±3.0).

Ozonolysis of (–)-α-pinene (1) and (+)-Δ^3-carene (2). An ozone-oxygen mixture was bubbled through a solution of 0.5 g (3.6 mmol) of alkene **1** or **2** in 20 mL of the solvent at 0°C until the absorption of 4 mmol of O_3. The reaction mixture was purged with argon. 11.0 mmol of isonicotinic **3** (1.5 g) or salicylic **4** (1.7 g) acid hydrazide was added at 0°C. The resulting mixture was stirred at room temperature until the disappearance of peroxides (control by iodine-starch test). After the solvent was distilled off, the residue was dissolved in $CHCl_3$, washed with saturated NaCl solution, dried

with Na_2SO_4, evaporated and chromatographed (SiO_2, petroleum ether–*tert*-butyl methyl ether, 20 : 1→1 : 1).

Ozonolysis in methanol. After chromatography of the residue (1.59 g) obtained by treatment of α-pinene **1** with isonicotinic acid hydrazide **3**, 1.05 g (71%) of acylhydrazone **5** and 0.07 g (10%) of methyl ester **9** were isolated. After chromatography of the residue (1.34 g) obtained from Δ^3-carene, 1.02 g (69%) of acylhydrazone **6** and 0.07 g (10%) of ketoester **10** were isolated.

After chromatography of the residue (1.17 g) obtained by treatment of α-pinene **1** with salicylic acid hydrazide **4**, 0.85 g (53%) of acylhydrazone **7** and 0.04 g (5%) of ketoester **9** were isolated. After chromatography of the residue (1.20 g) obtained from Δ^3-carene **2**, 0.83 g (52%) of acylhydrazone **8** and 0.11 g (15%) of methyl ester **10** were isolated.

Ozonolysis in tetrahydrofuran. After chromatography of the residue (1.43 g) obtained by treatment of α-pinene **1** with isonicotinic acid hydrazide **3**, 0.25 g (17%) of acylhydrazone **5** and 0.32 g (47%) of keto acid **11** were isolated. After chromatography of the residue (1.33 g) obtained from Δ^3-carene **2**, 0.31 g (21%) of acylhydrazone **6** and 0.45 g (67%) of keto acid **12** were isolated.

After chromatography of the residue (1.52 g) obtained from α-pinene **1** by treatment with salicylic acid hydrazide **4**, 1.07 g (67%) of acylhydrazone **7** and 0.10 g (14%) of keto acid **11** were isolated. After chromatography of the residue (1.68 g) obtained from Δ^3-carene **2**, 0.90 g (56%) of acylhydrazone **8** and 0.13 g (19%) of keto acid **12** were isolated.

Ozonolysis in DCM. After chromatography of the residue (1.15 g) obtained by treatment of α-pinene **1** with isonicotinic acid hydrazide **3**, 0.36 g (24%) of acylhydrazone **5** and 0.35 g (52%) of keto acid **11** were isolated. After chromatography of the residue (1.30 g) obtained from Δ^3-carene **2**, 0.30 g (20%) of acylhydrazone **6** and 0.35 g (52%) of keto acid **12** were isolated.

After chromatography of the residue (1.35 g) obtained by treatment of α-pinene **1** with salicylic acid hydrazide **4**, 1.12 g (70%) of acylhydrazone **7** and 0.11 g (16%) of keto acid **11** were isolated. After chromatography of the residue (1.49 g) obtained from Δ^3-carene **2**, 0.97 g (61%) of acylhydrazone **8** and 0.12 g (17%) of keto acid **12** were isolated.

