XVIII: mp 119–120° (lit.[6a] mp 121°); $\lambda_{max}^{CHCl_3}$ 2.90 (m), 3.1–3.4 (w), 5.80 (vs), 6.02 (s), 7.3 (s), 7.7 (w), 7.9 (m), 8.9 (s), 9.3 (w), and 10.3 (m) μ. The ultraviolet and nmr spectra were identical with those recorded by Moye and Sternhell.[10] A deep red solution was produced with aqueous ferric chloride. The correct elemental analysis (for a dichlorocyclopentanedione) was reported by Hantzsch.[6a]

Acknowledgment.—We are indebted to Dr. James N. Shoolery for obtaining and interpreting the earlier nmr spectra. We also thank Drs. C. J. Moye and S. Sternhell for helpful comments on the manuscript and Professor Herbert O. House for suggestions concerning mechanistic aspects of this work.

1,2,4-Triazoles. XV. Proton Magnetic Resonance Spectra of *s*-Triazolo[4,3-*a*]pyridine and *s*-Triazolo[1,5-*a*]pyridine Derivatives[1]

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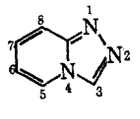
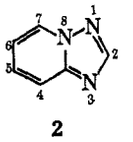
Proton magnetic resonance (pmr) spectral data at 60-Mc for 42 derivatives of the title ring systems are reported. Complete analyses of the spectra have been made and the mode and values of the various coupling constants have been determined. Long-range coupling involving protons separated by five and six bonds was observed. Data obtained for related 1-amino-2-imino-1,2-dihydropyridines are contrasted to those obtained for the bicyclic nuclei.

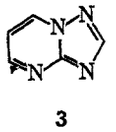
Interest in the chemistry of *s*-triazole and its various ring-fused derivatives has included a study[2,3] of the *s*-triazolo[4,3-*a*]pyridine nucleus (**1**) and the isomeric *s*-triazolo[1,5-*a*]pyridine nucleus (**2**), and in this communication we describe the proton magnetic resonance data for members of these systems. There has been considerable interest in relating proton magnetic resonance data to the various electronic properties associated with heteroaromatic molecules,[4] a logical extension of the extensive studies of the relationship between chemical shifts and π-electron densities in various benzenoid systems.[5] Pmr data for several bridgehead nitrogen systems of the indolizine type have been described in the recent literature[4] and the data for the two *s*-triazolopyridines are of considerable interest in relation to these studies. Closely related to the present system was an investigation[4b] of the *s*-triazolo[1,5-*a*]pyrimidine ring system (**3**).



1



2



3

Interpretation and Analysis of Spectra.—The spectrum of *s*-triazolo[4,3-*a*]pyridine is shown in Figure 1 and the spectral parameters of the members of this ring system studied are listed in Table I. Those of the *s*-triazolo[1,5-*a*]pyridine system are shown in Table II. A first-order analysis of the spectra based on a five-spin model gave a satisfactory explanation for the splitting patterns obtained in all cases and verification of the multiplet assignments was possible by C-methyl substitution around the periphery of the nucleus. The similarity between the spectra of the two isomeric systems[6] is clearly shown by the data in the tables. All *s*-triazolo[4,3-*a*]pyridines unsubstituted in the 3 position exhibited a low-field, concentration-dependent peak at τ 1.34–1.14, clearly attributable to the 3 proton as this peak was removed by substitution in the 3 position. In the *s*-triazolo[1,5-*a*]pyridines, the corresponding proton in the 2 position occurred at higher field (τ 1.65). The other assignments are in good agreement with those reported[4,7,8,15,16] for similar heterocyclic systems. Inter-ring coupling between the 3 and 8 proton was found to be present, as evidenced by the following considerations. Very slow passage through the 3-proton singlet revealed a reproducible, doublet splitting of the order of 1 cps. The τ 1.79 doublet of the 5 proton, which always absorbed at lower field relative to the other pyridine ring protons, had superimposed

(1) (a) Support of this work by Public Health Service Research Grant CA 05973-03,04 National Cancer Institute, is gratefully acknowledged; (b) present address, Department of Chemistry, Rensselaer Polytechnic Institute, Troy, N. Y. 12181; (c) taken in part from the Ph.D. thesis of S. W. Thomas, University of Louisville, 1964.

(2) K. T. Potts and H. R. Burton, *J. Org. Chem.*, **31**, 251 (1966); K. T. Potts, H. R. Burton, and J. Bhattacharyya, *ibid.*, **31**, 260 (1966).

(3) K. T. Potts, H. R. Burton, and S. K. Roy, *ibid.*, **31**, 265 (1966).

