ISSN 1070-3632, Russian Journal of General Chemistry, 2015, Vol. 85, No. 9, pp. 2030–2036. © Pleiades Publishing, Ltd., 2015.
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To the 85th Anniversary of birthday of late Yu.G. Gololobov

Chemoselective Oxidation of 1-Alkenylisatins with *m*-Chloroperbenzoic Acid. Synthesis of New Derivatives of Isatoic Anhydride

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Received July 17, 2015

Abstract—Oxidation of alkyl- and alkenylisatins with *m*-chloroperbenzoic acid proceeds with high chemoselectivity leading to the formation of 1-substituted isatoic anhydrides (benzo[*d*][1,3]oxazine-2,4-diones) without epoxidation of the double bond of the alkenyl substituent. This result is in accordance with the data of DFT quantum chemical calculations using the B3LYP functional in conjunction with the basis set of atomic orbitals 6-31G(d,p). The structure of the synthesized heterocyclic compounds was proved by NMR and X-ray diffraction data.

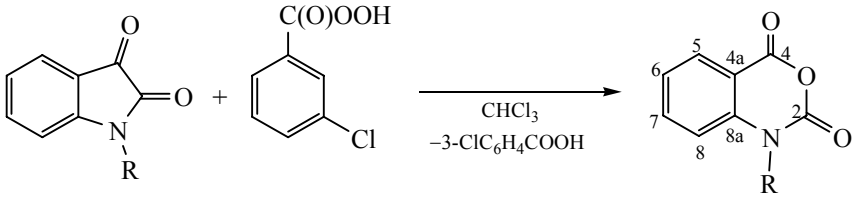
Keywords: isatin, ring expansion reaction, benzoxazinediones, X-ray diffraction

DOI: 10.1134/S1070363215090030

Isatoic anhydride (benzo[*d*][1,3]oxazine-2,4-dione) and its derivatives are convenient building blocks in organic synthesis. One of the main areas of their use is the synthesis of anthranilic acids used as corrosion inhibitors [1], in the production of pigments and dyes [2], etc. The high reactivity of 1,3-oxazine-2,4-dione moiety allows to use these compounds in the synthesis of various nitrogen-containing heterocyclic structures like quinazoline, quinazolone, quinazolinedione, benzodiazepines, quinolinone, and triptanthrin derivatives [3–6].

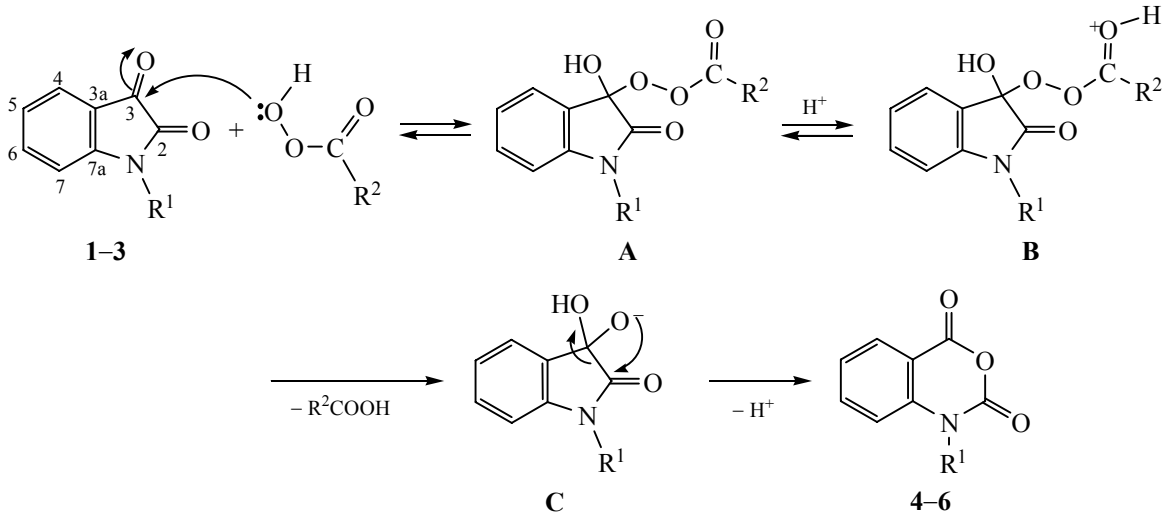
To date there are several approaches to the synthesis of benzo[*d*][1,3]oxazine-2,4-dione. The first isatoic anhydride synthesis was carried out in 1884 via isatin oxidation with chromium trioxide in acetic acid in the presence of acetic anhydride [7, 8]. Later, this approach was used for the synthesis of isatoic anhydride derivatives with benzo fragment containing halogen atoms [9, 10] or a trifluoroacetamide group [11]. Isatins with substituted aromatic moiety can be oxidized to the corresponding isatoic anhydrides by the action of various peroxides like hydrogen peroxide in acetic acid [12–14], peracetic [15, 16], monoperoxyphthalic [17] or *m*-chloroperbenzoic [18–20] acids. In contrast to the above examples, the oxidation of 1-methyl-4,5,6-tri-methoxyisatin with *m*-chloroperbenzoic acid in di-chloromethane afforded not the corresponding isatoic anhydride, but substituted 1,4-benzoxazine-2,3(4*H*)-dione [21]. The most popular method of the synthesis of the desired heterocycles is the reaction of anthranilic acid with phosgene or triphosgene. This approach allowed to obtain a number of substituted benzoxazinediones, which further were used the synthesis of heterocyclic and acyclic compounds exhibiting anti-allergic [22], anti-cancer [23–25], anticholinesterase [26, 27], antiviral [28, 29], antidiabetic [30, 31], and insecticidal [32] activity. Another simple method of the synthesis of isatoic anhydride involves the use of cyclic derivatives of phthalic acid like phthalimide and phthalic anhydride. In the first case, phthalimide is oxidized with sodium hypochlorite [33]; in the second case, reaction of phthalic anhydride with trimethylsilylazide occurring

Scheme 1.



