Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

Trisulfonamide Calix[6]arenes Catalysed Michael Addition to Nitroalkenes

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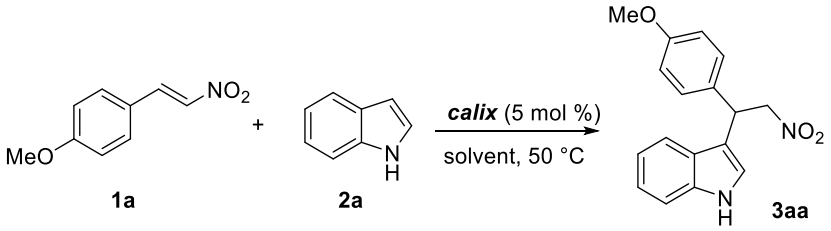
- **General Remarks and Materials**

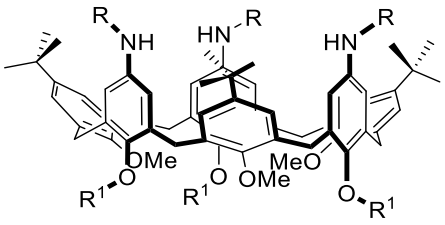
All chemicals those syntheses are not reported hereafter were purchased from commercial sources and used as received. Solvents were dried and stored over molecular sieves previously activated in an oven (450 °C overnight). Column chromatography was performed on silica gel 60 (70-230 mesh). NMR spectra were recorded on a Bruker 400 MHz and JEOL 600 MHz using solvents as internal standards (7.26 ppm for ^{1}H NMR and 77.00 ppm for ^{13}C-NMR for $CDCl_3$). The terms m, s, d, t, q and quint represent multiplet, singlet, doublet, triplet, quadruplet and quintuplet respectively, and the term br means a broad signal. TSA calixarenes **A-F** and sulfonamide **G** were synthesized according to a known procedure.[1,2] Nitroalkenes **1** and indoles **2** were purchased from commercially available sources or synthesized following common routes.[3] Single crystal data for calixarene **B** were collected at 200K with a Bruker D8 diffractometer equipped with Photon II area detector, using a CuKα microfocus radiation source (λ = 1.54184). The data collection strategy covered the sphere of reciprocal space. Absorption corrections were applied using the program SADABS.[4] The structure was solved with the SHELXT code.[5] Fourier analysis and refinement were performed by the full-matrix least-squares methods based on F2 using SHELXL-2014,[6] implemented in Olex2.[7] All the non-H atoms were refined with anisotropic displacement parameters. One of the terminal ethyl group was found disordered over two sites (0.45 and 0.55 site occupancy factors, respectively).

- **Optimisation of Reaction Conditions**

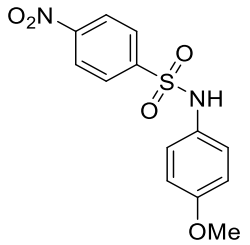


Entry[a]	*calix*	Solvent	Conv (%)	Yields (%)
1	**A**	toluene	8	6
2	**A**	$CHCl_3$	9	7
3	**A**	DMSO	--	--
4	**A**	MeOH	23	22
5	**--**	MeOH	28	26
6	**B**	MeOH	26	25
7	**C**	MeOH	28	22
8	**D**	MeOH	32	30
9	**E**	MeOH	43	42
10	**F**	MeOH	36	33
11[b]	**G**	MeOH	21	20
12[c]	**E**	MeOH	86	84 (81)
13[c]	**--**	MeOH	68	58
14[c]	**--**	*t*-BuOH	36	31
15[c]	**E**	*t*-BuOH	25	20
16[c]	**E**	H_2O	85	82

a) Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), ***calix*** (5 mol %), solvent (0.5 ml, 0.2 M), 50 °C, 24 hs. Yields calculated by ^{1}H-NMR integration using 1,3,5-trimethoxybenzene as internal standard. b) **G** (15 mol%) was employed. c) **2a** (0.3 mmol), solvent (0.25 ml, 0.4 M). In brackets, isolated yields.



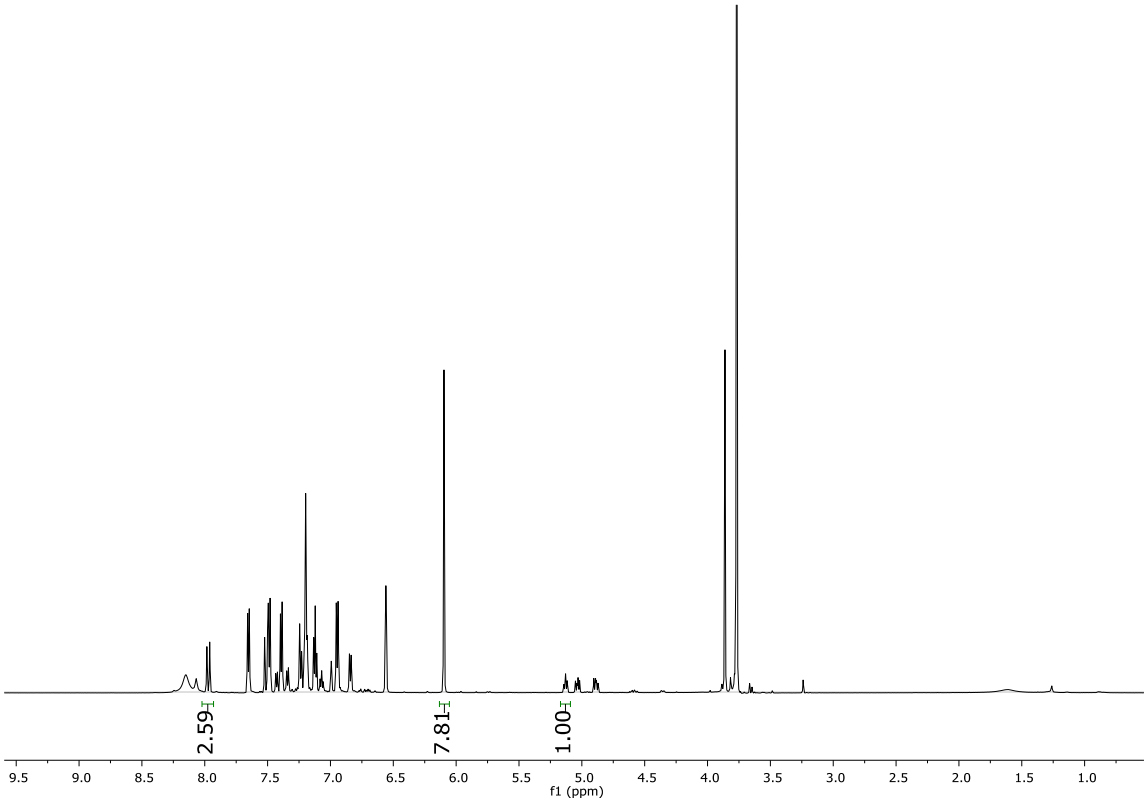
R = 4-$MeC_6H_4SO_2$ R^1 = *n*-Oct (**A**)
R = 4-$MeC_6H_4SO_2$ R^1 = $(CH_2)_2OEt$ (**B**)
R = 4-$MeOC_6H_4SO_2$ R^1 = *n*-Oct (**C**)
R = 4-$ClC_6H_4SO_2$ R^1 = *n*-Oct (**D**)
R = 4-$NO_2C_6H_4SO_2$ R^1 = *n*-Oct (**E**)
R = $C_6H_5NH(CO)$ R^1 = *n*-Oct (**F**)



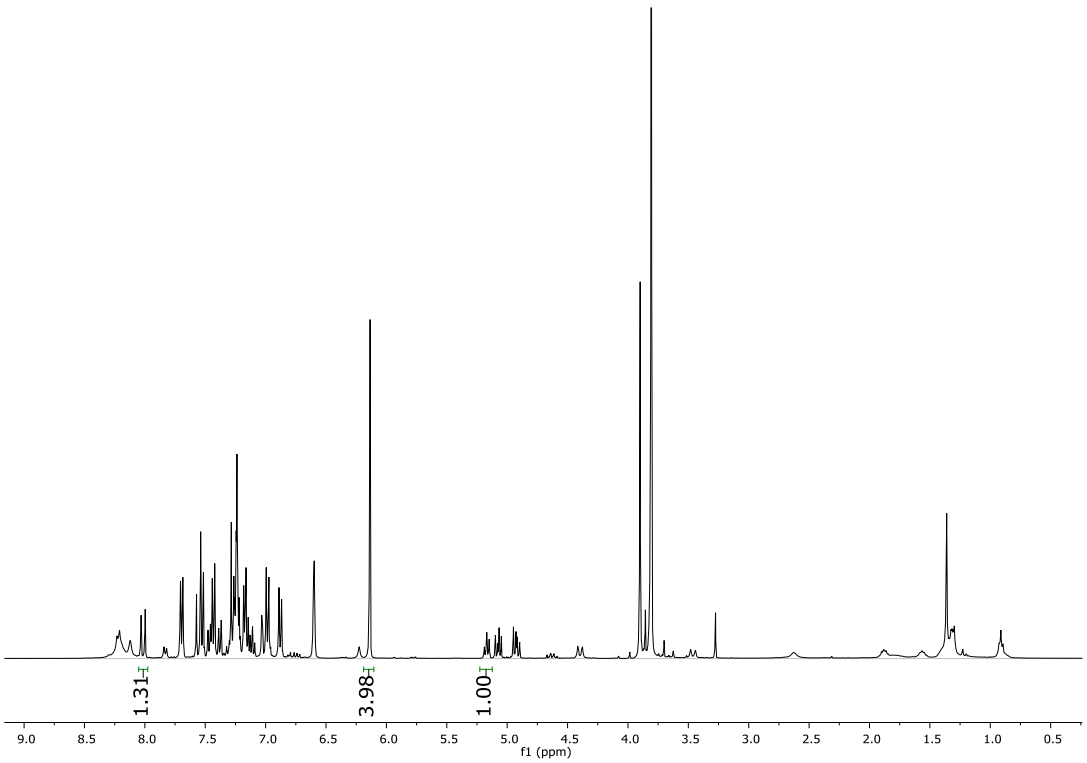
(**G**)

- **Key NMR Entries**

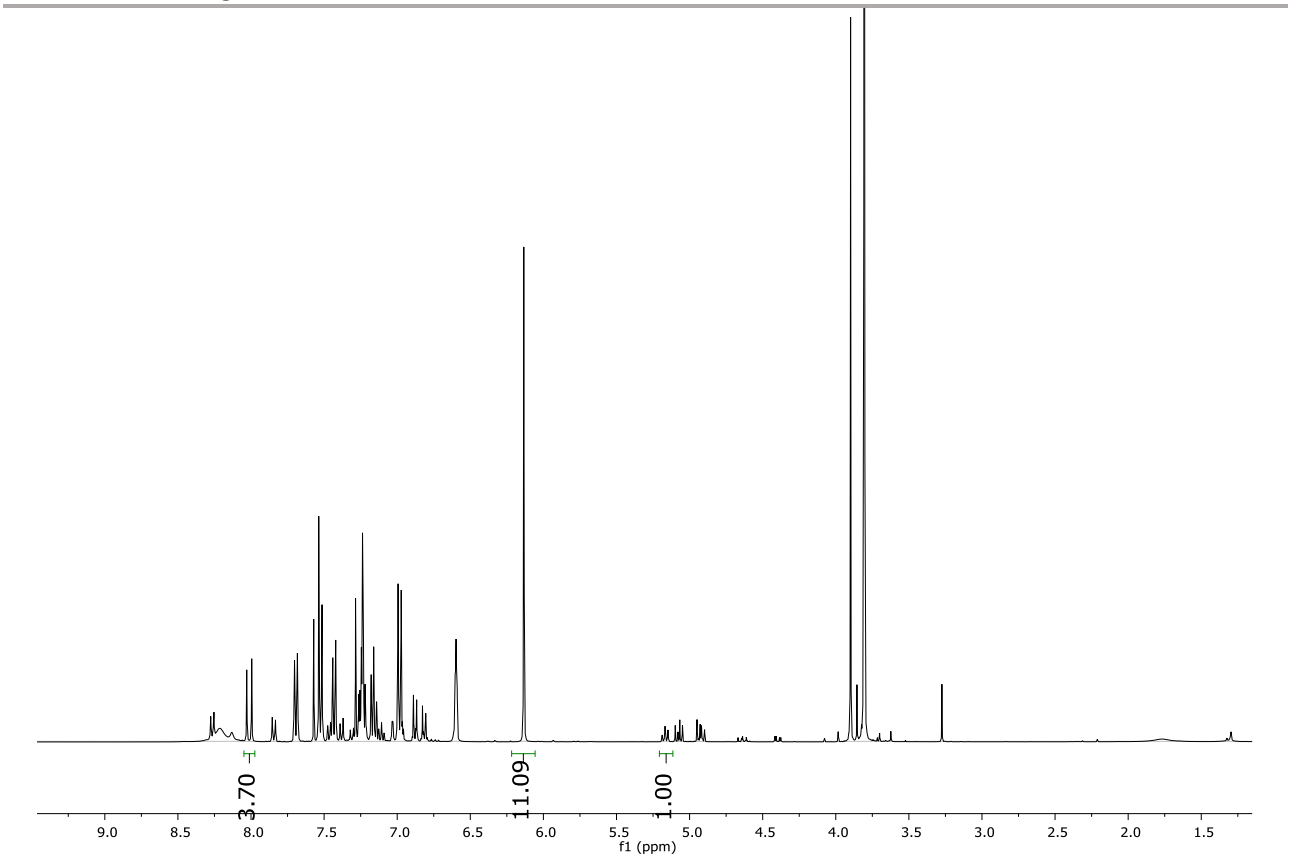
Entry 5. Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), MeOH (0.5 ml, 0.2 M), 50 °C, 24 hs. I.S. 11.6 mg



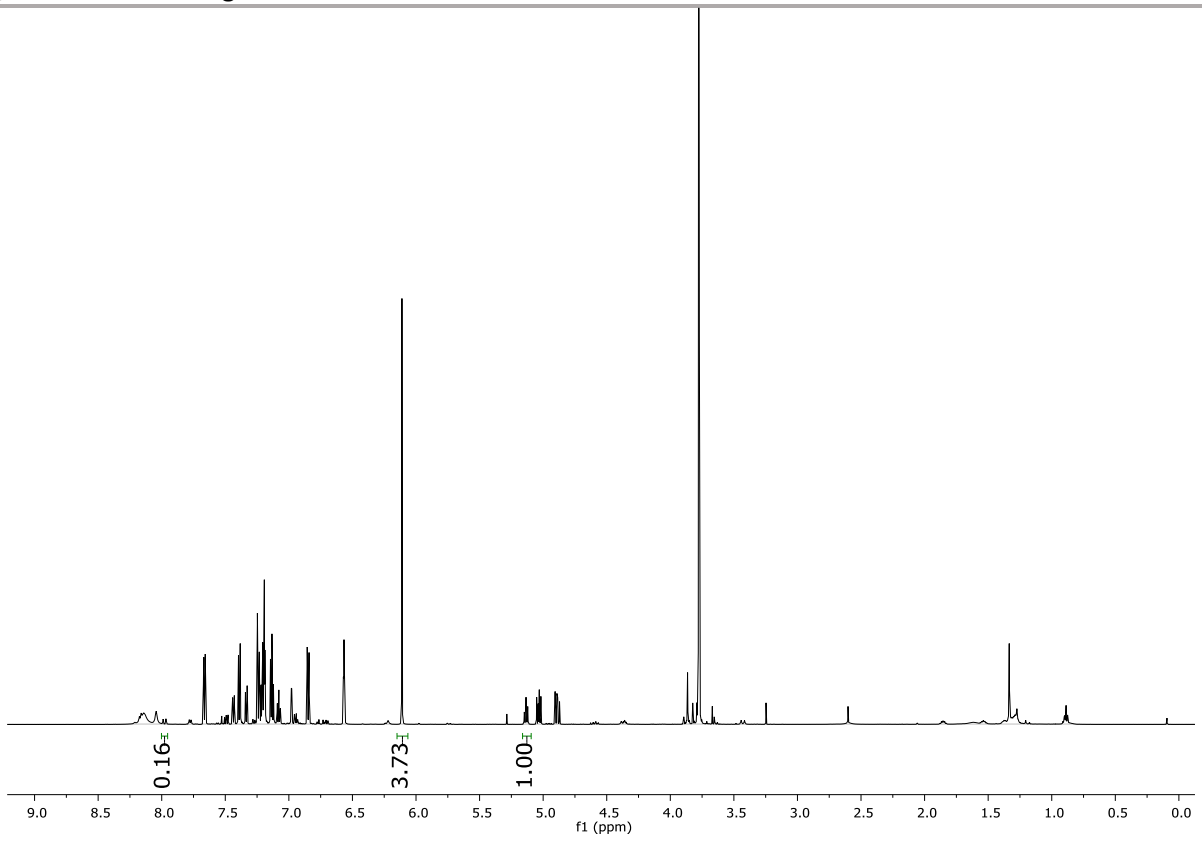
Entry 9. Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), **TSA E** (5 mol %), MeOH (0.5 ml, 0.2 M), 50 °C, 24 hs. I.S. 9.4 mg



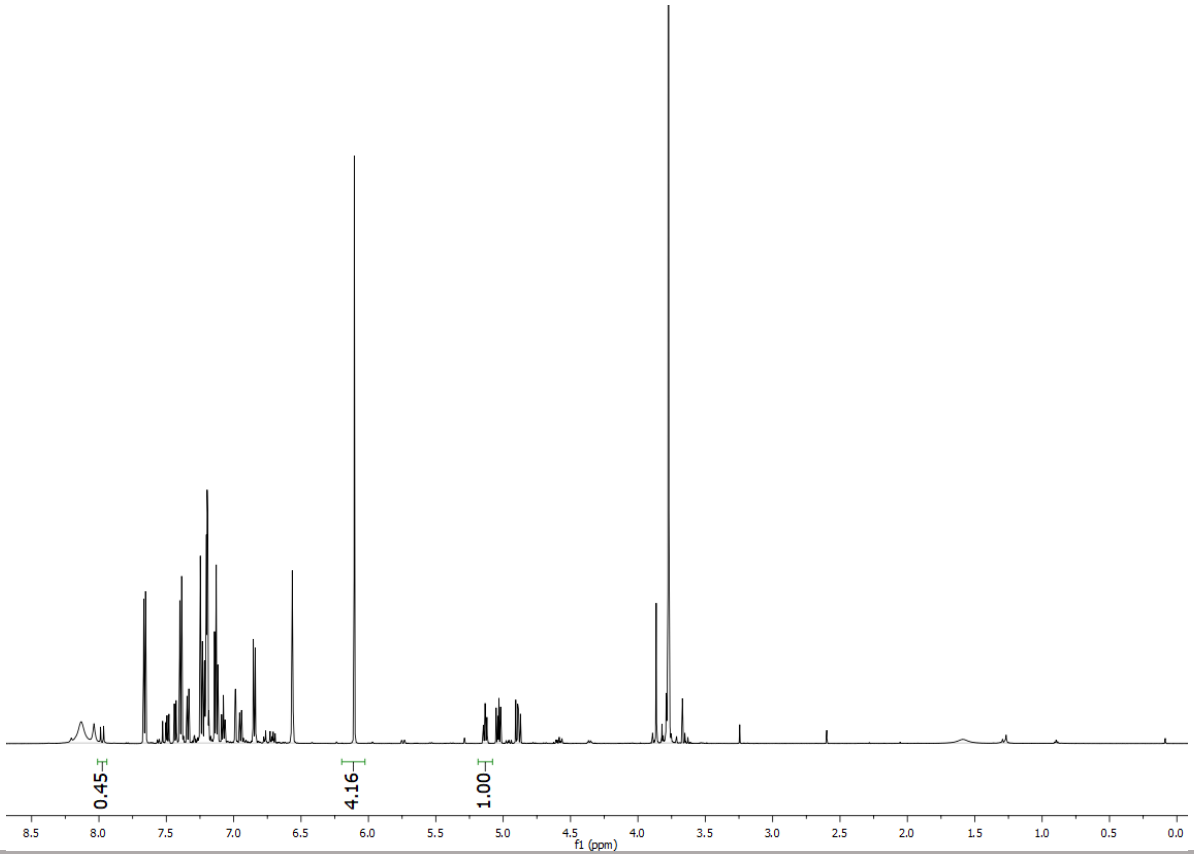
Entry 11. Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), **G** (15 mol %), MeOH (0.5 ml, 0.2 M), 50 °C, 24 hs. I.S. 12.3 mg



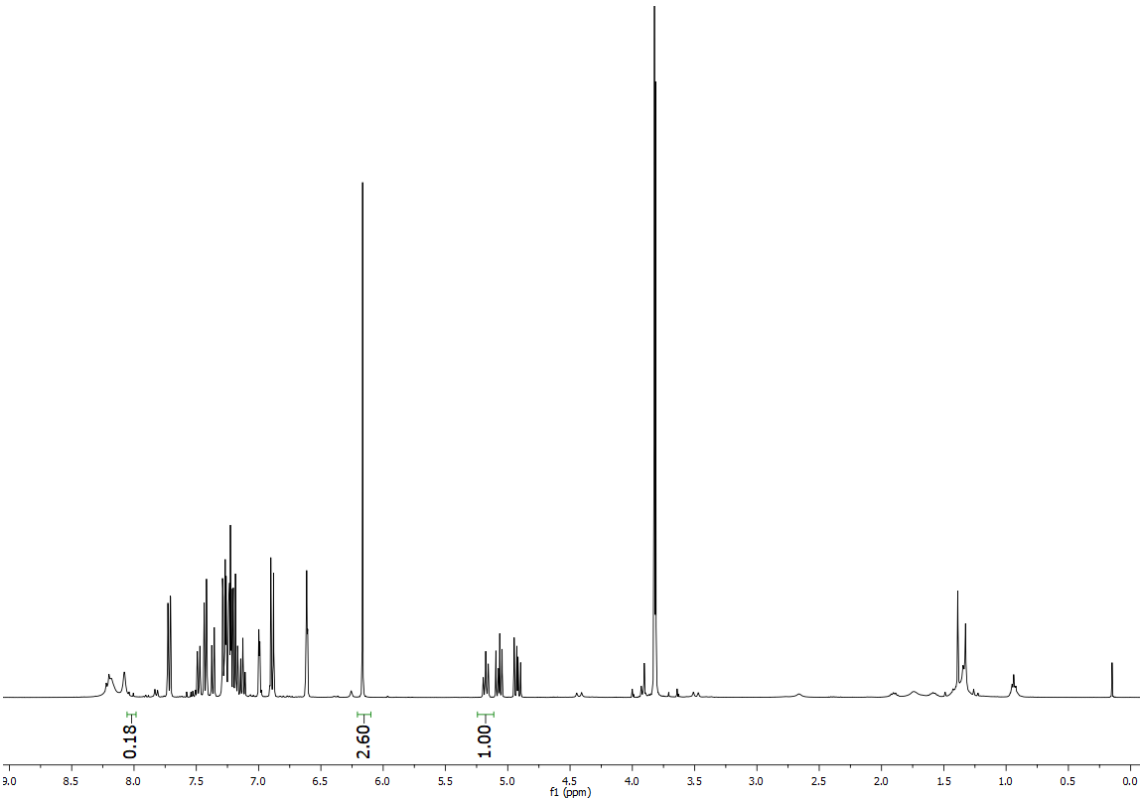
Entry 12. Reaction conditions: **1a** (0.1 mmol), **2a** (0.3 mmol), **TSA E** (5 mol %), MeOH (0.25 ml, 0.4 M), 50 °C, 24 hs. I.S. 17.6 mg



Entry 13. Reaction conditions: **1a** (0.1 mmol), **2a** (0.3 mmol), MeOH (0.25 ml, 0.4 M), 50 °C, 24 hs. I.S. 13.7 mg



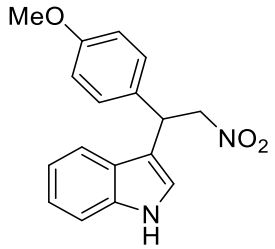
Entry 16. Reaction conditions: **1a** (0.1 mmol), **2a** (0.3 mmol), H_2O (0.25 ml, 0.4 M), 50 °C, 24 hs. I.S. 12.0 mg



- **General Procedure and Characterization Data for Compounds 3**

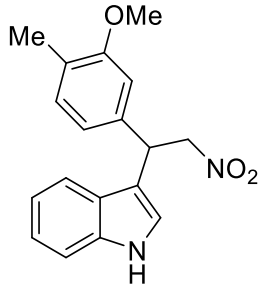
In a glass tube, **1** (0.1 mmol), **2** (0.3 mmol), and **E** (8.9 mg, 5 mol %) were subsequently added. Reagent grade MeOH (0.25 ml, 0.4 M) was added and the reaction placed in a pre-heated oil bath at 50 °C. After 24 hs the reaction mixture was cooled down at room temperature and CH_2Cl_2 (10 ml) was added. The mixture was concentrated under reduced pressure and the crude purified by column chromatography on silica gel.

