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# NMR investigation of hydrogen bonding and 1,3-tautomerism in 2-(2-hydroxy-5-substituted-aryl) benzimidazoles

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**The 1,3-tautomerism associated with 2-(2-hydroxy-5-substituted-aryl)benzimidazoles was studied in different solvents. The effect of hydrogen bonding involving the hydroxyl group of the 2-aryl ring on the tautomerism was investigated using NMR spectroscopy. The influence of the solvent concentration on 2-(2-hydroxy-5-chloroaryl)benzimidazole was studied in acetone-$d_6$ and DMSO-$d_6$.** 

**KEYWORDS:** NMR; $^1$H NMR; $^{13}$C NMR; 2D techniques; dynamic NMR; 5-substituted 2-(2-hydroxyaryl)benzimidazoles

## INTRODUCTION

The chemistry[1–4] of suitably substituted benzimidazoles is very important as some benzimidazole derivatives possess anticancer,[5] antiparasitic,[6] antitumour,[7] analgesic[8] and antipoliovirus[9] activities. The 1,3-tautomerism associated with benzimidazoles is a very popular topic and the existence of this tautomerism has been proved by several approaches, including NMR spectroscopy.[10] This 1,3-migration is not found when the imidazole hydrogen is replaced by other substituents such as an alkyl group[11] or under special circumstances where the hydrogen migration is affected by inter- and/or intramolecular hydrogen bonding.

We have recently synthesized a set of 2-(2-hydroxy-5-substituted-aryl)benzoxazoles[12] and showed the presence of hydrogen bonding in the compounds between the hydroxy hydrogen and oxazole nitrogen of the benzoxazole ring. It would be interesting to find out in analogous benzimidazoles whether (i) the hydroxyl hydrogen of the 2-aryl group is involved in hydrogen bonding with the imino nitrogen or (ii) the hydroxyl oxygen is involved in hydrogen bonding with the NH of benzimidazole or (iii) there is no hydrogen bonding, in which case the system will have a free tautomeric existence involving 1,3-hydrogen migration. To the best of our knowledge, no systematic study in this respect has been carried out on the related compounds. Hence we planned to prepare a set of 2-(2-hydroxy-5-substituted-aryl)benzimidazoles (**2**), most of which are new, and to investigate the NMR spectra in solution to address the above hypotheses.

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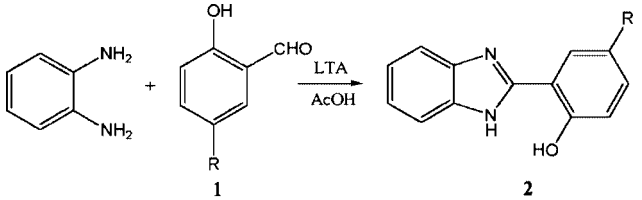
## RESULTS AND DISCUSSION

The target compounds **2** were synthesized by the lead tetraacetate oxidation of the imines prepared from 2-hydroxy-5-substituted-benzaldehydes (**1**) with *o*-phenylenediamine (Scheme 1). It has been shown that the simple benzaldehyde on reaction with *o*-phenylenediamine in a 1 : 1 molar ratio gives the monoimine, which was then subjected to lead tetraacetate oxidation to give benzimidazole.[13] However, in the case of 2-hydroxy-5-substituted-benzaldehydes, even in a 1 : 1 molar ratio of *o*-phenylenediamine and aldehydes, the diimine **3** and not the monoimine **4** was obtained in moderate yield.

The treatment of *o*-phenylenediamine and the aldehyde in a 1 : 2 ratio, of course, leads to the diimine **3** in very good yield. Upon treatment of the diimine with lead tetraacetate in acetic acid, surprisingly the target benzimidazole **2** was obtained in good yield. Probably the initial hydrolysis of the diimine **3** to monoimine **4** with acetic acid would have occurred, the latter subsequently being oxidized to the target compound **2**. The imine **3** has not been separated in many cases and the reaction product of 1 : 1 *o*-phenylenediamine and aldehyde has been treated with LTA–AcOH to obtain

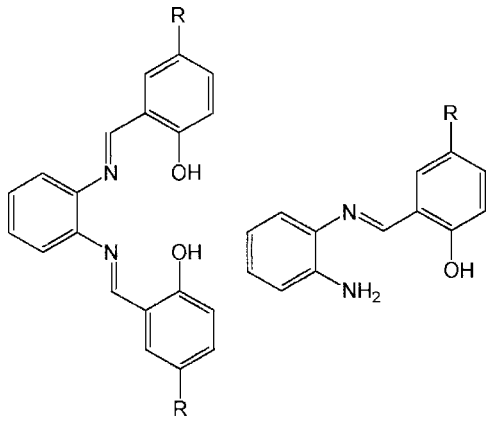



**1** **2**

| R | R |
|---|---|
| **a** *t*-Butyl | **e** Cumyl |
| **b** *i*-Propyl | **f** Ethyl |
| **c** *t*-Amyl | **g** Cl |
| **d** Ph | **h** Br |

**Scheme 1**

**2** directly. The monoimine **4** has not been separated in any case. The $^1$H NMR and $^{13}$C NMR spectral data for **2** are given in Tables 1 and 2, respectively.