(4) (a) P. J. Black, M. L. Heffernan, L. M. Jackman, Q. N. Porter, and G. R. Underwood, *Australian J. Chem.*, **17**, 1128 (1964), and references therein; (b) Y. Makisumi, H. Watanable, and K. Tori, *Chem. Pharm. Bull.* (Tokyo), **12**, 204 (1964); (c) G. S. Reddy and J. H. Goldstein, *J. Am. Chem. Soc.*, **83**, 2045, 5020 (1961); G. S. Reddy, R. T. Mobgood, and J. H. Goldstein, *ibid.*, **84**, 336 (1962); (d) H. A. P. de Jongh and H. Wynberg, *Tetrahedron*, **21**, 515 (1965); (e) W. W. Paudler and H. L. Blweitt, *ibid.*, **21**, 353 (1965); *J. Org. Chem.*, **30**, 4081 (1965); W. W. Paudler and J. E. Kuder, *ibid.*, **31**, 809 (1966); W. W. Paudler and H. L. Blewitt, *ibid.*, **31**, 1295 (1966); W. W. Paudler and D. E. Dunham, *J. Heterocyclic Chem.*, **2**, 410 (1965); W. W. Paudler and J. E. Kuder, *ibid.*, **3**, 33 (1966); (f) J. P. Paolini and R. K. Robins, *ibid.*, **2**, 53 (1965); J. G. Lombardino, *J. Org. Chem.*, **30**, 2403 (1965); J. P. Paolini and R. K. Robins, *ibid.*, **30**, 4085 (1965).

(5) T. K. Wu and B. P. Dailey, *J. Chem. Phys.*, **41**, 2796 (1964); B. P. Dailey, *ibid.*, **41**, 2304 (1964); J. A. Pople, *ibid.*, **41**, 2559 (1964).

(6) The numbering systems used are shown in **1** and **2**, respectively.

(7) P. J. Black and M. L. Heffernan, *Australian J. Chem.*, **16**, 1051 (1963).

(8) Couplings of this type in benzenoid systems[9] are of the order of 6–10 cps, whereas smaller values have been found for analogous couplings in heteroaromatic systems such as furan,[10] thiophene,[10,11] pyrrole,[12] indole,[13,14] and benzofuran.[14]

(9) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, pp 193, 148.

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(12) R. J. Abraham and H. J. Bernstein, *Can. J. Chem.*, **37**, 1056 (1959).

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(15) This deshielding has been reported in numerous heterocyclic systems, *e.g.*, E. B. Baker, *J. Chem. Phys.*, **23**, 1981 (1955); W. Brugel, *Z. Electrochem.*, **66**, 159 (1962).

(16) P. J. Black and M. L. Heffernan, *Australian J. Chem.*, **17**, 558 (1964).

TABLE I

CHEMICAL SHIFTS (PPM) AND COUPLING CONSTANTS (CPS) FOR VARIOUS s-TRIAZOLO[4,3-a]PYRIDINE DERIVATIVES (1)

