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Supplementary Materials

Synthesis of new water soluble β-Cyclodextrin@Curcumin conjugates and *in vitro* safety evaluation in primary cultures of rat cortical neurons

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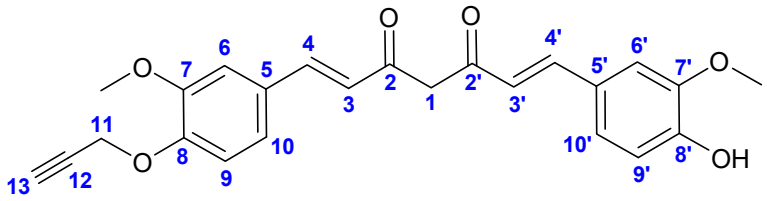
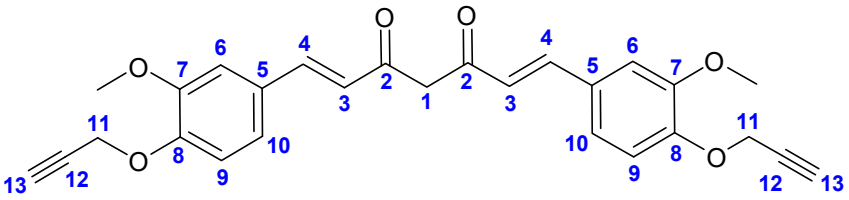
Characterization of Cur mono-alkyne 1



- ✓ **TLC**: R_f = 0.63 (EtOAc/Hexane = 50:50, v/v)
- ✓ **Analytical HPLC**: Rt = 12.62 min (ACN/H_2O, v/v) gradients from 10/90 to 100/0 in 25 min, then 100/0 for 10 min containing 0.1 % trifluoroacetic acid (TFA). A flow rate of 1.0 mL/min with UV detection at 254 nm and 420 nm.)
- ✓ **^{1}H NMR (300 MHz, DMSO-*d*$_6$)**: δ 3.59 (t, *J* = 2.1 Hz, 1H, H_{13}), 3.84 (s, 6H, $H_{7\text{-OMe}}$ and $H_{7'\text{-OMe}}$), 4.85 (d, *J* = 2.1 Hz, 2H, H_{11}), 6.10 (s, 2H, H_1), 6.79 (d, *J* = 1.8 Hz, 1H, H_6), 6.83 (d, *J* = 8.1 Hz, 1H, H_9), 6.87 (d, *J* = 1.8 Hz, 1H, $H_{6'}$), 7.08 (d, *J* = 8.4 Hz, 1H, $H_{9'}$), 7.16 (dd, *J* = 7.8 and 1.8 Hz, 1H, H_{10}), 7.27 (dd, *J* = 8.7 and 1.8 Hz, 1H, $H_{10'}$), 7.35 (d, *J* = 15.6 Hz, 2H, H_3 and $H_{3'}$), 7.57 (d, *J* = 15.6 Hz, 2H, H_4 and $H_{4'}$), 9.65 (s, 1H, $H_{8'\text{-OH}}$)
- ✓ **HRMS (ESI) for $C_{24}H_{22}O_6$**: $[M+H]^+$ calculated 407.1494, found 407.1867 and $[M+K]^+$ calculated 445.1053, found 445.1531

The physical data (NMR and HRMS) are in agreement with the values reported in the literature [1].

Characterization of Cur di-alkyne 2



- ✓ **TLC**: R_f = 0.72 (EtOAc/Hexane = 50:50, v/v)

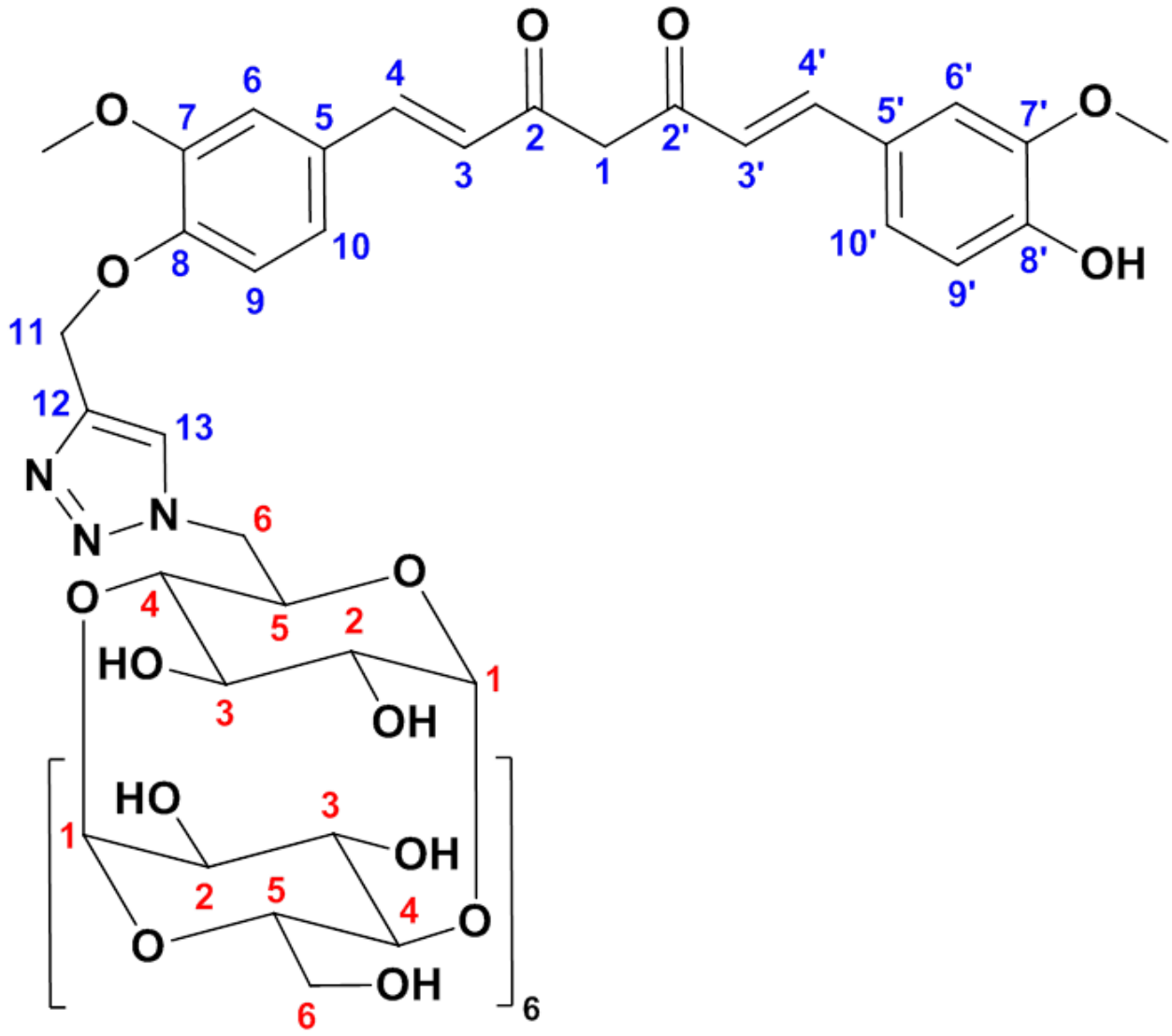
- ✓ **Analytical HPLC**: Rt = 13.64 min (ACN/H_2O, v/v) gradients from 10/90 to 100/0 in 25 min, then 100/0 for 10 min containing 0.1 % trifluoroacetic acid (TFA). A flow rate of 1.0 mL/min with UV detection at 254 nm and 420 nm.)

