Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Conjugates of titanocene with non-steroidal anti-inflammatory drugs: synthesis, unusual NMR characteristics, stability and cytotoxicity

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Supplementary information

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1. NMR Spectra of sodium salts 1-4.

All NMR spectra were recorded with Agilent 400 MR spectrometer in $CDCl_3$ or DMSO-d6; the residual signal of deuterated solvent was used as an internal standard.

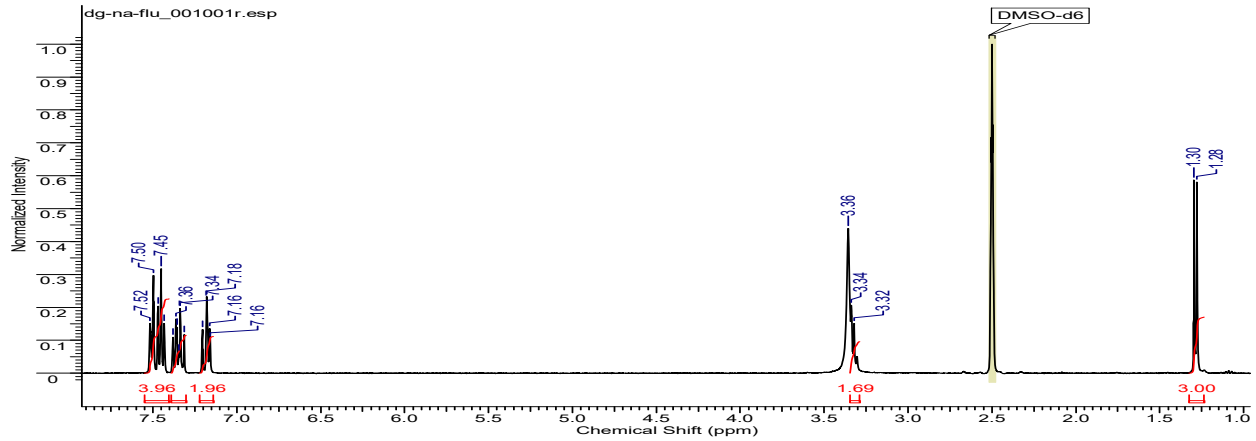


Fig. S1. ^{1}H NMR spectrum of salt **1**.

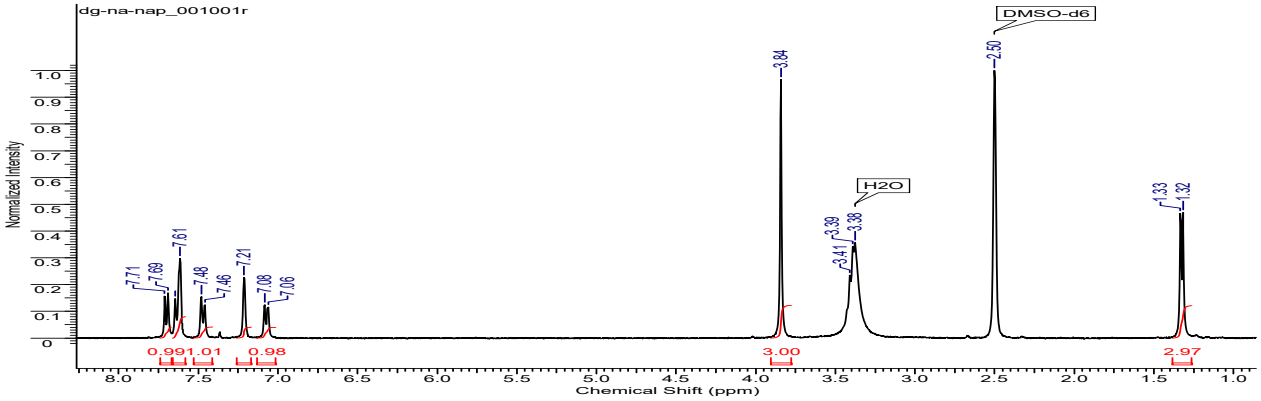


Fig. S2. ^{1}H NMR spectrum of salt **2**.

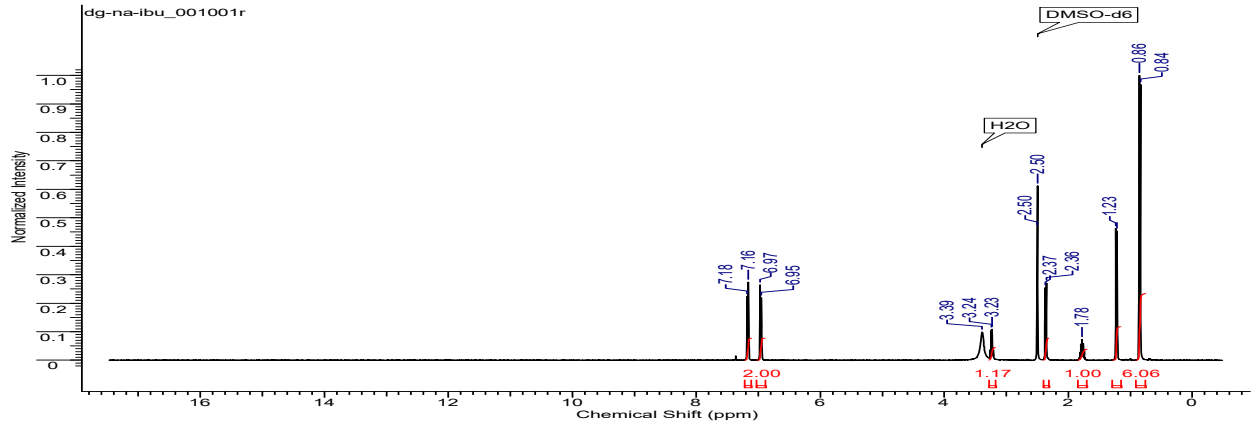


Fig. S3. ^{1}H NMR spectrum of salt **3**.

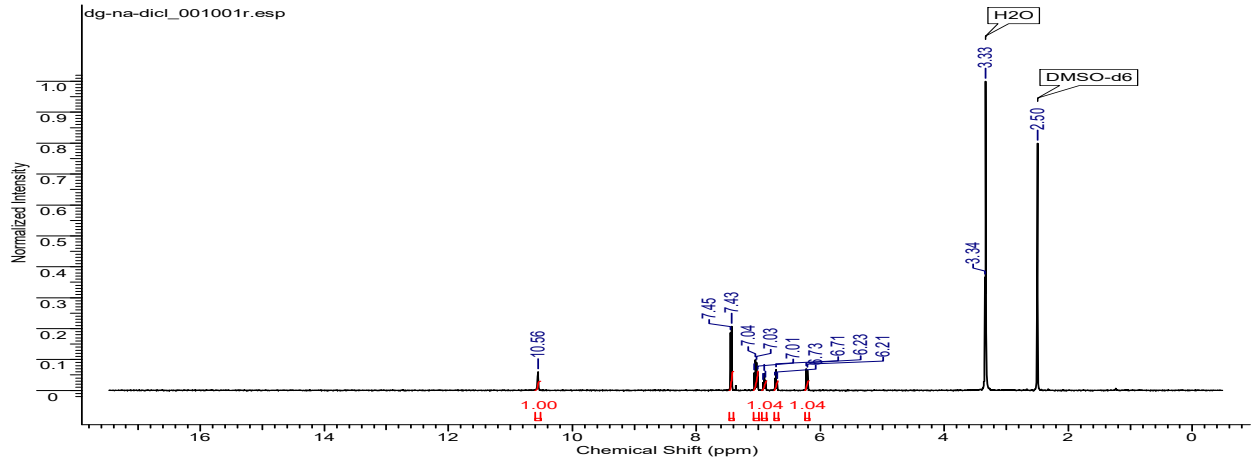


Fig. S4. ^{1}H NMR spectrum of salt **4**.

2. NMR Spectra of Titanocene conjugates 5-8.

2.1 NMR Spectra of conjugate 5.

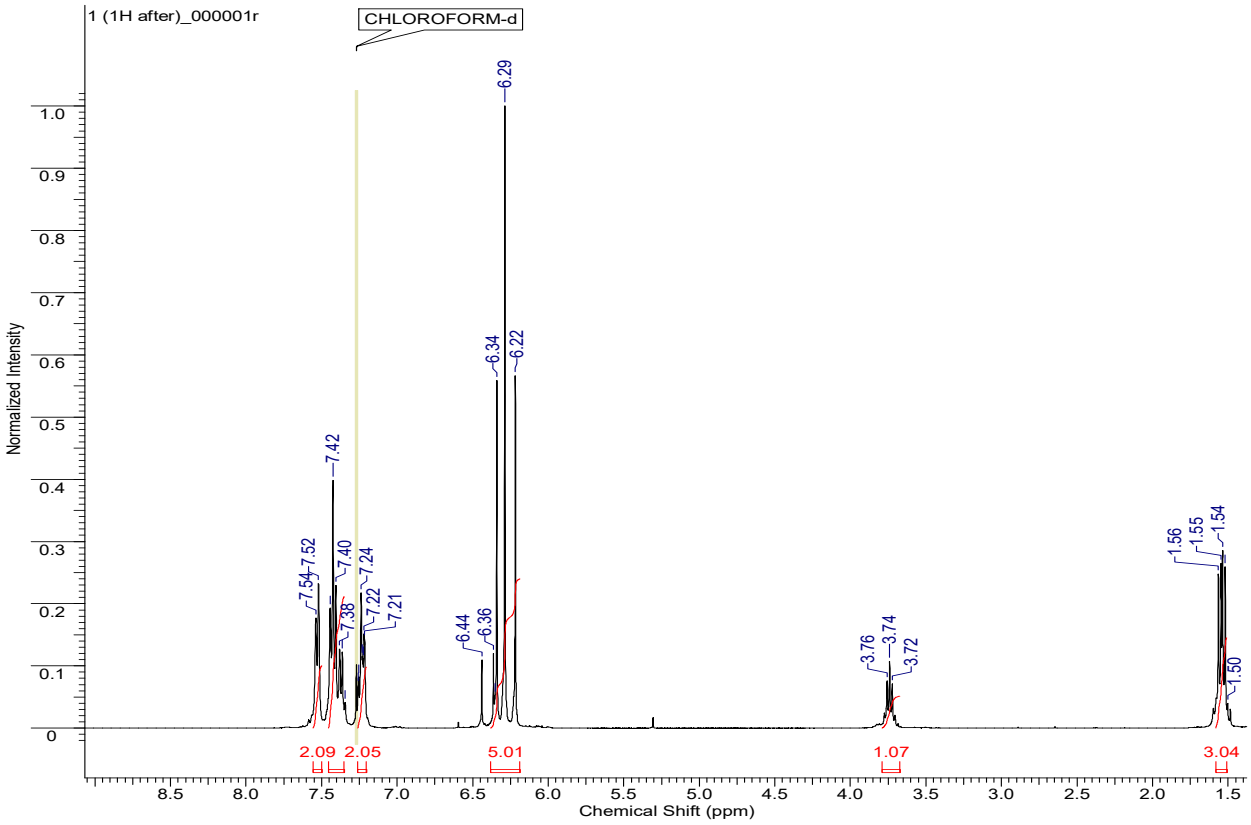


Fig. S5. ^{1}H NMR spectrum of conjugate **5**.

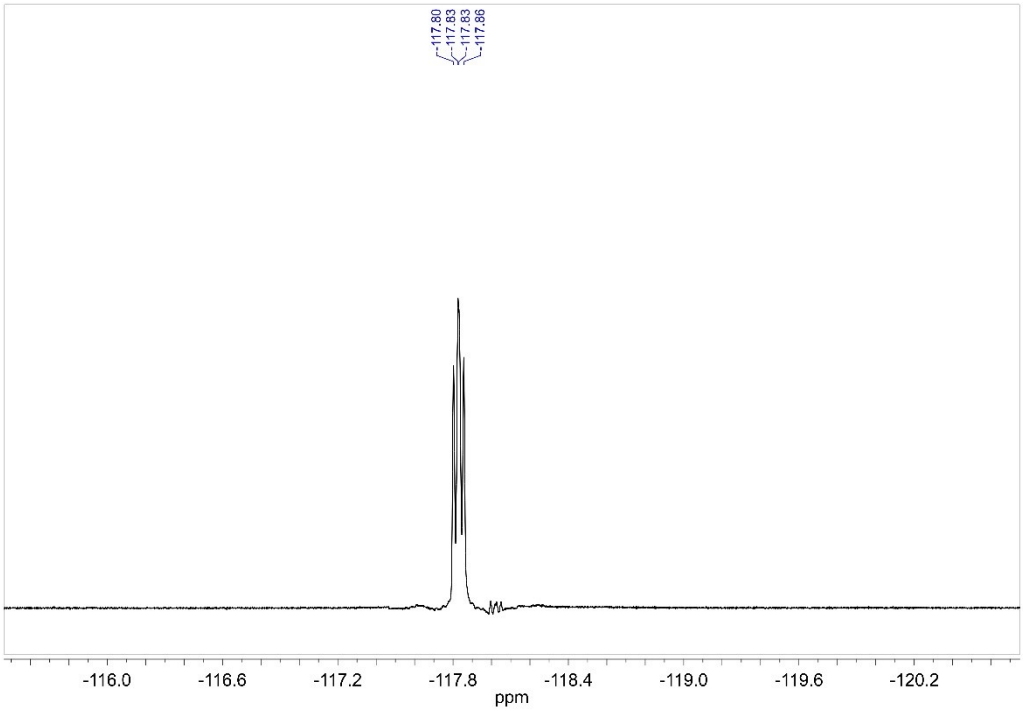


Fig. S6. ^{19}F NMR spectrum of conjugate **5**.