**3** **4**

To analyse the effect of hydrogen bonding, the 2-(2-methoxy-5-*tert*-butylaryl)benzimidazole **5** was also prepared by treating *o*-phenylenediamine with 5-*tert*-butyl-2-methoxybenzaldehyde, which in turn was prepared from 5-*tert*-butyl-2-hydroxybenzaldehyde by methylation with dimethyl sulfate. It must be mentioned that the treatment of *O*-methylated salicylaldehyde with *o*-phenylenediamine in a 1 : 2 ratio gives not the monoimine or diimine but a benzimidazole derivative, **6a**. The formation of **6a** has been accounted for by a reaction involving a hydride migration mechanism.[14] Treatment of 5-*tert*-butyl-2-methoxybenzaldehyde with *o*-phenylenediamine gives only 40% of **6b** (identified by the $^1$H NMR spectrum of the mixture of **5** and **6b** from the comparison of the intensity of the N-$CH_2$ signal at $\delta$ 5.23 ppm with that of the methoxy signals at $\delta$ 3.58, 3.78 and 4.05 ppm) and the remaining being oxidized product **5**. Formation of

**Table 1.** $^1$H NMR chemical shifts[a] of benzimidazoles **2** and **5**

| Compound | Solvent | 3′ | 4′ | 6′ | 4,7 | 5,6 | NH, OH[b] | R |
|---|---|---|---|---|---|---|---|---|
| **2a** | $CDCl_3$ | 7.08, d, (8.7 Hz) | 7.43, dd, (8.7, 2.4 Hz) | 7.56, d, (2.4 Hz) | 7.70, b | 7.31, dd, (6.0, 3.3 Hz) | 9.60, b 13.00, b | 1.37, s, 9H |
| | Acetone-$d_6$ | 6.98, d, (8.7 Hz) | 7.47, dd, (8.7, 2.4 Hz) | 8.05, d, (2.4 Hz) | 7.65, dd, (6.0, 3.3 Hz) | 7.29, dd, (6.0, 3.3 Hz) | 12.00, b | 1.36, s, 9H |
| | DMSO-$d_6$ | 7.00, d, (8.7 Hz) | 7.36, dd, (8.7, 2.4 Hz) | 7.99, d, (2.4 Hz) | 7.60, dd, (6.0, 3.3 Hz) | 7.25, dd, (6.0, 3.3 Hz) | 13.00, b | 1.38, s, 9H |
| **2b** | $CDCl_3$ | 7.07, d, (8.4 Hz) | 7.24, dd, (8.4, 2.1 Hz) | 7.45, d, (2.1 Hz) | 7.63, b | 7.30, dd, (6.0, 3.0 Hz) | 9.70, b 13.00, b | 1.27, d, 6H, (6.9 Hz) 2.90, sep, 1H, (6.9 Hz) |
| | Acetone-$d_6$ | 6.97, d, (8.4 Hz) | 7.27, dd, (8.4, 2.1 Hz) | 7.99, d, (2.1 Hz) | 7.65, b | 7.29, dd, (6.3, 3.3 Hz) | 12.70, b | 1.27, d, 6H, (6.9 Hz) 2.92, sep, 1H, (6.9 Hz) |
