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Efficient baseline suppression via TIP and modified DEPTH

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Abstract The baseline flattened NMR spectrum has been achieved by several methodologies including pulse manipulation with a series of phase cycling. The background signal inherent in the probe is also main source of baseline distortion both in solution and solid NMR. The simple direct polarization with 90° pulse flipping the magnetization from the *z*-axis onto the receiver coil requires the strong rf pulse enough to encompass the wide frequency range to excite the resonance of interest nuclei. Albeit the perfect polarization 90° pulse, the signal from the unwanted magnetic fields such as background signal can not be completely suppressed by suitable phase cycling. Moreover, slowly baseline wiggling signal from the low γ nuclei is not easy to eliminate with multiple pulse manipulation. So there is still need to contrive the new scheme for that purpose in an adroit manner. In this article new triple pulse excitation schemes for TIP and modified DEPTH pulse sequence are analytically examined in terms of arbitrary phase and flip angle of pulse. The suitable phase cycling for these pulse trains is necessary for the good sensitivity and resolution of the spectrum. It is observed that the ^{13}C sensitivity TIP experiment is almost equal to the CP/MAS with modified DEPTH sequence, both of which are applicable to both solid and solution state NMR.

Keywords DEPTH, TIP pulse sequence, polarization, baseline suppression, phase cycling.

Introduction

NMR is the most versatile tool to investigate the molecular structure as well as motional interaction in both solution and solid state. In addition to structure elucidation research, improved NMR instruments make it possible to do the precise quantitative measurements of small molecules to the ppm level in solution. The single pulse excitation gives a simple and direct polarization transfer that can be evidently interpreted by conventional NMR scheme. The radio-frequency hard pulse usually excites all the signals originating from the given pulse length, including the background from material in the probe circuit especially in solid NMR. For the low resonance frequency of hetero nuclei, the distorted baseline appears like a broad background signal in the spectrum even in the solution state NMR. Moreover, acoustic ringing of the radiofrequency pulse results in the wiggling of baseline due to the deadtime ringdown which is also observed in solid NMR. Acoustic ringing effect can be somewhat reduced just by using software treatment such as backward linear prediction together with large phase correction. But it has limitation to reproduce the lost first few fid data. Moreover, these spurious resonance signals make it hamper the quantitative analysis for many applications either academic or industrial field.

Many NMR schemes have been developed to suppress the background signal and acoustic ringing pattern. A Simple difference experiment with and without a

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sample in the probe is an alternative to avoid the two problems. But the separate probe tuning and phase correction for two independent NMR experiments gives another issue to overcome let alone the doubling the experiment time. Several pulse sequences have been proposed to eliminate these background signal.[1-4] DEPTH NMR method based on the multiple spin-echo by Bendall and Gordon is designed to select homogeneous regions of the radio-frequency field. The background resonance ^{13}C from the probe in solid and the glass resonance ^{29}Si in solution is sufficiently eliminated by DEPTH pulse sequence. A series of rf pulses with suitable phase cycling such as EXORCYCLE, composite 180 pulse have been designed by several authors. But the acoustic riniging effect in solid quadrupole nuclei has not been sufficiently removed albeit the sensitivity improvement.

Recently new pulse design called TIP (Triple Pulse Excitation) was proposed.[5] In this scheme the phase of pulse right before acquisition always remains the same in any two consecutive data acquisition while the receiver phase is alternated. Naturally the acoustic ringing effects from the last excitation pulse are cancelled through subtraction of two scan signals. These three pulses in TIP sequence generate an additional flip angle dependent scaling the single hard pulse excitation. When the flip angle is less than 90, the scaling is much less than one. So, the background signal with small flip angle the probe material can be significantly reduced with TIP sequence. The precise phase cycling of a given pulse sequence is important to trace out the magnetization vector of interest.[6]

In this article the exact pulse effect with corresponding phase cycling is examined to get a more precise angle dependence from TIP. And modified DEPTH pulse sequence is proposed to make a slight improvement in sensitivity and background suppression in solid and solution state NMR.

