^{35}Cl NQR Spectra of Substituted N-(phenyl)-2-chloroacetamides

B. Thimme Gowda, D. Krishna Bhat, H. Fuess[a] and Al. Weiss (†)

Department of Chemistry, Mangalore University, Mangalagangotri-574199, Mangalore, India
[a] Fachbereich Materialwissenschaft, TH Darmstadt, Petersenstrasse 23, D-64287 Darmstadt

Reprint requests to Prof. B. T. G.; Fax: 0091-824-742367. e mail: gowdabt@mnglr.ernet.in

Z. Naturforsch. **54a,** 679–684 (1999); received September 7, 1999

Fifteen methyl-, nitro-, or mixed substituted N-(phenyl)-2-chloroacetamides were investigated by ^{35}Cl NQR. The temperature dependence of the frequencies of the 3-methylphenyl and 2,6-dimethylphenyl derivatives were studied for the range 77 K<T<300 K. Only one ω C–Cl frequency was observed for the compound with the two exceptions. For N-(2-nitro,4-chlorophenyl)-2-chloroacetamide the observed values of 35.623 and 35.350 MHz were assigned to ω C–Cl and ring C–Cl, whereas the corresponding values are 36.254 and 34.815 MHz for N-(2-methyl, 3-chlorophenyl)-2-chloroacetamide. The experimental frequencies of all compounds have been compared with values estimated from NQR substituent parameters 'k' and the frequency of N-(phenyl)-2-chloroacetamide. The agreement is remarkably good with a maximum deviation of 1.64 MHz. Furthermore $\gamma(^{35}\mathrm{Cl})$ of all compounds has been correlated with $\sum k_i$ and with the Hammett constants.

Key words: Nuclear Quadrupole Resonance; Chloroacetamide.

Introduction

Amides are of fundamental chemical interest as conjugation between nitrogen lone pair electrons and the carbonyl π-bond results in distinct physical and chemical properties [1, 2]. Addition of a third hetero atom, either α or β, to the amino nitrogen of the amide group, as in hydroxamic acids, N-halo compounds and hydrazides increases their chemical complexity, which has required the advent of modern physical techniques to become unraveled. The amide moiety is an important constituent of many biologically significant compounds. Therefore an understanding of the formation, properties and reactions of amides is central to future development in such areas as polypeptide and protein chemistry. Many imides, hydroxamic acids and hydrazides exhibit pharmacological activity, which has further stimulated recent interest in their chemistry. Further, many acetanilides exhibit fungicidal, herbicidal and pharmacological activities [3–8].

NQR studies are done to provide evidence on the chemical bonding in molecules or crystals [9–13]. They are especially useful in the study of halogen compounds.

As part of our efforts in rationalising the correlations of ^{35}Cl NQR frequencies with chemical bond parameters, ^{35}Cl NQR studies of several substituted acetamides represented by the general formula $X_yC_6H_{5-y}$ NHCOR (where X = Cl, CH_3 or NO_2, y = 1, 2, or 3 and R = CH_2Cl) have been undertaken and reported in this paper.

Materials and Methods

The substituted N-(phenyl)-2-chloroacetamides were prepared [14, 15] from the respective anilines and chloroacetyl chloride (Aldrich, Germany). The commercial anilines were purified by either double distillation or zone refining. The respective anilines in acetone or benzene were treated with chloroacetyl chloride in acetone or benzene in the presence of excess 2 M NaOH with constant stirring. The solids separated were filtered under suction, washed thoroughly with water and dried. The amide samples were recrystallised several times from ethanol. The purity of the compounds was checked by elemental analysis for C, H, and N (Table 1). The compounds have been further characterised by recording their infrared spectra and by determining their melting points. All the chemicals employed in the preparation of acetanilides were of analytical grade.

^{35}Cl NQR Frequency Measurements

Polycrystalline samples of the title compounds were employed. The ^{35}Cl NQR of the substituted N-(phenyl)-2-chloroacetamides were measured at 77 K or as function of temperature T, ($77 \leq T/\mathrm{K} \leq 300$). The spectra were registered by the continuous wave method with a superregenerative spectrometer. This temperature at the sample site was produced by a stream of temperature and

Table 1. Elemental analysis of the acetanilides studied, $X_yC_6H_{5-y}NHCOCH_2Cl$ with X_y.

