Singlet Order Conversion and Parahydrogen-Induced Hyperpolarization of ^{13}C Nuclei in Near-Equivalent Spin Systems

Supporting Information

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1 Sample Preparation and Methods

All starting materials were bought from Sigma Aldrich.

1.1 Optimization Experiments

100 mg of fumaric acid was dissolved in 1 mL of DMSO solvent yielding a 0.86 M solution. 0.5 mL of this solution was subsequently transferred to a 5 mm NMR tube before bubbling with nitrogen gas at 30 $mLmin^{-1}$ for 20 minutes to remove the majority of dissolved molecular oxygen. The sample tube was then sealed.

1.2 Parahydrogen Experiments

To produce dimethyl acetylene dicarboxylate-d_6, dimethyl acetylene dicarboxylate was stirred in methanol-d_4 as described in Ref [1]. 2.4 μL dimethyl acetylene dicarboxylate-d_6 and 81.5 mg [Rh(dppb)(COD)]BF_4 were dissolved in 3.75 mL acetone-d_6. The solution was fully saturated with hydrogenation catalyst. 0.5 mL of the resulting solution was pipetted through glass wool into a 5 mm NMR tube. This catalyst is known to only hydrogenate the reactant once in acetone [2], consequently no dimethyl succinate-d_6 was formed. To parahydrogen at approx. 50% enrichment, an aluminium U-bend tube containing powdered charcoal was pressurized with 8 bar of hydrogen gas and submerged in liquid nitrogen for 2 hours. When the catalyst was sufficiently cool, hydrogen gas was slowly flowed through the U-bend using a Cole Parmer flow controller (flow rate = 70 $mLmin^{-1}$) before collection in a 2.7 L aluminium canister. Parahydrogen gas was flowed through a 1/16 inch PTFE capillary (flow rate = 15 $mLmin^{-1}$) into an NMR tube containing pre-prepared dimethyl acetylene dicarboxylate-d_6 and [Rh(dppb)(COD)]BF_4 solution, situated inside a 500 MHz magnet. After 15 s the flow was halted and the NMR experiment performed. All NMR experiments were performed on a Bruker Avance III 500 MHz spectrometer with a 5 mm liquid state BBO probe.

2 Pulse Sequences

2.1 SLIC Transfer Sequence

^{13}C SLIC duration and amplitude optimizations were performed with the pulse sequence detailed in Fig. 1. Pulse phases are denoted by letters, and specified in Table 1.

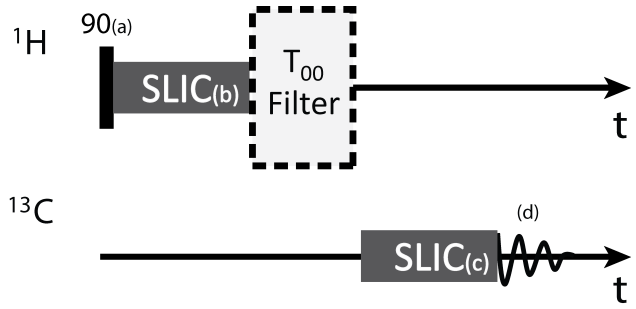

Figure 1: Pulse sequence used for SLIC optimization. Events a-d are indicated in parentheses.

Event	Event Description	Phase
a	^{1}H 90	0, 180
b	^{1}H SLIC	90
c	^{13}C SLIC	90
d	Acquire	0, 180

Table 1: Phase cycle used to ensure the observed signal came through the proton channel.

2.2 S2hM Transfer Sequence

S2hM delay and loop optimizations were performed with the pulse sequence in Fig. 2. The pulse phases are given by letters, and specified in Table 2.

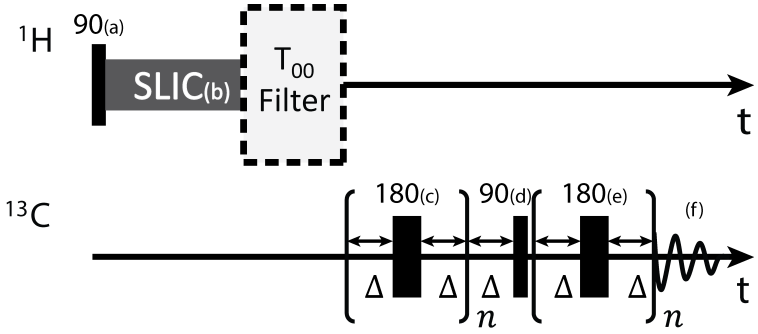

Figure 2: Pulse sequence used for S2hM optimization. Events a-f are indicated in parentheses.

