

A General Approach for Calculating Proton Chemical Shifts for Methyl, Methylene, and Methine Protons When There Are One or More Substituents within Three Carbons

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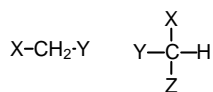
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Modern multidimensional NMR has elevated the importance of coupling constants (J or scalar) over chemical shift correlations (δ). The first chapter in a popular multidimensional NMR text provides the following emphasis (1):

“The exploitation of *coupling* is the basis for all the experiments described in this book. ...The predictable nature of couplings, and the fact that they indicate *pairwise relationships* between nuclei, make them a sensitive probe of molecular structure. Chemical shifts, in contrast, give only a crude indication of the environment of *individual nuclei*.”

Even so, chemical shift correlations remain important parameters in NMR, especially for beginning organic chemistry students.

Chemists have used Shoolery's rules to calculate approximate chemical shifts for decades (2). Shoolery's original list of 10 substituent parameters can be used to calculate the chemical shift of a methylene (CH_2) with two substituents or methine (CH) with 3 substituents. Only directly attached substituents are considered in the calculations, requiring two parameter values for a methylene and three parameter values for a methine (2).



$$\delta(\text{CH}_2) = 1.25 \text{ ppm} + (\text{X parameter}) + (\text{Y parameter}) \quad (1)$$

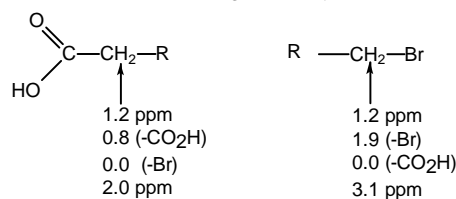
$$\begin{aligned} \delta(\text{CH}) &= 1.50 \text{ ppm} + (\text{X parameter}) \\ &+ (\text{Y parameter}) + (\text{Z parameter}) \quad (2) \end{aligned}$$

Shoolery's original list is expanded to a list of 23 α substituent parameters and a limited number of β substituent parameters in the fifth edition of Silverstein, Bassler, and Morrill (3). An extensive list of substituent parameters is provided for calculating methyl, methylene, and methine chemical shifts in two articles from this *Journal* (4, 5). Both actual and calculated chemical shifts are provided in those references.

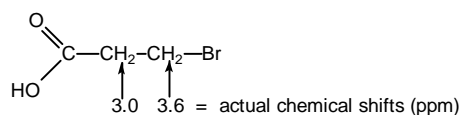
Additionally, 21 substituent parameters are listed with equations to calculate proton chemical shifts for methylene and methine hydrogens (6). Also listed in this reference are 29 common organic substituents on 5 common saturated carbon patterns (having methyl, primary, secondary, and tertiary carbons) (7).

In all these calculations of proton chemical shifts, the substituent parameter used is valid only if the substituent is directly attached to the carbon bonded to the hydrogens considered. A substituent on the adjacent carbon (β carbon) or subsequent carbon (γ carbon) is mostly ignored except for a limited number of β substituent parameters in Silverstein (3). For example, in the following molecule, each CH_2 would be considered attached to only one substituent and the chemical shift would be calculated as follows:

Chemical shift calculation using Shoolery parameters and eq 1:

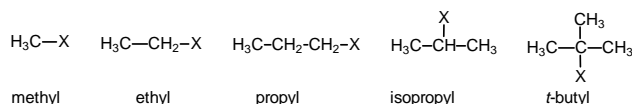


The actual chemical shifts are indicated below (δ):



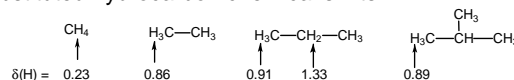
No account is taken of the diminished, but present, effect of other substituents once or twice removed. Also not accounted for in the Shoolery equations are multiple possibilities of either identical or different substituents at these same once- or twice-removed positions.

Our goal in writing this paper is to produce a simple, general approach, much like the Shoolery equations, to take account of these additional effects. Useful approximations can be made using the data provided in reference 6. The substituted carbon patterns listed include methyl, ethyl, propyl, isopropyl, and *t*-butyl. The symbol X represents 29 different possible substituent patterns. Where parameter values are missing, “The Aldrich Library of ^{13}C and ^1H FT NMR Spectra” was consulted to estimate values (8).

