



Centrosymmetric resonance-assisted intermolecular hydrogen bonding chains in the enol form of β -diketone: Crystal structure and theoretical study



Eduardo F. Franca^{a,*}, Silvana Guilardi^a, Drielly A. Paixão^a, Róbson R. Teixeira^{b,**}, Wagner L. Pereira^b, Javier A. Ellena^c

^a Instituto de Química, Universidade Federal de Uberlândia, 38.400-902, Uberlândia, MG, Brazil

^b Departamento de Química, Universidade Federal de Viçosa, 36.570-900, Viçosa, MG, Brazil

^c Instituto de Física de São Carlos, Universidade de São Paulo, 13560-970 São Carlos, SP, Brazil

ARTICLE INFO

Article history:

Received 17 March 2016

Received in revised form 8 June 2016

Accepted 9 June 2016

Available online 25 June 2016

Keywords:

Resonance assisted hydrogen bonds (RAHBs)

X-ray structure

Semi-empirical and DFT calculations

Phtalides

Isobenzofuranones

ABSTRACT

Isobenzofuran-1(3*H*)-ones (phtalides) are heterocycles that present a benzene ring fused to a γ -lactone functionality. This structural motif is found in several natural and synthetic compounds that present relevant biological activities. In the present investigation, the 3-(2-hydroxy-4,4-dimethyl-6-oxocyclohexen-1-yl)isobenzofuran-1(3*H*)-one was characterized by single-crystal X-ray analysis. In the crystal structure, there are two molecules per asymmetric unit. One of them exhibits resonance assisted hydrogen bonds (RAHBs). Semi-empirical and DFT calculations were performed to obtain electronic structure and π -delocalization parameters, in order to better understand the energy stabilization of RAHBs in the crystal packing of the studied molecule. The structural parameters showed good agreement between theoretical and experimental data. The theoretical investigation revealed that the RAHBs stabilization energy is directly related to the electronic delocalization of the enol form fragment. In addition, RAHBs significantly affected the HOMO and charge distribution around the conjugated system.

© 2016 Elsevier Inc. All rights reserved.

1. Introduction

The heterocyclic framework plays an important role in organic chemistry [1]. Heterocyclic compounds are widely available in nature and present a broad range of biological activities [2]. The vast majority of agrochemicals and pharmaceuticals (more than 70%) bears at least one heterocyclic ring [3,4]. Heterocycles are integrant part of several dyes, polymers and luminophores. Oxygen- and nitrogen- containing compounds constitute the largest and most varied group of heterocycles.

Heterocyclic compounds containing a benzene ring fused to a γ -lactone functionality are collectively termed isobenzofuran-1(3*H*)-ones (phtalides) (**1** in Fig. 1). This structural motif is an integrant part of several bioactive natural products isolated from plants, fungi, bacteria and liverworts [5]. In particular, isobenzofuranones that possess functionalization at the C-3 position of the lactone ring present several important medicinal properties [6–12].

* Corresponding author.

** Corresponding author.

E-mail addresses: eduardoffranca@ufu.br, eduardoffranca@yahoo.com.br (E.F. Franca), robsonr.teixeira@ufv.br (R.R. Teixeira).

furanones that possess functionalization at the C-3 position of the lactone ring present several important medicinal properties [6–12].

One of our research interests is on the synthesis and biological evaluation of isobenzofuranones. Within this context, we prepared several C-3 functionalized phtalides and reported their effects on photosynthetic electron transport [13] as well as their cytotoxicity [14]. *In vitro* biological assays carried out with isolated spinach chloroplast showed that the isobenzofuranone (**2**) (Fig. 1) is capable of inhibiting the photosynthetic electron flow in approximately 44% at 200 $\mu\text{mol L}^{-1}$ [13]. In addition, this compound also presented cytotoxic activity on cell lines K562 (myeloid leukemia; 49% inhibition of cell viability) and on U937 (lymphoma; 34% inhibition of cell viability) at 100 $\mu\text{mol L}^{-1}$ [14].

