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Synthesis of 1,3,4,6-Tetraoxo Compounds

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Anhydroustract—The two-step method of synthesis of 1,3,4,6-tetraoxocompounds with different terminal substituents is developed. By condensation of alkyl methyl ketones with dimethyl oxalate new 1,6-dialkyl-substituted 1,3,4,6-tetraoxohexanes are obtained. The esters of 3,4,6-trioxoalkanoic acids are synthesized by the condensation reaction of alkyl acetates with dialkyl oxalates and alkyl methyl ketones. By the reaction of ethyl acetate with diethyl oxalate and methyl acetate the mixed diester of 3,4-dioxo-1,6-hexanedioic (ketipic) acid has been first prepared. Specific structural features of the synthesized compounds are discussed basing on the data of the IR, NMR, and XRD diffraction (XRD) analysis.

Keywords: 1,6-dialkyl-1,3,4,6-tetraoxohexanes, esters of 3,4-dihydroxy-2,4-hexadiene-1,6-dioic and 3,4-dihydroxy-6-oxo-2,4-alkadienoic acids

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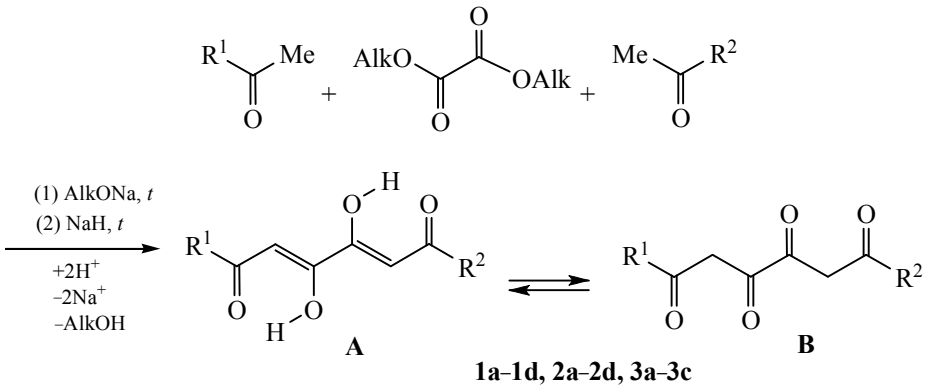
1,3,4,6-Tetraoxocarbonyl compounds are reactive species which are used in organic synthesis, including the synthesis of biologically active compounds [1–3]. The data on 1,3,4,6-tetracarbonyl compounds with different terminal substituents are limited to the methods of synthesis of 1,6-diarylsubstituted [4–8], 1-alkyl-6-arylderivatives of 1,3,4,6-tetraoxohexane [9, 10] or the esters of 6-aryl-3,4,6-trioxohexanoic acid [11]. The known methods are not universal and do not have preparative value [12].

The one-step condensation of two-fold excess of methylenecarbonyl compounds with dialkyl oxolates in the presence of excess of condensing agents is a well known preparative method for the synthesis of 1,3,4,6-tetracarbonyl compounds [1, 12, 13]. This method allows to obtain 1,6-diaryl- and 1,6-dialkyl-1,3,4,6-tetraoxohexanes or esters of 3,4-dioxo-1,6-hexanedioic (ketipic) acid in good yields, but it cannot be applied to the synthesis of 1,3,4,6-tetraoxosystems with different terminal substituents. Thus, we failed to prepare 1,6-dialkyl-1,3,4,6-tetraoxohexanes or esters of 3,4,6-trioxoalkanoic acids by one-step condensation of two different methylenecarbonyl compounds with dialkyl oxolates in the presence of two-fold excess of condensing agent. Performing the reaction in two steps with successive introduction of equimolar amounts of different methylenecarbonyl compounds and dialkyl oxolate was neither successful.

The formation of substantial amounts of by-products in the one-step method is due to the reaction of dialkyl oxolates with only one of the two methylene-carbonyl compounds that leads to the formation of the 1,3,4,6-tetracarbonyl compounds possessing C^3–C^4-axial symmetry. The presence of by-products in the two-step method is connected with the reversibility of the condensation reaction and the presence of both unreacted methylenecarbonyl compounds in the reaction mixture. Another possible reason of inapplicability or low efficiency of the above methods is the accumulation of alcohol in the reaction mixture

Scheme 1.



1a–1d, 2a–2d, 3a–3c

R^1 = Me (**1a**, **1b**), Et (**1c**, **1d**), OMe (**2a**, **2b**, **2c**, **3a**, **3b**), OEt (**2d**), R^2 = Me (**2a**, **2d**), Et (**1a**, **2b**), Pr (**1b**, **1c**, **2c**), C_5H_{11} (**1d**), OEt (**3a**, **3c**).

formed due to elimination of alkoxy groups. The molecules of alcohol prevent the anhydroustraction of proton from the methylele-active reagent by the alkoxide anion, shifting the equilibrium to the starting reagents. Thus, in alcohol medium, the condensation of a methylenecarbonyl compound with dialkyl oxolates proceeds smoothly only till the stage of formation of 1,2,4-tricarbonyl systems and does not give 1,3,4,6-tetracarbonyl compounds [14].

In the present work we describe a simple and convenient method for the synthesis of 1,3,4,6-tetracarbonyl compounds by two-step condensation of alkyl methyl ketones or alkyl acetates with dialkyl oxolates in the presence of condensing agents different in each stage. In such a method the effectiveness of the synthesis is increased due to a decrease in the accumulation of the alcohol in the reaction system, which allows the preparation of 1,3,4,6-tetracarbonyl compounds, both with identical and different terminal substituents, in preparative yields.

By the two-step reaction of different alkyl methyl ketones with dimethyl oxolate we have first synthesized 1,6-dialkyl-1,3,4,6-tetraoxohexanes **1a**–**1d** in 64–83% yields. The first stage was carried out by condensation of equimolar amounts of one alkyl methyl ketone with dimethyl oxolate and sodium methoxide, and the second step was performed by adding equimolar amount of another alkyl methyl ketone and sodium hydride to the mixture.

By the two-step reaction of different alkyl acetates with the corresponding dialkyl oxolates and alkyl methyl ketones the esters of 3,4-dihydroxy-6-oxo-2,4-alkadienoic (3,4,6-trioxo-alkanoic) acids **2a**–**2d** were synthesized in 57–68% yields (7–13% for compounds **2a**–**2c** [15, 16]). Note that compound **2d** was prepared for the first time.

By the reaction of ethyl acetate with diethyl oxolate and methyl acetate we have first synthesized the mixed diester of 3,4-dihydroxy-2,4-hexadiene-1,6-dioic (3,4-dioxo-1,6-hexanedioic) acid **3a** in 61% yield (Scheme 1). The reaction of alkyl acetates with dialkyl oxolates affords alkyl esters of 3,4-dihydroxy-2,4-hexadiene-1,6-dioic acid **3b, 3c** in 55–67% yield (42–49% [17, 18]).