- ✓ **^{1}H NMR (300 MHz, DMSO-*d*$_6$)**: δ 3.59 (t, *J* = 2.1 Hz, 2H, H_{13}), 3.85 (s, 6H, $H_{7\text{-OMe}}$), 4.86 (d, *J* = 2.1 Hz, 4H, H_{11}), 6.13 (s, 2H, H_1), 6.84 (d, *J* = 1.5 Hz, 2H, H_6), 6.95 (d, *J* = 7.9 Hz, 2H, H_9), 7.19 (dd, *J* = 8.1 and 1.5 Hz, 2H, H_{10}), 7.37 (d, *J* = 16.0 Hz, 2H, H_3), 7.60 (d, *J* = 16.0 Hz, 2H, H_4)

- ✓ **HRMS (ESI) for $C_{27}H_{24}O_6$**: $[M+H]^+$ calculated 445.1651, found 445.1962 and $[M+K]^+$ calculated 483.1209, found 483.1643

The physical data (NMR and HRMS) are in agreement with the values reported in the literature [1]..

1D and 2D NMR spectra (^{1}H, ^{13}C, HSQC and HMBC) of β-CD@Cur 4 nanoconjugate



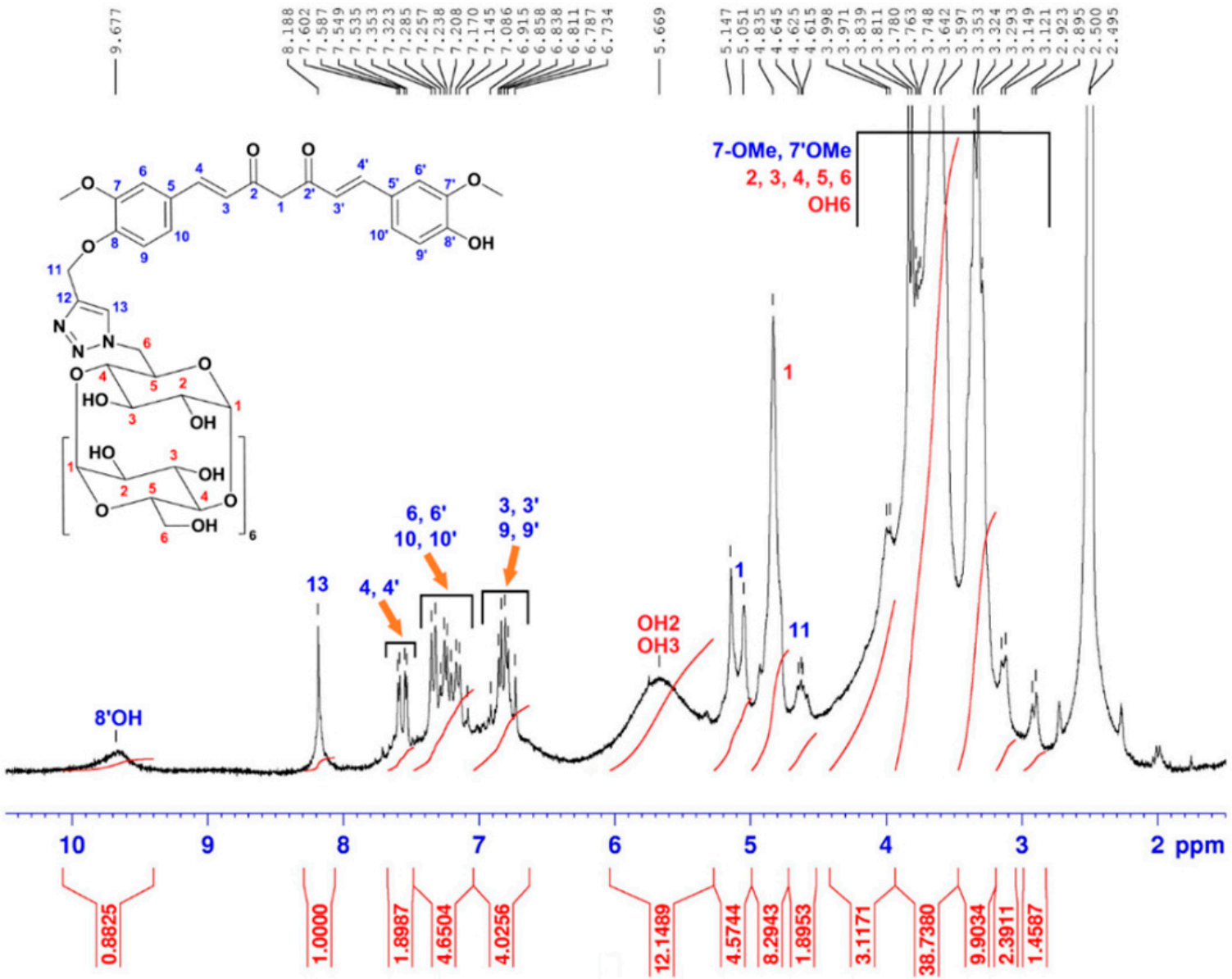


Figure S1. ^{1}H NMR spectrum (300 MHz, DMSO-d_6, 298K) of β-CD@Cur **4** nanoconjugate.

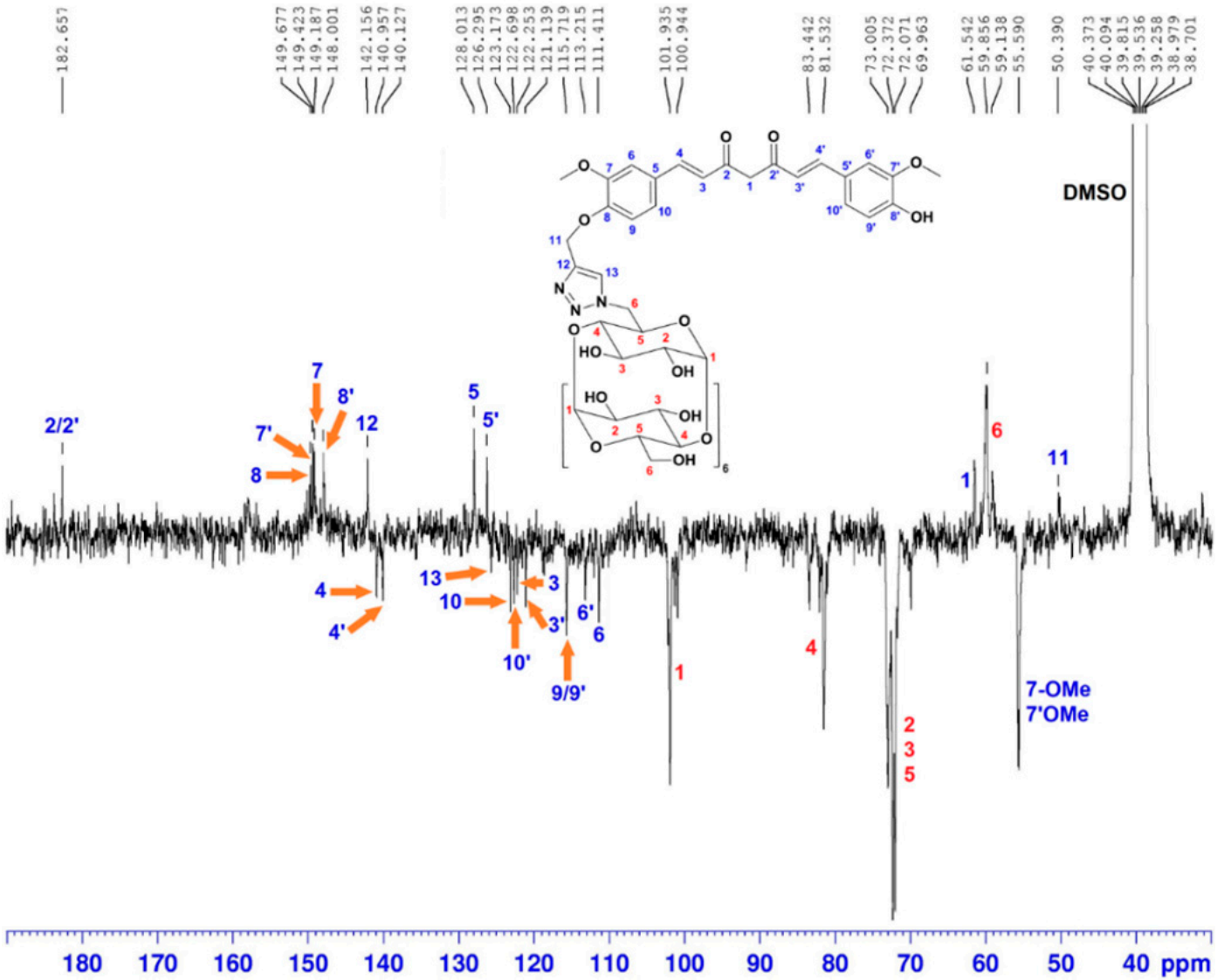


Figure S2. *J* mod ^{13}C NMR spectrum (75 MHz, DMSO-d_6, 298K) of β-CD@Cur **4** nanoconjugate (C and CH_2 up; CH_3 and CH down).

