Intrinsic $^2H/^1H$ NMR Isotope Effects on ^{13}C Chemical Shifts: Dependence on Carbon Hybridization and Substitution

Joachim R. Wesener, Detlef Moskau, and Harald Günther*

Contribution from Fachbereich 8, Organic Chemistry II, University of Siegen, D-5900 Siegen, Germany. *Received May 20, 1985*

Abstract: Deuterium-induced NMR isotope shifts of ^{13}C resonance frequencies, $^1\Delta(^{13}C)$, have been measured for a variety of deuterium-labeled hydrocarbons. One-bond effects in ethane, ethylene, and acetylene, as well as in the corresponding phenyl compounds, where found to correlate linearly with carbon hybridization. Upon introduction of α-substituents $^1\Delta(^{13}C)$ increases. For methyl- and phenyl-substituted methanes the substituent effect is additive. Data for 1-monodeuterated n-alkanes give support for the steric origin of the well-known γ-effect on ^{13}C chemical shifts. The torsional angle dependence of $^3\Delta(^{13}C)$-values shows maxima for dihedral angles of 0° and 180° and minima for 60° and 120°, respectively.

The availability of high-field NMR instruments today greatly facilitates the exact determination of $^2H/^1H$ isotope effects on ^{13}C chemical shifts, $^n\Delta(^{13}C)$, where n is the number of intervening bonds, and these parameters have emerged as valuable experimental data potentially useful for structural and mechanistic investigations. Presently, however, our knowledge of their dependence on chemical structure is still incomplete,[1] despite some interesting relationships formulated recently.[2]

In the following we report on three aspects of a systematic ^{13}C NMR investigation of a variety of saturated and unsaturated deuterium-labeled compounds: (1) The s-character dependence of deuterium-induced ^{13}C isotope shifts over one bond, $^1\Delta(^{13}C)$, (2) the additivity of substituent effects for these parameters, and (3) a correlation between isotope shifts and substituent effects on $\delta(^{13}C)$-values.

Results and Discussion

The compounds used for this study are summarized in Chart I and the experimental results are collected in Tables I–III; additional data for various model compounds are given in the text. All isotope effects were measured in solution at 100.61 MHz on mixtures of deuterated and nondeuterated material with ^1H decoupling and the highest possible resolution. High-field shifts are given as positive values. Assignments for ^{13}C resonances were either available from the literature or based on the characteristic magnitudes of $^{13}C,^2H$ spin–spin coupling constants. The $^{13}C,^2H$ coupling constants over one bond are also given in Table I. In a few cases additional ^2H decoupling was employed in order to resolve small shifts obscured by line-broadening due to long-range $^{13}C,^2H$ spin–spin interactions.

One-Bond Isotope Effects, $^1\Delta(^{13}C)$, and Carbon Hybridization.[3] There are a number of reports in the literature on the s-character dependence of $^1\Delta$.[4] In particular, calculations based on a vibrational model[5] as well as experimental data for cycloalkanes[6] have shown that $^1\Delta(^{13}C)$ decreases with increasing s-character of the corresponding CD bond hybrid. However, quantitative results from a study that includes aliphatic, olefinic, and acetylenic CD bonds have not yet been obtained. Doddrell and Burfitt[7] were the first to perform a systematic investigation in this direction. They measured $^1\Delta(^{13}C)$ in heptane-*1*-d_1, 1-heptene-*1*-d_1, and 1-heptyne-*1*-d_1, but they did not find the expected correlation with carbon hybridization. One reason for this failure can be seen in the lower accuracy of the experimental data attainable at that

Chart I

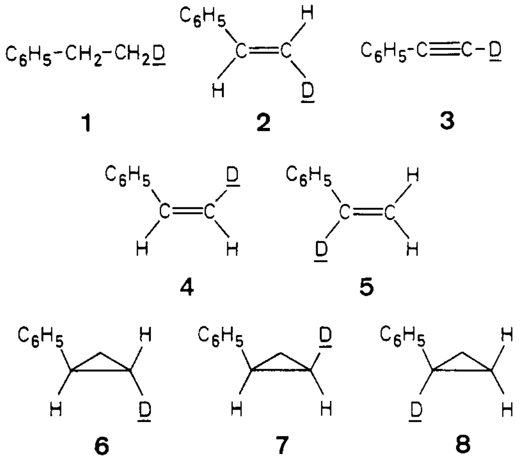

Table I. One-Bond $^2H/^1H$ Isotope Effects, $^1\Delta(^{13}C)$, on ^{13}C Chemical Shifts (ppb), $^1J(^{13}C,^2H)$ Coupling Constants (Hz), s-Character (in %) Calculated from Equation 2, and Isotope Effect (ppb) Calculated from Equation 1 for **1**–**8**

