The Proton Magnetic Resonance and ^{13}C–H Satellite Spectra of Aqueous Purine, and Their pH Dependence

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The behavior of purine in an acid medium has been studied by n.m.r. techniques. Both proton and ^{13}C–H satellite spectra have been examined. It was found that all spectral parameters demonstrate similar response to changes in pH in a way that suggests a simple acid–base equilibrium. Factors responsible for changes in the observed parameters in going from the neutral base to its conjugate acid are discussed. Also an attempt has been made to use the data to elucidate the protonation scheme in purine.

Introduction

The proton magnetic resonance (p.m.r.) spectra of purine and its derivatives have been reported by several investigators. In purine itself, the original assignments of the C-protons[1,2] were shown to be incorrect by Matsuura and Goto[3] and by Schweizer, *et al.*[4] Chan, *et al.*, examined the p.m.r. spectrum of purine at various concentrations in aqueous solution and concluded that the behavior of the chemical shifts could be accounted for by a sequence of associative equilibria involving purine *n*-mers.[5] These workers also observed the spectrum of aqueous purine under both acidic and basic conditions.

This communication describes the results of an extended study of purine in H_2O and D_2O solution, as a function of pH or pD (corresponding to $0 \leqq$ pH $\leqq 8$) at three different concentrations. Under these conditions the chemical shifts of the C-protons in H_2O were measured relative to an external reference and corrected for the bulk magnetic susceptibility of the medium. In addition, the ^{13}C–H satellite spectra of all the carbon protons were measured, using D_2O as the solvent to eliminate interference from the large water peak. These spectra were studied at one concentration (2.77 *m*) over a range of pD values ($\sim$0–6). It was also possible to observe the variations in the small H-2–H-6 splitting for most of the pH values employed.

All of the above spectral parameters exhibit a strikingly parallel behavior, and all turn out to be linear in the fraction, *f*, of total base present in the protonated form as calculated from the simple equilibrium $BH^+ \rightarrow B + H^+$, with the corresponding basic pK_a varying only moderately with concentration. If the pK_a values are extrapolated to zero concentration the result is in good agreement with the value obtained by spectrophotometric (ultraviolet) techniques.

Detailed examination of the results shows that they are consistent with a protonation scheme for purine involving all three basic centers, N-1, N-3, and N-7, with N-1 the principal site of protonation. As this result is at odds with the current interpretation, which limits protonation to N-1, the nature of the underlying assumptions in the two approaches has been examined briefly.

The effect of protonation on the spectroscopic parameters of purine is a matter of considerable interest. The factors involved here are understandably complex and difficult to isolate, but an effort has been made to enumerate them and to appraise their possible importance.

Experimental

A. Preparation of Samples. The purine used throughout this study was obtained from several commercial sources. It was found that these samples contained no spectroscopically observable impurities. Aqueous solutions of the compounds were prepared by dissolving weighed amounts of the base in water, adjusting the pH of the sample with HCl or NaOH, and diluting the sample to a specified weight. All concentrations are expressed on the molal basis (moles per 1000 g. of solvent). The pH measurements were made at 24° using a Radiometer TTT 1 pH meter which was periodically standardized against buffers of pH 1.68 and 6.50. Because the acidic purine solutions were found to decompose slightly on standing, samples were examined within 48 hr. of preparation. Although there was a 5° difference between probe and room temperatures, the pH of the samples was observed not to be significantly affected by this difference.

Samples used for the ^{13}C–H satellite spectra were prepared in a generally similar manner. However, strong interference by the water peak in this case made it necessary to use heavy-water solutions of d_9-purine. The latter was easily prepared by several cycles of dissolution and evaporation of purine in D_2O.[1] Adjustment of pD was made by addition of DCl or NaOD, as required. The pD values were determined by adding the constant value of 0.40 to each reading of the pH meter.[6,7]

B. Spectra. All spectra were recorded on a Varian Model A-60 n.m.r. spectrometer. The operating probe temperature was measured as 29° and was found to vary not more than ±1° for the duration of the study. Calibration of the spectra was performed by the usual side-band technique. A Hewlett-Packard Model 200-J audiooscillator and a Hewlett-Packard Model 522-B frequency counter were used for this

