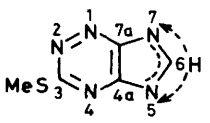
6-Azapurines. Part 1.[1] Determination of the Tautomeric Populations in 3-Methylthioimidazo[4,5-*e*]-*as*-triazine by ^{13}C and ^{15}N Nuclear Magnetic Resonance Spectroscopy

Jacques Riand and Marie-Therèse Chenon
LASIR, CNRS, 94320 Thiais, France
Cherng-Chyi Tzeng and Raymond P. Panzica*
Departments of Medicinal Chemistry and Chemistry, University of Rhode Island, Kingston, Rhode Island, 02881, U.S.A.

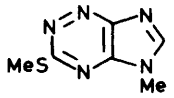
3-Methylthioimidazo[4,5-*e*]-*as*-triazine (**1**) was synthesized *via* ring closure of 5,6-diamino-3-methylthio-*as*-triazine. By using carbon-13 and nitrogen-15 chemical shifts and three-bond ^{13}C–^{1}H spin–spin coupling constants, the prototropic tautomerism in the imidazole moiety of this 6-azapurine was investigated. The data from these spectral techniques indicated that the 5*H*-tautomeric form predominates (69%). A critical evaluation of the three methods is provided.

We have been interested in the synthesis and chemical behaviour of novel, bicyclic, nitrogen heterocycles derived from *ortho*-diamino-*as*-triazines. Of particular concern to us are the 6-azapurine[2–8]† (imidazo[4,5-*e*]-*as*-triazine) and 4-azapteridine[9] (pyrazino[2,3-e]-*as*-triazine) ring systems. Recently, we described[9,10] an efficient, practical preparation of certain 5,6-diamino-*as*-triazines which can function as synthons for these fused heterocycles. By using one of them, we have now prepared 3-methylthioimidazo[4,5-e]-*as*-triazine (**1**). This heterocycle is the first 6-azapurine to be described in which all the nitrogen atoms are free of substituents.

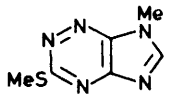
Being aware of the role which tautomerism plays in many biochemical functions of purines and other nucleic acid components, we decided to examine the prototropic tautomerism in the imidazole moiety of (**1**). For this investigation the 5- and 7-*N*-methylated analogues (**2**) and (**3**) were required and synthesized. Carbon-13 and nitrogen-15 n.m.r. techniques were employed to determine the predominant tautomeric form of 3-methylthioimidazo[4,5-e]-*as*-triazine (**1**) in solution, and the three techniques used were critically evaluated.



(**1**)



(**2**)



(**3**)

Results and Discussion

Synthesis.—Soon after we initiated our synthetic study of the 6-azapurine ring system, three preliminary accounts[2–4] appeared describing this heterocycle. Four other papers[5–8] recounting the preparation of this system appeared later. Three of these[6–8] presented detailed synthetic procedures. With one exception,[4] the 6-azapurines synthesized in these studies were obtained *via* ring contraction of pyrimido[4,5-e]-*as*-triazines[2,3,5–7] or their precursors.[8] Our approach, which involves cyclization of 5,6-diamino-*as*-triazines with selected one-carbon delivering reagents, is similar to the method described by Kaji and Kawase[4] and provides a greater versatility in constructing analogues of this system. Treatment of 5,6-diamino-3-methylthio-*as*-triazine[10] with triethyl orthoformate in the presence of a catalytic amount of concentrated hydrochloric acid furnished (**1**) in moderate yield. When 5,6-diamino-3-methylthio-*as*-triazine was replaced by either 6-amino-5-methylamino-3-methylthio-*as*-triazine[10] or 5-amino-6-methylamino-3-methylthio-*as*-triazine[9] the 5-methyl (**2**) or the 7-methyl (**3**) analogue was obtained, respectively, in comparable yield.

N.m.r. Spectral Studies.—Carbon-13 and nitrogen-15 n.m.r. spectroscopy have proved very useful for studying the tautomeric behaviour of aromatic nitrogen heterocycles. Carbon-13 chemical shifts,[11,12] three-bond ^{13}C–^{1}H spin–spin coupling constants,[13] and nitrogen-15 chemical shifts[14–18] have been employed to determine quantitatively populations of the predominant tautomeric forms of such heterocycles in solution. In an effort to ascertain the most stable tautomeric form of (**1**) and to evaluate the utility of the aforementioned techniques all three methods were employed in our study.

(A) *Assignment of carbon-13 chemical shifts.* The carbon-13 chemical shifts for (**1**)—(**3**) in dimethyl sulphoxide are summarized in Table 1. At ambient temperature, the rate of tautomeric exchange is high in comparison with the n.m.r. timescale; thus each carbon chemical shift of (**1**) is a weighted average of shifts of the contributing forms. In order to estimate the carbon chemical shifts of the 5*H*- and 7*H*-tautomeric forms, the methylated analogues (**2**) and (**3**) were prepared and their carbon chemical shifts determined.

