

Supplementary information for
Long-lived nuclear spin states far from magnetic equivalence

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I. SYNTHESIS OF LABELLED $^{13}\text{C}_2$ -AMD **3** AND $^{13}\text{C}_2$ -AFD **4**

$^{13}\text{C}_2$ -AMD **3** and $^{13}\text{C}_2$ -AFD **4** were synthesised from commercially available maleic anhydride-2,3- $^{13}\text{C}_2$ (**1**) in two steps and three steps, respectively (Scheme 1). Thus, treatment of maleic anhydride-2,3- $^{13}\text{C}_2$ (**1**) with $n\text{PrOH-}d_7$ and NEt_3 in refluxing CH_2Cl_2 for 10 min afforded half-ester **2** in 99% yield. The half-ester **2** was used directly in a Mitsunobu reaction with $\text{EtOH-}d_5$ to afford $^{13}\text{C}_2$ -AMD **3** in 86% yield (85% overall yield from **1**). Subsequent isomerisation of the double bond with diethylamine furnished $^{13}\text{C}_2$ -AFD **4** in 82% yield (70% overall yield from **1**).

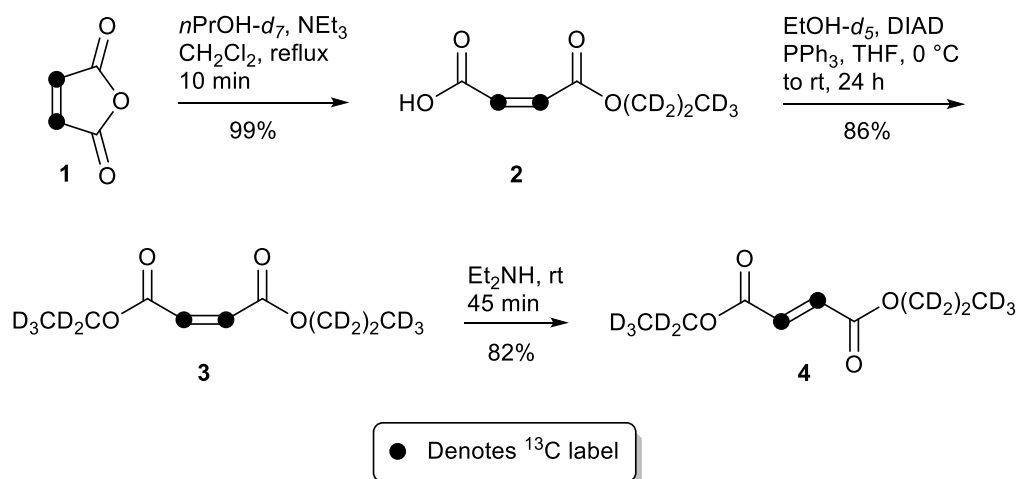


FIG. S1. Synthesis of $^{13}\text{C}_2$ -AMD **3** and $^{13}\text{C}_2$ -AFD **4**

A. Experimental

1. General experimental details

All air/moisture sensitive reactions were carried out under an inert atmosphere (N_2 or Ar), using oven or flame-dried glassware. The solvents THF (from Na/benzophenone) and CH_2Cl_2 (from CaH_2) were distilled before use. All other solvents and reagents were used as received from standard chemical suppliers unless otherwise stated. TLC was performed on aluminium plates pre-coated with silica gel 60 with an F_{254} indicator; visualised under UV light (254 nm) and/or by staining with KMnO_4 (10% aq.). Flash column chromatography was performed with Merck Kieselgel 60 silica gel. Fourier-transform infrared (FT-IR) spectra are reported in wavenumbers (cm^{-1}) and were collected on a Nicolet 380 spectrometer fitted with a Diamond platform, as solids or neat liquids. ^1H NMR and ^{13}C NMR spectra were recorded in CDCl_3 solutions using Bruker DPX400, Bruker AVII-400 or AVIIIHD-400 (400 and 100 MHz respectively) spectrometers. Chemical shifts are reported in δ units using CHCl_3 (δ 7.27 ppm ^1H , δ 77.0 ppm ^{13}C) or CH_3OH (δ 3.31 ppm ^1H , δ 49.1 ppm ^{13}C) as internal standards. ^2H NMR spectra were recorded in CHCl_3 solutions using a Bruker AVIIIHD-500 (76.8 MHz ^2H) spectrometer. Chemical shifts are reported in δ units using CDCl_3 as an internal standard (δ 7.27 ppm ^2H). Coupling constants (J) are reported in Hz and are rounded to the nearest 0.1 Hz. Matching coupling constants are corrected. For ^{13}C labelled compounds, only the signals corresponding to the labels are reported in the ^{13}C NMR data. High-resolution mass spectra (HRMS) were obtained using a MaXis (Bruker

Daltonics, Bremen, Germany) mass spectrometer equipped with a Time of Flight (TOF) analyser. HRMS were recorded using positive ion electrospray ionisation (ESI⁺).

