Electronic Supplementary Information

Optimized Polarization Build-Up Times in Dissolution DNP-NMR Using a Benzyl Amino Derivative of BDPA.

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1. Synthesis and characterization of compounds 1-7.

4-((9H-Fluoren-9-ylidene)methyl)benzonitrile (1)

To an oven-dried two necked 1000 ml round bottom flask containing a magnetic stir-bar 3.00 g (18 mmol, 1 eq) of fluorene and 5.56 g (49.6 mmol, 2.75 eq) of potassium tert-butoxide were added, followed by 300 ml of absolute ethanol. The flask was fitted with a watercooler reflux condenser and a rubber septum. The mixture was heated to reflux with vigorous stirring and then 2.8 g (21 mmol, 1.2 eq) of 4-formylbenzonitrile were added. The flask was allowed to reflux overnight. After cooling to room temperature, the mixture was poured into a flask containing excess of cold 1 M HCl. This mixture was extracted with 3 portions of ethyl acetate. The organic phase was dried over anhydrous magnesium sulfate and the solvent was removed under vacuum. The product was purified by column chromatography on silica gel eluting with a gradient from pure hexane to 98 Hx: 5 EtOAc. The pure product was isolated as a yellow powder (4.5 g, 90%). ^{1}H NMR (400 MHz, ^{6}d-dimethylsulfoxide): δ 7.07 (t, 1H, J= 8 Hz), 7.34 (t, 2H, J= 8Hz), 7.42 (t, 2H, J= 8 Hz), 7.58 (s, 1H), 7.68-7.77 (m, 7H) ppm. ^{13}C NMR (100 MHz, ^{6}d-dimethylsulfoxide): δ 141.9, 141.4, 139.0, 139.0, 137.5, 135.6, 133.0, 130.5, 129.8, 129.3, 127.8, 127.5, 126.7, 124.2, 121.5, 120.8, 120.4, 119.2, 111.0 ppm. MS (MALDI-TOF, positive mode): m/z 279 $[M+H]^{+}$. Calculated: $C_{21}H_{13}N$: 279. IR-ATR (cm^{-1}): 2223, 1602, 1502, 1446 and 1433.

4-(Bromo(9-bromo-9H-fluoren-9-yl)methyl)benzonitrile (2)

To an oven-dried 100 ml round-bottom flask equipped with a magnetic stir-bar, 2.5 g of compound **1** (8.9 mmol, 1 eq) and 50 ml of CCl_4 were added. The resulting suspension was introduced in an ultrasound bath for 5 minutes and then, bromine was added (1.83 ml, 5.7 g, 35.8 mmol, 4 eq). The solution became a homogeneous red solution and was stirred for 5 minutes at room temperature. After this time, the mixture was poured into a flask containing excess of cold 1 M $NaHSO_3$ in order to eliminate the excess of bromine. The pH was adjusted to 7 with Na_2CO_3, and the solution was extracted with dichloromethane. The organic phase was dried over anhydrous magnesium sulfate and the solvent was removed under vacuum. The product was purified by column chromatography on silica gel eluting with hexane. The pure product was isolated as white powder (3.8 g, 97%). ^{1}H NMR (400 MHz, ^{6}d-dimethylsulfoxide): δ 6.63 (s, 1H), 7.06 (d, 2H, J= 8 Hz), 7.31-7.33 (m, 2H), 7.49 (d, 2H, J= 8 Hz), 7.51-7.53 (m, 2H),

7.62-7.64 (m, 1H), 7.75-7.78 (m, 1H), 7.80-7.83(m, 1H), 8.23 (d, 1H, J= 8 Hz) ppm. ^{13}C NMR (100 MHz, CDCl3): δ 144.4, 144.3, 141.9, 139.0, 138.01, 137.99, 131.3, 130.4, 129.9, 129.7, 128.2, 126.5, 125.9, 120.7, 120.5, 118.1, 111.0, 65.8 and 59.7 ppm. MS (MALDI-TOF, positive mode): m/z 441 $[M+H]^+$. Calculated: $C_{21}H_{13}Br_2N$: 439. IR-ATR (cm^{-1}): 2223, 1602, 1502, 1446 and 1433.