(1) C. D. Jardetzky and O. Jardetzky, *J. Am. Chem. Soc.*, **82**, 222 (1960).
(2) G. S. Reddy, L. Mandell, and J. H. Goldstein, *J. Chem. Soc.*, 1414 (1963).
(3) S. Matsuura and T. Goto, *Tetrahedron Letters*, No. 22, 1499 (1963).
(4) M. P. Schweizer, S. I. Chan, G. K. Helmkamp, and P. O. P. Ts'o, *J. Am. Chem. Soc.*, **86**, 696 (1964).
(5) S. I. Chan, M. P. Schweizer, P. O. P. Ts'o, and G. K. Helmkamp; *ibid.*, **86**, 4182 (1964).
(6) P. K. Glasoe and F. A. Long, *J. Phys. Chem.*, **64**, 188 (1960).
(7) R. G. Bates, "Determination of pH, Theory and Practice," John Wiley and Sons, Inc., New York, N. Y., 1964, pp. 219, 220.

purpose. Generally, the proton frequencies represent the average calibration of two forward and two reverse 50-c.p.s. scans at 500 c.p.s./sec. The average deviation of any proton frequency from its mean was always less than 0.2 c.p.s.

The ^{13}C–H satellite spectra were recorded using an automatic integrator technique which has been described elsewhere.[8] The reported frequencies of the ^{13}C–H coupling constants represent the average of at least three calibrated spectra. Because of the low natural abundance of the ^{13}C nuclei, additional scans were sometimes necessary in order to identify the lines clearly. The deviation of an observed ^{13}C–H frequency from its mean was always less than 0.5 c.p.s. Assignment of satellite frequencies to their corresponding proton resonances was based largely on the requirement that each ^{13}C–H doublet be symmetrical about the parent line. At the higher pD values the differences in the three ^{13}C–H couplings are such as to make these assignments unambiguous, in spite of any slight dissymmetries in the spacings. As the pD of the solution is decreased the couplings for C-2 and C-8 tend to merge and finally cross over, but no difficulty was experienced in identifying the satellite lines.

The proton spectra were calibrated relative to external water contained in a capillary. For each sample, the bulk susceptibility was measured using nonrotating coaxial tubes and appropriate susceptibility corrections were applied.[9–12] Although water is not the ideal reference because of its temperature-dependent resonance, the probe was maintained at a relatively constant temperature throughout the studies and there was no indication of difficulties from this source. The choice of water as reference was made in order to optimize the experimental determination of the bulk susceptibility correction. These corrections are not listed separately, but they did vary by as much as 10 c.p.s. with pH and concentrations. The final corrected values were converted to an external benzene reference.

The ^{13}C–H satellite spectra were measured relative to external cyclohexane contained in a capillary, but since the values of J_{CH} represent differences the reference is of no relevance here. However, as it was desired to compare the variations of J_{CH} with those of the corresponding chemical shifts, and since observation of the satellite spectra was done at the natural abundance of ^{13}C, a slightly more concentrated solution was employed here than for the proton studies. The proton shifts in D_2O solution were recalibrated and corrected for the bulk susceptibility appropriate to the conditions employed.

Results

Table I summarizes the observed spectra of purine as a function of pH, in the range 0–8, for the three concentrations studied, 2.63, 0.531, and 0.205 *m*. Figure 1 is a plot of ν_i *vs.* pH at 0.531 *m*. Figure 2 shows the variation of one of the shifts (H-6) with pH at each of the concentrations employed. Similar curves are obtained for the other two shifts also. Figure 2 demonstrates that the shifts in aqueous purine become progressively less dependent on concentration as the pH decreases, a point which has previously been noted for the neutral and acidic solutions.[5]

Table I. Observed P.m.r. Spectra of Aqueous Purine as a Function of Concentration and pH[a]

pH	ν_6	ν_2	ν_8	δ_6[b]	δ_2[b]
		2.63 *m*			
0.04	−169	−156	−141	1.07	1.02
1.09	−162	−150	−134	1.01	0.96
1.53	−155	−143	−128	0.89	0.86
2.03	−139	−128	−115	0.59	0.64
2.30	−128	−119	−107	...	0.38
2.82	−111	−104	−93	...	...
4.03	−100	−95	−85	...	...
5.60	−100	−95	−85	...	...
8.01	−97	−93	−83	...	...
		0.531 *m*			
0.12	−170	−159	−144	1.03	0.85[c]
1.20	−166	−155	−139	1.04	0.98
1.56	−164	−153	−137	0.96	0.94
2.03	−154	−143	−127	0.80	0.75
2.47	−143	−133	−117	0.47	0.38
2.98	−127	−119	−104	...	...
4.00	−120	−112	−97	...	...
5.71	−119	−112	−97	...	...
8.03	−117	−109	−94	...	...
		0.205 *m*			
0.13	−170	−159	−144	1.03	1.06
1.13	−168	−157	−141	1.04	0.94
1.50	−166	−155	−139	1.00	0.90
2.03	−160	−149	−133	0.86	0.79
2.52	−151	−140	−123	...	...
2.92	−140	−130	−112	...	...
3.98	−131	−122	−105	...	...
5.80	−129	−120	−103	...	...
8.00	−129	−120	−102	...	...