B. Synthetic Procedures and Compound Characterisation Data

1. 1-(Ethyl-d₅) 4-(propyl-d₇) (Z)-but-2-enedioate-2,3-¹³C₂ (3)

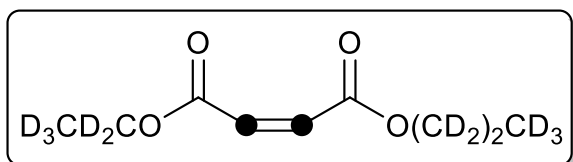


FIG. S2. maleate diester: The filled circles indicate ¹³C nuclei.

To a suspension of maleic anhydride-2,3-¹³C₂ (**1**) (229 mg, 2.29 mmol) in CH₂Cl₂ (4 mL) was added 1-propanol-1,1,2,2,3,3,3-d₇ (0.17 mL, 2.29 mmol) followed by Et₃N (0.35 mL, 2.52 mmol). The resulting solution was heated under reflux for 10 min. After cooling to rt, the reaction was quenched with 2M HCl (5 mL) and the layers separated. The aqueous layer was saturated with NaCl and extracted with CH₂Cl₂ (3 x 10 mL). The combined organic layers were dried (Na₂SO₄) before the solvent was removed in vacuo, affording half-ester **2** (378 mg, 2.26 mmol, 99%) as a colourless oil. The half-ester **2** (378 mg, 2.26 mmol) was immediately re-dissolved in THF (20 mL) whereupon Ph₃P (891 mg, 3.40 mmol) and ethanol-1,1,2,2,2-d₅ (0.16 mL, 2.72 mmol) were added. The mixture was cooled to 0 °C and DIAD (0.67 mL, 3.40 mmol) was added drop-wise over 20 min. After stirring at 0 °C for 10 min, the solution was warmed to rt and stirred for 24 h. The solvent was removed in vacuo and the residue purified by chromatography on silica gel (EtOAc:hexane 1:19) to afford the title compound **3** (388 mg, 1.94 mmol, 86%) as a colourless oil: ¹H NMR (400 MHz, CDCl₃) δ 6.23 (AB multiplet of ABXY system, ¹J_{CH} = 165.9 Hz, J_{CC} = 70.6 Hz, J_{HH} = 12.7 Hz, ²J_{CH} = 1.2 Hz, 2H) ²H NMR (76.8 MHz; CHCl₃) δ 4.24 (s, 2D), 4.14 (s, 2D), 1.66 (s, 2D), 1.28 (s, 3D), 0.92 (s, 3D); ¹³C NMR (100 MHz, CDCl₃) δ 129.7; IR (neat) ν 1719, 1586, 1380, 1222, 1169, 1088, 10729 cm⁻¹; HRMS (ESI⁺) m/z calcd for C₇¹³C₂H₂D₁₂O₄Na⁺ [M + Na]⁺ 223.1605, found 223.1606. **¹H and ¹³C NMR data for unlabelled maleate:** ¹H NMR (400 MHz, CDCl₃) δ 6.24 (s, 2H), 4.26 (q, J = 7.2 Hz, 2H), 4.16 (t, J = 6.8 Hz, 2H), 1.751.66 (m, 2H), 1.32 (t, J = 7.2 Hz, 3H), 0.97 (t, J = 7.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 165.3, 165.2, 129.8, 129.7, 66.9, 61.2, 21.8, 14.0, 10.3.

2. 1-(Ethyl-d₅) 4-(propyl-d₇) (E)-but-2-enedioate-2,3-¹³C₂ (4)

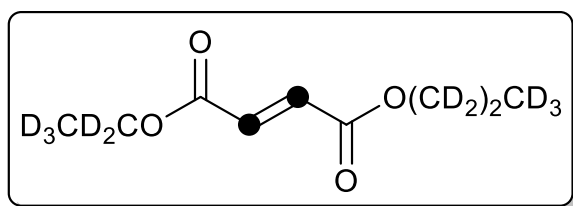


FIG. S3. fumarate diester: The filled circles indicate ¹³C nuclei.

Et₂NH (0.16 mL, 1.56 mmol) was added to maleate **3** (78 mg, 0.39 mmol) and the resulting mixture was stirred at rt for 45 min. The mixture was diluted with Et₂O (5 mL) and the reaction quenched by addition of 2M HCl (2 mL). The aqueous layer was extracted with Et₂O (3 x 5 mL) and the combined organic layers dried (Na₂SO₄). The solvent was removed in vacuo to afford the title compound **4** (64 mg, 0.32 mmol, 82%) as a colourless oil: ¹H NMR (400