X_y	% Nitrogen		% Carbon		% Hydrogen		m.p. (°C)
	calc.	found	calc.	found	calc.	found	
-H	8.26	8.23	56.65	56.56	4.72	4.70	134
2-CH_3	7.63	7.54	58.86	58.21	5.45	5.38	81
3-CH_3	7.63	7.53	58.86	58.87	5.45	5.55	84
4-CH_3	7.63	7.54	58.86	58.69	5.45	5.49	156
2-NO_2	13.05	13.12	44.77	44.65	3.29	3.16	88
3-NO_2	13,05	13.16	44.77	44.73	3.29	3.20	115
4-NO_2	13.05	13.16	44.77	44.68	3.29	3.18	182
2,3-$(CH_3)_2$	7.10	7.31	60.76	60.80	6.08	6.11	120
2,4-$(CH_3)_2$	7.10	7.98	60.76	60.68	6.08	6.10	144
2,5-$(CH_3)_2$	7.10	7.16	60.76	60.65	6.08	6.14	146
2,6-$(CH_3)_2$	7.10	7.21	60.76	60.86	6.08	6.20	141
2-CH_3, 3-Cl	12.25	12.26	42.01	46.97	3.94	3.84	120
2-NO_2, 4-Cl	11.25	11.25	38.55	38.38	2.41	2.37	111
2-NO_2, 4-CH_3	6.42	6.38	49.54	49.61	4.13	3.96	127

Table 2. ^{35}Cl NQR frequencies of acetanilides, $X_yC_6H_{5-y}NHCOCH_2Cl$ with X_y (Temp. 77 K).

X_y	γ_i	Assignment	*S/N*	γ(MHz)
-H	γ_1	w	30	35.333
2-CH_3	γ_1	w	15	36.026
3-CH_3	γ_1	w	38	36.590
	γ_2	w	35	35.766
4-CH_3	γ_1	w	20	35.150
2-NO_2	γ_1	w	5	34.793
3-NO_2	γ_1	w	6	36.566
4-NO_2	γ_1	w	7	36.335
2,3-$(CH_3)_2$	γ_1	w		No resonance
2,4-$(CH_3)_2$	γ_1	w	15	35.835
2,5-$(CH_3)_2$	γ_1	w		No resonance
2,6-$(CH_3)_2$	γ_1	w	60	35.723
2-CH_3, 3-Cl	γ_1	w	22	36.254
	γ_2	m	25	34.815
2-NO_2, 4-Cl	γ_1	w	30	35.623
	γ_2	p	35	35.350
2-NO_2, 4-CH_3	γ_1	w	25	34.810

flow regulated nitrogen gas or with a liquid nitrogen bath at 77 K. The temperatures at the sample site were measured by copper-constantan thermocouples to ±1 K. The resonance frequencies were measured via a frequency counter to an accuracy of ±5 kHz. The latter accuracy was determined by the line width of the resonances, which was between 10 and 20 kHz.

The parent compound N-(phenyl)-2-chloroacetamide and N-(2/3/4-nitrophenyl)-2-chloroacetamide were also prepared, characterised and their ^{35}Cl NQR frequencies were measured under identical conditions for comparison. All the corresponding N-(chlorophenyl)-2-chloroacetamides were prepared, characterised and their ^{35}Cl NQR frequencies were measured for the same purpose.

Results

The ^{35}Cl NQR frequencies of fifteen N-(methyl, nitro or mixed substituted phenyl)-2-chloroacetamides along with the available literature on ^{35}Cl NQR frequencies of the corresponding N-(chlorophenyl)-2-chloroacetamides are shown in Table 2. The temperature dependence of the ^{35}Cl NQR frequencies of N-(3-methylphenyl)-2-chloroacetamide and N-(2,6-dimethylphenyl)-2-chloracetamide were followed up to 300 K (Figure 1). The frequencies of N-(3-methylphenyl)-2-chloroacetamide corresponding to two crystallographically inequivalent states of the same ω-Cl, and that of N-(2,6-dimethylphenyl)-2-chloroacetamide decreased smoothly with increasing temperature as expected for molecular crystals,