	$^1\Delta(^{13}C)_{\text{exptl}}{}^a$	$^1J(^{13}C,^2H)$	s(i)	$^1\Delta(^{13}C)_{\text{calcd}}$
1	296.0	19.40	25.26	295.5
2	283.2	24.55	31.97	283.9
3	252.7	38.45	50.07	252.5
4	257.8	23.68	30.84	286.1
5	323.3	23.57	30.69	285.8
6	308.9	24.78	32.27	283.4
7	336.2	24.53	31.94	283.9
8	344.8	24.54	31.96	283.9

[a] Positive values denote high-field shifts.

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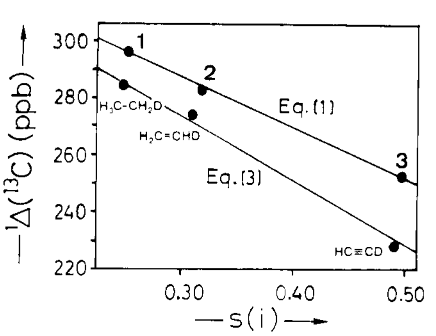

Figure 1. Correlation between $^{1}\Delta(^{13}C)$ (ppb) and fractional s-character (cf. text).

time. For example, they reported for heptane-*1-d*$_1$ $^{1}\Delta(^{13}C)$ = 280 ppb, whereas we find 300.9 ppb. The difference is already 50% of the total range observed for $^{1}\Delta(^{13}C)$ (Table I). Furthermore, the 1-heptene-*1-d*$_1$ studied was a mixture of the cis and trans isomer, a fact that introduced further ambiguities. On the other hand, Sergeyev[8] most recently emphasized that for the $^{1}\Delta(^{13}C)$ data of methane, benzene, and acetylene a correlation with the s-character of the respective CH bond hybrid is missing. It will become evident later that this comparison failed because substituent effects on $^{1}\Delta(^{13}C)$ were not considered.

For the deuterated β-carbon in ethylbenzene (**1**), (*E*)-styrene (**2**), and phenylacetylene (**3**) we now observed an excellent linear correlation between $^{1}\Delta(^{13}C)$ and the fractional s-character s(i), of the corresponding CD bond hybrid (Figure 1, correlation coefficient 0.9996):

$$^{1}\Delta(^{13}C)\ (\mathrm{ppb}) = -173.27s(i) + 339.27 \qquad (1)$$

s(i) was calculated from the one-bond $^{13}C,^{2}H$ coupling constant by the modified Muller–Pritchard relation[9]

$$s(i) = 6.5144\,{}^{1}J(^{13}C,^{2}H)/500 \qquad (2)$$

which takes into account the ratio $J(^{13}C,^{1}H)/J(^{13}C,^{2}H) = 6.5144$.[10] A possible primary isotope effect on the $^{1}J(^{13}C,^{2}H)$ data is thereby neglected, but recent studies[8,11] have shown that these effects are small and therefore well within the error limits of the empirical constant of eq 2. The $^{1}\Delta(^{13}C)$ data for **1**–**8** calculated from eq 1 are given in Table I.

A similar test for the parent systems ethane, ethylene, and acetylene was desirable. The monodeuterated species were prepared as mixtures with isotope-free material from suitable precursors (cf. experimental part) by reaction with H_2O/D_2O (1:3) and measured in solution at low temperature. The ^{1}H-decoupled ^{13}C spectra shown in Figure 2 yielded the following data:

	H_3C-CH_2D	$H_2C=CHD$	$HC\equiv CD$
$^{1}\Delta(^{13}C)$ (ppb)	284.0	273.6	226.7 (223)
$^{1}J(^{13}C,^{2}H)$ (Hz)	19.2	24.0	38.0 (38.16)
s(i) (%)	25.0	31.2	49.5