| | DMSO-$d_6$ | 7.01, d, (8.4Hz) | 7.19, dd, (8.4, 2.1 Hz) | 7.81, d, (2.1 Hz) | 7.60, b | 7.24, dd, (6.0, 3.0 Hz) | 12.80, b | 1.26, d, 6H, (6.9 Hz) 2.89, sep, 1H, (6.9 Hz) |
| **2c** | $CDCl_3$ | 7.07, d, (8.7 Hz) | 7.34, dd, (8.7, 2.1 Hz) | 7.52, d, (2.1 Hz) | 7.64, b | 7.31, dd, (6.0, 3.0 Hz) | — | 0.70, t, 3H, (7.5 Hz) 1.32, s, 6H, 1.66, q, 2H, (7.5 Hz) |
| | Acetone-$d_6$ | 6.99, d, (8.7 Hz) | 7.39, dd, (8.7, 2.1 Hz) | 8.00, d, (2.4 Hz) | 7.65, dd, (6.0, 3.3 Hz) | 7.28, dd, (6.0, 3.3 Hz) | 12.70, b | 0.70, t, 3H, (7.5 Hz) 1.32, s, 6H, 1.69, q, 2H, (7.5 Hz) |
| | DMSO-$d_6$ | 7.03, d, (8.7 Hz) | 7.30, dd, (8.7, 2.1 Hz) | 7.86, d, (2.1 Hz) | 7.60, dd, (6.0, 3.3 Hz) | 7.25, dd, (6.0, 3.0 Hz) | — | 0.69, t, 3H, (7.5 Hz) 1.31, s, 6H, 1.65, q, 2H, (7.5 Hz) |
| **2d** | $CDCl_3$ | 7.21, d, (8.4 Hz) | 7.61, m | 7.79, d, (2.1 Hz) | 7.85, b | 7.33, dd, (6.0, 3.0 Hz) | 9.60, b 13.2, b | *ortho*-7.61, m *meta*-7.46, t, (7.2 Hz) *para*-7.35, tt, (7.2, 1.2 Hz) |
| | Acetone-$d_6$ | 7.14, d, (8.4 Hz) | 7.65–7.72, m | 8.36, d, (2.4 Hz) | 7.65–7.72, m | 7.30, dd, (6.0, 3.3 Hz) | 12.90, b | *ortho*-7.65–7.72, m *meta*-7.44, t, (7.5 Hz) *para*-7.32, tt, (7.5, 1.2 Hz) |
| | DMSO-$d_6$ | 7.13, d, (8.7 Hz) | 7.56, dd, (8.7, 2.1 Hz) | 8.30, d, (2.1 Hz) | 7.61, dd, (6.0, 3.3 Hz) | 7.25, dd, (6.0, 3.3 Hz) | 12.50, b | *ortho*-7.65, dd, (7.8, 1.2 Hz) *meta*-7.42, t, (7.8 Hz) *para*-7.30, tt, (7.8, 1.2 Hz) |
| **2e** | $CDCl_3$ | 7.05, d, (8.4 Hz) | 7.26–7.31, m | 7.40, d, (2.1 Hz) | 7.60, b | 7.26–7.31, m | — | 1.72, s, 6H 7.26–7.31, 5H, m |
| | Acetone-$d_6$ | 6.81, d, (8.7 Hz) | 7.03, dd, (8.7, 2.4 Hz) | 7.88, d, (2.4 Hz) | 7.47, b | 7.10–7.15, m | 12.70, b | 1.56, s, 6H 7.10–7.15, 5H, m |
| | DMSO-$d_6$ | 6.90, d, (8.7 Hz) | 7.05, dd, (8.7, 2.4 Hz) | 7.84, d, (2.4 Hz) | 7.49, dd, (6.0, 3.0 Hz) | 7.11–7.20, m | | 1.61, s, 6H 7.11–7.20, m |

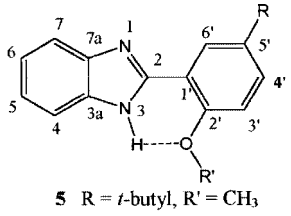
**Table 1.** (*Continued*)

