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Electronic Supplementary Information:

A 4-state acid-base controlled molecular switch based on a host-guest system

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General experimental methods

All solvents and reagents were obtained commercially. Solvents and chemicals were of reagent grade and were used without further purification.

^1H and ^{13}C NMR spectra were recorded either on a Bruker Avance 300, a Varian VNMRS 400 or 600 or a JEOL JNM-ECZ400R/S3 or JNM-ECZ600R/S3 spectrometer (at 300, 400 or 600 MHz for ^1H) equipped with a double or triple resonance 5 mm probe. The solvent was used as internal standard for both ^1H and ^{13}C chemical shift referencing. $CDCl_3$ was filtered through a short column of basic alumina to remove traces of DCl. NMR spectra were recorded at 298 K unless otherwise stated. Most of the ^1H NMR spectra signals were assigned through 2D NMR analyses (COSY, HSQC, HMBC). For the edited-HSQC and ROESY spectra, the blue signals are negatively phased and the red signals are positively phased. The ^1H NMR spectra were recorded using a spectral width of about 20.0 ppm centered at 5.00 ppm, 4.0 s relaxation delay, flip angle of 30° for high-power RF pulse width, 2.4 to 2.9 s acquisition time and 16 to 64 scans. Processing was performed using MestReNova 14.3.0–30573. For 1D ^1H spectra, it comprised zero-filling (total of 256k points), sine square apodization (90°) and Fourier transform of the free induction decay, followed by phase correction, baseline correction and chemical shift referencing of the spectrum. Chemical shifts are quoted on the δ scale and coupling constants (J) are expressed in Hertz (Hz). s: singlet, bs: broad singlet, d: doublet, bd: broad doublet, t: triplet, m: massif.

HRMS analyses were performed using methanol and 0.1% formic acid as solvent on an ESI-MS apparatus (Q-TOF 6520 Agilent Technology) equipped with a TOF detector.

IR spectra were recorded on a Bruker IFS 25 FTIR spectrometer on a NaCl pellet.

NMR Titration Experiments. All experiments were prepared following a similar protocol. A known volume (~600 µL) of a solution of known concentration of the host (~10^{-3} M) was placed in an NMR tube, and the ^1H NMR spectrum recorded. Aliquots of a stock solution of the guest were successively added, and the ^1H NMR spectrum recorded after each addition. In general, aliquots were added until no changes in the host signals were observed.

When ^1H NMR spectra revealed two sets of signals for the complex, the guest and for the free receptor in slow exchange on the NMR time scale, association constants (log K) were determined *via* integration of the signals of the different species. The association constants were determined as the mean values of the constants calculated based on different spectra and with the integration of different signals. The error was then estimated as the difference between the mean value with the smallest and largest association constants determined.

Molecular Modeling. Monte Carlo multiple minimum (MCMM)[1] conformational searches (100 steps per torsion angle, maximum 1000 steps in total) were performed in Schrödinger Release 2018-4, using the OPLS-2005 force field[2] without implicit solvation in Maestro MacroModel (version 11.8.012).

Dicationic complex [2.Zn]$^{2+}$

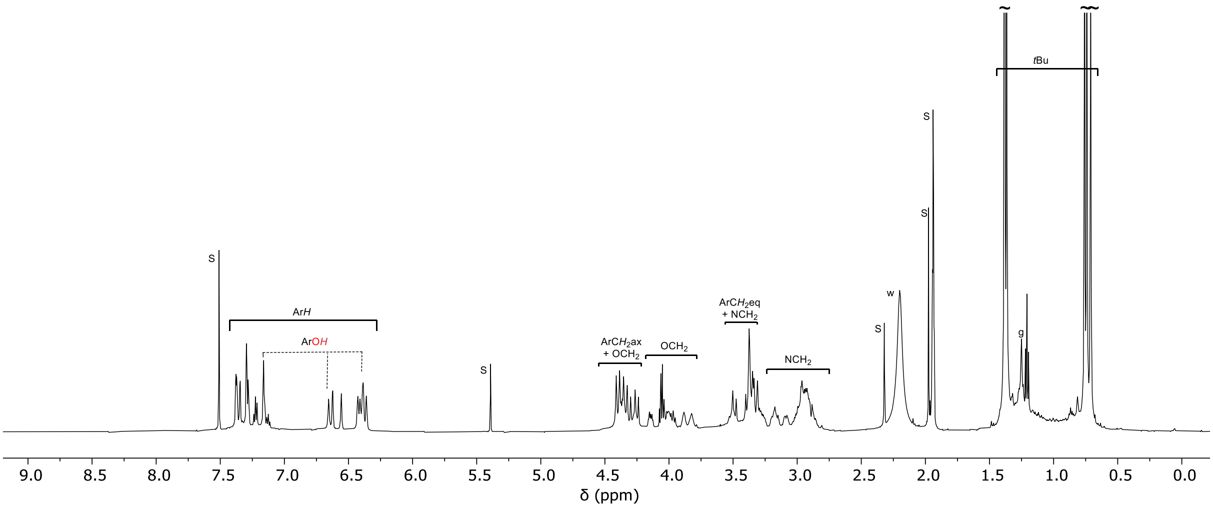

*Figure S 1: ^{1}H NMR spectrum (CDCl$_3$/CD$_3$CN 1:1, 600 MHz, 298 K) of complex [**2.Zn⊃CD$_3$CN**]$^{2+}$; S: solvent, w: water, g: grease.*

