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^{1}H- and ^{13}C-NMR Spectra of Phenyl-substituted Azole Derivatives. II. A Conformational Study

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^{13}C-NMR spectra of a number of phenyl-substituted pyrazolium bromides *1*, imidazolium bromides *2*, 1,2,3-triazolium bromides *4* and *5*, pyrazol-4-in-3-ones and -thiones *13* Z = O or S, imidazol-4-in-2-ones and -thiones *7* Z = O or S, 4-(1,2,3-triazolio)oxides and -sulfides *16*; Z = O or S, and 1,2,3-triazol-3-in-5-ones and -thiones *9*; Z = O or S have been recorded. Certain effects of substitution with methyl or chlorine have been measured. The magnitude of the chemical shifts of the benzene carbon atoms, particularly the *ortho*-carbon atoms, depends on the extent of interannular conjugation, and hence may provide information about the preferred conformation. Values for δ_{ortho}-C and the difference δ_{meta}-C − δ_{ortho}-C have been determined and their usefulness for assessing the extent of interannular conjugation in phenyl-substituted azoles with charged, zwitterionic, or partly aromatic heterocyclic rings has been demonstrated. ^{13}C-NMR data reveal that the heterocyclic ring of pyrazol-4-in-3-ones *13*; Z = O and triazol-3-in-5-ones *9*; Z = O, presumably takes up a twisted conformation, whereas the corresponding thiones are planar or nearly so. The ^{13}C-NMR-spectra render reliable information even in cases where ^{1}H-NMR-spectra fail to give correct results.

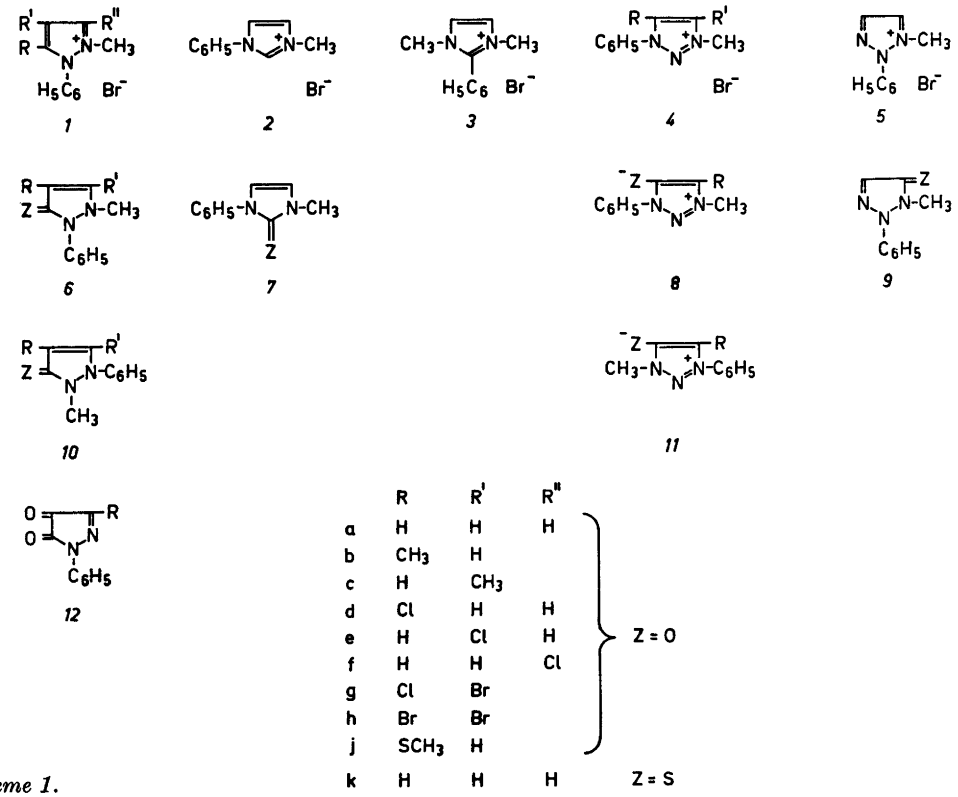
^{1}H- [1-6] and more recently ^{13}C-NMR-spectroscopy [7] has been employed for conformational studies of phenyl substituted heteroaromatic azoles. ^{1}H-NMR-spectra of unhindered compounds exhibit phenyl group multiplets, whereas phenyl substituted azoles with bulky substituents impeding interannular delocalization of the π-electrons give rise to phenyl group singlets or approximate singlets[1-3,5,6] When interannular conjugation in phenyl substituted azoles is extensive the electron density at C-2′ * increases leading to a high field shift of the C-2′ ^{13}C-NMR signal. Characteristic values for $\delta_{C-2'}$ and $\delta_{C-3'} - \delta_{C-2'}$ were found when interannular conjugation was extensive or impeded, respectively.[7] The ^{13}C-NMR method was found to yield unambiguous results even in cases where the ^{1}H-NMR method fails.

So far, ^{1}H- or ^{13}C-NMR spectroscopy has not been applied systematically to conformational analysis of phenyl substituted azoles with charged, zwitterionic, or non-aromatic heterocyclic rings.

The marked deshielding of the *o*-phenyl protons in unhindered systems may be caused by several factors the relative significance of which is poorly understood.[1,2,4-6,9,10] Presumably, anisotropy effects induced by the heteroaromatic ring play a major role.[11,12] Since phenyl substituted azoles with non-aromatic heterocyclic rings are devoid of a heterocyclic ring current, ^{1}H-NMR would not be expected to be useful for conformational analysis in these systems. Even in conformational analysis of phenyl substituted azoles with charged or zwitterionic heterocyclic rings the values of ^{1}H-NMR-shifts should be interpreted with caution due to the uncertain origin of the shifts and to known exceptions from the rules.[7] In contrast, the ^{13}C-NMR method provides direct information about the extent of delocalization. Hence, reliable information about the conformation is expected in phenyl substituted azoles with charged, zwitterionic or non-aromatic rings.

Results of a ^{1}H- and ^{13}C-NMR investigation

* In the present paper the heterocyclic carbon atoms are numbered according to the IUPAC nomenclature.[8] The phenyl carbon atoms are denoted with a dash. Counting starts with the substituted atom (C-1′).



Scheme 1.

of such compounds are reported in the present paper. As representatives of charged azoles, phenyl substituted pyrazolium bromides *1*, imidazolium bromides *3*, and 1,2,3-triazolium bromides *4* and *5* have been studied. Zwitterionic azoles are represented by the phenyl substituted 4(1,2,3-triazolio)oxides and -sulfides *16*; Z = O and S. Finally, 1,2-disubstituted pyrazol-4-in-3-ones *13*; Z = O, -thiones *13*; Z = S, 1,3-disubstituted imidazol-4-in-2-ones *7*; Z = O, -thiones *7*; Z = S, 1,2-disubstituted 1,2,3-triazol-3-in-5-ones *9*; Z = O, and -thiones *9*; Z = S have been investigated as representatives of azole derivatives with reduced heteroaromaticity.*

* Undoubtedly, the azolinones and -thiones, like 2-pyridone and -thione,[13] are heteroaromatically stabilized to a certain extent through resonance structures such as *14* and *15*. Estimates of heteroaromatic stabilization are available only for pyrazolones *13*; Z = O, contradictory results being reported.[14–17]

RESULTS

Most of the pertinent ^{1}H-NMR-data have been published previously.[18–23] ^{13}C-Signals arising from the phenyl groups are summarized in the Tables 1, 2, and 3.

Proton noise-decoupled ^{13}C-NMR data for pyrazolium, imidazolium, and 1,2,3-triazolium bromides are presented in Tables 1 and 2.

In the non-decoupled spectrum of *1a* (Table 4), the two signals at lowest field and that at the next highest field exhibited the largest splittings. Hence these signals were assigned to the heterocyclic carbon atoms.[24a]

In the off-resonance proton-decoupled spectra of *1d*, *1e*, and *1f*, with irradiating upfield from the aromatic protons (see Experimental), the signals showing the largest residual coupling were ascribed to the proton-carrying C-3 and C-5 atoms. The (sharp) non-shifted singlets in *1d*, or *1e*, when compared to *1f*, were attributed

Table 1. ^{13}C-NMR chemical shifts of phenyl substituted azolium salts in aqueous solution.

