

# Proton Detection of Carbon–Carbon Spin Coupling Constants in Symmetrical Molecules

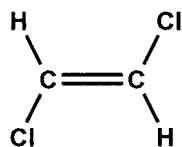
Stefan Berger

*Institute of Analytical Chemistry, University Leipzig, Linnéstr. 3 D-04103 Leipzig*

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**A new method is shown to determine C,C spin coupling constants in C<sub>2</sub> symmetric molecules by using proton detection with gradient selected 2QHMBC. It is shown that the pulse sequence proposed distinguishes between symmetric and antisymmetric eigenfunctions of the AA'XX' spin system.** © 2000 Academic Press

Carbon–carbon spin coupling constants provide basic understanding of the chemical bond in organic molecules (1, 2). The determination of C,C spin coupling constants in C<sub>2</sub> symmetric molecules, however, poses a spectroscopic challenge, because the nuclei in question have the same chemical shift. There are many examples in natural product chemistry or physical organic chemistry where such knowledge would be of large interest. Several years ago we demonstrated (3) a solution to this problem using <sup>13</sup>C INADEQUATE without proton decoupling. The idea was to measure in this way the XX' part of the AA'XX' spin system which is often present in such molecules as, for example, *trans*-1,2-dichloroethene **1** (Scheme 1).



**1**

$${}^1J(\text{C},\text{H}) 199.1$$

$${}^2J(\text{C},\text{H}) < 0.2$$

$${}^3J(\text{H},\text{H}) 12.1$$

$${}^1J(\text{C},\text{C}) 91.9$$

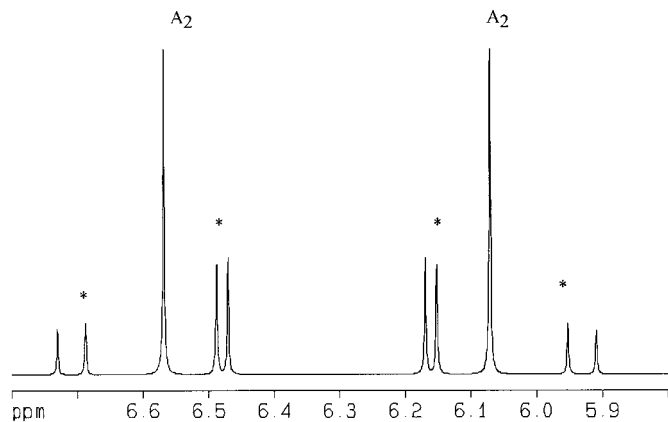
The AA' and XX' parts of an AA'XX' spin system are completely equivalent and if one would be able to measure either part one can extract the desired spin coupling constant. After it was shown by us that it is possible to measure the <sup>13</sup>C part of the spin system, this idea was applied by several authors (4–8). However, recording of proton coupled <sup>13</sup>C INADEQUATE spectra is possibly the least sensitive NMR method available and thus this technique cannot be applied in cases of

limited material. Furthermore, there was another drawback. From the 10 theoretical lines of the XX' part (see Fig. 1) the two A<sub>2</sub> lines were missing. This was explained by the fact that the A<sub>2</sub> subsystem of an AA'XX' spin system cannot generate double quantum coherences. After the availability of pulse simulation programs as SMART (9) or NMR-SIM (10), where any spin system can be studied under the action of a complicated pulse sequence, this experimental observation can now be corroborated by using such a pulse simulation program. Fortunately, the absence of the two A<sub>2</sub> lines did not prevent the extraction of the C,C spin coupling constant.

It is obvious that for sensitivity reasons one should try to measure the AA' part of the spin system by proton detection. However, simply applying proton INADEQUATE does not help because here the double quantum filter passes also the AA'X systems which dominate the experimental spectrum and the 100 times less sensitive, but desired, AA'XX' spin system is hidden as seen in the experimental spectrum of Fig. 2.

We therefore turned to the elegant gradient supported 2QHMBC technique recently communicated by Meissner *et al.* (11) We converted their pulse sequence to 1D and left everything off which was not necessary in our case. Figure 3 displays the details of the pulse sequence used. The first pulse on proton creates  $I_{\text{H}}^{+}$  and  $I_{\text{H}}^{-}$  coherences, whereas for the spin system involved, the first pulse on carbon creates the terms  $I_{\text{H}}^{+}I_{\text{C}}^{+}$  and others. For this, it is sufficient to use the delay  $d2 = \frac{1}{2}J(\text{C},\text{H}) = 2.51$  ms as demonstrated in the original paper by Meissner *et al.* (11). The 180° pulse  $p2$  on proton transforms this into  $I_{\text{H}}^{-}I_{\text{C}}^{+}$  corresponding to a sum of coherence orders of  $-2$ . This situation is dephased by gradient  $g1$  with a relative strength of 30 yielding a dephasing of  $-60$  units. The 180° pulse on carbon  $p4$  creates the term  $I_{\text{H}}^{-}I_{\text{C}}^{-}$  corresponding to a sum of coherence orders of  $-6$ . Therefore, gradient  $g2$  with the relative strength of  $-10$  refocuses the desired coherence and only signals of protons which are coupled to two carbon atoms are observed.

