Spectral editing with 2D E-HMQC NMR spectroscopy for CD\(_n\) groups: A theoretical study

İ Şaka*, S Gümüş & A Gençten

Department of Physics, Faculty of Arts and Sciences, Ondokuz Mayıs University, Samsun, Turkey

*E-mail: isaka@omu.edu.tr

Received 8 June 2009; accepted 14 May 2010

In order to get the simplified spectra for separation of carbonyl groups, the spectral editing of NMR signals has become a useful technique for complex molecules. E-HMQC is a \(^1\)H-detected, edited-pulse angle and two-dimensional NMR experiment which allows the selective detection of CH, CH\(_2\) and CH\(_3\) signals. The product operator theory is widely used for analytical description of the spectral editing NMR experiments for weakly coupled spin systems. In the present study, analytical descriptions of the 2D \(^2\)H-detected E-HMQC NMR experiment have been presented for weakly coupled IS\(_n\) (I=½; S=1; n=1, 2, 3) spin systems by using the product operator theory. By using obtained FID values, theoretical discussion and experimental suggestions for sub-spectral editing of CD, CD\(_2\) and CD\(_3\) groups have been made.

Keywords: NMR, E-HMQC, Product operator theory, CD\(_n\)

1 Introduction

Editing of NMR signals into sub-signals provides useful structural information, especially distinguishing of protonated and deuterated carbonyl groups in complex molecules. These experiments can be classified into two sub-groups as \(^{13}\)C- and \(^1\)H-detected NMR experiments. The well-known \(^{13}\)C editing NMR experiments are DEPT (Refs 1,2) and SEMUT (Refs 3,4). The edited-pulse \(^1\)H NMR experiments such as DEPT-HMQC (Refs 5,6), E-HMQC (Ref. 7) and MAXY (Ref. 8) are more useful than \(^{13}\)C-detected NMR experiments because of high natural abundance of \(^1\)H nucleus. Editing and selective detection methods for \(^1\)H NMR spectroscopy have been reviewed\(^9\). The basic HMQC is a two-dimensional NMR experiment which provides correlation between scalar coupled heteronuclei\(^10,11\). Modified forms of this experiment such as DEPT-HMQC and E-HMQC have been developed in order to edit the signals. The DEPT-HMQC pulse sequence has been designed by Kessler et. al\(^5\) to inverse detection of \(^1\)H nuclei using DEPT for multiplicity editing of CH\(_n\) signals into sub-signals. Zhang and Wang\(^7\) have presented an Editable Heteronuclear Multiple-Correlation (E-HMQC) experiment which allows detecting \(^1\)H nuclei for spectral editing of CH\(_n\) signals. The both (DEPT-HMQC and E-HMQC) experiments provide similar information and are called as two-dimensional, edited-pulse and \(^1\)H-detected NMR experiments. Liquid-state and solid-state \(^2\)H-detected NMR experiments are used to investigate the molecular properties of deuterated molecules\(^12-15\). Therefore, \(^2\)H-detected version of E-HMQC experiment can be used in deuterated molecules.

It is well known that the product operator theory as a quantum mechanical method is widely used for analytical description of multi-pulse NMR experiments having mostly two spin-½ system or spin-½ and spin-1 system in liquids\(^16-28\). A complete product operator theory for weakly coupled IS (I=½, S=1) spin system have been presented in our previous study\(^26\). By using product operator theory in NMR experiments, new experimental suggestions can be made and also experimental results can be confirmed\(^4,23\).

In the present study, by using product operator theory analytical descriptions of 2D \(^2\)H-detected E-HMQC experiment have been presented for weakly coupled IS\(_n\) (I=½; S=1; n=1, 2, 3) spin systems. For analytical description of the experiment, we have written a computer program in Mathematica which is very flexible for implementation and evolutions of the product operators under the Hamiltonians\(^29\). Then, a theoretical discussion and experimental suggestions for sub-spectral editing of CD, CD\(_2\) and CD\(_3\) groups have been presented. To the best of our knowledge, this will be the first application of product operator theory to 2D \(^2\)H-detected E-HMQC NMR spectroscopy for weakly coupled IS\(_n\) (I=½; S=1; n=1, 2, 3) spin systems.
2 Theory

