Proton Chemical Shifts in NMR. Part 15[1]. Proton chemical shifts in nitriles and the electric field and π electron effects of the cyano group.

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The proton resonance spectra of a number of nitriles of fixed geometry were recorded in dilute $CDCl_3$ solution and assigned. These were trans and cis-4-t-butyl cylohexanecarbonitrile, axial and equatorial cyclohexanecarbonitrile and ax-ax and eq-eq trans-1,4-dicyano cyclohexane, the latter compounds at -60^0C.The aromatic nitriles measured were benzonitrile, **o**, **m** and **p-** dicyanobenzene, 1 and 2-cyanonaphthalene and 9-cyanoanthracene. This data together with previous literature data allowed the determination of the cyano substituent chemical shifts (SCS) in a variety of molecules. These SCS were analysed in terms of the CN electric field, magnetic anisotropy and steric effects for protons more than three bonds removed together with a model (CHARGE7) for the calculation of the two-bond and three-bond SCS. For the aromatic nitriles ring current and π electron effects were included.

Analysis of the SCS showed that the anisotropic and steric effects of the cyano group were negligible in all the compounds investigated and in the aliphatic nitriles the SCS were due to only the electric field effect together with for near protons electronic effects.

For the aromatic nitriles the π electron effects were calculated using Huckel theory with the values of the exchange and resonance integrals involved adjusted so as to give π electron densities in agreement with those obtained by *ab initio* calculations. The ring current shifts of the cyano derivatives were assumed to be the same as those of the parent hydrocarbons.

The model gives the first comprehensive calculation of the SCS of the cyano group. For the data set of 93 proton chemical shifts spanning ca 9.0ppm the rms error of the observed vs calculated shifts was 0.088ppm. The breakdown of the CN SCS in the aromatic nitriles showed good agreement with the Swain/Lupton field and resonance (***F*** and ***R***) components of substituent effects.

Introduction

Nitriles are of considerable importance in all branches of chemistry. They are both versatile synthetic intermediates and important compounds *per se*. (see ref. 2 for a comprehensive treatment) and in consequence the proton resonance spectra of nitriles has been studied since the beginning of nmr spectroscopy. Despite this, there is still some controversy and uncertainty over the causes of the SCS of the cyano group. The cyano group is both strongly polar and also anisotropic and both of these factors have been proposed to account for cyano SCS. Early workers suggested that the CN magnetic anisotropy should be similar to that of the analogous C≡C bond and Reddy and Goldstein[3] using a correlation between C^{13}-H couplings and the proton chemical shift estimated $\Delta\chi$ as $-16.5\text{x}10^{-6}$ cm^3/mole for both the CN and the C≡C bond. Cross and Harrison[4] used the value of the CN anisotropy obtained by Reddy and Goldstein to calculate the shifts of the C-19 methyl groups in some 5α and 5β–cyano steroids. They found that the shifts were opposite to those predicted from the anisotropy and suggested that the CN electric field could be responsible. This early work has been well reviewed by Bothner-By and Pople[5].

Subsequently Zurcher[6] and ApSimon et al[7] conducted more detailed analyses of the CN SCS. They both used the McConnell equation[8] to calculate the magnetic anisotropy of the cyano group and the CN dipole to calculate the electric field. They did not consider any steric effects of the CN group in their calculations. They also assumed that the CN anisotropy could be calculated from the centre of the triple bond, although the π–electron system may be more or less displaced towards the more electronegative atom. Both studies came to the conclusion that the electric field effect was predominant. However both these studies used mainly the methyl groups of steroids to determine the SCS. When they extended their calculations to include nearer protons large differences between the observed and calculated shifts were found.

What is required for a definitive analysis is a sufficient data set of CN SCS using conformationally rigid molecules with fully assigned proton spectra. We present the complete assignment of the pmr spectra of both aliphatic and aromatic nitriles of fixed conformation. The aliphatic nitriles analysed are trans and cis-4-t-butylcylohexanecarbonitrile (**1a**,**1b**), axial and equatorial cyclohexanecarbonitrile (**2a, 2b**) and ax-ax and eq-eq trans-1,4-dicyano cyclohexane (**3a,3b**). Included also in the analysis are the pmr spectra of 2-exo and 2-endo norbornanecarbonitrile (**4a,4b**) and 1-adamantanecarbonitrile (**5**) recorded previously[9] and the proton shifts of acetonitrile (**6**), propionitrile (**7**), isobutyrocarbonitrile (**8**) and trimethylacetonitrile (**9**) from the Aldrich catalogue[10]. The aromatic nitriles recorded here are benzonitrile (**10**), **o**, **m** and **p-**di-cyanobenzene (**11**,**12**,**13**), 1 and 2-cyanonaphthalene (**14**,**15**) and 9-cyanoanthracene (**16**). The proton chemical shifts of acrylonitrile (**17**) were obtained from the Aldrich catalogue[10].

These results provides sufficient data for an analysis of cyano SCS using a previous model of proton chemical shifts[1,11]. In previous parts of this series this model which is based on simple charge calculations over one, two and three bonds and steric, electric field and anisotropic contributions over more than three bonds has been applied successfully to a variety of saturated hydrocarbons[12,13], haloalkanes[14], ethers[15] and ketones[16]. We shall show that this model provides a quantitative treatment for cyano SCS and that these are due solely to the CN electric field. The anisotropic and steric effects of the cyano group are negligible as far as the proton SCS are concerned.

Theory

A detailed account of the theory behind CHARGE can be seen in past references[1,11]. A brief account of the latest model (CHARGE7) will be given here. The theory distinguishes between substituent effects over one, two and three bonds which are attributed to the electronic effects of the substituents and longer range effects due to the electric fields, steric effects and anisotropy of the substituents. The CHARGE scheme calculates the effects of atoms on the partial atomic charge of the atom under consideration, based upon classical concepts of inductive and resonance contributions.