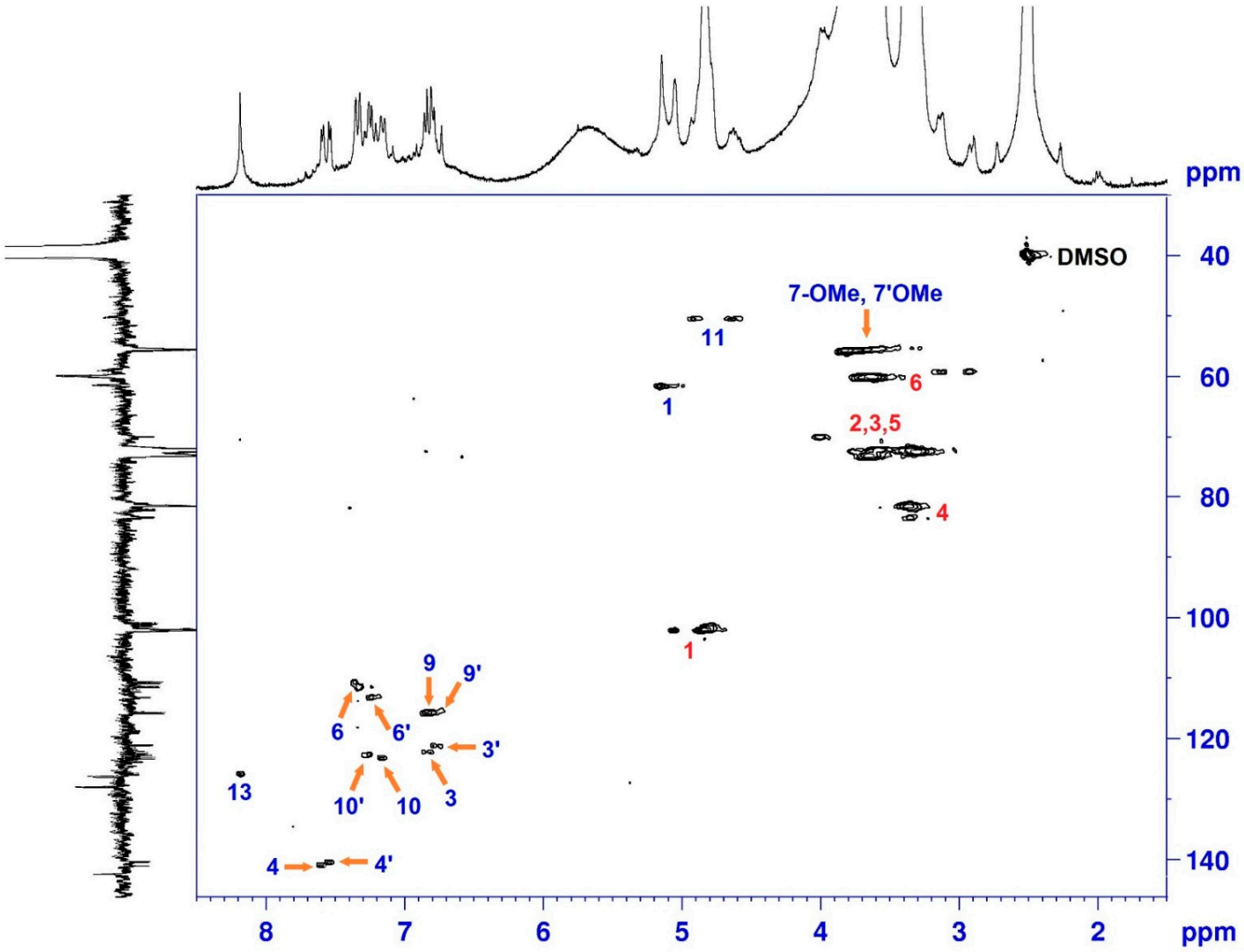


Figure S3. 2D HSQC NMR spectrum (300 MHz, DMSO-d_6, 298K) of β-CD@Cur **4** nanoconjugate.