MHz, CD₃Cl) δ 6.86 (AB multiplet of ABXY system, $^1J_{\text{CH}} = 165.9$ Hz, $J_{\text{CC}} = 70.6$ Hz, $J_{\text{HH}} = 15.7$ Hz, $^2J_{\text{CH}} = -2.8$ Hz, 2H) ^2H NMR (76.8 MHz; CH₂Cl₂) δ 4.25 (s, 2D), 4.15 (s, 2D), 1.67 (s, 2D), 1.29 (s, 3D), 0.93 (s, 3D); ^{13}C NMR (100 MHz, CD₃Cl) δ 133.6; IR (neat) ν 1715, 1592, 1300, 1161, 1079, 1055, 974, 772 cm⁻¹; HRMS (ESI⁺) m/z calcd for C₇¹³C₂H₂D₁₂O₄Na⁺ [M + Na]⁺ 223.1605, found 223.1609. **^1H and ^{13}C NMR data for unlabelled fumarate:** ^1H NMR (400 MHz, MeOD) δ 6.81 (s, 2H), 4.25 (q, J = 7.1 Hz, 2H), 4.17 (t, J = 6.6 Hz, 2H), 1.761.67 (m, 2H), 1.31 (t, J = 7.1 Hz, 3H), 0.98 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, MeOD) δ 166.4, 166.3, 134.6, 134.6, 68.1, 62.5, 23.0, 14.4, 10.7.

II. FITTING OF THE EXPERIMENTAL DATA

For $^{13}\text{C}_2$ -AFD when M2S and S2M occur on the same channel experimental points were fitted using a bi-exponential function of the form:

$$y = a_{\text{fast}}e^{-\frac{t}{T_{\text{fast}}}} + a_{\text{LLS}}e^{-\frac{t}{T_{\text{LLS}}}} \quad (1)$$

Parameters indicating the fitted values when using the ^1H and the ^{13}C channels are indicated in the table S1.

Parameters	^1H - ^1H	^{13}C - ^{13}C
a_{fast}	0.47 ± 0.1 s	0.45 ± 0.1 s
T_{fast}	5.60 ± 0.2 s	5.70 ± 0.2 s
a_{LLS}	0.52 ± 0.1 s	0.58 ± 0.1 s
T_{LLS}	63.20 ± 1.2 s	61.03 ± 1.5 s

TABLE S1. Table reports the fitting parameters of equation 1 when running experiments on $^{13}\text{C}_2$ -AFD using the same channel either ^1H or ^{13}C for excitation and detection.

When $^{13}\text{C}_2$ -AFD experiments involved alternative RF channels for excitation and detection (Fig. 5-c and Fig. 5-d in the main text) a single exponential decay function was used to fit the data.

$$y = b_{\text{LLS}}e^{-\frac{t}{T_{\text{LLS}}}} \quad (2)$$

Parameters indicating the fitted values when using both RF channels are indicated in the table S2.

Parameters	^1H - ^{13}C	^{13}C - ^1H
b_{LLS}	1.09 ± 0.1 s	1.42 ± 0.1 s
T_{LLS}	61.60 ± 1.2 s	59.88 ± 1.3 s

TABLE S2. Table reports the fitting parameters of equation 2 when running experiments on $^{13}\text{C}_2$ -AFD using ^1H and ^{13}C channels for excitation and detection.

III. THEORY AND SIMULATION

A. Torsional angle dependence of $\lambda_{\Delta_{gu}}$

The Liouvillian superoperator $\hat{\mathcal{L}}_{DD}$ is defined as:

$$\hat{\mathcal{L}}_{DD} = -i\hat{\mathcal{H}}_{\text{coh}} - \hat{\Gamma}_{DD} \quad (3)$$

$$\hat{\mathcal{L}}_{DD} = -i\hat{\mathcal{H}}_{\text{coh}} - \frac{6}{5}\tau_c \sum_{\{i,j,i',j'\}} b_{ij}b_{i'j'} D_{00}^2(\Omega^{ij,i'j'}) \sum_{m=-2}^2 (-1)^m \hat{T}_{2,m} \hat{T}_{2,-m} \quad (4)$$

Only the intra-molecular dipole-dipole interaction was considered. $\hat{\mathcal{H}}_{\text{coh}}$ is the commutation superoperator for the coherent hamiltonian \mathcal{H}_{coh} in the chemical equivalence regime, $\tau_c = 15$ ps is the molecular tumbling correlation time, b_{ij} is the dipolar coupling constant between nuclei i and j , $D_{00}^2(\Omega^{ij,i'j'})$ is the rank-2 Wigner matrix evaluated on the set of Euler angles specifying the angle between the principal axis of the pair i, j and the pair i', j' . Finally $\hat{T}_{2,m} \hat{T}_{2,-m}$ is the double commutation superoperator.

The coordinates, in m, of the nuclei in the spin system have been assigned as follows:

Coordinates :

10^{-10}

$\{\{-0.54, 0, 0\}, \{0.54, 0, 0\}, \{-1.08, -0.94, 0\}, \{1.08, -0.94 \cos(\theta), \sin(\theta)\}\}$, where the first two coordinates refer to ^{13}C and the other to ^1H . θ is the torsional angle shown in the text in Fig. 9-a. The rotation of the single bond ^{13}CH is assumed to occur around the axis specified by the double bond $^{13}\text{C}_2$. The diagonalisation of $\hat{\mathcal{L}}_{DD}$ returns a list of 256 complex eigenvalues for each geometric configuration defined by θ . Within each list has been selected the minimum non zero eigenvalue and plotted versus the value of θ .