| Compound | Solvent | 3′ | 4′ | 6′ | 4,7 | 5,6 | NH, OH[b] | R |
|---|---|---|---|---|---|---|---|---|
| **2f** | $CDCl_3$ | 7.06, d, (8.4 Hz) | 7.21, dd, (8.4, 2.1 Hz) | 7.42, d, (2.1 Hz) | 7.63, b | 7.31, dd, (6.0, 3.0 Hz) | 9.50, b 13.0, b | 1.26, t, 3H, (7.5 Hz) 2.65, q, 2H, (7.5 Hz) |
| | Acetone-$d_6$ | 6.97, d, (8.4 Hz) | 7.22, dd, (8.4, 2.1 Hz) | 7.85, d, (2.1 Hz) | 7.65, dd, (6.0, 3.3 Hz) | 7.28, dd, (6.0, 3.3 Hz) | 12.20, b | 1.23, t, 3H, (7.5 Hz) 2.63, q, 2H, (7.5 Hz) |
| | DMSO-$d_6$ | 7.00, d, (8.4 Hz) | 7.14, dd, (8.4, 2.1 Hz) | 7.78, d, (2.1 Hz) | 7.59, dd, (6.0, 3.0 Hz) | 7.23, dd, (6.0, 3.0 Hz) | 12.00, b | 1.24, t, 3H, (7.5 Hz) 2.61, q, 2H, (7.5 Hz) |
| **2g** | $CDCl_3$ | 7.08, d, (9.0 Hz) | 7.29, dd, (9.0, 2.4 Hz) | 7.59, d, (2.4 Hz) | 7.52, b(H-4) 7.78, b (H-7) | 7.35, dd, (6.3, 3.3 Hz) | 9.60, b | — |
| | Acetone-$d_6$ | 7.07, d, (8.7 Hz) | 7.38, dd, (8.7, 2.4 Hz) | 8.06, d, (2.4 Hz) | 7.69, dd, (6.0, 3.3 Hz) | 7.33, dd, (6.0, 3.3 Hz) | 12.90, b | — |
| | DMSO-$d_6$ | 7.01, d, (9.0 Hz) | 7.26, dd, (9.0, 2.4 Hz) | 8.06, d, (2.4 Hz) | 7.54, b (H-4) 7.69, b (H-7) | 7.28, dd, (6.0, 2.7 Hz) | 13.10, b | — |
| **2h** | $CDCl_3$ | 7.03, d, (8.7 Hz) | 7.44, dd, (8.7, 2.4 Hz) | 7.73, d, (2.4 Hz) | 7.51, b (H-4) 7.76, b (H-7) | 7.34, dd, (6.0, 3.0 Hz) | — | — |
| | Acetone-$d_6$ | 7.02, d, (9.0 Hz) | 7.51, dd, (9.0, 2.4 Hz) | 8.18, d, (2.4 Hz) | 7.64, b (H-4) 7.75, b (H-7) | 7.33, dd, (6.0, 3.3 Hz) | 12.50, b | — |
| | DMSO-$d_6$ | 6.96, d, (9.0 Hz) | 7.39, dd, (9.0, 2.4 Hz) | 8.20, d, (2.4 Hz) | 7.53, b (H-4) 7.68, b (H-7) | 7.27, dd, (6.0, 2.7 Hz) | 12.70, b 13.30, b | — |
| **5** | $CDCl_3$ | 7.00, d, (8.7 Hz) | 7.45, dd, (8.7, 2.4 Hz) | 8.62, d, (2.4 Hz) | 7.50, m (H-4) 7.84, m (H-7) | 7.26, dd, (6.0, 3.0 Hz) | 10.77, b | 1.38, s, 9H 4.05, s, 3H |

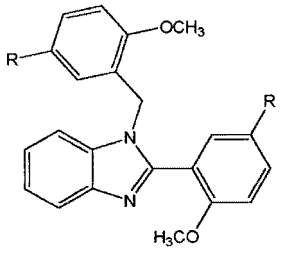
[a] Chemical shifts in ppm and coupling constants (Hz) in parentheses.

[b] In some cases the NH and OH protons merge together or are not seen.

such an oxidized product even in the absence of the oxidant is not unprecedented.[15] The NMR spectral data for **5** are included along with those of **2** in the respective tables. The assignments were made by a combination of one- and two-dimensional NMR techniques. Most of the quaternary carbons were assigned from the HMBC spectra, whereas the methine carbons were assigned from the HSQC spectra.



**5** R = *t*-butyl, R' = $CH_3$
**2** R' = H



**6a:** R = H; **6b:** R = *t*-Butyl

The compounds **2** are not very soluble in chloroform, so only very dilute solutions of **2** in $CDCl_3$ were prepared and the $^{13}C$ NMR spectra of these compounds could not be measured. The 2-aryl hydrogens are identified easily from their coupling pattern and hence assigned. Apart from these, a two-hydrogen doublet of doublets at $\delta\sim7.3$ ppm was observed which was assigned to protons 5 and 6. A broad band at $\delta\sim7.7$ ppm accounting for two hydrogens can be assigned to protons 4 and 7. The NH/OH hydrogens appear at $\delta$ 9.6/13.0 ppm. Although a single peak with fine coupling for protons 5 and 6 suggests that these two hydrogens are nearly isochronous, the distinct signals for hydrogens 4 and 7 clearly show that the 1,3-hydrogen shift is not very fast. In other words, the exchange is slowed, probably owing to intramolecular hydrogen bonding.

