Supporting Information

Isocyanide Incorporation Expands the Anticancer Potential of Diiron(I) Aminocarbyne Complexes

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IR and NMR spectra of diiron isocyanide complexes

Figure S1. Solid-state IR spectrum (650-4000 cm^{-1}) of $[Fe_2Cp_2(CO)(CNFc)(\mu\text{-}CO)\{\mu\text{-}CNMe_2\}]CF_3SO_3$, **2a** (*cis*/*trans* mixture).

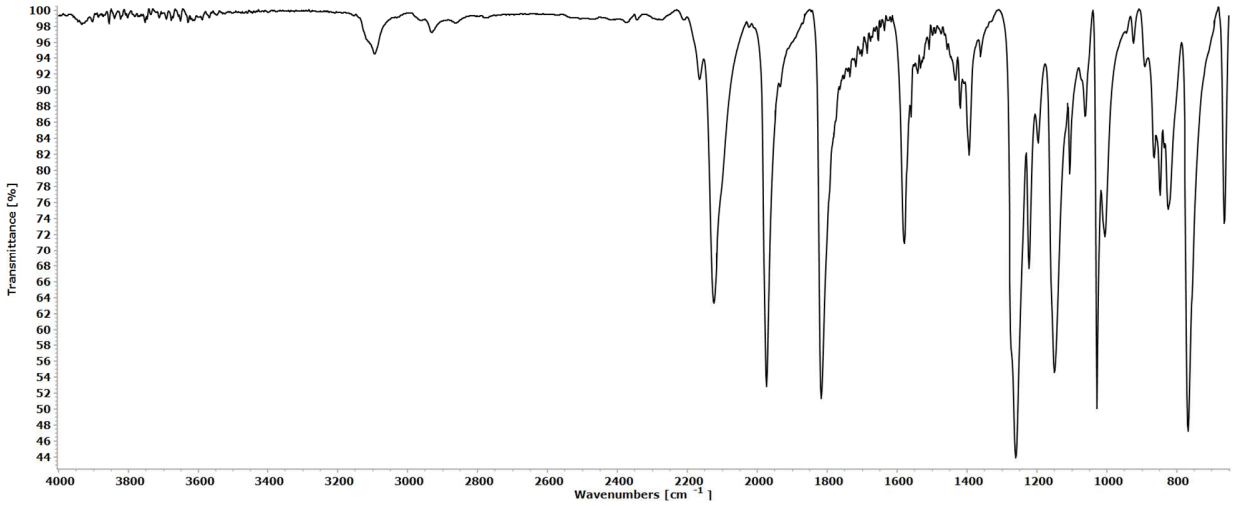


Figure S2. ^1H NMR spectrum (401 MHz, acetone-d_6) of **2a** (*cis*/*trans* ratio 7.7): full spectrum (top) and 4.0-5.0 ppm region (bottom). The corresponding signals of all isomers are integrated together; each Fe(I)-Cp integrates ≈ 4.5H due to low delay time.

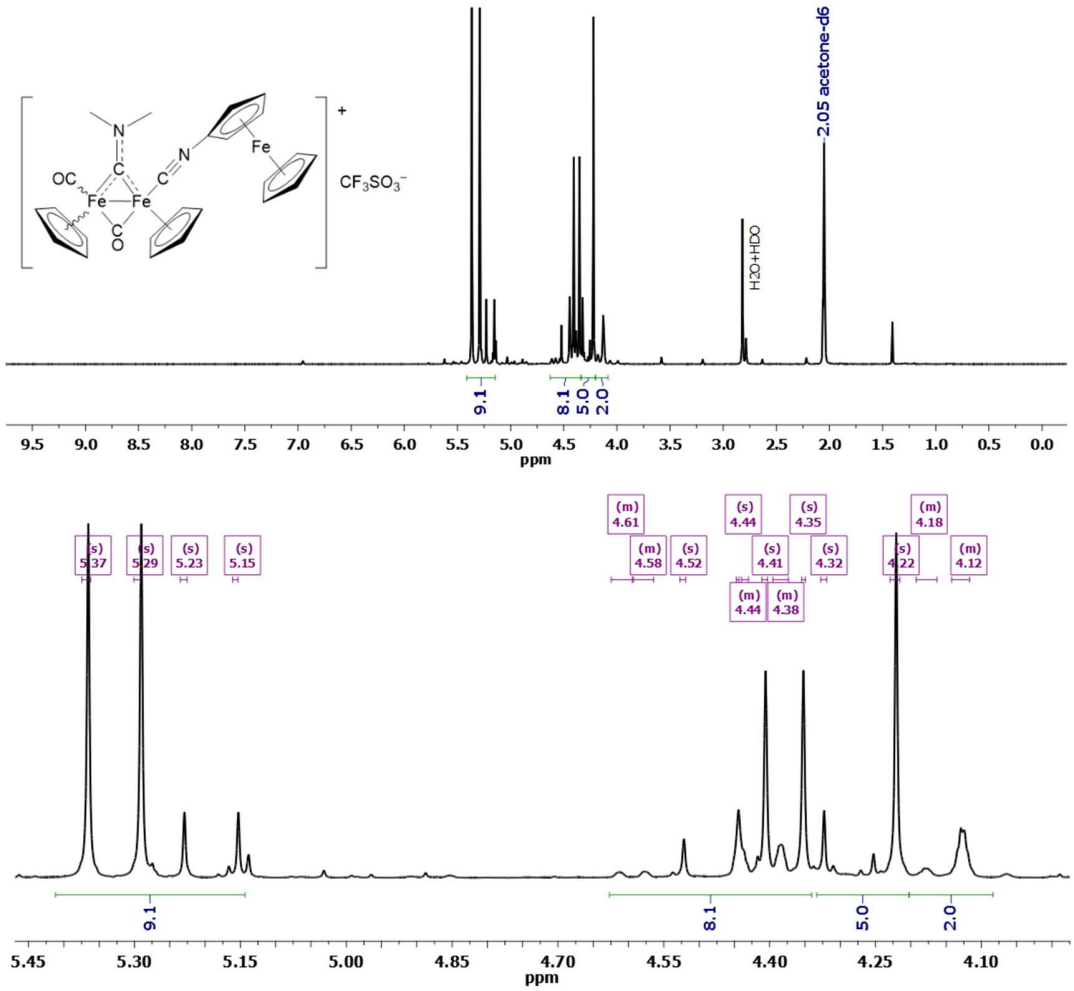


Figure S3. $^{13}C\{^{1}H\}$ NMR spectrum (101 MHz, $CDCl_3$) of **2a** (*cis*/*trans* ratio 7.7).

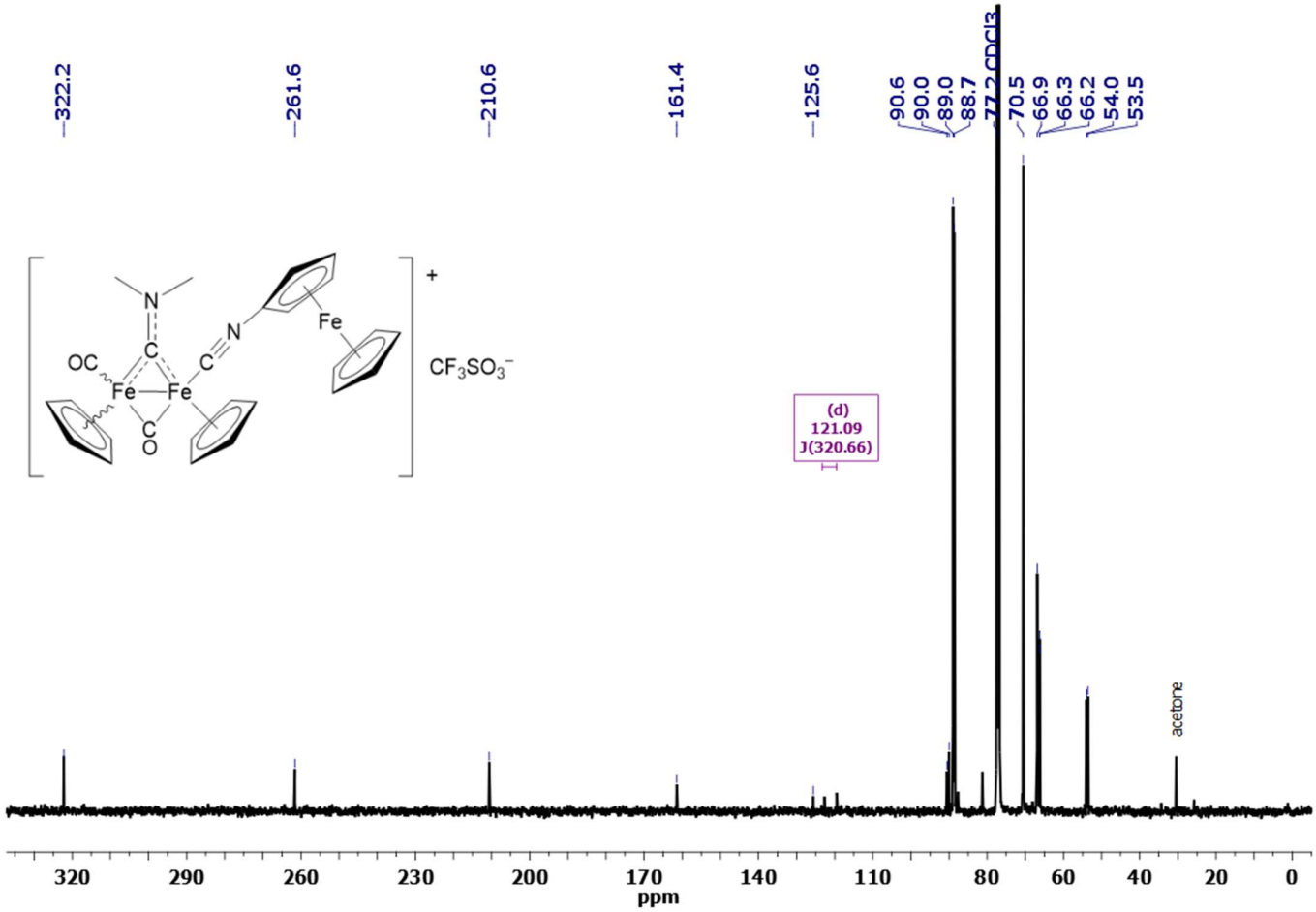


Figure S4. Solid-state IR spectrum (650-4000 cm^{-1}) of $[Fe_2Cp_2(CO)(CNFc)(\mu\text{-}CO)\{\mu\text{-}CNMe(Cy)\}]CF_3SO_3$, **2b** (*cis*-*E*/*Z* isomer mixture).

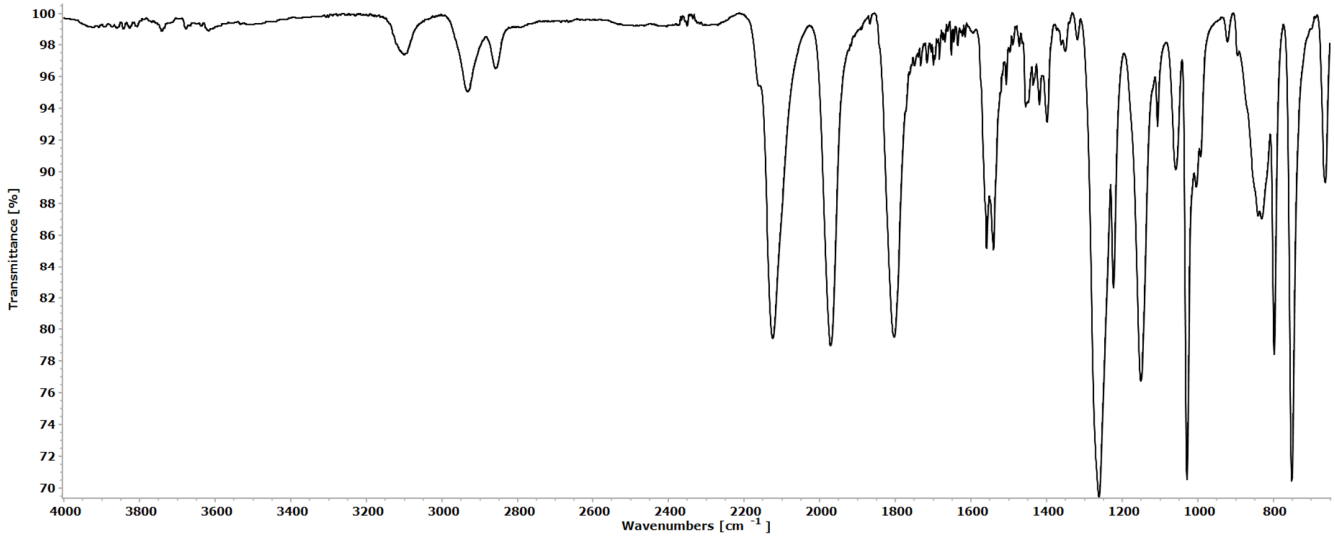


Figure S5. ^{1}H NMR spectrum (401 MHz, $CDCl_3$) of **2b** (*E*/*Z* ratio = 1.5). The corresponding signals of the two isomers are integrated together.

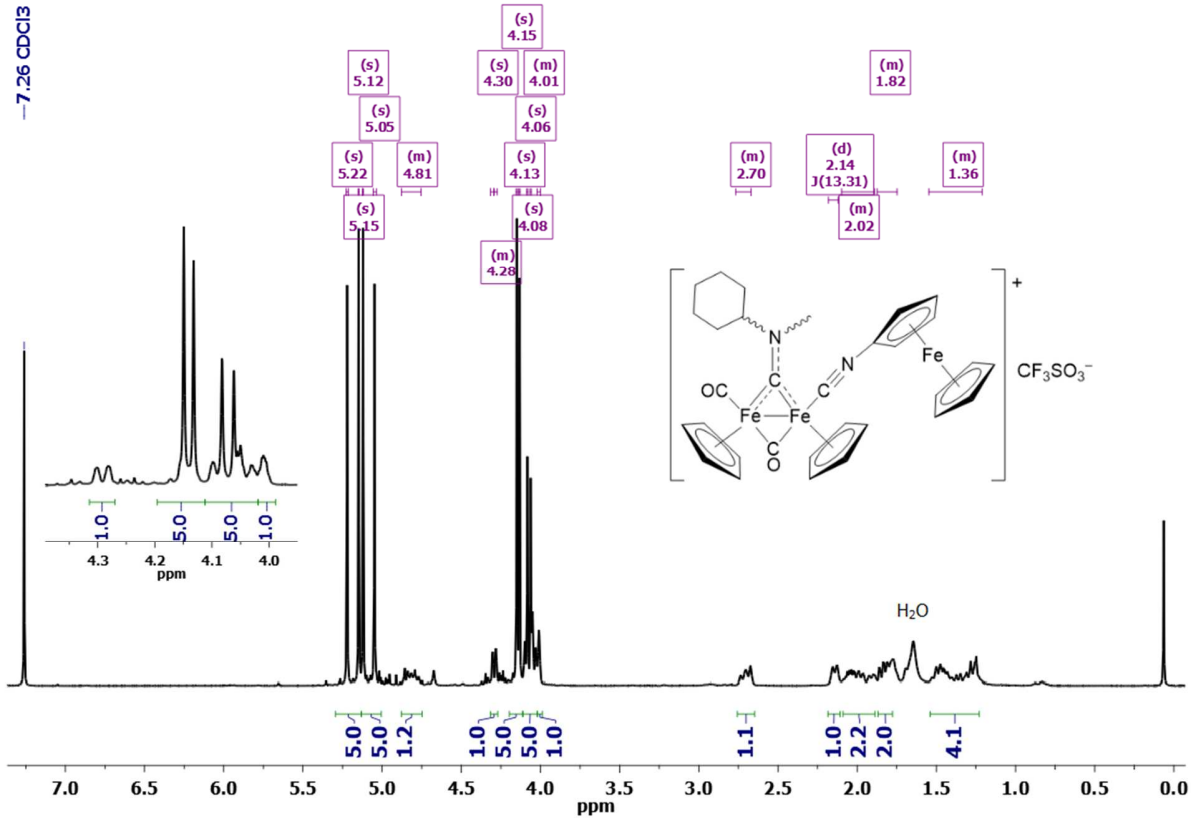


Figure S6. ^{1}H NMR spectrum (401 MHz, $CDCl_3$) of **2b**, highlighting the signals of the *cis*-*Z* isomer in the 5.30–4.00 ppm region.

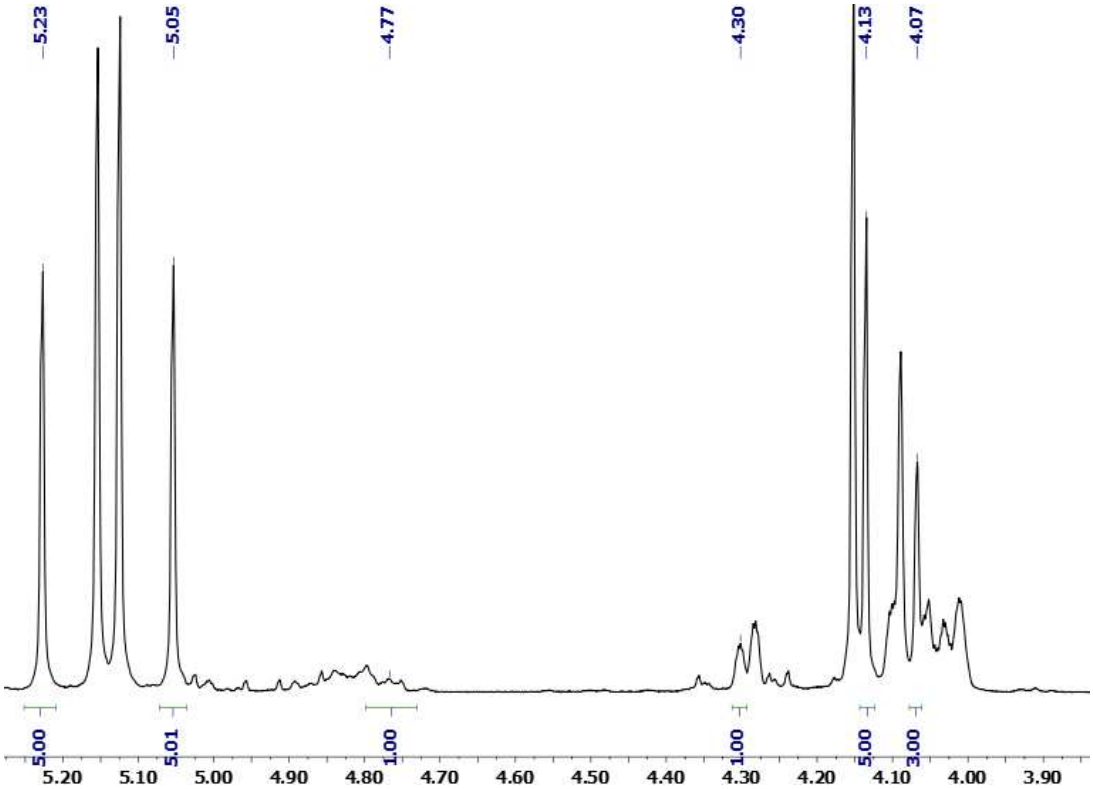


Figure S7. ^{1}H NMR spectrum (401 MHz, $CDCl_3$) of **2b**, highlighting the signals of the *cis-E* isomer in the 5.30–4.00 ppm region.

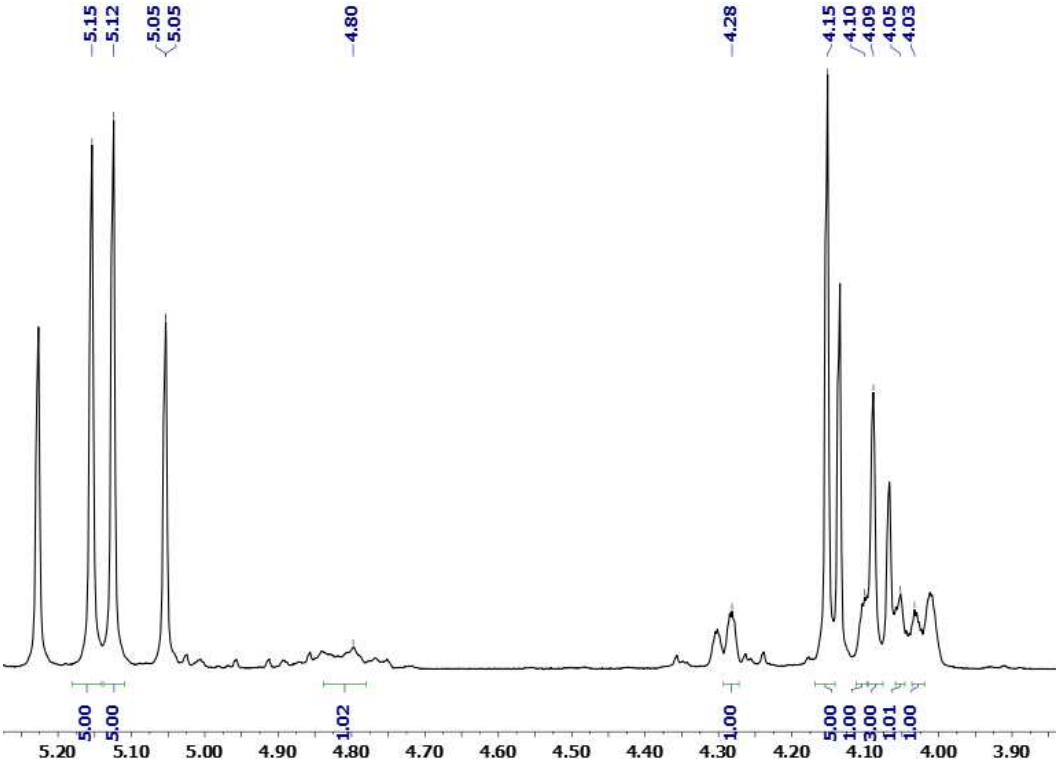


Figure S8. $^{13}C\{^{1}H\}$ NMR spectrum (101 MHz, $CDCl_3$) of **2b** (*E*/*Z* ratio = 1.5).

