

STRUCTURAL DIVERSITY OF 1,3,4,6-TETRACARBONYL COMPOUNDS, THEIR ANALOGUES AND NITROGEN CONTAINING DERIVATIVES (REVIEW)

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The article summarizes published data and provides new information concerning the synthesis, structural diversity and properties of 1,3,4,6-tetracarbonyl compounds. *Bis*-1,3-diketones are presented in solid state by (*E,E*)-isomer, and in solutions by dominant (*E,E*)- and minor (*Z,Z*)-isomers. Structure peculiarities and mass fragmentation of 1,6-dialkyl-3,4-dihydroxy-2,4-hexadiene-1,6-diones are investigated. Condensation of alkyl methyl ketones with diethyl oxalates and 1,2-diaminobenzene results in 2,3-*bis*-(2-oxoalkylidene)tetrahydro-1,2,3,4-quinoxalines. With the help of spectral methods isomeric forms of synthesized compounds are found. Compounds containing contiguous 1,2- and 1,3-dioxo fragments look promising for fine organic synthesis and structural chemical analysis.

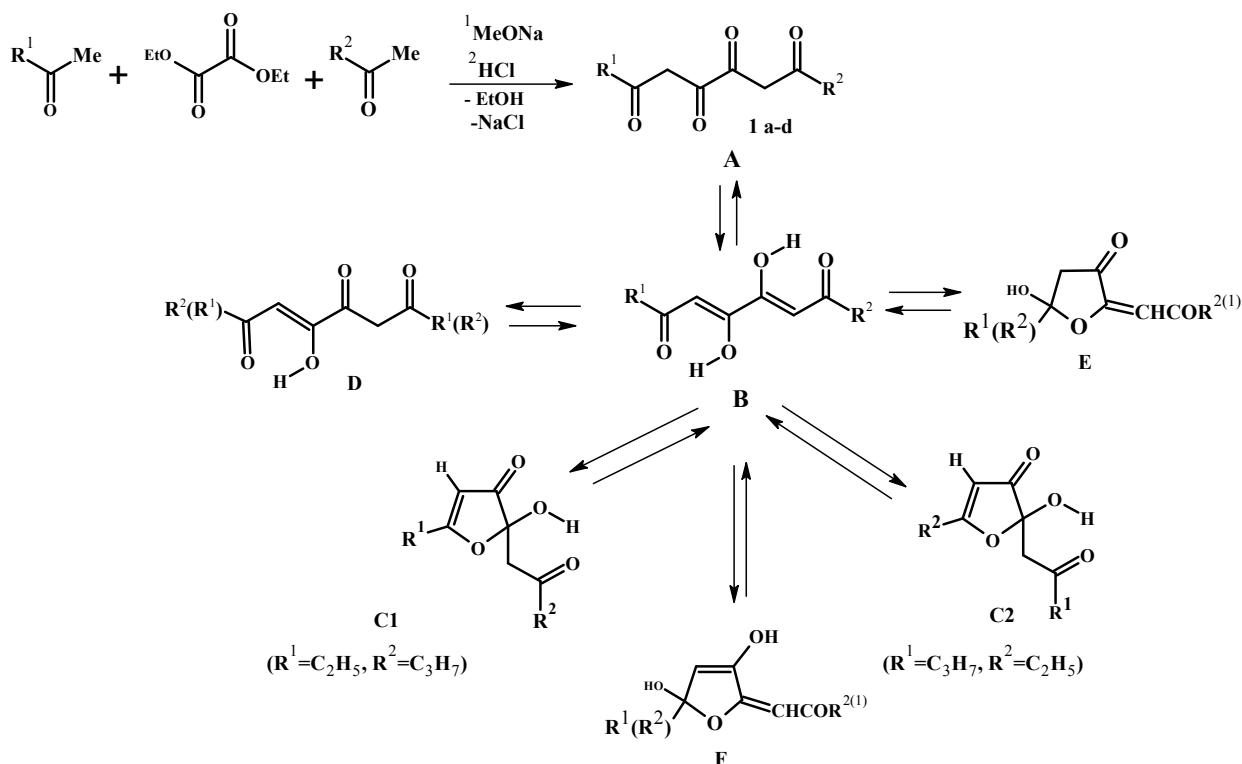
Ключевые слова: alkyl methyl ketones, oxalic condensation, 1,6-dialkyl-3,4-dihydroxy-2,4-hexadiene-1,6-diones, tautomeric forms, 2,3-*bis*-oxoalkylidene-1,3,4,6-tetrahydroquinoxalines.

