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Tautomeric polymorphism in salicylideneamine derivatives: an X-ray diffraction and solid-state NMR study

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Abstract

The crystal structure of the *N*-(3-hydroxysalicylidene)-4-methoxyaniline has been studied by single-crystal X-ray diffraction and solid-state NMR spectroscopy. This is the first example of a Schiff base derived from 3-hydroxysalicylaldehyde which displays in the asymmetric unit, four distinct molecules linked together in the crystal lattice by two types of intermolecular O–H···O hydrogen bonds and formed by two independent tetramers. The ^{13}C CPMAS NMR study corroborates the above results; the presence of different tautomeric equilibria in the same crystal structure is demonstrated and a qualitative estimation of the equilibrium mixture composition is given.

Keywords: Hydrogen bond; Polymorphism; ^{13}C MAS NMR; X-ray diffraction; Salicylideneamines

1. Introduction

N-salicylideneamines are compounds known to display proton transfer processes in the ground- and excited-states; extensive studies in both the solution and solid state can be found in the literature [1]. These derivatives exist in both phases as an equilibrium mixture of the enol-imine tautomer **a** and the keto-enamine form **b** (cf Fig. 1). In the solid state the influence on the proton transfer process of intermolecular interactions such as $\pi-\pi$ charge transfer [2] or hydrogen bonding [3–7] has been examined. This latter effect has been shown to be determinant in the tautomeric equilibrium of solid derivatives of 3-hydroxysalicylaldehyde [8,9]. These previous works also showed that the quinoid tautomer is the dominant species in compounds derived from alkyl amines. In the case of derivatives obtained from substituted anilines, the composition of the equilibrium mixture depends both on the nature of the substituents and type of intermolecular interactions. The compound *N*-(3-hydroxysalicylidene)-4-methoxyaniline (3MOSA) (Fig. 1) examined in this paper had been synthesized among others [8,9] in order to analyse the electronic effects of aniline substituents on the proton transfer process. Its unusual behaviour let us to carry out an extensive characterization by X-ray diffraction and high resolution ^{13}C solid-state NMR spectroscopy. The results obtained by both the methods are shown to be quite complementary and reveal the presence of

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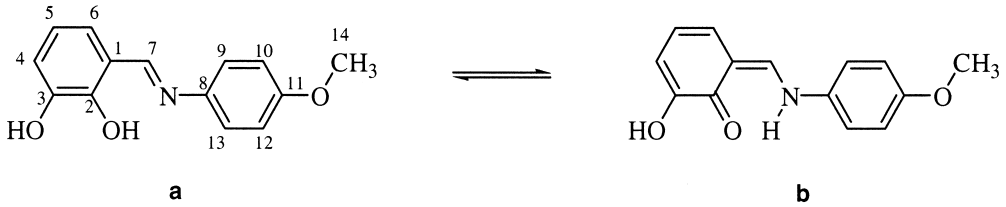

Fig. 1. Intramolecular hydrogen transfer in *N*-(3-hydroxysalicylidene)-4-methoxyaniline compound.

four molecular entities in the asymmetric unit each displaying a different contribution of phenol-imine and keto-enamine species.

2. Experimental

The compound 3MOSA was synthesized by condensation of 3-hydroxysalicylaldehyde with 4-methoxyaniline. Suitable crystals for X-ray analysis were obtained by slow evaporation of the solvent from a concentrated ethanolic solution. The X-ray measurements were performed on a Nonius Kappa CCD diffractometer [10] equipped with a graphite monochromated Mo-K_α radiation ($\lambda = 0.71073$ Å). The data were collected at room temperature using a phi scans method. The structure was solved and refined by using the maXus program [11]. Crystal data for 3MOSA: $C_{16}H_{13}NO_3$; $M_r = 243.26$ g mol^{-1}; triclinic P_{-1}; $a = 13.168(1)$, $b = 13.320(1)$, $c = 14.436(1)$ Å; $\alpha = 71.50(1)$, $\beta = 76.08(1)$, $\gamma = 82.85(1)°$; $V = 2327.0(9)$ Å^3; $Z = 8$; $D_0 = 1.388$ g cm^{-3}; and μ(Mo-K_α) $= 0.01$ mm^{-1}; $F(000) = 1024$; $T = 298$K; $R(F) = 0.039$; and $wR(F^2) = 0.050$; for 6656 observed reflections [$I > 3\sigma(I)$]. A list of fractional coordinates, anisotropic displacement parameters, bond lengths and angles in a CIF file has been deposited as Supplementary Material.

