Chlorine-35 Nuclear Quadrupole Resonance Spectra of Chlorodiazines

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The ^{35}Cl n.q.r. spectra of 17 chloroazines have been measured. The results are compared with values predicted by empirical methods. In general, they show it is not possible to extrapolate from chloropyridine to chlorodiazines since the effect of the additional nitrogen is mainly inductive rather than conjugative. Large solid-state splittings are observed in some chloropyridazines.

THE ^{35}Cl n.q.r. frequencies of chlorinated aromatic molecules provide measures of the charge distribution in such molecules. Quantitative calculations of the charge distributions within a chlorine–carbon bond are not routine at present and so qualitative correlations between the ^{35}Cl n.q.r. frequencies and other parameters sensitive to the charge distribution have been sought. The most common of these is Hammett's σ parameter. Bray and Barnes[1] found relationship (1) (for ^{35}Cl

$$\nu(^{35}\mathrm{Cl}) = (34.826 + 1.024\sum_i \sigma_i)\ \mathrm{MHz} \qquad (1)$$

n.q.r. frequencies at 77 K). The summation is taken over the whole ring and σ_i is the σ value of the ith substituent. The mean square deviation of the relationship is 360 kHz and may be explained by differences in molecular motion and by internal crystal fields, for the ^{35}Cl n.q.r. frequencies are also influenced by intermolecular effects such as the geometrical arrangement of neighbouring molecules in the crystal and the charge distribution within them.

A number of chlorinated heterocycles have been investigated by the n.q.r. method[2] but these have mainly been pyridines and pyrimidines. This paper reports measurements mainly on the pyrazine and pyridazine ring systems. Stidham and Farrell[3] have already reported data for 3,6-dichloropyrazine, tetrachloropyridazine, 2-chloropyrazine, and 2,6-dichloropyrazine. However, their data has been improved upon by measuring the ^{35}Cl n.q.r. spectra with an externally quenched super-regenerative spectrometer with sideband suppression.[4] Since the completion of this work Semin *et al.* have reported measurements (at 77 K only) on 2-chloropyrimidine[5] which agree well with those quoted here.

EXPERIMENTAL

The ^{35}Cl n.q.r. spectra were measured with the prototype of the Decca n.q.r. spectrometer by kind permission of Professor J. A. S. Smith. The sample size was 1 g. Initially a survey spectrum was recorded with maximum radio frequency level of the oscillator, high amplification, and lowest band width of the receiver network (time constant 10 s) without side-band suppression. The modulation normally used for this purpose was of the Zeeman type. After the line frequencies were roughly known, expanded spectra were run with sideband suppression and optimized radio frequency level to determine the line frequencies more precisely and to separate closely spaced lines. The samples were cooled slowly to liquid nitrogen temperature to avoid strain in the crystals of materials that are solid at room temperature and to avoid the formation of a glassy phase rather than a crystalline one for samples that are liquid at room temperature. Both these adverse conditions lead to broadening and loss of signal.

The temperature dependence of the spectra was measured by cooling in liquid nitrogen and allowing the sample to warm to room temperature. The sample temperature was measured with a thermocouple.

The materials were purified by either distillation, sublimation, or recrystallization, whichever was appropriate. 3-Chloropyridazine was prepared by conversion of 6-methyl-3-pyridazone hydrobromide to 3-oxopyridazine-6-carboxylic acid by chromic acid oxidation. This was decarboxylated by dry distillation to obtain 3-pyridazone which was chlorinated with phosphoryl chloride to yield 3-chloropyridazine.[6] 2-Chloropyrimidine was prepared by diazotization of 2-aminopyrimidine and decomposition of the resulting diazo-compound in hydrochloric acid.[7] 2-Amino-5-chloropyrimidine was prepared by reaction of 2-aminopyrimidine with chlorine gas.[8] 2-Chloropyrazine, 2,6-dichloropyrazine, 2,3-dichloropyrazine, 2-chloroquinoxaline, and 2,3-dichloroquinoxaline were samples donated by Dr. G. W. H. Cheeseman of this department. 3-Chloro-6-dimethylaminopyridazine, 4-amino-3,6-dichloropyridazine, and 3,6-dichloropyridazine were donated by Dr. R. F. Cookson of the Nicholas Research Institute. 3,4,6-Trichloropyridazine was donated by Dr. J. K. Landquist of I.C.I. Pharmaceutical Division. 3,4,5,6-Tetrachloropyridazine and 2,3,5,6-tetrachloropyrazine were donated by T. J. Jenkinson of Unilever Research.

