Electronic Supporting Information

Suppression of spin-spin coupling in nitroxyl biradicals by supramolecular host-guest interactions

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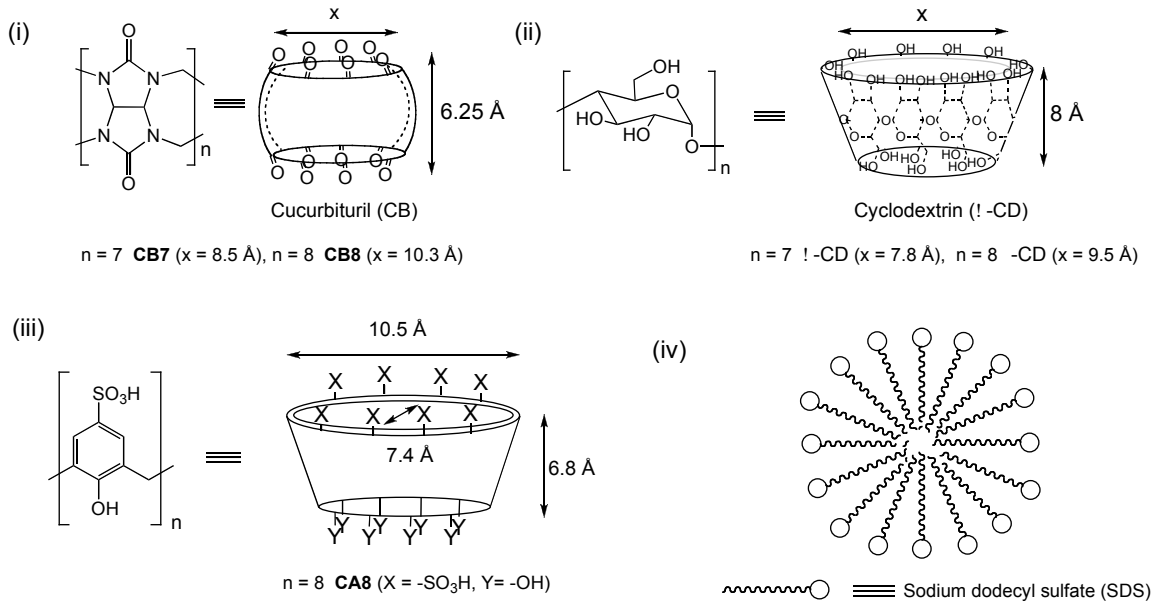
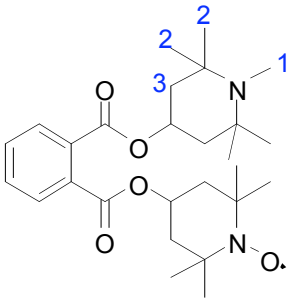


Figure S1 Investigated host structures. Dimensions of the hosts refer to atom-to-atom distance and do not include Van der Walls radii.



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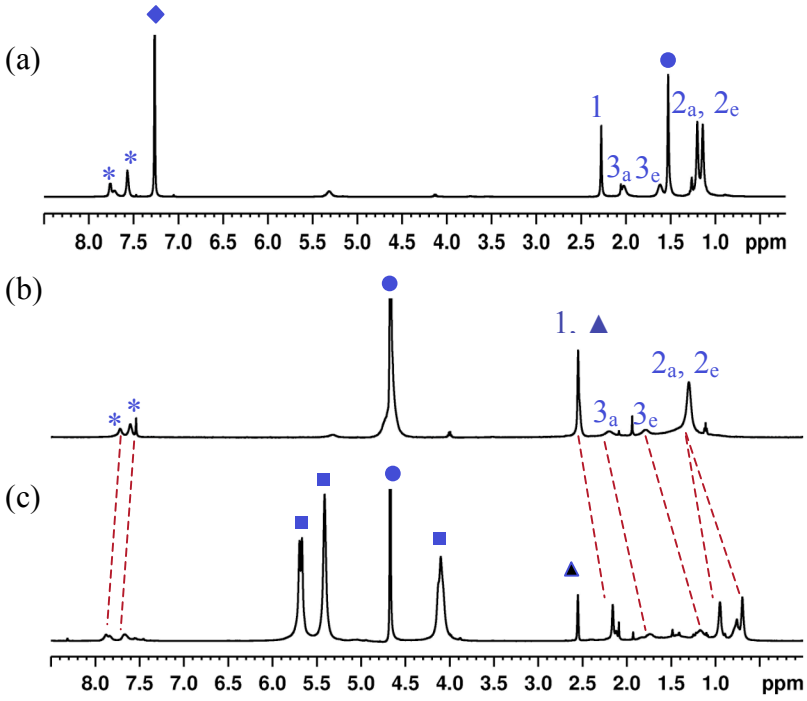


Figure S2 ^{1}H NMR spectra of **4** (a) in $CDCl_3$ (1mM, 500 MHz) (b) in D_2O (1mM, 500 MHz) and (c) **4**@CB8, (H:G = 1:1, [**4**] =1 mM, (500 MHz). Aliphatic guest resonances are represented with label 1-3 and aromatic guest protons are represented with label "*". The labels 'a' and 'e' represent axial and equatorial resonances. Host resonances are represented with label "■". The subscript 'a' and 'e' describes the 'axial' and 'equatorial' position in the piperidine moiety. The labels "♦", "▲" and "●"represent the residual $CHCl_3$, DMSO and H_2O resonances respectively.

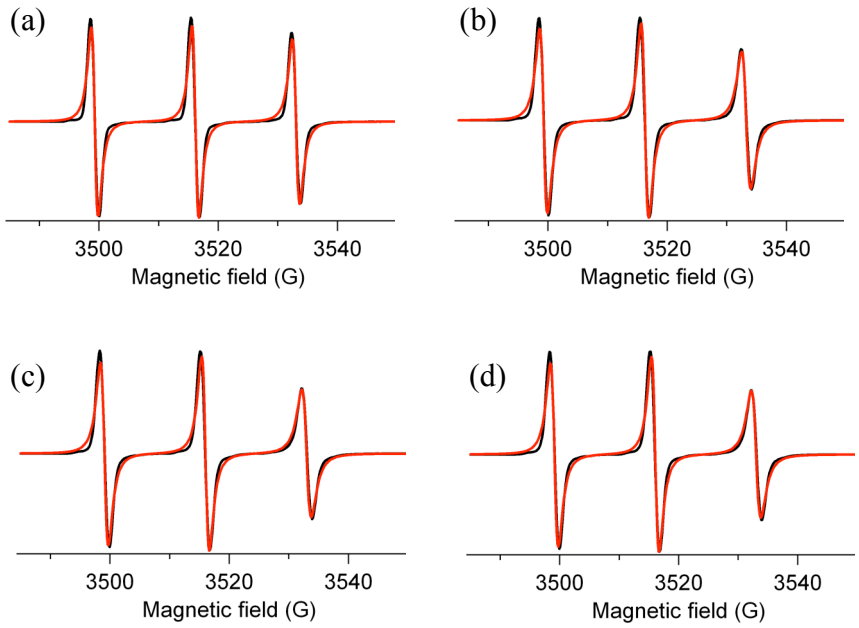


Figure S3 EPR spectra (black lines) and their simulations (red lines) for (a) **4** in water (1 mM), A_N = 16.9 G, τ_c = 0.042 ns (b) **4**/CB8 (1:1), A_N = 17 G, τ_c = 0.11 ns and (c) **4**/CB8 (1:2), A_N = 16.9 G, τ_c = 0.14 ns and (d) **4**/CB8 (1:3), A_N = 16.9 G, τ_c = 0.14 ns.