R = $CH_2CH=CH_2$ (**1**, **4**), $CH_2CH=CHPh$ (**2**, **5**), $C_{14}H_{29}$ (**3**, **6**).

Scheme 2.



through the intermediate formation of 2-carboxyphenylisocyanate is used [34–39]. The disadvantage of this approach is the formation of two regioisomeric isatoic anhydrides, when unsymmetrically substituted phthalic anhydrides were used as precursors.

In recent years, some approaches to the synthesis of this class of heterocycles were developed on the basis of palladium-catalyzed carbonylation of *o*-iodoaniline, anthranilic acids, or *N*-alkylanilines with carbon monoxide [40–42] or the oxidation of indole derivatives with oxone [43].

In this work we investigated the reaction of 1-alkenyl- and 1-alkyl-substituted isatins with *m*-chloroperbenzoic acid. Thus, reaction of isatins **1** and **2**, bearing alkenyl groups capable of epoxidation, with *m*-chloroperbenzoic acid led to the formation of the corresponding isatoic anhydride derivatives **4** and **5** as sole reaction products (Scheme 1). It should be noted that the formation of the corresponding products of the double bond epoxidation as described in [44, 45] was not observed.

Scheme 2 shows a plausible mechanism of the formation of compounds **4**–**6**. In the first stage the reaction proceeds probably according to the Bayer–Villiger reaction type and involves the formation of adduct **A** due to the addition of the peroxy acid to the carbonyl group of isatin. Further intermediate **A** undergoes protonation with *m*-chloroperbenzoic acid or 3-chloroperbenzoic acid followed by the elimination of carboxylic acid from its molecule to form intermediate **B**. Then intermediate **B** undergoes intramolecular nucleophilic attack of alkoxide anion at the carbonyl group followed by deprotonation and ring extension to give the final compound **4**–**6**.

The oxidation of the 1,2-dicarbonyl moiety instead of the alkenyl group may be due to the higher electrophilicity of the carbonyl group in position 3 of the heterocycle. Thus, quantum-chemical calculations of atomic charges in compounds **1** and **2** based on the density functional theory (DFT) with B3LYP functional in conjunction with the basis set of atomic orbitals 6-31G(d,p) showed that the largest positive

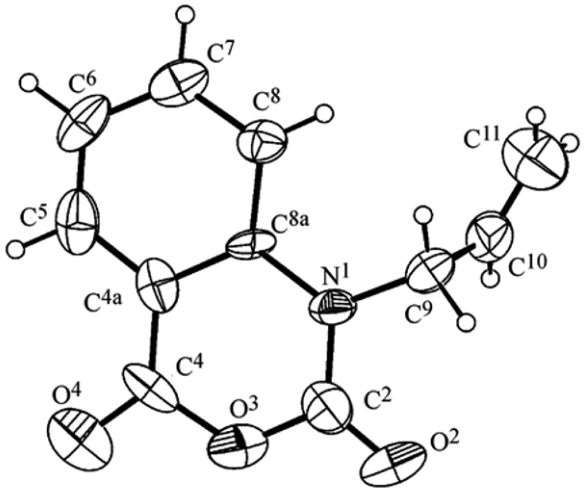


Fig. 1. Molecular geometry of compound **4** in a crystal. The selected bond lengths, bond and torsion angles: O^2–C^2 1.18(1), C^8–C^{8A} 1.40(1), O^3–C^2 1.36(1), C^9–C^{10} 1.55(1), O^3–C^4 1.42(1), C^{10}–C^{11} 1.22(1), O^4–C^4 1.20(1), N^1–C^2 1.37(1), N^1–C^{8A} 1.403(9), N^1–C^9 1.450(9), C^4–C^{4A} 1.40(1), C^{4A}–C^{8A} 1.401(9) Å; $C^2N^1C^{8A}$ 122.6(6)°, $C^2N^1C^9$ 114.6(6)°, $C^{8A}N^1C^9$ 122.8(5)°, $O^2C^2O^3$ 115(1)°, $O^2C^2N^1$ 127(1)°, $O^3C^2N^1$ 117.5(9)°, $O^3C^4O^4$ 110.2(9)°, $O^3C^4C^{4A}$ 119.3(7)°, $O^4C^4C^{4A}$ 130.5(9)°, $C^9N^1C^2O^2$ 8(2)°, $N^1C^9C^{10}C^{11}$ 134(1)°.

charge is localized on the atoms C^3, C^2 and C^{7a} (see table, positive charges shown in italics). Full geometry optimization of the studied molecular structures was carried out without restrictions on the symmetry by the program GAUSSIAN'03 [46]. Calculation and analysis of normal vibrations confirmed the compliance of the optimized structure to the energy minimum on the potential energy surface.