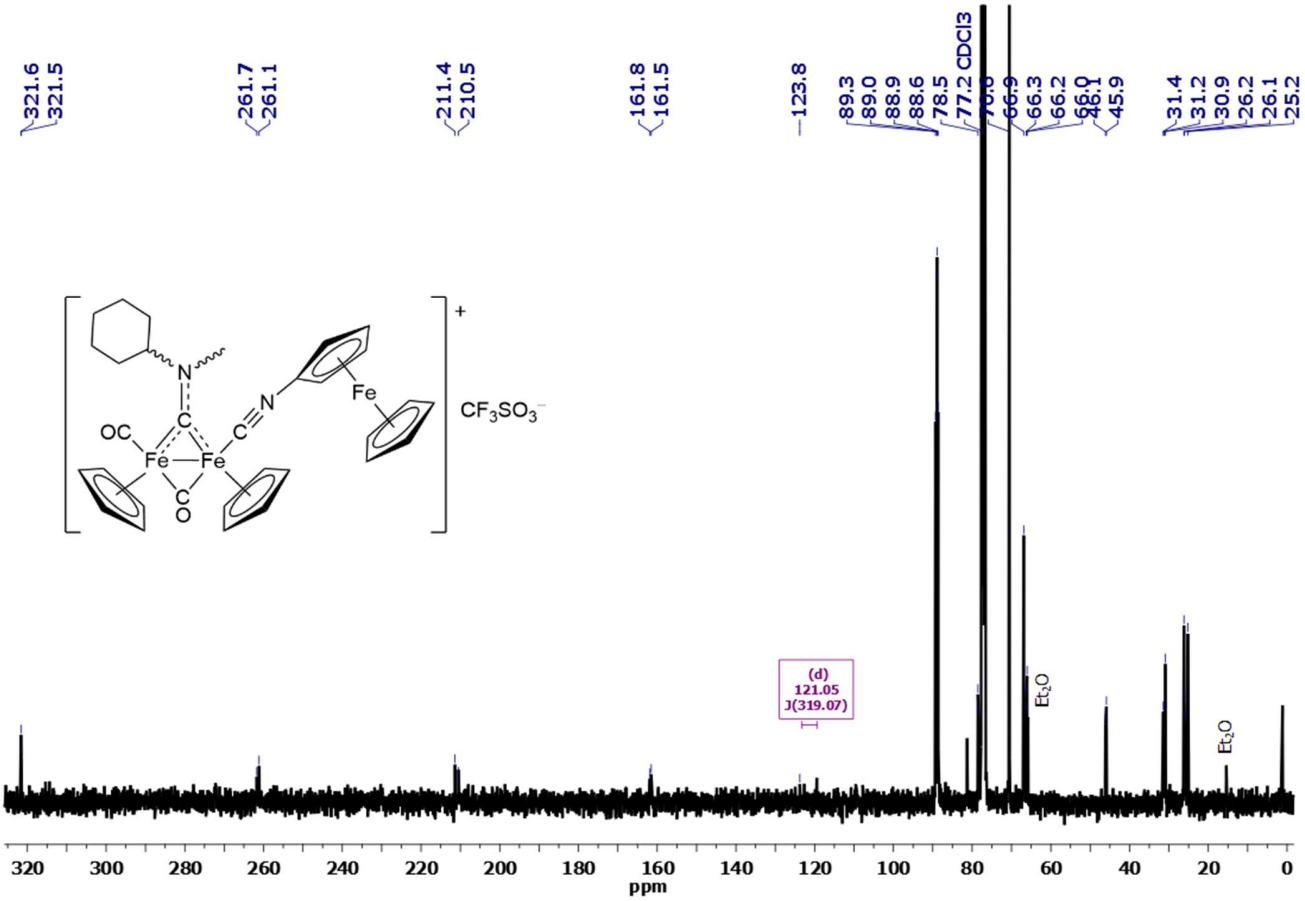
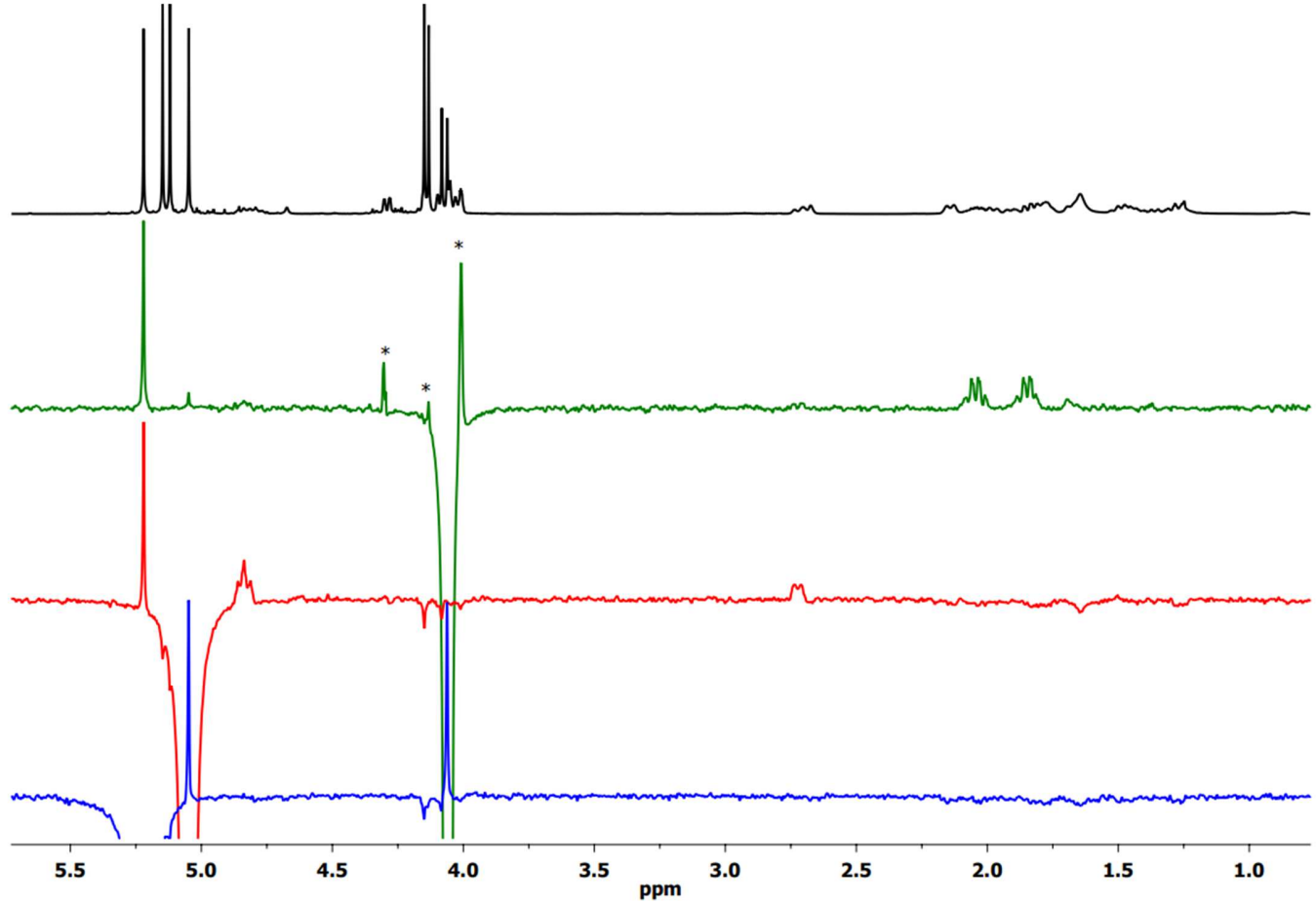


Figure S9. Black line: ^{1}H NMR spectrum (401 MHz, $CDCl_3$) of **2b**. Blue line: ^{1}H NOESY with irradiation at 5.05 ppm; red line: ^{1}H NOESY with irradiation at 5.22 ppm; green line: ^{1}H NOESY with irradiation at 4.06 ppm (Cp^{CO}, Cp^{CNR} and NMe of the *cis-Z* isomer, respectively). Observed NOEs are indicated by the arrows. The signals marked with asterisk are probably due to co-irradiation of N-methyl and ferrocenyl proton(s).



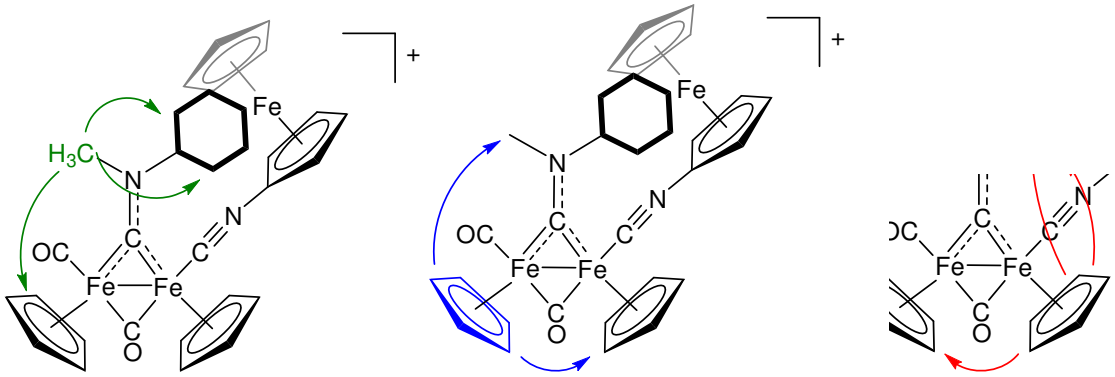


Figure S10. Black line: ^{1}H NMR spectrum (401 MHz, $CDCl_3$) of **2b**. Green line: ^{1}H NOESY with irradiation at 4.08 ppm (NMe of the *cis-E* isomer). Observed NOEs are indicated by the arrows.

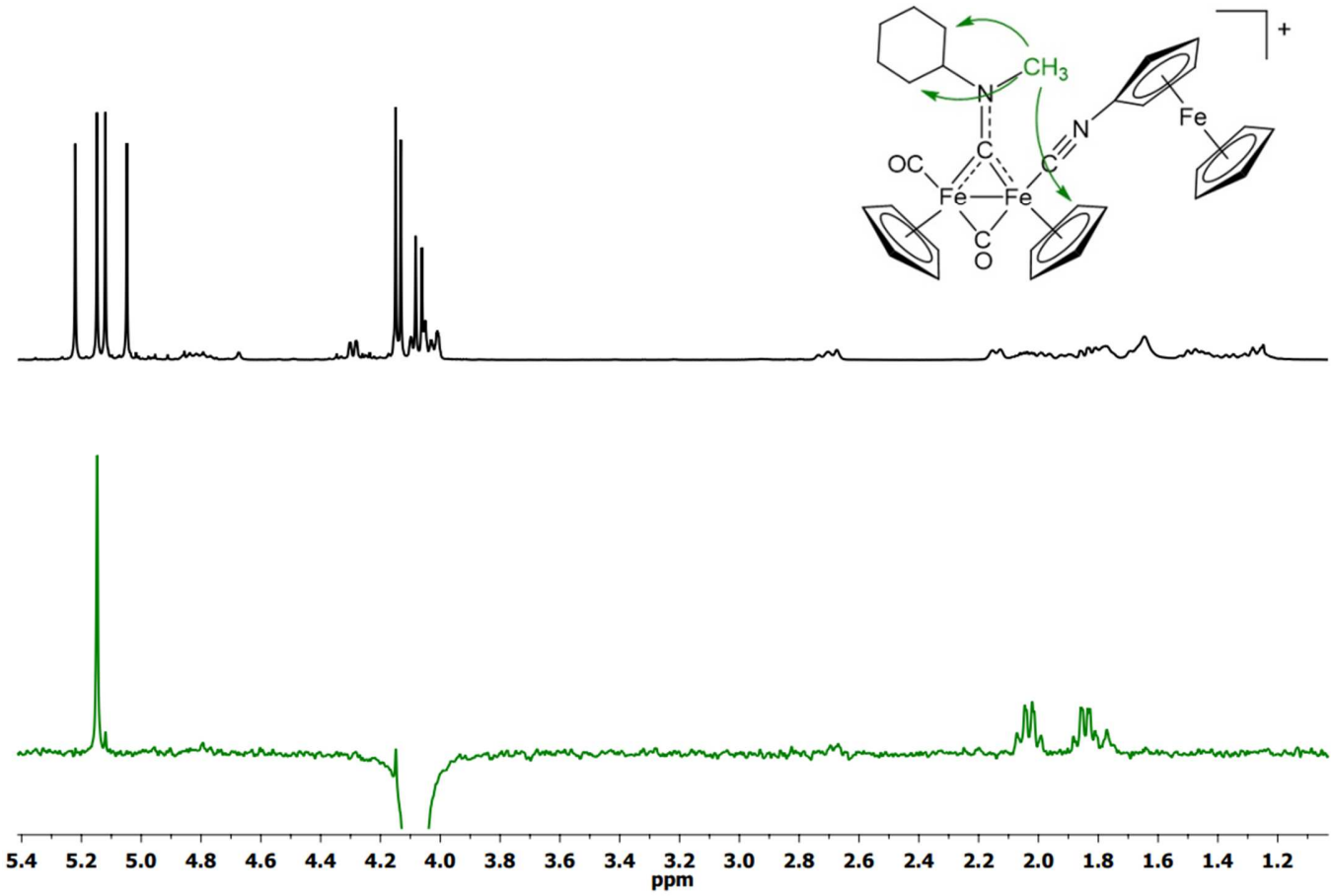


Figure S11. Solid-state IR spectrum (650-4000 cm^{-1}) of $[Fe_2Cp_2(CO)(CNFc)(\mu\text{-}CO)\{\mu\text{-}CNMe(4\text{-}C_6H_4OMe)\}]CF_3SO_3$, **2c** (cis-*E*/*Z* isomer mixture).

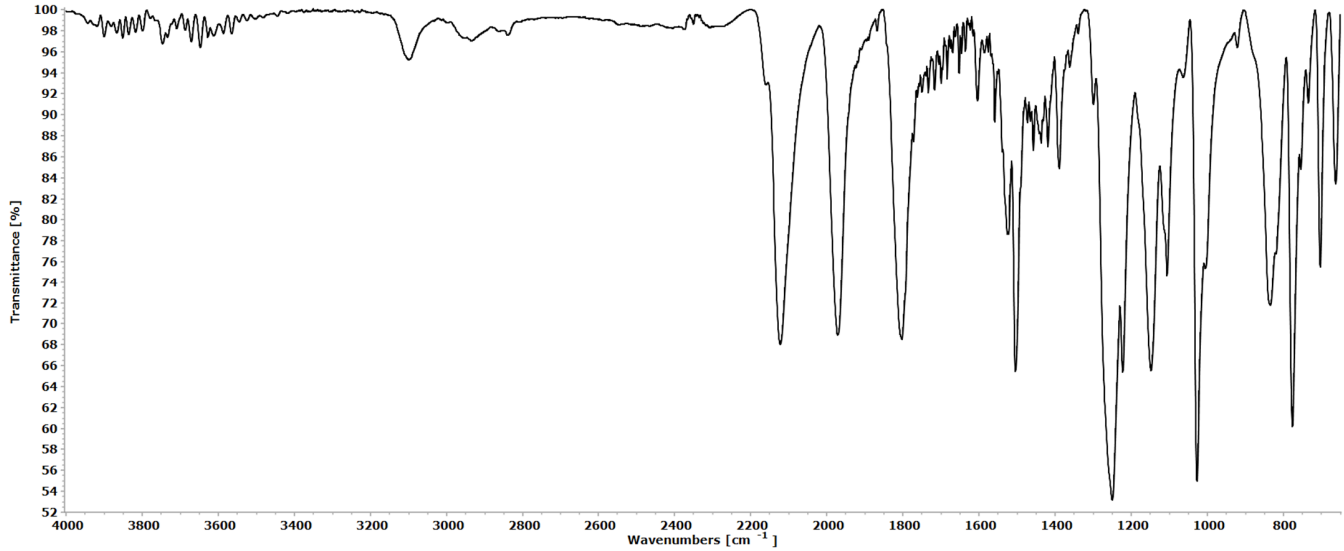


Figure S12. ^1H NMR spectrum (401 MHz, $CDCl_3$) of **2c** (*E*/*Z* isomer ratio 1.0). The corresponding signals of the two isomers are integrated together.

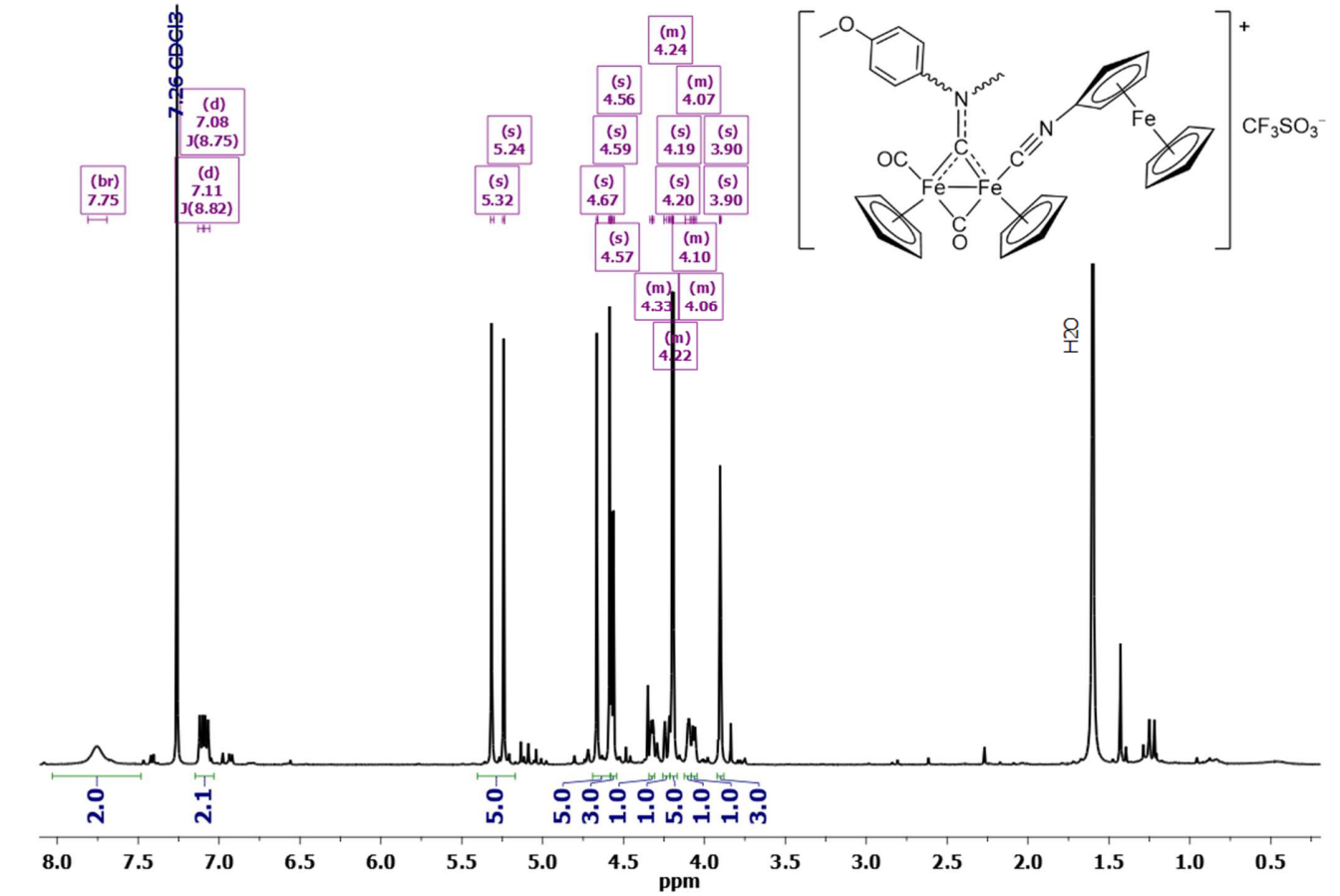


Figure S13. ^{1}H NMR spectrum (401 MHz, $CDCl_3$) of **2c** (*E*/*Z* isomer ratio 1.2), highlighting the signals of the *cis*-*E* isomer in the 5.30 – 3.80 ppm region.

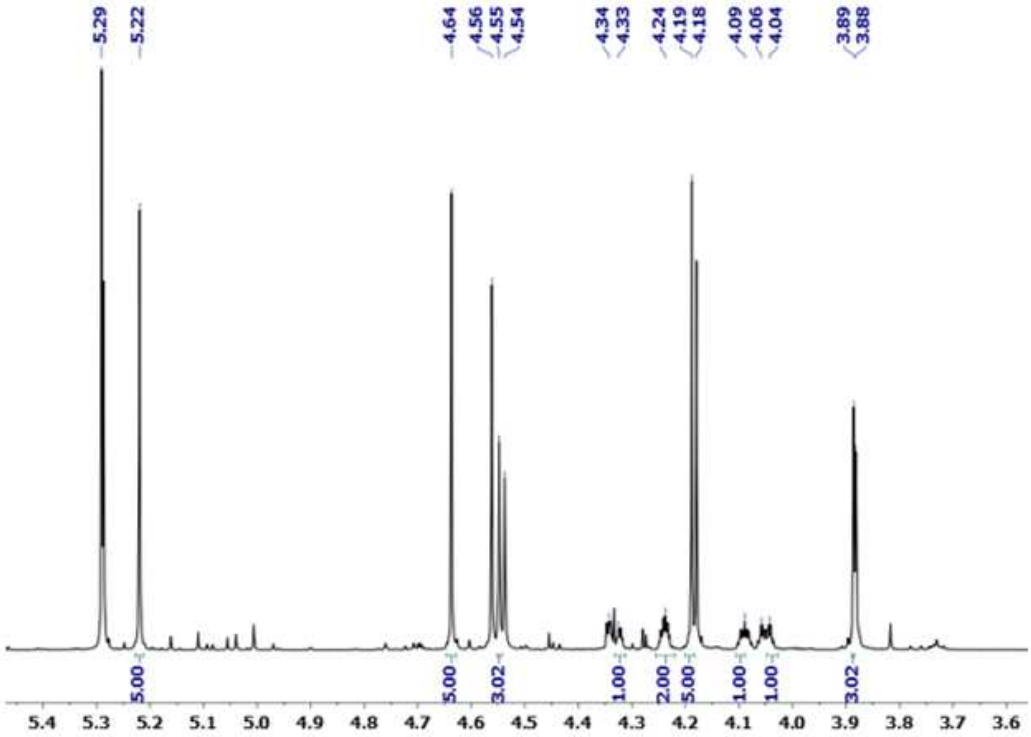


Figure S14. ^{1}H NMR spectrum (401 MHz, $CDCl_3$) of **2c** (*E*/*Z* isomer ratio 1.2), highlighting the signals of the *cis*-*Z* isomer in the 5.30 – 3.80 ppm region.

