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# Heteronuclear intermolecular single-quantum coherences in liquid nuclear magnetic resonance*

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This paper analyses the heteronuclear Cosy Revamped by Asymmetric Z-gradient Echo Detection pulse sequence. General theoretical expressions of the pulse sequence with arbitrary flip angles were derived by using dipolar field treatment and signals originating from heteronuclear intermolecular single-quantum coherences (iSQCs) in highly-polarized two spin-1/2 systems were mainly discussed in order to find the optimal flip angles. The results show that signals from heteronuclear iSQCs decay slower than those from intermolecular double-quantum coherences or intermolecular zero-quantum coherences. Magical angle experiments validate that the signals are from heteronuclear iSQCs and insensitive to the imperfection of radio-frequency flip angles. All experimental observations are in excellent agreement with theoretical predictions. The quantum-mechanical treatment leads to similar predictions to the dipolar field treatment.

**Keywords:** nuclear magnetic resonance, heteronuclear multiple-quantum coherences, distant dipolar field, highly-polarized system

**PACC:** 3240, 7660

## 1. Introduction

Intermolecular multiple-quantum coherences (iMQCs) in highly polarized spin systems have been a subject of interest in the NMR community since the 1990s.[1] Most of iMQC investigations today are confined to homonuclear intermolecular zero-quantum coherences (iZQCs), intermolecular double-quantum coherences (iDQCs) or intermolecular single-quantum coherences (iSQCs) originating from the two-spin terms in equilibrium density matrix.[2−11] For the homonuclear iSQCs from the two radio-frequency (RF) pulse Cosy Revamped by Asymmetric Z-gradient Echo Detection (CRAZED) sequence with $n$=1:±1 coherence selective gradients (CSGs), conventional SQC signals are hard to discard by phase cycling schemes.[12] On the other hand, the iDQC signals are not contaminated by conventional SQC signals, because the $n$=$G_1 : G_2 = 1 : \pm 2$ CSGs disperse all other coherences except for the iDQC signals. It means that pure homonuclear iSQC signals might be obtained by double-quantum-filtered and proper phase cycling schemes that discard the conventional SQC signals.[13] It also implies that pure heteronuclear iSQCs might be obtained due to the different gyromagnetic ratios of nucleus I and S, i.e. $\gamma_{\rm I} : \gamma_{\rm S} \neq \pm 1$. In other words, the CSGs with area ratio $G_1 : G_2 = \gamma_{\rm I} : \gamma_{\rm S} \neq \pm 1$ in the heteronuclear CRAZED pulse sequence will disperse the residual homonuclear SQC signals as the $G_1 : G_2 = 1 : \pm 2$ CSGs do in the homonuclear CRAZED pulse sequence. Theoretical formulations and quantitative experimental characterizations will help for understanding the heteronuclear iSQCs mechanisms. In our previous papers, we have studied the properties of homonuclear iSQCs and pure iSQC imaging theoretically and experimentally.[10,13] All experimental evidences were in good accord with theoretical predictions. In this paper, we will extend our work to heteronuclear iSQCs. Although there are studies on heteronuclear iMQCs or MSEs, they simply assumed the two first RF pulses in two channel to be 90°, or just ignored one of the first RF pulses in two different channels.[14−19] Here we further study how the four RF pulses influence the heteronuclear iSQCs and prove that pure and optimal heteronuclear

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iSQC signals can be obtained with proper flip angles, CSGs, and phase cycling. The results indicate that the four flip angles in the heteronuclear CRAZED pulse sequence only influence signal intensity, but not purity. Experimental observations are in good agreement with theoretical predictions.