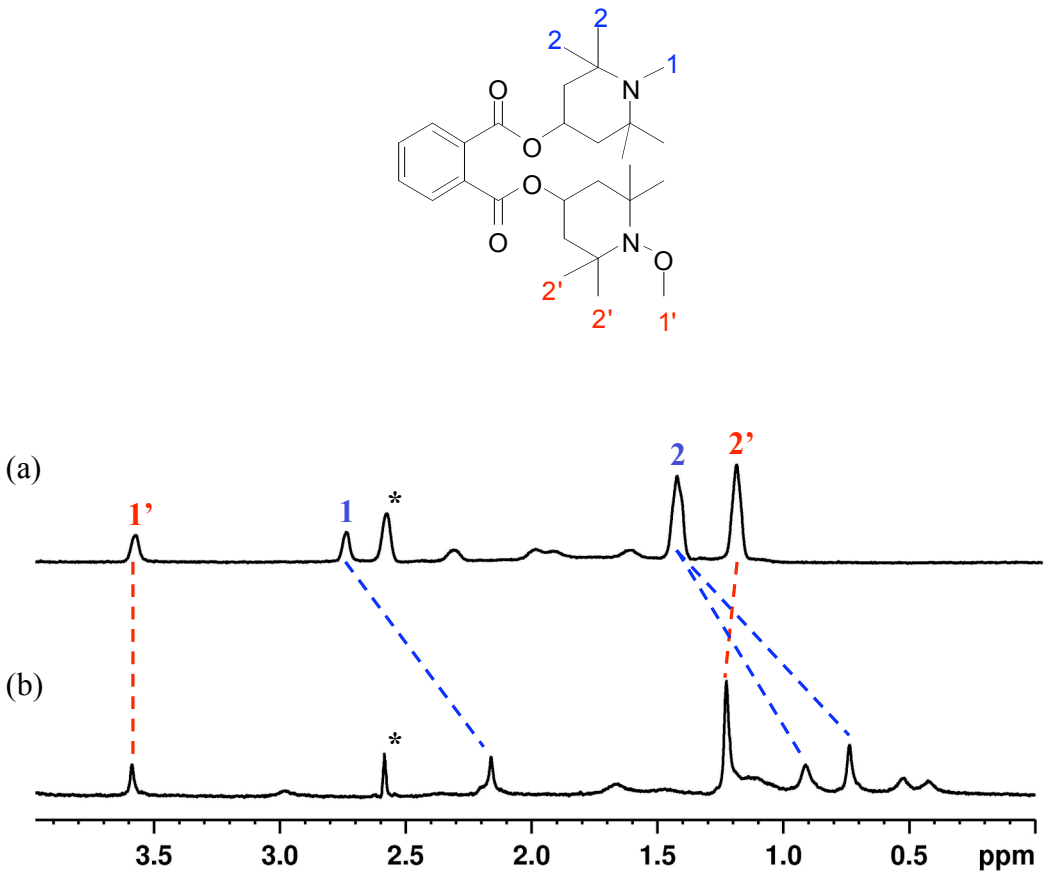


Figure S4. Partial ^{1}H NMR spectra of **5** (a) in D_2O (0.5 mM, 500 MHz) and (b) **5**@ CB8 (H:G = 1:1, [**5**] = 0.5 mM, (500 MHz). The label "*" represents residual DMSO resonance. Stock solution of guest was prepared in DMSO.

Note: In was observed that in presence of 1 eq. of CB8, -NOMe group of **5** was not upfield shifted whereas –NMe group is upfield shifted. This observation suggests that only piperidine moiety with N-Me group is encapsulated within CB8 whereas –NOMe resides in water.

