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Comparative Study of Models and Basis Sets in the Chemical Shifts Calculations of α-Mono-Substituted Acetonitriles

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Abstract: *^{1}H and ^{13}C NMR experimental chemical shifts for the α-CH_2 and CN groups of some α-monosubstituted acetonitriles are reported and compared to theoretical values. GIAO and CSGT models at DFT/B3LYP level of theory, using different basis sets, were employed for the chemical shifts calculations. The best agreement of theoretical with experimental data for α-CH_2 ^{1}H chemical shifts and for CN ^{13}C chemical shifts groups were obtained through cc-pVTZ basis set using GIAO and CSGT models, respectively. For the α-CH_2 ^{13}C chemical shifts the best agreement was obtained either through cc-pVDZ or 6-31G(d,p) basis set using GIAO or CSGT models, respectively.*

Introduction

Aliphatic Nitriles

Nitriles are versatile synthetic intermediates and are of considerable importance in all branches of chemistry.[1] The cyano group presents unique properties, when compared to other organic functional groups. The cyanide anion also has specific properties such as high toxicity, distinguishing it from other inorganic anions. This property is attributed to its ability to bind to hemoglobin, which blocks the respiratory cycle.[2] Although hydrocyanic acid is very weak (pk_a 9.21),[3] the cyano group presents a strong electron-withdrawing effect in comparison to other substituents (group electronegativity: CF_3 2.985; CN 3.208 and NO_2 3.421).[4] The cyano group presents a high dipole moment (3.44 D) as compared to other usual high dipole moments (C-F 1.43 D; C=O 2.25 D),[5] which confers high dielectric constants on nitriles and turn them into very useful polar aprotic solvents.

The classical description of the cyano group involves *sp* carbon and nitrogen atoms, making a σ and two π bonds, resulting in a linear arrangement. The large dipole moment of the cyano group has been attributed to the nitrogen electron lone pair directed along the CN axis, which has been also considered as a *sp* hybrid orbital.[1] A consequence of this arrangement is its small size, when attached to an alkyl chain, in comparison to NO_2 and CF_3. It is similar to a Br substituent. Taft's steric effect (-051) is the smallest among all the common substituents, with the exception of F (-0.46),[4] which precludes the occurrence of steric effects due to the CN group.

The high dipole moments are responsible for self-association, reflected in their high boiling points and high viscosity.[6]

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Allerhand and Schleyer showed that the basic properties of a series of aliphatic nitriles are correlated with Taft's $\sigma*$.[7] It was also observed that the introduction of a sulphur atom at the α-position leads to a decrease in their basic character, which is attributed to an orbital interaction between sulphur orbitals and the cyano group.[8]

Infrared and ultraviolet data of some cyano-derivatives showed that the cyano group effect is similar to that of other strong electron-withdrawing groups.[1] Infrared studies of α-alkylthionitriles have also indicated the occurrence of orbital interactions in these systems.[9]

The chemical shift of the CH_3 protons in acetonitrile is shielded, like in acetylenes, due to the anisotropic effect of the $C\equiv N$ group.[1] However, the ^{13}C chemical shift of the cyano carbon is deshielded (δ~120) in comparison to the acetylene carbon (δ ~70),[10] due to the polar effect of the nitrogen atom.

Several studies on molecular orbital calculation on aliphatic nitriles, through *semi-empirical* methods, were published in the 1980s. A first report on *ab initio* calculation gave a good agreement between microwave data and theoretically calculated rotational constants. It was observed that polar substituents lead to a bending in the C- C≡N system (*e.g.* bending angle of ~2° for F-C- C≡N).[11] Studies on the anomeric effect by an *ab initio* method showed that the *gauche* is more stable than the *trans* conformer of α-methoxyacetonitrile, in agreement with experimental data.[12]

NMR chemical shifts

It is well known that NMR spectroscopy is one of the most powerful and extensively used experimental technique to probe the electronic and molecular structure of organic compounds. A significant NMR spectral information is the chemical shift, used for structural assignments.[10] Relationships between chemical shifts and molecular structure have commonly been established by empirical rules.[13]

Recently, NMR chemical shift theoretical calculations have proved to be a useful tool for the interpretation of experimental data.[14-20] NMR experimental data, together with theoretical calculation, allows unequivocal structural assignments of the system under study. Chemical shift theoretical calculation exists since the 1970's, when electronic wave functions were expanded in terms of atomic orbitals.[21,22] The use of atomic basis sets of finite size yields a dependence of the chemical shift upon the chosen gauge origin of the vector potential, which describes the external magnetic field.[14] Many different methods were developed to solve this so-called gauge origin problem, where the most used method is the gauge-including atomic orbital (GIAO).[14] Other class of methods is the set of gauge transformation (SGT). This method includes the individual gauges for atoms in molecules method (IGAIM) and the continuous set of gauge transformation (CSGT).[23,24]