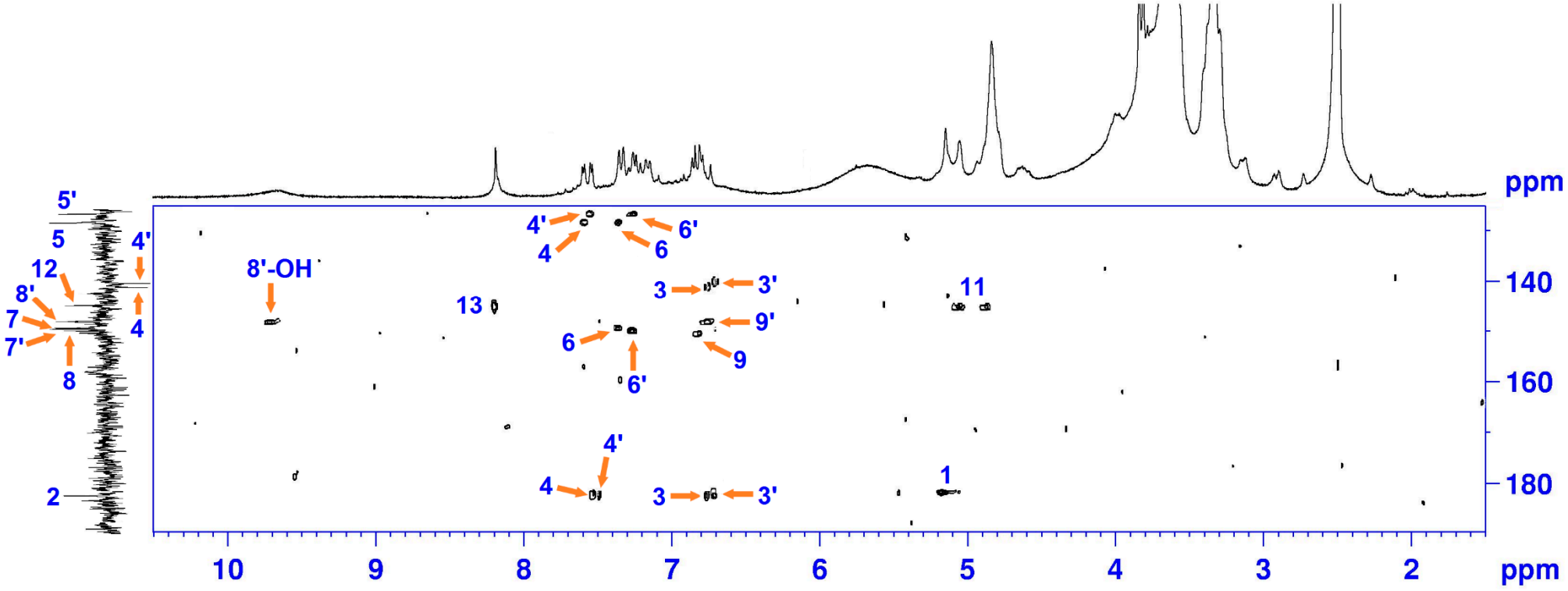
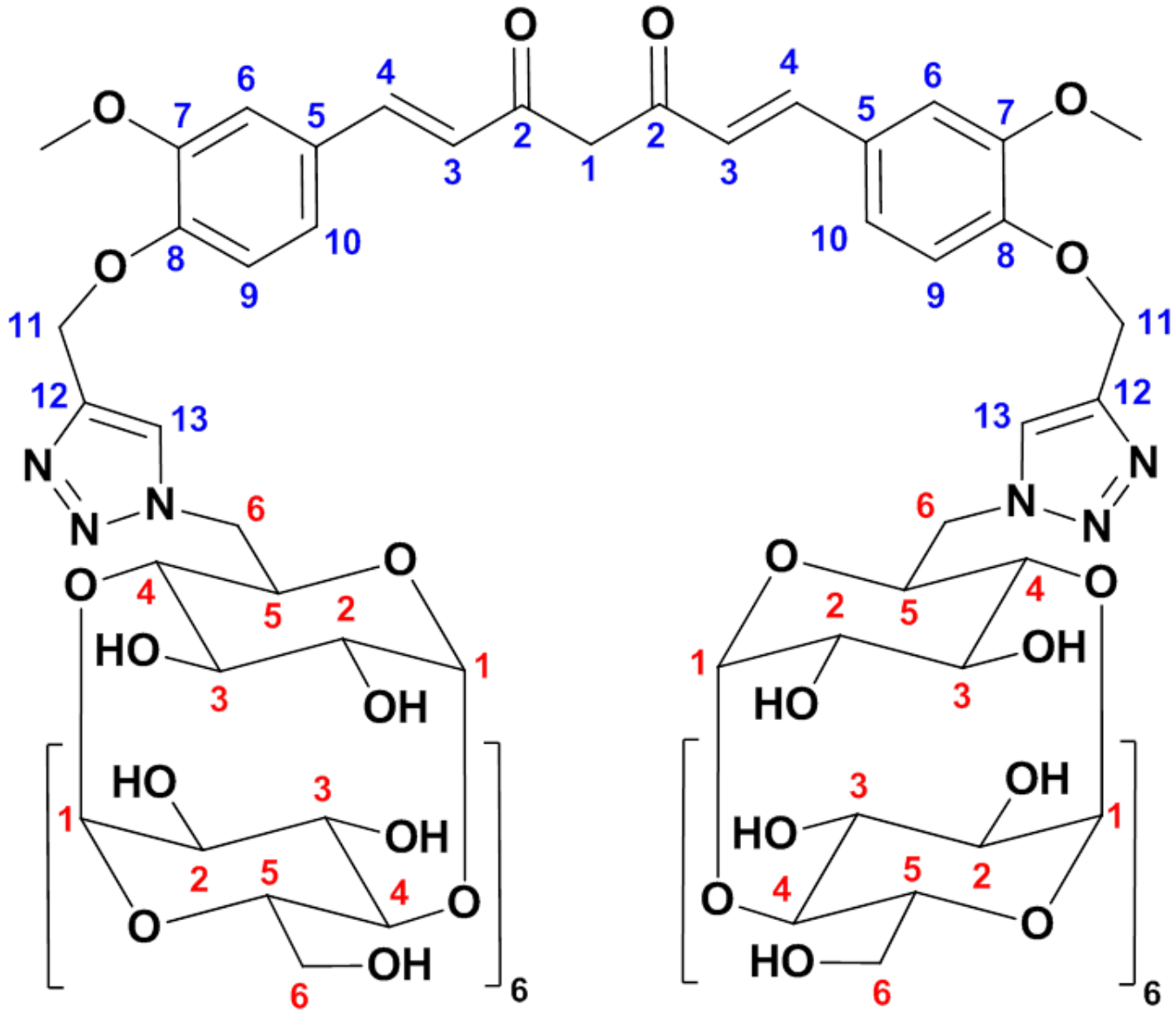


Figure S4. 2D HMBC NMR spectrum (300 MHz, DMSO-d_6, 298K) of β-CD@Cur **4** nanoconjugate.