Compounds **1a**–**1d**, **2a**–**2d**, **3a**–**3c** are colorless crystalline substances insoluble in water and readily soluble in most organic solvents. Their structure was determined by the methods of IR, ^{1}H NMR spectroscopy, mass spectrometry and XRD analysis. The IR spectra of compounds **1a**–**1d** contain broadened bands ν_{OH} in the range 3300–2400 cm^{-1}, broadened bands of oxo groups $C^{1(6)}$=O of the acyl fragments at 1623–1607 cm^{-1}, as well as wide bands of multiple bonds at 1568–1567 cm^{-1}, which is consistent with the enol structure **1A** (Scheme 2). Strong broadening and the shift to the low frequencies of the bands ν_{OH} are indicative of the presence of hydrogen bonds in the molecules of compounds **1a**–**1d**, while the low frequency of the C=O groups is due to the conjugation with the C=C bonds in the dioxodienol fragment. For comparison, the anhydrousorption bands of the C^3–C^4-axial symmetrical 1,3,4,6-tetraoxohexanes appear in similar ranges: at 3200–3253 (OH), 1556–1607 (C=O) and 1556–1607 cm^{-1} (C=C) [13, 19, 20].

The structure of compound **1c** was established by XRD method. In the crystal compound **1c** exists in the form (2*Z*,4*Z*)-1,6-dioxo-3,4-dienol **1A** (Scheme 2) with

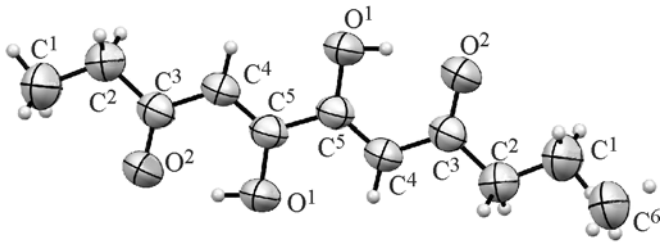


Fig. 1. XRD structure of compound **1c** with thermal ellipsoids of 50% probability.

the *s-trans* configuration of the C^3–C^4 bond (Fig. 1). Nonhydrogen atoms of molecule **1c** lie in one plane within 0.15Å, the carbonyl groups of the acyl fragments form with the enol hydroxy groups two six-membered OH-chelate rings closed by intramolecular hydrogen bonds with the OH···O=C.

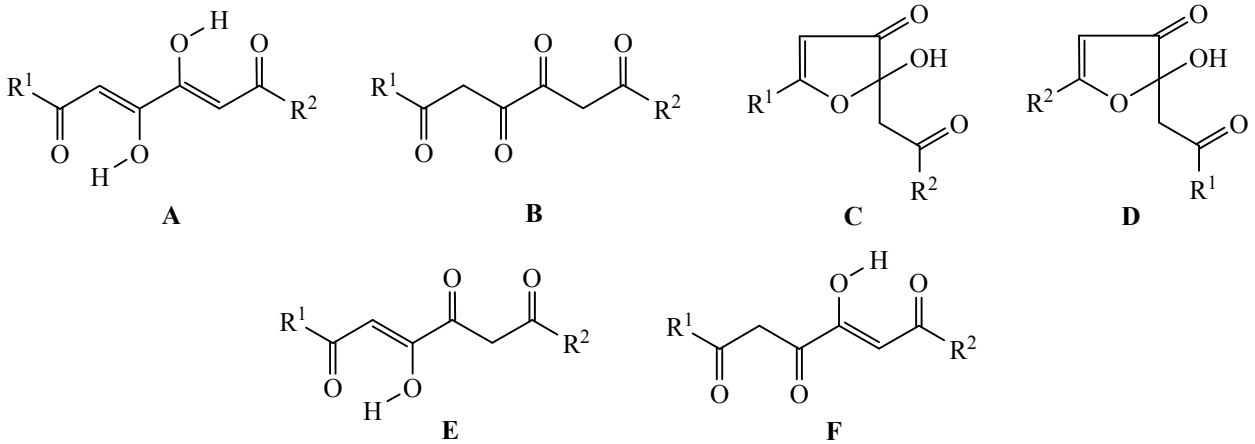
Two OH-chelate fragments in the 1,6-dioxo-3,4-dienol motif in molecule **1c** have practically equal bond lengths [C^3=O^2 1.247, C^3–C^4 1.441, C^4=C^5 1.346, C^5–O^1 1.334, O^1–H^1 0.89 Å].

The alkyl substituents in the bis-chelate fragment are statistically disordered between two positions with population coefficients 0.5, therefore, the final structure is the result of superposition of two molecules with different orientation of the alkyl substituents. The coordinates of the atoms, except for the terminal groups, practically coincide. Besides, practically equal are the coordinates of the carbon atoms of the methylene link of the *n*-propyl substituent and the methyl group of the ethyl substituent; therefore, the total population of this position and two protons connected with it are taken as 1, and proton H^{1A} located on the axis of bond C^1–C^6 was included in the refinement with population coefficient of 0.5. The arising disordering is, apparently, due to specific features of the crystal packing (Fig. 2).

In chloroform solution compounds **1a**–**1d**, as in the solid state exist in the dienol form **1A**, similar to the C^3–C^4-axial symmetrical 1,3,4,6-tetraoxohexanes [13, 19, 20]. In the ^{1}H NMR spectra of compounds **1a**–**1d**, apart from the signals of alkyl groups, a singlet of two olefin protons at 6.33 ppm and a broadened singlet of two protons of the enol hydroxy groups at 14.62–14.68 ppm are present, which confirms the structure of tautomer **1A**.

It should be specially noted that in solutions of compounds **1a**–**1d** in a nonpolar solvent (chloroform) the signals of the chemically different protons $C^{2(5)}$H or $C^{3(4)}$OH give singlets in the ^{1}H NMR spectrum. This is an unexpected result since in the spectra of the structurally similar and also having the bis-chelate structure esters of 3,4-dihydroxy-6-oxo-2,4-alkadienoic acids the $C^{2(5)}$H and $C^{3(4)}$OH protons are magnetically nonequivalent and have different chemical shifts: 5.83–6.25 (C^2H), 6.25–7.17 (C^5H), 11.52–12.18 (C^3OH), 14.65–16.22 ppm (C^4OH) [15, 16].

Scheme 2.



R^1 = Me, Et, R^2 = Et, Pr, C_5H_{11} (**1a**, **1d**), R^1 = OMe, OEt, R^2 = Me, Et, Pr (**2a**, **2d**), R^1, R^2 = OMe, OEt (**3a**, **3c**).

