Influence of the 1,1,3,3-Tetramethylguanidinyl Substituent on the Charge Distribution in Chlorobenzenes, Studied by ³⁵Cl NQR

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³⁵Cl NQR measurements were carried out on a series of chlorobenzenes with the 1,1,3,3-tetramethylguanidinyl substituent {TMG = $-N=C[N(CH_3)_2]_2$ }. The substituent constants σ_p , σ_m , σ_I and σ_R for the TMG group were estimated from the relationships between the NQR resonance frequencies, ν_Q , and substituent constant values, σ . The ν_Q value for 2-(4-chlorophenyl)-1,1,3,3-tetramethylguanidine is the lowest observed for all chlorobenzenes, and arises from the strong positive conjugative effect of the TMG group. This effect is attributed to the possible resonance stabilization of the positive charge. Steric inhibition of resonance is observed for the *ortho*-substituted isomers.

KEY WORDS Cl NQR 1,1,3,3-tetramethylguanidinyl-substituted chlorobenzenes Substituent constants Charge distribution

INTRODUCTION

In chlorobenzene derivatives the ³⁵Cl NQR frequency, ν_Q , can be treated as a measure of the electron charge distribution around the chlorine nucleus. This charge distribution depends on the nature and positions of substituents in the molecule studied. The substituents can interact with a carbon atom of the ring, bonded with chlorine conjugatively (π) and inductively (σ). These effects can increase (+C, +I) or decrease (-C, -I) the electron density in the aromatic ring, and on the carbon atom bonded with the chlorine atom, influencing the resonance frequency ν_Q .

Hammett¹ derived an equation which correlates the dissociation constants of derivatives of benzoic acid with the nature and position of the substituents. A number of other correlations have been derived which better describe the dependence in the case of particularly strong conjugative interactions using the σ^- and σ^+ substituent constants.^{2,3} Other relationships allow for the separation of the conjugative and inductive influences of substituents and the determination of the σ_R and σ_I constants.⁴ Since the resonance frequency, ν_Q , is a function of the substituents, it has been correlated with the σ values.⁵⁻⁷

We have attempted to determine the influence of the 1,1,3,3-tetramethylguanidinyl $(-N = C[N(CH_3)_2]_2)$ (TMG) group on the ν_Q value and to estimate its substituent constant. The exceptional properties of guanidine⁸ and its derivatives⁹ made the studied compounds particularly interesting. We expected an unusually strong +C influence from the TMG group because of resonance stabilization of the positive charge.

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EXPERIMENTAL

The compounds studied are shown in Table 1 and were synthesized by the Brederecks' method.¹⁰ N, N, N', N'-Tetramethylurea and appropriate chloroanilines were used as the starting materials. Because all chlorophenyl-1,1,3,3-tetramethylguanidines are very strong bases, the Brederecks' method was modified by extracting the products from the aqueous phase into benzene at pH 14. The structures and purities of the studied compounds were checked by MS, NMR and elemental analysis.¹¹

Preliminary measurements of the ³⁵Cl NQR frequencies were performed on a laboratory made super-regenerative spectrometer. Precise measurements were carried out with an ISSh 1-12 type pulse spectrometer equipped with an automatic frequency sweep.¹² The $\pi/2-\tau-\pi$ sequence was applied, with typical pulse widths of 15 and 30 μ s at the output RF power of the order of 1 kW. The second pulse triggered the boxcar integrator and the quadrupole echo, subsequent to the second pulse, proceeded to the recorder. As the frequency was swept, the whole NQR spectrum could be recorded. The values of the signal-to-noise ratio were between 25 and 38, so no accumulation was needed. The resonance frequency was measured by the beat method, involving the quadrupole spin-echo and an external generator, and reading the frequency of the latter from a digital frequency meter. The ³⁵Cl NQR frequency was measured with an accuracy of ±1 kHz.

The sample was placed inside a cylindrical tube with a diameter of 1 cm and a length of 4 cm. The sample was slowly cooled to 77 K and immersed in a liquid nitrogen Dewar vessel. All NQR measurements were recorded at 77 K.

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Table 1. ³⁵Cl NQR frequencies of chlorophenyltetramethylguanidines at 77 K

RESULTS AND DISCUSSION

The results of the resonance frequency, ν_Q , measurements for the studied chlorobenzene derivatives with a TMG group are given in Table 1.