3-(1-(4-methoxyphenyl)-2-nitroethyl)-1*H*-indole (3aa)[8]



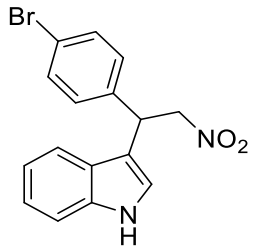
General procedure was followed using **1a** (0.1 mmol, 17.9 mg). Purification by column chromatography (*n*-Hex/EtOAc 95:5) yielded **3aa** (24.0 mg, 81%) as an off-white solid. **M. p.** = 154-157 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.11 (s, 1H), 7.46 (d, *J* = 8.1 Hz, 1H), 7.39 (d, *J* = 8.1 Hz, 1H), 7.27 (d, *J* = 8.6 Hz, 2H), 7.23 (t, *J* = 7.2 Hz, 1H), 7.10 (t, *J* = 7.6 Hz, 1H), 7.05 (d, *J* = 2.2 Hz, 1H), 6.92 – 6.84 (m, 2H), 5.17 (t, *J* = 7.9 Hz, 1H), 5.08 (dd, *J* = 12.2, 7.9 Hz, 1H), 4.92 (dd, *J* = 12.2, 7.9 Hz, 1H), 3.80 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 158.9 (C_q), 136.5 (C_q), 131.2 (C_q), 128.9 (CH), 126.1 (C_q), 122.7 (CH), 121.5 (CH), 120.0 (CH), 119.0 (CH), 114.8 (C_q), 114.3 (CH), 111.4 (CH), 79.8 (CH_2), 55.3 (CH_3), 40.9 (CH). **ESI-MS:** *m/z* $[M+H]^+$ calcd. for $C_{17}H_{17}N_2O_3$: 297.12; found: 297.10.

3-(1-(3-methoxy-4-methylphenyl)-2-nitroethyl)-1H-indole (3ba)



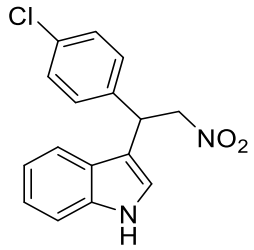
General procedure was followed using **1b** (0.1 mmol, 19.3 mg). Purification by column chromatography (*n*-Hex/EtOAc 95:5) yielded **3ba** (23.8 mg, 77%) as a yellow wax. **^{1}H NMR** (600 MHz, CD_2Cl_2) δ = 8.22 (s, 1H), 7.46 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.35 (dt, *J* = 8.3, 0.8 Hz, 1H), 7.18 – 7.15 (m, 1H), 7.08 – 7.02 (m, 3H), 6.82 (d, *J* = 1.7 Hz, 1H), 6.80 (s, 1H), 5.12 (t, *J* = 8.0 Hz, 1H), 5.06 (dd, *J* = 12.3, 8.0 Hz, 1H), 4.95 (dd, *J* = 12.3, 8.0 Hz, 1H), 3.75 (s, 3H), 2.14 (s, 3H). **^{13}C NMR** (150 MHz, CD_2Cl_2) δ = 158.1 (C_q), 138.4 (C_q), 136.6 (C_q), 130.8 (CH), 126.2 (C_q), 125.9 (C_q), 122.6 (CH), 121.6 (CH), 119.8 (CH), 119.2 (CH), 118.8 (CH), 114.6 (C_q), 111.4 (CH), 109.8 (CH), 79.7 (CH_2), 55.3 (CH_3), 41.6 (CH), 15.6 (CH_3). **ESI-MS**: *m/z* $[M+H]^+$ calcd. for $C_{18}H_{19}N_2O_3$: 311.14; found: 311.19. **HR-MS**: *m/z* $[M+Na]^+$ calcd. for $C_{18}H_{18}N_2NaO_3$: 333.1215, found: 333.1230.

3-(1-(4-bromophenyl)-2-nitroethyl)-1*H*-indole (3ca)[8]



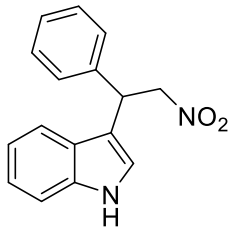
General procedure was followed using **1c** (0.1 mmol, 22.7 mg). Purification by column chromatography (*n*-Hex/EtOAc 95:5) yielded **3ba** (27.1 mg, 79%) as an off-white solid. **M. p.** = 121-123 °C. **^{1}H NMR** (400 MHz, CD_2Cl_2) δ = 8.32 (s, 1H), 7.54 – 7.48 (m, 2H), 7.43 (dd, *J* = 7.5, 3.2 Hz, 2H), 7.31 – 7.26 (m, 2H), 7.26 – 7.20 (m, 1H), 7.14 – 7.07 (m, 2H), 5.25 – 5.17 (m, 1H), 5.12 (dd, *J* = 12.3, 7.4 Hz, 1H), 4.98 (dd, *J* = 12.3, 8.4 Hz, 1H). **^{13}C NMR** (101 MHz, CD_2Cl_2) δ = 138.7 (C_q), 136.5 (C_q), 131.9 (CH), 129.6 (CH), 125.9 (C_q), 122.7 (CH), 121.6 (CH), 121.3 (C_q), 119.9 (CH), 118.7 (CH), 113.7 (C_q), 111.5 (CH), 79.3 (CH_2), 41.0 (CH). **ESI-MS**: *m/z* $[M+H]^+$ calcd. for $C_{16}H_{14}BrN_2O_2$: 345.02; found: 345.04.

3-(1-(4-chlorophenyl)-2-nitroethyl)-1*H*-indole (3da)[8]



General procedure was followed using **1d** (0.1 mmol, 18.3 mg). Purification by column chromatography (*n*-Hex/EtOAc 95:5) yielded **3ba** (24.9 mg, 83%) as an off-white solid. **M. p.** = 107-110 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.15 (s, 1H), 7.43 (d, *J* = 8.3 Hz, 1H), 7.40 (d, *J* = 8.1 Hz, 1H), 7.34 – 7.29 (m, 3H), 7.28 (s, 1H), 7.24 (t, *J* = 7.1 Hz, 1H), 7.14 – 7.09 (m, 1H), 7.05 (d, *J* = 2.0 Hz, 1H), 5.20 (t, *J* = 7.9 Hz, 1H), 5.08 (dd, *J* = 12.5, 7.9 Hz, 1H), 4.94 (dd, *J* = 12.6, 7.9 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 137.7 (C_q), 136.5 (C_q), 133.5 (C_q), 129.2 (CH), 129.1 (CH), 125.9 (C_q), 122.9 (CH), 121.5 (CH), 120.1 (CH), 118.9 (CH), 114.0 (C_q), 111.5 (CH), 79.3 (CH_2), 41.0 (CH). **ESI-MS**: *m/z* $[M+H]^+$ calcd. for $C_{16}H_{14}ClN_2O_2$: 301.07; found: 301.06.

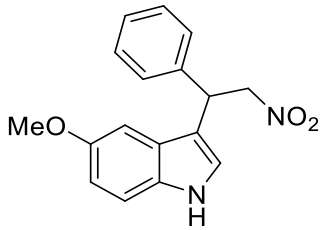
3-(2-nitro-1-phenylethyl)-1*H*-indole (3ea)[8]



General procedure was followed using **1e** (0.1 mmol, 14.9 mg). Purification by column chromatography (*n*-Hex/EtOAc 95:5) yielded **3ca** (21.4 mg, 80%) as an off-white solid. **M. p.** = 98-100 °C. **^{1}H NMR** (400 MHz, $CDCl_3$)

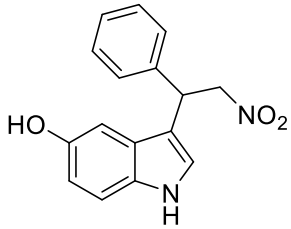
δ = 8.09 (s, 1H), 7.49 (d, *J* = 7.8 Hz, 1H), 7.40 – 7.35 (m, 5H), 7.33 – 7.28 (m, 1H), 7.28 – 7.21 (m, 1H), 7.17 – 7.09 (m, 1H), 7.02 (d, *J* = 2.0 Hz, 1H), 5.23 (t, *J* = 8.1 Hz, 1H), 5.10 (dd, *J* = 12.5, 8.1 Hz, 1H), 4.97 (dd, *J* = 12.5, 8.1 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 139.2 (C_q), 136.5 (C_q), 129.0 (CH), 127.8 (CH), 127.6 (CH), 126.1 (C_q), 122.7 (CH), 121.7 (CH), 120.0 (CH), 119.0 (CH), 114.4 (C_q), 111.5 (CH), 79.6 (CH_2), 41.6 (CH). **ESI-MS**: *m/z* $[M+H]^+$ calcd. for $C_{16}H_{15}N_2O_2$: 267.11; found: 267.13. *With H_2O*: General procedure was followed using **1e** (0.1 mmol, 14.9 mg) and H_2O (0.25 ml) as the solvent. Purification by column chromatography (*n*-Hex/EtOAc 95:5) yielded **3ca** (22.8 mg, 84 %) as an off-white solid.

5-methoxy-3-(2-nitro-1-phenylethyl)-1*H*-indole (3eb)[8]



General procedure was followed using **1e** (0.1 mmol, 14.9 mg). Purification by column chromatography (*n*-Hex/EtOAc 95:5) yielded **3cb** (25.9 mg, 88%) as a yellow solid. **M. p.** = 136-139 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.03 (s, 1H), 7.39 – 7.34 (m, 4H), 7.31 – 7.24 (m, 2H), 7.04 (d, *J* = 2.4 Hz, 1H), 6.90 – 6.85 (m, 2H), 5.17 (t, *J* = 7.9 Hz, 1H), 5.08 (dd, *J* = 12.2, 7.9 Hz, 1H), 4.96 (dd, *J* = 12.5, 7.9 Hz, 1H), 3.80 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 154.2 (C_q), 139.1 (C_q), 131.6 (C_q), 129.0 (CH), 127.8 (CH), 127.6 (CH), 126.6 (C_q), 122.3 (CH), 114.1 (C_q), 112.8 (CH), 112.1 (CH), 100.8 (CH), 79.5 (CH_2), 55.9 (CH_3), 41.5 (CH). **ESI-MS**: *m/z* $[M+H]^+$ calcd. for $C_{17}H_{17}N_2O_3$: 297.12; found: 297.15.

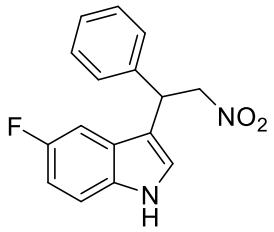
3-(2-nitro-1-phenylethyl)-1*H*-indol-5-ol (3ec)[9]



General procedure was followed using **1e** (0.1 mmol, 14.9 mg). Purification by column chromatography (*n*-Hex/EtOAc 95:5) yielded **3cc** (25.6 mg, 91%) as a yellow solid. **M. p.** = 122-124 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.03 (s, 1H), 7.38 – 7.26 (m, 5H), 7.23 (d, *J* = 8.8 Hz, 1H), 7.04 (d, *J* = 2.2 Hz, 1H), 6.83 (d, *J* = 2.2 Hz, 1H), 6.79 (dd, *J* = 8.7, 2.3 Hz, 1H), 5.11 (t, *J* = 7.8 Hz, 1H), 5.05 (dd, *J* = 12.2, 7.6 Hz, 1H), 4.93 (dd, *J* = 12.1, 7.9 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 149.6 (C_q), 139.1 (C_q), 131.8 (C_q), 129.0 (CH), 127.8 (CH), 127.6 (CH), 126.9 (C_q), 122.6 (CH), 113.8 (C_q), 112.6 (CH), 112.1 (CH), 103.5 (CH), 79.5 (CH_2), 41.6 (CH). **ESI-MS**: *m/z* $[M+H]^+$ calcd. for $C_{16}H_{15}N_2O_3$: 283.11; found: 283.08. *With H_2O*: General procedure was followed using **1e** (0.1 mmol,

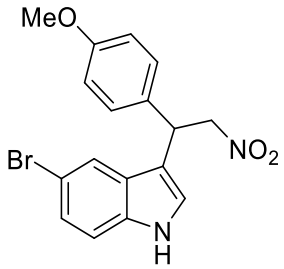
14.9 mg) and H_2O (0.25 ml) as the solvent. Purification by column chromatography (*n*-Hex/EtOAc 95:5) yielded **3ca** (24.9 mg, 88 %) as an off-white solid.

5-fluoro-3-(2-nitro-1-phenylethyl)-1H-indole (3ed)[9]



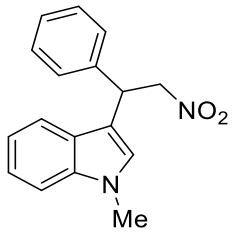
General procedure was followed using **1c** (0.1 mmol, 14.9 mg). Purification by column chromatography (*n*-Hex/EtOAc 95:5) yielded **3ce** (15.1 mg, 53%) as a yellow wax. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.15 (s, 1H), 7.40 – 7.24 (m, 6H), 7.12 (d, *J* = 2.4 Hz, 1H), 7.07 (dd, *J* = 9.5, 2.4 Hz, 1H), 6.96 (td, *J* = 9.0, 2.3 Hz, 1H), 5.14 (t, *J* = 7.9 Hz, 1H), 5.06 (dd, *J* = 12.2, 7.9 Hz, 1H), 4.95 (dd, *J* = 12.3, 7.9 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 157.8 (d, $^1J_{C\text{-}F}$ = 237 Hz, C_q) 138.9 (C_q), 133.0 (C_q), 129.1 (CH), 127.8 (CH), 127.7 (CH), 126.5 (d, $^5J_{C\text{-}F}$ = 9 Hz, C_q), 123.2 (CH), 114.5 (d, $^6J_{C\text{-}F}$ = 5 Hz, C_q), 112.2 (d, $^4J_{C\text{-}F}$ = 9 Hz, CH), 111.2 (d, $^2J_{C\text{-}F}$ = 26 Hz, CH), 104.0 (d, $^3J_{C\text{-}F}$ = 24 Hz, CH), 79.5 (CH_2), 41.5 (CH). **ESI-MS**: *m/z* $[M+H]^+$ calcd. for $C_{16}H_{14}FN_2O_2$: 285.10; found: 285.07.

5-bromo-3-(1-(4-methoxyphenyl)-2-nitroethyl)-1H-indole (3ae)



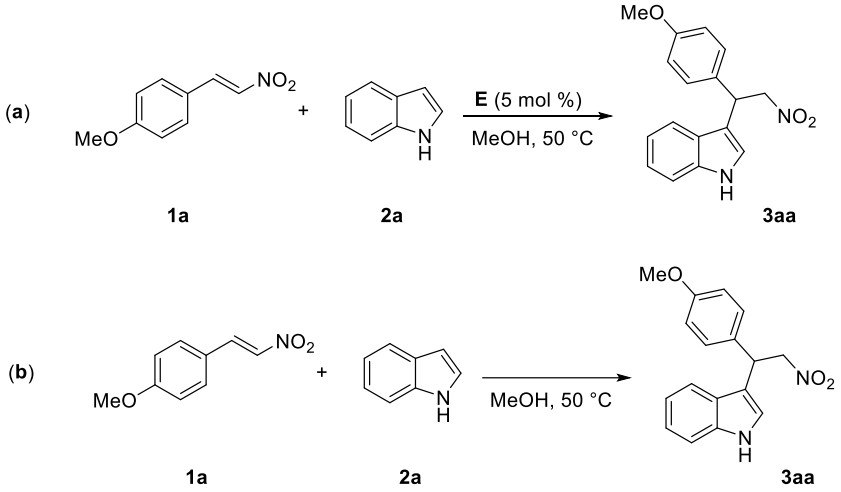
General procedure was followed using **1a** (0.1 mmol, 17.9 mg). Purification by column chromatography (*n*-Hex/EtOAc 95:5) yielded **3af** (21.3 mg, 57%) as a white solid. **M. p.** = 145-148 °C. **^{1}H NMR** (600 MHz, CD_2Cl_2) δ = 8.32 (s, 1H), 7.53 – 7.51 (m, 1H), 7.25 (dd, *J* = 3.0, 1.2 Hz, 2H), 7.22 – 7.18 (m, 1H), 7.10 (d, J = 2.1 Hz, 1H), 6.87 – 6.81 (m, 2H), 5.05 – 5.02 (m, 1H), 5.02 – 4.98 (m, 1H), 4.88 (dd, *J* = 11.6, 7.5 Hz, 1H), 3.74 (s, 3H). **^{13}C NMR** (151 MHz, CD_2Cl_2) δ = 159.2 (C_q), 135.2 (C_q), 130.9 (C_q), 128.8 (CH), 127.9 (C_q), 125.5 (CH), 122.8 (CH), 121.4 (CH), 114.4 (C_q), 114.3 (CH), 113.0 (CH), 112.9 (C_q), 79.7 (CH_2), 55.3 (CH_3), 40.6 (CH). **ESI-MS**: *m/z* $[M+H]^+$ calcd. for $C_{17}H_{16}BrN_2O_3$: 375.03; found: 375.07. **HR-MS**: *m/z* $[M+Na]^+$ calcd. for $C_{17}H_{16}BrN_2NaO_3$: 397.0164, found: 397.0182.

1-methyl-3-(2-nitro-1-phenylethyl)-1*H*-indole (3ef)[8]



General procedure was followed using **1e** (0.1 mmol, 14.9 mg). Purification by column chromatography (*n*-Hex/EtOAc 95:5) yielded **3cg** (24.1 mg, 86%) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.49 (d, *J* = 7.8 Hz, 1H), 7.40 – 7.33 (m, 4H), 7.32 – 7.23 (m, 3H), 7.11 (t, *J* = 7.5 Hz, 1H), 6.89 (s, 1H), 5.22 (t, *J* = 8.1 Hz, 1H), 5.08 (dd, *J* = 12.6, 8.1 Hz, 1H), 4.97 (dd, *J* = 12.5, 8.1 Hz, 1H), 3.78 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 139.4 (C_q), 137.2 (C_q), 129.0 (CH), 127.8 (CH), 127.6 (CH), 126.5 (C_q), 126.4 (CH), 122.3 (CH), 119.5 (CH), 119.0 (CH), 112.8 (C_q), 109.6 (CH), 79.6 (CH_2), 41.5 (CH), 32.9 (CH_3). **ESI-MS**: *m/z* $[M+H]^+$ calcd. for $C_{17}H_{17}N_2O_2$: 281.13; found: 281.14.

- **Kinetic profile of Michael addition to nitroolefin 1a.**



Experiments were performed running five parallel independent reactions. In five oven dried tubes, **1a** (17.9 mg, 0.1 mmol), **2a** (35.1 mg, 0.3 mmol), and **E** (8.9 mg, 5 mol %, **a**) (or no additive, **b**) were subsequently added. Reagent grade MeOH (0.5 ml) was added and the reaction placed in a pre-heated oil bath at 50 °C. After 30, 60, 90, 120 and 150 minutes, respectively, each reaction mixture was cooled down at room temperature and diluted with CH_2Cl_2 (10 ml). Sequentially, each mixture was concentrated under reduced pressure and the resulting crude was eventually analysed by ^{1}H-NMR spectroscopy using 1,3,5-trimethoxybenzene as the internal standard.

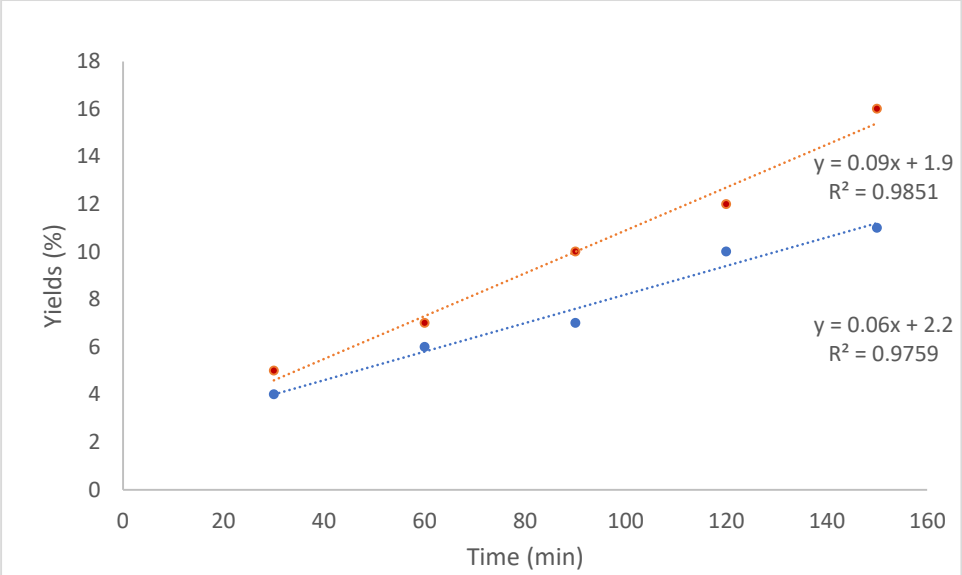
(**a**)

Entry	time (min)	I.S. (mg)	**3a**/ I.S.	Yields (%)
1	30	10.0	1/12.0	5
2	60	9.5	1/8.1	7
3	90	9.8	1/5.6	10
4	120	10.1	1/4.8	14
5	150	10.3	1/3.8	16

(**b**)

Entry	time (min)	I.S. (mg)	**3a**/ I.S.	Yields (%)
1	30	10.0	1/18.2	3
2	60	10.2	1/13.9	4
3	90	11.1	1/10.8	6
4	120	9.8	1/9.4	7
5	150	10.0	1/5.9	10

Kinetic profile of parallel reactions (MeOH, 0.02 M) in the presence of E (red line) and without E (blue line)



- **Experimental Mechanistic studies**

Figure S1. ^{1}H-NMR ($CDCl_3$, 400 MHz) of the reaction outcome w/wo MeOH

Two independent reactions were performed as follows:

1) in a glass tube, **1a** (27 mg, 0.15 mmol), **2a** (52 mg, 0.45 mmol), and **E** (13 mg, 0.0075 mmol, 5 mol %) were subsequently added. Reagent grade toluene (350 µl, 0.4 M) was added and the reaction placed in a pre-heated oil bath at 50 °C. After 1 h, an aliquot of the reaction mixtures (50 µl) was taken out and subsequently concentrated to dryness to be analysed by NMR (**C**). Hence, MeOH (6 µl, 0.15 mmol, 1 equiv) was added with a GC syringe and the reaction stirred for 1 h. After this time, 50 µl were taken out, concentrated and analyzed by NMR (**B**).
2) in a glass tube, **1a** (27 mg, 0.15 mmol) and **2a** (52 mg, 0.45 mmol) were subsequently added. Reagent grade toluene (350 µl, 0.4 M) and MeOH (6 µl, 0.15 mmol, 1 equiv, with a GC syringe) was added and the reaction placed in a pre-heated oil bath at 50 °C. After 2 hs, an aliquot of the reaction mixture (50 µl) was taken out and subsequently concentrated to dryness to be analysed by NMR (**A**).