## 2. Theoretical formalism

The pulse sequence depicted in Fig.1 was designed to detect heteronuclear iSQC signals in a two-component spin-1/2 system. The four RF pulses are denoted as $(\alpha)_{\phi_1}$,$(\beta)_{\phi_1}$,$(\theta)_{\phi_2}$, and $(\varphi)_{\phi_2}$ respectively. The subscript $\phi_1$ is the phase shift of the RF pulses $\alpha$ and $\beta$, and $\phi_2$ is the phase shift of the RF pulses $\theta$ and $\varphi$. The CSGs are applied with an area ratio of $G_1$:$G_2$, where $G_1$ and $G_2$ are the amplitudes and $\delta$ is the duration.

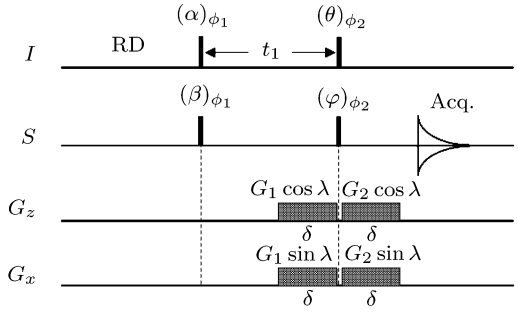



**Fig.1.** Heteronuclear iSQC CRAZED pulse sequence.

In order to optimize the RF flip angles for maximal pure heteronuclear iSQC signals, the modified Bloch equations with dipolar fields were employed to describe the heteronuclear two-component spin-1/2 systems without scalar coupling. It is assumed that the $I$ spin (corresponding to solvent) is abundant and the $S$ spin (corresponding to solute) is either abundant or dilute. Moreover, we define the same notation as we did before. $T_1^I$ and $T_1^S$ are the longitudinal relaxation times, $T_2^I$ and $T_2^S$ are the transverse relaxation times, $M_0^I$ and $M_0^S$ are the initial magnetizations, and $\gamma_I$ and $\gamma_S$ are the gyromagnetic ratios of $I$ and $S$ spins, respectively. At equilibrium state, the initial density operator is given by

$$\sigma(0^-) = I_z + S_z. \tag{1}$$

Assume that the four RF pulses are along $y$ direction. The density operator immediately after the first two RF pulses $\alpha$ and $\beta$ is then given by

$$\begin{aligned}\sigma(0^+) =&(I_z\cos\alpha + I_x\sin\alpha)\\ &+ (S_z\cos\beta + S_x\sin\beta).\end{aligned} \tag{2}$$

For simplification, only longitudinal and transverse relaxation efforts are considered during the evolution period $t_1$. Just before the last two RF pulses, i.e. $\theta$ and $\varphi$, the spin density operator under chemical shift and the first CSG could be written as

$$\begin{aligned}\sigma(t_1,z) =&[I_x\cos(\omega_I t_1+\gamma_I G_1\delta z) + I_y\sin(\omega_I t_1+\gamma_I G_1\delta z)]\sin\alpha\cdot \mathrm{e}^{-t_1/T_2^I} + I_z\cos\alpha\cdot\mathrm{e}^{-t_1/T_1^I}\\ &+ [S_x\cos(\omega_S t_1+\gamma_S G_1\delta z) + S_y\sin(\omega_S t_1+\gamma_S G_1\delta z)]\sin\beta\cdot\mathrm{e}^{-t_1/T_2^S} + S_z\cos\beta\cdot\mathrm{e}^{-t_1/T_1^S}.\end{aligned} \tag{3}$$

The last two pulses rotate the spin density operator into

$$\begin{aligned}\sigma(t_1,z) =&[(I_x\cos\theta - I_z\sin\theta)\cos(\omega_I t_1+\gamma_I G_1\delta z) + I_y\sin(\omega_I t_1+\gamma_I G_1\delta z)]\sin\alpha\cdot\mathrm{e}^{-t_1/T_2^I}\\ &+ [(S_x\cos\varphi - S_z\sin\varphi)\cos(\omega_S t_1+\gamma_S G_1\delta z) + S_y\sin(\omega_S t_1+\gamma_S G_1\delta z)]\sin\beta\cdot\mathrm{e}^{-t_1/T_2^S}\\ &+ (S_z\cos\varphi + S_x\sin\varphi)\cos\beta\cdot\mathrm{e}^{-t_1/T_1^S} + (I_z\cos\theta + I_x\sin\theta)\cos\alpha\cdot\mathrm{e}^{-t_1/T_1^I}.\end{aligned} \tag{4}$$