Chemical shifts for C-3 and C-6 in (**2**) and (**3**) were easily assigned by examination of their coupling constants with the methylthio group and H-6, respectively (Table 2). Similarly, long-range coupling with the *N*-methyl group provided a means to distinguish between C-4a and C-7a. The signal of the former appeared as a doublet of quartets in (**2**) and as a doublet in (**3**). The reverse was observed for C-7a. The chemical shift differences between (**2**) and (**3**) agree with those determined for the 7- and 9-methyl analogues of purine and adenine in the same solvent (see Table 3).

† The nomenclature and numbering used throughout this paper is that for the imidazo[4,5-*e*]-*as*-triazine ring system. The numbering of this ring system is depicted on structure (**1**).

Table 1. Carbon-13 chemical shifts for the 3-methylthioimidazo[4,5-*e*]-*as*-triazines[a]

Compound	C-3	C-4a	C-6	C-7a	N(5)Me	N(7)Me	SMe
(1)	166.5_3	145.9_8	151.0_6	151.0_6			13.6_6
(2)	166.2_1	143.1_2	152.0_7	153.6_4	29.5_5		13.6_9
(3)	167.3_0	151.7_0	155.2_9	145.1_4		30.5_2	13.5_0

[a] In p.p.m. with respect to Me_4Si. Solvent [$^2H_6$]dimethyl sulphoxide.

Table 2. $J(^{13}C, ^1H)$ coupling constants (Hz) for the 3-methylthioimidazo[4,5-*e*]-*as*-triazines

Compound	^1J(SMe)	^1J(NMe)	^3J(NMe, H-6)	^3J(C-3, SMe)	^3J(C-4a, H-6)	^3J[C-4a, N(5)Me]
(1)	141.6			4.4	7.7	
(2)	141.9	142.7	0.5	4.4	5.3	2.7
(3)	141.7	142.5	1.2	4.6	12.4	

	^1J(C-6, H-6)	^3J[C-6, N(5)Me]	^3J[C-6, N(7)Me]	^3J(C-7a, H-6)	^3J[C-7a, N(7)Me]
(1)	214.3			10.7	
(2)	216.2	3.4		13.0	
(3)	214.2		3.4	5.2	2.6

Table 3. Comparison of the carbon-13 chemical shift differences (Δδ) between the 5-methyl- and 7-methyl-3-methylthioimidazo[4,5-*e*]-*as*-triazines with those calculated for the 7- and 9-methyl derivatives of purine and adenine[a]

	Position				
Compound	C-3	C-4a	C-6	C-7a	NMe
(2) − (3)	−1.09	−8.58	−3.23	8.50	−0.97
	Position[b]				
	C-2	C-4	C-8	C-5	NMe
Purine[c] N(9)Me − N(7)Me	−0.18	−8.50	−2.34	7.67	−2.29
Adenine[c] N(9)Me − N(7)Me	0.19	−9.88	−4.47	6.95	−4.37

[a] In p.p.m.; solvent [$^2H_6$]dimethyl sulphoxide. [b] Since the numbering of purine differs from that of imidazo[4,5-*e*]-*as*-triazine, the data for the carbon atoms of each heterocycle have been placed in columns according to their analogous spatial positions. [c] Ref. 11.

Table 4. Nitrogen-15 chemical shifts for the 3-methylthioimidazo[4,5-*e*]-*as*-triazines[a,b]

Compound	N-1	N-2	N-4	N-5	N-7
(1)	4.8	−40.2	−131.1	n.a.	n.a.
(2)	11.7	−41.1	−139.5	−234.4	−141.0
(3)	−12.5	−41.3	−117.6	−144.2	−235.3

[a] In p.p.m. with respect to nitromethane; solvent [$^2H_6$]dimethyl sulphoxide. [b] na = not available (see text).

Table 5. Comparison of the nitrogen-15 chemical shift differences (Δδ) between the 5-methyl- and 7-methyl-3-methylthioimidazo[4,5-*e*]-*as*-triazines with those calculated for the 7- and 9-alkyl derivatives of purine and adenine[a]

	Position				
Compound	N-1	N-2	N-4	N-5	N-7
(2)—(3)	24.2	0.2	−21.9	−90.2	94.3
	Position[b]				
	N-1	N-3	N-9	N-7	
Purine[c] N(9)Me − N(7)Me	−1.1	−20.6	−93.8	96.8	
Adenine[d] N(9)Et − N(7)Et	−2.2	−17.9	−78.6	80.2	

[a] In p.p.m.; solvent [$^2H_6$]dimethyl sulphoxide. [b] Since the numbering of the purine ring differs from that of the imidazo[4,5-*e*]-*as*-triazine system, the data for the nitrogen atoms of each heterocycle have been placed in columns according to their analogous spatial positions. [c] Ref. 18. [d] Ref. 15.