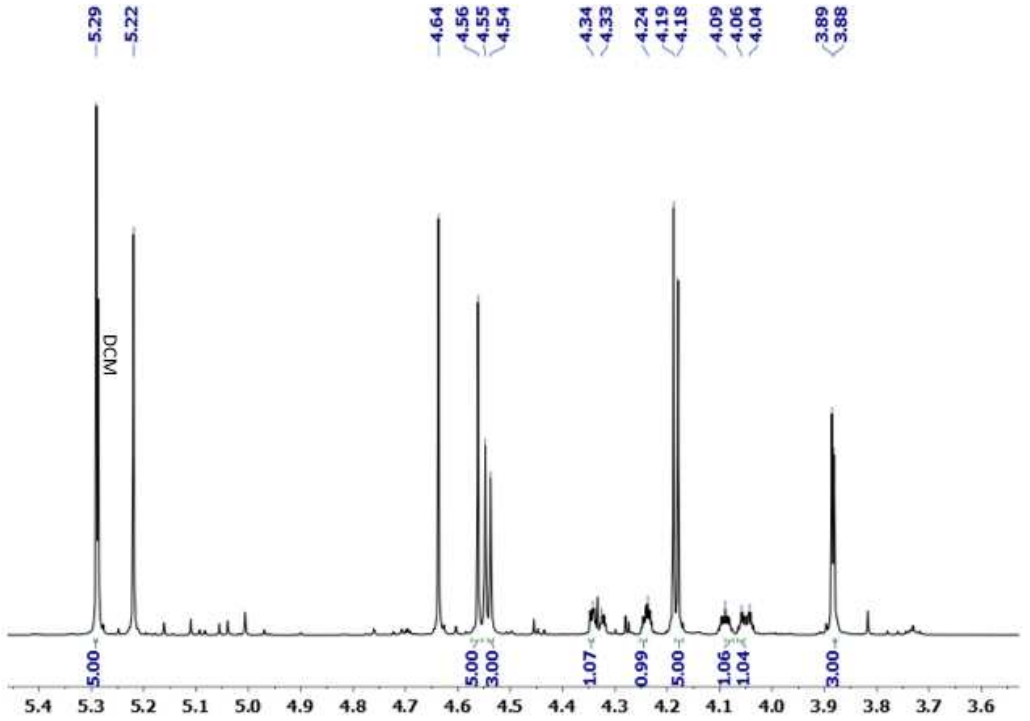


Figure S15. $^{13}C\{^{1}H\}$ NMR spectrum (101 MHz, $CDCl_3$) of **2c** (*E*/*Z* isomer ratio 1.2).

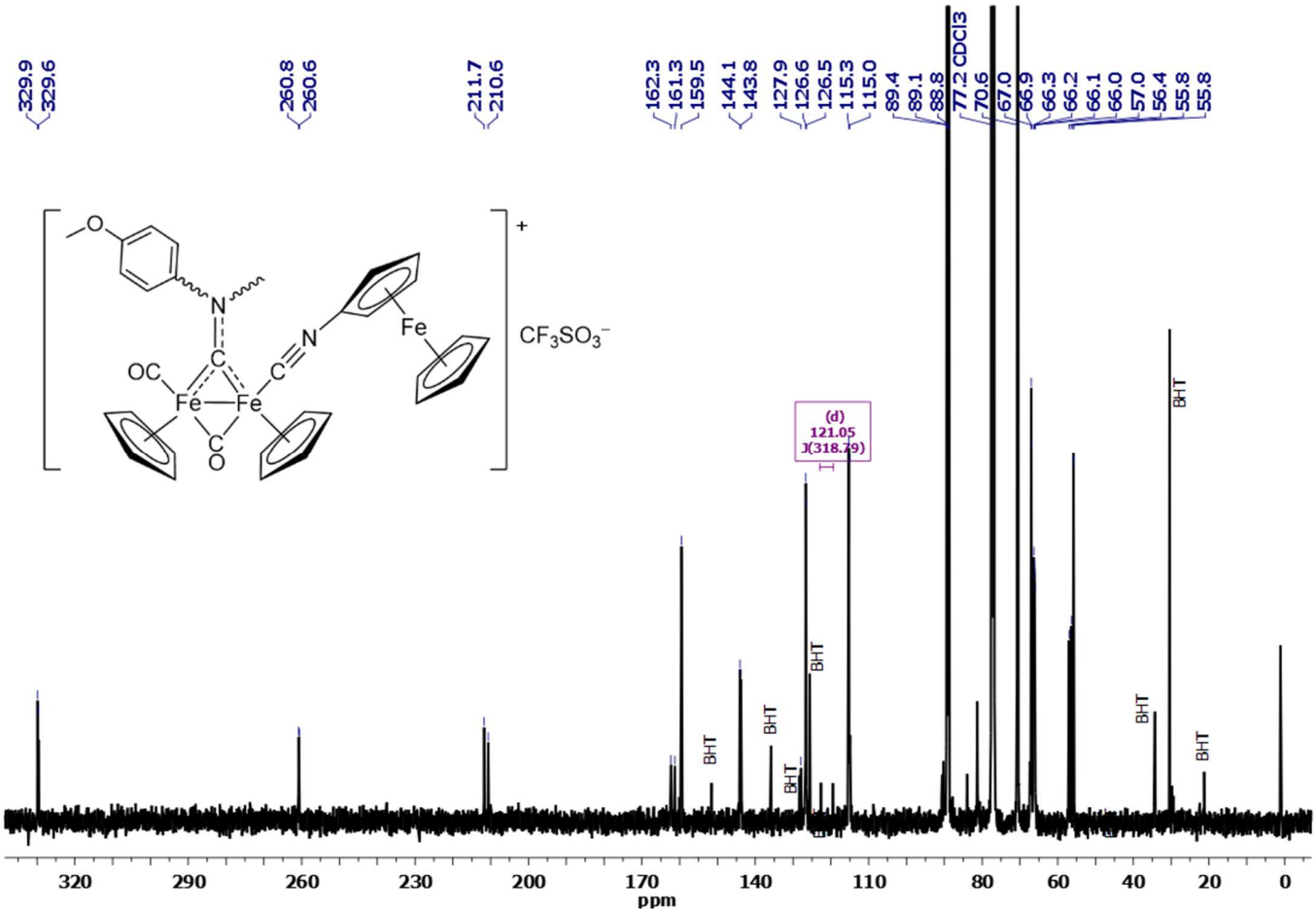
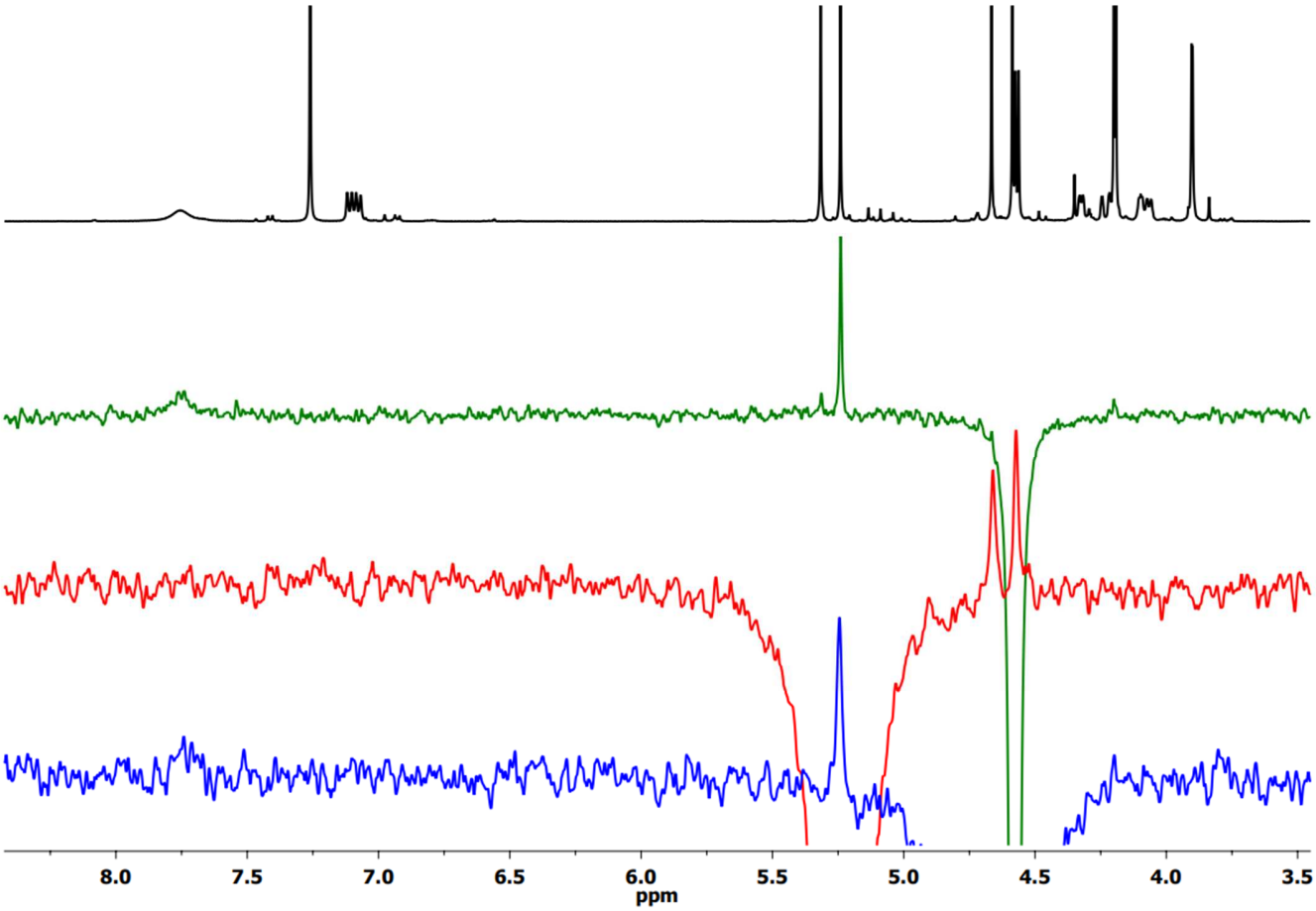


Figure S16. Black line: ^{1}H NMR spectrum (401 MHz, $CDCl_3$) of **2c**. Blue line: ^{1}H NOESY with irradiation at 4.67 ppm; red line: ^{1}H NOESY with irradiation at 5.24 ppm; green line: ^{1}H NOESY with irradiation at 4.57 ppm (Cp^{CO}, Cp^{CNR} and NMe of the *cis-E* isomer, respectively). Observed NOEs are indicated by the arrows (dashed line for weak NOE).



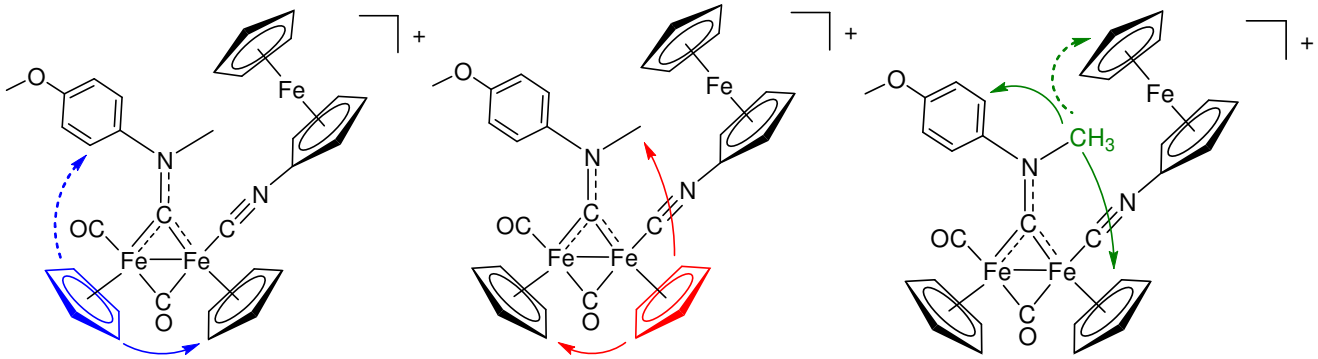
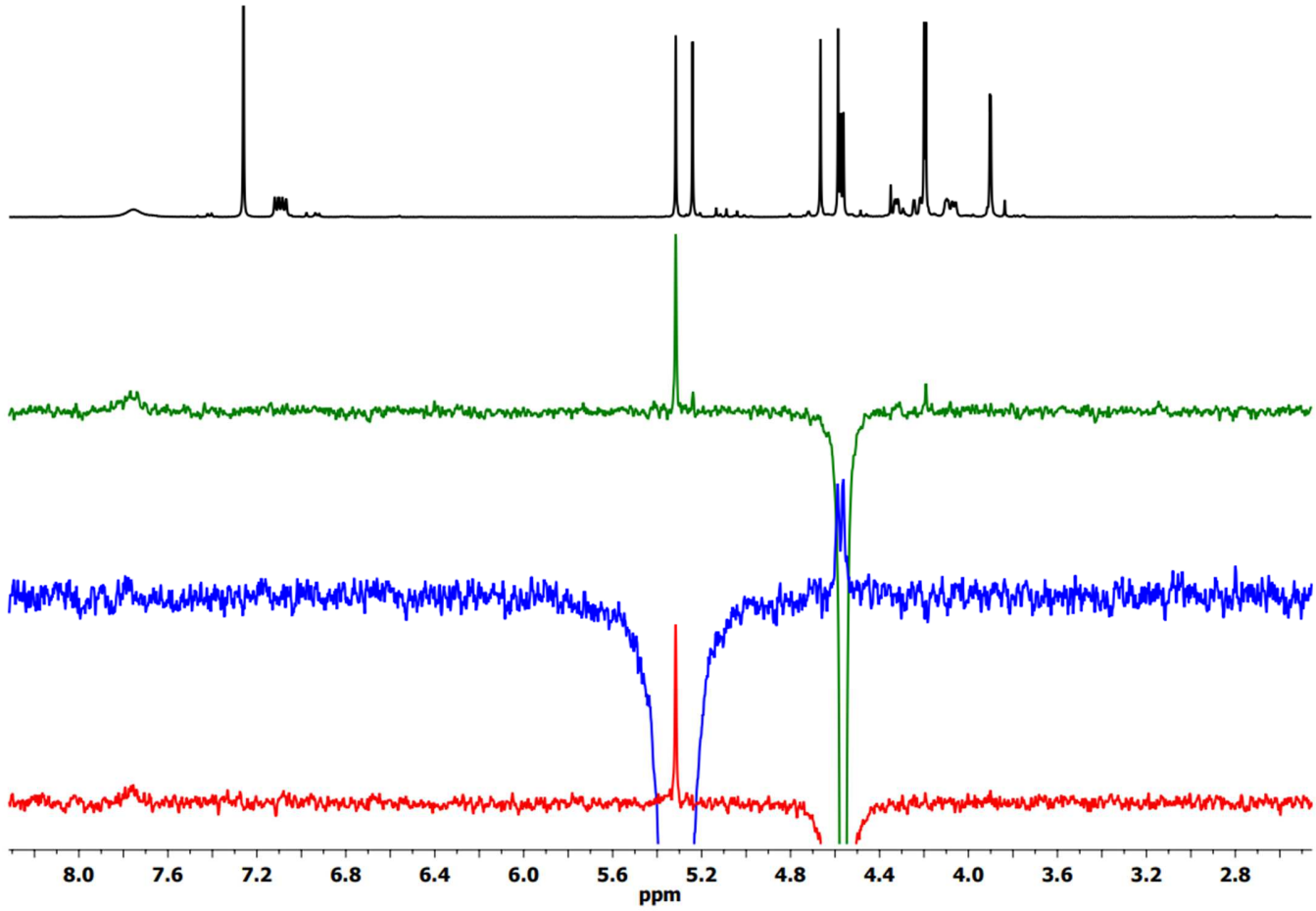


Figure S17. Black line: ^{1}H NMR spectrum (401 MHz, $CDCl_3$) of **2c**. Blue line: ^{1}H NOESY with irradiation at 5.32 ppm; red line: ^{1}H NOESY with irradiation at 4.57 ppm; green line: ^{1}H NOESY with irradiation at 4.56 ppm (Cp^{CO}, Cp^{CNR} and NMe of the *cis-Z* isomer, respectively). Observed NOEs are indicated by the arrows (dashed line for weak NOE).



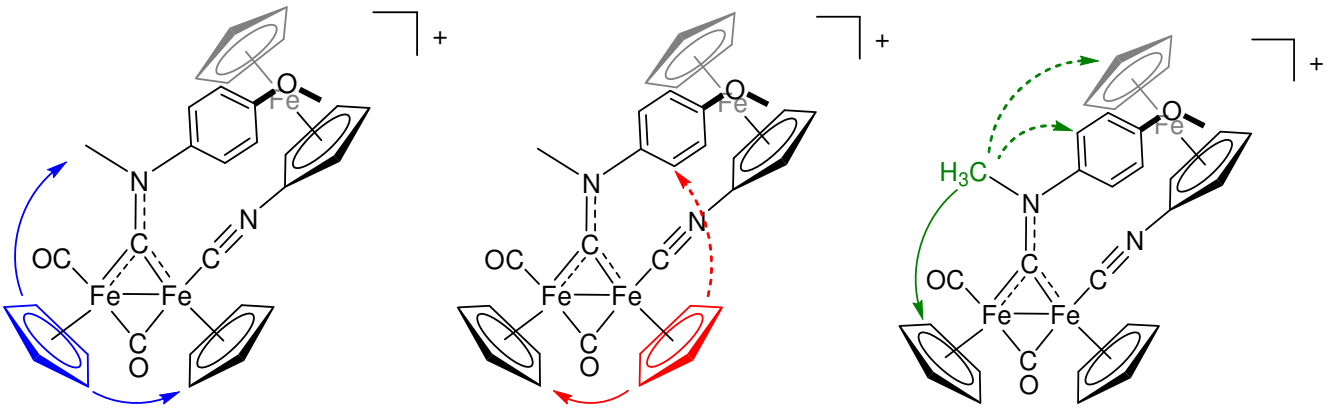


Figure S18. Solid-state IR spectrum (650-4000 cm^{-1}) of $[Fe_2Cp_2(CO)\{CN(4\text{-}C_6H_4OMe)\}(\mu\text{-}CO)\{\mu\text{-}CNMe(Cy)\}]CF_3SO_3$, **3b** (*E*/*Z* and *cis*/*trans* isomer mixture).

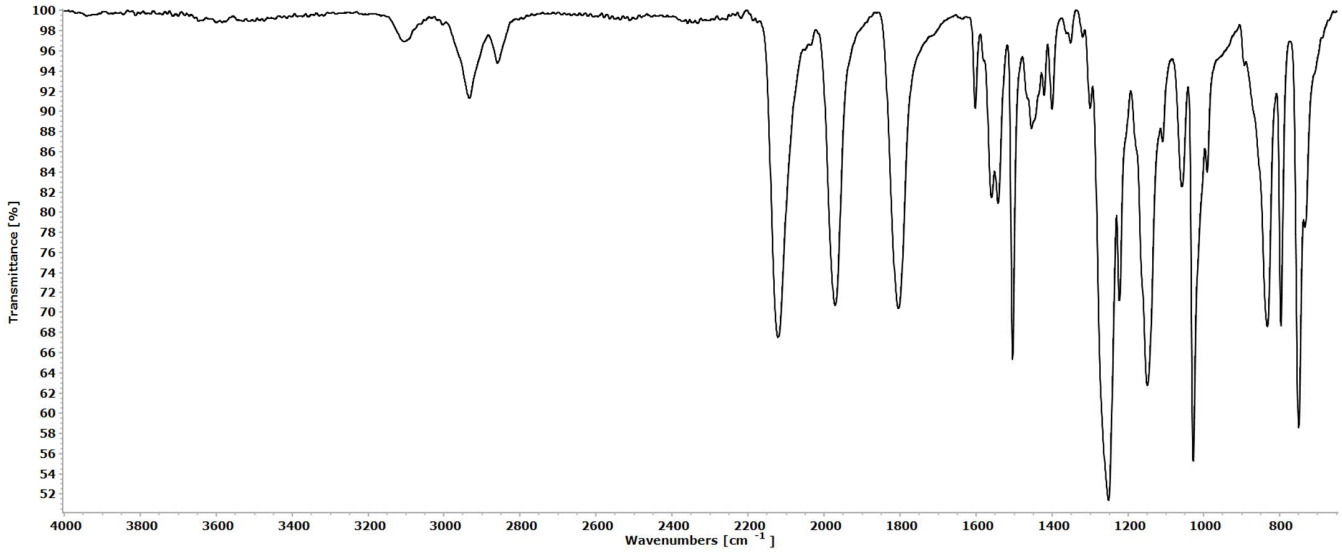


Figure S19. ^1H NMR spectrum (401 MHz, acetone-d_6) of **3b** (*cis*-*E*/*Z* isomer ratio 1.2 + 5 % *trans* isomers); signals due to *trans* isomers are not marked. The corresponding signals of all isomers are integrated together; each Cp integrates ≈ 4.6H due to low delay time.

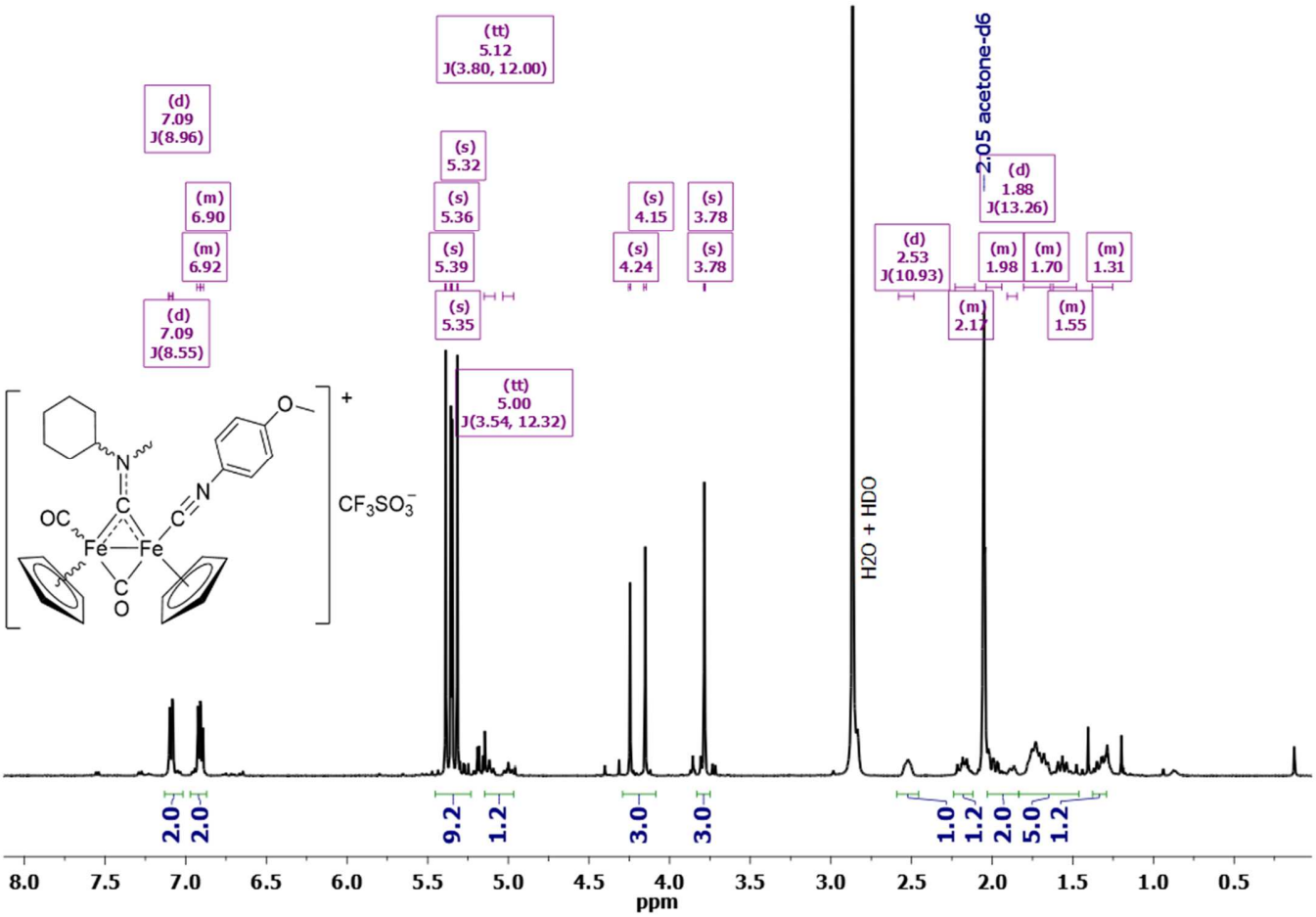


Figure S20. $^{13}C\{^{1}H\}$ NMR spectrum (101 MHz, acetone-d_6) of **3b** (*cis-E*/*Z* isomer ratio 1.2 + 5 % *trans* isomers); signals due to *trans* isomers are not marked.