The product operator formalism is the expansion of the density matrix operator in terms of matrix representation of angular momentum operators for individual spins. For IS \( I = \frac{1}{2}, \quad S = 1 \) spin system, four Cartesian spin angular momentum operators for \( I = \frac{1}{2}; \quad E_x, E_y, E_z, I \), and nine Cartesian spin angular momentum operators for \( S = 1; \quad E_x, S_x, S_y, S_z, S_x^2, (S_x, S_z), (S_y, S_z), (S_x, S_y, S_z), (S_x^2 - S_y^2) \) can be easily found.\(^{30}\)

So, \( 4 \times 9 = 36 \) product operators are obtained with direct products of these angular momentum operators for IS \( I = \frac{1}{2}, \quad S = 1 \) spin system. Depending on the pulse experiment, Cartesian spin operator \( (S_x^2 - S_y^2) \) is separated into two spin operators as \( S_x^2 \) and \( S_y^2 \). In this case, there exist 40 product operators.

Time dependency of the density matrix is given by\(^{21}\):

\[\sigma(t) = \exp(-iHt)\sigma(0)\exp(iHt) \quad \ldots (1)\]

where \( H \) is the total Hamiltonian which consists of radio frequency (rf) pulse, chemical shift and spin–spin coupling Hamiltonians and \( \sigma(0) \) is the density matrix at \( t = 0 \). After employing the Hausdorff formula\(^{21}\):

\[\exp(-iHt)A\exp(iHt) = A - (it)[H, A] + \frac{(it)^2}{2!}[H, [H, A]] - \frac{(it)^3}{3!}[H, [H, [H, A]]] + \Lambda \quad \ldots (2)\]

evolutions of the product operators under the rf pulse, chemical shift and spin–spin coupling Hamiltonians can easily be obtained.\(^{16,21,22}\) The effect of \( \alpha \)–axis rf pulse on some of Cartesian spin angular momentum operators for IS \( I = \frac{1}{2}, \quad S = 1 \) spin system are given in following equations\(^{26}\):

\[S_y \xrightarrow{H_{rf}} S_y c_0 + S_z s_0 \quad \ldots (3a)\]

\[S_z \xrightarrow{H_{rf}} S_z c_0 - S_y s_0 \quad \ldots (3b)\]

\[(S_y, S_z) \xrightarrow{H_{rf}} (S_y, S_z) c_0 + (S_y, S_z) s_0 \quad \ldots (3c)\]

\[(S_y, S_z) \xrightarrow{H_{rf}} (S_y, S_z) c_0 - (S_y, S_z) s_0 \quad \ldots (3d)\]

\[S_y^2 \xrightarrow{H_{rf}} \frac{1}{2} S_y^2 (c_{20} + 1) - \frac{1}{2} S_z^2 (c_{20} - 1) + \frac{1}{2} (S_y, S_z) c_{20} \quad \ldots (3e)\]

where the \( rf \) pulse Hamiltonian for \( \alpha \)-axes is \( H_{rf} = \omega_{rf} S_y, \quad \theta = \omega_{rf} t, \quad c_{ab} = \cos(n\theta) \) and \( s_{ab} = \sin(n\theta) \).

The effect of the spin–spin coupling Hamiltonian on some of product operators in a weakly coupled IS \( \Lambda = A \) \( I = \frac{1}{2}, \quad S = 1 \) spin system is given as following equations\(^{26}\):

\[I_x \xrightarrow{H_{rf}} I_y S_z s_{2j} + I_x [1 + S_y^2 (c_{2j} - 1)] \quad \ldots (4a)\]

\[I_y \xrightarrow{H_{rf}} I_x S_z s_{2j} + I_y [1 + S_x^2 (c_{2j} - 1)] \quad \ldots (4b)\]

\[I_z S_x \xrightarrow{H_{rf}} I_y S_z s_{2j} \quad \ldots (4c)\]

\[I_z S_y \xrightarrow{H_{rf}} I_x S_z s_{2j} - I_z S_x^2 s_{2j} \quad \ldots (4d)\]

\[I_z S_y \xrightarrow{H_{rf}} \frac{1}{2} I_x S_x^2 (c_{2j} + 1) - \frac{1}{2} I_y S_z^2 (c_{2j} - 1) + I_z (S_y, S_z) s_{2j} \quad \ldots (4e)\]

\[I_z S_y \xrightarrow{H_{rf}} -\frac{1}{4} (S_y, S_z) s_{2j} \quad \ldots (4f)\]

