

ON THE MODELS FOR DEUTERIUM LONG-RANGE ISOTOPE EFFECTS IN ^{13}C NMR SPECTROSCOPY

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Abstract

The long-range deuterium isotope effects on ^{13}C nuclear shielding are physically not yet completely understood. Two existing models for explaining these effects, vibrational and substituent, are compared here. The vibrational model is based on the Born–Oppenheimer approximation, but it can explain only one-bond deuterium effects. To the contrary, the substituent model may explain many long-range isotope effects, but it is controversial due to the assumption of some distinct electronic properties of isotopes. We explain how long-range deuterium isotope effects may be rationalized by the subtle electronic changes induced by isotope substitution, which does not violate the Born–Oppenheimer approximation.

1. Introduction

The isotope effects on nuclear shielding were theoretically predicted by Ramsey in 1952 [1]. Already in 1953, the effects were experimentally confirmed in deuterated hydrogen gas by Wimett [2]. Marshall calculated isotope shifts in H_2 , HD and D_2 , revealing nuclear shielding changes as a nonlinear function of interatomic distance [3]. The isotope effects on spin–spin coupling and on relaxation times are also known, but they are rather small in comparison to effects on nuclear shielding, i.e. chemical shifts. Because of this and due to their, in principle, simple determination, isotope effects on chemical shifts are most frequently investigated.

The most studied isotope is deuterium (D) because of the relative ease of its incorporation into the molecule as well as its large fractional change in mass on going from H to D, which induces large isotope effects.

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It has been thought that the isotope effects in NMR spectroscopy are almost completely understood; however, using high magnetic field spectrometers, a great number of unexpected D-effects have recently been observed. This includes isotope effects of unusual sign, i.e. the deshielding effect [4], through-space isotope effects [5] and long-range isotope effects (LRIE) [6]. These findings have challenged existing concepts of isotope effects.

2. The models for deuterium isotope effects

At the present time, two physically distinct models for deuterium isotope effects in ^{13}C NMR exist, excluding each other: the vibrational model based on the Born–Oppenheimer approximation, and the substituent model based on similarities of deuterium effects and substituent effects. The Born–Oppenheimer approximation allows one to separate the nuclear motion in rotation and vibration from the electronic motion [7]. Thus, within the Born–Oppenheimer approximation the electronic potential of a C–D bond is believed to be the same as the potential of a C–H bond. As a consequence, the isotope effects are assumed to originate from the anharmonicity of this potential and the lower zero point vibrational energy of the heavier isotope within this potential. In other words, the only important difference between isotopes is their mass difference, and all effects of isotopic substitution have to arise from it. Although the interpretation of isotope shifts is based on the consideration of the vibrational and rotational averaging of nuclear shielding, i.e. dynamical factors, it also involves electronic factors, i.e. changes of shielding with bond extension and/or bond angle deformation on isotopic substitution. In this respect, isotope shifts are closely related to the temperature dependence of nuclear shielding in the gas phase [8]. Within the Born–Oppenheimer approximation, one can consider a shielding surface which gives the values of nuclear shielding at rigidly fixed nuclear configurations and hence experimentally observed shielding must be explained by taking into account the potential energy surface and the nuclear shielding surface with simultaneous averaging on both of them. In fact, the motions involved in the averaging on the potential energy surface close to the equilibrium configuration correspond to averaging over small displacements on the shielding surface. Therefore, one can expand the nuclear shielding in terms of the normal coordinates Q_s :

$$\sigma = \sigma_e + \sum_s \left(\frac{\partial \sigma}{\partial Q_s} \right)_e Q_s + \frac{1}{2} \sum_{s,r} \left(\frac{\partial^2 \sigma}{\partial Q_r \partial Q_s} \right)_e Q_r Q_s + \dots, \quad (1)$$

where the shielding derivatives are at the equilibrium configuration. The nuclear shielding derivatives with respect to normal coordinates are not invariant to isotopic substitution and hence it is more convenient to expand the nuclear shielding in terms of internal coordinates:

$$\sigma = \sigma_e + \sum_i \left(\frac{\partial \sigma}{\partial \mathcal{R}_i} \right)_e \mathcal{R}_i + \frac{1}{2} \sum_{ij} \left(\frac{\partial^2 \sigma}{\partial \mathcal{R}_i \partial \mathcal{R}_j} \right)_e \mathcal{R}_i \mathcal{R}_j + \dots, \quad (2)$$