RESULTS

Table 1 shows the ^{35}Cl n.q.r. frequencies measured at 77 K and room temperature (*ca.* 298 K). Only two samples showed abnormal temperature dependences. For both 2-chloropyrimidine and 2,3-dichloroquinoxaline the two ^{35}Cl n.q.r. plots appear to cross at 225 and 205 K re-

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[1] P. J. Bray and R. G. Barnes, *J. Chem. Phys.*, 1957, **27**, 551.

[2] E. A. C. Lucken, ' Nuclear Quadropole Coupling Constants,' Academic Press, London, 1969, p. 181.

[3] H. D. Stidham and H. H. Farrell, *J. Chem. Phys.*, 1968, **49**, 2463.

[4] J. A. S. Smith and D. A. Tong, *J. Phys. E.*, 1968, **1**, 8.

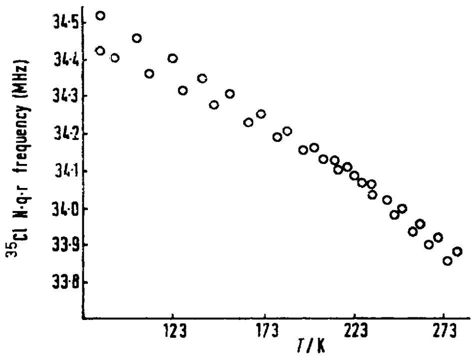
[5] G. K. Semin, T. A. Babushkina, V. P. Mamaev, and V. P. Krivopalov, *Izvest. Sib. otdel. Akad. Nauk S.S.R., Ser. Khim. Nauk*, 1971, 82 (*Chem. Abs.*, 1972, **76**, 39,820m).

[6] R. F. Homer, H. Gregory, W. G. Overend, and L. F. Wiggins, *J. Chem. Soc.*, 1948, 2195.

[7] I. C. Kogon, R. Minn, and C. G. Overberger, *Org. Synth.*, 1955, **35**, 34.

[8] J. P. English, J. H. Clark, J. W. Clapp, D. Seeger, and R. H. Ebel, *J. Amer. Chem. Soc.*, 1946, **68**, 453.

spectively. The Figure shows the measured temperature dependence of the ^{35}Cl n.q.r. spectrum of 2-chloropyrimidine. It may be seen from Table 1 that the three monochlorodiazines all contain two molecules in the asymmetric unit of the crystal. Of these three isomers, 3-chloropyridazine exhibits the largest solid-state splitting (800 kHz) reported for monochloroheterocyclic compounds. The solid-state splitting varies considerably in Table 1 and reaches a maximum of 1.2 MHz for the 3-chlorine of tetrachloropyridazine.



Plot of ^{35}C n.q.r. frequency of 2-chloropyrimidine against sample temperature (phase transition at *ca.* 225 K)

TABLE 1

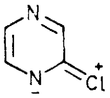
^{35}Cl N.q.r. frequencies measured at 77 K (liquid nitrogen) and 298 K (room temperature)