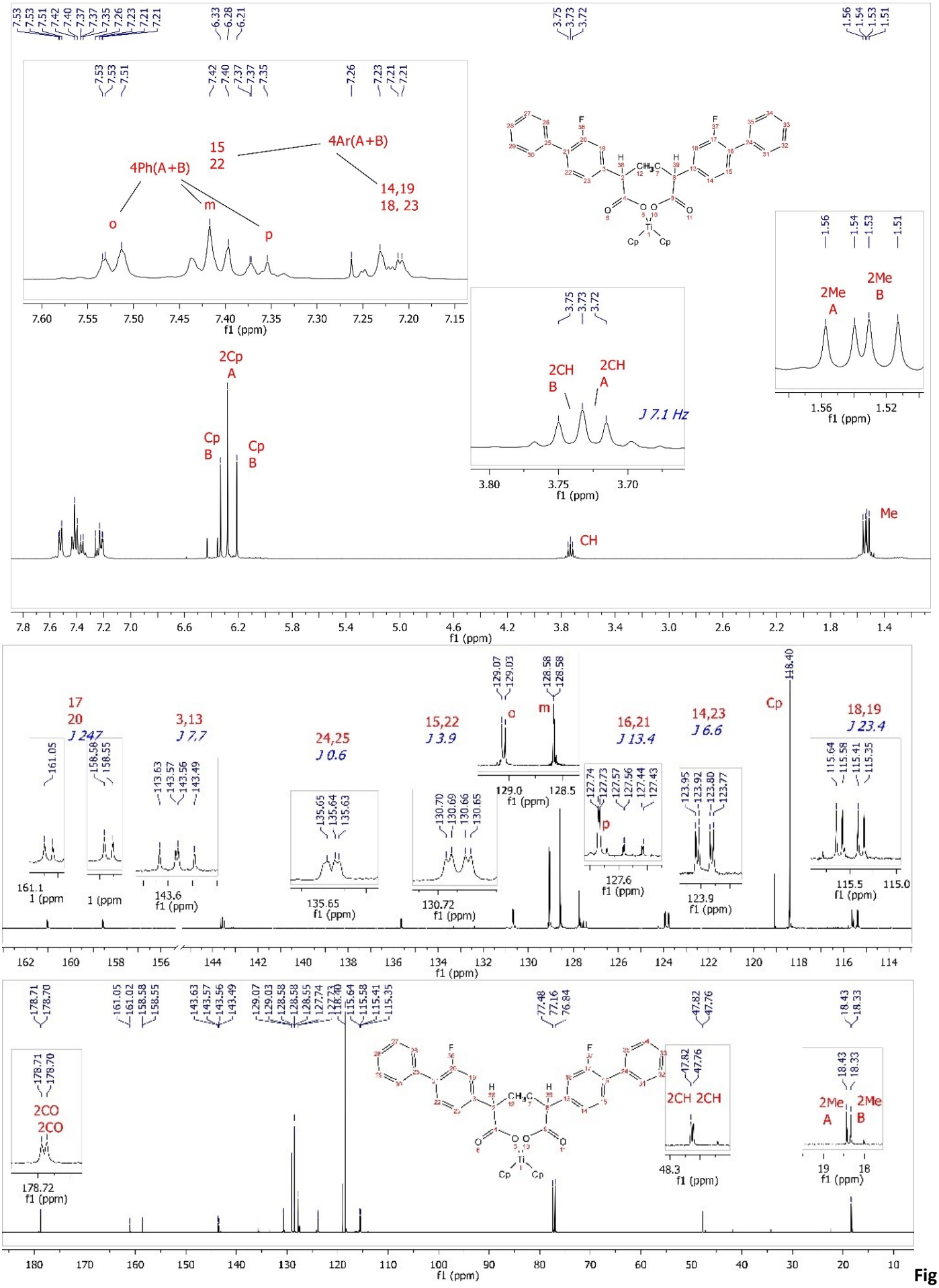


Fig. S7. Signal assignment in NMR spectra of **5** ^{1}H (Top), ^{13}C (Bottom).

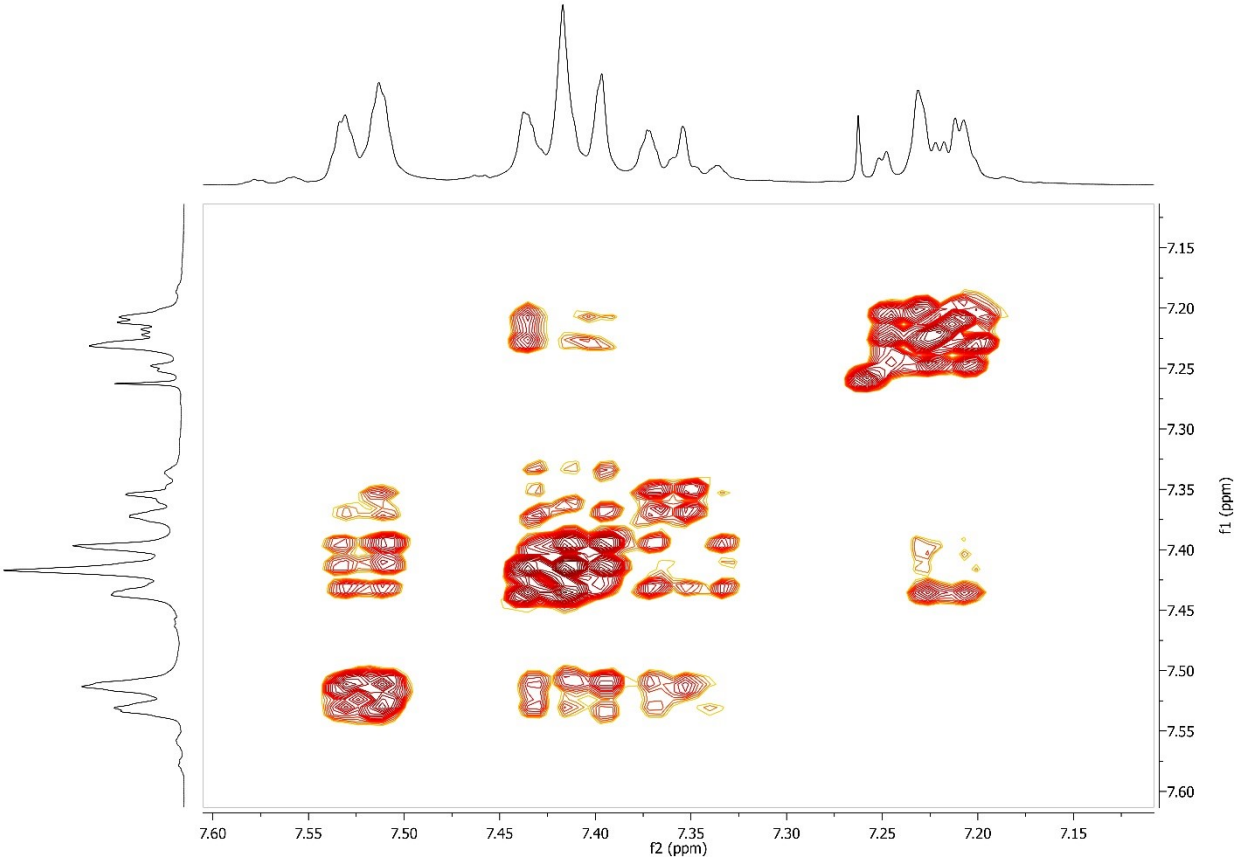


Fig. S8. COSY ^{1}H NMR spectrum of **5** ($CDCl_3$, 400 MHz, 298 K, aromatic region).

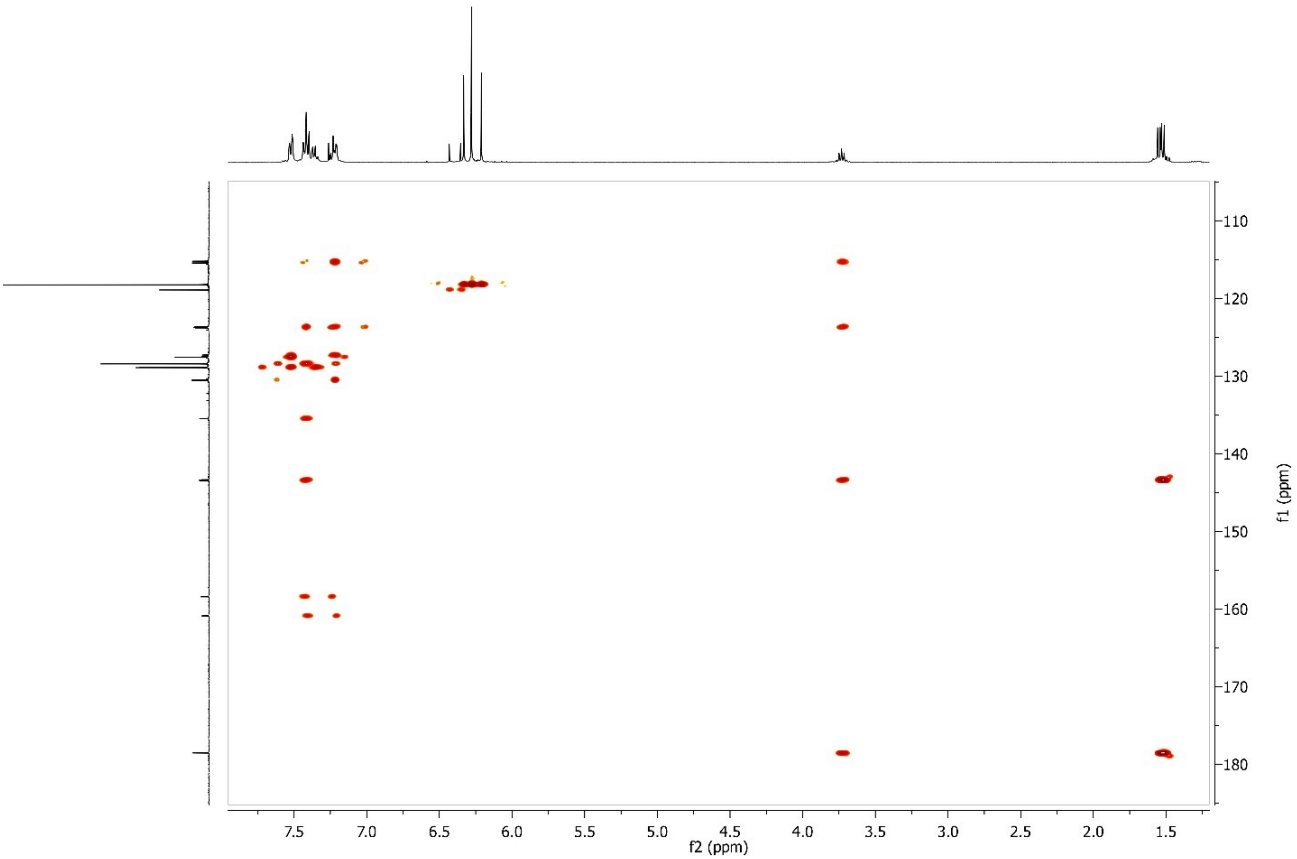


Fig. S9. gHMBCAD spectrum of **5** ($CDCl_3$, 400 MHz, 298 K).

