Approaches towards a Unified Empirical Treatment of Carbon-13 NMR Chemical Shifts: Part I—Correlation Analyses of Data on Alkanes & Aliphatic Alcohols & Amines

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The 13C NMR chemical shifts of alkanes and saturated aliphatic alcohols and amines can be reproduced by two parameters: the charge on the carbon atom as calculated by iterative partial equalization of orbital electronegativity and the number of hydrogen atoms three bonds away from the carbon atom under consideration. All data can be handled by a single linear equation with a correlation coefficient of 0.972 and a standard deviation of 3.38 ppm. Thus, the influence of C, H, O and N on 13C NMR chemical shifts in saturated systems is incorporated into a unified treatment.

Carbon-13 NMR spectroscopy is a valuable tool for structure determination of organic compounds. Elucidation of relationships between molecular structure and 13C NMR chemical shifts is, therefore, of considerable importance. The theoretical treatment of 13C NMR chemical shifts is rather complex; various attempts to simplify the problem have been made. However, the theoretical calculation of chemical shifts has not yet progressed far enough for it to be of general practical usefulness. In this situation recourse has been taken to empirical approaches for the prediction of 13C NMR chemical shifts, the methods most widely used being additivity schemes where the chemical shift of a carbon atom is obtained from a base value by adding increments for each substituent. Thus, the chemical shifts for the carbon atoms of aliphatic compounds can be obtained employing Eq. (1)

\[ \delta = -2.3 + \sum Z_i + S + K \]  

The increments \( Z_i \) have to be taken for each substituent in the \( x, y \) and \( \delta \) positions of the carbon atom considered; \( S \) and \( K \) are additional steric (S) and conformational (K) correction terms. Values for the various parameters have been obtained through regression analysis on experimental 13C NMR chemical shifts. Such additivity schemes are simple to apply and generally lead to rather accurate estimates, but this is no surprise as they are heavily parameterized. However, an additivity scheme must fail when there is no increment available for a given substituent. Furthermore, it should not be forgotten that most of the increments do not lend themselves to a physical interpretation and thus do not contribute to an understanding of the factors influencing 13C NMR chemical shifts.

In this paper the chemical shifts of the various carbon atoms of alkanes and aliphatic alcohols and amines are studied. Thus, the influence of H, O and N on 13C NMR shifts in saturated systems is investigated. Work is already in progress on aliphatic halides and on the effects of polysubstitution (unpublished data).

To put the problem in correct perspective, an analysis of previous correlations on alkanes, alcohols and amines is given in Table 1.

In their pioneering work Grant and Paul4 expressed the chemical shift \( \delta_{ik} \) of the \( k \)-th atom of a linear alkane by the linear equation (2)

\[ \delta_{ik} = B + \sum n_{ki} A_i \]  

\( n_{ki} \) is the number of carbon atoms in the \( i \)-th position relative to the \( k \)-th carbon, and \( A_i \) is the additive chemical shift parameter assigned to the \( i \)-th carbon atom. Correction terms for branched alkanes had to be introduced4 bringing the number of parameters to 13, 13C NMR measurements on more alkanes led to additional and revised parameters5 bringing their number to 22.

Beierbeck and Saunders6 investigated conformational effects on the 13C NMR chemical shifts in acyclic hydrocarbons. For the data set, of ref. 5 they could reproduce the 13C shifts with a standard deviation of 1.59 ppm using eleven parameters. For a smaller data set of alkanes a smaller number of parameters was suggested but only at the expense of a larger standard deviation7.
Table 1—Analysis of Additivity Schemes for Reproducing $^{13}$C NMR Chemical Shifts of Alkanes and Aliphatic Alcohols and Amines

