

Experimental and DFT studies on the IR spectra and structure of 4-acetamidobenzoic acid (acedoben), its oxyanion and dianion

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Dedicated to Acad. Ivan Juchnovski on the occasion of his 80th birthday

The spectral and structural changes taking place during the course of the conversion of 4-acetamidobenzoic acid, HOOC-C₆H₄-NH-COCH₃, into the corresponding oxyanion, -OOC-C₆H₄-NH-COCH₃, and dianion, -OOC-C₆H₄-N-COCH₃, have been followed by both infrared spectra in DMSO solution and DFT/B3LYP/6-311+G(2df,p) calculation. The solvent effect was simulated by using self-consistent integral equation formalism variant (IEFPCM) model. The *trans* conformers (with respect to phenylene and methyl groups) have been calculated to be more stable than the *cis* ones in all species studied. The changes accompanying the first deprotonation concern mainly the carboxylato fragment; those resulting from the second one are spread over the whole dianion. Analysis of the atomic charge changes shows that over 70% of the first (oxyanionic) charge remains localized within the carboxylato fragment. The second (nitranionic) charge delocalizes over the acetyl (0.42 e⁻) and phenylene (0.19 e⁻) groups, nitranionic center (0.34 e⁻) and (0.05e⁻) carboxylate group.

Key words: IR; DFT; 4-acetamidobenzoic acid (acedoben); oxyanion; dianion

INTRODUCTION

4-Acetamidobenzoic acid (acedoben) molecule, simultaneously a carboxamide and a carboxylic acid, is an important conjugated compound of biological and medicinal interest. Acedoben (or its sodium or potassium salts) is contained in a number of pharmaceutical products as antiviral drug Isoprinosine, Deanol acetamidobenzoate, Fibroderm, Perlinsol Cutaneo. In a human body acedoben is a metabolite of *p*-aminobenzoic acid [1], benzocaine [2], *etc.*, so its biological properties and metabolic transformations have been extensively investigated during the last few decades [3]. Acedoben has multifunctional coordination sites with chelating and bridging ability and it has been widely used in coordination chemistry and crystal engineering [4,5].

Acedoben was first prepared by Hofmann in 1876 [6]. The solid-state IR and Raman spectra of acedoben are accessible on-line [7]. Only the frequencies of the amide carbonyl (C=O) and amino (N-H) stretching bands in solutions of the title molecule have been reported, included in series of substituted acetanilides, and were found to correlate with both Hammett's substituent constants [8,9] and certain indices computed within DFT method [9].

ATR FTIR spectroscopy has recently been used to detection *p*-acetamidobenzoic acid and *p*-aminobenzoic acid in human skin treated with essential oil formulations [10]. Lanthanide complexes with 4-acetamidobenzoate have been characterized by their IR spectra [6]. No detailed interpretations of IR spectra of 4-acetamidobenzoic acid and of its carboxylate anion has been performed.

The conversions of neutral molecule into anions, radical-anions, carbanions, azanion, *etc.* are accompanied by essential changes in the vibration spectra. So, these changes are very informative for the structural variations caused by the same conversions [11]. The title compound is an interesting and convenient object of the molecule → anion → dianion conversions investigations, as it contains the (-COOH) and (-CO-NH-) characteristic groups and can be easily converted into a carboxylate anion and dianion, stable in dimethyl sulfoxide (DMSO). In the literature we have found neither IR spectra, nor theoretically calculations for the title anionic species. The structure of large series of organic molecules and their anions have been successfully studied recently on the basis of experimental IR spectra combined with DFT computations ([12-16] and references therein). The purpose of the present investigation is to follow the spectral and structural changes,

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caused by the conversion of 4-acetamidobenzoic acid molecule into the corresponding carboxylate anion and dianion, by means of both DFT computations and spectroscopic experiments.

EXPERIMENTAL AND COMPUTATIONS

Commercial 4-acetamidobenzoic acid (Aldrich, 98%) was used without further purification. The 4-acetamidobenzoate anion was prepared by adding solutions of the parent compound in dimethyl sulfoxide (DMSO) and DMSO- d_6 (Fluka) to an excess of dry sodium or potassium carbonate. The suspensions obtained were stirred for 1 min and then filtered through a syringe-filter. The conversion was practically complete (Fig. 1(A) and Fig. 1(B)). The dianion of 4-acetamidobenzoic acid was prepared by reacting DMSO and DMSO- d_6 solutions of the parent compound with an excess of dry alkali-metal methoxides and methoxides- d_3 . The conversion was also practically complete: in the spectra we found neither the bands of 4-acetamidobenzoic acid nor those of its anion (cf. Fig. 2(A-C)).

The IR spectra were recorded at a resolution of 1 cm^{-1} , by 50 scans on a Bruker Vector 22 FTIR spectrophotometer in a CaF_2 cell of 0.13 mm path length.

The quantum chemical calculations were performed using the Gaussian 09 package [17]. The geometry optimizations of the structures investigated were done without symmetry restrictions, using density functional theory (DFT). We employed B3LYP hybrid functional, which combines Becke's three-parameter nonlocal exchange with the correlation functional of Lee *et al.* [18,19], adopting 6-311+G(2df,p) basis sets. To estimate the effect of the solvent (DMSO) on the infrared spectra of studied species, we applied the integral equation formalism of polarizable continuum model (IEFPCM), proposed by Tomasi and coworkers [20,21].