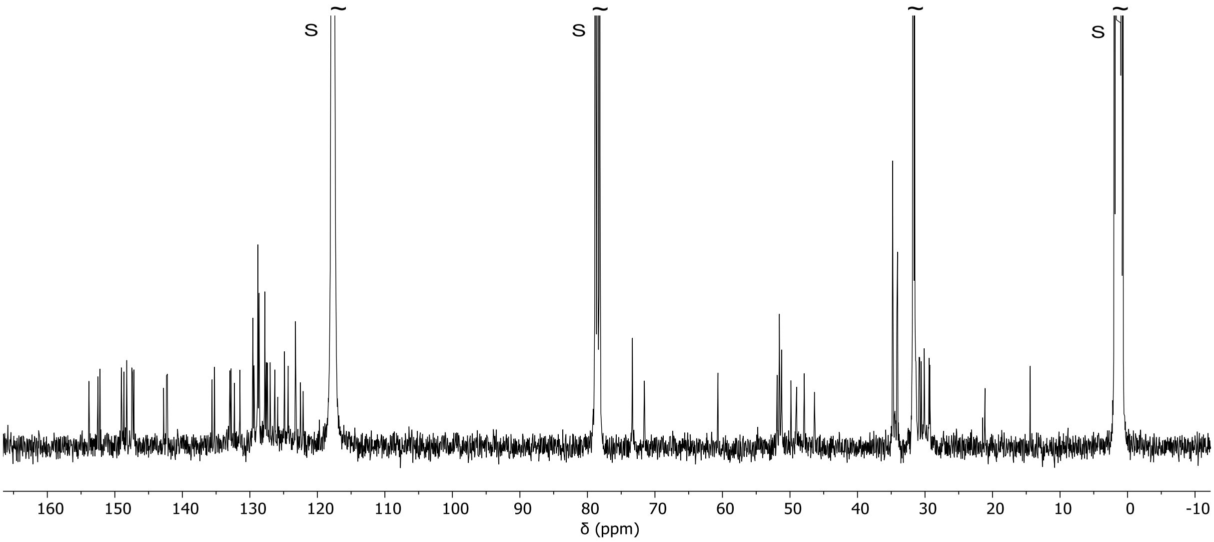

*Figure S 2: ^{13}C BBD NMR spectrum (CDCl$_3$/CD$_3$CN 1:1, 151 MHz, 298 K) of complex [**2.Zn⊃CD$_3$CN**]$^{2+}$; S: solvent.*

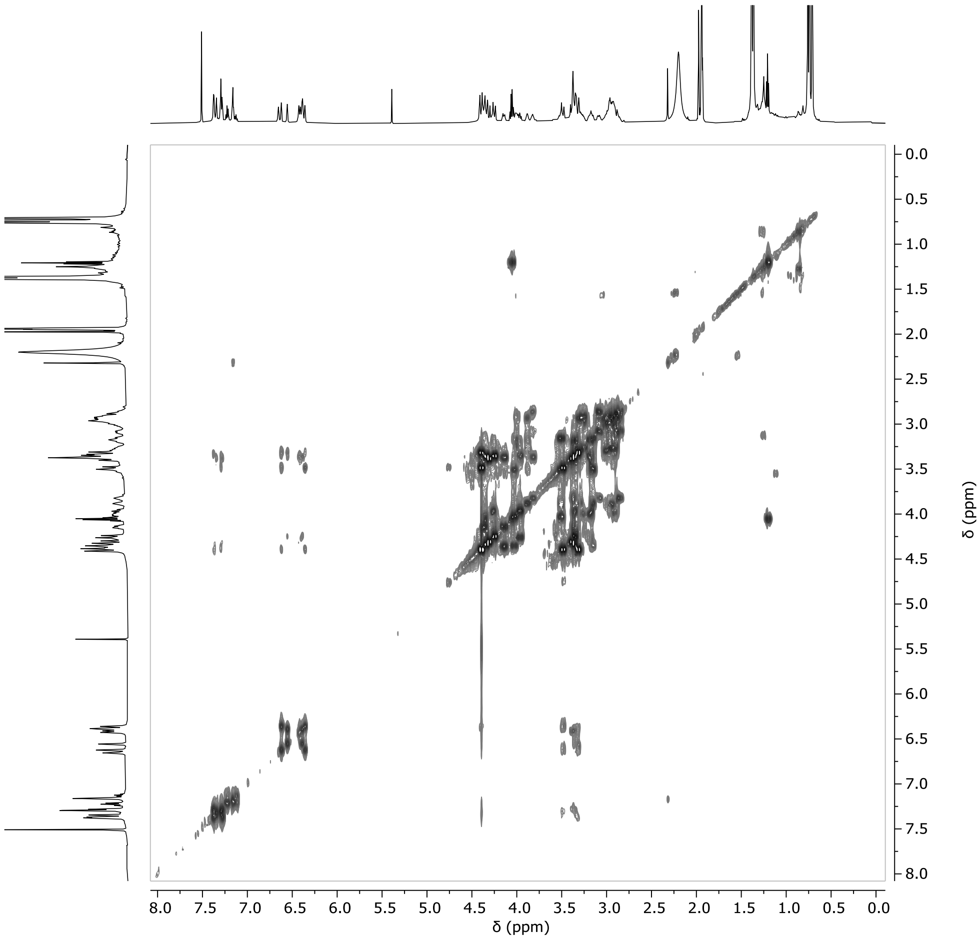

Figure S 3: gDQCOSY NMR spectrum ($CDCl_3$/CD_3CN 1:1, 600 MHz, 298 K) of complex [**$2.Zn\supset CD_3CN$**]$^{2+}$.

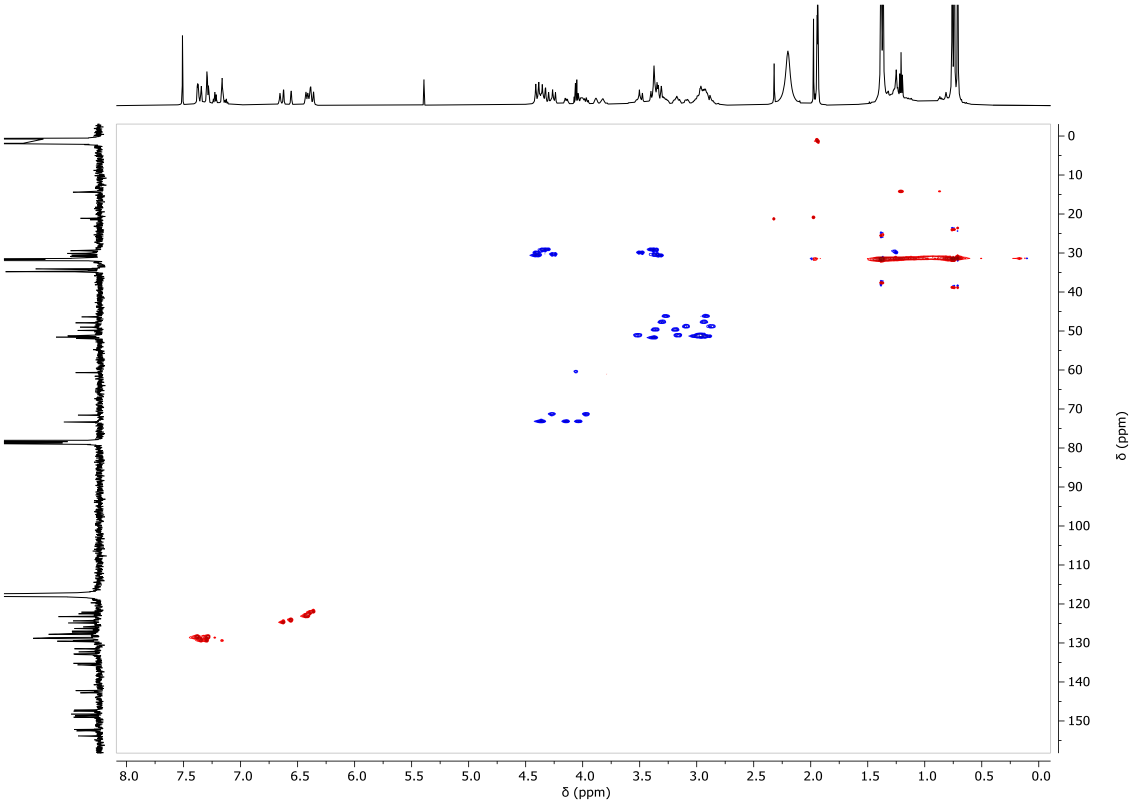

Figure S 4: Edited-gHSQCAD NMR spectrum ($CDCl_3$/CD_3CN 1:1, 600 MHz, 298 K) of complex [**$2.Zn\supset CD_3CN$**]$^{2+}$.

