Structure and Protonation Study of the Imidazo[2,1-*b*]-1,3,4-thiadiazole System: ^{1}H Nuclear Magnetic Resonance, Crystal and Molecular Structure of 5,6-Dimethylimidazo[2,1-*b*]-1,3,4-thiadiazole and its Hydrobromide

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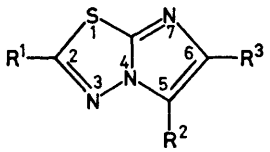
Crystal structure analysis of 5,6-dimethylimidazo[2,1-*b*]-1,3,4-thiadiazole (3) and its corresponding hydrobromide has shown that protonation occurs at N(7). Molecular properties, mainly aromaticity and basicity, of this system were interpreted on the basis of semi-empirically calculated ring-currents, which show that this molecule has a lower aromatic character than that of other fused heterocycles of imidazole with pyrimidine and thiazole rings. From ^{1}H n.m.r. measurements the protonation site in acidic solution could not be determined, but N(7) was found to be the site available for complex formation in the presence of a lanthanide shift reagent.

THE electronic character of fused heterocycles with a bridgehead nitrogen atom has been extensively studied [1-7] both by spectroscopic methods, mainly ^{1}H n.m.r., and from their reactivity. The relative electronic density of the two fused rings determines the reactivity of the carbon atoms, the basicity of the nitrogen atoms, and the proton chemical shift; this last quantity strongly depends on the electrons circulating in one of the rings, since they affect the screening of the protons of the other ring by a mutual effect.[1,3,6,7] The mutual effects of pyridine [1] and pyrimidine [3,6] on the imidazole ring, and of thiazole [7] on the imidazole ring have so far been studied. Also the reactivity in electrophilic substitution and the basicity of the nitrogen atoms have been determined experimentally and confirmed by theoretical calculations. In imidazo[1,2-*a*]-pyridine and -pyrimidine electrophilic substitution [3,8] occurs mainly on the carbon atom of the imidazo-ring adjacent to the bridgehead nitrogen atom, C(3), and this is true also for the imidazo[2,1-*b*]thiazole system,[7] C(5). As regards protonation in acidic solution, it seems that in the foregoing systems the nitrogen atom of the imidazo-ring is always the first site of protonation.[2,3,6] This information has not always been obtained directly, and especially when different nitrogen atoms are present doubts may arise. However, comparison with *N*-methylation behaviour is not a general criterion for unambiguously defining the site of protonation. Even the low-field shift produced by protonation of the molecule on different nitrogen atoms, as studied [6] in detail for imidazo[1,2-*a*]pyrimidine, does not turn out to be a reliable test for defining the protonation site.

We report here a study on the structure and properties of a relatively less-studied fused system, imidazo[2,1-*b*]-1,3,4-thiadiazole. To define the protonation site unambiguously the crystal structure of a protonated molecule was considered in order to evaluate critically the predictions which can be made from the electronic structure of these molecules. In fact, ^{1}H n.m.r. measurements were inconclusive in this respect, but they are of use in determining the aromatic character, when the



	R^1	R^2	R^3
(1)	H	H	H
(2)	H	H	Me
(3)	H	Me	Me
(4)	Me	H	Me

results are interpreted in the light of the ring-current model.[9]

RESULTS AND DISCUSSION

The ^{1}H n.m.r, spectra of compounds (1)—(4) were recorded for deuteriochloroform solutions (0.5M) and the parameters are listed in Table 1. The chemical shifts of the hydrogen atoms bonded to the ring show that in the fused system H(2) falls at higher field and H(5) and H(6) at lower field with respect to the parent thiadiazole [10] and imidazole or *N*-methylimidazole [11] heterocycles. Apparently the thiadiazole ring behaves qualitatively like the pyridine,[12] pyrimidine,[6] and thiazole [7] rings in the corresponding heterocycles fused with the imidazole ring,[6,7] but in the opposite direction to the imidazole ring itself: this effect will be analysed to see whether it can be attributed to ring-current circulations or to other effects and hence for a comparative analysis of the aromatic character of these systems.