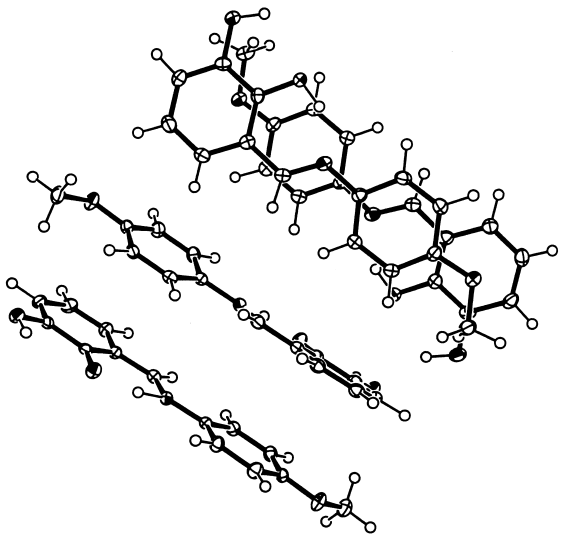

Fig. 2. ORTEP III view of the 3MOSA asymmetric unit.

^{1}H and ^{13}C solution measurements were performed on a Bruker AMX 400 NMR spectrometer operating at 400.13 and 100.62 MHz, respectively. Solid-state ^{13}C experiments with cross-polarization (CP) and magic angle spinning (MAS) were conducted at 75.49 MHz on a Bruker DSX 300 spectrometer using a high speed double bearing probe, zirconium rotors spun in dry air, at MAS rates around 5–6 kHz. The single-contact ^{13}C CPMAS spectra were recorded at room temperature with an optimized-contact time of 10 ms and also with a short-contact time of 20 μs. $\pi/2$ pulses of 3.8 μs and recycle delay of 10 s were used. The long CP time of 10 ms was optimized for this compound in order to obtain the best intensity ratios between the quaternary and protonated carbons. It is noteworthy that for these long-contact times the loss of polarization of the CH carbons is very small. For the short-contact time experiments, the CP time chosen for this derivative is much smaller than those usually used (about 200 μs); this was found necessary in order to avoid the presence of certain quaternary carbons still present after contact times of 100 μs in the spectra. The dipolar dephasing sequence with a refocusing π pulse was applied using a 40 μs dephasing window for the selective removal of signals from rigid protonated carbons. The calibration of the ^{13}C CPMAS spectra was realized by replacing the sample by a TMS filled rotor.

Table 1
Selected intramolecular interatomic distances and torsion angles with estimated standard deviations (ESDs) in parenthesis in 3MOSA molecules

