

H-D COUPLING CONSTANTS AND DEUTERIUM ISOTOPE EFFECTS ON THE PROTON CHEMICAL SHIFTS IN PARTIALLY DEUTERIATED METHANES

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Summary: Very accurate frequency measurements on 500 MHz ^1H NMR spectra of CH_4 , CH_3D , CH_2D_2 , and CHD_3 are reported. There are relatively large (up to 10%) solvent and temperature effects on the isotope shifts ($^2\Delta = -13.998$ to -15.555 ppb for CH_3D), which are non-additive by ca 0.2 ppb/deuterium; $^2J_{\text{HD}}$ (-1.929 ± 0.001 Hz, sign assumed, equivalent to $^2J_{\text{HH}} = -12.57$ Hz) is almost independent of solvent, temperature, and the number of deuterons present.

The effects of partial deuterium substitution on the chemical shifts of the remaining protons in a molecule have been extensively studied, both experimentally and theoretically.¹⁻⁵ In rigid and certain other molecules, where deuterium substitution does not perturb any rotameric or conformational equilibria, the observed shifts can be assigned to *intrinsic isotope effects*, in contrast to other cases where contributions from *equilibrium isotope effects* can be important.^{2,6} Questions concerning intrinsic isotope effects include (a) the additivity of the isotope effects when more than one deuterium is introduced in the molecule, (b) the temperature dependence of the isotope effect, and (c) the solvent dependence of the isotope effect.

In view of its position as the simplest saturated hydrocarbon, and being also very rigid, methane is of key importance in achieving an understanding of intrinsic chemical shift isotope effects. Deuterium isotope effects are known for both ^1H and ^{13}C in this molecule,^{7,8} and the origins of these effects in the gas phase have been explored from a theoretical point of view;⁹ possible solution effects have also been recently considered.¹⁰ In 1964 Bernheim and Lavery (BL) obtained 40 MHz sweep proton spectra on deuteriated methanes and reported that the deuterium isotope effects on the proton shifts were not additive,⁷ unlike those in ammonia.¹⁰⁻¹¹ Because subsequent experimental and theoretical work has shown that additivity in isotope effects is obeyed very well in general,¹⁻⁵ the extraordinary non-additivity in methane, which has been extensively quoted in the literature,^{1,2} has remained experimentally unchallenged for a surprisingly long time. Jameson and co-workers^{9, 10} have calculated theoretical non-additivities of only ca 0.03 ppb. They state that this "strict additivity" is in agreement with the experimental data, but they do not give any explicit justification for rejecting BL's claim of non-additivity.

We now report very accurate $^2J_{\text{HD}}$ and deuterium isotope effects¹² on ^1H chemical shifts for $\text{CH}_n\text{D}_{4-n}$ ($n = 1$ to 3)¹³ in various solvents (Table I). Nearly all the peaks in the mixtures of the four isotopomers were resolved at 500 MHz without deuterium decoupling (Figure 1).¹⁴ The influence of temperature was measured in acetone- d_6 as the solvent. Gas phase $^1\text{H}\{\text{D}\}$ NMR data on the deuteriated methanes at a pressure of about four atmospheres are also

reported and provide fairly accurate isotope effects on the chemical shifts because all the lines are well resolved.¹⁵

Table I ${}^2J_{HD}$ and Deuterium Isotope Effects (${}^2\Delta$'s) on the ${}^1\text{H}$ Chemical Shifts (δ) of CH_3D , CH_2D_2 , and CHD_3 (Errors Correspond to 90% Confidence Limits).