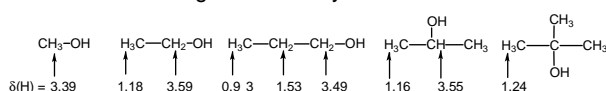


An example, from reference 6, showing the chemical shifts of the $-\text{OH}$ substituent is provided for each of the above carbon patterns. One can see that substituents do have an effect on hydrogens more removed than those directly on the substituted carbon.

Unsubstituted hydrocarbon chemical shifts



Chemical shift changes caused by an $-\text{OH}$ substituent



All methyls (CH_3) in the data from reference 6 are compared to the typical alkane methyl shift of 0.9 ppm. All methylenes (CH_2) are compared to the Shoolery starting

value of 1.2 ppm. Finally, all methines (CH) are compared to the Shoolery value of 1.5 ppm. The difference in chemical shift of each of these typical chemical shifts (CH₃, CH₂, and CH) and similar patterns in the substituted examples in reference 6 are tabulated three ways. If the hydrogens are directly attached to the same carbon as the substituent, they are grouped and averaged as α parameters. If the hydrogens are on an adjacent β carbon, they are grouped and averaged as β parameters. Finally, only the propyl pattern has hydrogens on a γ carbon and these produce γ parameters. The propyl skeleton, can generate all three parameters for each substituent (α , β , and γ). The ethyl skeleton provides values for the α and β parameters (as does isopropyl). Methyl can generate α parameters and *t*-butyl can generate β parameters. Additional comparisons were made from numerous examples in the Aldrich FT-NMR Library (8).

Using this approach, an approximate substituent parameter can be calculated for most of the 29 substituents listed, for directly attached substituents (α), and substituents once removed (β) or twice removed (γ) from the designated hydrogen and its carbon of consideration. The same example as above, of an alcohol substituent, is used to illustrate this approach.

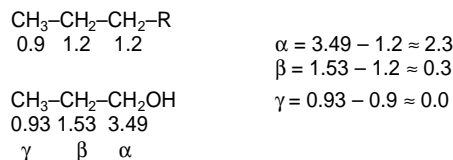
Table 1. Estimation of sp^3 C-H Chemical Shifts^a

α = directly attached substituent- α
 β = once-removed substituent- β
 γ = twice-removed substituent- γ

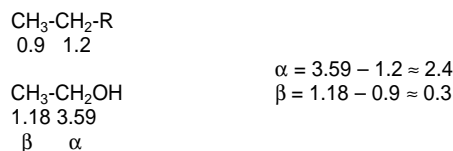
X	α	β	γ
R-	0.0	0.0	0.0
R ₂ C=CR-	0.8	0.2	0.1
RC≡C-	0.9	0.3	0.1
Ar-	1.4	0.4	0.1
F-	3.2	0.5	0.2
Cl-	2.2	0.5	0.2
Br-	2.1	0.7	0.2
I-	2.0	0.9	0.1
HO-	2.3	0.3	0.1
RO-	2.1	0.3	0.1
R ₂ C=CRO-	2.5	0.4	0.2
ArO-	2.8	0.5	0.3
RCO ₂ -	2.8	0.5	0.1
ArCO ₂ -	3.1	0.5	0.2
ArSO ₃ -	2.8	0.4	0.0
H ₂ N-	1.5	0.2	0.1
RCONH-	2.1	0.3	0.1
O ₂ N-	3.2	0.8	0.1
HS-	1.3	0.4	0.1
RS-	1.3	0.4	0.1
OHC-	1.1	0.4	0.1
RCO-	1.2	0.3	0.0
ArCO-	1.7	0.3	0.1
HO ₂ C-	1.1	0.3	0.1
RO ₂ C-	1.1	0.3	0.1
H ₂ NOC-	1.0	0.3	0.1
CIOC-	1.8	0.4	0.1
N≡C-	1.1	0.4	0.2
RSO-	1.6	0.5	0.3
RSO ₂ -	1.8	0.5	0.3

^aMultiple substituent parameters for protons within three carbons of consideration.

Propyl calculation of α , β , and γ correction parameters for an -OH substituent



Ethyl comparison calculation of α and β correction parameters for an -OH substituent



The α parameter is very similar to the Shoolery constants. The second correction parameter for substituents, once removed from the calculated hydrogens of interest, is an average of the carbon patterns listed in reference 6. This β correction is not normally made in the Shoolery calculation mentioned above. Finally, the third correction parameter for substituents twice removed is calculated from the propyl-substituted examples alone and is also not included in a typical Shoolery calculation. Three correction parameters are generated for most of the 29 substituents listed in reference 6. These are tabulated as α , β , and γ in Table 1. Three additional examples are included using examples from reference 8.