The choice of theory level, Hartree-Fock (HF) or DFT/B3LYP, and basis sets are crucial for a correct prediction of the theoretical chemical shift. It has been observed[21] for small molecules that HF and B3LYP at 6-31G* levels of theory predict ^{13}C chemical shifts with comparable accuracy. The RMS error for HF is 11.1 ppm, while for B3LYP is 12.5 ppm. When the theory was improved at B3LYP/6-311+G(2d,p) level an RMS error around 4.2 ppm was obtained.[21]

In the present study two different models, GIAO and CSGT,[14] and three different basis sets, 6-31G(d,p), cc-pVDZ and cc-pVTZ[25,26] were applied to predict NMR shielding tensor at the DFT/B3LYP[28,29] level of theory. α-Substituted acetonitriles (X = H, F, Cl, Br, I, OMe, OEt, SMe, SEt, NMe_2, NEt_2, Me and Et) (Scheme 1) were chosen for performing the calculations to check the best choice (GIAO or CSGT, and which basis sets) to calculate NMR shielding tensors on these systems, which present two functional groups attached to a methylene carbon. They involve the cyano group, which has been scarcely studied[30,31] and several substituents, some of which presenting the “heavy atom effect”.[32-34]

Experimental

Computational details

All structure optimisations were carried out with the Gaussian98 package of programs,[27] using the B3LYP hybrid functional.[28,29] The 6-31G(d,p), cc-pVDZ and cc-pVTZ basis sets[25,26] were employed to represent atomic orbitals.

All our calculations of NMR shielding tensors were done at the B3LYP level of theory using GIAO and CSGT models, which are fully described in the literature,[14,21,23,24]. The molecular structures optimised at the B3LYP/cc-pVTZ, B3LYP/cc-pVDZ and B3LYP/6-31G(d,p) levels were used as input . Three different types of basis sets were applied to perform these calculations. One of these is the Pople style basis set 6-31G(d,p),[35,36] which uses six Gaussian primitives to expand the 1s core of second period elements and one d-function and adds p-polarization functions to hydrogen atoms. The cc-pVDZ (correlation consistent polarised Valence Double Zeta) and cc-pVTZ (Triple Zeta) are standard Dunning basis sets,[25,26] where the correlation consistent (cc) basis sets is geared toward recovering the correlation energy of the valence electrons. Several different sizes of cc basis sets are available in terms of final number of contracted functions. The calculated NMR shielding tensors were converted into chemical shifts (δ) by using the same level of theory for the ^{13}C shielding tensor in TMS. The solvent effect was not included in the shielding tensor calculations.

NMR Measurements

^1H and ^{13}C NMR spectra of *ca.* 30 mg mL^{-1} solutions in CCl_4, were recorded at 300.13 and 75.48 MHz, respectively, on a Varian Gemini 300 spectrometer, at 25°C and referenced to Me_4Si. [$^2H_{12}$]-Cyclohexane was used as internal lock. Typical conditions for ^1H spectra were as follows: pulse width 7.8 μs, flip angle 30°, acquisition time 3.28 s, spectral width 3 530 Hz, number of transients 32 and number of data points 32K which were zero-filled to 64 K; for ^{13}C spectra the following conditions were employed: pulse width 6.0 μs, flip angle 30°, acquisition time 0.83 s, spectral width 20 000 Hz, number of transients 1000 and number of data points 32 K which were zero-filled to 64 K.

Results and Discussion

^{1}H and ^{13}C NMR chemical shift theoretical calculations for α-mono-substituted acetonitriles (Tables 1-3) were performed with GIAO and CSGT models, through B3LYP level of theory applying three different basis sets.

Methylene Hydrogens

As can be seen in Table 1, an excellent agreement is found between calculated and experimental chemical shifts for compounds **1**-**13**, using the GIAO model when cc-pVTZ basis set was applied (standard deviation 0.14). The results obtained from less expensive cc-pVDZ and 6-31G(d,p) basis sets gave also a reasonable agreement with the experimental data (SD=0.17 and SD=0.18, respectively).