	1	2	3	4
Bond lengths (Å)				
C1–C2	1.407(1)	1.401(1)	1.424(1)	1.423(1)
C2–C3	1.394(1)	1.388(1)	1.401(1)	1.406(1)
C3–C4	1.381(1)	1.381(1)	1.379(1)	1.375(1)
C4–C5	1.399(1)	1.399(1)	1.408(1)	1.402(1)
C5–C6	1.372(1)	1.372(1)	1.368(1)	1.362(1)
C1–C6	1.400(1)	1.409(1)	1.414(1)	1.418(1)
C2–O2	1.347(1)	1.359(1)	1.327(1)	1.325(1)
C3–O3	1.376(1)	1.379(1)	1.376(1)	1.377(1)
C1–C7	1.448(1)	1.445(1)	1.423(1)	1.416(1)
C7–N	1.285(1)	1.286(1)	1.305(1)	1.306(1)
N–C8	1.413(1)	1.420(1)	1.416(1)	1.416(1)
C8–C9	1.397(1)	1.395(1)	1.392(1)	1.389(1)
C9–C10	1.380(1)	1.380(1)	1.380(1)	1.384(1)
C10–C11	1.381(1)	1.383(1)	1.395(1)	1.388(1)
C11–C12	1.398(1)	1.395(1)	1.392(1)	1.394(1)
C12–C13	1.374(1)	1.374(1)	1.368(1)	1.381(1)
C13–C8	1.395(1)	1.393(1)	1.399(1)	1.395(1)
C11–O	1.368(1)	1.372(1)	1.365(1)	1.362(1)
O–C14	1.433(1)	1.437(1)	1.434(1)	1.438(1)
Hydrogen bond contacts (Å)				
O2···O3	2.723(1)	2.720(1)	2.751(1)	2.776(1)
O2···N	2.575(1)	2.592(1)	2.559(1)	2.595(1)
Torsion angle (°)				
C7–N–C8–C9	10.8(1)	1.0(1)	−18.1(1)	−3.2(1)

3. Results and discussion

3.1. X-ray diffraction analysis

The 3MOSA compound crystallizes in the triclinic P_{-1} space group with eight molecules constituting the unit cell. The presence in the asymmetric unit of four independent molecules (**1**–**4**) has, to our knowledge, never been reported in such types of derivatives. An ORTEP III [12] view of the asymmetric unit is shown in Fig. 2. Selected interatomic distances and torsion angles are collected in Table 1. An analysis of bond lengths and angles leads to the following results. The C–C bond lengths of the salicylidene ring of molecules **1** and **2** are comparable to those of an aromatic ring with electron delocalization; for molecules **3** and **4** however, [1.42 Å for C1–C2 and 1.36 Å for C5–C6] the presence of a localized double bond structure such as a quinoid ring seems probable. Similar variations are found for the C2–O2 distances. In molecules **1** and **2**, the measured values, 1.347(1) and 1.361(1) Å, respectively, are close to a C–O phenol distance [13], whereas shorter distances are found for molecules **3** and **4** [C2–O2: 1.327(1) and 1.325(1) Å, respectively]. For these two latter molecules, the smaller C2–O2 distance is accompanied by a shortening of C1–C7 [**3**: 1.423(1) and **4**: 1.416(1) Å] and a lengthening of C7–N. These variations suggest a significant increase of the quinoid character of entities **3** and **4**. The substituted aniline group, in all cases, keeps its aromatic character. The O2···N distances are in the range 2.559(1)–2.595(1) Å i.e. smaller than the sum of the van der Waals radii of oxygen and nitrogen [14]; this is indicative of the presence of strong intramolecular hydrogen bonds. No correlation between the values was observed for the O2···N distances and the different molecular structures can be established. Similarly, the very short O2···O3 distances (about 2.7 Å), suggest a second intramolecular hydrogen bond. These interactions ensure a quasi-planar conformation for the set formed by the salicylidene ring and the six-membered hydrogen-bonded pseudocycle N–C7–C1–C2–O2–H2. In all four cases, the dihedral angle between both the planes does not exceed 1°. Molecules **2** and **4** are nearly planar with a torsional angle C7–N–C8–C9 of 1.0(1) and −3.3(1)°, respectively, while the observed dihedral angles in **1** and **3** are equal to 10.3(1) and −18.1(1)°, respectively. It has been suggested that the planar conformation of *N*-salicylideneaniline molecules is a determining factor in the stabilization of keto-enamine tautomers [15]. In our case, the largest deviation from a planar structure is found for molecule **3** which, however, displays a contribution of quinoid species identical to that of planar molecule **4** (cf. similar C2–O2 distances, see Table 1). Generally, Schiff bases derived from 3-hydroxysalicylaldehyde exist as O3–H3···O2 hydrogen-bonded dimers in the solid state. Trimeric and polymeric associations have been found for cyclopropyl and *para*-tolyl R-groups [7]. In this case, the distinctive feature of our compound is the presence of four independent molecules with different molecular structures within the asymmetric unit. The resulting edifice is formed by two centrosymmetric tetramers, constituted by molecules **1**–**4**–**4**–**1** (Fig. 3a) and **2**–**3**–**3**–**2** (Fig. 3b), respectively. Each tetramer possesses two identical

