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Structural studies of 1-(2-hydroxy-4-bromophenyl)-4-methyl-4-imidazolin-2-ones

Michal K. Cyrański,[1]* Iwona Wawer,[2] Agnieszka Zielińska,[2] Agnieszka Mrozek,[3] Vera Koleva[4] and Christina Lozanova[4]

[1]Department of Chemistry, University of Warsaw, Pasteura 1, 02 093 Warsaw, Poland
[2]Department of Physical Chemistry, Faculty of Pharmacy, Banacha 1,02-097 Warsaw, Poland
[3]Institute of General and Ecological Chemistry, Technical University of Łódź, Żwirki 36, 90 362 Łódź, Poland
[4]Department of Chemistry, University of Sofia, Sofia 1126, Bulgaria

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ABSTRACT: The crystal structure of 1-(2-hydroxy-4-bromophenyl)-3-methyl-4-methyl-4-imidazolin-2-one was determined by x-ray diffraction. The structure is stabilized by intermolecular hydrogen bonds formed between the 2-hydroxy and central groups. Molecular modelling including *ab initio* calculations at the HF/6–31+G** level revealed that in the gas phase the molecule is stabilized by an intramolecular hydrogen bond. The derivatives with 3-alkyl, benzyl and phenyl substituents were studied by ^{13}C NMR including solid-state ^{13}C CP/MAS NMR [for 1-(2-hydroxy-4-bromophenyl)-3-methyl-4-methyl-4-imidazolin-2-one] and FT-IR methods. The differences in chemical shifts $\Delta = \delta$liquid $- \delta$solid are significant for aromatic carbons C(3) (−2.9 ppm), C(4) (3.6 ppm) and C(5) (−3.9 ppm) and, on the other side of the imidazoline ring, of C(7) (−1.5 ppm). These carbons are adjacent to N(1)—C(4), and are subject to the largest changes of the environment during reorientation of the imidazolin-2-one moiety.

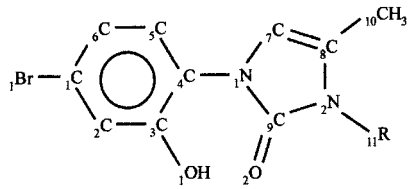
KEYWORDS: 1-aryl-4-imidazolin-2-ones; hydrogen bond; aromaticity; x-ray diffraction; *ab initio* calculations; ^{13}C solid-state NMR; infrared spectroscopy

INTRODUCTION

The aryl-4-imidazolin-2-ones with various substituents, including imidazoline rings, exhibit anticonvulsant activity.[1] They have multiple agrochemical and pharmaceutical applications.[2] Some of them exhibit bactericidal and herbicidal activity.[2] In order to relate the structural features of such compounds to their biological properties, a proper description of their conformational preferences is a useful first step. The crystal structures of only a few derivatives of imidazolin-2-ones have been reported so far.[2–12]

The derivatives of imidazolin-2-ones are interesting model compounds for the study of structural effects because their properties depend on the mutual orientation of the phenyl and imidazoline rings. Furthermore, the *o*-hydroxy group on the phenyl ring can be involved in intra- or intermolecular hydrogen bonding.

The structures and conformations in solution and in the solid state of four derivatives of (2-hydroxy-4-bromophenyl)-4-methyl-4-imidazolin-2-one (cf. Scheme **1**) were studied using ^{13}C NMR spectroscopy. Since the ^{1}H NMR spectra in the solid state were not sufficiently resolved, the information about hydrogen bonding was completed by solid-state Fourier transform infrared (FT-IR) spectroscopy. In the case of 1-(2-hydroxy-4-bromophenyl)-3-methyl-4-methyl-4-imidazolin-2-one (**1**) the information on the mutual orientation of the rings and possible stabilization of the molecule via hydrogen bonds was obtained from x-ray diffraction. Molecular modelling including *ab initio* calculations[13] completed the studies.



