

N-Methyl Chemical Shifts in Quaternized Azoles, Isazoles, Diazoles, and their Benzologs

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The *N*-methyl chemical shifts in the title compounds are reported. In the 1,3-orientation, the shift appears to be determined by resonance from the heteroatom, with the order of donating ability being $\text{NMe} > \text{O} > \text{S} \sim \text{Se}$. In the 1,2-orientation, electronegativity effects are also important as evidenced by a general downfield shift, and the order of donation is $\text{NMe} > \text{S} \sim \text{Se} > \text{O}$.

There is current interest (1,2) in determining the relative effects of nitrogen, oxygen and sulfur on the electron distribution in pyrrole, furan, and thiophen. It has been well established that the situation is complex, with the relative effects of sulfur and oxygen depending on the particular situation. For example, sulfur is a better donor than oxygen in the ground state, while the reverse is true during electrophilic substitution, *i.e.*, under conditions of strong electron demand.

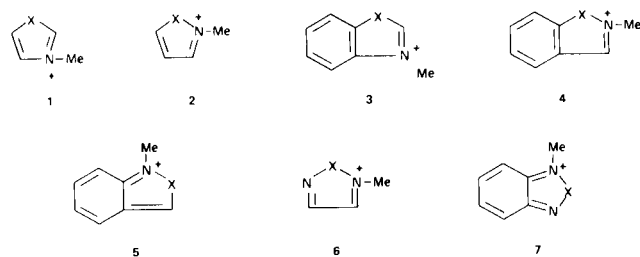
We wished to investigate a ground state probe that would parallel this reactivity order, *i.e.*, respond to the resonance effect of the heteroatom. It has been recently demonstrated (3) that, even with 2-substituted compounds, the *N*-methyl chemical shift in a ring substituted *N*-methylpyridinium compound is very dependent on the resonance effect of the substituent. We therefore thought it worthwhile to study the analogous situation in various series of quaternized azoles [1-7, X = NMe, S, O, and Se (3 and 7 only)]. The compounds were prepared in con-

donating effect is therefore represented by the largest downfield shift (positive).

In series 1, it appears that the probe is acting as in pyridinium compounds, where it responds to the π -electron density on the nitrogen. A situation of strong electron demand occurs with $\Delta\delta$ being a measure of the resonance response of the heteroatom to this demand. The order of donation $\text{NMe} > \text{O} > \text{S}$ is the same as that found (2) in electrophilic substitution in pyrrole, furan, and thiophen. This ground state probe therefore does parallel the situation encountered in the reactivity study and further illustrates that quaternary *N*-methyl chemical shifts can be a useful measure of 'substituent' resonance effects.

There is a large change evident in the results from series 2 where there is a downfield shift for each heteroatom relative to 1. This is particularly large for isoxazole and the order of donation in 2 is $\text{NMe} > \text{S} > \text{O}$, the "normal" ground state order. (The same $\text{S} > \text{O}$ order is found in 6). The fact that all chemical shifts in 2 are downfield from those of the analogous 1 means that the parallel with electrophilic substitution is lost. Pyrrole, furan and thiophen are all more reactive at the 2 than the 3 position. It is evident that removing the intervening atom between heteroatom and quaternary centre destroys the predominance and dependence of chemical shift on the resonance effect of the heteroatom. There is clearly a strong electronegativity component in the heteroatom effect in determining the chemical shift in 2. Thus the $\Delta\Delta\delta$ for 2-1 are in the electronegativity order $\text{O} > \text{N} > \text{S}$. Contributions from anisotropic effects would also be expected to be more important in 2.

The results for the various series of benzo derivatives (3, 4, 5, 7) show the same trends as 1 or 2 and the heteroatom effects do not require comment. In general, there is a downfield shift of ~ 10 Hz in the *N*-methyl signal produced by benzofusion. This is about the same as that



nection with kinetic studies of the quaternization reaction. (Reactivity order of parent heterocycles (4) is $\text{NMe} > \text{S} > \text{O}$ in series 1-4 and $1 > 2, 3 > 4$).