For $HC\equiv CD$ Sergeyev reported the values given in parentheses.[8] The $^{1}\Delta(^{13}C)$-values are now described by eq 3 (Figure 1, correlation coefficient 0.997):

$$^{1}\Delta(^{13}C)\ (\mathrm{ppb}) = -239.9s(i) + 349.9 \qquad (3)$$

These results clearly demonstrate the hybridization dependence of ^{13}C isotope shifts over one bond but at the same time show that quantitative relations are valid only for compounds of closely related structure. For instance, instead of methane it is important to use ethane as the sp^3 carbon model in order to keep the substitution pattern as close as possible to that in ethylene and acetylene. The differences found for the $^{1}\Delta(^{13}C)$-values in **1**–**3** and the parent compounds, respectively, could also originate—at least in part—from the fact that the measurements were made in different solvents and at different temperatures (cf. experimental part). However, the main reason for the different slopes and intercepts of eq 1 and 3 certainly must be seen in the β-substitution of the parent systems by phenyl. The $^{1}\Delta$-values found for **2** and **4** (cf. Table I) support this view since a simple change of the deuteration site from the trans to cis position with respect to the phenyl group completely destroys the correlation. Apparently already modest structural variations give rise to additional effects for $^{1}\Delta(^{13}C)$ that dominate the hybridization dependence. This view is further supported by the data from the series of phenyl-substituted cyclopropanes **6**–**8** (Chart I), where $^{1}J(^{13}C,^{2}H)$ and consequently the calculated s-character differs only slightly, while a strong variation of $^{1}\Delta(^{13}C)$ is found (Table I). It is also noteworthy that the $^{1}J(^{13}C,^{2}H)$ value for the olefinic compound **2** is identical with the corresponding values in **7** and **8**, whereas significant changes are observed for $^{1}\Delta(^{13}C)$. On the other hand, the data for the axial and equatorial CD bond in cyclohexane (% s(i) = 24.6, $^{1}\Delta_{ax}$ = 444.9 ppb and % s(i) = 25.4, $^{1}\Delta_{eq}$ = 396.4 ppb, respectively)[2j] are in line with the trend of eq 1 and 3.

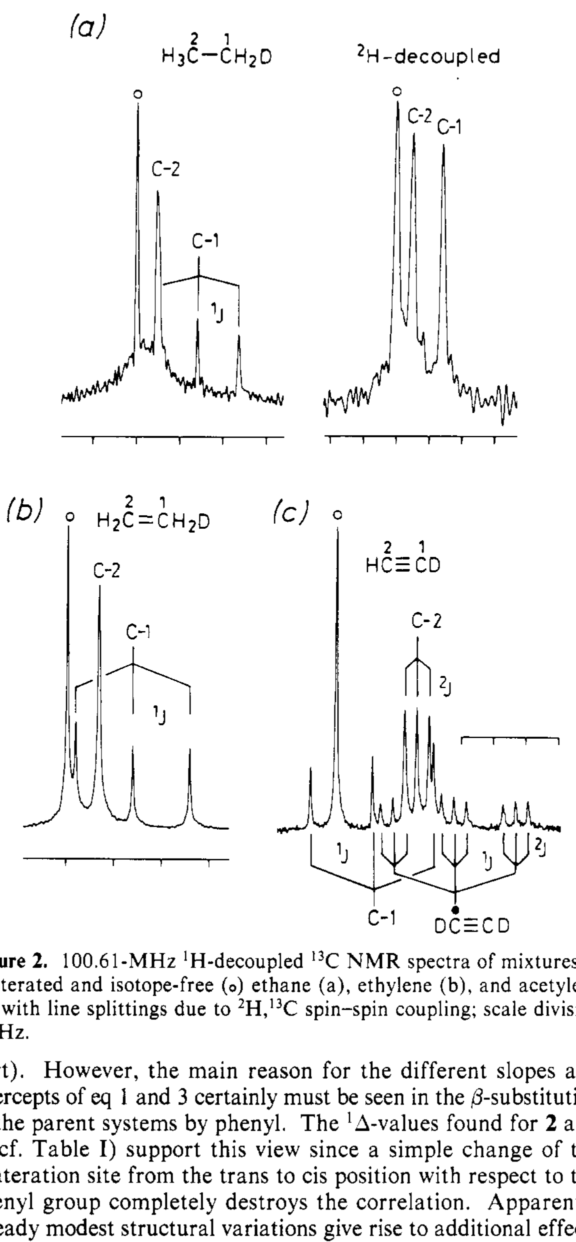

Figure 2. 100.61-MHz ^{1}H-decoupled ^{13}C NMR spectra of mixtures of deuterated and isotope-free (o) ethane (a), ethylene (b), and acetylene (c) with line splittings due to $^{2}H,^{13}C$ spin–spin coupling; scale division 20 Hz.