	τ_3	τ_5	τ_6	τ_7	τ_8	$J_{5,6}$	$J_{6,7}$	$J_{5,8}$	$J_{6,7}$	$J_{6,8}$	$J_{7,8}$
Unsubstituted	1.14	1.79	3.12	2.72	2.21	6.7	1.2	1.2	6.7	1.2	9.0
3-CH_3[a]	*7.26*	2.12	3.15	2.78	2.27	6.8	1.2	1.2	6.8	1.3	8.9
5-CH_3	1.27	*7.31*	3.33	2.76	2.30	...	...	...	6.9	Nr	9.2
6-CH_3	1.28	2.03	*7.65*	2.89	2.32	...	1.5	Nr	...	...	9.4
7-CH_3	1.26	1.94	3.29	*7.54*	2.52	7.2	...	Nr	...	1.4	...
8-CH_3	1.20	1.95	3.23	2.96	*7.33*	6.6	Nr	...	6.6	...	...
3-C_2H_5	*6.88*	2.08	3.15	2.76	2.28	6.5	1.2	1.2	6.5	1.3	9.3
	8.50										
3-*n*-C_3H_7		2.08	3.19	2.81	2.30	6.7	1.2	1.2	6.7	1.3	9.1
3-Ph	*2.21*	1.71	3.13	2.71	2.16	6.9	1.2	1.2	6.9	1.2	9.5
	2.40										
3-Cl		2.01	2.97	2.62	2.20	6.4	1.1	1.1	6.4	1.4	9.1
3-Br		1.94	3.02	2.66	2.25	6.8	1.1	1.1	6.8	1.4	9.4
3,5-$(CH_3)_2$	*6.98*	*7.16*	3.53	2.96	2.46	...	...	...	6.8	Nr	9.3
3,6-$(CH_3)_2$	*7.28*	2.44	*7.63*	2.93	2.40	...	1.8	Nr	...	...	9.3
3,7-$(CH_3)_2$	*7.29*	2.25	3.32	*7.57*	2.54	7.0	...	Nr	...	Nr	...
3,8-$(CH_3)_2$	*7.28*	2.25	3.24	2.97	*7.36*	6.5	Nr	...	6.5	...	...
3-C_2H_5, 5-CH_3	*6.60*	*7.15*	3.52	2.94	2.42	...	...	...	6.5	Nr	9.1
	8.47										
3-C_2H_5, 6-CH_3	*6.94*	2.38	*7.65*	2.93	2.32	...	1.5	1.5	...	...	9.6
	8.52										
3-C_2H_5, 7-CH_3	*6.94*	2.22	3.35	*7.61*	2.53	7.1	...	1.6	...	Nr	...
	8.53										
3-C_2H_5, 8-CH_3	*6.89*	2.26	3.27	3.01	*7.33*	6.7	Nr	...	5.7	...	...
	8.52										
3-Ph, 5-CH_3	*2.48*	*7.79*	3.40	2.79	2.29	...	...	...	6.5	Nr	9.2
3-Ph, 6-CH_3	*2.20*	1.95	*7.65*	2.86	2.27	...	1.5	Nr	...	...	9.7
	2.41										
3-Ph, 7-CH_3	*2.14*	1.82	3.27	*7.50*	2.59	7.1	...	Nr	...	1.6	...
	2.37										
3-Ph, 8-CH_3	*2.24*	1.88	3.20	2.96	*7.26*	6.7	Nr	...	6.7	...	...
	2.46										
5,7-$(CH_3)_2$	1.34	*7.34*	3.53	*7.58*	2.46	...	...	...	...	Nr	...
3,5,7-$(CH_3)_3$	*7.02*	*7.22*	3.69	*7.67*	2.73	...	...	...	...	1.0	...
3-C_2H_5, 5,7-$(CH_3)_2$	*6.67*	*7.23*	3.69	*7.69*	2.70	...	...	...	...	Nr	...
	8.50										
3-Ph, 5,7-$(CH_3)_2$	*2.48*	*7.84*	3.60	*7.61*	2.55	...	...	...	...	Nr	...

[a] Methyl, methylene, and phenyl proton absorptions italicized; Nr = not resolvable.

TABLE II

CHEMICAL SHIFTS (PPM) AND COUPLING CONSTANTS (CPS) FOR VARIOUS s-TRIAZOLO[1,5-a]PYRIDINE DERIVATIVES (2)

	τ_2	τ_4	τ_5	τ_6	τ_7	$J_{4,5}$	$J_{4,6}$	$J_{4,7}$	$J_{5,6}$	$J_{5,7}$	$J_{6,7}$
Unsubstituted	1.65	2.18	2.48	2.96	1.38	8.8	1.2	1.2	6.6	1.3	6.6
2-CH_3[a]	*7.26*	2.36	2.78	3.13	1.97	9.2	1.2	1.2	6.5	1.3	6.5
2-C_2H_5	*7.08*	2.31	2.67	3.07	1.49	8.4	1.4	1.4	6.6	1.4	6.6
	8.60										
2-Ph	*1.70*	2.20	2.50	3.00	1.37	8.7	1.3	1.3	6.9	1.5	6.9
	2.52										
2,4-$(CH_3)_2$	*7.39*	*7.37*	2.73	3.14	1.66	...	...	...	6.9	Nr	6.9
2,5-$(CH_3)_2$	*7.42*	2.59	*7.53*	3.23	1.67	...	Nr	Nr	...	...	7.1
2,6-$(CH_3)_2$	*7.43*	2.43	2.70	*7.61*	1.72	9.2	...	Nr	...	2.2	...
2,7-$(CH_3)_2$	*7.40*	2.39	2.53	3.10	*7.24*	7.8	Nr	...	6.3	...	...
2-C_2H_5, 4-CH_3	*7.05*	*7.37*	2.76	3.18	1.65	...	...	...	6.9	Nr	6.9
	8.57										
2-Ph, 4-CH_3	*1.67*	*7.27*	2.74	3.12	1.60	...	...	...	7.1	Nr	7.1
	2.53										
2-Ph, 5-CH_3	*1.71*	2.54	*7.54*	3.22	1.55	...	Nr	Nr	...	...	7.2
	2.54										
2-Ph, 6-CH_3	*1.75*	2.37	2.56	*7.61*	1.59	8.6	...	Nr	...	Nr	...
	2.50										
2-Ph, 7-CH_3	*1.65*	2.30	2.57	3.12	*7.17*	8.0	Nr	...	6.8	...	...
	2.42										
2,5,7-$(CH_3)_3$	*7.41*	2.75	*7.57*	3.41	*7.27*	...	Nr	...	...	...	...
2-Ph, 5,7-$(CH_3)_2$	*1.70*	2.59	*7.55*	3.33	*7.17*	...	Nr	...	...	...	...
	2.52										

[a] Methyl, methylene, and phenyl proton absorptions italicized; Nr = not resolvable.