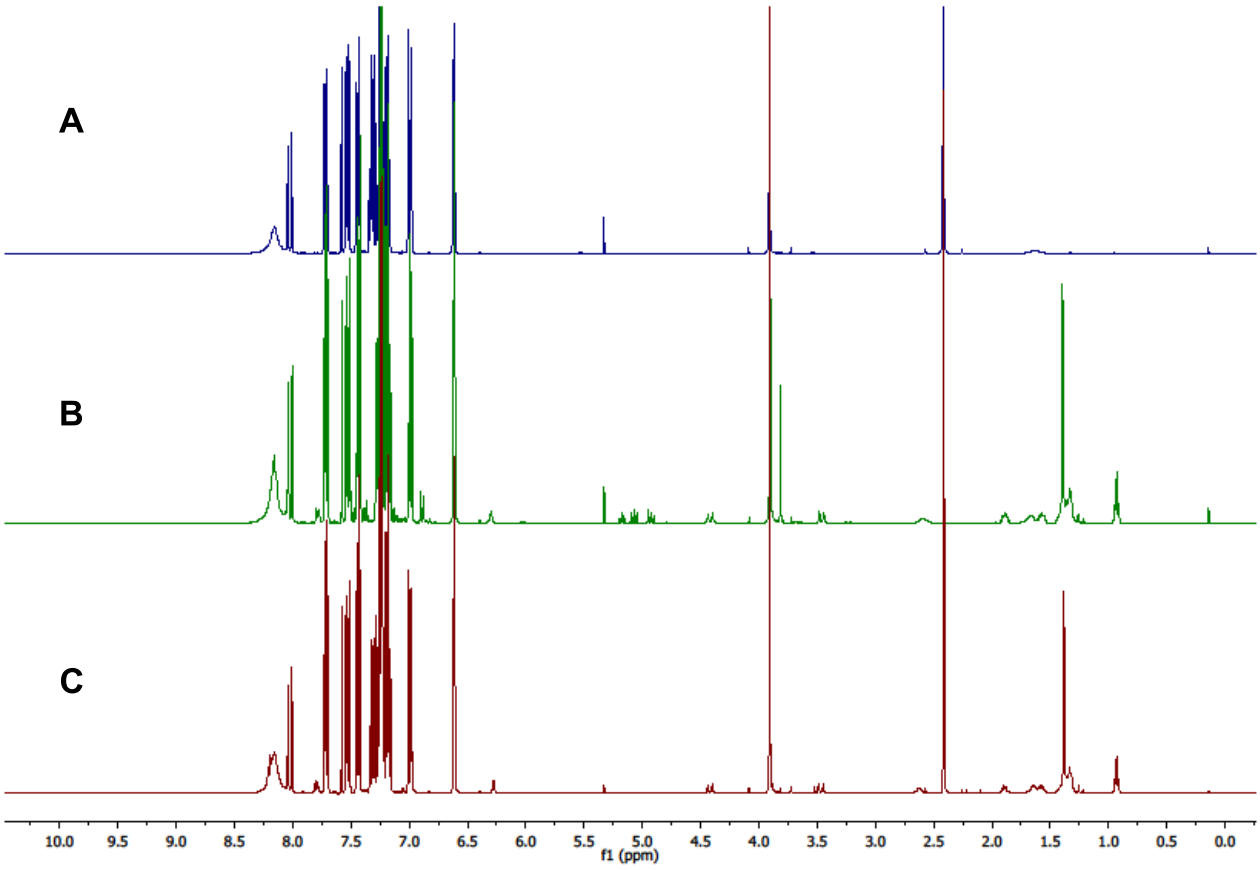


Figure S2. Low-field expanded region of the ^{1}H-NMR (MeOH-d_4, 400 MHz) of a) 1:1.5 mixture of TSA **E** and nitrostyrene **1a**; b) nitrosytrene **1a**.

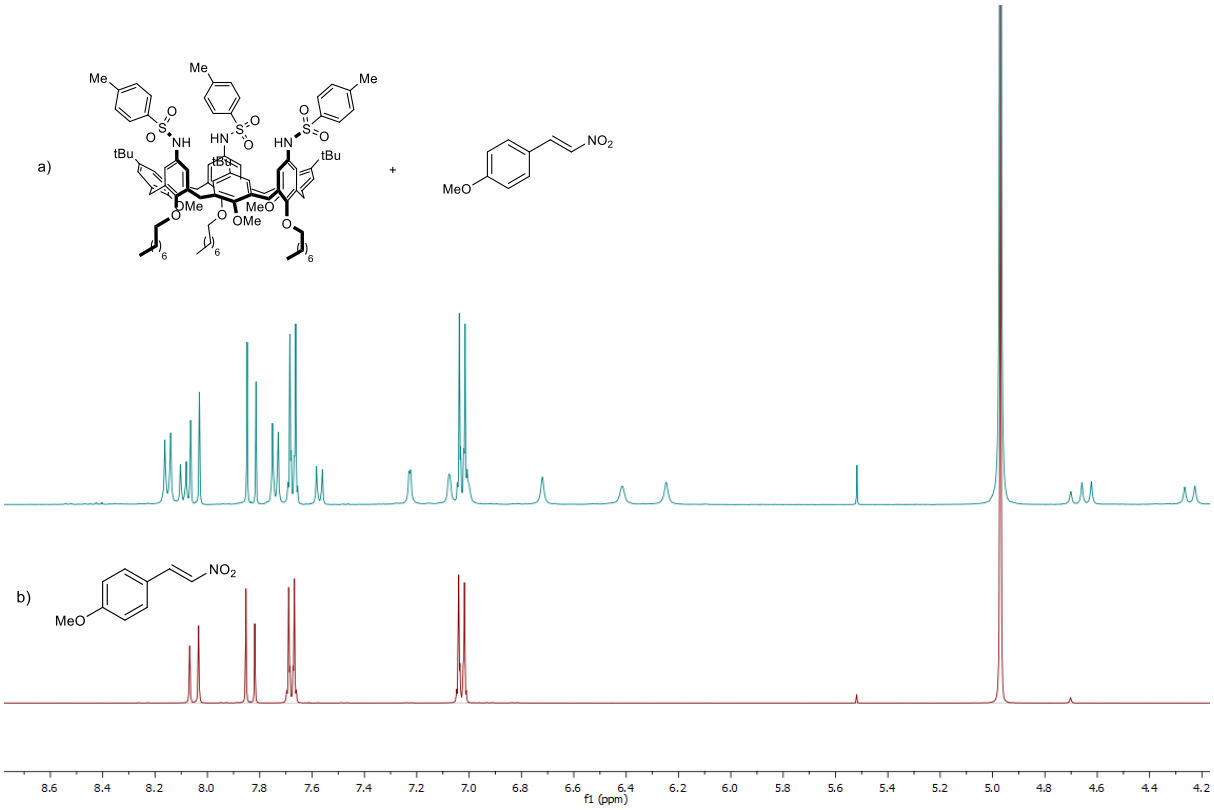
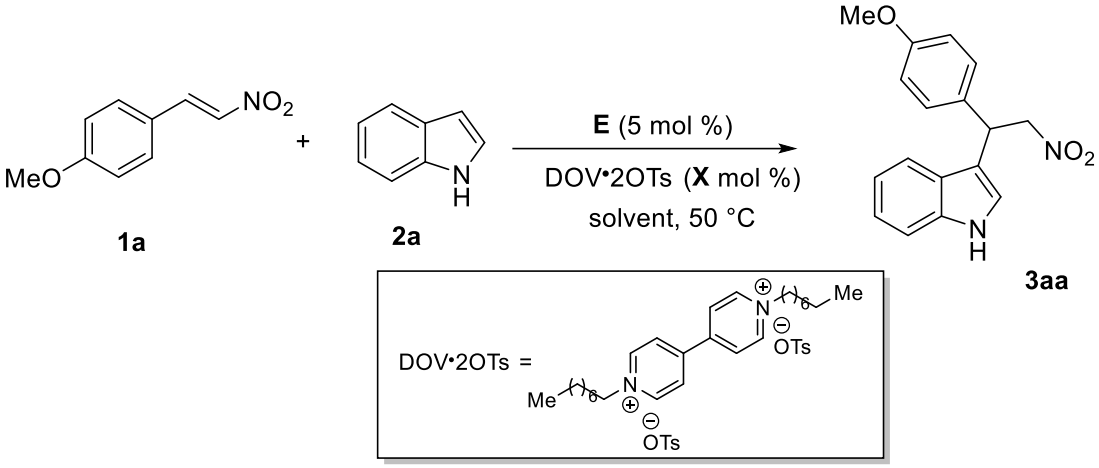


Figure S3. Experiments in the presence of competitive binders (DOV•2OTs).

In a glass tube, **1a** (17.9 mg, 0.1 mmol), **2a** (35.1 mg, 0.3 mmol), **E** (8.9 mg, 5 mol %) and DOV•2OTs (**X** mol %) were subsequently added. Solvent (0.25 ml, 0.4 M) was added and the reaction placed in a pre-heated oil bath at 50 °C. After 24 hs the reaction mixture was cooled down at room temperature and CH_2Cl_2 (10 ml) was added. The mixture was concentrated under reduced pressure and the crude analysed by ^{1}H-NMR spectroscopy using 1,3,5-trimethoxybenzene as internal standard.



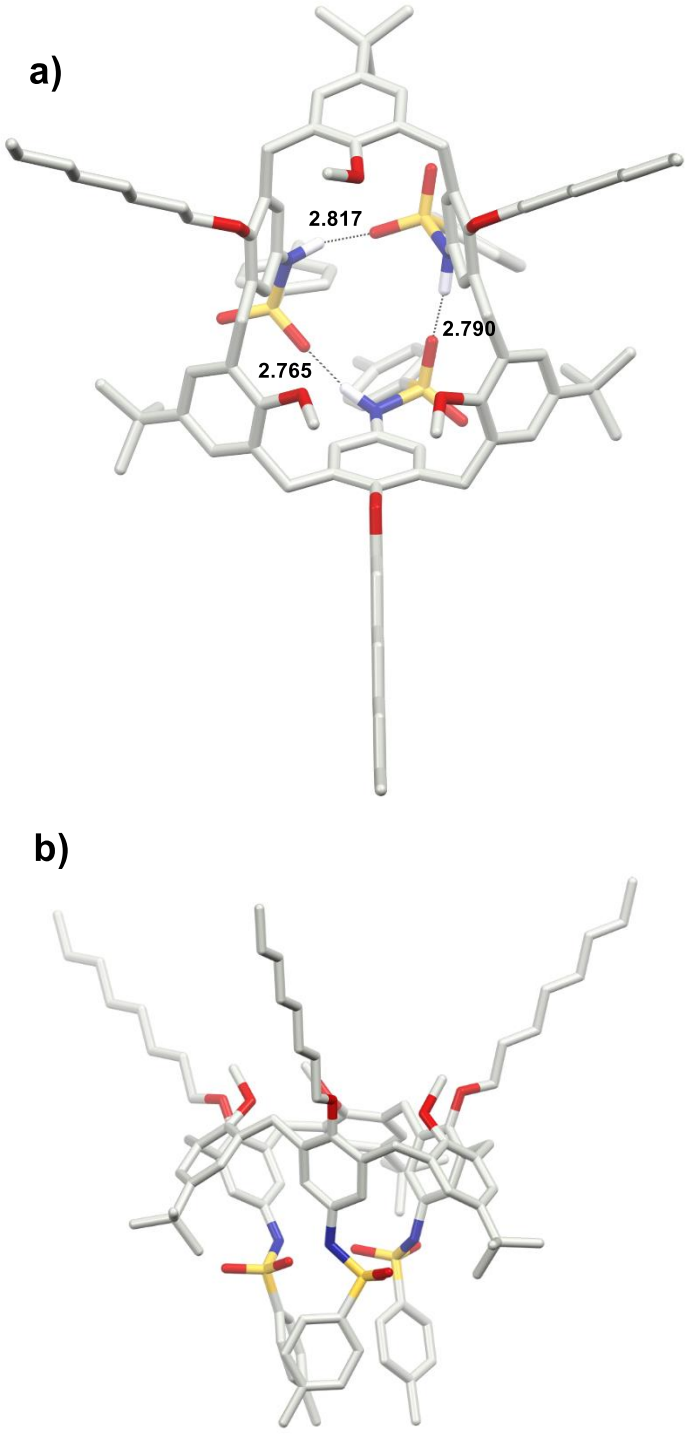
Entry	Solvent	DOV (mol %)	Yields (%)
1	MeOH	--	84
2	MeOH	30	74
3	toluene	--	32
4	toluene	30	13

Obs. The formation of TSA calixarene-based pseudorotaxanes, is established by weak acidic sulfonamide groups which efficiently separate the ion pair of bipyridinium salts, promoting threading of cationic axles inside the π-rich aromatic wheel, in low-polarity solvents (ref. 1 in SI). Hence, threading process is inefficient in polar media. For these reasons, results reported in entries 1,2 do not sufficiently support the hypothesis that TSAs are able to catalyse the reaction by using their cavity, in methanol. Contrarily, using toluene (entries 3,4), the observed poorer reactivity in the presence of DOV•2OTs could be expected since NH bonds of TSA are already engaged in H-bonding interactions with the tosylate counterions.

- **Molecular Mechanics Calculations**

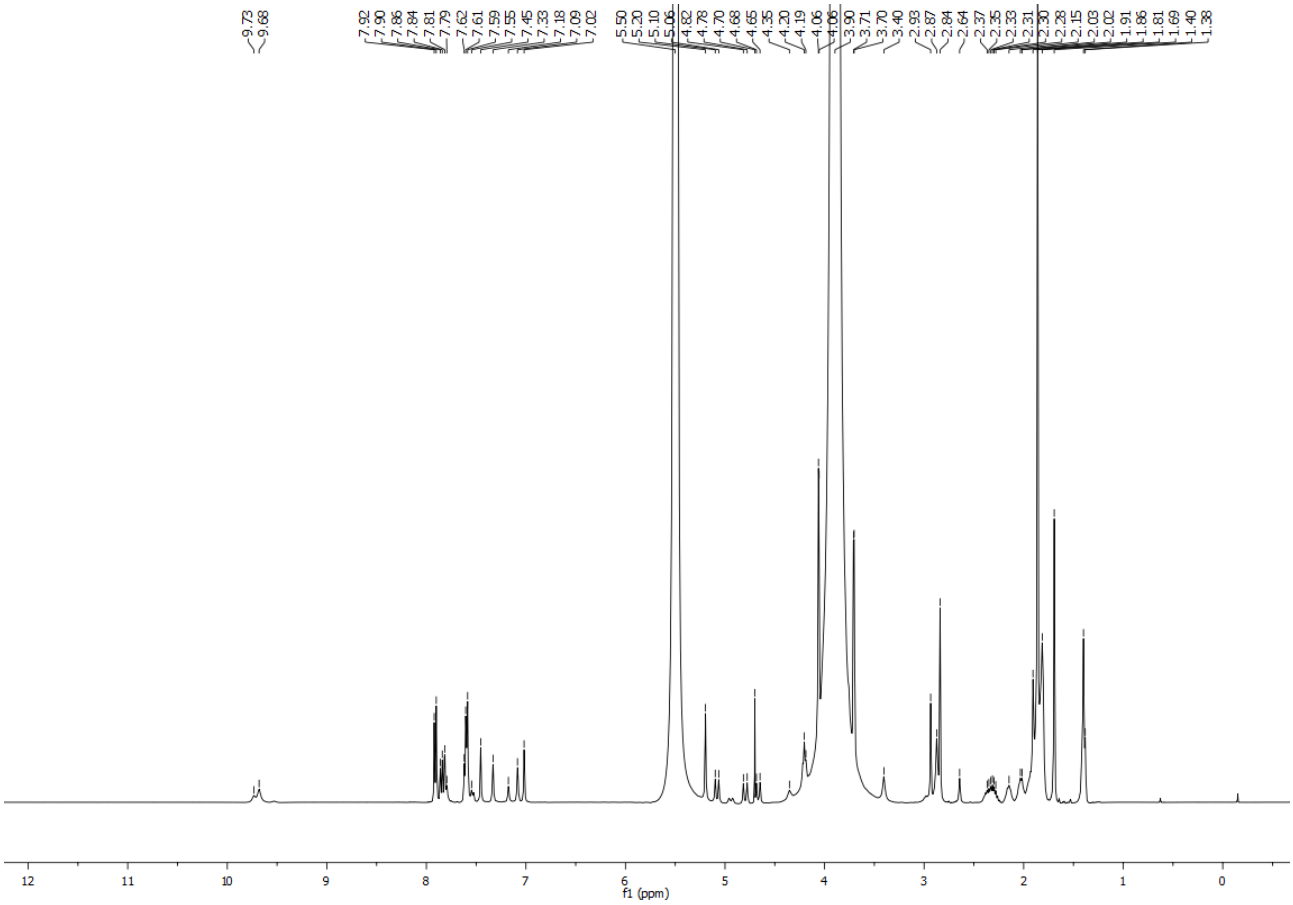
General: The geometry of **1a** was initially minimized with the MMFF94 force field[11] using the Avogadro software,[12] and then refined at PM6-DH+ and PM7 level[13,14] using the MOPAC2016 software.[15] The rendering of minimized structures was obtained using the Platon software.[16]

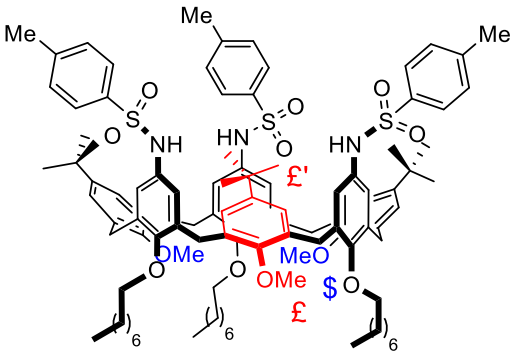
Figure S4. Bottom (**a**) and side (**b**) views of the minimized structures (PM7) of **1a** in a cone conformation. All hydrogen atoms except those participating in H-bonding have been omitted. Colors: C, gray; N, blue; O, red; H, white; S, yellow, H-bonds, dashed gray lines. Hydrogen bond distances in ångström (Å).



- **Detailed NMR analysis of model TSA calixarene A**

Figure S5. ^{1}H-NMR (D_2O, 400 MHz) spectrum of **A** in methanol.





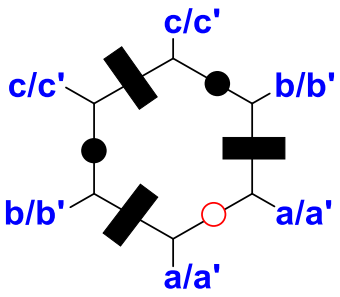


Figure S6. Mid-field expanded region of the 2D HSQC NMR (MeOH-d_4, 600 MHz) spectrum of **A**.

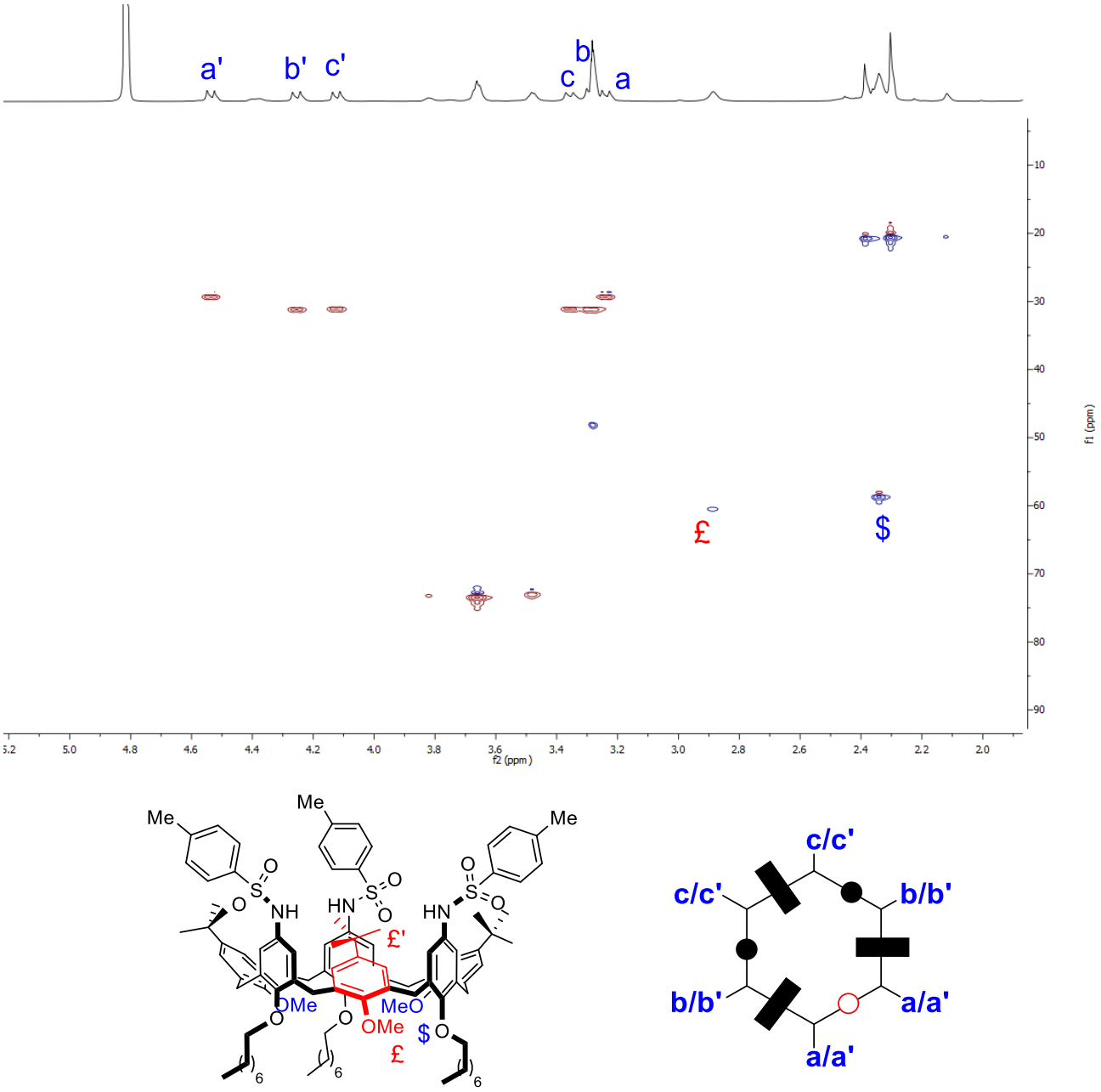
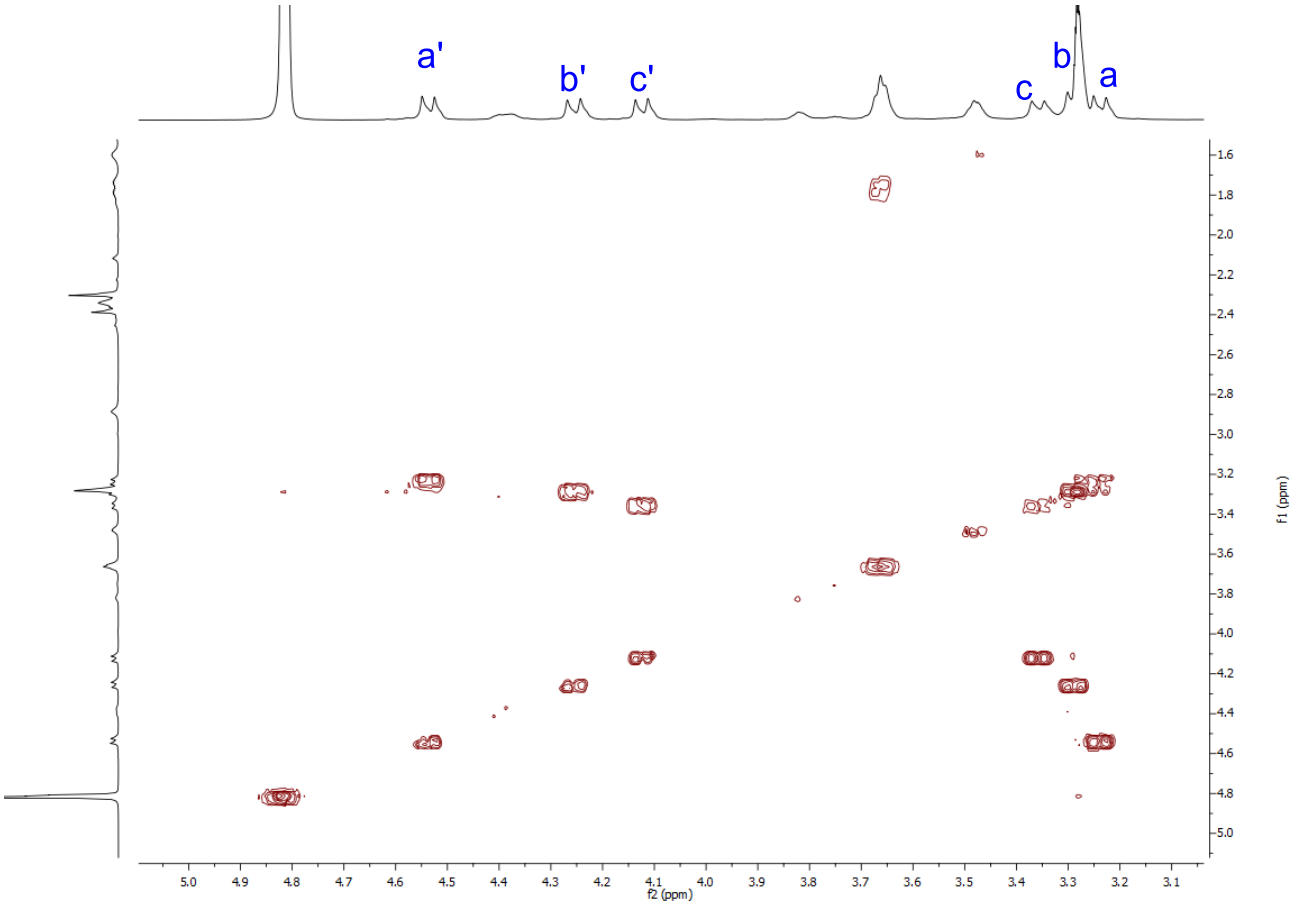
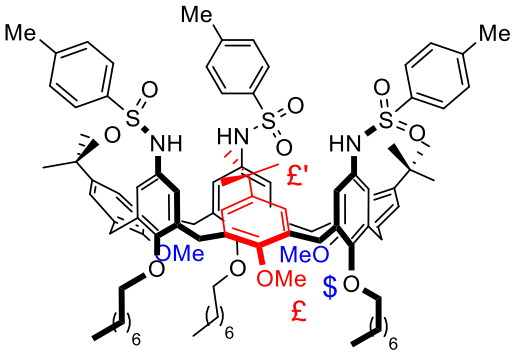


Figure S7. Mid-field expanded region of the 2D ^{1}H-^{1}H COSY NMR (MeOH-d_4, 600 MHz) spectrum of **A** showing the *J*-coupling correlations of the macrocycle "bridging" equatorial and axial methylene protons.