The stationary points found on the molecular potential energy hypersurfaces were characterized using standard harmonic vibrational analysis. The theoretical vibrational spectra were interpreted by means of potential energy distributions (PEDs) using VEDA 4 program [22]. For a better correspondence between experimental and calculated values, we modified the results using the empirical scaling factors.

RESULTS AND DISCUSSION

Energy analysis

The structures of the most stable conformers of the three species studied are shown in Scheme 1. All structures with a subscript 1 in Scheme 1 correspond to the *trans*-type conformers (with respect to phenylene and methyl groups). According to the B3LYP/6-311+G(2df,p) calculations the *cis* conformers of molecule are less stable than the *trans* form by 11.6 kJ mol^{-1} . The energy difference between two *trans* conformers of molecule (A_1 and A_{1a}), differing by the direction of the carboxyl group, is 0.7 kJ mol^{-1} and they seem to be present simultaneously in solutions. The presence of the conformer A_1 in solid state was established by crystallographic analysis [23]. According to both experimental and theoretical [24] data, the *trans* conformer of the unsubstituted acetanilide is also the more stable one. Our calculations predict the both *trans* conformers of the oxyanion and dianion are the more stable (Scheme 1).

The calculated total energies of the studied species are as follow:

$E_{\text{tot}} = -629.063365971$ H for the 4-acetamidobenzoic acid molecule (A_1 in Scheme 1);

$E_{\text{tot}} = -628.511829360$ H for the 4-acetamidobenzoic acid oxyanion (B_1 in Scheme 1);

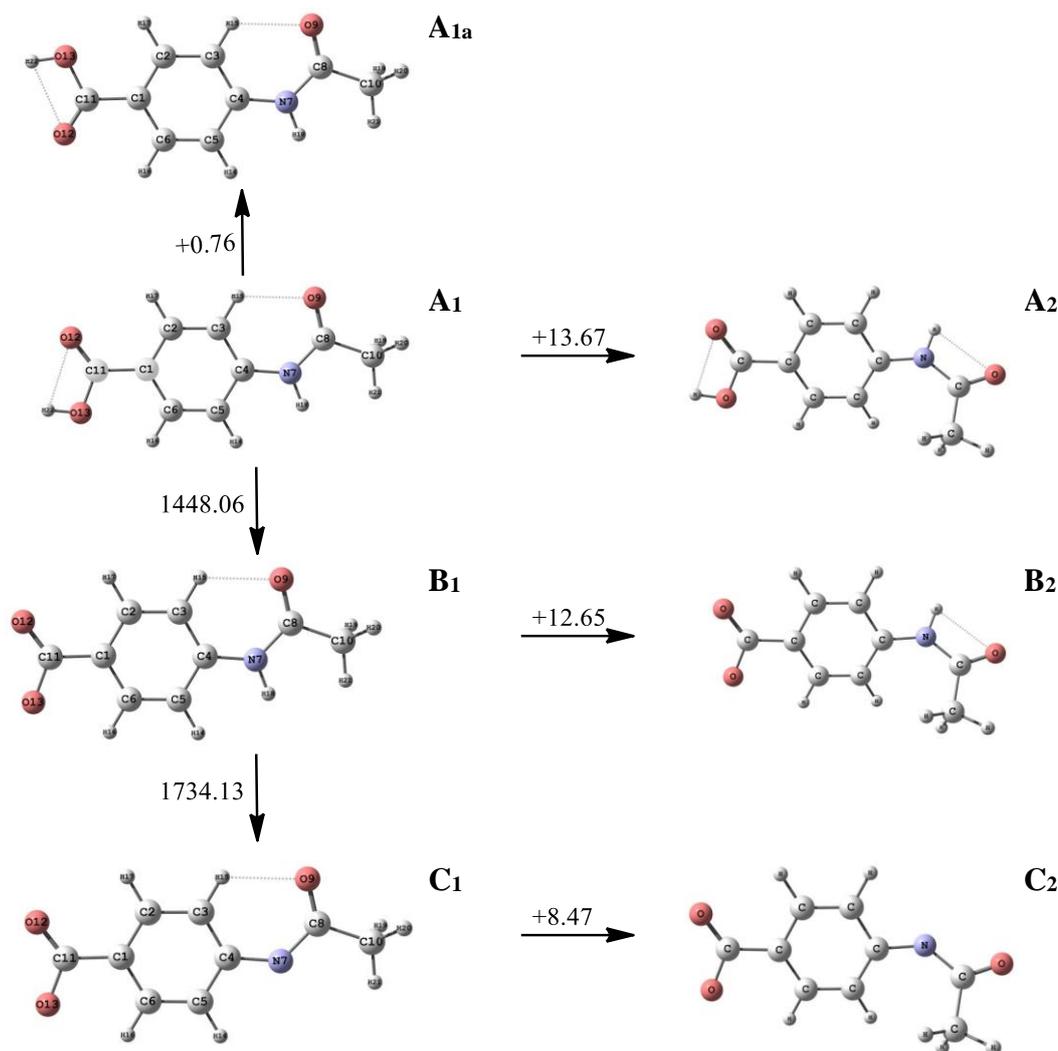
$E_{\text{tot}} = -627.851335706$ H for the 4-acetamidobenzoic acid dianion (C_1 in Scheme 1).