Theoretical Calculation of Pulse Excitation Profile

A radio-frequency pulse with rotation angle[β] rotates the initial magnetization Mo about the direction of the applied rf field axis. If we assume the sufficiently strong hard pulse, the resonance offset dependence is safely ignored. The basic pulse sequence of TIP and DEPTH are shown in Figure 1.[7-8] The TIP and DEPTH pulse is composed of three consecutive pulses with an arbitrary phase angle. It is necessary to track down on the magnetization when pulses are applied to the spin system. First we consider the rotation brought by general pulse. If we adopt a right handed convention, a positive rotation around the z-axis is easily verified. The corresponding rotation matrix about z-axis with angle α is given by[9,10]

$$\boldsymbol{R}_z(\alpha) = \begin{pmatrix} cos(\alpha) & -sin(\alpha) & 0 \\ sin(\alpha) & cos(\alpha) & 0 \\ 0 & 0 & 1 \end{pmatrix} \quad (1)$$

$$= \begin{pmatrix} sin(\phi) & cos(\phi) & 0 \\ -cos(\phi) & sin(\phi) & 0 \\ 0 & 0 & 1 \end{pmatrix} \quad (2)$$

In order to find the rotation due to the arbitrary phase of pulse we can use the simple relation

$$\boldsymbol{R}_{y'}(\beta) = \boldsymbol{R}_z(\alpha)\boldsymbol{R}_y(\beta)\boldsymbol{R}_z^{-1}(\alpha) \quad (3)$$

The rotation matrix for the general three pulse with different phase and offset is easily obtained by Eq.(1)

$$\boldsymbol{R} = \boldsymbol{R}_{\phi_3}(\beta_3)\boldsymbol{R}_{\phi_2}(\beta_2)\boldsymbol{R}_{\phi_1}(\beta_1) \quad (4)$$

The rotational matrix of $\boldsymbol{R}_\phi(\beta)$ can be estimated by the Eq.(3) The rotation matrix of TIP and DEPTH pulse can be easily constructed from Eq.(4). If the three angles of TIP pulse are equal to β and the phase of pulse are ϕ_1= 90°, ϕ_2= 270°, ϕ_3= 90°, then the corresponding rotation matrix is given by

$$\boldsymbol{R} = \boldsymbol{R}_{\phi_3}(\beta)\boldsymbol{R}_{\phi_2}(\beta)\boldsymbol{R}_{\phi_1}(\beta) \quad (5)$$

$$\boldsymbol{R}_{\phi}(\beta) = \begin{pmatrix} sin^2(\phi)\,cos(\beta) + cos^2(\phi) & -cos(\phi)\,sin(\phi)\,cos(\beta) + cos(\phi)\,sin(\phi) & sin(\phi)\,sin(\beta) \\ -cos(\phi)\,sin(\phi)\,cos(\beta) + cos(\phi)\,sin(\phi) & cos^2(\phi)\,cos(\beta) + sin^2(\phi) & -cos(\phi)\,sin(\beta) \\ -sin(\phi)\,sin(\beta) & cos(\phi)\,sin(\beta) & cos(\beta) \end{pmatrix} \quad (6)$$

$$\boldsymbol{R} = \boldsymbol{R}_y(\beta)\boldsymbol{R}_{-y}(\beta)\boldsymbol{R}_y(\beta) \quad (7)$$