The transverse magnetization of the spin $S$ can be written as

$$\begin{aligned}M_S^+(t_1,z) =&M_0^S[\cos\varphi\cos(\omega_S t_1+\gamma_S G_1\delta z)\sin\beta\mathrm{e}^{-t_1/T_2^S} + \sin\varphi\cos\beta\cdot\mathrm{e}^{-t_1/T_1^S}\\ &+ \mathrm{i}\sin(\omega_S t_1+\gamma_S G_1\delta z)\sin\beta\cdot\mathrm{e}^{-t_1/T_2^S}].\end{aligned} \tag{5}$$

The effective distant dipolar field (DDF) $B_d^S$ experienced by $S$ spins is given by

$$B_d^S(r) = -\frac{2}{3}\Delta_S\mu_0\hat{z}M_0^I\sin\theta\cos(\omega_I t_1+\gamma_I G_1\delta z)\sin\alpha\cdot\mathrm{e}^{-t_1/T_2^I}, \tag{6}$$

where $\mu_0$ is the magnetic vacuum permeability, $\hat{z}$ is the unit vector along z direction, and $\Delta_s = (3\cos^2\lambda - 1)/2$, $\lambda$ is the angle between the CSG and $z$ directions. When the gradient is along the $z$ direction, i.e. $\lambda$=0°, we have $\Delta_s = 1$. The magic-angle condition for the CSGs is determined by $3\cos^2\lambda - 1 = 0$, or $\lambda$=54.7°. Although $S$ spins also generate DDF acting on itself, the resulting homonuclear iMQCs will be filtered out by the CSGs with non-integral ratio. Therefore, this DDF can be ignored. In addition, since only the spin $S$ signals are detected, we abandon the part related to the spin $I$ signals. After the second CSG, the transverse magnetization of the $S$ spins can be written as

$$M_S^+(t_1,t_2,z) = M_0^S\{[\cos^2(\varphi/2)\exp(\mathrm{i}\omega_S t_1 + \mathrm{i}\gamma_S G_1\delta z) - \sin^2(\varphi/2)\exp(-\mathrm{i}\omega_S t_1 - \mathrm{i}\gamma_S G_1\delta z)]\sin\beta\cdot \mathrm{e}^{-t_1/T_2^S} + \sin\varphi\cos\beta\cdot\mathrm{e}^{-t_1/T_1^S}\}\exp(\mathrm{i}\omega_S t_2 + \mathrm{i}\gamma_S B_d^S t_2 + \mathrm{i}\gamma_S G_2\delta z)\mathrm{e}^{-t_2/T_2^S}. \quad (7)$$

Since most of our experiments satisfy the condition of small DDF effects, $\gamma\mu_0 M_0 t_2 \ll 1$,[20] the signal intensities of the heteronuclear iSQC as a function of the RF flip angles can be simplified to

$$M_S^+(t_1,t_2,z)(-\mathrm{iSQC}) = \frac{1}{3}\mathrm{i}\gamma_S t_2\Delta_S\mu_0 M_0^I M_0^S\sin\alpha\cos\beta\sin\theta\sin\varphi\exp(\mathrm{i}\omega_I t_1)\exp(\mathrm{i}\omega_S t_2)\cdot\mathrm{e}^{-t_1/T_2^I - t_1/T_1^S}\mathrm{e}^{-t_2/T_2^S} \quad (G_1 : G_2 = \gamma_S : -\gamma_I), \quad (8)$$