In DMSO-$d_6$ and acetone-$d_6$, the compounds **2** are fairly soluble. In fact, the addition of a drop of DMSO-$d_6$ to a $CDCl_3$ suspension of the compound dramatically changes the pattern of the signals. H-6′, the *meta*-coupled doublet, moves downfield to a larger extent (0.5 ppm) and interestingly the signal due to H-4 and H-7 is resolved, showing a neat doublet of doublets, experiencing an upfield shift of 0.1 ppm (in **2a**). This clearly shows that the 4,7-hydrogens and 5,6-hydrogens are equivalent, indicating the fast exchange of hydrogen

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**Table 2.** $^{13}$C NMR chemical shifts (ppm) of benzimidazoles **2** and **5**

| Compound | Solvent | 2 | 3a,7a | 4,7 | 5,6 | 1′ | 2′ | 3′ | 4′ | 5′ | 6′ | R |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **2a** | Acetone-$d_6$ | 153.79 | —[a] | 116.00 | 124.16 | 113.03 | 158.08 | 118.26 | 130.32 | 142.89 | 123.52 | 32.20, 35.26 |
| | DMSO-$d_6$ | 152.16 | —[a] | —[a] | 122.13 | 111.69 | 155.99 | 116.45 | 128.46 | 141.15 | 122.13 | 31.15, 33.88 |
| **2b** | Acetone-$d_6$ | 153.64 | —[a] | —[a] | 124.16 | 113.41 | 158.39 | 118.52 | 131.41 | 140.55 | 124.34 | 24.88, 34.56 |
| | DMSO-$d_6$ | 152.18 | —[a] | —[a] | 122.45 | 112.30 | 156.52 | 117.08 | 129.66 | 139.09 | 123.15 | 24.02, 33.22 |
| **2c** | Acetone-$d_6$ | 155.26 | —[a] | 117.00 | 124.31 | 114.50 | 159.47 | 118.24 | 130.91 | 142.49 | 124.31 | 11.31, 30.78, 39.26, 39.97 |
| | DMSO-$d_6$ | 152.43 | —[a] | 114.55 | 122.97 | 112.51 | 156.28 | 116.90 | 129.36 | 139.80 | 122.54 | 9.09, 28.51, 36.78, 37.37 |
| **2d** | Acetone-$d_6$ | 153.38 | —[a] | 116.00 | 124.35 | 114.16 | 159.85 | 119.22 | 131.39 | 133.16 | 125.37 | 127.66, 128.12, 130.11, 141.44 |
| | DMSO-$d_6$ | 151.71 | —[a] | 114.29 | 122.36 | 112.76 | 157.87 | 117.45 | 129.50 | 131.39 | 124.11 | 126.18, 126.38, 128.31, 139.97 |
| **2e** | Acetone-$d_6$ | 153.66 | —[a] | 115.92 | —[b] | 113.03 | 158.25 | 118.34 | 132.19 | 142.53 | 124.71 | 31.62, 43.51, 124.21, 126.83, 127.86, 129.29, 152.06 |
| | DMSO-$d_6$ | 152.76 | 138.00 | 114.54 | —[b] | 112.58 | 157.07 | 116.91 | 130.46 | 141.43 | 123.60 | 30.77, 42.30, 122.49, 125.38, 126.51, 127.83, 151.32 |
| **2f** | Acetone-$d_6$ | 153.54 | 138.66 | 115.95 | 124.19 | 113.46 | 158.33 | 118.56 | 132.71 | 135.82 | 125.83 | 16.58, 29.02 |
| | DMSO-$d_6$ | 151.99 | 137.08 | 114.38 | 122.40 | 112.25 | 156.39 | 117.01 | 130.93 | 134.22 | 124.55 | 15.53, 27.78 |
| **2g** | Acetone-$d_6$ | 151.98 | —[a] | —[a] | 124.63 | 115.12 | 158.92 | 120.42 | 132.57 | 124.49 | 126.42 | — |
| | DMSO-$d_6$ | 149.81 | —[a] | —[a] | 122.09 | 113.10 | 156.26 | 117.88 | 129.94 | 122.23 | 124.44 | — |
| **2h** | Acetone-$d_6$ | —[a] | —[a] | 112.70 (C-4) 119.80 (C-7) | 124.30[c] 125.16 | 115.74 | —[a] | 120.85 | 135.43 | 111.42 | 129.35 | — |
| | DMSO-$d_6$ | 150.11 | 140.44 —[a] | 110.80 (C-4) 117.63 (C-7) | 121.89[c] 122.76 | 114.12 | 157.16 | 118.73 | 133.11 | 109.72 | 127.66 | — |
| **5** | $CDCl_3$ | 150.33 | 133.62 (C-3a) 142.96 (C-7a) | 110.71 (C-4) 119.26 (C-7) | 122.15 122.58 | 117.19 | 154.73 | 111.16 | 128.16 | 144.57 | 126.95 | 31.43, 34.33, 55.98 |

[a] Not seen.

[b] Merged with the 5-substituted cumyl group.