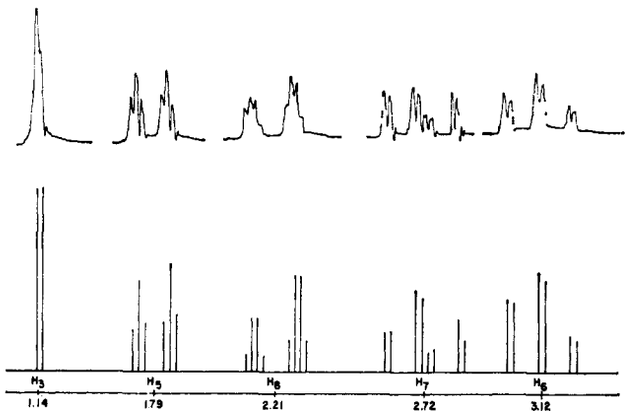

Figure 1.—*s*-Triazolo[4,3-*a*]pyridine.

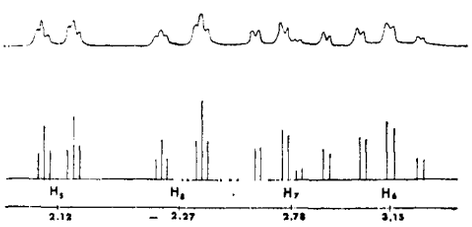

Figure 2.—3-Methyl-*s*-triazolo[4,3-*a*]pyridine.

on each peak triplet hyperfine splitting which was readily interpreted in terms of long-range *meta* and *para* coupling with the 7 and 8 protons. Long-range, cross-ring coupling resulting in a symmetrical triplet of this nature has been observed[12] previously in furan, thiophene, and pyrrole. The 8 proton is in an analogous spin interaction relationship with the other "pyridine ring" protons, but has quartet hyperfine splitting superimposed on each peak of the doublet at τ 2.21. The quartet character would be expected if the spin interaction between the 8 proton and the 3, 5, and 6 protons were equivalent and this appears to be so. No anomalous splitting occurred in the peaks assigned to the 6 proton and the 7 proton, precluding the existence of any measurable inter-ring spin interaction between these protons and the 3 proton. On methyl substitution at the 3 position, the quartet splitting of the 8-proton doublet was reduced to a triplet, further substantiating the 3,8 coupling. The peak of the 3 proton in the 8 methyl derivative was a singlet with no resolvable splitting at the same field homogeneity conditions under which the 3 proton of *s*-triazolo[4,3-*a*]pyridine was resolved. Deuteration of *s*-triazolo[4,3-*a*]pyridine resulted in replacement of the 3 proton only, and the absence of the 3,8 coupling led to a reduction of the complexity of the spectrum and confirmed the assignments made above. Inter-ring couplings of this type have been observed between the 4 and 8 protons of quinoline derivatives[16,17] ($J_{4,8}$ = 0.8 cps), and others have been found in benzofuran[14] ($J_{3,7}$ = 0.9 cps), various indenes ($J_{3,7}$ = 0.7 cps), and indolizines[4a,e] ($J_{3,8}$ = 0.5 cps). Paudler and Blewitt recently[4e] reported coupling between the 3 and 5 protons of imidazo[1,2-*a*]pyridine but we were not able to detect any such coupling in the present system. No inter-ring coupling was observed in the *s*-triazolo[1,5-*a*]pyridine system.

The spectra of *s*-triazolo[4,3-*a*]pyridine and its 3-methyl derivative have been calculated from the observed chemical shifts and coupling constants using the iterative method of Swalen and Reilly,[18] and these are shown in Figures 1 and 2, respectively. The chemical shifts and peak intensities of the calculated curve based on an ABCDE system are in close agreement with the experimental curve.

Influence of the Solvent on the Chemical Shift.—The largest solvent effect in the *s*-triazolo[4,3-*a*]pyridines was observed with the 3 proton which shifted to high field on dilution in every case. This may be explained in terms of an intermolecular hydrogen bond between the 3 proton and the 1 nitrogen atom which is the most basic nitrogen, protonation and salt formation occurring at this position.[3] Infrared studies[19] also indicate hydrogen bonding being associated with this nitrogen atom. Dilution would minimize this association and result in a shift of the 3 proton to high field.