For a long time the chemistry of 1,3,4,6-tetracarbonyl compounds (TCC) has remained virtually unexplored. Until recently, there has been a small number of papers concerning TCC that described the synthesis of some 1,6-disubstituted 1,3,4,6-hexanetetraones [1, 2]. TCC and their derivatives are noted for their diverse structure and high reactivity and are convenient to be used as structural blocks for the synthesis of various heterocyclic compounds. TCC (**1**) are unique *bis*- β -diketone molecules of which contain maximum contiguous 1,3-dicarbonyl units and are characterized by various physicochemical properties. Certain results of TCC (**1**) study are given in the papers [3, 4]. In the review of the current state of research into TCC we present the results of our own work. Scheme 1 shows the basic method of TCC (**1**) preparation used for compound preparative synthesis. The least studied 1,3,4,6-tetracarbonyl systems are 1,6-dialkyl derivatives, structural features of which have not been known before our research.

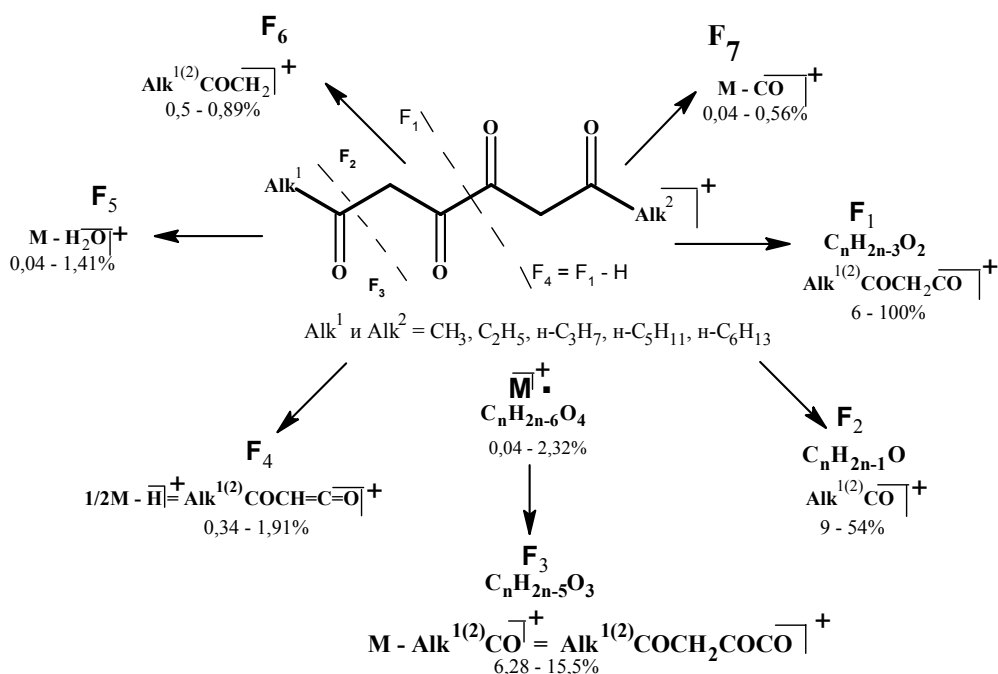
Published data on 1,6-dialkyl-1,3,4,6-tetraoxohexanes provide concise data on the synthesis of compounds having identical alkyl substituents [5]. TCC (**1**) (Scheme 1 shows the basic equilibrium structures **1A**, **1B**, **1C** which we take into account) in the solid state are marked by a stabilized intramolecular hydrogen bond (IHB) $OH \cdots O=C-$ inside two contiguous six-membered *OH*-chelates [3, 4, 6–12] in the linear 1,6-dioxo-3,4-dienol form **1B**. Thus, tetraketones (**1**) should in fact be regarded as a 1,6-disubstituted 3,4-dihydroxy-2,4-hexadiene-1,6-diones. TCC solutions contain not only tautomer **1B** but also appreciable amounts of ring oxofuran equilibrium form **1C** [13–15] (Scheme 1). Minor isomers (rated **1A** and its derivatives **1D**, **1E**, **1F**) were also found in the NMR 1H spectra, but their amount not exceed 3–5 % [3, 4, 14, 15]. In nonpolar solutions compounds (**1**) are mainly represented by dioxodienol tautomer **1B**, the amount of which always exceeds the sum of the remaining forms if any, and often reaches 100 % [3, 14, 9–12]. In polar solutions tetraketones (**1**) usually have much larger amount of cyclic tautomer **1C**, stabilized by IHB of *OH*-chelate type [3, 4, 10, 11]. The qualitative dynamic prototropic ring-chain transformations and ring-ring interconversions were thoroughly studied (for compounds (**1**) with different substituents R^1 and R^2) in TCC solutions [3, 4, 10, 11]. Operational databases were formed on the basis of NMR 1H and mass spectra of 1,3,4,6-tetraoxo systems, some of the results are presented in the publications dated by 2011–2012 [3, 4, 16–18]. The mass-decay processes of tetracarbonyl compounds with aliphatic substituents induced by electron impact using a chromatomass spectrometry (Scheme 2) have been studied. The two main dominant directions of fragmentation prevail for 1,6-dialkyl-3,4-dihydroxy-2,4-hexadiene-1,6-diones (**1**). The first direction F_1 involves C(3)O–C(4)O rupture which results in the formation of two equivalent alkanoylacetyl units. The second important trend of the fragmentation is the alkanoyl ion elimination along with the simultaneous formation of ion