The calculated Mulliken atomic charges in compounds **1** and **2**

Atom[a]	Compound	
	1	**2**
N	–0.590708	–0.589774
C^2	*+0.558318*	*+0.557511*
C^3	*+0.324226*	*+0.324236*
C^{3a}	+0.032433	+0.031750
C^4	–0.108488	–0.108703
C^5	–0.096359	–0.096400
C^6	–0.085514	–0.085628
C^7	–0.107445	–0.106277
C^{7a}	*+0.318995*	*+0.319937*
O^1	–0.469785	–0.470499
O^2	–0.431531	–0.432127

[a] The numbering of the atoms is given according to the Scheme 2.

The structures of compounds **4**–**6** were proved by ^{1}H and ^{13}C NMR spectroscopy methods. Thus, in the ^{13}C–{^{1}H} NMR spectra the signals at 158 ppm corresponded to the carbonyl group in the position 4 of the heterocycle. In the spectra of initial isatins the signal of this carbon atom appeared in a weak field (δ_C = 180–185 ppm) characteristic of the ketone carbonyl group. Comparing the ^{1}H NMR spectra of the starting compounds and isatins **4**–**6** the shift of the signal of H^5 proton from 7.63 to 8.16–8.18 ppm may be due to the occurrence of intramolecular hydrogen bond between the proton and the neighboring carbonyl group.

The spatial geometry of compounds **4** and **6** was established by X-ray diffraction analysis (Figs. 1 and 2). Suitable crystals were obtained by recrystallization from hexane–chloroform mixture. Six-membered heterocycles in compounds **4** and **6** are planar within 0.04(1) and 0.05(2) Å, respectively. The oxygen atoms of the carbonyl groups are in the plane of heterocycles. The substituents at the nitrogen atom in the crystals of compounds **4** and **6** are located orthogonally to the heterocycle plane: torsion angles $C^2N^1C^9C^{10}$ are 94.7(9)° and 92(1)°, respectively.

In summary, the oxidation of 1-alkyl- and 1-alkenyl isatins with *m*-chloroperbenzoic acid proceeded chemoselectively at the carbonyl group to form 1-substituted isatoic anhydrides as the sole reaction product.

EXPERIMENTAL

IR spectra were recorded on a Bruker Vector-22 spectrometer from the sample suspended in mineral oil or from KBr pellets. ^{1}H and ^{13}C NMR spectra ($CDCl_3$) were registered on a Bruker Avance-400 instrument (400 and 100.6 MHz, respectively). Melting points were measured on a SMP10 Stuart instrument. Elemental analysis was performed using a CHNS-3 analyzer.

Alkylisatins **1** and **3** were prepared according to procedures described in [47, 48].

1-Cinnamylindoline-2,3-dione (2). To a solution of 2.94 g (0.02 mol) of isatin in 20 mL of DMF with stirring at 10°C was slowly added 0.84 g (0.02 mol) of sodium hydride (60% suspension in mineral oil). After 30 min, 2.92 mL (0.02 mol) of cinnamyl chloride was added to the resulting purple solution followed by stirring at room temperature for 3 h. The reaction mixture was poured into 100 g of crushed ice. Next, the resulting precipitate was filtered off, washed with

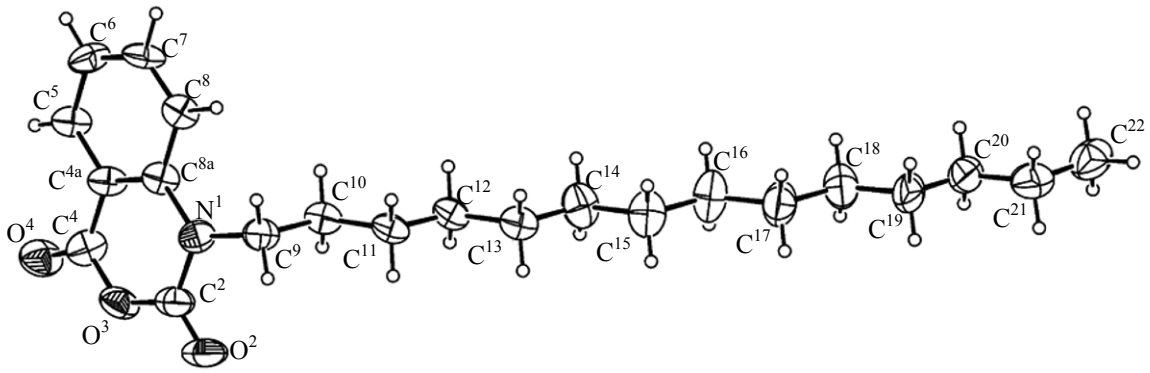


Fig. 2. Molecular geometry of compound **6** in a crystal. The selected bond lengths, bond and torsion angles: O^2–C^2 1.21(2), O^3–C^2 1.34(2), O^3–C^4 1.34(2), O^4–C^4 1.18(2), N^1–C^2 1.45(2), N^1–C^{8A} 1.39(2), N^1–C^9 1.48(2), C^4–C^{4A} 1.48(2), C^{4A}–C^{8A} 1.35(2) Å; C^2–N^1–C^{8A} 117(1)°, $C^2N^1C^9$ 119(1)°, $C^{8A}N^1C^9$ 124(1)°, $O^2C^2O^3$ 124(1)°, $O^2C^2N^1$ 118(1)°, $O^3C^2N^1$ 119(1)°, $O^3C^4O^4$ 117(1)°, $O^3C^4C^{4A}$ 116(1)°, $O^4C^4C^{4A}$ 127(1)°, $C^9N^1C^2O^2$ 9(2)°, $N^1C^9C^{10}C^{11}$ 169(1)°.