[a] Frequencies are in cycles per second at 60 Mc.p.s., relative to external benzene. [b] Splitting of H-6 and H-2 peaks due to $J_{2,6}$. [c] Poorly resolved.

The spectrum of neutral purine consists of three lines all broadened noticeably, presumably as a result of interaction with the adjacent nitrogen nuclei. However, below a pH of about 2.5, the peaks due to H-2 and H-6 exhibit a splitting, ascribable to the coupling, $J_{2,6}$, which increases as the pH is lowered (see Table I). It is to be expected that protonation at N-2 would decrease the inhomogeneities in the electric field gradients at the nitrogen nucleus and, in turn, decrease the quadrupolar line broadening at H-2 and H-6, thus permitting any effects of $J_{2,6}$ to become more readily observable. However, the pH dependence of this splitting is quite interesting and, as Figure 3 shows, it varies in roughly linear fashion with ν_6, due note being taken of the potentially large relative errors inherent in the measurement of this small splitting.

Figure 4 shows the appearance of one of the better quality integrated spectra obtained for the ^{13}C–H satellites. This is a small portion of one of the spectra showing only the high-field half of the ^{13}C–H doublet, at a pD of 1.09, reproduced here because it reveals so clearly the splitting produced by $J_{2,6}$. The distance between centers of the two peaks in Figure 4 is very nearly 1 c.p.s. (The values in Table II refer only to

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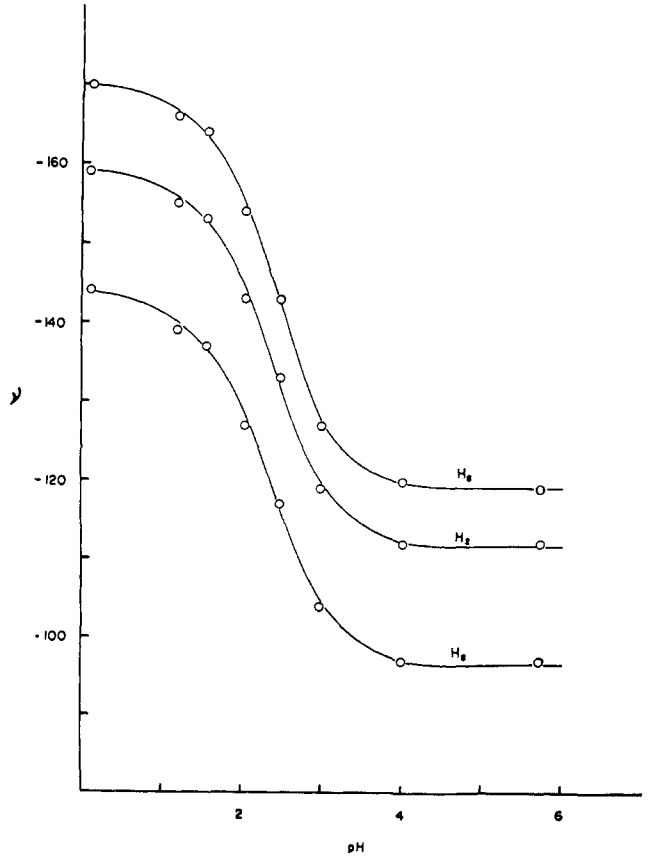

Figure 1. Chemical shifts of purine (0.531 *m*) *vs.* pH at 60 Mc.p.s.

