δ 3.48 (s, 3), 1.80 (s, 3), 2.1-1.1 (m, 14).

9-[1-(Methylthio)ethylidene]bicyclo[4.2.1]nonane (41). This compound is prepared and isolated as described for **15**; yield 68%. Extremely pure product was obtained with the aid of high-performance LC (hexane): MS, *m/e* 196; ^{1}H NMR ($CDCl_3$) δ 3.30 (m, 1), 3.03 (m, 1), 2.20 (s, 3), 1.97 (s, 3), 2.0-1.2 (m, 12).

***syn*-9-Acetyl-9-chlorobicyclo[4.2.1]nona-2,4,7-triene (44).** To a solution of vinyl ether **13** in SO_2 at -78 °C was added an excess (3 equiv) of SO_2ClF. The reaction was instantaneous. The reaction mixture was poured onto saturated aqueous $NaHCO_3$ and extracted into Et_2O. After the extract was dried ($MgSO_4$) and concentrated, hydrolysis of the intermediate ester was effected by passing the reaction mixture through a column of SiO_2 ($CHCl_3$ as eluent): ^{1}H NMR ($CDCl_3$) δ 6.0-5.7 (m, 4), 5.30 (d, 2), 3.53 (d, 2), 2.27 (s, 3); MS, *m/e* 194, 196.

Carbocation Generation. NMR samples were prepared by condensing SO_2 from a gas cylinder into an NMR tube containing the substrate and cooled in a dry ice/acetone bath. The concentration of the samples was about 100-200 mg/0.3 mL of solvent. To the cooled solution, was carefully added freshly prepared $HFSO_3/SbF_5$ (5:1) via the wall of the tube. In the case of the unsaturated substrates **13**, **15**, and **19**, 1 equiv of acid was used; the cations **47a-c** were generated with a twofold excess of acid. Mixing was effected by shaking the samples vigorously with the aid of a vibromixer. Samples were checked with 60-MHz ^{1}H NMR spectroscopy. Spectroscopic investigations were performed in the temperature range of -100 to -30 °C. Quenching was effected by pouring the samples onto saturated aqueous $NaHCO_3$.

Appendix

Tables IV and V contain collections of various ^{1}H and ^{13}C NMR spectral data, respectively.

Registry No. **2**, 38898-39-4; **3**, 83463-30-3; **4**, 83463-31-4; **5**, 34733-74-9; **10**, 70361-08-9; **11**, 70361-10-3; **12**, 83463-32-5; **13**, 83476-30-6; **14**, 83463-33-6; **15**, 83463-34-7; **16**, 83463-39-2; **17**, 83463-35-8; **19**, 83463-52-9; **20**, 83463-53-0; **21**, 83463-42-7; **22**, 83463-40-5; **23**, 83463-41-6; **24**, 83463-36-9; **25**, 83463-37-0; **26**, 83463-38-1; **27**, 83476-31-7; **28**, 83476-32-8; **30**, 83463-43-8; **31**, 83509-96-0; **32**, 83463-44-9; **36**, 83463-45-0; **37**, 83509-97-1; **38**, 83463-46-1; **39**, 83463-47-2; **40**, 83463-48-3; **41**, 83463-49-4; **44**, 83463-50-7; **46a**, 83463-57-4; **46b**, 83463-58-5; **46c**, 83486-34-4; **47a**, 83463-54-1; **47b**, 83463-55-2; **47c**, 83463-56-3; **52**, 64304-77-4; **56**, 83463-51-8.

^{15}N NMR Spectroscopy: Prototropic Tautomerism of Azoles

D. S. Wofford, D. M. Forkey,* and J. G. Russell*

Department of Chemistry, California State University, Sacramento, Sacramento, California 95819

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The ^{15}N NMR spectra of several azoles and their *N*-methyl derivatives were determined. The mole fractions of the NH tautomers were obtained from the ^{15}N chemical shifts of the NH tautomers and the corresponding *N*-methyl derivatives. With minor corrections in ^{15}N chemcial shifts, the *N*-methyl derivatives proved to be suitable models for the ^{15}N chemical shifts of the corresponding NH tautomers. As a result of the large chemical shift difference between the pyrrole-type and pyridine-type nitrogens, ^{15}N NMR provides a convenient, if not the most reliable, method for studying prototropic tautomerism in nitrogen heterocycles.

Introduction

Prototropic tautomerism of azoles has been extensively studied with use of NMR techniques.[1] However, in the case of ^{1}H NMR, the chemical shift substituent effect of the *N*-methyl group of the model compound is of the same magnitude as the differences in chemical shifts of the tautomeric species. Thus, interpolation between chemical shifts of the tautomeric species and the corresponding *N*-methyl model compounds is inconclusive. In a few cases low temperature[2,3] has permitted observation of the spectrum of each tautomer, which results in more definitive conclusions.

Application of ^{13}C NMR to the analysis of the tautomeric equilibria of azoles[4] by comparison of the shifts of *N*-methyl derivatives with the shifts of the tautomeric mixture is also not satisfactory. The substituent effect of the *N*-methyl is not only relatively large but sensitive to the azole. Thus, quantitative conclusions about the position of tautomeric equilibrium are usually unreliable.