Individual chlorine atoms are crystallographically equivalent, so the number of resonance lines equals the number of chlorine atoms in a molecule. The resonance frequency 33.924 MHz for **3**, to the best of our knowledge, is the lowest found so far for chlorobenzene derivatives. This proves that the C—Cl bond in this compound



Figure 1. The resonance structures for phenyltetramethylguanidine.

is the most ionic in character with the most negative charge at the chlorine atom. Thus, the TMG substituent has the most effect in increasing the electron density on the chlorine bonded to the phenyl ring in the *para* position. This is due to the exceptional property of the TMG group, viz. the resonance stabilization of positive charge (Fig. 1), which generates twice as many resonance structures for TMG as for other substituents. This results in an exceptionally strong conjugative effect (+C) of the TMG group.

From measurements on 52 chlorobenzene derivatives, Bray and Barnes⁶ derived Eqn (1), correlating the resonance frequency ν_Q (MHz) with the substituent constants σ_m and σ_p :

$$\nu_Q(^{35}\text{Cl}) = \left(34.826 + 1.024\sum_i \sigma_i\right)$$
 (1)

The values $\sigma_m = -0.62$ and $\sigma_p = -0.88$ for the TMG substituent were calculated using this equation with the measured resonance frequencies for 2 and 3 (Table 1).

Using separate correlations between ν_Q and the substituent constant values for *para*- and *meta*-substituted chlorobenzenes (Fig. 2), the following equations were obtained by computer analysis:

$$\nu_{O}(^{35}\text{Cl}) = 34.526 + 1.244\sigma_{m}$$
 (2)

$$\nu_O(^{35}\text{Cl}) = 34.634 + 0.532\sigma_n \tag{3}$$

The calculated values $\sigma_m = -0.27$ and $\sigma_p = -1.33$ are very different from those calculated from Eqn (1). This discrepancy is caused by using Eqn (1) for the excep-



Figure 2. ³⁵Cl NQR mean frequency versus Hammett constants, σ_p and σ_m , for substituted chlorobenzenes.^{5–7,13} Substituents R: 1 p-N(CH₃)₂; 2 p-NH₂; 3 p-COCH₃; 4 p-OCH₃; 5 p-CH₃; 6 H; 7 p-NHCOCH₃; 8 p-1; 9 p-CH₂Cl; 10 p-CHO; 11 p-Cl; 12 p-Br; 13 p-OCOCH₃; 14 p- COOH; 15 p-CN; 16 p-NO₂; 1' m-N(CH₃)₂; 2' m-NH₂; 3' m-CH₃; 4' m-OH; 5' m-NHCOCH₃; 6' m-F; 7' m-CHO; 8' m-COOH; 9' m-Br; 10' m-CF₃; 11' m-NO₂.



Figure 3. The plot of ³⁵Cl NQR mean frequencies¹³ versus σ_p^+ constants¹⁴ for chlorobenzene derivatives.

tionally strong conjugative substituent TMG. For such substituents the differences between the *para* and *meta* positions are too large to justify using the combined *meta-para* relationships. Equation (2) is very similar to Eqn (4) given by Tsvetkov *et al.*⁷:

$$\nu_Q(^{35}\text{Cl}) = 34.55 + 1.223\sigma_m$$
 (4)

which gave $\sigma_m = -0.29$ for the TMG substituent.

Taking into consideration the strong conjugative interaction of TMG with *para* substituents, we correlated appropriate resonance frequencies, ν_Q ,¹³ with the σ_p^+ constants¹⁴ (Fig. 3). This correlation is described by the equation

$$\nu_Q(^{35}\text{Cl}) = 34.731 + 0.464\sigma_p^+$$
 (5)

giving a value $\sigma_p^+ = -1.74$ for TMG.

Equation (4), originally derived for *meta* substituents, may also be applied to a series of *para* substituents which are not subject to strong conjugation with an aromatic ring.⁷ The deviation of the substituent constant calculated from Eqn (4) from its real value can be considered as a measure of the conjugative action of the substituent.⁷ The calculated value of the TMG substituent constant is $\sigma_{p \text{ calc}} = -0.51$ from Eqn (4). If we assume that $\sigma_p^+ = -1.74$ describes in the best way the interaction of the TMG substituent with a *p*-chlorine atom, the value $\sigma_R = -1.13$ can be calculated using Eqn (6) given by Tsvetkov *et al.*⁷:

$$\Delta \sigma = \sigma - \sigma_{\text{calc}} = (0.12 + 1.195\sigma_R) \pm 0.06 \tag{6}$$

The value of σ_I as a measure of the inductive action of the TMG substituent can be calculated from the follow-