1 R= CH_3 **3** R= CH_2-C_6H_5

2 R= C_4H_9 **4** R= C_6H_5

Scheme 1. The compounds studied with numbering of atoms

Correspondence to: M. K. Cyrański, Department of Chemistry, University of Warsaw, Pasteura 1, 02 093 Warsaw, Poland.
E-mail: chamis@chem.uw.edu.pl

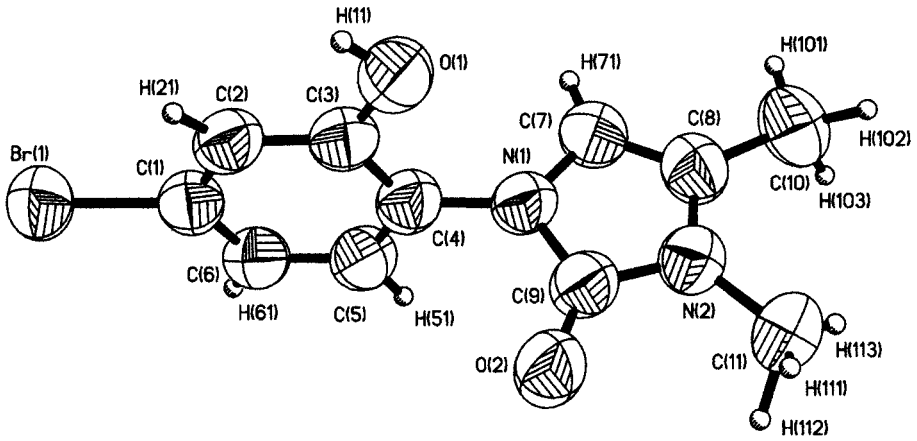


Figure 1. Molecular structure of 1-(2-hydroxy-4-bromophenyl)-3-methyl-4-methyl-4-imidazolin-2-one. Displacement ellipsoids are drawn at the 50% probability level

EXPERIMENTAL

The 1,3,4-substituted 4-imidazolin-2-ones were synthesized from aryloxazolon-3-yl-propanone, as reported previously.[14] Monocrystals of 1-(2-hydroxy-4-bromophenyl)-3-methyl-4-methyl-4-imidazolin-2-one suitable for further x-ray analysis were obtained by slow evaporation from a methanol solution. A single-crystal x-ray diffraction measurement was carried out using a KUMA diffractometer with graphite monochromatic Cu Kα radiation. The data were collected at room temperature using $\omega-2\theta$ scan techniques. The intensity of the control reflections for the compound varied by less than 5% and a linear correction factor was applied to account for this effect. The data were corrected for Lorentz and polarization effects, and an absorption correction (empirical) was also applied. The structure was solved by direct methods[15] and then refined by the full matrix least-squares technique on F^2 using SHELXL.[16] Hydrogen atoms were located from a difference map and refined isotropically. Atomic scattering factors were taken from the International Tables.[17] $C_{11}H_{11}BrN_2O_2$, colourless crystal, $0.2 \times 0.2 \times 0.25$ mm (grown from methanol), $M_1 = 283.13$, monoclinic, space group $P2_1/c$, $a = 10.869(2)$ Å, $b = 13.914(3)$ Å, $c = 7.467(1)$ Å, $\beta = 97.31(3)°$, $V = 1120.1(4)$ Å^3, $Z = 4$, $D_x = 1.679$ g cm^{-3}, absorption coefficient $\mu = 4.910$ mm^{-1}, absorption correction $T_{min} = 0.9522$, $T_{max} = 1.0202$. The collected data range was $4.10 < \Theta < 80.08$ ($0 \leq h \leq 13$, $-16 \leq k \leq 0$, $-8 \leq l \leq 8$); 2399 reflections collected, 2294 [R(int) = 0.0805] independent reflections, goodness-of-fit on $F^2 = 1.177$; final $R = 0.0602$, $wR^2 = 0.1955$ [for all 1939 $F_o > 4\sigma(F_o)$], $R = 0.0672$ and $wR^2 = 0.2156$ (for all data). Weight = $1/[\sigma^2(F_o^2) + (0.1558P)^2 + 0.00P]$, where $P = (F_o^2 + 2F_c^2)/3$. Minimum and maximum difference electron densities were 0.640 and -0.613 e A^{-3}. Structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry are deposited in the Cambridge Structural Database.