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$F_3 [M-Alk^{1(2)}CO]^+$. The most intense peaks are $[RCOCH_2CO]^+$ and $[RCO]^+$, formed by the α -cleavage of bonds in the molecule. The molecular ion in spectra of compounds (**1**) is always present, its intensity increases notably on transition from lower to higher alkyl substituents.



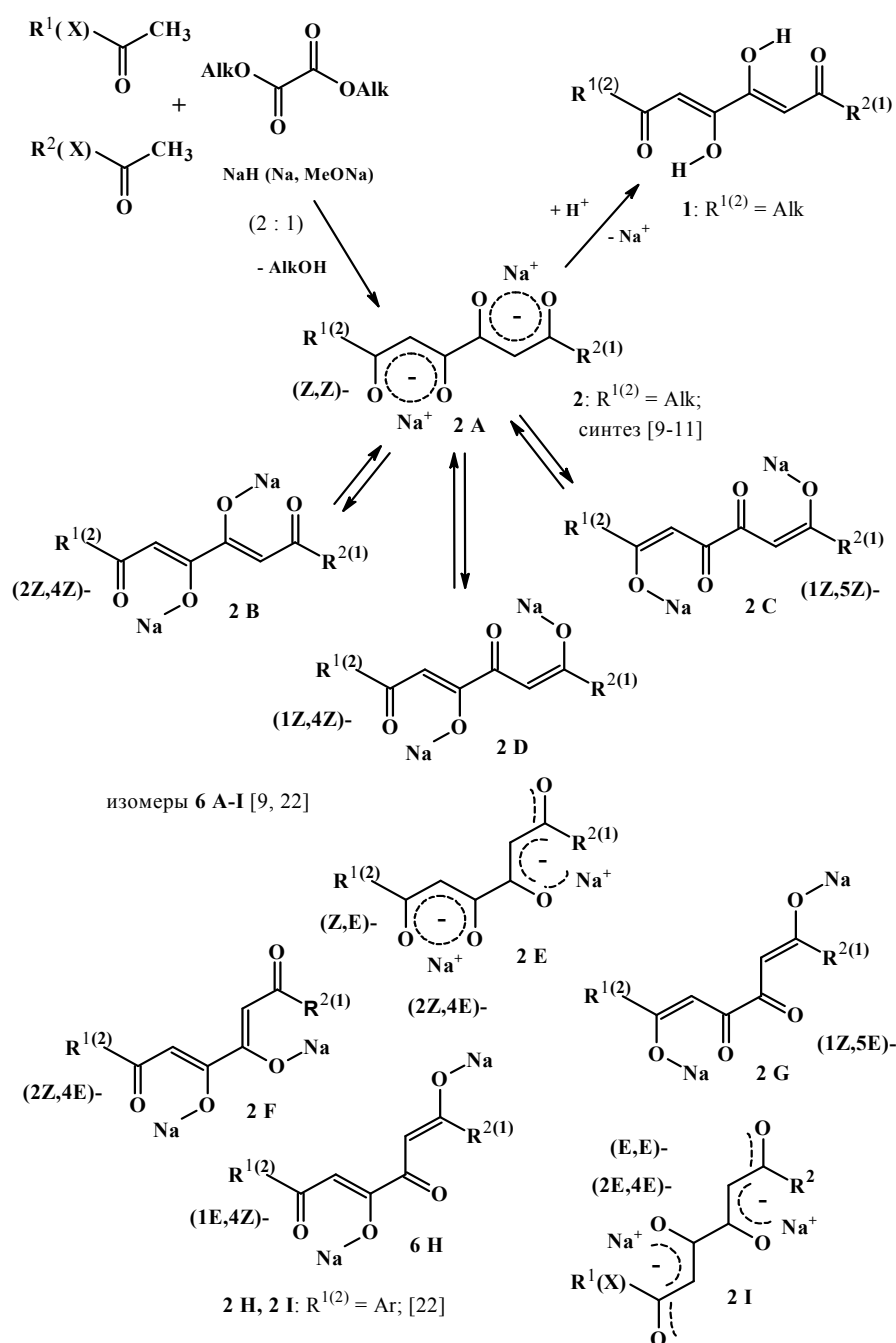
Scheme 1. Synthesis and structural diversity of 1,3,4,6-hexantetraones (**1**)