In a bid to contribute to the knowledge concerning the structural aspects of isobenzofuranones, we herein report the results of our investigation on the molecular structure of 3-(2-hydroxy-4,4-dimethyl-6-oxocyclohexen-1-yl)isobenzofuran-1(3*H*)-one (**2**) by single-crystal X-ray diffraction. It is demonstrated that the enol form of the β -diketone fragment exhibits resonance assisted hydrogen bonds (RAHBs). Gilli et al. [15–19] introduced this term to characterize strong and very strong intra or intermolecular hydrogen bonds in compounds containing delocalized

systems connecting the hydrogen-bond donor and acceptor groups. Hydrogen bonds (HBs) play an important role in stabilizing supramolecular arrangements and can be classified as positive or negative charge-assisted hydrogen bonds (\pm CAHBs), resonance-assisted hydrogen bonds (RAHBs), polarization-assisted hydrogen bonds (PAHBs), and isolated hydrogen bonds (IHBs) [18,20]. The resonance-assisted hydrogen bond (RAHB) is a synergistic interplay model, between H-bond strengthening and increased π -delocalization, used to explain the abnormally strong ($2.50 < d(\text{O}\cdots\text{O}) < 2.65 \text{ \AA}$) and very strong ($d(\text{O}\cdots\text{O}) < 2.50 \text{ \AA}$) O—H \cdots O hydrogen bonds formed by the fragment $\cdots\text{O}=\text{C}-\text{C}=\text{C}-\text{OH}\cdots$ which is the enol form typically associated with β -diketones [18]. This fragment can make intramolecular HBs closing 6-membered rings or intermolecular HBs in which the proton-donor and acceptor are linked through a chain of π -conjugated bonds (Fig. 2) [15]. In these chains, the calculated hydrogen-bond energies are within the range 20–66 kJ mol $^{-1}$, and the strict intercorrelation between hydrogen-bond strengthening and π -system delocalization is observed, in complete agreement with the intermolecular RAHB model [17].

The RAHBs formed by β -diketone enols display specific characteristics such as shortening of the distance $d(\text{O}\cdots\text{O})$, which is associated with a remarkable increase of delocalization in the $\cdots\text{O}=\text{C}-\text{C}=\text{C}-\text{OH}\cdots$ π -conjugated system. Thus, the O \cdots O distance become as short as 2.43–2.55 \AA for the intramolecular and 2.46–2.65 \AA for the intermolecular case [18]. This shortening of the distance O \cdots O is accompanied by changes in the distance $d(\text{O}-\text{H})$ ranging from 0.97 to 1.20 \AA [16]. These characteristics can be interpreted by recognizing that the π -system delocalization I \leftrightarrow II (Fig. 2) induce partial charges on the opposite O atoms, which have the correct signs for shortening of the O \cdots O and lengthening of the O—H distances, therefore giving rise to a synergistic mechanism between the resonance reinforcement and hydrogen bond strengthening. This is viewed as an increase in the donor and acceptor strengths through a charge flow in suitable polarizable π -bond systems which, in turn, are reflected in the very short donor–acceptor distances [15,17].

To evaluate the behavior of RAHBs, Gilli and collaborators proposed a comparison of the geometries of the molecular fragment (HO-CR=CR=O) associated with β -diketones, in order to understand what happens to the fragment geometry when it is perturbed by intramolecular or intermolecular RAHBs. These data are shown in Table 1 where standard distances are those tabulated for pure

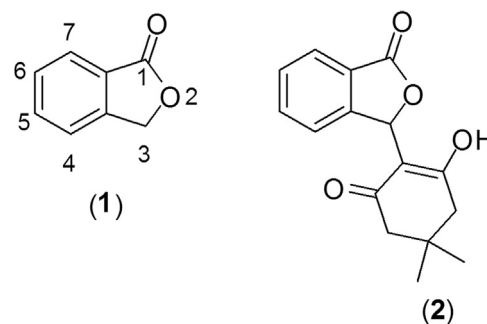


Fig. 1. Structures of isobenzofuranone nucleus **1** and 3-(2-hydroxy-4,4-dimethyl-6-oxocyclohexen-1-yl)isobenzofuran-1(3H)-one (**2**).