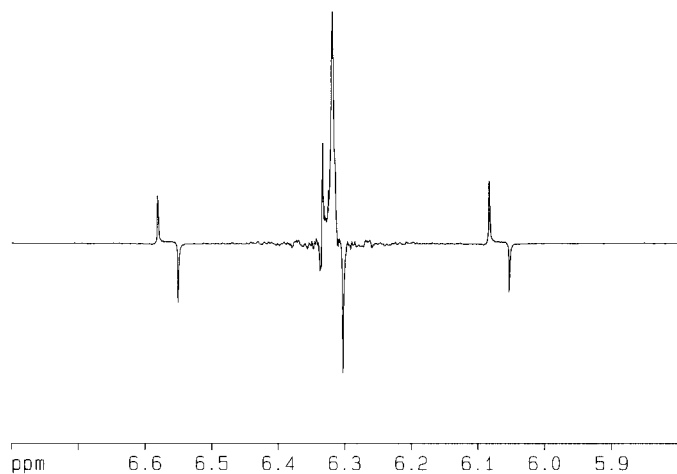
The resulting spectrum is given in Fig. 4 and was at first sight very surprising. The signals of the molecules containing two and one <sup>12</sup>C carbon atoms are very well suppressed. However, the spectrum is missing four lines, which comprise



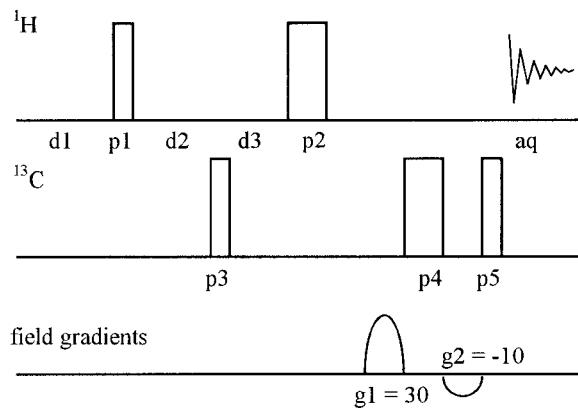
**FIG. 1.** Spin simulation of the AA'XX' System of **1**. The spectrum consists of two AX and one A<sub>2</sub> subspectra; transitions marked with an asterisk from antisymmetric submatrix B<sub>u</sub> (see Ref. (12)).

the inner of the two AX subspectra of the AA'XX' spin system. Again, the desired C,C spin coupling constant can be extracted manually or by spin simulation considering that the remaining AX subspectrum contains the sum of J(C,C) and J(H,H). The latter was taken from the <sup>1</sup>H INADEQUATE experiment shown in Fig. 2. We could reproduce the experimental results with the pulse simulation program NMR-SIM.

We interpret the missing of the inner AX subspectrum as follows. The Hamiltonian matrix of an AA'XX' spin system can be shown to factorize into two submatrices (12). One (symmetry A<sub>g</sub>) contains only symmetric eigenfunctions and is further factorized into five subsubmatrices of size 1 × 1, 2 × 2, 4 × 4, 2 × 2, and 1 × 1. The other (symmetry B<sub>u</sub>) contains only antisymmetric eigenfunctions and can be further factorized into three 2 × 2 subsubmatrices. In Fig. 5 the energy levels of the eigenfunctions of the spin system for **1** as calculated by spin simulation are given both for the two Hamiltonian