and

$$M_S^+(t_1,t_2,z)(+\mathrm{iSQC}) = \frac{1}{3}\mathrm{i}\gamma_S t_2\Delta_S\mu_0 M_0^I M_0^S\sin\alpha\cos\beta\sin\theta\sin\varphi\exp(-\mathrm{i}\omega_I t_1)\exp(\mathrm{i}\omega_S t_2)\cdot\mathrm{e}^{-t_1/T_2^I - t_1/T_1^S}\mathrm{e}^{-t_2/T_2^S} \quad (G_1 : G_2 = \gamma_S : \gamma_I), \quad (9)$$

where we have used the Bessel functions expansions. The values of high-order Bessel functions are neglected and only zero- and first-order Bessel functions were considered. The Bessel functions were approximated to the first term of Taylor expansion since the sample dimension in our experiments is much larger than the modulation length, $d_c = 2\pi/(\gamma G\delta)$. Effects of sample shape were also neglected.

Equations (8) and (9) provide the analytical expressions. They indicate that both pure negative and positive heteronuclear iSQC signals can be obtained with proper ratio of the two CSGs. According to Eqs.(8) and (9), the optimal RF pulse flip angles for both signals are $\alpha = \theta = \varphi = 90°$, $\beta = 0°$ (or 180°), similar to the homonuclear iSQC.[10]

As a complementary method, iMQC treatment is employed to intuitively demonstrate that the $S$ spin signals originate from heteronuclear intermolecular longitudinal two spin-orders. Since the SQC signal is filtered out by the CSGs with non-integral ratio, we only focus on the intermolecular longitudinal two-spin order, $I_zS_z$. After the first two RF pulses $\alpha$ and $\beta$, the reduced density operator becomes

$$I_zS_z \xrightarrow{\alpha_y(I)\beta_y(S)} (I^+S^+ + I^-S^- + I^-S^+ + I^+S^- + I^+S_z + I^-S_z + I_zS^+ + I_zS^- + I_zS_z), \quad (10)$$

in which the $I^+S_z$ and $I^-S_z$ correspond to positive and negative heteronuclear iSQCs, respectively. When $\alpha = \pi/2$ and $\beta = 0$ (or $\beta = \pi$), there are only $I^+S_z$ and $I^-S_z$ in Eq.(10). The $I^+S_z$ or $I^-S_z$ can be converted to observable $I_zS^-$ by $\theta_y(I)$ and $\varphi_y(S)$ with proper CSGs ($G_1 : G_2 = \gamma_S : \pm\gamma_I$). When $\theta = \pi/2$ and $\varphi = \pi/2$, maximal iSQC signal is achieved. Since only the density operator component with coherence order $p = -1$ of the $S$ spin in the final density operator contributes to observable signals, all components

with coherence order $p \neq -1$ can be disregarded. In contrast to the dipolar field treatment which provides completely quantitative predictions, the iMQC treatment presented herein provides qualitative predictions on the observed signals.

## 3. Experimental validation

All experiments were performed on a Varian NMR System 500 MHz spectrometer, equipped with a 5 mm $^{1}$H{$^{15}$N-$^{31}$P} XYZ indirect detection probe of 1.8 cm effective length. The pulse sequence depicted in Fig.1 was utilized. The sample is a mixture of 40 % water and 40% $H_3PO_4$ with 20% $D_2O$. The gradient amplitude was $G_1$ ≈0.08 T/m and the gradient duration $\delta$=1.2 ms. The relaxation delay (RD) was set to 8 s to allow the spin system return to its full equilibrium state and prevent any possible stimulated echoes. The acquisition time was 0.5 s. To suppress the effects of radiation damping, the width of a $\pi/2$ RF pulse for $^{1}$H was extended from 6.3$\mu$s to 98$\mu$s by deliberately detuning the probe. The $\pi/2$ RF pulse for $^{31}$P was 41$\mu$s. $^{31}$P signals were recorded at 298K. The $T_1$ relaxation times are 0.55 and 1.46 s for $^{1}$H and $^{31}$P respectively. The $T_2$ relaxation times are 0.21 and 0.08 s for $^{1}$H and $^{31}$P respectively.