Utilizing ^{14}N NMR[5] and the interpolation method to determine the position of the azole tautomeric equilibrium at first seems to be more reliable as a result of the very large chemical shift difference between the pyridine-type and pyrrole-type nitrogens. Unfortunately, the wide line widths and resulting overlapping of several different nitrogen resonances make ^{14}N NMR an unsatisfactory method.[1]

We have successfully used ^{15}N NMR and the chemical shift interpolation method to determine the position of azole tautomeric equilibria. The *N*-methyl derivatives were found to be suitable models for the corresponding tautomers. The ^{15}N spectra of the azoles exhibit the large chemical shift difference between pyridine-type and pyrole-type nitrogen atoms, but show the narrow lines expected for spin 1/2 nuclei. The narrow lines permitted the observation and assignment of a resonance for each nitrogen atom in the azoles that were studied. The ^{15}N chemical shifts for each azole and the *N*-methyl derivatives are collected in Table I.

Results and Discussion

The ^{15}N chemical shifts of the azoles collected in Table I compare favorably with the ^{14}N chemical shifts reported by Witanowski et al.[5] but only when there are two or fewer different nitrogen atoms. This is a result of overlapping of broad lines in the ^{14}N NMR spectra, which is not observed for the ^{15}N spectra. Thus, the previously reported ^{14}N chemical shifts and the ^{15}N chemical shifts are in agreement only for azoles **1-6**, **12**, **15**, **18**, and **19**.

The high-field resonance was assigned to the pyrrole-type nitrogen and the lower field resonances were assigned to the pyridine-type nitrogen atoms. The large downfield shift of the pyridine-type nitrogen atom is attributed to a large paramagnetic shielding term associated with the

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0022-3263/82/1947-5132$01.25/0

Table I. ^{15}N Chemical Shifts of Some Azoles

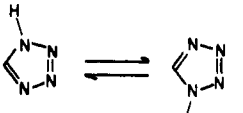
compound	no.	N atom no.	δ^{NH_3} ($DCCl_3$)[a]	δ^{NH_3} (Me_2SO)[a]
pyrrole	1	1	147.5	155.6
1-methylpyrrole	2	1	149.3	150.0
imidazole	3	1, 3	209.5	212.6
1-methylimidazole	4	1	160.7	162.2
		3	255.9	260.7
pyrazole	5	1, 2	248.0	
1-methylpyrazole	6	1	200.9	
		2	306.5	
indazole[13]	7	1		185.8
		2		314.6
1-methylindazole[13]	8	1		177.4
		2		323.7
2-methylindazole[13]	9	1		287.6
		2		219.3
1,2,3-triazole	10	1, 3	301.2	311.2
		2	318.3	304.3
1-methyl-1*H*-1,2,3-triazole	11	1	235.2	237.2
		2	363.9	364.0
		3	349.5	351.0
2-methyl-2*H*-1,2,3-triazole	12	1, 3	329.1	330.1
		2	247.4	248.8
benzotriazole	13	1, 3	276.8 ($W_{1/2}$ = 8.2 Hz, 47 °C)	283.5
		2	368.6	
			368.7 ($W_{1/2}$ = 1.4 Hz, 47 °C)	372.7
1-methyl-1*H*-benzotriazole	14	1	216.1	218.4
		2	378.0	379.3
		3	337.8	339.4
2-methyl-2*H*-benzotriazole	15	1, 3	317.1	317.7
		2	261.0	263.2
1,2,4-triazole	16	1, 2		252.8
		4	*b*	245.5
1-methyl-1*H*-1,2,4-triazole	17	1		208.9
		2		298.0
		4		252.1
4-methyl-4*H*-1,2,4-triazole	18	1,2		319.9
		4		163.1
tetrazole	19	1, 4		281.5
		2, 3	*b*	374.4
1-methyl-1*H*-tetrazole	20	1		228.8
		2		369.4
		3		392.5
		4		330.0
2-methyl-2*H*-tetrazole	21	1		307.0
		2		278.0
		3		379.3
		4		333.1

[a] The chemical shift was determined with respect to external nitromethane at 35 °C and corrected to external ammonia at 25 °C by addition of 380.2 ppm. [b] The azole was insoluble in $DCCl_3$.

nonbonding electron pair.[6] Thus, the *N*-methyl nitrogen, pyrrole-type, of 1-methylimidazole (**4**) is assigned to the line at 160.7 ppm, while the N3, pyridine-type, is assigned to the line at 255.9 ppm. The assignment of the pyridine-type nitrogen atoms, when there was more than one, was done by considering the number of adjacent nitrogen atoms and their accompanying downfield shifting effect. For example, the *N*-methyl nitrogen of 1-methylpyrazole (**6**) at 200.9 ppm is 40 ppm to low field of the *N*-methyl nitrogen of 1-methylimidazole (**4**) at 160.7 ppm. Similarly, the N2 resonance of **6** at 306.5 ppm exhibits a 51-ppm downfield shift relative to the N3 resonance of **4** at 255.9 ppm. Thus, for 1-methyl-1*H*-1,2,3-triazole (**11**), the resonance at 235.2 ppm is assigned to the *N*-methyl nitrogen, a pyrrole-type N. The pyridine-type nitrogen atoms of **11**, N2 and N3, are assigned to the resonances at 363.9 and 349.5 ppm, respectively. The N2 resonance is at lower field than the N3 resonance as a result of two neighboring nitrogen atoms for N2 but only one neighbor for N3.

