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# NOTE

# ISOTOPIC PERTURBATION OF RESONANCE—A TERM OF CONTROVERSY

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**The term ‘isotopic perturbation of resonance’ is critically reviewed. With the help of new data obtained from deuterium-labelled 1,3-dimethyl- and 1,3-di-*tert*-butylcyclopentenyl cations, it is shown that all observed deuterium isotope effects in these systems are purely intrinsic. The term ‘isotopic perturbation of resonance’ should no longer be used in the literature. © 1997 by John Wiley & Sons, Ltd.**

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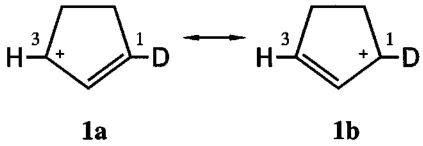
## INTRODUCTION

Nearly 20 years ago, Saunders and Kates[1] observed an intriguing signal splitting in the $^{13}C$ NMR spectra of deuterated cyclohexenyl and cyclopentenyl cations (**1**, Scheme 1). In contrary to the temperature-dependent isotope effects in equilibrating systems,[2, 3] these effects were essentially temperature independent and termed, in analogy with the isotopic perturbation of equilibrium or conformation,[4] ‘isotopic perturbation of resonance.’

In **1**, the chemical shift of the protonated carbon 3 was found to be at higher frequencies with respect to the undeuterated parent cation. This was explained with the assumption that ‘deuterium substitution increases the effective importance of one canonical form (**1a**) over the other (**1b**),’ because ‘the positive charge prefers to be on the carbon bearing the proton.’ The authors clearly differentiated between this novel effect and the well known intrinsic isotope effects. Subsequently, this effect was used to distinguish non-classical cations from equilibrating structures.[5–7] Other workers[7–9] expanded the term to ‘perturbation of hyperconjugation’ and Forsyth and co-workers even discussed[9] a ‘through space perturbation of resonance’ and used extensively the concept of isotopic perturbation of hyperconjugation by comparing different carbocations.[10] Similarly, for neutral aromatic compounds, hyperconjugation was used to explain isotope effects by different workers.[11, 12] Recently a perturbation of the $\pi$-electron frame in *N*-deuterated benzanilides was maintained.[13] This use of isotope effects in the context of the language of physical organic chemistry has been reviewed.[14] The vibrational theory of intrinsic isotope effects has been outlined mainly by Jameson and Osten,[15] who discouraged the use of terms such as hyperconjugation in connection with isotope effects, because this would imply a Born–Oppenheimer breakdown. In a later review, however, Jameson[16] stated that the isotope effects are a ‘convolution of electronic and dynamic parts’ and especially long range isotope effects correlate ‘with other purely electronic quantities which are dependent on the same electronic transmission path such as substituent effects.’ Here it is understood that the ‘electronic path’ stems from the sensitivity of the shielding of a given nucleus to a change in equilibrium geometry caused by isotopes.

In this work, we want to address the question of whether the term ‘isotopic perturbation of resonance’ is both necessary and useful to describe the isotope effects in **1** and related compounds. We wanted to investigate whether these isotope effects can be distinguished from normal intrinsic isotope effects and whether it is justified to state that one mesomeric form of **1** is favoured by isotopic substitution. For this purpose, we prepared the two closely related cations **2** and **3** (Scheme 2) and measured their isotope effects in $H_2SO_4$ solution.



Scheme 1

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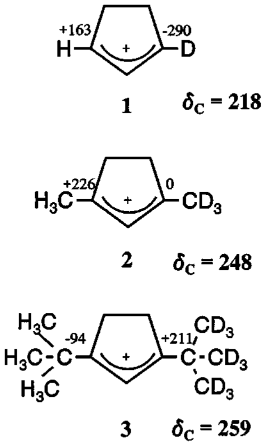
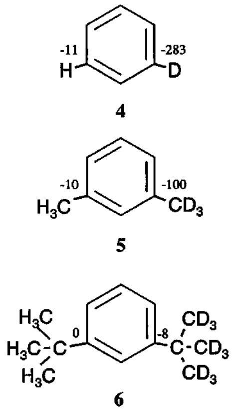


Scheme 2



Scheme 3

## RESULTS AND DISCUSSION

In **2**, methyl groups are placed at the ends of the allylic cation system, hence the deuterium atom is one bond further away; in **3**, *tert*-butyl groups terminate the allylic cation system and the deuterium is again one bond further away from the $\pi$-system. In **2** we measure a $^2\Delta$ isotope effect of essentially zero and a $^4\Delta$ isotope effect of $+226$ ppb (for the sign convention, see Ref. 14; positive isotope effects indicate that the carbon atom is deshielded with respect to the parent compound) (see Scheme 2, deuterium isotope effects given in ppb). A secure assignment could be achieved by admixture of the parent compound and the observed C–D spin coupling in the case of the neutral compounds. Within the framework of resonance perturbation, these results would mean that in **2**, similarly to **1**, the mesomeric form with the positive charge near the $CH_3$ group is favoured. Very striking are the results for **3**, where we observe the opposite polarization. Here we have a positive isotope effect over three bonds, $^3\Delta=211$ ppb, and a negative isotope effect over five bonds, $^5\Delta=-94$ ppb. Applying the above reasoning, this would mean that the other mesomeric form with the positive charge near the perdeuterated *tert*-butyl group is favoured. All isotope effects are essentially temperature independent in the available temperature range ($-30$ to $+20$ °C).