[c] Unambiguous assignment is not possible owing to poor correlation in 2D spectra.

and suggesting that the hydrogen bonding between the 2-hydroxyl and the benzimidazole ring is not strong enough to slow this exchange. The $^{13}$C spectra also support this observation. The exchange seems to be so fast that in most cases the C-3a/7a and C-4/7 carbons are not seen at all. However, in certain substituted benzimidazoles [**2a** (in acetone-$d_6$ only), **2c**, **2d**, **2e**, **2f** and **2h**], the C-4/7 carbon was observed as a broad signal. In one compound at least (**2f**), all the carbons are seen (Fig. 1).

It is interesting that **2h**, in both acetone-$d_6$ and DMSO-$d_6$ (at the same molar concentration as for the other compounds), shows distinctly different $^{13}$C signals for the 5,6- and 4,7-hydrogens. In the corresponding $^{1}$H NMR spectra, two distinct broad bands are noticed for the 4- and 7-hydrogens, though the 5- and 6-hydrogens are still indistinguishable. Hence in this bromo compound, the proton exchange rate seems to be slow, indicating possible intramolecular hydrogen bonding in this case.

In the case of 2-(2-methoxy-5-*tert*-butylphenyl)benzimidazole (**5**), H-4 and H-7 appear as two different sharp signals at $\delta$ 7.50 and 7.84 ppm, respectively, at all concentrations. This clearly indicates that in chloroform there exists strong intramolecular hydrogen bonding between the methoxy oxygen and the imidazole hydrogen, preventing the exchange of protons leading to separate signals for the 4- and 7-hydrogens and carbons. The carbons C-5 and C-6 also appear separately even though the corresponding protons appear together as a multiplet. The fact that there is strong hydrogen bonding with OMe and NH clearly suggests that similar bonding could exist in **2** and hence it may be concluded that N—H···OH may be the preferred hydrogen bonding in **2** rather than ═N···H—O. The hydroxyl hydrogen may be involved in hydrogen bonding with H-bond acceptor solvents such as DMSO and acetone.

The effect of solvent concentration on tautomerism was studied in the case of 2-(2-hydroxy-5-chlorophenyl)benzimidazole (**2g**) with acetone-$d_6$ and DMSO-$d_6$. At low concentration (0.0327 M) in acetone-$d_6$, the 1,3-tautomerism was fully arrested and **2g** exits as a single isomer so that the protons H-4 and H-7 appear as two different multiplets (Fig. 2, entry 1). When the concentration of the solution is raised, the rate of exchange of the imidazole hydrogen also

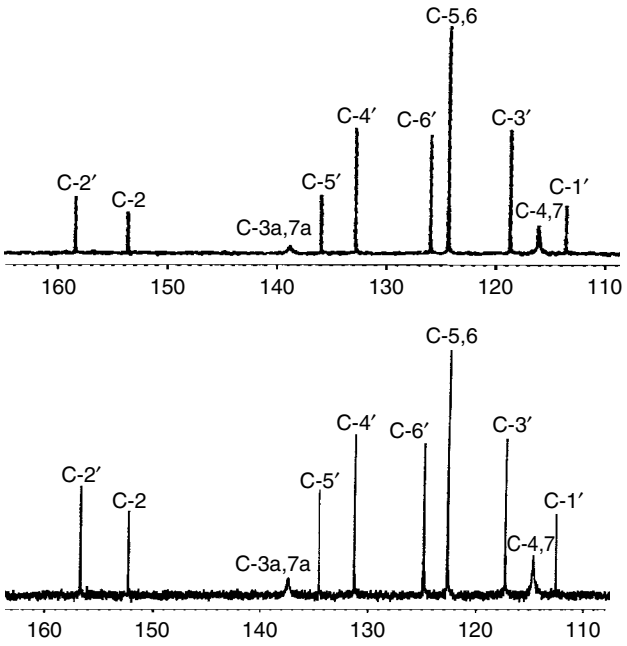


**Figure 1.** $^{13}$C NMR spectra of 2-(2-hydroxy-5-ethylphenyl)-benzimidazole (**2f**) in acetone-$d_6$ (top) and in DMSO-$d_6$ (bottom).

increases and as a result the hydrogens H-4 and H-7 appear as broad singlets coming closer (entry 2). As the concentration is increased further, the two broad bands merge to give a broad singlet (entries 3 and 4) due to the fast exchange rate of the imidazole hydrogen. In saturated solution (entry 5), both the protons H-4 and H-7 appear as a neat doublet of doublets with coupling constants 6.0 and 3.3 Hz, as NMR cannot distinguish these two protons because of very fast exchange. The same result was observed in DMSO-$d_6$. Probably, at lower concentration there is hydrogen bonding between the imidazole hydrogen and the hydroxyl oxygen. If the concentration of the solution increases, the intermolecular hydrogen bonding between the hydroxyl groups become dominant, accounting for the above trend.