4-(Bromo(9H-Fluoren-9-ylidene)methyl)benzonitrile (3)

To an oven-dried two necked 500 ml round-bottom flask equipped with a magnetic stir-bar, 3.5 g of compound **2** (8 mmol, 1 eq) and 85 ml of absolute ethanol were added. The flask was fitted with a water-cooler reflux condenser and a rubber septum. In a 250 ml round-bottom flask equipped with a magnetic stir-bar 16 g of NaOH (399 mmol, 50 eq) and 175 ml of absolute ethanol were added. After dissolution of NaOH in ethanol, were added into the 500 ml flask and refluxed for 15 minutes. After letting it to cool down to room temperature, the mixture was acidified with diluted hydrochloric acid and then extracted with dichloromethane. The organic phase was dried over anhydrous magnesium sulfate and the solvent was removed under vacuum. The product was purified by column chromatography on silica gel eluting with a gradient from pure hexane to Hx: EtOAc 95:5. The pure product was isolated as yellow powder (2. 56 g, 90%). ^{1}H NMR (400 MHz, ^{6}d-dimethylsulfoxide): δ 6.1 (d, 1H, J= 8 Hz), 6,97 (t, 1H, J= 8 Hz), 7.32 (t, 1H, J= 8 Hz), 7.47 (t, 1H, J= 8 Hz), 7.55 (t, 1H, J= 8 Hz), 7.74 (d, 2H, J= 8 Hz), 7.87 (d, 1H, J= 8 Hz), 7.95 (d, 1H, J= 8 Hz), 8.06 (d, 2H, J= 8 Hz), 8.77 (d, 1H, J= 8 Hz) ppm. ^{13}C NMR (100 MHz, ^{6}d-dimethylsulfoxide): δ 146.3, 140.8, 139.4, 136.8, 136.76, 135.8, 133.6, 130.0, 129.4, 129.0, 127.5, 127.4, 125.6, 124.1, 121.7, 120.3, 120.1, 118.4, 112.3 ppm. MS (MALDI-TOF, positive mode): m/z 359 $[M+H]^+$. Calculated: $C_{21}H_{12}BrN$: 357/359. IR-ATR (cm^{-1}): 2223, 1645, 1602, 1502 and 1444.

4-((9H-Fluoren-9-yl)(9H-Fluoren-9-ylidene)methyl)benzonitrile (4)

To an oven-dried 250 ml Schlenk flask equipped with a stir-bar and a rubber septum, 2.2 g (6.14 mmol, 1 eq) of compound **3** were added. The flask was evacuated under vacuum and refilled with argon for three times and then 32 mL of dry dimethylacetamide (DMA) were added. In a separate oven-dried 250 ml Schlenk flask equipped with a stir-bar and rubber septum, 1.53 g (9.2 mmol, 1.5 eq) of fluorene and 2.76 g (24.6 mmol, 4 eq) of potassium tert-butoxide were added. The flask was also evacuated under vacuum and refilled with argon for three times and 92 mL of dry