The ^{13}C NMR spectra were recorded in DMSO-d_6 on a Varian Gemini 200 spectrometer. The solid-state ^{13}C NMR spectrum was measured on a Bruker MSL 300 spectrometer at 75.5 MHz using cross-polarization (CP) and magic angle spinning (MAS) techniques. The powdered sample was placed in a ZrO_2 rotor and spun at 3.2–3.8 kHz. The chemical shifts were calibrated indirectly through the glycine CO signal observed at 176.3 ppm relative to TMS.

Infrared spectra were recorded from KBr pellets using a Nicolet Magna IR 550 spectrometer equipped with a data station.

The *ab initio* calculations of geometry optimization (at HF/6 – 31 + G**) and magnetic properties (at GIAO-HF/6 – 31 + G*) were performed using Gaussian 94.[13]

RESULTS AND DISCUSSION

The ORTEP view with the numbering of atoms and the crystal structure of the molecule are shown in Figs 1 and 2, respectively, while selected bond lengths with their estimated standard deviations are given in Table 1.

The crystal structure of 1-(2-hydroxy-4-bromophenyl)-3-methyl-4-methyl-4-imidazolin-2-one is stabilised by an O(1)—H(11)···O(2)′ intermolecular hydrogen bond with intermolecular distance O(1)˙O(2)′ = 2.666(4) Å, H(11)···O(2)′ = 1.90(6) Å and angle O(1)—H(11)···O(2)′ = 35.9(5)°. Other intermolecular contacts stabilizing the crystal structure are formed with distance C(11)···O(2)′ = 3.342(8) Å and angle C(11)—H(11)···O(2)′ = 60.7(2.1)°. Both fragments of the molecule, phenyl and imidazolin-2-one rings, are planar within experimental error. The angle between the best planes of these fragments is 88.9(2)°. The almost perpendicular orientation means that the conjugation of the π-electrons of the two systems is not efficient. The four carbon–nitrogen bonds are slightly shorter than the typical single bond and longer than the typical double CN