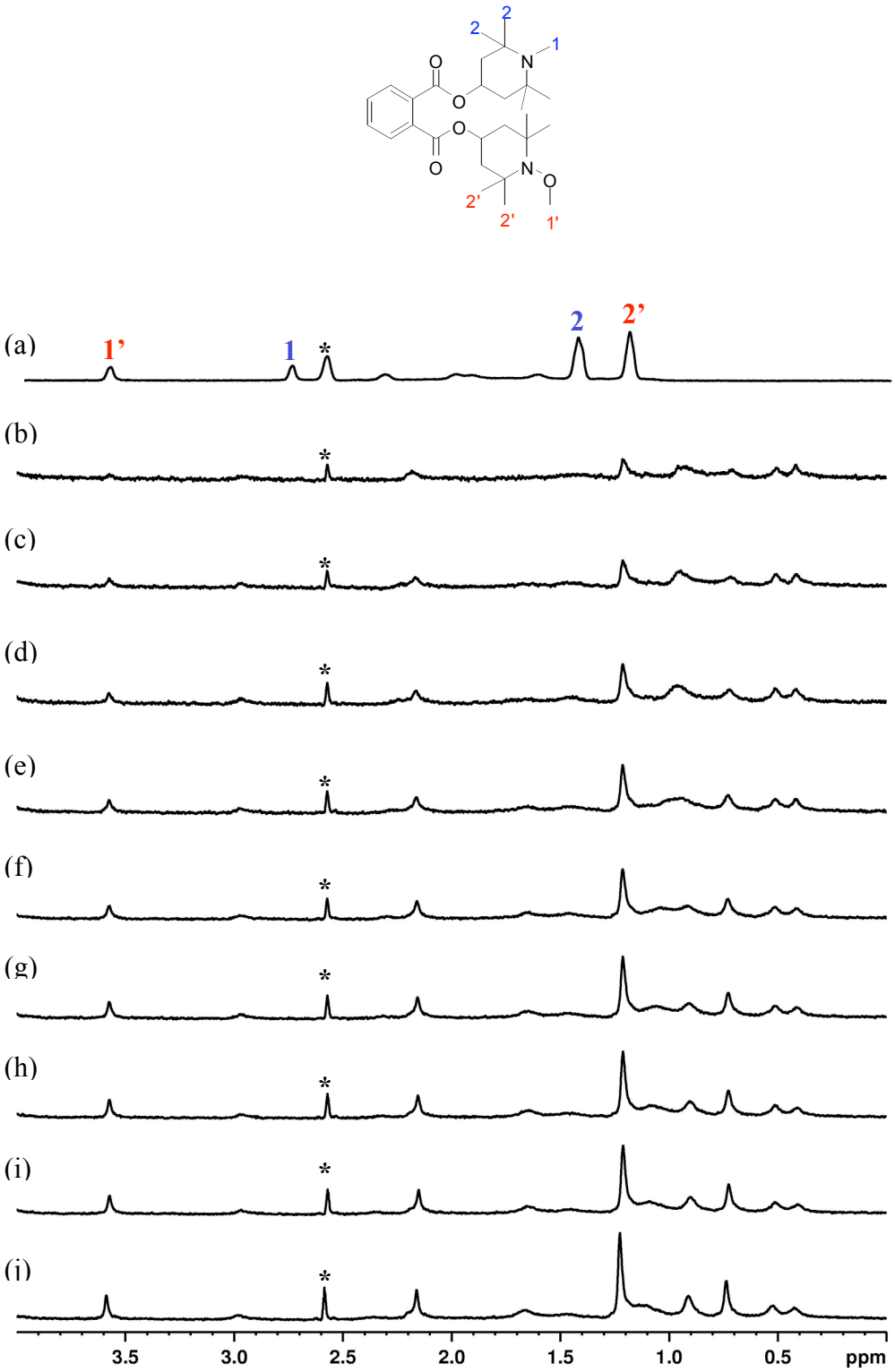


Figure S5. Partial ^{1}H NMR spectra of **5** (a) in D_2O (0.5 mM, 500 MHz) and (b) **5**:CB8 (1:0.1), (c) **5**:CB8 (1:0.2), (d) **5**:CB8 (1:0.3), (e) **5**:CB8 (1:0.4), (f) **5**:CB8 (1:0.5), (g) **5**:CB8 (1:0.6), (h) **5**:CB8 (1:0.7), (i) **5**:CB8 (1:0.8) and (j) **5**:CB8 (1:1),[**5**] = 0.5 mM, (500 MHz). The label "*" represents residual DMSO resonance.

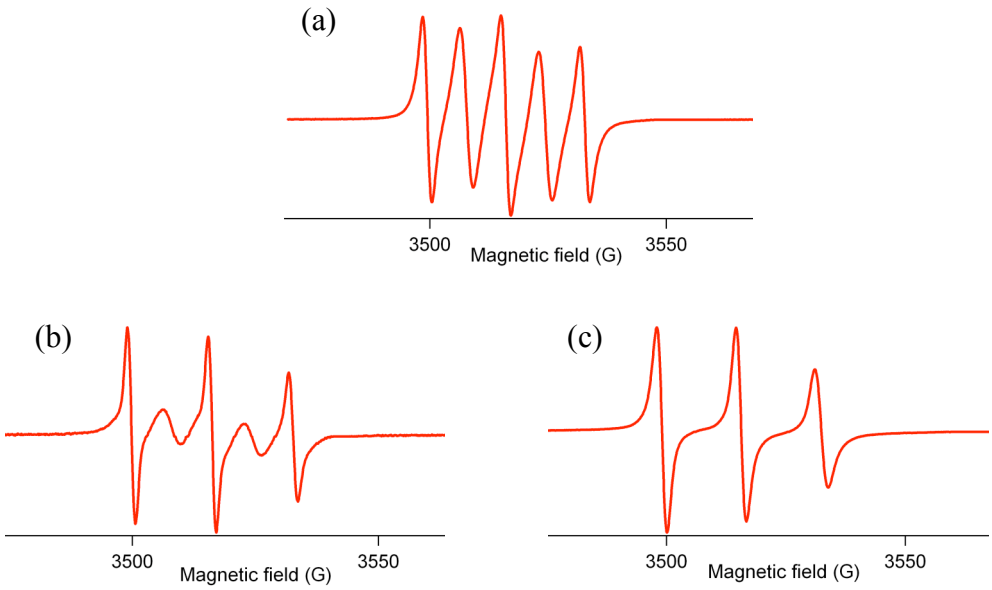


Figure S6. EPR spectra of (a) **3** in 50% MeOH/water, signal intensity by double integration = 1.42 x 10^8, (b) **3**/CB8 (1/0.5) in water, signal intensity by double integration = 1.46 x 10^8 and (c) **3**/CB8 (1/1) in water, signal intensity by double integration = 1.46 x 10^8, [**3**] = 0.1 mM.

Note: Because the signal intensities (from double integration of the EPR signal) of **3** in the absence and presence of CB8 are identical within experimental error, no nitroxyl groups in **3** are "lost" due to chemical reaction in the presence of CB8. It confirms that the change of five-line EPR spectra in solution to three-line EPR spectra in presence of 1 equivalent CB8 is only because of the restriction of spin-spin exchange between two radicals upon encapsulation. Spin-spin exchange gradually decreases with increase of CB8 concentration and stopps completely in presence of 1 eq. of CB8.

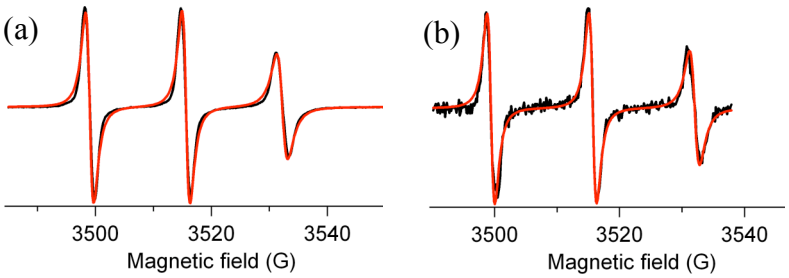


Figure S7 EPR spectra (black lines) and their simulations (red lines) for (a) **2**/CB8 (1:2), A_N = 16.6 G, τ_c = 0.22 ns and (b) **1**/CB8 (1:2), A_N = 16.3 G, τ_c = 0.27 ns.