dimethylacetamide (DMA) were added. The solution appeared dark red. The dark red solution was slowly added to the compound 18 flask by cannulation. The reaction turned deep green and was stirred for 2 hours at room temperature. After that, the flask was cooled down in an ice bath and then 1M HCl in diethyl ether was added until the green color disappeared. The solution was diluted with water and extracted with dichloromethane. The organic phase was dried over anhydrous magnesium sulfate, the solvent was removed under vacuum and then, with high vacuum to eliminate the dimethylacetamide. The product was purified by column chromatography on silica gel eluting with a gradient from pure hexane to Hx:EtOAc 95:5. The pure product was isolated as yellow powder (2.66 g, 97%). ^{1}H NMR (600 MHz, ^{8}d-tetrahydrofuran): δ 5.70 (d, 1H, J= 8 Hz, Hc), 6.50 (s, 1H, Hs), 6.84 (d, 2H, J= 8 Hz, Hb), 6.88 (t, 1H, J= 8 Hz, Hd), 7.28 (t, 1H, J= 8 Hz, He), 7.31 (t, 2H, J= 8 Hz, Hl , Hq), 7.39 (t, 2H, J= 8 Hz, Hm, Hp), 7.43 (t, 1H, J= 8 Hz, Hi), 7.54 (t, 1H, J= 8 Hz, Hh), 7.57 (d, 2H, J= 8 Hz, Ha), 7.62 (d, 2H, J= 8 Hz, Hk, Hr), 7.82 (d, 2H, J= 8 Hz, Hn, Ho), 7.92 (d, 1H, J= 8 Hz, Hf), 8.05 (d, 1H, J= 8 Hz, Hg), 8.54 (d, 1H, J= 8 Hz, Hj) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 144.5, 144.2, 143.4, 142.8, 142.2, 140.9, 139.1, 139.0, 137.1, 132.1, 130.3, 129.3, 128.5, 128.4, 128.1, 127.7, 127.1, 126.6, 126.0, 125.8, 120.7, 120.6, 119.9, 118.7, 112.2, 53.0 ppm. MS (MALDI-TOF, negative mode): m/z 444 $[M-H]^-$. Calculated: $C_{34}H_{21}N$: 443.5. IR-ATR (cm^{-1}): 2223, 1645, 1602, 1498 and 1445. UV-Vis (anion): 610 nm (ε = 21000 $M^{-1}cm^{-1}$).

4-((Fluoren-9-yl)(fluoren-9-ylidene)methyl)benzonitrile radical, CN-BDPA (5)

To an oven-dried 25 ml schlenk flask equipped with a stir-bar and a rubber septum, 100 mg (225 µmol, 1 eq) of CN-BDPA **4** was added. The flask was evacuated under vacuum and refilled with argon for three times and then 5mL of dry DCM were added. After that, 70 µL (451 µmol, 2 eq) of 1,8- Diazabicyclo[5.4.0]undec-7-ene (DBU) were slowly added. The reaction turned into deep green. The green solution was stirred at room temperature for five minutes. Then, a solution of $AgNO_3$ (153 mg, 902 µmol, 4 eq) in ACN were added, and the oxidation was monitored by UV-Visible. The organic phase was removed under vacuum and the organic solid obtained was purified by column chromatography on silica gel eluting with hexane to hexane:dichlorometane 8:2. The pure product was isolated as a red powder (97 mg, 97%). EPR (CH_2Cl_2): *g* = 2.0024; *a*(4H) = 1.928 G, *a*(4H) = 1.947 G, *a*(4H) = 0.492 G, *a*(4H) = 0.378 G; ΔHpp = 0.32 G. UV-Vis: 495 nm (ε = 33300 $M^{-1}cm^{-1}$), 860 nm (ε = 2300 $M^{-1}cm^{-1}$).

(4-((9H-Fluoren-9-yl)(9H-Fluoren-9-ylidene)methyl)phenyl)methanamine (6)

To an oven-dried 250 ml Schlenk flask equipped with a stir-bar and a rubber septum, 2.5 g (5.6 mmol, 1 eq) of CN-BDPA(H) **4** were added. The flask was evacuated under vacuum and refilled with argon for three times and 80 mL of dry tetrahydrofuran (THF) were added. The mixture was cooled in an ice bath and 22.54 mL of a solution of $LiAlH_4$ in THF 1 M (22.56 mmol, 4 eq) were slowly added. The reaction turned deep blue and was stirred for 4 hours at room temperature. After that, the flask was cooled in an ice bath and 1 M HCl in diethyl ether was added until the blue color disappeared. The solution was diluted with 1 M $KHCO_3$/DCM and extracted with dichloromethane. The organic phase was dried over anhydrous magnesium sulfate and the solvent was removed under vacuum. The product was purified by column chromatography on silica gel eluting with dichlorometane. The pure product was isolated as dark red powder (1.76 g, 70%). ^{1}H NMR (500 MHz, CD_2Cl_2): δ 3.77 (s, 2H, Ht), 5.85 (d, 1H, J= 8 Hz, Hc), 6.53 (s, 1H, Hs), 6.69 (d, 2H, J= 8 Hz, Hb), 7.84 (t, 1H, J= 8 Hz, Hd), 7.01 (d, 2H, J= 8 Hz, Ha), 7.23 (t, 1H, J= 8 Hz, He), 7.31 (t, 2H, J= 8 Hz, Hl , Hq), 7.36-7.41 (m, 3H, Hi , Hm, Hp), 7.51 (t, 1H, J= 8 Hz, Hh), 7.65 (d, 2H, J= 8 Hz, Hk, Hr), 7.71 (d, 2H, J= 8 Hz, Hk, Hr), 7.79 (d, 2H, J= 8 Hz, Hn, Ho), 7.92 (d, 1H, J= 8 Hz, Hg), 8.46 (d, 1H, J= 8 Hz, Hj) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.1, 144.3, 142.4, 141.4, 140.0, 139.1, 138.8, 137.0, 139.3, 128.7, 128.3, 127.59, 127.55, 127.4, 127.1, 126.8, 126.6, 126.1, 125.6, 125.23, 125.29, 120.1, 120.1, 119.2, 52.9, 45.9 ppm. MS (MALDI-TOF, positive mode): m/z 448 $[M+H]^+$. Calculated: $C_{34}H_{25}N$: 447.6. IR-ATR (cm^{-1}): 2926, 2855, 1610, 1510 and 1444. UV-Vis (anion): λ_{MAX} = 602 nm; (ε = 228000 $M^{-1}cm^{-1}$).