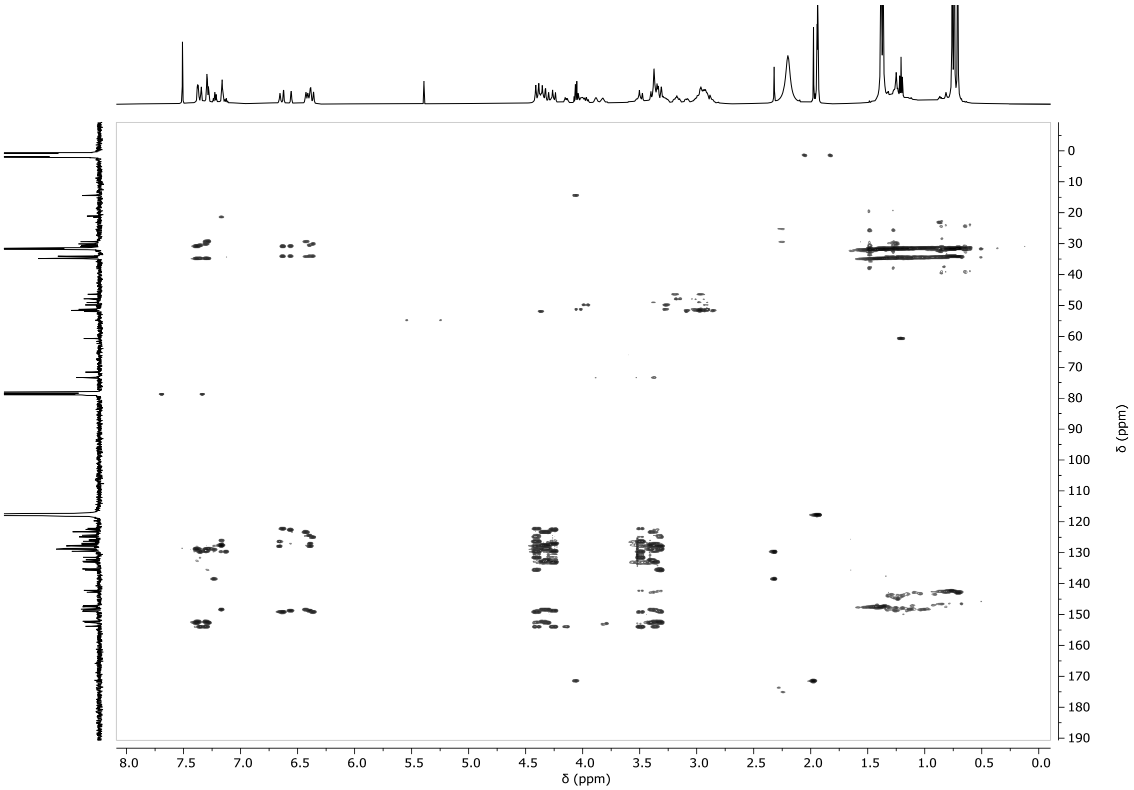

*Figure S 5: gHMBCAD NMR spectrum (CDCl$_3$/CD$_3$CN 1:1, 600 MHz, 298 K) of complex [**2.Zn⊃CD$_3$CN]$^{2+}$**.*

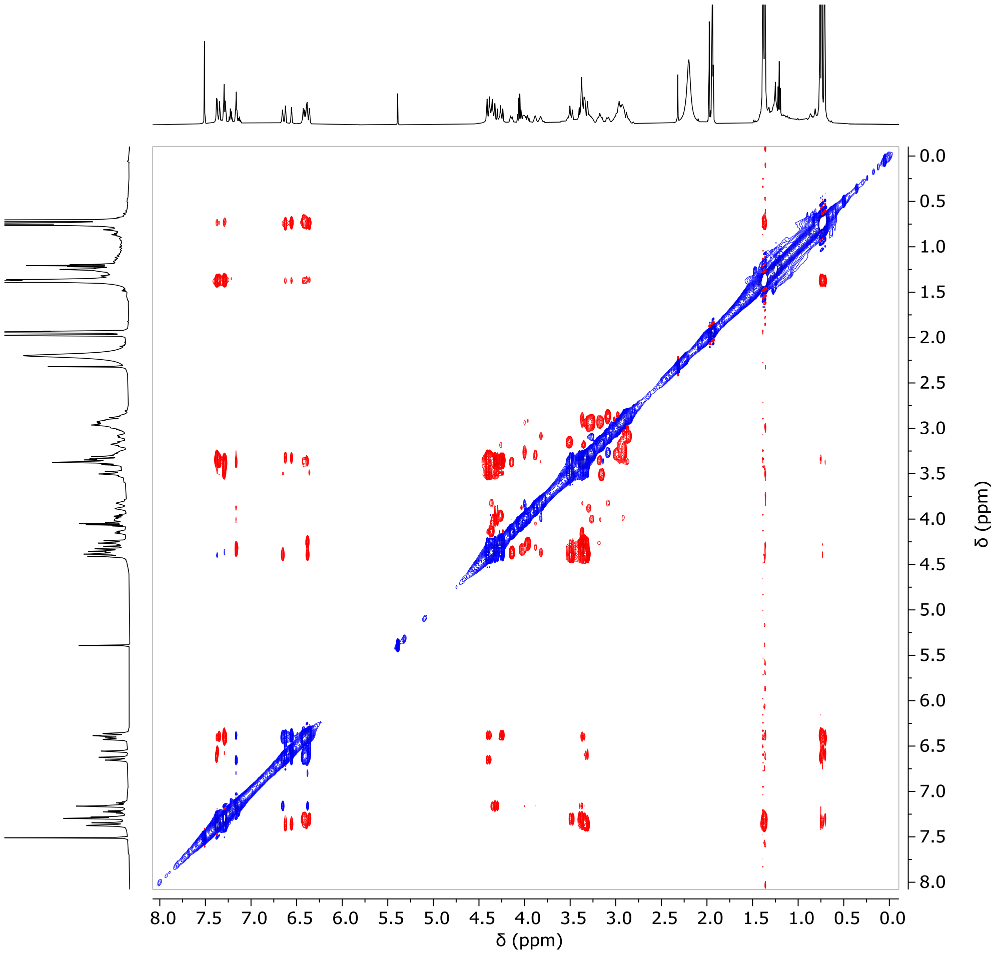

*Figure S 6: ROESYAD NMR spectrum (CDCl$_3$/CD$_3$CN 1:1, 600 MHz, 298 K, mixing time = 500 ms) of complex [**2.Zn⊃CD$_3$CN]$^{2+}$**.*