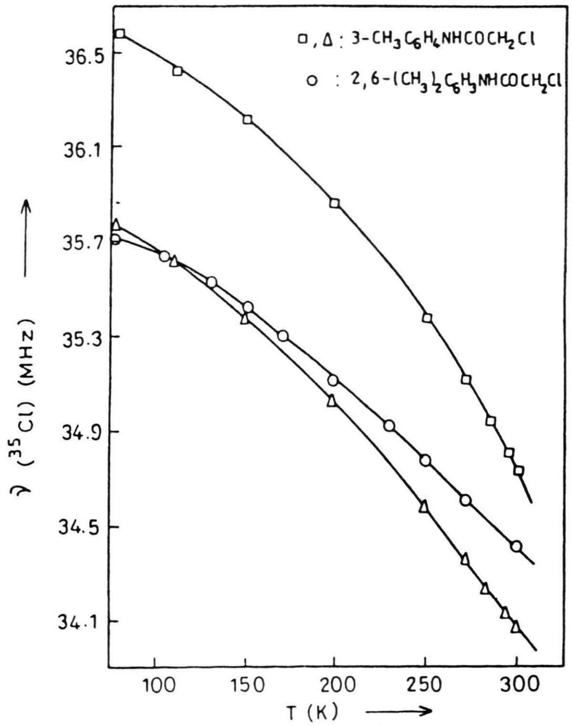

Fig. 1. Plot of (^{35}Cl NQR) vs. temperature.

Table 3. Coefficients of the power series development $\gamma(^{35}Cl) = f(T)$ for $3\text{-}CH_3C_6H_4NHCOCH_2Cl$ and $2,6\text{-}(CH_3)_2C_6H_3NHCOCH_2Cl$.

γ_i	z	σ (kHz)	a_0 MHz	a_{-1} MHz.K	$a_1 \cdot 10^3$ MHz.K^{-1}	$a_2 \cdot 10^6$ MHz.K^{-2}
			$3\text{-}CH_3C_6H_4NHCOCH_2Cl$			
γ_1	9	7.7	35.8595	5.7457	–86.3671	–0.1722
γ_2	9	1.6	35.8031	40.6769	5.9066	–0.3306
			$2,6\text{-}(CH_3)_2C_6H_3NHCOCH_2Cl$			
γ_1	10	7.1	36.4921	–24.9951	–5.4224	–4.2410

[a] Please see text.

obeying predictions of the Bayer theory [16] (Figure 1). The coefficients a_i of the power series development of the ^{35}Cl NQR frequencies as $f(T)$ have been computed according to equation (Table 3)

$$\gamma = \sum_i a_i T^i, -1 \le i \le 2. \tag{1}$$

Discussion

There is no problem in the assignment of the ^{35}Cl NQR frequencies as there is only one ω C–Cl frequency in all the substituted amides except in N-(2-methyl, 3-chlorophenyl)-2-chloroacetamide and N-(4-chloro, 2-nitrophenyl)-2-chloroacetamide. The two ^{35}Cl NQR frequencies of N-(2-methyl, 3-chlorophenyl)-2-chloroacetamides are 36.254 and 34.815 MHz compared to 36.026 MHz of N-(2-methylphenyl)-2-chloroacetamide. N-(3-chlorophenyl)-2-chloroacetamide did not show resonance in the NQR. Further, the ^{35}Cl NQR C–Cl ring frequencies of N-(3-chlorophenyl)-acetamide, N-(3-chlorophenyl)-2,2-dichloroacetamide and N-(3-chlorophenyl)-2,2,2-trichloroacetamide are 34.735, 34.564 and 34.954 MHz, respectively. Hence the frequency of 36.254 MHz in N-(2-methyl, 3-chlorophenyl)-2-chloroacetamide is assigned to ω C–Cl, and 34.815 MHz to the ring C–Cl. Similarly, the two ^{35}Cl NQR frequencies, 35.623 and 35.350 MHz of N-(2-nitro, 4-chlorophenyl)-2-chloroacetamide have been assigned to ω C–Cl and ring C–Cl, respectively. This is supported by ring C–Cl frequencies of N-(4-chlorophenyl)-acetamide, N-(4-chlorophenyl)-2-chloroacetamide, N-(4-chlorophenyl)-2,2-dichloroacetamide and N-(4-chlorophenyl)-2,2,2-trichloroacetamide of 34.788, 34.962, 34.636 and 34.564 MHz, respectively, which are lower than the ω C–Cl frequency of 35.745 MHz for N-(4-chlorophenyl)-2-chloroacetamide.

