

Notes

Pulsed Field Gradient NMR: Correction of t_1 artifacts in DQF-COSY, HMQC, and HMBC

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NMR techniques using multiple quantum transitions were mentioned in the literature as early as 1956.¹ Since then, many methods²⁻⁷ describing the excitation and detection of multiple-quantum transitions have been known. These methods give structural and dynamic information complementary to that of single quantum transition methods.

The general method⁴ to create multiple quantum (MQ) coherence introduces two non-selective 90° pulses separated by a small time interval τ . The coherence which is created then evolves during t_1 . After this, another 90° pulse as a read pulse is applied to transfer the MQ coherence to an observable single quantum (SQ) coherence. Thus, we collect MQ coherence signals in terms of SQ coherence during t_2 (See Figure 1-(a)). Sometimes a 180° pulse in the middle of t_1 is applied to cancel out the effect of chemical shifts.⁸ Selection of the order of coherence is achieved by an appropriate phase cycling.⁹

There is another way to select the coherence order, which makes use of the application of pulsed field gradients (PFG).¹⁰ There are several advantages when the PFG method is used. Firstly, there is a significant saving in experimental time because the phase cycling is no longer required. Secondly, most of t_1 artifacts are removed by PFG. Lastly, there is an extra benefit for the experiments done in H_2O ; PFG dephases out the huge H_2O peak.¹¹

Here, we apply PFG to the experiments of double quantum filtered correlated spectroscopy (DQF-COSY), heteronuclear multiple quantum coherence spectroscopy (HMQC), and heteronuclear multiple-bond correlation spectroscopy (HMBC). The spectra obtained by using the PFG method are compared with those obtained by using the phase cycling method.

The DQF-COSY^{9,12} gives simple and easily interpretable spectra by eliminating single quantum signals. It is particularly helpful in the analysis of large and complicated molecules because it eliminates the dispersive tailing of the diagonal peaks exhibited in normal COSY spectra, which interfere with the analysis of nearby cross peaks. The use of PFG can be extended to triple or higher order of quantum filtered spectroscopy simply by varying the ratios of PFG

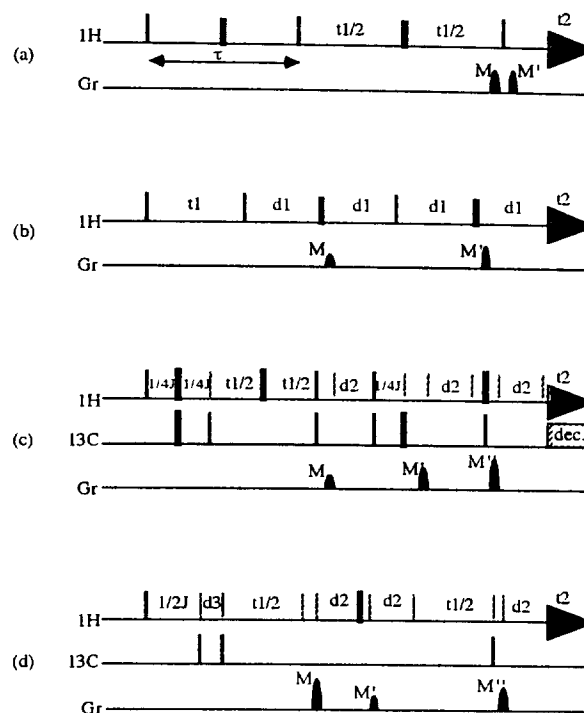


Figure 1. Pulse sequences of (a) a simple example of PFG-using multiple quantum spectroscopy, (b) DQF-COSY, (c) HMQC, and (d) HMBC. All the thin lines are 90° pulse and the thick lines are 180° pulse.

time lengths or pulse strengths during the evolution and the detection periods.¹³

PFG can also be utilized to proton-detected heteronuclear experiments^{14,15} such as HMQC or HMBC. With the PFG technique, it is possible to suppress all the signals except a set of echoes which correspond to a selectable order of quantum transitions,¹⁰ thus unwanted signals like water peak, t_1 noise, and proton signals attached to ^{13}C can be eliminated.