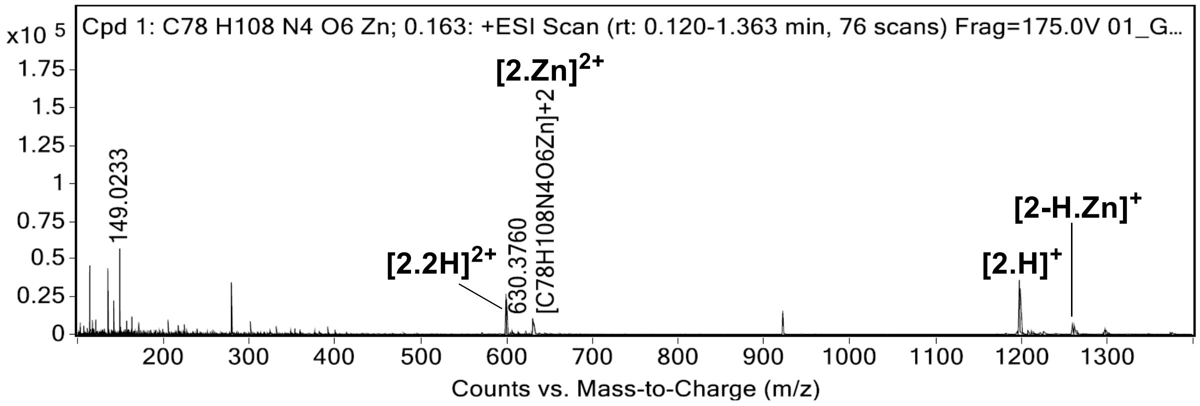

*Figure S 7: HRMS spectrum of complex [**2.Zn**]$^{2+}$.*

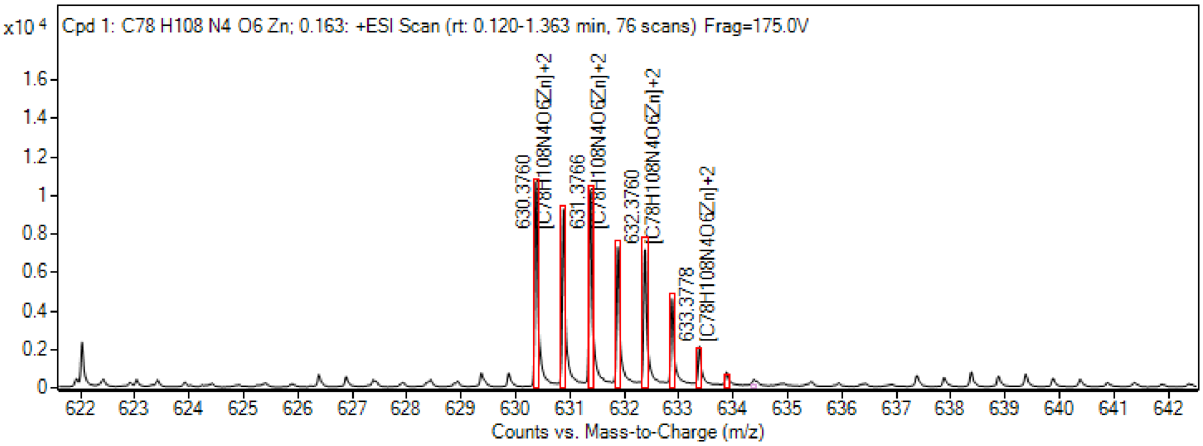

*Figure S 8: Region of HRMS spectrum of complex [**2.Zn**]$^{2+}$ (black) and calculated isotopic profile for formula $C_{78}H_{108}N_4O_6Zn$ (red).*

*Table S 1: Calculated and measured masses by HRMS and error for compound [**2.Zn**]$^{2+}$ $C_{78}H_{108}N_4O_6Zn$.*

Compound Label	RT	m/z	Mass	Abund	Formula	Tgt Mass	Diff (ppm)
Cpd 1: C78 H108 N4 O6 Zn	0.163	630.3760	1260.7535	10840	C78 H108 N4 O6 Zn	1260.756	-2.02

Monocationic complex [2-H.Zn]$^+$

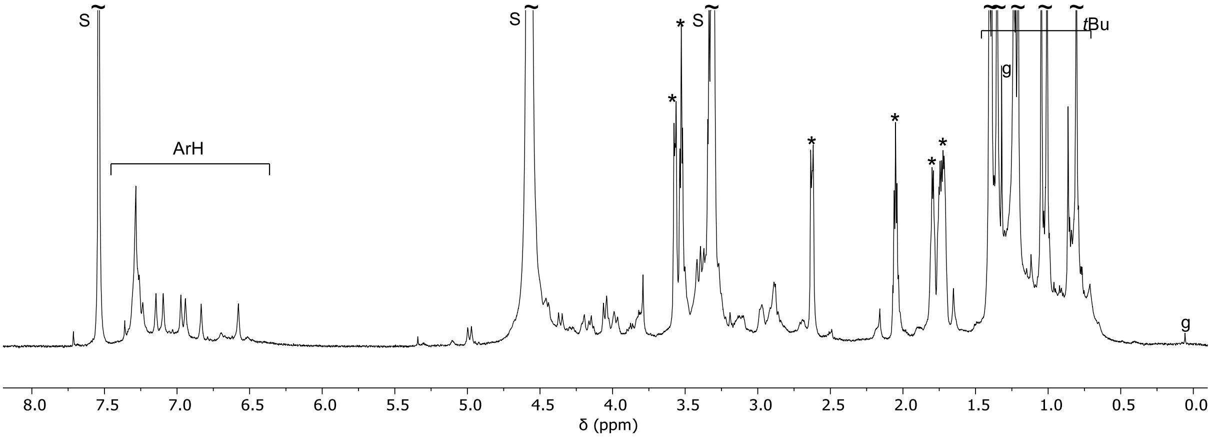

*Figure S 9: ^{1}H NMR spectrum (CDCl$_3$/CD$_3$OD 1:1, 600 MHz, 298 K) of complex [**2-H.Zn]**$^+$ in presence of 1.1 equiv. DBU (1,8-Diazabicyclo(5.4.0)undec-7-ene); *: DBU, S: solvent, g: grease.*