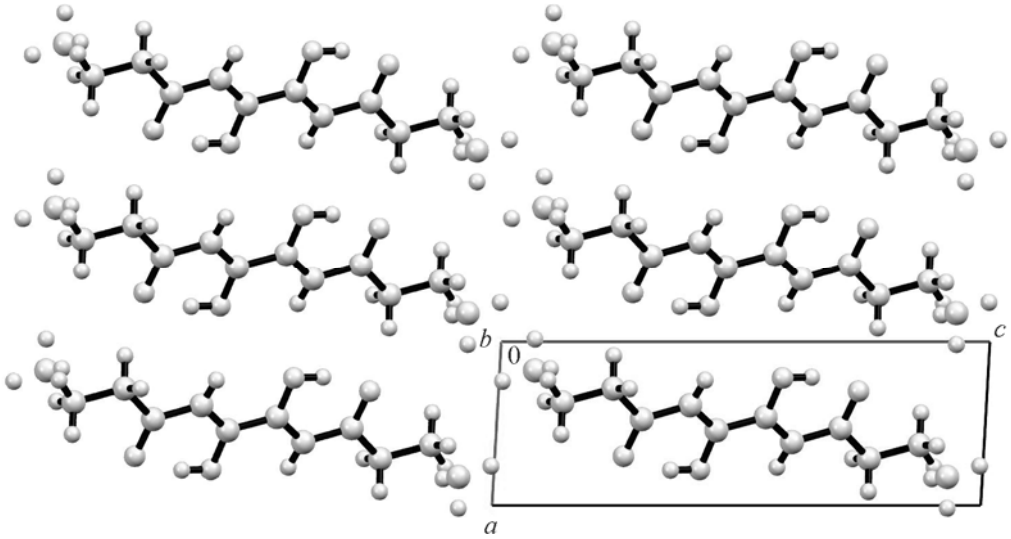


Fig. 2. Fragment of molecular packing in the crystal of compound **1c**.

Unlike the C^3–C^4-axial symmetrical 1,3,4,6-tetraoxohexanes, which in nonpolar chloroform exist in the form of several minor tautomers (linear and cyclic derivatives of ketoform **1B**, Scheme 2) [13, 20], compounds **1a**–**1d** in chloroform solution do not form these forms, as proved by the anhydrousence of the corresponding signals in the ^{1}H NMR spectra. In a polar solvent (DMSO-d_6), according to the ^{1}H NMR data, compounds **1a**–**1d** exist in the equilibrium between several forms (Scheme 2), among which the oxofuran regioisomeric structures **1C** (45–57%) and **1D** (27–39%) predominate, whereas the dienol form **1A** is present as a minor tautomer (14–19 %).

The structure of the cyclic regioisomers **1C** and **1D** is proved by the presence in the spectrum of two doublets at 2.87–2.88 and 2.98–3.01 ppm (J = 15.4–16.5 Hz), corresponding to the methylene protons of the Alk$^{1(2)}$COCH$_2$ group, the singlet of olefin proton of the oxofuran cycle at 5.47–5.53 ppm, and a broadened singlet of the hydroxyl proton of the hemiacetal fragment at 7.76–7.84 ppm.

The presence of the dienol form **1A** in solutions of compounds **1a**–**1d** in DMSO-d_6 is proved by the presence of proton signals of the alkyl groups and a singlet of two olefin protons at 6.38–6.44 ppm. The signals of the enol hydroxy groups cannot be observed due to the strong broadening caused, apparently, by fast exchange of protons with the solvent.

Earlier, we have established qualitative dynamic prototropic ring-chain transformations of compounds **2a**–**2d** in solutions in polar and nonpolar solvents. Thus, in nonpolar chloroform, compounds **2a**–**2d**, as well as the structurally similar 1,3,4,6-tetracarbonyl compounds **1a**–**1d**, exist exclusively in the dioxodienol form **2A**, whereas in DMSO solution, exclusively as the oxofuran tautomer **2D** (Scheme 2), whose structure was discussed earlier [13, 20]. Note that in the ^{1}H NMR spectra ($CDCl_3$) of triketoesters **2a**–**2d**, unlike tetraketones **1a**–**1d**, the chemical shifts of the proton signals of the C$^{2(5)}$H and C$^{3(4)}$OH groups are substantially different (C^{2}H and C^{5}H 0.09–0.31 ppm, C^{3}OH and C^{4}OH 3.02–3.14 ppm), suggesting essential difference in the magnetic surrounding (R^1 = OAlk, R^2 = Alk) between the two chelate fragments of the molecule [15, 16].

In the solid phase the structure of compounds **2a**–**2d** was earlier studied only by IR spectroscopy [15, 16]. To prove the structure of triketoesters **2** we determined the structure of compounds **2a**, **2b** by XRD analysis. According to XRD analysis the molecules of compounds **2a**, **2b** exist in the form of (2*Z*,4*Z*)-1,6-dioxo-3,4-dienol **2A** (Fig. 3, Scheme 2), having the structure similar to that of the known tetraketones **1** [21, 22]. Molecules **2a** and **2b** are planar (within 0.2 Å), the C$^{1(6)}$=O carbonyl groups form with the C$^{3(4)}$OH hydroxyl groups two six-membered OH-chelate rings closed by intramolecular hydrogen bonds of the OH···O=C type. The chelate fragments in the molecules of compounds **2a**, **2b** are turned out to the *trans*-configuration with respect to each other, similar to the known structural analogs **1** [19, 21, 22]. As distinct from tetraketone **1c**, the effect of two different substituents (R^1 = OAlk, R^2 = Alk) in the molecules of

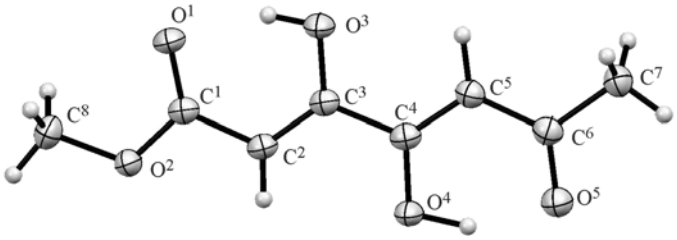


Fig. 3. XRD structure of compound **2a** with thermal ellipsoids of 50% probability.

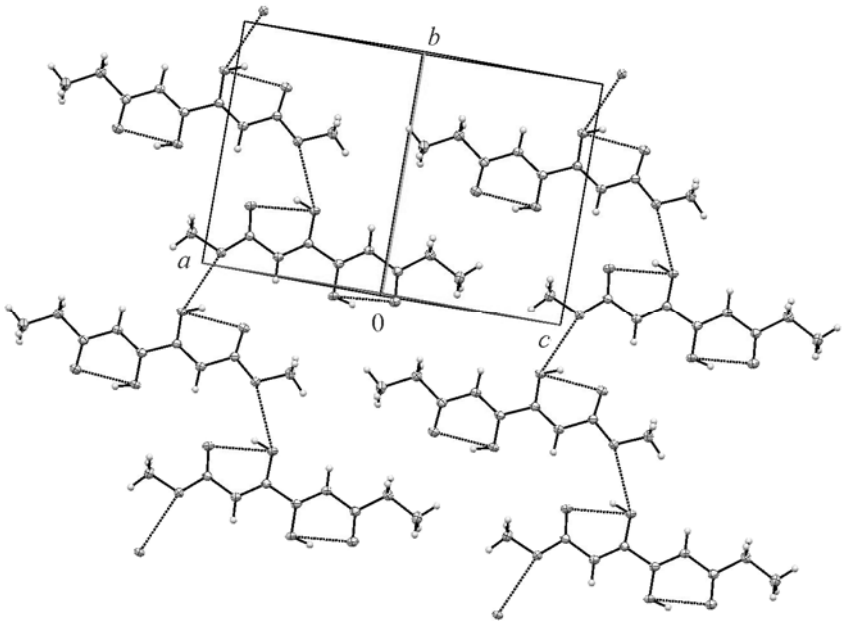


Fig. 4. XRD structure of compound **2b** with thermal ellipsoids of 50% probability.

compounds **2a**, **2b** on the bis-chelate fragment is more clearly pronounced, as proved by the values of the bond lengths in the two OH-chelate rings (see the table). The differences are, however, small, thus indicating the formation of a common π-system in the bis-chelate fragment of the molecule.