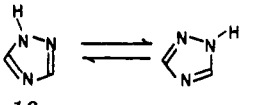
With use of these considerations, it is generally possible to assign all the resonances to a particular nitrogen atom or equivalent group of atoms for the azoles studied. However, in order to assign the N1 and N4 resonances for 2-methyl-2*H*-tetrazole (**21**), it is necessary to consider whether the adjacent nitrogen atom is a pyrrole-type or pyridine-type nitrogen. The closest analogues to **21** from which to qualitatively estimate the different effects are the *N*-methyl derivatives **11** and **12** of 1,2,3-triazole and **14** and **15** of 1,2,3-benzotriazole. The N3 atom in 1-methyl-1*H*-1,2,3-triazole (**11**) has a pyridine-type neighbor and is 20 ppm to low field of N1 and N3 in 2-methyl-2*H*-1,2,3-triazole (**12**), each with a pyrrole-type neighbor. A similar 20-ppm downfield shift is found for N3 of 1-methyl-1*H*-benzotriazole (**14**) relative to N1 and N3 of 2-methyl-2*H*-benzotriazole (**15**). Thus, for 2-methyl-2*H*-tetrazole (**21**), N1 with an adjacent pyrrole-type nitrogen is assigned to the resonance at 307.0 ppm, while N4 with an adjacent pyridine-type nitrogen is assigned to the resonance 26 ppm to lower field at 333.1 ppm. This is in agreement with the assignments arrived at by considering ^{14}N line widths.[7]

The nitrogen atoms in the NH azoles may be assigned with the additional consideration that rapid prototropic tautomerism will result in averaged chemical shifts weighted by the mole fractions of the various tautomers. Thus, as a result of rapid proton exchange between the two 1*H* tautomers, vide infra, tetrazole (**19**) has two sets of equivalent nitrogen atoms,[5] N1 and N4, and N2 and N3, which give rise to two resonances at 281.5 and 374.4 ppm, respectively.



19a 19b

With continuous broadband ^1H decoupling the spectrum of 1,2,4-triazole (**16**) gave only one line at 252.8 ppm.



16a 16b

However, with gating of the ^1H decoupler to suppress the nuclear Overhauser effect and addition of $Cr(Acac)_3$ to ensure ^{15}N relaxation, two resonances at 252.8 and 245.5 ppm with relative intensities of 2:1 were observed. The more intense resonance at 252.8 ppm was assigned to the two equivalent nitrogen atoms N1 and N2 and the resonance at 245.5 ppm was assigned to N4. The nitrogen atoms of 1,2,3-triazole (**10**) were assigned by the same method.

Prototropic Tautomerism. Rapid prototropic tautomerism in azoles can be examined by NMR techniques. The observed parameters, p^{obsd}, are averaged according to eq 1, in which X_a and X_b are the respective mole fractions and P_a and P_b are chemical shifts or coupling constants. However, this approach requires suitable model com-

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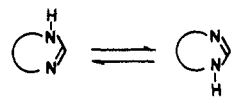

a b (1)

$$p^{obsd} = X_a P_a + X_b P_b$$

pounds to provide values for P_a and P_b. In the case of the azoles, the *N*-methyl derivatives of the tautomers were selected as appropriate models for the ^{15}N chemical shifts of the NH tautomers, despite the unsuitability of the ^{1}H and ^{13}C chemical shifts.[1,4] This is illustrated by the example of imidazole (**3**) and 1-methylimidazole (**4**) for which the ^{1}H, ^{13}C, and ^{15}N chemical shifts are collected in Table II.

As imidazole is rapidly equilibrating between two equivalent tautomers the $^{1}H4$ and H5, $^{13}C4$ and C5, and $^{15}N1$ and N3 chemical shifts are averaged. The corresponding average of the chemical shifts in 1-methylimidazole should be the same, if the effect of the methyl group is small relative to the pertinent chemical shift difference.

For the ^{1}H NMR, not only is the chemical shift difference between H4 and H5 in 1-methylimidazole (**4**) a small 0.10 ppm but the exchange averaged H4 and H5 chemical shift of the NH tautomers is outside the range defined by the *N*-methyl compound. The chemical shift effects of the methyl group are of the same magnitude as the chemical shift difference expected for the tautomers. The case of ^{13}C chemical shifts is better with a C4 and C5 chemical shift difference of 9.3 ppm in **4**. However, the exchange averaged C4 and C5 chemical shift for the NH tautomers is 1.2 ppm less than the C4 and C5 average chemical shift for the *N*-methyl compound, an error of more than 10%. The ^{15}N chemical shifts give the best results. The N1 and N3 chemical shift difference in **4** is 98.5 ppm with an exchange averaged chemical shift for the imidazole NH tautomers 1.9 ppm less than the N1 and N3 average for *N*-methylimidazole, a 1.9% error. The substitution of a methyl group has a relatively small effect on the ^{15}N chemical shifts.