A detailed description of the effect of the magnetic field gradients on MQT coherence has been given by A. A. Maudsley *et al.*¹³ and A. Bax *et al.*¹⁰ According to them the separation of the different orders of multiple quantum transitions by the use of PFG is based on the fact that the rate of defocusing and refocusing of the magnetization in an inhomogeneous magnetic field is proportional to the order of coherence. In the experiment of Figure 1-(a), the magnetization $M_{y(kl;mn)}(t_1, t_2)$ of coherence between the levels m and n during the evolution period and the levels k and l during the detection period in a completely homogeneous magnetic field is given by

$$M_{y(kl;mn)}(t_1, t_2) = 2\exp(-t_2/T_{2kl})\exp(-t_1/T_{2mn}) \\ \times [Re(A_{kl;mn})\cos(\Delta_{kl;mn}) \\ - Im(A_{kl;mn})\sin(\Delta_{kl;mn}) \\ + Re(A_{kl;mn})\cos(\Sigma_{kl;mn})]$$

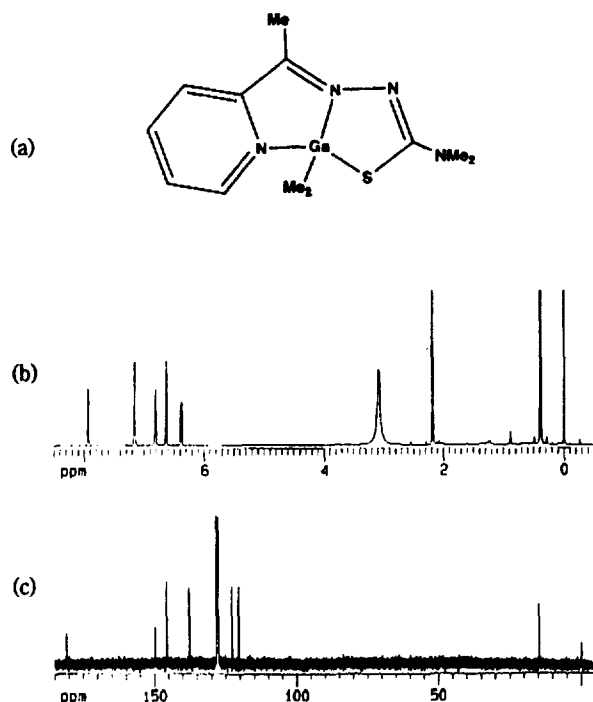


Figure 2. (a) The structure of the sample used in the experiments. (b) 1D proton spectrum. (c) 1D carbon spectrum.

$$+Im(A_{kl,mn})\sin(\Sigma_{(kl,mn)})] \quad (1)$$

where $A_{kl,mn}$ is a mixing coefficient which measures the amount of (mn) -coherence being transferred to (kl) -magnetization, and

$$\begin{aligned} \Delta_{(kl,mn)} &= \omega_{0kl}t_2 - \omega_{0mn}t_1 \\ \Sigma_{(kl,mn)} &= \omega_{0kl}t_2 + \omega_{0mn}t_1 \end{aligned} \quad (2)$$

If there is a time-dependent gradient $\Delta B(r, t)$, the magnetic field can be described as

$$B(r, t) = B_0 + \Delta B(r, t) \quad (3)$$

In a homonuclear coupled spin system of nuclei which have gyromagnetic ratio γ , if we apply magnetic field gradients $\Delta B(r, t)$ as a constant gradient of $\Delta B_1(r)$ for a time τ_1 during the evolution period and $\Delta B_2(r)$ for a time τ_2 at the beginning of the detection period, the resonance frequencies are changed, and therefore equation (2) becomes

$$\begin{aligned} \Delta_{(kl,mn)} &= \omega_{0kl}t_2 - \omega_{0mn}t_1 - \gamma[\Delta M_{kl}\tau_2\Delta B_2(r) - \Delta M_{mn}\tau_1\Delta B_1(r)] \\ \Sigma_{(kl,mn)} &= \omega_{0kl}t_2 + \omega_{0mn}t_1 - \gamma[\Delta M_{kl}\tau_2\Delta B_2(r) + \Delta M_{mn}\tau_1\Delta B_1(r)] \end{aligned} \quad (4)$$

Now, it is clear from equation (4) that only $\Delta_{(kl,mn)}$ terms are not influenced by these gradients applied in the condition of

$$\Delta B_2(r)\tau_2 = \Delta B_1(r)\tau_1 p \quad (5)$$

where $p = \Delta M_{mn}/\Delta M_{kl}$.

According to A. Bax *et al.*, this means that if the gradient pulse is sufficiently strong, only the p-quantum coherence transfer echo will appear, while all the other signals will be eliminated because of the dephasing.