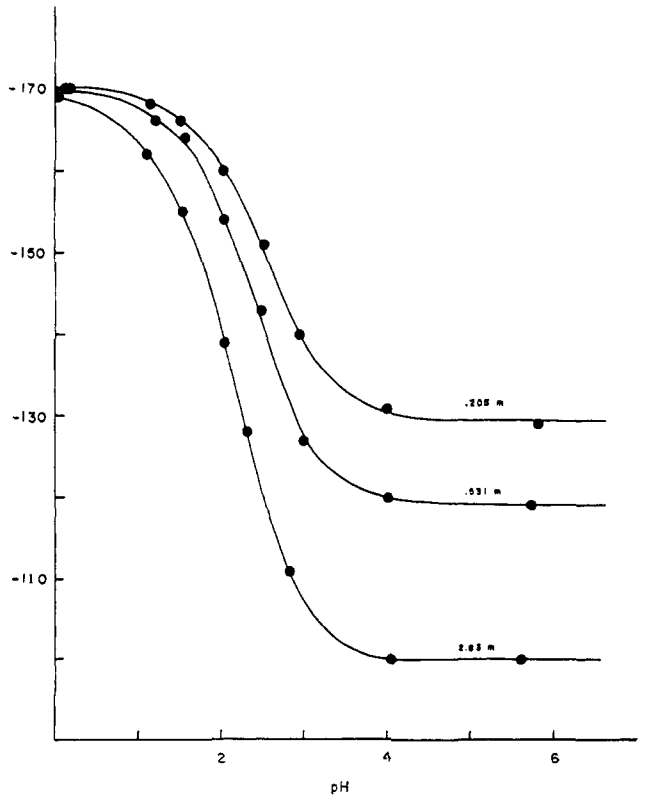

Figure 2. Proton resonance frequencies of H-6 *vs.* pH. Frequencies are relative to external benzene at 60 Mc.p.s. Ascending the graph the concentrations are 2.63, 0.531, and 0.205 *m*.

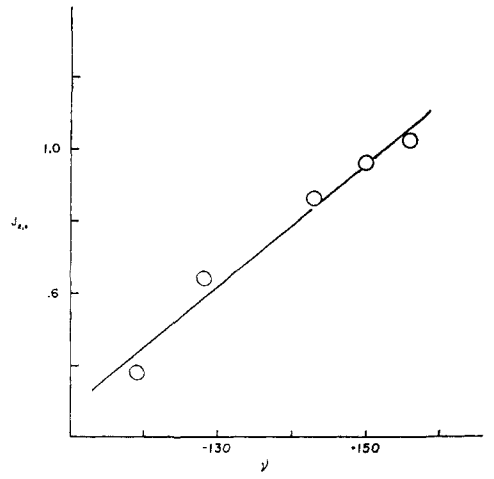

Figure 3. Graph of $J_{2,6}$ plotted against ν_2.

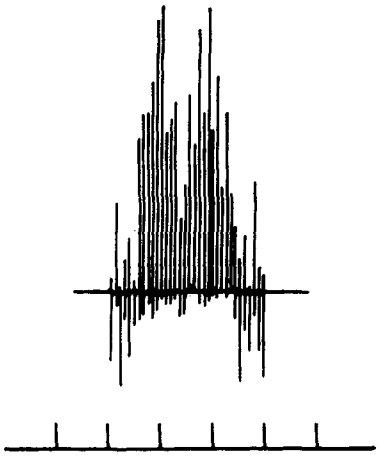

Figure 4. Integrator spectrum of upfield ^{13}C–H satellite of H_2 at pD 1.09. Each chart division represents 1.0 c.p.s.

those resonances arising from protons directly bonded to ^{13}C. For each isotopic species the remaining protons give rise to resonances very close to the parent lines but only about 1% as intense. They are, therefore, virtually unobservable and, in any case, are not expected in the present study to provide new information of any value.)

Table II. Chemical Shifts[a] and ^{13}C–H Coupling Constants[b] for d_0-Purine (2.77 *m*) in D_2O

pD	ν_i			J^{13}_{C-H}		
	H_6	H_2	H_8	H_6	H_2	H_8
0.15	−488	−475	−459	196.6	219.1	218.5
1.09	−484	−472	−455	196.1	218.8	217.3
2.72	−449	−439	−427	191.4	211.5	215.2
3.22	−430	−422	−413	188.8	208.6	213.8
5.63	−417	−411	−402	187.4	207.0	213.5

[a] In cycles per second from external cyclohexane at 60 Mc.p.s. (corrected for bulk susceptibility). [b] In c.p.s.