In the Eqs 4(a–f), \( H_{rf} = 2\pi JH I S_z \) is the weak coupling Hamiltonian, \( c_{ab} = \cos(n\pi Jt) \) and \( s_{ab} = \sin(n\pi Jt) \). All evolutions under the \( rf \) pulse, spin–spin coupling and chemical shift Hamiltonians can be found elsewhere\(^{26}\).

The product operators are the direct products of the spin angular momentum operators, e.g., \( I_x S_y \) is \( I_y S_z \). At any time during the experiment, the ensemble averaged expectation value of the spin angular momentum, e.g., for \( I_y \), is:

\[M_y(t) \propto \langle I_y \rangle \equiv \text{Tr}[I_y \sigma(t)] \quad \ldots (5)\]

where \( \sigma(t) \) is the density matrix operator calculated from Eq. (1) at any time. As \( \langle I_y \rangle \) is proportional to the magnitude of the \( y \)-magnetization, it represents the signal detected on \( y \)-axis. So, in order to estimate the free induction decay (FID) signal of a multiple-pulse NMR experiment, density matrix operator should be obtained at the end of the experiment.

3 Results and Discussion

For the product operator description of the 2D E-HMQC NMR experiment for CD\(_6\) groups, the pulse sequence is shown in Fig. 1, is used. The density matrix operator at each stage of the experiment is labeled with numbers and \(^13\)C is treated as spin \( I \) and \(^2\)H (D) as spin \( S \). In the pulse sequence; \( \Delta \) is the
coupling evolution delay, \( \tau \) delay is applied for recovery of magnetic field homogeneity, \( t_1 \) and \( t_2 \) delays are the chemical shift evolution period for \( I \) and \( S \), respectively. Optimum value of \( \Delta \) is \( 1/(4J) \) for the 2D E-HMQC experiment. Starting from the density matrix operator at thermal equilibrium, one should apply the required Hamiltonians during the pulse sequence and obtain the density matrix operator at the end of the experiment. For multi-pulse NMR experiments and multi-spin systems, to follow these processes by hand becomes too difficult. In order to overcome this problem, a home made computer program written in Mathematica is used. Thus, the density matrix operators for every stage and at the end of the experiment are obtained for different spin systems such as \( IS, IS_2 \) and \( IS_3 \) (\( I=\frac{1}{2}, S=1 \)).

For \( IS \) spin system, the density matrix at thermal equilibrium is \( \sigma_0 \propto S \). The density matrices evolutions under Hamiltonians for some labeled point are obtained as follows:

\[
\sigma_0 \xrightarrow{90^\circ,(S)} S_y \xrightarrow{H,(\Delta=1/4J)} -\sqrt{2}I_xS_x + \frac{1}{\sqrt{2}}S_y \equiv \sigma_2 
\]

\[
\sigma_2 \xrightarrow{180^\circ,(S)+180^\circ,(I)} -\sqrt{2}I_xS_x - \frac{1}{\sqrt{2}}S_y \xrightarrow{H,(\Delta)} -2I_xS_x 
\]

Applying the procedure, the following density matrices are obtained in steps 11, 17 and 22:

\[
\sigma_{11} = -2I_x(S_x,S_z)c_0 + 2I_x(S_x,S_y)_+s_0 
\]

\[
\sigma_{17} = 2I_xS_xc_0c_i - 2I_x(S_x,S_y)_+s_qc_i - 2I_xS_xc_0s_i - 2I_x(S_x,S_y)_+s_qS_i 
\]

\[
\sigma_{22} = S_y(c_qc_ic_s - 2I_x(S_x,S_y)_+s_qc_i - 2I_x(S_x,S_y)_+c_0s_i + 2I_x(S_x,S_y)_+s_qS_i - S_yc_0c_sS_i) 
\]