The n.m.r. spectra of the compounds were also recorded for deuterium oxide solutions and with increasing amounts of deuterium chloride: by following the chemical shift of the single protons of compound (2) as a function of the molar ratio of compound to acid only

one protonation step was observed, as in the case of imidazo[1,2-*a*]pyrimidine, while the chemical shift of the protons remained constant for values of this ratio >1. The n.m.r. spectra of protonated forms were also measured by employing solutions of the compounds in trifluoroacetic acid (0.5M) and spectral parameters are

TABLE 1

Chemical shifts (δ) and coupling constants (Hz) of imidazo[2,1-*b*]-1,3,4-thiadiazole derivatives [a]

Cpd.	Solvent [b]	δ_2	δ_5	δ_6	$J_{5,6}$	$J_{2,6}$
(1)	A	8.56	7.82	7.38	1.42	0.97
(2)	A	8.47	7.54	2.36	0.92	
(3)	A	8.44	2.43	2.31	0.67	
(4)	A	2.66	7.41	2.33	0.93	
(1)	B	9.22	8.20	7.80	2.45	1.24
		(0.66)	(0.38)	(0.42)		
(2)	B	9.15	7.91	2.60	1.12	
		(0.68)	(0.37)	(0.24)		
(2)	C	9.16	7.88	2.45	1.09	
		(0.69)	(0.34)	(0.09)		
(2)	C [c]	9.39	8.10	2.57	1.17	
		(0.92)	(0.56)	(0.21)		
(3)	B	9.11	2.63	2.52	0.73	
		(0.67)	(0.20)	(0.21)		
(4)	B	2.91	7.80	2.56	1.06	
		(0.25)	(0.39)	(0.23)		

[a] Solutions are 0.5M in all solvents. Values in parentheses are differences between measurements for trifluoroacetic acid or acidified aqueous solution and those for deuteriochloroform. [b] Solvents: A, $CDCl_3$; B, $CF_3{\cdot}CO_2H$; and C, 0.25N DCl in D_2O. [c] Chemical shifts measured relative to the methyl peak of internal t-butyl alcohol and translated to the tetramethylsilane scale by employing δ_{Me} 1.31.

also reported in Table 1. The differences in chemical shift relative to the free base suggest that the effect of protonation is highest on H(2), followed by H(5) and H(6). This behaviour was not conclusive for determining the site of protonation.

A test for locating the basicity of the nitrogen atoms was also made by examining the complex-formation effect in the presence of a lanthanide shift reagent, $Eu(fod)_3$, with compound (4). The shift induced on the different protons, extrapolated from plots obtained [13] from measurements in the presence of different ratios of shift reagent to substrate, showed that the effect is a maximum on the methyl group attached to C(6) (24.35 p.p.m.), very small on that on C(2) (0.94 p.p.m.), and medium on the proton on C(5) (6.07 p.p.m.). Location of the lanthanide on N(7) may be unequivocally demonstrated by employing known theories.[14] This nitrogen atom thus proves to be the molecular site with the highest basicity, at least in the sense of having a higher availablity of electrons for complex formation.

In order to determine unequivocally the site of *N*-protonation in the monocation of this heterocyclic system we performed an *X*-ray analysis of 5,6-dimethylimidazo[2,1-*b*]-1,3,4-thiadiazole, compound (3), and of its corresponding hydrobromide derivative (3a). Bond distances and angles for both compounds are reported in Table 2, while details of some molecular planes are given in Table 3. Geometrical parameters for similar molecules with a bridgehead nitrogen atom are reported in ref. 15. The *X*-ray analysis suggests that protonation in compound (3) occurs at N(7): in fact a significant residual peak was located on a difference-Fourier map of height 0.7 eÅ^{-3} over a background of 0.2 eÅ^{-3} and at 1.15(10) Å from N(7): moreover the endocyclic angle at N(7) is significantly larger [108.3(6)°] in the protonated molecule (3a) than in the unprotonated one [103.3(5)°]. Similar behaviour is observed in other protonated five-membered heterocyclic compounds containing nitrogen.[16]