In the crystal the molecules of compounds **2a**, **2b** are organized in a layer packing formed due to an extended system of intermolecular hydrogen bonds of the type OH···O=C between the protons of the hydroxyl groups and carbonyl oxygen of the ester group, as well as due to weak van der Waals interactions between the alkyl fragments.

The structure of compounds **2a**–**2d** was also confirmed by the data of high-resolution mass spectrometry obtained in the electrospray mode in acetonitrile solution, where characteristic signals of ions $[M + H]^+$ or $[M + Na]^+$ as well as cluster ions $[2M + H]^+$ and $[2M + Na]^+$ were observed.

By the IR spectroscopy data, compound **3a** in the crystal, like esters **3b**, **3c** [17, 18], has the enol structure. The IR spectrum of compound **3a** contains a broadened ν_{OH} band in the range 3300–2600 cm^{-1}, the

Selected bond lengths in compounds **2a** and **2b**

2a		**2b**	
$C^1=O^1$	1.228	$C^1=O^5$	1.226
$C^6=O^5$	1.246	$C^6=O^3$	1.246
$C^1–C^2$	1.454	$C^1–C^2$	1.456
$C^5–C^6$	1.444	$C^5–C^6$	1.450
$C^2=C^3$	1.340	$C^2=C^3$	1.348
$C^4=C^5$	1.352	$C^4=C^5$	1.357
$C^3–O^3$	1.346	$C^3–O^2$	1.343
$C^4–O^4$	1.334	$C^4–O^4$	1.333
$O^3–H^3$	0.89	$O^2–H^2$	0.85
$O^4–H^4$	1.02	$O^4–H^4$	0.84

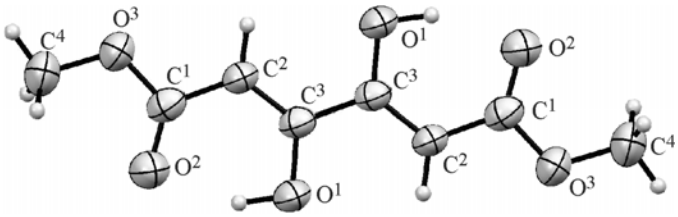


Fig 5. XRD structure of compound **3b** with thermal ellipsoids of 50% probability.

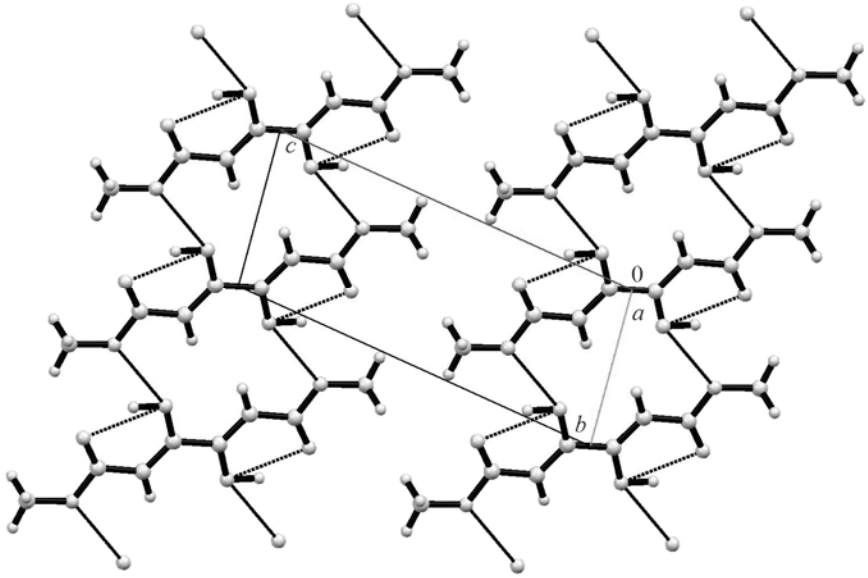


Fig. 6. Hydrogen bonds in the crystal of compound **3b**.

band of ester carbonyl groups $C^{1(6)}$=O at 1645 cm^{-1}, a broadened band of multiple bonds at 1590 cm^{-1}, and the $\nu_{C–OR}$ band at 1182 cm^{-1}, proving the enol structure of the compound. Broadening of the OH group bands and their shift to the low-frequency field are indicative of the presence of hydrogen bonds in the molecule of compound **3a**, and the low frequency of the carbonyl groups, of their conjugation with the C=C bonds in the enol fragments. Note that the corresponding anhydrousorption bands of the known ketipinates **3** existing in the solid state in form **3A** (Scheme 2) appear in a close region: 3480–3380 (OH), 1660–1638 (C=O), 1630–1589 cm^{-1} (C=C), and 1194–1166 cm^{-1} (C–OAlk) [14, 17, 18].

To prove the structure of ketipinates **3** we determined the structure of compound **3b** by XRD analysis (for compound **3a** we failed to prepare crystals suitable for the XRD analysis). From XRD analysis (Fig. 5), compound **3b** in the crystal exists in the form of symmetric (2*Z*,4*Z*)-1,6-dioxo-3,4-dienol **3A** (Scheme 2). The molecule is planar (within 0.2 Å), the six-membered chelate cycles formed with the participation of the ester carbonyl groups and the enol hydroxyls are in the *trans*-configuration to each other and are closed by intramolecular hydrogen bonds OH···O=C. The lengths of the double (C=C, C=O) and ordinary bonds (C–C, C–O) in the OH-chelate fragments in compound **3b** are slightly shorter (by 0.08–0.19 Å) than those in compound **2a**, formed with participation of the ester carbonyl group of the MeOC=O fragment, which is indicative of a stronger degree of conjugation in the bis-chelate system of compound **3b** (C^1=O^2 1.220, C^1–C^2 1.435, C^2=C^3 1.329, C^3–O^1 1.337 Å). The enol hydroxyl protons in compound **3b** are located at the central oxygen atoms, as in **2a**, as witnessed by the values of bond lengths of the ketoenol fragments (O^1–H^1 0.97 and O^3–H^3 0.89 Å).

In the crystal, the molecules of compound **3b** are organized in a layer packing (Fig. 6) formed due to an extended system of intermolecular hydrogen bonds between the hydroxyl protons and the ester oxygens as well as between the olefin protons and the hydroxyl oxygens.