An estimate of the effect of substitution of NH by a methyl group can be obtained by noting in Table I that the ^{15}N chemical shifts for pyrrole (**1**) and 1-methylpyrrole (**2**) in $CDCl_3$ are 147.5 and 149.3 ppm, respectively. Thus, in $CDCl_3$ N-methylation causes a downfield shift of 1.8 ppm. However, for Me_2SO-d_6 there is a 5.6-ppm upfield shift.

These differences in ^{15}N chemical shifts between **1** and **2** will be used as correction terms to δNCH_3 for the *N*-methyl derivative model compounds when the mole fractions of the NH tautomers are calculated, −1.8 ppm for chloroform and +5.6 ppm for Me_2SO-d_6 solvent. We will refer to this correction as the "pyrrole *N*-methyl correction".

It should be noted that the correction in chloroform solvent is small and is of the magnitude of changes in chemical shifts resulting from solution magnetic susceptibility differences[9] or $Cr(Acac)_3$ magnetic susceptibility effects.[10]

The difference in the chemical shift of a pyridine-type nitrogen adjacent to NH vs. *N*-methyl can be obtained from the spectra of pyrazole (**5**) and 1-methylpyrazole (**6**). The N1 (N2) chemical shift of **5** is 248.0 ppm and the average chemical shift of N1 and N2 of **6** is 253.7 ppm.

Table II. ^{1}H,[a] ^{13}C,[a] and ^{15}N[b] Chemical Shifts for Imidazole and 1-Methylimidazole

atom	imidazole	1-methyl-imidazole	av δ
H-4[s]	7.25	7.08	6.98
H-5[s]		6.88	
C-4[4]	122.8	129.6	125.0
C-5[4]		120.3	
N-1	209.5	162.2	211.4
N-3		260.7	

[a] Chemical shifts in parts per million from Me_4Si. [b] Chemical shifts in parts per million relative to external liquid ammonia.

Using the "pyrrole *N*-methyl correction" of −1.8 ppm in $CDCl_3$, we can calculate δ_{NH} for pyrazole to be 199.1 ppm. With use of mole fractions of 0.5 for the two tautomers, p^{obsd} of 248.0 ppm and a δ_{N1} of 199.1 ppm, eq 1 can be solved to obtain a value for δ_{N2} of 296.9 ppm. This is 9.6 ppm to high field of δ_{N2} for 1-methylpyrazole (**6**). Thus the substitution of a methyl group for hydrogen deshields an adjacent pyridine-type nitrogen by 9.6 ppm. We will term this the "adjacent methyl correction".

Consideration of δ_{N2} for benzotriazole (**13**) and 1-methyl-1*H*-benzotriazole (**14**) further substantiate this conclusion. On the basis of electronic considerations benzotriazole (**13**) is expected to be equilibrating between equivalent 1-NH and 3-NH tautomers, with no 2-NH tautomer present. This has been verified by dipole moment[11] and ^{1}H NMR studies.[2,12] The δ value of 378.0 ppm for N2 in 1-methyl-1*H*-benzotriazole (**14**) is 9.4 ppm to lower field than the δ value of 368.6 ppm for N2 in benzotriazole (**13**) and is the result of the methyl substitution. Thus, in order to estimate the chemical shifts for pyridine-type nitrogens in the NH tautomers from the corresponding *N*-methyl derivative, a −9.5-ppm correction, the "adjacent methyl correction", will be applied if the pyridine-type nitrogen is adjacent to a *N*-methyl nitrogen.

Finally, a recent report of the ^{15}N chemical shifts of indazole (**7**)[13] in Me_2SO-d_6 solution is in good agreement with the conclusions reached here on the effects of methyl substitution. The chemical shift of N1 for indazole (**7**) is 8.4 ppm to low field of δ_{N1} for 1-methylindazole (**8**), while the indazole δ_{N2} is 9.1 ppm to high field of δ_{N2} for 1-methylindazole.

Tautomer Mole Fractions. Knowing the changes in chemical shift that result when the NH hydrogen is replaced by a methyl group, it is possible to estimate the tautomeric composition of the azoles. Equation 1 may be applied to imidazole (**3**), which is undergoing rapid prototropic tautomerism. It shows one nitrogen resonance, p^{obsd}, which is a weighted average of δ_{NH} and $\delta_{N'}$. The value for $\delta_{N'}$, the chemical shift of the pyridine-type N, is taken as δ_{N3} of 1-methylimidazole (**4**) and the value for δ_{NH} is taken as δ_{N1} for **4**, corrected by the "*N*-methyl correction", −1.8 ppm or +5.6 ppm for $DCCl_3$ or Me_2SO-d_6 solvent, respectively. The expected mole fraction is 0.50 and a mole fraction of 0.50 ± 0.02 is obtained on solving eq 1 for the mole fraction.