Compound [a]		Position of carbon atoms in ppm C-2	C-3	C-4	C-5	C-1′	C-2′	C-3′	C-4′	$\frac{N\text{-}CH_3}{C\text{-}CH_3}$	[b]
1-Methyl-2-phenyl-pyrazolium bromide	*1a*		138.8	108.9	139.7	132.8	127.9	131.0	133.1	38.5	bs
1-Methyl-2-phenyl-3-chloro-pyrazolium bromide	*1d*		138.4	108.8	139.9	133.9	129.2	131.4	133.9	39.7	s
1-Methyl-2-phenyl-4-chloro-pyrazolium bromide	*1e*		136.9	113.6	138.0	132.3	127.9	131.0	133.5	39.1	s
1-Methyl-2-phenyl-5-chloro pyrazolium bromide	*1f*		139.0	109.2	139.4	133.1	128.0	131.1	133.5	36.1	nm
1-Methyl-3-phenyl-imidazolium bromide	*2a*	135.8		122.2	125.3	134.4	122.8	131.2	130.9	37.2	s
1,3-Dimethyl-2-phenyl-imidazolium bromide	*3*			123.6	123.6	121.7	130.2	130.8	133.1	36.5	bs
1-Methyl-3-phenyl-1,2,3-triazolium bromide	*4a*			129.5	132.5	135.3	122.0	130.8	132.5	41.2	m
1,4-Dimethyl-3-phenyl-1,2,3-triazolium bromide	*4b*			142.0	130.3	133.7	125.9	130.8	132.7	40.9 10.2	s
1,5-Dimethyl-3-phenyl-1,2,3-triazolium bromide	*4c*			127.0	142.2	135.2	121.8	130.9	132.3	38.4 9.4	m
1-Methyl-3-phenyl-4-chloro-1,2,3-triazolium bromide	*4d*			130.8	130.5	132.7	126.0	130.8	133.3	42.3	bs
1-Methyl-3-phenyl-5-chloro-1,2,3-triazolium bromide	*4e*			127.3	133.4	135.2	122.0	131.0	132.9	39.0	2+3
1-Methyl-2-phenyl-1,2,3-triazolium bromide	*5*			135.4	137.5		131.1	133.4	134.0	40.5	s

[a] The compounds were prepared as described in the experimental section. [b] Appearance of the phenyl group in the ^{1}H-NMR spectrum, bd (broad doublet), bs (broad singlet), m (multiplet), nm (narrow multiplet), s (singlet), 2+3 (a low field multiplet containing two protons plus a high field multiplet containing three protons).

to C-1′. In *1f*, the signal at lowest field, in *1d*, the signal at next lowest field, and in *1e*, the signal at next highest field appeared as (broad) singlets. Hence these signals were assigned to the chlorine-substituted carbon atoms C-5, C-3, and C-4, respectively. Consequently, the order $\delta_{C-5} > \delta_{C-3} > \delta_{C-4}$ was deduced for 1-methyl-2-phenyl-pyrazolium bromide *1a*.

Identification of the phenyl carbon atoms of *1a* through the fine structure of the undecoupled signals as described previously [7] proved unsuccessful since the spectra were indistinct and unresolvable and did no allow an unequivocal distinction between C-2′ and C-3′.* However, in all phenyl-substituted azole derivatives where a definite assignment, through undecoupled spectra, has been carried out (see Ref. 7 and below) the intensity of the signals decreases in the order C-3′ > C-2′ > C-4′. The same order of intensity was suggested by the identification of C-2′, C-3′, and C-4′ in *1a*, 1*d*, 1*e*, and

* The change in fine structure may be due to a change in the ratio between $^3J_{CCCH}$ and $^2J_{CCH}$ [7] or to the presence of a more strongly coupled spin system in the phenyl group of *1a* — and in other azolium salts as well — than in the azoles.

Table 2. ^{13}C-NMR chemical shifts of phenyl substituted azolium salts in deuteriochloroform solution.

Compound		Position of carbon atoms in ppm C-2	C-3	C-4	C-5	C-1′	C-2′	C-3′	C-4′	$\frac{N\text{-}CH_3}{C\text{-}CH_3}$	[b]
1-Methyl-2-phenyl-pyrazolium bromide	*1a* [a]		137.3	108.5	140.7	131.9	127.7	130.5	132.7	38.9	bd
1-Methyl-2-phenyl-3-chloro-pyrazolium bromide	*1b*		136.8	107.7	140.6	132.8	129.1	130.4	128.7	39.7	bs
1-Methyl-2-phenyl-5-chloro-pyrazolium bromide	*1f*		138.5	108.9	132.4		127.9	130.1	132.1	36.5	2+3
1-Methyl-3-phenyl-imidazolium bromide	*2a* [a]	135.8		120.7	124.5	134.2	121.7	130.3	130.0	37.2	m
1-Methyl-3-phenyl-1,2,3-triazolium bromide	*4a*			128.9	133.0	134.1	120.9	129.8	131.1	41.1	2+3
1,4-Dimethyl-3-phenyl-1,2,3-triazolium bromide	*4b*			140.4	131.2	132.7	125.7	129.9	131.9	40.3 10.0	s
1,5-Dimethyl-3-phenyl-1,2,3-triazolium bromide	*4c*			127.4	141.6	134.1	120.6	129.9	131.2	38.8	2+3

[a] Solution saturated at room temperature. [b] Appearance of the phenyl group in the ^{1}H-NMR spectrum.

1f, as well as in the other azolium bromides *2*, *3*, *4*, and *5*.

The ^{13}C-NMR-signals of 1-methyl-3-phenyl-1,2,3-triazolium bromide *4a*, its 4- and 5-methyl derivatives *4b* and *4c*, as well as its 4- and 5-chloro derivatives *4d* and *4e* (Table 1), were identified similarly. The off-resonance spectra indicated that δ_{C-5} in *4b* and *4d* was larger than δ_{C-4} in *4c* and *4e*, respectively. Conversely, δ_{C-5} in *4c* and *4e* was larger than δ_{C-4} in *4b* and *4d*, respectively. Hence, δ_{C-5} was assumed to be larger than δ_{C-4} in 1-methyl-3-phenyl-1,2,3-triazolium bromide *4a*, a supposition confirmed by its undecoupled spectrum (Table 4) in which C-4 appeared with sharp doublet fine structure due to coupling to H-5. The fine structure of C-5 was a doublet with unresolved hyperfine structure. The doublet part is explained by coupling to H-4, the hyperfine structure by coupling to the methyl protons.

In the undecoupled spectrum of 1-methyl-3-phenyl-imidazolium bromide *2a* (Table 4) the fine structure of the three signals with large splittings, from low to high field, was a narrow, quartet-like pattern, an extended double doublet with broad peaks, and an extended double doublet with narrow peaks. The two high field signals were attributed to C-4 and C-5, the extended fine structure was attributed to large $^2J_{CCH}$ couplings. The signal with the broad peaks was attributed to C-5, the broadening arising from long range coupling to the methyl protons. The narrow, fine splitting of C-2 is the result of small $^3J_{CNCH}$ couplings. The strong deshielding of C-2 is caused by the two adjacent nitrogen atoms.

C-4 and C-5 in 1-methyl-2-phenyl-1,2,3-triazolium bromide *5a* could be distinguished, since the latter signal in the undecoupled spectrum (Table 4) appeared with unresolved hyperfine structure due to weak coupling to the methyl protons.

The ^{13}C-NMR signals of [1-methyl-3-phenyl-4-(1,2,3-triazolio)]-oxide *8a* and of [1-phenyl-3-methyl-4-(1,2,3-triazolio)]oxide *11a* (Table 3) were identified through the proton undecoupled spectra (Table 5). The signal exhibiting solely doublet fine structure was attributed to C-4. The doublet arises from coupling to H-5. C-4 of *8a* and *11a*, like common carbonyl carbon atoms,[24b] absorb at very low field. The signal with the largest splitting was attributed to C-5. C-5 of *8a* and *11a* resonate at higher field than the other aromatic carbon atoms. The signals of the

Table 3. ^{13}C-NMR chemical shifts of phenyl substituted pyrazol-4-in-3-ones *13*; Z = O, pyrazol-4-in-3-thiones *13*; Z = S, imidazol-4-in-2-ones *7*; Z = O, imidazol-4-in-2-thiones *7*; Z = S, 4-(1,2,3-triazolio)oxides *16*; Z = O, 4-(1,2,3-triazolio)sulfides *16*; Z = S, 1,2,3-triazol-3-in-5-ones *9*; Z = O, and 1,2,3-triazol-3-in-5-thiones *9*; Z = S.