As the concentration of the substrate is increased, not only do H-4 and H-7 become merged, but also OH and NH in the above cases. This clearly shows that at this concentration, the fast tautomeric proton exchange between N-1 and N-3 is facilitated owing to poor hydrogen bonding and also there is an exchange between NH and OH. This could be due to a zwitterionic form of the type shown in Fig. 3.

## CONCLUSIONS

The tautomerism present in **2** was studied in the light of the nature of hydrogen bonding present in **2**. It was found that in **5**, the hydrogen bonding between hydrogen of the imidazole ring and the oxygen of the methoxy can be attributed to the arrest of the tautomerism in that compound. This is in $CDCl_3$, where the solvent may not form any appreciable hydrogen bonding with NH. A similar argument is extended to **2**, in which it is suggested that the hydrogen of the imidazole group may be involved in the intramolecular hydrogen bonding with the hydroxyl oxygen

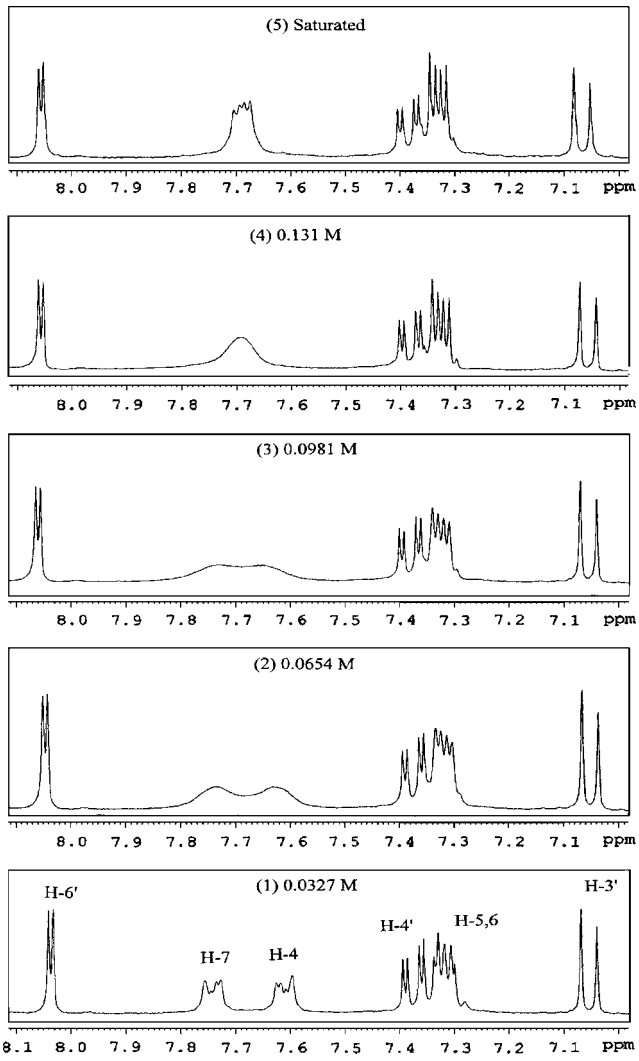


**Figure 2.** Effect of solvent concentration on H-4 and H-7 in 2-(2-hydroxy-5-chlorophenyl)benzimidazole (**2g**) in acetone-$d_6$.

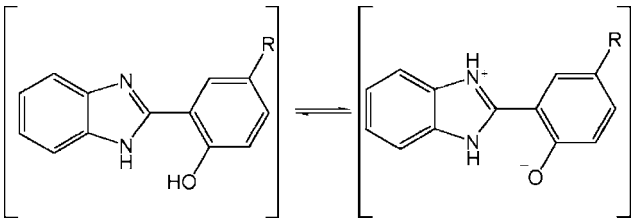


**Figure 3.** Possible zwitterionic form.

(not the hydroxyl hydrogen with the ring imino nitrogen). In hydrogen bond acceptor solvents such as DMSO and acetone, the hydroxyl hydrogen may have hydrogen bonding with the solvent.