where \mathcal{R}_i includes the bond displacement (Δr_i) and the bond angle deformations ($\Delta \alpha_{ij}$). Therefore, the isotope effects on chemical shifts in NMR involve mass-independent electronic contributions which describe the change of shielding with bond extension and/or angle deformation $(\partial \sigma / \partial \mathcal{R})_e = (\partial \sigma / \partial \Delta r)_e, (\partial \sigma / \partial \Delta \alpha)_e, \dots$, and the mass-dependent thermal averages due to vibrations and rotations, given by $\langle \Delta r \rangle^T, \langle \Delta \alpha \rangle^T, \dots$ and $\langle \mathcal{R}_i \mathcal{R}_j \rangle^T$ which are $\langle (\Delta r)^2 \rangle^T, \langle (\Delta \alpha)^2 \rangle^T, \langle \Delta r \Delta \alpha \rangle^T, \dots$. The equation for the isotope shift is hence:

$$\begin{aligned} \sigma - \sigma^* &= \sum_i \left(\frac{\partial \sigma}{\partial \mathcal{R}_i} \right)_e \left[\langle \mathcal{R}_i \rangle^T - \langle \mathcal{R}_i \rangle^{T*} \right] \\ &+ \frac{1}{2} \sum_{ij} \left(\frac{\partial^2 \sigma}{\partial \mathcal{R}_i \partial \mathcal{R}_j} \right)_e \left[\langle \mathcal{R}_i \mathcal{R}_j \rangle^T - \langle \mathcal{R}_i \mathcal{R}_j \rangle^{T*} \right] + \dots \end{aligned} \quad (3)$$

The electronic factor, which is subtle indeed, is very often overlooked in the consideration of long-range deuterium isotope effects. In fact, the electronic factor may be the reason for the existence of long-range isotope effects since it seems unlikely that a change in the normal mode of vibrations upon the isotopic substitution at a given site could have an effect on distances many bonds away.

The substituent model for deuterium effects in ^{13}C NMR is based on the similarities between isotope effects and substituent effects [9]. This concept was introduced more than twenty years ago by Halevi [10]. He found that kinetic isotope effects can be nicely explained supposing that deuterium behaves like a real substituent with its own electronic properties different from those of H. Therefore, strictly taken, the substituent model is against the Born–Oppenheimer approximation. However, at the moment this model is the only one which can rationalize a large number of unexpected deuterium isotope effects. On the basis of the substituent model, it is postulated that deuterium has its own inductive, hyperconjugative and steric effects. The deuterium "isotope-induced" inductive effect is assumed to be the consequence of a shorter C–D than C–H bond. Hence, the C–D bond has greater electron density than the C–H bond and it seems as if D is more electropositive than H [11]. Within the substituent model, it is supposed that the CD_3 group has a lower hyperconjugative ability than the CH_3 group. Hence, CD_3 causes deshielding of corresponding C-atoms. In fact, for most deuterium isotope effects two opposite mechanisms are supposed to be present: a "normal" effect which gives rise to shielding, and a hyperconjugative effect which gives deshielding [12]. The different steric effect of D as compared to H is explained by the shorter C–D than C–H bond and hence the smaller amplitude of vibrations of the former. It implies that the C–D bond has smaller steric requirements than the C–H bond [13]. The shortening of the C–D bond, amounting to 0.007 Å

in the gas phase, has been detected by microwave and Raman spectroscopies as well as by electron diffraction [14]. Neutron diffraction in the solid state showed a C–D bond shorter than the C–H bond by 0.012 Å [15].

There are some interesting correlations between isotope effects and hybridization, pi bond order, etc., which are in fact pure electronic terms. However, one cannot say that the isotope effects are "real" electronic effects because this would imply that the isotopes are substituents. If this were so, the potential energy surfaces of isotopomers would be different, but we know they are identical. In spite of its controversial nature, the substituent model of isotope effects still remains very attractive.