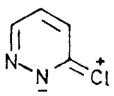
	N.q.r. frequency	
	77 K	298 K
2-Chloropyrazine	35.02	*a*
	35.09	
2-Chloropyrimidine	34.42	33.72
	34.52	33.80 [b]
3-Chloropyridazine	34.52	*c*
	35.33	
3-Chloro-6-methylpyridazine	34.75	34.04
3-Chloro-6-dimethylaminopyridazine	34.33	33.80
2-Amino-5-chloropyrimidine	35.95	35.23
2-Chloroquinoxaline	34.22	33.58
2,6-Dichloropyridine	34.66	*d*
3,5-Dichloropyridine	35.62	*d*
2,6-Dichloropyrazine	35.22	34.52
	35.69	34.88
2,3-Dichloropyrazine	36.10	*e*
3,6-Dichloropyridazine	35.91	35.10
	36.02	35.22
	36.44	35.44
	36.45	35.54
2,3-Dichloroquinoxaline	35.66	34.93
		35.30 [f]
4-Amino-3,6-dichloropyridazine	35.05	*e*
	35.85	
3,4,6-Trichloropyridazine	36.50	35.85
	36.92	36.20
	37.60	36.72
3,4,5,6-Tetrachloropyridazine	36.82	36.35
	38.10	37.49
	38.12	37.60
	38.71	38.20
2,3,5,6-Tetrachloropyrazine	36.86	36.10
	36.90	36.22

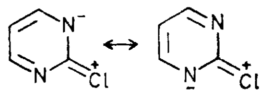
[a] Liquid at room temperature. [b] Phase transition at 225 K. [c] Low m.p. 308 K. [d] See ref. 2 for values at room temperature. [e] Very weak signal, unobservable at room temperature. [f] Phase transition at 205 K.

DISCUSSION

2-Chloropyrimidine resonates at a frequency *ca.* 1 MHz lower than the other two isomers (average values). This can be explained by π-bonding in the carbon–chlorine bond. For, in valence bond terms, the chlorine in both 2-chloropyrazine and 3-chloropyridazine can conjugate with one nitrogen and not the other. However in 2-chloropyrimidine the chlorine can conjugate with either nitrogen.







In Table 2, the measured ^{35}Cl n.q.r. frequencies are compared with those predicted on the basis of ' additivity principles.' The predicted values are based on comparisons between chloropyridines and chlorobenzene as a datum. The predicted values are all lower than the measured ones, demonstrating that the introduction of the second nitrogen into the ring has a greater inductive than conjugative effect.

TABLE 2

Comparison of values predicted by additivity and measured values of ^{35}Cl n.q.r. frequency for monochloroazines

	Resonance frequencies (average) (MHz)		
Compound	Predicted	Measured	Notes
2-Chlorobenzene		34.622	Datum
2-Chloropyridine		34.194	thus *ortho*-effect of nitrogen −428 kHz
3-Chloropyridine		35.234	thus *meta*-effect of nitrogen +612 kHz
4-Chloropyridine		34.739	thus *para*-effect of nitrogen +117 kHz
2-Chloropyrimidine	33.77	34.47	*ortho* + *ortho*
2-Chloropyrazine	34.81	35.05	*ortho* + *meta*
3-Chloropyridazine	34.81	34.92	*ortho* + *meta*

Biedenkapp and Weiss[9] have found that the Bray–Barnes relation can be somewhat improved by using Taft's σ_i and σ_r parameters; they give relation (2) (in MHz at 77 K). Tupitsyn *et al.*[10] have applied this relationship to nitrogen-containing heterocycles by estimating a σ_i and σ_r value for ring nitrogen. They were forced to adopt different σ values for nitrogen in different relative positions to the chlorine whose n.q.r. frequency was being measured. First, for nitrogen *ortho* to chlorine they chose $\sigma_i = -0.15$ except for the 2-position in pyrimidine (where chlorine is *ortho* to two nitrogens) they chose $\sigma_i = -0.04$. For nitrogen in any other

$$\nu_{^{35}\mathrm{Cl}} = 34.540 + 2.978\Sigma\sigma_i\,(ortho) + 0.470\Sigma\sigma_r\,(ortho) + 1.310\Sigma\sigma_i\,(meta) + 0.360\Sigma\sigma_r\,(meta) + 0.940\Sigma\sigma_i\,(para) + 0.056\Sigma\sigma_r\,(para) \quad (2)$$

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[9] D. Biedenkapp and A. Weiss, *J. Chem. Phys.*, 1968, **49**, 3933.

