Deuterium Isotope Effects as a Probe for C – C Hyperconjugation

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In several aromatic compounds bearing a perdeuterated *tert*-butyl the $^4\Delta$-deuterium isotope effects on their ^{13}C-chemical shifts are shown to correlate linearly with π bond orders. The sign of this effect changes when the deuterated *tert*-butyl group is replaced by a deuterated methyl group and thus is indicative of C – C hyperconjugation. By comparison with substituent-induced shifts of a *tert*-butyl and a methyl group, the Taft σ_I and σ_R constants for the deuterated *tert*-butyl and methyl group were determined.

Deuterium-Isotopeneffekte als Sonde für C – C-Hyperkonjugation

Die Deuterium-Isotopeneffekte auf die ^{13}C-NMR-Signale einiger aromatischer Verbindungen, die eine perdeuterierte *tert*-Butylgruppe tragen, werden beschrieben. Die $^4\Delta$-Deuterium-Isotopeneffekte korrelieren linear mit den π-Bindungsordnungen. Das Vorzeichen dieser Effekte ändert sich, wenn die deuterierte *tert*-Butylgruppe durch eine deuterierte Methylgruppe ersetzt wird und zeigt somit C – C-Hyperkonjugation an. Durch Vergleich mit den Substituenteninkrementen der *tert*-Butyl- und der Methylgruppe wurden die σ_I- und σ_R-Konstanten nach Taft für die deuterierten *tert*-Butyl- und Methylgruppen bestimmt.

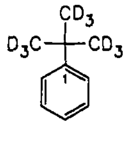
The study of deuterium isotope effects on ^{13}C-chemical shifts is an area of considerable interest[1]. Several recent papers deal with the physical cause of these small but accurately measurable chemical shift differences within a variety of compounds[2]. Although deuterium isotope effects are ultimately of vibrational origin, the results can be described conveniently in electronic terms[3]. The lower internuclear distance in the CD bond compared with the CH distance causes a redistribution of the electron density and therefore is responsible for chemical shift differences. Thus, deuterium isotope effects offer an ideal possibility to investigate the relation between electron density and chemical shift without interference from the strong perturbations usually encountered in studies of substituent chemical shifts.

In an intriguing study Ernst et al.[4] have shown that isotope effects of deuterated methyl groups over three bonds ($^3\Delta$) in aromatic molecules correlate closely with π bond orders. This was explained by less efficient hyperconjugative electron release of the deuterated methyl group compared with its proton analogue. Furthermore, Ernst[4] and Günther[5] have demonstrated, that the deuterium isotope effects in these compounds are probably caused by a dual mechanism of which the hyperconjugational part is opposite to the intrinsic contribution.

In an extension of our earlier studies of long-range deuterium isotope effects on ring-deuterated aromatic systems[6] and the calculation of substituent constants for deuterium[7], we present in this work a comparative study addressing the different behaviour of the deuterated methyl group versus a deuterated *tert*-butyl group.

Results and Discussion

We have measured the deuterium isotope effects for the *tert*-butylated aromatic compounds **1** – **9** bearing a deuterated *tert*-butyl group and for 3-methylthiophene **10**, deuterated at the methyl group. Our results are given in Table 1.



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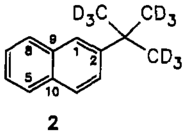

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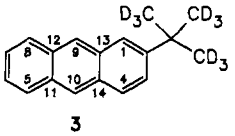

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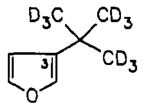

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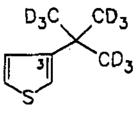

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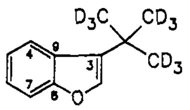

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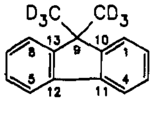

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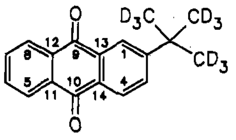

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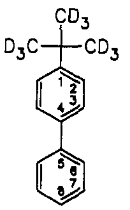

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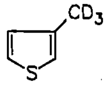