<table>
<thead>
<tr>
<th>Data Set</th>
<th>Number of Data points</th>
<th>Parameters</th>
<th>St. dev. (ppm)</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkanes (linear)</td>
<td>30</td>
<td>5</td>
<td>0.21</td>
<td>4</td>
</tr>
<tr>
<td>Alkanes (linear &amp; branched)</td>
<td>53</td>
<td>13</td>
<td>0.30</td>
<td>4</td>
</tr>
<tr>
<td>Alkanes (linear &amp; branched)</td>
<td>344</td>
<td>13</td>
<td>2.00</td>
<td>5</td>
</tr>
<tr>
<td>Alkanes (linear, branched &amp; cyclic)</td>
<td>57</td>
<td>8</td>
<td>1.96</td>
<td>7</td>
</tr>
<tr>
<td>Alcohols</td>
<td>184</td>
<td>b</td>
<td>0.8-1.0</td>
<td>8</td>
</tr>
<tr>
<td>Alkanes (linear) + Alcohols (linear)</td>
<td>30+36</td>
<td>5+4</td>
<td>c</td>
<td>9</td>
</tr>
<tr>
<td>Alkanes + Alcohols</td>
<td>344+255</td>
<td>22+8+20</td>
<td>0.27-0.74</td>
<td>10</td>
</tr>
<tr>
<td>Alkanes + Amines</td>
<td>344+711</td>
<td>22+18</td>
<td>0.30-1.6</td>
<td>13</td>
</tr>
<tr>
<td>Alkanes + Amines</td>
<td>344+711</td>
<td>22+18+17</td>
<td>0.26-0.63</td>
<td>13</td>
</tr>
</tbody>
</table>

(a) The four values for the diamagnetic corrections also have to be taken as parameters
(b) Not directly comparable as the shifts of the alcohols were given relative to the ones of alkanes by introducing four additional parameters
(c) Not given; approximately 1.0 ppm
(d) Separate correlations both for $\alpha$, $\beta$, $\gamma$ and $\delta$-C and for primary, secondary and tertiary alcohols (altogether 10 different correlations)
(e) Separate correlations both for $\alpha$, $\beta$, $\gamma$-carbons and for primary, secondary and tertiary amines (altogether 9 different correlations)

Roberts et al. found that the $^{13}$C shifts in alcohols can be correlated with the $^{13}$C shifts in the corresponding substituted hydrocarbon with CH$_3$ in place of a OH group through Eq.(3).

\[ \delta_{C\text{ROH}} = c_1 \cdot \delta_{C\text{RCH}_3} - c_0 \]  

(3)

Different correlations had to be given for the $\alpha$, $\beta$ and $\gamma$ carbon atoms. For carbon atoms in the $\delta$ position and further away from the substituent (OH or CH$_3$) the chemical shifts are about equal. These regularities led to additivity schemes covering both alkanes and alcohols, but whereas for linear systems the number of parameters could be kept to nine, inclusion of branched systems required a sizeable number of parameters. Even with 30 parameters, correlations of the type of Eq.(3) had values for $c_0$ and $c_1$ which depended both on the type of alcohol (primary, secondary, or tertiary) and the site of the carbon atom ($\alpha$, $\beta$, $\gamma$ or $\delta$). As 10 different correlations of the above type were found, the simultaneous treatment of all alkanes and alcohols would need 50 parameters.

In extensions of these studies to include more derivatives, e.g. additionally incorporating primary amines, primary and secondary alkyl groups still had to be treated differently.

Alcohols and amines are almost similarly placed. Equations analogous to Eq.(3) can be set up, but again the values of $c_0$ and $c_1$ are different for primary, secondary and tertiary amines, and within these series of compounds, for the $\alpha$, $\beta$ and $\gamma$ carbon atoms, resulting in 9 different correlations. Thus, the unified treatment of alkanes and amines requires 40 parameters. Reductions in the standard error of estimation can be achieved only by including 17 additional terms.

However simple an additivity scheme for estimating $^{13}$C NMR chemical shifts might appear at the outset, practise has shown that a large number of parameters has to be considered in order to achieve a certain accuracy for the estimated value. Thus, to achieve a standard error of about 1.0 ppm in a unified treatment of the alkanes, alcohols and amines of references 5, 8 and 13, 60 parameters are needed, whereas 85 parameters are required to bring the standard deviation down to about 0.5 ppm. This high number of
parameters makes an additivity scheme for this level of accuracy of questionable practical usefulness.