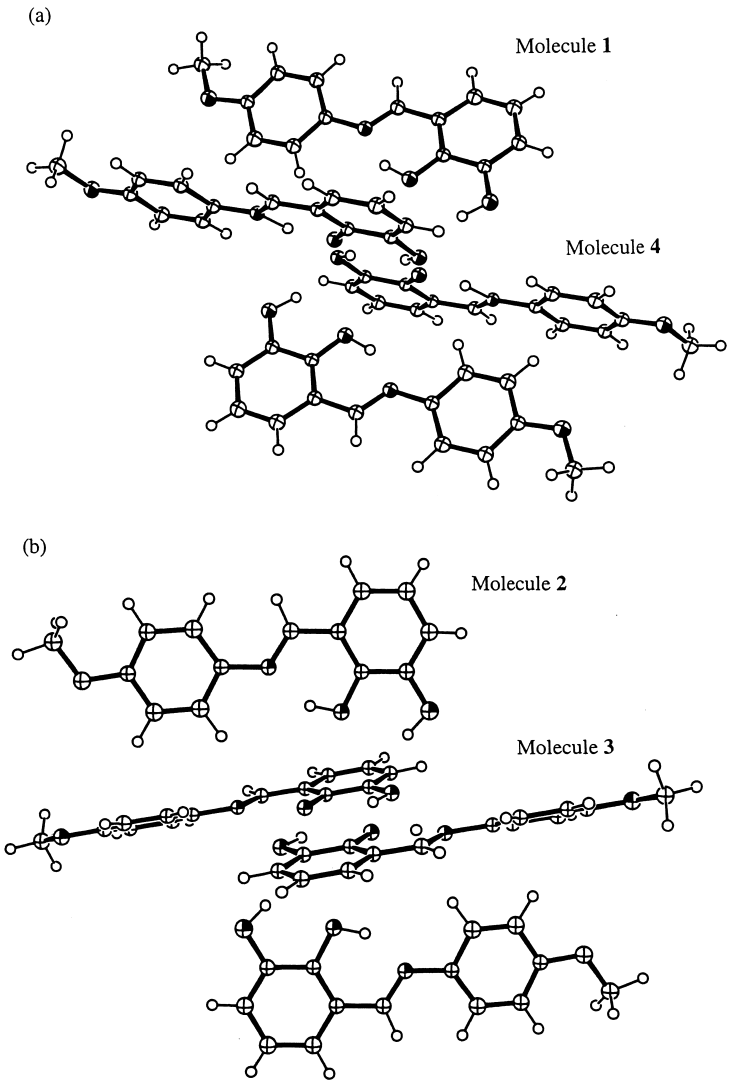

Fig. 3. ORTEP III representation of the tetramers constituted by. (a) Molecules **1** and **4**. (b) Molecules **2** and **3**.