Results and Discussion

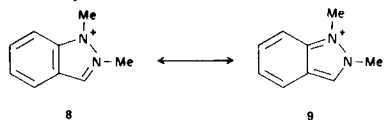
The *N*-methyl chemical shifts ($\Delta\delta$), in sulfolane, are listed in Table I and are quoted in Hz relative to dimethylsulfate (the internal reference at δ 4.0 ppm). The weakest

Table I
N-Methyl Chemical Shifts of Quaternized Azoles,
 in Sulfolane Relative to Me₂SO₄

Azole	Anion	Series	$\Delta\delta$ (Hz)
1-Methylimidazole	I ⁻	1	5
Oxazole	ClO ₄ ⁻	1	4
Thiazole	I ⁻	1	18
1-Methylpyrazole	I ⁻	2	9
Isothiazole	I ⁻	2	23
Isoxazole	ClO ₄ ⁻	2	29
1-Methylbenzimidazole	I ⁻	3	9
Benzoazole	ClO ₄ ⁻	3	18
Benzoselenazole	I ⁻	3	27
Benzothiazole	I ⁻	3	29
1,(2)-Methylindazole	I ⁻	5,4	18,27
1,2-Benzisothiazole	I ⁻	4	31
1,2-Benzisoxazole	ClO ₄ ⁻	4	39
2,1-Benzisothiazole	I ⁻	5	28
2,1-Benzisoxazole	ClO ₄ ⁻	5	37
1,2,5-Thiadiazole	I ⁻	6	38
1,2,5-Osadiazole	ClO ₄ ⁻	6	49
2-Methylbenzotriazole	ClO ₄ ⁻	7	37,50
2,1,3-Benzoselenadiazole	MeSO ₄ ⁻	7	44
2,1,3-Benzothiadiazole	I ⁻	7	46
2,1,3-Benzoxadiazole	ClO ₄ ⁻	7	60

observed (5) in going from pyridine to quinoline or isoquinoline. The addition of another pyridine type nitrogen in a 1,3-orientation with respect to the quaternizing centre (6-7) produces a downfield shift of ~ 20 Hz.

In the cases of the methylindazoles and methylbenzotriazole, a complication exists because there are two non-equivalent *N*-methyl peaks. Both 1- and 2-methylindazole give the same quaternary product which can be represented as a resonance hybrid of **8** and **9**. The major contributing



form would be **8**, which has the benzenoid structure and the high field signal is from the N₁-Me. This has been demonstrated by isotopic labelling (6). The 18 Hz value therefore belongs to series **5** and the 27 Hz value to series **4**. The higher field signal in the spectrum of 1,2-dimethyltriazolium fluorosulfonate has been assigned to the N₁-Me group (7) and this assignment will also hold in the 1,2-dimethylbenzotriazolium compound. The 37 Hz value (N₁-Me) therefore pertains to series **7** to give the order NMe > Se \sim S > O.

The very similar effect of sulfur and selenium in series **3** and **7** is of interest. The rates of quaternization of the two parent compounds in series **3** are very similar (4a). However, dipole moment (8) and quaternization studies (4c) show that, in series **7**, selenium is a much better donor than sulphur. The nmr data afford no clue as to the origin

of this unexplained selenium donor effect in the 2,1,3-benzodiazole.

EXPERIMENTAL

The figures quoted in Table I were obtained on a Varian A-60D spectrometer for 0.1 *M* solutions of the appropriate salt at the probe temperature (54°). Each result is the average of three determinations and is quoted to the nearest Hz. Measurements were carried out in sulfolane since some of the compounds decomposed in DMSO, the solvent used in the previous study. Chemical shifts were obtained by direct measurement on 100 Hz sweep width, relative to dimethyl sulfate (δ 4.0 ppm) as internal standard.

The lack of any significant counterion or concentration effects in chemical shifts of related quaternary compounds has been demonstrated previously (3). This was shown to also be the case with *N*-methyl-2,1-benzisothiazolium salts.

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