However, CSGT model led to large standard deviations, when compared with GIAO model, for all basis sets used, namely [SD=0.65 for 6-31G(d,p), SD=0.47 for cc-pVDZ and SD=0.21 for cc-pVTZ].

The best correlation between theoretical and experimental ^{1}H chemical shifts obtained for cc-pVTZ basis set (Table 1) can be attributed to the fact that this basis set has 5s,2p,1d primitive functions, while cc-pVDZ and 6-31G(d,p) basis sets have only 4s,1p primitive functions for hydrogen atoms.[37] Thus, comparing the cc-pVTZ with the cc-pVDZ basis set, the former describes hydrogen atoms much better than the latter.

Table 1. Experimental (δ_{exp}) and theoretical α-methylene hydrogen chemical shifts, calculated by GIAO and CSGT methods for some α-mono-substituted acetonitriles (**1**-**13**) at B3LYP level of theory.

			GIAO			CSGT		
Comp.	Y	δ_{exp}	6-31G(d,p	cc-pVDZ	cc-pVTZ	6-31G(d,p	cc-pVDZ	cc-pVTZ
1	H	2.00	1.70	1.60	1.76	0.68	1.11	1.64
2	F	5.16	4.94	4.69	4.94	2.76	3.53	4.77
3	Cl	4.66	3.75	3.63	3.98	1.24	1.99	3.63
4	Br	3.79	3.59	3.36	3.69	0.51	1.64	3.25
5	I	3.54	3.27	3.03	3.28	1.58	2.11	3.11
6	OMe	4.16	3.97	3.79	4.06	2.23	2.84	3.95
7	OEt	4.20	4.07	3.88	4.13	2.24	2.88	4.03
8	SMe	3.26	2.89	2.67	3.01	1.40	1.75	2.85
9	SEt	3.26	2.87	2.69	3.04	1.29	1.69	2.87
10	NMe_2	3.65	3.21	3.06	3.33	1.70	2.20	3.25
11	NEt_2	3.50	3.21	3.06	3.20	1.59	2.16	3.21
12	Me	2.34	2.13	1.98	2.16	1.14	1.44	2.10
13	Et	2.28	1.99	1.81	1.98	1.02	1.29	1.97
SD[a]			0.18	0.17	0.14	0.65	0.47	0.21

[a] Standard deviation was calculated from $\Delta\delta=\delta_{theor}-\delta_{expt}$

α-Methylene Carbon

Table 2 shows the theoretical values for the α-methylene carbon chemical shifts of compounds **1**-**13**. They were obtained using GIAO and CSGT models at B3LYP level of theory applying three different basis sets.

Table 2. Experimental (δ_{exp}) and theoretical α-methylene carbon chemical shifts, calculated by GIAO and CSGT methods for some α-mono-substituted acetonitriles (**1**-**13**) at B3LYP level of theory.

			GIAO			CSGT		
Comp.	Y	δ_{exp}	6-31G(d,p	cc-pVDZ	cc-pVTZ	6-31G(d,p	cc-pVDZ	cc-pVTZ
1	H	1.49	2.06	1.59	0.38	3.74	2.28	0.56
2	F	70.69	65.50	64.93	70.61	68.78	69.73	71.33
3	Cl	24.49	30.31	31.93	32.74	23.98	27.15	31.85
4	Br	5.13	22.32	22.94	23.37	20.11	17.95	22.34
5	I	-32.01	5.26	6.00	7.35	5.36	5.22	6.04
6	OMe	58.70	56.50	56.93	60.45	59.09	60.52	60.96
7	OEt	56.00	56.35	56.07	59.24	58.47	59.50	59.59
8	SMe	18.82	23.04	24.59	24.34	19.70	21.04	23.59
9	SEt	16.43	22.53	23.98	23.87	19.38	20.36	22.96
10	NMe_2	48.62	46.24	46.86	48.36	46.62	44.85	48.77
11	NEt_2	40.06	47.66	49.87	49.96	50.46	50.99	50.24
12	Me	10.67	13.35	14.17	13.30	13.67	12.70	14.30
13	Et	18.78	20.62	21.75	21.32	20.29	20.10	22.27
SD[a]			2.52	3.37	3.42	3.43	3.51	3.17

[a] Standard deviation was calculated from $\Delta\delta=\delta_{theor}-\delta_{expt}$, excluding data for compounds **4** and **5**.