As for the physical cause of the observed effect, it seems reasonable to relate the decreasing isotope shift in ethane, ethylene, and acetylene to the decreasing CH bond lengths of these systems.[12] Recent theoretical findings established the dependence of isotope shifts in diatomic molecules AB on the anharmonicity of the AB bond potential.[13] Assuming that the potential is less anharmonic for the shorter and stronger bonds, the presumably smaller fractional bond shortening upon replacement of hydrogen

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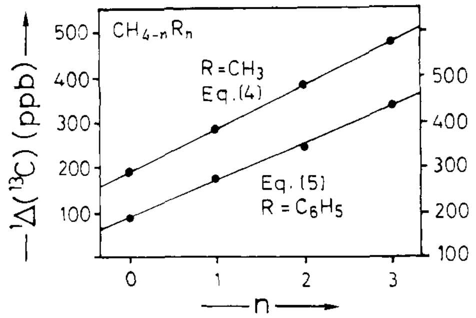


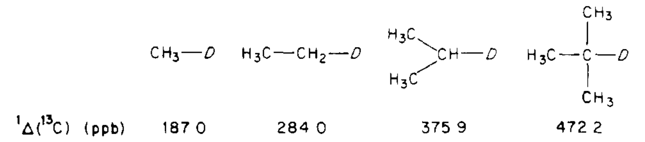
Figure 3. Correlation between $^1\Delta(^{13}C)$ (ppb) and the number, n, of substituents in methyl- and phenyl-substituted methanes $CH_{4-n}R_n$ (cf. text): left scale eq 4, right scale eq 5.

by deuterium should then result in a diminished isotope shift. However, for heavier elements than ^2H Gombler[14] reported the opposite trend, i.e., increasing isotope shifts with decreasing bond lengths. The reason for this different behavior is presently not clear.

An interesting side aspect is illustrated by the two pairs of stereoisomers **2**/**4** and **6**/**7**. In both pairs the $^1\Delta$ values found for the cis and the trans compounds differ considerably. However, for **2**/**4** $^1\Delta_{cis} < {}^1\Delta_{trans}$ holds, whereas for **6**/**7** the reverse is true. These are again examples of stereospecific isotope effects,[2h–n] but the results also emphasize that empirical $^1\Delta(^{13}C)$/structure correlations are of limited scope.

The largest isotope effect in both series of compounds is found for α-substitution by phenyl (data for **5** and **8**). Relative to the parent compounds with $^1\Delta(^{13}C)$-values of 273.6 ppb (ethylene) and 308.7 ppb (cyclopropane),[6] the effect of phenyl substitution is +49.7 and +36.1 ppb, respectively. Hence, $^1\Delta(^{13}C)$ increases with carbon substitution, a finding that parallels observations to be discussed in the following section.

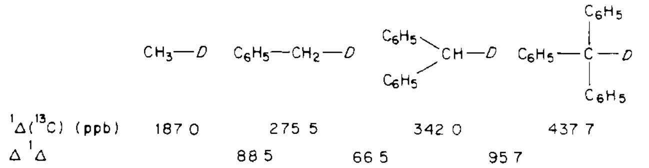
Additivity of Substituent Effects on $^1\Delta(^{13}C)$ and Correlation with $\delta(^{13}C)$. All investigations so far have shown that isotope effects are additive in the sense that for a particular methyl group $^1\Delta(^{13}CD_3) = (^3/_2)^1\Delta(CHD_2) = (3)^1\Delta(CH_2D)$ holds. This was most clearly demonstrated by the findings made for the deuterated methanes.[15] Puzzled by the large difference observed for $^1\Delta(^{13}C)$ in methane[15] and C-2 in propane[16] (see below), respectively, we investigated the complete series of methyl-substituted methanes and found that the substituent effect on $^1\Delta(^{13}C)$-values in these compounds is also additive:



The observed isotope effects are linearly correlated to the number, n, of methyl groups, as shown in Figure 3. The appropriate equation is

$$^1\Delta(^{13}C)\ (ppb) = (94.98)n(CH_3) + 186.74 \qquad (4)$$

with a correlation coefficient of 0.9999. A similar relation sholds for phenyl substitution:



The correlation is now expressed by

$$^1\Delta(^{13}C)\ (ppb) = (81.1)n(C_6H_5) + 189.7 \qquad (5)$$

Table II. $^2H/^1H$ NMR Isotope Effects for ^{13}C Chemical Shifts in n-Alkanes (ppb) (experimental error ±0.5 ppb)

compd	$^1\Delta$	$^2\Delta$	$^3\Delta$	$^4\Delta$
methane	187.0[a]			
ethane	284.0	93.5		
propane	299.5	90.5	31.6	
butane	298.2	88.7	29.1	-5.1
pentane	301.0	87.9	27.8	-5.3
hexane	300.7	87.7	28.2	-5.6
heptane	300.9	88.1	28.2	-5.7
octane	301.3	88.3	28.3	-5.7
nonane	301.0	87.9	28.4	-5.1
decane	300.9	87.8	28.1	-5.4

[a] Reference 15.

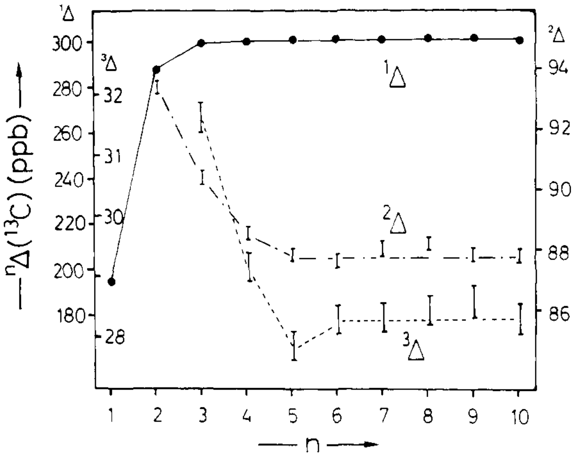


Figure 4. Intrinsic ^2H-induced isotope shifts in n-alkanes (cf. text; note different scales).

(Figure 3, correlation coefficient 0.996).

Since substituent effects on ^{13}C chemical shifts are within certain limits additive, especially in the case of alkyl substituents,[17] our results suggest that the observed isotope shifts to some extent reflect the normal substituent effects for ^{13}C chemical shifts. In other words, the NMR isotope effect of a particular carbon responds to the introduction of substituents in an analogous way as the NMR shielding constant does. This view was also expressed by Jameson.[18] Forsyth in his recent review[1b] also noted that $^1\Delta(^{13}C)$-values increase upon substitution.

Our finding is contrasted, however, by the opposite trend reported for $^3\Delta(^{13}C)$-values in D–O–C–C_γ bond fragments in polysaccharides,[20] where $^3\Delta$ decreases with substitution of the γ-carbon. This discrepancy can be related to the fact that in this case substitution and isotopic replacement occur at different positions, while in our case the same carbon is involved.

In this context it seemed of interest to extend NMR isotope effect measurements to larger alkanes where the additivity of substituent effects on ^{13}C chemical shifts has been studied extensively. The results for compounds that contain a terminal CH_2D group, up to decane and including long-range effects, are summarized in Table II and Figure 4. One finds that isotope shifts over one, two, and three bonds are subject to substituent effects that arise from chain prolongation. This influence ceases with pentane, and the $^n\Delta(^{13}C)$-values are constant for the larger alkanes. Up to pentane, $^1\Delta$ increases with the introduction of additional methyl groups, while $^2\Delta$ and $^3\Delta$ decrease. A closer inspection of the $^1\Delta$-data, however, shows that the substituent-induced change is slightly negative in going from propane to butane (cf. Table II). This structural change corresponds to the intro-

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Table III. Geminal and Long-Range ^{13}C Isotope Shifts (ppb) for **1–8** and Other Model Compounds Mentioned in the Text

	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**
$^2\Delta$	83.0 $(84.1)^a$	104.4	427.2	80.6	69.0 (C-2) 147.0 (C-α)	97.0 (C-1) 101.0 (C-3)	89.8 (C-1) 92.4 (C-3)	50.9 (C-α) 79.4 (C-2)
$^3\Delta$	3.9 $(3.8)^a$	8.4	0.0	9.4	19.4	0.0	6.6	43.2
$^6\Delta$	4.4 $(4.2)^a$	4.9	7.6	11.6		3.9	6.4	