In Eqs (8-10) and following equations, \( H_I=2\pi IJ,S_z \), \( c_{0I} = \cos(n\theta) \), \( s_{0I} = \sin(n\theta) \), \( c_{nI} = \cos(n\Omega_{d1}) \), \( s_{nI} = \sin(n\Omega_{d1}) \), \( c_{nS} = \cos(n\Omega_{d2}) \) and \( S_{nS} = \sin(n\Omega_{d2}) \). In the last density matrix operator in Eq. (10), only the first term contributes to the signals since acquisition is taken along \( y \)-axes for spin \( S \). Then, the magnetization along the \( y \)-axis is proportional to \( \sum_{i=1}^{n}\langle S_y \rangle \) and

\[
M_y(t_1,t_2) \propto \sum_{i=1}^{n}\langle S_y \rangle = \sum_{i=1}^{n}\text{Tr}(S_y \sigma_{22}) 
\]

Now, it is necessary to obtain the \( \sum_{i=1}^{n}\text{Tr}(S_y O) \) values of observable product operators indicated by \( O \). For the IS \( \sim (I=\frac{1}{2}, S=1; n=1, 2, 3) \) spin systems, \( \sum_{i=1}^{n}\text{Tr}(S_y O) \) values of observable product operators are calculated by using Mathematica and results are given in Table 1. Using Table 1 for the IS spin system:

\[
M_y(t_1,t_2) \propto \langle S_y \rangle \text{Tr}(S_y \sigma_{22}) = 4c_qc_ic_s \] is obtained.

For \( IS_2 \) spin system, the density matrix at thermal equilibrium is \( \sigma_0 \propto S_1+2S_2 \). At the end of the experiment, following observable terms are obtained using the computer program:

\[
\sigma_{22} = \frac{1}{2}(2S_{1y} + 2S_{2y} - S_{1y}S_{2x} - S_{1y}S_{2y} - S_{1y}S_{2y}) 
\]

\[
+ S_{1y}S_{2y}c_0c_sc_s + \frac{1}{2}(S_{1y}S_{2x} + S_{1y}S_{2y} + S_{1y}S_{2y}) 
\]

\[
+ S_{1y}S_{2y}c_0c_sc_s + \frac{1}{2}(S_{1y}S_{2x} + S_{1y}S_{2y} - S_{1y}S_{2y}) 
\]

\[
- S_{1y}S_{2y}c_0c_sc_s 
\]

\[
- S_{1y}S_{2y}c_0c_sc_s 
\]

\[
- S_{1y}S_{2y}c_0c_sc_s 
\]
Spin system | Product operators (O) | \( \sum_{n=1}^{n} \text{Tr}(S_{n} \sigma_{22}) \)
--- | --- | ---
\( IS \) | \( S_{y} \) | 4
\( IS_{2} \) | \( S_{y} + S_{z} \) | 24
\( IS_{3} \) | \( S_{y} + S_{z} + S_{x} \) | 108

Using trace values for the observable terms given in Table 1:

\[
M_{y}(t_{1},t_{2}) \propto \sum_{i=1}^{2} \langle S_{y} \rangle = \sum_{i=1}^{2} \text{Tr}(S_{y} \sigma_{22}) = 8c_{0}c_{j}c_{s} + 16c_{20}c_{0}c_{j}c_{s} \quad \ldots (14)
\]

is found.

For \( IS_{3} \) spin system, applying the same procedure:

\[
M_{y}(t_{1},t_{2}) \propto \sum_{i=1}^{2} \langle S_{y} \rangle = \sum_{i=1}^{2} \text{Tr}(S_{y} \sigma_{22}) \quad \ldots (15)
\]

\[
2c_{6}c_{j}c_{s} + 48c_{20}c_{6}c_{j}c_{s} + 48c_{20}^{2}c_{0}c_{j}c_{s}
\]

is obtained.