1D and 2D NMR spectra (^{1}H, ^{13}C, HSQC and HMBC) of (β-CD)$_2$@Cur 5 nanoconjugate



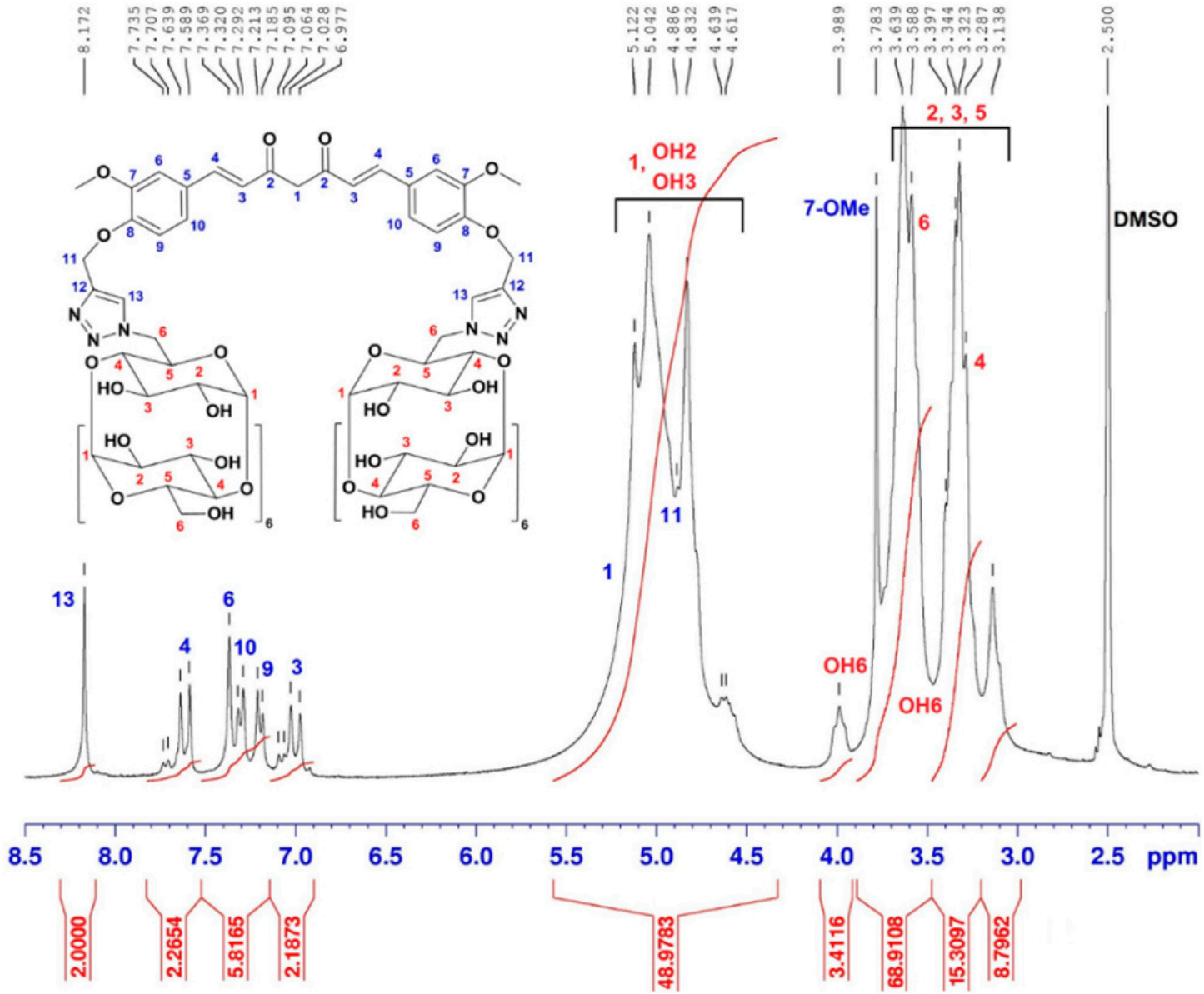


Figure S5. ^{1}H NMR spectrum (300 MHz, DMSO-d_6, 298K) of (β-CD)$_2$@Cur **5** nanoconjugate.