Molecule (solvent)	Temp. °C	${}^2J_{HD}$ ^a (Hz)	Isotope Effect on δ , ^b ${}^2\Delta$ (ppb)	Increment in ${}^2\Delta$ (ppb) ^c	Non-Additivity in the Incre- ment (ppb) ^d
CH_3D (gas)	22		-14.93 ± 0.02		
CH_2D_2 (gas)	22		-29.66 ± 0.02	-14.73 ± 0.02	0.20 ± 0.02
CHD_3 (gas)	22		-44.17 ± 0.02	-14.51 ± 0.02	0.22 ± 0.02
CH_3D (CCl_4) ^e	22	-1.9286 ± 0.0006	$-15.117^f \pm 0.001$		
CH_2D_2 (CCl_4) ^e	22	-1.9282 ± 0.0004	$-30.022^g \pm 0.001$	-14.905 ± 0.001	0.211 ± 0.001
CHD_3 (CCl_4) ^e	22	-1.9275 ± 0.0006	$-44.750^h \pm 0.001$	-14.728 ± 0.001	0.171 ± 0.001
CH_3D (CDCl_3)	22	-1.927 ± 0.006	-15.14 ± 0.01		
CH_2D_2 (CDCl_3)	22	-1.926 ± 0.003	-30.095 ± 0.006	-14.96 ± 0.01	0.18 ± 0.01
CHD_3 (CDCl_3)	22	-1.926 ± 0.005	-44.818 ± 0.01	-14.78 ± 0.01	0.17 ± 0.01
CH_3D (C_6D_6)	22	-1.9272 ± 0.0006	-13.988 ± 0.001		
CH_2D_2 (C_6D_6)	22	-1.9270 ± 0.0006	-27.780 ± 0.001	-13.792 ± 0.001	0.196 ± 0.001
CHD_3 (C_6D_6)	22	-1.926 ± 0.003	-41.391 ± 0.006	-13.611 ± 0.006	0.181 ± 0.006
CH_3D (Acetone)	22	-1.9361 ± 0.0008	-15.555 ± 0.002		
CH_2D_2 (Acetone)	22	-1.9364 ± 0.0006	-30.907 ± 0.001	-15.352 ± 0.002	0.202 ± 0.002
CHD_3 (Acetone)	22	-1.936 ± 0.005	-46.08 ± 0.01	-15.170 ± 0.01	0.18 ± 0.01
CH_3D (Acetone)	-50	-1.931 ± 0.001	-15.430 ± 0.002		
CH_2D_2 (Acetone)	-50	-1.931 ± 0.002	-30.655 ± 0.004	-15.225 ± 0.004	0.204 ± 0.004
CHD_3 (Acetone)	-50	-1.930 ± 0.004	-45.697 ± 0.008	-15.04 ± 0.01	0.18 ± 0.01
CH_3D (CD_3OD)	22	-1.936 ± 0.002	-15.300 ± 0.004		
CH_2D_2 (CD_3OD)	22	-1.937 ± 0.004	-30.410 ± 0.008	-15.11 ± 0.01	0.19 ± 0.01
CHD_3 (CD_3OD)	22	-1.946 ± 0.010	-45.33 ± 0.02	-14.92 ± 0.02	0.19 ± 0.02

^a Assumed to be negative. ^b $\delta(\text{deuteriated methane}) - \delta(\text{CH}_4)$. ^c $\delta(\text{CH}_2\text{D}_2) - \delta(\text{CH}_3\text{D})$ for CH_2D_2 and $\delta(\text{CHD}_3) - \delta(\text{CH}_2\text{D}_2)$ for CHD_3 . ^d The reference is the isotope effect on δ of CH_3D . ^e Locked on internal (ca 2%) CD_2Cl_2 . ^f -19 ± 1 ppb (reference 7). ^g -27 ± 3 ppb (reference 7). ^h -45 ± 4 ppb (reference 7).

The *large* non-additivity reported by BL in the deuteriated methanes (Table I, footnotes f, g, and h) is clearly the result of an underestimation of the error in the isotope effect in CH_3D .¹⁶ The present work shows that there is a *small* non-additivity, as the isotope effect increment per deuterium decreases (in absolute value) with increasing numbers of deuterium atoms on the molecule. The theoretically predicted non-additivity effects based on rotational and vibrational contributions⁹ are an order of magnitude too small, although solvent effects have been suggested to induce large non-additivities.¹⁰ However, in the present molecules, the non-additivities are almost independent of solvent and temperature. Although the accuracy of the gas phase data is substantially lower than that of the solution data,¹⁵ the non-additivities (ca 0.21 ± 0.02 ppb) of the deuterium isotope effects on the chemical shifts are very similar to those found in solution (Table I).

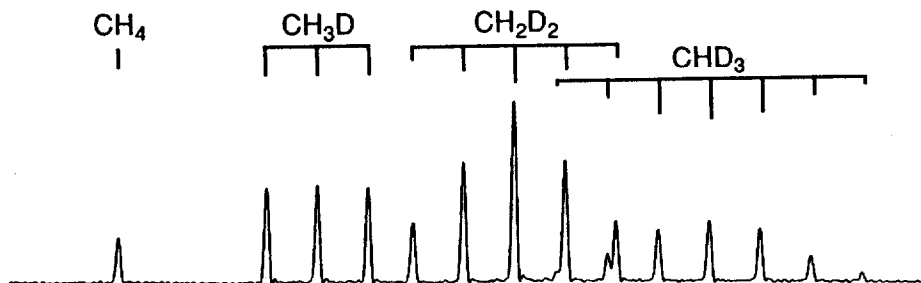


Figure 1 500 MHz ^1H NMR spectrum of a mixture of CH_4 , CH_3D , CH_2D_2 , and CHD_3 in CDCl_3 at 22 °C measured with resolution enhancement (0.006 Hz/point, Bruker parameters: LB = -0.4 Hz, GB = 0.5, AQ = 7 s).

It is conceivable that bending vibrations, which have been neglected in theoretical treatments of isotope effects on chemical shifts, are not negligible, especially concerning non-additivity effects in proton shifts. Whether bending or other effects, such as deviations from the Born-Oppenheimer approximation, can explain the present data remains to be determined.

The isotope effect on the ^1H shift in CH_3D shows a surprisingly large solvent and temperature dependence (Table I), e.g., the isotope effects in acetone and benzene differ by 10%. However, the non-additivity with increasing number of deuterons is remarkably constant. There is probably some weak but slightly selective association of the deuteriated methanes, which by symmetry cannot have zero dipole moments, with the magnetically anisotropic benzene and acetone molecules, and this may explain why the isotope effects in these two solvents deviate the most from the gas phase and CCl_4 values.