The 16 phase cycling of TIP is given in reference 5. For each pulse scan the total rotation matrix can be constructed. In Figure 3 triple pulse excitation efficiency is plotted along with the single pulse excitation(SIP) profile. The efficiency of TIP is proportional to cos($\beta 1$)cos($\beta 2$)sin($\beta 3$), while that of single pulse is sin(β), which is shown in Figure 3. The excitation efficiency for TIP scheme is strongly dependent upon the receiver phase(ϕ_R).
If we change the receiver from 0, 180, 180, 0 to 0, 180, 0, 180 the total excitation efficiency is completely disappeared when the 90 pulse is applied to the spin system. The scaling factor between the TIP and normal single pulse is evidently deduced from the two curve in Figure 3. The efficiency below the 30 degree pulse is huge different between two pulse sequences. So the low RF flip angle originating the background signal can be successfully suppressed by TIP sequence. The DEPTH pulse sequence and corresponding phase cycling are shown in Figure 1 (left), and Table 1. The fourth column in Table 1 is the modified phase cycling with the same receiver phase.

Experimental Methods

All the NMR experiments were performed on a JEOL ECXS-500 spectrometer operating at the resonance frequency 500.16 MHz for ^{1}H corresponding to magnetic field 11.727 T. For solution TIP measurement of ^{11}B NMR [160.47 MHz] Boric Acid was used. 90 pulse for ^{11}B NMR is 9 μsec. Delay time was taken as 5 sec. For solid measurement the adamantane from Aldrich Chemical Co. was used. The pulse width of ^{13}C NMR was 2.9 μsec and relaxation delay is 10 sec. The MAS with and without DEPTH pulse is 6 kHz.

Results and Discussion

The NMR signal intensity in the normal single pulse excitation for spin I = 1/2 varies with the sine curve of nutation frequency depending on the RF pulse width. As shown previous section, the TIP pulse gives the different nutation angle dependence instead of sin(β). In order to eliminate the acoustic ringing effect, at least 4 phase cycling is needed for TIP pulse. The first two pulses of TIP change the spin magnetization in such an opposite way that magnetization vector behaves cos(2β) dependence. The third pulse with constant phase along with alternating receiver phase assures that the cancellation of acoustic ringing effect reduced. Thus the TIP excitation efficiency shows the sin(β_3) multiplied by sine and/or cosine modulation with respect to the receiver phase.

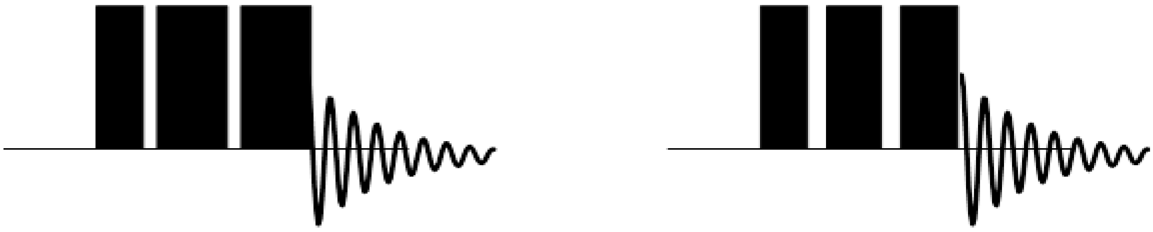

Figure 1. DEPTH pulse (left) and triple pulse excitation sequence (right)