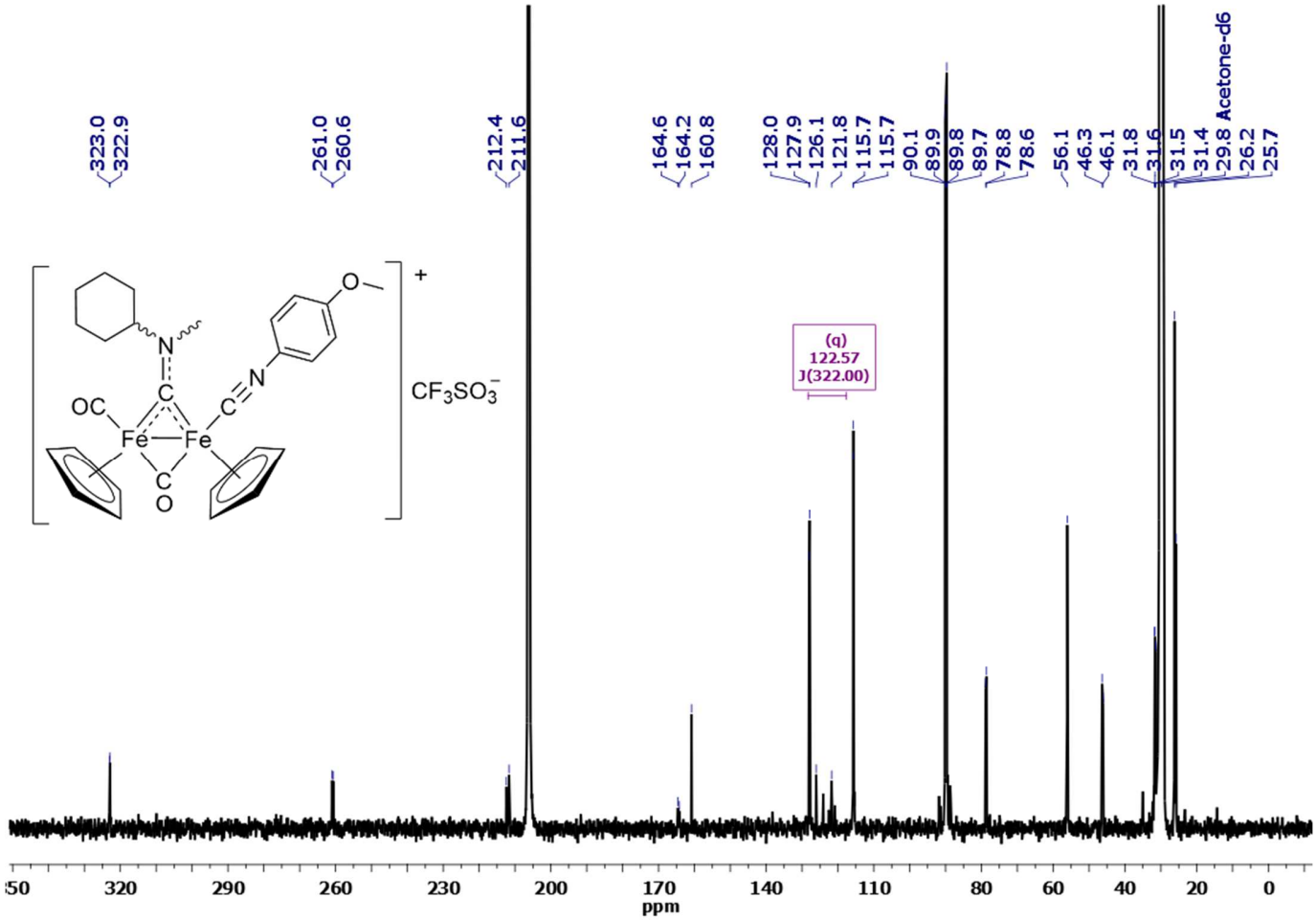
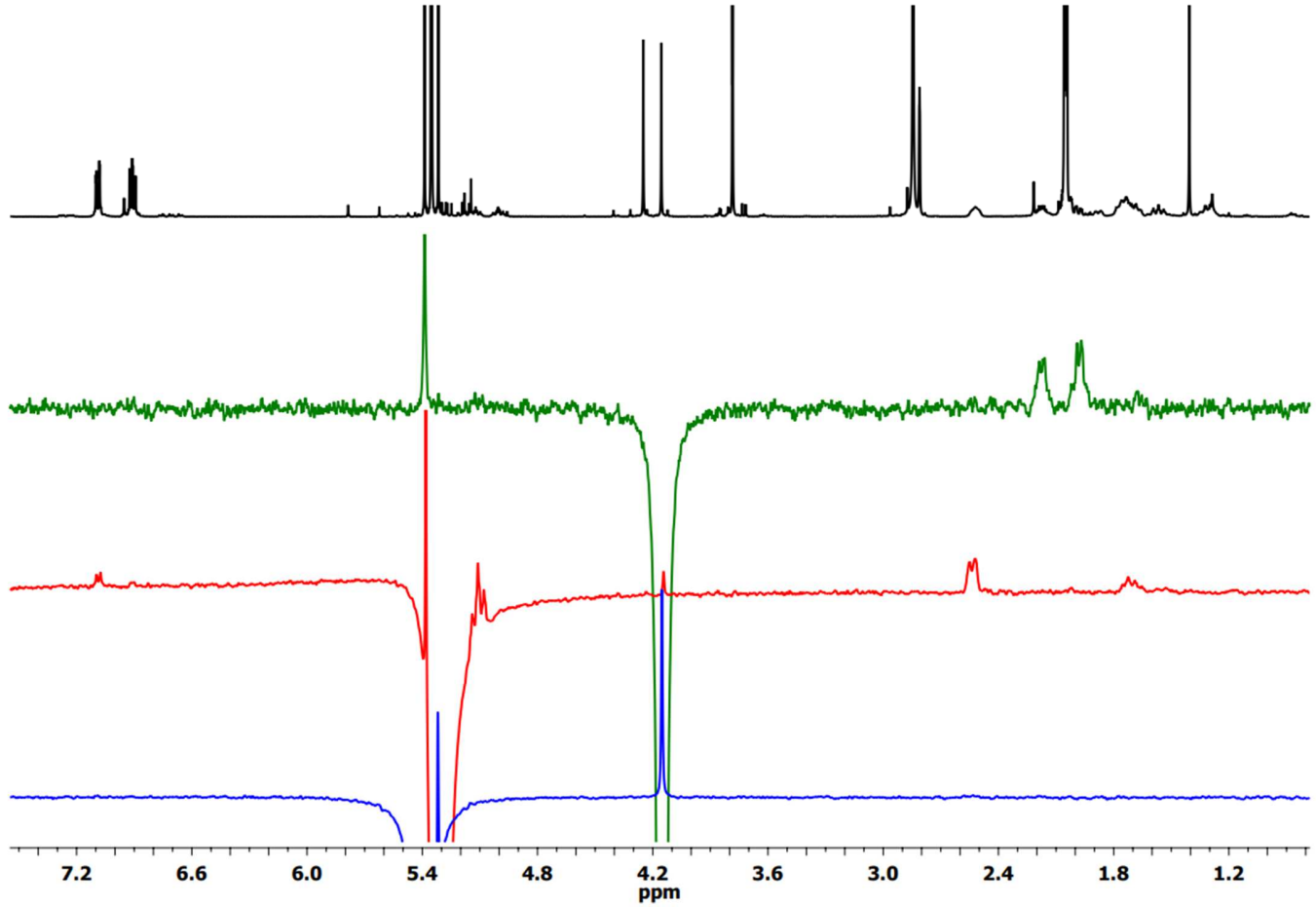


Figure S21. Black line: ^{1}H NMR spectrum (401 MHz, acetone-d_6) of **3b**. Blue line: ^{1}H NOESY with irradiation at 5.39 ppm; red line: ^{1}H NOESY with irradiation at 5.32 ppm; green line: ^{1}H NOESY with irradiation at 4.15 ppm (Cp^{CO}, Cp^{CNR} and NMe of the *cis-Z* isomer). Observed NOEs are indicated by the arrows (dotted lines for weaker effects).



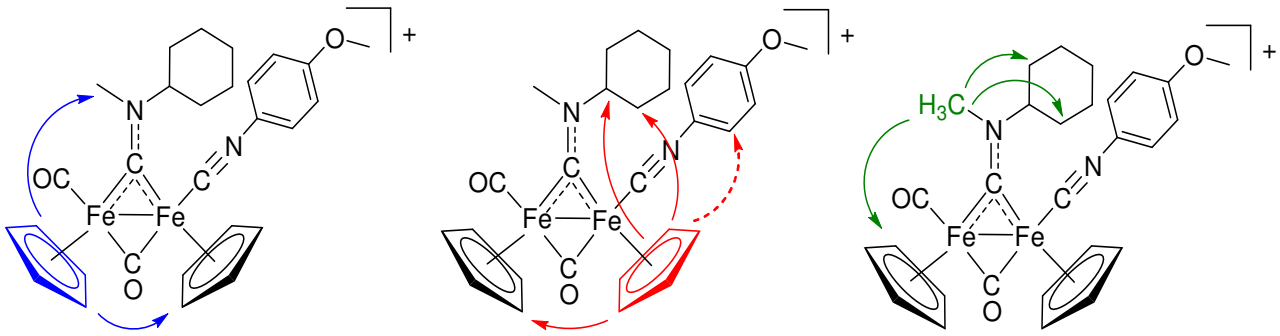
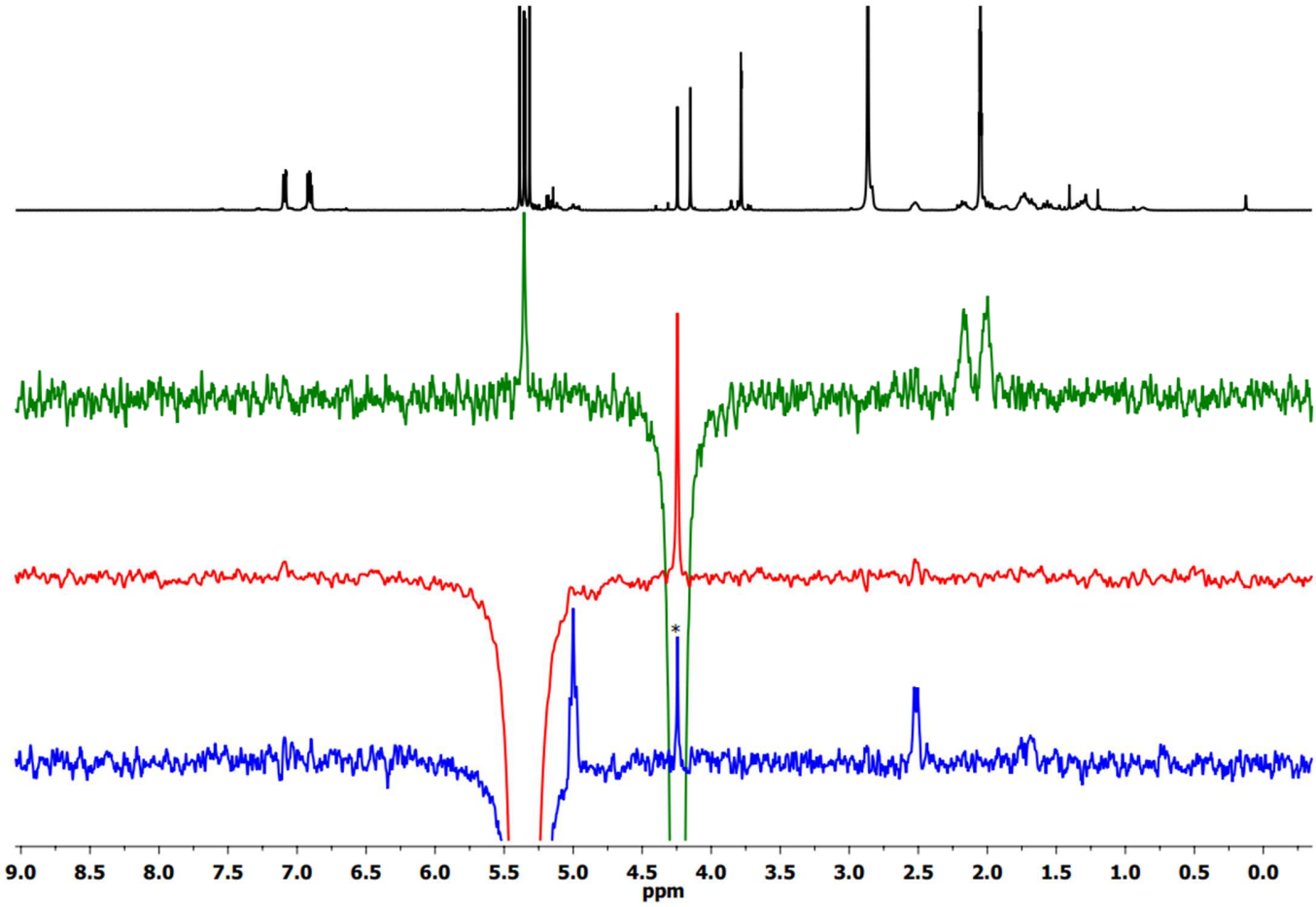


Figure S22. Black line: ^{1}H NMR spectrum (401 MHz, acetone-d_6) of **3b**. Blue line: ^{1}H NOESY with irradiation at 5.35 ppm; red line: ^{1}H NOESY with irradiation at 5.36 ppm; green line: ^{1}H NOESY with irradiation at 4.25 ppm (Cp^{CO}, Cp^{CNR} and NMe of the *cis-E* isomer). Observed NOEs are indicated by the arrows (dotted lines for weaker effects). The lack of mutual NOE effects between the Cp ligands as well as the signal marked with asterisk are probably due to partial co-irradiation.



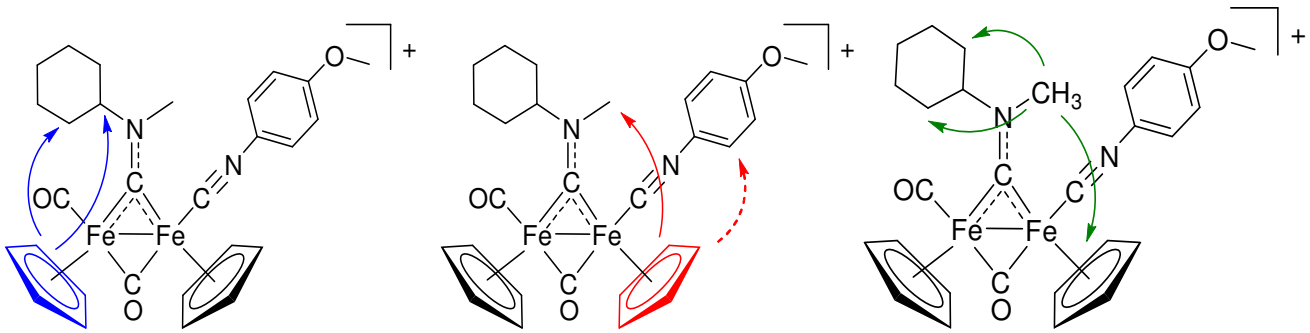


Figure S23. Solid-state IR spectrum (650-4000 cm^{-1}) of $[Fe_2Cp_2(CO)(CNCy)(\mu\text{-}CO)\{\mu\text{-}CNMe(4\text{-}C_6H_4OMe)\}]CF_3SO_3$, **3c** (*E*/*Z* and *cis*/*trans* isomer mixture).

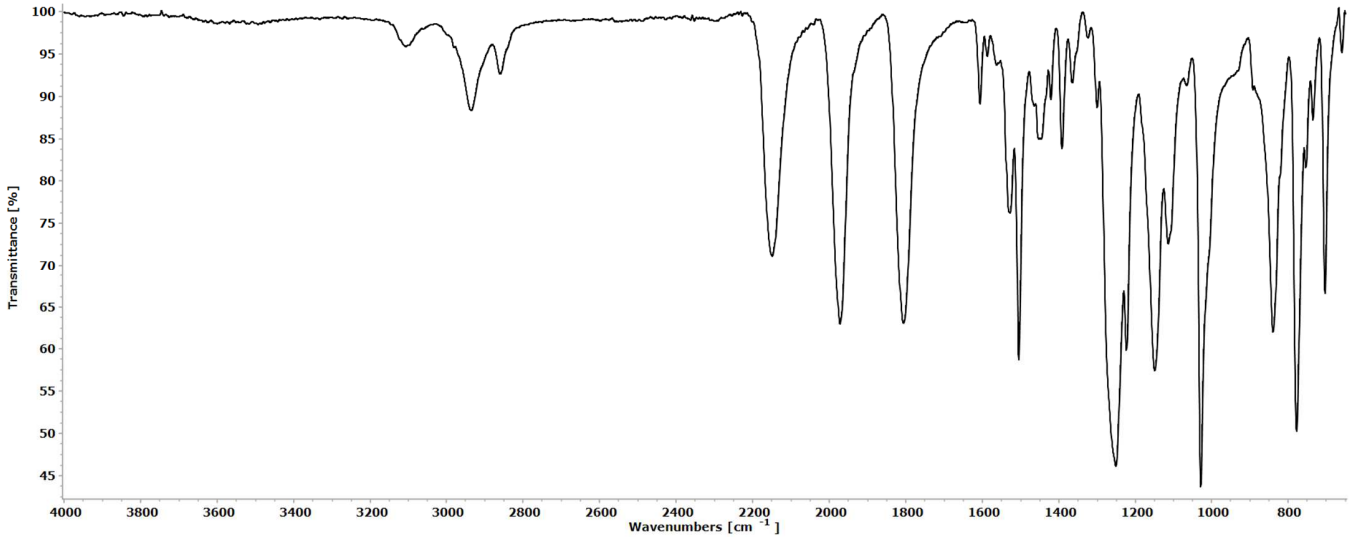


Figure S24. ^1H NMR spectrum (401 MHz, acetone-d_6) of **3c** (*cis*-*E*/*Z* isomer ratio 1.3 + 8 % *trans* isomers); signals due to *trans* isomers are not marked. The corresponding signals of all isomers are integrate together; each Cp integrates ≈ 4.5H due to low delay time.

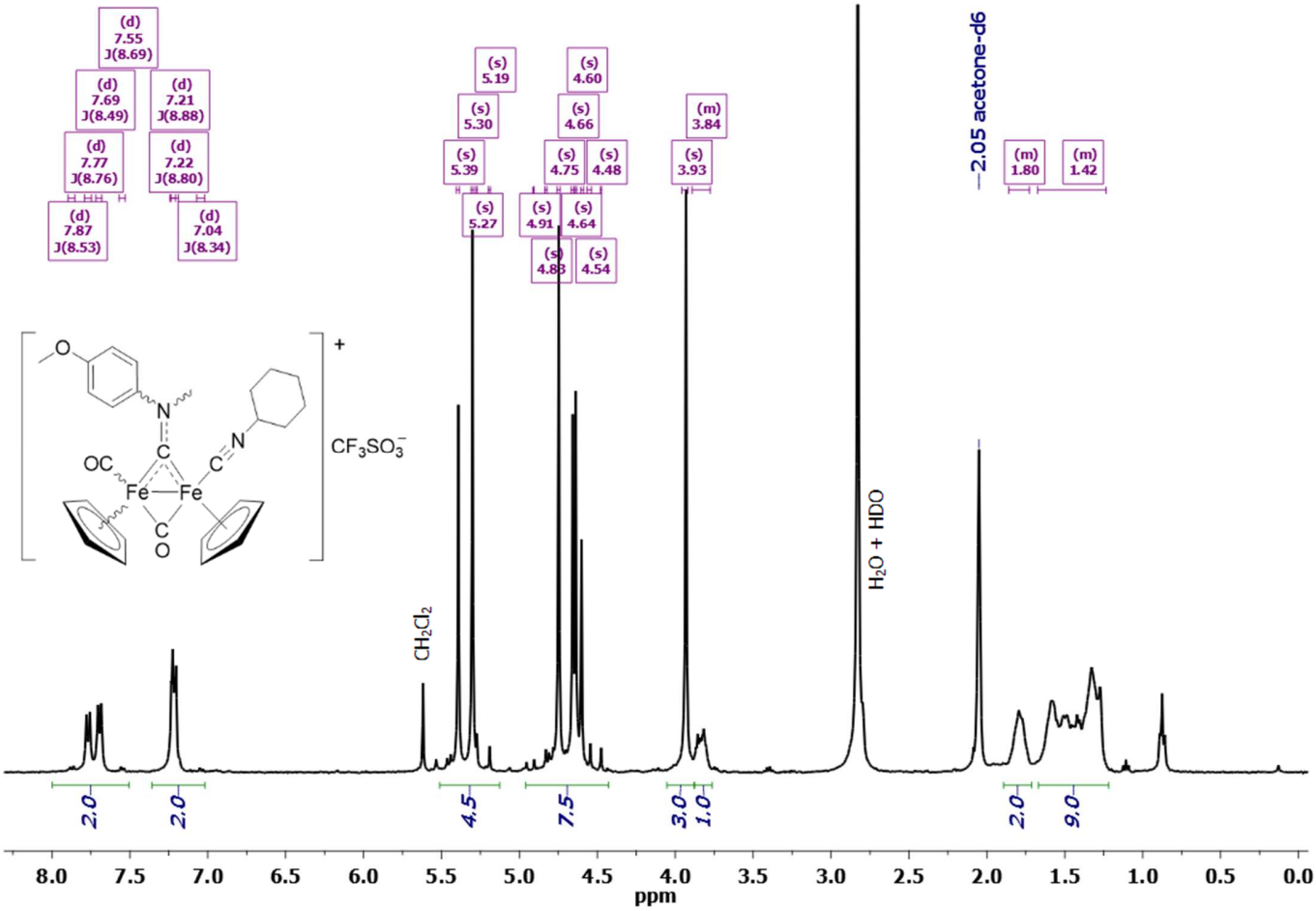


Figure S25. $^{13}C\{^{1}H\}$ NMR spectrum (101 MHz, acetone-d_6) of **3c** (*cis-E*/*Z* isomer ratio 1.3 + 8 % *trans* isomers); signals due to *trans* isomers are not marked.