Furthermore, the need to include more and more "correction" parameters in the additivity schemes clearly points out that these parametrizations cannot help in elucidating the foundations of $^{13}$C NMR chemical shifts. What would be needed is some systematic scheme which would give guidelines as to which parameters to consider and how the contribution of such a parameter to the chemical shift could be derived. Starting with the number of carbon atoms in the $\alpha,\beta,\gamma$ etc. positions is apparently not the appropriate procedure.

As an alternative to additivity schemes, empirical correlations have been sought between $^{13}$C NMR chemical shifts and parameters from other sources like charge values, electronegativities or Hammett type substituent constants. As these parameters are measures of electronic effects, such correlations could further an understanding of the factors contributing to $^{13}$C chemical shift. Quite a number of investigations have been reported using charge values on unsaturated or aromatic systems. However, for aliphatic systems, the material is rather scarce. Two reasons can be given. Firstly, there is a problem in choosing a reliable method for calculating charges in aliphatic systems. The methods investigated were: Excess 2p-electron densities, Del Re method, SGBO method, o-HMO method and modified population analysis.

Secondly, the results were generally disappointing in that the correlations had limited validity only. Thus, the slopes of these correlations change not only with the method used for calculating charges, but, what is more severe, in going from one type of compound to another. That is, when various types of compounds have been studied, the slopes for different carbon atoms ($\alpha,\beta,\gamma$ etc.) are all different. In other words, in studying R-X compounds, correlations were obtained when changing either $R$ or $X$, but no correlations were found when both $R$ and $X$ were changed.

The conclusion to be drawn is that either the methods for calculating atomic charges are unsatisfactory, or that there is no simple global correlation between the charge on a carbon atom and its $^{13}$C NMR chemical shift.

It will be evident from the above perspective that further attempts are necessary to find ways of expressing $^{13}$C NMR chemical shifts in a global manner. In other words, the chemical shifts of all carbon atoms for series of compounds where both skeleton and substituents have been changed should be given by a single equation. This should lay the foundation for an automatic predictor system: a computer program that, starting from the molecular structure, can give the chemical shift of all carbon atoms of that molecule. Clearly, this would constitute a valuable tool for the structure elucidation of molecules.

In a first approach only the nature of the constituent atoms and the network of bonds—the topology of a molecule—should be considered. As pointed out consideration of the constitution of a molecule only may result in an oversimplification of the problem, since quite often conformational and steric factors have been invoked in explaining $^{13}$C NMR chemical shifts.

In our endeavour we used multilinear regression analysis on known chemical shifts to derive linear equations expressing these data, at the same time, keeping the number of parameters to a minimum. An important incentive for this study was to investigate again the influence of charge on $^{13}$C NMR chemical shifts. To this end, methods to quantify these factors had to be developed. For each individual parameter algorithms have been defined which allow their calculation directly from the structural formula.

Parameters

Structural parameters

For reasons that become clearer later, the number of hydrogen atoms directly attached to the carbon atom considered ($N_{1H}$), as well as those two ($N_{2H}$) and three bonds away ($N_{3H}$) were taken as parameters. The values for these parameters can simply be obtained by inspection. However, as we were aiming at an automatic system we had to develop programs that derive the values for these parameters directly from the constitution of the molecule. For this purpose a spanning tree is grown for the molecule with the carbon atom considered as the root of this tree. The hydrogen atoms at the first, second, and third level of that tree are then counted.