J.-M. Tyburn *et al.*¹⁵ has analyzed the gradient-enhanced,

Table 1. Number of scans and experimental time for the phase-cycling and the PFG methods

Experiment	DQF-COSY		HMQC		HMBC	
	No. of Scans	Exp. Time	No. of Scans	Exp. Time	No. of Scans	Exp. Time
Phase -Cycling	16	2 h 30 m	8	1 h 50 m	16	3 h 42 m
PFG	4	38 m	4	38 m	8	1 h 52 m

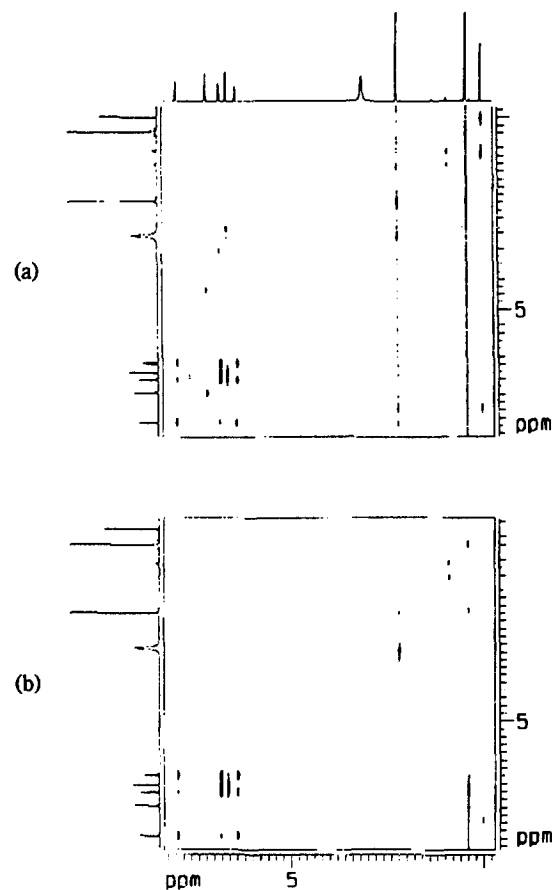


Figure 3. DQF-COSY spectra of the sample shown in Figure 2-(a) with (a) phase-cycling and (b) PFG methods.

heteronuclear, chemical shift correlation experiment in terms of product operators. For a heteronuclear two spin system, with angular momentum operators I and S in the sequence of Figure 1-(a), the refocusing condition is as follows:

$$\Delta B_2(r)\tau_2 = \Delta B_1(r)\tau_1 \frac{\gamma_I}{\gamma_S} p \quad (6)$$

As above, we can select any order of coherence by varying the gradient pulse strength or the pulse length.

Here, we show the DQF-COSY, HMQC, and HMBC spectra of a synthetic organometallic compound taken by using the PFG method, and compare them with the spectra obtained by the usual phase-cycling method. The structure of the sample is presented in Figure 2-(a). The sample was dissolved in benzene- d_6 and sealed.

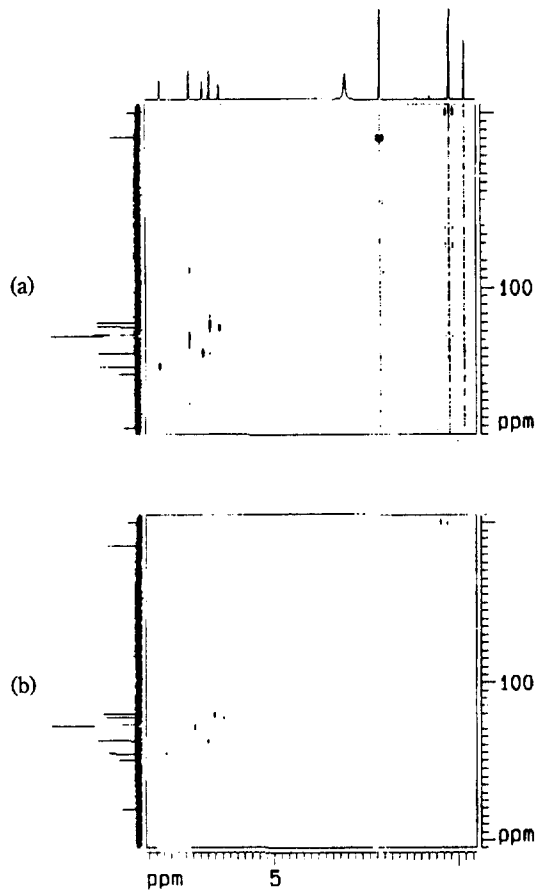


Figure 4. HMQC spectra of the sample shown in Figure 2-(a) with (a) phase-cycling and (b) PFG methods.