The variation of all three ^{13}C–H couplings with pH is shown in Figure 5 and reveals the same general behavior as do the chemical shifts (Figure 1). However, it should be noted that the coupling constants for H-2 and H-8 cross over at the low end of the pH range.

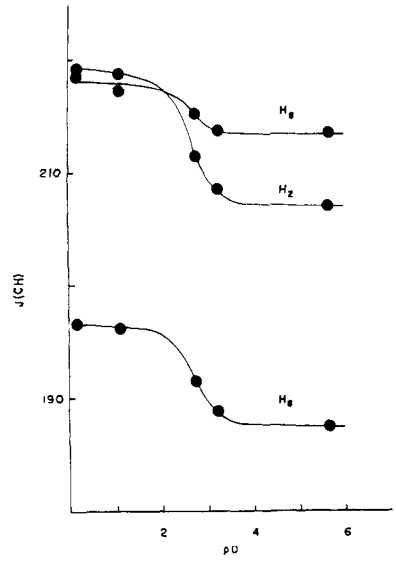

Figure 5. Graph of ^{13}C–H coupling constants *vs.* pD.

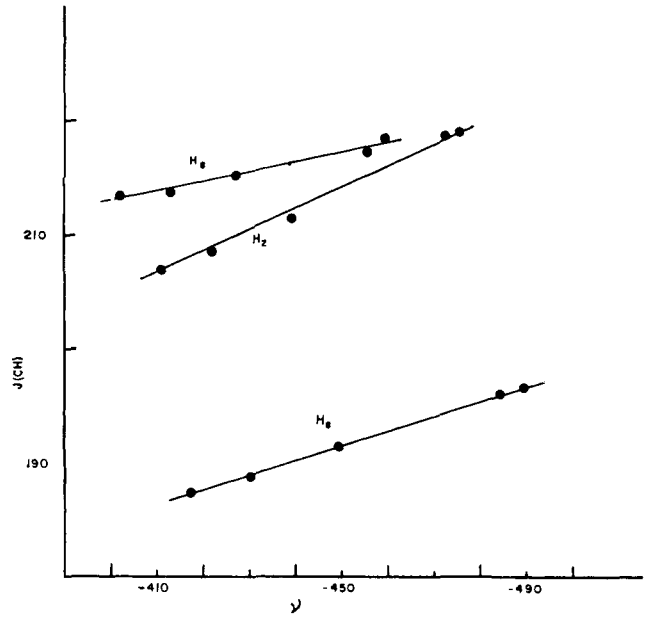

Figure 6. ^{13}C–H coupling constants *vs.* corresponding proton resonance frequencies at 60 Mc.p.s.

Furthermore, as is shown in Figure 6, each J_{CH} and its corresponding shift are in a linear relation to each other as the pH varies, although the slope for H-2 is noticeably greater than those of H-6 and H-8. The shifts employed in Figure 6 are those measured at the same concentration employed for the ^{13}C–H coupling constants (see Table II).

Discussion

The behavior of both the chemical shifts and the ^{13}C–H couplings in purine with pH (or pD) at a given concentration suggests the applicability of the simple equilibrium

$$BH^+ \rightleftharpoons B + H^+ \qquad (1)$$

with a corresponding (basic) dissociation constant K_a. If we define f as the fraction of base protonated, which is related to pK_a by

$$f = [1 + \text{antilog}\,(pH - pK_a)]^{-1} \qquad (2)$$

the observed value of each chemical shift, ν_i, can be expressed as

$$\nu_i = f\nu_i^+ + (1 - f)\nu_i^0 \qquad (3)$$

where ν_i^+ and ν_i^0 are the corresponding shifts in the species BH^+ and B, respectively. Analogous expressions hold for the ^{13}C–H coupling parameters. The validity of eq. 3 requires that proton exchange between species represented as B and BH^+ be sufficiently rapid to produce a single, average spectrum, which is, indeed, the experimentally determined situation. Either or both of B and BH^+ may involve a sequence of associative equilibria,[5] but it can be assumed, again, that under conditions of rapid exchange ν_i^0 and ν_i^+ will represent the corresponding averages for their respective associated species.

On this basis it is expected that a plot of ν_i *vs.* f will yield a straight line for each ν_i if the value of pK_a is suitably chosen for a given concentration. Although these are not expected to be identical with the thermodynamic pK_a, extrapolation to the limit $m = 0$ should provide a result reasonably near the latter.