Compound [a]	Position of carbon atoms in ppm								$\frac{N\text{-}CH_3}{C\text{-}CH_3}$	$\frac{O\text{-}CH_3}{S\text{-}CH_3}$	[b]
	C-2	C-3	C-4	C-5	C-1′	C-2′	C-3′	C-4′			
2-Phenyl-5-methyl-pyrazol-5-in-3,4-dione *12b* [46]		183.9	148.7	144.0	136.5	117.4	128.7	125.8	11.0		2+3
2-Phenyl-4-methoxy-carbonyl-pyrazol-4-in-3-one *13l* [c,d]		166.3		138.2	137.2	121.1	128.8	126.7		51.5	m
1-Methyl-2-phenyl-pyrazol-4-in-3-one *6a* [13]		165.9	98.3	145.6	133.9	124.4	128.9	126.8	37.5		bs
1,5-Dimethyl-2-phenyl-pyrazol-4-in-3-one *6c* [48]		165.7	98.1	156.0	134.8	123.8	128.6	126.1	35.3 12.9		s
1-Methyl-2-phenyl-5-chloro-pyrazol-4-in-3-one *6e* [44,49]		164.1	99.6	147.5	134.3	123.9	128.9	126.9	36.7		bs
1-Methyl-2-phenyl-4-chloro-5-bromo-pyrazol-4-in-3-one *6g* [14]		159.7	108.1	134.0	133.8	123.8	129.1	127.3	38.7		s
1-Methyl-2-phenyl-4,5-dibromo-pyrazol-4-in-3-one *6h* [14]		156.1	95.7	136.5	134.1	123.8	129.0	127.3	38.7		s
1-Methyl-2-phenyl-pyrazol-4-in-3-thione *6k* [41]		170.1	111.1	136.2	133.2	128.4	129.2	129.9	37.2		s
1-Phenyl-2-methyl-pyrazol-4-in-3-one *10a* [13]		167.9	97.8	142.1	137.5	122.6	129.6	127.4	30.1		m
1-Phenyl-2,5-dimethyl-pyrazol-4-in-3-one *10c* [50]		167.1	97.8	152.5	136.9	126.3	129.4	128.6	30.0 13.2		m
1-Phenyl-2-methyl-5-chloro-pyrazol-4-in-3-one *10e* [44,49]		165.4	99.0	143.6	135.8	126.5	129.2	129.2	30.2		m
1-Phenyl-2-methyl-4-chloro-5-bromo-pyrazol-4-in-3-one *10g* [14]		161.0	107.7	130.0	136.6	126.9	129.4	129.7	31.1		m
1-Phenyl-2-methyl-4,5-dibromo-pyrazol-4-in-3-one *10h* [14]		162.0	95.2	132.6	136.7	126.8	129.3	129.7	31.3		m
1-Phenyl-2-methyl-pyrazol-4-in-3-thione *10k* [44]		170.0	112.2	134.8		125.6	129.7	129.9	33.3		m
1,2-Diphenyl-pyrazol-4-in-3-one *13m* [51]		166.6	98.9	145.3	138.9 135.1	120.8 123.2	129.3 128.4	126.2 125.9			nm nm
1,2-Diphenyl-4-methyl-pyrazol-4-in-3-one *13n* [e]		166.9	109.1	143.3	140.1 135.7	120.4 122.3	129.2 128.4	125.6 125.4	7.8		
1,2-Diphenyl-5-methyl-pyrazol-4-in-3-one *13o* [52]		166.0	98.9	155.9	138.6 135.4	125.1 123.2	128.9 128.2	127.6 125.4	 13.7		s m
1-Methyl-3-phenyl-imidazol-4-in-2-one *7a* [41]	152.1		108.8	112.4	137.0	121.1	128.7	125.3	30.4		m
1-Methyl-3-phenyl-imidazol-4-in-2-thione *7k* [41]	163.0		117.2	118.1	137.9	125.4	128.5	127.7	35.1		m

Table 3. Continued.

{1,3-Dimethyl-5-phenyl-4-(1,2,3-triazolio)}oxide	*16p*	155.6	126.7		127.8	128.6	127.8	38.8; 31.0		m
{1-Methyl-3-phenyl-4-(1,2,3-triazolio)}oxide	*8a* [16]	157.8	107.9	135.4	120.8	128.7	127.5	39.6		2+3
{1,5-Dimethyl-3-phenyl-4-(1,2,3-triazolio)}oxide	*8b* [16]	155.6	115.8	135.7	120.7	128.6	127.1	37.4 7.6		2+3
{1-methyl-3-phenyl-5-bromo-(1,2,3-triazolio)}oxide	*8h* [16]	154.1	92.8	135.7	120.3	128.8	128.6	38.9		2+3
{1-Methyl-3-phenyl-4-(1,2,3-triazolio)}sulfide	*8k* [43]	158.8	128.0	135.2	124.7	128.4	129.2	39.0		2+3
{1-Phenyl-3-methyl-4-(1,2,3-triazolio)}oxide	*11a* [16]	157.8	103.6	136.2	119.7	129.3	129.6	31.3		nm
{1-Phenyl-3,5-dimethyl-4-(1,2,3-triazolio)}oxide	*11b* [16]	156.3	115.0		124.1	129.3	130.0	31.0 8.6		bs
{1-Phenyl-3-methyl-5-bromo-4-(1,2,3-triazolio)}oxide	*11h* [16]	155.7	92.1	135.5	124.4	129.2	130.5	32.0		s
{1-Phenyl-3-methyl-5-methylthio-4-(1,2,3-triazolio)}oxide	*11j* [53]	157.6	111.5	135.6	124.5	128.8	130.1	31.7	17.9	s
{1-Phenyl-3-methyl-4-(1,2,3-triazolio)}sulfide	*11k* [53]	158.3	123.8	134.8	120.1	129.6	130.3	35.4		nm
1-Methyl-2-phenyl-triazol-3-in-5-one	*9a* [17]	130.1	160.0	137.6	123.4	129.5	128.7	30.4		m
1-Methyl-2-phenyl-triazol-3-in-5-thione	*9k* [41]	140.2	165.2	135.5	124.9	129.7	130.4	34.1		m

[a] The compounds were prepared as described in the references given. [b] Appearance of the phenyl group signal in the ^{1}H-NMR spectrum. See footnote *b*, Table 1. [c] The material was prepared analogous to the ethoxycarbonyl compound.[47] [d] The solution was saturated at room temperature. [e] The material was prepared analogous to *13m*.[51]

latter were identified through the undecoupled spectra as described previously.[7] The intensities of the proton noise decoupled signals of *8a* and *11a* decrease in the order C-3′ > C-2′ > C-4′ > C-5 > C-4 and C-1′. The order of intensities was used to identify the phenyl carbon signals of the 5-substituted 4(1,2,3-triazolio)oxides *8b*, *8h*, *11b*, *11h*, *11j*, and *16p* and those of the 4(1,2,3-triazolio)sulfides *8k* and *11k* (Table 3). The C-4 and C-5 signals of the 5-substituted 4(1,2,3-triazolio)oxides were assigned by their characteristic low field and high field positions, respectively. The 4(1,2,3-triazolio)sulfides *8k* and *11k* like the analogous oxygen compounds *8a* and *11a*, showed a low field and a high field ^{13}C-NMR signal (Table 3). Hence these signals were attributed to C-4 and C-5, respectively.

The ^{13}C-NMR signals (Table 3) of the pyrazol-4-in-3-ones *13*; Z = O, imidazol-4-in-2-ones *7*; Z = O, and 1,2,3-triazol-3-in-5-ones *9*; Z = O or S were identified analogously through undecoupled spectra (Table 5). Low field signals exhibiting only fine structure were ascribed to C = O carbon atoms and signals with large splittings to proton-carrying heterocyclic carbon atoms. Benzene carbon atoms were identified in the usual way.[7] C-5 of the pyrazol-4-in-3-one *6a* was identified as the heterocyclic carbon signal at the next lowest field since it appeared with quartet hyperfine structure due to a small long-range coupling to the methyl protons. In *10a* only broadening of the C-5 signal due to coupling to the methyl protons is observed.

C-3 and C-4 of the 4- and 5- substituted

Table 4. ^{13}C-^{1}H NMR coupling constants of phenyl substituted azolium bromides [a].

Compound		The carbon to which the coupling takes plane C-2	C-3	C-4	C-5	C-1′	C-2′	C-3′	C-4′	*N*-CH_3 / *C*-CH_3
				$^{1}J_{CH}$ / $^{2}J_{CCH}$ / $^{3}J_{CXCH}$ Hz						
				190			167	167	168	146
1-Methyl-2-phenyl-pyrazolium bromide	*1a*		7;7[b]	7;7					9	
1-Methyl-3-phenyl-imidazolium bromide	*2a*	220 5;10		12[b] 5	210[b] 6		166	165		145
1-Methyl-3-phenyl-1,2,3-triazolium-bromide	*4a*			211 13	212 13		165	166 8	165 8	146
1-Methyl-2-phenyl-1,2,3-triazolium-bromide	*5*			211 10	15			166		148

[a] All coupling constants have been obtained by first order analysis. [b] The $^{3}J_{CXCH}$ coupling constants were distinguished from the $^{2}J_{CCH}$ coupling constants since the latter are of the same order of magnitude as $^{2}J_{CCH}$ in the triazolium bromides *4a* and *5a* and from C-4 of the pyrazolium bromide *1a*.