The chemical shift of the 5 proton was less concentration dependent and did not always shift to high field, the parent compound showing the largest concentration dependence for both the 3 and the 5 protons. 3-Phenyl-*s*-triazolo[4,3-*a*]pyridine and its 6-, 7-, and 8-methyl derivatives exhibited shifts to low field for the 5 proton on dilution. This may be due to a steric effect or a mesomeric effect reducing the intermolecular association described above, especially if the molecular association takes the form of "stacking" of layers of these planar molecules, as frequently occurs in aromatic systems. The induced secondary magnetic field of the ring systems would then be minimized on dilution and shifts to low field would result. Concentration effects on the 6 and 7 protons were small and no apparent trend in direction of shift was detected. The chemical shift of the 8 proton, on dilution, moved to low field consistently in all derivatives examined, an effect that could be due to the breakdown of the hydrogen bonding associated with the nitrogen atom at position 1. Concentration effects for all protons in the *s*-triazolo[1,5-*a*]pyridines were minimal.

3-Substituted *s*-Triazolo[4,3-*a*]pyridines.—In 3-phenyl-*s*-triazolo[4,3-*a*]pyridine, the 3-phenyl group is coplanar with the bicyclic nucleus but with a 5-methyl substituent the steric requirements can only be satisfied by the phenyl group adopting a conformation skew to the nucleus. This is clearly shown by the hypsochromic shift in the ultraviolet absorption spectrum of 5-methyl-3-phenyl-*s*-triazolo[4,3-*a*]pyridine when compared to the corresponding 3-phenyl product[19] and a similar effect has been observed in other fused systems of this type with analogous substitution patterns.[20] This steric interaction has some interesting consequences on the pmr spectra of these derivatives.[21] The chemical shift of the 5 proton (τ 1.71–1.95) in each of the 3-phenyl compounds investigated was found to occur at lower field (0.08–0.43 ppm) than the chemical shift of the 5 proton (τ 1.79–2.38) in the other members of the series. A planar conformation would place the 5 proton in the plane of and at the edge of the 3-phenyl

(17) F. A. L. Anet, *J. Chem. Phys.*, **32**, 1274 (1960).

(18) J. D. Swalen and C. A. Reilly, *ibid.*, **37**, 21 (1962).

(19) K. T. Potts and H. R. Burton, unpublished observations.

(20) S. Schneller, M.S. Thesis, University of Louisville, 1965.

(21) Similar effects have been observed in other ring systems with substituent phenyl groups and are of considerable importance in structural determinations. We have studied the *s*-triazole and *s*-triazolo[4,3-*a*]pyrazine systems, and the pyrazole system has been investigated by L. G. Tensmeyer and C. Ainsworth [*J. Org. Chem.*, **31**, 1878 (1966)] and by B. M. Lynch and Y. Y. Hung [*Can. J. Chem.*, **42**, 1605 (1964)].

group and would, consequently, shift the resonance absorption of this proton to lower field.[22] In the absence of the 3-phenyl group, the chemical shifts of the 5-methyl protons are τ 7.15–7.35 but in the 3-phenyl-5-methyl compound, the methyl protons absorb at τ 7.79. The effect of the phenyl group on methyl protons at the 6 and 7 positions is essentially 0, while the 8-methyl protons are shifted to low field by 0.07 ppm. The anomalously high-field shift of the 5-methyl protons may be explained in terms of the nonplanar conformation forced on the 3-phenyl group, with the result that the 5-methyl protons would be shielded by the 3-phenyl group. Further confirmation is obtained from the absorption pattern of the 3-phenyl protons. Instead of the characteristic, split phenyl protons, the 3-phenyl protons of the 5-methyl compounds absorb as a sharp singlet, a consequence of the nonplanar conformation removing the *ortho* protons from the influence of the magnetic anisotropic effect of the nucleus.

Alkyl substituents in the 3 position of the s-triazolo[4,3-*a*]pyridine nucleus produced expected high-field shifts (0.03–0.09 ppm) of the 6, 7, and 8 protons, while the 5 proton experienced an extremely large shift of 0.30 ppm to high field. The shift is comparable to those undergone by the protons adjacent to methyl substituents in the "pyridine ring," except in the case of a 6-methyl group and the 7 proton, and a 7-methyl group and the 6 proton where the shift was about 0.17 ppm only. In the 3,5-dimethyl-substituted compounds both methyl groups absorbed at lower field than either did in the respective monomethyl derivatives. The 3-methyl group was shifted 0.28 and 0.24 ppm to lower field in the 3,5-dimethyl- and 3,5,7-trimethyl-s-triazolo[4,3-*a*]pyridine derivatives, respectively. In addition, the absorption of the methylene protons of the 3-ethyl-5-methyl derivatives is shifted (0.28 ppm) to low field relative to its position in the 3-ethyl compound, and the methyl protons of the ethyl group are essentially unaffected. The influence of the 3-alkyl group on the 5-methyl protons's absorption is smaller than the reciprocal effect just discussed and was in the range of 0.16–0.12 ppm. The deshielding influence of the 3-methyl group on the 5-methyl group may, perhaps, best be explained as resulting from the extensive overlap of these two groups, clearly shown in models. Dailey and Martin,[23] in a discussion of the effects observed in some *ortho*-disubstituted benzenes, suggest that certain anomalies may arise through the interactions of neighboring groups held in close proximity to each other, especially when they approach the sum of their van der Waals radii, and the rapid diminution of these effects suggests that they are not transmitted through the bonding orbital of the molecule. The overlap of the 3- and 5-methyl groups is considerably greater than that of *o*-methyl groups and these substituents are well within their van der Waals radii of each other. It seems reasonable that such extensive overlap would produce a significantly asymmetric charge distribution in these perturbed substituents and result in the "anomalously" low chemical shift values for the 3- and 5-methyl protons. It is especially interesting to compare these results with those obtained by Paudler and Kuder[4e] with 3,5-dimethylimidazo[1,5-*a*]pyridine. Here it was found that a similar *peri* interaction was most likely operative and that both methyl groups absorbed at lower field than was predicted.