Table 4. NQR substituent parameters (k) and Hammett σ values.

Group	k	σ
o-Cl	1.206 ± 0.047	–
m-Cl	0.499 ± 0.035	0.373
p-Cl	0.329 ± 0.072	0.227
o-Br	0.975 ± 0.204	–
p-Br	0.312 ± 0.173	0.232
o-I	0.917 ± 0.196	–
p-I	0.199 ± 0.173	0.276
o-NH_2	–0.534 ± 0.119	–
m-NH_2	–0.103 ± 0.130	–0.161
p-NH_2	–0.119 ± 0.133	–0.660
o-NO_2	2.096 ± 0.087	–
m-NO_2	1.069 ± 0.093	0.710
p-NO_2	0.067 ± 0.125	0.778/1.270
o-CH_3	–0.392 ± 0.054	–
m-CH_3	–0.207 ± 0.161	–0.069
p-CH_3	–0.004 ± 0.126	–0.170
m-CF_3	0.611 ± 0.147	0.415
p-CF_3	0.740 ± 0.207	0.551
o-OH	0.442 ± 0.101	–
m-OH	0.140 ± 0.140	–0.002 ± 0.106
p-OH	0.286 ± 0.143	–0.357 ± 0.104
o-COOH	1.704 ± 0.162	–
m-COOH	0.377 ± 0.153	0.355
p-COOH	0.409 ± 0.148	0.265 ± 0.126
o-OCH_3	0.917 ± 0.172	–
p-OCH_3	0.122 ± 0.145	–0.268
o-OC_2H_5	0.793 ± 0.172	–
p-OC_2H_5	–0.027 ± 0.157	–0.250

Table 5. Comparison of computed and experimental ω C–Cl ^{35}Cl NQR frequencies of substituted N-(phenyl)-2-chloroacetamides, $X_yC_6H_{5-y}NHCOCH_2Cl$.

X_y	γ(MHz)		X_y	γ(MHz)	
	calc.	obsd.		calc.	obsd.
-H	–	35.333	-H	–	35.333
2-CH_3	34.941	36.026	2-Cl	36.539	36.278
3-CH_3	35.126	36.178	3-Cl	No resonance	
4-CH_3	35.290	35.150	4-Cl	35.662	35.745
2,3-$(CH_3)_2$	No resonance		2.3-Cl_2	37.038	36.725
2,4-$(CH_3)_2$	34.937	35.835	2,4-Cl_2	No resonance	
2,5-$(CH_3)_2$	No resonance		2,5-Cl_2	37.038	35.584
2,6-$(CH_3)_2$	34.549	35.723	2,6-Cl_2	37.745	36.674
2-CH_3, 3-Cl	35.440	36.254	3,4-Cl_2	37.038	36.589
2-NO_2, 4-Cl	37.748	35.623	2,4,5-Cl_3	37.367	37.730
2-NO_2, 4-CH_3	37.425	34.810	2-NO_2	37.429	34.793
4-NO_2	35.940	36.335	3-NO_2	36.402	36.566

Biedenkapp and Weiss [17] have deduced NQR substituent parameters for various groups (Table 4) solely from $\gamma(^{35}Cl\ NQR)$.

$$\gamma(^{35}Cl) = \gamma_0 + \sum k_i, \text{ with } k(H) = 0.$$

i distinguishes the different groups with regard to the Cl-atom considered. The reference frequency,