Table 2
Intermolecular hydrogen bonds, distances in Å

Interaction	**3**–**3**[a]	**4**–**4**[b]	**3**–**2**[c]	**4**–**1**[d]
O2···O2	2.706(1)	2.701(1)	3.021(1)	2.868(1)
O2···O2	3.303(1)	3.456(1)		
O3···O3	4.344(1)	4.250(1)	2.843(1)	2.826(1)

[a] Symmetry code: $(-x, 1-y, 1-z)$.
[b] Symmetry code: $(1-x, 2-y, -z)$.
[c] Symmetry code: (x, y, z).
[d] Symmetry code: $(x, 1+y, z)$.

molecules (**4**–**4** and **3**–**3**) coupled by intermolecular O3–H3···O2 bridges. On each of these monomers, a third molecule (**1** on **4**, and **2** on **3**) is associated by an intermolecular O3–H3···O3 hydrogen bond. Distances between the atoms implicated in intermolecular hydrogen bonds are collected in Table 2. The shorter C2–O2 distances [1.327(1) Å for **3** and 1.325(1) Å for **4**] correspond to molecules associated as cyclic dimers by intermolecular hydrogen bond O3–H3···O2. The intermolecular O3–H3···O3 interactions present in molecules **1** and **2** give rise to a

Table 3
^{13}C NMR solution spectra assignment. Chemical shifts in ppm relative to TMS

Carbon	δ (ppm)
1	118.6
2	148.6
3	145.5
4	117.4
5	119.0
6	122.2
7	160.2
8	141.2
9–13	122.2
10–12	114.6
11	159.0
14	55.1

molecular structure closely related to a phenolic form; these molecules do not benefit from an interaction which stabilizes the keto-amine tautomer.

3.2. NMR results in solution

The ^{13}C spectral assignment of 3MOSA in solution (CCl_4) (see Table 3) was carried out by comparison with derivatives which have been previously studied [8,9]. The spectra are characteristic of a phenol-imine molecular structure, exclusive in aprotic, apolar solution. ^{1}H NMR spectra clearly show the different natures of both hydroxyl groups. The broad resonance observed at 12.5 ppm is characteristic of the H2 intramoleculary labile proton. The H3 proton signal is observed at 5.6 ppm as a broad line independent of concentration. This chemical shift indicates a less acidic character for H3 than for H2 and shows that H3 is involved in a weak intramolecular hydrogen bond.

3.3. Solid-state NMR

The ^{13}C CPMAS spectra illustrated in Fig. 4 are described in Table 4. The assignment of the ^{13}C lines was performed by using short-contact time and dipolar dephased CP spectra.

In the range 50–60 ppm, the four peaks with equal intensities ascribed to methoxy groups confirm the presence of four independent molecules in the asymmetric unit. In the short-contact time spectra, the overlapping resonances located between 110 and 130 ppm correspond to CH aromatic carbons. One observed at 154.7 and 156.5 ppm, two equally intense peaks assigned to the proton bearing carbon C7; they are indicative of two different electronic environments at the same molecular site. Thanks to the dipolar dephased CP spectra, the C1 signal is easily isolated from the overlapping CH aromatic peaks. It is consisted of four equally intense resonances, at 117.5, 118.0, 118.9 and 119.2 ppm. Consequently, the remaining lines observed between 130 and 160 ppm correspond to quaternary carbons: C2, C3, C8 and C11. In solution, carbon C8 is found at 141.2 ppm. An increase of quinoid tautomer contribution would move its chemical shift upfield [16]. Consequently, the two lines of equal intensity at 134.7 and 137.0 ppm will be ascribed to C8. In the region above 140 ppm, eight lines can be extracted by signal decomposition. The two intense lines at 159.5 and 159.8 ppm are assigned to the C11 carbons (bearing the methoxy groups) by comparison with their chemical shift values observed in solution. The six remaining signals in the region 144–158 ppm are consequently related to the C2 and C3 carbons. These results obtained for lines C1, C7 and C8 agree with the X-ray results and reveal the presence at the same atomic site of two different electronic environments. This suggests the presence of two molecular structures each characterized by different amounts of phenolic and quinoid tautomers. The chemical shift values of C2 and C3 should also be very indicative and allow a distinction between the two OH groups, O3–H3 and O2–H2. Because O3–H3 is involved in centrosymmetric dimers, the observed chemical shift of C3 should be of the order of 146–149 ppm as found in derivatives of substituted anilines [8,9]. It is then possible for molecules **3** and **4** to locate this line among the overlapping resonances found between 147.8 and 150 ppm. For molecules **1** and **2** however, the O3–H3 groups are involved in much weaker intermolecular hydrogen bonds so in this case a reasonable assignment would be to attribute the lines found at 144.1 and 145.8 ppm to C3 which is in accordance with values found in solution ($\delta = 145.5$ ppm, cf. Table 3). Concerning C2, previous results showed that its chemical shift is very sensitive to the tautomeric equilibrium position [17] and shifts to higher values as the contribution of the quinoid form increases. Therefore, the intense peak located at