Both models, GIAO and CSGT, led to a good agreement (standard deviation around 3) between calculated and experimental chemical shifts (Table 2). It was observed large deviations for chloro- (**3**), bromo- (**4**) and iodo-derivative (**5**) calculated values in relation to the experimental chemical shifts (Table 2), which must be due to the spin-orbit contribution.[38] A heavy halogen can induce large upfield shifts on NMR nuclei, bound to them.[39]

The cc-pVTZ is a standard Dunning basis set;[25] the correlation consistent (cc) basis sets are geared toward recovering the correlation energy of valence electrons, which was not observed for Pople 6-31G(d,p). The results presented in Table 2 show almost the same standard deviation for all basis sets used here.

However, better accuracy between calculated and experimental ^{13}C chemical shifts for the methylene carbon was observed when 6-31G(d,p) basis set was applied. An important point that should be mentioned here is that while the cc-pVTZ basis set gives 148 basis functions for compound **2** (fluoroacetonitrile), the 6-

31G(d,p) basis set gives 70 basis functions and cc-pVDZ gives 66 basis functions. This fact leads to a shorter computational time with the same accuracy level for ^{13}C NMR chemical shifts.

Cyano Carbon

The theoretical calculations of cyano ^{13}C NMR chemical shifts for α-mono-substituted acetonitriles (**1**-**13**) were performed with GIAO and CSGT models applying 6-31G(d,p), cc-pVDZ and cc-pVTZ basis set (Table 3).

An excellent agreement between calculated and experimental chemical shifts was observed when CSGT model for 6-31G(d,p) basis set (SD=1.28) was used. In the GIAO model, only the cc-pVTZ basis set showed a good agreement between calculated and experimental chemical shifts (SD=1.45). For the other two basis sets, 6-31G(d,p) and cc-pVDZ, the difference between theoretical and experimental value obtained in the calculation was around 7-10 ppm for all compounds of the series. The better response obtained through cc-pVTZ basis set is due to the quality of this basis.[25]

Table 3. Experimental (δ_{exp}) and theoretical cyano carbon chemical shifts, calculated by GIAO and CSGT methods for some α-mono-substituted acetonitriles (**1**-**13**) at B3LYP level of theory.

			GIAO			CSGT		
Comp.	Y	δ_{exp}	6-31G(d,p	cc-pVDZ	cc-pVTZ	6-31G(d,p	cc-pVDZ	cc-pVTZ
1	H	117.10	104.80	107.38	116.47	114.55	112.17	116.34
2	F	118.63	105.25	107.92	115.78	115.75	113.55	115.56
3	Cl	114.22	104.59	107.40	116.46	113.68	112.12	115.72
4	Br	114.08	105.34	108.03	117.33	114.49	112.40	116.46
5	I	115.56	105.73	110.58	119.06	116.91	115.42	119.44
6	OMe	115.79	106.18	108.80	117.05	116.85	114.70	117.05
7	OEt	116.18	106.58	109.21	117.50	117.14	114.99	117.49
8	SMe	115.41	105.58	108.26	117.43	115.36	113.48	117.19
9	SEt	116.36	106.06	108.70	117.95	115.64	113.79	117.64
10	NMe_2	118.77	107.79	106.97	115.51	116.04	113.24	115.82
11	NEt_2	113.47	107.60	109.26	118.80	117.40	114.89	118.95
12	Me	120.24	109.5	112.03	121.22	118.78	112.94	120.76
13	Et	118.08	108.48	111.30	120.60	118.43	116.32	120.36
SD[a]			2.00	3.13	1.45	1.28	1.93	1.59

[a] Standard deviation was calculated from $\Delta\delta=\delta_{theor}-\delta_{expt}$

For CN carbon chemical shifts calculated at the CSGT model with the less expensive 6-31G(d,p) basis set, the same accuracy was obtained in comparison with those observed with more expensive GIAO/cc-pVTZ model. The CSGT is a better model than GIAO to evaluate the gauge origin of the vector potential describing the external magnetic field for this type of carbon.

Conclusion

Data from Tables 1 to 3 indicate that the NMR shielding tensor can be predicted from DFT/B3LYP theory. For methylene carbon, the lesser correlation consistent basis sets, cc-pVDZ, was applied, while for the ^{1}H (CH_2 group) and ^{13}C (CN group) a good correlation between experimental and theoretical data were obtained when a higher-order polarisation function is added, like cc-pVTZ.

The CSGT is a more adequate model for calculation of the NMR shielding tensor only for the cyano carbon, whereas the GIAO model is more appropriate for describing the chemical shifts of the methylene hydrogens. The values of NMR shielding for the methylene carbon showed a best agreement when small basis sets were used, independent of the model.

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