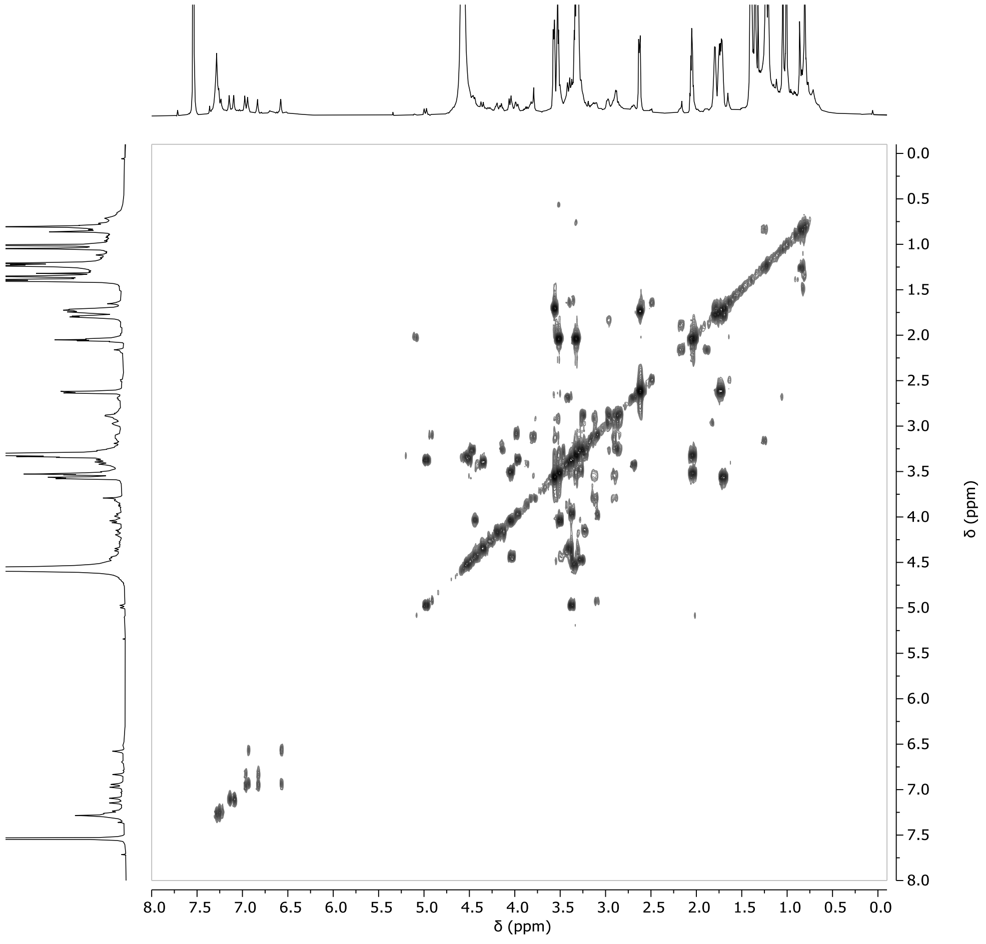

*Figure S 10: gDQCOSY NMR spectrum (CDCl$_3$/CD$_3$OD 1:1, 600 MHz, 298 K) of complex [**2-H.Zn]**$^+$ in presence of 1.1 equiv. DBU.*

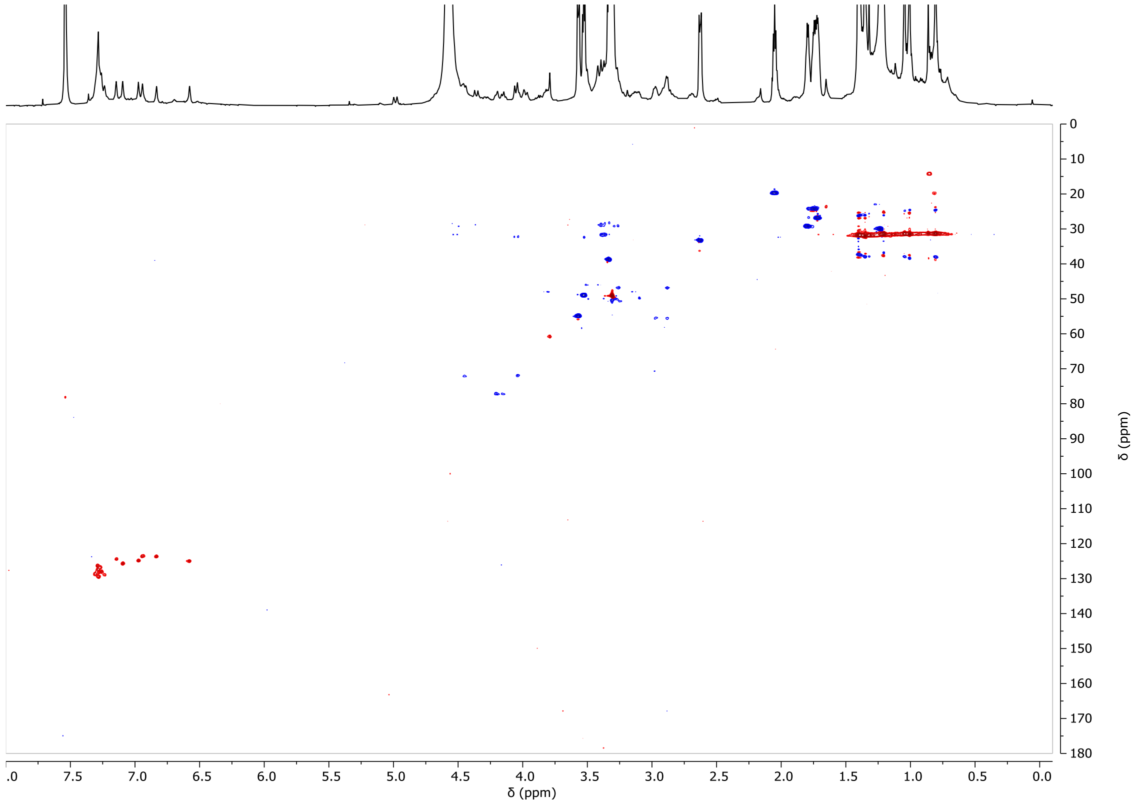

*Figure S 11: Edited gHSQCAD NMR spectrum ($CDCl_3$/CD_3OD 1:1, 600 MHz, 298 K) of complex [**2-H.Zn**]$^+$ in presence of 1.1 equiv. DBU.*

