Strong intramolecular hydrogen bonding within the dimedone–aldehyde adducts

Mark Sigalov [a,*], Radion Vainer [a], Vladimir Khodorkovsky [b,**]

[a] Department of Chemistry, Ben-Gurion University of the Negev, Beer-Sheva 84105, Israel
[b] Interdisciplinary Center of Nanoscience CINaM (CNRS UPR 3118), 13288 Marseille Cedex 9, France

ABSTRACT

Ionization of the well-known 2:1 dimedone–aldehyde adducts in polar solvents leads to the respective monoanions involving the intramolecular ionic hydrogen bond. These anions feature the short $O \cdots H_a \cdots O$ distance (2.403 Å for **4**, R=p-ClC$_6$H$_4$) and the strong downfield shift of the corresponding signal (δH_a = 17.0 ppm, in dichloromethane-d$_2$). The negative charge is delocalized over the two dimedone moieties. This phenomenon is also reproduced by quantum mechanical calculations. The dynamic NMR spectra provide an estimate of the hydrogen bond energy as high as 16 kcal/mol.

© 2010 Elsevier B.V. All rights reserved.

1. Introduction

Ionic hydrogen bonds are the focus of numerous theoretical and experimental studies [1]. These bonds are characterized by the short distances between the involved heteroatoms (2.4–2.55 Å for O⋯H⋯O bonds) and high energies that can reach 40 kcal/mol [2]. The quantum mechanical calculations (HF, B3LYP and MP2) for the simplest pair formic acid/formate anion in the gas phase yielded 22–27 kcal/mol depending on the level of theory [3]. The ionic hydrogen bonds within the carboxylic acid/carboxylate pairs exhibit low-field ^{1}H NMR chemical shifts (16–22 ppm) of the bonded protons, as observed at low temperatures in thoroughly dried solvents [4].

The most accurately studied systems are dicarboxylic acid derivatives, which involve the intramolecular ionic hydrogen bonds [5–10]. Thus, malonic acid derivatives **1** exhibit pK_{a1} lower than usually observed for carboxylic acids and pK_{a2} higher than usual so that the difference between both values (ΔpK_a) varies between 2.9 and 5.4 depending on the substituents. These large differences can only partially be explained by the electrostatic repulsion within the dianions formed upon ionization of the monoanions [6]. The ΔpK_a for maleic acid is 4.3, whereas it is only 1.4 for fumaric acid. The hydrogen maleate salts (**2**) were investigated in detail by diffraction, computational methods and the NMR spectroscopy [7]. In the solid state, the monoanion is found to be symmetrical and the deviation from the C$_{2v}$ symmetry is negligible over the wide range of temperatures (300–5 K) [8]. The sin-

gle molecule calculations afford the C$_s$ structure as the global minimum, whereas the structure with the symmetric hydrogen bond is a transition state, by about 0.7 kcal/mol less stable than the asymmetrical structure. Calculations of the ionic hydrogen bonding energy in the gas phase yield 27–29 kcal/mol and it is still predicted to be strong by calculations in water [9]. The monoanions of a large variety of mono-^{18}O-labeled dicarboxylic acids, including hydrogen phthalate anion, were studied in water and several organic solvents (DMSO-d$_6$, THF-d$_8$, CD$_2$Cl$_2$, and CDCl$_3$) [10]. The results indicate that the hydrogen bonds in the monoanions of dicarboxylic acids are asymmetric in water and all organic solvents [10a]. Theoretical calculations of hydrogen phthalate by QM/MM method taking into account the interactions with the solvent are in agreement with this conclusion [10b].

Another important feature of the systems with strong intramolecular hydrogen bonding is delocalization [11]. The symmetricity of **2** suggests delocalization of the negative charge between the both carboxylate groups over the bridging ethylene moiety, as indeed follows from the experimental bond lengths.