(4-((Fluoren-9-yl)(fluoren-9-ylidene)methyl)phenyl)methanamine radical, BAm-BDPA (7)

To an oven-dried 25 ml Schlenk flask equipped with a stir-bar and a rubber septum, 100 mg (223 µmol, 1 eq) of (H)BDPACH_2NH_2 **6** was added. The flask was evacuated under vacuum and refilled with argon for three times and then 5mL of dry DCM were added. After that, 67 µL (447 µmol, 2 eq) of 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) were slowly added. The reaction turned into deep blue. The blue solution was stirred at room temperature for five minutes, then, a solution of $AgNO_3$ (152 mg, 894 µmol, 4 eq) in ACN were added, and the oxidation was monitored by UV-Visible. The organic phase was removed under vacuum and the organic solid obtained was purified by column chromatography on silica gel eluting with hexane to dichlorometane: methanol 98:2.

The pure product was isolated as a red powder (98 mg, 98%). EPR (CH_2Cl_2): *g* = 2.0023; *a*(4H) = 2.002 G, *a*(4H) = 1.835 G, *a*(4H) = 0.465 G, *a*(4H) = 0.394 G; ΔHpp = 0.25 G. UV-Vis: λ_{MAX} = 493 nm (ε = 32300 $M^{-1}cm^{-1}$), 855 nm (ε = 1150 $M^{-1}cm^{-1}$).