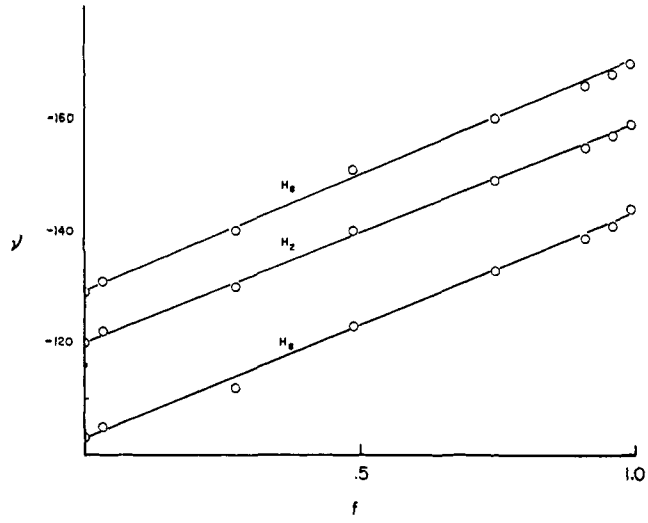

Figure 7. Plot of proton resonance frequencies against fraction protonated, f, at 0.205 m.

For the ν_i given in Table I, it is found that a satisfactorily linear plot (Figure 7) is obtained for eq. 3 using least squares, adjusted pK_a values of 2.10, 2.40, and 2.50, when m = 2.63, 0.531, and 0.205, respectively. The extrapolated value, pK_a (m = 0), is 2.57 which is to be compared with reported values for purine of 2.39[13] and 2.52.[14]

As can be seen from Figures 3 and 6, $J_{2,6}$ and all the ^{13}C–H couplings vary linearly with the corresponding chemical shifts; consequently, these parameters must also depend on f in a linear manner. (This observation should be taken cautiously as far as $J_{2,6}$ is concerned, because of the small magnitude, possible errors, and limited variation of this parameter. In the plot of J_{CH_i} *vs.* ν_{H_i}, both sets of data were obtained at the same concentration in D_2O; hence, both are to be referred to

(13) A. Albert and D. J. Brown, *J. Chem. Soc.*, 2060 (1954).
(14) A. Bendich, D. J. Russell, and J. J. Fox, *J. Am. Chem. Soc.*, 76, 6073 (1954).

the pK_a applicable to $BD^+ \rightleftarrows B + D^+$, in D_2O.) The parallel behavior of these three types of parameters, especially since their dependence on structural detail and environment are certainly dissimilar, provides further support for the simple interpretation involved in eq. 1–3.

Arguing from basic pK_a data for the 2-methyl- and 6-methylmercaptopurines, Albert has concluded that protonation can occur only at N-1.[15] In support of this conclusion can be cited the differences in the ultraviolet spectra of the cations of 7-methyl- and 9-methylpurine, reported by Bendich, Russell, and Fox,[14] and the much greater base weakening evident in 6-trifluoromethylpurine as compared with the 8-trifluoromethyl derivative, as determined by Bendich, Giner-Sorolla, and Fox.[16] Such conclusions, however, necessarily presuppose that protonation occurs exclusively at one site. Lynch, Robinson, and Cheng[17] have used resonance-stabilization arguments to also establish N-1 as the predominant site of protonation, but this approach admits the possibility that multiple sites are involved.

Qualitatively, at least, the effect of protonation on the chemical shifts seems to be more in accord with the idea that all the basic sites in purine (N-1, N-3, and N-7–N-9) participate. The effect of protonation on the observed shifts, expressed as $\nu_i^+ - \nu_i^0$, is −39, −41, and −41 c.p.s., at 0.205 *m*, for H-2, H-6, and H-8, respectively, which is at first glance difficult to reconcile with protonation at N-1 exclusively. However, the interpretation of these protonation effects becomes much more complex and imprecise when paramagnetic,[18] dipolar,[18] and dielectric reaction field[19,20] contributions to the proton screenings are taken into account. Counterion effects, which have been considered in nonaqueous solutions of protonated pyridine,[21] are not expected to be a significant factor in this present case.

The ^{13}C–H couplings, while certain to be sensitive to changes in both the polar dielectric and the intramolecular fields, should not be significantly influenced by changes in paramagnetic susceptibility of the nitrogen atoms. It is true that J_{CH_i} and ν_i exhibit a linear dependence as pH is varied, but, as Figure 6 shows, the slopes are not the same for all protons.