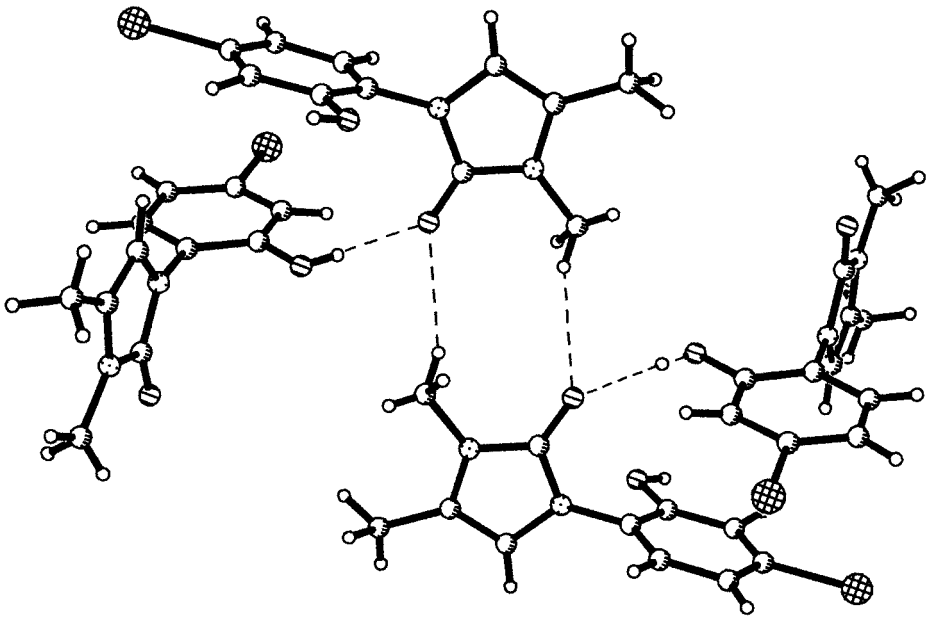


Figure 2. Intermolecular interactions in the crystal lattice

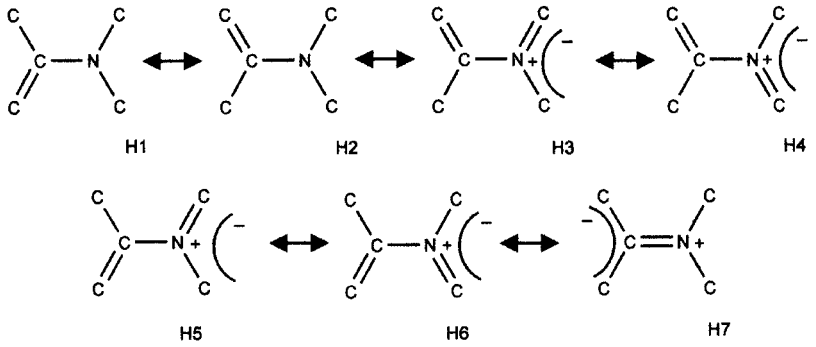
bond indicating, that the N(1)—CO—N(2) fragment contains delocalized electrons similarly as in the urea fragment. The comparison of CN bond lengths with their optimal values[18] may be a measure of delocalization of π-electrons over a C(7)—N(1)—CO—N(2)—C(8) fragment. Applying the geometry-based HOMA index[19] to check the aromatic character of the imidazolin-2-one ring yields a value of 0.767, indicating its substantial aromaticity (the HOMA index is normalized in such a way as to give 1 for a fully aromatic system and 0 for a non-aromatic system). The dearomatization of the ring is mainly due to the GEO term,[19] which means that the bond alternation is the main factor which is responsible for the lowering of aromaticity. Also, the magnetic index NICS developed by Schleyer *et al.*[20] calculated at the imidazoline ring center at GIAO-HF/6 – 31 + G* shows a highly aromatic character of the fragment: NICS = −9.2 ppm compared with the phenyl fragment, NICS = −11.2 ppm. [NICS is defined as the negative value of the absolute shielding computed at a ring centre (or some other interesting point of the system); rings with negative NICS values qualify as aromatic, and the more negative is NICS, the more aromatic are the rings]

In the case of the N(1) nitrogen atom, the lone electron pair interacts strongly with π-electrons of CO and may additionally interact with the π-electrons of the phenyl ring, which diminishes the interaction with the CO group. The double bond character of N(1)—C(4) is therefore of special interest, since it can be related to the rotational barrier around this bond and to the flexibility of this molecular fragment. Application of the HOSE model[21,22] enabled us to estimate the relative weight of a structure with a double bond between C(4) and N(1) among seven canonical structures describing this molecular fragment (Scheme **2**). The contribution of H(7) of 8.7% appeared to be the smallest one, indicating that the π-electron interactions between the phenyl and imidazoline rings do not seem to be very effective.

In order to establish the preferred conformation of the rings, a full 10° steps conformational analysis was performed for 1-(2-hydroxy-4-phenyl)-3-methyl-4-methyl-4-imidazolin-2-one (starting from the experimen-

Table 1. Selected bond lengths (Å), angles (°) and torsion angles (°) with standard deviations (in parentheses) for 1-(2-hydroxy-4-bromophenyl)-3-methyl-4-methyl-4-imidazolin-2-one

N(1)—C(9)	1.367(5)	N(2)—C(9)—N(1)	105.2(3)
C(9)—O(2)	1.240(5)	C(9)—N(2)—C(8)	110.5(3)
N(2)—C(9)	1.367(5)	C(7)—C(8)—N(2)	107.4(4)
N(2)—C(8)	1.373(6)	C(8)—C(7)—N(1)	107.3(4)
C(8)—C(7)	1.345(6)	C(7)—N(1)—C(4)—C(3)	−91.7(5)
N(1)—C(7)	1.394(5)	C(7)—N(1)—C(4)—C(5)	87.7(6)
N(1)—C(4)	1.426(4)	C(9)—N(1)—C(4)—C(5)	−85.5(5)
C(9)—N(1)—C(7)	109.5(3)	C(9)—N(1)—C(4)—C(3)	95.1(5)



