Journal of Molecular Structure 1122 (2016) 48–61

Contents lists available at ScienceDirect

Journal of Molecular Structure

journal homepage: http://www.elsevier.com/locate/molstruc

Theoretical and vibrational spectroscopic approach to keto-enol tautomerism in methyl-2-(4-methoxybenzoyl)-3-(4-methoxyphenyl)-3-oxopropanoylcarbamate

Hatice Arı [a], Talat Özpozan [b, *], Zeki Büyükmumcu [b], Yiğit Kabacalı [b], Mustafa Saçmaci [a]

[a] Bozok University, Faculty of Arts and Sciences, Department of Chemistry, Yozgat, Turkey
[b] Erciyes University, Faculty of Sciences, Department of Chemistry, Kayseri, Turkey

ARTICLE INFO

Article history:
Received 10 March 2016
Received in revised form
15 May 2016
Accepted 17 May 2016
Available online 20 May 2016

Keywords:
Carbamate
Keto-enol tautomerism
Transition state
Vibrational analysis
DFT

ABSTRACT

A carbamate compound having tricarbonyl groups, methyl-2-(4-methoxybenzoyl)-3-(4-methoxyphenyl)-3-oxopropanoylcarbamate (BPOC) was investigated from theoretical and vibrational spectroscopic point of view employing quantum chemical methods. Hybrid Density Functionals (B3LYP, X3LYP and B3PW91) with 6-311 G(d,p) basis set were used for the calculations. Rotational barrier and conformational analyses were performed to find the most stable conformers of keto and enol forms of the molecule. Three transition states for keto-enol tautomerism in gas phase were determined. The results of the calculations show that enol-1 form of BPOC is more stable than keto and enol-2 forms. Hydrogen bonding investigation including Natural bond orbital analysis (NBO) for all the tautomeric structures was employed to compare intra-molecular interactions. The energies of HOMO and LUMO molecular orbitals for all tautomeric forms of BPOC were predicted. Normal Coordinate Analysis (NCA) was carried out for the enol-1 to assign vibrational bands of IR and Raman spectra. The scaling factors were calculated as 0.9721, 0.9697 and 0.9685 for B3LYP, X3LYP and B3PW91 methods, respectively. The correlation graphs of experimental versus calculated vibrational wavenumbers were plotted and X3LYP method gave better frequency agreement than the others.

1. Introduction

Carbamates are one of the important groups of carbamic esters [1]. Many applications of carbamates have been published in various areas such as insecticides [2], antiparasitics [1,3] and pharmaceuticals [4]. N-acyl carbamates are typical examples of such compounds that undergo a rapid development as pesticides [5,6] and pharmaceuticals [7] due to their biological activity [8]. Several carbamates have been synthesized as anticancer agents recognizing their inhibiting effects for some carbamates on endothelial cell proliferation *in vitro* and tumor induced angiogenesis *in vivo* as well as tumor growth in mice [9].

Keto-enol tautomerism is critical for the biological effect of carbamates in most cases. β,β′-tricarbonyl compounds can exist in different tautomeric forms. Examination of tautomeric equilibrium in carbonyl compounds can be very important to rationalize their biological activity [10–16] and to recognize biochemical changes in which they take part [17]. Keto-enol tautomerism has been widely studied by several experimental [18–30] and theoretical methods [31–36] in literature.

BPOC molecule investigated here is a carbamate compound with tricarbonyl group and also indicates keto enol tautomerism. The two carbonyl groups are similar in chemical environment. Both of the two carbonyls have aromatic rings and connected the same carbon. Therefore, two enol and one keto tautomers can be expected for BPOC. The keto form (KF), enol form-1 (EF-1), transition state for keto form to enol form-1 (TS-1), enol form-2 (EF-2), transition state for keto form to enol form-2 (TS-2) and transition state for enol form-1 to enol form-2 (TS-3) were depicted in Fig. 1. Rotational barrier analysis and conformer analysis were made to find the conformers of these tautomers. The most stable conformers of tautomers and the transition states of the tautomerism were obtained in gas phase. Hydrogen bondings were examined through NBO, structural and vibrational analyses. Frontier orbital analysis was performed to search for the kinetically most stable conformers of the keto and the two enol forms and the transition

* Corresponding author.
E-mail address: ozpozant@erciyes.edu.tr (T. Özpozan).