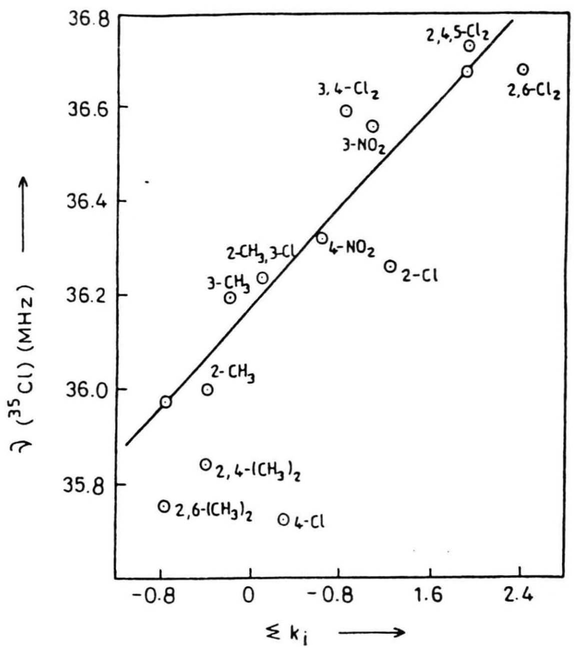

Fig. 2. Plot of $\gamma(^{35}$Cl NQR) vs. $\sum k_i$.

$\gamma_0 = 34.695$ MHz was obtained by a least squares adjustment of the available ^{35}Cl NQR frequencies of chlorobenzene derivatives, which in the limit of the crystal field effect is equal to the ^{35}Cl NQR frequency of chlorobenzene (34.622 MHz at 77 K).

Using the k values [17] listed in Table 4 and 35.333 MHz (^{35}Cl NQR) of ω C–Cl for N-(phenyl)-2-chloroacetamide [15], the corresponding ^{35}Cl NQR frequencies of N-(methyl, chloro and mixed substituted phenyl)-2-chloroacetamides have been estimated. These values along with the experimental frequencies are shown in Table 5. Despite the fact that the listed k values for various groups in Table 4 were deduced based on the effects of these groups on the ^{35}Cl NQR frequencies of the ring C–Cl, the calculated frequencies of ω C–Cl of N-(methyl or mixed substituted phenyl)-2-chloroacetamides measured in this study and those of N-(chloro or nitrophenyl)-2-chloroacetamides reported in the literature agree remarkably well with the experimental frequencies.

The maximum deviation of 1.64 MHz is observed for N-(2-nitrophenyl)-2-chloroacetamide, while N-(4-chloro and 4-methylphenyl)-2-chloroacetamides showed minimum deviation. Further $\gamma(^{35}$Cl) of all the substituted acetanilides have been correlated with $\sum k_i$ (Fig. 2), assuming the additivity i of the substituent effects. The deviations are understandable considering the fact that the effect of substitution is not immediately next to the ω C–Cl bond. The effect has to be transmitted through the peptide linkage –NHCO–. As may be seen, the deviation is unsystematic, although generally electron withdrawing groups in the ring increased the $\gamma(^{35}$Cl) of ω C–Cl. For example the nitro group in the ortho position is an exception to this behaviour. Unsystematic be-

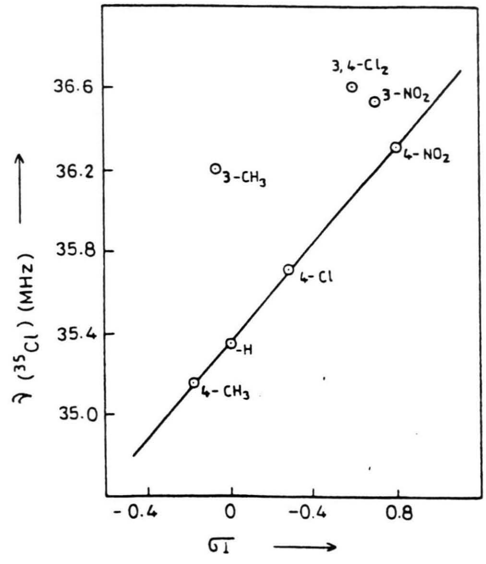

Fig. 3. Plot of $\gamma(^{35}$Cl NQR) vs. Hammett σ.