## EXPERIMENTAL

### Spectra

The $^1$H, $^{13}$C and related 2D NMR spectra were recorded on a Bruker 300 MHz (UltraShield) NMR spectrometer at room temperature. The $^1$H NMR spectra were measured with a spectral width of 5000 Hz, a 90° flip angle and 2 s

**Table 3.** Melting-points, yields and elemental analysis data for compounds **2** and **5**

| Compound | Yield (%) | M.p. (°C) | Formula | Found (%) | | | Calc. (%) | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | C | H | N | C | H | N |
| **2a** | 78 | 284–285 (282–284)[16] | — | — | — | — | — | — | — |
| **2b** | 70 | 224–225 | $C_{16}H_{16}N_2O$ | 76.20 | 6.45 | 11.25 | 76.16 | 6.39 | 11.10 |
| **2c** | 77 | 238–239 | $C_{18}H_{20}N_2O$ | 77.25 | 7.15 | 9.95 | 77.11 | 7.19 | 9.99 |
| **2d** | 69 | 240–241 | $C_{19}H_{14}N_2O$ | 79.81 | 4.85 | 7.75 | 79.90 | 4.93 | 9.78 |
| **2e** | 76 | 208–209 | $C_{22}H_{20}N_2O$ | 80.40 | 6.08 | 8.41 | 80.46 | 6.14 | 8.53 |
| **2f** | 73 | 210–211 | $C_{15}H_{14}N_2O$ | 75.55 | 5.85 | 11.65 | 75.61 | 5.92 | 11.76 |
| **2g** | 75 | 306–307 (305–306)[17] | — | — | — | — | — | — | — |
| **2h** | 72 | 298–299 (286–288)[17] | — | — | — | — | — | — | — |
| **5** | 47 | 258–259 | $C_{18}H_{20}N_2O$ | 77.20 | 7.10 | 10.11 | 77.11 | 7.19 | 9.99 |

relaxation delay in 32 scans for ~0.05 M solution in acetone-$d_6$/DMSO-$d_6$ with TMS as internal reference. For $^{13}C$ NMR spectra, a pulse angle of 37.5° (5 μs), an acquisition time of 0.75 s and a repetition time of 3.72 s with a spectral width of 17 000 Hz were used. The one- and two-dimensional NMR spectra reported in this work were recorded using Bruker 'icon NMR' software. IR spectra were recorded in a Jasco FT-IR instrument in KBr pellets and mass spectra were recorded with a Finnigan GC–MS instrument.

## Compounds

Analytical data are collected in Table 3. Melting-points are uncorrected.

### *Preparation of 2-(2-hydroxy-5-substituted-aryl)-benzimidazoles (**2**)*

A 0.01 mol solution of 5-substituted-2-hydroxybenzaldehydes (**1**) was refluxed with 1.08 g (0.01 mol) of *o*-phenylenediamine in 50 ml of ethanol for 1.5 h and then the solution was concentrated and cooled. Without isolating the imine intermediate, the reaction mixture was stirred with 30 ml of acetic acid and 0.01 mol of lead tetraacetate at room temperature for 15 min. After completion of the reaction, the mixture was poured into water and extracted with ethyl acetate. The pure product of **2** was obtained after evaporation of the solvent followed by silica column chromatography and recrystallized from light petroleum–ethyl acetate.

**2b**: IR, 3457, 3261, 3056, 2960, 1598, 1504, 1390, 1253 $cm^{-1}$; MS, *m/z* (intensity, %) 252 (58), 237 (100), 236 (70), 207 (10). **2c**: IR, 3415, 3251, 3058, 2964, 1594, 1504, 1388, 1257 $cm^{-1}$; MS, *m/z* (intensity, %) 280 (20), 251 (100), 236 (20), 207 (26). **2d**: IR, 3467, 3303, 3050, 1606, 1486, 1390, 1278, 1253 $cm^{-1}$. **2e**: IR, 3438, 3266, 3058, 2967, 1596, 1498, 1384, 1267 $cm^{-1}$; MS, *m/z* (intensity, %) 328 (4), 295 (82), 294 (100), 279 (92). **2f**: IR, 3438, 3241, 3058, 2956, 1589, 1502, 1382, 1257 $cm^{-1}$; MS, *m/z* (intensity, %) 238 (82), 223 (100), 193 (12).

### *Preparation of 2-(2-methoxy-5-tert-butylphenyl)-benzimidazoles (**5**)*

5-*tert*-Butyl-2-methoxybenzaldehyde was prepared from 0.02 mol (3.56 g) of 5-*tert*-butyl-2-hydroxybenzaldehyde, 0.03 mol (3.78 g) of dimethyl sulfate and 4 g of potassium hydroxide. A solution of 0.01 mol (1.08 g) of *o*-phenylenediamine and 0.01 mol (1.92 g) of 5-*tert*-butyl-2-methoxybenzaldehyde in 50 ml of ethanol was refluxed for 2 h. After completion of the reaction, the solvent was evaporated and pure **5** was obtained by the recrystallization from light petroleum–ethyl acetate.

**5**: IR, 3430, 3058, 2956, 1614, 1488, 1446, 1253 $cm^{-1}$; MS, *m/z* (intensity, %) 280 (100), 265 (14), 250 (30), 235 (74), 119 (76).

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