http://dx.doi.org/10.1016/j.molstruc.2016.05.060
0022-2860/

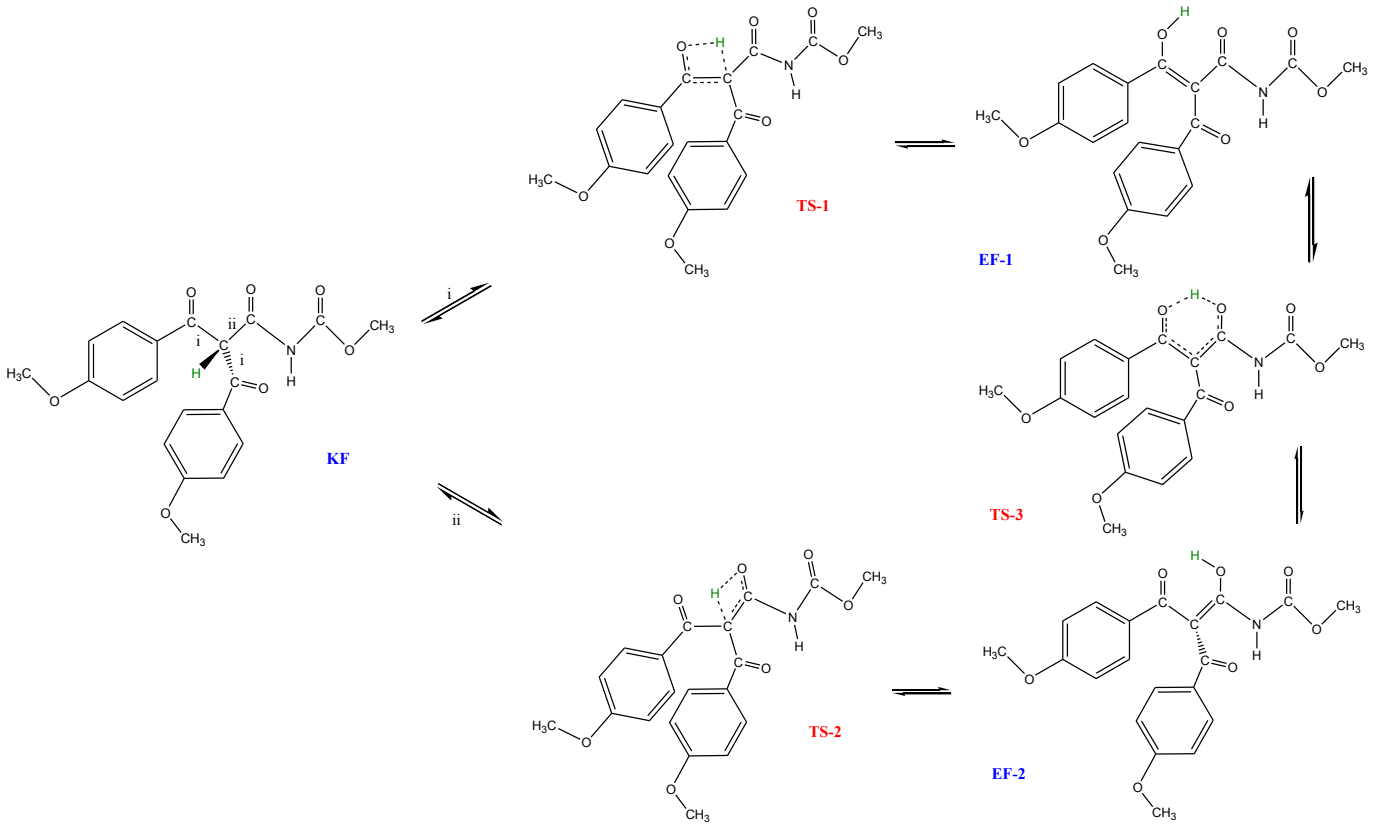

Fig. 1. Tautomeric (KF, EF-1 and EF-2) and transition state (TS-1, TS-2 and TS-3) structures of BPOC.

states of BPOC. Vibrational assignments of the observed IR and Raman bands were proposed for EF-1 which was calculated to be the most stable structure.

2. Instrumental and computational methods

2.1. Instrumentation

BPOC was previously synthesized by one of us [37] and characterized by elemental analysis, IR, ^{1}H and ^{13}C NMR spectroscopic techniques. The IR spectrum of BPOC was recorded by Perkin-Elmer Spectrum 400 FT-IR Spectrometer in the 400-4000 cm^{-1} region with a resolution of 4 cm^{-1}. The Raman spectrum of BPOC was measured in the range 100–4000 cm^{-1} with a resolution of 0.5 cm^{-1} using Renishaw inVia Raman microscope equipped with Peltier-cooled CCD detectors (−70 °C) and 785 nm diode laser as the excitation source. All the spectra were recorded at room temperature.

2.2. Computational methods

Rotational barrier and conformational analyses were carried out first through relaxed scan around easily twistable single bonds using B3LYP of DFT for KF, EF-1 and EF-2. Relaxed scans were performed with 4° increments to get full rotation. All the structures obtained near to minima of the scan curves were re-optimized. The structures obtained in this way were compared geometrically to eliminate identical structures. This way of obtaining the most stable conformer was given in our previous studies [38–40]. The population of different tautomers follows Boltzmann distribution like conformers;

$$\frac{N_i}{N_{total}} = \frac{e^{-E_{rel}/RT}}{\sum_{k=1}^{N_{total}} e^{-E_k/RT}} \quad (1)$$

The left hand side of the equation is the equilibrium ratio of *i*-th tautomer to the total number of tautomers. E_{rel} is the relative energy of the *i*-th tautomer with respect to the minimum energy tautomer. *T* is the absolute temperature and *R* is the universal gas constant. The % population of the tautomer i ($\%P_i$) can be given as;

$$\%P_i = \left(\frac{N_i}{N_{total}}\right) \times 100 \quad (2)$$

The transition state of keto − enol forms were obtained using direct TS optimizations. All the calculations after conformer analysis including NBO-, hydrogen bonding- and HOMO-LUMO analyses were performed using B3LYP, X3LYP and B3PW91 methods level with 6-311G(d,p) basis set. The most stable tautomer EF-1 was used later in vibrational analysis. All the calculations were carried out on Gaussian 09 package [41]. The Potential Energy Distributions (PED)'s of the normal frequencies were calculated using VEDA4 program [42,43].

3. Results and discussion

3.1. Rotational barriers and conformational analyses of BPOC

BPOC has the three carbonyl groups and the two of them are identical in chemical environment. To find the most stable conformers of keto, enol-1 and enol-2 tautomers of BPOC the critical torsional angles were determined as $C_3O_2C_1H_{29}$, $C_1O_2C_3C_4$, $C_5C_6C_9C_{11}$, $C_6C_9C_{11}C_{12}$, $C_9C_{11}C_{12}C_{14}$, $C_9C_{11}C_{22}C_{24}$, $O_{13}C_{12}C_{14}C_{15}$,