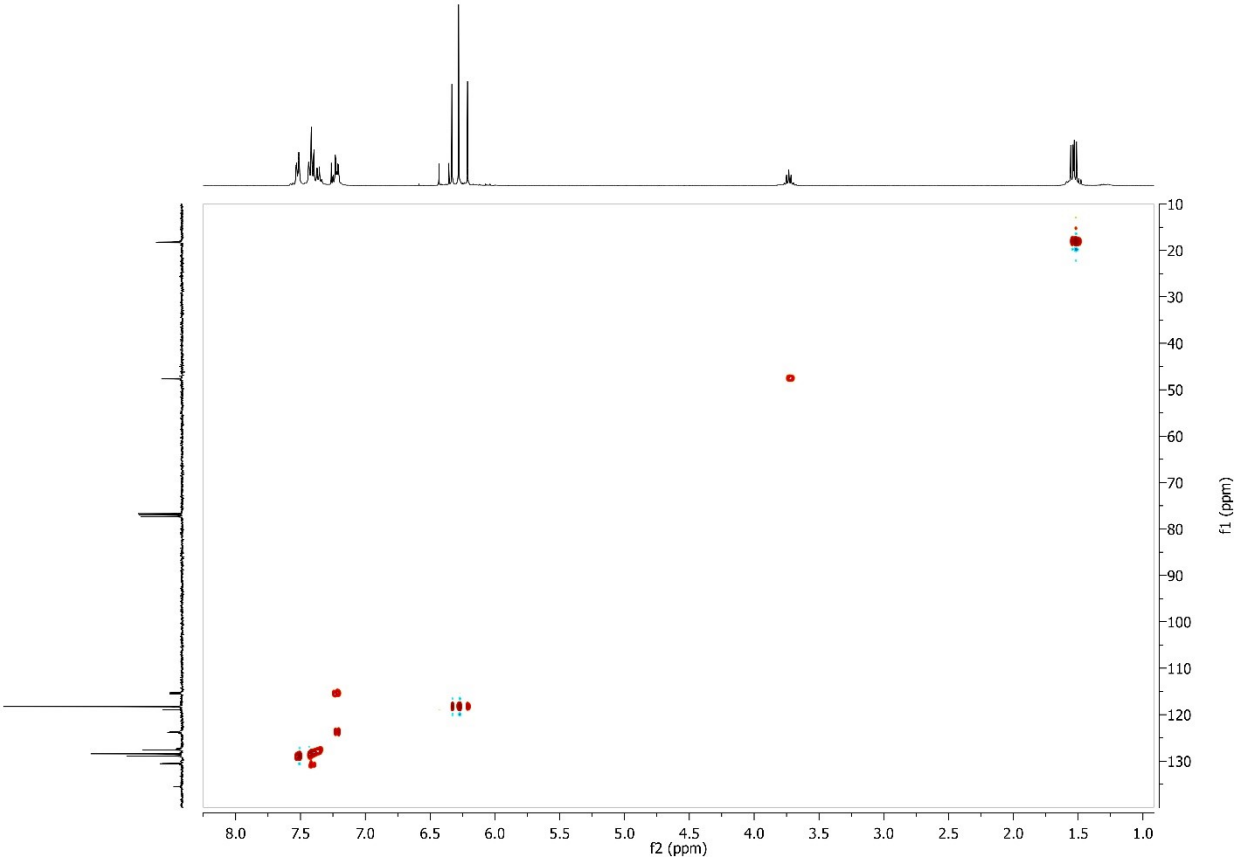


Fig. S10. gHSQCAD spectrum of **5** ($CDCl_3$, 400 MHz, 298 K).

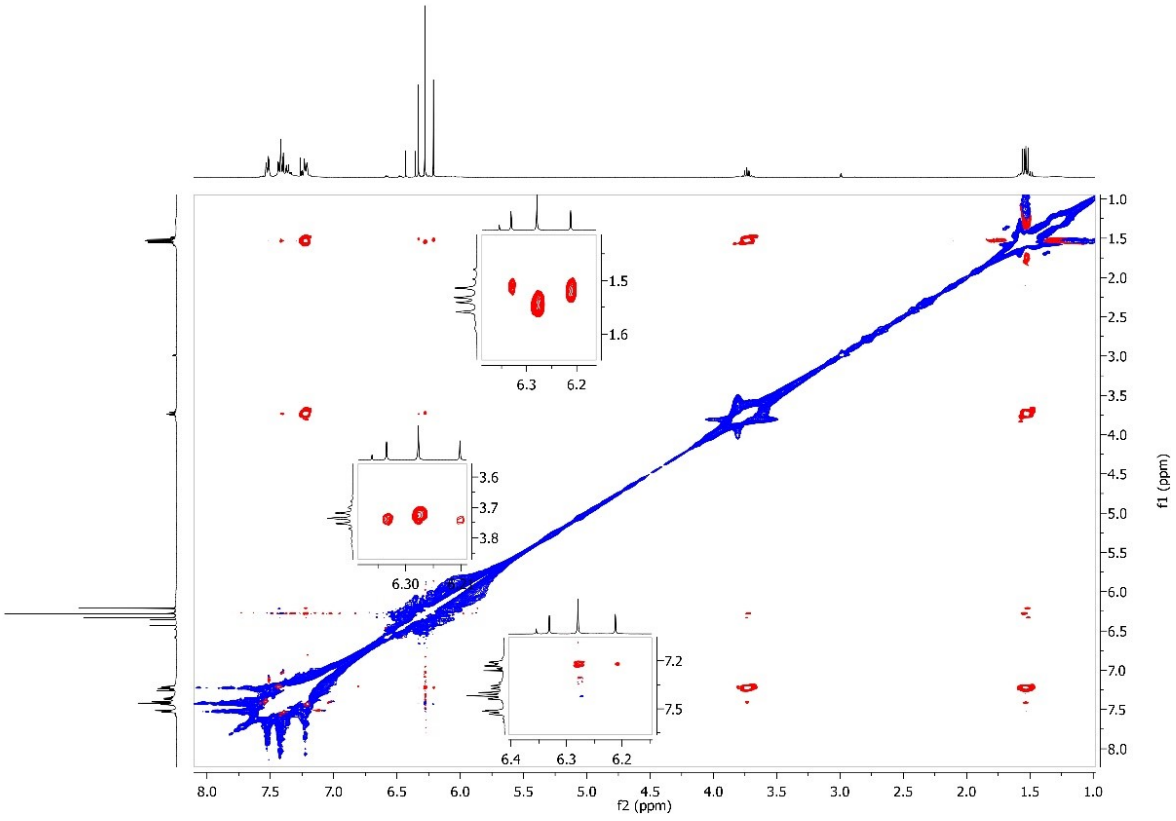


Fig. S11. NOESY spectrum of **5** ($CDCl_3$, 400 MHz, 298 K).

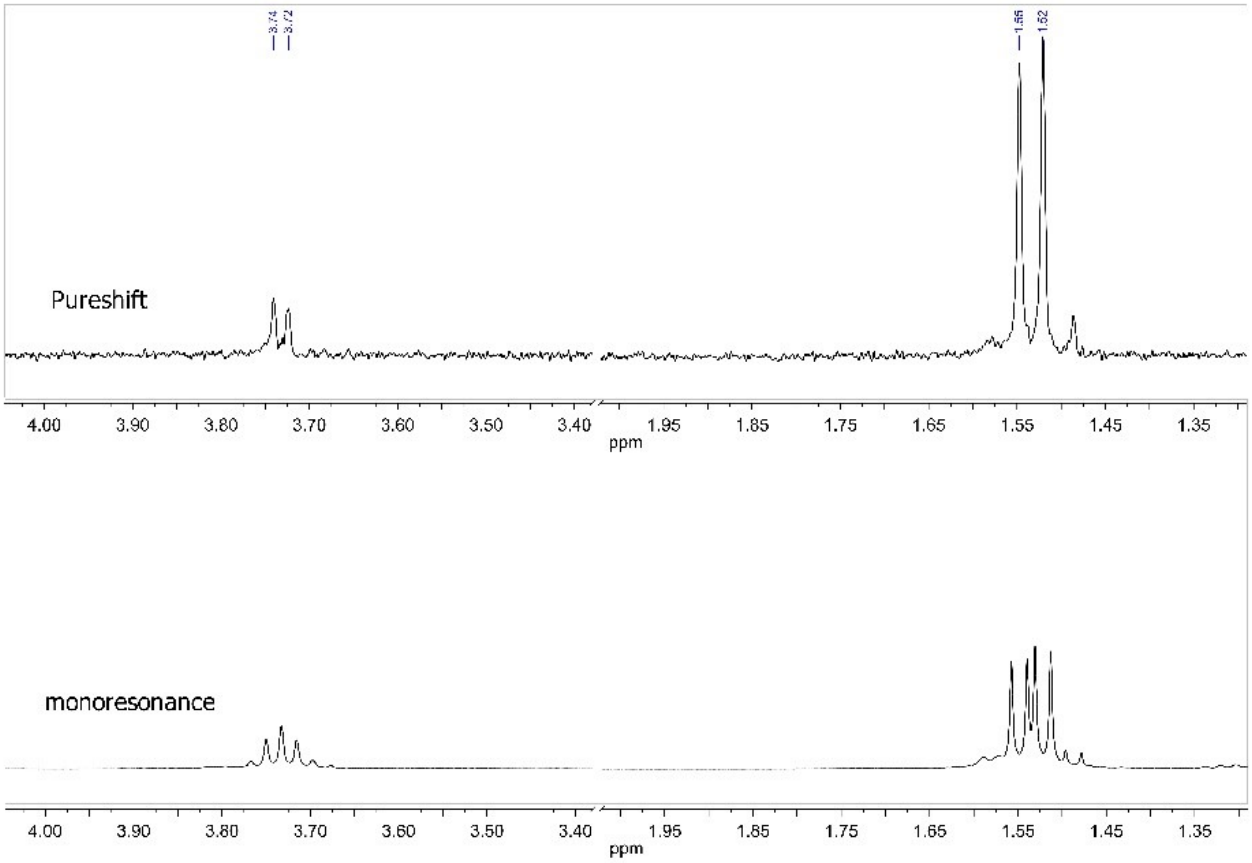
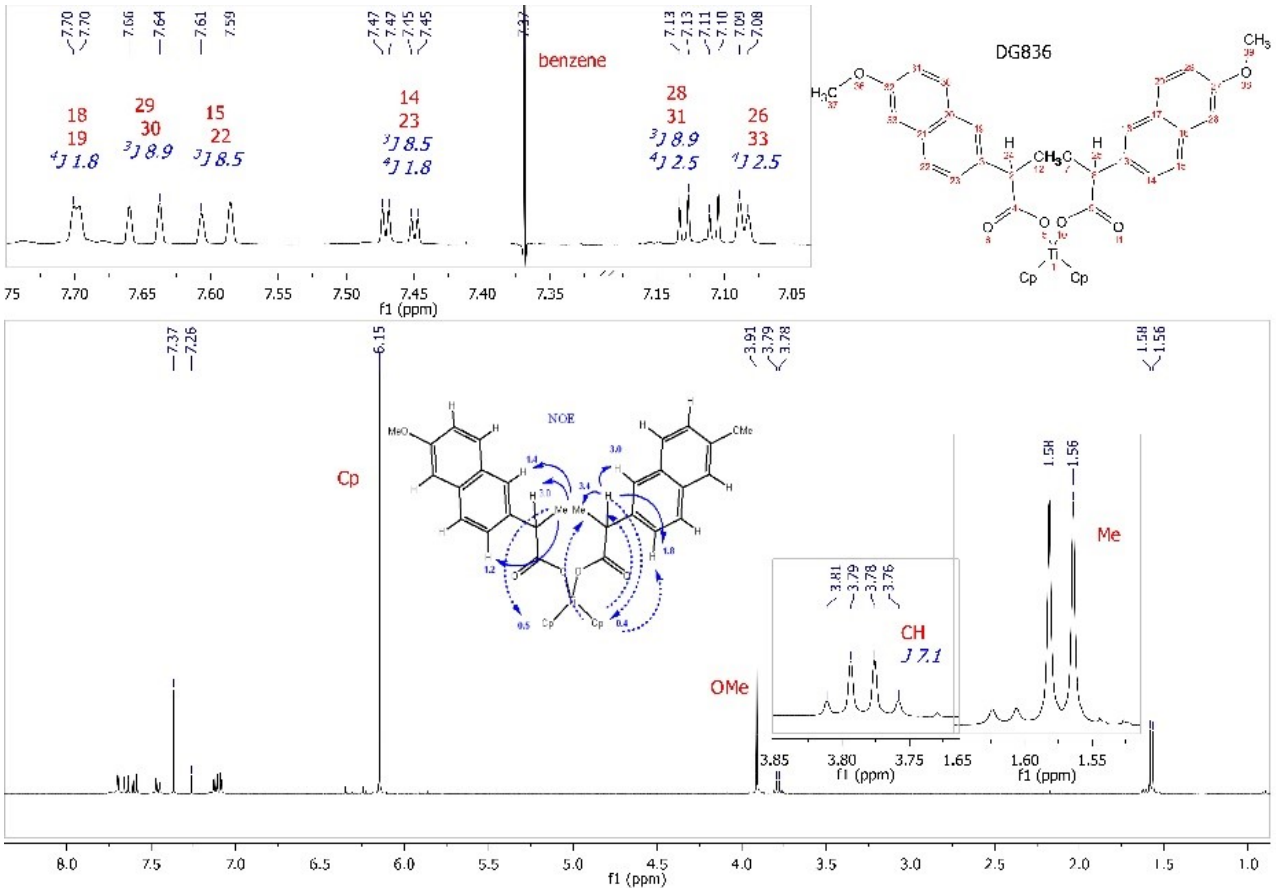


Fig. S12. PSYCHE spectrum (highfield region) of **5** ($CDCl_3$, 400 MHz, 298 K).