Table 5. ^{13}C-^{1}H NMR coupling constants of phenyl substituted pyrazol-4-in-3-ones *13*; Z=O, imidazol-4-in-2-ones *7*; Z=O, 4-(1,2,3-triazolio)oxides *16*, Z=O, and 1,2,3-triazol-3-in-5-ones *9*; Z=O.[a]

Compound	The carbon to which the coupling takes place C-2	C-3	C-4	C-5	C-1′	C-2′	C-3′	C-4′
			$^{1}J_{CH}$ / $^{2}J_{CCH}$ / $^{3}J_{CXCH}$ Hz					
1-Methyl-2-phenyl-pyrazol-4-in-3-one *6a*		9[b] 7	183 6	186 8[b] 2	7	163 6	161 8	160 7
1-Phenyl-2-methyl-pyrazol-4-in-3-one *10a*			183 6	189 9		161 6	162 6	164 8
1-Methyl-3-phenyl-imidazol-4-in-2-one *7*			196 10	196 7[b] 2		163 6	161 7	161 7
{1-Methyl-3-phenyl-4-(1,2,3-triazolio)}oxide *8a*			11	200	9	165 6	162 9	161 9
{1-Phenyl-3-methyl-4-(1,2,3-triazolio)}oxide *11a*			11	201		165 5	163 4	162 5
1-Methyl-2-phenyl-1,2,3-triazol-3-in-5-one *9*			201		10	165	163	163

[a] All coupling constants have been obtained by first order analysis. [b] The $^{3}J_{CXCH}$ coupling constants were distinguished from the $^{2}J_{CCH}$ coupling constants since the latter are of the same order of magnitude as $^{2}J_{CCH}$ in the triazole-derivatives *8a* and *11a*.

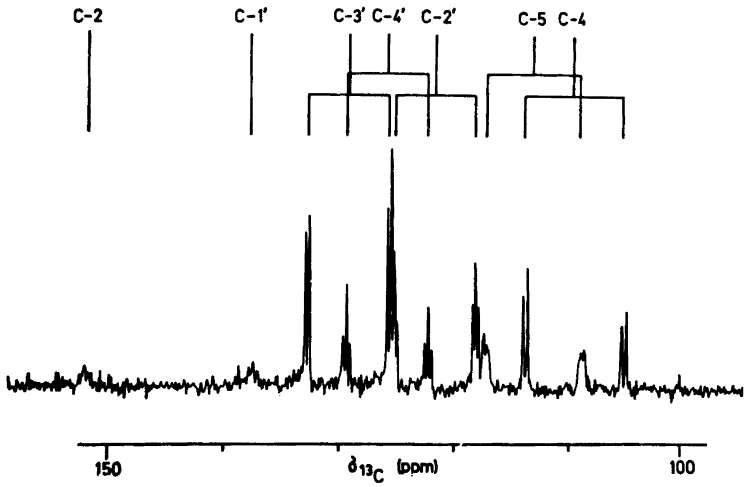


Fig. 1. Proton undecoupled ^{13}C-NMR spectrum of 1-methyl-3-phenyl-4-in-2-one *7a*.

pyrazol-4-in-3-ones *6c*, *6e*, *6g*, *6h*, *10c*, *10e*, *10g*, *10h*, *12b*, *13l*, *13m*, and *13o* were identified through their characteristic positions. C-4 in *12b* was identified as the second lowest field signal since its intensity, like that arising from C-3, was particularly low. Low intensity as the result of long relaxation time, T_1, is characteristic of carbonyl carbon atoms.[25a]

C-5 and the benzene ring carbon atoms of the substituted pyrazol-4-in-3-ones were identified, assuming the same order of intensities, C-3′ > C-2′ > C-4′ > C-4, C-5 > C-1′ > C-3, as observed in *6a* and *10a* and taking into account that substituent-carrying carbon atoms appear with strongly reduced intensity.[7]

The two sets of phenyl carbon signals of *13m* and *13n* were assigned by comparison with the phenyl carbon signals of *6a* and *10a*. For example, $\delta_{C-1'}$ of *10a* > $\delta_{C-1'}$ of *6a*. Hence, the low and high field C-1′ signals of *13m* were ascribed to the 1- and 2-phenyl groups, respectively. Similarly, the two sets of phenyl carbon signals of *13o* were identified by comparison with the phenyl carbon signals of *6c* and *10c*.

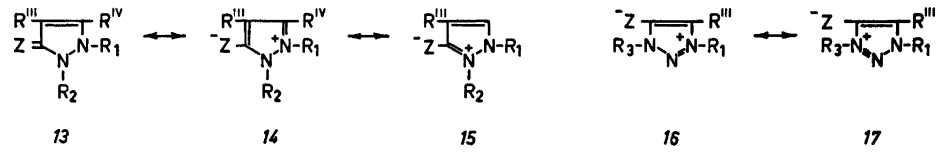
C-5 of 1-methyl-3-phenyl-imidazol-4-in-2-one *7a* was distinguished from C-4 as the signal which shows multiplet hyperfine structure due to coupling to the methyl protons (Fig. 1).

The ^{13}C-NMR signals of the thiones *6k* and *10k* were assigned comparing δ-values and relative intensity of signals with those of the corresponding oxygen analogues. The signals of the thiones *7k* and *9k* were identified through their undecoupled spectra as described for the corresponding oxygen analogues.

Superficially, δ^{13}_{C} of azolium ring carbon atoms is expected to increase when the number of ring nitrogen atoms, particularly in α-position or positively charged, increases. However, the observed ^{13}C chemical shifts are not in keeping with this assumption. (Thus δ_{C-5} of *1a* > δ_{C-5} of *5* > δ_{C-2} of *2a*). Nor are these shifts larger the faster the proton on the appropriate carbon atom is exchanged with deuterium in basic solution.[18,21,22]

According to calculations [26] and ^{13}C-NMR of the protonated azoles [27] or azines,[28] the electron density of α-carbon atoms increases when a heterocyclic ring nitrogen adopts a positive charge. This effect may account for the unexpected order in the present case.

In each of the methylphenylazolium bromides *1a*, *2a*, *4a*, and *5a* the chemical shift of a carbon atom adjacent to an *N*-methyl group is larger than that of a carbon atom adjacent to an *N*-phenyl group, indicating that the electron density is higher at the latter carbon atom. The protons at the appropriate carbon atoms absorb in the reverse order, which also corresponds to the relative acidity of the protons, as reflected by the rate of the base catalyzed deuterium exchange.[18,21] In *1a*, *2a*, *4a*, and *5a* $\delta^{13}_{CH_3N-1}$ is



13 14 15 16 17

	R_1	R_2	R^{III}	R^{IV}	
l	H	C_6H_5	$COOCH_3$	H	Z = O
m	C_6H_5	C_6H_5	H	H	
n	C_6H_5	C_6H_5	CH_3	H	
o	C_6H_5	C_6H_5	H	CH_3	
p	CH_3	CH_3	C_6H_5	H	

Scheme 2.

larger the more electron attracting the ring is. (Thus δ_{CH_3N-1} of *4a* and *5a* > δ_{CH_3N-1} of *1a* > δ_{CH_3N-1} of *2a*).

Methyl carbon atoms at N-1 in 1,3-disubstituted 4(1,2,3-triazolio)oxides *16*; Z = O, absorb at 6.8 – 8.7 ppm lower field than methyl carbon atoms at N-3. This indicates that N-1 is more electron deficient than N-3, suggesting that the resonance structure *16*; Z = O (Scheme 2) is the major contributor to the 4(1,2,3-triazolio)oxide hybrid. The chemical shifts of C-4, C-5, and the N-1 methyl carbon atoms in the 4(1,2,3-triazolio)sulfides *8k* and *11k* are similar to those in the corresponding 4(1,2,3-triazolio)-oxides *8a* and *11a*, respectively. In contrast, δ_{CH_3N-3} is 4.1 ppm larger in the 4(1,2,3-triazolio)sulfide *11k* than δ_{CH_3N-3} in the corresponding 4(1,2,3-triazolio)oxide *11a*. δ_{CH_3N-1} in *8k* is larger than δ_{CH_3N-3} in *11k*, again indicating that *16*; Z = S, is the major contributor to the hybrid. This has recently been confirmed in the solid by X-ray studies of [1,3-dimethyl-4-(1,2,3-triazolio)] sulfide *16*; $R_1 = R_3 = CH_3$, Z = S.[29]

Methyl carbon atoms at N-1 in 1,2-disubstituted pyrazol-4-in-3-ones *13*; Z = O, absorb at 7.4 – 8.2 ppm lower field than N-2 methyl carbon atoms. This indicates that N-1 is more electron deficient than N-2, suggesting that the dipolar structure *14*; Z = O, contributes appreciably to the pyrazol-4-in-3-one hybrid. Arguments for [14] and against [15–17] the importance of zwitterionic structures have been presented, and some of the arguments have been critically analyzed.[30,31] It should be emphasized that the present data are only suggestive.

The ^{13}C-NMR chemical shifts of the heterocyclic ring- and the *N*-methyl carbon atoms of the thiones *6k*, *10k*, *7k*, and *9k* are quite different from those of the corresponding oxygen analogues.

A methyl group deshields the methyl carrying carbon atom 10.4 – 11.5 ppm in 1,3-disubstituted 1,2,3-triazolium salts *4*, 1,3-disubstituted 4(1,2,3-triazolio)oxides *16*; Z = O, and 1,2-disubstituted pyrazol-4-in-3-ones *13*; Z = O. Carbon atoms adjacent to the methyl-substituted carbons are shielded 1.5 – 2.1 ppm in 1,2,3-triazolium salts *4* and 4(1,2,3-triazolio)-oxides *16*; Z = O.