hexane, and dried in a vacuum (18 mmHg). Yield 4.94 g (94%), orange powder, mp 133–135°C. IR spectrum (KBr), ν, cm^{-1}: 3091, 3037, 2918, 2853, 1725, 1607, 1469, 1370, 1347, 1172, 1094. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 4.54 d.d (2H, NCH_2, $^3J_{HH}$ 6.0, $^4J_{HH}$ 1.5), 6.20 d.t (1H, C=CH, $^3J_{HH}$ 6.0, $^3J_{HH}$ 15.9), 6.70 br.d (1H, C=CH, $^3J_{HH}$ 15.9), 6.99 d (1H, H^7, $^3J_{HH}$ 7.9), 7.13 m (1H, H^5, $^3J_{HH}$ 7.5, $^3J_{HH}$ 7.6, $^4J_{HH}$ 0.7), 7.25–7.38 m (5H, Ph), 7.58 d.d.d (1H, H^6, $^3J_{HH}$ 7.8, $^3J_{HH}$ 7.9, $^4J_{HH}$ 1.3), 7.63 d.d (1H, H^4, $^3J_{HH}$ 7.5, $^4J_{HH}$ 0.8). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm (*J*, Hz) (the data given in parentheses are for the ^{13}C–{^{1}H} spectra): 42.10 t.d.d (s) (NCH_2, $^1J_{HC}$ 139.9, $^1J_{HC}$ 140.3, $^3J_{HC}$ 7.6, $^2J_{HC}$ 4.0, $^2J_{HC}$ 4.4), 110.81 d.d.d.d (s) (C^7, $^1J_{HC}$ 164.5, $^3J_{HC}$ 8.0, $^4J_{HC}$ 1.6, $^4J_{HC}$ 1.2), 117.61 d.d.t (s) (C^{ipso}, $^3J_{HC}$ 6.7, $^3J_{HC}$ 5.6, $^2J_{HC}$ 1.2), 121.45 d.d.t (s) (CH=CH_2, $^1J_{HC}$ 156.2, $^2J_{HC}$ 5.6, $^2J_{HC}$ 1.6), 123.74 d.m (s) (C^4, $^1J_{HC}$ 164.5), 125.32 d.d.d.d (s) (C^5, $^1J_{HC}$ 165.3, $^3J_{HC}$ 8.6, $^2J_{HC}$ 1.6, $^2J_{HC}$ 1.2), 126.44 d.m (C^o, $^1J_{HC}$ 158.2, $^3J_{HC}$ 6.4), 128.16 d.d.t (s) (C^p, $^1J_{HC}$ 160.9, $^3J_{HC}$ 7.2, $^2J_{HC}$ 1.2), 128.61 d.d.d (s) (C^m, $^1J_{HC}$ 160.5, $^3J_{HC}$ 8.0, $^2J_{HC}$ 1.2), 134.0 d.m (s) (=CH–Ph, $^1J_{HC}$ 151.8, $^3J_{HC}$ 5.2, $^3J_{HC}$ 4.8), 135.72 m (s) (C^{3a}, $^3J_{HC}$ 6.0), 138.31 d.d.d (s) (C^6, $^1J_{HC}$ 161.3, $^3J_{HC}$ 7.9, $^2J_{HC}$ 2.0), 150.76 m (s) (C^{7a}), 157.88 t (C^2=O, $^3J_{HC}$ 3.2), 183.20 d.t (s) (C^3=O, $^3J_{HC}$ 3.2, $^4J_{HC}$ 1.2). Found, %: C 77.32; H 4.69; N 5.27. $C_{17}H_{13}NO_2$. Calculated, %: C 77.55; H 4.98; N 5.32.

General procedure for the preparation of compounds 4–6. To a solution of 2.9 mmol of substituted isatin in 20 mL of chloroform while stirring at 0°C was slowly added 0.6 g (3.5 mmol) of *m*-chloroperoxybenzoic acid followed by stirring at 60°C for 2 h. After cooling, a saturated aqueous potassium carbonate solution (10 mL) was added to the reaction mixture. The organic layer was separated and evaporated. The residue was recrystallized from chloroform–hexane mixture (9 : 1).