## 4. Results and discussion

The 1D experimental spectra of the $H_3PO_4$ in water sample are displayed in Fig.2, obtained from the pulse sequence shown in Fig.1. The dependences of the heteronuclear iSQC signals on the RF flip angles $\alpha$, $\beta$, $\theta$, and $\varphi$ were measured individually to determine the optimal values from 0 to $\pi$ in an increment of $\pi/20$. When one flip angle was studied, the other three were fixed at their theoretical optimal values. The results suggest that the four optimal RF flip angles for the maximal signal intensity for both negative and positive heteronuclear iSQCs are $\alpha = \theta = \varphi$=90° and $\beta$=0° (or 180°).

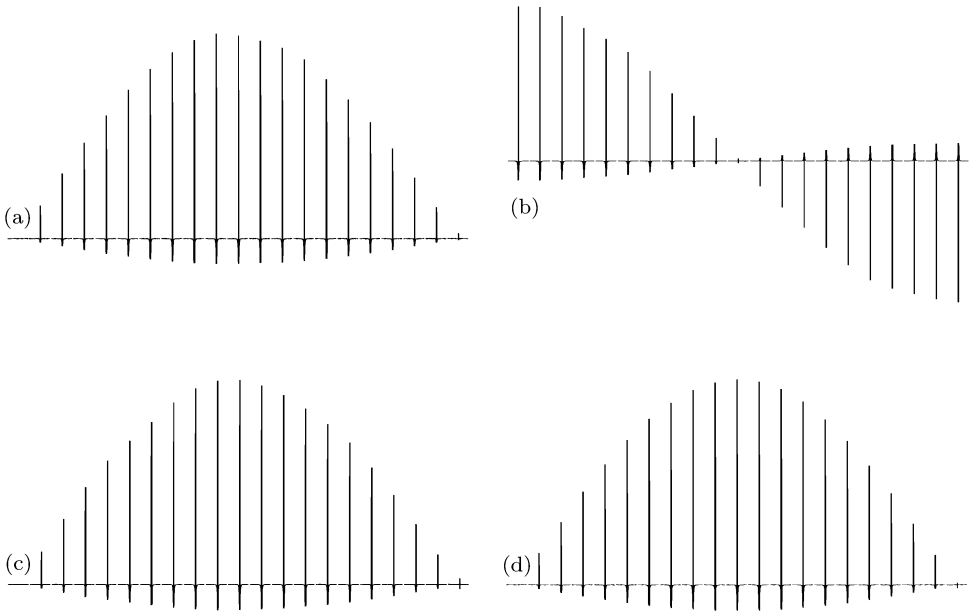



**Fig.2.** Variation of positive heteronuclear iSQC signal intensities with RF flip angles of $\alpha$ (a), $\beta$ (b), $\theta$ (c), and $\varphi$ (d).

Equations (8) and (9) provide the analytical expressions for the signal intensities of $S$ spins related to the negative and positive heteronuclear iSQCs, respectively. Unlike the signal expression for homonuclear iSQCs, there is only one iMQC term in Eq.(8) or (9), which means that the signals of the heteronuclear iSQC are not contaminated by conventional SQC signals.[10] This is understandable. The residual SQC signals cannot be dispersed by the CSGs in a homonuclear iSQC sequence since $G_1 : G_2 = \pm 1$ for $n = 1{:}\pm 1$, while the CSGs with $G_1 : G_2 \neq \pm 1$ in the heteronuclear iSQC sequence can filter out the residual con-

ventional SQC signals.

To further demonstrate that the observed signals are from the heteronuclear iSQCs and insensitive to the imperfection of the RF pulse flip angles, magic angle experiments were carried out with the flip angles purposely deviated 2/9 from their optimal values, i.e. 90° and 180° were replaced by 70° and 140°, respectively. The results (Fig.3) show that there is only a tiny signal at magic angle, verifying our theoretical predictions.