Scheme 2. Canonical structures for the linkage of two rings

tal geometry of the bromo derivative) allowing rotation around the C(4)—N(1) and C(3)—O(1) bonds. The revealed eight conformers next used as starting points for *ab initio* optimizations (at HF/6 – 31 + G**) led to only one conformer, the lowest energy system allowing the formation of an intramolecular hydrogen bond. For comparison, we also calculated the conformer with perpendicular imidazoline and phenyl rings (in the frozen conformation similarly to the crystal structure). No imaginary wavenumbers were found in either case. The difference in energy between the fully optimised and the perpendicular (frozen) conformation is as high as 23.8 kJ mol^{-1} (zero point energy corrected), indicating the possibility of an additional competitive structure stabilisation via intramolecular H-bond formation. The H(11)···O(2) distance is very short (1.847 Å) and the angle between the best planes of the rings is 45.3°. *Ab initio* calculations were performed for isolated system, i.e. the results refere to the gas phase and might be compared with the conformations present in a dilut solution in a non-polar, weak interacting solvent. Unfortunately, because of insolubility of the compounds in less polar solvents such as $CDCl_3$, the ^{13}C NMR spectra were recorded in DMSO. This solvent is a strong proton acceptor and the intermolecular hydrogen bonds present in the solid state are probably broken in this solvent and the OH groups are bonded to the oxygen atom of the solvent.

The ^{13}C NMR chemical shifts for compounds **1** –**4** are given in Table 2. The resonances of phenyl carbons bearing the substituents are easily recognized, and the remaining CH carbons were assigned using the 2D $^{1}H/^{13}C$ HETCOR spectra analysed only for a narrow range of aromatics. The chemical shifts of aromatic carbons are in agreement with those found for the 2-hydroxy-4-bromophenyl substituent of ureas.[23] Some influence of the substituent at N(2) can be seen on the aromatic carbon chemical shifts; the largest changes appear for the imidazolin-2-one carbons upon introducing a phenyl ring, because its π-electrons conjugate with those of the imidazolin-2-one ring. A corresponding increase in shielding of the neighbouring C(9) and C(8) and deshielding of C(7) of ca 1.5 ppm is observed.

A comparison of the solid-state and solution chemical shifts allows the identification of rigid and flexible fragments of the structure. For rigid systems, the similar aromatic ring and also the imidazoline ring [with a C(7)═C(8) double bond and a delocalized N(1)—CO—N(2) fragment], the solution conformation should be close to that in the solid state, whereas the flexible fragments are assumed to undergo larger changes of screening. Inspection of solid-state chemical shifts for **1** shows that the differences $\Delta = \delta_{liquid} - \delta_{solid}$ are significant for aromatic carbons near to C(4)—N(1), which are subject to the largest changes of the environment during reorientation of the imidazolin-2-one residue. Frozen rotation around the C(4)—N(1) bond results in deshielding of C(3) (−2.9 ppm) and C(5) (−3.9 ppm), increased shielding of C(4) (3.6 ppm) and on the other side deshielding of C(7) (−1.5 ppm) of the imidazoline ring.

Table 2. Selected ^{13}C chemical shifts of 1-aryl-4-methyl-imidazolin-2-ones **1** –**4** in DMSO-d_6 solution and in the solid state (in parentheses), and differences Δ(ppm) = $\delta_{liquid} - \delta_{solid}$

Compound	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	C(7)	C(8)	C(9)	C(10)
1	119.46	120.12	152.14	124.34	127.70	122.17	107.28	120.08	152.14	9.70
	(120.8)	(120.8)	(155.0)	(120.8)	(131.6)	(120.8)	(108.8)	(120.8)	(152.8)	(10.2)
Δ	−1.3	−0.7	−2.9	3.6	−3.9	1.4	−1.5	−0.7	−0.7	−0.5
2	119.84	121.9	151.21	122.09	123.75	123.47	107.0	123.04	154.03	10.18
3	119.84	121.09	151.21	122.18	123.75	123.15	107.00	123.04	154.03	9.81
4	119.90	119.58	151.52	121.96	127.72	123.68	109.23	118.82	152.68	10.62

The other source of differences in chemical shifts may be due to different intra- and intermolecular contacts in the two phases.

The FT-IR spectra of solid compounds **1–4** were recorded in order to monitor the hydrogen bond network. No sharp OH stretching band at ca 3600 cm^{-1} characteristic of monomeric OH was observed, and the broad and strong absorption in the range 2500–3400 cm^{-1}, with a maximum at approximately 3000 cm^{-1}, confirms that in all the compounds studied the OH group is involved in hydrogen bonding. It is possible that this hydrogen bond is intermolecular, as in **1**.

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