All the experiments were carried out on a Bruker DMX600 NMR spectrometer operating at a proton frequency of 600.13 MHz and at a carbon frequency of 150.90 MHz. Field gradients were generated by pulsing the actively shielded Z gradient coil. The filed gradients corresponded to 17-50% of the maximum strength (50 G/cm). An inverse probehead was used to enhance the proton sensitivity.

1D proton and carbon spectra are presented in Figure 2-(b) and 2-(c). Assignments and characterization of the molecule will be reported elsewhere.¹⁶

The pulse sequences¹⁷ used for DQF-COSY, HMQC, and HMBC are shown in Figure 1-(b), 1-(c), and 1-(d), respectively. The acquisition time for these experiments was 0.190 sec. The number of t_1 data points was 256. The gradient pulse length was 1000 μ sec. The delay for lock recovery was 500 μ sec. The gradient pulse strengths denoted by the percentage of the maximum strength are $M : M' = 20 : 40$ for DQF-COSY, $M : M' : M'' = 34 : 40 : 50$ for HMQC, and $M : M' : M'' = 50 : 30 : 40$ for HMBC, respectively (See Figure 1).

A comparison between the phase-cycling and the PFG method is given in Table 1. When PFG is used, the time required for the experiment is only one half or one quarter of the time required for the phase-cycling method. If the sample is more concentrated, only two scans (single scan for DQF-COSY) per t_1 would be enough, and thus the experimental time would be much shorter.

As shown in Figures 3-5, another benefit of the PFG

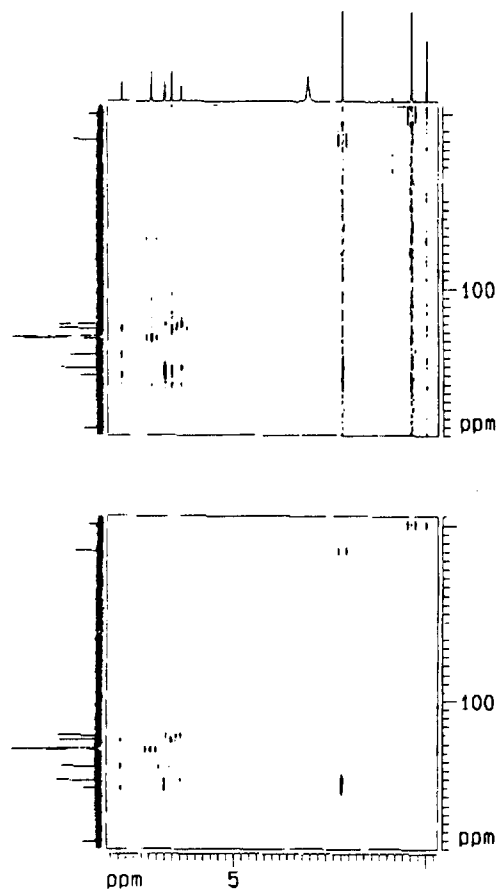


Figure 5. HMBC spectra of the sample shown in Figure 2-(a) with (a) phase-cycling and (b) PFG methods.

method is the reduction of t_1 artifacts which are streaks of spurious signals parallel to the ν_1 axis of strong resonances, e.g., solvent peaks. They are revealed at 2.4 ppm, 1.7 ppm, and 0 ppm in the spectra of phase-cycling method (See Figure 3-(a), 4-(a), and 5-(a)) and are remarkably reduced when the PFG method is used (See Figure 3-(b), 4-(b), and 5-(b)). Also, noises at $\nu_1 = 3-5$ ppm of DQF-COSY spectrum and at $\nu_1 = 75-100$ ppm of HMQC and HMBC spectra by phase-cycling method are not shown in the PFG spectra. Since the t_1 artifacts do not diminish by signal averaging, the noise reduction is very helpful in the analysis of complicated spectra.

In conclusion, we recommend the use of the pulsed field gradients for the selection of coherence orders instead of the phase-cycling because of significant reduction in experiment time and improved spectrum quality.

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 - Bruker pulse programs have been used.