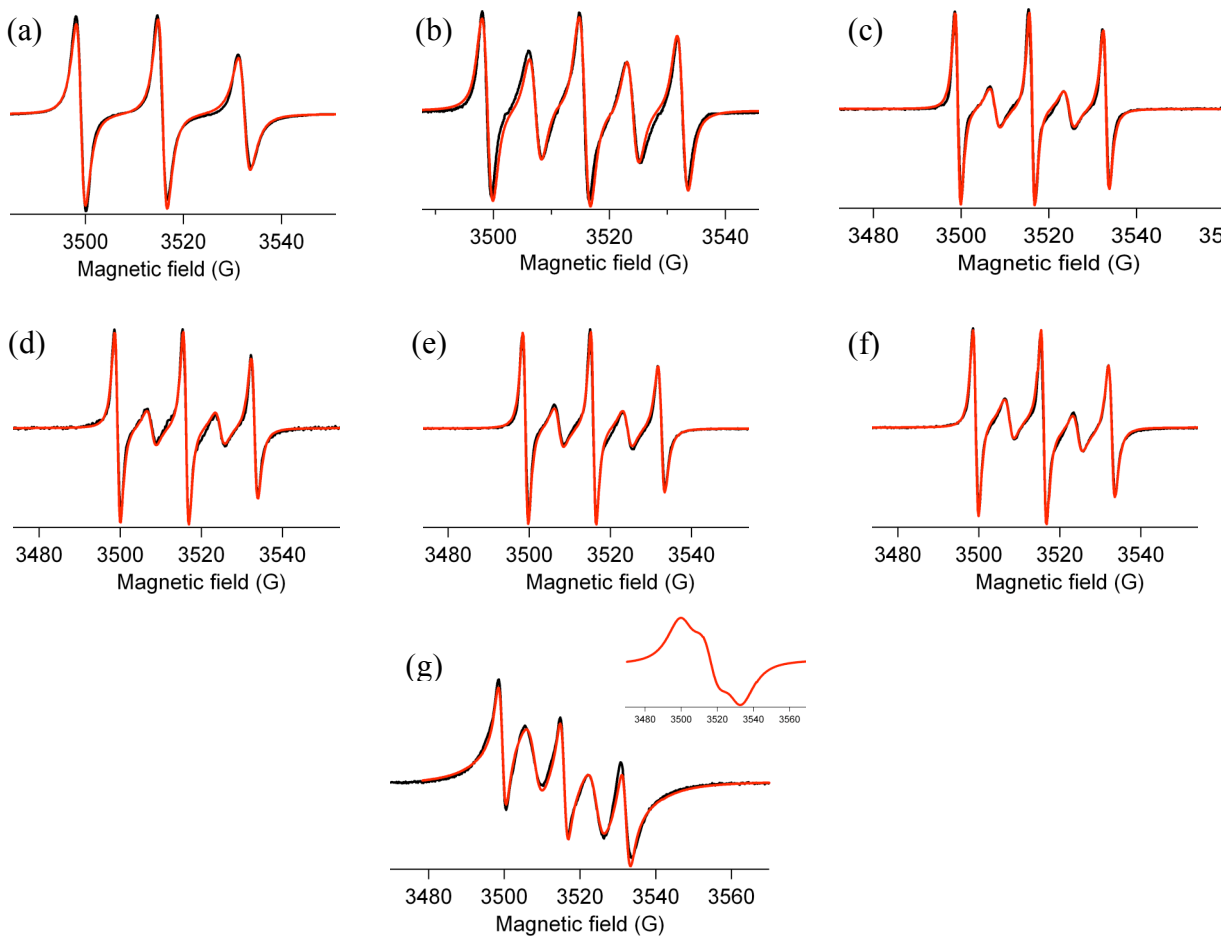


Figure S8 EPR spectrum (black lines) and its simulation (red lines) for (a) **3** /CB8 (1:2), A_N = 16.7 G, τ_c = 0.24 ns, (b) **3** /CB7 (1:1), A_N = 16.9 G, τ_c = 0.07 ns, (c) **3** /CB7 (1:2), A_N = 16.9 G, τ_c = 0.06 ns, (d) **3** /CA8 (1:2), A_N = 16.9 G, τ_c = 0.1 ns, (e) **3** /β-CD (1:2), A_N = 16.7 G, τ_c = 0.15 ns, (f) **3** /γ-CD (1:2), A_N = 16.8 G, τ_c = 0.12 ns, (g) **3** @ SDS, [**3**] = 0.1 mM, [SDS] = 200 mM, A_N = 16.3 G, τ_c = 0.12 ns, in the insert (44% on the total): $\omega_{exchange} = 2x10^8\ s^{-1}$; line width = 3 G. From (a) to (f), [**3**]=1mM.

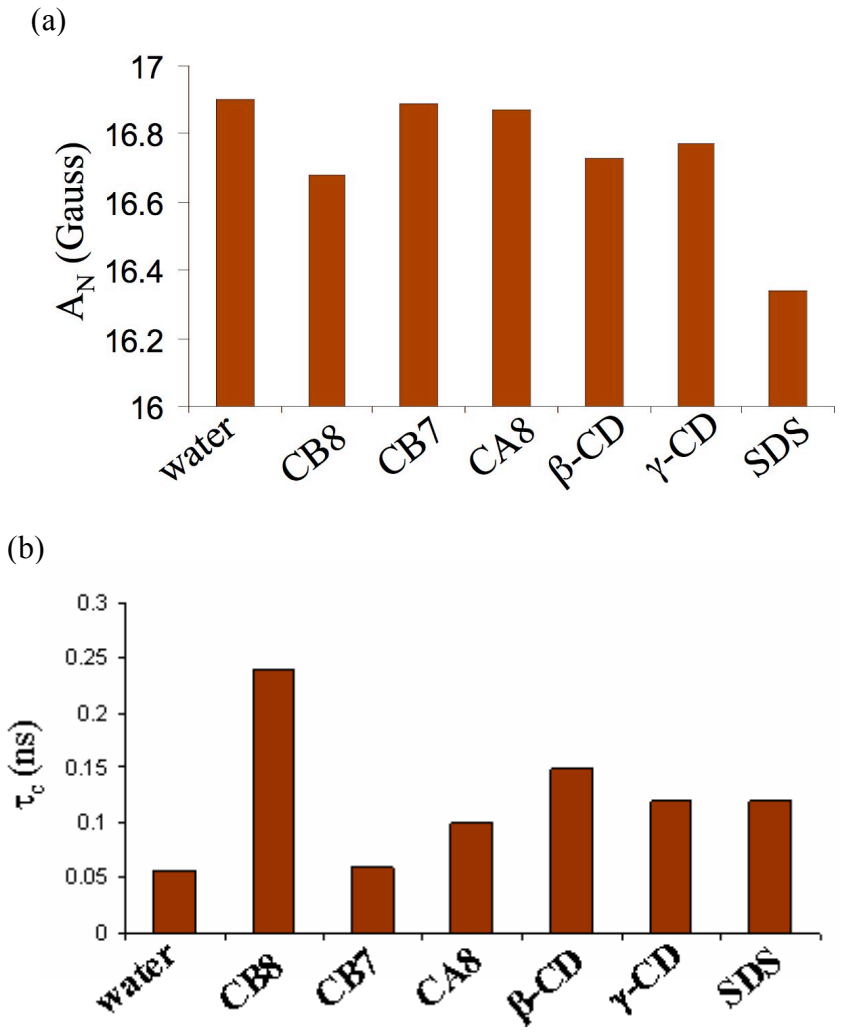


Figure S9 Comparison of (a) hyperfine splitting (A_N) and (b) rotational correlation time (τ_c) of **3** in absence and presence of different hosts.

Experimental section:

Materials and Methods: Cucurbit[7]uril (CB7) and cucurbit[8]uril (CB8) were synthesized by following a published procedure[1]. β-cyclodextrin (β-CD) and γ-cyclodextrin (γ-CD) were purchased from Sigma-Aldrich. Calixarene[8]octa sulfonic acid (CA8) was synthesized from the published procedure[2,3,4].

Synthesis of the compounds used in the study:

Compound 1:

Terephthalic acid (0.3 g) was mixed with 4-hydroxy-2,2,6,6-tetramethyl piperidine-N-oxyl (0.8 g) and DMAP (cat.) in dry dichloromethane (20 mL) at 0 ^{o}C. A suspension of EDCI (0.83 g) in dichloromethane was added to the above reaction mixture at 0 ^{o}C, it was allowed to warm up to rt and stirred for 15 h. The reaction mixture was washed with water and dried over Na_2SO_4 and purified by column chromatography to afford the corresponding ^{14}N-*para*-^{14}N biradical (**1**).