Any substituent directly attached to a methyl is a unique value; there are no additional bonds for further consideration. Almost any common methyl pattern and chemical shift can be found directly in the list of values provided in reference 6. However, these chemical shifts can also be calculated using equation 3 below.

$$\delta_{\text{CH}_3} = 0.9 + \alpha \quad \begin{array}{c} \text{CH}_3\text{-} \\ \alpha \end{array} \quad (3)$$

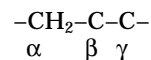
If a methyl is part of a longer chain with an additional substituent (or several substituents) on a β or γ position (or both positions), no general formula exists to predict such a chemical shift. Using the 0.9-ppm chemical shift for a simple methyl as a starting point, we can correct for any number of substituents within three carbons as follows:

$$\delta_{\text{CH}_3} = 0.9 + \sum (\beta + \gamma) \quad \begin{array}{c} \text{CH}_3\text{-C-C-} \\ \beta \quad \gamma \end{array} \quad (4)$$

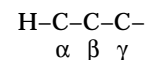
where \sum is the summation symbol for all substituents considered.

In a similar fashion, we can calculate chemical shifts for methylenes and methines using the following formulas.

$$\delta_{\text{CH}_2} = 1.2 + \sum (\alpha + \beta + \gamma) \quad (5)$$



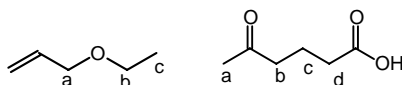
$$\delta_{\text{CH}} = 1.5 + \sum (\alpha + \beta + \gamma) \quad (6)$$



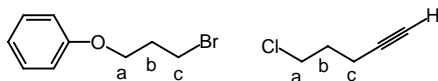
The following examples are included to demonstrate the process. This approach can extend the useful Shoolery equations to polysubstituted carbon skeletons. It does so in a way analogous to Shoolery's original equations. Most chemists and students familiar with the Shoolery's approach should be able to use the equations in this article with minimal effort. The calculated chemical shifts are often

quite close to the experimental values. However, like Shoolery's original equations, these calculations of chemical shift should be considered no more reliable than ± 0.5 ppm. The reliability also decreases with greater numbers of substituents included in the calculations.

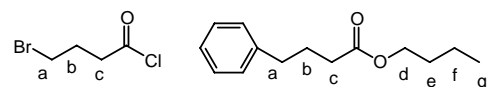
Calculated versus experimental chemical shifts



	a	b	c	a	b	c	d	
Actual δ (ppm)	4.0	3.5	1.2	2.1	2.6	1.9	2.4	
Calculated δ (ppm)	1.2	1.2	0.9	0.9	1.2	1.2	1.2	
C=C-	0.8	0.2	0.1	O=C	1.2	1.2	0.3	0.0
R-O-	<u>2.1</u>	<u>2.1</u>	<u>0.3</u>	HO ₂ C-	-	<u>0.1</u>	<u>0.3</u>	<u>1.1</u>
Total	4.1	3.5	1.3	2.1	2.5	1.8	2.3	



	a	b	c	a	b	c	
Actual δ (ppm)	4.1	2.3	3.6	3.7	2.0	2.4	
Calculated δ (ppm)	1.2	1.2	1.2	1.2	1.2	1.2	
ArO-	2.8	0.5	0.3	Cl-	2.2	0.5	0.2
Br-	<u>0.2</u>	<u>0.7</u>	<u>2.1</u>	C \equiv C-	<u>0.1</u>	<u>0.3</u>	<u>0.9</u>
Total	4.2	2.4	3.6	3.5	2.0	2.3	



	a	b	c	a	b	c	d	e	f	g	
Actual δ (ppm)	3.4	2.2	3.1	2.6	2.0	2.3	4.1	1.6	1.4	0.9	
Calculated δ (ppm)	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	0.9	
Br-	2.1	0.7	0.2	Ar-	1.4	0.4	0.1	0.0	0.0	0.0	
ClOC-	<u>0.1</u>	<u>0.4</u>	<u>1.8</u>	RO ₂ C-	0.1	0.3	1.1	0.0	0.0	0.0	
Total	3.4	2.3	3.2	RCO ₂ -	<u>0.0</u>	<u>0.0</u>	<u>0.0</u>	<u>2.8</u>	<u>0.5</u>	<u>0.1</u>	<u>0.0</u>
				Total	2.7	1.9	2.4	4.0	1.7	1.3	0.9

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