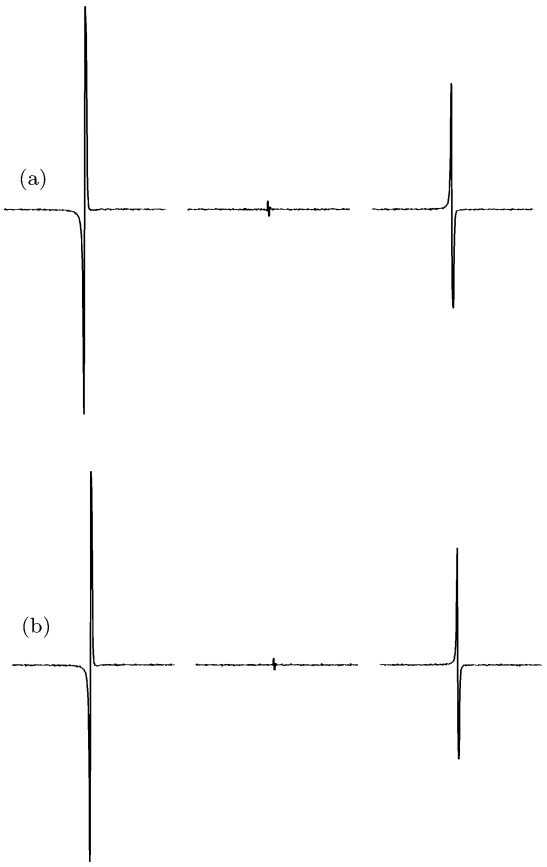



**Fig.3.** (a) Heteronuclear positive iSQC signals with exact optimal RF flip angles and different CSG orientations:$\lambda =$ 0° (left), $\lambda = 54.7°$ (middle), $\lambda = 90^o$ (right); (b) signals corresponding to (a) with the RF flip angles deviated by a factor of 2/9 from the optimal values.

Equations (8) and (9) also indicate that the heteronuclear iSQC signals decay as an exponential function of the spin $I$ transverse relaxation time, i.e. $\mathrm{e}^{-t_1/T_2^I - t_1/T_1^S}$, during $t_1$ evolution. Similar theoretical deductions suggest that the heteronuclear iDQC and iZQC signals decay as $\mathrm{e}^{-t_1/T_2^I - t_1/T_2^S}$. [5,21] As $T_1^S > T_2^S$, the heteronuclear iDQC and iZQC signals will decay faster than the heteronuclear iSQC signal. For a short $T_2^S$, increment of the $t_1$ evolution time will result in much faster decay of the heteronuclear iDQC and iZQC signals. Experimental results shown in Fig.4 confirm the theoretical predictions.

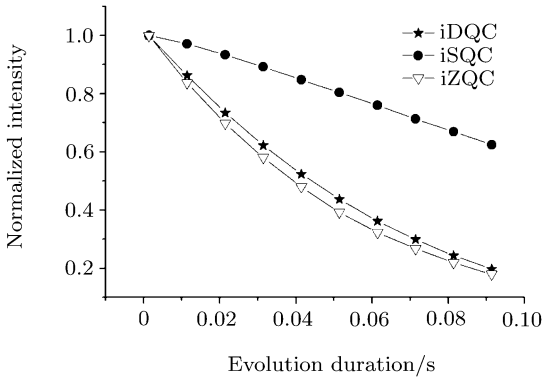



**Fig.4.** Variation of heteronuclear iMQC signal intensities vs evolution time $t_1$ using the sequence of Fig.1.

In addition, Eqs.(8) and (9) demonstrate that the heteronuclear iSQCs have the same signal intensity as the heteronuclear iDQCs and iZQCs with their respective optimal RF flip angles.[19] Experimental results of the relative signal intensities with different coherence orders shown in Fig.5 are in excellent agreement with the above-given theoretical predictions.