The remaining azoles, **7**, **10**, **13**, **16**, and **19**, all show two different exchange averaged nitrogen resonances. The mole fractions of the tautomers calculated from each different nitrogen resonance must be in agreement. Thus, the values of the *N*-methyl correction terms can be

(8) G. B. Barlin and T. J. Batterham, *J. Chem. Soc. B*, 516 (1967).
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(10) A. J. DiGioia and R. L. Lichter, *J. Magn. Reson.*, **27**, 431 (1977).
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Table III. Azole Tautomer Mole Fractions Estimated from ^{15}N Chemical Shifts

compound	NH tautomer	av mole fraction[a]	range	solvent
indazole (7)	2H	0.02[b]	±0.02[b]	Me_2SO
benzotriazole (13)	2H	0.02	±0.02	$DCCl_3$
	2H	0.02	±0.05	Me_2SO
1,2,3-triazole (10)	2H	0.34	±0.01	$DCCl_3$
	2H	0.55	±0.05	Me_2SO
1,2,4-triazole (16)	4H	0.05	±0.03	Me_2SO
tetrazole (19)	2H	0.01	±0.03	Me_2SO

[a] Average of the mole fractions obtained from the exchange averaged chemical shifts for the two different nitrogen atoms. [b] Calculated from the ^{15}N chemical shifts reported in ref 13.

qualitatively confirmed by this agreement. The mole fractions of the 2-NH tautomer for **7**, **10**, **13**, and **19** and the 4-NH tautomer mole fraction for **16** are collected in Table III. The mole fractions are the averages of the mole fractions derived from the two different nitrogen atoms. The range is the difference in mole fraction between the average mole fraction and that obtained from one nitrogen atom chemical shift. The range is ±0.05 mole fraction or less in each case, an agreement that qualitatively confirms the appropriateness of the two methyl correction terms.

The simplest case of rapid prototropic tautomerism that shows two different nitrogen resonances is indazole (**7**) given below.

7a **7b**

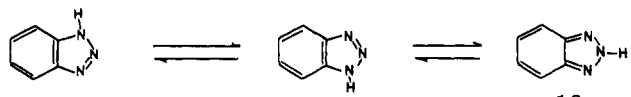
Indazole prototropic tautomerism is a rapid proton exchange between **7a** and **7b**. With use of eq 1, the mole fraction of **7b**, X_b, can be expressed in terms of the observed nitrogen chemical shifts and those of the corresponding *N*-methyl derivatives (corrected for *N*-methyl effects) of **7a** and **7b**, which are **8** and **9**, respectively. Utilizing the chemical shift of N2 for indazole, the mole fraction X_b is given by eq 2 where $\delta_{N2} = \delta_{N2}$ for **7**, $\delta_{NH} =$

$$X_b = (\delta_{N2} - \delta_{N'})/(\delta_{NH} - \delta_{N'}) \quad (2)$$

δ_{N2} for **9** +5.6 ppm (Me_2SO), and $\delta_{N'} = \delta_{N2}$ for **8** −9.5 ppm. The "pyrrole *N*-methyl correction" of 5.6 ppm is added to δ_{N2} for **9** and the "adjacent methyl correction", 9.5 ppm, is subtracted from δ_{N2} for **8** to give $\delta_{N'}$. After these corrections are made, a value of zero (0.00) is found for the 2-NH mole fraction, X_b.

An expression similar to eq 2 may be written for X_b in terms of δ_{N1} for indazole (**7**). When δ_{N1} for **7** and the appropriate NCH_3 corrections are applied to δ_{N1} for **8** and **9**, a value of 0.03 for X_b is obtained. The results from both δ_{N2} and δ_{N1} are in excellent agreement with each other and those reported in the literature.[13] Indazole exists almost exclusively as the 1-NH tautomer.

The triazoles **10**, **13**, and **16** equilibrate between three possible tautomers, which can be exemplified by benzotriazole (**13**) and tautomers **13a**–**13c**. The chemical shift



13a **13b** **13c**

of N2 for **13** will be a mole fraction weighted average of the chemical shifts of N2 in **13a**,**b**,**c** as in the following equation:

$$\delta_{N2} = X_a\delta_{N'a} + X_b\delta_{N'b} + X_c\delta_{NH} \quad (3)$$

Since $X_a = X_b$ and $\delta_{N'a} = \delta_{N'b}$

$$X_c = (\delta_{N2} - \delta_{N'})/(\delta_{NH} - \delta_{N'}) \quad (4)$$

where $\delta_{N2} = \delta_{N2}$ for **13**; $\delta_{NH} = \delta_{N2}$ for **15**, −1.8 ppm ($HCCl_3$); $\delta_{N'} = \delta_{N2}$ for **14**, −9.5 ppm. Thus eq 4 provides a value for mole fraction of the 2-NH tautomer, X_c. Using the values of δ_{N2} for the *N*-methyl derivatives **14** and **15** and correcting for the effect of the *N*-methyl group, a value of zero (0.00) for X_c is obtained for benzotriazole in $HCCl_3$ solution.

The chemical shift of N1 for **13** is similarly an average of chemical shifts weighted by mole fractions X_a, X_b, X_c and given by eq 5, where $\delta_{N1} = \delta_{N1}$ for **13**; $\delta_{NH} = \delta_{N1}$ for

$$\delta_{N1} = X_a\delta_{NH} + X_b\delta_{N} + X_c\delta_{N'} \quad (5)$$

$$X_c = \frac{2\delta_{N1} - (\delta_{NH} + \delta_{N})}{2\delta_{N'} - (\delta_{NH} + \delta_{N})} \quad (6)$$

14, −1.8 ppm ($HCCl_3$); $\delta_N = \delta_{N3}$ for **14**; $\delta_{N'} = \delta_{N1}$ for **15**, −9.5 ppm. On noting that X_a and X_b are equal, due to symmetry, X_c will be given by eq 6. Using the chemical shifts of the appropriate nitrogen atoms in the *N*-methyl derivatives **14** and **15** and correcting for the effects of the methyl group, a value of 0.03 for X_c is obtained for **13** in $HCCl_3$ solution. This value determined from δ_{N1} of **13** is in excellent agreement with that obtained from δ_{N2}.