The assignment of the C-3 and C-6 chemical shifts of (**1**) was straightforward. On the other hand, the C-4a and C-7a resonances could not be assigned from only an analysis of their spin–spin coupling constants; the values obtained could fit either. However, only the assignments presented in Tables 1 and 2 lead to coherent results for the tautomeric populations when calculated from either the carbon chemical shifts or coupling constant data.

(B) *Assignment of nitrogen-15 chemical shifts.* The nitrogen-15 chemical shifts for (**1**)—(**3**) are given in Table 4. The *N*-methyl group in (**2**) and (**3**) is expected to have a small effect on the chemical shift of N-2. Therefore, the resonances at −41.1 in (**2**) and −41.3 p.p.m. in (**3**) have been assigned to N-2. The chemical shifts of N-5 and N-7 in (**2**) and (**3**) were assigned by examining their coupling constants. In (**2**), the N-5 line (Figure 1) appeared at −234.4 p.p.m. as a doublet [^2J(N-5,H-6) 8 Hz], broadened by coupling with the methyl protons. On the other hand, N-7 resonated at −141.0 p.p.m. as a sharp doublet [^2J(N-7,H-6) 12 Hz]. These coupling constants are similar to those observed for analogous purines.[18] As expected, the reverse was found for the N-5 and N-7 chemical shifts of (**3**). The N-5 signal appeared at −144.2 p.p.m. as a sharp doublet [^2J(N-5,H-6) 12 Hz] and the N-7 signal as an unresolved multiplet at −235.3 p.p.m. (Figure 2). The N-4 chemical shift was assigned by comparing the effect of the *N*-methyl substituents in (**2**) and (**3**) with the effect for the corresponding N-3 of the 7- and 9-*N*-alkylated purine and adenine derivatives.[15,18] These effects were similar and are listed in Table 5 with those observed for the aforementioned purines. Lastly, the N-1 resonance was assigned by default.

The nitrogen chemical shifts for (**1**) were assigned by analogy with data obtained for (**2**) and (**3**). The resonances at 4.8, −40.2,

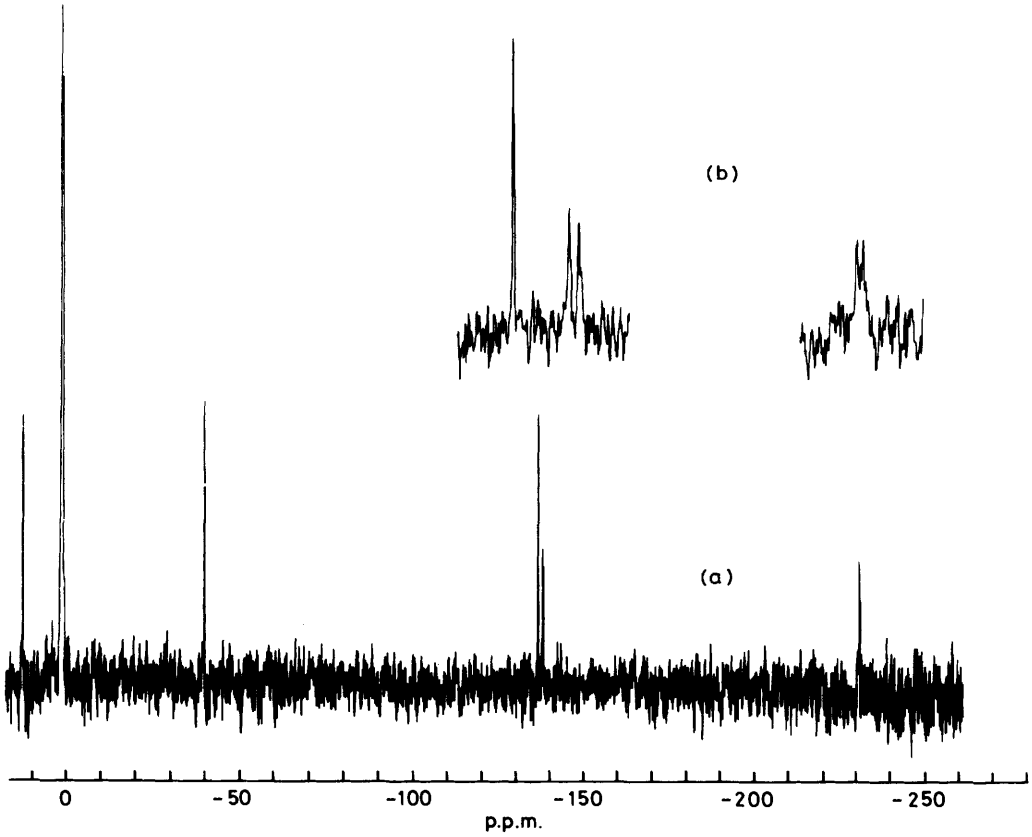


Figure 1. ^{15}N N.m.r. spectra of 5-methyl-3-methylthioimidazo[4,5-*e*]-*as*-triazine in dimethyl sulphoxide with (a) and without (b) gated proton broad-band decoupling