1   **2**
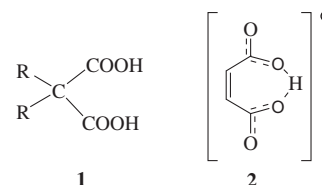
The geometrical factors, in particular, proximity of the carboxylic groups, facilitate hydrogen bonding in dicarboxylic acids [12], making estimations of the bonding energies complicated. Whereas the dicarboxylic acids remain the focus of the current researches,

* Corresponding author.
** Corresponding author.
   E-mail address: msigalov@bgu.ac.il (M. Sigalov).

the enol–enolate complexes are practically not investigated, although quantum mechanical calculations predict that the hydrogen bonding energy can reach 19–35 kcal/mol [13]. From this point of view, it deemed purposeful to investigate a system in which the two acidic enol functional groups are linked by a non-conjugated bridge without constraining possible geometries of each moiety.

Here we report on the results of our investigation on the well-known 2:1 adducts of dimedone with aldehydes **3** (2,2′-(methylene)-bis-(3-hydroxy-5,5-dimethylcyclohex-2-en-1-ones), which exist as double enols stabilized by two hydrogen bonds both in the solid state and in solution [14]. These compounds are easily available [15] and behave as diacids (pK_{a1} = 6.57, pK_{a2} = 12.37 measured in 1:1 water–ethanol mixture) with the ΔpK_a of 5.8, which is even larger than observed for most of the dicarboxylic acids [16].

2. Results and discussion
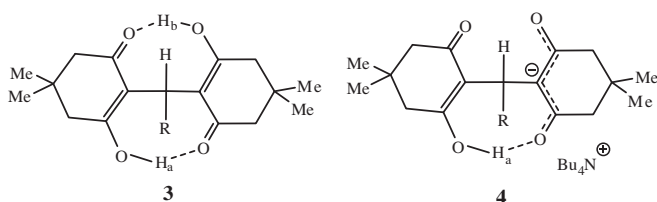
Salts **4** can easily be prepared by dissolving **3** in dichloromethane and adding a methanolic solution of tetrabutylammonium hydroxide. The UV absorption spectrum of the salt features a characteristic band at 266 nm in dichloromethane (268 nm in water), whereas the neutral species **3** absorb at 261 nm. The neutral species **3** is completely ionized in water and its spectrum in this solvent is fully identical to the spectrum of **4**. The neutral species **3** can be generated by addition of an acid to the water solution, whereas formation of the corresponding dianion with the maximum at 288 nm occurs only upon addition of a large excess of NaOH (Fig. 1).

We made preliminary quantum mechanical calculations for simpler cyclohexane-1,3-dione analogs **5** and **6** [17].