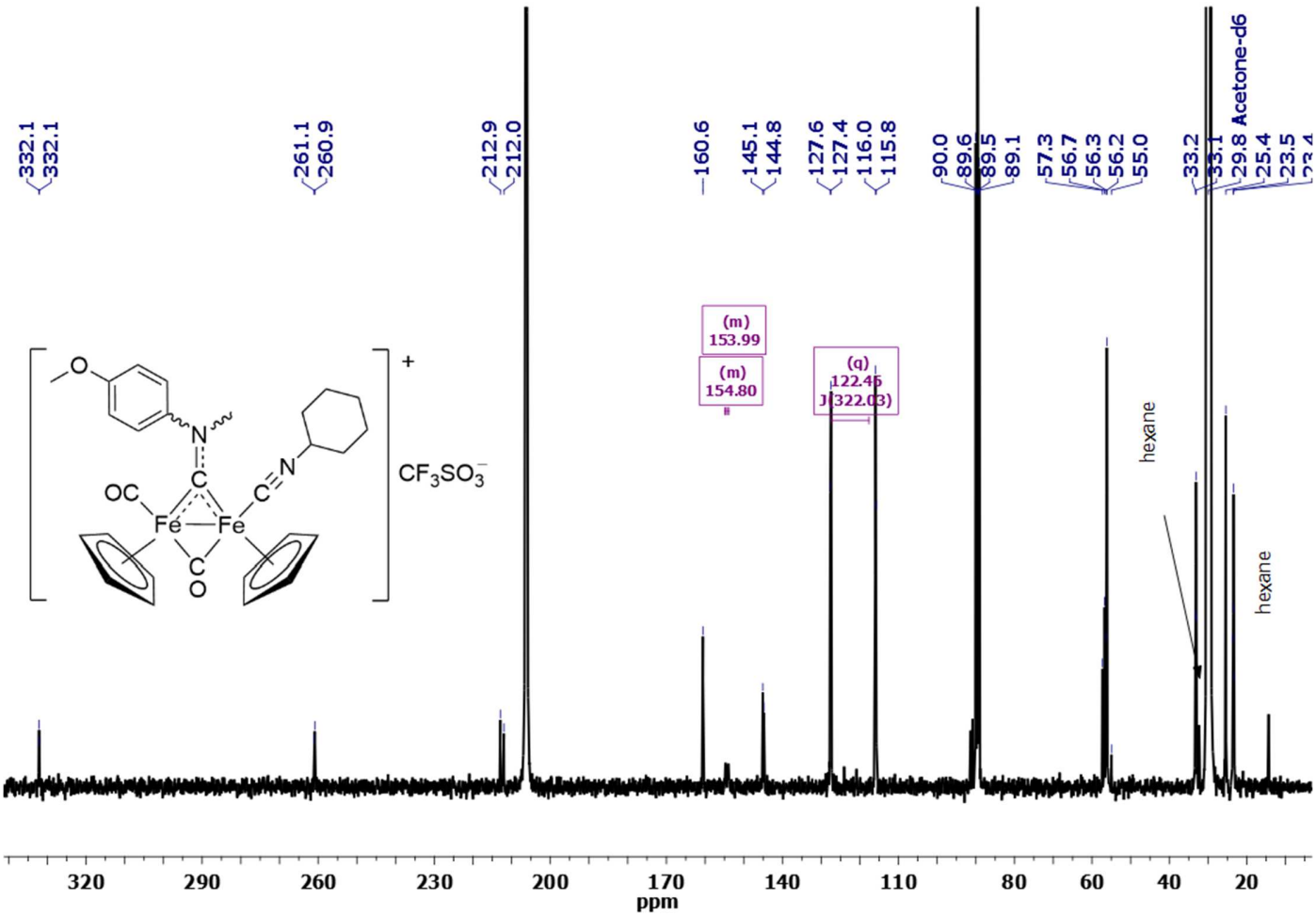
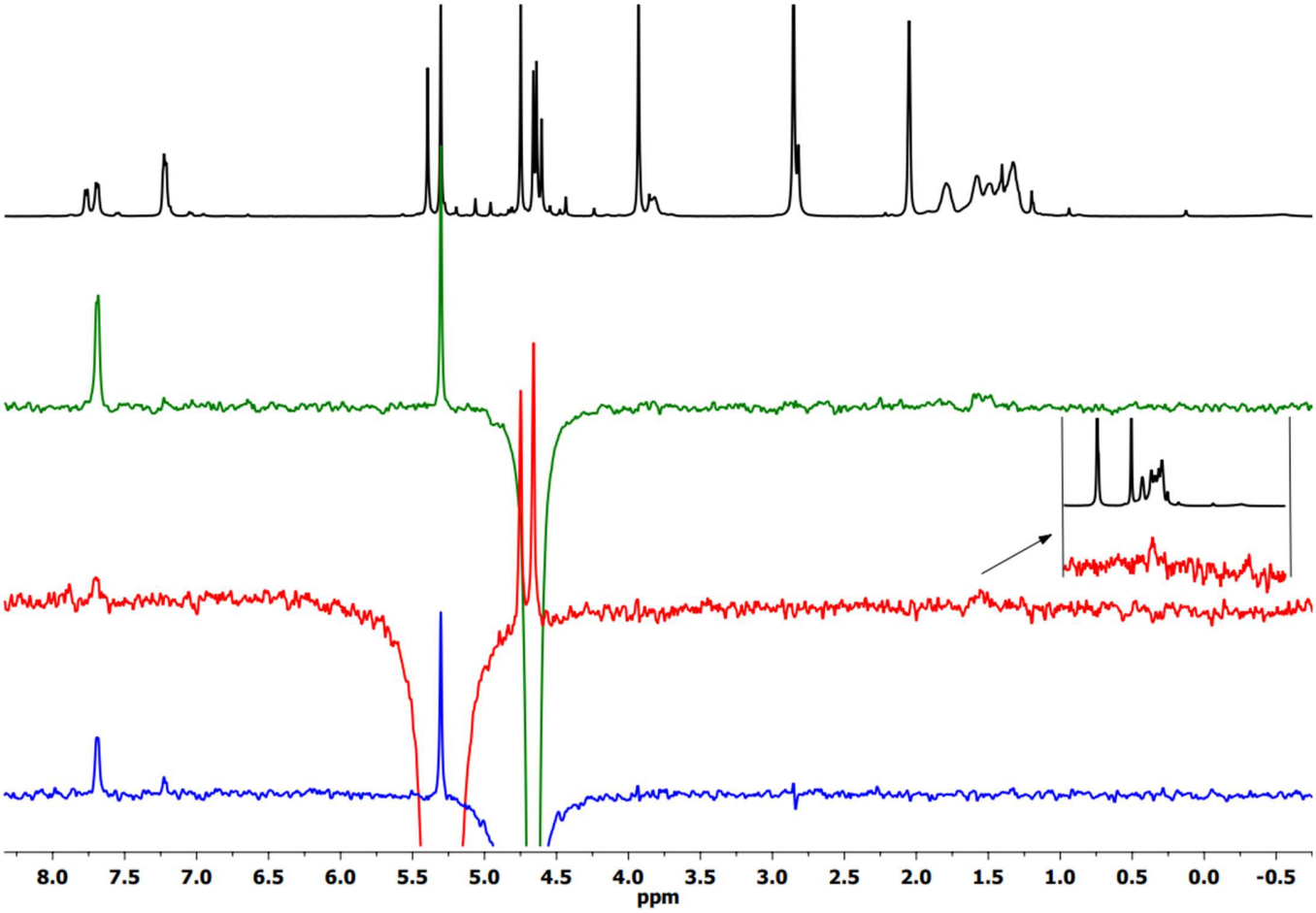


Figure S26. Black line: ^{1}H NMR spectrum (401 MHz, $CDCl_3$) of **3c**. Blue line: ^{1}H NOESY with irradiation 4.75 ppm; red line: ^{1}H NOESY with irradiation at 5.30 ppm; green line: ^{1}H NOESY with irradiation at 4.66 ppm (Cp^{CO}, Cp^{CNR} and NMe of the *cis-E* isomer, respectively). Observed NOEs are indicated by the arrows (dashed line for weak NOE).



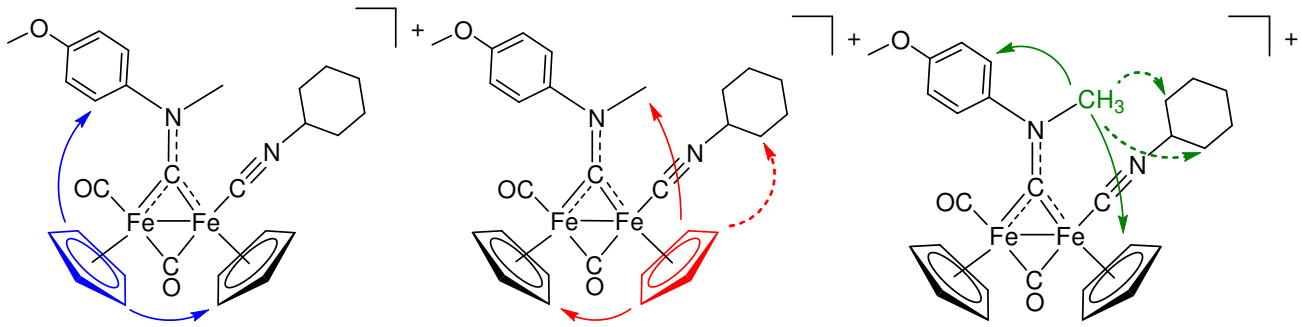
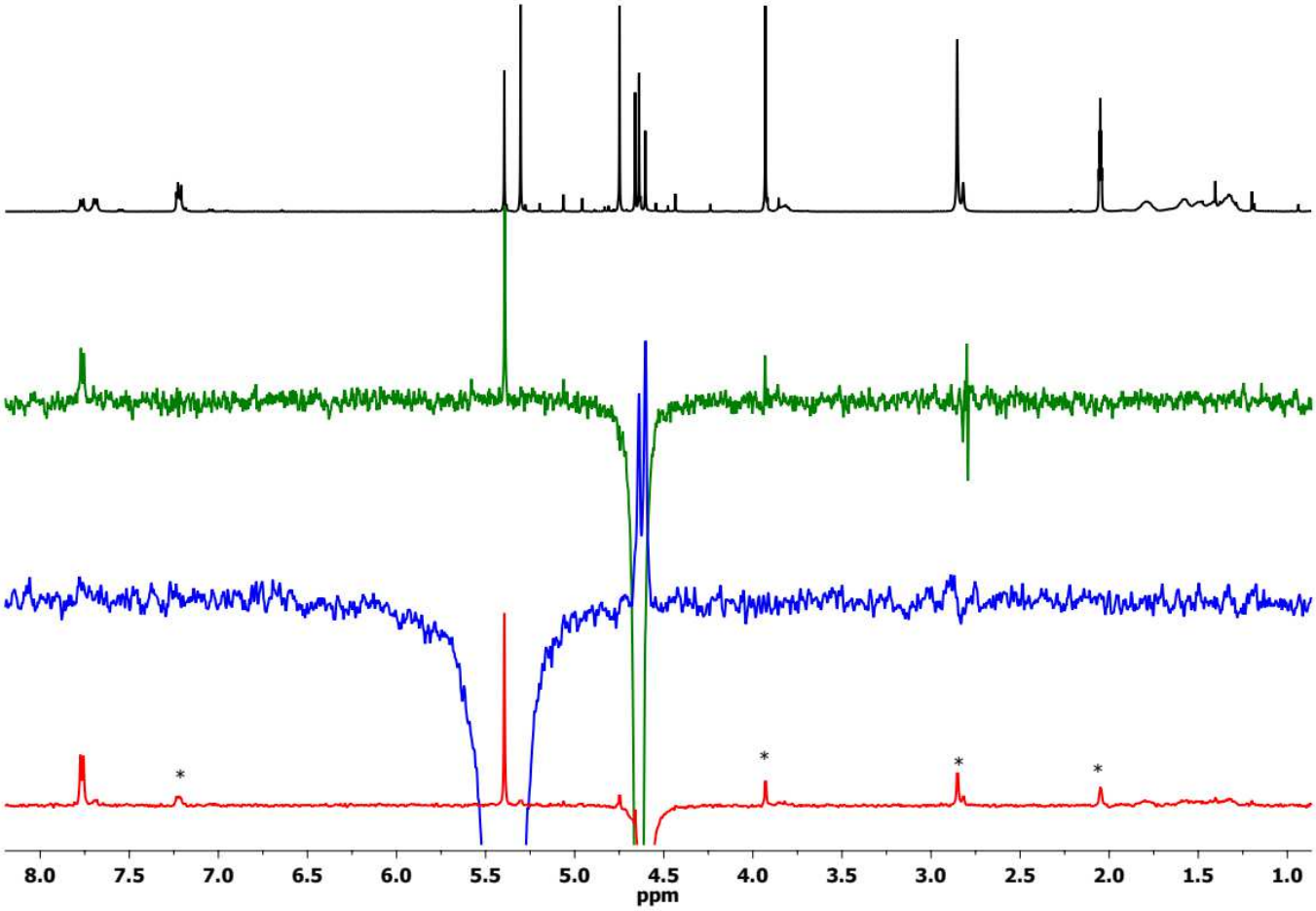


Figure S27. Black line: ^{1}H NMR spectrum (401 MHz, $CDCl_3$) of **3c**. Blue line: ^{1}H NOESY with irradiation 5.40 ppm; red line: ^{1}H NOESY with irradiation at 4.64 ppm; green line: ^{1}H NOESY with irradiation at 4.60 ppm (Cp^{CO}, Cp^{CNR} and NMe of the *cis-Z* isomer, respectively). Observed NOEs are indicated by the arrows (dashed line for weak NOE). Signals marked with asterisk are due to FID acquisition errors (NOE effects with HDO, acetone-d_6, etc.)



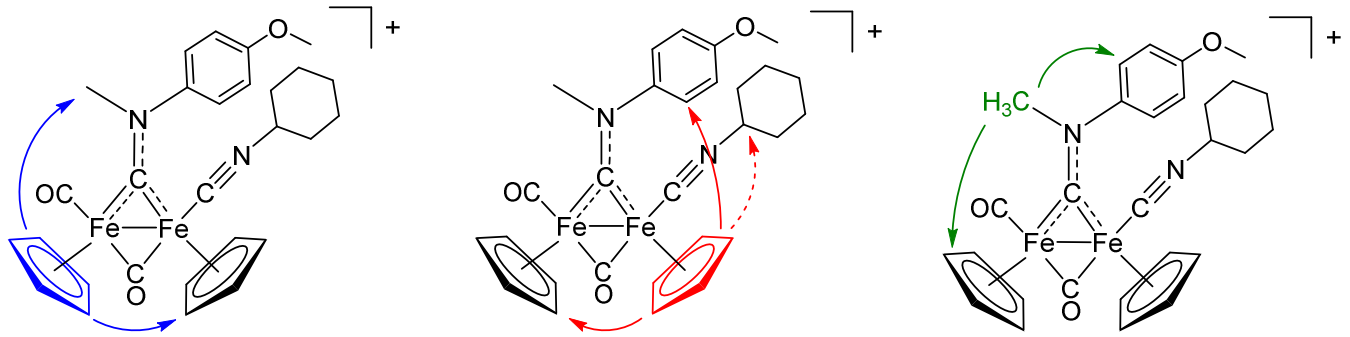


Figure S28. Solid-state IR spectrum (650-4000 cm^{-1}) of $[Fe_2Cp_2\{CN(4\text{-}C_6H_4OMe)\}_2(\mu\text{-}CO)\{\mu\text{-}CNMe(Cy)\}]CF_3SO_3$, **4b** (*cis*/*trans* isomer mixture)

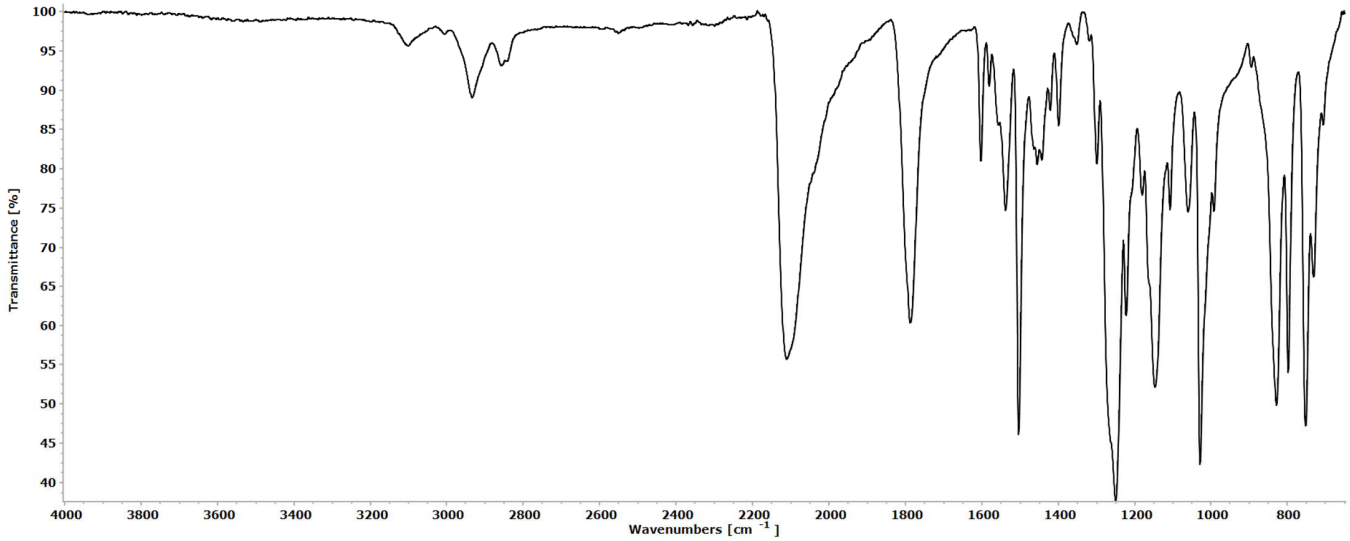


Figure S29. ^1H NMR spectrum (401 MHz, acetone-d_6) of **4b** (*cis/trans* ratio 6.5). The corresponding signals of all isomers are integrated together; each Cp integrates ≈ 4.7H due to low delay time.

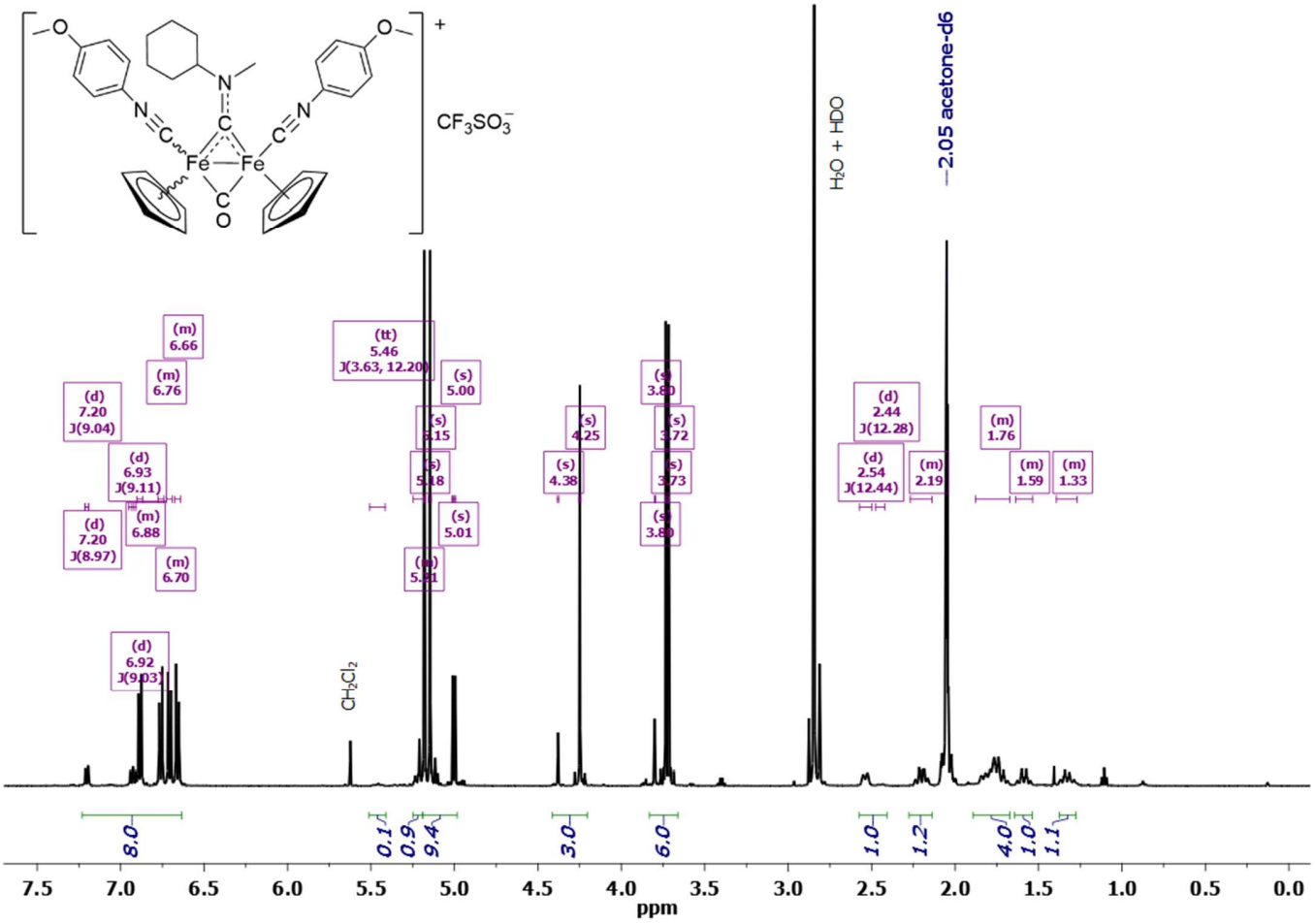


Figure S30. $^{13}C\{^{1}H\}$ NMR spectrum (101 MHz, acetone-d_6) of **4b** (*cis/trans* ratio 6.5).