Scheme 2. Mass fragmentation of compounds (**1**)

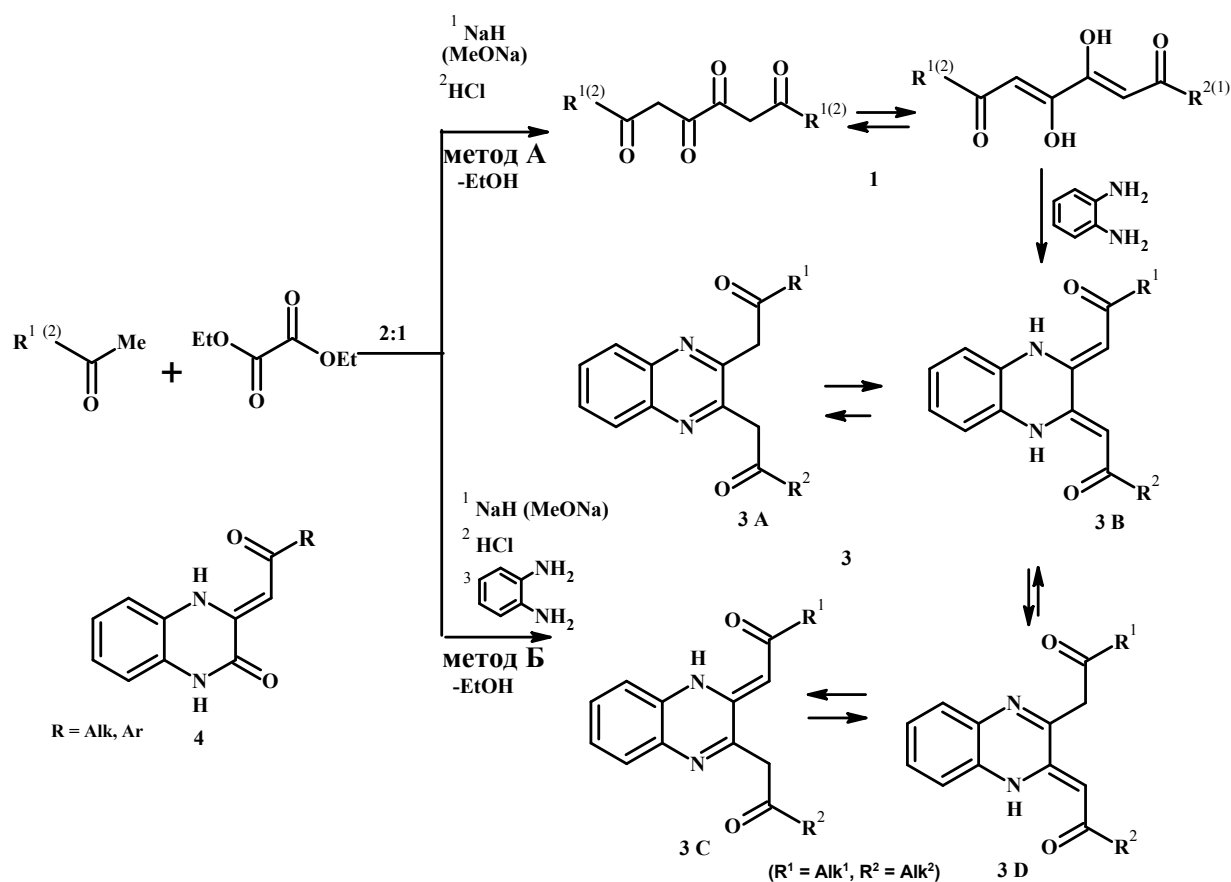
During the one-pot or performed stepwise oxalyl condensation of oxalates with a twofold excess of the similar methyl ketones or equimolar amounts of different methyl ketone substituents R^1 and R^2 in the presence of bases easily extracted and fairly steady *bis*-sodium-1,3-diketonates are formed first [9–11, 19–22] (Scheme 3). The latter if acidified easily turn into the designated dioxo dienols (**1**). Spectral data