Earlier it was shown that compounds **3** exist in solution in the equilibrium tautomeric forms (**3A**, **3E**)

[14, 17], which are the enol derivatives of tetraoxo form **3B** (Scheme 2). Cyclic oxofuran tautomers, which are typical for compounds **1**, **2**, were not detected in solutions of compounds **3b, 3c**.

From the ^{1}H NMR spectroscopy data, in nonpolar solvents compound **3a** exists exclusively in the dienol form **3A**, whereas in polar solvents several equilibrium tautomeric forms (**3A**, **3B**, **3E**, **3F**, Scheme 2) are present. In the ^{1}H NMR spectrum of compound **3a** in $CDCl_3$, apart from the signals of alkoxy groups, a singlet of two olefin protons at 5.88 ppm and a broadened singlet of two protons of the enol hydroxy groups at 11.74 ppm are observed, corresponding to tautomer **3A**. As in compounds **1a**–**1d**, the signals of chemically nonequivalent protons $C^{2(5)}H$ or $C^{3(4)}OH$ are present in the spectrum as singlets. No other equilibrium tautomeric forms of compound **3a**, or its homologs **3b** or **3c** were found in the chloroform solution.

In the ^{1}H NMR spectrum in DMSO-d_6 of compound **3a**, in addition to the signals of alkoxy groups and the signals of form **3A** [30%, $C^{2(5)}H$ 5.82 ppm, $C^{3(4)}OH$ 11.61 ppm], the singlets of olefin protons C^2H 5.76 ppm (**3F**, 20%) and 5.78 ppm (**3E**, 15%), methylene protons C^5H_2 3.89 ppm (**3F**) and δ 3.92 ppm (**3E**), and hydroxyl protons C^3OH 11.35 (**3F**) and 11.52 ppm (**3E**) are observed, corresponding to two regioisomeric ketoenol tautomers **3E**, **3F**, as well as a singlet of methylene protons $C^{2(5)}H_2$ 3.82 ppm of tautomer **3B**.

In the mass spectra of compounds **3a**–**3c** characteristic signals of ions $[M + H]^+$ or $[M + Na]^+$, as well as of cluster ions $[2M + H]^+$ and $[2M + Na]^+$ are observed.

Therefore, the investigated 1,3,4,6-tetraoxo compounds is a typical example of substituted polyenes. All studied compounds exist in the planar bis-1,3-ketoenol form with enolizable oxo groups in positions 3, 4 and *s-trans* arrangement of the double bonds in the system of conjugation of the tetraoxo compound.

EXPERIMENTAL

IR spectra were taken on a Bruker Alpha IR Fourier spectrometer in the attenuated total reflection mode with ZnSe windows. ^{1}H NMR spectra were registered on a Bruker AVANCE II spectrometer (400 MHz), internal reference tetramethylsilane. High resolution mass spectra were recorded on a quadruple time-of-flight mass spectrometer maXis impact HD, Bruker Daltonik GmbH. The samples were dissolved in acetonitrile and injected with the rate 240 μL/h by a syringe pump 100 (KD Scientific Inc.). Positive ions were registered in the electrospray mode with standard ionic source in the range of masses 50–1300 Da using parameters of the pre-installed method Direct Infusion 100–1000. Elemental analysis was performed on a LECO CHNS-932 instrument. Purity of the obtained products was confirmed by TLC on Sorbfil UV-254 plates in the systems hexane–acetone 5 : 1; 3 : 1; chloroform–hexane 10 : 1; chloroform.

XRD analysis was performed on an automated difractometer Xcalibur 3, ω-scanning with 1° step, monochoromator MoK_α. For compounds **2a**, **2b**, **3b** empirical correction for extinction was introduced, for compound **1c** no correction was made. The structures were determined by the direct method and refined by the full-matrix least-squares method with respect to F^2 in the anisotropic approximation for all nonhydrogen atoms. CH hydrogen atoms were placed in the geometrically calculated positions and refined in the isotropic approximation, the positions of OH protons were refined independently. All calculations were performed using the program package Olex2 [23, 24].

Compound 1c: triclinic, *P*-1, *T* 295(2) K, *a* 4.6434(9), *b* 4.7505(12), *c* 13.583(3) Å, α 92.703(19)°, β 92.638(17)°, γ 101.701(19)°, μ 0.091 mm^{-1}. 2643 total reflections (3.01° < θ < 26.34°), 1122 independent reflections (R_{int} 0.0248), including 537 with $I > 2\sigma(I)$. Final refinement parameters: R_1 0.0981, wR_2 0.1520 (on all reflections), R_1 0.0496, wR_2 0.1388 [on reflections with $I > 2\sigma(I)$], *S* 1.005.

Compound 2a: monoclinic, $P2_1/c$, *T* 150(1) K, *a* 8.0551(5), *b* 13.3557(10), *c* 8.0649(6) Å, β 103.458(8)°, μ 0.124 mm^{-1}. 4757 total reflections (6.02° < 2θ < 56.56°), 2096 independent reflections (R_{int} 0.0216), including 2423 with $I > 2\sigma(I)$. Final refinement parameters: R_1 0.0517, wR_2 0.1406 (on all reflections), R_1 0.0780, wR_2 0.1625 [on reflections with $I > 2\sigma(I)$], *S* 1.007.

Compound 2b: monoclinic, $P2_1/c$, *T* 120(1) K, *a* 10.1363(9), *b* 9.9888(7), *c* 9.4856(7) Å, β 98.458(8)°, μ 0.115 mm^{-1}. 3900 total reflections (5.76° < 2θ < 56.56°), 2287 independent reflections (R_{int} 0.0216), including 1579 with $I > 2\sigma(I)$. Final refinement parameters: R_1 0.0817, wR_2 0.1579 (on all reflections), R_1 0.0510, wR_2 0.1345 [on reflections with $I > 2\sigma(I)$], *S* 1.001.

Compound 3b: triclinic, *P*-1, *T* 295(2) K, *a* 3.9776(8), *b* 5.0316(9), *c* 11.646(2) Å, α 98.990(14)°, β 90.864(15)°,

γ 103.671(15)°, μ 0.131 mm^{-1}. 2164 total reflections (3.55° < θ < 28.27°), 1107 independent reflections (R_{int} 0.0210), including 415 with $I > 2\sigma(I)$. Final refinement parameters: R_1 0.0443, wR_2 0.0811 (on all reflections), R_1 0.1016, wR_2 0.0839 [on reflections with $I > 2\sigma(I)$]. Full set of structural data is deposited to the Cambridge Crystallographic Database Center (CCDC 1043555, 1405972, 1406315, 1030426 for compounds **1c**, **2a**, **2b**, **3b,** respectively).