10

The values obtained for compound **10** serve to enhance the validity of the equation (1)[4].

$$^{3}\Delta\,(\text{ppb}) = -88.4\,P_\pi + 54.9 \qquad (1)$$

The $^1\Delta$ isotope effects of the *tert*-butylated compounds fall into the range of 1030 to 1110 ppb. These values can be understood from a threefold additive contribution of the $^1\Delta$ isotope effect in ethane (284 ppb)[8] and a sixfold contribution of $^2\Delta$ in alkanes (30 ppb)[8]. Thus one calculates for the methyl carbon atom in a deuterated *tert*-butyl group a value of 1032 ppb in good agreement with the results in Table 1.

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Table 1. Deuterium isotope effects on ^{13}C-chemical shifts of the compounds **1**–**10**[a]

Compound	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**[d]	**10**
C-Atom										
1	−25	6	9				0		−25	
2	0	−23	−24	14	19	20	−14	−46	0	10
3	0	−7	−6	18	10	17	−16	5	0	89
4	26	3	0	0	0	29	0	4	24	−22
5	−11	0	14	9	0	0			−13	8
6		20	8[b]			10	−16	3	0	
7		10	7[b]			0	−14	4	0	
8		0	8			0	0		9	
9		−10	0			−29	381	−6		
10		−6	0				12	−8		
11			0				−26			
12			−11				−26			
13			10				12	13		
14			0							
Me	1107	1105	1091	[c]	[c]	1034	797		1110	771
C_q	667	663	[c]	[c]	[c]	[c]		652	679	

[a] Given in ppb, measured in diluted [D_6]acetone solutions, positive values mean upfield deuterium isotope effects. — [b] Assignment tentative. — [c] Not observed due to overlap with solvent signal or intensity problems. — [d] Data from ref.[6c].

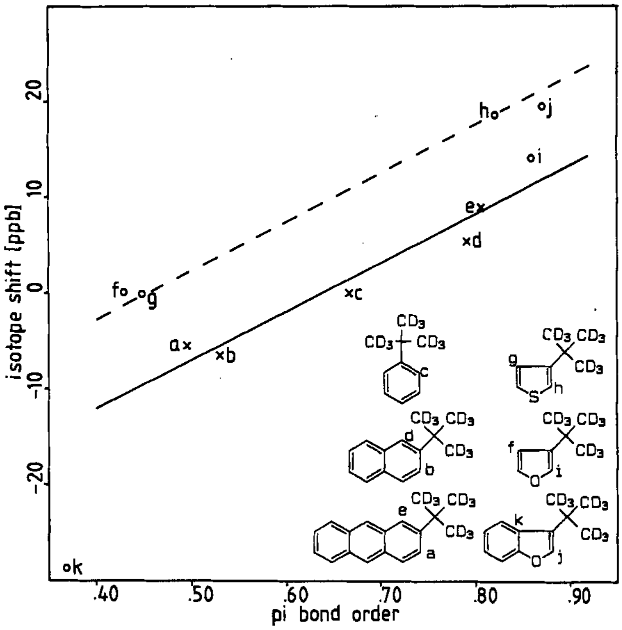


Figure 1. Plot of $^4\Delta$ isotope effects on ^{13}C-NMR chemicals shifts in compounds **1**–**6** versus π bond order

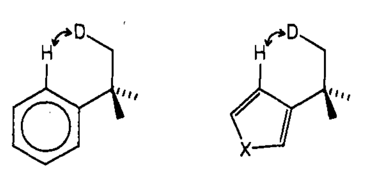
The $^2\Delta$ isotope effects can similarly be rationalized. A ninefold contribution of $^2\Delta$ in *n*-alkanes[8] yields 810 ppb. However, reduction by the effect of double substitution has to be considered. We have shown[9] for aromatic carbon atoms that substitution by one methyl group reduces the $^2\Delta$ isotope effects by about 27 ppb, thus the expected values are in the range of the results in Table 1. However, the $^3\Delta$ isotope effects are unprecedented. We find three negative values in the compounds **1**–**3** and small positive values in the remaining examples.