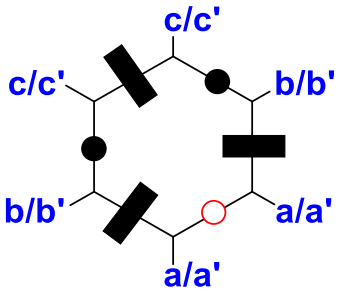
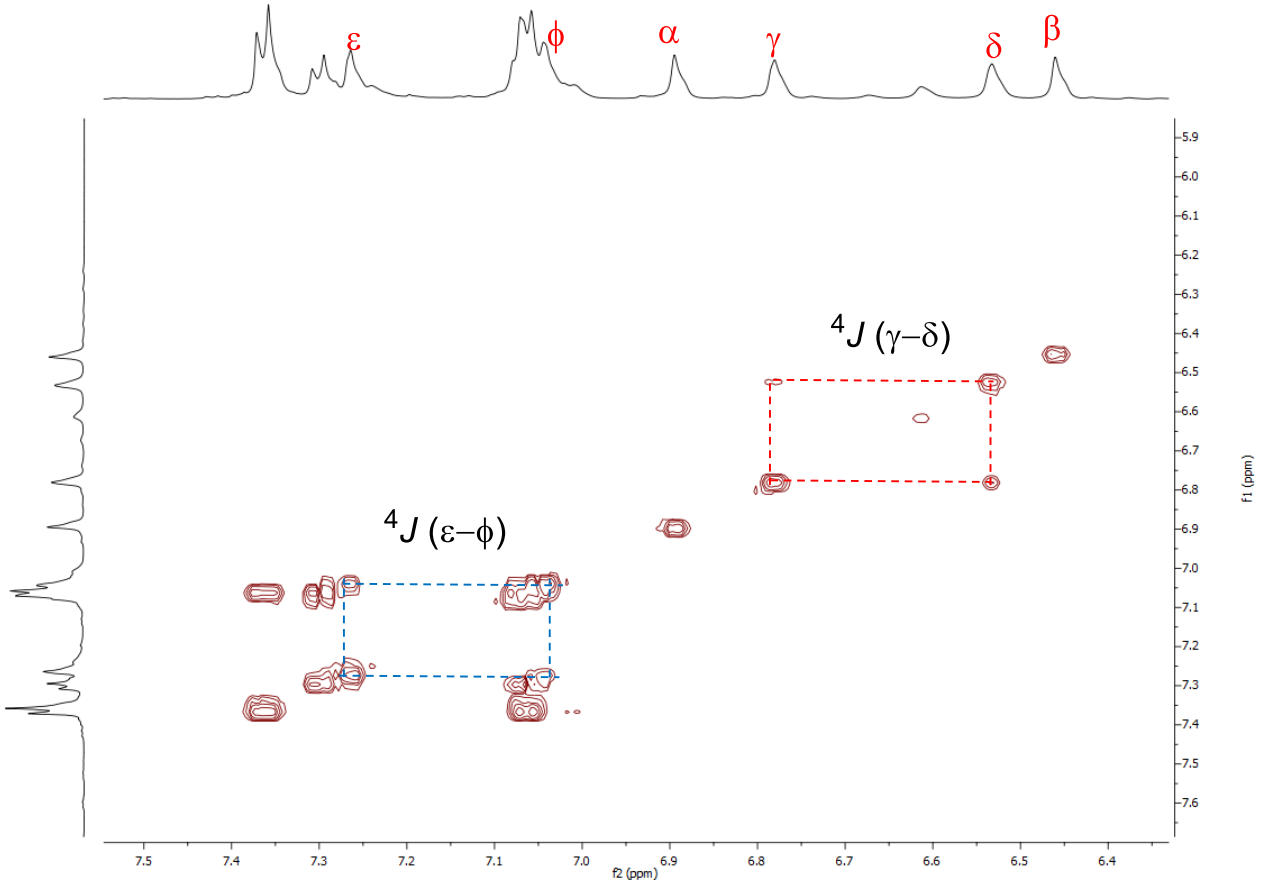
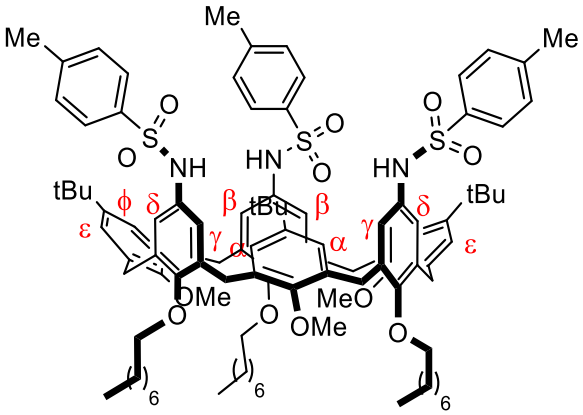


Figure S8. Low-field expanded region of the 2D ^{1}H-^{1}H COSY NMR (MeOH-d_4, 600 MHz) spectrum of **A** showing the *J*-coupling correlations between the aromatic protons.





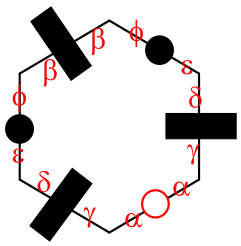
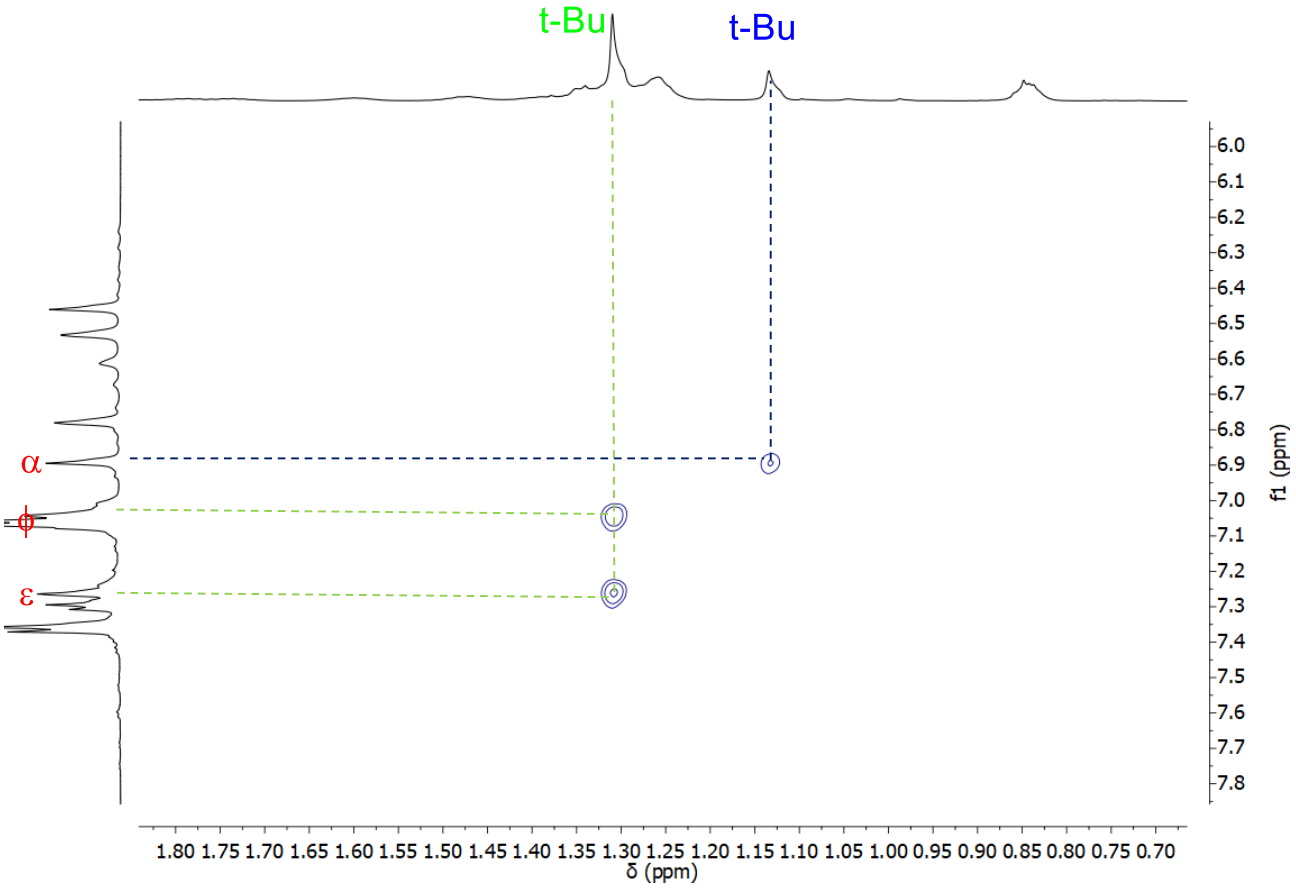
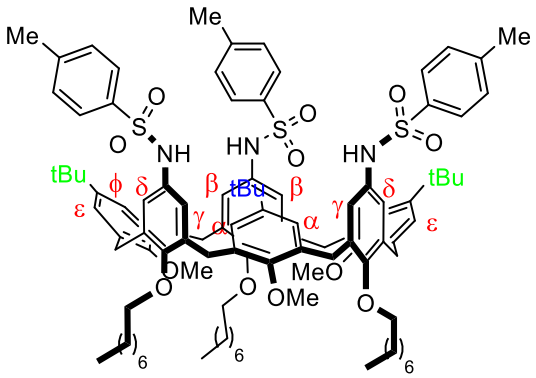


Figure S9. Low-field expanded region of the 2D ROESY-NMR (MeOH-d_4, 600 MHz, spin-lock = 200 ms) spectrum of **A** showing the dipolar correlations of the aromatic protons of calixarene with t-Bu groups.





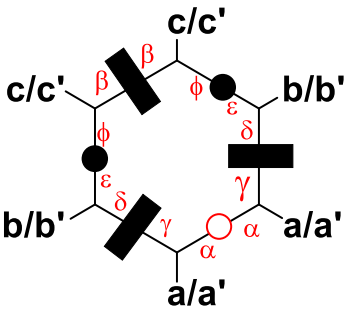
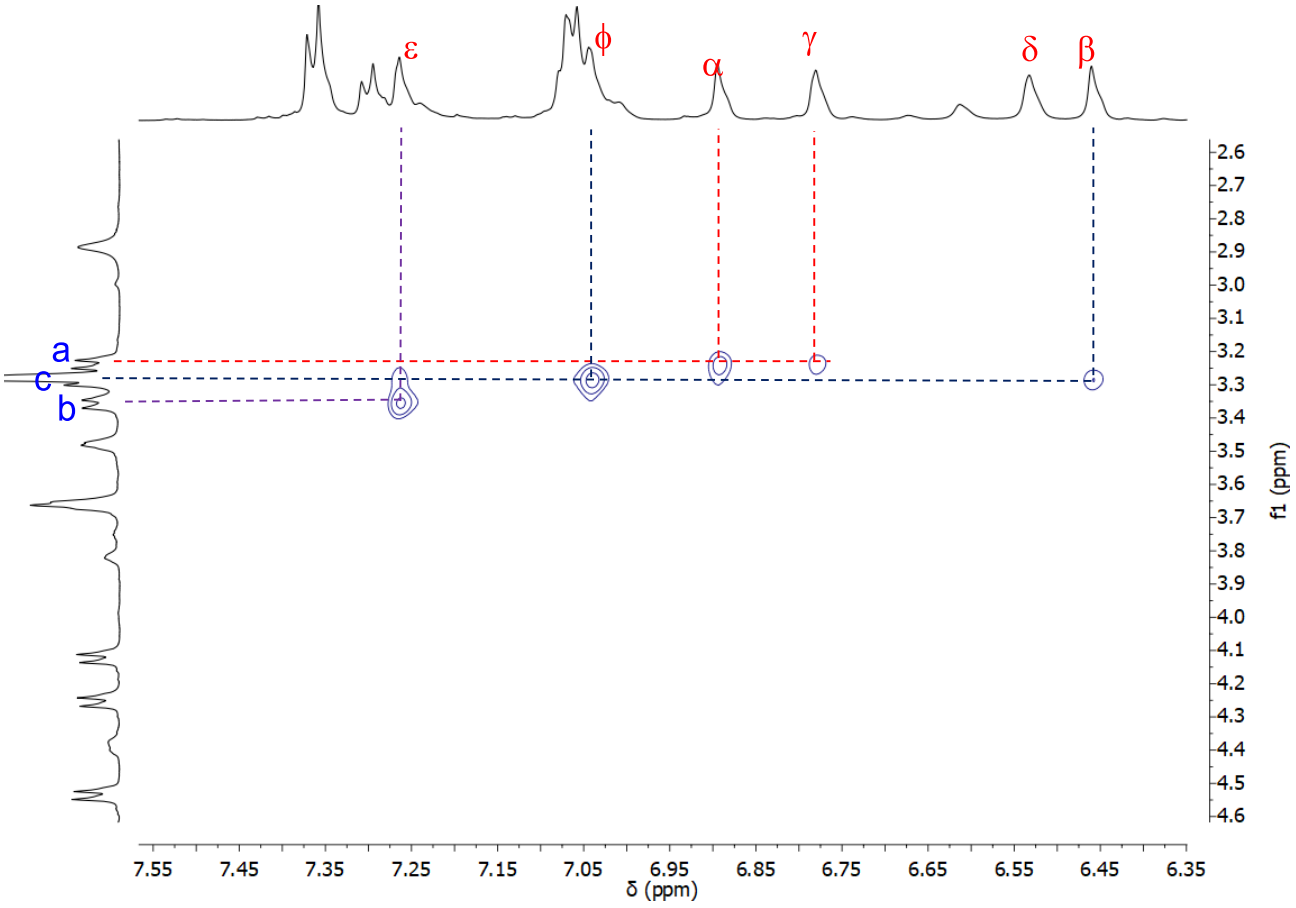
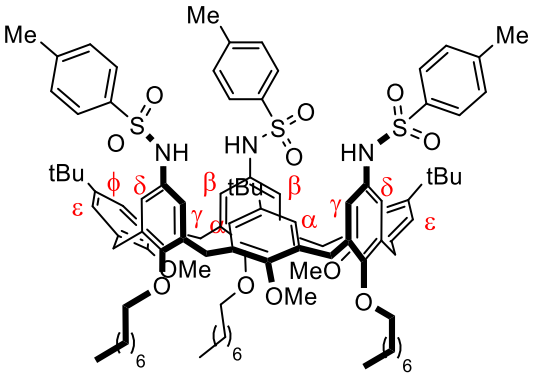
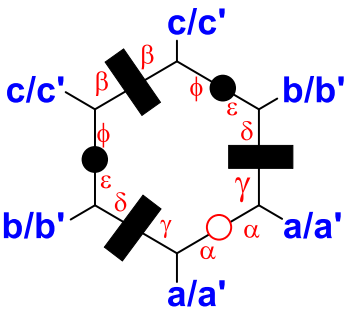


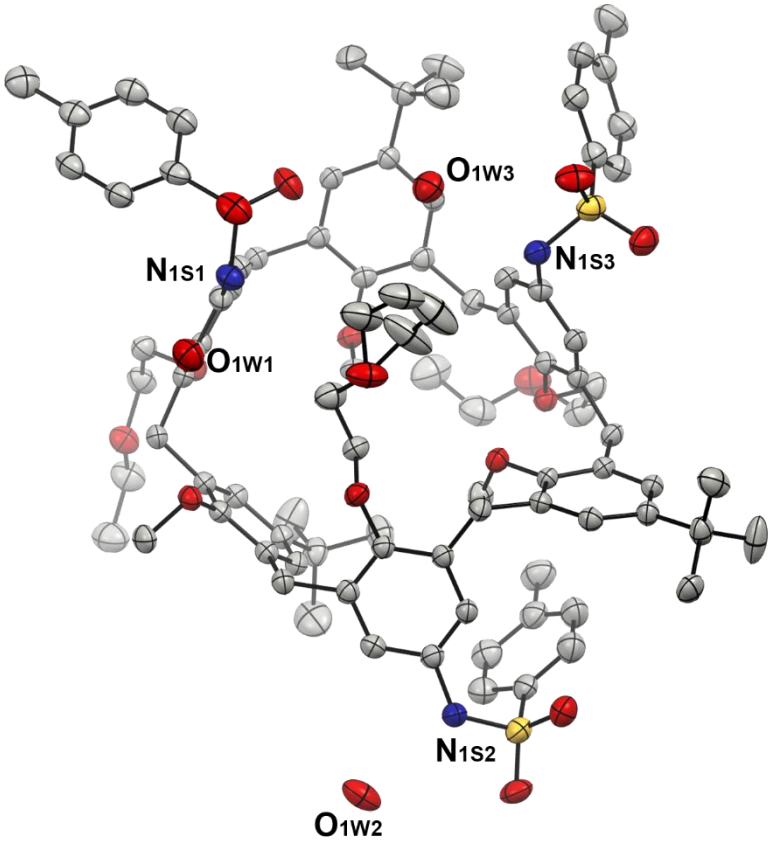
Figure S10. Low-field expanded region of the 2D ROESY-NMR (MeOH-d_4, 600 MHz, spin-lock = 200 ms) spectrum of **A** showing the dipolar correlations of the aromatic protons of calixarene with methylene protons.







- **Crystallographic Data**



Ortep representation of the asymmetric unit of calixarene **B**, (thermal ellipsoids are drawn at 30% probability level), hydrogen atoms are omitted for clarity. Colour code: C, gray; O, red; N, blue; S, yellow. The disordered ethyl fragment is depicted at the center of the drawing.

Table S1. Crystal data and structure refinement for calix B.	
Empirical formula	$C_{90}H_{117}N_3O_{18}S_3$
Formula weight	1625.04
Temperature/K	200.0
Crystal system	triclinic
Space group	P-1
a/Å	15.5420(6)
b/Å	16.5195(6)
c/Å	20.2175(7)
α/°	74.481(2)
β/°	69.188(2)
γ/°	67.602(2)
Volume/Å^3	4433.3(3)
Z	2
ρ_{calc}g/cm^3	1.217
μ/mm^{-1}	1.311
F(000)	1740.0
Crystal size/mm^3	0.07 × 0.06 × 0.04
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	6.416 to 140.398
Index ranges	-16 ≤ h ≤ 18, -19 ≤ k ≤ 19, -24 ≤ l ≤ 23
Reflections collected	36476
Independent reflections	16505 [R_{int} = 0.0917, R_{sigma} = 0.1253]
Data/restraints/parameters	16505/48/1073
Goodness-of-fit on F^2	1.003
Final R indexes [I>=2σ (I)]	R_1 = 0.0698, wR_2 = 0.1540
Final R indexes [all data]	R_1 = 0.1658, wR_2 = 0.1963
Largest diff. peak/hole / e Å^{-3}	0.30/-0.30

$R_1 = \Sigma||F_O|-|F_C||/\Sigma|F_O|$, $wR_2 = [\Sigma[w(F_O^2-F_C^2)^2]/\Sigma[w(F_O^2)^2]]^{½}$, $w = 1/[\sigma^2(F_O^2) + (aP)^2 + bP]$, where

$$P = [\max(F_O^2,0) + 2F_C^2]/3$$

Figure S11. Intermolecular hydrogen bond interactions involving water molecule O1W1 and calixarene **B**.

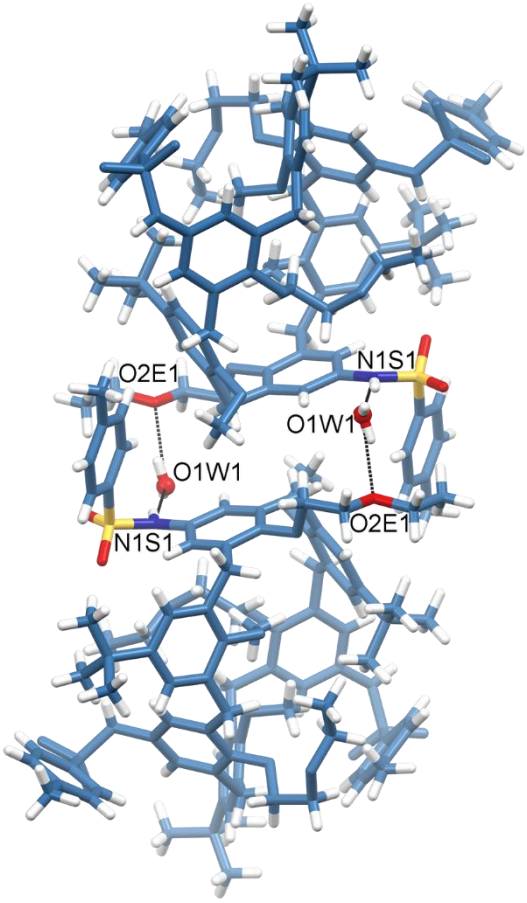


Figure S12. Intermolecular hydrogen bond interactions involving water molecule O1W2 and calixarene **B**.

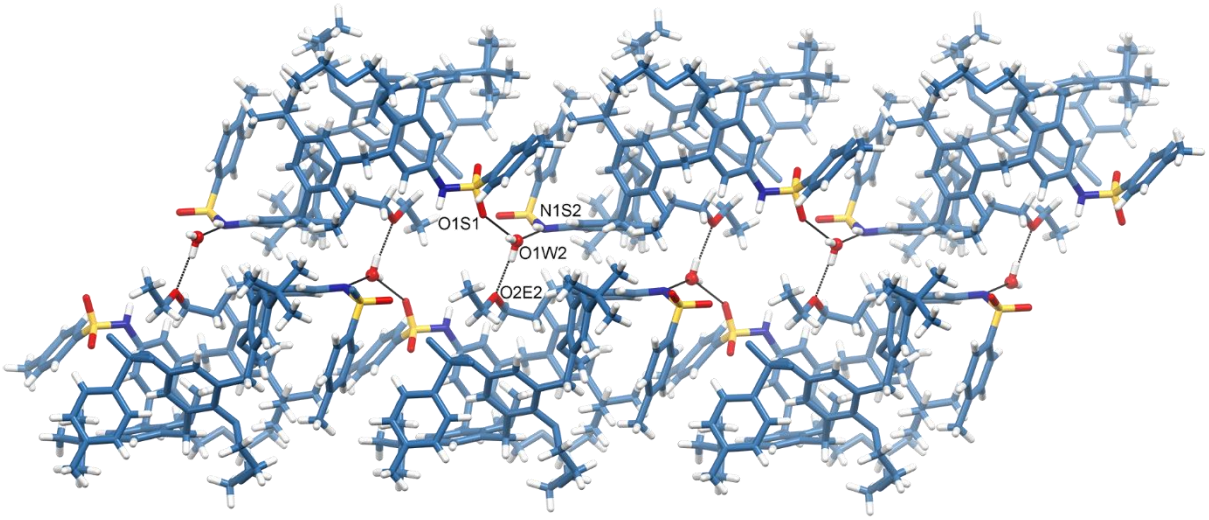


Figure S13. Intermolecular hydrogen bond interactions involving water molecule O1W3 and calixarene **B**.

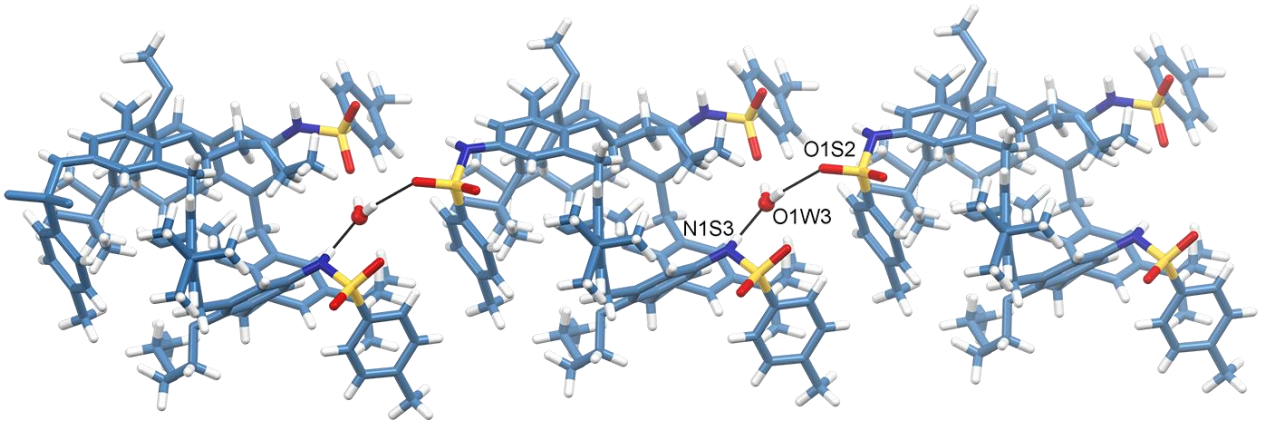


Figure S14. View of the selected intramolecular weak contacts for calixarene **B**, with partial labelling scheme for the atoms involved in the CH-π interactions (calculated centroids are plotted as shaded orange sphere).