2.2 NMR Spectra of conjugate 6.



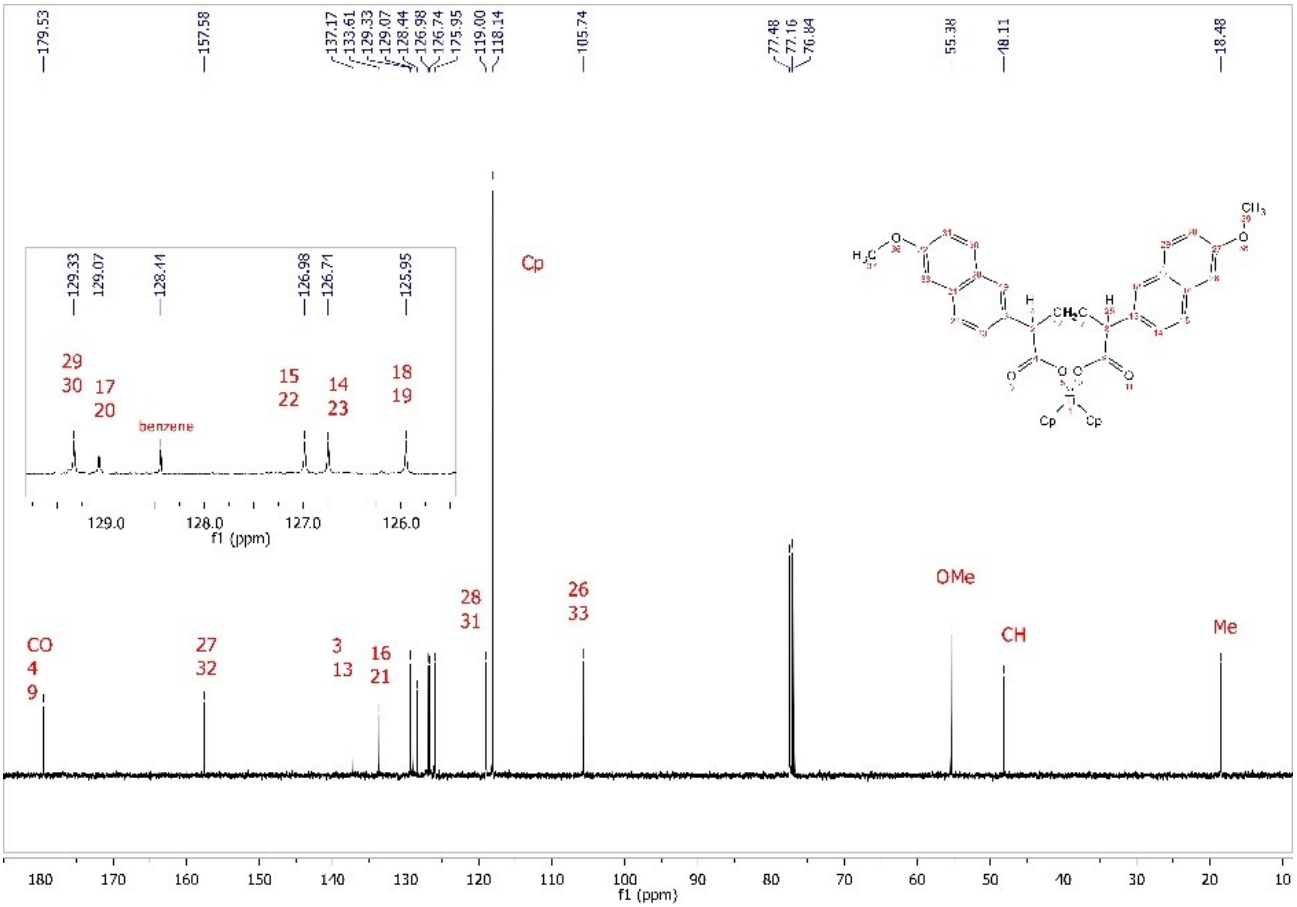


Fig. S13. Signal assignment in NMR spectra of **6** ^{1}H (Top), ^{13}C (Bottom).

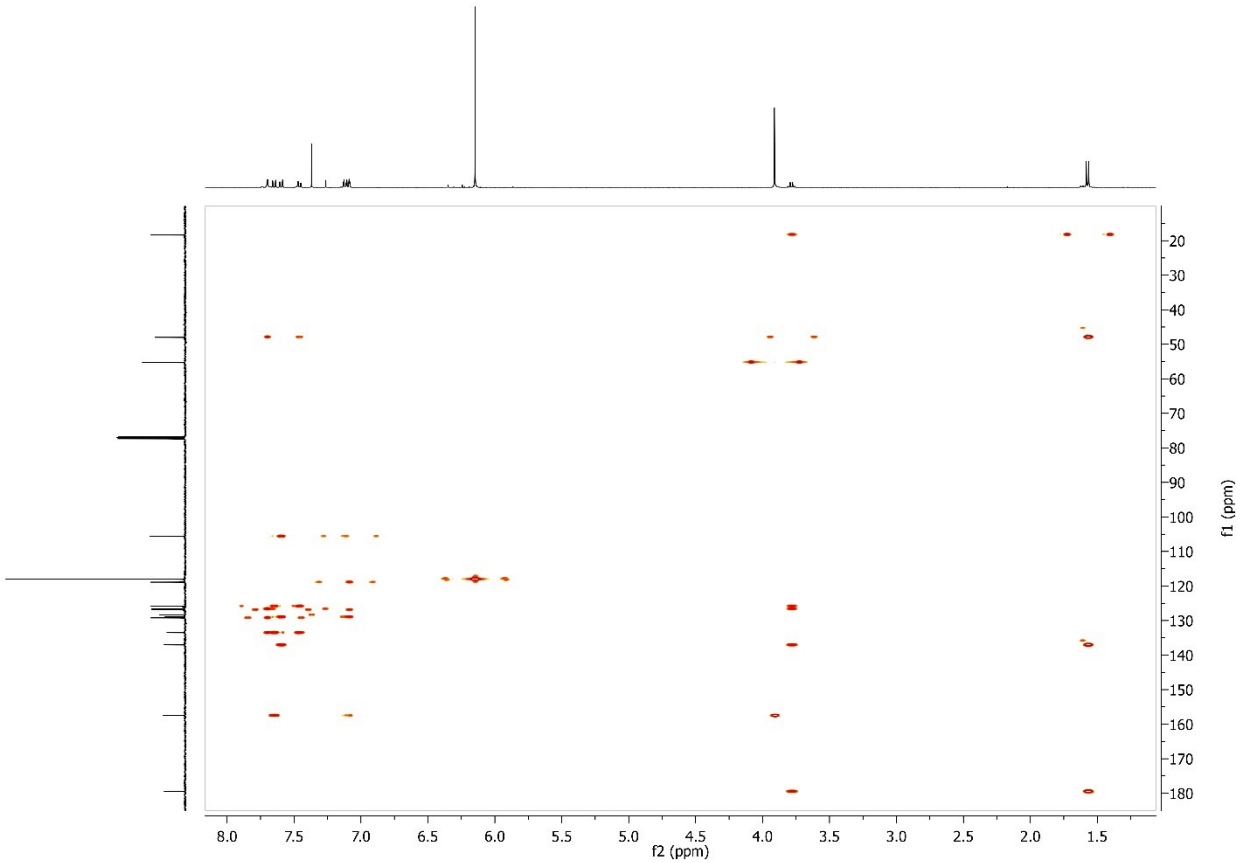


Fig. S14. gHMBCAD spectrum of **6** ($CDCl_3$, 400 MHz, 298 K).

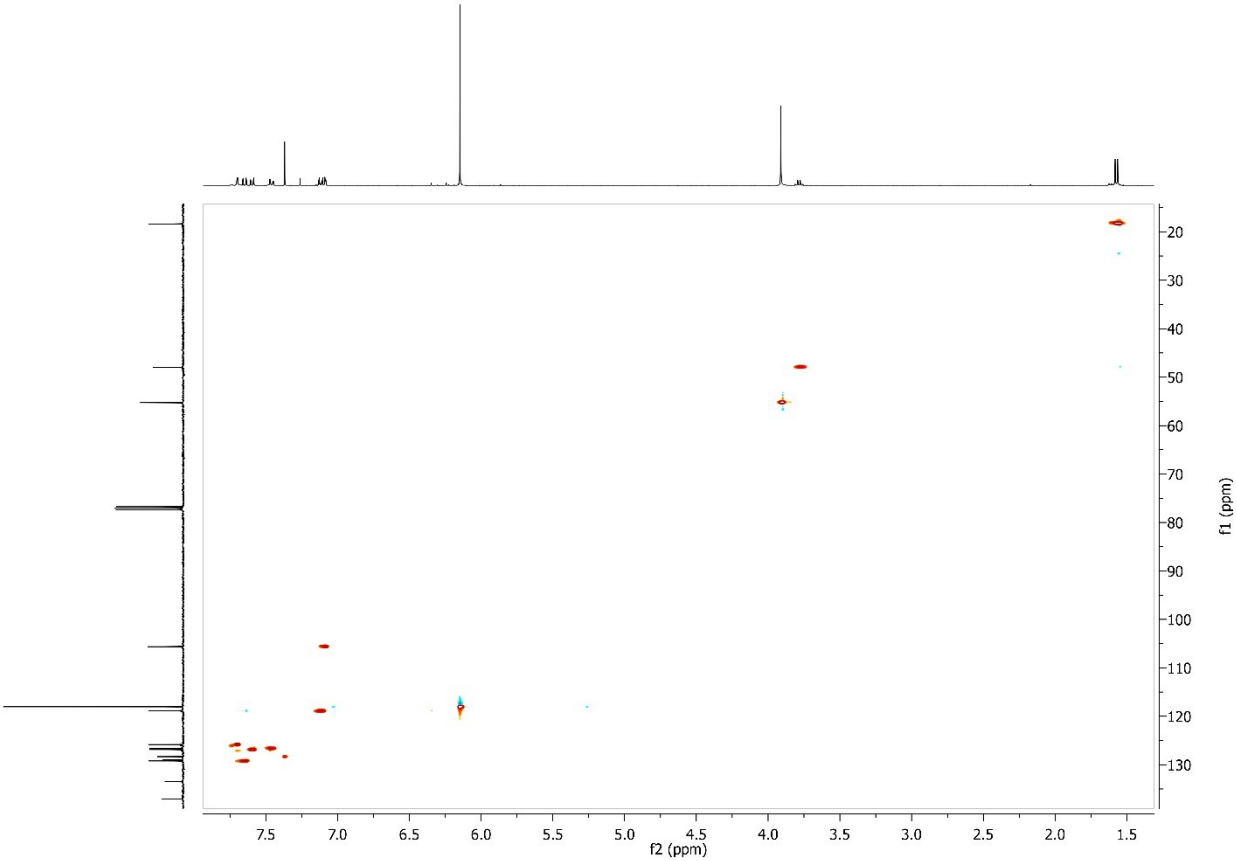


Fig. S15. gHSQCAD spectrum of **6** ($CDCl_3$, 400 MHz, 298 K).

