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Intrinsic Deuterium Isotope Effects of Deuteriated *tert*-Butyl Groups on the ^{13}C NMR Spectra of Aromatic Compounds

Hartmut H. Balzer and Stefan Berger*
Fachbereich Chemie der Universität Marburg, Hans Meerwein Strasse, D-3550 Marburg, FRG

The $^3\Delta$-deuterium isotope effects of partially and fully deuteriated *tert*-butyl groups on the ^{13}C NMR spectra of *tert*-butylbenzene and derivatives are discussed in detail. It is shown that they correlate with the chemical shift of C-1 of the aromatic ring. It has been demonstrated that when deuterium is replaced with some other substituents, the SCS values of these substituents show a parallel behaviour to the deuterium isotope effects. It is concluded that, for the compounds studied, deuterium isotope effects and substituent chemical shifts can be described on a common basis.

KEY WORDS Deuteriated *tert*-butyl groups ^{13}C NMR $^3\Delta$-Deuterium isotope effects Substituent chemical shifts

INTRODUCTION

Current understanding of deuterium isotope effects

$$\Delta = \delta_{C(D)} - \delta_{C(H)}$$

on ^{13}C NMR chemical shifts is based on the vibrational model and most of these values are well understood.[1,2] In a recent review,[3] however, it was shown that the language of physical organic chemistry, using terms such as isotope inductive and hyperconjugational effects as introduced by Halevi *et al.*,[4,5] have even better descriptive and predictive power in complex organic molecules for isotope effects over more than one bond. In earlier work we had established substituent constants for the deuteriated *tert*-butyl and methyl groups[6,7] and had shown that in carbonyl compounds $^2\Delta$-isotope effects of both signs behave like SCS values.[8] Earlier, Wesener *et al.*[9] had shown a parallelism between $^1\Delta$-isotope and substituent effects, which has recently been reviewed by Jameson.[10] In this work we focus on $^3\Delta$-isotope effects of a *tert*-butyl group, starting from the unusual observation that in *tert*-butylbenzene (**1**) the perdeuteriated *tert*-butyl group exerts a positive isotope effect at C-1 of the aromatic ring (for a discussion of the sign of isotope effects, see Refs 3 and 8 and references cited therein).

This observation is at first sight without precedent, since conformational reasons, equilibrium isotope effects and other influences which can cause positive isotope effects are not obvious for this molecule. We wish to show that this positive isotope effect is indeed normal and to be expected from a detailed analysis of a set of analogous compounds.

* Author to whom correspondence should be addressed.

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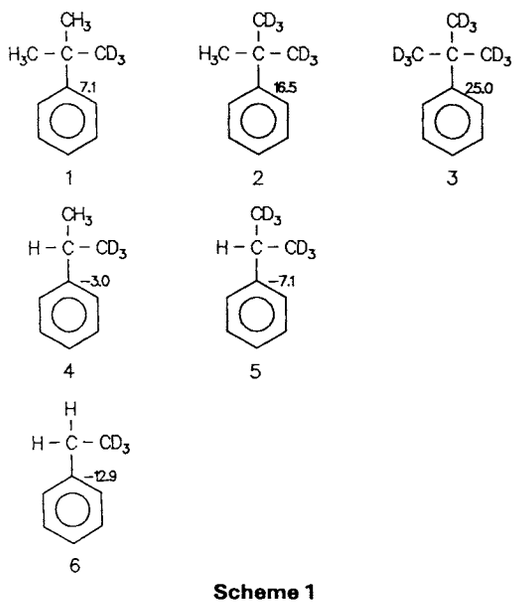
RESULTS AND DISCUSSION

Alkylbenzenes

The results for the alkylbenzenes studied are given in Scheme 1. As can be seen, we varied the number of deuterium atoms from left to right and the number of attached methyl groups from bottom to top in this scheme. Within the limits of the accuracy of the measurements the deuterium isotope effects are additive



Scheme 1

from left to right, both for the 'normal' negative isotope effects in the isopropylbenzenes **4** and **5** and for the unusual positive isotope effects in the *tert*-butylbenzenes **1–3**. The signals for C-1 in **1–3** are shown as examples in Fig. 1. The corresponding signal in **3** is broad owing