The \( \sum_{i=1}^{n} \text{Tr}(S_{y} \sigma_{22}) \) values obtained for \( IS, IS_{2} \) and \( IS_{3} \) spin systems represent the FID signals of the 2D \(^{2}H\)-dedected E-HMQC experiment for CD, CD\(_{2}\) and CD\(_{3}\) groups, respectively. These \( \sum_{i=1}^{n} \text{Tr}(S_{y} \sigma_{22}) \) values for \( IS_{n} \) (\( n = 1, 2, 3 \)) spin systems can be generalized as following:

\[
\sum_{i=1}^{n} \text{Tr}(S_{y} \sigma_{22})(CD_{n}) = 4n(1 + 2c_{20})c_{0}c_{j}c_{s} \quad \ldots (16)
\]

These normalized \( \sum_{i=1}^{n} \text{Tr}(S_{y} \sigma_{22}) \) values can be also written in a generalized form as:

\[
\sum_{i=1}^{n} \text{Tr}(S_{y} \sigma_{22})(CD_{n}) = \frac{1}{4^{n}}(1 + 2c_{20})^{n-1}c_{0}c_{j}c_{s} \quad \ldots (20)
\]

The plots of these FID functions are shown in Fig. 2. As seen in Fig. 2, the relative signal intensities of CD, CD\(_{2}\) and CD\(_{3}\) groups vary as functions of \( \theta \).

In 2D the \(^{3}H\)-dedected E-HMQC experiment, as the observed nuclei is \(^{3}H\), Eq. (20) is multiplied by \( n \) for the real relative signal intensities of CD\(_{n}\) groups. Then, the obtained real relative signal intensities for several angles are given in Table 2. As seen in Table 2 and in Figure 2, when the experiment is performed for the angle of 60\(^{\circ}\), only CD groups will be observed as positive signals. For the angle of 75\(^{\circ}\), CD and CD\(_{2}\) groups will give positive signals and CD\(_{2}\) groups will give negative signals. By comparing the signs and the relative intensities of signals for the angles of 60\(^{\circ}\) and 75\(^{\circ}\), one can easily identify all CD, CD\(_{2}\) and CD\(_{3}\) groups from each other. Therefore, 2D...
**Table 2**—Real relative signal intensities of the $^2$H-dedected E-HMQC experiment of CD$n$ groups for several pulse angles of $\theta$

<table>
<thead>
<tr>
<th>Spin System</th>
<th>$\theta=60^\circ$</th>
<th>$\theta=75^\circ$</th>
<th>$\theta=180^\circ$</th>
</tr>
</thead>
<tbody>
<tr>
<td>IS(CD)</td>
<td>0.5</td>
<td>0.26</td>
<td>-1</td>
</tr>
<tr>
<td>IS$_2$(CD$_2$)</td>
<td>0</td>
<td>-0.19</td>
<td>-2</td>
</tr>
<tr>
<td>IS$_3$(CD$_3$)</td>
<td>0</td>
<td>0.14</td>
<td>-3</td>
</tr>
</tbody>
</table>

$^2$H-dedected E-HMQC experiment can be used for the sub-spectral editing of CD, CD$_2$, and CD$_3$ groups. In deuterium labeling, it is of interest to determine whether the methyl–group is transferred as a whole leading to $^{13}$CD$_3$– containing compounds or leading to $^{13}$CD$_2$H– or $^{13}$CDH$_2$– containing compounds$^{13,14}$. So, 2D $^2$H-dedected E-HMQC experiment of CD$n$ groups can be also used for this purpose.

## 4 Conclusions

Multi–pulse NMR experiments including editing pulse angles have become a powerful technique for selective detection of protonated and deuterated carbonyl groups in complex molecules. The product operator theory is a useful technique for the analytical description of multi–pulse and editing pulse NMR experiments for weakly coupled spin systems$^{16-28}$. In this study, by using product operator theory, an analytical description of 2D $^2$H-dedected E-HMQC NMR experiment is presented for IS$_n$ ($I=\frac{1}{2}$; $S=1$; $n=1$, 2, 3) spin systems. Then, it is shown this experiment can be easily used for the identification of CD, CD$_2$ and CD$_3$ groups from each other.

**References**