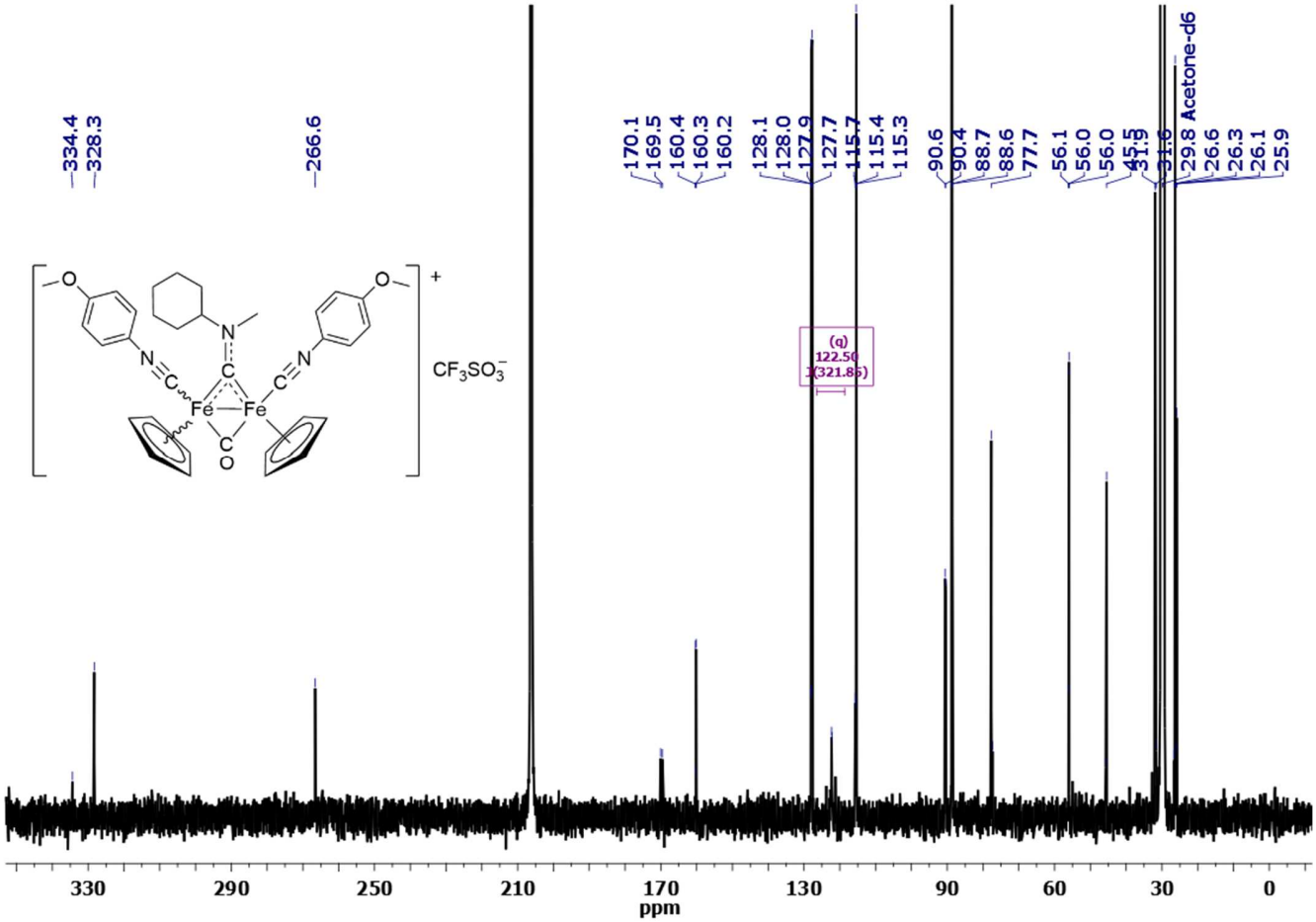


Figure S31. Solid-state IR spectrum (650-4000 cm^{-1}) of $[Fe_2Cp_2(CNCy)_2(\mu\text{-}CO)\{\mu\text{-}CNMe(4\text{-}C_6H_4OMe)\}]CF_3SO_3$, **4c** (*cis/trans* isomer mixture).

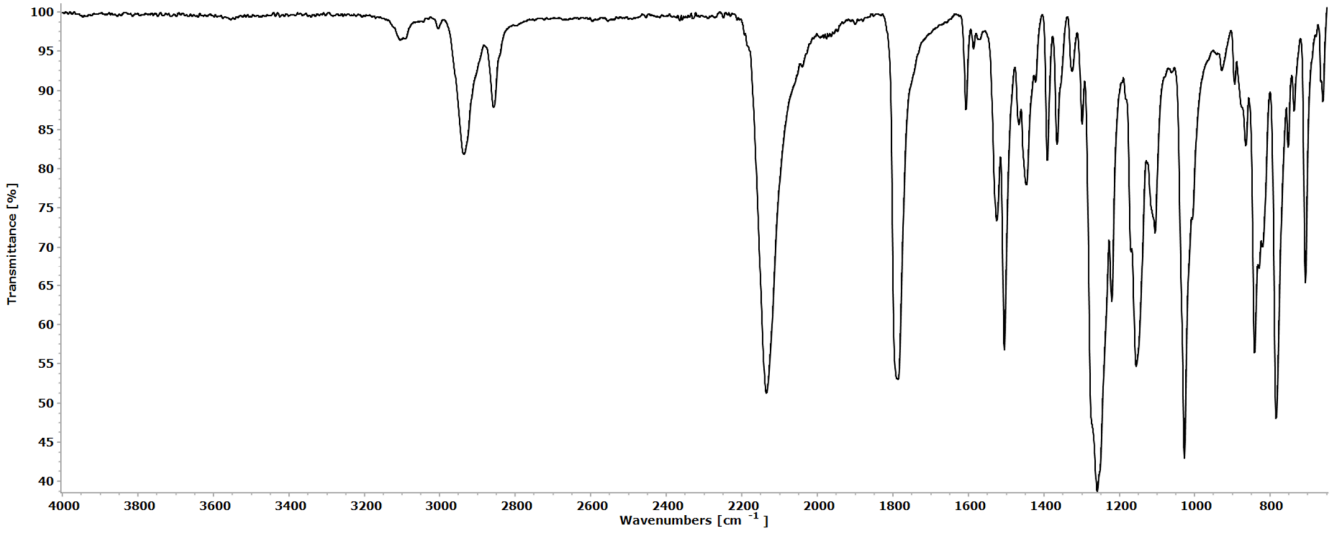


Figure S32. ^{1}H NMR spectrum (401 MHz, acetone-d_6) of $[Fe_2Cp_2(CNCy)_2(\mu\text{-}CO)\{\mu\text{-}CNMe(4\text{-}C_6H_4OMe)\}]CF_3SO_3$, **4c** (*cis/trans* ratio 1.6). The corresponding signals of all isomers are integrated together.

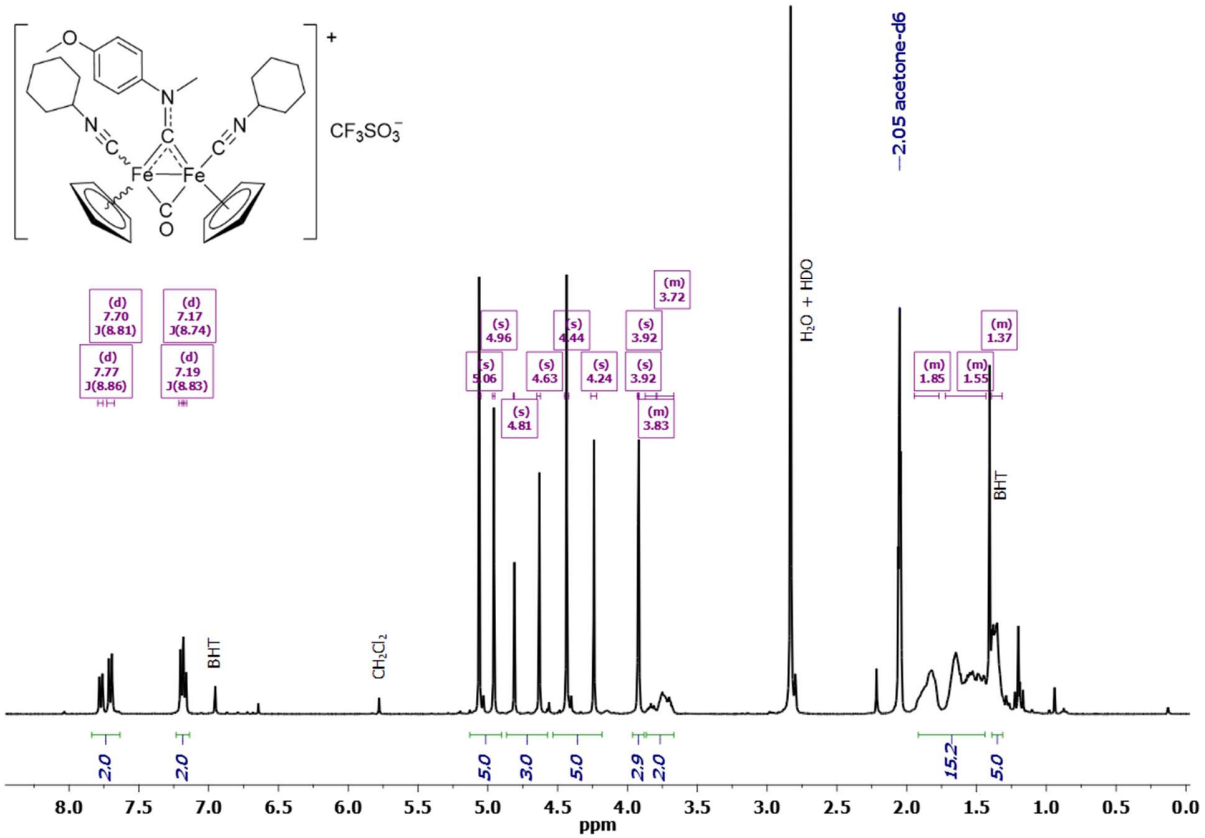


Figure S33. $^{13}C\{^{1}H\}$ NMR spectrum (101 MHz, acetone-d_6) of **4c** (*cis/trans* ratio 1.6).

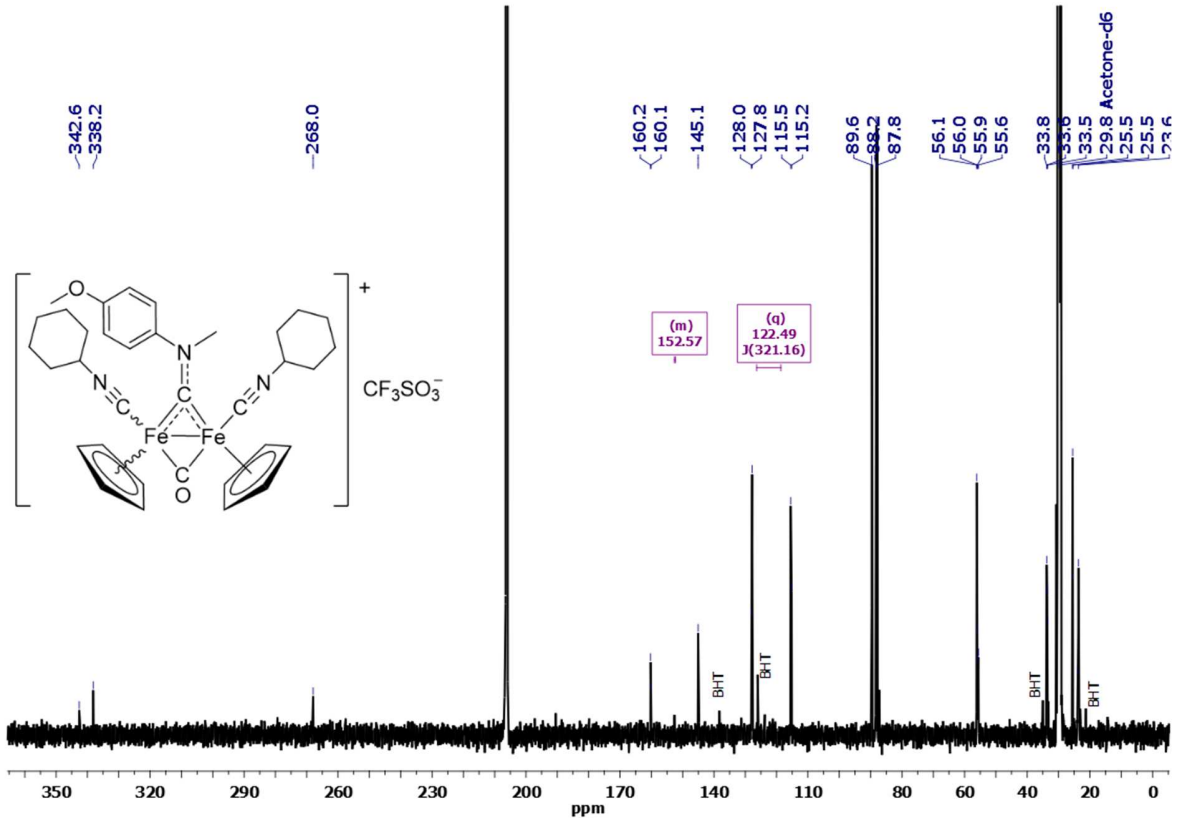
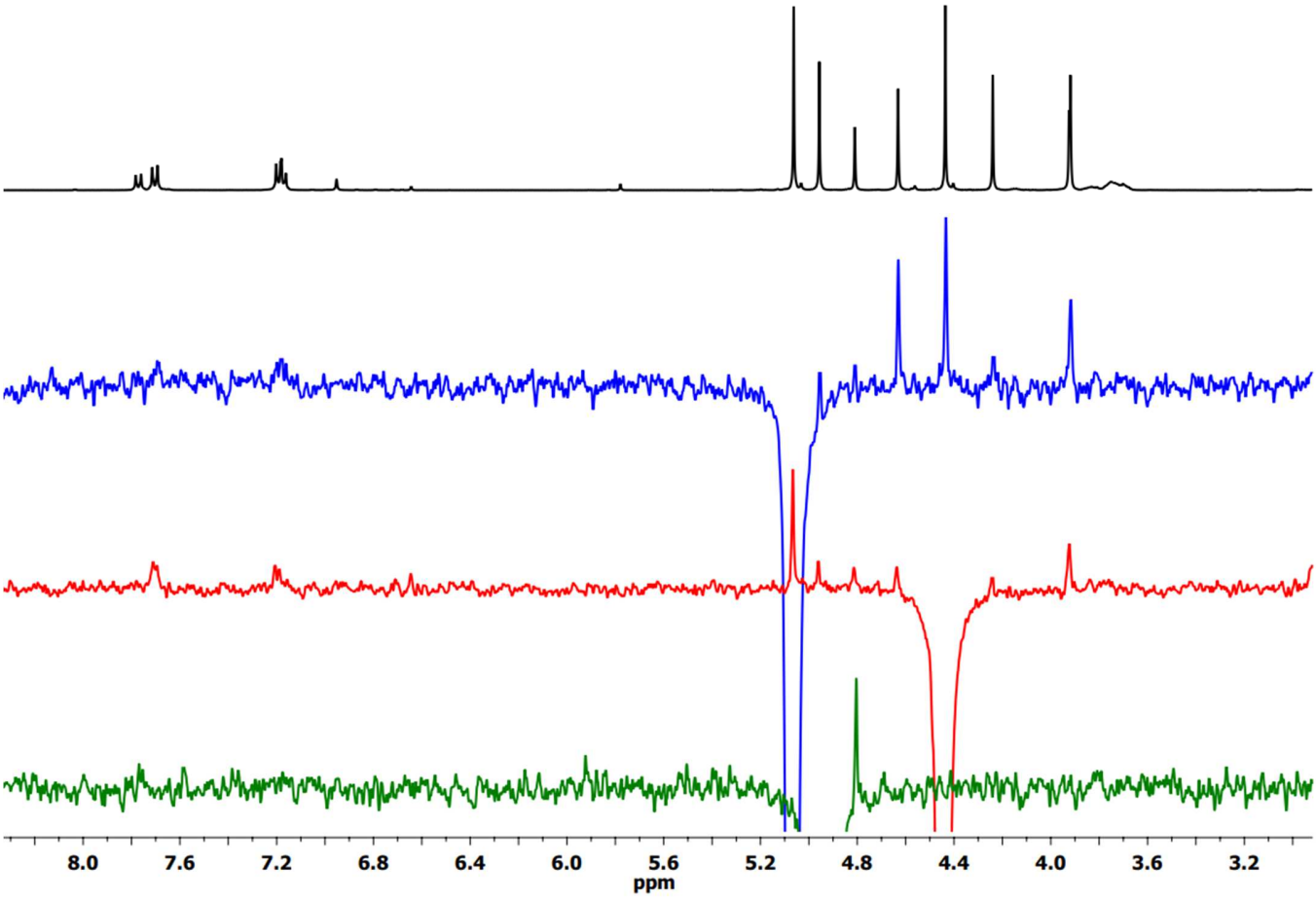
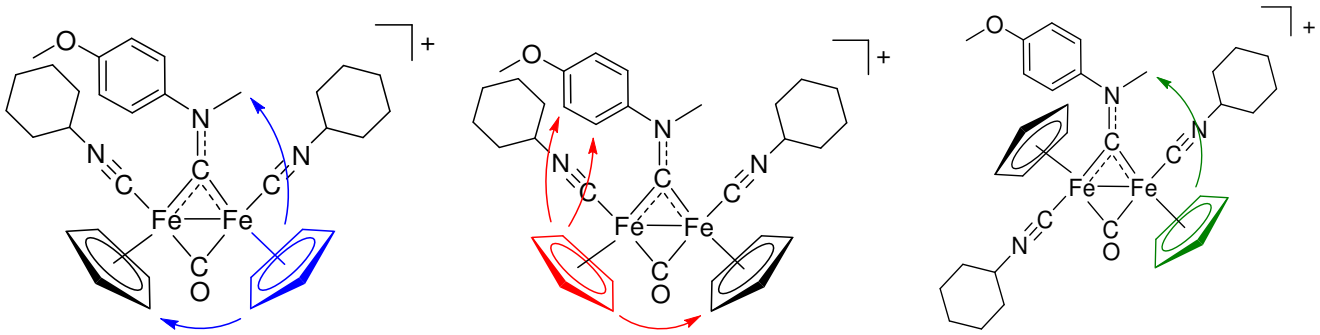


Figure S34. Black line: ^{1}H NMR spectrum (401 MHz, acetone-d_6) of **4c**. Blue line: ^{1}H NOESY with irradiation at 5.06 ppm; red line: ^{1}H NOESY with irradiation at 4.44 ppm (both Cp ligands of the *cis* isomer). Green line: ^{1}H NOESY with irradiation at 4.95 ppm (Cp ligand of the *trans* isomer). Observed NOEs are indicated by the arrows.





Solid state IR data

$[Fe_2Cp_2(CO)(CNFc)(\mu\text{-}CO)(\mu\text{-}CNMe_2)]CF_3SO_3$, 2a. IR (solid state): ῡ/cm^{-1} = 3115w, 3095w, 2931w, 2165w; 2125s, 2101m-sh (t-CN); 1974s (t-CO), 1817s (μ-CO), 1579m (μ-CN), 1433w, 1418w, 1394m, 1271s-sh, 1259s (SO_3), 1222m-sh (SO_3), 1196w-sh, 1149s (SO_3), 1105m, 1062w, 1028s, 1004m, 923w, 890w-sh, 865m, 846m, 823m, 766s, 663m.

$[Fe_2Cp_2(CO)(CNFc)(\mu\text{-}CO)\{\mu\text{-}CNMe(Cy)\}]CF_3SO_3$, 2b. IR (solid state): ῡ/cm^{-1} = 3100w, 2932w, 2858w, 2124s (t-CN), 1971s (t-CO), 1803s (μ-CO), 1558m (μ-CN), 1540m, 1455w, 1419w, 1399w, 1270s-sh, 1261s (SO_3), 1222s-sh (SO_3), 1151s (SO_3), 1106w-sh, 1058m, 1029s, 1004m-sh, 992w-sh, 921w, 840m, 830m, 797s, 751s, 662m.

$[Fe_2Cp_2(CO)(CNFc)(\mu\text{-}CO)\{\mu\text{-}CNMe(4\text{-}C_6H_4OMe)\}]CF_3SO_3$, 2c. IR (solid state): ῡ/cm^{-1} = 3099w, 293m, 2838w, 2122s (t-CN), 1971s (t-CO), 1803s (μ-CO), 1604w, 1586w, 1558w, 1526m (μ-CN), 1504s, 1472w, 1457w, 1437w, 1419w, 1389m, 1299w-sh, 1272s-sh, 1250s-br (SO_3), 1222s-sh (SO_3), 1148s (SO_3), 1113m-sh, 1105m-sh, 1063w, 1027s, 1004m-sh, 921w, 834m, 818m-sh, 776s, 754w, 734w, 702m, 662w.

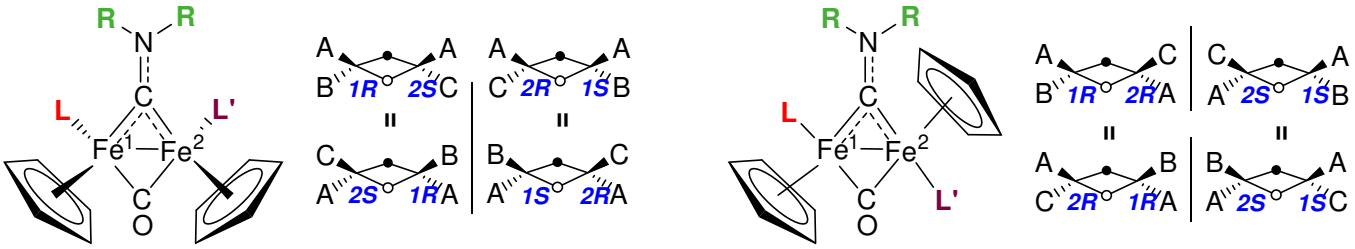
$[Fe_2Cp_2(CO)\{CN(4\text{-}C_6H_4OMe)\}(\mu\text{-}CO)\{\mu\text{-}CNMe(Cy)\}]CF_3SO_3$, 3b. IR (solid state): ῡ/cm^{-1} = 3105w, 2934w, 2859w, 2121s (t-CN), 1971s (t-CO), 1804s (μ-CO), 1602w, 1559m (μ-CN), 1542m, 1504s, 1454w, 1421w, 1400w, 1351w, 1300w, 1270s-sh, 1251s (SO_3), 1222s-sh (SO_3), 1149s (SO_3), 1109w-sh, 1058m, 1028s, 991w-sh, 833s, 797s, 750s, 733m-sh.