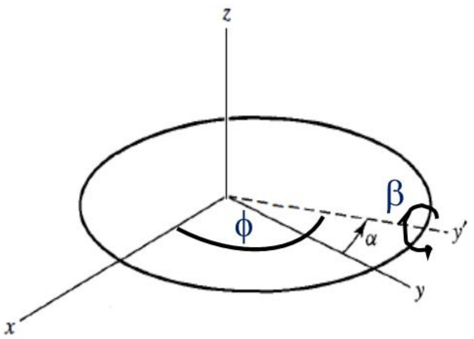

Figure 2. Phase angle of rotation in 3-dimension

Riqiang Fu showed the $\sin(2\pi\nu_1\tau_p)[1-\cos(4\pi\nu_1\tau_p)]/2$ excitation profile with *x,-x,-x,x* receiver phase cycling. With this sequence the ^{13}C of adamantane spectra of TIP and single 90 pulse are shown in Figure 4. The background signal around the 110~120 ppm is sufficiently suppressed while the that of adamantine is almost same in peak intensity. The background signal from the probe material contributed from the low rf flip angle can be easily estimated via sinusoidal dependence of TIP and single pulse. Since $\sin(\beta) \sim \beta$ at below 30 degrees, the rf nutation angle dependence of TIP over single pulse is β^2. So the background signal reduction at 20 degree pulse is roughly estimated about 12%. The signal probe responding to 10 degree pulse gives only 3%, which is thought to be sufficiently suppressed by TIP sequence. The background signal in the ^{11}B Boric Acid spectrum in solution state is also greatly reduced via TIP pulse sequence. The spectrum difference between SIP and TIP pulse is evidently observed in Figure 5. The upper brown ^{11}B signal around 50 ppm by SIP is greater than the lower green signal by TIP, thus convincing the validity of TIP on the solution state NMR.

Moreover, it has been well known fact that the background signal in solid phase is successfully diminished by DEPTH pulse sequence.[1] The multiple spin echo 180 pulses in the DEPTH sequence has been used to eliminate the acoustic ringing effect even when there is no delay between the π pulses. In this scheme it is necessary to implement the π refocusing pulses providing the suitable 4 phase cycling with respect to two π pulses. The original DEPTH pulse sequence with phase cycling is given in Table. 1. The fid signal of original DEPTH is given as follow

$$\text{FID[Original]} \sim [\cos(\beta_1)\sin(\beta_2)\cos(\beta_3) -\cos(\beta_1)\cos(\beta_2)\sin(\beta_3)]\cos(\omega t) + \sin(\beta_1)\sin(\omega t) \quad (8)$$

The 16 phase cycling of DEPTH experiment sufficiently reduce the background signal. When the phase of second π pulse is changed into as 180 out of phase, the resulting FID may be slightly modified to result in a small amount of difference in the gain in sensitivity.

$$\text{FID[Modified]} \sim [\cos(\beta_1)\sin(\beta_2)\cos(\beta_3) + \cos(\beta_1)\cos(\beta_2)\sin(\beta_3)]\cos(\omega t) + \sin(\beta_1)\sin(\omega t) \; (9)$$

The difference between the original and modified DEPTH in FID is evidently $2\cos(\beta_1)\cos(\beta_2)\sin(\beta_3)$.

In order to see the modified pulse phase effect of DEPTH sequence, the modified pulse phase scheme is applied to the solid NMR spectrum. The background signal is considerably decreased compared to the single pulse experiment for each DEPTH sequence. As shown in Figure 6 the sensitivity improvement is observed in the modified DEPTH along with almost same background uppression. From the Figure 6. We can observe that the upper spetrum from modified DEPTH shows more then 5% peak intensity increament over the original DEPTH spectrum. In Figure 6 the *y*-axis intensity is plotted in a same scale for two spectra. The 6 kHz of MAS and 4 k dapa point with 10 sec delay is given. The baselines of both spectra are almost flat while the sensitivity of spectra are almost flat while the sensitivity of modified DEPTH goes up about 5% in ^{13}C Adamantane signal. In terns of sensitivity and background supperssion the modified DEPTH pulse sequence is slighltly superior to the original one. With regard to the I >1/2 spin the TIP excitation pulse sequence is applicable to quadrupolar nuclei in solid in a such way that wide baseline and wiggling is effectively removed.