Event	Event Description	Phase
a	^{1}H 90	0, 180
b	^{1}H SLIC	90
c	^{13}C Composite 180 (90, 180, 90)	(0, 90, 0)
d	^{13}C 90	90
e	^{13}C Composite 180 (90, 180, 90)	(0, 90, 0)
f	Acquire	0, 180

Table 2: Phase cycle used to ensure the observed signal came through the proton channel.

2.3 Goldman Transfer Sequence

Goldman sequence offset dependence experiments were performed with the pulse sequence in Fig. 3. The pulse phases are given by letters, and specified in Table 3.

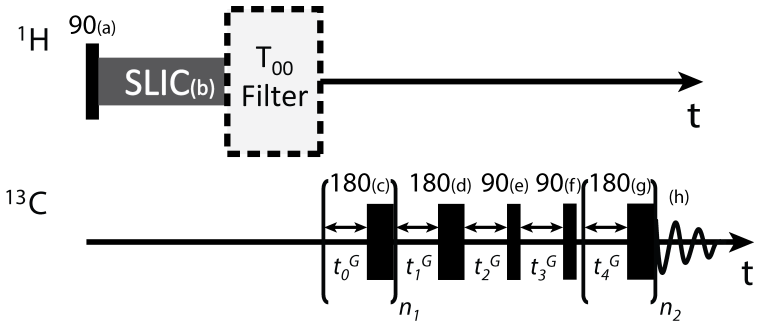

Figure 3: Pulse sequence used for Goldman sequence optimization. Events a-h are indicated in parentheses. Delays used were t0G=t1G=t3G=t4G=31.6 ms, t2G=15.8 ms. n1=5, n2=7.

Event	Event Description	Phase
a	^{1}H 90	0, 180
b	^{1}H SLIC	90
c	^{13}C Composite 180 (90, 180, 90)	(0, 90, 0)
d	^{13}C Composite 180 (90, 180, 90)	(0, 90, 0)
e	^{13}C 90	0
f	^{13}C 90	90
g	^{13}C Composite 180 (90, 180, 90)	(0, 90, 0)
h	Acquire	0, 180

Table 3: Phase cycle used to ensure the observed signal came through the proton channel.

2.4 Kadlecek 2b Transfer Sequence

Kadlecek 2b sequence offset dependence experiments were performed with the pulse sequence in Fig. 4. The pulse phases are given by letters, and specified in Table 4.

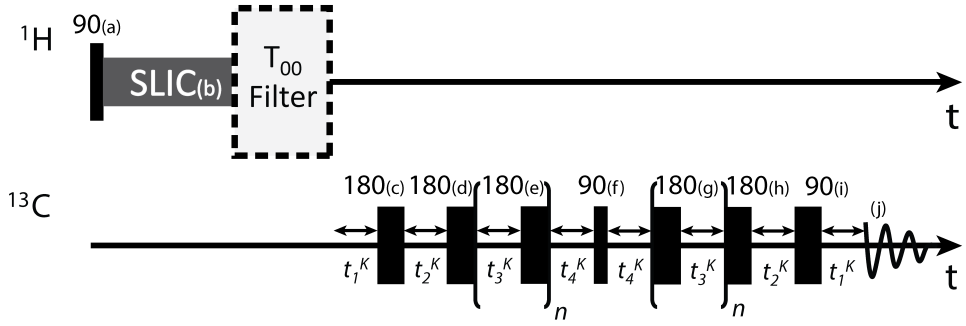

Figure 4: Pulse sequence used for Kadlecek 2b sequence optimization. Events a-j are indicated in parentheses. Delays used were t1K=t2K=t3K=31.6 ms, t4K=7.9 ms. n=5.

