Directionality of Intrinsic Deuterium Isotope Effects in ^{13}C NMR Spectra of Molecules Containing One or Two Phenyl Groups

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Intrinsic deuterium-induced isotope effects have been measured and analyzed for compounds having one or two phenyl groups specifically labelled at different positions in a molecule. Some typical examples of directional and orientational dependence of the effects have been given. Different magnitudes of isotope effects that are transmitted in opposite directions have been observed. Thus, in *p*-^{2}H-*cis*-stilbene, the effect over six bonds at C-α of 8.7 ppb is found, while the corresponding effect in α-^{2}H-*cis*-stilbene at C-4 is only 1.4 ppb. Similarly, in *o'*-^{2}H-*trans*-*N*-benzylideneaniline, the effect over six bonds at C-2,6 is 1.7 ppb, whereas that in *o*-^{2}H-*trans*-*N*-benzylideneaniline at C-2',6' is equal to zero. Similar behaviour was observed in other molecules and at other positions as well. Additional factors contributing to the magnitude and sign of isotope effects, such as π-electron delocalization, conformation, steric hindrance and lone pair electrons are also discussed.

INTRODUCTION

Isotope effects in NMR spectra provide a wealth of information about molecular structural properties, but also appear to be a sensitive probe to gauge perturbations in chemical equilibria in solution. A number of papers have reported relations between isotope effects and molecular parameters, such as dihedral angles,[1,2] conformation,[3–5] hybridization or bond-lenght.[6,7] Although it has been established that isotope effects are of a rovibrational origin,[8] empirical relations are still very useful in understanding this phenomenon. This is especially so for effects transmitted over many bonds

away from the isotopic substitution site (so called long-range isotope effects), which provide a better insight into the behaviour of molecules in solution.

P. Novak *et al.*[3,9–11] have recently observed a variety of intrinsic isotope effects in NMR spectra of benzene derivatives and they have thoroughly discussed their structural and conformational dependence. However, little has been said about the directionality and orientational dependence of isotope effects, which seems to have a great impact on the sign and the magnitude of some isotope effects observed at specific sites in a molecule. In papers discussing isotope effects,[3,9–11] the importance of the position of the isotopic nuclei within a molecule was stressed. It is the aim of the present article to throw more light on the directional and orientational behaviour of isotope effects in molecules containing one or two phenyl groups.

EXPERIMENTAL PART

The preparation of deuteriated isotopomers was described elsewhere.[3,9,12] Intrinsic deuterium isotope effects were determined in the conventional way, *i.e.* from mixtures of labelled and unlabelled species, prepared in different ratios. Positive sign denotes an upfield deuterium-induced chemical shift (shielding effect).

^{13}C NMR spectra with the Waltz-16 decoupling sequence were recorded with Varian Gemini 300, XL-400 and Unity Inova 600 spectrometers operating at 75.4, 100.6 and 150.9 MHz for ^{13}C nuclei, respectively. Acetone-d_6 and chloroform-d_1 were used as solvents and also for the internal lock signal. Spectra were obtained from 0.2–0.3 M solutions in 5 mm NMR tubes at ambient temperature. Narrow-region spectra with spectral widths of 500–2000 Hz were zero-filled to 64 K, thus giving a digital resolution better than 0.05 Hz per point after Fourier transformations. Resolution enhancement functions were used where necessary. Standard deviations were less than 0.5 ppb.