The $^4\Delta$ isotope effects are the central theme of this investigation. In Figure 1 a plot of these values versus the π bond order of the aromatic bonds leading from the point of substitution are given. We have used the same numerical values[4] of π bond orders from an INDO calculation[10]. For benzene, naphthalene, anthracene, biphenyl, and anthraquinone we observe exactly the same pattern as shown by Ernst et al., however, with the opposite sign of the linear correlation. The best fit is given by equation (2) with a correlation coefficient of $r = 0.9847$.

$$^4\Delta\ (\text{ppb}) = 49.2\ P_\pi - 31.9 \tag{2}$$

The five-membered ring systems furan, thiophene, and the benzofuran derivative **6** deviate clearly. No such discrepancy was observed in the presence of deuterated methyl groups. From Figure 1 our data reveal that the slope of the linear correlation is the same, but the Y intercept has changed. We believe that the Y intercepts of the equations (1) and (2) contain steric information. Consideration of steric interactions can explain the difference in behaviour of the *tert*-butyl group in the two situations encountered. The interaction between the hydrogen atoms of a single methyl group and the two hydrogen atoms in *ortho* position of the aromatic ring is almost negligible and therefore similar in six-membered and five-membered ring systems. As indicated in Scheme 1 this is not true for a *tert*-butyl group since there is a larger steric interaction of the hydrogen atoms of a *tert*-butyl group with the *ortho* hydrogen atoms and thus a considerable difference between five-membered and six-membered rings can be expected. Consequently we find a large deviation for the isotope effect of carbon atom 9 in **6**. Furthermore, this carbon atom is the only quaternary one in the above correlations. The sensitivity of isotope effects on a particular environment of a carbon atom is demonstrated in compound **7** where the two deuterated methyl groups represent two thirds of a *tert*-butyl group in a fixed conformation. The isotope effects on C-10 and C-11 deviate clearly from what would be expected by analogy with the other six-membered ring systems.

Scheme 1



The correlation for the isotope effects of the CD_3 group was explained by a less effective hyperconjugative overlap of the CD-σ bond with the aromatic π system. Higher π bond order leads to a stronger deuterium isotope effect since better conjugation enhances the difference between the CH_3 and the CD_3 group. If we place the deuterated methyl group one bond further away from the aromatic π system one should expect a different situation: Due to the shorter CD distance higher electron density builds up in the bond between the quaternary carbon atom and the methyl groups of the *tert*-butyl group. Therefore, this bond is more likely to be in hyperconjugation with the aromatic system compared with the parent *tert*-butyl group. The higher π bond order of the aromatic bond causes an isotope effect of opposite sign since in contrast to the deuterated methyl group the deuterated *tert*-butyl group acts as hyperconjugative donor. Thus, our findings constitute strong experimental evidence[11] for C−C hyperconjugation in neutral compounds.

Determination of Substituent Constants for the Deuterated *tert*-Butyl and Methyl Croups

If the interpretation given above is correct, one should be able to quantify this substituent character of the deuterated *tert*-butyl group and to show by Taft σ_I and σ_R constants, that the deuterated methyl group behaves electronically in a different manner. For these calculations[12] we have adopted the following procedure: From a recent extensive compilation of the various substituent constants[13] we have chosen a likely consistent set of σ_I and σ_R values, which was shown to give good correlations with ^{13}C-NMR chemical shifts[14]. About 20 substituents were selected, not, however, including the methyl and *tert*-butyl group. With the known ^{13}C-chemical shifts for C-4 in 1-substituted benzenes[15], for C-6 and C-8 in 2-substituted naphthalenes[16], for C-1, C-1′, and C-4′ in 4-substituted biphenyls[17], for C-5 in 3-substituted thiophenes[18], for C-14 in 2-substituted anthraquinones[19], and for C-9 and C-14 in 2-substituted anthracenes[20] a dual parameter correlation was performed to obtain the ϱ_I and ϱ_R values of these carbon atoms. These carbon atoms were selected to avoid proximity effects known for the *tert*-butyl group[21]. With the ϱ_I and ϱ_R values obtained in this manner the σ_I and σ_R substituent constants for the *tert*-butyl group and the methyl group were calculated using the known substituent chemical shifts for the above-mentioned carbon atoms. Subsequently, using the deuterium isotope effects on these carbon atoms σ_I and σ_R constants for the deuterated *tert*-butyl group and the deuterated methyl group were determined. The results of the calculations with the statistical parameters are given in Table 2. The σ_I and σ_R substituent constants for the methyl group and for the *tert*-butyl group are:

Methyl group	$\sigma_I = 0.1896$	$\sigma_R = -0.1769$
tert-Butyl group	$\sigma_I = 0.3162$	$\sigma_R = -0.2139$

It is noteworthy that the σ_I values we obtained for the methyl and *tert*-butyl group deviate clearly from the literature (σ_I reported[13] from +0.02 to −0.08), whereas the σ_R values are similar (σ_R reported[13] from −0.13 to −0.17). The deviation for σ_I could stem from the relatively small data base, however, there have been extensive discussions on the electronic nature of the methyl group[22] with both electropositive and electronegative group behaviour documented. Within the context of this work the absolute values are not of prime importance, but rather the relative outcome of σ_I and σ_R values of the deuterated methyl group and the deuterated *tert*-butyl group versus the undeuterated ones obtained on the same data base. Thus we find for the isotope effects:

[D$_3$] Methyl group	$\Delta\sigma_I = -0.0027$	$\Delta\sigma_R = +0.0012$
[D$_9$] *tert*-Butyl group	$\Delta\sigma_I = -0.0025$	$\Delta\sigma_R = -0.0005$

These quantitative results document what qualitatively was already found in the interpretation of the slope of the correlation between deuterium isotope effects and π bond orders. σ_R of the deuterated methyl group is less negative than σ_R of the parent methyl group whereas σ_R of the deuterated *tert*-butyl group is more negative than σ_R of the parent *tert*-butyl group. Thus we document quantitatively the less efficient hyperconjugative electron release of the deuterated methyl group compared with the parent methyl group and the more efficient C−C hyperconjugative electron release of the deuterated *tert*-butyl group compared with the parent *tert*-butyl group. The inductive behaviour of both groups is, as expected, of the +I type.

Deuterium isotope effects in ^{13}C-NMR spectra reflect the behaviour of substituents on a smaller scale without the

Table 2. Statistical parameters for the Taft-type correlations.
Chemical shift data taken from the literature as indicated in the text.
N = Number of individual entries. − R = Multible correlation coefficient. − f = Standard deviation in ppm for each data set.

Data set	N	σ_I	σ_R	ϱ_I	ϱ_R	R	f
C-4 of 1-X-benzenes	17			4.2335	20.5694	0.9942	0.60
C-6 of 2-X-naphthalenes	15			4.3891	8.1475	0.9787	0.55
C-8 of 2-X-naphthalenes	15			1.4971	4.8517	0.8738	0.79
C-1 of 4-X-biphenyls	12			4.8881	21.4713	0.9836	1.08
C-1’ of 4-X-biphenyls	12			−3.2093	−1.6520	0.9815	0.16
C-4’ of 4-X-biphenyls	12			1.8794	2.9818	0.9838	0.17
C-5 of 3-X-thiophenes	11			5.1081	3.1216	0.8835	0.55
C-14 of 2-X-anthraquinones	10			2.9683	19.9494	0.9072	1.74
C-9 of 2-X-anthracenes	7			2.7112	6.8298	0.9609	0.53
C-14 in 2-X-anthracenes	7			0.5017	6.9410	0.9418	0.65
SCS values of the methyl group	8	0.1896	−0.1769			0.9767	0.29
SCS values of the *tert*-butyl group	10	0.3162	−0.2139			0.8761	0.79
Isotope effects of the CD$_3$ group	8	−0.0027	0.0012			0.8990	0.0034
Isotope effects of the [D$_9$]*tert*-butyl group	10	−0.0025	−0.0005			0.8774	0.0059

large electronic perturbations. We have shown in this paper that qualitative ideas on hyperconjugative behavior of the methyl group and the *tert*-butyl group find a correspondence by fitting the deuterium isotope effects with a Taft-type dual parameter equation. C – C Hyperconjugation and steric interaction are likely to account for the isotope effects observed for deuterated *tert*-butyl groups.