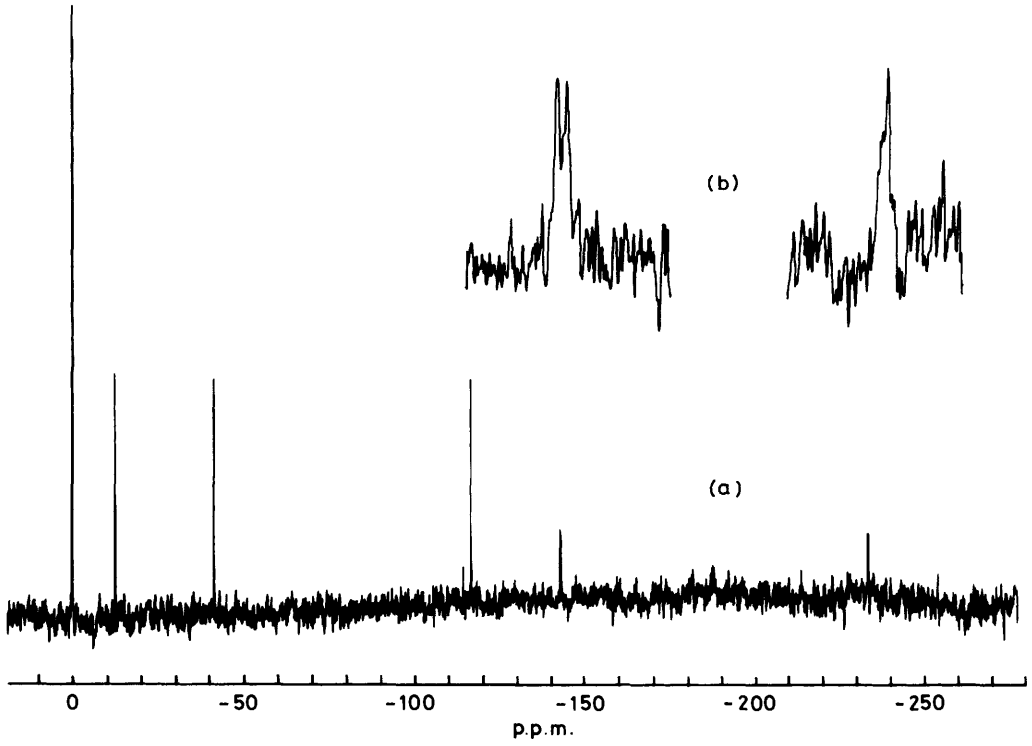


Figure 2. ^{15}N N.m.r. spectra of 7-methyl-3-methylthioimidazo[4,5-*e*]-*as*-triazine in dimethyl sulphoxide with (a) and without (b) gated proton broad-band decoupling