Synthesis of 1,6-dialkyl-1,3,4,6-tetraketones (1a–1d), esters of 3,4,6-trioxoalkanoic (2a–2d) and 3,4-dioxo-1,6-hexanedioic acids (3a–3c). Mixture of 50 mL of tetrahydrofuran, 2.0 g (50 mmol) of 60% suspension of sodium hydride in mineral oil, 2.0 mL of anhydrous methanol (for compounds **1a**–**1d**, **2a**–**2c**, **3b**) or 2.9 mL of anhydrous ethanol (for compounds **2d**, **3a**, **3c**) and refluxed for 30 min for the formation of the corresponding sodium alkoxide. Then the mixture of 5.9 g (50 mmol) of dimethyl oxolate (for compounds **1a**–**1d**, **2a**–**2c**, **3b**) and 4.5 mL (50 mmol) of 2-butanone (for compounds **1a**, **1c**) or 5.3 mL (50 mmol) of 2-pentanone (for compound **1b**) or 7.1 mL (50 mmol) of 2-heptanone (for compound **1b**) or 4.0 mL (50 mmol) of methyl acetate (for compound **2a**–**2c**, **3b**) or the mixture of 6.8 mL (50 mmol) of diethyl oxolate and 4.6 mL (50 mmol) of ethyl acetate (for compounds **2d**, **3a**, **3c**) was added and refluxed for 30 min. After that, to the reaction mixture was added 2.0 g (50 mmol) of 60% suspension of sodium hydride in mineral oil and 3.7 mL (50 mmol) of acetone (for compounds **1a**, **1b**, **2a**, **2d**) or 5.3 mL (50 mmol) of 2-pentanone (for compounds **1c**, **2c**) or 4.5 mL (50 mmol) of 2-butanone (for compounds **1d**, **2b**) or 4.0 mL (50 mmol) of methyl acetate (for compounds **3a**, **3b**) or 4.6 mL (50 mmol) of ethyl acetate (for compound **3c**) and refluxed for 1 h. The solvent was removed, to the residue 100 mL of cooled 15% hydrochloric acid was added, the formed precipitate was filtered, dried, and crystallized from ethanol or ethyl acetate.

(2*Z*,4*Z*)-1-Methyl-6-ethyl-3,4-dihydroxy-2,4-hexadiene-1,6-dione (1a). Yield 5.89 g (64%); mp 43–44°C. IR spectrum, ν, cm^{-1}: 3300–2400 br (OH), 3110 (CH), 1623 (C=O), 1567 (C=C), 1463, 1377, 1244, 1184, 1140, 1095, 1056, 991, 921, 895, 806. ^{1}H NMR spectrum, δ, ppm: 1.16 t (3H, $CH_2\underline{CH_3}$, J = 7.5 Hz), 2.24 s (3H, CH_3), 2.52 q (2H, $\underline{CH_2}CH_3$, J = 7.5 Hz), 6.33 s (2H, =CH), 14.62 br.s (2H, OH), form **1A** (100%). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 0.90 t (3H, $CH_2\underline{CH_3}$, J = 7.2 Hz, form **1C**, 47%), 0.91 t (3H, $CH_2\underline{CH_3}$, J = 7.3 Hz, form **1D**, 32%), 1.10 t (3H, $CH_2\underline{CH_3}$, J = 7.5 Hz, form **1A**, 17%), 2.17 s (3H, CH_3, form **1A**), 2.19 s (3H, CH_3, form **1C**), 2.20 s (3H, CH_3, form **1D**), 2.44 q (2H, $\underline{CH_2}CH_3$, J = 7.5 Hz, form **1A**), 2.48 q (2H, $\underline{CH_2}CH_3$, J = 7.3 Hz, form **1D**), 2.50 q (2H, $\underline{CH_2}CH_3$, J = 7.2 Hz, form **1C**), 2.88 d, 2.98 d (2H, CH_2, J = 16.0 Hz, forms **1C**, **1D**), 5.52 s (1H, CH, form **1C**), 5.53 s (1H, CH, form **1D**), 6.43 s (2H, =CH, form **1A**), 7.84 s (1H, OH, forms **1C**, **1D**). Found, %: C 58.60; H 6.61. $C_9H_{12}O_4$. M 184.19. Calculated, %: C 58.69; H 6.57. M 184.19.

(2*Z*,4*Z*)-1-Methyl-6-propyl-3,4-dihydroxy-2,4-hexadiene-1,6-dione (1b). Yield 6.73 g (68%); mp 69–70°C. IR spectrum, ν, cm^{-1}: 3300–2400 (OH) 3101 (CH), 1607 (C=O), 1568 (C=C), 1463, 1377, 1247, 1188, 1145, 1095, 1084, 1040, 1027, 989, 900, 841. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.96 t (3H, $CH_2CH_2\underline{CH_3}$, J = 7.8 Hz), 1.68 m (2H, $CH_2\underline{CH_2}CH_3$), 2.24 s (3H, CH_3), 2.46 t (2H, $\underline{CH_2}CH_2CH_3$, J = 7.8 Hz), 6.33 s (2H, =CH), 14.68 br.s (2H, OH), form **1A** (100 %). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 0.81 t (3H, $CH_2CH_2\underline{CH_3}$, J = 7.5 Hz, form **1A**, 19%), 0.84 t (3H, $CH_2CH_2\underline{CH_3}$, J = 7.8 Hz, form **1C**, 46%), 0.87 t (3H, $CH_2CH_2\underline{CH_3}$, J = 7.8 Hz, form **1D**, 34%), 1.42 m (2H, $CH_2\underline{CH_2}CH_3$, form **1A**), 1.58 m (2H, $CH_2\underline{CH_2}CH_3$, forms **1C**, **1D**), 2.12 s (3H, CH_3, form **1A**), 2.14 s (3H, CH_3, form **1C**), 2.15 s (3H, CH_3, form **1D**), 2.45 t (2H, $\underline{CH_2}CH_2CH_3$, J = 7.8 Hz, form **1C**), 2.46 t (2H, $\underline{CH_2}CH_2CH_3$, J = 7.8 Hz, form **1D**), 2.87 d, 3.00 d (2H, CH_2, J = 16.5 Hz, forms **1C**, **1D**), 5.47 s (1H, =CH, form **1C**), 5.48 s (1H, =CH, form **1D**), 6.38 s (2H, =CH, form **1A**), 7.76 s (1H, OH, forms **1C**, **1D**). Found, %: C 60.63; H 7.15. $C_{10}H_{14}O_4$. M 198.22. Calculated, %: C 60.59; H 7.12. M 198.22.