The thiadiazole ring in the two compounds shows no significant differences as far as bond distances and angles are concerned. In both molecules the S–C distances from the imidazole ring [S(1)–C(8) 1.720(3) and 1.711(4)] are significantly shorter than those involving C(2) [S(1)–C(2) 1.740(4) and 1.737(5) Å]. This fact suggests that π-delocalization is more favoured through C(8)

TABLE 2

Bond distances and angles for compounds (3) and (3a) *

	(3)	(3a)
(*a*) Intramolecular distances (Å)		
S(1)–C(2)	1.740(4)	1.737(5)
S(1)–C(8)	1.720(3)	1.711(4)
C(2)–N(3)	1.288(5)	1.276(6)
N(3)–N(4)	1.383(3)	1.375(4)
N(4)–C(5)	1.376(4)	1.405(6)
N(4)–C(8)	1.354(4)	1.328(5)
C(5)–C(5′)	1.480(6)	1.486(6)
C(5)–C(6)	1.374(5)	1.353(6)
C(6)–C(6′)	1.502(6)	1.502(6)
C(6)–N(7)	1.399(4)	1.379(6)
N(7)–C(8)	1.322(4)	1.326(6)
(*b*) Bond angles (°)		
C(2)–S(1)–C(8)	87.7(3)	86.3(4)
S(1)–C(2)–N(3)	117.7(5)	119.1(6)
C(2)–N(3)–N(4)	107.3(5)	106.0(6)
N(3)–N(4)–C(5)	133.2(6)	131.5(7)
N(3)–N(4)–C(8)	117.8(5)	118.2(7)
C(5)–N(4)–C(8)	108.9(5)	110.3(6)
N(4)–C(5)–C(5′)	122.6(7)	122.6(7)
N(4)–C(5)–C(6)	103.4(5)	104.0(5)
C(5′)–C(5)–C(6)	134.0(8)	133.4(8)
C(5)–C(6)–N(7)	112.2(5)	109.3(6)
C(5)–C(6)–C(6′)	127.7(7)	129.4(8)
C(6′)–C(6)–N(7)	120.1(6)	121.3(7)
C(6)–N(7)–C(8)	103.3(5)	108.3(6)
S(1)–C(8)–N(4)	109.4(4)	110.5(4)
S(1)–C(8)–N(7)	138.4(5)	141.5(6)
N(4)–C(8)–N(7)	112.2(5)	108.1(6)
(*c*) Distances (Å) involving hydrogen atoms		
C(2)–H(2)	0.99(5)	0.82(10)
C(5′)–H(51)	1.04(8)	0.89(12)
C(5′)–H(52)	0.98(8)	1.09(5)
C(5′)–H(53)	0.87(6)	1.00(6)
C(6′)–H(61)	1.05(5)	1.14(12)
C(6′)–H(62)	1.12(7)	1.08(10)
C(6′)–H(63)	0.91(8)	0.96(10)
N(7)–H(7)		1.15(10)
O–H[O(W)]		0.97(10)

* The prime refers to the carbon atom of the methyl groups.

than through C(2); C(2)–N(3) [1.288(5) and 1.276(6) Å] is close to the value for a localized double bond. The same effect is observed in cyclic sulphones [17] where unsymmetric conjugation of the sulphonyl group seems to be favoured.

Protonation causes significant modifications in the π-delocalization within the imidazole ring as shown by the differences in the bond distances N(4)–C(5), N(4)–C(8), and C(6)–N(7), and it seems evident that there is a

more pronounced bond-length alternation. Moreover, the remarkable enlargement of the angle at N(7) significantly perturbs the other endocyclic angles.