3. Results and discussions

Deuterium isotope effects of the longest extent were observed in extended π -electron systems. Hence, one can assume that the π -electrons play an important role in the transmission of isotope perturbations in such molecules. To throw some light on the behaviour of deuterium in π -systems, we have synthesized and scrutinized by ^{13}C NMR a series of differently deuterated compounds which consist of two benzene rings linked with different bridging groups B . The nature of B determines the transmittivity and conformation of a given molecule. The following deuterated molecules were studied: trans-stilbenes (tSB, $B = -\text{CH}=\text{CH}-$), cis-stilbenes (cSB, $B = -\text{CH}=\text{CH}-$), trans-N-benzylideneanilines (tBA, $B = -\text{CH}=\text{N}-$), trans-azobenzenes (tAB, $B = -\text{N}=\text{N}-$), tolanes (TOL, $B = -\text{C}\equiv\text{C}-$), benzophenones (BPN, $B = >\text{C}=\text{O}$), etc. We observed all kinds of unusual D isotope effects, i.e. deshielding effects, steric effects and long-range effects. The latter include deuterium isotope effects through five, six, seven, eight and even ten bonds. The deuterium isotope effects on ^{13}C chemical shifts in some tBA molecules (I, II, III and IV) are displayed in fig. 1. As one can see, the longest D-effect in tBA molecules was found in II, where D is placed at the para position of the C-phenyl ring. This seven-bond deshielding effect amounts to 2.9 ppb (the digital resolution was 0.25 ppb). In III, where D is placed at the para position of the N-phenyl ring, the maximal observed D-effect was a six-bond effect. We concluded that this difference in extent of long-range D-effects arises from the rather different C-phenyl and N-phenyl dihedral angles, which are 10–20° and 40–50°, respectively [16]. In fact, if D-effects are transmitted mainly by π -electrons, then in conjugated molecules where π -delocalization and conformation are related, D long-range effects have to be conformationally dependent. We found additional proofs for the unusual behaviour of deuterium in tSB [17], cSB, tAB and BPN [18] molecules. In these compounds, the extent and the magnitudes of long-range deuterium effects are also related to molecular conformation, i.e. the molecular dihedral angle [19]. So, for instance in 4-D-tSB, which is a nearly planar molecule, a ten-bond deuterium isotope effect was observed. In addition to the conformational dependence, we have observed some other interesting features of long-range D isotope effects in the compounds investigated. So, the absence of D

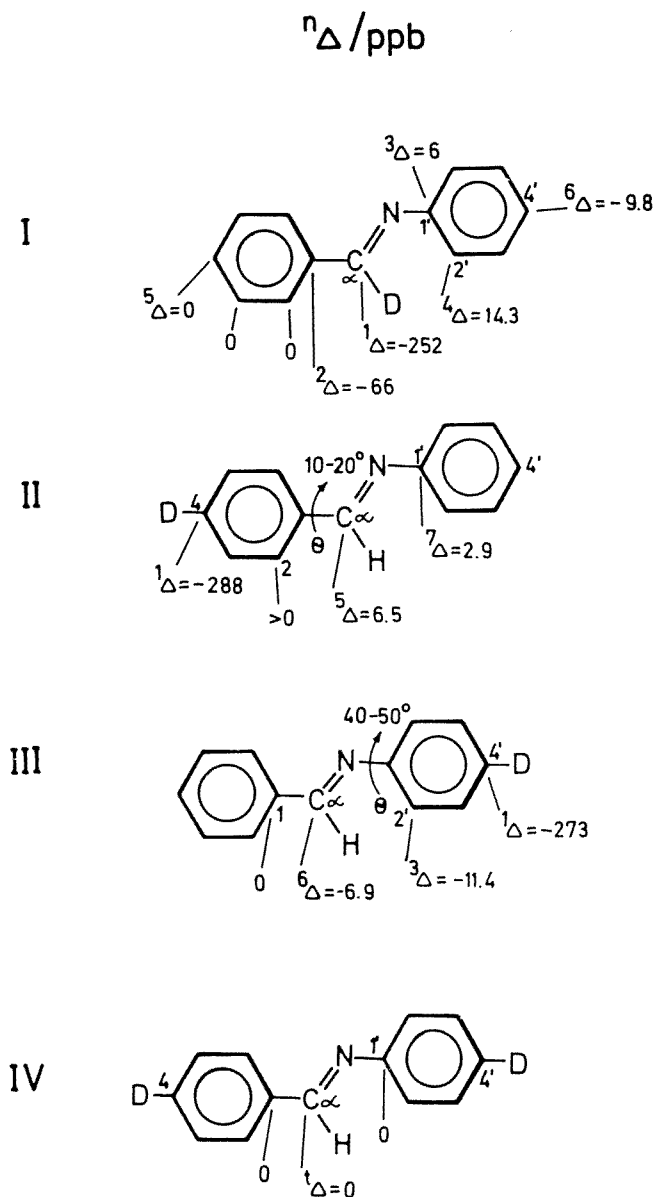


Fig. 1. Deuterium isotope effects $n\Delta$ (ppb), n denotes the number of intervening bonds, on ^{13}C chemical shifts in some trans-N-benzylideneanilines.