If we consider an atom I in a four atom fragment I-J-K-L the partial atomic charge on I is due to three effects. There is an α effect from atom J given by the difference in the electronegativity of atoms I and J. A β effect from atom K proportional to both the electronegativity of atom K and the polarisability of atom I. There is also a γ effect from atom L given by the product of the atomic polarisabilities of atoms I and L. This was shown to be true for I = H and L = F,Cl,Br,I,S. However for the second row atoms (C,O,etc.) the γ effect (i.e. C.C.C.H) is parameterised separately and is given by eqn 1. where θ is the C.C.C.H dihedral angle.

$$\begin{aligned} \mathrm{GSEF} &= A+B_1\cos\theta && 0^0 \le \theta \le 90^0 && (1)\\ &= A+B_2\cos\theta && 90^0 \le \theta \le 180^0 && \end{aligned}$$

and A and B empirical parameters. There are also routines for the methyl γ effect and for the decrease in the γ effect of the electronegative oxygen and fluorine atoms for CX_2 and CX_3 groups.

The total charge is given by summing these effects and the partial atomic charges (q) converted to shift values using eqn. 2

$$\delta = 160.84q - 6.68 \qquad (2)$$

The effects of more distant atoms on the proton chemical shifts are due to steric, anisotropic and electric field contributions. H..H steric interactions in alkanes were found to be shielding and X..H (X = C, F, Cl, Br, I) interactions deshielding according to a simple r^{-6} dependence (eqn 3).

$$\delta_{\text{steric}} = a_S / r^6 \qquad (3)$$

Furthermore any X..H steric contributions on a methylene or methyl proton resulted in a push-pull effect (shielding) on the other proton(s) on the attached carbon.

The effects of the electric field of the C-X bonds (X= H,F,Cl,Br,I,O) were calculated from eqn. 4 where A_Z was determined as 3.67×10^{-12} esu (63 ppm au) and E_Z is the component of the electric field along the C-H bond. The electric field for a univalent atom (e.g. fluorine) is calculated

$$\delta_{\text{el}} = A_Z\ E_Z \qquad (4)$$

as due to the charge on the fluorine atom and an equal and opposite charge on the attached carbon atom. The vector sum gives the total electric field at the proton concerned and the component of the electric field along the C-H bond considered is E_Z in eqn. 4. This procedure is both simpler and more accurate than the alternative calculation using bond dipoles.

The magnetic anisotropy of a bond with cylindrical symmetry such as CN is obtained from eqn. 5, where R is the distance from the perturbing group to the nucleus of interest in Å, φ is

$$\delta_{\text{an}} = \Delta\chi^{\text{CN}}(3\cos^2\varphi - 1)/\ 3R^3 \qquad (5)$$

the angle between the vector R and the symmetry axis and $\Delta\chi^{\text{C-N}}$ the molar anisotropy of the CN bond. ($\Delta\chi^{\text{C-N}} = \chi^{\text{CN}}_{\text{parl}} - \chi^{\text{CN}}_{\text{perp}}$) where $\chi^{\text{CN}}_{\text{parl}}$ and $\chi^{\text{CN}}_{\text{perp}}$ are the susceptibilities parallel and perpendicular to the symmetry axis respectively. This is illustrated in figure 1.

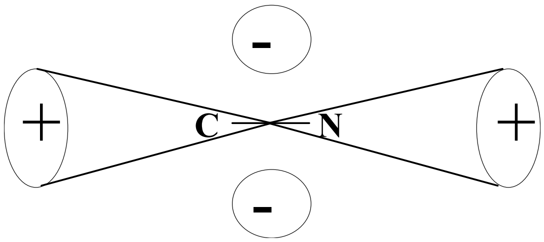


Figure 1: Representation of the anisotropy in an axially symmetric molecule

Aromatic Compounds. For aromatic compounds it is necessary to include the shifts due to the aromatic ring current and the π electron densities in the aromatic ring. The aromatic ring current density is calculated in CHARGE from the Pauling theory and the equivalent dipole approximation is then used to calculate the ring current shifts[1]. This treatment reproduces the proton chemical shifts of a wide range of aromatic hydrocarbons and is incorporated unchanged here.

The π electron densities are calculated from Huckel theory[17]. The standard coulomb and resonance integrals for the Huckel routine are given by eqn. 6, where α_0 and β_0

$$\alpha_r = \alpha_0 + h_r\beta_0$$

$$\beta_{rs} = k_{rs}\beta_0 \qquad (6)$$

are the coulomb and resonance integrals for a carbon $2p_Z$ atomic orbital and h_r and k_{rs} the factors modifying these integrals for orbitals other than sp^2 carbon. For alternant aromatic hydrocarbons this calculation gives π electron densities at every carbon equal 1.0 as in benzene and this is in agreement with the results of more sophisticated calculations[1].

For substituted aromatics the appropriate values of the coefficients h_r and k_{rs} in eqn 6 for the orbitals involving hetero atoms have to be found. These are now obtained in CHARGE so that the π densities calculated from the Huckel routine reproduce the π densities given from ab initio calculations.

The effect of the excess π electron density at a given carbon atom on the proton chemical shifts of the neighbouring protons is given in CHARGE by eqn. 7. Δq_α and Δq_β are the excess π electron density at the α and β carbon atoms and the values of the coefficients a_1 and a_2 were found to be 10.0 and -2.0 res[1].

$$\Delta\delta = a_1\,\Delta q_\alpha + a_2\,\Delta q_\beta \qquad (7)$$

The above contributions are added to the shifts of eqn. 1 to give the calculated shift of eqn 8.

$$\delta_{total} = \delta_{charge} + \delta_{steric} + \delta_{anisotropy} + \delta_{el} + \delta_{\pi} \qquad (8)$$

Application to the cyano Group

The cyano group has in principle steric, electric field and anisotropic effects on protons more than three bonds away plus for aromatics a large effect on the π electron densities. All these have to be incorporated into the model. The electric field of the cyano group is calculated in an identical manner to any other C-X bond. The electric field is calculated as being due to the charge on the nitrogen atom of the CN and an equal and opposite charge on the carbon atom of the CN bond. The charge on the nitrogen atom is already calculated in CHARGE and the coefficient in eqn.4 is known so the electric field is given without any further parameterisation.