	$H_3C—CH_2D$	$H_2C=CHD$	$HC \equiv CD$	$(CH_3)_2CHD$	$(CH_3)_3CD$
$^2\Delta$	93.5	131.2	500.4	113.0	124.8

	$C_6H_5—CH_2D$	$(C_6H_5)_2CHD$	$(C_6H_5)_3CD$		$C_6H_5—CH_2D$	$(C_6H_5)_2CHD$	$(C_6H_5)_3CD$
$^2\Delta$	34.1	32.1	48.5	$^5\Delta$	−3.9	−2.6	0.0
$^3\Delta$	−0.2	10.3	19.8				

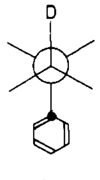
^{a}Values derived from the d_3 compound.

duction of a γ-methyl group with respect to C-1 and the sign change of the $^1\Delta$ increment parallels the sign change observed for $\Delta\delta(^{13}C)$ in alkanes where γ-effects are negative (upfield shift), while α- and β-effects are positive.[17] If indeed the γ-effect is of steric origin—as seems generally accepted[19]—the effectively smaller size of the CD bond[20] should diminish these interactions and thus reduce the upfield shift resulting from the introduction of a γ-methyl group. The small decrease found for $^1\Delta(^{13}C)$ in butane-d_1 supports this view that was also advanced in order to explain a low-field intrinsic isotope shift over four bonds.[21]

The three isotope effects discussed so far are of positive sign (high-field shift). On the other hand, $^4\Delta(^{13}C)$ is negative (low-field shift) and within experimental error of constant magnitude, suggesting again a steric origin of the observed change. As above, the slightly smaller CH_2D group as compared to the CH_3 group should reduce steric repulsion in the γ-position. The shielding of the γ-carbon resonance should therefore decrease, as is indeed observed. The experimental findings thus once more strongly support the idea that the γ-shielding effect for $\gamma(^{13}C)$ in *n*-alkanes is of steric origin.

Geminal, Vicinal, and Long-Range Isotope Shifts for 1-8 and the Other Model Compouds. The isotope effects over two and more bonds measured in this study and summarized in Table III display several interesting features that can be related to a number of observations discussed by other research groups. For **1–3** as well as for the parent systems ethane, ethylene, and acetylene we note a dramatic increase for $^2\Delta$ in going to the acetylenic compound. This leads to the unusual situation that $^2\Delta > {}^1\Delta$. The $^2\Delta$-values for **3** and for acetylene substantiate earlier findings for 1-heptyne-*1-d*$_1$.[7] The large two-bond effect in acetylene was recently compared with the fairly strong substituent effects on $\delta(^{13}C)$ over two bonds found in acetylenes.[8] A similar exceptional behavior is shown for $^2J(^{13}C,^1H)$ in acetylene, which has the largest geminal $^{13}C,^1H$ coupling constant measured so far.[22]

The three-bond effects for **1**, **2**, and **4** are of interest with respect to the torsional angle dependence of $^3\Delta(^{13}C)$.[2h–n] $^3\Delta(\mathbf{4}) > {}^3\Delta(\mathbf{2})$ agrees with other observations that showed $^3\Delta(0°) > {}^3\Delta(180°)$.[2h]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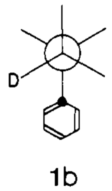
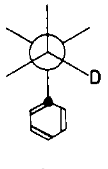

1b


1c

For **1**, the measured effect is the average for the three conformations **1a–c**. Neglecting isotope effects on rotamer populations it can be expressed by

$$^3\Delta_{\text{obsd}} = (1/3)^3\Delta(180°) + (2/3)^3\Delta(60°) \qquad (6)$$

With 8.4 ppb from **2** as an estimate for $^3\Delta(180°)$, $^3\Delta(60°) = 1.7$ ppb results. The $^3\Delta(180°)/^3\Delta(60°)$ ratio is thus similar to that observed in adamantane (26:8).[2h] For **6** and **7** the three-bond effects for C-α correspond to $^3\Delta(120°)$ and $^3\Delta(0°)$, respectively, and the observed values now indicate a minimum for $^3\Delta(^{13}C)$ around torsional angles of 120°.