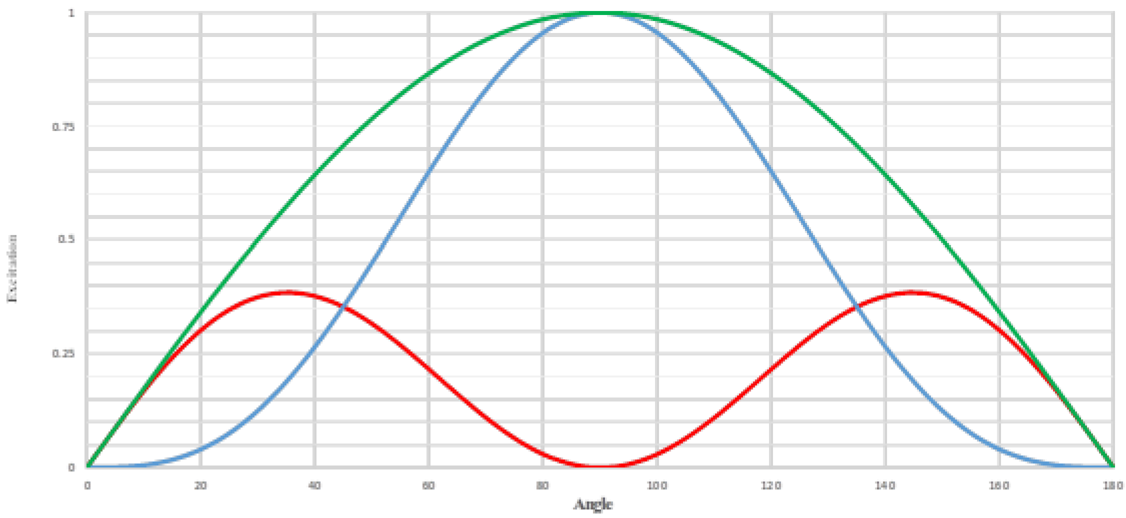

Figure 3. TIP and SIP pulse profile as a function of flipping angle. Top (green : SIP), middle (blue : TIP, $\phi_R = x,-x,-x,x$), bottom (red: TIP, $\phi_R = x,-x,x,-x$).

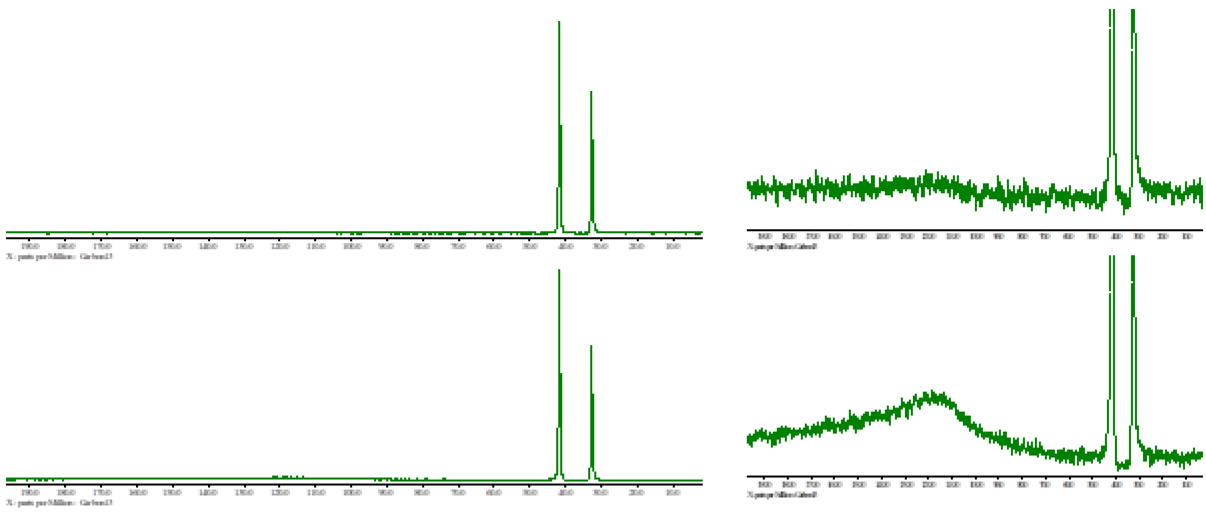

Figure 4 . ^{13}C adamantane spectrum with SIP (down) and TIP (up) pulse profile.