(2*Z*,4*Z*)-1-Ethyl-6-propyl-3,4-dihydroxy-2,4-hexadiene-1,6-dione (1c). Yield 7.42 g (70%); mp 103–105°C. IR spectrum, ν, cm^{-1}: 3300–2400 (OH), 3098 (CH), 1609 (C=O), 1568 (C=C), 1460, 1378, 1292, 1144, 1095, 1058, 1000, 878, 807. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.96 t (3H, $CH_2CH_2\underline{CH_3}$, J = 7.8 Hz), 1.16 t (3H, $CH_2\underline{CH_3}$, J = 7.8 Hz), 1.68 m (2H, $CH_2\underline{CH_2}CH_3$), 2.46 t (2H, $\underline{CH_2}CH_2CH_3$, J = 7.8 Hz), 2.52 q (2H, $\underline{CH_2}CH_3$, J = 7.8 Hz), 6.33 s (2H, =CH), 14.62 br.s (2H, OH), form **1A** (100%). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 0.85 t (3H, $CH_2CH_2\underline{CH_3}$, J = 7.2 Hz, form **1C**, 45%), 0.90 t (3H, $CH_2\underline{CH_3}$, J = 7.2 Hz, form **1D**, 39%), 0.94 t (3H, $CH_2CH_2\underline{CH_3}$, J = 7.5 Hz, form **1A**, 14%), 0.96 t (3H, $CH_2\underline{CH_3}$, J = 7.3 Hz, form **1D**), 1.09 t (3H, $CH_2\underline{CH_3}$, J = 7.4 Hz, form **1A**), 1.16 t (3H, $CH_2\underline{CH_3}$, J = 7.3 Hz,

form **1C**), 1.45 m (2H, $CH_2\underline{CH_2}CH_3$, form **1A**), 1.46 m (2H, $CH_2\underline{CH_2}CH_3$, form **1C**), 1.61 m (2H, $CH_2\underline{CH_2}CH_3$, form **1D**), 2.46 t (2H, $\underline{CH_2}CH_2CH_3$, J = 7.2 Hz, form **1C**), 2.48 t (2H, $\underline{CH_2}CH_2CH_3$, J = 7.2 Hz, form **1D**), 2.51 q (2H, $\underline{CH_2}CH_3$, J = 7.3 Hz, form **1D**), 2.52 q (2H, $\underline{CH_2}CH_3$, J = 7.3 Hz, form **1C**), 2.58 t (2H, $\underline{CH_2}CH_2CH_3$, J = 7.5 Hz, form **1A**), 2.63 q (2H, $\underline{CH_2}CH_3$, J = 7.4 Hz, form **1A**), 2.87 d, 2.99 d (2H, CH_2, J = 15.6 Hz, forms **C**, **1D**), 5.52 s (1H, =CH, forms **1C**, **1D**), 6.43 s (2H, =CH, form **1A**), 7.79 s (1H, OH, forms **1C**, **1D**). Found, %: C 62.29; H 7.55. $C_{11}H_{16}O_4$. *M* 212.24. Calculated, %: C 62.25; H 7.60. *M* 212.24.

(2*Z*,4*Z*)-1-Ethyl-6-pentyl-3,4-dihydroxy-2,4-hexadiene-1,6-dione (1d). Yield 9.96 g (83%); mp 40–42°C. IR spectrum, ν, cm^{-1}: 3300–2400 (OH), 3098 (CH), 1615 (C=O), 1568 (C=C), 1464, 1378, 1246, 1143, 1094, 1058, 1003, 886, 810. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.84 t (3H, $(CH_2)_4\underline{CH_3}$, J = 7.0 Hz), 1.14 t (3H, $CH_2\underline{CH_3}$, J = 7.8 Hz), 1.12–1.34 m [8H, $\underline{(CH_2)_4}CH_3$], 2.52 q (2H, $\underline{CH_2}CH_3$, J = 7.8 Hz), 6.33 s (2H, =CH), 14.65 br.s (2H, OH), form **1A** (100%). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 0.88 t [3H, $(CH_2)_4\underline{CH_3}$, J = 7.2 Hz, form **1C**, 57%], 0.91 t [3H, $(CH_2)_4\underline{CH_3}$, J = 6.0 Hz, form **1D**, 27%], 0.92 t [3H, $(CH_2)_4\underline{CH_3}$, J = 7.0 Hz, form **1A**, 16%], 1.09 t (3H, $CH_2\underline{CH_3}$, J = 7.0 Hz, form **1A**), 1.13 t (3H, $CH_2\underline{CH_3}$, J = 6.0 Hz, form **1D**), 1.16 t (3H, $CH_2\underline{CH_3}$, J = 7.2 Hz, form **1C**), 1.19–1.68 m [8H, $\underline{(CH_2)_4}CH_3$, forms **1A, 1C**, **1D**], 2.42–2.68 m (2H, $\underline{CH_2}CH_3$, forms **1A, 1C**, **1D**), 2.88 d, 3.01 d (2H, CH_2, J = 15.4 Hz, forms **1C**, **1D**), 5.51 s (1H, CH, form **1C**), 5.52 s (1H, CH, form **1D**), 6.44 s (2H, =CH, form **1A**), 7.79 s (1H, OH, forms **1C**, **1D**). Found, %: C 64.90; H 8.45. $C_{13}H_{20}O_4$. *M* 240.30. Calculated, %: C 64.98; H 8.39. *M* 240.30.

Methyl (2*Z*,4*Z*)-3,4-dihydroxy-6-oxo-2,4-heptadienoate (2a). Yield 6.32 g (68%); mp 98–100°C. Found: *m/z* 209.0420 $[M + Na]^+$. Calculated for $C_8H_{10}NaO_5^+$: 209.0420.

Methyl (2*Z*,4*Z*)-3,4-dihydroxy-6-oxo-2,4-octadienoate (2b). Yield 5.70 g (57%); mp 76–78°C. Found: *m/z* 201.0761 $[M + H]^+$. Calculated for $C_9H_{13}O_5^+$: 201.0757.

Methyl (2*Z*,4*Z*)-3,4-dihydroxy-6-oxo-2,4-nonadienoate (2c). Yield 6.85 g (64%); mp 67–68°C. Found: *m/z* 237.0737 $[M + Na]^+$. Calculated for $C_{10}H_{14}NaO_5^+$: 237.0733.

Ethyl (2*Z*,4*Z*)-3,4-dihydroxy-6-oxo-2,4-heptadienate (2d). Yield 5.90 g (59%); mp 61–62°C. IR spectrum, ν, cm^{-1}: 3300–2400 (OH), 2995 (CH_3), 2911 (CH_2), 2855, 1633 (C^1=O), 1607 (C^6=O), 1575 (C=C), 1475, 1374, 1222, 1084, 1030, 981, 908, 795, 727. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.33 t (3H, $OCH_2\underline{CH_3}$, J = 7.2 Hz), 2.25 s (3H, CH_3), 4.27 q (2H, $O\underline{CH_2}CH_3$, J = 7.2 Hz), 5.97 s (1H, C^2H), 6.26 s (1H, C^5H), 11.73 s (1H, C^3OH), 14.75 s (1H, C^4OH), form **2A** (100%). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.13 t (3H, $OCH_2\underline{CH_3}$, J = 7.2 Hz), 2.17 s (3H, CH_3), 2.81 d, 2.87 d (2H, C^2H_2, J = 15.3 Hz), 4.00 q (2H, $O\underline{CH_2}CH_3$, J = 7.2 Hz), 5.50 s (1H, $C^{5'}$H), 7.84 s (1H, $C^{3'}$OH), form **2D** (100 %). Found: *m/z* 201.0758 $[M + H]^+$. Calculated for $C_9H_{13}O_5^+$: 201.0757.