The nitrogen chemical shifts of benzotriazoles **13**, **14**, and **15** in Me_2SO were also determined. The average value of the mole fractions for the 2-NH tautomer, X_c, obtained from consideration of δ_{N2} and δ_{N1} was 0.02 with a range of ±0.05. As a result of the solvent effects, in particular hydrogen bonding, in Me_2SO the *N*-methyl compounds and the correction terms might be expected to be more approximate and vary more from one azole to another. However, the agreement is still quite reasonable.

Thus, it can be concluded that benzotriazole exists almost exclusively as the 1-NH tautomer. This is in agreement with the more qualitative conclusions drawn on the basis of the benzene ring vicinal proton coupling constants[12] and the change of the benzene ring proton spectrum from an AA′BB′ at room temperature to an ABCD type of spectrum at low temperature.[2]

The prototropic tautomerism of 1,2,3-triazole (**10**) may be analyzed by applying eq 4 and 6 to the chemical shifts of N2 and N1, respectively. The *N*-methyl model compounds for the NH tautomers are triazoles **11** and **12**. When the chemical shifts for the 1,2,3-triazole compounds are treated as described for the benzotriazole compounds, the $HCCl_3$ solution mole fraction of 2-NH tautomer for **10** is found to be 0.34 with a range of ±0.01 mole fraction. This is in good agreement with a 2-NH tautomer mole fraction of 0.4 determined by considering the one bond ^{13}C–^{1}H coupling constants.[14]

The 2-NH tautomer mole fraction for 1,2,3-triazole (**10**) was also determined in Me_2SO solution and found to be 0.55 ± 0.05 mole fraction of 2-NH tautomer. The range of ±0.05 mole fraction is again larger than that of ±0.01 mole fraction found for the $HCCl_3$ solution.

It is, however, notable that the increase in 2-NH tautomer mole fraction in Me_2SO is definitely greater than the uncertainty in the technique. The value of 0.34 mole fraction of 2-NH tautomer in $HCCl_3$ is essentially a statistical tautomer distribution, thus the 1-NH and 2-NH

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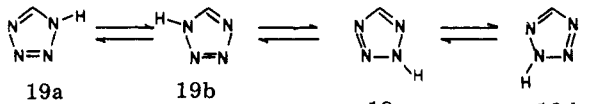
tautomers in $HCCl_3$ are of equal free energy. In Me_2SO, a polar solvent to which the triazole may also hydrogen bond, the equilibrium shifts in favor of the 2-NH tautomer. As a result of the inductive effect of two adjacent nitrogen atoms the 2-NH tautomer might be expected to form the stronger hydrogen bond, and thus be favored in Me_2SO.

The prototropic tautomeric equilibrium of 1,2,4-triazole (**16**) may also be treated by eq 4 and 6, using the *N*-methyl derivatives of the tautomers, triazoles **17** and **18**. However, δ_{N4} for **16** is used with eq 4 to arrive at the mole fraction of 4-NH tautomer. Further, δ_{NH} is taken as δ_{N4} for triazole **18** corrected by 5.6 ppm and $\delta_{N'}$ is taken as δ_{N4} for triazole **17**. This yields a mole fraction of 0.08 for the 4-NH tautomer. With use of δ_{N1} to report the position of equilibrium and eq 6 with the changes in nitrogen atom ring positions, a value of 0.02 mole fraction for the 4-NH tautomer is obtained. The average value of 0.05 ± 0.03 mole fraction for the 4-NH tautomer is consistent with the results obtained by low-temperature proton NMR.[3] On the basis of the low-temperature proton NMR it was concluded that 1,2,4-triazole (**16**) exists exclusively as the 1-NH tautomer. While on the border of experimental uncertainty, these ^{15}N results indicate there may be as much as 0.08 mole fraction of the 4-NH tautomer present for 1,2,4-triazole in Me_2SO solution.

The prototropic tautomerism of tetrazole (**19**) is an equilibrium involving the four tautomers **19a–19d**, for which the mole fractions of **19a** and **19b** are equal and **19c** and **19d** are equal as a result of symmetry.

The chemical shift of N1 may be utilized to report on the position of equilibrium.