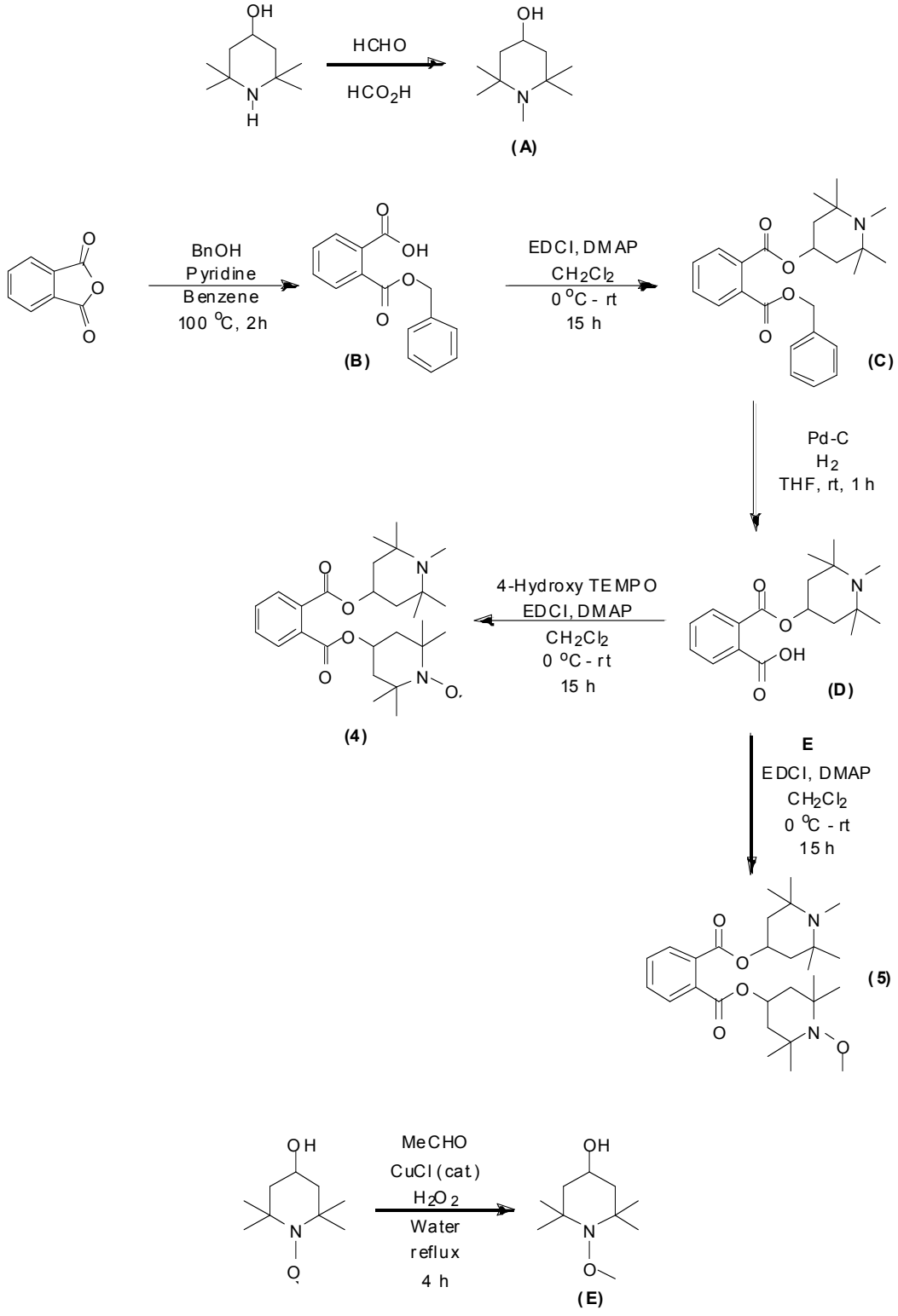
FAB-MS (m/z): 475 $(M+H)^+$

By comparing the EPR signal intensity (double integrating the EPR spectra) of the known concentration of the compound against a standard solution of 4-hydroxy TEMPO (1 mM in EtOH), the purity was ascertained.

Compound 2: A similar procedure was followed as described for compound **1** with isophthalic acid to afford the ^{14}N-*meta*-^{14}N biradical (**2**).

Compound 3: ^{14}N-*ortho*-^{14}N biradical (**3**) was synthesized by following the procedure reported in the literature.[5]

Compounds 4 and 5:



Scheme S1. Synthesis of compounds **4** and **5**.

1,2,2,6,6-Pentamethylpiperidine-4-ol **(A):**

2,2,6,6-Tetramethylpiperidine-4-ol (1.5 g) was mixed with 2 mL of formalin (37 % formaldehyde) solution and 0.5 mL of formic acid and refluxed for 7 h. The solution was poured in to ice and the solution was made basic with KOH and extracted with diethyl ether to afford the required 1,2,2,6,6-pentamethylpiperidine-4-ol (**A**) in 85 % yield.

^{1}H NMR (500 MHz, $CDCl_3$) □: 1.01 (6 H, s), 1.15 (6 H, s), 1.36 (dd, 2 H), 1.83 (d, 2 H), 2.22 (3 H, s) 3.91 (1 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) □: 20.54, 28.04, 33.28, 50.06, 55.34, 63.91. GC-MS (m/z): 171 (M^+, 10 %), 156 (M-15, 100 %).

Mono-benzyl-phthalate **(B):**

A solution containing 10 mmol of benzylalcohol and phthalicanhydride in 10 mL of pyridine and 50 mL of benzene was heated at 100 ^{o}C for 2 h. The reaction mixture was cooled and poured in to ice-water mixture, acidified with conc. HCl and extracted with $CHCl_3$ and washed with 5% aqueous sodium carbonate solution. The aqueous solution was further acidified with conc. HCl and extracted with $CHCl_3$ to afford the required mono-benzyl-phthalate in quantitative yield.

^{1}H NMR (500 MHz, $CDCl_3$) □: 5.37 (2 H, s), 7.29 – 7.9 (9 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) □: 67.9, 128.45, 128.56, 128.63, 128.87, 129.9, 129.97, 130.94, 132.36, 133.24, 135.24, 167.95, 172.32.

Benzyl-4-(1,2,2,6,6-pentamethylpiperidinyl) phthalate **(C):** Mono-benzyl-phthalate (0.68 g) was mixed with 1,2,2,6,6-pentamethylpiperidine-4-ol (0.35 g) and DMAP (cat.) in dry dichloromethane (20 mL) at 0 ^{o}C. A suspension of EDCI (0.55 g) in dichloromethane was added to the above reaction mixture at 0 ^{o}C, it was allowed to warm up to rt and stirred for 15 h. The reaction mixture was diluted with chloroform, washed with water and dried over Na_2SO_4. The crude reaction mixture was purified by column chromatography to afford the product **C** in 60 % yield.