Much larger $^3\Delta(^{13}C)$-values are found for **5** and **8**. In both compounds the preferred conformation brings the CD bond in the plane of the phenyl ring, since **5** is planar[23] and **8** has a bisectic arrangement of both rings.[24] The $^3\Delta$-effects are then the arithmetic mean of $^3\Delta(0°)$ and $^3\Delta(180°)$, and both effects are presumably larger than the corresponding values discussed above. While the general conclusion $^3\Delta(0°,180°) > {}^3\Delta(60–120°)$ finds support, a detailed torsional angle dependence for $^3\Delta$ that includes all compounds cannot be formulated.

From the long-range effects those over four and five bonds were not resolved (exception compound **5**); $^6\Delta$ is observed for **1**, **6**, and **7**, as well as for the π-systems **2**, **3**, and **4**, a finding which is of interest with respect to the polar mechanism recently advanced to explain long-range $^n\Delta(^{13}C)$-values.[2g,25] The same is true for the observation of $^5\Delta$ in **8** and the stereospecific magnitudes of $^6\Delta$ in **2**, **4**, **6**, and **7** with $^6\Delta(\mathbf{2}) < {}^6\Delta(\mathbf{4})$ and $^6\Delta(\mathbf{6}) < {}^6\Delta(\mathbf{7})$. As in other cases,[21,m] the possibility that vibrational coupling is responsible for the observed effects should also be considered. In this respect we note that $^6\Delta$ shows a systematic increase in going from **1** to **3** (Table I). However, considering the experimental error, the significance of this trend remains to be established.

The data of the phenyl-substituted systems are of interest with respect to the conformational dependence of hyperconjugative interactions.[2a] Compared to toluene, introduction of phenyl groups in diphenyl- and triphenylmethane favors conformations with twisted phenyl rings[26] where overlap between the π-system and the benzylic CD bond is reduced. Accordingly, the negative hyperconjugative contributions to $^3\Delta$ and $^5\Delta$[2a] decrease and these isotope shifts become increasingly positive.

Conclusions

The results presented in this paper demonstrate that an s-character dependence of $^1\Delta(^{13}C)$ does exist for compounds of closely related structure. For the first time, quantitative relations for substituent effects on $^1\Delta(^{13}C)$ were derived. The data for *n*-alkanes strongly support the idea that steric effects contribute to the observed isotope shifts in cases where van der Waals interactions are important. $^3\Delta(^{13}C)$-values show maxima for torsional angles of 0° and 180° and minima for 60° and 120°.

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Experimental Section

Compounds. The synthesis of the compounds followed standard procedures and deuteration was mostly achieved by deuteriolysis of organometallic precursors with D_2O or deuterated acid. The following reaction pathways were used. **1**: from β-phenylethylmagnesium bromide. **2**,[27] **3**: from phenylacetylene with *n*-butyllithium followed by deuteriolysis. **4**: from **3** following ref 27. **5**: 1-phenylethanol-*1*-d_1 was prepared from acetophenone with $LiAlD_4$ and dehydrated by destillation over $KHSO_4$. **6**: from **2** by Simmons–Smith reaction[28] with CH_3I. **7**: from **4** as before. **8**: from phenylcyclopropane by reaction with NaH in Me_2SO-d_6. Ethane-d_1: from ethyl magnesium bromide by deuteriolysis. Ethylene-d_1: from vinyl magnesium bromide as before. Acetylene-d_1: from CaC_2 as before. In the last three cases the 3:1 mixture of deuterated and isotope-free material was directly prepared by reaction with D_2O/H_2O (3:1). The gaseous products were passed through two cooling traps (−50 °C) in order to remove solvent traces and condensed into the NMR tube filled with the appropriate solvent (see below). In the case of acetylene the product mixture contained C_2H_2, C_2HD, and C_2D_2 in a ratio of 1:2:2 as determined by integration of the ^1H-decoupled ^{13}C NMR spectrum. The deuterated methylmethanes as well as the deuterated *n*-alkanes were prepared via the corresponding Grignard compounds, while the phenylmethanes were generated from benzylmagnesium chloride, diphenylmethyllithium, and triphenylmethylmagnesium bromide, respectively, by deuteriolysis.