A possible deuterium isotope effects on $^2J_{\text{HD}}$ is barely discernable for the most accurate data in Table I, i.e., that for CCl_4 , and if real is about 0.5 mHz per deuterium. There is little doubt that the difference (2 to 3 mHz) in $^2J_{\text{HD}}$ between CCl_4 and acetone- d_6 is real as is also the temperature variation (0.075 mHz/deg.) of $^2J_{\text{HD}}$ in acetone between 22 and -50 °C. For CH_4 in CCl_4 $^2J_{\text{HH}}$ is calculated to be -12.564 ± 0.004 Hz, provided that there is no primary isotope effect on the coupling constant.

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12. The convention for the sign of the deuterium isotope effect used in references 1 and 2 is the opposite of that used in the present paper, which follows the more rational convention of defining the effect as $\delta_D(H) - \delta_H(H)$, where the $\delta_D(H)$ refers to the proton shift in the deuteriated molecule (Jameson, C. J. *Nucl. Magn. Res.* **1986**, *15*, 1-27; Hawkes, G. E. *Nucl. Magn. Res.* **1986**, *15*, 28-80). This definition is consistent with that used for substituent effects in NMR spectroscopy. The non-additivity in the isotope effect, as used in this paper, is defined in Table I, footnote d.

13. The deuteriated hydrocarbons were prepared by the zinc-copper couple reduction in D_2O of CH_3I , CH_2Br_2 , or $CHBr_3$ in a flask fitted with a rubber septum (the Zn-Cu couple was prepared by adding a few percent of $CuCl_2$ to zinc dust in D_2O). After evacuation of the flask at Dry Ice temperature, shaking for a few minutes at room temperature resulted in the evolution of gas. A plastic syringe connected to a long stainless needle was used to withdraw samples of the gas. The contents of the syringe were passed through a drying tube and then into the desired cold solvent in a 5 mm NMR tube. The tubes were vigorously shaken to ensure uniform concentrations of the methanes, which is critically important in obtaining high resolution, especially in C_6D_6 . For gaseous samples NMR tubes fitted with screw caps were cooled with liquid N_2 and injected by syringe to give a pressure of four atmospheres at 22 °C.

14. The acquisition times used to obtain the FID's varied from 5 to 12 s. A line narrowing of 0.15 to 0.4 Hz was applied, and only the frequencies of *non-overlapping* lines were used in the spectral analysis. Accurate measurements of line frequencies require an appropriately high signal-to-noise ratio (including a flat base line) and correct frequency-dependent phasing; extremely sharp lines are helpful, but are not an absolute requirement. Fortunately, there is an internal check on the accuracy of the data because all the parameters for the solution spectra can be obtained in *at least two independent ways*. Additionally, $^2J_{HD}$ is virtually independent of solvent and the number of deuterons: this could not be the case if the data had larger errors than those given. The best data is for the CCl_4 solution, where much effort was spent on getting excellent resolution, line shape, and signal-to-noise ratio. The lower accuracy for some of the CHD_3 data arises because the concentration was not high enough to provide the same signal-to-noise ratio as for the other isotopomers. Because of a referee's comment, new measurements for a $CDCl_3$ solution were made. Different ratios of isotopomers and a somewhat higher total solute concentration were employed and gave the following values: $^2J_{HD} = 1.9276 \pm 0.0003$, 1.9275 ± 0.0003 , 1.9270 ± 0.0004 Hz, and for the two non-additivity parameters 0.1890 ± 0.0006 and 0.1717 ± 0.0010 in excellent agreement with the previous results and their errors ($^2\Delta$ is distinctly concentration dependent as probably are also the non-additivity parameters).

15. The acquisition times were in the range of 1.5 to 2.0 s and sums of 128 or 256 FID's were acquired without a lock; the raw line widths were 2.0 to 2.5 Hz. Resolution enhancements with $LB = -1.0$ to -2.0 Hz and $GB = 0.6$ to 0.75 were used. The spin-rotation interaction, which is the dominant relaxation mechanism in the gas phase, gives rise to broad lines that become sharper at higher gas pressures. The $^1H\{D\}$ resonances of the methane isotopomers increase slightly in sharpness as the number of deuterium atoms is increased, as expected.

16. The errors given by BL for the chemical shift isotope effect (-17 ppb) in CH_3D is only ± 1 ppb (± 0.04 Hz), whereas in the case of CH_2D_2 and CHD_3 , the errors are given as 3 and 4 ppb. Strangely, the error quoted for J_{HD} (1.91 Hz) in CH_3D is ± 0.21 Hz, i.e., five times larger than the error in the isotope effect! It appears that the error given for the isotope effect in CH_3D was unrealistically low for some reason. BL's paper gives no information on the temperature, the solvent, or the actual measurement method; however, the solvent (CCl_4) is given in reference 1.

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