Both molecules show small but significant deviations from planarity (see Table 3), whereas the individual rings are planar. The out-of-plane distances of the two methyl substituents are interesting and more relevant in the unprotonated compound.

The packing of the two compounds is shown in Figures 1 and 2. For compound (3) all the contacts are consistent with van der Waals radii. In the protonated compound the water molecule is involved in contacts with N(7) [O(W) . . . N(7^{I}) 2.76, O(W) · · · H(7) 1.65 Å; I is at x, $3/2 - y$, $1/2 + z$], with bromine {O(W) · · · Br^{II} 3.23, H[O(W)] · · · Br^{II} 2.38 Å; II is at $1 - x$, $3/2 - y$, $1/2 + z$; O(W) · · · Br^{III} 3.21 Å; III is at $1 - x$, $2 - y$, $1 - z$} and with S(1) [O(W) · · · S(1^{IV}) 3.15 Å; IV is at $1 - x$, $1 - y$, $1 - z$] and the stereographic projection of the environment is shown in Figure 3. O(W)H · · · Br hydrogen bonds form infinite (H_2O · · · Br · · · H_2O) chains running parallel to [010], so that the organic cations are linked by zig-zag NH · · · O(W) interactions. The O(W) · · · S(1) contact is slightly shorter than the sum of the van der Waals radii and this is imposed by the orientation of the cation along the chain.

The analysis of the aromatic character of the whole heterocyclic system according to the ring-current model [9] was performed within the framework of coupled Hartree–Fock perturbation theory,[18] with a parameter set previously tested [19] and by employing experimental geometries. The ring-current contributions (p.p.m.) amount to: 1.00 on H(2), 2.26 on H(5), and 2.30 on H(6). These values, when compared with those of the equivalent positions of 1,3,4-thiadiazole [1.26 on H(2)] and *N*-methylimidazole [2.31 on H(4) and 2.17 on H(5)] show that only ring currents from the imidazole ring, behaving as an electron-rich system, make a significant contribution to the shielding of proton H(2) (−0.26 p.p.m.), whereas H(5) and H(6) are poorly affected by the thiadiazole system. Comparison of the differences in chemical shift between corresponding positions of imidazo[2,1-*b*]-1,3,4-thiadiazole and those of the parent single heterocycles [10,11] [$\Delta\delta$(2) −0.72, $\Delta\delta$(5) 0.94, $\Delta\delta$(6)

TABLE 3

Analysis of the planarity of compounds (3) and (3a). Equations of least-squares planes are in the form $lX + mY + nZ = p$ where X, Y, and Z are related to the crystallographic orthogonal axes by the transformation matrix

$$//10 \cos\beta/010//00 \sin\beta//.$$

Distance (Å × 10^3) of atoms from the planes are given in square brackets, those for compound (3) preceeding those for compound (3a)

Plane (1): S(1), C(2), N(3), N(4), C(5), C(6), N(7), C(7a)

$0.9689X + 0.1807Y - 0.1691Z = -0.1597$ (3)
$-0.4456X + 0.7110Y - 0.5440Z = 0.2829$ (3a)

[S(1) 4(2), 0(1); C(2) −1(5), 14(5); N(3) −11(5), 2(4); N(4) 1(4), −14(3); C(5) 21(5), −3(4); C(6) 17(5), 13(4); N(7) −13(4), −5(4); C(7a) −17(5), −6(4); C(5′) 79(3), 44(6); C(6′) 68(7), 10(6)]

Plane (2): S(1), C(2), N(3), N(4), C(7a)

$0.9701X + 0.1788Y - 0.1640Z = -0.1540$ (3)
$-0.4374X + 0.7161Y - 0.5440Z = 0.3251$ (3a)