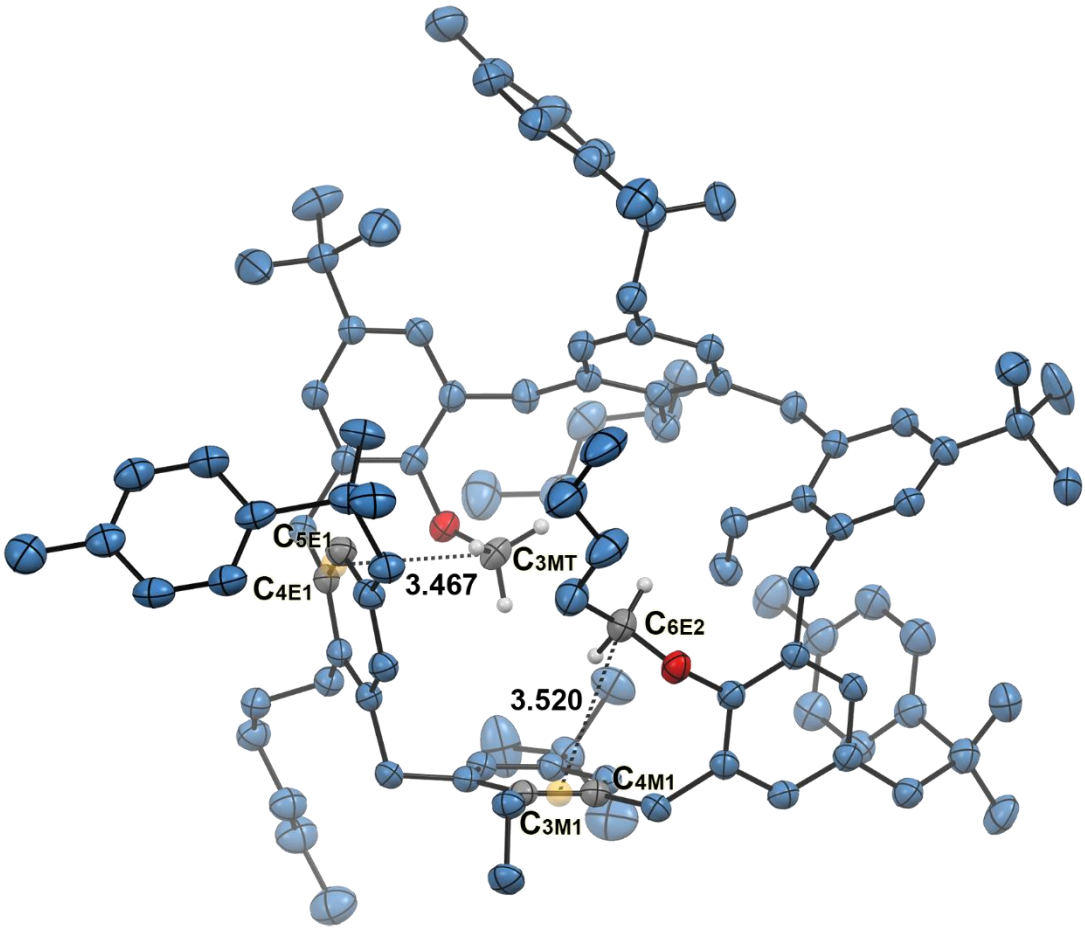


Figure S15. Intermolecular CH-π interactions for calixarene **B**, with partial labelling scheme (calculated centroids are plotted as shaded orange sphere).

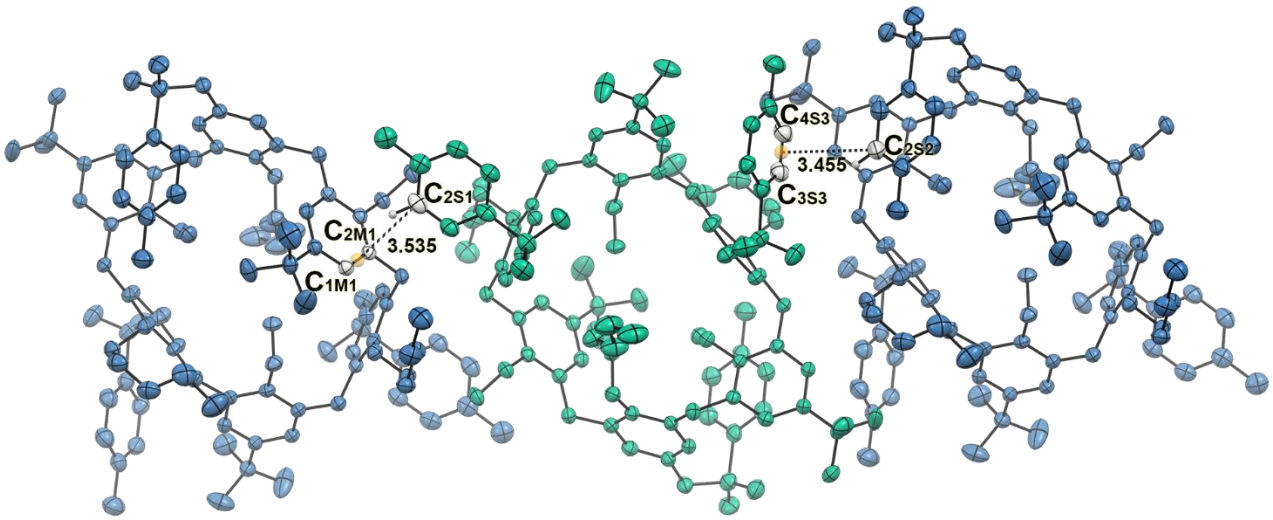


Figure S16. Stick view and phenyl labelling scheme for calixarene **B**.

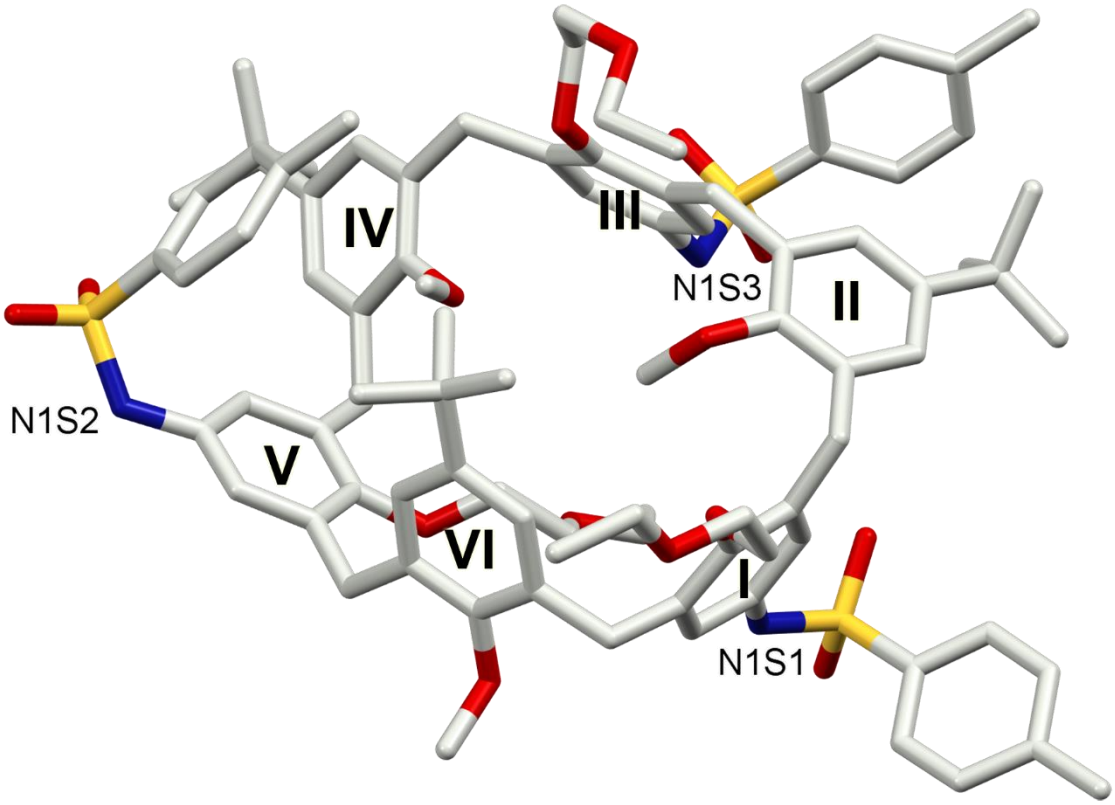


Figure S17. View of mean plane R (light blue colour) passing through the six methylene bridges (light blue spheres), and the mean plane passing through the aromatic ring I (yellow colour).

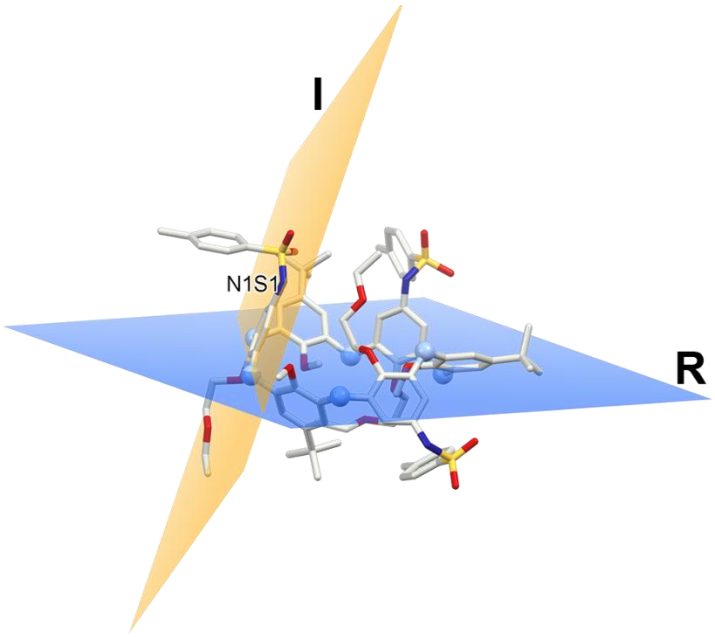


Figure S18. Torsion angles ϕ (C1-C2-C3-C4) and χ (C2-C3-C4-C5).

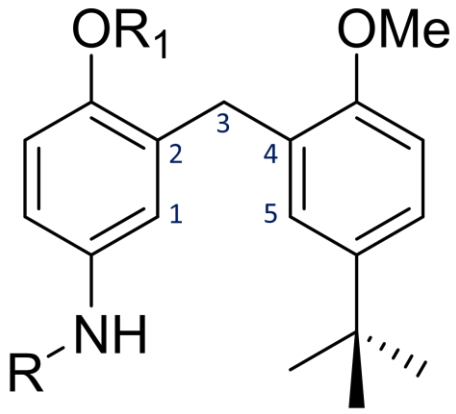
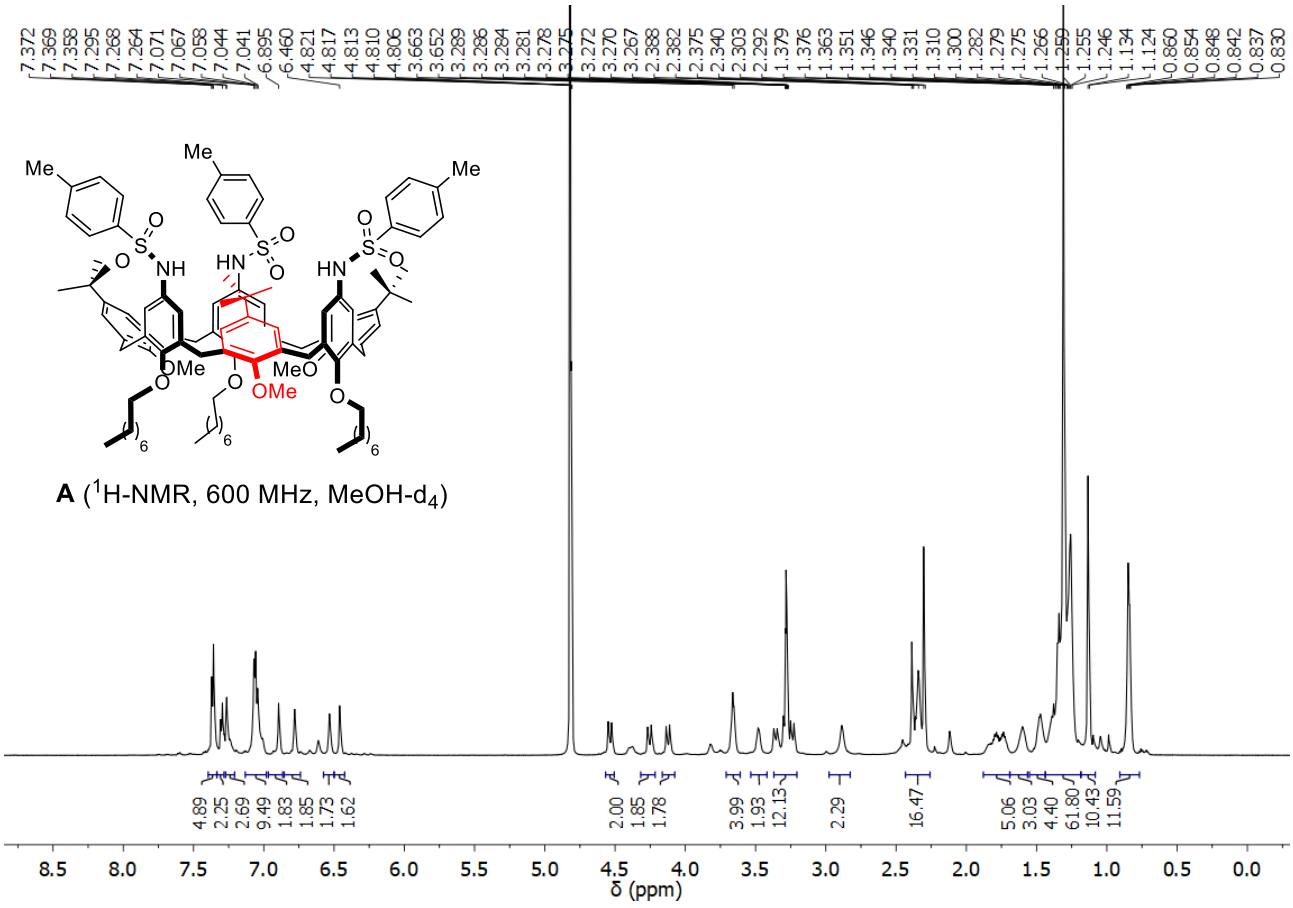


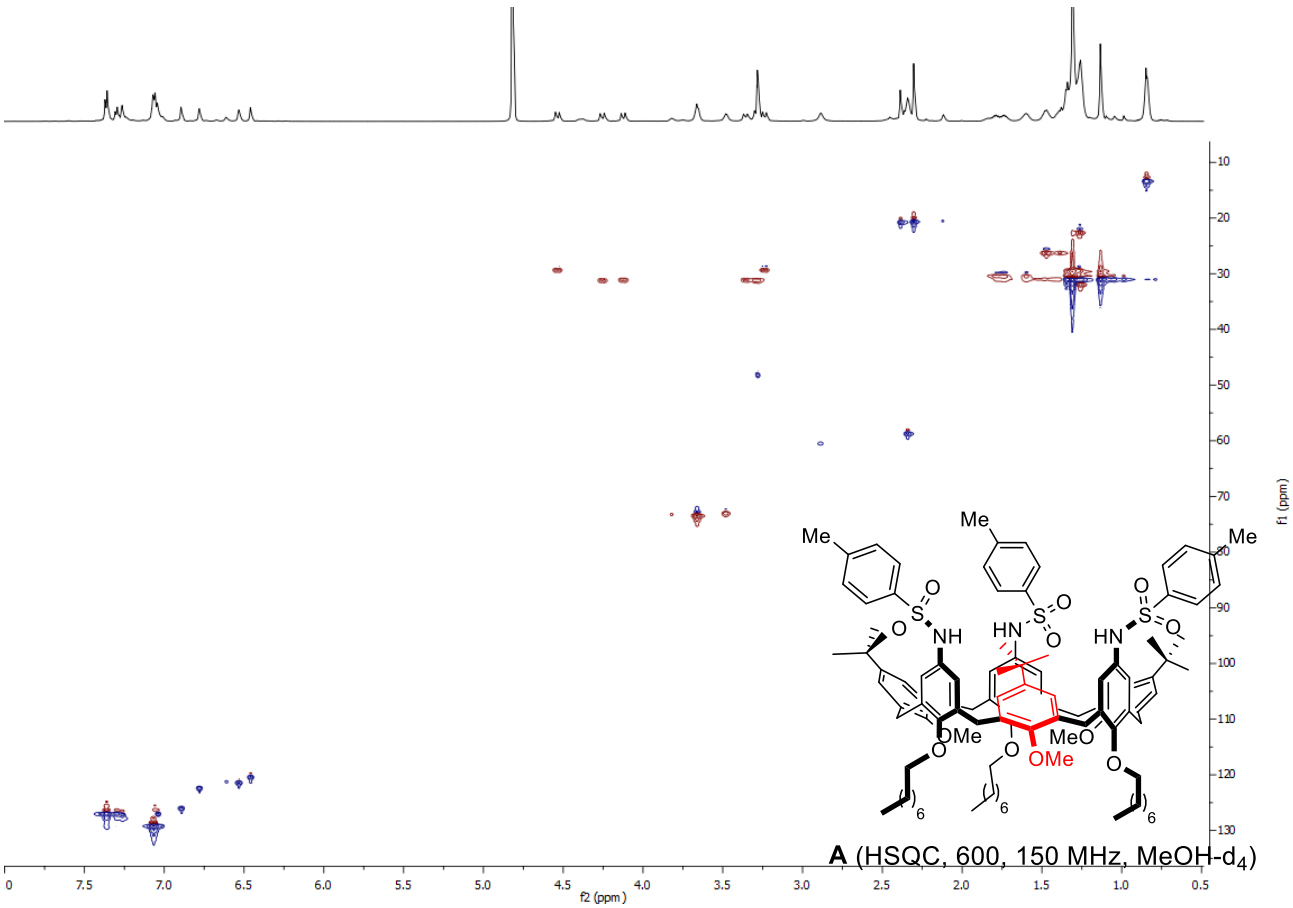
Table S2. Summary of dihedral angles δ and conformational parameters ϕ and χ in the structure of **B**.[15,16] The symbolic representation which accounts for the point symmetry of calixarene **B** (Schöenflies symbol) is C_1 – –, + –, + –, – +, – +, – +.

Diedral angles δ			**Torsion Angles ϕ**	**Torsion Angles χ**
	(°)		**(°)**	**(°)**
I-R	69.1	I-II	-86.9(5)	-83.1(5)
II-R	53.9	II-III	37.2(6)	-99.1(5)
III-R	57.2	III-IV	46.7(6)	-109.7(5)
IV-R	25.2	IV-V	-128.4(5)	41.9(6)
V-R	89.0	V-VI	-15.9(7)	72.4(6)
VI-R	47.4	VI-I	-105.1(5)	43.6(6)

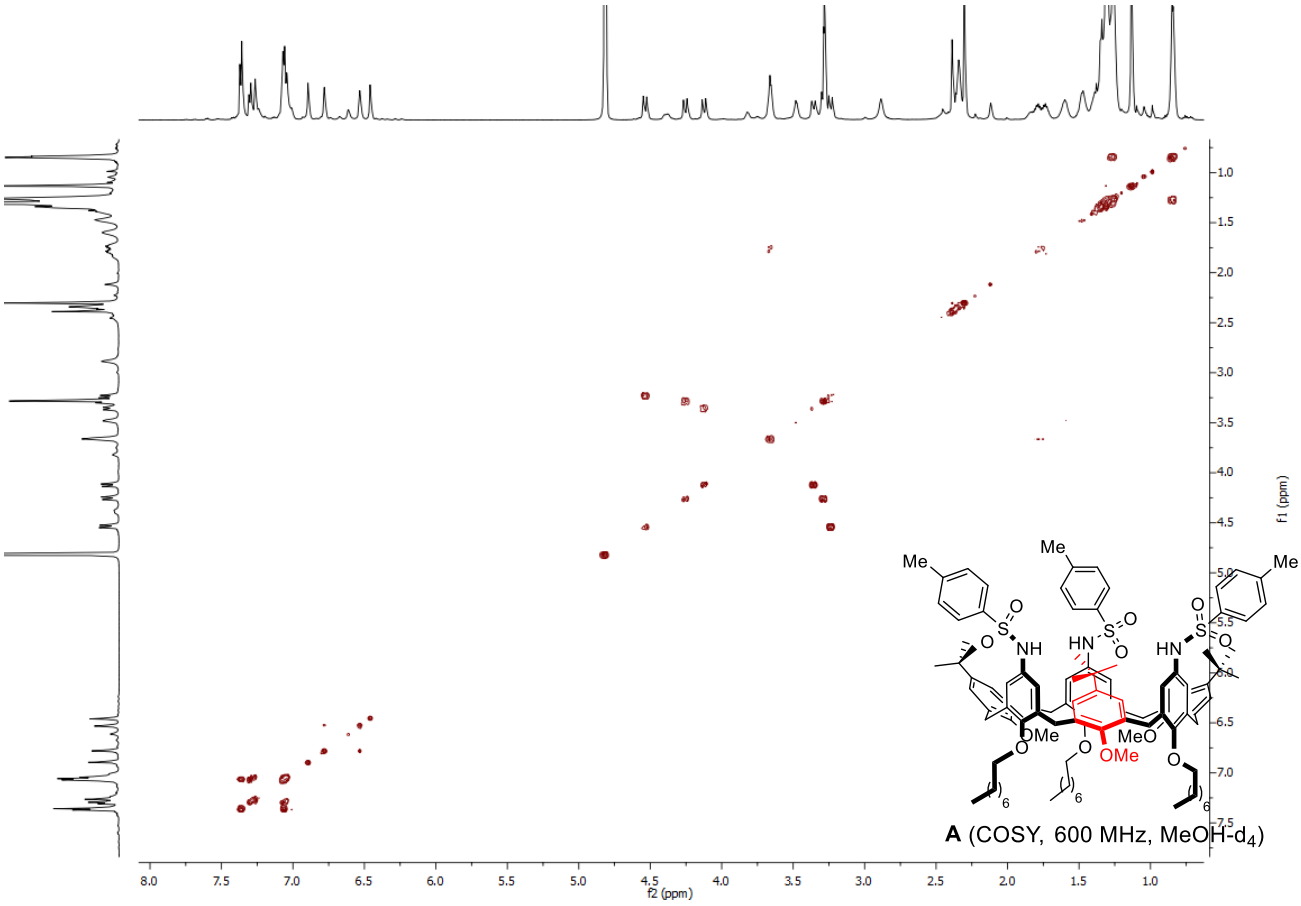
- **NMR Spectra**



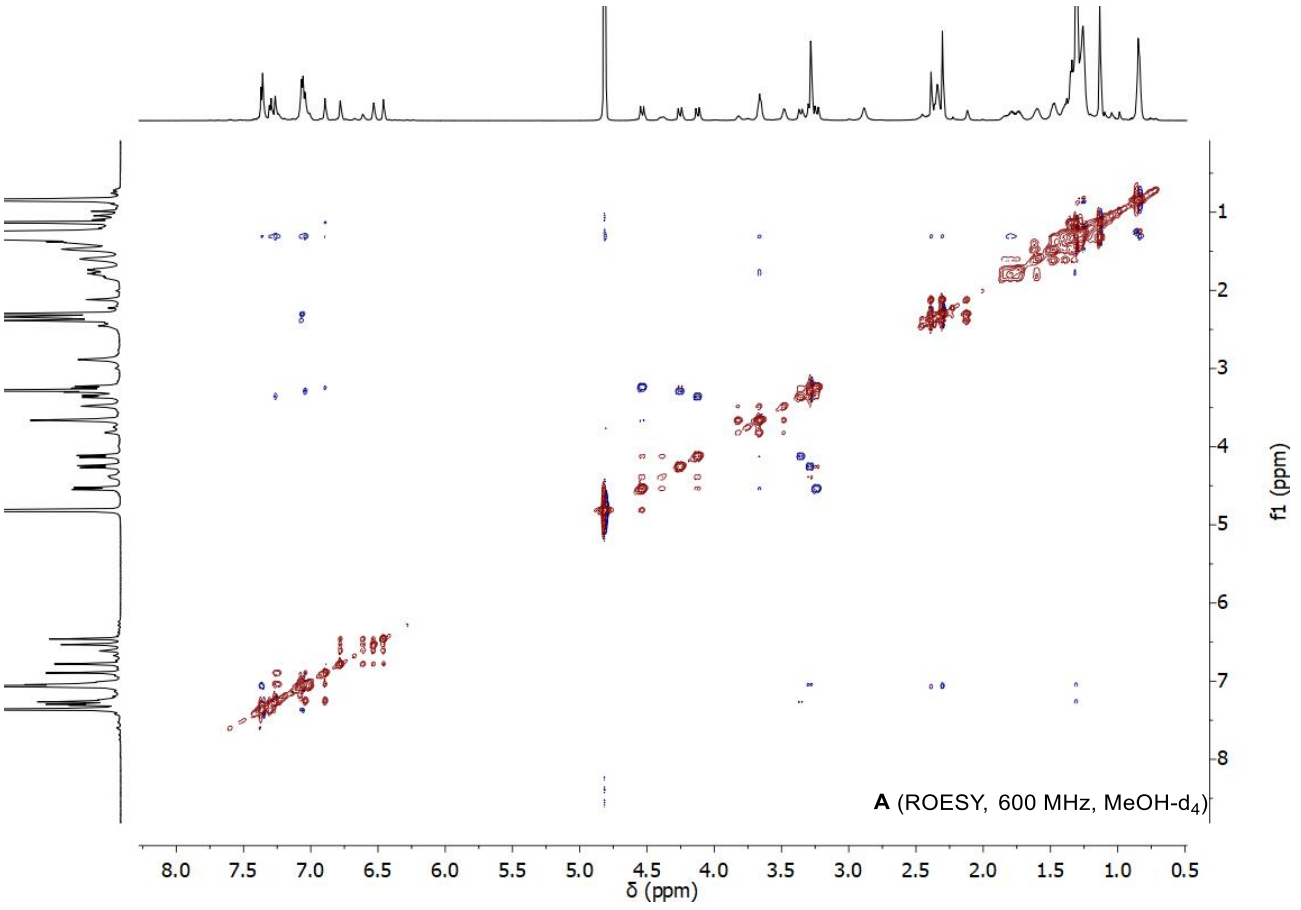
A (^{1}H-NMR, 600 MHz, MeOH-d_4)