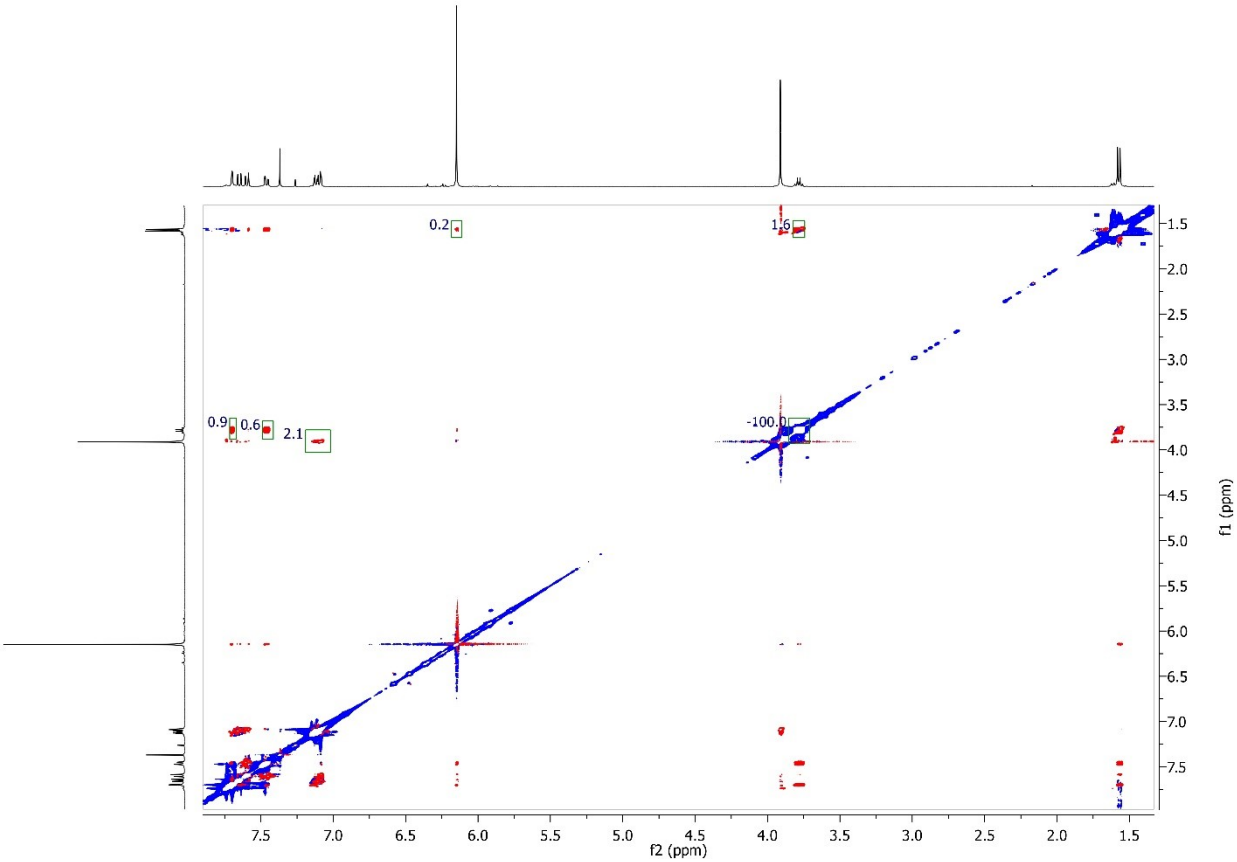


Fig. S16. NOESY spectrum of **6** ($CDCl_3$, 400 MHz, 298 K).

2.3 NMR Spectra of conjugate 7.

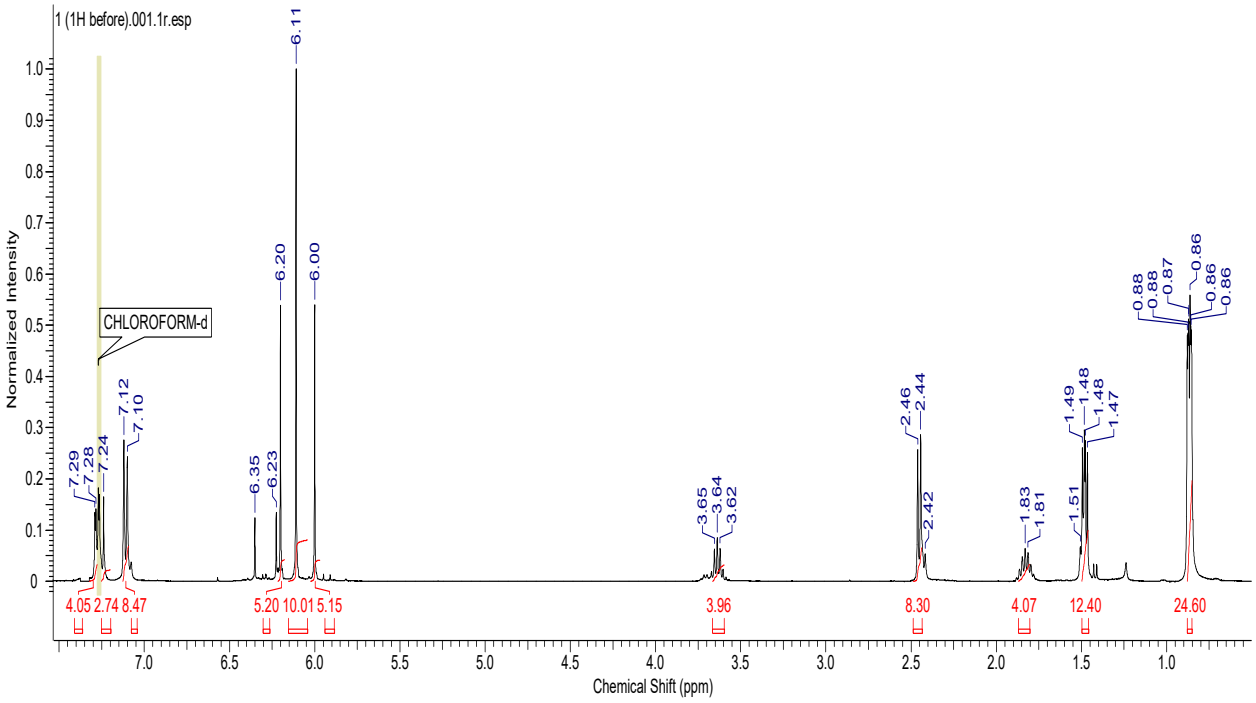


Fig. S17. ^{1}H NMR spectrum of conjugate **7.**

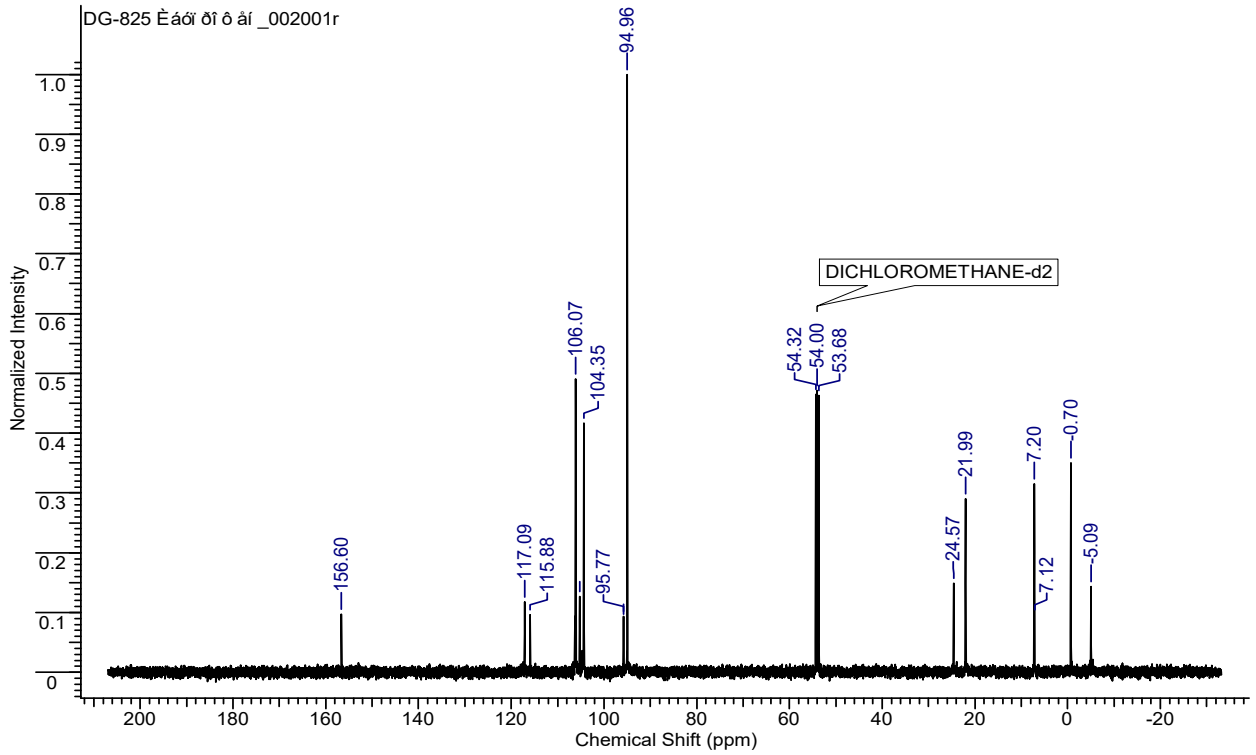


Fig. S18. ^{13}C NMR spectrum of conjugate **7**.