2. EPR spectra of CN-BDPA (5) and BAm-BDPA (7) radicals.

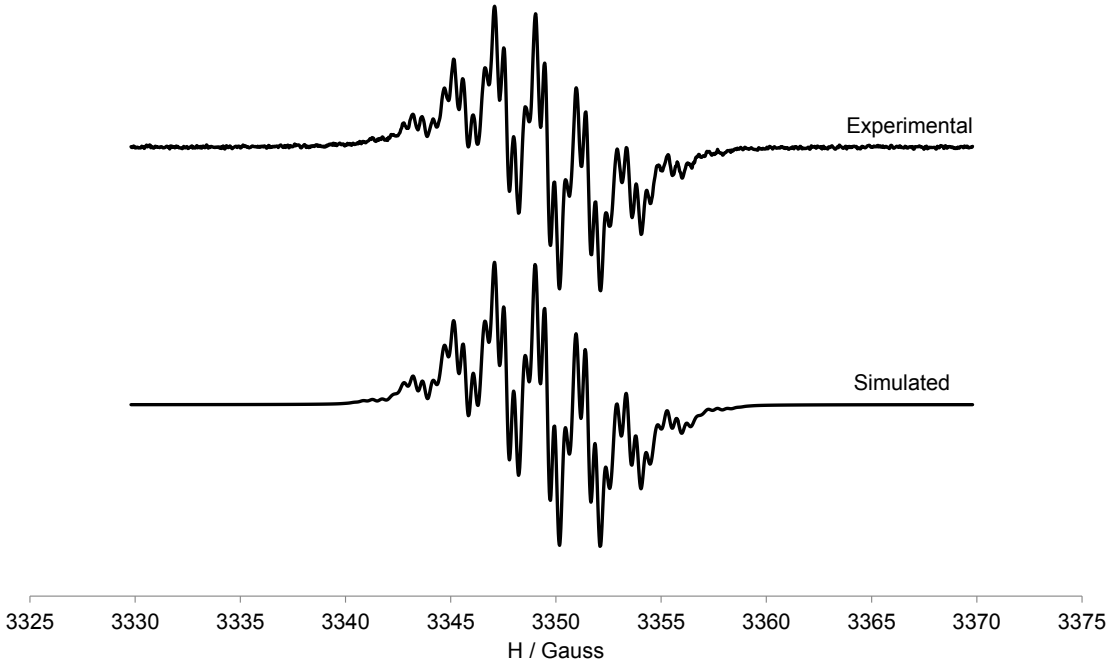

Fig. S1. EPR spectra of CN-BDPA (**5**) in CH_2Cl_2 at 298 K: experimental (up) and simulated (down). EPR simulation data: *g* = 2.0024; *a*(4H) = 1.928 G, *a*(4H) = 1.947 G, *a*(4H) = 0.492 G, *a*(4H) = 0.378 G; ΔHpp = 0.32 G.

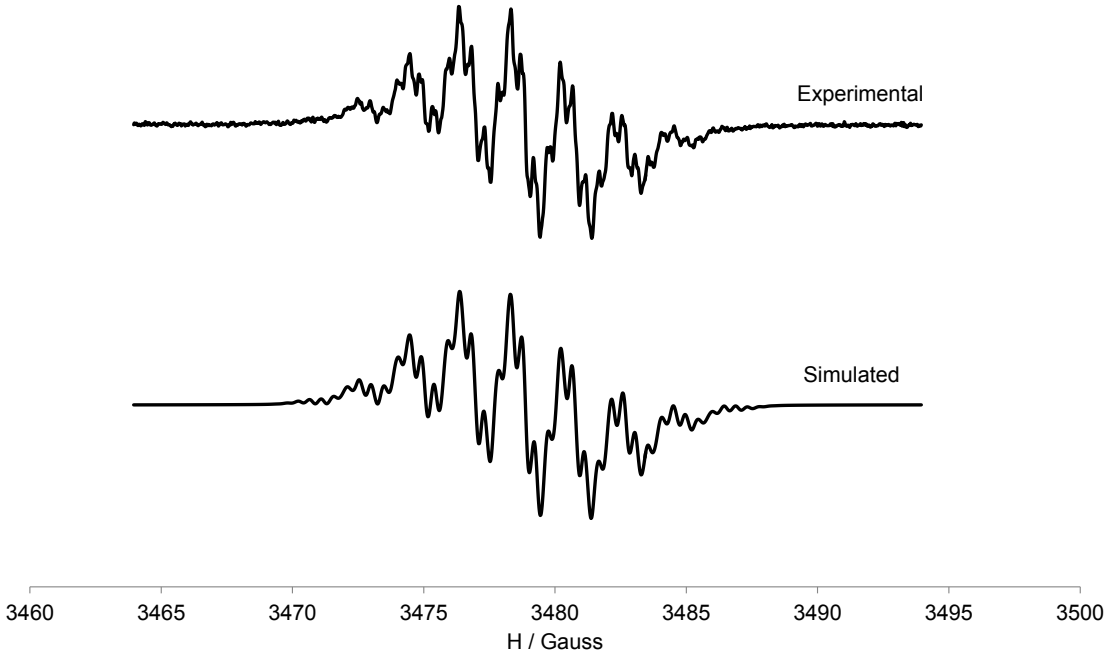

Fig. S2. EPR spectra of BAm-BDPA (**7**) in CH_2Cl_2 at 298 K: experimental (up) and simulated (down). EPR simulation data: g = 2.0023; a(4H) = 2.002 G, a(4H) = 1.835 G, a(4H) = 0.465 G, a(4H) = 0.394 G; ΔHpp = 0.25 G.