Charge

We recently developed a method and an associated algorithm for the calculation of partial atomic charges in molecules. An attractive feature of this empirical method, iterative partial equalization of orbital electronegativity (PEOE) is the short computation times involved. Correlations with physical and chemical data demonstrated the significance of the charge values thus obtained. Chemical shifts in C-1s ESCA and $^1$H NMR data could be reproduced. Whereas these correlations indicated that the charge values reproduce trends in physical data, the calculation of dipole moments showed that the magnitude of the charge values is also correct. Of particular interest for the studies reported here is that for monosubstituted benzene deriva-
tives a simple correlation was found between \(^{13}\text{C}\) NMR chemical shifts and charge values\(^2\) of \(m\)and \(p\)-carbon atoms.

As carbon has a higher orbital electronegativity than hydrogen electron density is transferred from hydrogen to carbon. Figure 1 gives atomic charges on carbons for some representative molecules.

Comparison of the data on \(n\)-hexanol with those of \(n\)-hexane shows the influence of the heteroatom and its attenuation through a sequence of bonds. The data on \(2,2,4\)-trimethylpentane illustrate the sensitivity of the method to the structure of the molecule.

**Data Sets**

**Alkanes**

The \(^{13}\text{C}\) NMR chemical shift data on alkanes were taken from literature\(^4\). Data on all isomeric alkanes up to the octanes and those on \(n\)-nonane and \(n\)-decane were included in the analysis. Thus, the data set comprised 183 \(^{13}\text{C}\) NMR chemical shift values on methane, primary, secondary, tertiary and quaternary carbon atoms in the range of \(-2.3\) ppm to 53.3 ppm.

**Alcohols**

The \(^{13}\text{C}\) NMR chemical shift data on alcohols of Table 1 were those reported in literature\(^8\). These include values on all carbon atoms of primary, secondary and tertiary acyclic alcohols, altogether 184 \(^{13}\text{C}\) NMR chemical shift values in the range of 8.8 ppm to 75.1 ppm.

**Amines**

The \(^{13}\text{C}\) NMR chemical shift data on amines were also taken from literature\(^13\). All data on compounds up to a carbon content of eight were included in the data set. Thus, values on 124 \(^{13}\text{C}\) shifts from primary amines, 76 from secondary amines and 37 from tertiary amines were studied, altogether 237 \(^{13}\text{C}\) NMR chemical shift values from 8.36 ppm to 60.92 ppm.

In summary, in the selection of data care was taken to have an unbiased, homogeneous and statistically balanced set covering all bonding situations of carbon met in alkanes, alcohols and amines.

**Results and Discussion**

First we deal with investigations using structural parameters. This is done in order to accentuate the merits and problems inherent in structural parameters. For \(^{13}\text{C}\) NMR chemical shifts of the carbon atoms in \(n\)-alkanes from methane up to \(n\)-decane Grant and Paul\(^4\) used five parameters, i.e. the number of carbon atoms in the \(a,\beta,\gamma,\delta\) and \(e\)-positions, respectively. Thereby, the 30 data points could be reproduced with a correlation coefficient of 0.9998 and a standard deviation of 0.21 ppm (cf. Table 1). An equally good correlation could be achieved by using three parameters only, i.e. the number of hydrogen atoms in the \(a,\beta\) and \(\gamma\)-positions \((N_1H, N_2H, N_3H\) respectively). With the same 30 \(^{13}\text{C}\) NMR shifts, the equation obtained presently (Eq. 4) had a regression coefficient of 0.9995 and a standard deviation of 0.29 ppm.

\[
\delta = 64.39 - 16.75 N_1H - 2.55 N_2H + 2.28 N_3H \ldots\ldots (4)
\]

Some representative examples are given in Table 2. Note that this equation also takes account of the \(\gamma\)-effect\(^4\), particularly through the \(N_3H\) parameter.

The attractiveness of Eq.(4) lies in its simplicity; the three parameters, i.e. the number of hydrogen atoms one, two and three bonds away from the carbon atom under consideration, can easily be obtained by inspection.