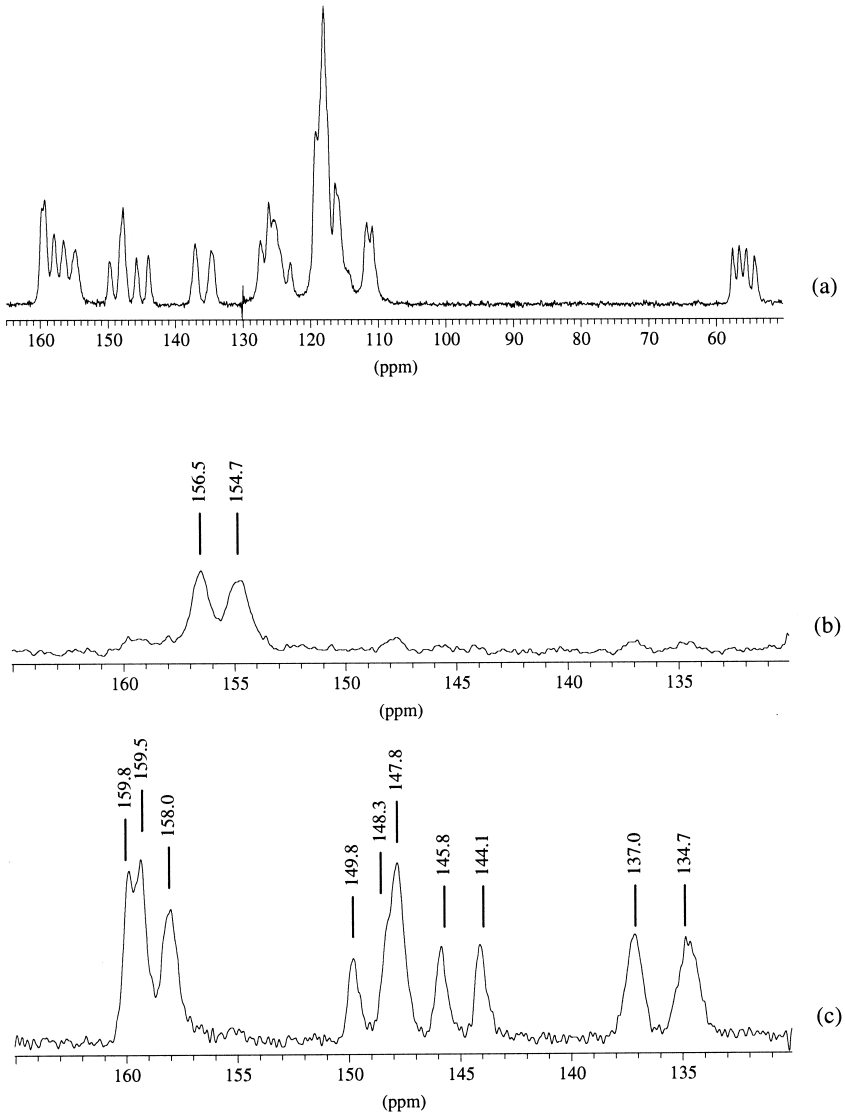

Fig. 4. ^{13}C CPMAS spectra of 3MOSA (a); short-contact time; (b) and dipolar dephasing (c) spectra of the region 130–165 ppm.