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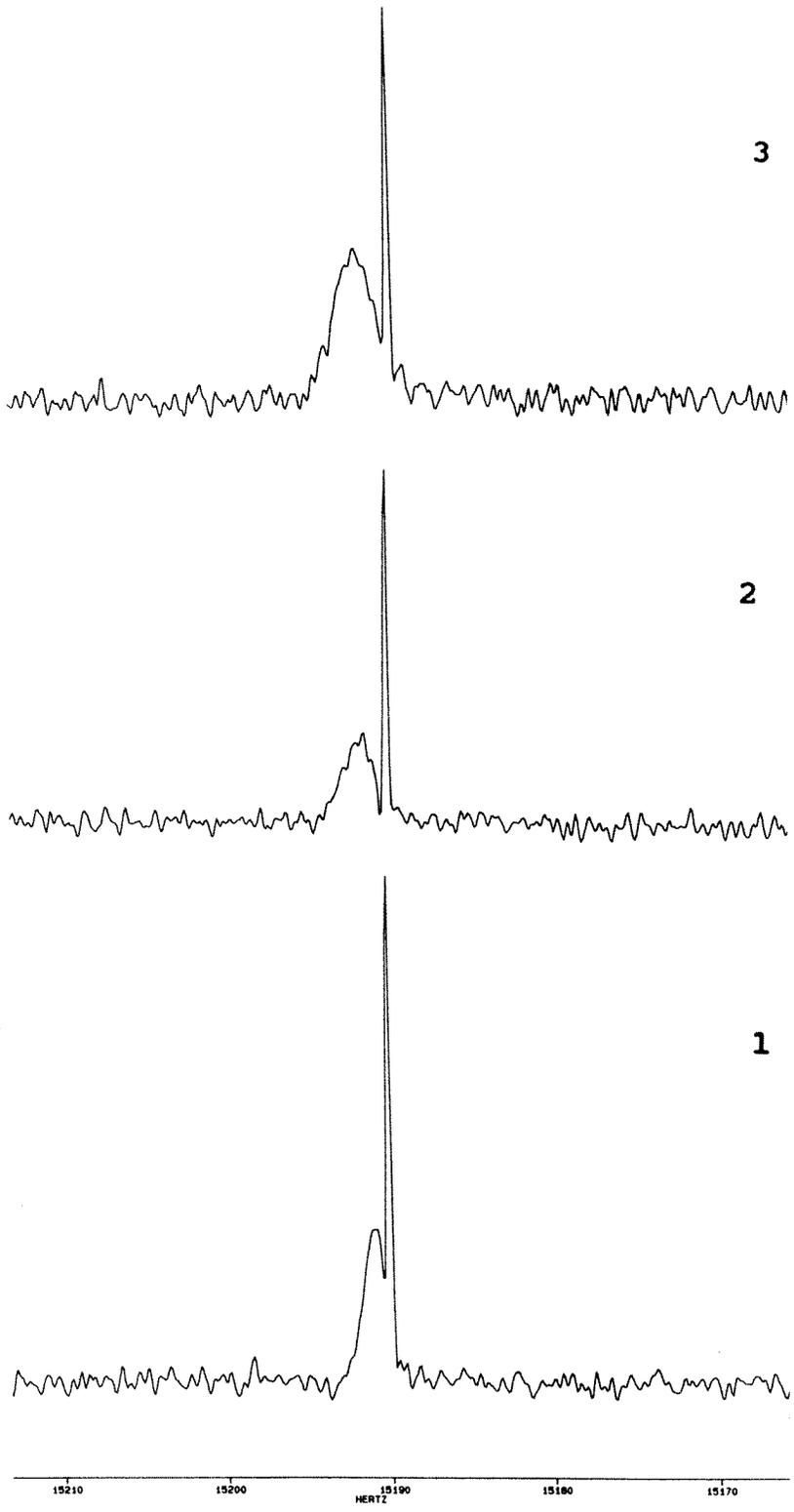


Figure 1. Signal of C-1 of **1–3** with unlabelled *tert*-butylbenzene as internal reference. Line broadening due to spin coupling with three, six or nine deuterium atoms.

to the spin coupling with nine deuterium atoms. The positive isotope effects are as additive as all other known deuterium isotope effects, which probably excludes any particular conformational origin.