This of course assumes that the charges used in eqn 4 provide a reasonable measure of the electric field of the cyano group. The partial atomic charges obtained in the CHARGE programme have been derived from the observed molecular dipole moments and the extent of the agreement provides one check on the electric field calculation. The calculated vs observed (in parenthesis) dipole moments[18] (in debye) of acetonitrile, propionitrile, t-butylcarbonitrile, **1a**, **1b**, acrylonitrile and benzonitrile are 3.81 (3.97), 3.77 (4.02), 3.82 (3.95), 3.87 (3.82), 3.65 (3.76) , 4.11 (3.89) and 4.15 (4.14) and the good agreement provides strong support for the electric field calculation.

The CN group has cylindrical symmetry and eqn.5 may be used to calculate the contribution of the anisotropy to the proton chemical shifts. The steric effects of the CN group are calculated by use of eqn.**3**. The unknowns to be obtained are $\Delta\chi$, the molar anisotropy of the CN bond and the steric coefficient $\mathbf{a_s}$.

For protons of three bonds or less from the CN group it is necessary to determine the orientational dependence of the γ proton chemical shift w.r.t. the cyano carbon. This is simulated by a γ substituent effect (GSEF) from the cyano carbon following eqn 1, in which the coefficients A and B may differ for the CN group in aromatic vs saturated compounds. There is also a possible effect from the nitrogen atom which affects the β protons and as this has no orientation dependence it may be considered as dependent only on the polarisability of the nitrogen atom.

For the aromatic cyanides it is first necessary to obtain the appropriate values of the factors h_r and k_{rs} which give the Huckel integrals for the CN group (eqn 6). An iterative least mean square programme (CHAP8)[19] was used to obtain the best fit values of these parameters from π electron densities obtained from GAUSSIAN94[20] calculations. The π electron densities and dipole moments from these *ab initio* calculations are very dependent on the basis set used. As the 3-21G basis set gave the best agreement with the observed dipole moment, the π densities from this basis set were used to parameterise the Huckel calculations. Values of h_r of -0.12 and 0.19 for C(sp) and N(sp) and of k_{rs} of 1.05 for (Csp^2-Csp) and 1.20 for (Csp-Nsp) gave π electron densities for the aromatic nitriles in reasonable agreement with those from the ab initio calculations. The electron densities (total and π) and dipole moments calculated for benzonitrile by CHARGE and GAUSSIAN94 are given in table.1

Table 1. Total and π (in parenthesis) charges (me), and dipole moments for benzonitrile

Atom	Method				
	STO-3G	3-21G	6-31G	CHARGE	Obs
N(sp)	-200 (-49)	-504 (-87)	-273 (-63)	-484 (-137)	
C(sp)	73 (26)	338 (31)	21 (52)	390 (109)	
C_1	2 (-56)	-58 (-77)	10 (-76)	13 (-9)	
C_o	-42 (24)	-194 (37)	-148 (37)	-47 (14)	
C_m	-58 (2)	-232 (0)	-212 (1)	-72 (-1)	
C_p	-49 (28)	-227 (36)	-180 (34)	-66 (11)	
μ (D)	*3.65*	*4.55*	*4.82*	*4.15*	*4.14*

Experimental

Trans and cis-4-t-butylcyclohexanecarbonitrile (**1a,1b**) were synthesised by dehydration of the corresponding amide by reaction with phosphorus oxychloride[21]. Cyclohexanecarbonitrile (**2**), trans-1,4-dicyanocyclohexane (**3**) , acetonitrile(**6**), benzonitrile (**10**), o, m and p-dicyanobenzene (**11**,**12**,**13**), 1 and 2-naphthalenecarbonitrile (**14**,**15**) and 9-anthracenecarbonitrile (**16**) were obtained commercially[22,23].

^{1}H and ^{13}C NMR were obtained on a Bruker AMX400 spectrometer operating at 400MHz for proton and 100.63MHz for carbon. The spectra for **1a** and **1b** were recorded on a Varian 750MHz spectrometer at GlaxoWellcome[24]. HMQC, HMBC and NOE experiments were also performed with this spectrometer.

The spectra were recorded in 10mg cm^{-3} solutions (^{1}H) and ca.50mg cm^{-3} (^{13}C) with a probe temperature of ca.25°C in CDCl$_3$ and referenced to TMS. Typical running conditions of the spectrometers were 128 transients, spectral width 3300Hz and 32k data points to give AT of 5s. The FID were zero-filled to 128k to give a digital resolution of 0.025Hz.

The 2D experiments were conducted using the Bruker AMX400 and Varian 750MHz machines using the standard Bruker COSY-DQF and HXCO-BI and the standard Varian HMQC and GHMQC-DA pulse sequences[25,26]. The geometry of the compounds investigated were obtained by use of the program PC MODEL Version 7.0[27] and were also optimised using the GAUSSIAN 94W programme at the RHF/6-31G* and MP2/6-31G* levels[20]. The GAUSSIAN 94W and CHARGE calculations were performed on a PC.

Spectral Assignments

The spectral assignments of the compounds examined are given in tables 3-7 along with the calculated values from the CHARGE7 model.

Trans and cis- 4-t-butylcyclohexanecarbonitrile (1a,1b). The ^{1}H, ^{13}C, 2-D and NOE spectra for the 4-t-butylcyclohexanes were recorded at both 400 and 750MHz. The cis and trans isomers were not separated and the spectra recorded together. This was not a problem as the spectra are well resolved and all the resonance's may be distinguished from each other.

(1a). The 750MHz ^{1}H NMR spectrum of this compound consists of six proton resonance's, excluding the methyl resonance's. The 1a, 2e and 2a protons are readily assigned but the resonance's at ca.1.50ppm and 1.0ppm contain 2 and 3 protons respectively and it was necessary to perform 2-D and NOE experiments. By examination of the ^{1}HCosy, the resonance at ca.1.5ppm is shown to contain the H-2a proton and this was confirmed by NOE experiments. Further NOE experiments assigned H-3e, H-3a and H-4a. A HetCor plot plus the known assignments of the ^{13}C spectra for the cis and trans compounds[28] further confirmed these assignments.