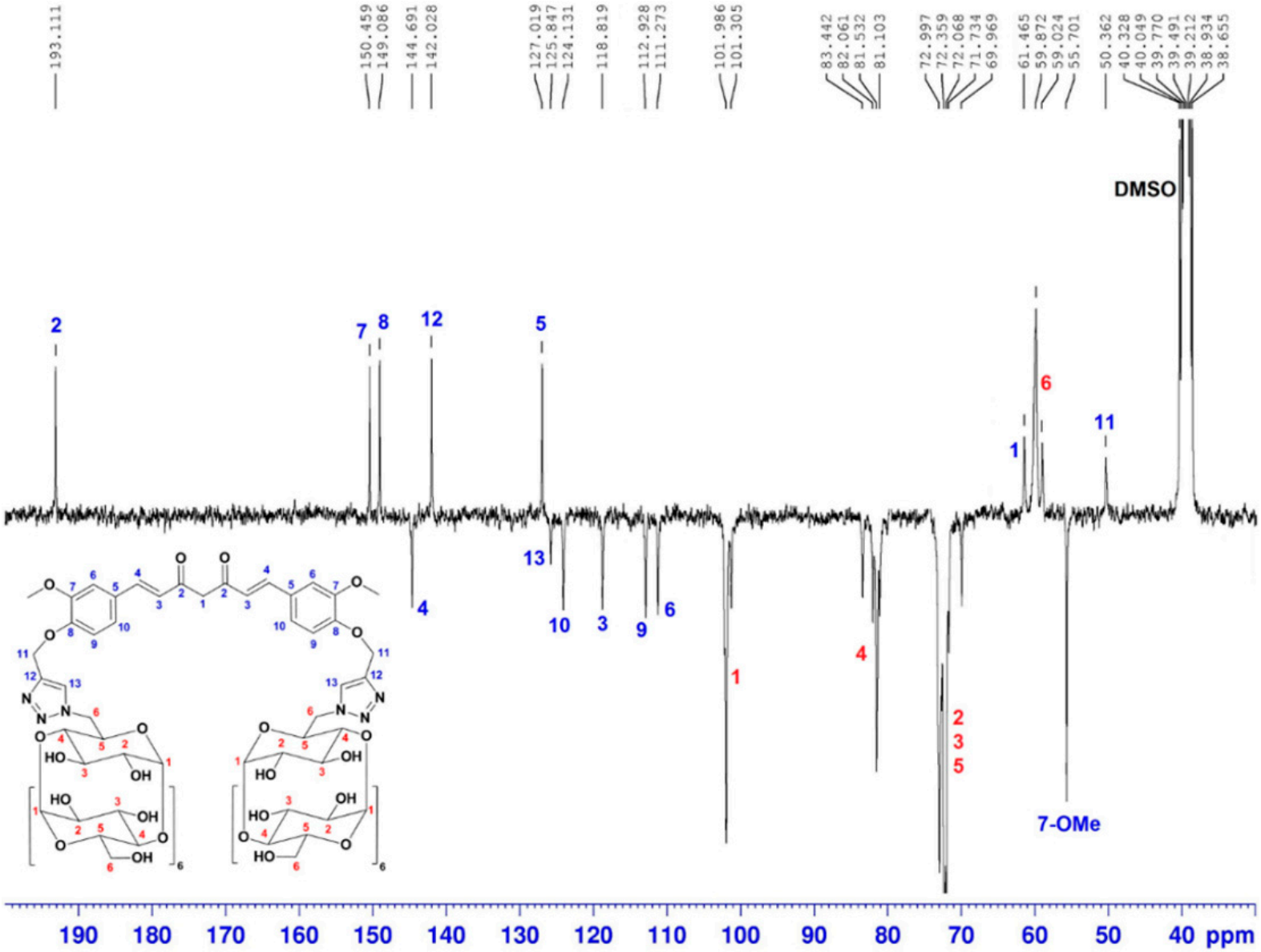


Figure S6. *J* mod ^{13}C NMR spectrum (75 MHz, DMSO-d_6, 298K) of (β-CD)$_2$@Cur **5** nanoconjugate (C and CH$_2$ up; CH$_3$ and CH down).

