^{13}C NMR STUDY OF ANNULAR TAUTOMERISM OF AZOLES IN THE SOLID STATE

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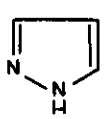
Abstract - The ^{13}C chemical shifts of 1,2,4-triazole, tetrazole, indazole, benzimidazole, and benzotriazole have been obtained from solid samples using the CP-MAS technique. They are discussed in connection with the annular prototropic tautomerism of these azoles and benzazoles. A case of functional tautomerism, that of benzoxazolidin-2-thione, and a case of non-prototropic tautomerism, that of 1-trimethylsilylbenzimidazole, are also studied.

The CP-MAS ^{13}C nmr spectroscopy opens a new entry to the study of the structure of organic compounds in the solid state.[1,2] Amongst the structural problems, tautomerism occupies an important place.[3] Its study in solution is complicated due to temperature dependent proton exchange phenomena. On the other hand, solid state studies suffer from the possible existence of several independent molecules in the crystal lattice and from ^{14}N quadrupole effects.[4]

In the case of pyrazole 1 and imidazole 2 it has been shown that CP-MAS ^{13}C experiments are coherent with results obtained from X-ray crystallography. Moreover, the chemical shifts of the solid and those of the solution are closely related if the tautomerism is frozen using low temperatures or N-methyl derivatives.



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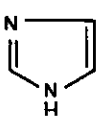

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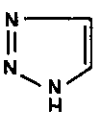

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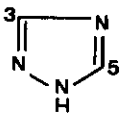

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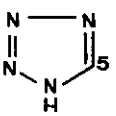

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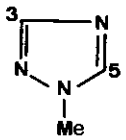
In order to explore further the problem of the annular tautomerism of azoles in the solid state we have selected another five compounds, for which both the X-ray structures and the ^{13}C chemical shifts in solution are known. Since 1,2,3-triazole 3 is a liquid at room temperature, we have studied 1,2,4-triazole 4 and tetrazole 5. Both structures have been determined by radiocrystallography[3] and exist as represented in the crystal: 1H-1,2,4-triazole[6] and 1H-1,2,3,4-tetrazole.[7] The chemical shifts of the solid samples[8] appear at 148.0 (C_3) and 143.9 (C_5) for 4 and at 144.0 (C_5) for 5, values close to the solution chemical shifts: 150.4 (C_3) and 143.5 (C_5) for 1-methyl-1,2,4-triazole 6 (DMSO-d_6),[9] 142.1 (C_5) for tetrazole 5 (DMSO-d_6),[9] and 143.4 (C_5) for 1-methyltetrazole 7 (DMSO-d_6).[9]



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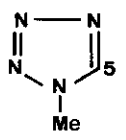

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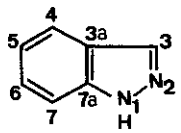
Amongst the three benzazoles,[10] indazole 8, benzimidazole 9, and benzotriazole 10, indazole exists in solution as such, 1H-indazole 8, whereas the two others exist in solution as rapid equilibrating mixtures of tautomers 1-H and 3-H (autotropic tautomerism).[3] In the solid state, the X-ray structures have been determined for all of them[10,11] and the tautomeric proton located without ambiguity on N_1.



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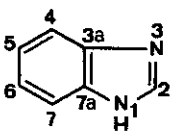

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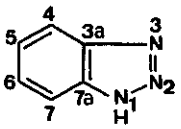

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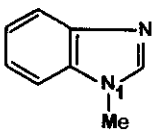

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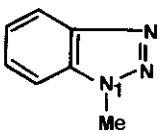

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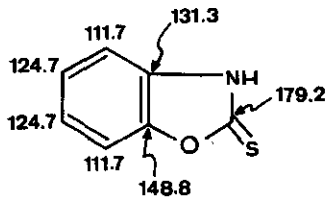
In the following table the ^{13}C chemical shifts in the solid state along with those previously determined in solution are gathered. Due to the $N_1H \rightleftharpoons N_3H$ tautomerism, in the last two cases the model compounds will be 1-methylbenzimidazole 11 and 1-methylbenzotriazole 12.