***N′*-{(1*E*)-1-[(1*R*,3*R*)-2,2-Dimethyl-3-{(2*E*)-2-[2-(pyridin-4-ylcarbonyl)hydrazinylidene]ethyl}-cyclobutyl]ethylidene}pyridine-4-carbohydrazide (5)** [6]. R_f 0.25 (hexane–*tert*-butyl methyl ether, 2 : 1). White crystals, mp 173–174°C, $[\alpha]_D^{20}$ –14° (*c* = 0.192, CH_2Cl_2). IR spectrum (KBr), ν, cm^{-1}: 1599 (C=N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (hereinafter, the numbering of atoms is arbitrary, see Scheme 1): 0.75–0.90 m (2H, H^1, H^3), 0.95 s (3H, H^9), 1.05 s (3H, H^{10}), 2.15 s (3H, H^6), 2.20–2.35 m (4H, H^4, H^7), 7.45 m (1H, H^8), 7.50–7.70 m (4H, $H^{3',3'',6,6''}$), 8.40–8.70 m (4H, $H^{4',4'',5',5''}$), 9.25 br. s (2H, 2NH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.55 (C^6), 19.10 (C^2), 20.04 (C^{10}), 23.01 (C^1), 23.23 (C^3), 29.17 (C^9), 29.86 (C^7), 32.86 (C^4), 121.24 (121.35) ($C^{3',3'',6',6''}$), 139.90 ($C^{2',2''}$), 149.22 (C^8), 150.14 (150.29) ($C^{4',4'',5',5''}$), 163.34 (C^5), 164.34 ($C^{1',1''}$). Mass spectrum, *m/z* (I_{rel}, %): $[M + H]^+$ 407 (100.0). Found, %: C 65.12; H 6.40; N 20.61. $C_{22}H_{26}N_6O_2$. Calculated, %: C 65.01; H 6.45; N 20.68. *M* 406.48.

***N′*-{(2*E*)-1-[(1*S*,3*R*)-2,2-Dimethyl-3-{(2*E*)-2-[2-(pyridin-4-ylcarbonyl)hydrazinylidene]ethyl}cyclopropyl]propan-2-ylidene}pyridine-4-carbohydrazide (6)** [6]. White crystals, mp 170–171°C, $[\alpha]_D^{20}$ –5° (*c* = 1.1, CH_2Cl_2), R_f 0.25 (hexane–*tert*-butyl methyl ether, 2 : 1). IR spectrum (KBr), ν, cm^{-1}: 1601 (C=N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.10 s (3H, H^{10}), 1.15 s (3H, H^9), 1.60–1.70 m (2H, H^4), 1.85 s (3H, H^6), 1.90–2.05 m (1H, H^1), 2.10–2.35 m (2H, H^7), 2.50–2.70 m (1H, H^3), 7.40–7.60 m (4H, $H^{3',3'',6,6''}$), 7.70–7.80 m (1H, H^8), 8.40–8.70 m (4H, $H^{4',4'',5',5''}$), 10.10 br. s (2H, 2NH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 18.29 (C^6), 22.48 (C^{10}), 24.22 (C^7), 26.70 (C^9), 30.43 (C^1), 34.59 (C^4), 43.44 (C^2), 49.14 (C^3), 121.32 (121.53) ($C^{3',3'',6',6''}$), 139.95 ($C^{2',2''}$), 150.16 (150.33) ($C^{4',4'',5',5''}$), 153.27 (C^8), 162.41 (C^5), 162.91 ($C^{1',1''}$). Mass spectrum, *m/z* (I_{rel}, %): $[M + H]^+$ 407 (100.0). Found, %: C 65.10; H 6.39; N 20.63. $C_{22}H_{26}N_6O_2$. Calculated, %: C 65.01; H 6.45; N 20.68. *M* 406.48.

***N′*-{(1*E*)-1-[(1*R*,3*R*)-3-{(2*E*)-2-[2-(2-Hydroxybenzoyl)hydrazinylidene]ethyl}-2,2-dimethylcyclobutyl]ethylidene}-2-hydroxybenzohydrazide (7)**. R_f 0.30 (hexane–*tert*-butyl methyl ether, 2 : 1), white crystals, mp 161–162°C. $[\alpha]_D^{20}$ 5° (*c* = 0.68, CH_2Cl_2). IR spectrum (KBr), ν, cm^{-1}: 3225 (OH), 3062 (NH), 1652, 1645 (C=N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.89 s (3H, H^{10}), 1.05 s (3H, H^9), 1.85 s (3H, H^6), 2.10–2.75 m (2H, H^4), 2.60–2.75 m (2H, H^7), 4.18–4.39 m (1H, H^3), 5.22–5.31 m (1H, H^1), 7.02–7.16 m (4H, $H^{4',4'',6',6''}$), 7.37–7.43 m (4H, $H^{3',3'',5',5''}$), 7.90 br. s and 8.03 br. s (2H, 2NH + 2H, 2OH), 8.18–8.22 m (1H, H^8). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 13.99 (C^6), 20.01 (C^{10}), 23.93 (C^4), 28.92 (C^7), 30.01 (C^9), 40.55 (C^2), 43.07 (C^3), 50.57 (C^1), 113.54 ($C^{2',2''}$), 119.18 ($C^{6',6''}$), 120.06 ($C^{4',4''}$), 129.44 ($C^{3',3''}$), 134.41 ($C^{5',5''}$), 145.61 (C^8), 154.3 (C^5), 159.58 ($C^{7',7''}$), 165.99 ($C^{1',1''}$). Mass spectrum, *m/z* (I_{rel}, %):