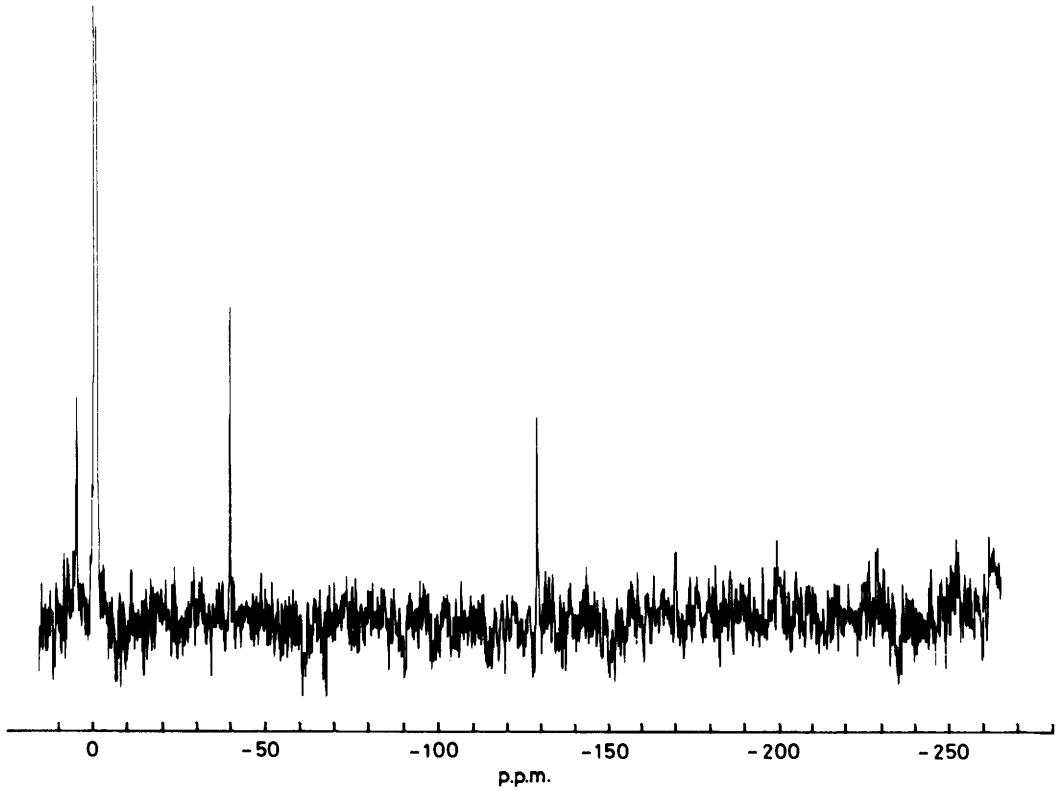


Figure 3. ^{15}N N.m.r. gated proton-decoupled spectrum of 3-methylthioimidazo[4,5-*e*]-*as*-triazine in dimethyl sulphoxide

and −131.1 p.p.m. correspond to N-1, N-2, and N-4, respectively. Unlike the chemical shift of N-2, the chemical shifts of N-1 and N-4 are influenced by the tautomeric equilibrium. The shielding pattern for these nitrogen atoms agrees with that recently reported for 3-methylthio-*as*-triazine.[19] The signals for N-5 and N-7 were not observed (Figure 3) because the labile hydrogen was exchanging between these positions at an intermediate rate under the experimental conditions employed. The difference between the chemical shifts for these nitrogen atoms in the two tautomeric forms is *ca.* 4 500 Hz (Table 4). Two methods could be used to observe the N-5 and N-7 signals: either accelerating the exchange or reducing it. In the first case, the exchange rate can be increased by raising the temperature. Unfortunately, (**1**) was found to be unstable in Me_2SO solutions at temperatures higher than 70 °C. We therefore tried to reduce the exchange rate. Such a reduction had been successful in another study[12] when hexamethylphosphoric triamide (HMPA) was employed as solvent. In our case, this method proved unsatisfactory. When (**1**) was dissolved in HMPA and the spectrum run at ambient temperature, the N-1 and N-4 lines broadened to the extent that they disappeared into the base line, indicating that the exchange process slowed down, but not sufficiently to narrow the N-5 and N-7 resonances so that they could be detected. Lastly, the limited solubility of these heterocycles in solvents other than Me_2SO (m.p. 18.4 °C) and HMPA (m.p. 7 °C), both of which are unsuitable for low-temperature work, prevented their thorough examination at lower temperatures.

(C) *Determination of the tautomeric population of* (**1**). The percentages of the 5*H*- and 7*H*-tautomeric forms of (**1**) were calculated from the chemical shifts of C-4a and C-7a, their spin–spin coupling constants with H-6, and the chemical shifts of N-1 and N-4. In the first and third methods, the tautomeric populations are determined by the differences in chemical shifts[11,12,14–18] of the aforementioned atoms between the two tautomeric forms, whereas the second method relies on the decrease of the vicinal three-bond [^3J(C, H)] coupling constants through a pyridine- *vs.* a pyrrole-type nitrogen atom.[13,20–22]

As already stated, the calculation of tautomeric populations, *e.g.* the percentages of the 5*H*- and 7*H*-tautomers of (**1**), requires the use of *N*-substituted derivatives. Therefore any change in the chemical shift resulting from the *N*-substituent must be taken into account and a correction made. In our work, for a given n.m.r. parameter, this effect, or correction, was considered identical for C-4a and C-7a (or N-1 and N-4) since these atoms are in similar spatial positions with respect to the positions undergoing prototropic exchange. The magnitude of this correction factor was expected to be small and therefore the β-effect on carbon (and the γ-effect on nitrogen) was considered negligible.

Equations (1) and (2) permit the calculation of the two

$$P_{obs.} = \chi[P_{N(5)Me} - \Delta P_{NH}^{NMe}] + (1 - \chi)P_{N(7)Me} \quad (1)$$

$$P'_{obs.} = P'_{N(5)Me} + (1 - \chi)[P'_{N(7)Me} - \Delta P_{NH}^{NMe}] \quad (2)$$

unknowns, namely the population χ of the 5*H*-tautomer of (**1**) and the corrective term* ΔP_{NH}^{NMe} which is defined as $\Delta P_{NH}^{NMe} = P_{NMe} - P_{NH}$; P and P' are the experimental n.m.r. parameters of (**1**) and correspond, respectively, to C-4a (or N-4) and to C-7a (or N-1); $P_{N(5)Me}$, $P'_{N(5)Me}$, $P_{N(7)Me}$, and $P'_{N(7)Me}$ are the corresponding parameters of the *N*-methylated analogues (**2**) and (**3**).

The results are presented in Table 6. The three sets of data

* The corrective term ΔP_{NH}^{NMe} represents either the α-effect on carbon or the β-effect on nitrogen.