1-Allyl-1*H*-benzo[*d*][1,3]oxazine-2,4-dione (4). Yield 81%, colorless crystalline powder, mp 103°C. IR spectrum (paraffin oil), ν, cm^{-1}: 1770, 1722, 1683, 1603, 1493, 1379, 1319, 1247, 1028. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 4.71 d.t (2H, NCH_2, $^3J_{HH}$ 5.1, $^4J_{HH}$ 1.7), 5.27–5.35 m (2H, $=CH_2$), 5.87–5.97 м (1H, =CH), 7.16 br.d (1H, H^8, $^3J_{HH}$ 8.4), 7.30 d.d.d (1H, H^6, $^3J_{HH}$ 7.8, $^3J_{HH}$ 7.4, $^4J_{HH}$ 0.9), 7.73 d.d.d (1H, H^7, $^3J_{HH}$ 7.4, $^3J_{HH}$ 7.4, $^4J_{HH}$ 1.6), 8.16 d.d.d (1H, H^5, $^3J_{HH}$ 7.9, $^4J_{HH}$ 1.6, $^5J_{HH}$ 0.4). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm (*J*, Hz): 158.33 d (s) (C^4, $^3J_{HC}$ 4.0), 147.72 d.d (s) (C^2, $^3J_{HC}$ 3.7, $^3J_{HC}$ 4.0), 141.35 m (s) (C^{8a}), 137.10 d.d.d (s) (C^7, $^1J_{HC}$ 162.1, $^3J_{HC}$ 8.8, $^2J_{HC}$ 1.5), 130.84 d.d (s) (C^5, $^1J_{HC}$ 167.3, $^3J_{HC}$ 8.4), 130.07 d.m (s) (=CH, $^1J_{HC}$ 158.5), 124.05 d.d (s) (C^6, $^1J_{HC}$ 166.2, $^3J_{HC}$ 7.7), 118.66 t.d.d (s) ($=CH_2$, $^1J_{HC}$ 154.8, $^3J_{HC}$ 5.5, $^3J_{HC}$ 5.1), 114.44 d.d (s) (C^8, $^1J_{HC}$ 163.6, $^3J_{HC}$ 7.3), 111.76 d.d (s) (C^{4a}, $^3J_{HC}$ 7.7, $^3J_{HC}$ 7.4), 47.11 t.m (s) (NCH_2, $^1J_{HC}$ 141.2). Found, %: C 64.87; H 4.28; N 6.69. $C_{11}H_9NO_3$. Calculated, %: C 65.02; H 4.46; N 6.89.

1-Cinnamyl-1*H*-benzo[*d*][1,3]oxazine-2,4-dione (5). Yield 89%, beige powder, mp 193–195°C (decomp.). IR spectrum (KBr), ν, cm^{-1}: 3085, 3042, 1715, 1655, 1630, 1452, 1378, 1132, 1061. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 4.87 d.d (2H, NCH_2, $^3J_{HH}$ 5.9, $^4J_{HH}$ 1.5), 6.25 d.t (1H, C=CH, $^3J_{HH}$ 6.0, $^3J_{HH}$ 16.0), 6.68 br.d (1H, C=CH, $^3J_{HH}$ 16.0), 7.25–7.37 m (6H,

Ph, H^8), 7.41 t (1H, H^6, $^3J_{HH}$ 7.9), 7.74 d.d.d (1H, H^7, $^3J_{HH}$ 7.4, $^3J_{HH}$ 7.4, $^4J_{HH}$ 1.6), 8.18 d.d (1H, H^5, $^3J_{HH}$ 7.9, $^4J_{HH}$ 1.5). Found, %: C 72.80; H 4.47; N 4.83. $C_{17}H_{13}NO_3$: Calculated, %: C 73.11; H 4.69; N 5.02.

1-Tetradecyl-1*H*-benzo[*d*][1,3]oxazine-2,4-dione (6). Yield 78%, beige powder, mp 90°C. IR spectrum (KBr), ν, cm^{-1}: 2916, 2849, 1783, 1722, 1603, 1478, 1372, 1324, 1250, 1031. ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.88 t (3H, CH_3, $^3J_{HH}$ 7.2), 1.26–1.47 m (22H, $11CH_2$), 1.72–1.79 m (2H, CH_2), 4.05 t (2H, NCH_2, $^3J_{HH}$ 7.8), 7.16 d (1H, H^8, $^3J_{HH}$ 8.5), 7.29 m (1H, H^6, $^3J_{HH}$ 7.4), 7.75 d.d.d (1H, H^7, $^3J_{HH}$ 7.4, $^3J_{HH}$ 7.4, $^3J_{HH}$ 1.6), 8.16 d.d (1H, H^5, $^3J_{HH}$ 7.9, $^4J_{HH}$ 1.6). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm (*J*, Hz): 158.52 d.d (s) (C^4, $^3J_{HC}$ 4.4, $^4J_{HC}$ 1.1), 147.70 t (c) (C^2, $^3J_{HC}$ 4.0), 141.40 m (s) (C^{8a}), 137.13 d.d.d (s) (C^7, $^1J_{HC}$ 161.8, $^3J_{HC}$ 8.8, $^2J_{HC}$ 1.8), 130.98 d.d.d.d (s) (C^5, $^1J_{HC}$ 166.5, $^3J_{HC}$ 8.1, $^2J_{HC}$ 2.2, $^4J_{HC}$ 1.1), 123.80 d.d (s) (C^6, $^1J_{HC}$ 166.2, $^3J_{HC}$ 7.7), 113.83 d.d.t (s) (C^8, $^1J_{HC}$ 162.9, $^3J_{HC}$ 7.7, $^4J_{HC}$ 1.5), 111.88 d.d.d (s) (C^{4a}, $^3J_{HC}$ 8.1, $^3J_{HC}$ 5.5, $^2J_{HC}$ 1.1), 45.02 t.m (s) (NCH_2, $^1J_{HC}$ 141.5, $^3J_{HC}$ 4.8), 31.90 m and 29.65 m (s) ($2CH_2$), 29.62 m (s) (CH_2), 29.59 m (s) (CH_2), 29.51 m (s) (CH_2), 29.47 m (s) (CH_2), 29.33 m (s) (CH_2), 29.23 m (s) (CH_2), 26.88 m (s) (CH_2), 26.65 m (s) (CH_2), 22.66 m (s) (CH_2), 14.08 q.m (s) (CH_3, $^1J_{HC}$ 124.4). Found, %: C 73.29; H 9.07; N 3.71. $C_{22}H_{33}NO_3$. Calculated, %: C 73.50; H 9.25; N 3.90.