(IR, NMR) indicate the presence of (*Z,Z*)-isomer structure **2A** with the “aligned” π -bonds in enolates (**2**) due to the delocalization of electron density in the solution solvation. Solid-state *bis*-enolates (**2**) exist in the form of (*E,E*)-isomer **2B** with delocalized double bonds, as evidenced by the intense, broad, relatively low-frequency absorption band in the region at 1605–1655 cm^{-1} in the IR spectra of compounds (**2**). Solid-state compounds (**2**) have an axisymmetric structure along the 3,4-dienolate (*2Z,4Z*)-**2B** bond of C (3)–C(4) and possibly along the isomeric 1,6-dienolate (*1Z,5Z*)-**2C** bond. In some cases, the presence of 1,4-*ONa*-dienolate (*1Z,4Z*)-**2D** is possible in the solutions [9, 20–22]. Solutions of compounds (**2**) were recorded to have additional equilibria with (*Z,E*)- and (*E,E*)-isomers. For example, the source of such equilibria is isomeric structure (*Z,E*)-**2E** with delocalized double bonds. The most likely (*2Z,4E*)-**2F**-isomer, as well as possible (*1Z,5E*)-**2G**- and (*1E,4Z*)-**2H**-geometric forms here serve as specific structures [9, 20, 21]. The final individual choice in favor of a particular dienolate isomer is now quite difficult, since the amorphous compounds (**2**) can not be cleaned sufficiently with the desired result, and their dissolution is accompanied by side reactions such as solvolysis.



Scheme 3. Synthesis and structure of *bis*-sodium 1,3-diketonates (dienolates) (**2**)

TCC and ringed oxotautomers (**1**) are widely used in organic synthesis as highly reactive substrates that are easy to get into a variety of nucleophilic transformations. Thus, the reaction of TCC (**1**) with 1,2-diaminobenzene leads to the formation of 2,3-bis-oxoylidene derivatives of 1,3,4,6-tetrahydroquinoxalines (**3**) [13, 15] (Scheme 4).