Table 2. Estimated values of the substituent constants for the TMG group obtained from NQR measurements						
$\sigma_p^{\ a}$	$\sigma_m^{\ \ 8}$	$\sigma_{\rho}^{\ b}$	σ _m ^b	σ_p^{+c}	σ_{R}	σ_{l}
-0.88	-0.62	-1.33	-0.27	-1.74	-1.13	0.08
^a Values [†] ^b Values [†] ^c Calculat	found from found usin ted from I	m Eqn (1) ng separa Eqn (5).	6 te Eqns (2	2) and (3).		

ing equation:15

$$\sigma_m = \sigma_I + 0.33 \sigma_R \tag{7}$$

The value $\sigma_m = -0.29$ calculated from Tsvetkov *et al.* Eqn (4) and the estimated value $\sigma_R = -1.13$ then yield $\sigma_I = 0.08$ for the TMG substituent. This value is close to $\sigma_I = 0.11$ for amine and dimethylamine groups,¹⁶ which supports the validity of our calculations.

The calculated substituent constants for the TMG group are given in Table 2. Thus the TMG group is a substituent which conjugatively releases electrons to the benzene ring (+C) and inductively withdraws electrons from the ring (-I).

Figure 4 shows the dependence of the resonance frequency on the mutual position of Cl and TMG groups in a benzene ring. For comparison, the analogous dependence for NH₂ and N(CH₃)₂ groups are also included. For all the substituents in Fig. 4, a change in mutual position from *para* to *meta* is reflected in an increase in the resonance frequency. This is mainly a consequence of the reduced conjugative action of these groups toward a *m*-Cl compared with a *p*-Cl substituent. The inductive influence of the NH₂, N(CH₃)₂ and TMG groups dominates in the *meta* position.¹⁴

For compounds with a chlorine atom ortho to these groups one would expect a decrease in the resonance frequencies because of the reappearance of a strong conjugative interaction of the substituents. This is observed for o-chloroaniline, but in 1 it is diametrically opposed to that expected. This may be due to the presence of hindrance to the conjugative interaction of the TMG group with the phenyl ring in the presence of a chlorine atom at the neighbouring carbon atom. Taking into account the size of the substituents and the flatness of the TMG group when conjugated with the phenyl ring, this hindrance seems to be of a steric character. It precludes the achievement of a planar structure by the whole molecule. Such a situation means that only an inductive (-I) effect operates and ν_Q increases. Even though the inductive effect is the strongest for the ortho



Figure 4. The change of the ³⁵Cl NQR mean frequency (ν_a) with the relative position of NH₂*, N(CH₃)₂* and TMG groups against chlorine atoms in chlorobenes. *—values from Ref. 13.

position, the resonance frequency for 1, $\nu_0 =$ 34.629 MHz, is still only slightly higher than that for unsubstituted chlorobenzene, $\nu_Q = 34.621$ MHz.¹³ This confirms the validity of our calculations, showing that the TMG group is characterized by a weak -I type of interaction with $\sigma_I = 0.08$ (Table 2).

In order to check the hypothesis of steric inhibition of mesomeric interactions in 1, we synthesized 4 and 5 with two chlorine atoms per molecule (Table 1). Two pairs of compounds, 3-4 and 2-5 (Table 1), show similar structural properties, viz. the presence of a chlorine atom in the ortho position with respect to the TMG group in the second member of each pair. One can predict, on the grounds of Biedenkapp and Weiss's data,¹⁷ the influence of this structural change on the resonance frequency for p-Cl with respect to the TMG group. In the case of p-Cl (3-4) this predicted change is $0.499 \pm$

0.035 MHz, but an increase in ν_0 of 1.041 MHz (Table 1) is observed. This change, so much higher than predicted, is evidence that the o-Cl present in 4 destroys the conjugative interaction of the TMG group. The same effect at the *m*-Cl with respect to the TMG group (2-5) should give a much smaller discrepancy between the predicted and observed Δv_Q . This is so; whereas an increase of $\nu_Q = 0.329 \pm 0.072 \text{ MHz}^{17}$ is expected, the observed value is 0.439 MHz. The destruction of conjugation of the TMG group is appreciable at m-Cl, although it is much less than at p-Cl.

The comparison of the discrepancies between the observed and predicted changes in the resonance frequencies for the p-Cl and m-Cl groups may lead to a quantitative estimation of the meaning of the conjugation influence of the TMG substituent at the meta position in the benzene ring.

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