The following deprotonation energies correspond to the above values (see Scheme 1):

$E^d = E_{\text{tot}}(B_1) - E_{\text{tot}}(A_1) = 1448.05948249$ kJ mol^{-1} ;

$E^d = E_{\text{tot}}(C_1) - E_{\text{tot}}(B_1) = 1734.12622068$ kJ mol^{-1} .

The energy differences E^d is related to the gas-phase Brønsted acidities, and can be used as approximate measure of these acidities in polar aprotic solvents [25]: low $E^d \rightarrow$ high acidities \rightarrow low pKa values. For comparison, the first deprotonation energy is lower than E^d of paracetamol (1537.9 kJ mol^{-1} [24]) and higher than E^d of stronger acid acesulfame (1324.31 kJ mol^{-1} [12]). The second deprotonation energy is essentially higher, and can be compared with the second deprotonation energy of paracetamol (1880.2 kJ mol^{-1} [26]). This result is not surprising, having in mind that the products of the second deprotonation are in fact dianions.



Scheme 1. Conformers of the 4-acetamidobenzoic acid molecule, oxyanion and dianion. The values the arrows are the means energy differences in kJ mol⁻¹.

Infrared analysis

A fragment of the infrared spectrum of 4-acetamidobenzoic acid in DMSO-d₆ solution is shown in Fig. 1(A). The numeric data for the frequencies of the bands are listed in Table 1 together with the corresponding theoretical values for the most stable conformers of molecules. As can be seen, there is a good agreement between the scaled theoretical and experimental IR frequencies. The mean deviation between them is 11.1 cm⁻¹. No experimental data for the $\nu(\text{OH})$ and $\nu(\text{NH})$ bands were given in Table 1, as they are very broad because of the formation of hydrogen bonds mainly with solvent, like other carboxamides in DMSO [18,20]. The assignment of the experimental bands to the calculated normal modes in the C–H stretching region (3100–2800 cm⁻¹) is not obvious

because there are fewer bands in the experimental spectrum than predicted by the calculations.

The highest frequency experimental bands observed in the IR spectrum (3200–3000 cm⁻¹) are assigned to the aromatic C–H stretches, while the lower frequency bands are attributed to the methyl group motions. The $\nu(\text{C–H})$ bands are of low intensity in both the experimental and theoretical spectra.

The calculations resolved and located well the two carbonyl stretching vibrations, those of the carboxy and the amido group, at 1693 cm⁻¹ and 1683 cm⁻¹, respectively. The shifting expected in this case should amount to a 10 cm⁻¹ and it is in agreement with the experimental measured after having decomposed the complex band into components (1702 cm⁻¹, 1691 cm⁻¹, Table 1).

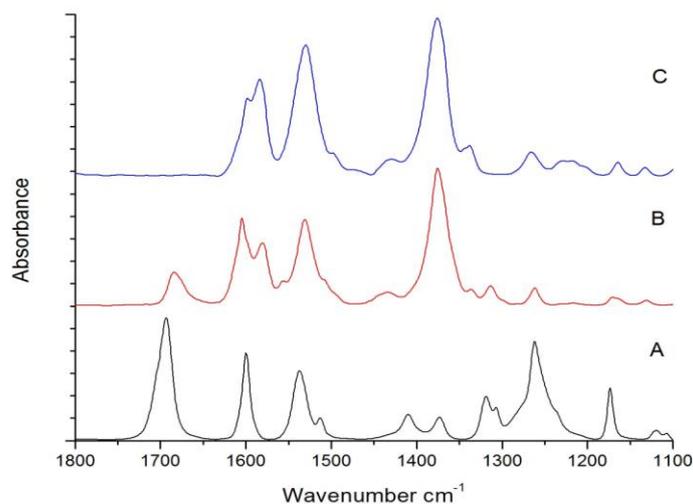


Fig. 1. Infrared spectra of : (A) 4-acetamidobenzoic acid, (B) its anion (with counter ion Na⁺) and (C) its dianion (with counter ions Na⁺), 0.09 mol l⁻¹ in DMSO-d₆.

Table 1. Theoretical (B3 LYP/6-311+G(2df,p) and experimental (solvent DMSO-d₆) vibrational frequencies (in cm⁻¹) and IR integrated intensities (A in km.mol⁻¹) of 4-acetamidobenzoic acid.