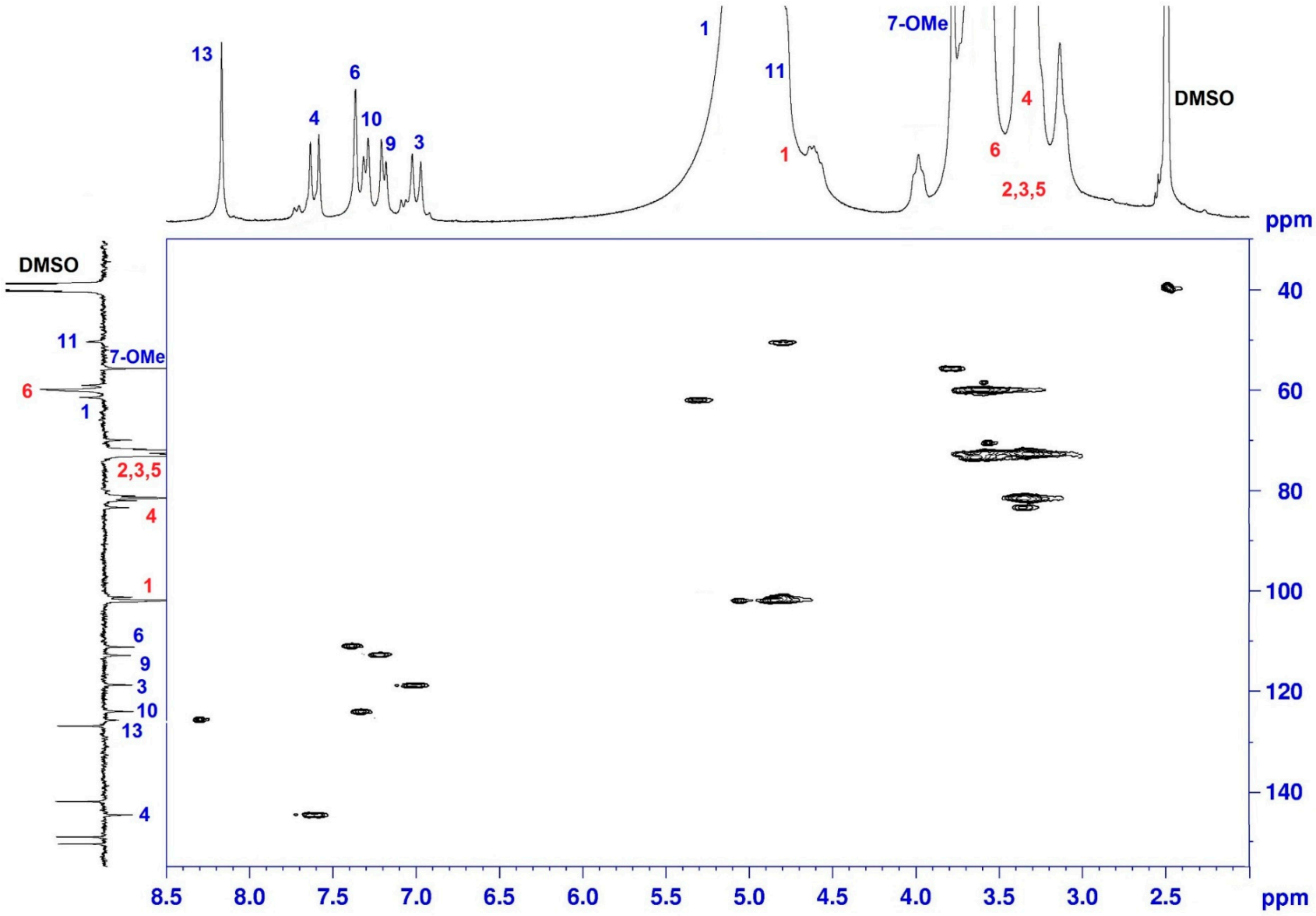


Figure S7. 2D HSQC NMR spectrum (300 MHz, DMSO-d_6, 298K) of (β-CD)$_2$@Cur **5** nanoconjugate.

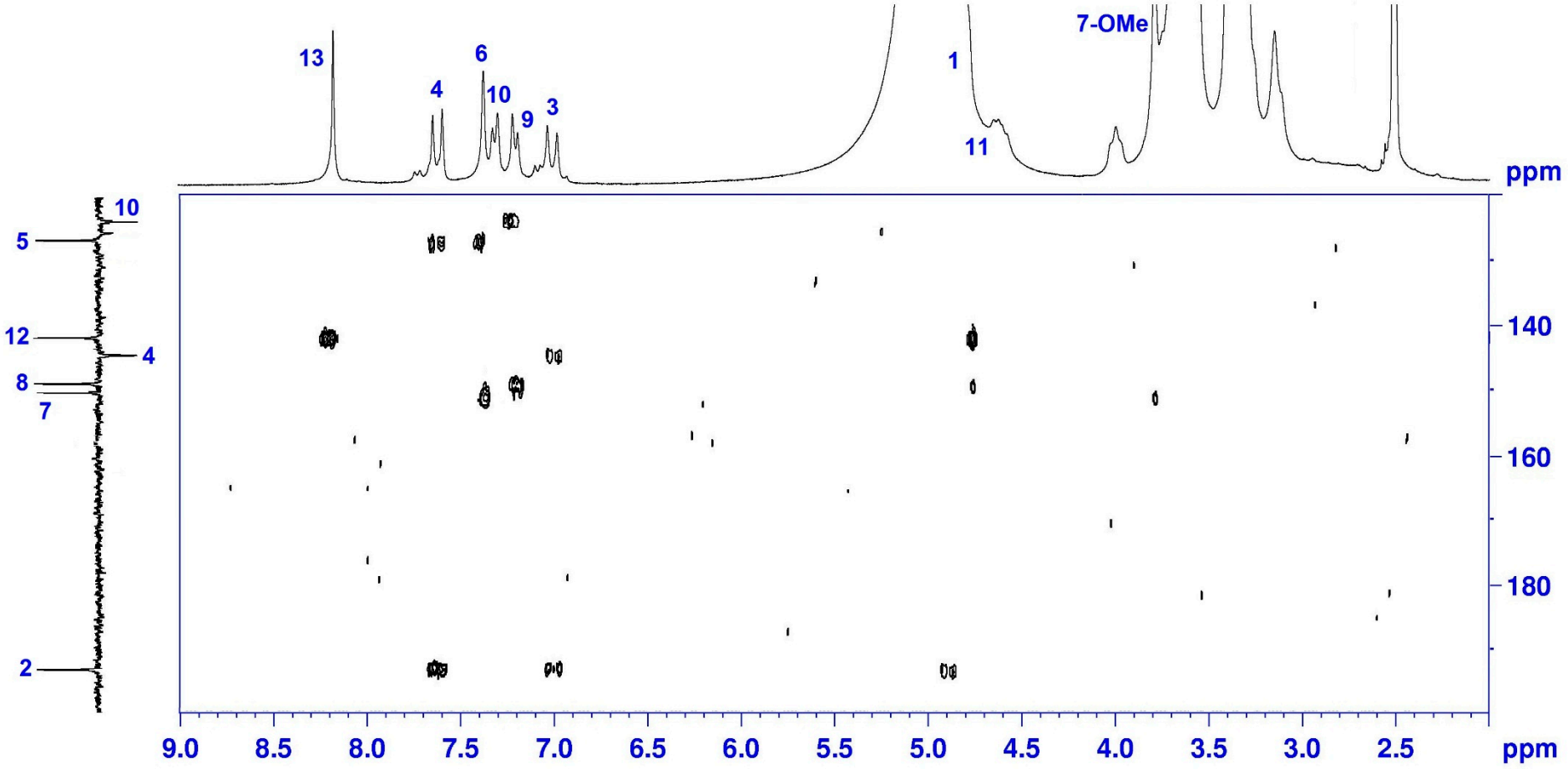


Figure S8. 2D HMBC NMR spectrum (300 MHz, DMSO-d_6, 298K) of (β-CD)$_2$@Cur **5** nanoconjugate.

References

1. Raja, K.; Alonso, A.; Banerjee, P.; Dolai, S.; Corbo, C.; Averick, S.; Mogha, A.; Debnath, S. Curcumin derivatives. WO2011106691A2.**2011**. https://patentimages.storage.googleapis.com/44/6a/79/e7561b802ebbd8/WO2011106691A2.pdf