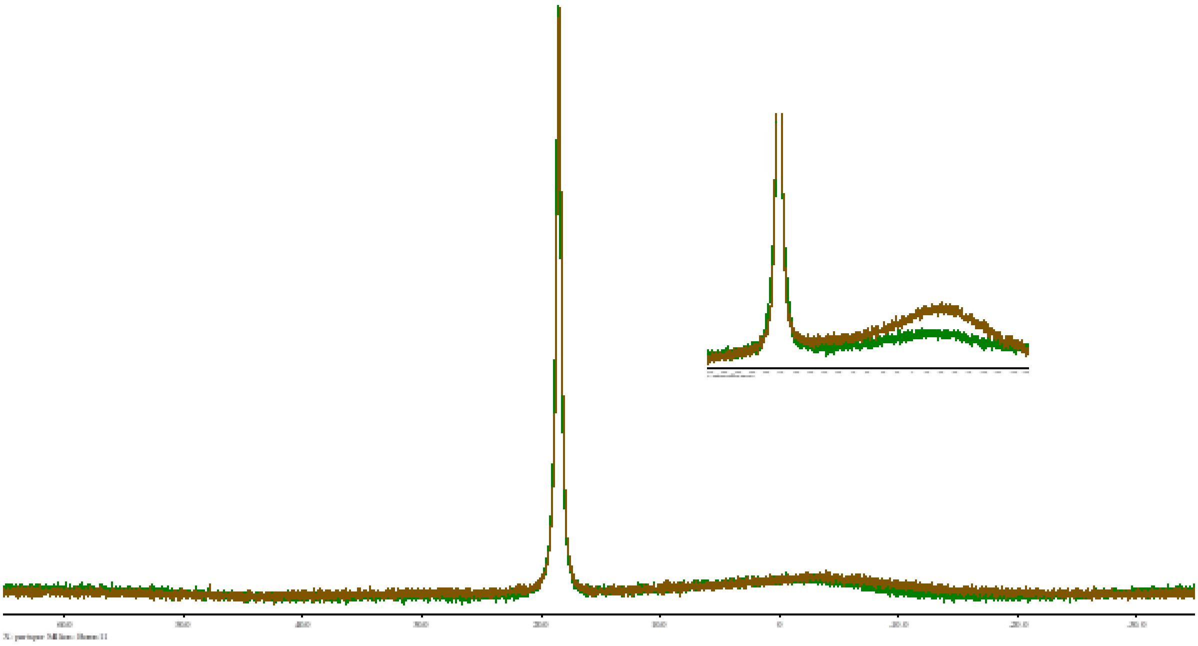

Figure 5. ^{11}B boric acid spectrum with SIP (brown) and TIP (green) pulse profile.

The central transition of quarapolar nuclei with the RAPT (rotor assisted population transfer) results in higher sensitivity with TIP scheme. The simple three pulse trains with suitable phase cycling can be a good NMR method to both sensitivity and resolution. Thus TIP and Modified DEPTH pulse offer us a convinient and reliable NMR sepctra without the baseline distortion problems in solid and solution state.

Conclusion

Triple pulse excitation profile for an arbitrary phase and flipping angle has been investigated in a quantitative way. From the rf flip angle dependence of a given pulse trains it can be deduced that the phase cycling for suitable magnetization transfer is important for getting the specific modulated magnetization signal of the compounds. Spin echo based DEPTH pulse sequence is also re-examined and modified the the phase of third pulse and receiver resulting in the slight sensitivity increment and background baseline suppression. Although TIP scheme does not increase the sensitivity compared to spin-echo based DEPTH it is one of the most efficient way to suppress the background signal as well as acoustic ringing effect. Scaling factor for excitation angle of TIP shows how to choose the excitation angle for the good spectrum. It is also observed that TIP scheme enables us to enlarge the scope to the quadrupole system both in solution and solid state and do the quantitative measurement at a low molecular concentration level. The combination of these sequences with conventional pulse methods can be a good footstep to more advanced experiments. Moreover, new pulse sequence such as inverted DEPTH and arbitrary flip angle TIP pulse sequence can be another candidate for the better resolution and sensitivity in NMR, which are underway in our laboratory.