X-Ray diffraction analysis was performed on a Bruker Smart APEX II CCD and Bruker Kappa APEX II CCD automated diffractometers [graphite monochromator, λ(MoK_α) 0.71073 Å, ω-scanning, 150 K]. Semi-empirical correction for extinction was performed using SADABS software [49]. The structure was solved by the direct method and refined first in isotropic and then in anisotropic approximation using SHELX software [50]. Hydrogen atoms were placed in the geometrically calculated positions and involved into refinement with a *rider* model. All calculations were performed using WinGX software [51]. Data collection, indexing and processing were performed using APEX2 software package [52]. The figures were drawn using ORTEP software [53].

The crystals of compound **4** were rhombic, $C_{11}H_9NO_3$, *M* 203.19; parameters of the unit cell: *a* = 6.984(13), *b* = 9.148(17), *c* = 15.48(3) Å; *V* = 989(3) $Å^3$, *Z* = 4; space group $P2_12_12_1$, *F*(000) = 424, $2\theta_{max}$ = 54°, *R* = 0.0845, *wR*(F^2) = 0.2807 (for 2140 independent reflections). The crystallographic data were deposited at the Cambridge Crystallographic Data Center (CCDC 1 415 507).

The crystals of compound **6** were monoclinic, $C_{22}H_{33}NO_3$, *M* = 359.49; parameters of the unit cell: *a* = 26.83(8), *b* = 4.903(15), *c* = 15.79(5) Å; β = 93.52(4)°; *V* = 2073(11) $Å^3$, *Z* = 4; space group $P2_1/c$, *F*(000) = 784, $2\theta_{max}$ = 54°, *R* = 0.1656, *wR*(F^2) = 0.3764 (for 4517 independent reflections). The crystallographic data were deposited at the Cambridge Crystallographic Data Center (CCDC 1,415,508).

ACKNOWLEDGMENTS

This work was financially supported by the Russian Science Foundation (grant no. 14-50-00014).

REFERENCES

1. US Patent 3947416, 1976.
2. Pummerer, R., Fiesselmann, H., and Muller, O., *Lieb. Ann*., 1940, vol. 544, p. 206. DOI: 10.1002/jlac.19405440113.
3. Brouillette, Y., Martinez, J., and Lisowski, V., *Eur. J. Org. Chem*., 2009, no. 21, p. 3487. DOI: 10.1002/ejoc.200801007.
4. Tucker, A.M. and Grundt, P., *Arkivoc*, 2012, vol. i, p. 546.
5. Coppola, G.M., *Synthesis*, 1980, vol. 7, p. 505. DOI: 10.1055/s-1980-29110.
6. Kappe, T. and Stadlbauer, W., *Adv. Heterocycl. Chem*., 1981, vol. 28, p. 127. DOI: 10.1016/S0065-2725(08)60042-2.
7. Kolbe, H., *J. Prakt. Chem*., 1884, vol. 30, p. 84. DOI: 10.1002/prac.18840300105.
8. Kolbe, H., *J. Prakt. Chem*., 1884, vol. 30, p. 467. DOI: 10.1002/prac.18850300144.
9. Colotta, V., Catarzi, D., Varano, F., Cecchi, L., Filacchioni, G., Galli, A., and Costagli, Ch., *Arch. Pharm*., 1997, vol. 330, p. 129. DOI: 10.1002/ardp.19973300504.
10. Castle, R.N., Adachi, K., and Guither, W.D., *J. Heterocycl. Chem*., 1965, vol. 2, p. 459. DOI: 10.1002/jhet.5570020426.
11. Norcini, G., Allievi, L., Bertolini, G., Casagrande, C., Miragoli, G., Santangelo, F., and Semeraro, C., *Eur. J. Med. Chem*., 1993, vol. 28, p. 505. DOI: 10.1016/0223-5234(93)90018-A.
12. US Patent 4316020, 1982.
13. US Patent 5597922A, 1997.
14. Lahm, G.P., Stevenson, Th.M., Selby, Th.P., Freudenberger, J.H., Cordova, D., Flexner, L., Bellin, Ch.A.,

Dubas, Ch.M., Smith, B.K., Hughes, K.A., Hollingshaus, J.G., Clark, Ch.E., and Benner, E.A., *Bioorg. Med. Chem. Lett*., 2007, vol. 17, p. 6274. DOI: 10.1016/j.bmcl.2007.09.012.