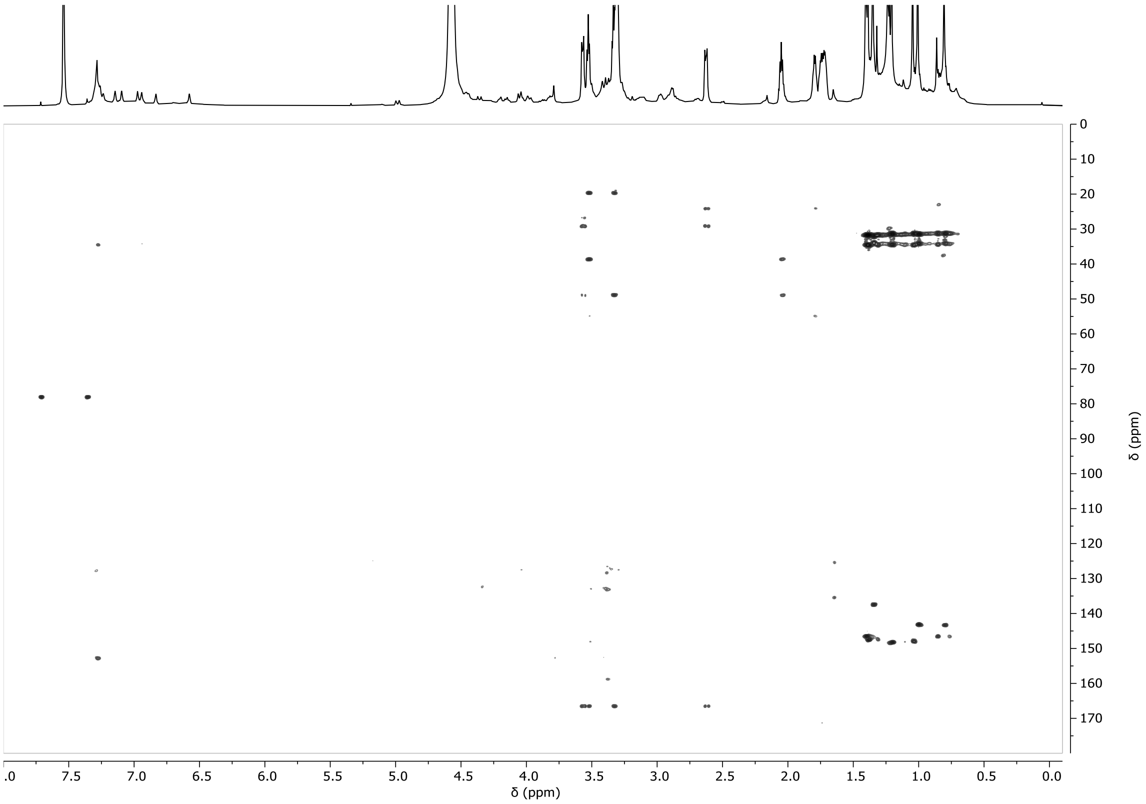

*Figure S 12: gHMBCAD NMR spectrum ($CDCl_3$/CD_3OD 1:1, 600 MHz, 298 K) of complex [**2-H.Zn**]$^+$ in presence of 1.1 equiv. DBU.*

Neutral complex [2-2H.Zn]

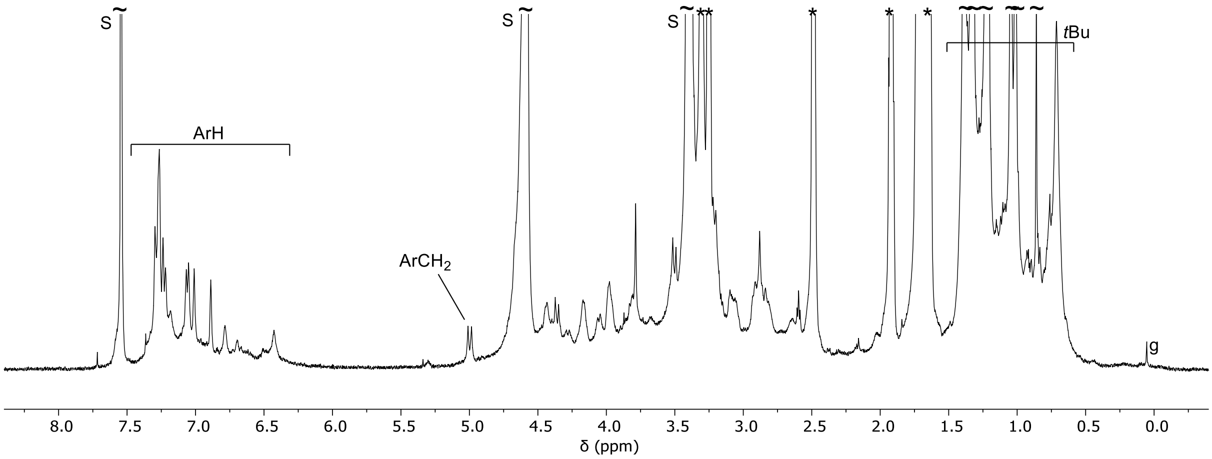

*Figure S 13: ^{1}H NMR spectrum (CDCl$_3$/CD$_3$OD 1:1, 600 MHz, 298 K) of complex [**2-H.Zn**]$^+$ in presence of 5.2 equiv. DBU (1,8-Diazabicyclo(5.4.0)undec-7-ene); *: DBU, S: solvent, g: grease.*