The effect of chlorine on the ^{13}C chemical shifts of azolium salts depends on the type of ring and the position of the substituent. Thus chlorine deshields the substituted carbon atom 0.9 – 1.3 ppm in the 1,2,3-triazolium bromides *4d* and *4e*. The adjacent carbon atom is shielded 2.0 – 2.2 ppm. Chlorine in the 4-position of the pyrazolium salt *1e* has a similar effect but chlorine in the 3- or 5-position of the pyrazolium salts *1d* and *1f* affects the ^{13}C chemical shift of the substituted and the adjacent carbon atom less than 0.4 ppm (Table 1). Chlorine in the 5-position of the pyrazolones *13*; Z = O, deshields the substituted and the adjacent carbon atom 1.5 – 1.9 and 1.2 – 1.3 ppm, respectively.

Bromine shields the substituted carbon atom *ca* 14.6 ppm in the 4(1,2,3-triazolio)oxides *16*; Z = O. The adjacent carbon atom is deshielded *ca* 3.0 ppm.

The effects of the substituents are similar to

Table 6. The ^{13}C chemical shift of C-2′ and the ^{13}C chemical shift difference between C-3′ and C-2′ for *C*- and *N*-phenyl substituted azole derivatives.

Type of compound	Hindered/unhindered[a]		Representative compounds	$\delta_{C-2'}$[b] ppm	$\delta_{C-3'} - \delta_{C-2'}$[b] ppm
1-Phenyl-pyrazoles[c]	unhindered			118.5 – 118.8	10.5
	hindered			124.6 – 125.4	3.3 – 4.0
1-Methyl-2-phenyl-pyrazolium bromides *1*	hindered			127.7 – 129.1	1.3 – 2.6
1,2-Disubstituted pyrazol-4-in-3-ones *13*; Z = O	C_6H_5	*unhindered*	*13m*	120.8	8.5
	O		*13l*	121.1	7.7
	CH_3		*10a*	122.6	7.0
	$O + C_6H_5$		*13m*	123.2	5.2
	$O + CH_3$	↓	*6a*	123.8 – 124.4	4.5 – 5.3
	$CH_3 + CH_3$ or Br	*hindered*	*10c*	126.3 – 126.9	2.5 – 3.1
1,2-Disubstituted pyrazol-4-in-3-thiones *13*; Z = S	CH_3	*hindered*	*10k*	125.6	4.1
	$S + CH_3$	*hindered*	*6k*	128.4	0.8
1-Phenyl-imidazoles[c]	unhindered			121.0	9.4
1-Methyl-3-phenyl-imidazolium bromide *2*	unhindered			121.7	8.6
1-Methyl-3-phenyl-imidazol-4-in-2-one or -thione *7*; Z = O or S	O	*unhindered*	*7a*	121.1	7.6
	S	*hindered*	*7k*	125.4	3.1
2-Phenyl-imidazoles[c,e]	unhindered			125.2	3.2
	hindered			128.0	0
1,3-Dimethyl-2-phenyl-imidazolium bromide *3*[e]	hindered			130.2[d]	0.6[d]
1-Phenyl-1,2,3-triazoles[c]	unhindered			120	9.4
	hindered			124.5	4.6
1-Methyl-3-phenyl-1,2,3-triazolium bromides *4*	unhindered			120.6 – 120.9	8.9 – 9.3
	hindered			125.7	4.2
1,3-Disubstituted 4-(1,2,3-triazolio) oxides or sulfides *16*; Z = O or S	unhindered		*11a*	119.7 – 120.1	9.5 – 9.6
	O	*unhindered*	*8a*	120.3 – 120.8	7.9 – 8.5
	hindered		*11b*	124.1 – 124.5	4.3 – 5.2
	S	*hindered*	*8k*	124.7	3.7
{1,3-Dimethyl-5-phenyl-4-(1,2,3-triazolio)}oxide[e] *16p*	hindered			127.8	0.8
2-Phenyl-1,2,3 triazole[c]	unhindered			118.3	10.6
1-Methyl-2-phenyl-1,2,3-triazolium bromide *5*	hindered			131.1[d]	2.3[d]
1-Methyl-2-phenyl-1,2,3-triazol-3-in-5-one *9a*	CH_3	*hindered*		123.4	6.1
1-Methyl-2-phenyl-1,2,3-triazol-3-in-5-thione *9k*	CH_3	*hindered*		124.9	4.8

[a] See the footnote p. 71. The indications are typed in italics when the extent of hindrance has been estimated from the ^{13}C-NMR data and the substituents adjacent to the *N*-phenyl groups are stated in cases where a more exact specification is considered necessary. [b] When not otherwise stated the δ-values given are for deuteriochloroform solution with TMS as an internal standard. [c] The data have been published previously [7] but are shown for comparison. [d] The δ-values given are for deuterium oxide solution with *p*-dioxane as an internal standard. [e] Notice that the compound is *C*-phenyl substituted.

Table 7. $^1J^{13}_{CH_3N}$ coupling constants of *N*-methyl substituted azoles in deuteriochloroform.[a]

Compound	$^1J^{13}_{CH_3N}$ Hz
1-Methyl-pyrazole	140.0
1-Methyl-imidazole	140.9
1-Methyl-1,2,3-triazole	142.2
2-Methyl-1,2,3-triazole	142.0

[a] The values were determined by 60 MHz ^{1}H-NMR spectroscopy.

those observed in the phenyl substituted azoles.[7]

The $^1J^{13}_{CH}$ coupling constants of the heterocyclic carbon atoms in the azolium bromides *1*, *2*, *4*, and *5* are 12 – 20 Hz larger than the corresponding coupling constants of the parent 1-phenyl substituted azoles [7] (Table 4). The long range coupling constants are similar in *1*, *2*, *4*, and *5* and in the parent 1-phenyl-azoles. The $^1J^{13}_{CH_3N}$ coupling constants are 2 – 4 Hz larger in *1*, *2*, *4*, and *5* than in the parent 1-methyl substituted azoles (Table 7). The larger $^1J^{13}_{CH}$ coupling constants observed in the azolium salts, compared with the corresponding azoles, are explained by the increased electron deficiency of the azolium systems.

The $^1J^{13}_{CH}$ and $^2J^{13}_{CCH}$ coupling constants of the 1,2,3-triazol-3-in-5-one *9a*; the 4(1,2,3-triazolio)oxides *8a* and *11a*, imidazol-4-in-2-one *7a*, and the pyrazol-4-in-3-ones *6a* and *10a* (Table 5) are similar to the values found in the parent *N*-phenyl substituted compounds.[7] (Thus the $^1J^{13}_{CH}$ coupling constants decrease in the order $^1J_{CH-4}$ in *9a* and $^1J_{CH-5}$ in *8a* and *11a* > $^1J_{CH-4}$ in *7a* > $^1J_{CH-5}$ in *6a* and *10a* > $^1J_{CH-4}$ in *6a* and *10a*. Similarly, $^2J_{HCC-4}$ in *8a* and *11a* > $^2J_{HCC-4}$ in *7a* > $^2J_{HCC-3}$ and $^2J_{HCC-5}$ in *6a* and *10a* > $^2J_{HCC-4}$ in *6a* and *10a*).

DISCUSSION

The ^{13}C chemical shift of C-3′. In simple *N*-phenyl substituted azoles, $\delta_{C-3'} = 128.5 - 129.8$ ppm is the parameter least sensitive to ring type and substitution.[7] Similarly, C-3′ of the 4-(1,2,3-triazolio)oxides *16*; Z = O, 4-(1,2,3-triazolio)-sulfides *16*; Z = S, pyrazol-4-in-3-ones *13*; Z = O, pyrazol-4-in-3-thiones *13*; Z = S, 1,2,3-triazol-3-in-5-one *9a*, 1,2,3-triazol-3-in-5-thione *9k*, imidazol-4-in-2-one *7a*, and imidazol-4-in-2-thione *7k*, consistently resonate between 128.2 and 129.7 ppm (Table 3). The shifts of C-3′ of the azolium salts *1*, *2*, *4*, and *5* are slightly larger [129.8 – 130.5 ppm in deuteriochloroform solution (Table 2) and 130.8 – 133.4 ppm in deuterium oxide solution (Table 1)], presumably due to strong inductive electron attraction from the positively charged azolium ring.