long-range effects in IV, i.e. a para dideuterated molecule, could be explained by the additivity of isotope effects. We found that the additivity rule holds for other dideuterated molecules as well. In molecule I, where D is spatially close to the C-atom four bonds away, the four-bond D-effect is twice as large as the three-bond

effect. This indicates significant through-space participation to the four-bond D-effect, i.e. steric interaction of D.

In the same type of compounds, besides the long-range deuterium isotope effects, we have observed long-range substituent effects and also long-range coupling constants. Moreover, we recognized the parallelism of long-range interactions of different origins, e.g. isotope effects and coupling constants, etc. [19, 20]. We rationalized this by the same transmission of information for different effects, which exist in the molecules due to the π -electrons. Already in 1957, McConnell pointed out the importance of π -electron transmission for spin–spin coupling, in spite of the fact that the π -electron density vanishes at the site of the nucleus [21]. On the basis of our data and data from the literature, one can assume that transmission by π -delocalization, which gives rise to long-range couplings and long-range substituent effects, may enable subtle shielding changes through many bonds; in other words, long-range deuterium isotope effects on deuteration. The fact that some relationships between deuterium isotope effects and substituent parameters exist does not necessarily imply that both phenomena are intrinsically the same. In our opinion, there is no need to ascribe some distinct electronic properties to deuterium. In fact, long-range deuterium isotope effects may be explained within the vibrational model as well. As mentioned before (eq. (3)), the vibrational model implies two contributing factors, dynamical and electronic, to isotope effects in NMR. The dynamical factor is due to the rotational and vibrational averaging changes on isotopic substitution. The electronic factor is due to the bond extension and bond angle deformation which may be reflected through the local changes on the electronic potential energy surface, but not affecting the gross potential surface of the molecule. For isotopomers, this surface remains the same. The electronic changes mentioned, which are subtle indeed, may be transmitted by π -electrons as electronic changes for other types of long-range interactions in π -molecules. Therefore, there are many similarities among isotope effects, substituent effects, coupling constants, etc., in π -compounds. One can say that a given molecule determines how perturbations behave in it, i.e. the pattern of this behaviour is coded in a molecule.

Since the isotope and substituent effects both produce electronic perturbations, although on a rather different scale of magnitude, they could be similar in the same types of compounds.

4. Conclusions

The substituent model of isotope effects, although very attractive due to the familiar language of physical organic chemistry, cannot exactly explain the real nature of long-range isotope effects. However, this model is very useful for rationalizing and classifying a huge number of unusual D-effects. On the other hand, the vibrational model within the Born–Oppenheimer approximation can quantify only one-bond isotope effects, but it can also qualitatively explain long-range isotope effects on the basis of electronic terms inherent to this model, which is very often overlooked.

5. Experimental

The ^1H (and some ^{13}C) NMR measurements were performed on a Bruker WH-270 spectrometer in Bangalore, India. The ^{13}C (and some ^1H) NMR measurements were done on a Varian XL-400 spectrometer in Budapest, Hungary. All samples were dissolved in deuterated acetone and measured at ambient temperatures. The digital resolution attained in ^{13}C NMR spectra was 0.25 ppb, using very long acquisition times (up to 20 s) and zero filling. The techniques used were: broadband proton decoupling, off-resonance decoupling, gated decoupling and semiselective 2D-J. Other experimental details will be published elsewhere.

6. Comments

The calculations of long-range deuterium isotope effects are unfortunately still somewhat out in the future. Semi-empirical INDO and CNDO/2 methods failed to reproduce isotope effects through more than one bond [15]. Therefore, ab initio methods may be the choice for calculating long-range isotope effects. However, the limiting factor is the size of molecules (molecular weights from 150 up) in which these effects exist. In a small molecule such as acetone, the two-bond isotope effect was successfully calculated using an ab initio method with the GAUSSIAN-70 program [22]. This two-bond effect is the longest deuterium isotope effect ever calculated until now. Anyway, a greater interest of physicists and mathematicians is badly needed in the field of isotope effects.

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