$[Fe_2Cp_2(CO)(CNCy)(\mu\text{-}CO)\{\mu\text{-}CNMe(4\text{-}C_6H_4OMe)\}]CF_3SO_3$, 3c. IR (solid state): ῡ/cm^{-1} = 3106w, 2936m, 2860w, 2149s (t-CN), 1972s (t-CO), 1806s (μ-CO), 1606w, 1587w, 1563w, 1528m (μ-CN), 1505s, 1456w, 1447m, 1421w, 1391m, 1365w, 1324w, 1300w-sh, 1272s-sh, 1251s (SO_3), 1223s-sh (SO_3), 1149s (SO_3), 1114m-sh, 1106m-sh, 1066w, 1029s, 1010m-sh, 894s, 778s, 750w, 735w, 704s, 660w.

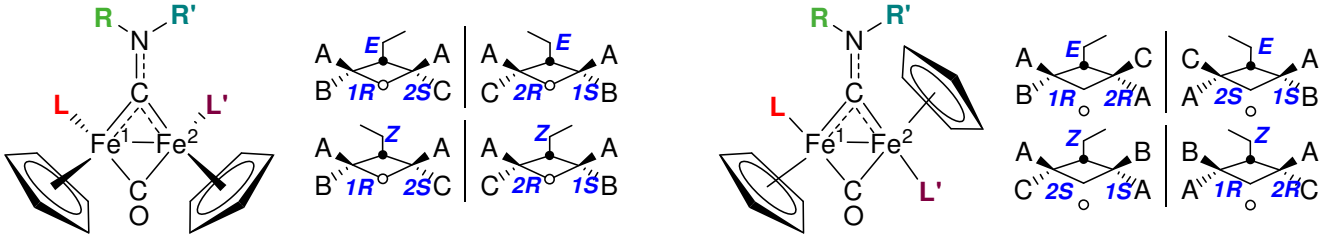
$[Fe_2Cp_2\{CN(4\text{-}C_6H_4OMe)\}_2(\mu\text{-}CO)\{\mu\text{-}CNMe(Cy)\}]CF_3SO_3$, 4b. IR (solid state): ῡ/cm^{-1} = 3101w, 2934w, 2857w, 2842w; 2110s, 2098s-sh, 2036m-sh (t-CN); 1787s (t-CO), 1602m, 1581w, 1557w, 1538m (μ-CN), 1504s, 1464w, 1455w, 1443w, 1421w, 1399w, 1351w, 1319w, 1299m, 1264s-sh, 1250s (SO_3), 1222m-sh (SO_3), 1180m-sh, 1164m, 1147s (SO_3), 1107m, 1060m, 1029s, 993m-sh, 829s, 798s, 753s, 732m-shm 707w-sh.

$[Fe_2Cp_2(CNCy)_2(\mu\text{-}CO)\{\mu\text{-}CNMe(4\text{-}C_6H_4OMe)\}]CF_3SO_3$, 4c. IR (solid state): ῡ/cm^{-1} = 3104w, 3094w, 3004w, 2936m, 2857m, 2135s (t-CN), 1788s (t-CO), 1607w, 1587w, 1570w, 1525m-sh (μ-CN), 1505s, 1466m, 1447m, 1422w-sh, 1391m, 1365m, 1325w, 1299w, 1275s-sh, 1259s (SO_3), 1220s-sh (SO_3), 1170m-sh, 1156s (SO_3), 1112m-sh, 1105m, 1028s, 1006m-sh, 928w, 894w, 865w, 841m, 830m, 821m, 784s, 752w, 736w, 707s, 661w.

Isomerism and NMR spectra

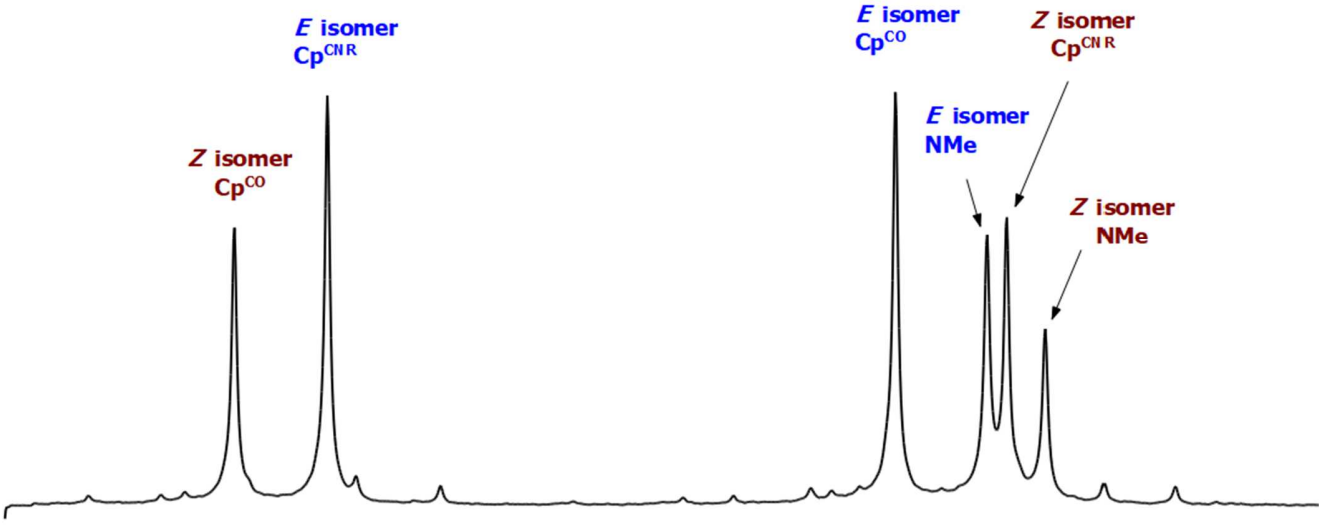


Scheme S1. Isomerism in $[Fe_2Cp_2(L)(L')(\mu\text{-}CO)(\mu\text{-}CNR_2)]^+$ complexes (L ≠ L'): *cis* and *trans* diastereomers each one existing as a pair of enantiomers (*RS*/*RS* and *RR*/*SS* configurations at the iron centres, respectively). NMR spectra show a set of signals for each diastereomer with non-equivalent Cp and R groups.



Scheme S2. Isomerism in $[Fe_2Cp_2(L)(L')(\mu\text{-}CO)(\mu\text{-}CNRR')]^{0/+}$ complexes (L ≠ L'): *cis*-E, *cis*-*Z*, *trans*-*E*, *trans*-*Z* diastereomers each one existing as a pair of enantiomers with different *R*/*S* configurations at the iron centres. NMR spectra show a set of signals for each diastereomer with non-equivalent Cp and R groups.

Figure S35. Common pattern ^{1}H NMR resonances for Cp and NMe groups in *cis*-*E*/*Z* isomers of compounds of the type $[Fe_2Cp_2(CO)\{CNR\}(\mu\text{-}CO)\{\mu\text{-}CNMe(R')\}]CF_3SO_3$ (**2** and **3**).



Comparison of selected IR and NMR data

Table S1. Salient IR and NMR data of carbonyl, aminocarbyne and isocyanide ligands in compounds of the type $[Fe_2Cp_2(L)(L')(\mu\text{-}CO)\{\mu\text{-}CNMe(R)\}]CF_3SO_3$ (L, L': CO or isocyanide).

Cpd. [a]	R	L	L'	IR:[b] ũ / cm^{-1}				$^{13}C\{^1H\}$ NMR:[c] δ / ppm			
				t-CN	t-CO	μ-CO	μ-CN	t-CN	t-CO	μ-CO	μ-CN
1a [1,2]	Me	CO	CO	-	2022s 1990w	1835m	1602m	-	207.6	255.4	315.7
2a	"	"	CNFc	2132s	1985s	1818s	1591m	161.4	210.7	261.6	322.3
5a [3]	"	"	CNMe	2174	1985	1809	1591	154.0	210.2	262.1	332.4
4a [3]	"	CNMe	CNMe	2177	-	1795	1577	*n.r.*	*n.r.*	*n.r.*	*n.r.*
1b [1]	Cy	CO	CO	-	2020s 1988w-sh	1835m	1567w	-	208.5, 207.6	255.3	316.4
2b	"	"	CNFc	2131s	1984s	1819s	1560m	*161.8*, 161.5	211.4, *210.5*	*261.7*, 261.1	321.6, *321.5*
3b	"	"	CNAnis	2130s	1985m	1821m	1560m	164.6, *164.2*	*212.4*, 211.7	261.0, *260.6*	*323.0*, 322.9
4b	"	CNAnis	CNAnis	2124s 2100m-sh	-	1803m	1537w	170.1, 169.5	-	266.6	*334.4*, 328.3
1c [1]	Anis	CO	CO	-	2021s 1989w	1836m	1540w	-	208.6, 207.6	254.5	324.3
2c	"	"	CNFc	2133s	1986s	1820s	1530m	162.3, *161.3*	211.7, *210.6*	*260.8*, 260.6	329.9, *329.6*
3c	"	"	CNCy	2155s	1984s	1817s	1530m-sh	*154.8*, 154.0	212.9, *212.0*	*261.1*, 260.9	332.2, *332.1*
4c	"	CNCy	CNCy	2147m-sh, 2134s	-	1799s	1518m-sh	152.5	-	268.0	*342.6*, 338.2
1d [1]	Xyl	CO	CO	-	2023s 1992w	1840m	1530w	-	208.6	253.9	327.8
5d [4]	"	"	CNXyl	2120vs	1991vs	1824s	1524m	167.3 166.9	210.5 210.2	258.8 259.2	332.0 330.9
6d [4]	"	"	CN^{t}Bu	2149vs	1988vs	1822s	1524m	*n.r.*	210.8	259.1	332.4
4d [5]	"	CNXyl	CNXyl	2115vs 2085sh	-	1805s	1517m	172.1 171.5	-	265.0	336.2
4d' [5]	"	CN^{t}Bu	CN^{t}Bu	2128vs	-	1803s	1505m	160.9 158.3	-	267.3	337.3

[a] Numbering extended to previously-reported compounds. [b] All IR data refer to CH_2Cl_2 solutions except for **5a** ($CHCl_3$ solution). [c] NMR data refer to $CDCl_3$ (**1a-d**, **2a-c**, **4d**, **4d'**, **5a,d**, **6d**) or acetone-d_6 (**3b-c**, **4b-c**) solutions; in italics for minor isomers. Abbreviation list. Cy = C_6H_{11}; Anis = *p*-C_6H_4OMe; Fc = $FeCp(\eta^5\text{-}C_5H_4)$; Xyl = 1,3-$C_6H_3Me_2$. *n.r.* = not reported.

Table S2. Salient IR and NMR changes upon replacing terminal carbonyl(s) with isocyanide ligands on compounds of the type $[Fe_2Cp_2(L)(L')(\mu\text{-}CO)\{\mu\text{-}CNMe(R)\}]CF_3SO_3$ (based on data in Table S1).

Transformation	IR (CH_2Cl_2): $\Delta\tilde{\nu}$ / cm^{-1}			$^{13}C\{^1H\}$ NMR: $\Delta\delta$ / ppm		
	t-CO [a]	μ-CO	μ-CN	t-CO [b]	μ-CO	μ-CN
1a → 2a	– 37	– 17	– 11	+ 3.1	+ 6.2	+ 6.6
1a → 5a	– 37	– 17	– 11	+ 2.6	+ 6.7	+ 16.7
1a → 4a	-	– 40	– 25	-	-	-
1b → 2b	– 36	– 16	– 7	*+* 3.4, *+ 2.5*	+ *6.4*, + 5.8	*+* 5.2, + *5.1*
1b → 3b	– 35	– 14	– 7	+ *4.4*, + 3.7	+ 5.7, + *5.3*	+ *6.6*, + 6.5
1b → 4b	-	– 32	– 30	-	+ 11.3	+ *18.0*, + 11.9
1c → 2c	– 35	– 16	– 10	+ 3.6, + *2.5*	+ *6.3*, + 6.1	*+* 5.6, *+ 5.3*
1c → 3c	– 37	– 19	– 10	*+* 4.8, *+ 3.9*	+ *6.6*, + 6.4	+ 7.9, + *7.8*
1c → 4c	-	– 37	– 22	-	+ 13.5	+ *18.3*, + 13.9
1d → 5d	– 32	– 16	– 6	+ 1.9, + 1.6	+ 5.3, + 4.9	+ 4.2, + 3.1
1d → 6d	– 35	– 18	– 6	+ 2.2	+ 5.2	*+* 4.6
1d → 4d	-	– 35	– 13	-	+ 11.1	+ 8.4
1d → 4d'	-	– 37	– 25	-	+ 13.4	+ 9.5

[a] Calculated with respect to the more intense asymmetric CO stretching band. [b] Calculated with respect to an average value of the two resonances for the inequivalent terminal carbonyls in **1a-d.**

Stability studies in aqueous medium

Figure S36. ^{1}H NMR spectra (401 MHz) of a freshly-prepared solution of **2a** in D_2O/CD_3OD 1:1 *V*/*V* (top, blue line) and after 72 h at 37 °C (bottom, red line). The height of the Me_2SO_2 signal is normalized.

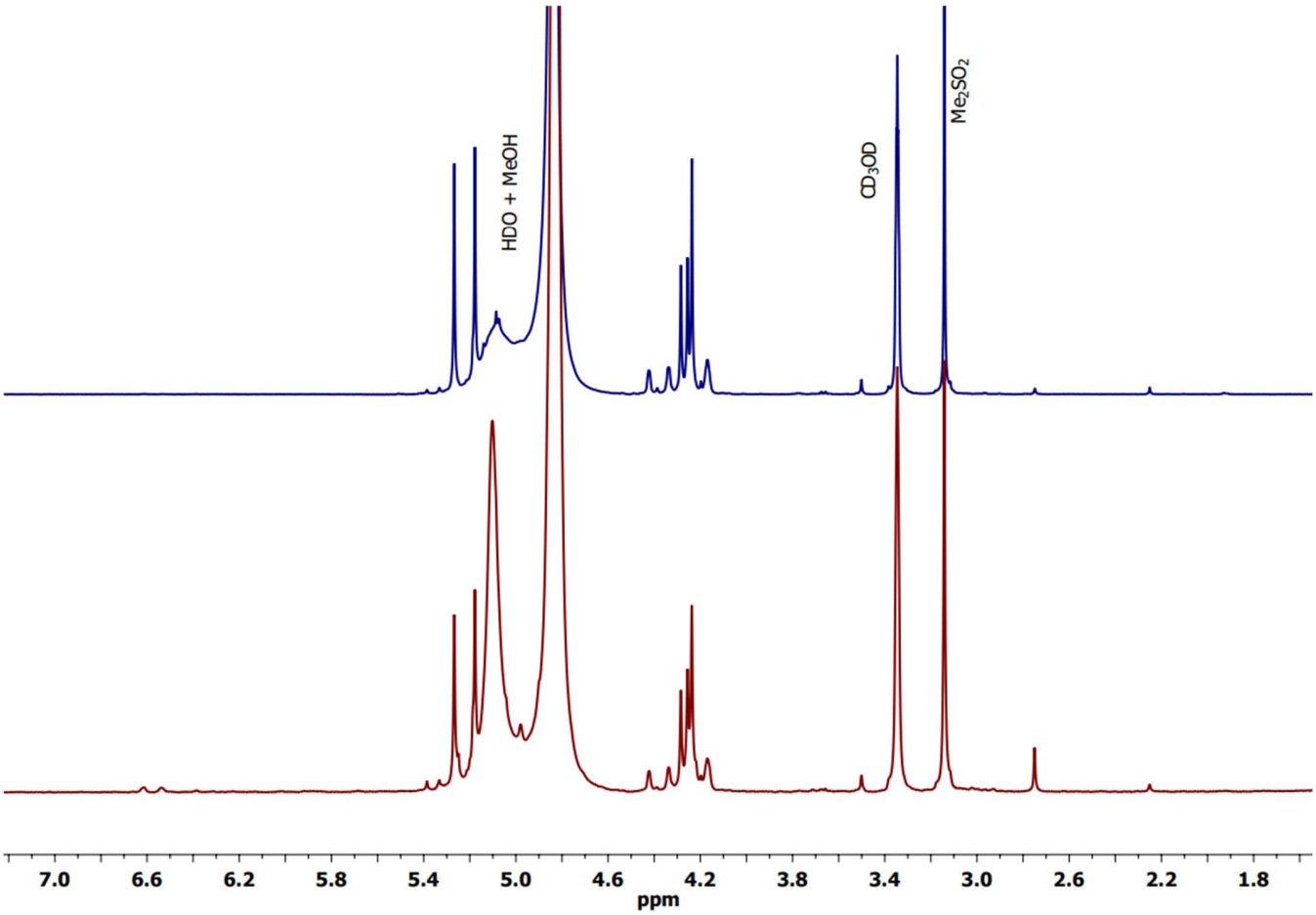


Figure S37. ^{1}H NMR spectra (401 MHz) of a freshly-prepared solution of **2b** in D_2O/CD_3OD 1:1 *V*/*V* (top, blue line) and after 72 h at 37 °C (bottom, red line). The height of the Me_2SO_2 signal is normalized.

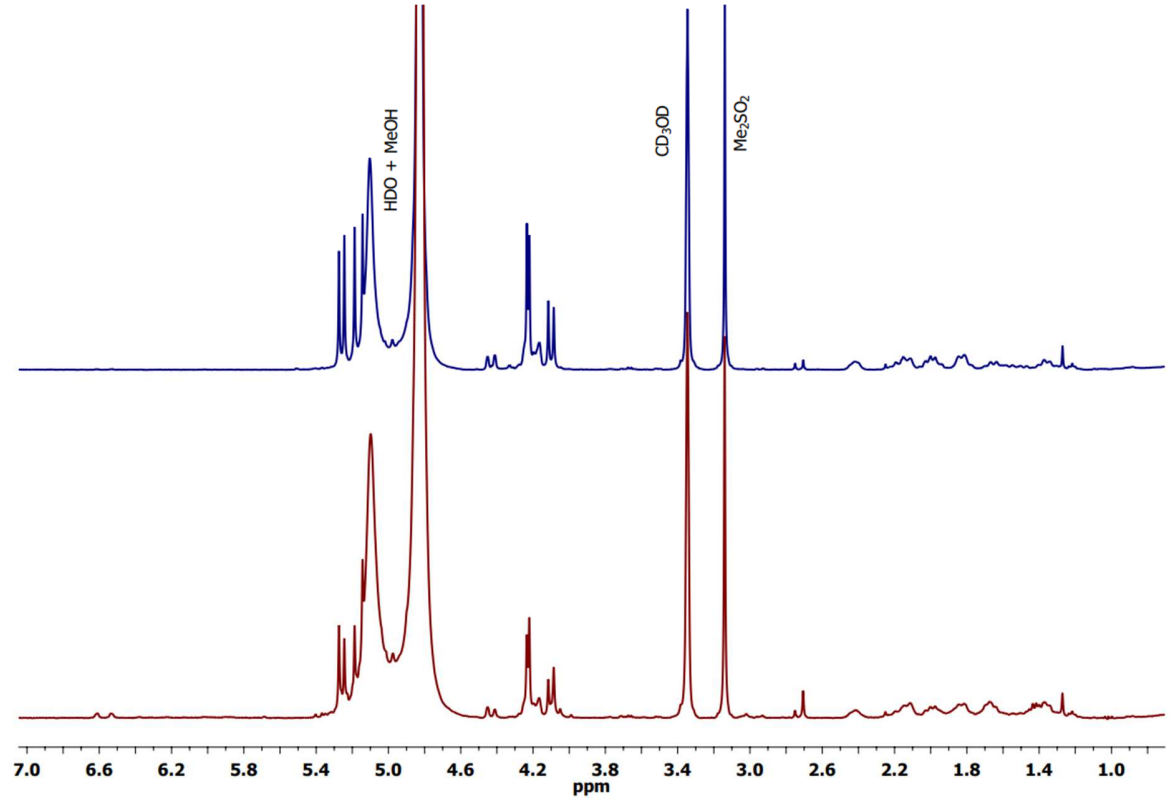


Figure S38. ^{1}H NMR spectra (401 MHz) of a freshly-prepared solution of **2c** in D_2O/CD_3OD 1:1 *V*/*V* (top, blue line) and after 72 h at 37 °C (bottom, red line). The height of the Me_2SO_2 signal is normalized.

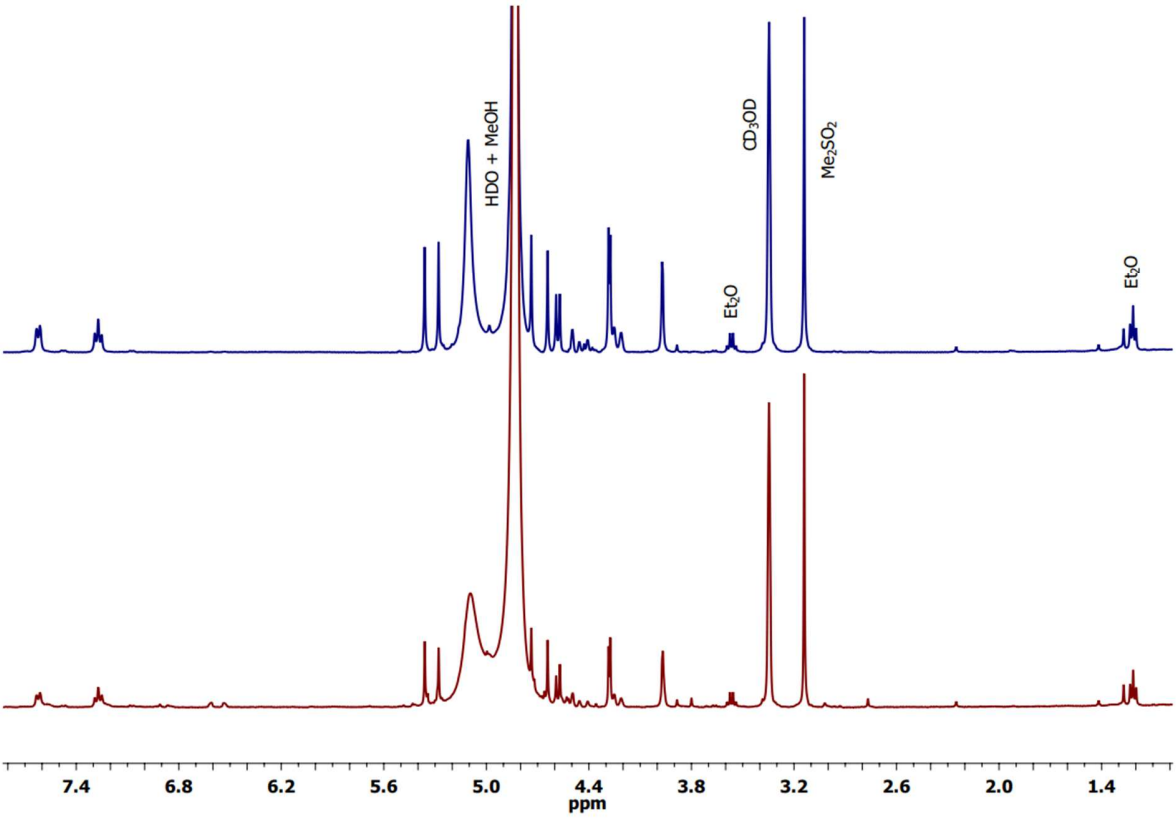


Figure S39. ^{1}H NMR spectra (401 MHz) of a freshly-prepared solution of **3b** in D_2O/CD_3OD 1:1 *V*/*V* (top, blue line) and after 96 h at 37 °C (bottom, red line). The height of the Me_2SO_2 signal is normalized.