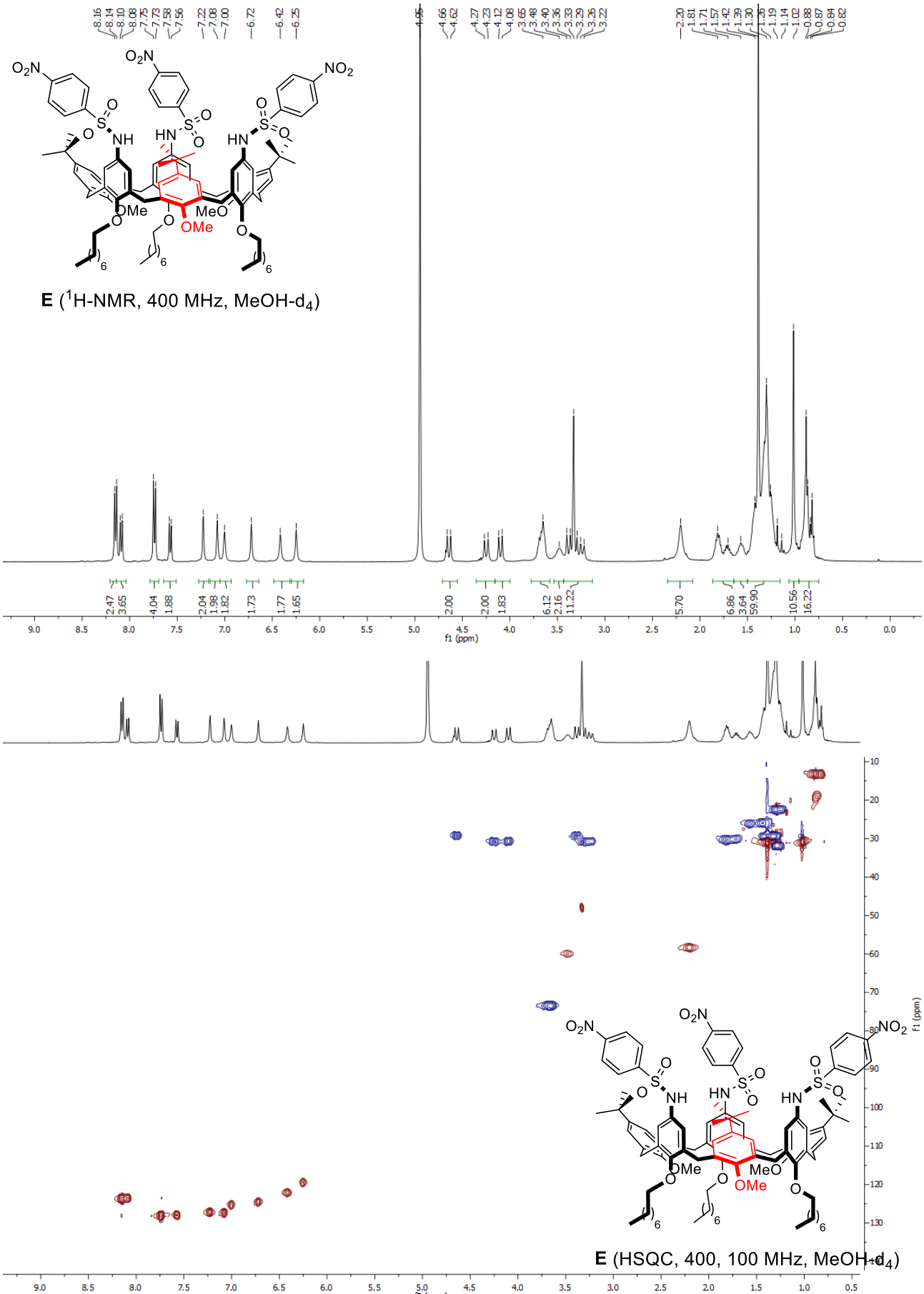
A (HSQC, 600, 150 MHz, MeOH-d_4)



A (COSY, 600 MHz, MeOH-d_4)

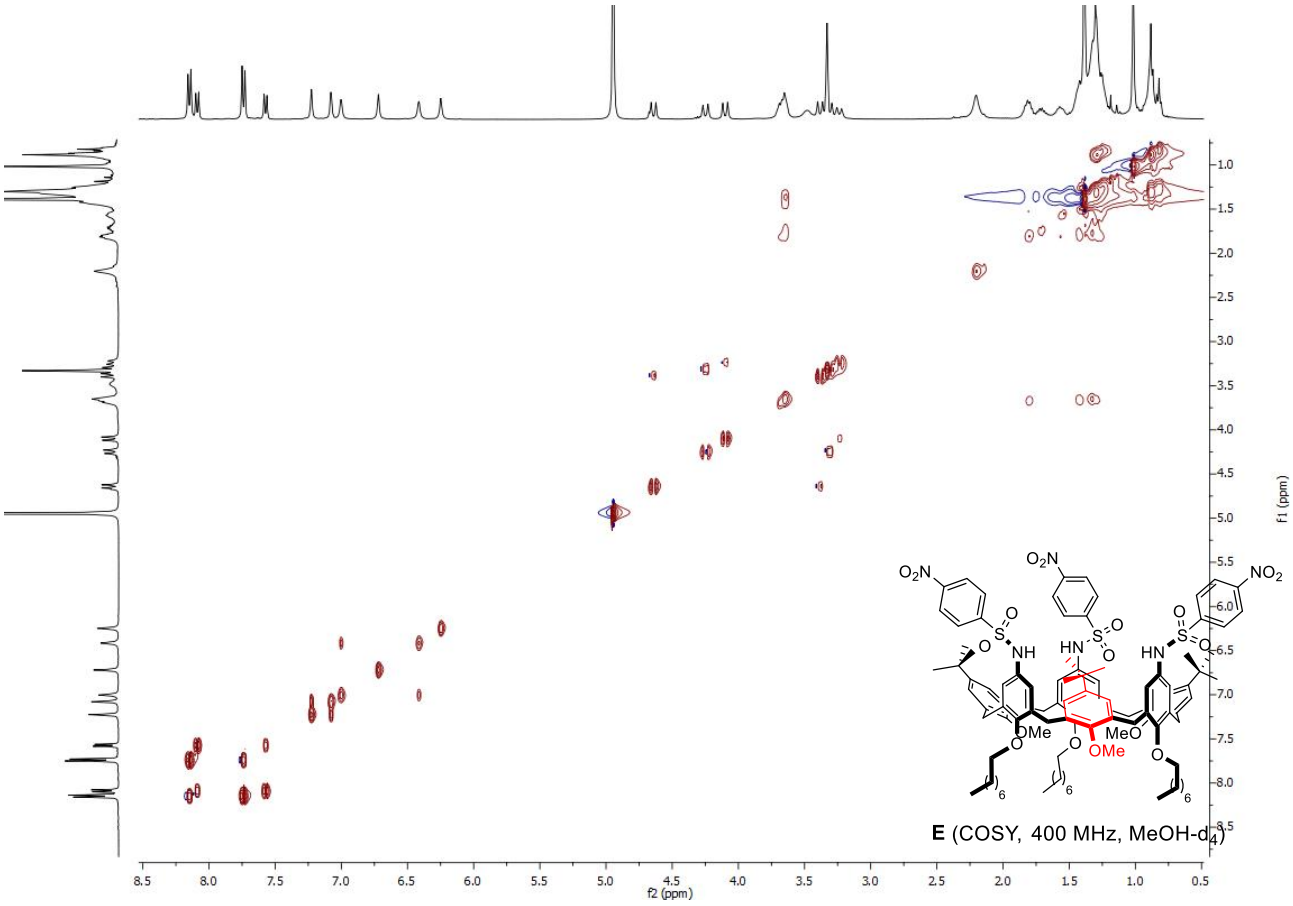


A (ROESY, 600 MHz, MeOH-d_4)

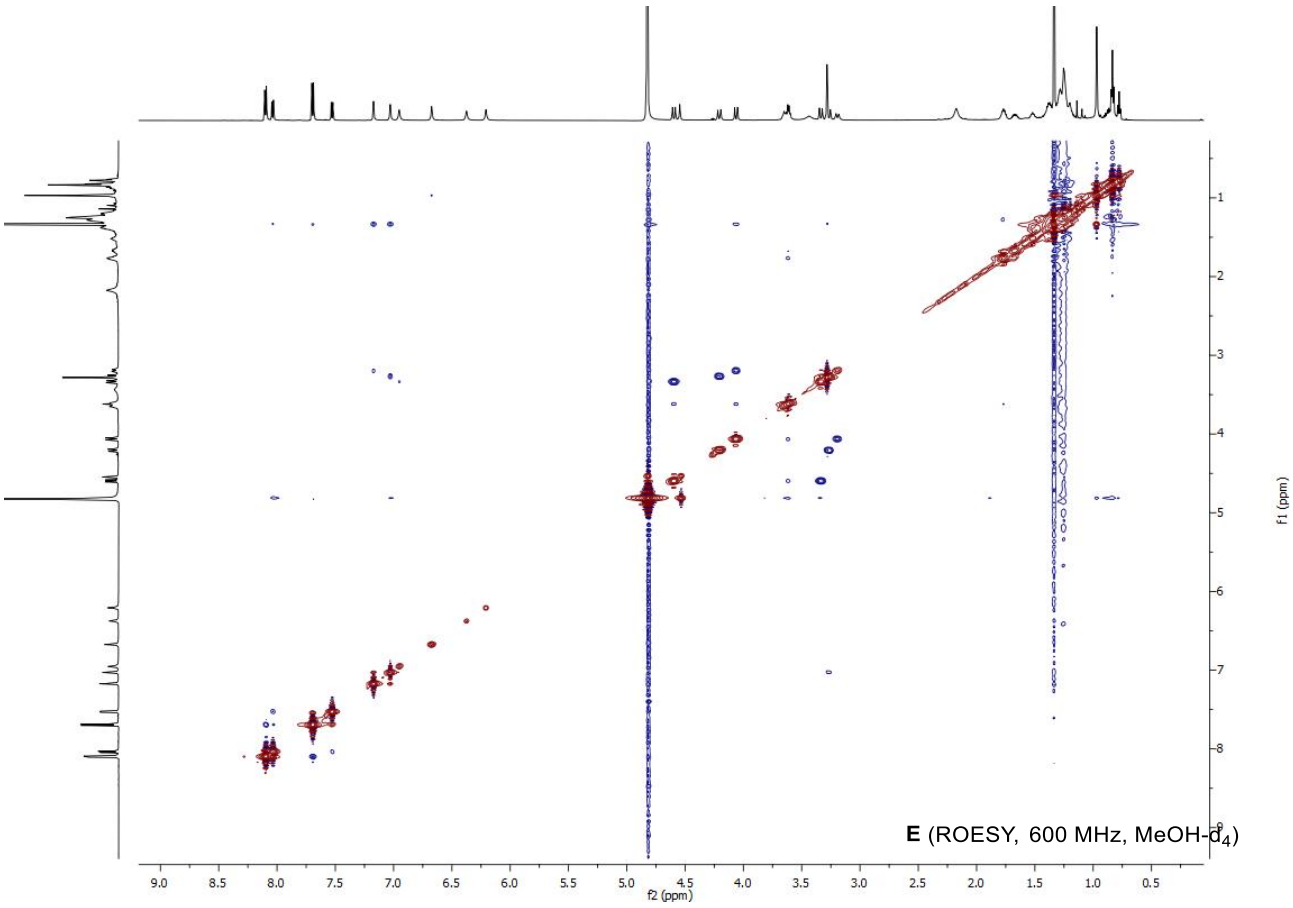


E (^{1}H-NMR, 400 MHz, MeOH-d_4)

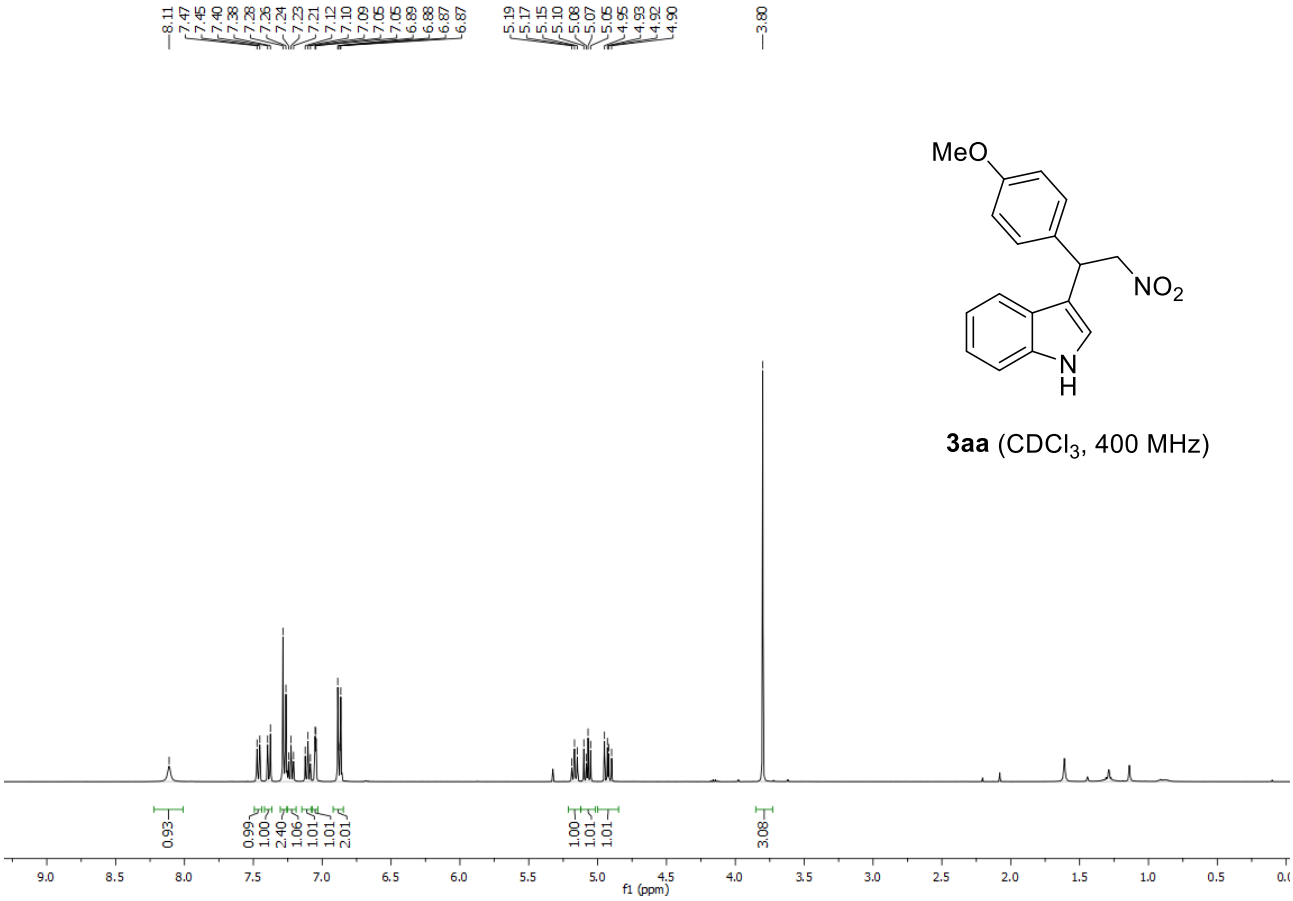
E (HSQC, 400, 100 MHz, MeOH-d_4)



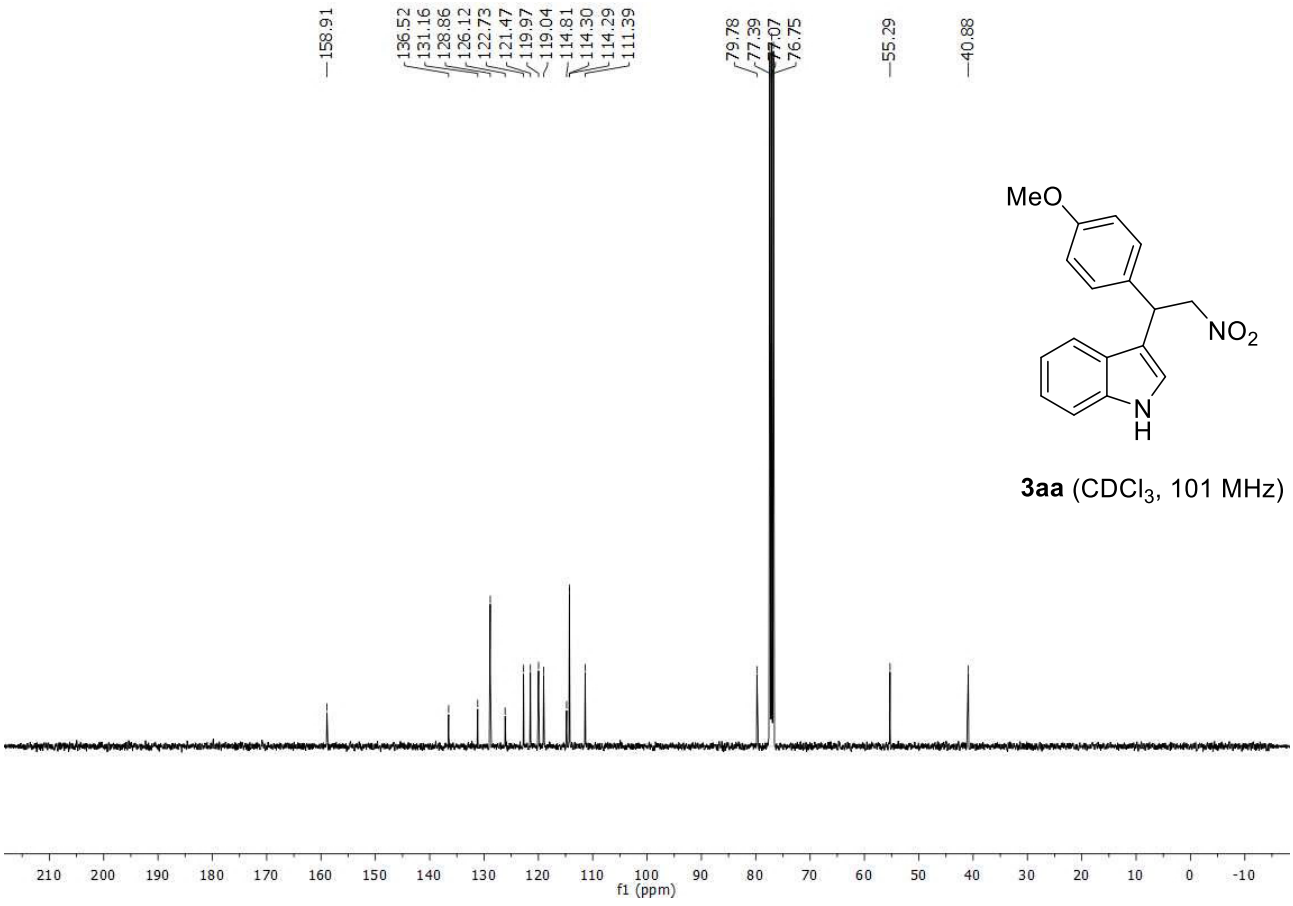
E (COSY, 400 MHz, MeOH-d_4)



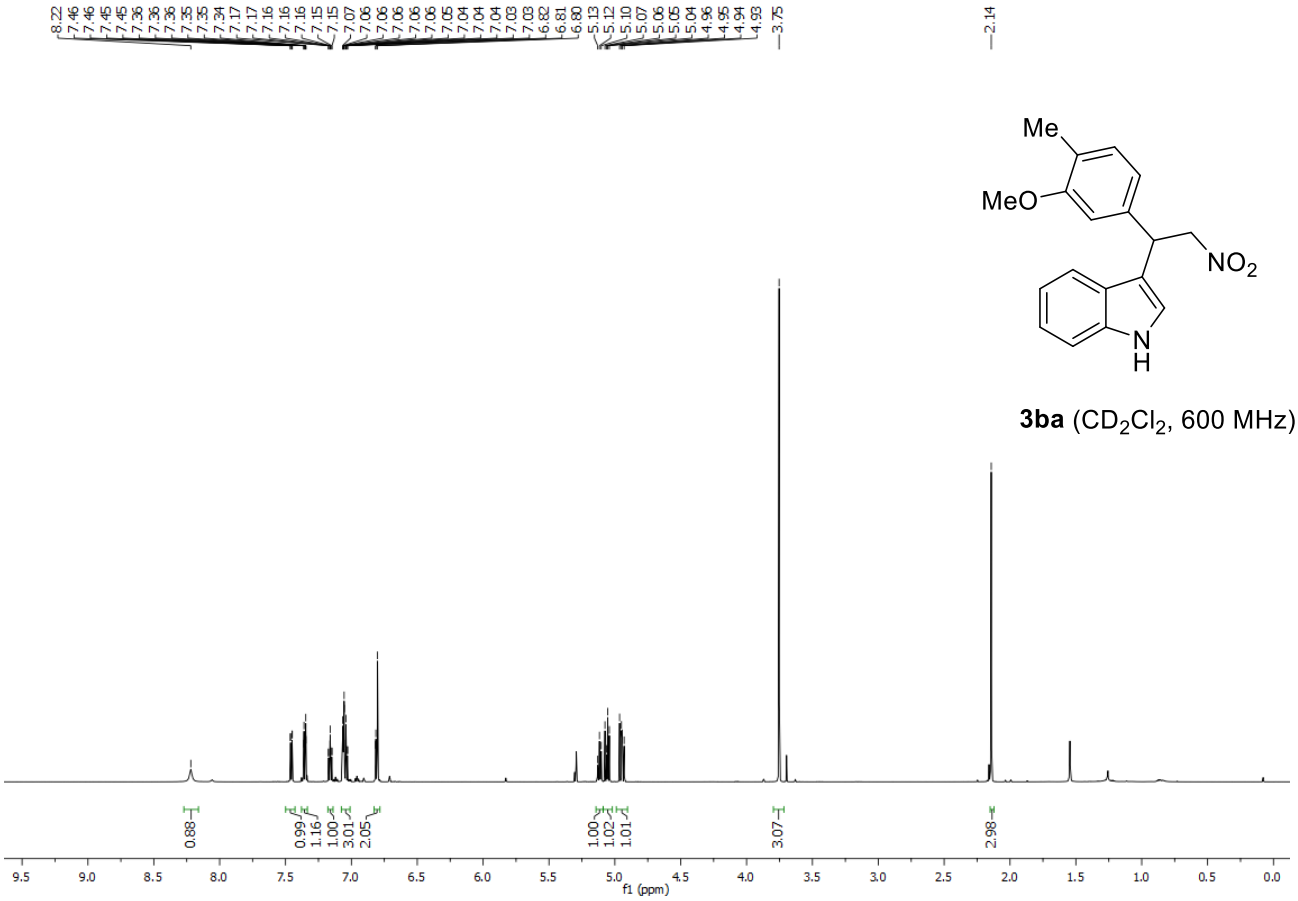
E (ROESY, 600 MHz, MeOH-d_4)