15. US Patent 3238201, 1966.
16. Chen, W.-M. and Wan, Sh.-H., *Synth. Commun*., 2007, vol. 37, p. 53. DOI: 10.1080/00397910600978085.
17. Singh, Sh.K., Govindan, M., and Hynes, J.B., *J. Heterocycl. Chem*., 1990, vol. 27, p. 2101. DOI: 10.1002/jhet.5570270746.
18. US Patent 4218464A, 1980.
19. Tojo, T., Spears, G.W., Tsuji, K., Nishimura, H., Ogino, T., Seki, N., Sugiyama, A., and Matsuo, M., *Bioorg. Med. Chem. Lett*., 2002, vol. 12, p. 2427. DOI: 10.1016/S0960-894X(02)00377-3.
20. Kurkin, A.V., Bernovskaya, A.A., and Yurovskaya, M.A., *Tetrahedron Asym*., 2010, vol. 21, p. 2100. DOI: 10.1016/j.tetasy.2010.07.001.
21. Coppola, G.M. and Schuster, H.F., *J. Heterocycl. Chem*., 1989, vol. 26, p. 957. DOI: 10.1002/jhet.5570260414.
22. Sirkar, J.C., Capiris, Th., and Kesten, S.J., *J. Med. Chem*., 1981, vol. 24, p. 735. DOI: 10.1021/jm00138a019.
23. Raffa, D., Maggio, B., Plescia, F., Cascioferro, S., Plescia, S., Raimondi, M.V., Daidone, G., Tolomeo, M., Grimaudo, S., Di Cristina, A., Pipitone, R.M., Bai, R., and Hamel, E., *Eur. J. Med. Chem*., 2011, vol. 46, p. 2786. DOI: 10.1016/j.ejmech.2011.03.067.
24. Dong, G., Wang, Sh., Miao, Zh., Yao, J., Zhang, Y., Guo, Z., Zhang, W., and Sheng, Ch., *J. Med. Chem*., 2012, vol. 55, p. 7593. DOI: 10.1021/jm300605m.
25. Henderson, E.A., Bavetsias, V., Theti, D.S., Wilson, S.C., Clauss, R., and Jackman, A.L., *Bioorg. Med. Chem*., 2006, vol. 14, p. 5020. DOI:10.1016/j.bmc.2006.03.001.
26. Tomassoli, I., Ismaili, L., Pudlo, M., de los Rios, C., Soriano, E., Colmena, I., Gandia, L., Rivas, L., Samadi, A., Marco-Contelles, J., and Refouvelet, B., *Eur. J. Med. Chem*., 2011, vol. 46, p. 1. DOI: 10.1016/j.ejmech.2010.08.054.
27. Darras, F.H., Pockes, S., Huang, G., Wehle, S., Strasser, A., Wittmann, H.-J., Nimczick, M., Sotriffer, Ch.A., and Decker, M., *ACS Chem. Neurosci*., 2014, vol. 5, p. 225. DOI: 10.1021/cn4002126.
28. Carter, M.C., Alber, D.G., Baxter, R.C., Bithell, S.K., Budworth, J., Chubb, A., Cockerill, G.S., Dowdell, V.C.L., Henderson, E.A., Keegan, S.J., Kelsey, R.D., Lockyer, M.J., Stables, J.N., Wilson, L.J., and Powell, K.L., *J. Med. Chem*., 2006, vol. 49, p. 2311. DOI: 10.1021/jm051185t.
29. Tedesco, R., Shaw, A.N., Bambal, R., Chai, D., Concha, N.O., Darcy, M.G., Dhanak, D., Fitch, D.M., Gates, A., Gerhardt, W.G., Halegoua, D.L., Han, Ch., Hofmann, G.A., Johnston, V.K., Kaura, A.C., Liu, N., Keenan, R.M., Lin-Goerke, J., Sarisky, R.T., Wiggall, K.J., Zimmerman, M.N., and Duffy, K.J., *J. Med. Chem*., 2006, vol. 49, p. 971. DOI: 10.1021/jm050855s.
30. Miyamoto, Y., Banno, Y., Yamashita, T., Fujimoto, T., Oi, S., Moritoh, Y., Asakawa, T., Kataoka, O., Yashiro, H., Takeuchi, K., Suzuki, N., Ikedo, K., Kosaka, T., Tsubotani, Sh., Tani, A., Sasaki, M., Funami, M., Amano, M., Yamamoto, Y., Aertgeerts, K., Yano, J., and Maezaki, H., *J. Med. Chem*., 2011, vol. 54, p. 831. DOI: 10.1021/jm101236h.
31. Maezaki, H., Banno, Y., Miyamoto, Y., Moritoh, Y., Asakawa, T., Kataoka, O., Takeuchi, K., Suzuki, N., Ikedo, K., Kosaka, T., Sasaki, M., Tsubotani, S., Tani, A., Funami, M., Yamamoto, Y., Tawada, M., Aertgeerts, K., Yano, J., and Oi, S., *Bioorg. Med. Chem*., 2011, vol. 19, p. 4482. DOI: 10.1016/j.bmc.2011.06.032.
32. Zhou, Y., Wang, B., Di, F., Xiong, L., Yang, N., Li, Y., Li, Yuxin, and Li, Zh., *Bioorg. Med. Chem. Lett*., 2014, vol. 24, p. 2295. DOI: 10.1016/j.bmcl.2014.03.077.
33. Rao, Y.R., Bapuji, M., and Mahapatra, S.N., *Org. Prep. Proc. Int*., 1982, vol. 14, p. 199. DOI: 10.1080/00304948209354906.
34. Pfaendler, H.R. and Weisner, F., *Heterocycles*, 1995, vol. 40, p. 717. DOI: 10.3987/COM-94-S58.
35. Norman, M.H., Rigdon, G.C., Hall, W.R., and Navas III, F., *J. Med. Chem*., 1996, vol. 39, p. 1172. DOI: 10.1021/jm950551d.
36. Sarmiento-Sanchez, J.I., Montes-Avila, J., Ochoa-Teran, A., Delgado-Vargas, F., Wilson-Corral, V., Diaz-Camacho, S.P., Garcia-Paez, F., and Bastidas-Bastidas, P., *Quim. Nova*, 2014, vol. 37, p. 1297. DOI: 10.5935/0100-4042.20140201.
37. Guillonneau, C., Nault, A., Raimbaud, E., Leonce, S., Kraus-Berthier, L., Pierre, A., and Goldstein, S., *Bioorg. Med. Chem*., 2005, vol. 13, p. 175. DOI: 10.1016/j.bmc.2004.09.047.
38. Moder, K.P. and Leonard, N.J., *J. Am. Chem. Soc*., 1982, vol. 104, p. 2613. DOI: 10.1021/ja00373a046.
39. Nagasaka, T. and Koseki, Y., *J. Org. Chem*., 1998, vol. 63, p. 6797. DOI: 10.1021/jo972158g.
40. Guan, Zh.-H., Chen, M., and Ren, Zh.-H., *J. Am. Chem. Soc*., 2012, vol. 134, p. 17490. DOI: 10.1021/ja308976x.
41. Gao, Sh., Chen, M., Zhao, M.-N., Du, W., Ren, Zh.-H., Wang, Y.-Y., and Guan, Zh.-H., *J. Org. Chem*., 2014, vol. 79, p. 4196. DOI: 10.1021/jo500417u.
42. Chen, M., Ren, Zh.-H., Wang, Y.-Y., and Guan, Zh.-H., *J. Org. Chem*., 2015, vol. 80, p. 1258. DOI: 10.1021/jo502581p.
43. Nelson, A.C., Kalinowski, E.S., Czerniecki, N.J., Jacobson, T.L., and Grundt, P., *Org. Biomol. Chem*., 2013, vol. 11, p. 7455. DOI: 10.1039/c3ob41802b.
44. Nisha Mehra, V., Hopper, M., Patel, N., Hall, D., Wrischnik, L.A., Land, K.M., and Kumar, V., *Med. Chem. Commun*., 2013, vol. 4, p. 1018. DOI: 10.1039/c3md00057e.