[S(1) 1(2), −1(1); C(2) 0(5), 4(5); N(3) −3(5), −3(4); N(4) 12(4), −6(3); C(7a) −11(5), 6(4); C(5) 35/5) 16(4); N(7) −3(4), 20(4)]

Plane (3): N(4), C(5), C(6), N(7), C(7a)

$0.9650X + 0.1835Y - 0.1874Z = -0.2240$ (3)
$-0.4532X + 0.7051Y - 0.5454Z = 0.2065$ (3a)

[N(4) 0(4), −1(3); C(5) −2(5), −2(4); C(6) 2(5), 5(4); N(7) −2(4), −7(4); C(7a) 2(5), 5(4); S(1) 50(2), 26(1); N(3) −6(5), 27(4); C(5′) 31(3), 44(6); C(6′) 37(7), −13(6)]

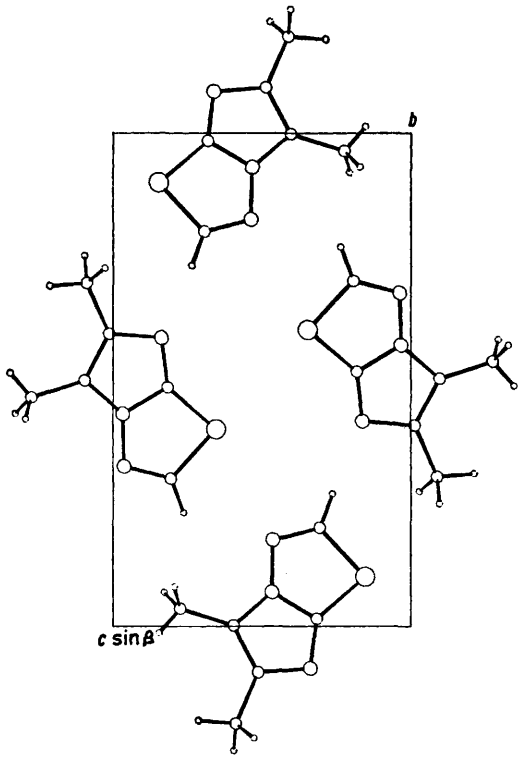


FIGURE 1 Compound (3): projection of the structure along [100]

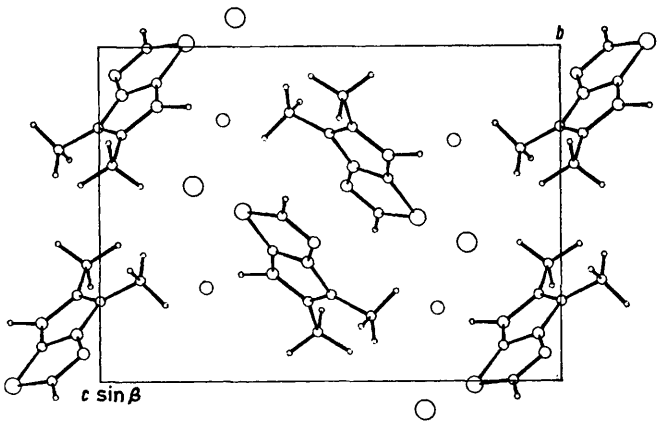


FIGURE 2 Compound (3a): projection of the structure along [100]

0.33 p.p.m.] shows that these quantities are not caused only by the mutual ring-current contributions of the two rings on the protons of the other. In particular, only the effect of the imidazole ring on H(2) is found qualitatively, whereas the low-field shift of H(5) and H(6) relative to *N*-methylimidazole should also account for other effects. The analysis of π-electron charge densities, calculated from the SCF MO [20] employed for the evaluation of ring-currents, indicates that in comparison with the parent *N*-methylimidazole, while C(6) is slightly positive, C(5) is negatively charged; hence the low-field shift of the proton on C(5) can not be attributed to a decreased electron density there. On the other hand, from a comparison of the proton chemical shifts [21] of H(3) between indolizine and pyrrolo[1,2-*b*]pyridazine, and between imidazo[1,2-*a*]pyridine and imidazo[1,2-*b*]-pyridazine, proton H(3) in these systems can be compared with H(5) in our system, and the introduction of a second