No.	$\nu_{\text{calc.}}^{\text{a}}$	A_{calc}	Approximative description ^b	$\nu_{\text{exp.}}^{\text{c}}$	
1.	3667	175.8	100 $\nu(\text{OH})$		
2.	3530	62.9	100 $\nu(\text{NH})$		
3.	3176	4.5	97 $\nu(\text{PhH})$		
4.	3134	1.6	97 $\nu(\text{PhH})$		
5.	3130	3.8	97 $\nu(\text{PhH})$	3048	w
6.	3098	10.7	97 $\nu(\text{PhH})$	3006	w
7.	3063	20.1	100 $\nu(\text{CH}_3)$		
8.	3044	4.7	100 $\nu(\text{CH}_3)$	2934	w
9.	2983	5.8	100 $\nu(\text{CH}_3)$	2856	w
10.	1693	645.8	78 $\nu(\text{C=O})$ (carboxy)	1702 ^d	s
11.	1683	558.9	61 $\nu(\text{C=O})$ (amid)	1691 ^d	vs
12.	1609	209.0	52 $\nu(\text{CC})$	1599	s
13.	1589	179.7	52 $\nu(\text{CC})$, 10 $\delta(\text{PhH})$		
14.	1516	256.7	54 $\delta(\text{HNC})$, 10 $\nu(\text{NC})$	1537	s
15.	1503	338.1	78 $\delta(\text{PhH})$, 10 $\delta(\text{CCC})$	1512	m
16.	1453	39.9	72 $\delta(\text{CH}_3)$, 12 $\nu(\text{PhH})$		
17.	1434	12.7	93 $\delta(\text{CH}_3)$		
18.	1408	88.5	30 $\nu(\text{CC})$, 26 $\delta(\text{PhH})$	1409	m
19.	1370	65.9	90 $\delta(\text{CH}_3)$		
20.	1337	188.7	28 $\nu(\text{C-O})$, 25 $\delta(\text{HOC})$, 13 $\nu(\text{C-COOH})$	1373	m
21.	1318	303.1	37 $\nu(\text{NC})$, 15 $\delta(\text{HNC})$, 13 $\nu(\text{CC})$	1318	m
22.	1308	169.3	69 $\delta(\text{PhH})$	1307	m
23.	1247	311.3	36 $\delta(\text{PhH})$, 20 $\nu(\text{Ph-C})$, 12 $\delta(\text{HNC})$,	1261	s
24.	1217	118.6	23 $\nu(\text{Ph-N})$, 22 $\nu(\text{NC})$, 19 $\nu(\text{C-CH}_3)$		
25.	1188	42.7	32 $\delta(\text{PhH})$, 22 $\delta(\text{HOC})$, 12 $\nu(\text{CC})$	1173	m
26.	1149	503.9	34 $\delta(\text{CCC})$, 28 $\delta(\text{PhH})$	1119	w
27.	1119	21.0	78 $\delta(\text{PhH})$, 15 $\nu(\text{CC})$	1108	
28.	1099	398.4	55 $\nu(\text{C-O})$, 13 $\nu(\text{CC})$, 12 $\delta(\text{HOC})$		
29.	1055	12.6	67 $\delta(\text{CH}_3)$, 19 $\delta(\text{NC=O})$		

^aScaled by 0.98. ^bVibrational modes: ν , stretching; δ , bendings. The numbers before the mode symbols indicate % contribution (10 or more) of a given mode to the corresponding normal vibration, according to the potential energy distribution. ^cRelative intensity: s, strong; m, moderate; w, weak; v, very. ^dMeasured after having decomposed the complex hands into components.

The theory reproduce qualitatively well the high integral intensities for the bands in the experimental spectrum, namely $\nu(\text{C}=\text{O})$ (carboxy) and $\nu(\text{C}=\text{O})$ (amid-I). DFT calculations predicted well also the IR frequencies measured in DMSO of the amide-II and amide-III vibrations. The amide-II mode $\delta(\text{HNC})$ is predicted to appear at 1516 cm^{-1} as a very intense band. Experimentally, a very strong

band was detected at 1537 cm^{-1} in DMSO. The stretching $\nu(\text{N}-\text{C})$ coupled with $\delta(\text{HNC})$ and $\nu(\text{CC})$, denoted as amide-III was predicted and measured as an intensity band at 1318 cm^{-1} .

The experimental spectrum of anion is shown on Fig. 1(B) and its numerical data are compared with theoretical values in Table 2.

Table 2. Theoretical (B3 LYP/6-311+G(2df,p) and experimental (solvent DMSO- d_6) vibrational frequencies (in cm^{-1}) and IR integrated intensities (A in $\text{km}\cdot\text{mol}^{-1}$) of 4-acetamidobenzoic acid.

No.	$\nu_{\text{calc.}}^a$	A_{calc}	Approximative description ^b	$\nu_{\text{exp.}}^c$	
1.	3538	55.8	100 $\nu(\text{NH})$		
2.	3172	1.2	97 $\nu(\text{PhH})$		
3.	3129	8.6	97 $\nu(\text{PhH})$		
4.	3122	7.2	97 $\nu(\text{PhH})$		
5.	3089	21.7	97 $\nu(\text{PhH})$	3049	w
6.	3064	23.4	100 $\nu(\text{CH}_3)$	2972	w
7.	3048	6.5	100 $\nu(\text{CH}_3)$		
8.	2987	8.8	100 $\nu(\text{CH}_3)$	2930	w
9.	1675	432.7	73 $\nu(\text{C}=\text{O})$, 10 $\delta(\text{HNC})$	2910	w
10.	1605	43.3	63 $\nu(\text{CC})$	1684	s
11.	1593	617.2	72 $\nu^{\text{as}}(\text{OCO})$	1604	vs
12.	1545	405.1	39 $\nu(\text{CC})$, 14 $\delta(\text{PhH})$	1580	s
13.	1507	656.5	38 $\delta(\text{HNC})$, 12 $\nu(\text{NC})$, 10 $\delta(\text{PhH})$		
14.	1497	98.7	68 $\delta(\text{PhH})$, 14 $\delta(\text{CCC})$	1531	vs
15.	1451	31.9	89 $\delta(\text{CH}_3)$	1512	w
16.	1433	12.4	92 $\delta(\text{CH}_3)$		
17.	1391	62.3	44 $\nu(\text{CC})$, 14 $\delta(\text{PhH})$	1435	w
18.	1369	680.0	72 $\nu^{\text{s}}(\text{OCO})$		
19.	1333	54.5	90 $\delta(\text{CH}_3)$	1375	vs
20.	1309	419.2	58 $\nu(\text{CC})$, 18 $\nu(\text{Ph-N})$		
21.	1293	40.0	83 $\delta(\text{PhH})$	1313	m
22.	1244	273.1	37 $\nu(\text{NC})$, 15 $\delta(\text{HNC})$, 13 $\nu(\text{CC})$		
23.	1211	3.2	36 $\nu(\text{Ph-N})$	1261	m
24.	1166	47.8	54 $\delta(\text{PhH})$, 14 $\nu(\text{CC})$		
25.	1115	33.3	44 $\delta(\text{CCC})$, 28 $\delta(\text{PhH})$	1170	w
26.	1100	19.3	76 $\delta(\text{PhH})$, 14 $\nu(\text{CC})$	1131	w
27.	1033	11.9	40 $\delta(\text{NCC})$, 33 $\delta(\text{CH}_3)$		
28.	1009	18.0	54 $\delta(\text{CCC})$		