(1b). The ^{1}H NMR spectra for this compound was easy to assign as all the proton resonance's are separate. The only uncertainty was for H-2a (ca.1.52ppm) and H-4a (ca.0.9ppm) which overlap with the H-3a and H-4a protons of the trans compound. These were assigned from the ^{1}HCosy spectrum and NOE experiments on H-1e, H-2e and H-3e confirmed these assignments.

Axial and equatorial-cyclohexanecarbonitrile (2a,2b). The spectra of the separate conformers were obtained by obtaining the spectra at -60°C. The equatorial conformer was the more favoured with ΔE (ax - eq) = 0.27 kcal mol^{-1} in agreement with literature values (0.2 kcal mol^{-1}) [29]. A ^{1}H Cosy spectrum was recorded at -60°C to fully assign the two conformations. Because of the number of different protons within these conformers, the exact chemical shifts could only be approximated due to much overlapping of the resonance's.

(**2a**). Protons 1e, 2e are easily assigned and inspection of the ^{1}HCosy spectrum plus the integrals of the ^{1}H spectrum gave the assignments of the remaining protons, but due to much overlapping of the resonance's the exact chemical shifts can only be approximated.

(**2b**). The same can be said for the equatorial conformer. H-1a and H-2e can be clearly identified and also H-2a, H-3e and H-3a from the COSY plot. However, as with the axial carbonitrile the chemical shifts of the H-4 protons are less accurate.

ax-ax and eq-eq trans-1, 4-dicyanocyclohexane (3a,3b). The commercial sample of 1,4-dicyanocyclohexane was identified as the trans isomer from the m.pt. of 140-141°C. (cf lit. 139-140°C[30]). This was further confirmed by the pmr spectrum The spectrum has three distinct signals at room temperature and each conformer has three distinct signals at low temperature. The cis conformer would be expected to show three separate resonance's at room temperature and six resonance's from the one conformer at low temperature.

The -60°C spectra was assigned by recording spectra every 20°C and following the coalescence of the peaks and finally the emergence of the individual conformers at -60°C. From these experiments and the integration of the peaks the low temperature spectra was assigned as there are only 3 inequivalent protons in each conformer. The di-equatorial conformer was the more stable (1.5/1.0 ratio) with ΔE (ax - eq) = 0.17 kcal mol^{-1}.

The proton chemical shifts of the individual conformers of compounds **2** and **3** were measured at low temperatures (-60^{0}C). Thus it was of interest to determine whether there was an intrinsic temperature dependance of their chemical shifts. This was achieved by measuring the spectra of **1a** and **1b** at various temperatures and the results are shown in table 2. It can be seen that the only protons experiencing a significant (> 0.05ppm) change in their chemical shifts on going from RT to -60^{0}C are the H-1 protons in both **1a** and **1b**. δ (H1eq) changes by 0.098ppm and δ (H1ax) changes by 0.072ppm. and the corresponding protons in compounds **2** and **3** are corrected by these amounts subsequently.

Table 2. Proton chemical shifts (δ) of trans and cis-4-t-butyl-cyclohexanecarbonitrile (**1a,1b**) as a function of temperature.

^{1}H Number	Trans			Cis		
	R.T	-20^{o}C	-60^{o}C	R.T	-20^{o}C	-60^{o}C
1e	------------	------------	------------	2.921	2.973	3.019
1a	2.314	2.347	2.388	------------	------------	------------
2e	2.161	2.179	2.192	2.037	2.059	2.077
2a	1.529	1.535	1.550	1.516	1.520	1.528
3e	1.855	1.856	1.862	1.771	1.782	1.794
3a	0.981	0.985	0.990	1.367	1.341	1.324
4a	1.023	1.025	1.030	0.986	0.986	0.987

Aromatic Nitriles. The full analysis and assignment of benzonitrile (**10**) and ortho (**11**) and meta (**12**) dicyanobenzene have been given previously[31,32] and our analyses follow these assignments. The 400MHz pmr spectra of (**10**) and (**11**) were analysed using the LAOCOON programme[33] to give accurate chemical shifts. The pmr spectrum of (**12**) is first order and that of para dicyanobenzene is a single line. The pmr spectra of 1 and 2-naphthalenecarbonitrile (**14,15**) have not been analysed previously. The spectrum of both (**14**) and (**15**) at 400MHz consist of seven well separated resonance's and both assignments were made with the help of COSY and particularly HETCOR plots together with the known assignments of the ^{13}C spectra[28].

The assignment of both the proton and ^{13}C spectrum of 9-anthracenecarbonitrile (**16**) has been given previously[34] and our analysis confirmed this assignment. The proton chemical shifts for propionitrile (**7**), iso-butyronitrile (**8**), trimethylacetonitrile (**9**) and acrylonitrile (**17**) were measured directly from the Aldrich ^{1}H NMR catalogue[10].

Results and Discussion

The data for the aromatic nitriles obtained here in dilute $CDCl_3$ solution is in excellent agreement with the earlier data obtained in CCl_4 solution[32]. For example the ortho, meta and para proton shifts in benzonitrile in $CDCl_3$ and in CCl_4 solution (in parentheses) are 7.660 (7.631), 7.482 (7.452) and 7.559 (7.552). As found previously for the aromatic hydrocarbons[1] there is a small almost constant shift to higher δ values in $CDCl_3$ compared to CCl_4. Thus the proton SCS for the cyano group obtained by earlier investigations may be used unchanged for the $CDCl_3$ solutions used here.

The data obtained for the cyano compounds may be combined with the proton chemical shifts of the parent compounds given previously[1,12] to give the cyano SCS in these compounds. These are shown in figure 2 for the 4-t-butyl cyclohexanecarbonitriles (**1a, 1b**) and 1 and 2 cyanonaphthalene (**14,15**), together with the corresponding SCS found earlier for 2-exo and 2-endonorbornane (**4a, 4b**) and are of some interest. The SCS are invariably deshielding. The SCS on the β protons (H.C.CN) is almost constant at 1.24 (± 0.04) ppm. The γ effect of the CN group (i.e. H.C.C.CN) is also deshielding with for the saturated nitriles little orientational dependance. E.g. the 2ax and 2eq protons in **1a** and **1b** and the 3-exo and 3-endo protons in **4a** and **4b** all give almost identical SCS of 0.41 (± 0.02) ppm.