2.4 NMR Spectra of conjugate 8.

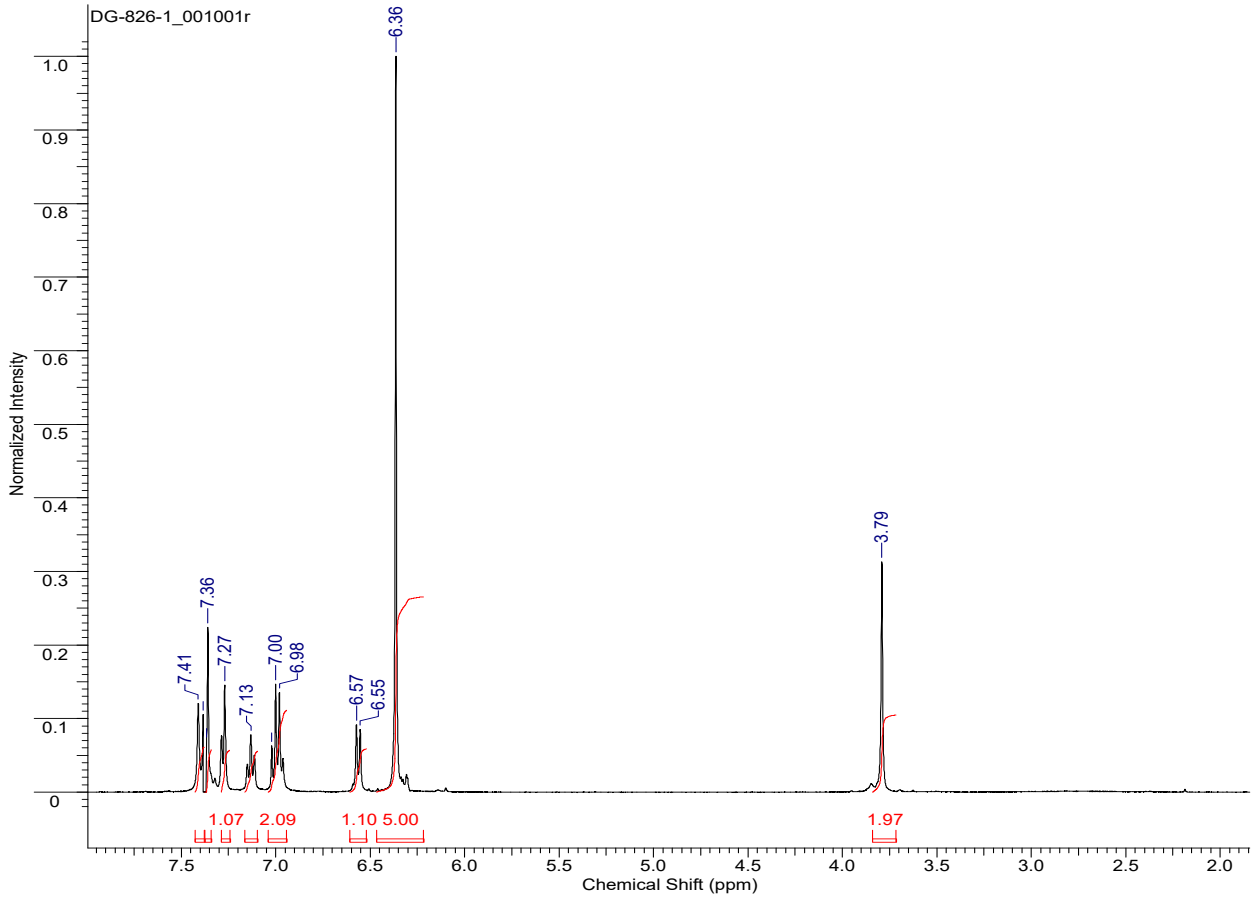


Fig. S19. ^{1}H NMR spectrum of conjugate **8.**

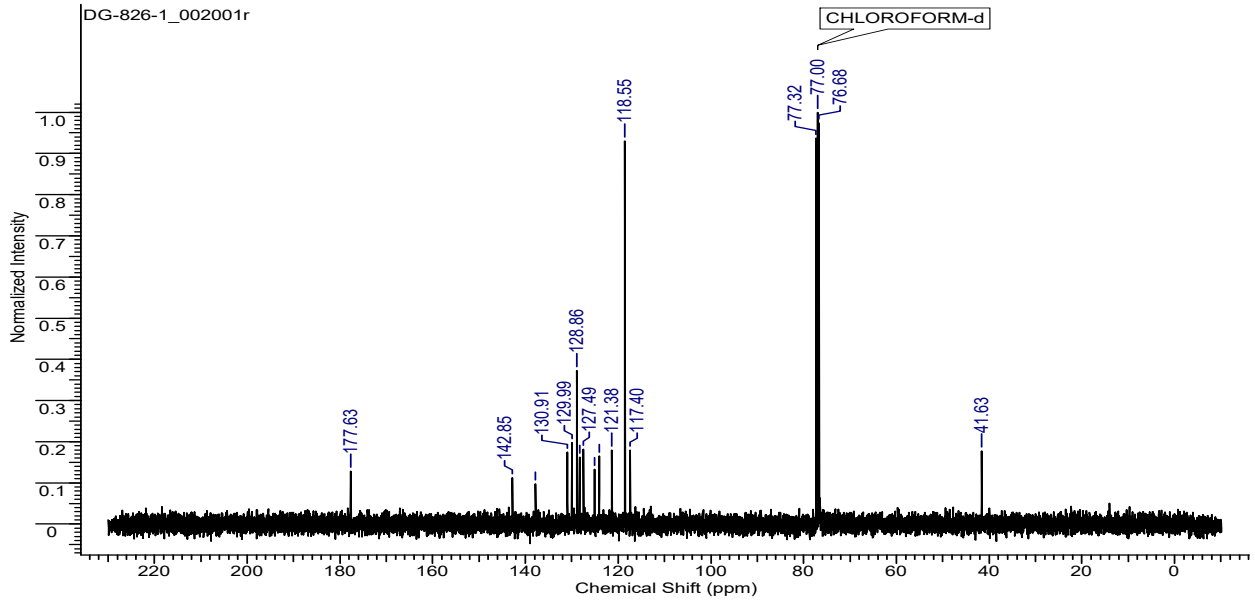


Fig. S20. ^{13}C NMR spectrum of conjugate **8**.

3. IR Spectra of Titanocene conjugates 5-8.

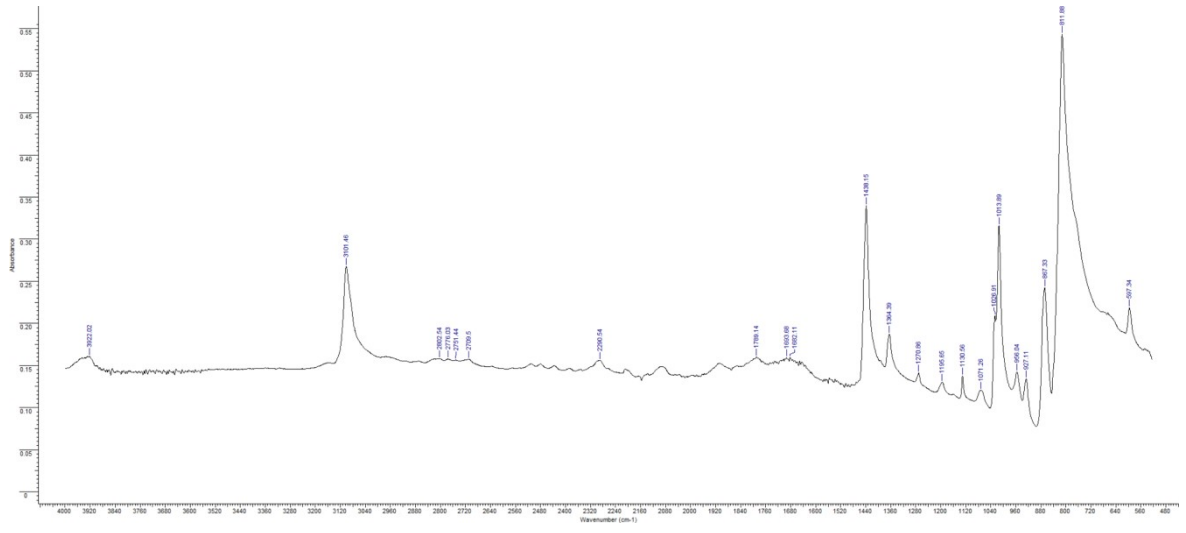


Fig. S21. IR spectrum of Cp_2TiCl_2.

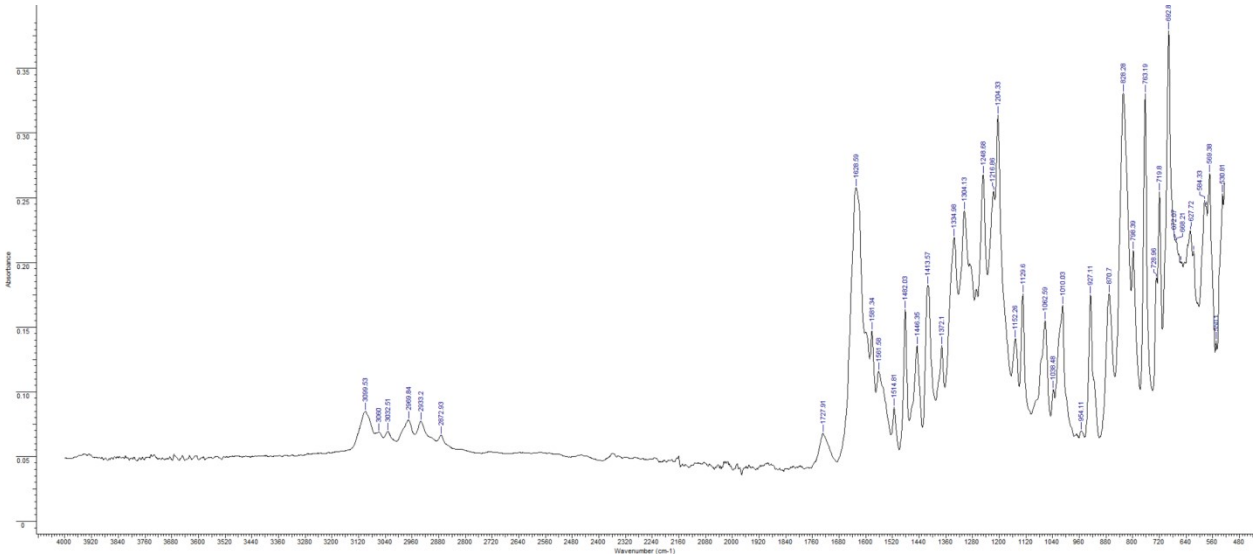


Fig. S22. IR spectrum of Conjugate **5**.

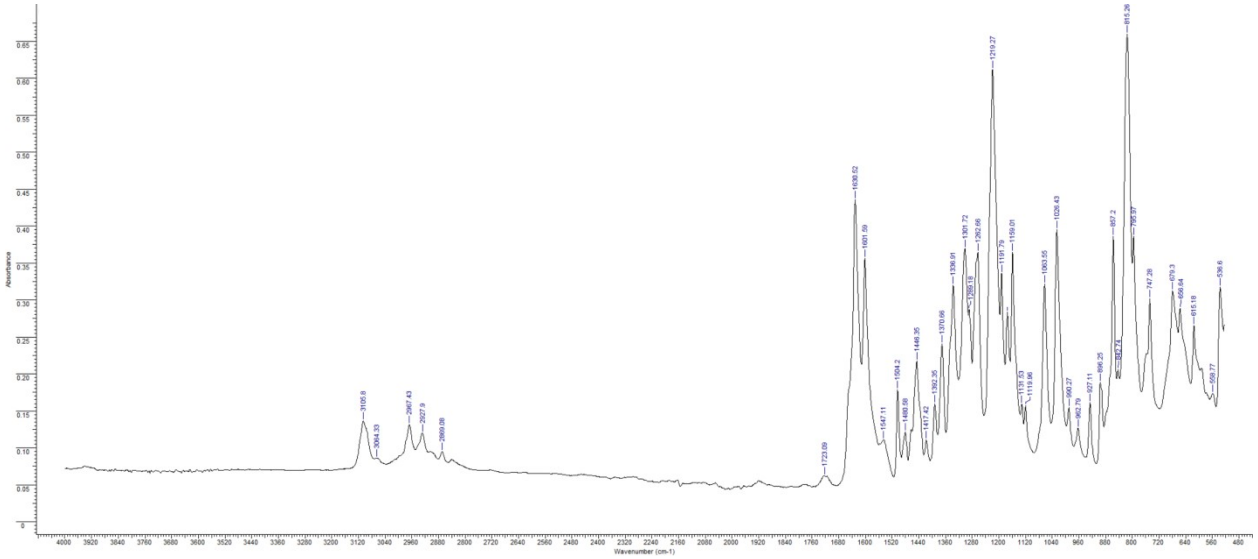


Fig. S23. IR spectrum of Conjugate **6**.

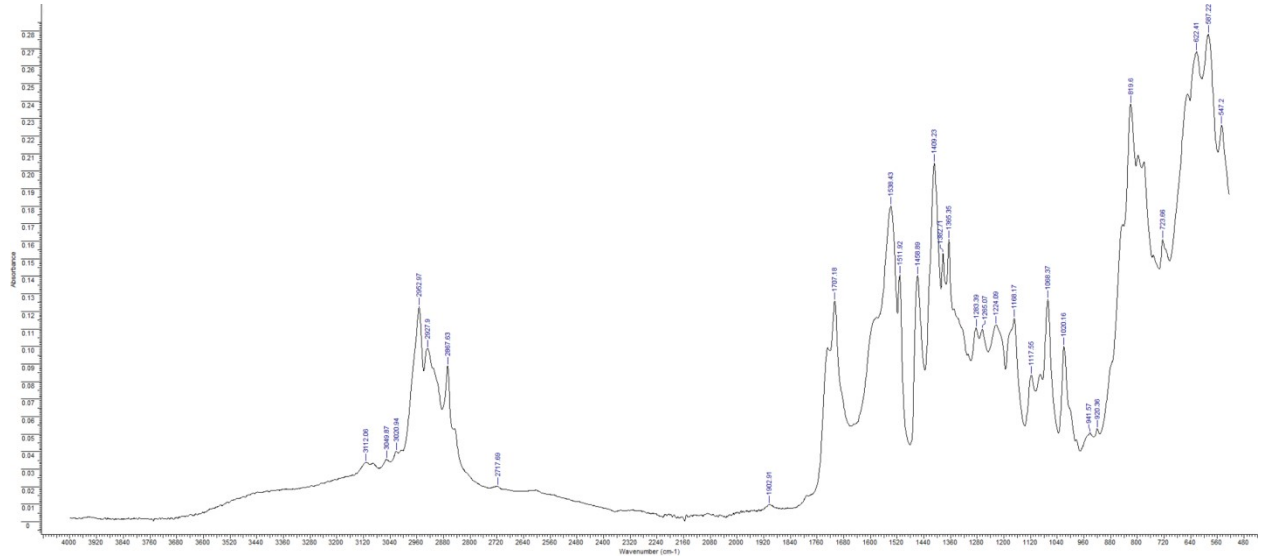


Fig. S24. IR spectrum of Conjugate **7**.

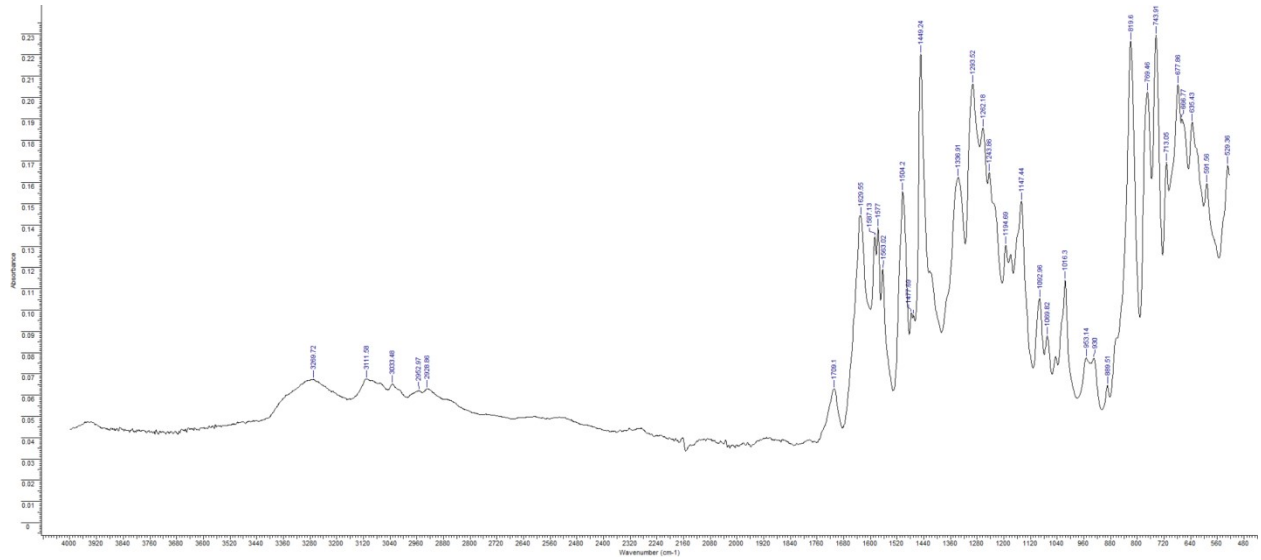


Fig. S25. IR spectrum of Conjugate **8**.