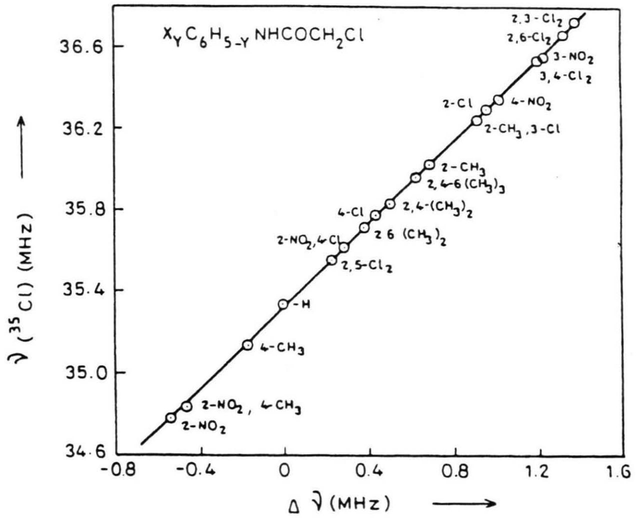

Fig. 4. Plot of $\gamma(^{35}$Cl NQR) vs. $\Delta\gamma$.

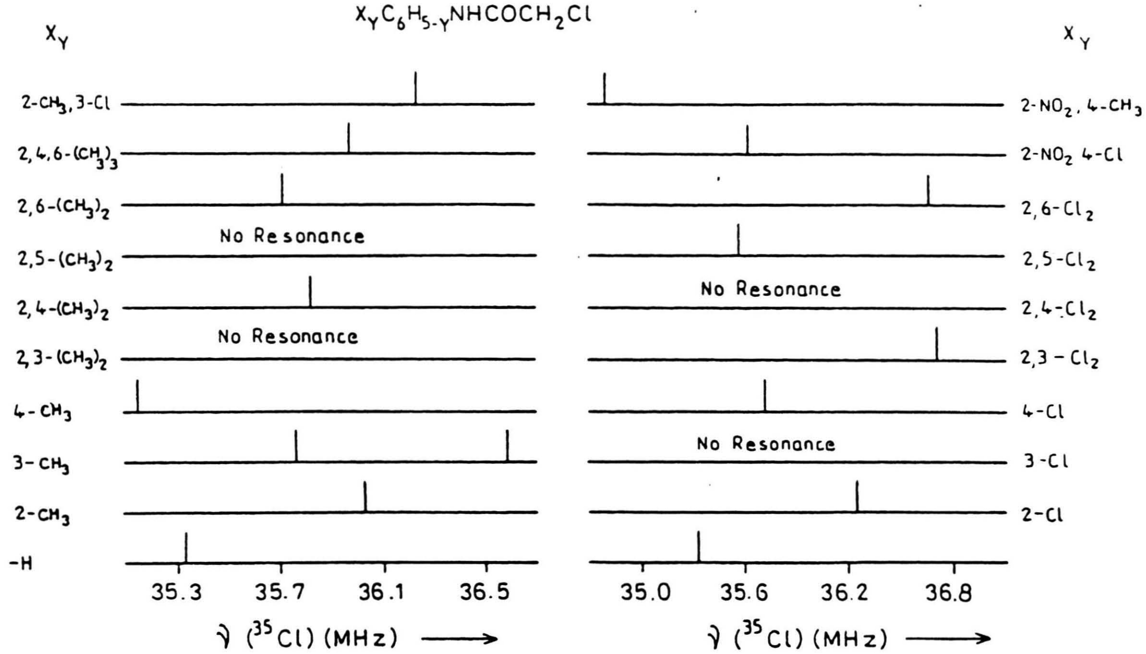

Fig. 5. Plot of $\gamma(^{35}$Cl NQR) vs. substitution.

haviour is due to chemically equivalent chlorine atoms which may exhibit different NQR frequencies due to the crystal field effect [18, 19]. Further, introduction of a steric parameter adds to the deviation due to the steric inhibition of mesomerism [20]. Intramolecular hydrogen bonding may also partly contribute. In the absence of complete crystal structures of the compounds studied and reported in literature, a quantitative prediction of either the frequency or deviation becomes extremely difficult.

Available $\gamma(^{35}$Cl NQR) of parasubstituted ω-monochloroacetanilides have also been correlated with the Hammett constants (Figure 3). The correlation is extremely good. Further, frequencies of all the compounds are correlated with the changes in frequencies on substitution in the ring, taking $\gamma(^{35}$Cl) of N-(phenyl)-2-chloroacetamide (Figure 4) as reference. Variation in $\gamma(^{35}$Cl) with substitution is also diagrammatically shown in Figure 5.