The long range (> 3bonds) effects of the cyano group are also large and extend over both the cyclohexane and bicycloheptene system. For **1a** the CN-SCS decreases with increasing distance of the proton from the CN, with the equatorial protons generally displaying a greater CN-SCS than the axial protons. However for **1b** the SCS of H-3a is very large. Similar large effects are observed at the 7syn protons in **4a** and the 6-endo protons in **4b**. All these protons are in a similar environment to the cyano group, i.e. essentially orthogonal to the CN bond. Although these SCS can be due to either the CN anisotropy or electric field, significantly the CN SCS at protons situated along the CN bond (e.g. the 3ax and 3eq protons in **1a**, the 7syn protons in **4b** etc.) is also deshielding which would not be the case if the SCS were primarily due to the CN anisotropy. This suggestion will be shown to be verified by the detailed analysis in terms of the CHARGE model. Similar CN SCS are observed for the aromatic nitriles **14** and **15** though in these compounds π electron effects will be present. Again all the SCS are deshielding and they are considerable even for the protons in the non-substituted aromatic ring.

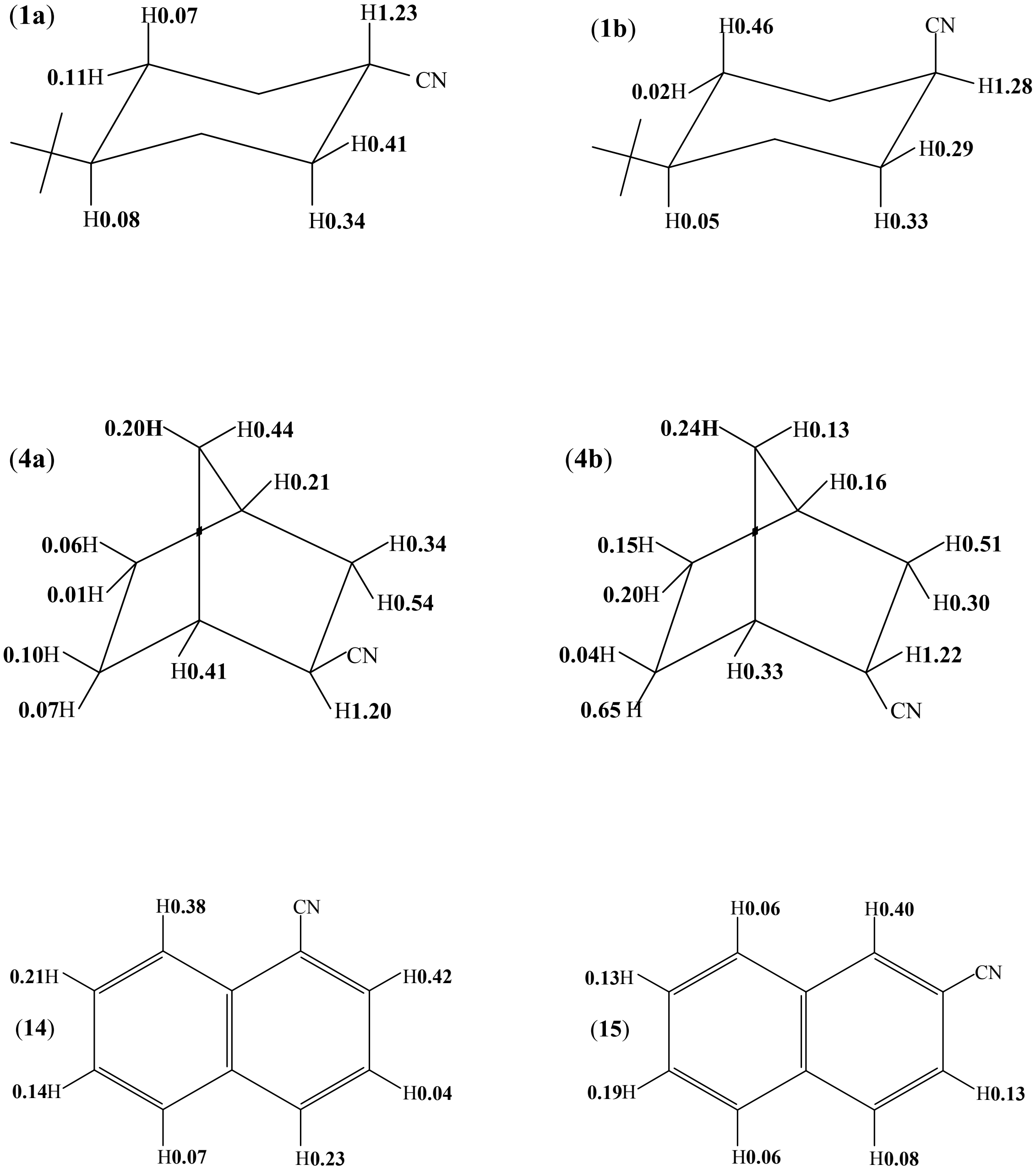


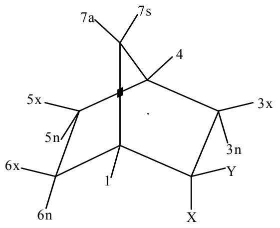
Figure 2: Cyano SCS in aliphatic and aromatic molecules

Table 3. Observed vs calculated proton chemical shifts (δ) in trans and cis 4-t-butyl-cyclohexanecarbonitrile (**1a,1b**), axial and equatorial cyclohexanecarbonitrile (**2a,2b**) and ax-ax and eq-eq trans-1,4-dicyanocyclohexane (**3a,3b**)

H no.	1a		1b		2a [a]		2b [a]		3a [a]		3b [a]	
	Obs	Calc	Obs	Calc	Obs	Calc	Obs	Calc	Obs	Calc	Obs	Calc
1e	------	------	2.921	2.886	2.960	2.859	------	------	3.040	2.999	------	------
1a	2.314	2.416	------	------	------	------	2.386	2.342	------	------	2.445	2.440
2e	2.161	2.067	2.037	2.076	2.000	2.035	2.076	2.034	2.009	2.196	2.208	2.184
2a	1.529	1.646	1.516	1.641	1.538	1.587	1.521	1.591	1.918	1.990	1.582	1.695
3e	1.855	1.807	1.771	1.824	1.700	1.788	1.760	1.776	------	------	------	------
3a	0.981	0.985	1.367	1.290	1.500	1.575	1.220	1.284	------	------	------	------
4e	------	------	------	------	1.700	1.763	1.700	1.730	------	------	------	------
4a	1.023	1.095	0.986	1.078	1.200	1.254	1.220	1.277	------	------	------	------

a). -60°C, protons 1e and 1a have been corrected by 0.098 and 0.072ppm res.