[10] I. F. Tupitsyn, N. N. Zatsepina, N. S. Kolodina, and A. V. Kirova, *Reaks. Sposobnost. Org. Soedinenii*, 1972, **9**, 1075 (*Chem. Abs.*, 1973, **79**, 114,718b).

position they chose $\sigma_i = 0.45$. They used the same value of σ_r for nitrogen throughout, namely $\sigma_r = 0.25$. The results of using their σ values for ring nitrogen in the Biedenkapp–Weiss relation are shown in Table 3.

TABLE 3

Comparison of measured values and calculated values (based on Taft's σ_i and σ_r parameters) or n.q.r. frequency of chloroazines

	N.q.r. frequency (MHz) Measured (average)	Calculated	Error (Meas. − Calc.)
2-Chloropyrazine	35.05	34.89	0.16
2-Chloropyrimidine	34.47	34.54	−0.07
3-Chloropyridazine	34.93	34.89	0.04
3-Chloro-6-methylpyridazine	34.75	34.84	−0.09
2-Amino-5-chloropyrimidine	35.95	35.95	0.00
2,6-Dichloropyridine	34.66	34.74	−0.08
3,5-Dichloropyridine	35.62	35.75	−0.13
2,6-Dichloropyrazine	35.45	35.42	0.03
2,3-Dichloropyrazine	36.10	36.18	−0.08
3,6-Dichloropyridazine	36.21	35.32	0.89
4-Amino-3,6-dichloropyridazine			
3-Cl	35.85	35.26	0.59
6-Cl	35.05	35.18	−0.13
3,4,6-Trichloropyridazine			
3-Cl	36.92	36.61	0.31
4-Cl	37.60	36.71	−0.11
6-Cl	36.50	35.85	−0.35
Tetrachloropyridazine			
3-Cl	37.46	37.14	−0.32
4-Cl	38.42	37.90	0.52
Tetrachloropyrazine	36.88	37.14	−0.26

The correlation coefficient is 0.950, somewhat worse than the original correlation coefficient of Biedenkapp and Weiss (0.976).

The major deviations from the relationship are positive and occur for pyridazines; they reach a maximum at 3,6-dichloropyridazine where the error is 890 kHz. Stidham and Farrell, in their study of this molecule used a modified form (3) of the Bray–Barnes relationship [11] adapted to allow for π-bonding between carbon and chlorine. $\Delta\nu_{db}$ is a double-bond contribution. For

$$\nu_{^{35}Cl} = 34.826 + 1.024\Sigma\sigma - \Delta\nu_{db} \qquad (3)$$

pyridines and pyrimidines Bray *et al.*[11] report $\Delta\nu_{db} =$ 1.23 MHz, while for *s*-triazine it is twice this. Stidham and Farrell found their results produce a negative double-bond contribution for any physically reasonable choice of σ values. This they suggest indicates an unusually large crystal-packing defect. The magnitude of the solid-state splitting in 3-chloropyridazine tends to support this. However, this is only a partial explanation since pyridazines are expected to be most different from pyridine of all the diazines. Crystal structure determinations [12] of two pyridazine derivatives have revealed that the N–N bond length is close to a value for a N–N single bond.

Guibé and Lucken [13] have studied the ^{14}N n.q.r. spectra of 3,6-dichloropyridazine and found the axis of the electric field gradient of the nitrogen atom must be rotated by 90° from that in pyridazine itself if the difference between the average σ and π orbital populations in the dichloro-compound is to be less than that in the parent heterocycle, which would be expected from data on pyridines.

From the data reported here it is evident that the pyridazine ring system has the most interesting crystal structure of the diazines, but further work is necessary to elucidate this point.

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[11] P. J. Bray, S. Moskowitz, H. O. Hooper, R. G. Barnes, and S. L. Segal, *J. Chem. Phys.*, 1958, **28**, 99.

[12] R. N. Castle, 'Pyridazines,' in 'The Chemistry of Heterocyclic Compounds,' Wiley, New York, 1973, vol. 28.

[13] L. Guibé and E. A. C. Lucken, *Mol. Phys.*, 1968, **14**, 79.