However, these parameters—and this is true for any structural parameter—do not without further investigations provide insights into the physical mechanisms responsible for the success of Eq.(4). Furthermore, the validity of Eq.(4) is limited. It can still be applied with reasonable success to the larger cycloalkanes \((\delta_{\text{obs}} - \delta_{\text{calc}} \text{ in ppm})\): cycloctane \((-3.2)\), cycloheptane \((-1.0)\), cyclohexane \((-2.7)\), cyclopentane \((-3.5)\), cyclobutane \((-2.1)\). However, it fails badly with cyclopropane \((-23.5)\). In addition, with branched alkanes, the differences between observed and estimated \(^{13}\text{C}\) NMR shifts increase remarkably. A correlation analysis on 102 \(^{13}\text{C}\) NMR shifts of linear and branched alkanes only gave a correlation coefficient of 0.936 and a standard deviation of 3.49 ppm. The picture could only be improved by including more parameters (cf. in an analogous way, Grant and Paul\(^4\) increased their parameters from 5 to
Several criteria are offered for determining the quality of the results: (i) The statistical parameters, regression coefficient (r), and standard deviation (s), (ii) The coefficients, \( c_0 \), \( c_1 \) and \( c_2 \), of the correlation equations should be similar in the separate MLRA (a-c) and in the MLRA on the entire data set, (iii) The coefficient \( c_1 \) for the charge dependence of \(^{13}\text{C} \) NMR shift should be in the range of 300 to 500 ppm/electron\(^{19,20}\).

It must be clear from the very beginning that charge data alone will not suffice in satisfactorily reproducing \(^{13}\text{C} \) NMR chemical shifts. Some observations are clearly at variance with an intuitive understanding of charge distribution. For example, in \( n \)-alkanes one observes a discontinuity for the shift of the \( \gamma \)-carbon atom (cf. \( n \)-octane, 1, in Table 4). This certainly has no counterpart in the electron distribution of \( n \)-alkanes.

Consequently, charge data alone do not reproduce \(^{13}\text{C} \) shifts of alkanes very well (Eq. Sa, Table 4), for \( n \)-alkanes the largest deviation being that for the \( \gamma \)-carbon atom, as expected. A critical analysis of the largest deviations obtained with Eq. (Sa) for alkanes led us to choose the number of hydrogen atoms three bonds away from the carbon atom under consideration (N3H) as a second parameter. 2,2-Dimethylpropane (2) (Table 4), most vividly demonstrates the improvement obtained by including N3H as a second parameter, thus going from Eq. (Sa) to Eq. (6a). However, the other examples in Table 4 also illustrate the merits of the additional parameter N3H. Thus, the deviations for C-1, C-2, and C-3 in 3 and 4 (the 20.1 ppm error for C-3 of 4 was the largest deviation in the entire data set!) as well as that for C-4 of 4 are largely removed without introducing drastic deviations for the other carbon atoms. Even for \( n \)-alkanes, as exemplified by 1, the situation has improved. Although the error in estimation for the \( \gamma \)-carbon is still high (4.4 ppm), the trends in the \(^{13}\text{C} \) chemical shifts are now well reproduced. Whereas with Eq. (Sa) the changes in the deviations in going from the \( \beta \)- to the \( \gamma \)- and then to the \( \delta \)-carbon atom were +6.7 and -2.7 ppm, respectively, these values have decreased with Eq. (6a) to +1.7 and -0.7 ppm. The improvement obtained by including N3H as a parameter is also reflected in the statistical results contained in Table 3.

However, there is still a sizeable standard deviation of 3.13 ppm. The largest deviations occur for quaternary carbon atoms adjacent to another quaternary or tertiary carbon atom. We consider that as evidence for a steric effect which is not modelled by our topological approach. We believe that any drastic improvement in the quality of predictions of \(^{13}\text{C} \)
### Table 3—Results of Multilinear Regression Analysis of $^{13}$C NMR Chemical Shifts of Alkanes (183 data points), Alcohols (184), Amines (237) and Combined Data Set (604)