45. Nisha Gut, J., Rosenthal, Ph.J., and Kumar, V., *Eur. J. Med. Chem*., 2014, vol. 84, p. 566. DOI: 10.1016/ j.ejmech.2014. 07.064.

46. Frisch, M.J., Trucks, G.W., Schlegel, H.B., Scuseria, G.E., Robb, M.A., Cheeseman, J.R., Montgomery, Jr., J.A., Vreven, T., Kudin, K.N., Burant, J.C., Millam, J.M., Iyengar, S.S., Tomasi, J., Barone, V., Mennucci, B., Cossi, M., Scalmani, G., Rega, N., Petersson, G.A., Nakatsuji, H., Hada, M., Ehara, M., Toyota, K., Fukuda, R., Hasegawa, J., Ishida, M., Nakajima, T., Honda, Y., Kitao, O., Nakai, H., Klene, M., Li, X., Knox, J.E., Hratchian, H.P., Cross, J.B., Adamo, C., Jaramillo, J., Gomperts, R., Stratmann, R.E., Yazyev, O., Austin, A.J., Cammi, R., Pomelli, C., Ochterski, J.W., Ayala, P.Y., Morokuma, K., Voth, G.A., Salvador, P., Dannenberg, J.J., Zakrzewski, V.G., Dapprich, S., Daniels, A.D., Strain, M.C., Farkas, O., Malick, D.K., Rabuck, A.D., Raghavachari, K., Foresman, J.B., Ortiz, J.V., Cui, Q., Baboul, A.G., Clifford, S., Cioslowski, J., Stefanov, B.B., Liu, G., Liashenko, A., Piskorz, P., Komaromi, I., Martin, R.L., Fox, D.J., Keith, T., Al-Laham, M.A., Peng, C.Y., Nanayakkara, A., Challacombe, M., Gill, P.M.W., Johnson, B., Chen, W., Wong, M.W., Gonzalez, C., and Pople, J.A., *GAUSSIAN'03*, Revision A.1, Gaussian, Inc., Pittsburgh PA, 2003.

47. Tacconi, G., Righetti, P.P., and Desimoni, G., *J. Prakt. Chem*., 1973, vol. 315, p. 339. DOI: 10.1002/ prac.19733150221.

48. Shimazawa, R., Kuriyama, M., and Shirai, R., *Bioorg. Med. Chem. Lett*., 2008, vol. 18, p. 3350. DOI: 10.1016/ j.bmcl.2008. 04.027.

49. Sheldrick, G.M., SADABS, 1997, Bruker AXS Inc., Madison, WI-53719, USA.

50. Sheldrick, G.M., *Acta Crystallogr. (A)*, 2008, vol. 64, p. 112. DOI: 10.1107/S0108767307043930.

51. Farrugia, L.J., *J. Appl. Crystallogr*., 1999, vol. 32, p. 837. DOI: 10.1107/S0021889899006020.

52. *APEX2* (Version 2.1), SAINTPlus. Data Reduction and Correction Program (Version 7.31A, Bruker Advansed X-Ray Solutions, BrukerAXS Inc., Madison, Wisconsin, USA, 2006.

53. Farrugia, L.J., *J. Appl. Crystallogr*., 1997, vol. 30, p. 565. DOI: 10.1107/S0021889897003117.