^aScaled by 0.98. ^bVibrational modes: ν , stretching; δ , bendings; superscripts: s, symmetrical; as, asymmetrical.. The numbers before the mode symbols indicate % contribution (10 or more) of a given mode to the corresponding normal vibration, according to the potential energy distribution. ^cRelative intensity: s, strong; m, moderate, w, weak; v, very. ^dMeasured after having decomposed the complex bands into components.

As above we can find there a good agreement between experimental and scaled theoretical frequencies. The mean deviation between them is 10.2 cm^{-1} within the corresponding interval of $9\text{--}25 \text{ cm}^{-1}$, typical for DFT calculations of frequencies for series of anions [12-16] (and references therein). Removing the proton after the conversion of the carboxy group into the carboxylate anion leads to equalization of the two CO bonds in the anion (and hence the disappearance of bands 10, Table 1). Two strong bands at 1583 and 1338 cm^{-1} , corresponding to the $\nu^{\text{as}}(\text{OCO})$ and $\nu^{\text{s}}(\text{OCO})$ vibrations appear instead of the $\nu(\text{C=O})$ (carboxy)

band at 1702 cm^{-1} and the formal $\nu(\text{C-O})$ band at 1373 cm^{-1} . In full agreement between theory and experiment, conversion of the studied molecule into the oxyanion has only a weak effect on the $\nu(\text{C=O})$ (amide-I) frequency: predicted decrease 8 cm^{-1} , measured 7 cm^{-1} . The conversion causes also a decrease in the $\delta(\text{HNC})$ (amide-II) frequency: predicted 13 cm^{-1} , measured 6 cm^{-1} (Tables 1 and 2). The $\nu(\text{C-N})$ (amide-III) band also undergoes a frequency decrease: predicted 9 cm^{-1} , measured 6 cm^{-1} (Tables 1 and 2). Theoretical and experimental IR data for the 4-acetamidobenzoic acid dianion are compared in Table 3.

Table 3. Theoretical (B3 LYP/6-311+G(2df,p) and experimental (solvent DMSO- d_6) vibrational frequencies (in cm^{-1}) and IR integrated intensities (A in $\text{km}\cdot\text{mol}^{-1}$) of 4-acetamidobenzoic acid dianion.

No.	$\nu_{\text{calc.}}^{\text{a}}$	$A_{\text{calc.}}$	Approximative description ^b	$\nu_{\text{exp.}}^{\text{c}}$	
1.	3153	3.3	97 $\nu(\text{PhH})$		
2.	3107	27.2	97 $\nu(\text{PhH})$		
3.	3095	19.0	97 $\nu(\text{PhH})$	3052	w
4.	3077	32.9	97 $\nu(\text{PhH})$	3026	w
5.	3042	47.8	100 $\nu(\text{CH}_3)$		
6.	2998	39.0	100 $\nu(\text{CH}_3)$	2936	w
7.	2951	68.1	100 $\nu(\text{CH}_3)$	2902	w
8.	1610	98.0	63 $\nu(\text{CC})$	1598	vs
9.	1567	528.6	42 $\nu^{\text{as}}(\text{O-C-O}), 16 \nu(\text{CC})$	1583	vs
10.	1522	409.8	41 $\nu^{\text{as}}(\text{O-C-O}), 21 \nu(\text{CC})$	1535 ^d	
11.	1519	1054.2	40 $\nu(\text{C=O}), 16 \nu(\text{Ph-N})$	1528 ^d	vs
12.	1496	703.9	68 $\delta(\text{PhH})$	1496	sh
13.	1455	8.5	80 $\delta(\text{CH}_3)$	1469	vw
14.	1440	202.2	98 $\delta(\text{CH}_3)$	1429	w
15.	1411	32.7	39 $\delta(\text{CCC}), 22\delta(\text{PhH})$		
16.	1378	356.3	30 $\nu(\text{C-N}), 17 \nu(\text{C=O})$	1376	vs
17.	1351	55.2	90 $\delta(\text{CH}_3)$		
18.	1332	2115.0	71 $\nu^{\text{s}}(\text{O-C-O})$	1338	m
19.	1297	46.2	75 $\delta(\text{PhH})$		
20.	1284	5.9	73 $\nu(\text{CC})$	1266	m
21.	1214	39.6	30 $\nu(\text{Ph-N}), 20 \delta(\text{CCC})$	1230	w
22.	1163	111.4	55 $\delta(\text{PhH}), 24 \nu(\text{CC})$	1164	w
23.	1124	192.4	55 $\delta(\text{PhH}), 24 \nu(\text{CC})$	1132	w
24.	1099	21.4	76 $\delta(\text{PhH})$		
25.	1027	4.2	55 $\delta(\text{NCC}), 20 \delta(\text{CH}_3)$		
26.	997	1.9	77 $\delta(\text{CCC})$		