^{1}H NMR (500 MHz, $CDCl_3$) □: 1.09 (6 H, s), 1.17 (6 H, s), 1.70 (dd, 2 H), 1.94 (d, 2 H), 2.26 (3 H, s), 5.26 (1 H, m), 5.37 (2H, s), 7.36-7.73 (9 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) □: 20.71, 28.02, 33.25, 45.58, 55.34, 67.43, 69.38.

Mono-4-(1,2,2,6,6-pentamethylpiperidinyl)phthalate **(D):** The compound **C** was dissolved in THF and degassed with nitrogen for 15 min, charged with Pd-C (5 % on carbon, 10 % by weight) cautiously and purged with hydrogen gas for 1 h, Pd-C was removed by filtration over celite pad and the solution was concentrated to give the product in quantitative yield.

^{1}H NMR (500 MHz, $CDCl_3$) □: 1.38 (6 H, s), 1.56 (6 H, s), 2.26 (dd, 2 H), 2.44 (dd, 2 H), 2.68 (3 H, s), 5.34 (1 H, m), 7.36-7.77 (4 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) □: 22.72, 28.96, 41.99, 46.27, 63.59, 65.95, 129.06, 129.18, 131.53, 133.52, 134.04, 139.08, 169.14, 171.12.

4-(2,2,6,6-tetramethylpiperidine-N-oxyl)-4-(1,2,2,6,6-pentamethylpiperidinyl)phthalate **(4):** Compound **D** (0.22 g) was mixed with 4-hydroxy TEMPO (0.16 g,) and DMAP (cat.) in dry dichloromethane (15 mL) at 0 ^{o}C. A suspension of EDCI (0.19 g) in dichloromethane was added to the above reaction mixture at 0 ^{o}C and stirred at rt for 15 h, washed with water and dried over Na_2SO_4. The crude reaction mixture was purified by column chromatography to afford the product **4** in 50 % yield. FAB-MS (m/z): 473 (M+)
By comparing the EPR signal intensity (double integrating the EPR spectra) of the known concentration of the compound against a standard solution of 4-hydroxy TEMPO (1 mM in EtOH), the purity was ascertained.

^{1}H NMR (500 MHz, $CDCl_3$) □: 1.14 (6 H, s), 1.2 (3 H, s), 1.62 (2H, s), 2.0 (2H, s), 5.32 (1H, s), 7.57 (2H, s), 7.76 (2H, s).

4-(1-Methoxy-2,2,6,6-tetramethylpiperidinyl)-4-(1,2,2,6,6-pentamethylpiperidinyl)-phthalate **(5):** Compound **D** (0.3 g) was mixed with compound 1-Methoxy-2,2,6,6-tetramethylpiperidin-4-ol **(E)** (0.19 g) and DMAP (cat.) in dry dichloromethane (15 mL) at 0 ^{o}C.[6] A suspension of EDCI (0.23 g) in dichloromethane was added to the above reaction mixture at 0 ^{o}C and stirred at rt for 15 h, washed with water and dried over Na_2SO_4. The crude reaction mixture was purified by column chromatography to afford the product **5** in 37 % yield.

^{1}H NMR (500 MHz, $CDCl_3$) □: 1.14 (6 H, s), 1.2 (3 H, s), 1.14 (6 H, s), 1.23 (6 H, s), 1.24 (6 H, s), 1.63 (4H, m), 2.0 (4H, dd), 2.27 (3H, s), 3.62 (3H, s), 5.28 (2H, m), 7.52

(2H, s), 7.69 (2H, s); ^{13}C NMR (125 MHz, $CDCl_3$) □: 21.09, 21.18, 28.45, 30.11, 33.49, 33.69, 44.35, 46.16, 55.71, 60.41, 65.89, 68.55, 69.63, 76.99, 129.22, 131.21, 131.3, 133.02, 167.46

Preparation of host/guest complex: Stock solution (20 mM) of guest was prepared in $CHCl_3$. Host stock solution (5 mM) was prepared in H_2O. Required amount of guest solution in $CHCl_3$ was added in a vial and the solvent was evaporated by shaking in a mechanical shaker. Then calculated amount of host solution and water were added and shacked by the mechanical shaker for 15 h. The same procedure was adopted for all guests.

EPR study: EPR spectra were recorded at room temperature in Bruker EMX spectrometer at 9.5 GHz (X band) employing 100 KHz of field modulation frequency. Spectrometer setting: Power, 1.997 mW; amplitude modulation, 0.50 G; time constant, 163.84 ms; conversion time, 163.84 ms. Samples were loaded to quartz (CFQ) EPR tubes from Wilmad LabGlass (2 mm OD, 0.5 mm wall thickness, 10 cm height) for the EPR experiments

Protocol for NMR study: A ^{1}H NMR spectrum of 600 μL of 1 mM CB8 in D_2O was recorded. To this solution 1 equivalent of guest (10 μL of 60 mM solution of **4** in DMSO) was added. The mixture was shaken well for about 5 min and the spectra were recorded.