158.0 ppm correspond to C2 of molecules **3** and **4**. It was previously discussed that this chemical shift is the parameter of choice in order to study the position of the tautomeric equilibrium **a** = **b**. [8,9,16–18] For this purpose, the knowledge of the intrinsic values for the pure tautomeric forms is required. In the case of a fast exchange process, as IR results on crystalline 3-hydroxysalicylideneamines have shown [19,20], a standard procedure in order to obtain these values is to isolate the exchanging species by running low temperature NMR experiments. In our case, this proton transfer was found to be so fast, that these values could not be obtained [8,9]. Therefore, an estimation of the characteristic δ(C2) value of each tautomer has been made. In the *N*-salicylideneanilines, carbon C2 appears at 161 ppm in **a** form,

Table 4
^{13}C CPMAS spectra attribution. Chemical shifts in ppm relative to TMS

δ (ppm)	Assignment
54.3 55.5 56.5 57.5	C14 (molecules **1**–**4**)
117.5 118.0	C1(**3**) + C1(**4**)
118.9 119.2	C1(**1**) + C1(**2**)
134.7	C8(**3**) + C8(**4**)
137.0	C8(**1**) + C8(**2**)
144.1 145.8	C3(**1**) + C3(**2**)
147.8 148.3 149.8	C3(**3**) + C3(**4**) + C2(**1**) + C2(**2**)
154.7	C7(**3**) + C7(**4**)
156.5	C7(**1**) + C7(**2**)
158.0 159.3 159.9	C2(**3**) + C2(**4**) C11 (molecules **1**–**4**)

whereas the corresponding value in the **b** form is ca. 180 ppm [17]. These values cannot be used here owing to the substituent influence of the second OH group. For this substituent, a shielding effect of about −12 ppm can be assumed on the C2 chemical shift, as the observed chemical shift value found in solution is around 149 ppm for a phenol structure ($\delta =$ 148.6 ppm, cf. Table 3). So, a correction of the estimated quinoid value gives a chemical shift of about 168 ppm. With these assumptions the observed chemical shift provides a quinoid tautomer concentration for molecules **3** and **4** of the order of 47%. In solution, O2–H2 forms part of an intramolecular resonance-assisted hydrogen bond and the C2 line for a phenol-imine form usually appears at 149–150 ppm. Therefore for molecules **1** and **2** the two peaks at 148.3 and 149.8 ppm, respectively can be assigned to C2.

4. Conclusions

Compound 3MOSA displays a complex crystal structure constituted by centrosymmetric hydrogen-bonded tetramers which in the case of 3-hydroxysalicylideneamine derivatives has never been reported. These associations clearly illustrate the determining role of the intermolecular O2···H3–O3 hydrogen bonds in the stabilization of the keto-enamine tautomer. Our detailed structural analysis reveals the presence in the same crystal of four tautomeric equilibria for which X-ray diffraction only gives an average composition weighted by the concentration of each tautomer. For molecules **1** and **2**, which do not benefit of intermolecular interaction involving O2, the phenol-imine tautomer is dominant if not unique. In the case of molecules **3** and **4**, the quinoid tautomer concentration is significant and can be estimated to be around 47% according to the C2 chemical shift value. Moreover, it is noteworthy that the non-planarity of molecule **3** does not prevent the stabilization of the quinoid species whose concentration is similar to that of planar molecule **4**. A destabilization of the quinoid tautomer induced by a non-planar molecular conformation seems to be compensated by intermolecular interactions. Finally, these results compared to those obtained for compounds of a same derivatives series [8,9] highlight the important variation in tautomeric equilibrium position which can be expected in the solid state.

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Supplementary Data relating to this article are deposited with the B.L.L.D. as Supplementary Publication No. SUP26642.

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