$[M + H]^+$ 437 (100.0). Found, %: C 66.03; H 6.46; N 12.83. $C_{24}H_{28}N_4O_2$. Calculated, %: C 66.07; H 6.41; N 12.84. *M* 436.51.

***N′*-{(2*E*)-1-[(1*S*,3*R*)-3-{(2*E*)-2-[2-(2-Hydroxybenzoyl)hydrazinylidene]ethyl}-2,2-dimethylcyclopropyl] propan-2-ylidene}-2-hydroxybenzohydrazide (8)**. R_f 0.30 (hexane–*tert*-butyl methyl ether, 2:1), white crystals, mp 165–166°C, $[\alpha]_D^{20}$ 7° (*c* = 0.62, $CHCl_3$,). IR spectrum, ν, cm^{-1}: 3225 (OH) , 3062 (NH), 1652, 1645 (C=N). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.95 s (3H, H^{10}), 1.10 s (3H, H^9), 1.20–1.35 m (1H, H^1), 1.40–1.50 m (1H, H^3), 1.82 s (3H, H^6), 1.95–2.25 m (2H, H^7), 2.28–2.48 m (2H, H^4), 6.78–7.00 m (4H, $H^{4',4'',6',6''}$), 7.30–7.45 m (4H, $H^{3',3'',5',5''}$), 7.71 br. s and 7.73 br. s (2H, 2NH + 2H, 2OH), 7.82–7.86 m (1H, H^8). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.18 (C^{10}), 17.07 (C^6), 19.25 (C^2), 25.45 (C^3), 26.37 (C^1), 27.97 (C^7), 28.62 (C^9), 33.48 (C^4), 114.87 ($C^{2',2''}$), 117.01 ($C^{6',6''}$), 119.00 ($C^{4',4''}$), 127.51 ($C^{3',3''}$), 133.52 ($C^{5',5''}$), 143.79 (C^8), 155.52 (C^5), 159.21 ($C^{7',7''}$), 168.59 ($C^{1',1''}$). Mass spectrum, *m/z* (I_{rel}, %): $[M + H]^+$ 437 (100.0). Found, %: C 66.03; H 6.46; N 12.83.$C_{24}H_{28}N_4O_2$. Calculated, %: C 66.05; H 6.50; N 12.81. *M* 436.51.

Methyl [(1*R*,3*R*)-3-acetyl-2,2-dimethylcyclobutyl]-acetate (9). R_f 0.44 (hexane–*tert*-butyl methyl ether, 2 : 1), $[\alpha]_D^{23}$ –24.8° (*c* = 0.73, CH_2Cl_2).

Methyl [(1*S*,3*R*)-2,2-dimethyl-3-(2-oxopropyl)-cyclopropyl]acetate (10). R_f 0.36 (hexane–*tert*-butyl methyl ether, 5 : 1), $[\alpha]_D^{20}$ –19.9° (*c* = 16.5, $CHCl_3$). IR and NMR spectra of compounds **9** and **10** matched those given in [13].

[(1*R*,3*R*)-(3-Acetyl-2,2-dimethylcyclobutyl)]acetic acid (8). R_f 0.21 (hexane–*tert*-butyl methyl ether, 4 : 1), $[\alpha]_D^{20}$ –39.8° (*c* = 0.8164, CH_2Cl_2).

{(1*R*,3*S*)-[2,2-Dimethyl-3-(2-oxopropyl)cyclopropyl]}acetic acid (11). R_f 0.19 (hexane–*tert*-butyl methyl ether, 4 : 1), $[\alpha]_D^{20}$ –14° (*c* = 2.23, CH_2Cl_2). IR and NMR spectra of compounds **11** and **12** matched those given in [14].