19a 19b 19c 19d

The mole fraction of **19d**, X_d, can then be obtained from eq 8 and the appropriate nitrogen chemical shifts for the NH tautomers estimated from the *N*-methyl derivatives **20** and **21**, where $\delta_{N1} = \delta_{N1}$ for **19**; $\delta_{NH} = \delta_{N1}$ for **20** +5.6 ppm (Me_2SO); $\delta_{Nb} = \delta_{N4}$ for **20**; $\delta_{Nc} = \delta_{N1}$ for **21**, –9.5 ppm; $\delta_{Nd} = \delta_{N4}$ for **21**.

$$\delta_{N1} = X_a\delta_{NH} + X_b\delta_{Nb} + X_c\delta_{Nc} + X_d\delta_{Nd} \quad (7)$$

$$X_d = \frac{\delta_{N1} - 0.5(\delta_{NH} + \delta_{Nb})}{(\delta_{Nc} + \delta_{Nd}) - (\delta_{NH} + \delta_{Nb})} \quad (8)$$

In a similar fashion, eq 9 and the chemical shift for N2 of tetrazole (**19**) will yield a value for the mole fraction of **19d**, X_d, where $\delta_{N2} = \delta_{N2}$ for **19**; $\delta_{Nb} = \delta_{N3}$ for **20**; $\delta_{Nd} = \delta_{N2}$ for **21**, –9.5 ppm; $\delta_{Na} = \delta_{N2}$ for **20**, –9.5 ppm; $\delta_{NH} = \delta_{N1}$ for **21**, +5.6 ppm (Me_2SO). The appropriate nitrogen chemical shifts are estimated from the chemical shifts of the *N*-methyl derivatives **20** and **21**.

$$X_d = \frac{\delta_{N2} - 0.5(\delta_{Na} + \delta_{Nb})}{(\delta_{NH} + \delta_{Nb}) - (\delta_{Na} + \delta_{Nb})} \quad (9)$$

The mole fraction of 2-NH tautomer for tetrazole (**19**) will be twice the value estimated for **19d**. The average of 0.01 ± 0.03 mole fraction from δ_{N1} and δ_{N2} is thus obtained. This result, that tetrazole is almost exclusively in the 1-NH tautomer, is in agreement with the qualitative conclusions based on the ^1H NMR of several substituted tetrazoles[15] and the more quantitative ^{13}C NMR results of Roberts et al.[4]

A final observation on prototropic tautomerism and its' consequences in ^{15}N NMR spectra of nitrogen heterocyclic compounds comes from the ^{15}N spectrum of benzotriazole (**13**). At a probe temperature of 35 °C only the N2 resonance at 368.6 ppm is observed. However, on warming to 47 °C, a broad line appears at 276.8 ppm, which is the N1 (N3) resonances now averaged by more rapid proton exchange. The N1 and N3 resonance was not observable at 35 °C because the large chemical shift difference in hertz between the pyrrole-type N1 nitrogen and the pyridine-type N3 nitrogen results in 35 °C being close to the coalescence temperature. Thus, broadening the N1 (N3) resonance into the base line noise.

An estimate of the rate constant for tautomerization may be obtained by using the approximate expression[16] for an exchange broadened line above the coalescence temperature given by eq 10. The approximate rate constant may

$$k = \pi(\Delta\nu)^2/2(W_{1/2}) \quad (10)$$

in turn be used to obtain an estimate of $\Delta G^\ddagger$ for the prototropic tautomerism of benzotriazole (**13**). The chemical shift difference, in hertz, for the two nuclei in the absence of exchange is $\Delta\nu$. The chemical shift difference between N1 and N3 for benzotriazole (**13**) was taken as equal to the difference between N1 and N3 for methyl benzotriazole **14**. This is equal to a $\Delta\nu$ of 995.3 Hz, after correcting for the methyl group. The exchange contribution to the width at one-half maximum peak height, $W_{1/2}$, was obtained by subtracting the nonexchange contributions to the line width from the width at one-half maximum, 8.2 Hz, of the N1 (N3) resonance of **13**. The nonexchange line width contribution was taken as 1.4 Hz, the width at one-half maximum for the N2 resonance of **13**. This yields a value of $W_{1/2}$ equal to 6.8 Hz and results in a rate constant, k, of 2.3×10^5 s^{-1} for the tautomerism. At 47 °C this corresponds to $\Delta G^\ddagger$ of 11 kcal/mol for prototropic tautomerism of benzotriazole. The $\Delta G^\ddagger$ for prototropic tautomerism of 1,2,4-triazole[3] obtained by low-temperature ^1H NMR is 13.4 kcal/mol, a value that is comparable to that reported here for benzotriazole.

In conclusion, the large ^{15}N chemical shift differences between pyrrole-type and pyridine-type nitrogen atoms in nitrogen heterocycles result in the *N*-methyl compounds being suitable model compounds for the ^{15}N chemical shifts of their respective NH tautomers. This may now be conveniently exploited to obtain quantitative mole fraction estimates for the NH tautomers. Since this is not generally the case for ^1H and ^{13}C spectra of heterocyclic compounds, ^{15}N NMR may well be the method of choice for studying prototropic tautomerism in nitrogen heterocyclic compounds.

Experimental Section

Materials. The azoles **2–5**, **13**, **16**, and **19** were obtained from commercial sources and were used without further purification. A commerical sample of pyrrole (**1**) was distilled just prior to use. The remaining azoles, **6**,[17] **10**,[18] **11**,[19] **12**,[19] **14**,[20] **15**,[20] **17**,[21] **18**,[21] and **21**[8] were synthesized according to published procedures. Samples for NMR spectra determinations of **11**, **12**, **14**, **15**, and **21** were purified by preparative GLC, using a Varian-Aerograph A90-P3

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gas chromatograph equipped with a 10 ft by 0.25 in. column packed with 8% SE-30 on 80–100-mesh Chromosorb Q. 1-Methyl-1*H*-tetrazole (**20**) was synthesized by deamination[22] of 5-amino-1-methyl-1*H*-tetrazole.[23] The structures and purity of the compounds studied were verified by their ^1H and ^{13}C NMR spectra.