Transition Metal-Mediated Carbon Insertion Reaction of *arachno*-6,8-C₂B₇H₁₃: Synthesis and Characterization of *nido*-6-R-5,6,9-C₃B₇H₁₀

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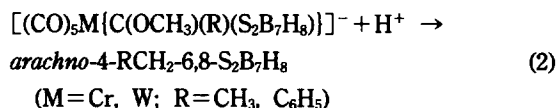
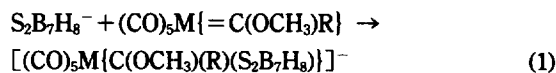
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We previously reported our results concerning the metal-mediated alkylation reaction of a boron hydride, in which Fischer-type carbene complexes were found to promote the conversion of *arachno*-S₂B₇H₈⁻ to the alkylated cage com-

ound, *arachno*-4-RCH₂-6,8-S₂B₇H₈ as shown in equation 1 and 2.¹

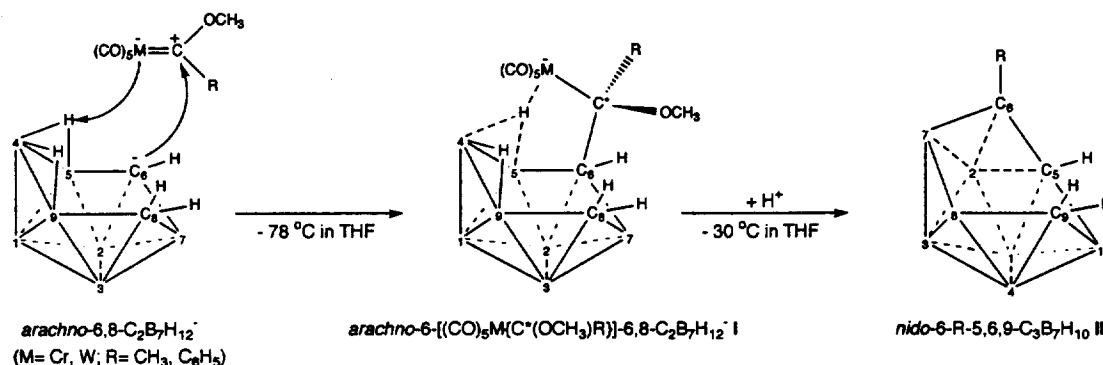


The result of the foregoing reactions suggests that isoelectronic *arachno*-C₂B₇H₁₂⁻ anion might also attack Fischer-type carbene complexes. Consequently, we have found that *arachno*-C₂B₇H₁₂⁻ anion readily reacted with Fischer-type carbene complexes² at room temperature. But, in contrast to the reactions with *arachno*-S₂B₇H₈⁻, carbene-carbon insertion into the cage results in the production of new tricarbon carborane *nido*-6-R-5,6,9-C₃B₇H₁₀ (**IIa**: R = CH₃; **IIb**: R = C₆H₅) in good yields.

The reaction of *arachno*-6,8-C₂B₇H₁₃ with NaH in THF at room temperature produces a faint yellow solution of *arachno*-C₂B₇H₁₂⁻. This anion was treated with (methoxy)(alkyl) metal carbene complexes for 6 h, producing the anionic complexes I (Scheme 1). After removing the solvent *in vacuum*, the residue was diluted in dry dichloromethane and treated with the anhydrous hydrogen chloride at -78 °C. The reaction mixture was stirred for 1 h at -10 °C, affording after workup (see experimental section) and purification the tricarbon carborane **II**.

The compound **IIa** was first prepared *via* thermal reaction of nitriles with *arachno*-Na⁺C₂B₇H₁₂⁻ in 35% yield.^{3,4} The reaction required at least 2 weeks to reach completion in refluxing nitrile solution. It was found that our synthesis allow routine production of **IIa** in yields of 50% or better at room temperature and shortened the reaction time dramatically to 6 h-14 h. Thus, a more efficient procedure for production of **IIa** was developed.

Exact mass measurement and elemental analysis support the proposed composition of *nido*-6-C₆H₅-5,6,9-C₃B₇H₁₀ **IIb**. The ¹¹B spectrum of **IIb** (Figure 1b) is also consistent with the proposed cage skeleton, showing seven different doublets of intensity 1, with the peak at -1.2 ppm having a narrow line width characteristic of a boron (B10) located between two heteroatoms (C5 and C9). The assignment of these resonances to the B8, B7, B10, B1, B2, B3, and B4 borons, respectively, (as shown in Scheme 1) is consistent with the assign-



Scheme 1.