On going from ethylbenzene[11] (**6**) via isopropylbenzene (**4**) to *tert*-butylbenzene (**1**) there is a linear change in the isotope effect with increasing number of methyl groups in the side-chain. The chemical shift at C-1 is changed on increasing the number of methyl groups, and the correlation of the isotope effect with the number of methyl groups is given in Fig. 2. It can be seen from this series that the positive isotope effect in **1–3** is not an isolated entity, but the result of the continuously changing chemical shift of C-1. The isotope

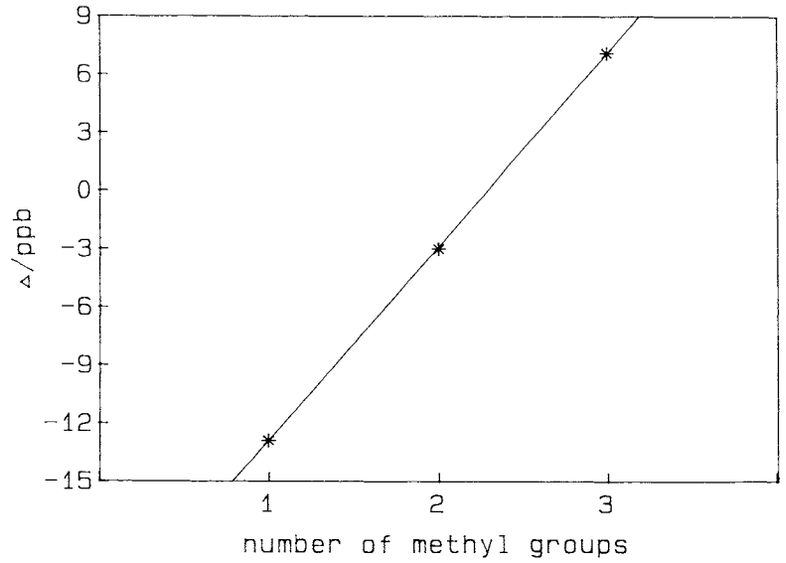


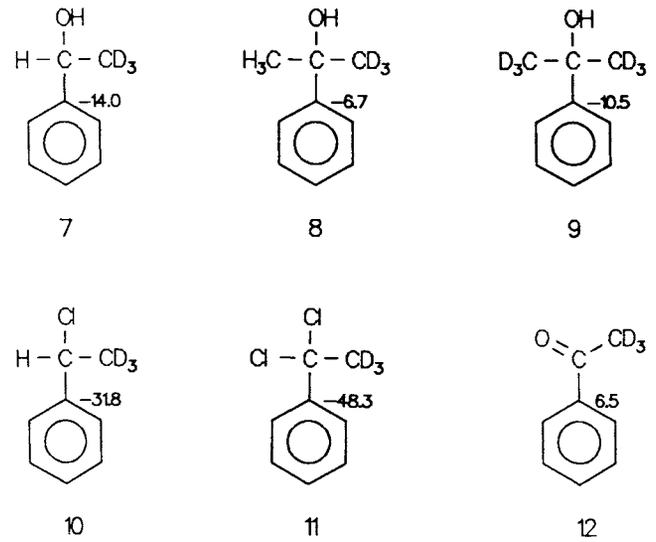
Figure 2. Dependence of deuterium isotope effects on the number of methyl groups for **1**, **4** and **6**.

effect in **5** can be predicted from the results for **4** by the additivity rule.

Hydroxy, chloro and keto derivatives

If the conclusion given above is correct, a similar picture must apply for these compounds if one replaces one methyl group by a different substituent. This substituent will introduce a chemical shift change at C-1 and the deuterium isotope effects should display corresponding changes. The results are given in Scheme 2.