Spectra. The CW ^1H NMR spectra were determined at 60 MHz with a Perkin-Elmer R-20 or at 100 MHz with a Varian HA-100 NMR spectrometer. The ^{13}C NMR spectra were recorded at 20 MHz, using a Varian FT-80A NMR spectrometer. The ^{13}C spectra were determined at a spectral width of 4 kHz with a 16K data table, applying a 45° pulse with a repetition rate of 2 s and continuous broad-band ^1H decoupling.

The ^{15}N NMR spectra were determined at 8.059 MHz with the Varian FT-80A instrument, using solutions of 750 mg of the azole dissolved in 2 mL of $DCCl_3$ or Me_2SO-d_6. ^{15}N spectra of the NH azoles were recorded with the following conditions: 4 kHz spectral width, 8K data table, 15° or 30° pulse angle, 1-s pulse repetition, and continuous broad-band ^1H decoupling. Then 30 mg of Cr(Acac)$_3$ was added to the NH azole sample and the spectrum was determined with a 4-kHz spectral width, 4K data with 4K of zeros, 15° or 30° pulse angle, 0.5-s aquisition time, and 2.5-s pulse repetition rate. The broad-band ^1H decoupler was on only during the aquisition time to ensure maximum supression of the NOE. The spectra of the *N*-methylazoles were determined in the presence of Cr(Acac)$_3$ and with the appropriate spectrometer conditions. In all cases, it was necessary to accumulate 30 000–60 000 transients in order to obtain spectra with an acceptable signal-to-noise ratio.

The chemical shifts were determined with respect to external nitromethane contained in a 2-mm capillary held concentrically in the sample tube. The nitrogen chemical shifts referenced to nitromethane, $\delta_{CH_3NO_2}$, were then converted to a chemical shift relative to liquid ammonia, δ_{NH_3}, using the following expression:[9,24]

$$\delta_{NH_3} = \delta_{CH_3NO_2} + 380.2 \text{ ppm}$$

No effort was made to correct the chemical shifts for solution magnetic susceptibility differences[9] or magnetic susceptibility changes resulting from the Cr(Acac)$_3$[10] as these result in chemical shift changes that are small in relation to the differences in chemical shifts between the pyrrole- and pyridine-type of nitrogen atoms.

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Registry No. **1**, 109-97-7; **2**, 96-54-8; **3**, 288-32-4; **4**, 616-47-7; **5**, 288-13-1; **6**, 930-36-9; **7**, 271-44-3; **10**, 288-36-8; 11, 16681-65-5; **12**, 18922-69-5; **13**, 95-14-7; **14**, 13351-73-0; **15**, 16584-00-2; **16**, 288-88-0; **17**, 6086-21-1; **18**, 10570-40-8; **19**, 288-94-8; **20**, 16681-77-9; **21**, 16681-78-0.

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On the Mechanism of Ester Aminolysis in the Presence of Alkylammonium Carboxylate Reversed Micelles

Monica I. El Seoud, Rita C. Vieira, and Omar A. El Seoud*

Instituto de Quimica, Universidad de São Paulo, 01000 São Paulo, SP, Brazil

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The mechanism of ester aminolysis by alkylammonium carboxylate reversed micelles was examined. There are two possible pathways, one involving the carboxylate group of the surfactant acting as a general base and another in which it is acting as a nucleophile. The latter mechanism involves the formation of a mixed anhydride (derived from the surfactant and the ester) leading, on aminolysis, to two amides. It was not possible to detect the formation of the intermediate anhydride. Careful analysis of the reaction products showed that only one amide, that derived from the ester, is formed. Thus the second mechanism is in error. The nature of the slow step was explored by studying the aminolysis of a series of esters: *p*-X-phenyl acetates (where X = CH_3O, CH_3, H, Br, CN, and NO_2) by dodecylammonium propionate (DAP) and by dodecylamine plus DAP in benzene and in cyclohexane. Excellent correlations between the logarithm of the rate constant and the Hammett (σ^-) values were obtained. This implies that the phenoxide ion is the leaving group and that the slow step probably involves the collapse of the tetrahedral intermediate formed by the attack of the amine on the ester. Thus it appears that ester aminolysis in the micellar pseudophase and that in aprotic solvents proceed with the same mechanism and rate-limiting step.

Catalysis by detergent aggregates in organic solvents (termed reversed micelles) is a subject of increasing importance because of the catalytic efficiency of these species.[1] Reversed micellar catalysis is also relevant to the enzymatic counterpart since the active sites of proteolytic as well as lipolytic enzymes contain hydrophobic regions,[2] whose polarity is similar to that in the micellar water "pools".[1,3] The substrates usually concentrate in the micellar "core" (made of the surfactant hydrophilic groups) where enhanced reactivities, concerted proton transfer, and favorable entropies of activation contribute to the catalysis.[1,3,4]

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