Another interesting result was obtained with the 3-chloro- and 3-bromo-s-triazolo[4,3-*a*]pyridines. Substitution of either of these atoms into a ring system generally produces a low-field shift of the remaining ring protons.[11] The 6, 7, and 8 protons of these halogen-substituted derivatives did show small shifts to low field (0.10–0.15 ppm); however, the 5 proton moved to high field in both the 3-chloro product (0.20 ppm) and in the 3-bromo product (0.15 ppm). Previous studies of *ortho*-disubstituted benzenes have shown that halogens exert a strongly deshielding effect on *ortho* protons.[23] However, in s-triazolo[4,3-*a*]pyridine, there is more overlap of the van der Waals radii of the 3 halogen and the 5 proton than for a proton *ortho* to a halogen atom in benzene. It would be surprising if this difference in overlap alone could account for a reversal of the usually observed effect.

A possible, alternative explanation for the 3,5-dimethyl deshielding may be found in a purely steric argument. It is conceivable that in the unhindered molecule a methyl group at either the 3 or the 5 position might not be orientated relative to the deshielding ring currents in a geometry that produces maximum deshielding. Introduction of the second alkyl group could cause some deformation of the molecule and consequently move each alkyl group into a region of stronger deshielding. No X-ray investigation of this ring system has been made but in the related s-triazolo[1,5-*c*]pyrimidine system, X-ray analysis has shown the planar five- and six-membered rings to be inclined to each other at an angle of 6.1° in the solid state.[24] The structural similarity between both systems is immediately apparent and this small deviation from over-all planarity probably influences to some extent the chemical shifts of the 3,5 substituents though, of course, the translation of solid state X-ray data into solution cannot be done with certainty.

The chemical shift values obtained for the various ring protons on introduction of methyl substituents into the nucleus are shown in Table I. These data are consistent with those obtained in related systems and it is not possible to relate the position of methyl substitution in the pyridine ring with the magnitude of the 3-proton shift. The effect of methyl substitution upon the chemical shift of a 3-methyl group (Table I) was also as expected, with the 7-methyl substituent causing a greater high-field shift (0.03 ppm) than the 6- and 8-methyl substituents (0.02 ppm). Similar results were obtained with a series of 3-ethyl-substituted products (Table I). No long-range inter-ring coupling involving either a 3-methyl or 3-ethyl substituent was observed.

The effect of various substituents on the chemical shift of the 5 proton of s-triazolo[4,3-*a*]pyridine can be seen in Table I and is as expected for such substitution patterns. In 8-methyl-s-triazolo[4,3-*a*]pyridine and its 3-substituted derivatives, the 5 proton was also split into the characteristic doublet which was broadened with respect to the same doublet in the 7-methyl product, but it was not possible to effect any further resolu-

(22) A recent list of references on this topic can be found in ref 4d.
(23) J. S. Martin and B. P. Dailey, *J. Chem. Phys.*, **39**, 1722 (1963).
(24) P. G. Owston and J. M. Rowe, *Acta Cryst.*, **15**, 231 (1962); G. W. Miller and F. L. Rose, *J. Chem. Soc.*, 5642 (1963).