Table 4. Obs. vs Calc. Proton Chemical shifts (δ) for 2-exo **(4a)** and 2-endo **(4b)** norbornanecarbonitrile**,**

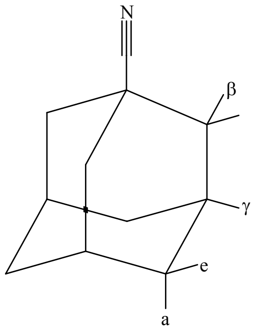


(**4a**) X=H, Y=CN (Exo)
(**4b**) X=CN, Y=H (Endo)

^{1}H Number	4a		4b	
	Observed [a]	Calculated	Observed [a]	Calculated
1	2.599	2.402	2.520	2.373
2x	------------------	------------------	2.694	2.873
2n	2.360	2.539	------------------	------------------
3x	1.810	1.947	1.982	1.928
3n	1.697	1.664	1.458	1.631
4	2.397	2.204	2.348	2.182
5x	1.528	1.643	1.619	1.641
5n	1.171	1.328	1.356	1.400
6x	1.570	1.620	1.505	1.639
6n	1.225	1.402	1.814	1.835
7s	1.621	1.533	1.308	1.290
7a	1.381	1.356	1.417	1.335

a) ref 9.

Table 5. Obs. vs Calc. Proton Chemical shifts (δ) for 1-adamantanecarbonitrile(**5**) and the acyclic nitriles.



(5)

Compound		Obs[a]	Calc	Compound		Obs[b].	Calc.
(5)	β	2.04	1.97	CH_3CN		2.03	2.07
	γ	2.04	2.12	CH_3CH_2CN	Me	1.30	1.22
	e	1.74	1.76		CH_2	2.47	2.44
	a	1.74	1.77	Me_2CHCN	Me	1.35	1.28
acrylonitrile	gem	5.66	5.86		CH	2.78	2.80
	cis	6.24	6.09	t-BuCN	Me	1.40	1.33
	trans	6.10	5.94				

a) ref 9, b) ref 10

Table 6. Observed vs Calculated Proton chemical shifts (δ) of benzonitrile(**10**), o, m and p-dicyanobenzene(**11**,**12**,**13**)

	(**10**)		(**11**)		(**12**)		(**13**)	
Proton	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.
H2	7.660	7.684	--------	--------	7.971	8.042	7.806	7.876
H3	7.482	7.550	7.850	7.888	--------	--------	7.806	7.876
H4	7.615	7.576	7.782	7.775	7.916	7.916	--------	--------
H5	7.482	7.550	7.782	7.775	7.671	7.760	7.806	7.876
H6	7.660	7.684	7.850	7.888	7.916	7.916	7.806	7.876

Table 7. Observed vs Calculated Proton chemical shifts (δ) for 1 and 2-naphthalenecarbonitrile (**14**,**15**) and 9-anthracenecarbonitrile (**16**)

	(14)		**(15)**		**(16)**	
Proton	Observed	Calculated	Observed	Calculated	Observed	Calculated
H1	------------	------------	8.245	8.245	8.431	8.362
H2	7.900	7.897	------------	------------	7.728	7.779
H3	7.512	7.721	7.611	7.779	7.596	7.699
H4	8.069	8.112	7.925	8.012	8.089	8.181
H5	7.916	7.928	7.908	7.895	------------	------------
H6	7.612	7.564	7.663	7.566	------------	------------
H7	7.685	7.624	7.610	7.548	------------	------------
H8	8.226	8.133	7.907	7.935	------------	------------
H10	------------	------------	------------	------------	8.691	8.956

The data collected in tables 3-7 provide a rigorous test of the application of both the CHARGE model and also of present theories of cyano SCS. All the molecules considered are of fixed conformation and the geometries calculated by ab initio calculations, thus the only empirical parameters to be determined are those required for the model. These have been given earlier and are the anisotropy and steric coefficient of the cyano group and the factors involved in the γ effect (eqn 1). The anisotropy of the CN bond $\Delta\chi^{CN}$ was taken from the centre of the CN bond and the steric effect of the sp carbon atom from the atom considered. The nitrogen atom was considered to be of a sufficient distance from the protons of the molecules considered here to have no noticeable steric interaction with them. There is however a possible γ-effect from the nitrogen of the CN group (i.e.H.C.CN) which was considered as a polarisability effect (see theory).

Thus the entire data set of tables 3-7 is calculated with a total of ten possible parameters which are the anisotropy of the CN bond, the carbon steric effect, the γ effect of the sp carbon atom (coefficients A and B eqn 1) which may differ for aliphatic and aromatic nitriles and the nitrogen polarisability.

An iterative programme (CHAP8[19]) was used to determine the best fit values of all these parameters using all the above data a total of 93 shifts. Iterations were carried out including both the steric and anisotropy terms, the anisotropy alone and the steric term alone. All iterations performed yielded little or no improvement of the calculated chemical shifts than those calculations performed with no steric or anisotropic terms present. It was therefore concluded that the steric and anisotropic terms of the cyano group were negligible and the major factor influencing the long range proton chemical shifts was the electric field effect.

The final parameterisation of the cyano group therefore included electronic effects for protons 2 or 3 bonds removed and the electric field effect for protons 3 or more bonds away. It was found that eqn. 1 could be further simplified with $B_1=B_2$. Thus the entire data set was reproduced with only five parameters.The values of the coefficients A and B in eqn 1 were obtained as 0.110 and -0.047 for the saturated nitriles and -0.185 and 0.030 for the unsaturated nitriles. The orientation dependance of the γ CN effect (H.C.C.CN) is very small in both the saturated and unsaturated compounds. The nitrogen polarisability was obtained as 0.19 somewhat less than the value used previously (0.44).