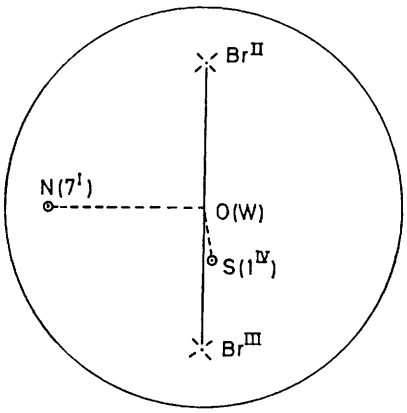


FIGURE 3 Compound (3a): stereographic projection of the environment of the water molecule

nitrogen atom in the nearby ring is seen to produce a marked low-field shift (0.4—0.5 p.p.m.) on this proton. The effect can most probably be attributed to the local magnetic anisotropy of the lone-pair of this added nitrogen atom. The ring-current model shows on the other hand, that imidazo[1,2-*b*]-1,3,4-thiadiazole still possesses aromatic character, but a lower one than that of imidazo[2,1-*b*]thiazole and imidazo[1,2-*a*]pyrimidine; also the magnetic susceptibility normal to the molecular plane is of the order -2.55×10^{-5}, -3.12×10^{-5}, -5.36×10^{-5} c.g.s. e.m.u. for the three systems, thus showing that the first-named should be the least aromatic molecule.[22]

The analysis of π-electron charge-densities also indicated that N(7) is the most negative nitrogen atom, whereas, within the carbon atoms, electrons tend to prefer C(5), and to some slight extent C(6), over C(2): C(5) is the most negative site. The same trend of π-electron charge densities is shown by the all-valence electrons CNDO/2 method,[23] while this method also indicates that N(7) has the highest total electron density. These results agree with the experimental indication that in the monocation protonation occurs at N(7), that this position should be the one with a higher electron availability for complex formation, and further that electrophilic reactions should mainly occur at C(5), as a number of experiments do in fact bear out.[24]

By employing the experimental geometry of the heterocyclic ring determined for compound (3), the CNDO/2 method was applied to a calculation of the relative stability of the different protonated forms of compound (1), namely monoprotonated at N(7) and N(3) and diprotonated at N(7) and N(3). Comparison of the resulting binding energies gives the monoprotonated form at N(7) as the most stable.

Conclusions.—Electronic delocalization, as deduced from experimental measurements, both n.m.r. and *X*-ray analysis and MO calculations, involves electrons moving from thiadiazole to the imidazole ring. In the same context theoretical calculations, made by semi-empirical methods, indicate N(7) as the most basic atom, and the relative stability of the protonated forms indicates substantial preference for the one monoprotonated at N(7). We should thus conclude that in heteroaromatic systems having more than one basic centre in the ring, the chemical shift behaviour of the protons as a function of the acidity of the solution is not a reliable tool for defining the protonation site, owing to the delocalization of the electrons and of the positive charge over the whole molecular frame. This is no longer true for aliphatic or non-conjugated systems, where the protonation behaviour of different dissociating groups in the molecule may be followed by the proton chemical shift of vicinal groups.[25]

EXPERIMENTAL

^{1}H N.m.r. spectra were recorded on a JEOL JNM C60 HL spectrometer. The shift changes produced by the lanthanide shift reagent, $Eu(fod)_3$, were extrapolated from linear plots obtained at different molar concentrations of the shift reagent relative to that of compound (4).

Compounds.—Compounds (2), (3), and (4) were prepared as described in ref. 24.