The effect of N-chlorination on the ω C–Cl ^{35}Cl NQR frequencies of various ring chlorosubstituted acetanilides is shown in Table 6, in comparison with those of the corresponding chloro and methylsubstituted acetanilides.

Table 6. Comparison of ω C–Cl ^{35}Cl NQR frequencies of substituted acetanilides and their N-chloro analogues at 77 K.

$X_yC_6H_{5-y}NHCOCH_2Cl$				$X_yC_6H_{5-y}$ NClCOCH$_2$Cl	
X_y	γ(MHz)	X_y	γ(MHz)	X_y	γ(MHz)
-H	35.333	–H	35.333	-H	37.004
2-Cl	36.278	2-CH_3	36.026	2-Cl	35.969
3-Cl	No resonance	3-CH_3	36.590 36.766	3-Cl	37.017
4-Cl	35.745	4-CH_3	35.150	4-Cl	34.935
2,3-Cl_2	36.725	2,3-$(CH_3)_2$	No resonance	2,3-Cl_2	37.568
2,4-Cl_2	No resonance	2,4-$(CH_3)_2$	35.835	2,4-Cl_2	36.728
2,5-Cl_2	35.584	2,5-$(CH_3)_2$	No resonance	2,5-Cl_2	36.625
2,6-Cl_2	36.674	2,6-$(CH_3)_2$	35.723	2,6-Cl_2	36.303
2-NO_2	34.793			2-NO_2	36.402

Acknowledgement

B. T. G. is grateful to the Alexander von Humboldt Foundation, Bonn, Germany, for a Research Fellowship. Support of the Fonds der Chemischen Industrie is gratefully acknowledged.

[1] P. A. S. Smith, Open-Chain Nitrogen Compounds, Benjamin, New York 1966, Vols. 1 and 2.
[2] The Chemistry of Amides, ed. J. Jabicky, Interscience, London 1970.
[3] J. C. Sheehan and E. J. Corey, Org. Reaction **9,** 7388 (1957)
[4] E. H. White and D. W. Grisley, J. Amer. Chem. Soc. **83,** 1191 (1961).
[5] M. K. Hargreaves, J. G. Pritchard, and H. R. Dave, Chem. Rev. **70,** 439 (1970).
[6] W. E. Stewart and T. H. Siddal, Chem. Rev. **70,** 517 (1970).
[7] S. R. Sandler and W. Karo, Organic Functional Group Preparations, Academic Press, London 1972, Vol. 3.
[8] N. S. Isaacs, Chem. Soc. Rev. **5,** 181 (1976).
[9] E. A. C. Lucken, Nuclear Quadrupole Coupling Constants, Academic Press, New York 1969.
[10] H. G. Dehmelt and H. Kruger, Naturwiss. **37,** 111 (1950).
[11] T. P. Das und E. L. Hahn, Nuclear Quadrupole Resonance Spectroscopy, Academic Press, New York 1958.
[12] G. K. Semin, T. A. Babushkina, and G. G. Yakobson, Nuclear Quadrupole Resonance in Chemistry, John Wiley, New York 1975.
[13] J. A. S. Smith (Ed.), Advances in Nuclear Quadrupole Resonances, John Wiley, London 1974–83, Vols. 1–5.
[14] W. Pies, H. Rager and Al. Weiss, Org. Mag. Reson. **3,** 147 (1971).
[15] B. T. Gowda and Al. Weiss, Z. Naturforsch. **49a,** 695 (1994).
[16] H. Bayer, Z. Physik. **130,** 227 (1951).
[17] D. Biedenkapp and Al. Weiss, J. Chem. Phys. **49,** 3933 (1968).
[18] M. J. S. Dewar and E. A. C. Lucken, J. Chem. Soc. 426 (1959).
[19] D. Biedenkapp and Al. Weiss, Ber. Bunsenges. Physik. Chem. **70,** 788 (1966).
[20] B. M. Webster, in Progress in Stereochemistry, Academic Press, New York 1958, Vol. 2.