Spectra. ^{13}C NMR spectra were measured under ^1H broadband decoupling at 100.61 MHz on a Bruker WH-400 FT NMR spectrometer equipped with an ASPECT 2000 data system. Isotope shifts were determined from 3:1 or 4:1 mixtures of deuterated and isotope-free material either prepared directly or by mixing. Ethane and ethylene were measured at 173 K in CD_2Cl_2/CS_2 (20 vol %), while acetylene was measured at 213 K in acetone-d_6 (50 vol %). All other compounds were measured as 1 M solutions in $CDCl_3$ (1% Me_4Si) at 310 K, except for propane and butane, which were measured at 215 and 265 K, respectively. Spectral assignments were available from the literature[22a,29] and supported by intensity ratios and line splittings due to $^{13}C,^2H$ spin–spin coupling. Ambiguities in the assignments of isotope shifts were removed by increasing the concentration of one of the components in the test mixture. In order to achieve highest possible resolution, selected portions of the spectrum were recorded separately with use of sweep widths of 100–300 Hz and zero-filling resulting in an experimental error of $<\pm 0.5$ ppb for the isotope shifts and $>\pm 0.05$ Hz for the coupling constants. Where necessary, resolution enhancement and/or ^2H decoupling was employed in order to remove signal overlap due to line-broadening effects.

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Registry No. Ethylbenzene, 100-41-4; styrene, 100-42-5; phenylacetylene, 536-74-3; phenylcyclopropane, 873-49-4; heptane, 142-82-5; octane, 111-65-9; nonane, 111-84-2; decane, 124-18-5; methane, 74-82-8; ethane, 74-84-0; propane, 74-98-6; butane, 106-97-8; pentane, 109-66-0; hexane, 110-54-3; deuterium, 7782-39-0.

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Dynamics of Phenylalanine in the Solid State by NMR

M. H. Frey,[†] J. A. DiVerdi,[‡] and S. J. Opella*

Contribution from the Department of Chemistry, University of Pennsylvania, Philadelphia, Pennsylvania 19104.
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Abstract: The dynamics of the amino acid phenylalanine in the solid state at room temperature are characterized by ^2H and ^{13}C NMR experiments. Samples crystallized from water at neutral pH and samples crystallized from ethanol/water solution have two identifiable types of molecules. About half of the phenylalanine molecules crystallized from water have immobile rings, and the rest have rings that undergo rapid 2-fold flips about the C_β–C_γ bond axis. Analysis of the ^2H and ^{13}C relaxation rates indicates that the frequency of ring flips for phenylalanine crystallized from water is approximately 10^9 Hz. Both types of phenyl rings in the sample crystallized from ethanol/water are immobile on time scales slower than about 10^2 Hz. In contrast, phenylalanine hydrochloride samples have only a single type of molecule with a ring undergoing relatively slow ($\approx 10^2$ Hz) reorientation about the C_β–C_γ bond axis.

Large amplitude motions are present in many crystalline and amorphous solid materials at room temperature.[1] These motions can be readily characterized by solid-state NMR because motional averaging strongly influences spectral manifestations of the nuclear spin interactions. A wide range of amplitudes and frequencies of intramolecular motions can be examined through experiments that measure spectroscopic properties of the chemical shift, dipolar, and quadrupolar interactions.

In solid-state NMR, the amplitudes and directions of rapid motions can be deduced from the analysis of powder pattern line shapes. Motions alter powder patterns through the averaging of the spin interaction tensors. The effects of specific types of motions on powder pattern line shapes can be readily calculated when these motions occur frequently compared to the NMR time scale defined by the frequency breadth of the static powder pattern resulting from the spin interaction. Isotropic chemical shift spectra typically reflect motions slower than about 10^2 Hz, chemical shift anisotropy powder patterns are averaged by motions that occur more rapidly than 10^3 Hz, ^1H–^{13}C heteronuclear dipolar couplings are averaged by motions faster than 10^4 Hz, and the ^2H quadrupole interaction is sensitive to motions that are faster than 10^6 Hz. Relaxation measurements reflect events that occur near the 10^9-Hz Larmor frequencies. The averaging of powder patterns requires large amplitude fluctuations, while efficient relaxation can be induced by both relatively small as well as large amplitude fluctuations.

The dynamics of phenylalanine in the solid state are suprisingly complex.[2,3,5,11] The phenyl side chains of the aromatic amino

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[†] Present address: JEOL (USA), Inc., Peabody, MA 01960.

[‡] Present address: Smith, Kline & French Laboratories, Philadelphia, PA 19101.

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