With one exception, all $^3\Delta$-isotope effects in these compounds are negative, because in none of these compounds is the chemical shift at C-1 higher than 148 ppm and, as shown in Fig. 3, a chemical shift of about 150 ppm is required to change the sign of the isotope effect. The additivity of the isotope effects can be seen on going from **8** to **9**. The influence of the substituent, for example on comparing **6** with **10** and **11**, is also addi-



Scheme 2

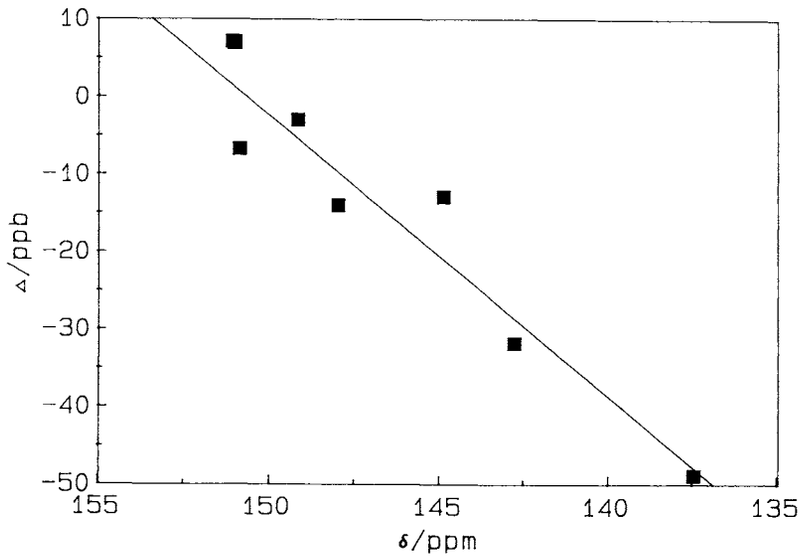
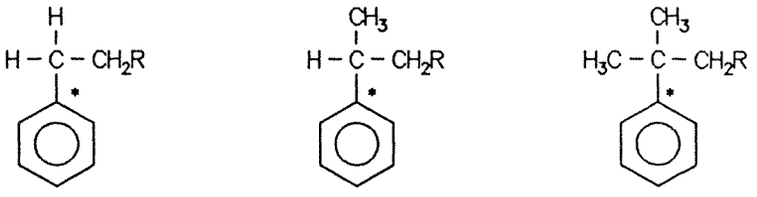


Figure 3. Correlation of $^3\Delta$-deuterium isotope effects for **1**–**11** with the chemical shift of C-1.



13 14 15

a)	R = Cl	*	−6.1	−5.4	−5.0
b)	R = Br	*	−5.4	−5.2	−2.6
c)	R = OH	*	−5.7	−5.1	−2.3
d)	R = COOH	*	−11.0	−9.1	−7.2

Scheme 3

tive. The overall correlation between isotope effects and chemical shifts for all compounds shown in Schemes 1 and 2 is shown in Fig. 3, and is acceptable allowing for the range of possible conformational changes and the different electronic influences of the substituents. The results for acetophenone (**12**) do not fit into this scheme, probably because an sp^2-hybridized carbon atom causes a large electronic deviation compared with the compounds having an aliphatic side-chain.

Substituent chemical shifts (SCS) values

If the deuterium isotope effects discussed above are dependent on the chemical shifts, one would expect the SCS values of other substituents to behave similarly; these are, however, on a ppm scale whereas the deuterium isotope effects are on a ppb scale. We therefore prepared the series of compounds shown in Scheme 3 and measured their C-1 chemical shifts.