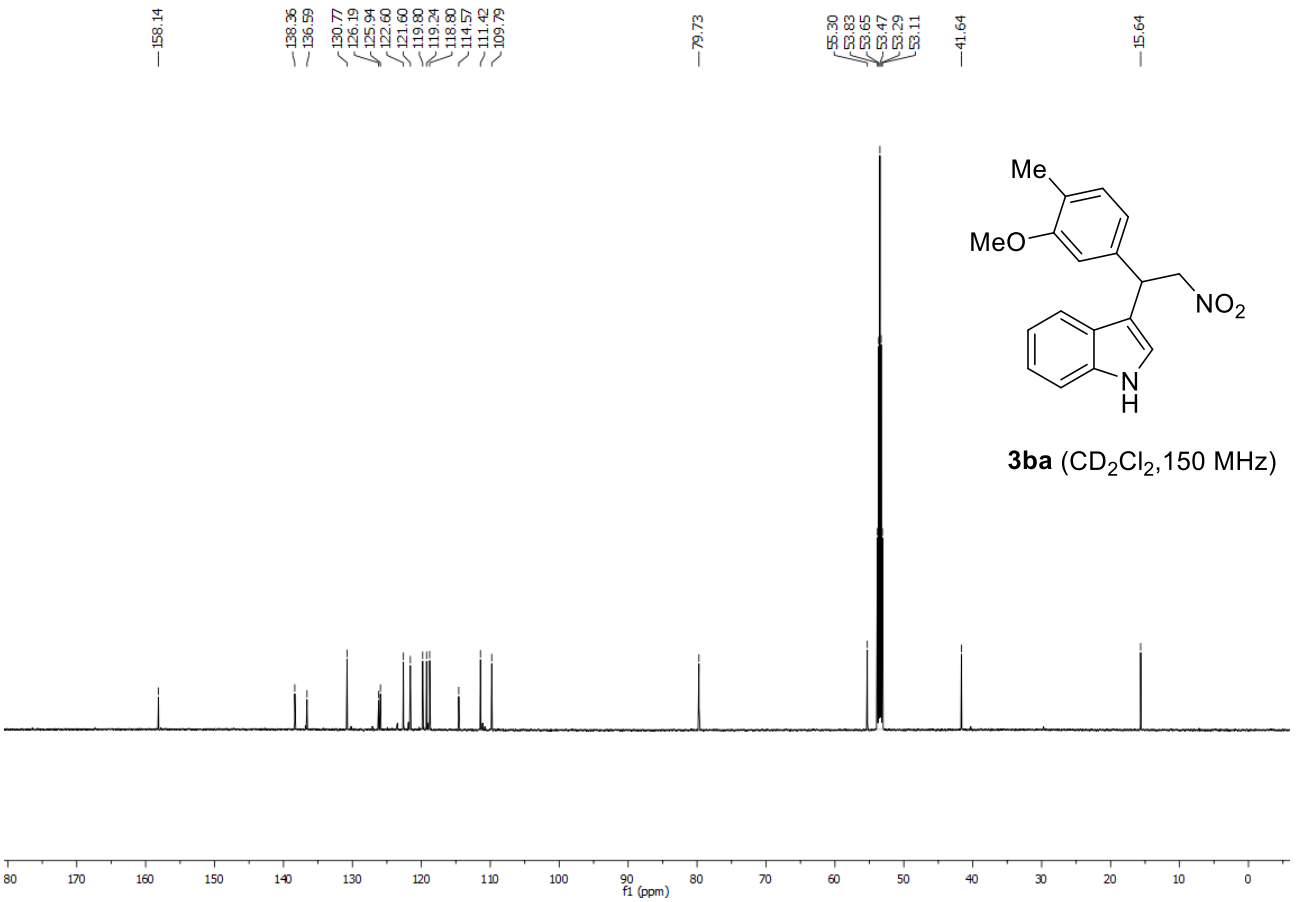
3aa ($CDCl_3$, 400 MHz)



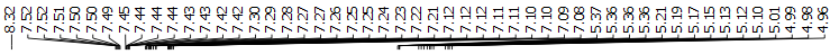
3aa ($CDCl_3$, 101 MHz)

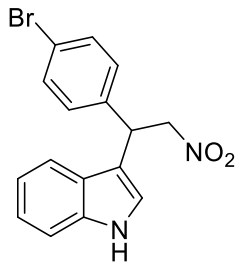


3ba (CD_2Cl_2, 600 MHz)

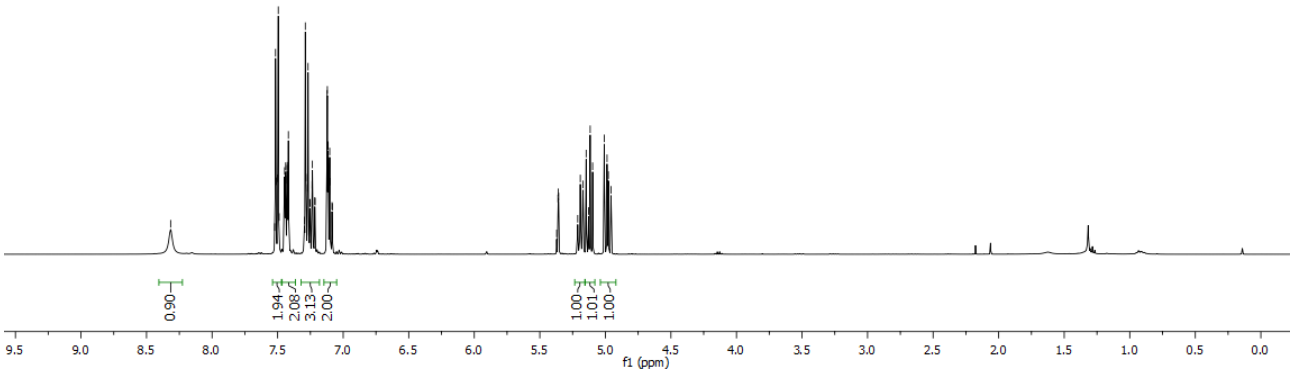


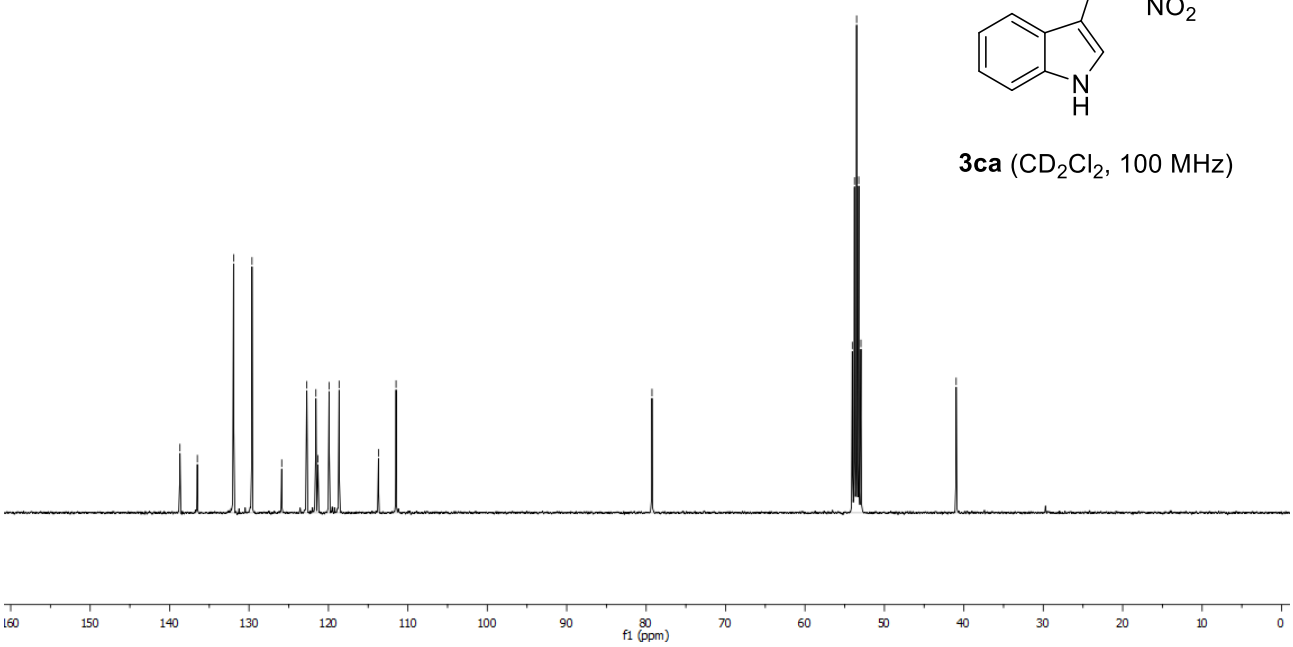
3ba (CD_2Cl_2,150 MHz)

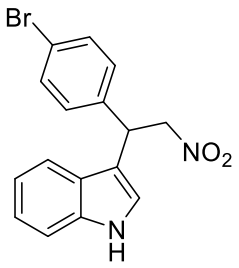




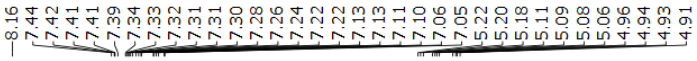
3ca (CD_2Cl_2, 400 MHz)

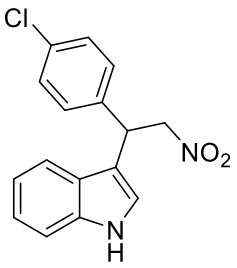




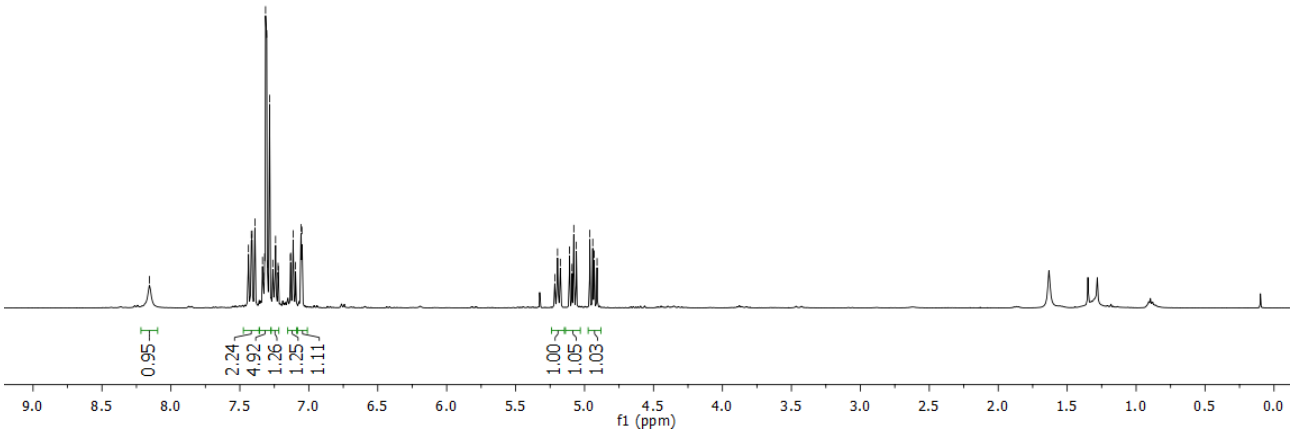


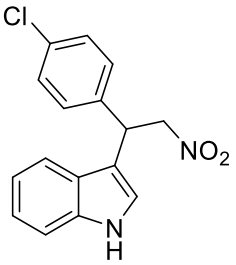
3ca (CD_2Cl_2, 100 MHz)



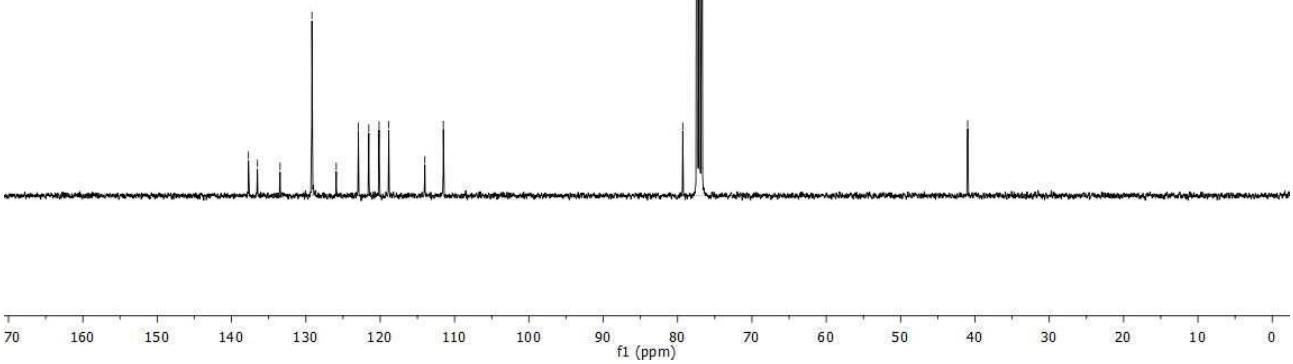


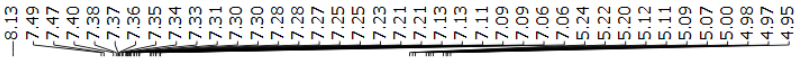
3da ($CDCl_3$, 400 MHz)

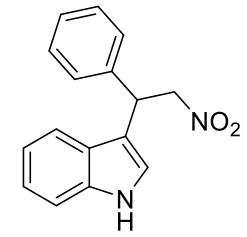




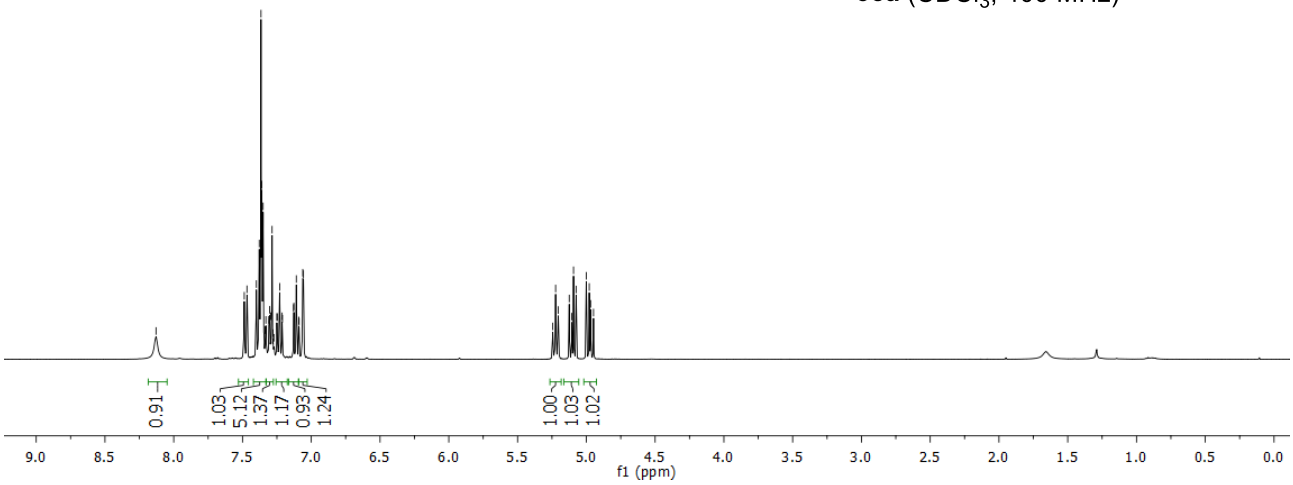
3da ($CDCl_3$, 101 MHz)

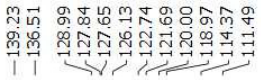


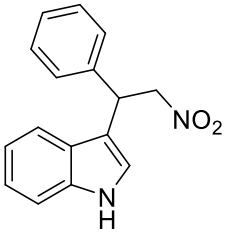




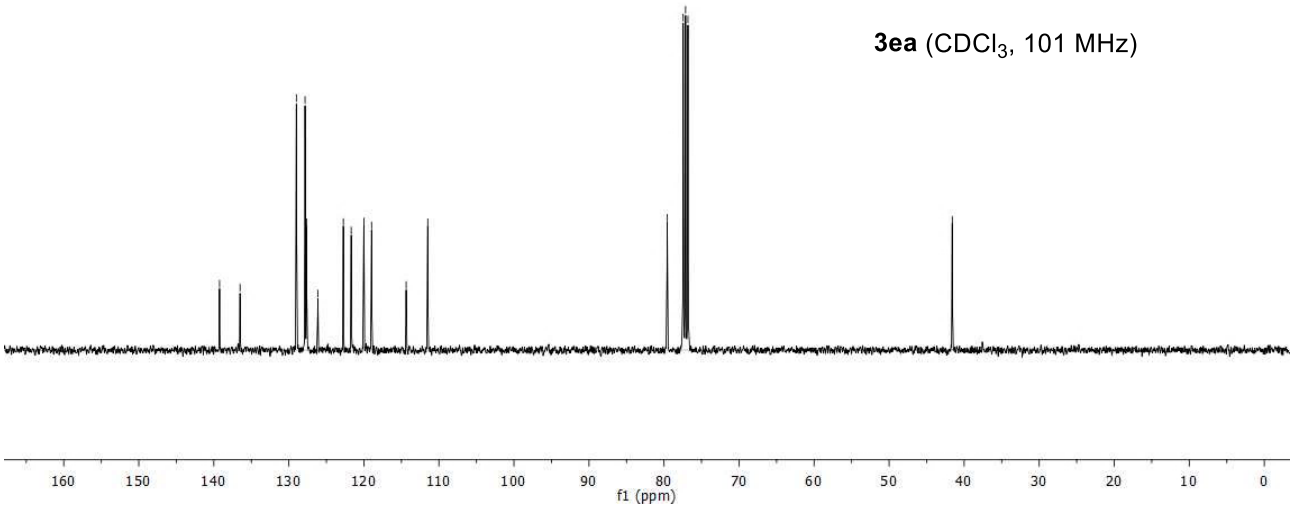
3ea ($CDCl_3$, 400 MHz)

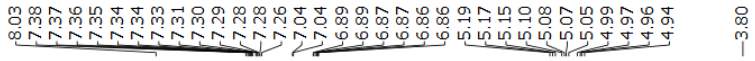


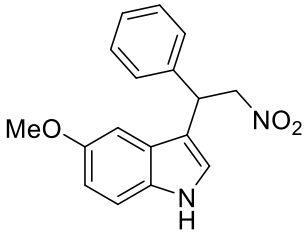




3ea ($CDCl_3$, 101 MHz)







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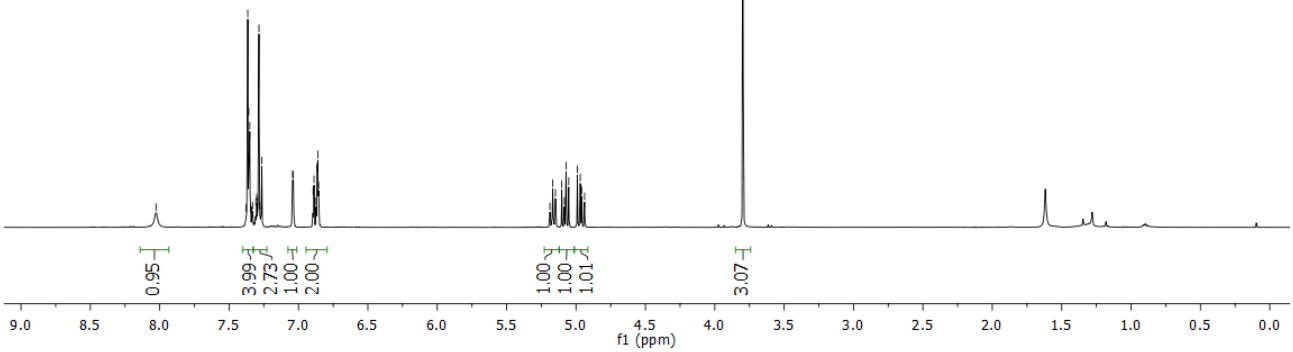
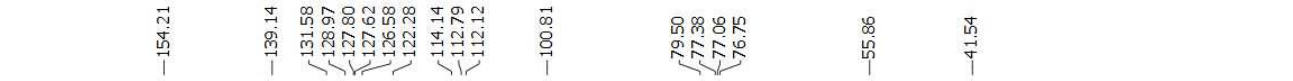
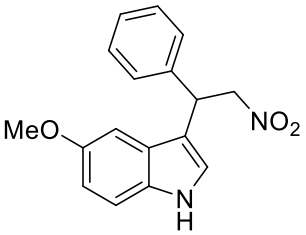
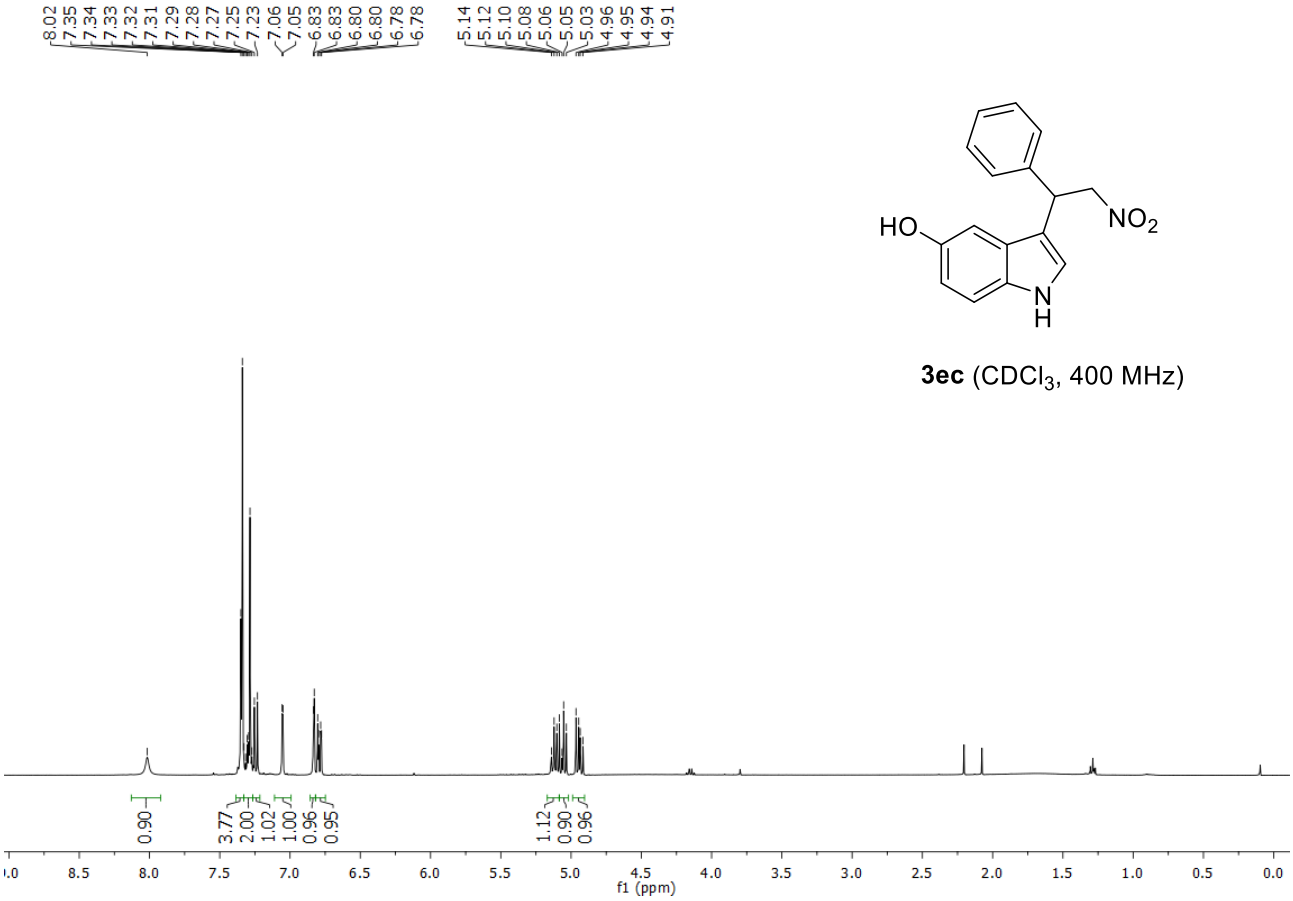