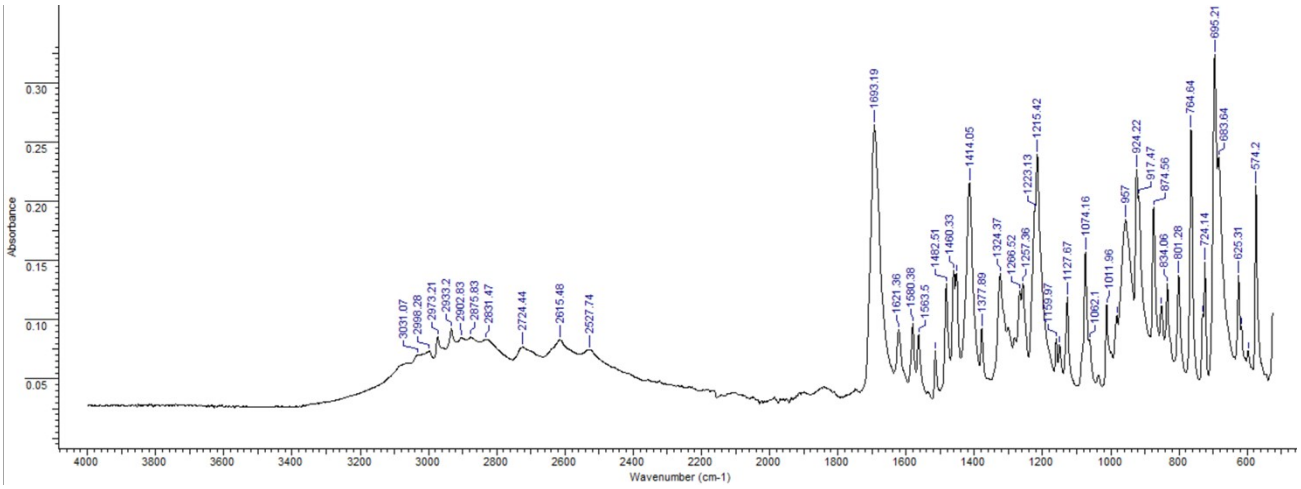


Fig. S26. IR spectrum of Flurbiprofen.

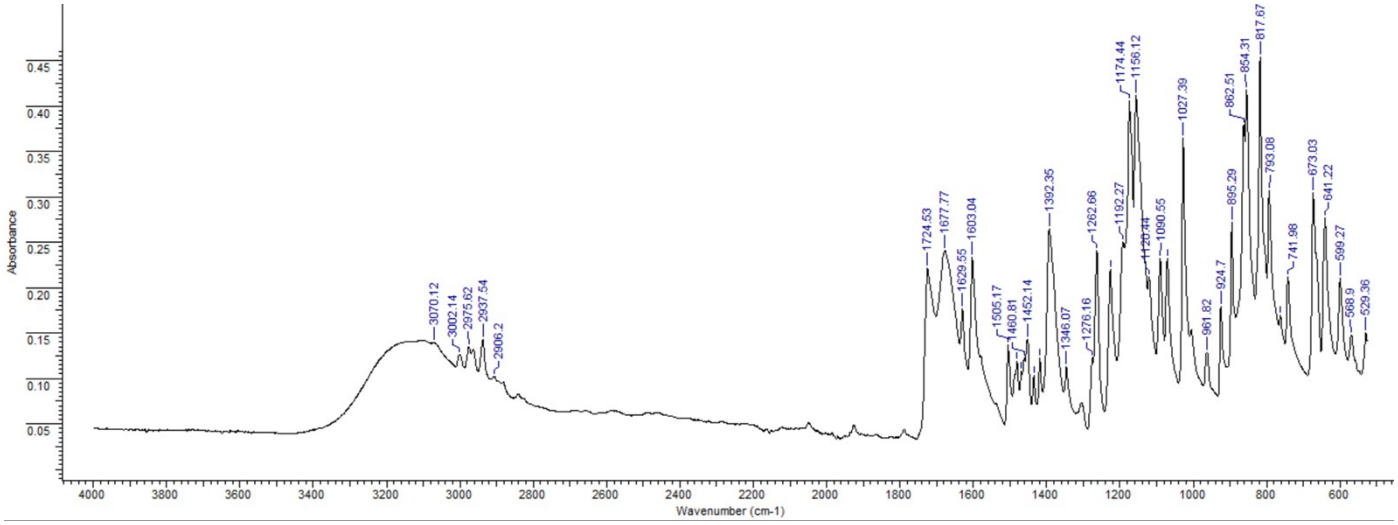


Fig. S27. IR spectrum of Naproxen.

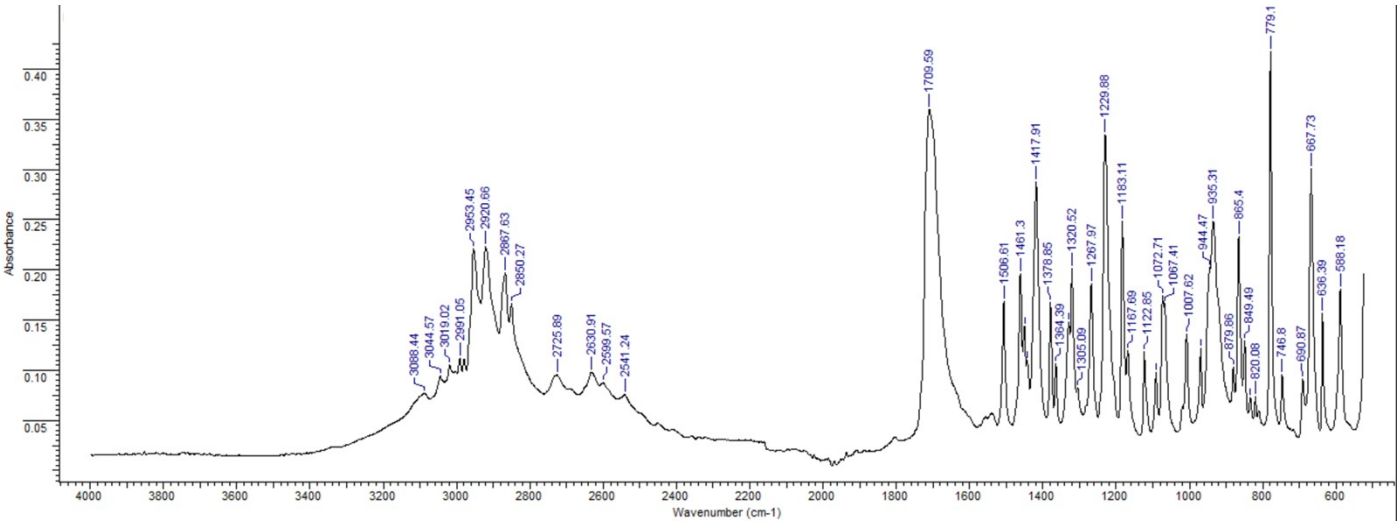


Fig. S28. IR spectrum of Ibuprofen.

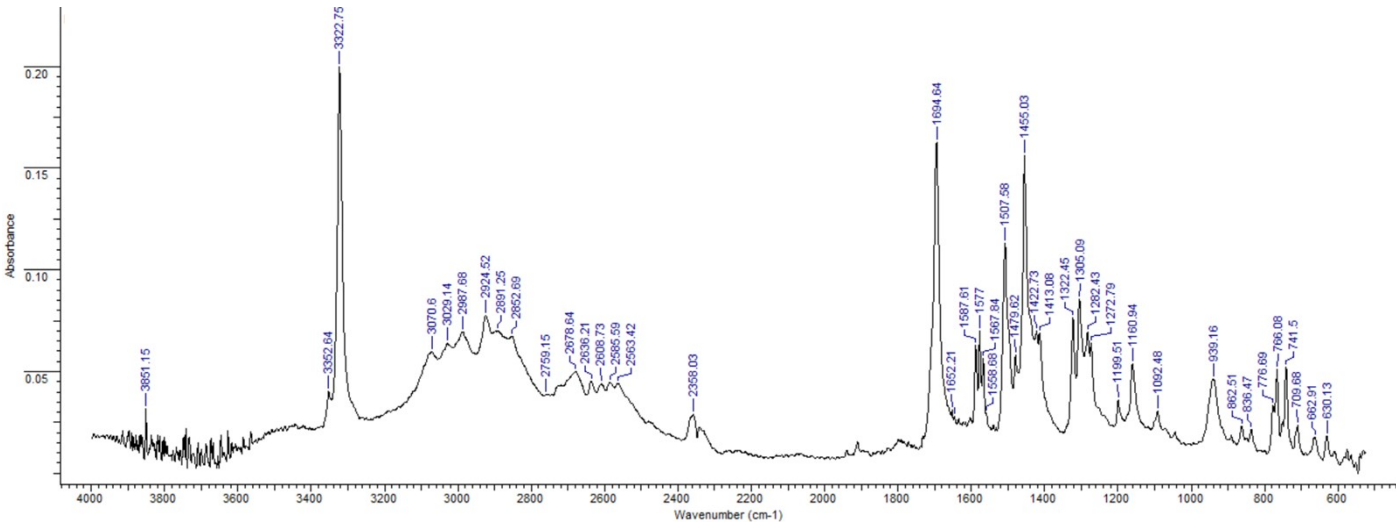


Fig. S29. IR spectrum of Diclofenac.

4. Chiral chromatography data for naproxen and flurbiprofen

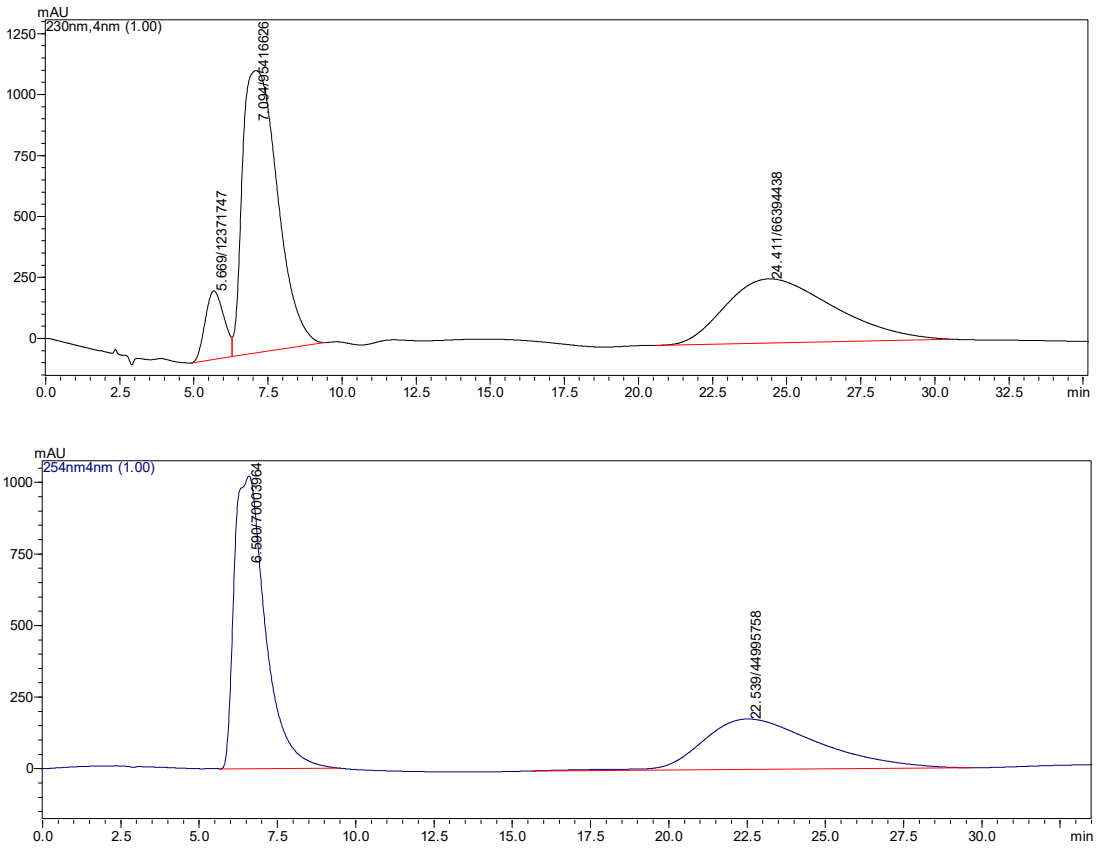


Fig. S30. Chromatograms on the chiral stationary phase for R/S-naproxen (top) and commercially available R/S-flurbiprofen (bottom).