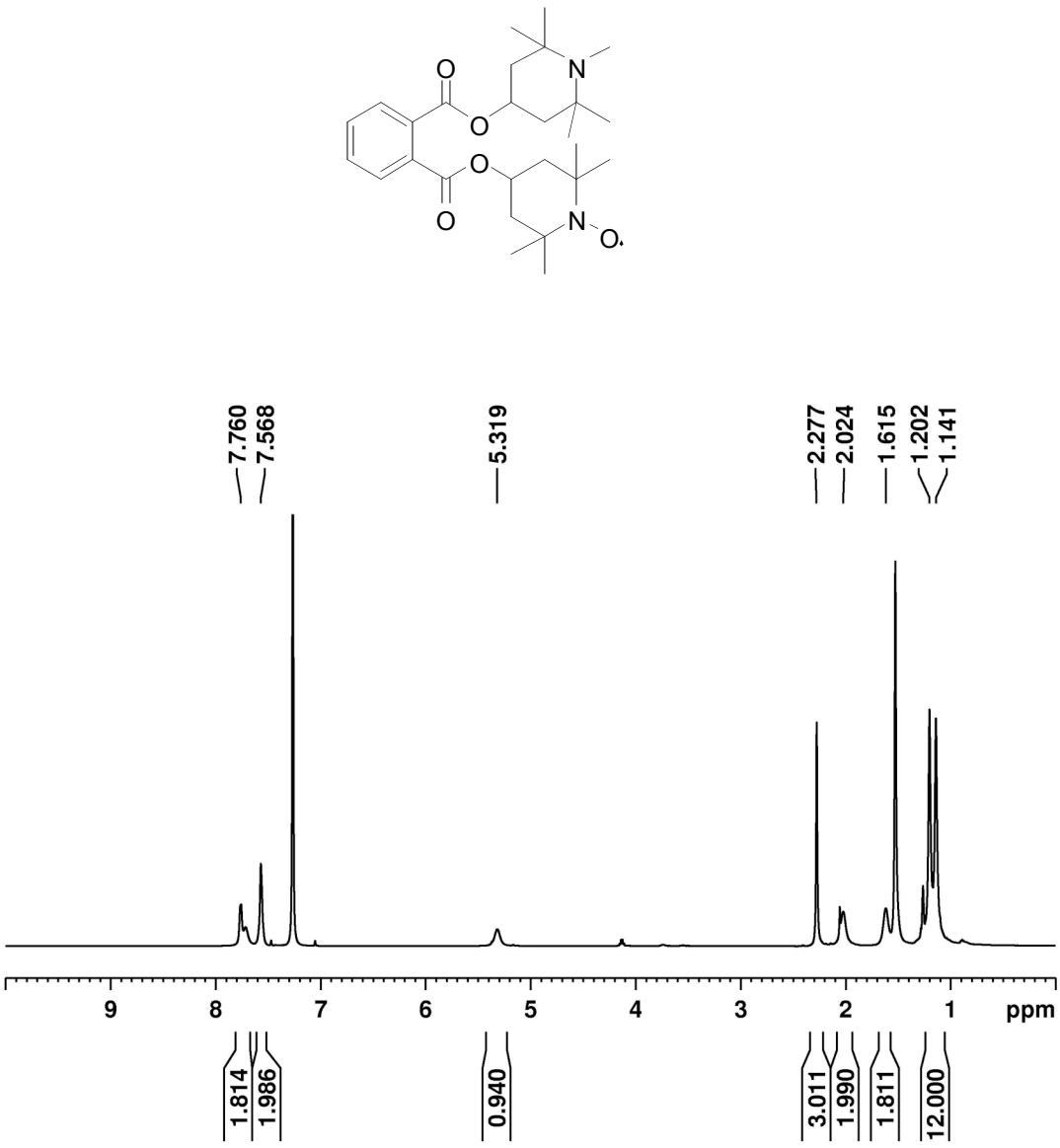


Figure S10 ^{1}H NMR of **4** in $CDCl_3$ (500 MHz)

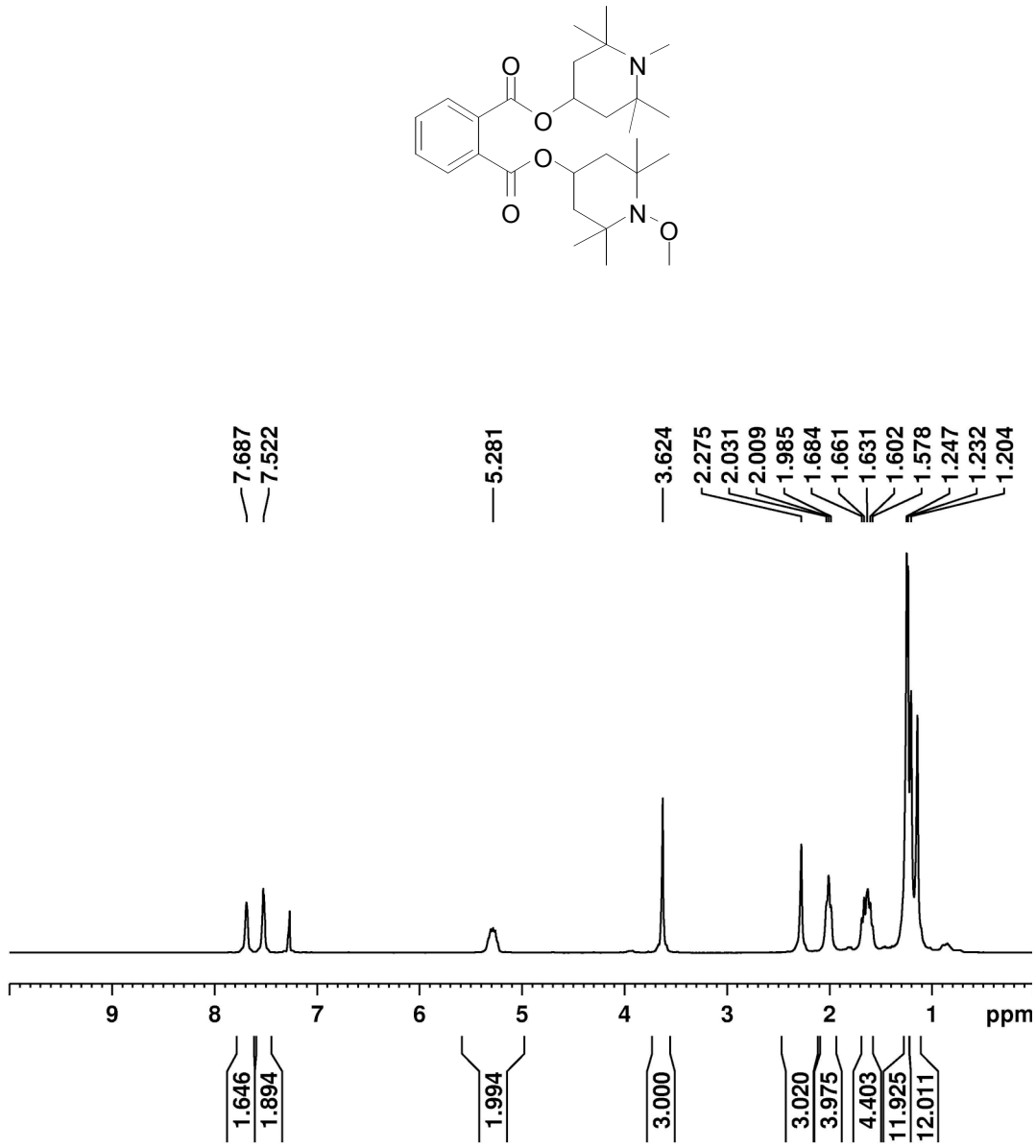


Figure S11 ^{1}H NMR of **5** in $CDCl_3$ (500 MHz)