TABLE III

CHEMICAL SHIFTS (PPM) AND COUPLING CONSTANTS (CPS) FOR 1-AMINO-2-IMINO-1,2-DIHYDROPYRIDINE AND ITS METHYL DERIVATIVES

	τ_5	τ_6	τ_7	τ_8	$J_{5,6}$	$J_{6,7}$	$J_{6,7}$	$J_{6,8}$	$J_{7,8}$
Unsubstituted	2.74	4.34	3.21	3.67	6.4	1.8	6.4	1.9	9.0
	(0.95)[a]	(1.22)	(0.49)	(1.46)					
5-CH_3	*7.67*[b]	4.39	3.29	3.72	...	...	6.4	Nr	9.0
	(0.36)	(1.06)	(0.52)	(1.42)					
6-CH_3	2.96	*8.07*	3.33	3.71	...	2.2	...	...	9.2
	(0.93)	(0.42)	(0.44)	(1.39)					
7-CH_3	2.83	4.47	*7.97*	3.83	6.9	...	...	2.0	...
	(0.89)	(1.18)	(0.43)	(1.31)					

[a] Values in parentheses represent the difference between the chemical shifts of corresponding protons in the free base and the *s*-triazolo[4,3-*d*]pyridine. [b] Methyl protons are italicized.

tion. This broadening is most likely the result of a long-range coupling of about 0.3 cps with the 7 proton, as coupling with the 8-methyl protons would involve six bonds and the 3 proton has been shown to couple only with the 8 proton. This splitting pattern is of interest in view of the 3,5 coupling observed in the imidazo[1,2-*a*]pyridines mentioned earlier.[4e]

From Table I it can be seen that the same general effects hold on introduction of methyl substituents for the relative chemical shifts of the 7 proton that held for the 5 and 6 protons. Methyl substitution in the 8 position had a more pronounced effect (high-field shift of 0.29 ppm) on the chemical shift of the 7 proton than did the corresponding substitution in the 6 position (high-field shift 0.17 ppm), indicating a greater degree of π-electron localization in the 7,8 bond than in the 6,7 bond. In 6-methyl-*s*-triazolo[4,3-*a*]pyridine, the 7 proton was split into a doublet by the 8 proton (J = 9.3–9.7 cps) and superimposed on this splitting pattern was a doublet owing to the long-range coupling of the 7 and 5 protons (J = 1.5–1.8 cps). The magnitude of this latter coupling was generally greater than that for the other couplings observed through four bonds and, though there has been no definite relationship established to date, it is possible that this reflects a more localized arrangement of the electrons in the bonds concerned.

The chemical shifts of the 8-methyl protons (Table I) correlate well with the kind and position of the substituent in the ring system. In 8-methyl and 3,8-dimethyl-*s*-triazolo[4,3-*a*]pyridine, the absorption of the 8-methyl protons occurred as a single, broad peak which could not be resolved.

Numerous attempts have been made to interpret the observed effect on the chemical shifts of the protons attached to a ring when methyl groups are introduced into the ring, and of particular interest to this present work are the study[4b] of the *s*-triazolo[1,5-*c*]pyrimidine system (**3**) and the recent data reported by Abraham, *et al.*,[25] and Elvidge[26] regarding the ring current associated with furan and thiophene.

Abraham's data indicate that the addition of a methyl group at the 2 position of furan produces a high-field shift of 0.43 ppm for the 3 proton relative to its chemical shift in the unsubstituted furan, while a 2-methyl group added to the nonaromatic 4,5-dihydrofuran produces a shift of the 3 proton of only 0.38 ppm. In the analogous set of thiophene compounds the effects are almost identical on methyl substitution, the proton shifts observed being of the order of 0.41 and 0.38 ppm, respectively. On the basis of Makisumi's work, it would be expected that localization of the π electrons in the dihydro compounds would support a larger methyl substituent effect than would be expected for the aromatic furan and thiophene nuclei.

In an attempt to obtain some indication of the possible aromatic character associated with the *s*-triazolo-[4,3-*a*]pyridine and *s*-triazolo[1,5-*a*]pyridine ring systems, we have studied a series of methyl-substituted 1-amino-2-imino-1,2-dihydropyridines (**6**) and the data for these compounds are shown in Table III. From the data in Tables I and II it can be seen that the effects of methyl substitution on the chemical shifts of the ring protons are in general agreement with those obtained by Makisumi, except that the total methyl substituent effect is larger in the *s*-triazolopyridines than in *s*-triazolo[1,5-*c*]pyrimidine. As there is one additional ring position available for methyl substitution in the pyridine series however, the differences in total effect are not strictly comparable. On the basis of Makisumi's argument, it would appear that there is considerable double-bond character present in the 5,6 and 7,8 bonds of the pyridine ring in the [4,3-*a*] series and in the 4,5 and 6,7 bonds of the [1,5-*a*] series.