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Experimental

The preparations of the unlabeled compounds *tert*-butylbenzene[23], 2-*tert*-butylnaphthalene[24], 2-*tert*-butylanthracene[25] 3-*tert*-butylthiophene[26], 3-*tert*-butylbenzofuran[27], 9,9-dimethylfluorene[28] 2-*tert*-butylanthraquinone[25], and 2-methylthiophene[29] have been described in the literature. The viability of each published procedure was first tested in the synthesis of the unlabeled material which was subsequently needed as internal reference for the determination of isotope effects. The same procedures served for the preparation of the labeled compounds **1 – 3**, **5 – 8**, **10** starting from commercially available [D_9]*tert*-butyl alcohol.

3-*tert*-Butylfuran could not be synthesized by direct alkylation. The synthesis followed the sequence given by Miller[30] with some modification as given below.

1-Trimethylsilyl-3-chloromethyl-4,4-dimethyl-1-pentyn-3-ol: A flame-dried two-necked flask was charged with 30 mmol of *tert*-butylmagnesium chloride in THF and cooled to −78°C. To this solution, 5.22 g (30 mmol) of 4-trimethylsilyl-1-chloro-3-butyn-2-one[30] was added, and the temperature was raised to −10°C. After stirring for 20 min the mixture was worked up with water, extracted with ether, and the organic phase dried with $MgSO_4$. The compound was isolated by prep. GLC (see below) to yield 2 g (29%) of the product. – ^{1}H NMR ([D_6]Acetone): δ = 0.14 [s, 9 H, $Si(CH_3)_3$], 1.08 (s, 9 H, *tert*-butyl), 3.75 (AB pattern, J = 10.8 Hz, 2 H, CH_2Cl), 2.77 (s, 1 H, OH). – ^{13}C NMR ([D_6]Acetone): δ = 90.08 (C-1), 107.26 (C-2), 76.79 (C-3), 38.07 (C-4), 24.73 (C-5), 51.85 (chloromethyl) 1.10 ($SiMe_3$).

$C_{11}H_{21}ClOSi$ (232.8) Calcd. C 56.74 H 9.09
Found C 56.67 H 9.00

3-tert-Butylfuran: To remove the trimethylsilyl group, the above described pentyn-3-ol (2.25 g, 9.7 mmol) was dissolved in ether and treated with one equivalent of tetrabutylammonium fluoride and 0.5 g of NaOH. The compound rearranges to yield 1 g (83%) of 2-*tert*-butyl-2-ethynyl oxirane[30] which was purified by prep. GLC. This oxirane was transformed into **4** according to the literature[30].

The prep. *GLC work* was performed with an A 90-P3 Aerograph, column 5% SE 30 on Chromosorb G, AW-DMCS, 60 – 80 mesh, 1.8 m, 1/4 inch, helium flow rate (120 – 130 ml/min). The anthracene derivatives were recrystallized from aqueous ethanol. – *NMR Measurements:* The 100.6-MHz ^{13}C-NMR spectra were taken at 305 K on a Bruker WH-400 spectrometer equipped with an 80 K Aspect 2000 computer using [D_6]acetone solutions or in some cases $CDCl_3$, with no detectable difference of the deuterium isotope effects. The measurements were performed first with the pure deuterated compounds and then repeated after subsequent addition of small amounts of the unlabeled material. The spectral width was set as narrow as possible and separate for the aromatic and aliphatic regions, typically between 2000 and 4000 Hz. Zero filling to 64 K gave a digital resolution better than 0.1 Hz/pt after the Fourier transform. Gaussian multiplication was used to increase the resolution. The statistical computations were performed on a Sperry 11/750 computer of the Hochschulrechenzentrum Marburg.

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