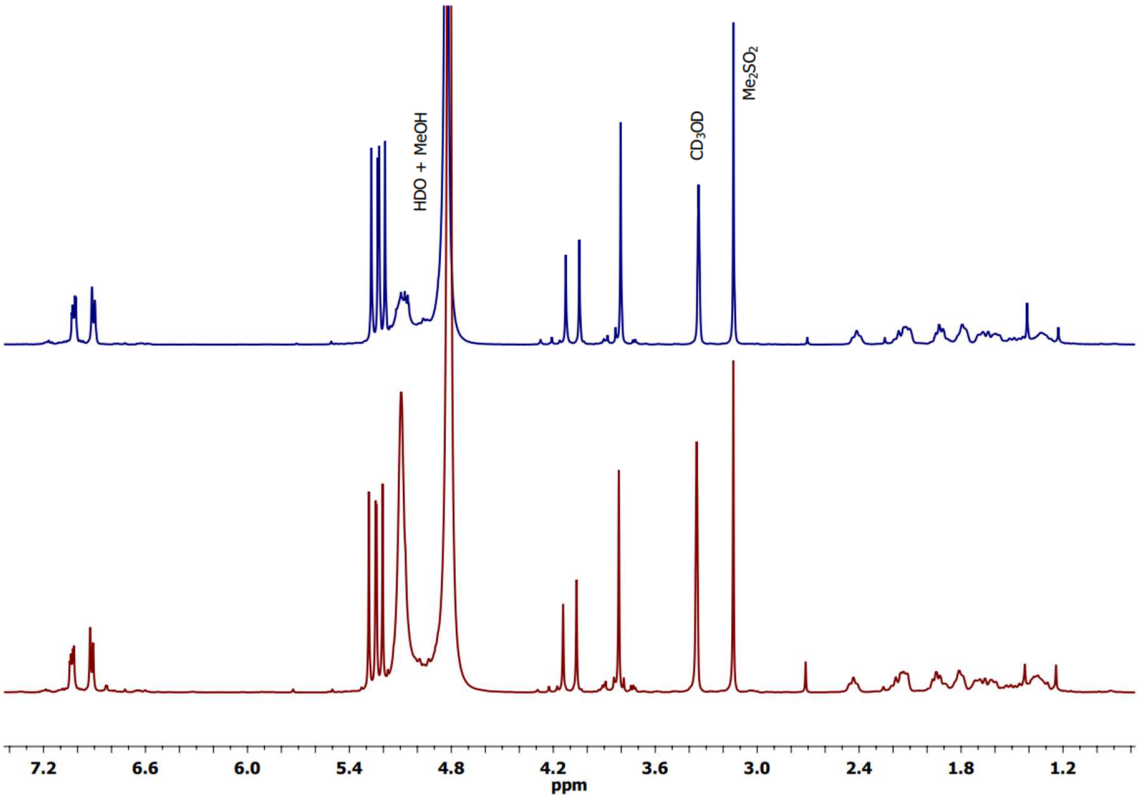


Figure S40. ^{1}H NMR spectra (401 MHz) of a freshly-prepared solution of **3c** in D_2O/CD_3OD 1:1 *V*/*V* (top, blue line) and after 96 h at 37 °C (bottom, red line). The height of the Me_2SO_2 signal is normalized.

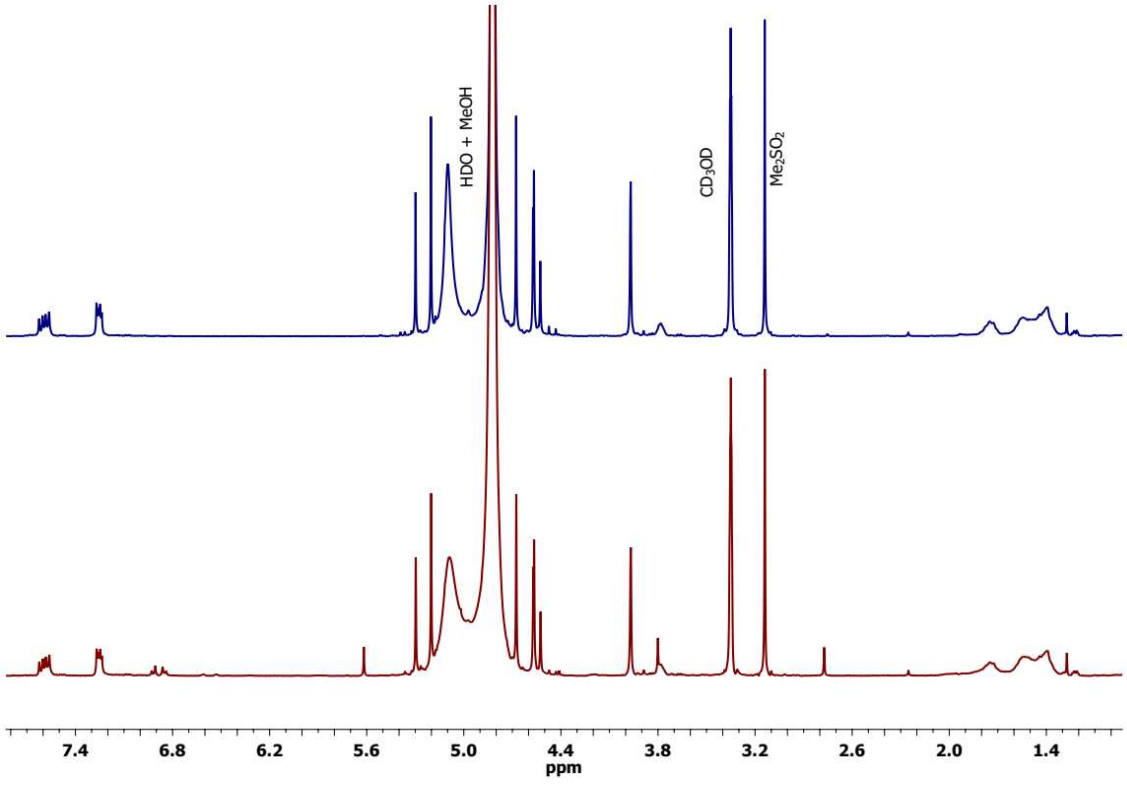


Figure S41. ^{1}H NMR spectra (401 MHz) of a freshly-prepared solution of **4b** in D_2O/CD_3OD 1:1 *V*/*V* (top, blue line) and after 96 h at 37 °C (bottom, red line). The height of the Me_2SO_2 signal is normalized.

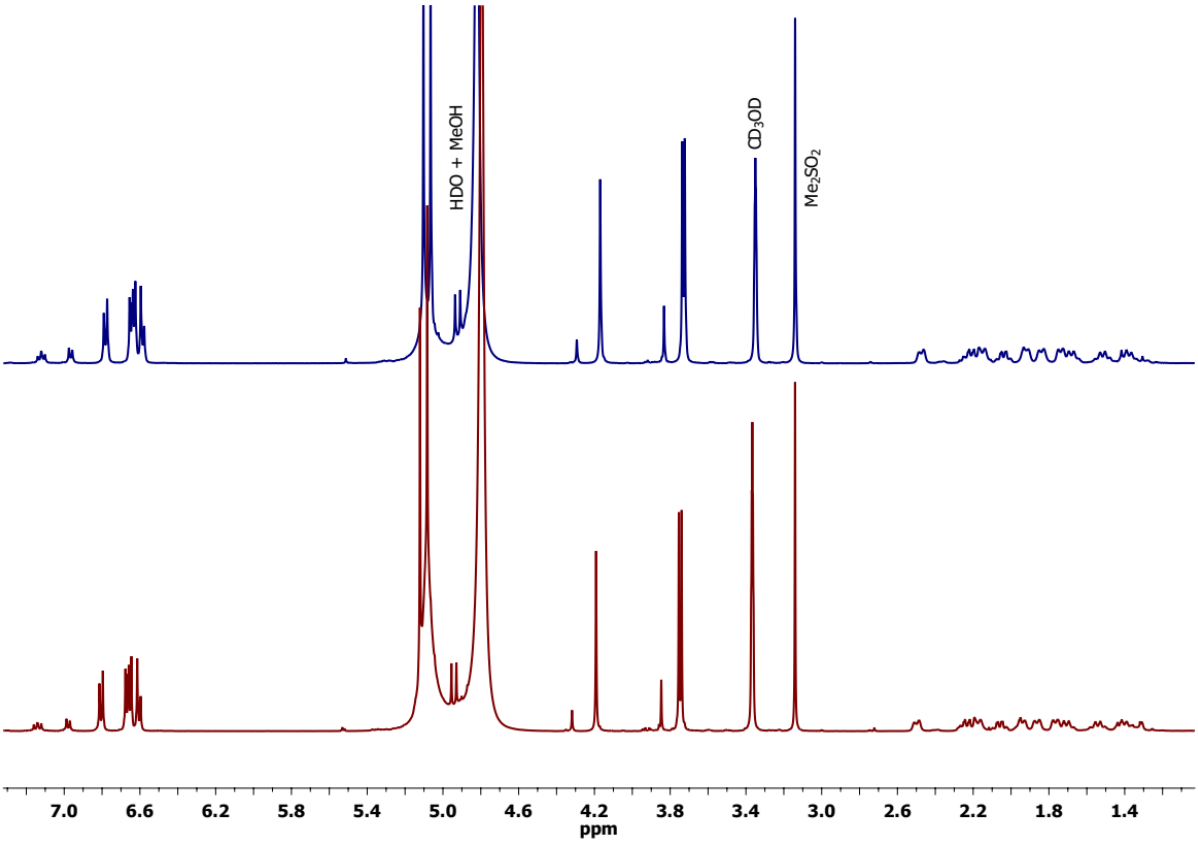
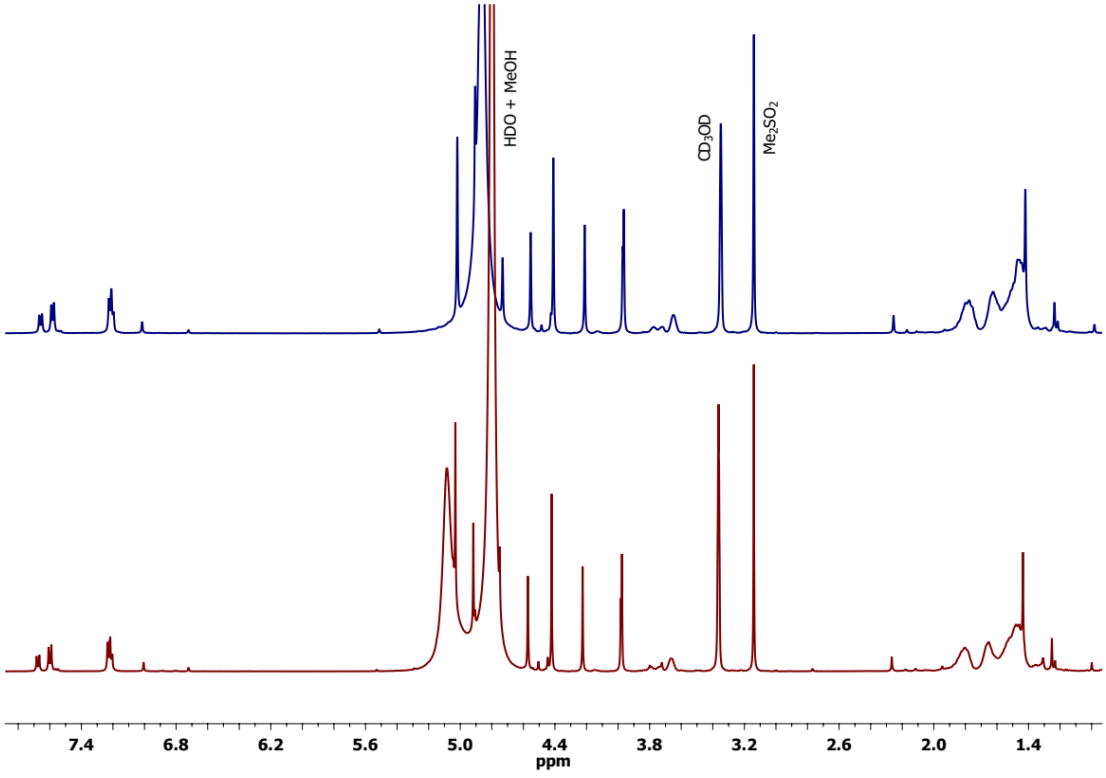


Figure S42. ^{1}H NMR spectra (401 MHz) of a freshly-prepared solution of **4c** in D_2O/CD_3OD 1:1 *V*/*V* (top, blue line) and after 96 h at 37 °C (bottom, red line). The height of the Me_2SO_2 signal is normalized.



NMR data in aqueous solutions

Chemical shifts are referenced to Me_2SO_2 as in pure D_2O [δ/ppm = 3.14]. Negligible differences were observed in the set of signals and isomer ratios between parallel experiments in D_2O/CD_3OD and DMEM/CD_3OD solutions.

2a. Ocher-brown solution. ^{1}H NMR (D_2O): δ/ppm = 5.23, 5.16, 5.15, 5.05 (s, 10H, Cp); 4.43, 4.38, 4.34-4.30, 4.16 (m, 4H) (C_5H_4); 4.25, 4.21, 4.19, 4.14 (s, 6H, NMe); 4.23 (s, 5H, Cp^{Fc}); *cis*/*trans* isomer ratio ≈ 1. ^{1}H NMR (D_2O/CD_3OD 1:1 *V*/*V*): δ/ppm = 5.27, 5.18 (s, 10H, Cp); 4.42 (m, 1H), 4.34 (m, 1H), 4.17 (m, 2H) (C_5H_4); 4.28, 4.26 (s, 6H, NMe); 4.24 (s, 5H, Cp^{Fc}). Signals of the *trans* isomer not detectable due to their low amount and overlaps.

Other species detected (72 h): CpH, Me_2NH; ^{1}H NMR (D_2O/CD_3OD 1:1 *V*/*V*): δ/ppm = 4.22 (s), 5.25 (s).

2b. Ocher-brown solution. ^{1}H NMR (D_2O/CD_3OD 1:1 *V*/*V*): δ/ppm = *5.27*, 5.24, 5.19, *5.14* (s, 10H, Cp); *4.45*, 4.41 (m, 1H), 4.25, 4.20, 4.17 (m, 3H) (C_5H_4); 4.23, *4.22* (s, 5H, Cp^{Fc}); 4.12, *4.09* (s, 3H, NMe); 2.43 (m, 1H); 2.20-1.30 (m, 9H) (CH_2^{Cy}); *cis*-*E*/*cis*-*Z* isomer ratio = 1.1 (0 h), *cis*-*Z*/*cis*-*E* isomer ratio = 1.3 (72 h). Other species detected (72 h): CpH, CyMeNH and ^{1}H NMR (D_2O/CD_3OD 1:1 *V*/*V*): δ/ppm = 4.10 (s), 4.05 (s).

2c. Ocher-brown solution. ^{1}H NMR (D_2O/CD_3OD 1:1 *V*/*V*): δ/ppm = 7.62 (d, *J* = 7.3 Hz, 2H, C_6H_4); 7.28, *7.26* (d, *J* = 7.3 Hz, 2H, C_6H_4); *5.36*, 5.28, 4.74, *4.64* (s, 10H, Cp); *4.59*, 4.57 (s, 3H, NMe); 4.50 (m, 1H), 4.45, 4.40 (m, 1H), 4.25, 4.21 (m, 2H) (C_5H_4); 4.28, *4.27* (s, 5H, Cp^{Fc}); 3.97, *3.96* (s, 3H, OMe); *cis*-*Z*/*cis*-*E* isomer ratio = 1.0 (0 h), 1.3 (72 h). Other species detected (72 h): CpH, AnisMeNH and ^{1}H NMR (D_2O/CD_3OD 1:1 *V*/*V*): δ/ppm = 7.47 (d), 7.07 (d), 5.34 (s), 4.66 (s), 4.53 (s), 4.52 (s).

3b. Red-brown solution. ^{1}H NMR (D_2O): δ/ppm = 7.08–7.01 (m, 2H), 6.87 (d, *J* = 8.5 Hz, 2H); 5.23, 5.21 (s, 5H); 5.19, 5.17 (s, 5H); 4.09, 4.00 (s, 3H), 2.44–2.30, 2.20–2.00, 1.82–1.56 (m). ^{1}H NMR (D_2O/CD_3OD 1:1 *V*/*V*): δ/ppm = 7.05–7.01 (m, 2H), 6.92 (d, *J* = 8.5 Hz, 2H) (C_6H_4); 5.29, *5.25* (s, 5H, Cp); *5.24*, 5.20 (s, 5H, Cp'); *4.14*, 4.06 (s, 3H, NMe); 3.81 (s, 3H, OMe); 2.43 (t, *J* = 11 Hz, 1H), 2.22–2.11 (m, 2H), 2.01–1.88 (m, 2H), 1.85–1.76 (m, 2H), 1.74-1.57 (m, 3H) (CH_2^{Cy}); *cis*-*Z*/*cis*-*E* isomer ratio = 1.1 (0-24 h in

DMEM-d); 1.2 (96 h in D_2O). Other species detected (96 h): CyMeNH and ^{1}H NMR (D_2O/CD_3OD 1:1 *V*/*V*): δ/ppm = 6.83 (d, *J* = 9.3 Hz, 2H), 6.80 (d, *J* = 9.3 Hz, 2H), 3.77 (s, 3H).

3c. Red-brown solution. ^{1}H NMR (D_2O): δ/ppm = 7.61, 7.56 (d, *J* = 8.4 Hz), 7.27–7.20 (m); 5.26, 5.17 (s); 4.65, 4.55 (s); 4.54, 4.48 (s); 3.93 (s); 3.78–3.66 (m); 1.74–1.59, 1.56– 1.38, 1.38–1.23 (m). ^{1}H NMR (D_2O/CD_3OD 1:1 *V*/*V*): δ/ppm = *7.61*, 7.57 (d, $^3J_{HH}$ = 8.7 Hz, 2H); 7.28–7.20 (d, $^3J_{HH}$ = 8.8 Hz, 2H); *5.30*, 5.20 (s, 5H, Cp); 4.68, *4.567* (s, 5H, Cp'); 4.572, 4.53 (s, 3H, NMe); 3.97 (s, 3H, OMe); 3.78 (m, 1H; CH^{Cy}); 1.87–1.67 (m, 2H), 1.64–1.33 (m, 8H) (CH_2^{Cy}); *cis*-*E*/*Z* isomer ratio = 1.3 (0-96 h).

Other species detected (96 h): CpH, AnisMeNH and ^{1}H NMR (D_2O/CD_3OD 1:1 *V*/*V*): δ/ppm = 5.62 (s).

4b. Green-brown solution. ^{1}H NMR (D_2O/CD_3OD 1:1 *V*/*V*): δ/ppm = *7.15–7.09* (m), *6.97* (d, *J* = 9.0 Hz), 6.78 (d, *J* = 9.0 Hz), 6.67–6.56 (m) (8H, C_6H_4); 5.10, 5.07, *4.94*, *4.91* (s*, Cp); *4.29*, 4.17 (s, 3H, NMe); *3.83*, 3.74, 3.72 (s, 6H, OMe); 2.47, *2.37* (d, *J* = 12 Hz, 1H), 2.28–1.30 (m, 9H) (CH_2^{Cy}); *cis*/*trans* isomer ratio: 6.8 (0 h), 8.2-8.3 (24 h in DMEM-d and 96 h in D_2O). *Over OH peak.

4c. Green-brown solution. ^{1}H NMR (D_2O/CD_3OD 1:1 *V*/*V*): δ/ppm = *7.67*, 7.60 (d, *J* = 8.8 Hz, 2H); 7.23, *7.21* (d, *J* = 8.7 Hz, 2H) (C_6H_4); 5.03, *4.92* (s*, Cp); *4.75*, 4.52 (s, 3H, NMe); 4.42, *4.22* (s, 5H, Cp'); *3.99*, 3.98 (s, 3H, OMe); 1.87–1.72 (m, 4H); 1.70–1.57 (m, 4H), 1.56–1.39 (m, 12H); *cis*/*trans* isomer ratio: 1.5 (0 h), 1.6 (24 h in DMEM-d), 1.7 (96 h in D_2O).

Other species detected in the final solutions

Cyclopentadiene, **CpH**. ^{1}H NMR (D_2O/CD_3OD 1:1 *V*/*V*): δ/ppm = 6.61 (m, 2H), 6.54 (m, 2H), 3.07-2.99 (m, 2H).

Me_2NH.[6] ^{1}H NMR (D_2O/CD_3OD 1:1 *V*/*V*): δ/ppm = 2.75 (s).

MeCyNH.[6] ^{1}H NMR (D_2O/CD_3OD 1:1 *V*/*V*): δ/ppm = 3.04 (m, 1H), 2.71 (m, 3H).

(4-C_6H_4OMe)NHMe. ^{1}H NMR (D_2O/CD_3OD 1:1 *V*/*V*): δ/ppm = 6.92 (d, *J* = 8.9 Hz, 2H), 6.85 (d, *J* = 8.9 Hz, 2H), 3.80 (s, 3H), 2.77 (s, 3H).

Notes and references

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6 Presumably as ammonium salts in D_2O/CD_3OD solutions, considering their pK_b in water.