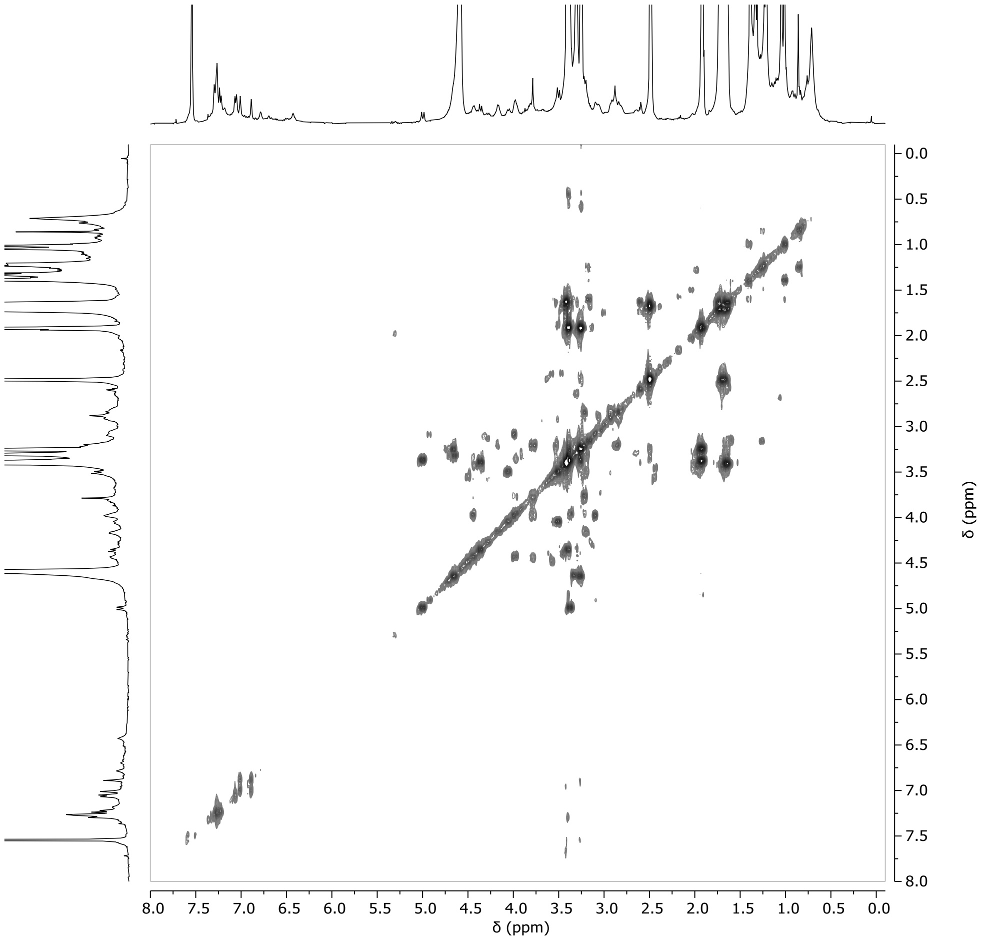

*Figure S 14: gDQCOSY NMR spectrum (CDCl$_3$/CD$_3$OD 1:1, 600 MHz, 298 K) of complex [**2-2H.Zn**] in presence of 5.2 equiv. DBU (1,8-Diazabicyclo(5.4.0)undec-7-ene).*

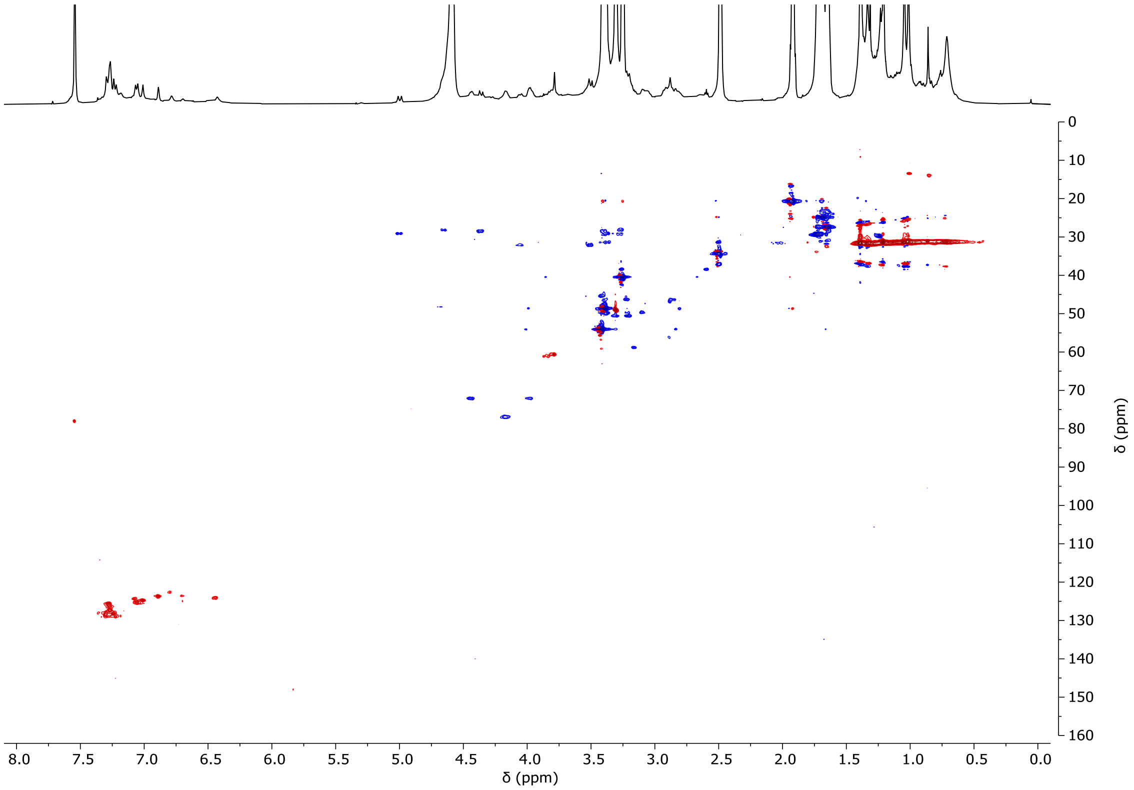

Figure S 15: Edited-gHSQCAD *NMR* spectrum ($CDCl_3/CD_3OD$ 1:1, 600 MHz, 298 K) *of* complex [**2-2H.Zn]** *in presence of 5.2 equiv. DBU (1,8-Diazabicyclo(5.4.0)undec-7-ene).*

Host-guest studies of $[2.Zn]^{n+}$

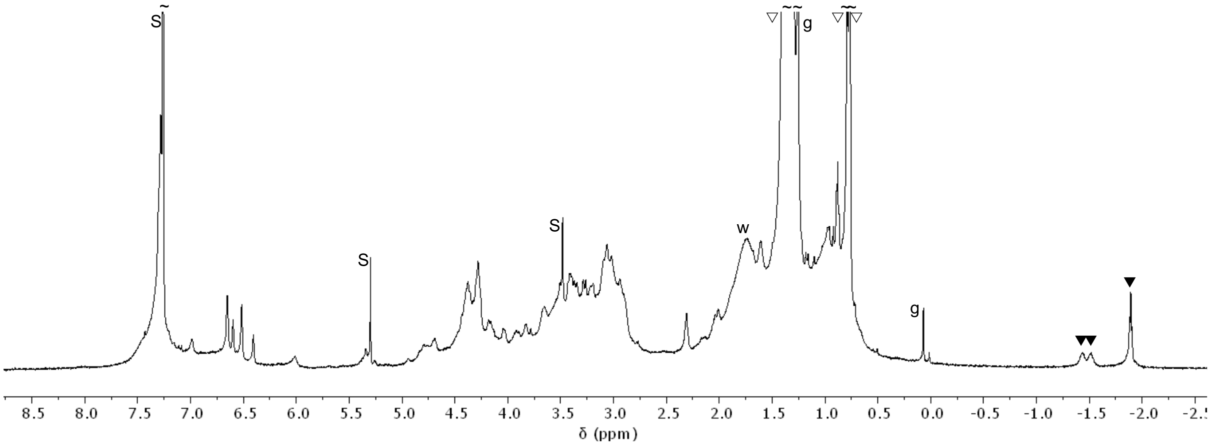

Figure S 16 : ^{1}H NMR spectrum (CDCl$_3$, 600 MHz, 298 K, C ≈ 2.10^{-3} M) of ***$[2.Zn \supset PrNH_2]^{2+}$*** in presence of 1 equiv. of PrNH$_2$; ▼*:* PrNH$_{2in}$*,* ▽*:* PrNH$_{2out}$*, S: solvent, w: water, g: grease.*