^aScaled by 0.98. ^bVibrational modes: ν , stretching; δ , bendings; superscripts: s, symmetrical; as, asymmetrical. The numbers before the mode symbols indicate % contribution (10 or more) of a given mode to the corresponding normal vibration, according to the potential energy distribution. ^cRelative intensity: s, strong; m, moderate, w, weak; v, very. ^dMeasured after having decomposed the complex bands into components.

Again there is good agreement between experimental and scaled theoretical frequencies. The mean deviation between them is 9.1 cm⁻¹, this value being lower than these in case of the dianion of paracetamol [20]. The experimental spectrum of the dianion studied is shown in Fig. 2(C). Comparison with the other spectra of Fig. 2 shows that fundamental spectral changes accompany the second deprotonation of 4-acetamidobenzoic acid. There is no longer carbonyl band $\nu(\text{C}=\text{O})$ at the usual place. The theory predicts two new bands characterizing the carboxamido group in the dianion: very strong bands at 1519 cm⁻¹ and 1378 cm⁻¹. These very strong bands are actually present in the experimental spectrum (Fig. 2(C)): i.e., at 1531 cm⁻¹ and 1376 cm⁻¹. The approximate description of the corresponding normal vibrations (Table 3, nos. 11 and 16) are in agreement with the literature data. For the nitranions of acetanilide and of a series of ring-substituted acetanilides, Ognyanova *et al.* have assigned the very strong bands in the 1518-1533 cm⁻¹ spectral region as $\nu(\text{C}=\text{O})$ (amide-I) and the medium-to-strong bands at 1373-1382 cm⁻¹ $\nu(\text{C}-\text{N})$ (amide-III). In agreement

between theory and experiment, the second deprotonation of 4-acetamidobenzoic acid causes an increase in C-N stretching frequency $\nu(\text{C}-\text{N})$ and essential increase in the corresponding intensity $A(\text{C}-\text{N})$. The shift of this coordinate to higher frequency is obviously due to the significant shortening of the C-N bond, caused by the conversion of the acetanilide molecule into the azanion.

Structural analysis

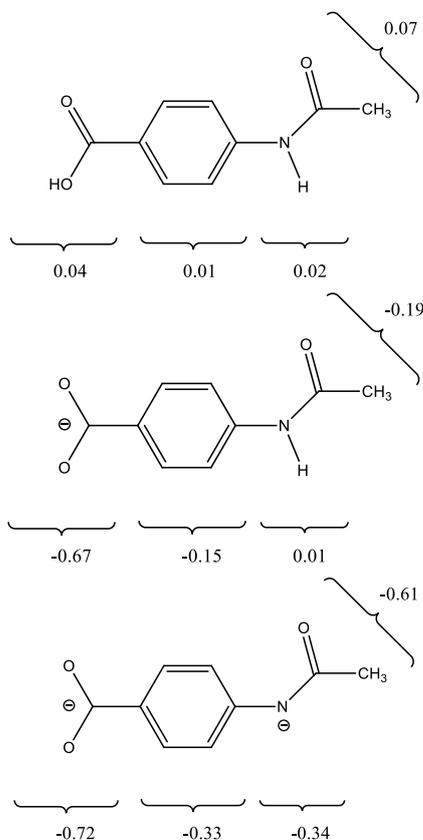
According to X-ray diffraction the plane of the acetamide group is oriented at 40.4° with respect to the benzene ring, whereas the plane of the carboxylic acid group is essentially coplanar with the benzene ring [21]. According to the calculations in the most stable conformers of the isolated molecule these groups are planar. The same groups in the isolated oxyanion and dianion have been predicted to be again planar. The theoretical and experimental bond lengths and angles in the 4-acetamidobenzoic acid and its oxyanion and dianion are listed in Table 4.

Table 4. Theoretical (B3LYP/6-311+G(2df,p)) and experimental bond lengths R (Å) and bond angles A (°) in the 4-acetamidobenzoic acid molecule, its oxyanion and dianion.