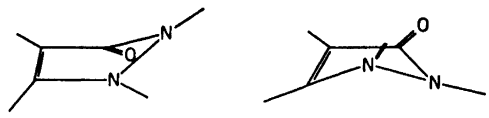
The ^{13}C chemical shift of C-2′. In simple *N*-phenyl substituted azoles, $\delta_{C-2'}$ and $\delta_{C-3'} - \delta_{C-2'}$ are the parameters most susceptible to hindrance of interannular conjugation.[7] In Table 6, these parameters of simple phenyl substituted azoles are compared with those extracted from Tables 2 and 3 of the phenyl substituted derivatives with charged, zwitterionic, or partly aromatic heterocyclic rings. In the unhindered imidazolium salt *2* and triazolium salts *4a*, *4c*, and *4e*, $\delta_{C-2'}$ ($CDCl_3$) = 120.6 – 121.7 ppm and $\delta_{C-3'} - \delta_{C-2'}$ ($CDCl_3$) = 8.6 – 9.3 ppm. [In deuterium oxide solution $\delta_{C-2'} = 121.8 - 122.8$ ppm and $\delta_{C-3'} - \delta_{C-2'} = 8.4 - 9.1$ ppm (Table 1)]. These values correspond to those of the unhindered azoles indicating that interannular conjugation is extensive in these salts. In the hindered * pyrazolium bromides *1a*, *1d*, *1e*, and *1f* and 1,2,3-triazolium bromides *4b*, *4d*, and *5a*, $\delta_{C-2'}$ ($CDCl_3$) = 125.7 – 129.1 ppm and $\delta_{C-3'} - \delta_{C-2'}$ ($CDCl_3$) = 1.3 – 4.2 ppm. [In deuterium oxide solution $\delta_{C-2'} = 125.9 - 131.1$ ppm and $\delta_{C-3'} - \delta_{C-2'} = 2.1 - 4.9$ ppm (Table 1).] These values are similar to those of the hindered azoles. In the hindered *C*-phenyl substituted imidazolium salt *3*, $\delta_{C-2'} = 130.2$ ppm and $\delta_{C-3'} - \delta_{C-2'} = 0.6$ ppm, *i. e.* values similar to those of the hindered *C*-phenyl substituted imidazoles.

In the unhindered [1-phenyl-3-methyl-4-(1,2,3-triazolio)]oxide *11a* and -sulfide *11k* the values of $\delta_{C-2'}$ and $\delta_{C-3'} - \delta_{C-2'}$ correspond to those of the unhindered 1-phenyl substituted 1,2,3-triazoles indicating that interannular conjugation is extensive in *11a* and *11k*. Methyl, bromine, or methylthio in the 5-position of *11*; Z = O, impedes interannular conjugation as reflected by $\delta_{C-2'}$ and $\delta_{C-3'} - \delta_{C-2'}$ which are

* In the following discussion it is assumed that the steric effects of substituents are similar to those in the azoles and that the steric effect of an *N*-methyl group and a *C*-methyl group are similar.

similar to those of the hindered 5-substituted 1,2,3-triazoles. In the [1-methyl-3-phenyl-4-(1,2,3-triazolio)]oxides *8*; Z=O, $\delta_{C-2'}$ and $\delta_{C-3'} - \delta_{C-2'}$ deviate slightly from the values observed in the unhindered 1,2,3-triazoles indicating that the oxygen atom adjacent to the phenyl group impedes interannular conjugation insignificantly. In contrast, the sulfur atom of [1-methyl-3-phenyl-4-(1,2,3-triazolio)]sulfide *8k* impedes interannular conjugation as effectively as a methyl group, as evident from the similarity between $\delta_{C-2'}$ and $\delta_{C-3'} - \delta_{C-2'}$ in *8k* (Table 3) and in 1-phenyl-5-methyl-1,2,3-triazole.[7] In the hindered *C*-phenyl substituted 4-(1,2,3-triazolio)-oxide *16p* $\delta_{C-2'}$ and $\delta_{C-3'} - \delta_{C-2'}$ values correspond to those of the hindered *C*-phenyl substituted azoles.[7]

In 2-phenyl-5-methyl-pyrazol-5-in-3,4-dione *12b* and 2-phenyl-4-carbomethoxy-pyrazol-4-in-3-one *13l*, $\delta_{C-2'}$ and $\delta_{C-3'} - \delta_{C-2'}$ values are similar to those of the unhindered 1-phenyl-pyrazoles indicating that the oxygen atom adjacent to the phenyl group does not impede interannular conjugation at all in *12b* and only slightly in *13l*. According to the ^{13}C-NMR data of 1-phenyl-5-methyl-pyrazole [7] and 1-methyl-2-phenyl-pyrazolium bromide *1a* (Table 2), the methyl group of 1-phenyl-2-methyl-pyrazol-4-in-3-one *10a* is expected to impede interannular conjugation. However, $\delta_{C-2'}$ and $\delta_{C-3'} - \delta_{C-2'}$ values are roughly between those of the unhindered and hindered heteroaromatic pyrazoles. This implies that interannular conjugation in *6a* is impeded to a minor extent, due to the fact that the extent of interannular conjugation is a cos^2-function of the angle between the 2*p*-orbitals of the *N*-atom and the π-orbitals of the attached phenyl group.[32-34] Inspection of Dreiding models reveals that minor impediment of interannular conjugation is possible only if the pyrazole ring of *6a* is not planar but in isotropic phase takes up a conformation like that shown in Fig. 2. By replacement of oxygen in *6a* with sulfur, $\delta_{C-2'}$ increases to values similar to those of the hindered heteroaromatic pyrazoles. The sulfur atom cannot influence the phenyl group through space. Hence, the hindrance must be due to the *N*-2 methyl group. This seems possible only if the pyrazole ring is planar or almost so in the pyrazolthione *10k*. By introduction of methyl or bromine in the 5-position of the pyrazolone *10a*, $\delta_{C-2'}$ increases, and $\delta_{C-3'} - \delta_{C-2'}$ decreases to values similar to those of hindered 1-phenyl-pyrazoles. A similar effect of a 5-methyl group is observed in *13o*. The effect of a 5-methyl group is much larger than that of the *N*-2 methyl group (compare $\delta_{C-2'}$ and $\delta_{C-3'} - \delta_{C-2'}$ values of *10a* and *10c*). This implies that the angle between the exocyclic bonds of *C*-5 and *N*-1 is smaller than that between the exocyclic bonds of *N*-1 and *N*-2. This in turn suggests that the 5-substituted 1-phenyl-2-methyl-pyrazol-4-in-3-ones *10b*, *10g*, and *10h* take up a skew conformation (Fig. 2). The strong impediment of 5-substituents indicates that the pyrazolones *6c*, *6e*, *6g*, *6h*, and *13o* in solution apparently do not adopt the conformation with a planar pyrazole ring and with the 5-substituent out of the plane, which has been observed by an X-ray study of 1,5-dimethyl-2-phenyl-4-bromo-pyrazol-4-in-3-one.[35]



18 *19*

Fig. 2. Possible nonplanear conformations of 1,2-disubstituted pyrazol-4-in-3-ones. *18* and *19* have been selected as the ideal envelope conformations with the least distorted conjugated carbonyl system. *18* seems more likely than *19* both for 1-methyl-2-phenyl-pyrazol-4-in-3-ones *6*; Z=O where the N-2 phenyl group is least hindered in the former, and for 1-phenyl-2-methyl-pyrazol-4-in-3-ones *10*; Z=O as discussed in the text.

In the 1-methyl-2-phenyl-pyrazol-4-in-3-ones *6a*, *6c*, *6g*, and *6h*, $\delta_{C-2'}$ and $\delta_{C-3'} - \delta_{C-2'}$ values are not far from those of the hindered 1-phenyl-pyrazoles, indicating that interannular conjugation is impeded in the pyrazol-4-in-3-ones *6a*, *6c*, *6g*, and *6h*. In these, however, the combined effects of the *N*-1 methyl group and the *C*-3 oxygen atom are smaller than that of the single methyl group in 1-phenyl-5-methyl-pyrazole.[7] This again may be explained by assuming that the heterocyclic ring in the pyrazol-4-in-3-ones *6a*, *6c*, *6g*, and *6h* is not planar (see Fig. 2). A conformation like that observed for 1,5-dimethyl-2-phenyl-4-bromo-pyrazol-4-in-3-one in the crystal phase [35] seems more improbable. $\delta_{C-2'}$ in the pyrazol-4-in-3-thione *6k* is larger and $\delta_{C-3'} - \delta_{C-2'}$ is smaller than those of the

oxygen analog *6a* (Table 3). This indicates that replacement of an oxygen atom adjacent to the phenyl group with a sulfur atom increases the impediment of interannular conjugation. In *6k* the combined effects of the *N*-1 methyl group and the *C*-3 sulfur atom are similar to the combined effects of a methyl group and a sulfur atom in heteroaromatic compounds. (Thus the difference between $\delta_{C-2'}$ of *6k* and 1-phenylpyrazole [7] is 9.7 ppm and the difference between $\delta_{C-2'}$ of 1-phenyl-5-methyl-pyrazole [7] and 1-phenyl-pyrazole [7] plus the difference between $\delta_{C-2'}$ of *8k* and 1-phenyl-1,2,3-triazole [7] is 10.0 ppm. The corresponding difference for $\delta_{C-3'} - \delta_{C-2'} = -9.5$ and -11.6 ppm, respectively). This suggests that the heterocyclic ring of the pyrazol-thione *6k* is probably planar, or nearly so.

According to $\delta_{C-2'}$ and $\delta_{C-3'} - \delta_{C-2'}$ values of *13m* and *13n*, an *N*-phenyl group impedes the interannular conjugation of an adjacent phenyl group to a smaller extent than an oxygen atom.