The simulation of the frozen solution EPR spectra of both radicals is very similar, as an example we show the corresponding to the BAm-BDPA (**7**) in CH_2Cl_2 at 120 K.

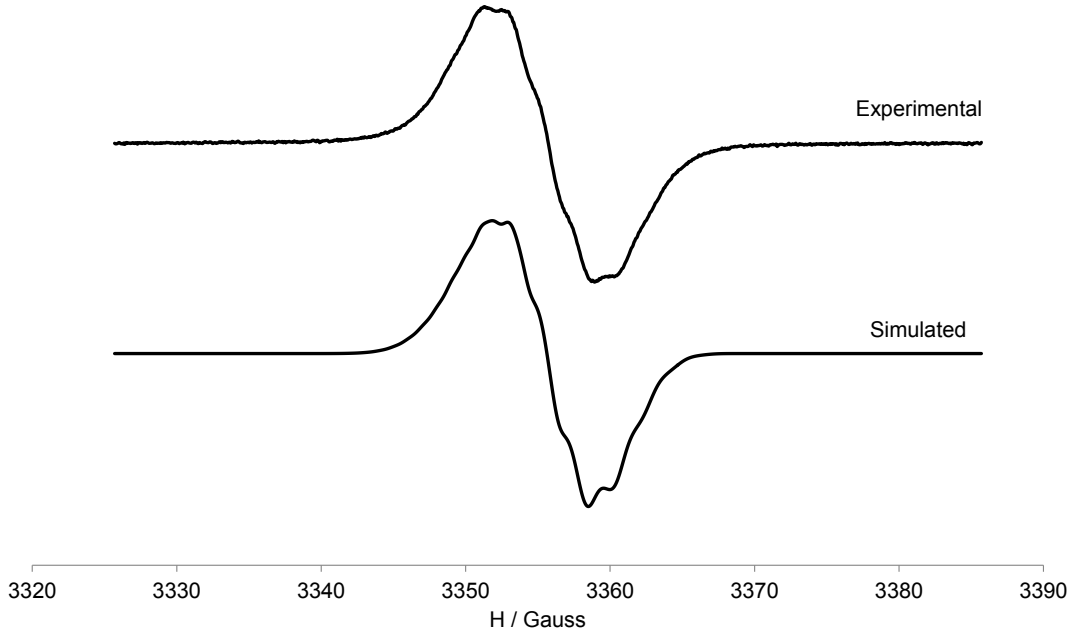

Fig. S3. Frozen solution EPR spectra of BAm-BDPA (**7**) in CH_2Cl_2 at 120 K: experimental (up) and simulated (down). EPR simulation data: g_{xx} = 2.0010; g_{yy} = 2.0026; g_{zz} = 2.0048; $a(8H_a)$: a_{xx} = 1.85 G, a_{yy} = 1.85 G, a_{zz} = 2.00 G; $a(8H_b)$: a_{xx} = 0.45 G, a_{yy} = 0.45 G, a_{zz} = 0.90 G; ΔHpp = 1.0 G.

3. Dissolution DNP studies of CN-BDPA (5) radical.

Due to the insolubility of the CN-BDPA radical **5** in neat [1-^{13}C]pyruvic acid (PA), the samples were prepared using sulfolane as a co-solvent, as described for the BDPA radical. Thus, once radical **5** was completely dissolved in 100 µl of sulfolane, the same amount of PA (100 µl) was added, obtaining a final 40 mM concentration of the radical in the mixture. The ^{13}C microwave DNP spectrum was acquired with 100 µl of the previously prepared solution which was frozen at 1.4 K at the pressure of 3 mbar. The frequency was scanned from 93.950 GHz to 94.250 GHz with 5 MHz steps and irradiating for 300 s at each step in order to determine the optimum polarization positive P(+) and negative P(-) peaks, and hence the optimum irradiation frequency for the DNP experiments. It can be observed from the microwave spectrum (Fig. S4a) that the positive polarization peak is located at 94.080 GHz and the negative one at 94.120 GHz, so the frequency of work was set as the positive peak polarization, P(+) = 94.080 GHz. The separation between the polarization peaks (|P(+) - P(-)|= 94080 - 94120) was 40 MHz which is close to that of the non-functionalized BDPA radical (50 MHz). Therefore, this radical fulfills the requirements to polarize ^{13}C nuclei by the thermal mixing mechanism, as commercial BDPA radical does. The polarization build-up curve (Fig. S4b) was performed with a 30 µl aliquot of the frozen sample (40 mM) irradiated at the optimal frequency of 94.080 GHz. The sample was introduced in the DNP equipment, and before starting the polarization, the sample remained inside the variable temperature insert until the pressure and temperature became stable at 3.2 mbar and 1.4 K. Data were acquired every 1 minute and the total time of polarization was 3.5 h.