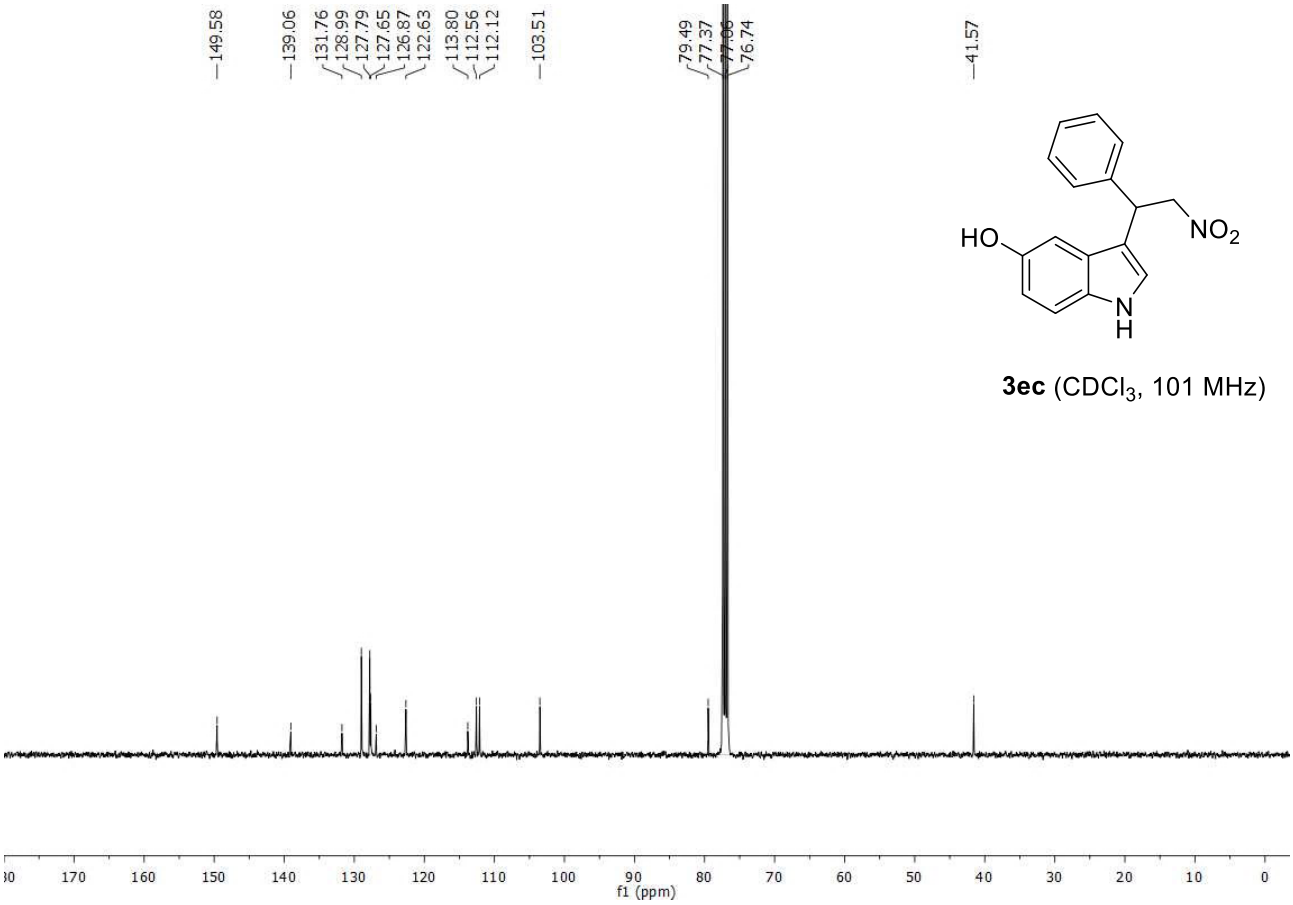




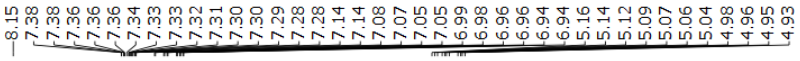
3eb ($CDCl_3$, 101 MHz)

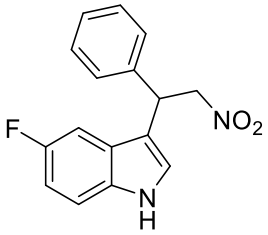


3ec ($CDCl_3$, 400 MHz)

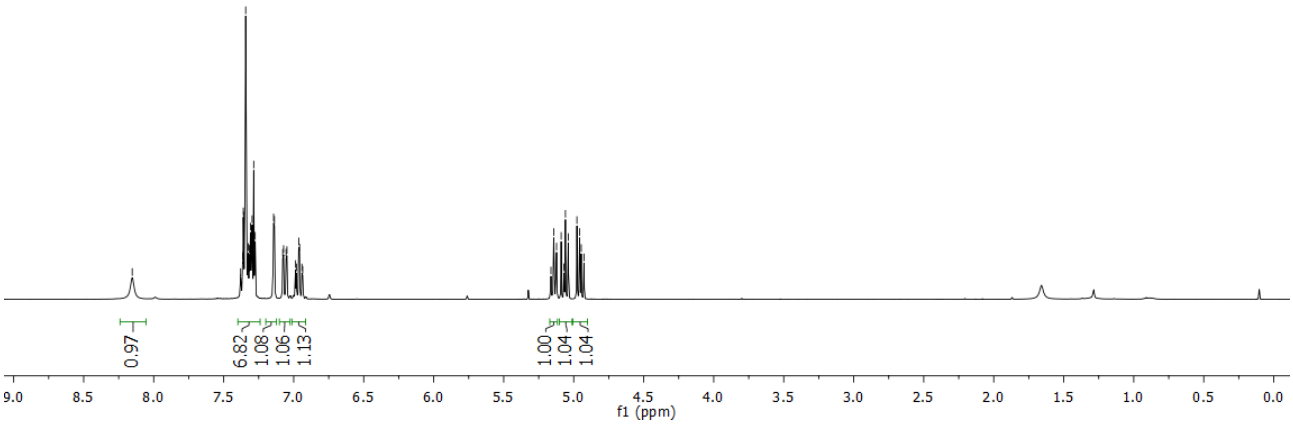


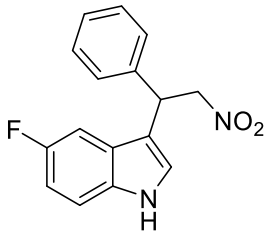
3ec ($CDCl_3$, 101 MHz)



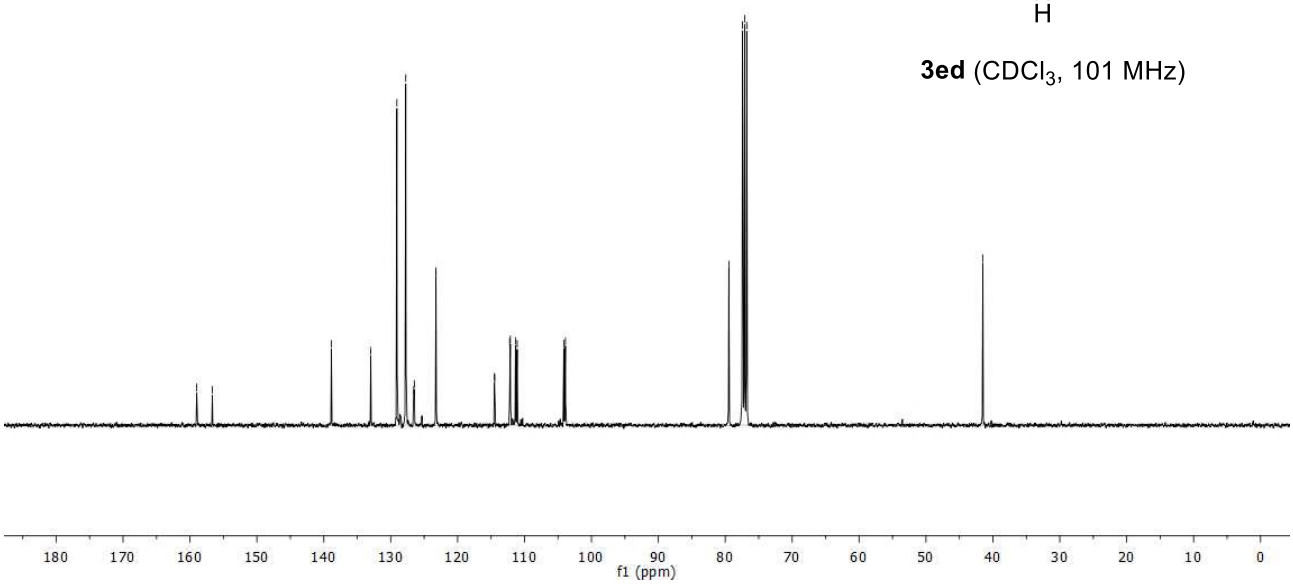


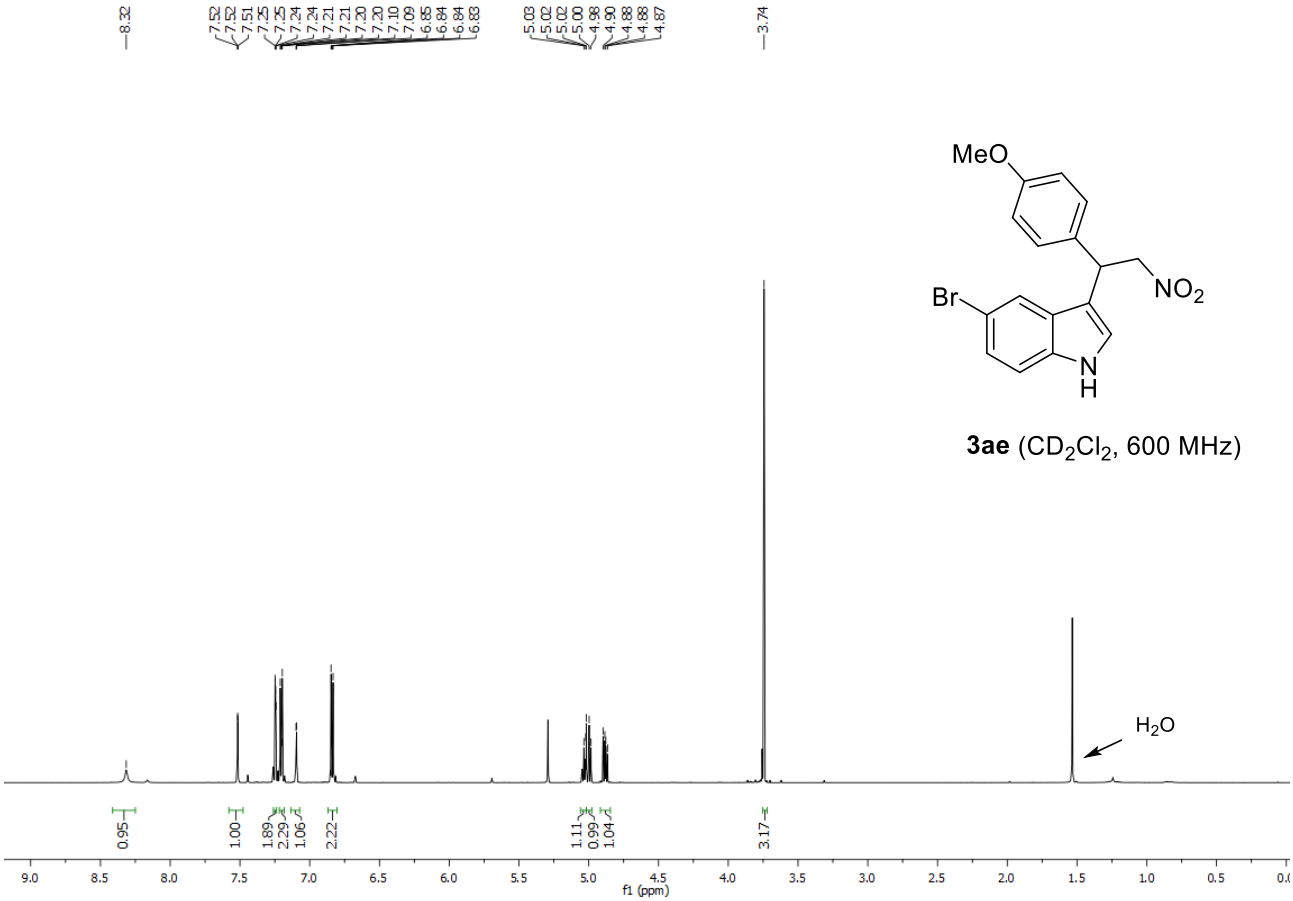
3ed ($CDCl_3$, 400 MHz)



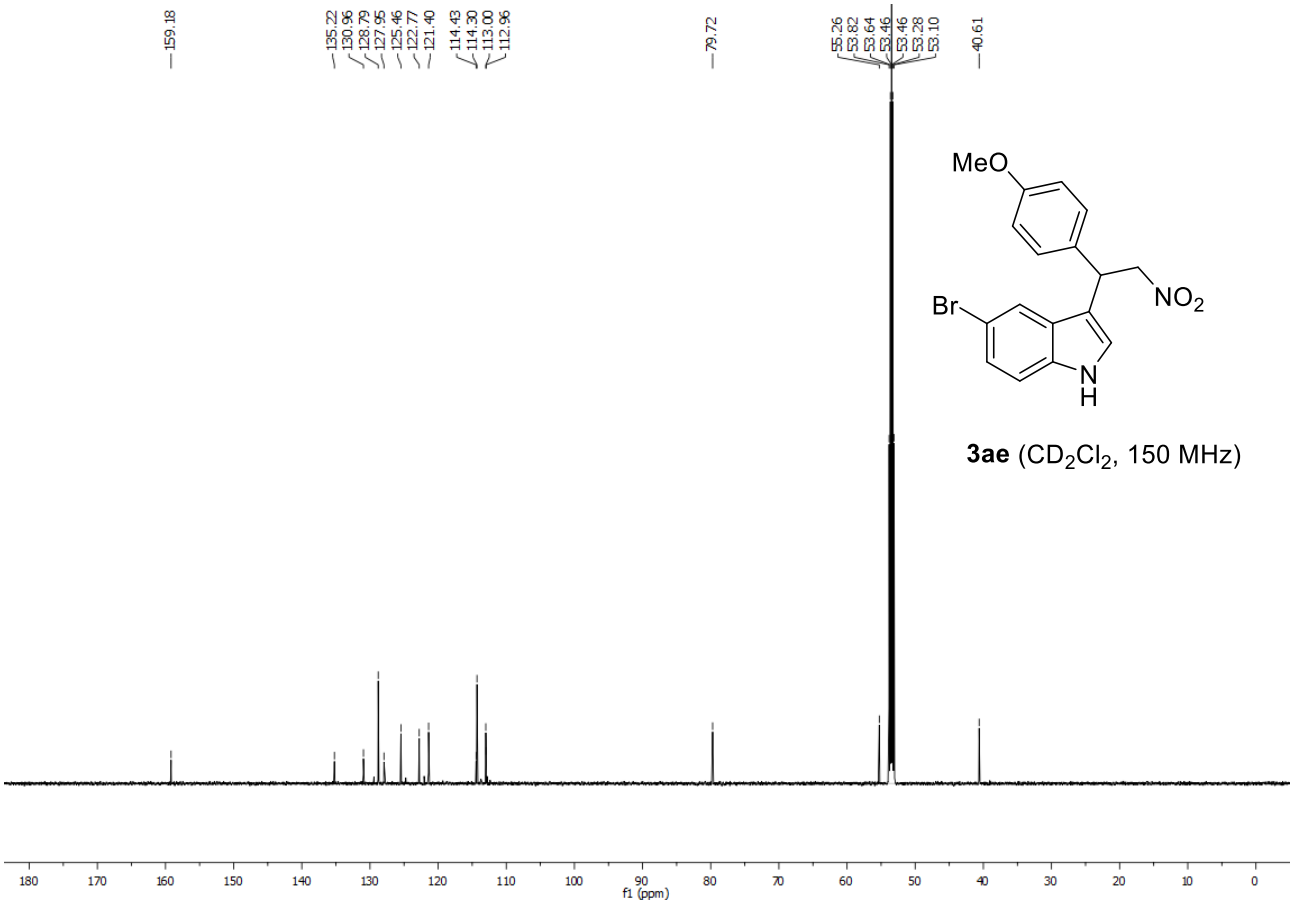


3ed ($CDCl_3$, 101 MHz)

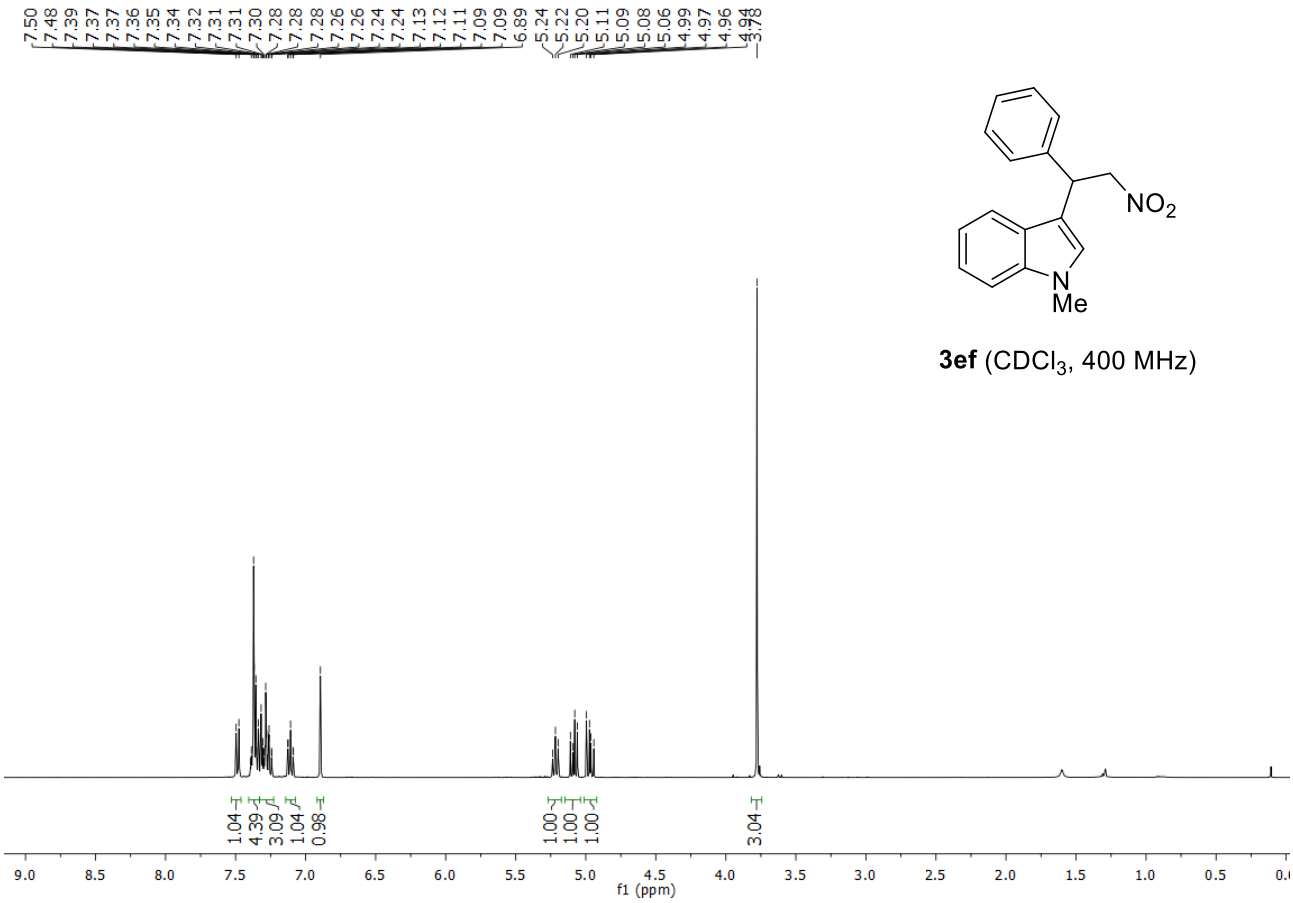




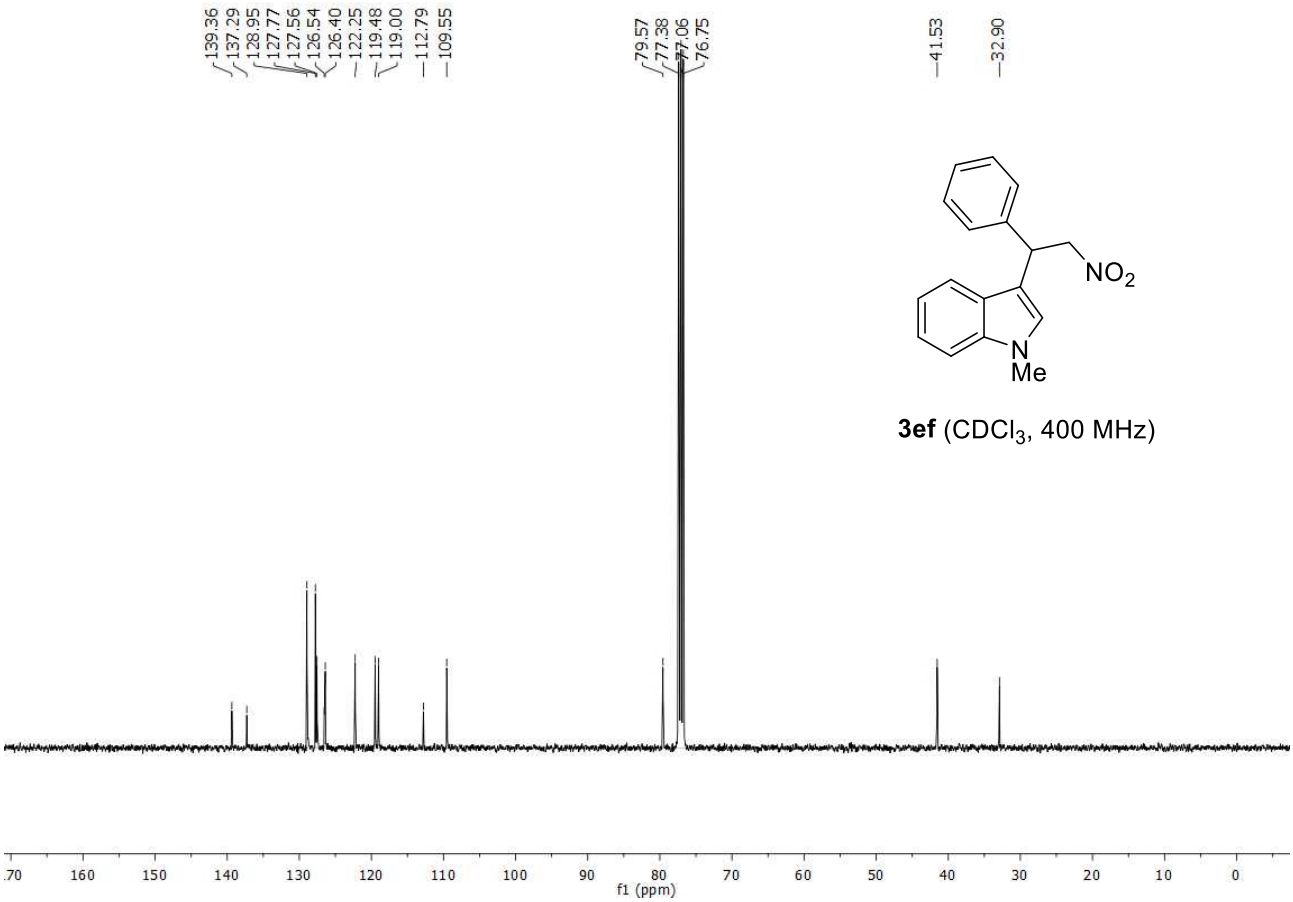
3ae (CD_2Cl_2, 600 MHz)



3ae (CD_2Cl_2, 150 MHz)



3ef ($CDCl_3$, 400 MHz)



3ef ($CDCl_3$, 400 MHz)

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