However, as is known for isotopic perturbation of equilibria,[3] the observed signal splittings have to be corrected by the intrinsic isotope effects. We therefore have to look for suitable model systems which give a reliable estimate. This is very difficult, since it was shown that isotope effects are dependent on the chemical shifts[7, 17–19] and for cations intrinsic isotope effects are expected to be larger than for neutral compounds. We chose to compare the values with those in analogously substituted benzenes (**4**–**6**) which were partly available to us from earlier work[20, 21] and by a new preparation of **6** (see Scheme 3).

If we compare the values of **1** with **4**, we observe for the deuterated carbon atoms essentially the same isotope effects. This already points to an interpretation that the signal splitting observed by Saunders is not a special new effect but is at least partly due to the normal high-field shift of the deuterated carbon atom. The only unusual observation is the isotope effect at C-3 in the cation of $+163$ ppb compared with $-11$ ppb in the neutral benzene.

Similar observations hold for the methylated compounds **2** and **5**. The carbon atoms bearing the deuterated methyl group experience in the neutral benzene derivative **5** only a weak upfield $^2\Delta$ isotope effect; in the corresponding cation this is hardly observable, probably owing to the larger linewidth. The carbon atom 3 of the cation is even more deshielded compared with **1** and of course is very different from the value in **5**. However, for comparison reasons, one must divide the experimental value by three, since isotope effects are known to be additive. The $^4\Delta$ isotope effect at C-3 in **2** of 75 ppb per deuterium atom would then be about half of the $^3\Delta$ value found in **1**, a not unusual result.

As already mentioned, we observe in **3** a sign reversal of the isotope effects compared with **1** and **2**, however, this sign reversal is also found in the neutral *tert*-butylbenzene.[17] The reference compound **6** prepared for this work reveals a very small $^3\Delta$ isotope effect of $-8$ ppb for nine deuterium atoms at carbon atom 1; a $^5\Delta$ isotope effect at C-3 is not observable. Dividing the $^5\Delta$ value found in **3** by 9, we obtain a small effect per deuterium atom of $-10$ ppb. Thus, on going from **1** (163 ppb) via **2** (75 ppb per deuterium) to **3** ($-10$ ppb per deuterium) we find a constant increment of about 86 ppb per deuterium atom for the isotope effects at carbon atoms 3, revealing the typical attenuation of isotope effects over three, four and five bonds. At the same time, the chemical shift of the three cations changes from $\delta=215$ in **1** to $\delta=248$ in **2** and $\delta=259$ in **3**. This accounts for the sign change, since it has been shown that the sign of both substituent increments and deuterium isotope effects is dependent on the chemical shift of the carbon atom in question.[7, 18, 19] Comparing the deuterium isotope effects in the cations **1**, **2** and **3** with the neutral reference systems **4**,

**5** and **6**, we feel safe in interpreting the observed values of these carbon atoms as a simple reflection of the large chemical shifts of the cationic carbon atoms.

## CONCLUSION

As a conclusion of this study, the term isotopic perturbation of resonance, its implications and expansions to hyperconjugation should no longer be used in the literature. It is not justified to interpret the observed signal splittings in cations of type **1** with reasonings such as the 'effective importance of one canonical form over the other,'[1] the observed signal displacements can be understood as normal intrinsic isotope effects in cations which are difficult to compare with neutral compounds owing to their unusual chemical shift.

## EXPERIMENTAL

The $^{13}C$ NMR spectra were recorded on either a Bruker AM-400 or a Bruker AMX-500 spectrometer; the cations **2** and **3** were measured in a 5:1 $H_2SO_4$–$CDCl_2$ solution, whereas the reference compounds **4**–**6** were measured in acetone-$d_6$. The measurements were always performed first with the labelled species alone and then on mixtures of labelled and unlabelled compounds to provide unequivocal assignments. The spectral widths were kept to a minimum. Zero filling to 64 K gave a digital resolution of better than 0·1 Hz per point after Fourier transformation.

Methylcyclopentenone was reacted with methyllithium-$d_3$ to give 1-trideuteromethyl-3-methylcyclopenten-1-ol;[22] **2** was prepared by dissolving this alcohol in $H_2SO_4$. The preparation of **3** started with $d_9$-*tert*-butyl-$d_9$ chloride,[17] which was reacted with *tert*-butylcyclopentadiene to yield a mixture of deuterated di-*tert*-butylcyclopentadienes.[23] Protonation of this mixture by concentrated $H_2SO_4$ yielded a single cation **3**. Compound **6** was obtained by Friedel–Crafts alkylation of *tert*-butylbenzene with *tert*-butyl-$d_9$ chloride to yield deuterated *p*-di-*tert*-butylbenzene, which was isomerized[24] to a mixture of *m*- and *p*-di-*tert*-butylbenzene. Separation of **6** from this mixture was achieved by preparative GLC.

### ACKNOWLEDGEMENTS

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