FUNDING

This work was supported by the Russian Foundation for Basic Research (project no. 19-33-90083) using the equipment of the Center for Collective Use "Chemistry" of the Ufa Institute of Chemistry, Russian Academy of Sciences and the Regional Center for Collective Use "Agidel" of the Ufa Federal Research Center of the Russian Academy of Sciences.

CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

REFERENCES

1. Andreeva, O.V., Sharipova, R.R., Strobykina, I.Y., Lodochnikova, O.A., Dobrynin, A.B., Babaev, V.M., Mironov, V.F., Kataev, V.E., and Chestnova, R.V., *Russ. J. Gen. Chem*., 2011, vol. 81, no. 8, p. 1643. https://doi.org/10.1134/S1070363211080111
2. Rogoza, L.N., Salakhutdinov, N.F., and Tolstikov, G.A., *Mini-Rev. Org. Chem*., 2009, vol. 6, no. 2, p. 135. https://doi.org/10.2174/157019309788167657
3. Popiolek, L., *Med. Chem. Res*., 2017, vol. 26, no. 2, p. 287. https://doi.org/10.1007/s00044-016-1756-y
4. Khan, M.Sh., Siddiqui, S.P., and Tarannum, N., *Hygeia J. Drugs Med*., 2017, vol. 9, no. 1, p. 61. https://doi.org/10.15254/H.J.D.Med.9.2017.165
5. Legostaeva, Yu.V., Garifullina, L.R., Nazarov, I.S., Kravchenko, A.A., Ishmuratova, N.M., and Ishmuratov, G.Yu., *Chem. Nat. Compd*., 2017, vol. 53, no. 5, p. 891. https://doi.org/10.1007/s10600-017-2149-2
6. Legostaeva, Yu.V., Garifullina, L.R., Nazarov, I.S., and Ishmuratov, G.Yu., *Russ. J. Org. Chem*., 2018, vol. 54, no. 1, p. 146. https://doi.org/10.1134/S1070428018010165
7. Myasoedova, Yu.V., Garifullina, L.R., Nurieva, E.R., Ishmuratova, N.M., and Ishmuratov, G.Yu., *Chem. Nat. Compd*., 2020, vol. 56, no. 2, p. 259. https://doi.org/10.1007/s10600-020-03002-5
8. Kudryashova, O.S. and Buzmakova, U.A., *Vestn. Permsk. Univ. Ser. Khimiya*, 2018, vol. 8, no. 1, p. 6. https://doi.org/10.17072/2223-1838-2018-1-6-28
9. Tyutyugina, A.V., Andreeva, O.V., and Garieva, F.R., *Vestn. Kazansk. Tekhnol. Univ.*, 2012, vol. 15, no. 12, p. 119.
10. Tinkov, O.V., Grigor'ev, V.Yu., Polishchyuk, P.G., Yarkov, A.V., and Rayevskii, O.A., *Biomed. Khim*., 2019, vol. 65, no. 2, p. 123. https://doi.org/10.18097/PBMC20196502123
11. Kovalishyn, V., Hodyna, D., Sinenko, V.O., Blagodatny, V., Semenyuta, I., Slivchuk, S.R., Brovarets, V., Poda, G., and Metelytsia, L., *Curr. Drug Discov. Technol*., 2020, vol. 17, no. 3, p. 365. https://doi.org/10.2174/1570163816666190411110331
12. Kovalishyn, V., Grouleff, J., Semenyuta, I., Sinenko, V.O., Slivchuk, S.R., Hodyna, D., Brovarets, V., Blagodatny, V., Poda, G., Tetko, I.V., and Metelytsia, L., *Chem. Biol. Drug Design*, 2018, vol. 92, no. 1, p. 1272. https://doi.org/10.1111/cbdd.13188
13. Ishmuratov, G.Yu., Legostaeva, Yu.V., Botsman, L.P., Yakovleva, M.P., Shakhanova, O.O., Muslukhov, R.R., and Tolstikov, G.A., *Chem. Nat. Compd*., 2009, vol. 45, no. 3, p. 318. https://doi.org/10.1007/s10600-009-9354-6
14. Ishmuratov, G.Yu., Legostaeva, Yu.V., Garifullina, L.R., Botsman, L.P., Muslukhov, R.R., and Tolstikov, G.A., *Russ. J. Org. Chem*., 2014, vol. 50, no. 8, p. 1075. https://doi.org/10.1134/S1070428014080016