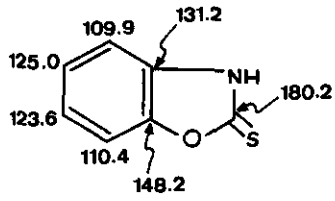
	Medium	C_2	C_3	C_4	C_5	C_6	C_7	C_{3a}	C_{7a}
Indazole 8	Solid[8]	---	134.4	121.6	121.6	126.7	111.6	123.0	141.4
	DMSO-d_6 8[12]	---	133.4	120.4	120.1	125.8	110.0	122.8	139.9
Benzimidazole 9	Solid[8]	143.1	---	{118.3 120.4	123.0	123.0	112.9	143.1	136.4
	DMSO-d_6 9[13]	142.0	---	115.5	121.6	121.6	115.5	138.1	138.1
	DMSO-d_6 9[14]	142.0	---	119.3	121.0	122.2	111.7	142.1	134.1
	$CDCl_3$ 11[15]	143.1	---	119.7	121.5	122.4	108.9	143.2	134.1
Benzotriazole 10	Solid[8]	---	---	115.5	123.4	123.4	110.7	{140.8 144.2	132.7
	DMSO-d_6 10[16]	---	---	115.1	125.7	125.7	115.1	139.2	139.2
	DMSO-d_6 12[17]	---	---	119.1	123.8	127.1	110.4	145.4	133.5
	$CDCl_3$ 12[15]	---	---	119.3	123.4	126.8	108.8	145.5	133.1

Here, a clear parallelism still exists between the solid state and the solution ^{13}C chemical shifts. However two signals appear splitted in the CP-MAS spectra, those of C_4 (benzimidazole) and C_{3a} (benzotriazole). Both concern carbons near the nitrogen atom hydrogen-bonded with the NH of other molecules in the crystal lattice.[11,18,19] The splitting seems too large to be due to the ^{14}N quadrupole effect[4] or to the existence of different molecules in the cell (four independent molecules in the case of benzotriazole).[10,19] Until a more detailed study (for instance, using substituted benzazoles) could explain these splittings, it can be concluded from the study of the five azoles, 4,5,8,9, and 10, that CP-MAS ^{13}C nmr spectroscopy is a powerful tool to determine the tautomeric structure of heterocycles in the solid state.

An example of non-annular tautomerism and another of non-prototropic tautomerism have been studied to extend further the applications of the technique. The first one concerns the functional tautomerism of benzoxazolidin-2-thione. The chemical shifts obtained[8] in the solid state 13a proves that, like in solution 13b (DMSO-d_6),[20] the equilibrium thiol/thione is completely shifted towards the thione tautomer 13. An interesting consequence of these results is that, for tautomeric studies in solution, the solid state ^{13}C chemical shifts can be used instead of the chemical shifts of one of the blocked tautomers, i.e., the N-methyl derivative of benzoxazolidin-2-thione.

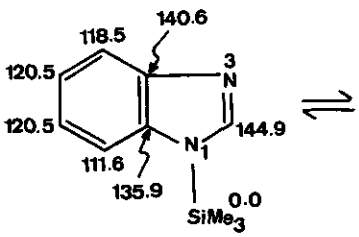


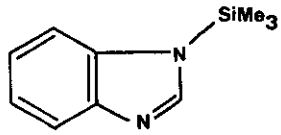
13a

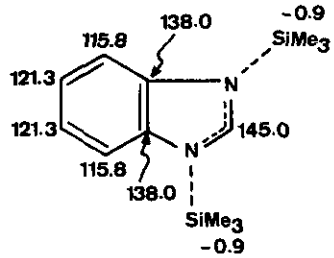


13b

The second one concerns the silylotropy[21] of 1-trimethylsilylbenzimidazole 14. The trimethylsilyl group exchanges quickly between nitrogens N_1 and N_3 of benzimidazole and only average signals are obtained for all the carbons but C_2 at room temperature 14b.







14a[22]

14b

In the solid state[8] the metallotropy no longer occurs and the molecule appears without symmetry, 14a. The mean value of the ^{13}C chemical shifts of 14a are very close to those of 14b: C_4 and C_7, 115.0 (115.8), C_{3a} and C_{7a}, 138.2 (138.0).

In conclusion, the ^{13}C-CP-MAS method affords much information about all tautomeric equilibria involving or not the proton.

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