We define, by analogy with the deuterium isotope effect, an SCS value for the given substituent as the difference between its C-1 chemical shift and that in the corresponding ethylbenzene (144.2 ppm), isopropylbenzene (148.8 ppm) or *tert*-butylbenzene (151.0 ppm):

$$SCS = \delta_{C\text{-}1}(X) - \delta_{C\text{-}1}(H)$$

The SCS values are given in Scheme 3; the ^{13}C NMR chemical shifts are listed in the experimental section. As shown in Fig. 4, the important result is that the SCS values themselves are not constant, but are a function of the chemical shift. This was pointed out in an earlier contribution on $^2\Delta$-isotope effects and the corresponding SCS values effective over two bonds.[8] Apparently, the result for the effects over three bonds shown in Fig. 4 is similar and could have implications for the discussion of substituent increment systems. It can be seen from Fig. 4 that the incremental displacement of a ^{13}C signal caused by a substituent is a function of the chemical shift. This new conclusion, which was achieved by inspection of the deuterium isotope effects, seems not to be widely recognized in the huge mass of carbon chemical shift literature, although similar ideas have

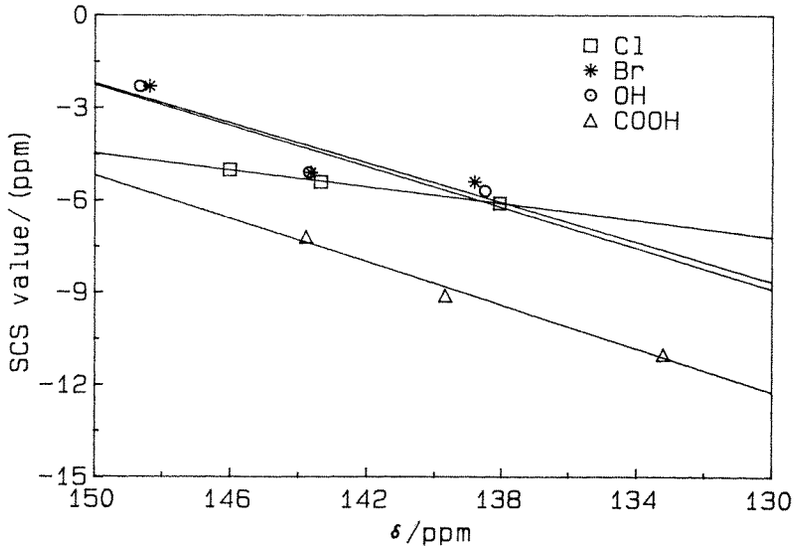


Figure 4. Correlation of SCS values for bromine, carboxyl, chlorine and hydroxyl in **13a–d**, **14a–d** and **15a–d** with the chemical shift of C-1.

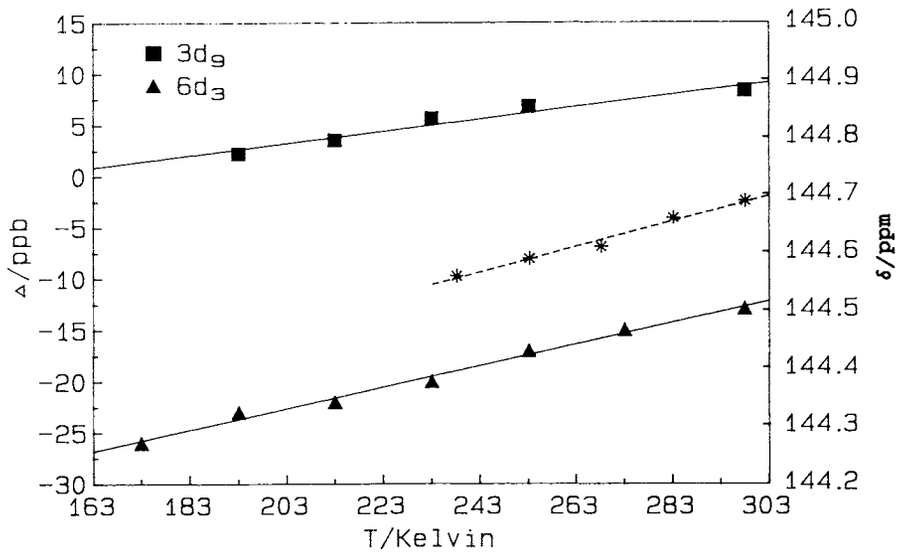


Figure 5. Temperature dependence of $^3\Delta$-deuterium isotope effects in **3** normalized to three deuterium atoms and **6** (left-hand scale) and temperature dependence of the chemical shift of C-1 in unlabelled *tert*-butylbenzene (right-hand scale).