Scheme 4. Synthesis of 2,3-bis-(2-oxoylidene)-1,2,3,4-tetrahydroquinoxalines (**3**)

One-pot alkyl methyl ketone condensation with diethyl oxalate in the presence of sodium methylate in a 2:1 ratio, followed by neutralization and the 1,2-diaminobenzene action was first successfully carried out, as a result of which new bis-(oxoylidene)quinoxalines (**3**) were extracted (method **B**). The main advantage of method **B** is the fact that the process of 2,3-bis-(2-oxoylidene)-1,2,3,4-tetrahydroquinoxaline (**3**) extraction is more technologically advanced than in method **A** and it is the one-stage reaction. The structure of the synthesized quinoxaline derivatives (**3**) of 1,6-dialkyl-3,4-dihydroxy-2,4-hexadiene-1,6-diones (**1**) is determined on the basis of IR and NMR ^1H spectroscopy. In polar solvents of the compounds (**3**) **2B** is the dominant and most stable form, stabilized by two *NH*-chelate cycles. The presence of **3B** form is also confirmed by the presence of the signals of two magnetically equivalent *N(1,4)H*-protons of the predominant isomer **3B** bis-chelate fragments in the δ 13.95–14.03 ppm in the NMR ^1H spectra of compounds (**3**).

There are signals of equal integral intensity of the two magnetically nonequivalent *NH* protons of predominant isomer **3B** in the NMR ^1H spectrum of compound (**3**) which has various alkyl substituents at the acyl units ($\text{R}^1 = \text{Alk}^1$, $\text{R}^2 = \text{Alk}^2$), which is caused by the fact that these units propyl and ethyl fragments have different influences. Maximum *NH*-proton deshielding should be observed when the carbonyl group *NH*-chelate fragment carbon atom has maximum positive charge and, therefore, when acyl-unit alkyl substituent has minimum positive inductive effect. The chemical shift of *N(1,4)H*-proton of the compound (**3**) isomer **3B** is much more high field (δ 0.7 ppm), compared with a chemical shift of *N(4)H*-proton of minor isomers of **3D** and **3C**. The reason probably lies in larger coupling of the aromatic heterocycle with *NH*-monochelate fragment of isomers **3C** and **3D** due to the presence of *N(1)=C(2)-endocyclic* double bond in comparison with bis-chelate isomers **3B**. The greater coupling of *NH*-chelate

and the aromatic ring leads to the anisotropic deshielding effect increase and to the lower field shift of the *NH* proton signal.

Thus, 1,3,4,6-tetracarbonyl compounds resulting from the Claisen ester condensation, their analogues and nitrogen-containing derivatives, look promising and are accessible for further study of their physicochemical properties and structural diversity.

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ОСОБЕННОСТИ СТРУКТУРНОГО РАЗНООБРАЗИЯ 1,3,4,6–ТЕТРАКАРБОНИЛЬНЫХ СОЕДИНЕНИЙ, ИХ АНАЛОГОВ И АЗОТСОДЕРЖАЩИХ ПРОИЗВОДНЫХ (ОБЗОР)

Обобщены литературные данные и приводятся новые сведения, касающиеся синтеза, структурного разнообразия и свойств 1,3,4,6-тетракарбонильных соединений. Бис-1,3-дикетонаты в твердом состоянии представлены (*E,E*)-изомером, а в растворе преобладающим (*E,E*)- и минорным (*Z,Z*)-изомерами. Обсуждаются структурные особенности и масс-фрагментация 1,6-диалкил-3,4-дигидрокси-2,4-гексадиен-1,6-дионов. Конденсацией алкилметилкетонов с диэтилоксалатом и 1,2-диаминобензолом получены 2,3-бис-(2-оксоалкилиден)тетрагидро-1,2,3,4-тетрагидрохиноксалины. С помощью спектральных методов выявлены изомерные формы полученных соединений. Соединения, содержащие сближенные 1,2- и 1,3-диоксофрагменты, являются перспективными для тонкого органического синтеза и структурного химического анализа.

Ключевые слова: алкилметилкетоны; оксалильная конденсация; 1,6-диалкил-3,4-дигидрокси-1,6-гексадиен-1,6-дионы; таутомерные формы; бис-1,3-дикетонаты; 2,3-бис-оксоилиден-1,3,4,6-тетрагидрохиноксалины

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