Methyl Ethyl (2*Z*,4*Z*)-3,4-dioxo-1,6-hexanedioate (3a). Yield 6.59 g (61%); mp 64–66°C. IR spectrum, ν, cm^{-1}: 3300–2600 (OH), 3128 (CH), 2982, 2951, 2854, 1645 (C=O), 1590 (C=C), 1447, 1375, 1182, 1083, 1014, 829. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.33 t (3H, $OCH_2\underline{CH_3}$, J = 7.6 Hz), 3.82 s (3H, OCH_3), 4.28 q (2H, $O\underline{CH_2}CH_3$, J = 7.6 Hz), 5.88 s (2H, =CH), 11.74 s (2H, OH), form **3A** (100%). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.19 t (3H, $CH_2\underline{CH_3}$, J = 7.3 Hz, form **3B**, 35%), 1.20 t (3H, $CH_2\underline{CH_3}$, J = 7.3 Hz, forms **3E**, **3F**), 1.26 t (3H, $CH_2\underline{CH_3}$, J = 7.3 Hz, form **3A**, 30%), 3.65 s (3H, CH_3, form **3B**), 3.75 s (3H, CH_3, form **3F**, 20%), 3.76 s (3H, CH_3, form **3E**, 15%), 3.79 s (3H, CH_3, form **3A**), 3.82 s (4H, CH_2, form **3B**), 3.89 s (2H, C^5H_2, form **3F**), 3.92 s (2H, C^5H_2, form **3E**), 4.11 q (2H, $\underline{CH_2}CH_3$, J = 7.3 Hz, forms **3E**, **3F**), 4.12 q (2H, $\underline{CH_2}CH_3$, J = 7.3 Hz, form **3B**), 4.23 q (2H, $\underline{CH_2}CH_3$, J = 7.3 Hz, form **3A**), 5.76 s (1H, C^2H, form **3F**), 5.78 s (1H, C^2H, form **3E**), 5.82 s (2H, =CH, form **3A**), 11.35 s (1H, C^3OH, form **3F**), 11.52 s (1H, C^3OH, form **3E**), 11.61 s (2H, OH, form **3A**). Found: *m/z* 217.0703 $[M + H]^+$. Calculated for $C_9H_{13}O_6^+$: 217.0707.

Dimethyl (2*Z*,4*Z*)-3,4-dioxo-1,6-hexanedioate (3b). Yield 5.56 g (55%); mp 120–122°C. Found: *m/z* 225.0370 $[M + Na]^+$. Calculated for $C_8H_{10}NaO_6^+$: 225.0367.

Diethyl (2*Z*,4*Z*)-3,4-dioxo-1,6-hexanedioate (3c). Yield 7.71 g (67%); mp 77–78°C. Found: *m/z* 253.0674 $[M + Na]^+$. Calculated for $C_{10}H_{14}NaO_6^+$: 253.0671.

REFERENCES

1. Koz'minykh, V.O., Goncharov, V.I., Koz'minykh, E.N., and Mukovoz, P.P., *Vest. Orenburg. Gos. Univ.*, 2007, vol. 73, no. 9, p. 134.

2. Koz'minykh, E.N., Mukovoz, P.P., Koz'minykh, V.O., Kirillova, E.A., Shcherbakov, Yu.V., Vinogradov, A.N., and Karmanova, O.G., *Vest. Orenburg. Gos. Univ.*, 2008, vol. 91, no. 9, p. 185.
3. Koz'minykh, V.O., Mukovoz, P.P., and Kirillova, E.A., *Vest. Orenburg. Gos. Univ.*, 2009, vol. 111, no. 5, p. 155.
4. Balenović, K., Deljac, A., Gašpert, B., and Štefanac, Z., *Monatsh. Chem*., 1967, vol. 98, no. 4, p. 1344.
5. Balenović, K. and Poje, M., *Tetrahedron Lett*., 1979, no. 23, p. 2175.
6. Laćan, M., Vukićević, M., Džanić, H., and Stefanović, D., *Org. Mass Spectrom*., 1975, no. 10, p. 899.
7. Inhoffen, H.H., Bohlmann, F., and Bartram, K., *Ann.,* 1948, vol. 561, p. 13.
8. Kozminykh, V.O., Igidov, N.M., and Konshina, L.O., *J. Prakt. Chem*., 1993, vol. 8, p. 714.
9. Schmitt, J., *Liebigs Ann. Chem*., 1950, vol. 569, p. 17.
10. Balenović, K. and Poje, M., *J. Heterocycl. Chem*., 1979, vol. 16, p. 417.
11. Shurov, S.N., Pavlova, E., Livantsova, L.I., Zaitseva, G.S., and Andreichikov, Yu.S., *Russ. J. Org. Chem*., 1993, vol. 29, no. 11, p. 1890.
12. Koz'minykh, E.N., Mukovoz, P.P., and Koz'minykh, V.O., *Tekh. Nauki – ot Teor. k Prakt*., 2014, no. 40, p. 157.
13. Shironina, T.M., Igidov, N.M., Koz'minykh, E.N., Kon'shina, L.O., Kasatkina, Yu.S., and Koz'minykh, V.O., *Russ. J. Org. Chem*., 2001, vol. 37, no. 10, p. 1486. doi 10.1023/A:1013431407273
14. Mukovoz, P.P., *Cand. Sci. (Chem.) Dissertation*, Yaroslavl, 2010.
15. Mukovoz, P.P., Koz'minykh, V.O., and Tarasova, V.A., *Russ. J. Org. Chem*., 2014, vol. 50, no. 11, p. 1687. doi 10.1134/S1070428014110244
16. Tarasova, V.A., Mukovoz, P.P., and Koz'minykh, V.O., *Vest. Yuzh.-Ural. Gos. Univ*., 2014, vol. 6, no. 3, p. 11.
17. Mukovoz, P.P., Dvorskaya, O.N., and Koz'minykh, V.O., *Izv. Vuzov, Ser. Khim. Khim. Tekhnol*., 2011, vol. 54, no. 5, p. 96.
18. Löw, N., *Dissertation*, Erlangen-Nürnberg, 1997.
19. Tarasova, V.A., Kuz'min, A.V., Mukovoz, P.P., and Koz'minykh, V.O., *Bashkir. Khim. Zh*., vol. 21, no. 4, p. 15.
20. Kirillova, E.A., Mukovoz, P.P., Vinogradov, A.N., Koz'minykh, V.O., and Dvorskaya, O.N., *Izv. Vuzov, Ser. Khim. Khim. Tekhnol*., 2011, vol. 54, no. 4, p. 18.
21. Chetkina, L.A., *Kristallograf*., 1992, vol. 37, no. 1, p. 212.
22. Shigorin, D.N., Rudenko, N.A., Chetkina, L.A., Kon'shina, L.O., Andreichikov, Yu.S., Kozlov, A.P., Muromtsev, V.I., Barashkov, N.N., and Lebedev, S.A., *Zh. Fiz. Khim.,* 1992, vol. 66, no. 8, p. 2128.
23. Sheldrick, G.M., *J. Appl. Cryst*. *A*, 2008, vol. 64, p. 112.
24. Dolomanov, O.V., Bourhis, L.J., Gildea, R.J., Howard, J.A.K., and Puschmann, H., J. *Appl. Cryst. A*, 2009, vol. 42, p. 339. doi 10.1107/S0021889808042726