Event	Event Description	Phase
a	^{1}H 90	0, 180
b	^{1}H SLIC	90
c	^{13}C Composite 180 (90, 180, 90)	(0, 90, 0)
d	^{13}C Composite 180 (90, 180, 90)	(0, 90, 0)
e	^{13}C Composite 180 (90, 180, 90)	(0, 90, 0)
f	^{13}C 90	90
g	^{13}C Composite 180 (90, 180, 90)	(0, 90, 0)
h	^{13}C Composite 180 (90, 180, 90)	(0, 90, 0)
i	^{13}C Composite 180 (90, 180, 90)	(0, 90, 0)
j	Acquire	0, 180

Table 4: Phase cycle used to ensure the observed signal came through the proton channel.

2.5 Parahydrogen Experiment

The parahydrogen ^{13}C SLIC experiment was performed with the pulse sequence shown in Fig. 5. The resulting spectrum was acquired with a single transient.

Figure 5: Pulse sequence used for parahydrogen experiment.

2.6 T_{00} Filter

The T_{00} gradient filter used in experiments only allows NMR signals passing through singlet order to be observed.[3] A schematic of the SLIC optimization pulse sequence is shown in Fig. 6, with T_{00} filter shown in full. The relevant paraneters are summarized in Table. 3.

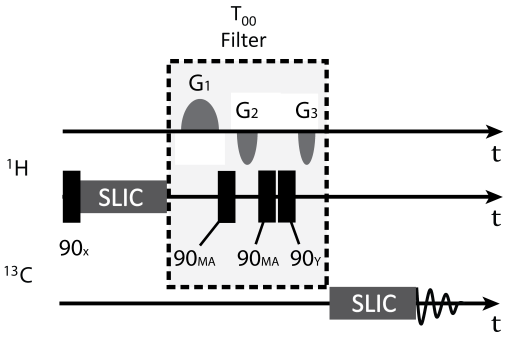

Figure 6: Graphical depiction of the T_{00} filter used to remove proton magnetization.

PFG	Shape	Strength / G cm^{-1}	Duration / ms
G1	SINE.100	10	8.8
G2	SINE.100	-10	4.8
G3	SINE.100	-15	4.0

Table 5: Parameters used for the T_{00} filter.

2.7 Refocused INEPT

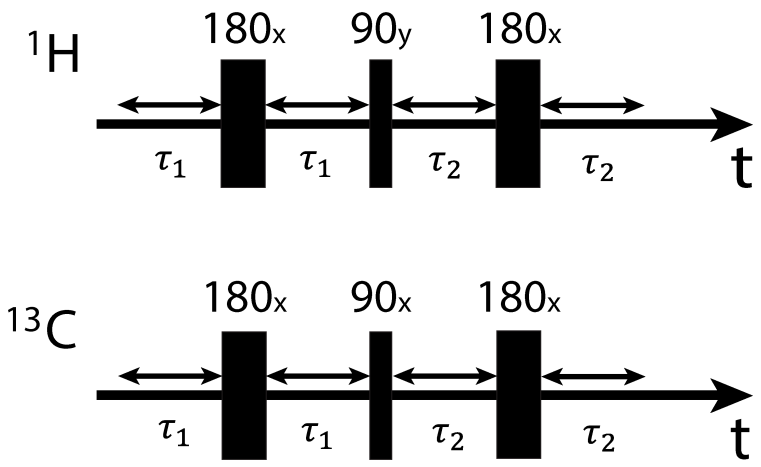

Figure 7: The refocused INEPT block used in the Figure 6 pulse sequences. The pulse phases assume the initial 90 pulse on the proton channel has phase x. The evolution delays used were $\tau_1 = 51\ ms$ and $\tau_2 = 34\ ms$. The values were determined by the formulae $\tau_1 = 1/4J_{CH}$ and $\tau_2 = 1/6J_{CH}$, where the average proton-carbon J coupling of 4.9 Hz was used. Using a refocused INEPT allows us to decouple on the proton channel during acquisition.

References

[1] E. H. Huntress, T. E. Lesslie, J. Bornstein, *Org. Synth.* **32**, 55 (1952)

[2] R. R. Schrock, J. A. Osborn, *J. Am. Chem. Soc.* **98**, 2143-2147 (1976)

[3] M.C.D. Tayler, M. H. Levitt, *J. Am. Chem. Soc.* **135**, 2120-2123 (2013)