Table 6. Calculations of the percentage of the 5*H*-tautomeric form 3-methylthioimidazo[4,5-*e*]-*as*-triazine (**1**) from chemical shift and coupling constant data

N.m.r. parameter	$\Delta P^{N(5)Me}_{N(7)Me}$ [a]	ΔP^{NMe}_{NH} [b]	% 5*H*
δ(C-4a) and δ(C-7a)	−8.58 p.p.m. and 8.50 p.p.m.	−0.26 p.p.m.	69
^3J(C-4a, H-6) and ^3J(C-7a, H-6)	−7.1 Hz and 7.9 Hz	−0.3 Hz	69
δ(N-1) and δ(N-4)	24.2 p.p.m. and −21.9 p.p.m.	−2.2 p.p.m.	69

[a] Difference between the values of the n.m.r. parameters defined in column one for (**2**) − (**3**). [b] Substituent effect of a methyl group for a hydrogen on the n.m.r. parameters defined in column one.

give identical population percentages and this indirectly corroborates our initial assignments of C-4a and C-7a. The population of the 5*H*-tautomeric form (69%) is similar to those calculated for the analogous 9*H*-tautomeric forms of certain purines which possess a substituent at C-6 that does not strongly perturb the bond order of the pyrimidine moiety, *i.e.* H, 60%; OCH_3, 68%; SCH_3, 82%; NH_2, 85%.[11] On the other hand, when the C-6 substituent can participate in either a lactim–lactam or a thiol–thione process, in which the latter species predominates, the proportion of the 9*H*-tautomeric species decreases to 42 and 21%, respectively.[11]

Although the three methods gave identical results, it is important to keep in mind the large differences in their precision. The experimental errors in the carbon-13 and nitrogen-15 chemical shifts were approximately 0.05 and 0.1 p.p.m. respectively. That for the three-bond coupling constants ^3J(C,H) was of the order of 0.3 Hz. The ratios of these limits to the corresponding $\Delta P^{N(5)Me}_{N(7)Me}$ values (Table 6) are 0.6% for the carbon chemical shifts, 0.4% for the nitrogen chemical shifts, and 4% for ^3J(C,H). This clearly indicates that for a precise, quantitative determination of the tautomeric populations, ^3J(C,H) must be within the error limits of 0.05 Hz in order to be reliable, which places a severe limitation on the use of this parameter.

Another critical point is the importance of the nitrogen substituent effects (ΔP^{NMe}_{NH}) with respect to the magnitude of the variation of P [$\Delta P^{N(5)Me}_{N(7)Me}$] of the methylated analogues. For the carbon chemical shifts, this substituent effect is −0.26 p.p.m., in agreement with the value (−0.2 p.p.m.) determined for C-4 and C-5 of purine.[11] Even though this correction is minor, since it only corresponds to approximately 3% of the $\Delta P^{N(5)Me}_{N(7)Me}$ value, it was taken into consideration for better precision. The substituent effect on ^3J(C,H) was determined to be −0.3 Hz. This value is similar to that reported for purine.[13] For the nitrogen-15 chemical shifts, the correction is −2.2 p.p.m., and must be considered since it represents approximately 10% of $\Delta P^{N(5)Me}_{N(7)Me}$. We cannot compare this two-bond (β) correction factor on a nitrogen atom in an adjacent ring with any other examples in the literature because, to our knowledge, none has been reported. This effect, which leads to an upfield shift, appears to be reminiscent of the *peri*-effect[23] observed for carbon.

Conclusion

Three n.m.r. procedures were employed in the evaluation of the tautomeric populations of 3-methylthioimidazo[4,5-e]-*as*-triazine (**1**). All three led to the same result, *i.e.* the predominance of the 5*H*-tautomer (69%). Of the three spectroscopic techniques used, the ^{13}C–^1H coupling constant method appears the least reliable, since a very high degree of precision is required to calculate the percentage of the tautomeric forms in question. The carbon chemical shift approach seems the more reliable ^{13}C n.m.r. method and consumes less spectrometer time. Unfortunately, this method also has its limitations, because it requires a carbon atom α to the site undergoing exchange. Thus for (**1**), both bridgehead carbon atoms (C-4a and C-7a) were necessary. At first glance, the nitrogen-15 chemical shift method appears the method of choice, but it too has drawbacks. Either a concentrated solution is required or a high-field spectrometer is needed to obtain a spectrum with adequate signal-to-noise within a reasonable time frame. Even when these conditions are met, problems can arise from broadening of the nitrogen signals due to an unfavourable exchange rate of the labile hydrogen. Furthermore, if ^{15}N-labelled compounds are required to assign some of the nitrogen chemical shifts, the time and expense of their preparation greatly diminish the utility of this method. Therefore the carbon-13 chemical shift method still appears the most convenient and least time consuming, and is the one which gives consistent quantitative results. As instrumental techniques improve, however, nitrogen-15 n.m.r. should become the method of choice for studying tautomeric equilibria of nitrogen heterocycles in solution.