Imidazo[2,1-b]-1,3,4-*thiadiazole*, (1). A solution of 2-amino-1,3,4-thiadiazole (2 g) and bromoacetaldehyde (2.4 g) in absolute ethanol (30 ml) was heated under reflux for 5 h. On cooling, light brown crystals separated; a cold aqueous solution of the precipitate was saturated with KOH and extracted with $CHCl_3$. Solvent was evaporated off and a benzene solution of the residue chromatographed on SiO_2. Colourless needles from ligroin had m.p. 107 °C (Found: C, 38.55; H, 2.10; N, 33.35. Calc. for $C_4H_3N_3S$: C, 38.39; H, 2.42; N, 33.58%).

5,6-*Dimethylimidazo*[2,1-b]-1,3,4-*thiadiazole hydrobromide*, (3a). 45% Hydrogen bromide (1 ml) was added to a solution of free base (3) (200 mg) in acetonitrile (10 ml) at room temperature. The hydrobromide (3a) was obtained quantitatively by addition of diethyl ether; m.p. 230 °C (from CH_3CN/Et_2O) (Found: C, 30.90; H, 3.50; Br 34.05; N, 17.75. Calc. for $C_6H_8N_3BrS$: C, 30.78; H, 3.44; Br 34.13; N, 17.95%.

Crystal Structure of 5,6-*Dimethylimidazo*[2,1-b]-1,3,4-*thiadiazole* (3).—Crystals were colourless prisms elongated along [100]. Preliminary cell dimensions and space group were obtained from rotation and Weissenberg photographs. Lattice parameters were refined by least-squares

from seventeen $(\theta, \chi, \phi)_{hkl}$ measurements taken on a Siemens single-crystal diffractometer.

Crystal data. $C_6H_7N_3S$, $M = 153.2$. Monoclinic, $a = 7.344(2)$, $b = 12.792(2)$, $c = 8.192(2)$ Å, $\beta = 108.3(1)°$, $Z = 4$, $D_c = 1.39$ g cm^{-3}, $U = 730.7$ Å^3, Cu-K_α radiation. $\lambda = 1.541\,8$ Å; μ(Cu-K_α) = 31.8 cm^{-1}. Space group $P2_1/c$ from systematic absences.

Intensity data were collected up to θ 70° by use of the ω—2θ scan method and the five-points technique [26] with nickel-filtered Cu-K_α radiation on the same single-crystal diffractometer. Of 1 372 independent reflections measured, 356 were not used in the crystal analysis because they had intensity $I \leqslant 2[\sigma^2(I) + 10^{-4}I^2]^{1/2}$, where I is the relative intensity and $\sigma^2(I)$ its variance. The dimensions of the crystal used were 0.40 × 0.17 × 0.26 mm. No absorption correction was applied.

Structure analysis and refinement. The structure was solved by direct methods by use of the system of computer programs written by Sheldrick.[27] The structure was refined by a few cycles of full-matrix anisotropic least-squares up to R 0.084. A difference-Fourier synthesis was then computed and revealed significant residual peaks near all the positions where hydrogen atoms were expected to occur. Further least-squares cycles were then computed with hydrogen atoms included with isotropic thermal parameters; and a final R of 0.052 was obtained. Positional parameters together with their standard deviations are given in Table 4.

TABLE 4

Atom fractional co-ordinates (× 10^4, × 10^3 for hydrogen) for compound (3), with estimated standard deviations in parentheses

	x	y	z
S(1)	276(2)	1 004(1)	1 536(1)
C(2)	762(7)	1 999(3)	3 061(6)
N(3)	1 668(6)	1 755(2)	4 632(5)
N(4)	2 048(5)	695(2)	4 669(4)
C(5)	2 989(6)	16(3)	5 961(5)
C(5′)	3 917(11)	362(5)	7 754(7)
C(6)	2 846(6)	−928(3)	5 131(5)
C(6′)	3 657(9)	−1 962(4)	5 885(8)
N(7)	1 838(5)	−847(2)	3 376(4)
C(7a)	1 398(6)	157(3)	3 174(5)
H(2)	20(6)	269(4)	264(6)
H(51)	294(10)	69(5)	828(8)
H(52)	505(11)	80(6)	794(9)
H(53)	447(9)	−13(5)	846(8)
H(61)	463(8)	−190(4)	713(8)
H(62)	249(9)	−251(5)	596(7)
H(63)	437(10)	−226(6)	528(9)