been advanced for the explanation of the increment systems in doubly substituted aromatic compounds.[12]

Temperature dependence of intrinsic isotope effects

The temperature dependence of the intrinsic isotope effects in **3** and **6** is shown in Fig. 5. Both lines have a slope of the same sign and of similar magnitude if one normalizes the results for **3** to three deuterium atoms. If the intrinsic isotope effects were caused by a conformational equilibrium, the temperature dependence in **6** should have been larger than in **3**, since the rotation potential of the ethyl group is certainly not as symmetrical as the potential in **3**. The temperature dependence in **3** must therefore have other causes. We therefore measured the temperature dependence of the chemical shift in unlabelled *tert*-butylbenzene. Indeed, we find a significant temperature dependence for this signal, whereas the other signals of the aromatic ring do not show a temperature dependence. It is shown in Fig. 5 that this temperature dependence of the chemical shift has the same sign as the temperature dependence of the isotope effects. Hence we conclude that the temperature dependence of intrinsic isotope effects can resemble the temperature dependence of the corresponding chemical shift, but on a smaller scale. This is in agreement with the vibrational model of isotope effects.[2,10]

CONCLUSION

We have demonstrated that $^3\Delta$-deuterium isotope effects in a series of alkylated benzenes show complete parallelism with the behaviour of the chemical shifts of the corresponding carbon atom. A similar result was found earlier for $^2\Delta$-isotope effects. These findings led to a re-examination of SCS values, and it was shown that the latter are not constant but are dependent on the chemical shift range. This is the reason why chemical shift increment systems always operate only for a specific class of compounds, where the chemical shift range is limited.

EXPERIMENTAL

Compounds **1–3** were prepared from the correspondingly deuteriated *tert*-butanols via Friedels–Crafts alkylation of benzene. The deuteriated *tert*-butanols were prepared from the correspondingly deuteriated acetone and methyl iodide. The isopropylbenzenes **4** and **5** were prepared by reduction of **8** and **9** with lithium in liquid ammonia.[13] Ethylbenzene (**6**) was similarily prepared from **7**. The hydroxy compounds **7–9** were prepared by addition of deuteriated methyl iodide to benzaldehyde or ethyl benzoate. Compound **10** was obtained by chlorination of **7** with $SOCl_2$,[14] and **11** by chlorination of **12** with PCl_5 in toluene.[15] Oxidation of **7** with chromic acid gave **12**.

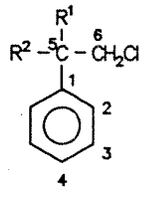
Purification of the compounds was achieved by preparative gas–liquid chromatography [90-P3 Aerograph column (1.8 m × $\frac{1}{4}$ in i.d.), 5% SE-30 on Chromosorb G AW DMCS, 60–80 mesh, carrier gas helium at a flow-rate of 120–130 ml min^{-1}].

Compounds **13a–d**, **14a–d** and **15a–d** were either commercially available or synthesized by standard procedures. The ^{13}C chemical shifts of these compounds are given in Table 1.

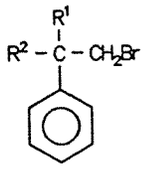
NMR measurements

The room-temperature 100.6-MHz ^{13}C NMR spectra were recorded at 303 K on a Bruker AM-400 spectrometer equipped with a 256K Aspect 3000 computer using acetone-d_6 solutions or, in some cases, $CDCl_3$, with a small detectable difference in the deuterium isotope effects. The measurements were always performed on mixtures of labelled and unlabelled compounds as described above. The spectral width was set

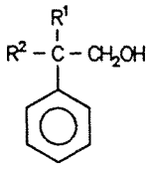
Table 1. ^{13}C NMR chemical shifts (δ, $CDCl_3$) of 13a–d, 14a–d and 15a–d



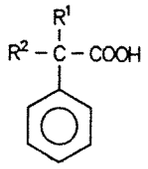
	13a $R^1=H$, $R^2=H$	14a $R^1=H$, $R^2=CH_3$	15a $R^1=CH_3$, $R^2=CH_3$
1	138.1	143.4	146.0
2	128.8	127.2	125.9
3	128.5	128.6	128.3
4	126.8	126.9	126.5
5	39.2	42.3	39.8
6	44.9	50.8	56.3
7		18.9	26.4