1-Amino-2-imino-1,2-dihydropyridine and its methyl derivatives (**6**) have been studied on the premise that they are nonaromatic, and have a sufficiently close, structural relationship to the *s*-triazolopyridine series.[27] The chemical shift data for the ring protons of **6** and its derivatives indicate that they do not appear to be aromatic in character and this is supported by their chemical behavior. Table III shows that the ring protons occurred consistently at higher fields than do the corresponding protons of the *s*-triazolopyridines and their methyl derivatives, as well as those of pyridine and its methyl derivatives. The protons at the 7 position in the dihydropyridine series absorb in the chemical shift region of olefinic protons, and the 6- and 7-methyl protons fall in the region of the spectrum where methyl groups attached to diene systems have been assigned.[28] All of the methyl protons of the free bases occur at significantly higher fields than the corresponding methyl protons of the *s*-triazolopyridines or, indeed, than those

(25) R. J. Abraham, R. C. Sheppard, W. A. Thomas, and S. Turner, *Chem. Commun.*, 43 (1965); R. J. Abraham and W. A. Thomas, *J. Chem. Soc.*, 127 (1966).

(26) J. A. Elvidge, *Chem. Commun.*, 160 (1965).

(27) It is recognized that a more suitable system would be the appropriately reduced bicyclic system. However, the synthesis of such a system is extremely complex. The 1-amino-2-imino-1,2-dihydropyridines have been numbered in a partial sequence for purposes of relating the ring positions with those of the *s*-triazolo[4,3-*a*]pyridines.

(28) R. H. Wiley, F. G. Nau, and T. H. Crawford, *J. Org. Chem.*, **26**, 4285 (1961).

of any methyl group attached to an aromatic ring.[29] This high-field absorption for both the ring protons and the methyl protons in these dihydropyridines suggests that the aromatic ring current in this system is minimal and considerable localization of electron density around the ring is suggested by the large chemical shift difference (1.13 ppm) between the 6-H and the 7-H of the free base, while the difference in the *s*-triazolo[4,3-*a*]-pyridine series is only 0.40 ppm. The differences in the chemical shift values of the 7 protons of the free base and the *s*-triazolo[4,3-*a*]pyridine series are significantly less than the differences observed for the other ring protons and similar effects are observed for corresponding protons in the *s*-triazolo[1,5-*a*]pyridine series. This may be indicative of the importance to the ground state of the canonical form represented by **7**.

6 **7**

For purposes of comparing the methyl-substituent effect on the methyl derivatives of **1** and **6**, the shifts of only the pyridine ring protons were considered. Table III shows the effects of each methyl group on the various protons as well as the total effect over all three protons. In all cases the total effect is significantly less in the dihydropyridine series. Comparison of the methyl substituent effect across the 5,6, 6,7, and 7,8 bonds for the two series indicates a smaller effect in the dihydropyridine series than in the *s*-triazolo[4,3-*a*]-pyridine series and similar results were obtained in the *s*-triazolo[1,5-*a*]pyridine series. These results are in general agreement with the data reported by Abraham, *et al.*, for the methyl substituent effect in related dihydro, nonaromatic systems which was only 88–93% of that observed in the aromatic furan and thiophene nucleus. The effect in the dihydropyridines varies from 23 to 92% of that observed in the *s*-triazolo[4,3-*a*]-pyridine series, the diminution of the methyl substituent effect being more pronounced in the two present series than that which appeared in the furan and thiophene series. In the dihydro furans and thiophenes and also in the dihydropyridines, there should have been extensive π-electron localization as compared to that present in the appropriate aromatic analogs used in both studies, and the double-bond character should have been greater in the nonaromatic compounds at $C_{5,6}$ and $C_{7,8}$. On the basis of Makizumi's results, the methyl substituent effect across these bonds should have been greater than that observed in the aromatic series; it was actually found to be less. It appears from these observations that the explanation for this effect must involve more than the π-bond order of the bond through which the effect is transmitted and it seems reasonable to conclude that while localization of the π-electron density may be involved in the mechanism of the methyl substituent effect, some delocalization and the presence of some ring current appears to be necessary to optimize the effect.

(29) N. S. Bhacca, L. F. Johnson, and J. N. Shoolery, "N.M.R. Spectrum Catalog," Varian Associates, Palo Alto, Calif., 1962, Spectrum No. 2; however, Paudler and Blewitt[4e] have reported the methyl protons of 6-methylimidazo[1,2-*a*]pyridine absorb at τ 8.02, a value higher than that for most other aromatic ring methyl groups.

Experimental Section

Pmr spectra were measured with a Varian Associates HR-4302 high-resolution spectrometer with a 60-Mc oscillator fitted with super stabilizer and field homogeneity controls. Samples were examined in deuteriochloroform solution (normal operating temperature, 30°) at an initial concentration of 10% w/v. All τ values reported here are the results of several dilutions (a minimum of four) of each sample with the chemical shifts plotted against relative concentration and extrapolated to infinite dilution. The plots were generally linear and the best straight line was used in all cases. Tetramethylsilane was used as an internal standard. Spectra were calibrated using the side-band technique and chemical shift data were readily reproducible and accurate to ±0.5 cps. Coupling constants were determined directly from the spectra and are reproducible to ±0.5 cps. The syntheses of all the compounds examined were carried out as described earlier.

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