Crystal Structure of 5,6-Dimethylimidazo[2,1-b]-*1,3,4-thiadiazole Hydrobromide Monohydrate* (3a).—The compound was recrystallized from ethanol as pale yellow prisms, elongated along [101]. Cell parameters were derived as before and lattice parameters refined from sixteen $(\theta, \chi, \phi)_{hkl}$ measurements.

Crystal data.—$C_6H_{10}BrN_3O$, $M = 220.1$. Monoclinic, $a = 6.843(5)$, $b = 10.170(5)$, $c = 14.104(5)$ Å, $\beta = 94.1(1)°$, $U = 979.1$ Å^3, $Z = 4$, $D_c = 1.49$ g cm^{-3}, Cu-K_α radiation; μ(Cu-K_α) = 70.2 cm^{-1}. Space group $P2_1/c$ from systematic absences.

Intensity data were collected as before. Of 1 859 independent reflections measured, 1 699 were used in the crystal analysis. The dimensions of the crystal used were 0.71 × 0.30 × 0.24 mm. No absorption correction was applied.

Structure analysis and refinement. The structure was solved by use of the same program routine as before, and refined by cycles of full-matrix anisotropic least-squares (hydrogen atoms isotropically) up to R 0.067. Only one of the hydrogen atoms of the water molecule was located in the difference-Fourier map. Positional parameters together with their standard deviations are given in Table 5. For

TABLE 5

Atom fractional co-ordinates (× 10^4, × 10^3 for hydrogen) for compound (3a), with estimated standard deviations in parentheses

	x	y	z
S(1)	3 345(2)	4 899(1)	3 108(1)
C(2)	1 634(8)	5 040(5)	3 954(4)
N(3)	1 958(6)	5 845(4)	4 641(3)
N(4)	3 727(5)	6 429(3)	4 501(2)
C(5)	4 794(6)	7 407(4)	5 015(3)
C(5′)	4 084(8)	8 033(6)	5 878(4)
C(6)	6 385(7)	7 601(4)	4 515(3)
C(6′)	8 089(8)	8 516(6)	4 716(4)
N(7)	6 295(6)	6 768(4)	3 742(3)
C(7a)	4 652(6)	6 076(4)	3 744(3)
Br	2 353(1)	9 145(0)	2 961(0)
O(W)	8 777(6)	7 807(4)	7 314(3)
H(2)	72(15)	454(10)	403(6)
H(7)	712(13)	679(7)	306(6)
H(51)	474(15)	879(10)	594(8)
H(52)	387(9)	729(5)	642(4)
H(53)	274(9)	834(5)	565(4)
H(61)	800(15)	910(10)	540(9)
H(62)	810(12)	914(9)	410(8)
H(63)	910(12)	786(9)	480(6)
H[O(W)]	890(12)	867(9)	704(6)

both compounds atomic scattering factors were from ref. 28 for non-hydrogen atoms and from ref. 29 for hydrogen.

Observed and calculated structure factors and thermal parameters are given in Supplementary Publication No. SUP 22643 (12 pp., 1 microfiche).* All calculations relating to the crystal structures and to properties related to MO wavefunctions were carried out on the CDC Cyber 76 of Consorzio per la Gestione del Centro di Calcolo Interuniversitario dell' Italia Nord-Orientale, Casalecchio, Bologna, Italy. Bibliographic searches were carried out using the Cambridge Crystallographic Data Files through the Servizio Italiano di Diffusione dei Dati Cristallografici, Parma, Italy.

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