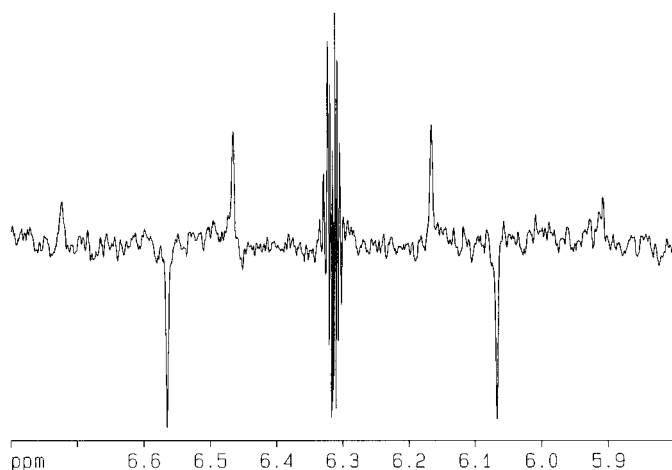


**FIG. 2.** Experimental <sup>1</sup>H-INADEQUATE of **1**, only AA'X spectra can be seen (20% solution of **1** in CDCl<sub>3</sub>, Bruker DRX-400 Spectrometer).

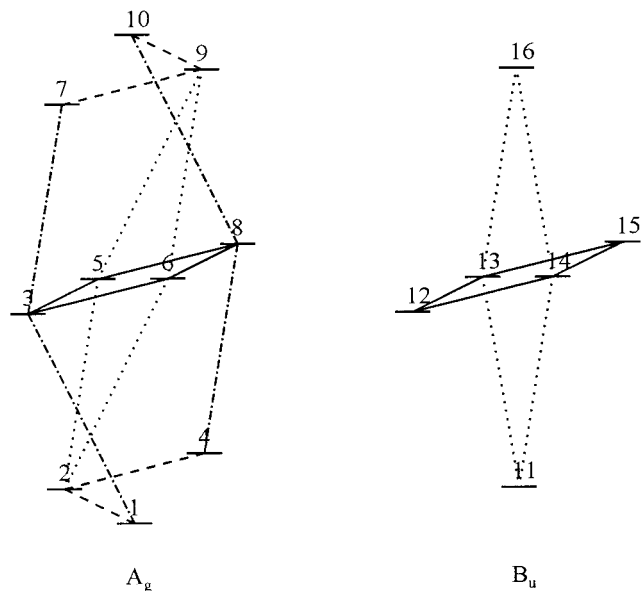


**FIG. 3.** 1D 2QHMBC sequence derived from Meissner *et al.* (11) Pulse phases: p1, p3, p4 = x; p2 = x<sub>16</sub>, y<sub>16</sub>, -x<sub>16</sub>, -y<sub>16</sub>; p5 = x<sub>4</sub>, y<sub>4</sub>, -x<sub>4</sub>, -y<sub>4</sub>; aq = (x, -x, x, -x, -x, x, -x, x)<sub>2</sub>, (-x, x, -x, x, x, -x, -x)<sub>2</sub>.

submatrices A<sub>g</sub> and B<sub>u</sub>. The distances between the energy levels correspond to the actual frequencies in **1**. It can be seen that the antisymmetric submatrix B<sub>u</sub> contains the lines of the inner AX subsystem both for <sup>1</sup>H and <sup>13</sup>C, whereas the symmetric matrix A<sub>g</sub> contains the A<sub>2</sub> lines and those of the outer AX subsystem, again both for <sup>1</sup>H and <sup>13</sup>C. In Fig. 5 the lines for the proton AX subsystems are drawn solid, the lines for the proton A<sub>2</sub> transitions are dashed, those for the carbon AX spin systems are dotted, and those for the carbon A<sub>2</sub> subsystems are dashed-dotted. Apparently, the selection process of one proton and two carbons (coherence I<sub>H</sub><sup>+</sup>I<sub>C</sub><sup>+</sup>I<sub>C</sub><sup>+</sup>) by the pulsed field gradients in the 2QHMBC sequence described above corresponds to a selection of the Hamiltonian submatrix with symmetrical eigenfunctions leading to a absence of those four transitions contained in the submatrix B<sub>u</sub>.



**FIG. 4.** Experimental 1D 2QHMBC result of **1**; (20% solution of **1** in CDCl<sub>3</sub>, Bruker DRX-400 Spectrometer, d1 = 3 s, d2 = 2.51 ms, d3 equal to effective gradient length = 1.05 ms, spectral width 1000 Hz on 4 k data points, total experiment time ca. 5 h).



**FIG. 5.** Energy level diagram and transitions of the AA'XX' spin system of **1** as calculated by spin simulation. Solid transitions, proton AX lines; dashed transitions, proton A<sub>2</sub> lines; dotted transitions, carbon AX lines; dashed-dotted transitions, carbon A<sub>2</sub> lines.

## CONCLUSIONS

We have shown in this work that it is possible to measure carbon-carbon spin coupling constants with proton sensitivity provided higher order spin systems are present. This enables these measurements for compounds which are only present in minor quantities.

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