	Molecule		Δ^b	Anion	Δ^c	Dianion	Δ^d
	Experimental ^a	Theoretical		Theoretical		Theoretical	
<i>Bond lengths</i>							
R(C ⁴ ,C ⁵)	1.383(3)	1.400	0.017	1.398	-0.002	1.414	0.016
R(C ⁵ ,C ⁶)	1.379(2)	1.379	-0.001	1.385	0.007	1.387	0.002
R(C ¹ ,C ⁶)	1.382(3)	1.398	0.016	1.394	-0.004	1.399	0.005
R(C ¹ ,C ²)	1.392(3)	1.396	0.004	1.392	-0.004	1.396	0.004
R(C ² ,C ³)	1.384(3)	1.386	0.002	1.392	0.006	1.394	0.002
R(C ⁴ ,N ⁷)	1.420(3)	1.400	-0.020	1.420	0.02	1.394	-0.026
R(N ⁷ ,C ⁸)	1.350(2)	1.372	0.022	1.361	-0.011	1.326	-0.035
R(C ⁸ ,O ⁹)	1.219(2)	1.220	0.001	1.221	0.001	1.259	0.038
R(C ⁸ ,C ¹⁰)	1.505(3)	1.511	0.006	1.524	0.013	1.543	0.019
R(C ¹ ,C ¹¹)	1.481(3)	1.477	-0.004	1.549	0.072	1.539	-0.010
R(C ¹¹ ,O ¹²)	1.254(2)	1.214	-0.040	1.251	0.037	1.260	0.009
R(C ¹¹ ,O ¹³)	1.279(2)	1.349	0.070	1.250	-0.099	1.259	0.009
<i>Bond angles</i>							
A(C ⁴ ,C ⁵ ,C ⁶)	119.6(2)	120.5	0.9	120.4	-0.1	122.5	2.1
A(C ⁵ ,C ⁶ ,C ¹)	120.2(2)	120.5	0.3	121.0	0.5	121.4	0.4
A(C ⁶ ,C ¹ ,C ²)	119.4(2)	118.7	-0.7	117.7	-1	116.3	-1.4
A(C ¹ ,C ² ,C ⁶)	120.4(2)	121.2	0.8	122.2	1	122.7	0.5
A(C ⁶ ,C ¹ ,C ¹¹)	120.2(2)	119.7	-0.5	120.6	0.9	121.4	0.8
A(N ⁷ ,C ¹ ,C ²)	118.6(2)	116.9	-1.7	116.5	-0.4	116.3	-0.2
A(C ⁸ ,N ⁷ ,C ¹)	127.6(2)	129.7	2.1	130.8	1.1	123.5	-7.3
A(N ⁷ ,C ⁸ ,O ⁹)	123.3(2)	123.5	0.2	125.2	1.7	131.5	6.3
A(N ⁷ ,C ⁸ ,C ¹⁰)	115.0(2)	114.8	-0.2	114.4	-0.4	113.0	-1.4
A(C ¹ ,C ¹¹ ,O ²⁰)	119.7(2)	124.8	5.1	115.1	-9.7	116.4	1.3
A(C ⁴ ,C ¹¹ ,O ²¹)	117.2(2)	113.4	-3.8	115.3	1.9	116.4	1.1
A(O ²¹ ,C ¹¹ ,O ²²)		121.7		126.2	-5.5	125.2	1.0

^aSee Ref. [23]. ^bAlgebraic deviations between experimental and theoretical values. ^cAlgebraic deviations between theoretical values of the anion and molecule. ^dAlgebraic deviations between theoretical values of the dianion and anion.

As seen, there is a good agreement between the experimental and the theoretical values. Exceptions (deviations of 0.04 Å or more) are typical only for the carboxy group itself, whose atoms participate directly in hydrogen bond formation. The data in the Table 4 make it possible to conclude that the conversion of the molecule studied into corresponding anion are localized within the corboxy/carboxylate groups and the adjacent C-Ph bond. As in the carboxylate anion has two equal C-O bonds, the C=O bond undergo a lengthening of 0.037 Å and the C-O one undergo shortening of 0.099 Å. The C-Ph bond in the anion is with 0.072 longer than the same bonds in the molecule, as the carboxylate group is much less conjugated with the aromatic ring that the carboxy group. The OCO bond angel in the anion is with 7.8° larger than those in the molecule, because of the repulsion of the electronic densities in the carboxylate groups. The bond length changes that accompany the conversion of the oxyanion into the dianion are take place both at the azanionic center and next to it - shortening of the Ph-N and N-C and bonds and lengthening of the C=O and C-CH₃ bonds (Table 4). The net electric charges of certain fragments of the species studied are shown in Scheme 2.



Scheme 2. Mulliken net electric charges over fragments of 4-acetamidobenzoic acid molecule, its anion and dianion.

The corresponding charge changes accompanying the conversion molecule - oxyanion - dianion (Table 5) are also quite informative, and show that:

1. The first (oxyanionic) charge remains localized mainly within the carboxylate group while.
2. The second (nitranionic) charge spreads over the whole species.

Table 5. Electric charge changes accompanying the conversion of the 4-acetamidobenzoic acid molecule into the oxyanion and of the oxyanion into the dianion.

Charge changes of the fragments	-COOH/ Ph	COO ⁻	NH/N-	COCH ₃
$q_{\text{oxyanion}} - q_{\text{molecule}}$	-0.71	-0.16	-0.01	-0.12
$q_{\text{dianion}} - q_{\text{oxyanion}}$	-0.05	-0.18	-0.35	-0.42

CONCLUSION

The spectral and structural changes, caused by the conversion of the 4-acetamidobenzoic acid into the corresponding anion and dianion have been studied by IR spectra and calculations at B3LYP/6-311+G(2df,p) level of theory. A comparison of calculated with measured infrared data can be used as a test for the reliability of the structural predictions for various molecules and anions of this and similar types. These predictions can be very useful in cases of molecules and ions for which experimental structural parameters are inaccessible or unknown. IR spectral changes, which take place as a result of the conversion of molecule into anions, were adequate predicted by same theoretical method.