In 1-methyl-2-phenyl-1,2,3-triazol-3-in-5-one *9a*, $\delta_{C-2'}$ and $\delta_{C-3'} - \delta_{C-2'}$ values fall between those of the hindered and unhindered 1-phenyl-1,2,3-triazoles or 1,2,3-triazolium bromides *4*, implying that interannular conjugation is impeded to a smaller extent in *9a* than in the hindered aromatic triazoles. This may be explained assuming that the heterocyclic ring of *9a* is not planar but takes up a skew conformation like the pyrazol-4-in-3-ones *13*; Z = O (see Fig. 2). Like in *13*, interannular conjugation vanishes in *9* by replacement of oxygen with sulfur as indicated by $\delta_{C-2'}$ and $\delta_{C-3'} - \delta_{C-2'}$ of *9k*.

$\delta_{C-2'}$ and $\delta_{C-3'} - \delta_{C-2'}$ values of the imidazol-4-in-2-one *7a* correspond to those of 1-phenylimidazole indicating that interannular conjugation prevails in *7a*. When oxygen is replaced by the larger sulfur atom interannular conjugation vanishes as indicated by $\delta_{C-2'}$ and $\delta_{C-3'} - \delta_{C-2'}$ values of *7k*.

The ^{13}C chemical shift of C-4'. The chemical shift of C-4' varies much less than $\delta_{C-3'}$ with the extent of interannular conjugation. In the azolium bromides, the pyrazol-4-in-3-ones *13*; Z = O, and the pyrazol-4-in-3-thiones *13*; Z = S, C-4' is shifted to low field, and $\delta_{C-3'} - \delta_{C-4'}$ decreases when conjugation vanishes (Tables 1, 2, and 3). In the hindered and unhindered 4-(1,2,3-triazolio)oxides *16*; Z = O, only small variations in $\delta_{C-4'}$ and $\delta_{C-3'} - \delta_{C-4'}$ values are observed.

The ^{13}C chemical shift of C-1'. C-1' in *C*-phenyl substituted compounds is more shielded than C-1' of *N*-phenyl substituted compounds (compare $\delta_{C-1'}$ of *3* and *16p* with $\delta_{C-1'}$ of *2* and *11a*, respectively). $\delta_{C-1'}$ depends little on the extent of interannular conjugation. Generally, $\delta_{C-1'}$ and $\delta_{C-1'} - \delta_{C-3'}$ values decrease when conjugation vanishes. Conceivably, this high field shift of C-1' reflects increased electron density at the phenyl-substituted *N*-atom due to reduced delocalization of the *N*-lone pair in the hindered compounds. $\delta_{C-1'}$ and $\delta_{C-1'} - \delta_{C-3'}$ values of the unhindered 1,2,3-triazolium bromides *4a*, *4c*, and *4e* are slightly larger than those of the unhindered diazolium bromide *2*. Similarly, $\delta_{C-1'}$ and $\delta_{C-1'} - \delta_{C-3'}$ values of the hindered 1,2,3-triazolium bromides *4b*, *4d*, and *5* are slightly larger than those of the hindered diazolium bromides *1a*, *1d*, *1e*, and *1f* (Tables 1 and 2).

In the pyrazol-4-in-3-ones *13*; Z = O, $\delta_{C-1'}$, like $\delta^{15}_{CH_3N}$ (see above) depends primarily on the position of the phenyl group. Secondly, $\delta_{C-1'}$ depends on the extent of conjugation as described above.

Comparison between ^1H- and ^{13}C-NMR data. The phenyl groups of all of the hindered and unhindered *N*- and *C*-phenyl substituted azolium salts studied appear as singlets and multiplets, respectively, with two exceptions (Tables 1 and 2). The phenyl group of the hindered 1-methyl-2-phenyl-5-chloro-pyrazolium bromide *1d* appears as a multiplet both in deuteriochloroform and deuterium oxide solution. Secondly, the unhindered 1-methyl-3-phenyl-imidazolium bromide *2a* exhibits a phenyl group singlet in aqueous solution but a multiplet in deuteriochloroform solution. More inconsistencies between ^1H- and ^{13}C-NMR spectra are observed in the 4-(1,2,3-triazolio)oxides *16*; Z = O. Thus the unhindered [1-phenyl-3-methyl-4-(1,2,3-triazolio)]oxide *11a* and -sulfide *11k* exhibit phenyl group singlets or doublets, whereas the ^{13}C-NMR data indicate extensive interannular conjugation.

The hindered [1-methyl-3-phenyl-4-(1,2,3-triazolio)]sulfide *8k* exhibits a phenyl group multiplet, whereas the ^{13}C-NMR data imply that conjugation has vanished. In the 5-substituted [1-phenyl-3-methyl-4-(1,2,3-triazolio)]-oxides *11b*, *11h*, and *11i*, as well as in [1-methyl-3-phenyl-4-(1,2,3-triazolio)]oxide *8a*, the ^1H- and ^{13}C-NMR data are consistent. The observed

discrepancies between the ^{1}H- and ^{13}C-NMR data of 4-(1,2,3-triazolio)oxides and -sulfides may be explained by assuming that the major factor influencing the *o*-phenyl proton shifts is anisotropy by the *C*-oxygen or *C*-sulfur bonds. Hence, phenyl groups adjacent to these bonds appear as multiplets in the ^{1}H-NMR spectra, independent of the extent of conjugation. The appearance of the *C*-phenyl group of the hindered [1,3-dimethyl-5-phenyl-4-(1,2,3-triazolio)] oxide *16p* as a multiplet is in keeping with this assumption. In the [1-phenyl-3-methyl-4-(1,2,3-triazolio)]oxides (*11*; Z = O) or -sulfide *11k* the net anisotropy effect on the *o*-phenyl protons is zero, yielding phenyl group singlets in the ^{1}H-NMR spectra, independent of the extent of conjugation.

In compounds with reduced heteroaromaticity, ring current effects become of minor importance and other factors may determine the appearance of the phenyl group ^{1}H-NMR signal. The phenyl groups of the hindered 1-methyl-2-phenyl-pyrazol-4-in-3-ones *6c*, *6g*, and *6h* and -thione *6k* appear as singlets in the proton spectra. In contrast, the hindered 5-substituted 1-phenyl-2-methyl-pyrazol-4-in-3-ones *10c*, *10g*, and *10h* exhibit phenyl group multiplets in the ^{1}H-NMR spectra, while ^{13}C-NMR data reveal that conjugation has vanished. Like in the 4-(1,2,3-triazolio)oxide series, the position of the phenyl group and not the extent of interannular conjugation determines the appearance of the phenyl group in the ^{1}H-NMR spectra. A comparison of the ^{1}H-NMR spectra of *10a* and its 4,2′,4′,6′-tetradeuterio derivative (see Experimental) proved that it is the *o*-protons of *10a* which are deshielded relative to the *m*- and *p*-protons. Most likely, this is the case, too, in the 5-substituted derivatives *10*; Z = O, and the pyrazol-4-in-3-thione *10k*. The reason for the deshielding of the *o*-protons in *10*; Z = O, and *10k* is not clear.

The 1-methyl-2-phenyl-1,2,3-triazol-5-one *9a* and -thione *9k* behave like the analogous 1-phenyl-2-methyl-pyrazol-4-in-3-ones and -thione (*10*; Z = O or S), exhibiting a phenyl group multiplet in the ^{1}H-NMR spectra.

1-Methyl-3-phenyl-imidazol-4-in-2-one *7a* and -thione *7k* both exhibit a phenyl group multiplet in the ^{1}H-NMR spectra, whereas the ^{13}C-NMR data reveal that interannular conjugation is extensive in *7a* but vanishes in *7k*.

CONCLUSION

The results reveal that ^{13}C-NMR spectroscopy can be used for assessing the extent of interannular conjugation in *C*- and *N*-phenyl substituted azoles with charged, zwitterionic, or heterocyclic rings with reduced aromaticity. Comparison of the ^{1}H- and ^{13}C-NMR data demonstrates that ^{13}C-NMR spectroscopy apparently provides unambiguous information about the extent of interannular conjugation even in cases where ^{1}H-NMR spectroscopy leads to erroneous results or in azole derivatives with reduced heteroaromaticity where ^{1}H-NMR, as expected, provides no information about the extent of conjugation.

The ^{13}C-NMR data indicate that extensive interannular conjugation is present in unhindered *N*-phenyl substituted imidazolium salts *2*, 1,2,3-triazolium salts *4*, and 4-(1,2,3-triazolio)oxides *16*; Z = O, or sulfides *16*; Z = S. The data further imply that a given substituent in the partly heteroaromatic pyrazol-4-in-3-ones *13*; Z = O, or 1,2,3-triazol-5-ones *9*; Z = O, impedes interannular conjugation much less than in heteroaromatic systems. Therefore, the heterocyclic rings of *13*; Z = O and *9*; Z = O are believed to adopt a twisted conformation (Fig. 2).

An oxygen atom adjacent to a phenyl group impedes interannular conjugation only slightly, even in the heteroaromatic systems *8*; Z = O. In contrast, however, a sulfur atom adjacent to a phenyl group impedes interannular conjugation strongly. The ^{13}C-NMR data seem to indicate that the partly aromatic heterocyclic rings of the thiones *6k*, *10k*, *7k*, and *9k* are planar or nearly so, in contrast to the oxygen analogues.