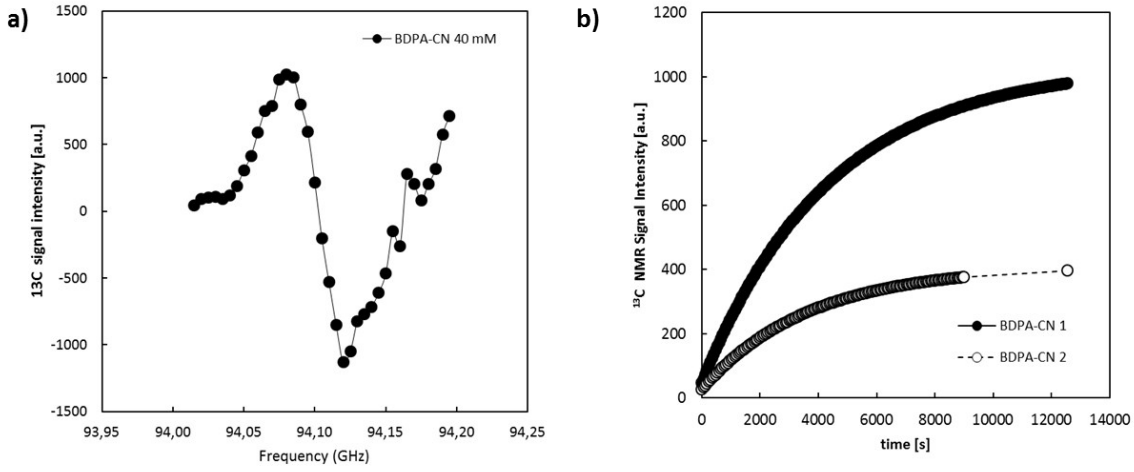

Fig. S4 a) ^{13}C microwave spectrum of 100 µl of a 1:1 (v/v) [1-^{13}C]pyruvic acid:sulfolane doped with 40 mM CN-BDPA **5** at 3.35 T and 1.4 K. b) ^{13}C polarization build-up curves of 30 µl 1:1

(v/v) [1-^{13}C]pyruvic acid:sulfolane doped with 40 mM CN-BDPA **5**, freshly prepared (filled circles) and after being stored 2 hours at -20◦C in the freezer (open circles).

The polarization build-up curve (Fig. S4b) was performed with a 30 µl aliquot of the frozen sample (40 mM) irradiated at the optimal frequency of 94.080 GHz. We obtained a slow polarization build-up curve with low polarization level, and, in addition, the sample was not stable with time, because it was observed that the ^{13}C polarization achieved for the same sample after some time changed, even if the sample was stored in the freezer at -20◦C. As can be observed in Fig. S4b, the solid-state polarization level achieved by the sample after being stored 2 hours in the freezer was approximately a 40% of the value of the freshly prepared one. Since the decomposition of the radical could be the origin of such behavior, as occurs for BDPA radical, we repeated the experiments with equimolar quantities of radical and benzene. Thus, a new sample of radical **5** was prepared dissolving the radical in 100 µl of sulfolane and benzene at 80 mM. Once the radical was completely dissolved, 100 µl of PA were added, obtaining a final solution where the concentration of both radical and benzene was 40 mM. As with the previous sample, the polarization build-up curve was performed with an aliquot of 30 µl irradiating the frozen sample at the same frequency, 94.080 GHz. The data obtained by the build-up curves were similar to those obtained in the previous case with a freshly prepared CN-BDPA radical.