Experimental

M.p.s were determined with a Thomas-Hoover apparatus. U.v. absorption spectra were recorded with a Beckman DB-GT grating spectrophotometer. Elemental analyses were performed by M-H-W Laboratories, Phoenix, Arizona, U.S.A.

N.m.r. Spectra.—The natural-abundance spectra were obtained for solutions in [$^2H_6$]dimethyl sulphoxide and [$^2H_{18}$]hexamethylphosphotriamide in the concentration range 0.6—1 mol dm^{-3}.

^1H Spectra were obtained with a Varian EM-390 spectrometer (U.R.I.), using [$^2H_6$]dimethyl sulphoxide as solvent and Me_4Si as standard.

^{13}C Spectra were recorded with Varian CFT-20, Bruker WH-90 (CNRS, Thiais) and Bruker WM-500 (Centre de Spectrochimie, Universite Paris 6) spectrometers. The normal operating conditions involved a 30° pulse flip angle and a pulse repetition time of *ca.* 3 s. In a typical experiment 8 500 (decoupled spectra) to 60 000 (coupled spectra) transients were accumulated. The digital resolution was better than 0.6 Hz; however, the observed coupling constant values are precise to ±0.2 Hz when determined from well resolved multiplets. The temperature of the probe was *ca.* 30 °C.

^{15}N Spectra were obtained at 50.68 MHz with a Bruker WM-500 spectrometer, under gated proton decoupling conditions to suppress the nuclear Overhauser effect. A capillary tube containing a 0.01M-solution of [^{15}N]nitromethane in [$^2H_3$]nitromethane provided the reference standard; deuteriated solvents were used as internal field-frequency lock. The samples were run at *ca.* 30 °C {also at 70 °C for compound (**1**) in [$^2H_6$]dimethyl sulphoxide}. Typical acquisition parameters were: spectral width, 15 200 Hz; pulse flip angle, 40°; acquisition time, 2.1 s; pulse delay, up to 10 s. Adequate signal-to-noise ratio required 2 000—7 000 scans. The reported nitrogen-15 chemical shifts (±0.1 p.p.m.) are positive when downfield from the resonance line of external [^{15}N]nitromethane. No bulk susceptibility correction (0.92 p.p.m. for [$^2H_6$]dimethyl sulphoxide with respect to nitromethane) was applied.

3-*Methylthioimidazo*[4,5-e]-as-*triazine* (**1**).—To a well stirred suspension of 5,6-diamino-3-methylthio-*as*-triazine[10] (785 mg, 5 mmol) in triethyl orthoformate (40 ml) was added concentrated hydrochloric acid (2.0 ml). The mixture was then heated at reflux (oil-bath) for 3 h during which time dissolution was achieved. After this period, the solution was allowed to cool and kept at 4 °C for 16 h. The crystalline precipitate was collected by filtration, washed with cold absolute ethanol, and air-dried to give the azapurine (**1**) (542 mg). Concentration of the filtrate under diminished pressure (to *ca.* 10 ml) provided a second crop (140 mg). Recrystallization of the combined crops from absolute ethanol furnished 635 mg (76%); m.p. 208—210 °C; δ_H 2.65 (3 H, s, SCH_3) and 8.65 (1 H, s, H-6); $\lambda_{max.}$ (pH 1) 250 nm (ε 19 340); $\lambda_{max.}$ (MeOH) 343 (ε 4 080) and 244 nm (20 460); $\lambda_{max.}$ (pH 11) 340 (ε 2 940), 303 (4 680), and 245 nm (18 220)(Found: C, 35.9; H, 3.0; N, 42.05; S, 19.2. Calc. for $C_5H_5N_5S$: C, 35.9; H, 3.0; N, 41.9; S, 19.2%).

5-*Methyl*-3-*methylthioimidazo*[4,5-e]-as-*triazine* (**2**).—The procedure for the preparation of (**2**) was similar to that for (**1**) except that the starting heterocycle was 6-amino-5-methylamino-3-methylthio-*as*-triazine[10] (513 mg, 3 mmol). This was suspended in triethyl orthoformate (18 ml) containing concentrated hydrochloric acid (1.0 mol). Recrystallization from absolute ethanol afforded 402 mg (74%) of the *product* (**2**), m.p. 149—151 °C; δ_H 2.7 (3 H, s, SCH_3), 3.8 (3 H, s, NCH_3), and 8.8 (1 H, s, H-6); $\lambda_{max.}$ (pH 1) 257.5 nm (ε 27 900); $\lambda_{max.}$ (MeOH) 344 (ε 5 620) and 247 nm (23 400); $\lambda_{max.}$ (pH 11) 323 (ε 7 790), 272sh (12 320), 252sh (15 580), and 236 nm (16 880) (Found: C, 39.7; H, 4.1; N, 38.8; S, 17.7. $C_6H_7N_5S$ requires C, 39.8; H, 3.9; N, 38.65; S, 17.7%).