The ^{13}C-NMR data for the unhindered and hindered charged or zwitterionic azoles, and species with reduced heteroaromaticity are summarized in Table 6. When these data are combined with those previously measured for phenyl-substituted azoles with aromatic uncharged heterocyclic rings, it may be concluded that in any *N*-phenyl substituted pyrazole derivatives of the types studied interannular conjugation is extensive if $\delta_{C-2'} = 118.5 - 118.8$ ppm and $\delta_{C-3'} - \delta_{C-2'} = 10.5$ ppm but strongly impeded if $\delta_{C-2'} = 124.6 - 129.1$ ppm and $\delta_{C-3'} - \delta_{C-2'} = 1.3 - 4.0$ ppm. Intermediate values signify a smaller hindrance to conjugation. Similarly, interannular conjugation is extensive in

imidazoles if $\delta_{C-2'} = 121.0 - 121.7$ ppm and $\delta_{C-3'} - \delta_{C-2'} = 8.6 - 9.4$ ppm. In *N*-phenyl-1,2,3-triazole derivatives interannular conjugation is extensive if $\delta_{C-2'} = 118.3 - 120.9$ ppm and $\delta_{C-3'} - \delta_{C-2'} = 8.9 - 10.6$ ppm but impeded if $\delta_{C-2'} = 124.1 - 125.7$ ppm* and $\delta_{C-2'} - \delta_{C-3'} = 3.7 - 5.2$ ppm. If these data are further combined it appears that in any *N*-phenyl substituted azole of the types studied, interannular conjugation is extensive if $\delta_{C-2'} = 118.3 - 121.7$ ppm and $\delta_{C-3'} - \delta_{C-2'} = 8.6 - 10.6$ ppm but strongly impeded if $\delta_{C-2'} = 124.1 - 129.1$ ppm and $\delta_{C-3'} - \delta_{C-2'} = 1.3 - 5.2$ ppm. In *C*-phenyl substituted azoles interannular conjugation is extensive if $\delta_{C-2'} = 124.7 - 126.4$ ppm and $\delta_{C-3'} - \delta_{C-2'} = 2.1 - 3.8$ ppm but impeded if $\delta_{C-2'} = 127.8 - 128.1$ ppm ** and $\delta_{C-3'} - \delta_{C-2'} = 0 - 0.8$ ppm. Since the values in case of interannular conjugation do not overlap with values in case of strongly impeded conjugation the ^{13}C-NMR method is a powerful method for assessing the extent of interannular conjugation, and hence for conformational analysis, of phenyl substituted azole derivatives. In addition, the values presented in Table 6 may be useful for distinguishing between positional isomers. For example, 1-phenyl-3,4-disubstituted 1,2,3-triazolium salts *4c* may be distinguished from the 1-phenyl-3,5-disubstituted isomers *4b*. Furthermore, the size and possibly the orientation of a substituent adjacent to a phenyl group may be evaluated.

The compounds studied in the present and preceding papers may be taken as representative for a bulk of other compounds. Thus, the results become generally applicable to all *C*- and *N*-phenyl substituted azole derivatives. In the light of the results obtained, an investigation of the use of the ^{13}C-NMR method for conformational analysis of phenyl substituted azines with neutral, charged, zwitterionic, or with nonaromatic heterocyclic rings seems obvious.

* Extreme values ($\delta_{C-2'} = 131.1$ ppm and $\delta_{C-3'} - \delta_{C-2'} = 2.3$ ppm) have been observed for 1-methyl-2-phenyl-1,2,3-triazolium bromide *5* in aqueous solution.

** An extreme value ($\delta_{C-2'} = 130.2$ ppm) has been observed for 1,3-dimethyl-2-phenyl-imidazolium bromide *3* in aqueous solution.

EXPERIMENTAL

^{1}H-NMR spectra were obtained on a Varian A-60 instrument. Position of signals are given in ppm (δ-values) relative to tetramethylsilane (TMS) when deuteriochloroform was used as the solvent. When deuterium oxide was used as the solvent 2,2-dimethyl-2-silapentane-5-sulfonate (DSS) was used as an internal standard.

^{13}C-NMR spectra were obtained using 0.695 mmole of compound dissolved in 1.20 ml of solvent (10 mm tube), when not otherwise stated. When deuteriochloroform was used as the solvent position of signals were measured relative to the center peak of the deuteriochloroform triplet (δ 76.9 ppm) [25b] and are given in ppm (δ-values) relative to TMS. When deuterium oxide was used as the solvent position of signals were measured relative to *p*-dioxane (δ 67.4 ppm) [25b] and are given in ppm (δ values) relative to TMS. The ^{13}C-NMR spectra were obtained on a Bruker WH-90 instrument using Fast Fourier Transform pulse technique. Unless otherwise stated, 1 000 scans were accumulated with 6000 Hz sweep using 8K computer memory. This corresponds to an accuracy of ± 0.07 ppm in the chemical shifts and of ± 3 Hz in the coupling contants. The repetition time was 3.0 sec. The decoupled spectra were obtained using proton-noise-decoupling. The undecoupled spectra were measured by the gated decoupling technique.[36] in order to maintain part of the Overhauser enhancement of the signals. Thus, the proton-noise decoupling was interrupted after 1.0 sec. After a delay of 0.4 sec, the pulse (4 μsec) was turned on again. This cycle was repeated every 3.0 sec, 6000 scans being accumulated. Off resonance decoupled spectra [24c,37-41] were measured irradiating with a low power (2 Watt) continuous wave radio frequency at 800 Hz to high field of the chloroform proton signal.

Preparation of azolium bromides

1-Methyl-2-phenyl-pyrazolium bromide 1a. 1-Methyl-2-phenyl-pyrazolium tosylate [42] (1.00 g) was dissolved in water and passed through Amberlite IRA 400 ion exchanger (65 ml) regenerated with aqueous hydrogen bromide. The eluate was filtered through activated carbon. The water was removed *in vacuo* and the residue was recrystallized from methanol-ether. This gave 0.70 g (98 %) of 1-methyl-2-phenyl-pyrazolium bromide *1a* as colourless crystals, m.p. 174°. The NMR-spectrum was identical with that of the corresponding pyrazolium tosylate, except that the tosylate ion signal had disappeared.

Similarly, the pyrazolium bromides *1d*, *1e*, and *1f* were prepared from the corresponding tosylates,[18] and the 1,2,3-triazolium bromides *4a*, *4b*, *4c*, *4d*, and *4e* from their tosylates.[21,43,44] The 1,2,3-triazolium bromide *5* was prepared in

an analogous manner from the corresponding fluorosulfonate.[22] Finally, the imidazolium bromides *2a* and *3* were prepared in the same way from the corresponding tosylates.[44] In all cases the yield was 95 – 100 %. The purity was controlled by ^{1}H-NMR spectroscopy. Further purification and combustion analysis of all azolium bromides was omitted since all of the corresponding tosylates (or fluorosulfonates) are well characterized compounds.

4,2′,4′,6′-Tetradeuterio-1-phenyl-2-methyl-pyrazol-4-in-3-one. 1-Phenyl-2-methyl-pyrazol-4-in-3-one *10a*[18] (142 mg) and conc. dideuterio sulfuric acid (99 % enriched) (0.44 ml) were heated with stirring to 140° for 3 h. Deuterium oxide (4.4 ml) was then added and the solution was neutralized with potassium carbonate, freshly dried at 140° for 24 h. The solvent was then removed *in vacuo* and the residue was extracted with boiling chloroform (5 × 10 ml). After removal of the chloroform the treatment with dideuterio sulfuric acid was repeated. After the chloroform extraction and removal of the chloroform the residue was extracted with boiling ethyl acetate (5 × 10 ml). The solution was filtered through activated carbon and the ethyl acetate was removed affording 69 mg (47 %) of crude 4,2′,4′,6′-tetradeuterio-1-phenyl-2-methyl-pyrazol-4-in-3-one, m.p. 93 – 96°. Recrystallizations from ethyl acetate-hexane raised the melting point to 109 – 112°. A comparison of the ^{13}C-NMR spectra of the starting material *10a* and the tetradeuterio derivative showed that the latter compound was devoid of absorptions due to C-4 and C-4′. The signal due to C-2′ was strongly reduced. In contrast, the signals due to C-3, C-5, and C-3′ showed no loss in intensity. Replacement of hydrogen with deuterium at a carbon atom gives rise to a prolongation of the relaxation time, T_1, and hence to loss in intensity of the ^{13}C-signal.[45] Consequently, the ^{13}C-NMR data indicate that H-4, H-2′, H-4′, and H-6′ have been replaced with deuterium. The ^{1}H-NMR spectrum of the starting material *10a* exhibits a phenyl group multiplet at 7.2 – 7.6 ppm. In contrast, the ^{1}H-NMR spectrum of the tetradeuterio derivative exhibits two broad singlets at 7.58 and 7.55 ppm corresponding to H-5 and the two *m*-protons, respectively.

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