Table 1
Selected bond lengths (\AA) for the enol form of the β -diketone fragment [15].

	d_1	d_2	d_3	d_4
Standart	1.37	1.33	1.48	1.20
Unperturbed	1.353(4)	1.344(3)	1.454(5)	1.225(3)
Perturbed by intramolecular RAHB	1.281(4)	1.398(4)	1.410(4)	1.279(4)
Perturbed by intermolecular RAHB	1.316(2)	1.372(2)	1.431(2)	1.238(2)

single and double bonds, while the unperturbed distances are related to resonant systems that do not present RAHBs. The perturbed distances are related to resonant systems which have intra or intermolecular RAHBs, and the interatomic distances d_1 , d_2 , d_3 , and d_4 , displayed in Fig. 2, result in changes which are consistent with an increased contribution of the polar form II to the limits of 48% or 29% for the intra or intermolecular case, respectively [15].

In order to identify the existence of RAHBs, one can use the Q parameter [$Q=(d_1-d_4)+(d_3-d_2)$] to describe the electronic delocalization. The Q values show good correlation with other parameters that describe hydrogen bonds, such as O \cdots O and O \cdots H distances. For RAHBs, the lower the Q value, the more intense is the hydrogen bond and greater is the electron delocalization [17]. Furthermore, many articles have reported this unusual HB in order to better understand this phenomenon termed RAHB [21–30].

In this paper, comparisons are made among experimental results related to compounds **2** (Fig. 1) with those predicted

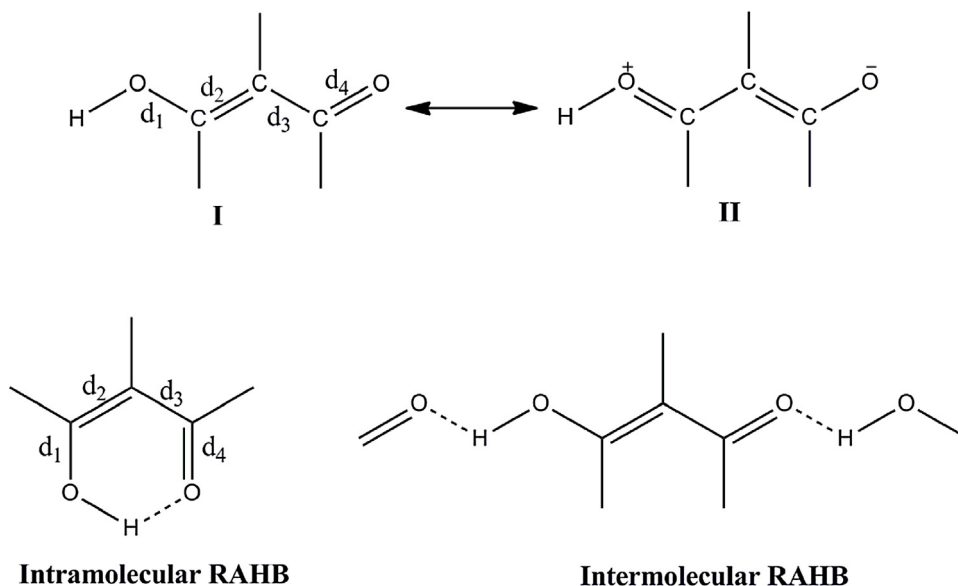


Fig. 2. The main structures of Gilli's first paper [15].

Download English Version:

<https://daneshyari.com/en/article/443224>

Download Persian Version:

<https://daneshyari.com/article/443224>

[Daneshyari.com](https://daneshyari.com)