7-*Methyl*-3-*methylthioimidazo*[4,5-e]-as-*triazine* (**3**).—The synthetic procedure for (**3**) was similar to that described for (**1**) with the exception that 5-amino-6-methyamino-3-methylthio-*as*-triazine[9] (513 mg, 3 mmol) was used as starting material. Recrystallization of the crude crystalline product (435 mg) from absolute ethanol provided 410 mg (76%) of pure material (**3**), m.p. 185—187 °C; δ_H 2.6 (3 H, s, SCH_3), 3.92 (3 H, s, NCH_3), and 8.92 (1 H, s, H-6); $\lambda_{max.}$ (pH 1) 256 nm (ε 26 440); $\lambda_{max.}$ (MeOH) 356 (ε 3 760), 284 (4 160), and 246 nm (24 240); $\lambda_{max.}$ (pH 11) 353 (ε 5 160), 287sh (13 760), and 266 nm (20 620) (Found: C, 39.5; H, 3.75; N, 38.9; S, 17.8. $C_6H_7N_5S$ requires C, 39.8; H, 3.9; N, 38.65; S, 17.7%).

Acknowledgements

We thank Mr. D. Davoust for recording the ^{15}N n.m.r. spectra and Professor Elie Abushanab for discussions. C.-C. T. acknowledges a University of Rhode Island Graduate Fellowship, 1983—1984.

References

1 Presented in part at the Joint Great Lakes and Central Regional Meeting of the American Chemical Society, Kalamazoo, Michigan, May 1984, Abstract ORG 331.
2 F. Yoneda, T. Nagamura, and M. Kawamura, *J. Chem. Soc., Chem. Commun.*, 1976, 658.
3 F. Yoneda, M. Kawamura, T. Nagamatsu, K. Kuretani, A. Hoshi, and M. Iigo, *Heterocycles*, 1976, **4**, 1503.
4 K. Kaji and M. Kawase, *Chem. Pharm. Bull.*, 1976, **24**, 2274.
5 M. Ichiba, S. Nishigaki, and K. Senga, *J. Org. Chem.*, 1978, **43**, 469.
6 F. Yoneda, M. Noguchi, M. Noda, and Y. Nitta, *Chem. Pharm. Bull.*, 1978, **26**, 3154.
7 T. Kametani, M. Higuchi, M. Noguchi, Y. Hashiguchi, and F. Yoneda, *Heterocycles*, 1980, **14**, 1295.
8 F. Yoneda, M. Higuchi, and Y. Nitta, *J. Heterocyl. Chem.*, 1980, **17**, 869.
9 C.-C. Tzeng and R. P. Panzica, *J. Heterocycl. Chem.*, 1983, **20**, 1123.
10 C.-C. Tzeng, N. C. Motola, and R. P. Panzica, *J. Org. Chem.*, 1983, **48**, 1271.
11 M.-Th. Chenon, R. J. Pugmire, D. M. Grant, R. P. Panzica, and L. B. Townsend, *J. Am. Chem. Soc.*, 1975, **97**, 4627, 4636.
12 M.-Th. Chenon, C. Coupry, D. M. Grant, and R. J. Pugmire, *J. Org. Chem.*, 1977, **42**, 659.
13 M. Schumacher and H. Günther, *J. Am. Chem.* Soc., 1982, **104**, 4167.
14 N. C. Gonnella and J. D. Roberts, *J. Am. Chem. Soc.*, 1982, **104**, 3162.
15 N. C. Gonnella, H. Nakanishi, J. B. Holtwick, D. S. Horowitz, K. Kanamori, N. J. Leonard, and J. D. Roberts, *J. Am. Chem. Soc.*, 1983, **105**, 2050.
16 D. S. Wofford, D. M. Forkey, and J. G. Russell, *J. Org. Chem.*, 1982, **47**, 5132.
17 G. Tóth, A. Szöllösy, C. Szántay, I. Hermecz, A. Horváth, and Z. Mészáros, *J. Chem. Soc., Perkin Trans. 2*, 1983, 1153.
18 M. Schumacher and H. Günther, *Chem. Ber.*, 1983, **116**, 2001.
19 M. V. Jovanovic, *Spectrochim. Acta, Part A*, 1984, **40**, 637.
20 J. Riand, *J. Chem. Soc., Chem. Commun.*, 1983, 105.
21 J. Riand, C. Coupry, and M.-Th. Chenon, *J. Chem. Soc., Perkin Trans. 2*, 1981, 783.
22 M. C. Vitorge, M.-Th. Chenon, C. Coupry, and N. Lumbroso-Bader, *Org. Magn. Reson.*, 1983, **21**, 20.
23 N. Platzer, J. J. Basselier, and P. Demerseman, *Bull. Soc. Chim. Fr.*, 1974, 905.

Received, 1*st April* 1985; *Paper* 5/546