Discussion

Aliphatic nitriles. The 62 proton chemical shifts of the saturated nitriles in tables 3-5 range from ca.0.70 to 3.50δ and are predicted with an rms error of 0.087ppm. and the generally good agreement between the observed and calculated shifts can be seen from the tables. The agreement for the cyclohexane derivatives shown in table 3 is excellent with the largest error ca 0.15ppm and the great majority of shifts reproduced to <0.1ppm.

The agreement for the norbornanes (table 4) is not as good and this is due to the larger errors in the observed vs calculated shifts in the parent compounds than for the cyclohexanes due to the difficulty of reproducing the proton shifts in these highly strained molecules with a simple model. This is confirmed by the much better agreement between the observed and calculated SCS for these compounds (table 8).

Table 8. Obs. vs Calc. SCS for 2-exo **(4a)** and 2-endo **(4b)** norbornanecarbonitrile

^{1}H Number	4a		4b	
	Observed	Calculated	Observed	Calculated
1	0.41	0.43	0.33	0.40
2x	------------------	------------------	1.22	1.34
2n	1.20	1.30	------------------	------------------
3x	0.40	0.41	0.51	0.39
3n	0.54	0.42	0.30	0.45
4	0.21	0.23	0.16	0.21
5x	0.06	0.11	0.15	0.11
5n	0.01	0.09	0.19	0.16
6x	0.10	0.09	0.09	0.10
6n	0.06	0.16	0.65	0.60
7s	0.44	0.30	0.13	0.06
7a	0.20	0.12	0.24	0.10

In particular the SCS for H-1,H-2 and H-4 are in good agreement with the observed SCS confirming that the calculations of the CN SCS given are accurate even for these systems. The large deshielding of the H-6endo in **2b** is particularly well reproduced showing that this simple electric field model gives excellent agreement with the observed SCS.

The calculated chemical shifts for the acyclic molecules (table 5) are also in good agreement with the observed shifts. This is of some interest as Zurcher[6] could not predict the α-proton chemical shifts in these compounds (H.C.CN) or in norbornenecarbonitrile using only the electric field effects of the CN and concluded that other effects besides the linear electric field effect must be present. Zurcher also found that the calculated chemical shifts of protons three bonds from the CN group (H.C.C.CN) in 2-endo/exo-norbornenecarbonitrile and 1-adamantanecarbonitrile were very different from the observed chemical shifts and again suggested that factors other than linear electric field effects must be present. He suggested the different steric environments of particular protons and their interactions with the solvent molecules.

ApSimon et al[7] came to similar conclusions. They examined the long range shielding effects of the CN group on methyl protons in several cyano-steroids and also on the ring protons in 2-endo/exo-norbornenecarbonitrile. They obtained a poor correlation between the observed and calculated shifts and they also concluded that a modification of the solvent-solute interaction may be responsible for the poor correlation of some protons.

However it is clear from the present analysis that all these effects can be quantitatively explained in terms of the carbon and nitrogen γ effects outlined above. It is of interest to consider the actual magnitudes of the contributions to the cyano SCS and Table 9 gives the observed vs calculated CN-SCS for **1a** and **1b** with the calculated electric field and steric contributions. The contributions to the CN-SCS include effects due to the removal of the hydrogen in forming the CN derivative. These are the C-H electric field and the steric effect of the hydrogen. However the dominant effect for all long range protons can be seen to be the CN electric field effect.

For protons that are >3 bonds away from the cyano group the sum of the components gives the total calculated SCS. For the H-2e/H-2a protons the components do not add up to give the calculated value of the CN-SCS as these protons experience γ-electronic effects (eqn 1.) Even in these cases the electric field effect is the major effect.

Table 9. Observed vs calculated CN-SCS with the C-CN/C-H electric field and H-steric contributions for trans (**1a)** and cis **(1b**) 4-t-butylcyclohexanecarbonitrile.

Compound	Proton No.	Obs. SCS	Calc. SCS	C-CN Electric Field	C-H Electric field	H-Steric
(**1a**)	2e	0.411	0.413	0.332	-0.001	0.000
	2a	0.339	0.413	0.336	-0.001	0.000
	3e	0.105	0.153	0.120	0.027	0.006
	3a	0.071	0.108	0.079	0.017	0.012
	4a	0.083	0.090	0.061	0.022	0.007
(**1b**)	2e	0.287	0.408	0.344	-0.001	0.000
	2a	0.326	0.422	0.262	-0.001	0.000
	3e	0.021	0.170	0.153	0.005	0.012
	3a	0.457	0.413	0.270	0.040	0.103
	4a	0.046	0.073	0.070	-0.005	0.009

Aromatic Nitriles.

The aromatic nitriles have other mechanisms which may affect the proton chemical shifts, in particular the ring current and π electron effects. The ring currents in the aromatic hydrocarbons are calculated in CHARGE on the basis of the Pauling theory in which the emf of a current loop is proportional to the area enclosed and the resistance proportional to the number of bonds in the circumference[1]. In this treatment the ring current intensity of the naphthalene, anthracene and benzene rings are all different. The further assumption is made here that the introduction of the cyano group has no effect on the parent hydrocarbon ring current. Thus there are no ring current effects on the CN SCS. In contrast the CN group does affect the π electron densities and this has a significant effect on the CN SCS.

The observed versus calculated proton chemical shifts for the aromatic nitriles are given in tables 6 and 7 and the observed vs calculated SCS for benzonitrile (**10**) , 1 and 2-naphthalene carbonitrile (**14,15**) and 9-cyanoanthracene (**16**) in table 10 together with the calculated contributions to the CN SCS.

There is again generally good agreement between the observed and calculated shifts with the majority of shifts predicted to 0.1ppm. and the majority of SCS to <0.05ppm. The large deshielding of the peri protons H-8 in **14** and H-1 in **16** is well predicted, again demonstrating the accuracy of the electric field calculation even at these short interatomic distances. There are also some discrepancies. The difference between the observed and calculated shift for H-3 in **14** is 0.21ppm. whereas the corresponding meta proton in benzonitrile is predicted quite well (7.48 vs 7.55).