Studies of substituent effects on J_{CH} indicate that the additivity relation of Malinowski, $J_{CH} = \Sigma \zeta_{\alpha\beta}$ (where α and β designate the atoms α and β to the C-atom), is generally valid over a wide range of compounds,[22,23] and values of ζ are available for many heterocyclic aromatic compounds.[23,24] Using the values $\zeta_{CN}' = 84.5$, $\zeta_{NC}' = 103$, $\zeta_{CN}'' = 87.0$, and $\zeta_{NC}'' = 105.5$, where the prime and double prime indicate six- and five-membered rings, respectively, the calculated couplings for purine are $J_{CH_8} = 187.5$ c.p.s., $J_{CH_2} = 206.0$ c.p.s., and $J_{CH_8} = 211.0$ c.p.s., in close agreement with the corresponding values of 187.4, 207.0, and 213.5 for neutral purine.

Although there appears to be no previously established procedure for treating a branched carbon, it was assumed that, of the two atoms at the branch point, N-7 rather than C-4 provides the dominant contribution to J_{CH_6}. Accordingly, only ζ_{NC}' and ζ_{CN}' were used to calculate this coupling. Support for this approach is provided by the good agreement with the observed parameter and the fact that J_{CH_6} in purine is greater than the corresponding value in pyrimidine by approximately 4 c.p.s.[25]

In order to extend the above calculations to the species BH^+ some additional notation is required: (1) the change in ζ_{NC} produced by complete protonation is designated as Θ; (2) the fractions of time a proton spends at N-1, N-2, and on the imidazole ring are represented by a, b, and c, respectively. Changes in J_{CH} on protonation are then given by the equations

$$\begin{aligned} a + b + c &= 1 \\ a\Theta &= \Delta J_{CH_6} = 9.2 \text{ c.p.s.} \\ (a + b)\Theta &= \Delta J_{CH_2} = 12.1 \text{ c.p.s.} \\ c\Theta &= \Delta J_{CH_8} = 5.0 \text{ c.p.s.} \end{aligned} \quad (4)$$

Solving for a, b, and c, the per cent of protonation at each site is found to be: N-1, 54 ± 12%; N-3, 17 ± 12%; N-7–N-9, 29 ± 7%; and Θ = 17 c.p.s.

The listed uncertainties reflect only the experimental uncertainties in the coupling constants. The validity of even such an approximate calculation would be further impaired by any factor which affected the additivity of the $\zeta_{\alpha\beta}$ values in the protonated structure. As a rough test of this possibility, Θ might perhaps be compared with the difference between ζ_{OC} and ζ_{NC}. The latter difference turns out to be 16 c.p.s.,[24] whereas the experimentally determined value of Θ is 17 c.p.s.

In addition, upon protonation of pyrimidine it has been found that J_{CH_2} changes ~13 c.p.s. and J_{CH_4} changes ~9 c.p.s.[25] which agrees moderately well with values of 17 and 8.5 c.p.s., which were calculated using Θ = 17.0 c.p.s.

The above computation does not include the β-substituent contribution to J_{CH_8} when the protonated form is N-7–H^+. This contribution amounts to approximately $^1/_2[\zeta_{CO}'' - \zeta_{CN}''] = 4$ c.p.s.[24] with the factor $^1/_2$ reflecting the fact that the positive charge in the imidazole ring is assumed to be equally divided between N-7 and N-9. Inclusion of such a contribution changes the previous results to 47, 24, and 29% with the same uncertainties as before.

The occurrence of the splitting, $J_{2,6}$, with a final value of approximately 1.0 c.p.s. in the fully protonated form seems to indicate exclusive protonation at N-1. However, this conclusion is not necessarily valid since the observed splitting could represent only a fraction of the total coupling that should hold for the species N-1–H. On this basis we might expect a value of about 1.7 c.p.s. for this species. Moreover, it is not an *a priori* requirement that the molecule be fully pro-

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(21) G. Kotowycz, T. Schaefer, and E. Bock, *Can. J. Chem.*, **42**, 2541 (1964).
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(23) E. R. Malinowski, L. Z. Pollara, and J. P. Larmann, *ibid.*, **84**, 2649 (1962).
(24) K. Tori and T. Nakagawa, *J. Phys. Chem.*, **68**, 3163 (1964).
(25) H. B. Evans and J. H. Goldstein, unpublished results.

tonated at N-1 in order to completely eliminate the quadrupolar effects on $J_{2,6}$. The relative size of the errors possible here are such that one cannot entirely rule out the likelihood that the plot of Figure 3 should flatten out near the maximum of J_{HH}.