5. CV-Curves Titanocene conjugates 5-8.

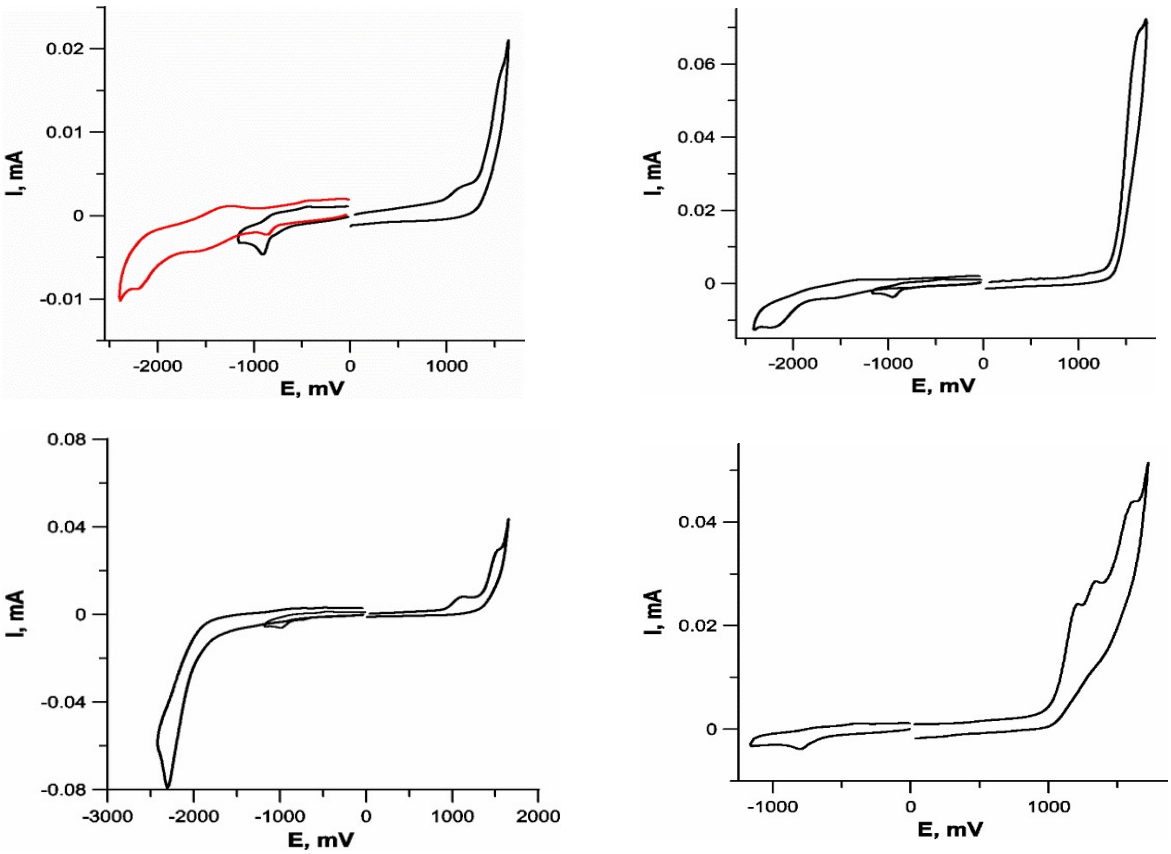


Fig. S31. CV-Curves for compounds **5** (top left), **6** (top right), **7**(bottom left), **8** (bottom right), in DMF, C = 1 × 10–4 mol L^{-1}.

6. Optical absorption spectra for aqueous solutions of Titanocene conjugates 5-8.

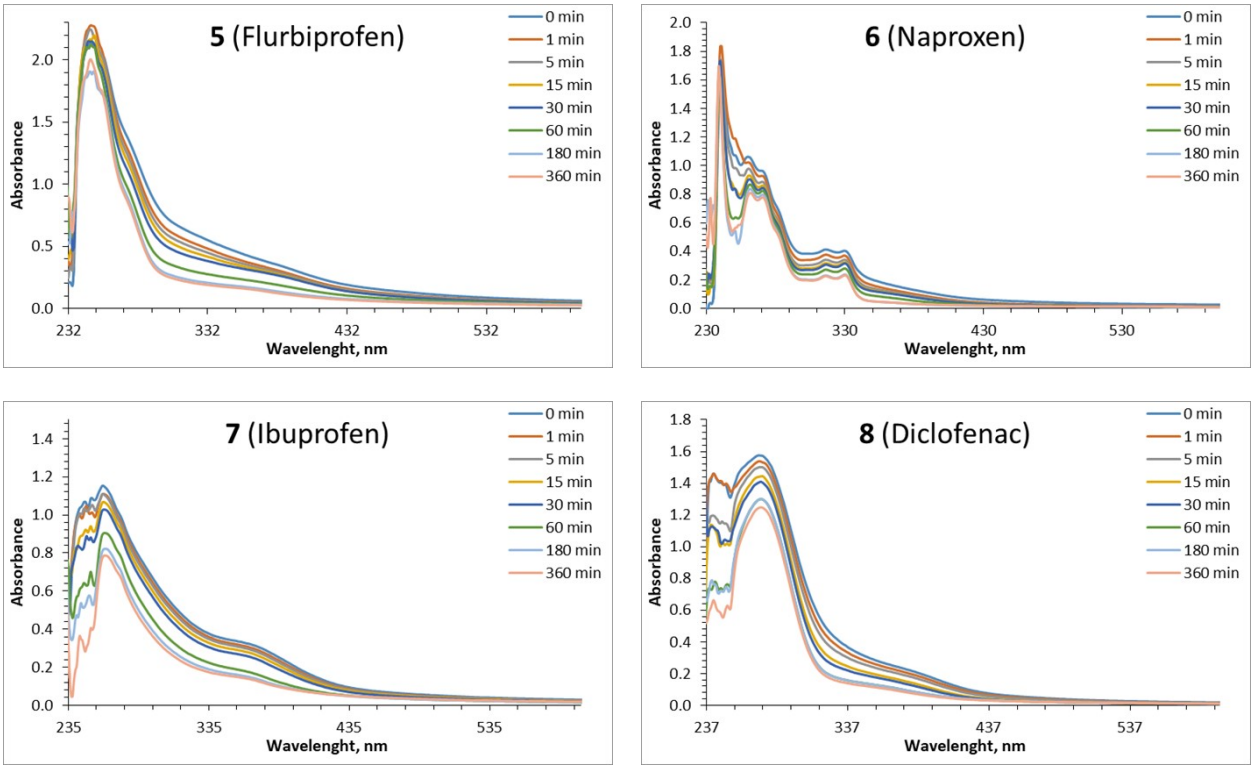


Fig. S32. Optical absorption spectra of compounds **5**-**8** in 10%DMSO aqueous solution, C = 0.4 mM in time.

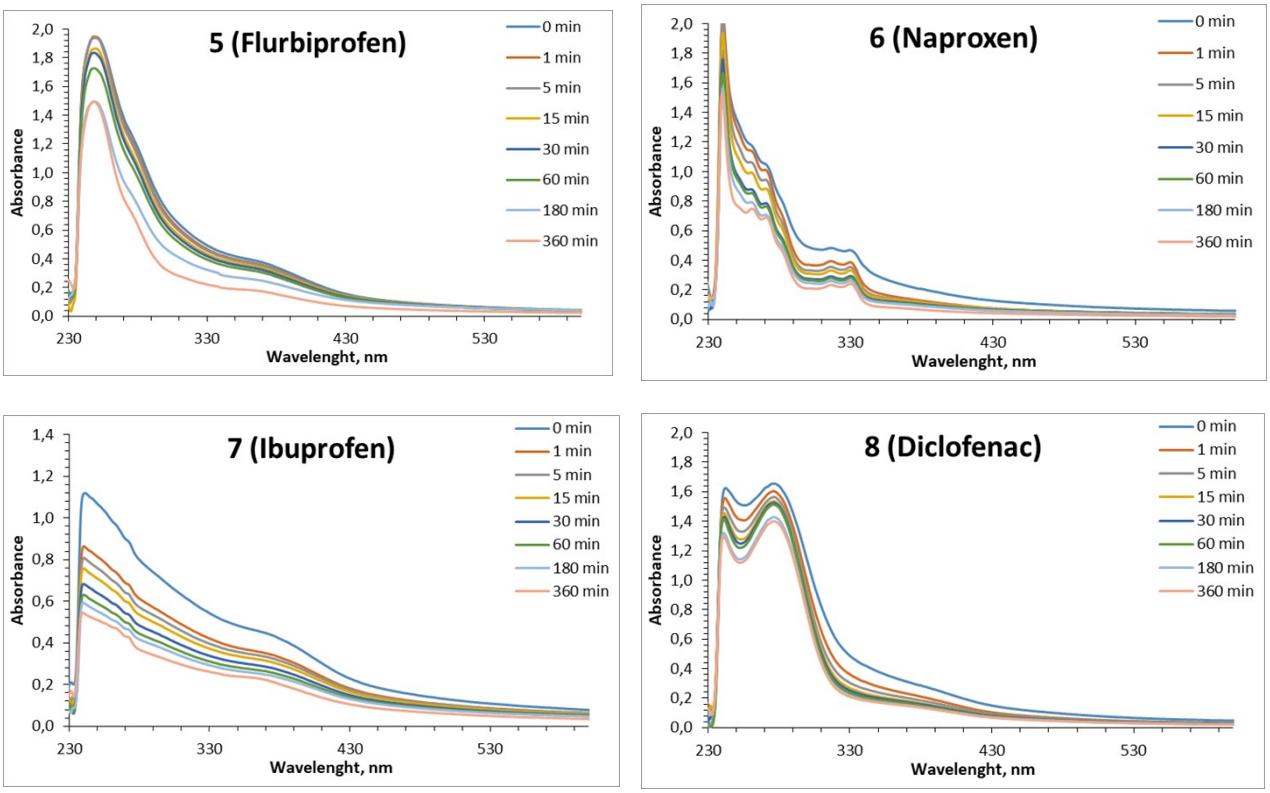


Fig. S33. Optical absorption spectra of compounds **5**-**8** in PBS buffer solution, C = 0.4 mM in time.

7. Cell viability in MTT-test for Titanocene conjugates 5-8.

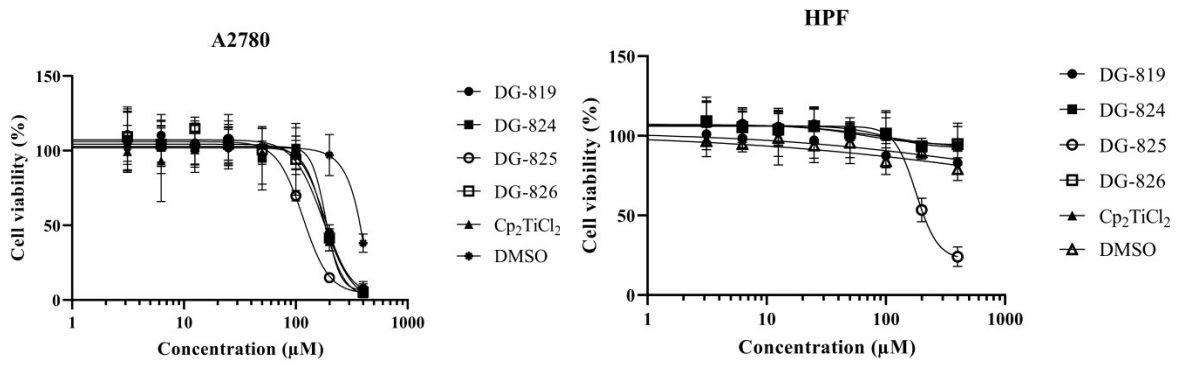


Fig. S34. Cell viability curves for compounds **5**-**8** on A2780 (Left) and HPF (Right) cell lines.