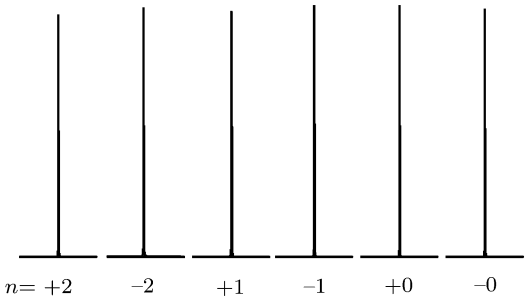



**Fig.5.** 1D absolute-value spectra for heteronuclear iMQCs with different coherence orders.

## 5. Conclusions

In summary, modified Bloch equations with DDF were utilized to derive analytical expressions. The heteronuclear CRAZED sequence was analysed, and the optimal RF flip angles for the heteronuclear iSQCs were discussed. Magic angle experiments with exact or 2/9 deviated the optimal RF flip angles were performed to validate that the signals are from the heteronuclear iSQCs and insensitive to the imperfection of RF pulses. The deviation of the RF flip angles only influences the signal intensity but not purity. In addition, the heteronuclear iSQC signal decays slower than the heteronuclear iDQC or iZQC signals. This effect is useful in the short $T_2^S$ situation. All experimental results shown in this paper are in good agreement with the theoretical predictions.

# References


[1] Warren W S, Richter W, Andreotti A H and Farmer B T II 1993 *Science* **262** 2005

[2] Vathyam S, Lee S and Warren W S 1996 *Science* **272** 92

[3] Warren W S, Ahn S, Mescher M, Garwood M, Ugurbil K, Richter W, Rizi R R, Hopkins J and Leigh J S 1998 *Science* **281** 247

[4] Ahn S, Lisitza N and Warren W S 1998 *J. Magn. Reson.* **133** 266

[5] Chen Z, Chen Z W and Zhong J H 2001 *J. Chem. Phys.* **115** 10769

[6] Faber C 2005 *J. Magn. Reson.* **176** 120

[7] Lee S, Richter W, Vathyam S and Warren W S 1996 *J. Chem. Phys.* **105** 874

[8] Chen Z, Chen Z W and Zhong J H 2001 *Chem. Phys. Lett.* **333** 126

[9] Chen Z, Chen Z W and Zhong J H 2004 *J. Am. Chem. Soc.* **126** 446

[10] Chen Z, Chen Z W and Zhong J H 2002 *J. Chem. Phys.* **117** 8426

[11] Zhu X Q, Cai C B, Chen Z and Zhong J H 2005 *Chin. Phys.* **14** 516

[12] Charles-Edwards G D, Payne G S, Leach M O and Bifone A 2004 *J. Magn. Reson.* **166** 215

[13] Chen Z, Zhu X Q, Zheng B W, Cai S H and Zhong J H 2006 *Chem. Phys. Lett.* **429** 611

[14] Bachiller P R, Ahn S and Warren W S 1996 *J. Magn. Reson.* A **122** 94

[15] Ahn S, Warren W S and Lee S 1997 *J. Magn. Reson.* **128** 114

[16] Ahn S, Lee S and Warren W S 1998 *Mol. Phys.* **95** 769

[17] Ardelean I, Kossel E and Kimmich R 2001 *J. Chem. Phys.* **114** 8520

[18] Granwehr J, Urban J T, Trabesinger A H and Pines A 2005 *J. Magn. Reson.* **176** 125

[19] Jiang B, Liu H L, Liu M L, Ye C H and Mao X A 2007 *J. Chem. Phys.* **126** 054502

[20] Ramanathan C and Bowtell R 2001 *J. Chem. Phys.* **114** 10854

[21] Xu F, Liu T Y and Huang Y R 2006 *Acta Phys. Sin.* **55** 3054 (in Chinese)