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REFERENCES

1. C. Nortje, P. Jansen Van Rensburg, C. Cooke, E. Erasmus, *Bioanalysis*, **7**, 1211 (2015).
2. A. Szoke, W. L. Hayton, I. R. Schultz, *J. Pharm. Biomed. Anal.*, **16**, 69 (1997).
3. <https://www.wikigenes.org/e/chem/e/19266.html>
4. X. Yin, J. Fan, Z. H. Wang, S. R. Zheng, J. B. Tan, W. G. Zhang, *J. Solid State Chem.*, **184**, 1850 (2011) (and references therein).
5. J. Arriñez-Soriano, J. Albalad, J. Pérez-Carvajal, I. Imaz, F. Busqué, J. Juanhuix, D. Maspoch, *Cryst. Eng. Comm.*, **18**, 4196 (2016).

6. A. W. Hofmann, *Ber. Dtsch. Chem. Ges.*, **9**, 1302 (1876).
7. <http://sdbs.db.aist.go.jp>
8. J. Bennett, J. C. Maire, *J. Chem. Soc. B*, 309 (1971).
9. S. Ilieva, B. Hadjieva, B. Galabov, *J. Org. Chem.*, **67**, 6210 (2002).
10. L. H. Wang, J. X. Chen, *Microchim. Acta*, **168**, 93 (2010).
11. N. Juchnovski, I. G. Binev, in: The chemistry of functional groups, Suppl. C, S. Patai, Z. Rappoport (eds.), Wiley, New York, 1983.
12. A. D. Popova, E. A. Velcheva, B. A. Stamboliyska, *J. Mol. Struct.*, **1009**, 23 (2012).
13. E. A. Velcheva, B. A. Stamboliyska, P. J. Boyadjieva, *J. Mol. Struct.*, **963**, 57 (2010).
14. D. Popova, M. K. Georgieva, O. I. Petrov, K. V. Petrova, E. A. Velcheva, *Int. J. Quant. Chem.*, **107**, 1752 (2007).
15. S. Stoyanov, J. A. Tsenov, D. Y. Yancheva, *J. Mol. Struct.*, **42**, **1009** (2012).
16. S. Stoyanov, *J. Phys. Chem.*, **114**, 5149 (2010).
17. M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox, Gaussian 09, Revision A1, Gaussian Inc., Wallingford CT, 2009.
18. A. D. Becke, *J. Chem. Phys.*, **98**, 5648 (1993).
19. C. Lee, W. Yang, G. R. Parr, *Phys. Rev.*, **B37**, 785 (1998).
20. J. Tomasi, M. Perisco, *Chem. Rev.*, **94**, 2027 (1994).
21. J. Tomasi, B. Mennucci, E. J. Cancès, *J. Mol. Struct. (THEOCHEM)*, **464**, 211 (1999).
22. H. J. Michal, VEDA 4, Warsaw, 2004.
23. S. Kashino, T. Matsushita, T. Iwamoto, K. Yamaguchi, M. Haisa, *Acta Crystallogr.*, **C42**, 457 (1986).
24. E. Velcheva, Z. Glavcheva, B. Stamboliyska, *Bulg. Chem. Commun.*, **48**(3), 514 (2016).
25. V. M. Vlasov, L. A. Oshkina, *Org. React.*, **28**, (1993) 47.
26. I. G. Binev, P. J. Boyadjieva, Y. I. Binev, *J. Mol. Struct.*, **447**, 235 (1998).

ЕКСПЕРИМЕНТАЛНО И ТЕОРЕТИЧНО ИЗСЛЕДВАНЕ НА ИЧ СПЕКТРИ И СТРУКТУРА НА 4-АЦЕТАМИДОБЕНЗОЕНА КИСЕЛИНА (АЦЕДОБЕН), НЕЙНИТЕ ОКСИАНИОН И ДИАНИОН

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(Резюме)

Спектралните и структурни промени, протичащи от превръщането на 4-ацетамидобензоена киселина, $\text{HOOC-C}_6\text{H}_4\text{-NH-COCH}_3$, в съответния оксианион, $^-\text{OOC-C}_6\text{H}_4\text{-NH-COCH}_3$ и дианион, $^-\text{OOC-C}_6\text{H}_4\text{-N}^-\text{-COCH}_3$ са проследени посредством ИЧ спектри в ДМСО разтворител и DFT/B3LYP/6-311+G (2df,p) изчисления. Ефектът на разтворителя е отчетен по IEFPCM модела. Установено е, че *транс*-формите (по отношение на фениленовите и метиловите групи) са по-стабилни от *цис*-формите при всички изследвани частици. Промените, придружаващи първото депротониране, засягат главно карбоксилатния фрагмент, докато тези, които произтичат от второто депротониране, са разпределени върху целия дианион. Анализът на промените в атомните заряди показва, че над 70% от първия (оксианионен) заряд остава локализиран в карбоксилатния фрагмент. Вторият (азанионен) заряд се делокизира върху ацетилната ($0.42 e^-$), фенилната ($0.19 e^-$) и карбоксилатната ($0.05 e^-$) групи и азанионения център ($0.34 e^-$).