	13b $R^1=H$, $R^2=H$	14b $R^1=H$, $R^2=CH_3$	15b $R^1=CH_3$, $R^2=CH_3$
1	138.8	143.6	148.4
2	128.6	127.0	125.5
3	128.5	128.5	127.3
4	126.8	126.9	126.7
5	39.3	42.1	40.1
6	32.8	39.8	43.2
7		19.9	27.9



	13c $R^1=H$, $R^2=H$	14c $R^1=H$, $R^2=CH_3$	15c $R^1=CH_3$, $R^2=CH_3$
1	138.5	143.7	148.7
2	128.9	127.4	126.9
3	128.5	128.6	128.7
4	126.3	126.3	126.3
5	39.1	42.4	40.5
6	63.5	68.6	72.6
7		17.5	25.8



	13d $R^1=H$, $R^2=H$	14d $R^1=H$, $R^2=CH_3$	15d $R^1=CH_3$, $R^2=CH_3$
1	133.2	139.7	143.8
2	129.3	127.6	125.8
3	128.6	128.6	128.4
4	127.3	127.4	126.9
5	41.0	45.4	46.3
6	178.2	185.4	183.3
7		18.0	26.2

as narrow as possible and separately for the carbonyl and aliphatic regions, typically between 1000 and 4000 Hz. Zero filling to 64K gave a digital resolution better than 0.1 Hz per point after Fourier transformation. Gaussian multiplication was used to increase the resolution. The lines are sometimes broadened owing to spin coupling with the deuterium over three bonds; in these cases the accuracy is only 1.5 ppb.

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REFERENCES

1. P. E. Hansen, *Annu. Rep. NMR Spectrosc.*, edited by G. A. Webb, Academic Press, New York, **15**, 105 (1983); P. E. Hansen, *Prog. Nucl. Magn. Reson. Spectrosc.*, edited by J. W. Emsley, J. Feeney and L. H. Sutcliffe, Pergamon Press, Oxford, **20**, 207 (1988).
2. C. J. Jameson and H. J. Osten, *Annu. Rep. NMR Spectrosc.*, edited by G. A. Webb, Academic Press, New York, **17**, 1 (1986).
3. S. Berger, in *Nuclear Magnetic Resonance, Basic Principles and Progress*, edited by H. Günther, **22**, 2 (1990). Springer, Berlin.
4. E. A. Halevi, *Progr. Phys. Org. Chem.* **1**, 109 (1963).
5. E. A. Halevi, M. Nussim and A. Ron, *J. Chem. Soc.* 866 (1963).
6. S. Berger, B. W. K. Diehl and H. Künzer, *Chem. Ber.* **120**, 1059 (1987).
7. H. Künzer and S. Berger, *J. Am. Chem. Soc.* **107**, 2804 (1985).
8. S. Berger and B. W. K. Diehl, *J. Am. Chem. Soc.* **111**, 1240 (1989).
9. J. R. Wesener, D. Moskau and H. Günther, *J. Am. Chem. Soc.* **107**, 7307 (1985).
10. C. J. Jameson, in *Isotopes in the Physical and Biomedical Sciences*, edited by E. Buncel, in press. Elsevier, Amsterdam.
11. J. R. Wesener and H. Günther, *Tetrahedron Lett.* 2845 (1982).
12. D. J. Craik, *Annu. Rep. NMR Spectrosc.* edited by G. Webb, Academic Press, New York, **15**, 2 (1983).
13. G. H. Small, A. E. Minella and S. S. Hall, *J. Org. Chem.* **40**, 3151 (1975).
14. A. R. Bassindale, R. J. Ellis, J. C. Y. Lau and D. G. Taylor, *J. Chem. Soc., Perkin Trans. 2* 593 (1986).
15. J. Kagan, S. K. Arora, M. Bryzgin, S. N. Dhawan, K. Reid, S. P. Singh and L. Tow, *J. Org. Chem.* **48**, 703 (1983).