The observed variations with protonation of the chemical shifts in purine ($\nu_i^+ - \nu_i^0$) are difficult to interpret reliably because of the number and complexity of the factors that can be involved. In the case of pyridine and its cation, Gil and Murrell were able to obtain a reasonable correlation of shifts with π-electron densities only after correcting the former for the paramagnetic and lone-pair dipole contributions of the nitrogen atom.[18] It would appear that similar corrections would be applicable to purine as well. Since in purine there are four different nitrogen atoms (or three, if those in the imidazole ring are considered to exhibit an average behavior), the required calculations, with appropriate weighting of all the structures, for both the base and its conjugate acid are considerably more involved. Nevertheless, this is a factor which should be incorporated into any comprehensive attempt to interpret and correlate the chemical shift data, which is outside the scope of the present investigation.

The various factors involved in interpreting the n.m.r. parameters suggest that the ^{13}C–H couplings probably provide the least ambiguous basis for a postulated protonation pattern of purine. The distribution of protonated sites deduced above is one which is at least consistent with all of the n.m.r. data. Although it may not necessarily rigorously rule out exclusive protonation at N-1, it provides new grounds for consideration of an alternative such as that presented here.

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Nuclear Magnetic Resonance Studies of 1,3-Butadienes. I. The Spectra of Halogenated Butadienes

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Contribution from Mellon Institute, Pittsburgh, Pennsylvania 15213.
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The nuclear magnetic parameters are presented for fluoroprene, chloroprene, and the three isomers of 1,4-dichloro-1,3-butadiene. Comments are made about the mathematical analysis of the spectra. The chemical shifts and H,F coupling constants are discussed.

Introduction

In general there have been few detailed n.m.r. studies of butadiene derivatives, largely because of the complexity of the spectra. Heavily substituted butadienes, which would give simpler spectra, cannot be readily obtained. The only comprehensive study of high accuracy published so far is that of Hobgood and Goldstein,[2] who reported the nuclear magnetic parameters of 1,3-butadiene itself and a number of derivatives. Among these compounds was one halogenated derivative, namely, 2,3-dichlorobutadiene. This report gives the results of investigations on fluoroprene (2-fluoro-1,3-butadiene) and four chlorinated butadienes. The *s-trans* conformations of these molecules are shown in Figure 1, together with the chemical shifts (τ-values) obtained by the present work. Microwave and infrared spectroscopy have shown that the *s-trans* conformation is indeed the stable form in both fluoroprene[3] and chloroprene.[4] There is every reason to suppose this is also true for the three isomeric 1,4-dichloro-1,3-butadienes.[5] It may be noted that hexachlorobutadiene has been shown to be nonplanar.[4]

Nomenclature

The numbering system for the substituents of 1,3-butadiene used in this paper is illustrated for butadiene itself in Figure 2. This retains the normal numbering for the carbon atoms of the skeleton and extends it to the substituents, using a prime to distinguish between the two substituents bonded to C-1 and to C-4. A new nomenclature has been introduced for the coupling constants in the butadiene molecule in order to facilitate comparisons between molecules. The method of Musher and Corey[6] is used to designate by means of a numerical prefix the number of chemical bonds through which coupling occurs. A subscript *c* or *t* indicates that the path of the coupling is through bonds oriented *cis* or *trans*, respectively, about one of the double bonds, ^3J_c and ^3J_t being the usual vicinal vinylic coupling constants. The extension to the ^4J values is self-explanatory. For the long-range coupling through five bonds two suffixes are necessary since the coupling path extends across two double bonds. Thus the symbol $^5J_{tc}$ indicates coupling between protons at positions 1 and 4′. The same symbol is used for the analogous coupling between protons at 1′ and 4. Similarly in some molecules there may be two coupling constants each of types ^2J, ^3J_c, ^3J_t, ^4J_c, and ^4J_t. Finally the symbol ^3J_s designates coupling between protons at positions 2 and 3, the *s* indicating that this is a formal single-bond vicinal coupling.

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