RESULTS AND DISCUSSION

An analysis of the directional properties of isotope effects can only be made if a series of molecules specifically labelled at different sites are available. Thus, *ortho*-, *meta*-, *para*- and *alpha*-deuteriated benzene derivatives have been prepared and their sign and magnitudes compared and analyzed. Some typical examples of the dependence of deuterium isotope effects on the site of deuteriation are shown in Figures 1–2. It is demonstrated here that, within the same molecular framework, differences in *e.g.* $^4\Delta$, $^5\Delta$ and $^6\Delta$ in o'-^{2}H and m'-[2]H-*trans*-N-benzylideneaniline are a consequence of the C-[2]H
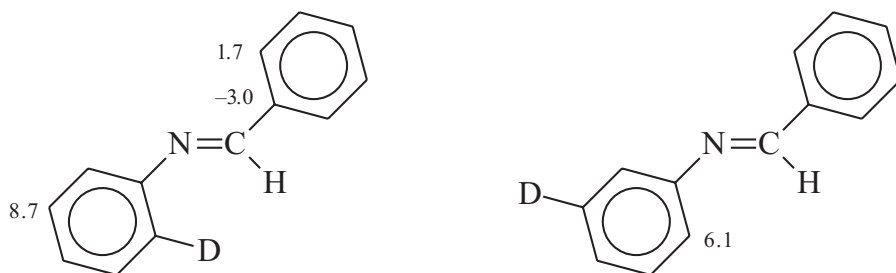
Figure 1. Deuterium-induced isotope effects over four, five and six bonds in o'-^{2}H and m'-^{2}H isotopomers of *trans*-*N*-benzylideneaniline.
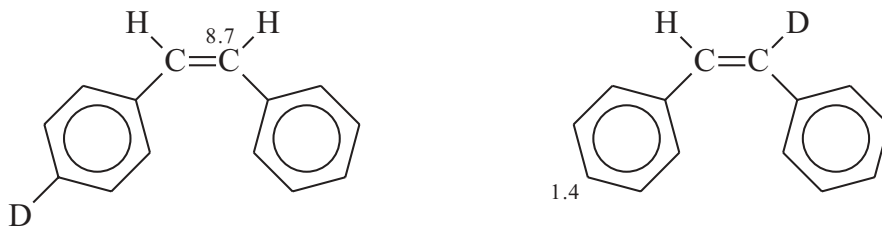

Figure 2. Deuterium-induced isotope effects over six-bonds in p-^{2}H and α-^{2}H-*cis*-stilbene.

bond direction (Figure 1). The same property should be responsible for significantly different values of $^6\Delta$ in p-^{2}H- and α-^{2}H-*cis*-stilbene (Figure 2).

It has already been pointed out that isotope effects over three bonds, $^3\Delta$, observed in monodeuteriated isotopomers of toluene,[9] benzaldehyde,[13] benzoic acid[9] and benzophenone,[9] strongly depend on the position of isotopic nuclei in the molecule, with respect to the site of observation. This dependence is even more pronounced in the case of certain long-range effects: $^4\Delta$, $^5\Delta$ and $^6\Delta$. Moreover, quite different values are obtained when the effects transmitted over the same number of bonds, but through different path, are compared. Many of examples can be found for benzene derivatives, but attention will be restricted only to the most significant and straightforward cases. For instance, $^3\Delta$ and $^4\Delta$ differ substantially in o'-^{2}H- and m'-^{2}H-*trans*-*N*-benzylideneaniline (Figure 1). Namely, $^4\Delta$ in o'-^{2}H-*trans*-*N*-benzylideneaniline observed at the *meta′*-position (C-5') has the value of 8.7 ppb, while that $^4\Delta$ in m'-^{2}H-*trans*-*N*-benzylideneaniline found at the *ortho′*-position (C-6') amounts to 6.1 ppb. It is important to note here that, although the through-bond distance between ^{2}H and the observed carbon site is the same, the two effects act in different directions (Figure 1). Similarly, it has been found that $^5\Delta$ and $^6\Delta$, observed in o'-^{2}H-*trans*-*N*-benzylideneaniline at C-1 and C-2,6 (Figure 1), are different from the respective effects in o-^{2}H-*trans*-*N*-benzylideneaniline,[14] which are transmitted in the opposite di-