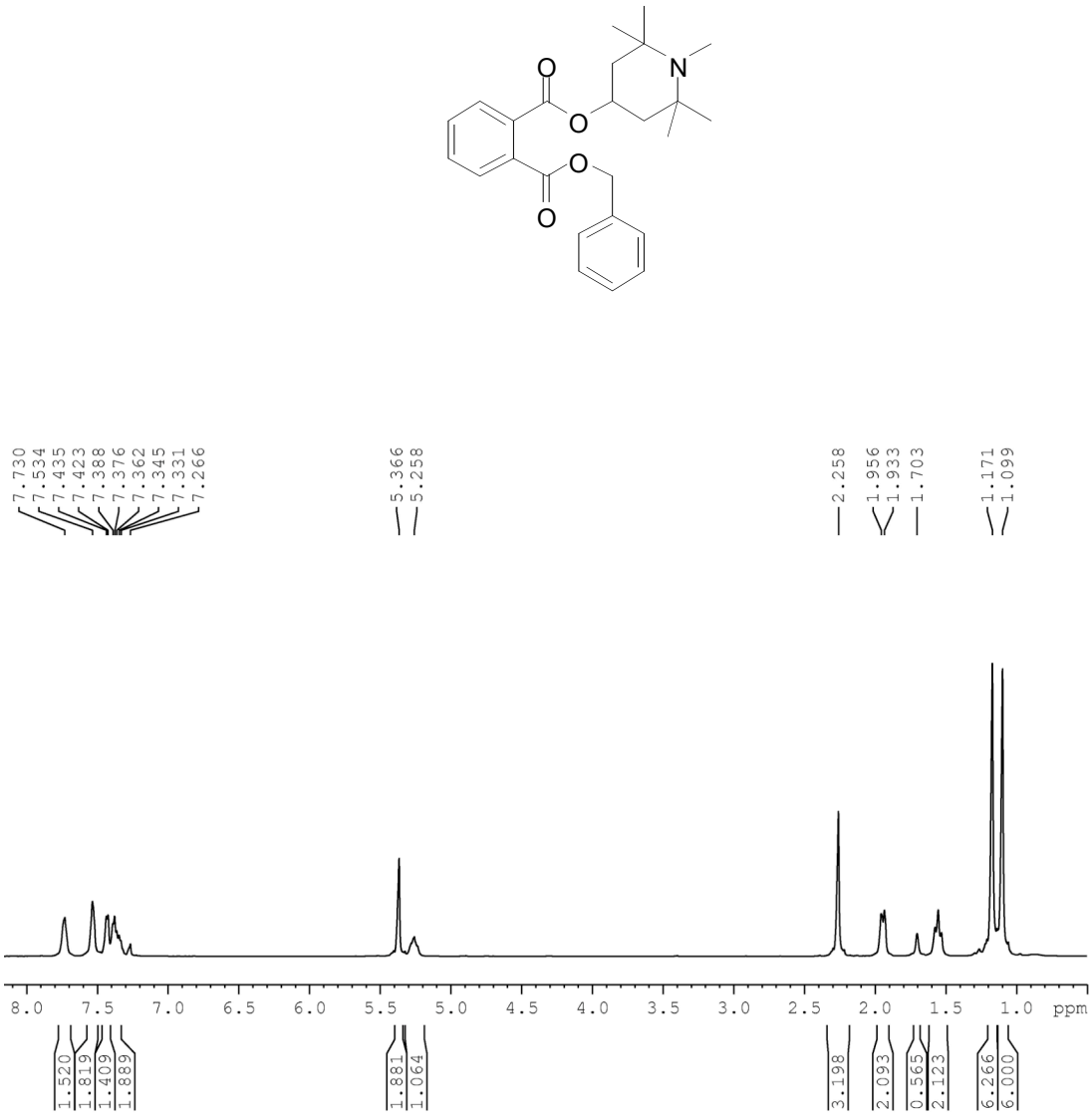


Figure S12 ^{1}H NMR of benzyl-4-(1,2,2,6,6-pentamethylpiperidinyl)phthalate (**C**) in $CDCl_3$ (500 MHz).

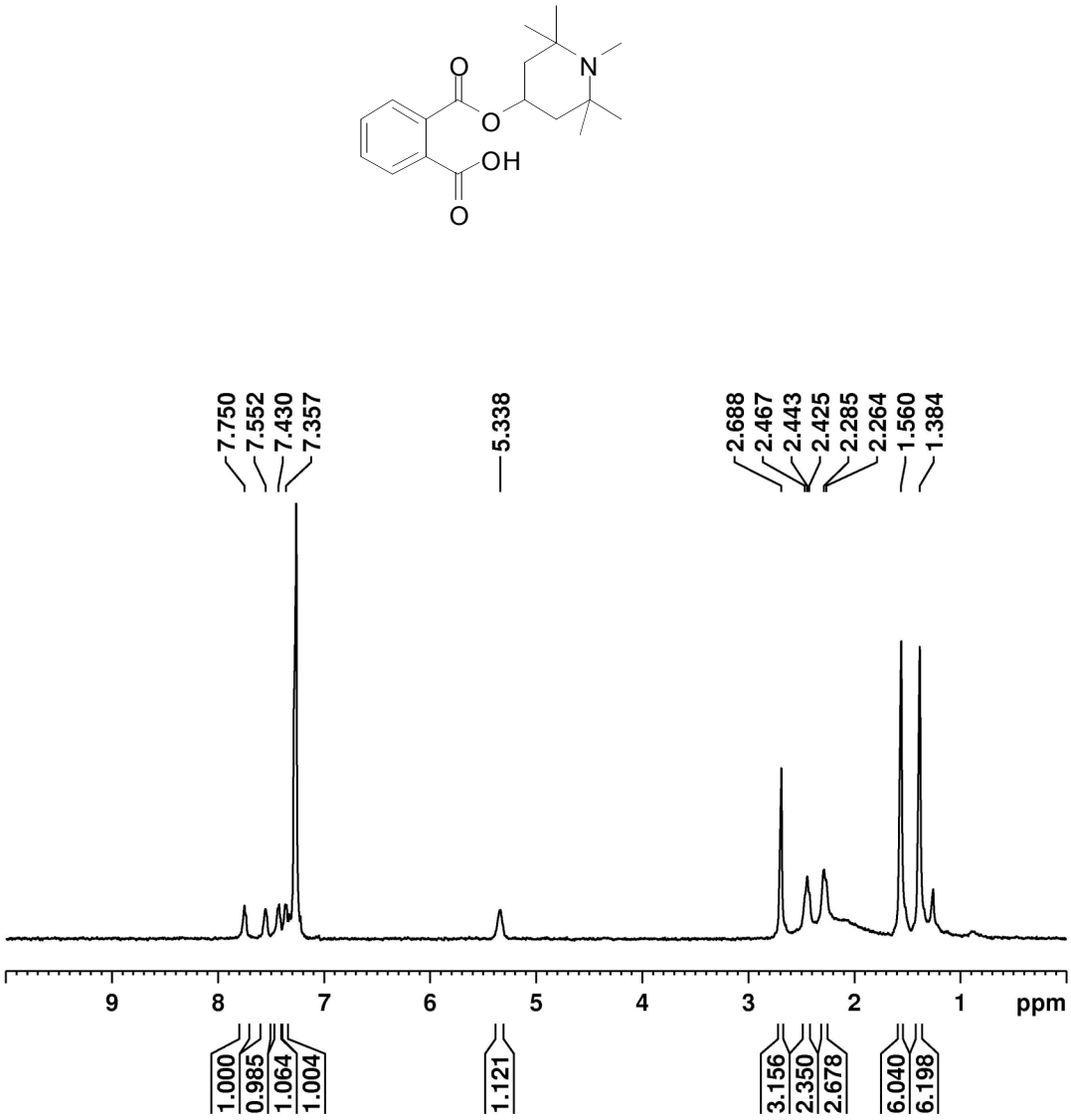


Figure S13 ^{1}H NMR of mono-4-(1,2,2,6,6-pentamethylpiperidinyl) phthalate (**D)** in $CDCl_3$ (500 MHz).

References

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