Table 10. Observed vs Calculated CN SCS with the electric field and π electron contributions for benzonitrile(**10**) and 1and 2-naphthalenecarbonitrile(**14,15**) and 9-cyanoanthracene (**16**).

Compound	Proton No.	Observed	Calculated	CN El. Field	C-H El. field	π Shift
(**10**)	2,6	0.319	0.347	0.370	0.000	0.116
	3,5	0.141	0.213	0.127	0.046	0.044
	4	0.274	0.239	0.096	0.036	0.107
(**14**)	2	0.423	0.404	0.375	0.000	0.169
	3	0.035	0.228	0.126	0.046	0.059
	4	0.225	0.283	0.096	0.035	0.154
	5	0.072	0.099	0.058	0.014	0.028
	6	0.135	0.071	0.054	0.010	0.008
	7	0.208	0.131	0.089	0.012	0.032
	8	0.382	0.304	0.333	0.074	0.001
(**15**)	1	0.401	0.416	0.376	0.000	0.180
	3	0.134	0.286	0.367	0.000	0.059
	4	0.081	0.183	0.127	0.046	0.014
	5	0.064	0.066	0.040	0.013	0.012
	6	0.186	0.073	0.035	0.000	0.037
	7	0.133	0.055	0.039	0.000	0.015
	8	0.063	0.106	0.050	0.021	0.037
(**16**)	1	0.422	0.416	0.336	0.070	0.000
	2	0.261	0.226	0.092	0.010	0.055
	3	0.129	0.146	0.055	0.008	0.011
	4	0.080	0.235	0.059	0.010	0.048
	10	0.260	0.549	0.099	0.027	0.252

Table 10 shows that the observed SCS for H-3 in benzonitrile is 0.14 whereas the observed SCS for H-3 in **14** is 0.04. The calculated SCS for these protons are very similar as would be expected. It would appear that the CN SCS differ significantly in the naphthalene and benzene rings, an interesting effect. The calculated shift of the H-10 proton in **16** is also too large by 0.27ppm. and table 10 shows that this error is due to the calculated SCS for this proton. This is probably due to the approximations in the Huckel treatment used which tends to overestimate the π-electron changes in substituted condensed aromatics such as anthracene.

A number of investigators have attempted to explain the proton SCS in aromatic molecules in terms of the π and σ effects of the substituent groups and it is of some interest to consider their results in the light of the above calculations. Hehre et al[35] reviewed the early work in this area and attempted to interpret proton and carbon SCS in substituted benzenes in terms of the charge distributions as calculated by ab initio theory. They like other investigations only considered the meta and para protons as the ortho protons “are subject to other effects”.

The para carbon in benzonitrile had a decreased π electron density (wrt benzene) and an slight increase in the σ electron density. In the meta carbon in contrast the π electron density is the same as in benzene but the σ electron density increases. They correlated the chemical shift of the meta proton with the sum of the σ-charges at the proton and at the attached carbon. The chemical shift of the para proton was correlated with the total charge density at the carbon atom but displayed little dependence on the charges at the hydrogen atom. They also found that the proton SCS could be approximately correlated with the hydrogen atom charge densities plus a term in the total π-charge density transferred from the substituent to the benzene ring. This π-charge transfer was presumed to account for the ring current effects.

These investigations could not find any direct link between the electron densities at the specific atoms and the proton chemical shifts. They concluded that the proton SCS depend on factors other than the electron densities at the hydrogen atom and adjoining carbon atom. It is a pity that these investigations did not attempt to correlate the proton SCS with the π-charge density at both the attached and neighbouring carbon atoms (cf eqn. 7) as this approach has been successful for both the cyano derivatives studied here and a range of monosubstituted benzenes[1].

An alternative investigation of proton SCS in benzenes is by the use of the field and resonance components of substituent effects (***F*** and ***R***) obtained by Swain and Lupton[36]. The proportions of field and resonance effects on the CN SCS at any proton can be obtained from eqn 11 used by Swain and Lupton to determine the substituent constant, σ:

$$\sigma = \boldsymbol{f}\mathrm{F} + \boldsymbol{r}\mathrm{R} \tag{11}$$

Where σ is the substituent constant and *f* and *r* are weighting factors. Replacing σ with the proton SCS and using the values of F and R for the CN group of 0.847 and 0.184 from ref 36 allows the determination of the coefficients ***f*** and ***r*** . This was done by an iterative least means square analysis using all the data of tables 5 and 6. This gave values of 0.098 and 0.376 res. for the meta proton SCS and 0.142 and 0.946 for the para proton SCS. The field and resonance contributions to the proton SCS ($\boldsymbol{f}\mathrm{F}$ and $\boldsymbol{r}\mathrm{R}$) are thus given from eqn 11 as 0.083 and 0.069 for the meta protons and 0.120 and 0.174 for the para protons.

It is of some interest to compare these values with the calculated contributions to the proton SCS in table 10. For benzonitrile the meta proton SCS has electric field and π charge contributions of 0.121 and 0.044 res. and for the para proton SCS the calculated contributions are 0.092 and 0.107 res. These values are in very good agreement with the values obtained by the Swain and Lupton treatment although they are based on a totally different conceptual treatment and this gives strong support for the model used in these calculations.

Conclusions

The CN-SCS over more than three bonds is determined by linear electric field effects only, without the need to include any steric or anisotropic effects. The short range CN SCS (≤ 3bonds) requires the inclusion of a γ effect from both the carbon and nitrogen of the CN substituent and these contributions plus the electric field effect for the γ protons (H.C.C.CN) are used to calculate the chemical shifts of the α and β protons respectively. The γ effect of the cyano carbon atom has a very small orientational dependence. The γ effect of the nitrogen (H.C.CN) which cannot have an orientation effect, is modelled by adjusting the nitrogen polarisability. In the aromatic nitriles the field effect of the cyano group is much larger than the resonance (π electron) effects at the ortho and meta protons but the two effects are almost equal at the para protons.

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