The optimized geometry of **5** shows the presence of two hydrogen bonds and this structure is by 23.5 kcal/mol (or 21.6 kcal/mol in terms of $\Delta G°$ (298 K)) more stable than **5a**, in which both hydrogen bonds are 'switched off', providing thus 11.8 (10.9) kcal/mol per hydrogen bond. The optimized geometry of **6** afforded a somewhat asymmetric structure with one hydrogen bond, which can be classified as a 'double well' strong hydrogen bond judging by the
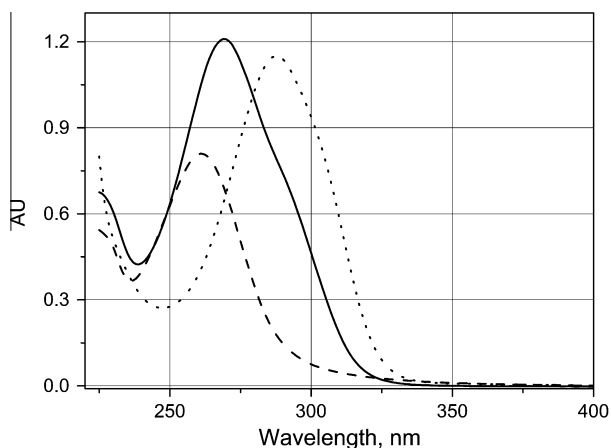
geometrical parameters. However, as it happened in other cases [13], the optimized symmetrical structure with the hydrogen atom fixed in the middle between two oxygen atoms becomes by 1.1 kcal/mol more stable after ZPE correction. Structure **6** is by 22.8 kcal/mol (by 21.6 kcal/mol in term of $\Delta G°$ (298 K)) more stable than structure **6a**. Thus, hindered by hydrogen bonds rotation is expected to exist in all derivatives of this type and should be manifested, in particular, in their NMR spectra.
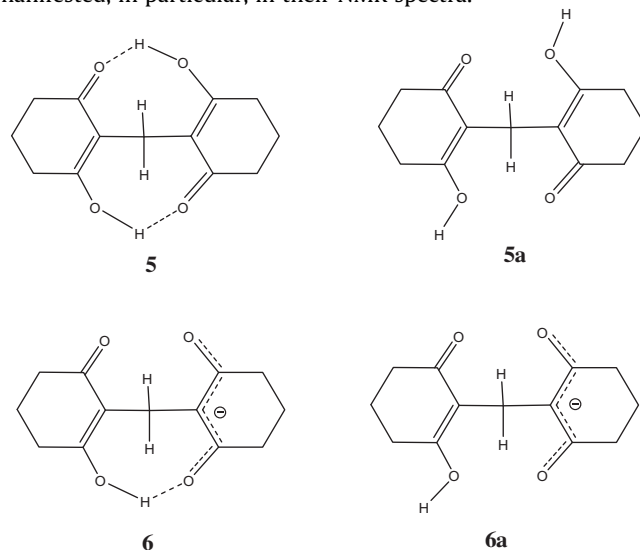
The potential energy surface scan calculations reveal that the cyclohexane-1,3-dione moieties in **5a** and **6a** can be rotated without experiencing considerable steric hindrance. Indeed, the barrier to rotation in **5a** does not exceed 2 kcal/mol (for configurations in which the two moieties are almost perpendicular) and amounts to 1.3 kcal/mol for the configuration in which the hydrogen bonds can form (Fig. 2). Therefore, it is the hydrogen bonding that contrib-
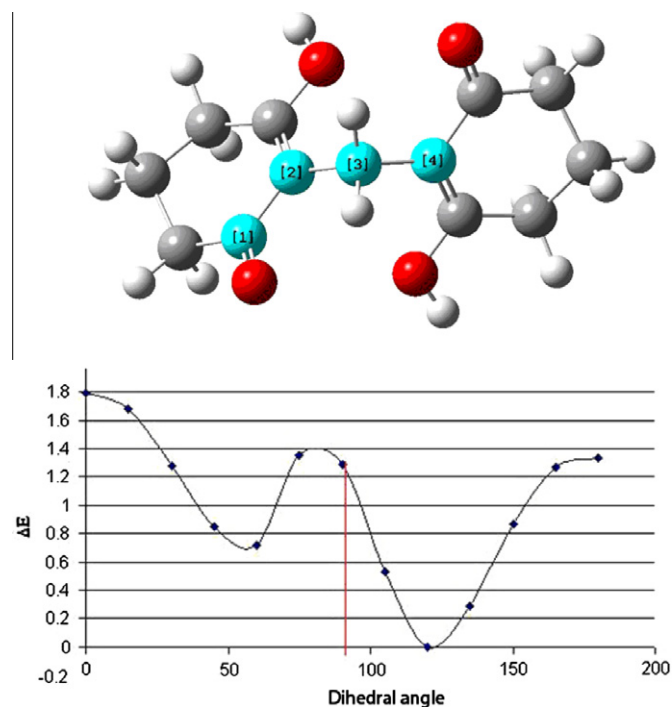

Fig. 1. Absorption of **3** (R=*p*-Cl-C₆H₄) in water: solid line (identical to absorption of **4**); after acidification by HCl: dashed line; after addition of an excess of NaOH: dotted line.

Fig. 2. The potential energy (ΔG) surface scan of **5a** along the dihedral angle 1–2–3–4 between the 1,3-cyclohexane-dione moieties. The red vertical line corresponds to the conformation with the hydrogen bond (the dihedral angle is the same as in **5**). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)