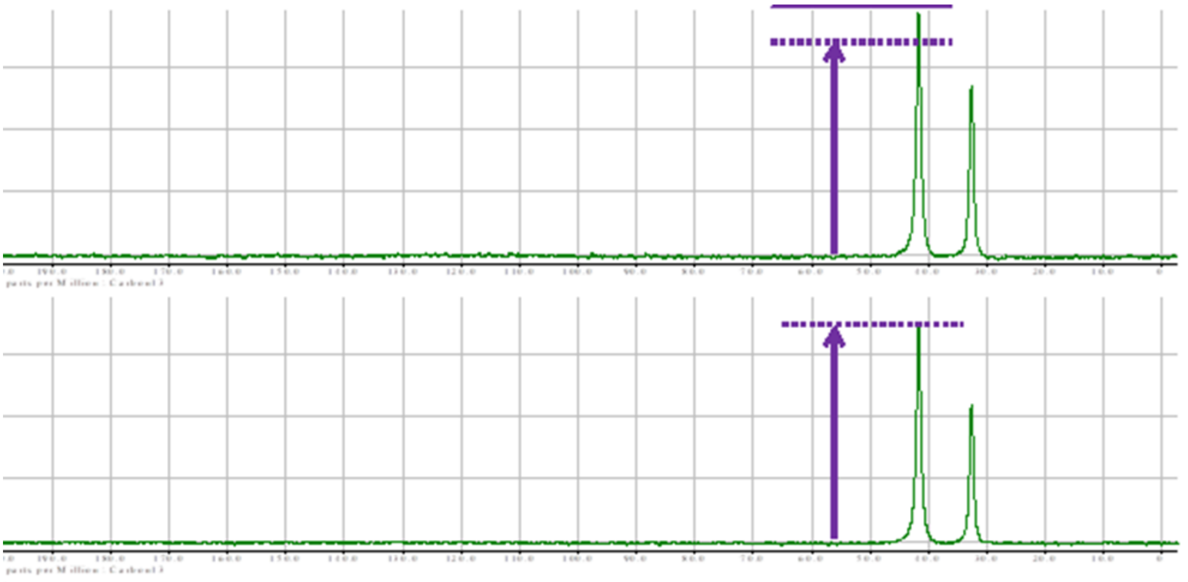

Figure 6. ^{13}C solid NMR spectrum with DEPTH (bottom) and modified DEPTH (top) pulse sequence

Table 1. DEPTH pulse phase cycling (ϕ_3) and modified DEPTH pulse phase cycling ($\phi_{3'}$)

ϕ_1	ϕ_2	ϕ_3	$\phi_{3'}$	**Receiver(ϕ_R)**
x	*x*	*x*	*x*	*x*
-y	*-y*	*y*	*y*	*-y*
-x	*-y*	*-y*	*-y*	*-x*
y	*-x*	*x*	*-x*	*y*
x	*-x*	*x*	*x*	*x*
-y	*y*	*y*	*y*	*-y*
-x	*y*	*-y*	*-y*	*-x*
y	*x*	*x*	*-x*	*y*
-x	*-x*	*-y*	*-y*	*x*
y	*y*	*x*	*-x*	*-y*
x	*y*	*x*	*x*	*-x*
-y	*x*	*y*	*y*	*y*
-x	*x*	*-y*	*-y*	*x*
y	*-y*	*x*	*-x*	*-y*
x	*-y*	*x*	*x*	*-x*
-y	*-x*	*y*	*y*	*y*

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