<table>
<thead>
<tr>
<th>Parameter(s)</th>
<th>Alkanes</th>
<th>Alcohols</th>
<th>Amines</th>
<th>Combination</th>
</tr>
</thead>
<tbody>
<tr>
<td>$q_c$</td>
<td>0.798</td>
<td>0.961</td>
<td>0.895</td>
<td>0.901 6.27</td>
</tr>
<tr>
<td>$q_c, N_{3H}$</td>
<td>0.950</td>
<td>3.13</td>
<td>0.982</td>
<td>3.38</td>
</tr>
</tbody>
</table>

$r$ = regression coefficient; $s$ = standard deviation in ppm; $c, c, c = coefficients of Eqs. (5) and (6)

### Table 4—Observed $^{13}$C NMR Chemical Shifts and Values Calculated by Eqs (5a) and (6a) with Charge and $N_{3H}$ Parameters for Representative Alkanes

<table>
<thead>
<tr>
<th></th>
<th>$\delta_{obs}$</th>
<th>$\delta_{obs}$</th>
<th>$\delta_{obs}$</th>
<th>$\delta_{obs}$</th>
<th>$\delta_{obs}$</th>
<th>$\delta_{obs}$</th>
<th>$\delta_{obs}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$q_c$</td>
<td>-0.065</td>
<td>-0.056</td>
<td>-0.053</td>
<td>-0.053</td>
<td>-0.060</td>
<td>-0.041</td>
<td>9.9</td>
</tr>
<tr>
<td>$N_{3H}$</td>
<td>2 2 5 4</td>
<td>9 0</td>
<td>10.9</td>
<td>-9.7</td>
<td>0.1</td>
<td>2.9</td>
<td>0.1</td>
</tr>
<tr>
<td>$\Delta$ (Eq 5a)</td>
<td>-2.3</td>
<td>-1.4</td>
<td>5.3</td>
<td>2.6</td>
<td>10.9</td>
<td>-9.7</td>
<td>0.1</td>
</tr>
<tr>
<td>$\Delta$ (Eq 6a)</td>
<td>-1.1</td>
<td>2.7</td>
<td>4.4</td>
<td>3.7</td>
<td>10.9</td>
<td>-9.7</td>
<td>0.1</td>
</tr>
</tbody>
</table>

$r$ = regression coefficient; $s$ = standard deviation in ppm; $c, c, c = coefficients of Eqs. (5) and (6)
NMR chemical shifts of alkanes will only result from a consideration of three-dimensional structure of these molecules.

More or less the same qualitative and quantitative picture as just discussed for the alkanes emerges from the MLRA on the data on aliphatic alcohols and amines. The consistency of the results as reflected in the values of $r$, $s$, $c_0$, $c_1$ and $c_2$ (see Table 3) is further underscored by the successful analysis of the combined set of 604 $^{13}$C NMR chemical shift data on alkanes, alcohols and amines. Eq. (6d) reproduces these shifts with a regression coefficient, $r=0.972$, and a standard deviation, $s=3.38$ ppm.

$$\delta_{13C}[\text{ppm}] = 39.41 + 427.3 \cdot q_c + 2.10 \cdot N_{3H} \quad \ldots(6d)$$

This shows that our approach handles the influence of hydrogen, carbon, oxygen and nitrogen atoms on the $^{13}$C NMR chemical shifts in aliphatic systems in a balanced manner with fair accuracy. Moreover, the sensitivity of shift to charge at 427 ppm/electron is in the expected range$^{19,20}$.

As typical examples for the application of Eq. (6d) results for the calculation of $^{13}$C NMR chemical shifts on changing the substituent in position 4 of 2-methylpentane from H to CH$_3$, OH and NH$_2$ are given in Table 5.

Although some of the errors are fairly high it should be kept in mind that all carbon atoms are treated simultaneously by one equation, not each position represented by a separate correlation. Thus, changes both in the skeleton (H $\rightarrow$ CH$_3$) and in heteroatom substitution are handled in a unified treatment.