rection, *i.e.* they act at C-1' and C-2',6'. The effects in the former isotopomer have the values of -3.0 ppb and 1.7 ppb, respectively (Figure 1), while in the latter both effects are equal to zero.[14] However, in the case of $^5\Delta$ effects, one has to take into account different interacting pathways, *i.e.* in *o'*-^{2}H-*trans*--*N*-benzylideneaniline the transmission path includes the torsional C=C-N=C angle, while in *o*-^{2}H-*trans*-*N*-benzylideneaniline it includes the torsional C=C-C=N angle, which is significantly different. Our *ab initio* calculations have shown that the former angle is 45°, while the latter one is close to zero.[15] On the other hand, the transmission of $^6\Delta$ effects in both *o*-^{2}H- and *o'*-^{2}H-*trans*-*N*-benzylideneaniline is associated with the same structural framework and steric effects, so the difference in their values should arise from factors other than conformation itself. The same reasoning applies to the two isotopomers of *cis*-stilbene: *p*-^{2}H- and α-^{2}H-*cis*-stilbene (Figure 2). The effects over six bonds are considered here, *i.e.* one transmitted from the *para*- to the *alpha'*-position and the other from the *alpha'*- to the *para*-position. Both effects are transmitted through the same structural moiety, but in the opposite direction. However, their magnitudes differ by almost an order of magnitude (Figure 2). The value of 8.7 ppb has been determined for *p*-^{2}H-*cis*-stilbene, whereas only 1.4 ppb has been observed for α-^{2}H-*cis*-stilbene.[16] Similar differences in values have been found for the corresponding effects in structurally related benzene derivatives containing two phenyl rings connected via the bridging C=C or C=N group, such as α-^{2}H- and *p*-^{2}H-*trans*-stilbene or α-^{2}H- and *p*-^{2}H-*trans*-*N*-benzylideneaniline. In the two isotopomers of *cis*-stilbene discussed above, conformational and steric influences are the same, but the measured isotope effects are quite different (Figure 2). Therefore, one has to consider the relative orientation of the particular C-D σ-bond orbital with respect to the π-bond orbital of the observed carbon atom, which modifies the isotope effect transmission. Furthermore, in the case of *p*-^{2}H isotopomers of *cis*-stilbene, *trans*-stilbene or *trans*-*N*-benzylideneaniline (Scheme 1), the direction of the C-D σ-bond is along the axes of phenyl rotation, while in the case of α-^{2}H
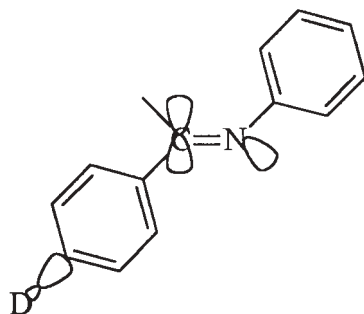
Scheme 1.

Figure 3. HOMO orbital description of *trans-N*-benzylideneaniline as calculated by the *ab initio* 63-1G* basis set.

isotopomers it is at a certain angle to it. In isotopomers of *trans-N*-benzylid-eneaniline an additional contributing factor is operative, *i.e.* the influence of nitrogen electron lone-pairs. Relative orientation of the lone-pair orbital with respect to the C-D bond and to the observed carbon atom play an important role as well (Figure 3). It is clearly seen that the HOMO C_{para}-H or C_{para}-D orbital interacts with the imino moiety of the *trans-N*-benzyliden-eaniline molecule and also with the C'_{para}-carbon orbital of the neighbouring phenyl ring (Figure 3). This can explain why long-range effects over nine[9] and ten bonds[16,17] were observed in *p*-^{2}H-molecules of a related type. Usually, lone pair electrons decrease the magnitude and are the main cause of the negative sign of some isotope effects.[9] Similar arguments for explaining magnitudes of deuterium isotope effects over three and four bonds observed in the deuteriated ring of the respective molecules[9,13] can be applied.

In conclusion, one can postulate several factors that govern the observed magnitude and sign of isotope effects in these π-electron systems: i) π-electron delocalization, ii) conformational and steric effects, iii) orientation and direction of the C-D σ-bond and iv) lone-pairs, when they are present in the molecule. Although directionality plays an important role, as shown above,

it has not yet been firmly established which factor predominates for a particular isotope effect. In order to separate individual contributions of each, it is necessary to involve high level quantum chemical calculations.

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SAŽETAK

Usmjerenost intrinzičnih deuterijskih izotopnih efekata u ^{13}C NMR spektrima molekula koje sadrže jednu ili dvije fenilne skupine

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Izmjereni su i analizirani intrinzični deuterijski izotopni efekti u molekulama koje sadržavaju jednu ili dvije fenilne skupine specifično obilježene deuterijem na različitim mjestima. Dani su neki tipični primjeri usmjerenosti i orijentacijske ovisnosti izotopnih efekata. Opaženi su različiti iznosi efekata koji se prenose u suprotnim smjerovima. Tako je u *p*-^{2}H-*cis*-stilbenu izmjeren efekt kroz šest veza na atomu C-α u iznosu od 8,7 ppb, dok odgovarajući efekt u *a*-^{2}H-*cis*-stilbenu iznosi samo 1,4 ppb. U *o'*-^{2}H-*trans*-*N*-benzilidenanilinu efekt kroz šest veza na atomima C-2,6 iznosi 1,7 ppb, dok u *o*-^{2}H-*trans*-*N*-benzilidenanilinu taj je efekt nula. Slično ponašanje deuterijskih efekata primijećeno je i za ostale istraživane izotopomere. Razmatrani su i dodatni čimbenici koji utječu na iznos i predznak izotopnih efekata, kao što su π-elektronska delokalizacija, konformacija, sterički efekti te utjecaj slobodnih parova elektrona.