It is interesting to note the influence of the $N_{3H}$ parameter on the central carbon atom (C-3). Although its rather high $^{13}$C shift in 2-methylpentane is not quite reproduced, the increase of $^{13}$C shift on going to 2,4-dimethylpentane is nearly exactly given. The increase of $N_{3H}$ from 9 to 12 is of predominant influence. Note also that in calculating $N_{3H}$ hydrogen atoms on carbon, oxygen, and nitrogen are counted with equal weight. The increase in chemical shift of carbon atom bearing the substituent (C-4) is solely and nicely handled by the change in charge value.

As a further illustration of the application of Eq. (6d), results are given in Table 6 for compounds obtainable from 2-methylbutane through substitution of H by CH$_3$, OH, or NH$_2$ at various positions. This example has been chosen as most of the relevant data were present in the data set.

Both here and in the previous examples the influence of charge on $^{13}$C NMR chemical shifts can be deciphered, particularly in alcohols and amines. It follows from our previous work$^{22-25}$ that the charge parameter calculated by the PEOE method represents the charge distribution in the molecules considered. Until further work, we refrain from a physical interpretation of the $N_{3H}$-parameter. The magnitude of its coefficient casts doubt on whether it represents a direct magnetic interaction between protons and $^{13}$C-nuclei. Amongst other results it takes account of the $\gamma$-effect. Therefore, in light of the steric interpretation$^{26}$ of the $\gamma$-effect the $N_{3H}$-parameter could as well be some measure of steric influence on $^{13}$C shifts. We expect any marked improvement in the accuracy of the predictive power of our approach only when explicit consideration is taken on the three-dimensional structure of the molecules. However, this goal is still elusive, even with approaches based on large numbers

| \begin{tabular}{lcccccc}
| Substitution & \multicolumn{3}{c}{CH$_3$} & \multicolumn{3}{c}{OH} & \multicolumn{3}{c}{NH$_2$} \\
| C & q_c & $N_{3H}$ & $\delta_{obs}$ & q_c & $N_{3H}$ & $\delta_{obs}$ & q_c & $N_{3H}$ & $\delta_{obs}$ \\
| C-1 & -0.043 & 5 & 22.7 & -0.3 & -0.043 & 5 & 23.1 & 0.1 & -0.042 & 5 & 23.37 & -0.1 \\
| C-2 & -0.047 & 2 & 27.9 & 4.4 & -0.046 & 1 & 25.7 & 3.8 & -0.044 & 1 & 25.1 & 2.4 \\
| C-3 & -0.051 & 9 & 41.9 & 5.4 & -0.048 & 12 & 49.0 & 4.9 & -0.025 & 10 & 49.2 & -0.6 \\
| C-4 & -0.056 & 1 & 20.8 & 3.2 & -0.046 & 1 & 25.7 & 3.8 & +0.053 & 1 & 45.5 & 1.3 \\
| C-5 & -0.045 & 2 & 14.3 & -1.5 & -0.043 & 5 & 22.7 & -0.3 & -0.039 & 3 & 24.3 & -4.7 \\
| \end{tabular} |

Values of the parameters, observed data and errors obtained through Eq 6d.
of parameters. Here we have achieved a description with a single linear equation using only two parameters of the influence of H, C, N and O on 13C NMR chemical shifts of aliphatic systems.

Of particular merit is that procedures have been developed to calculate the two parameters directly from constitutional information. Thus, 13C NMR chemical shifts can automatically be calculated, within the accuracy achieved here, for all carbon atoms of saturated structures containing H, C, N and O.

In this manner the approach outlined here provides an alternative, to the coding of 13C NMR spectra according to substructural features27,28 and makes it of interest to work on systems for the automatic prediction of 13C NMR spectra20,29,30.

Conclusion

Obviously, the results presented here are far from reproducing 13C NMR chemical shifts within experimental accuracy. However, they are to be regarded as a novel inroad to a unified empirical treatment of 13C NMR chemical shifts. We hope that further work along these lines will help in elucidating the factors influencing 13C NMR chemical shifts.

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References