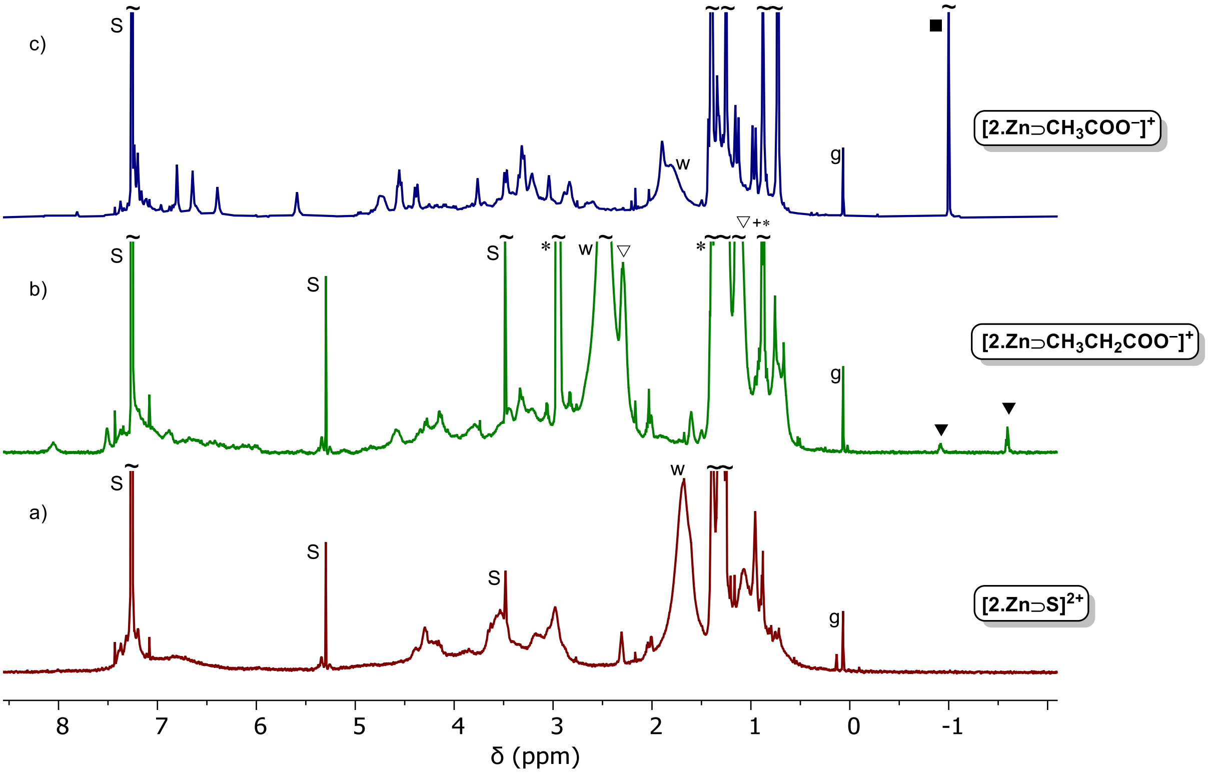

Figure S 17: ^{1}H NMR spectra (CDCl$_3$, 600 MHz, 298 K, C ≈ 2.10^{-3} M) of complex ***$[2.Zn \supset S]^{2+}$*** *(a) before and (b) after addition of 3 equiv. of propanoic acid and of 4 equiv. of Et$_3$N; (c) 1:1 mixture of ligand* ***2*** *and Zn(OAc)$_2$;* ▼*: $CH_3CH_2COO^-_{in}$,* ▽*: $CH_3CH_2COO(H)_{out}$,* ■*: $CH_3COO^-_{in}$, *: Et$_3$N, S: solvent, w: water, g: grease.*

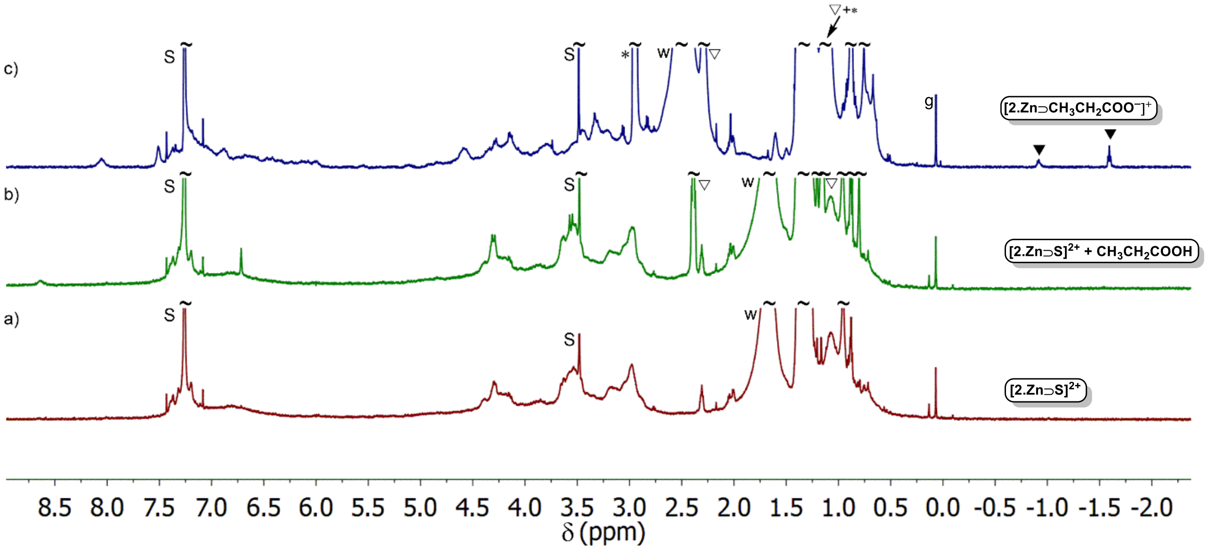

*Figure S 18: ^{1}H NMR spectra (CDCl$_3$, 600 MHz, 298 K, C ≈ 2.10^{-3} M) of the complex **[2.Zn⊃S]$^{2+}$** (a) before addition, (b) after addition of 3 equiv. of propanoic acid, (c) after addition of 3 equiv. of propanoic acid and of 4 equiv. of TEA ; ▼: CH$_3$CH$_2$COO$^-$$_{in}$, ▽: CH$_3CH_2$COO(H)$_{out}$, *: Et$_3$N, S: solvent, w: water, g: grease.*

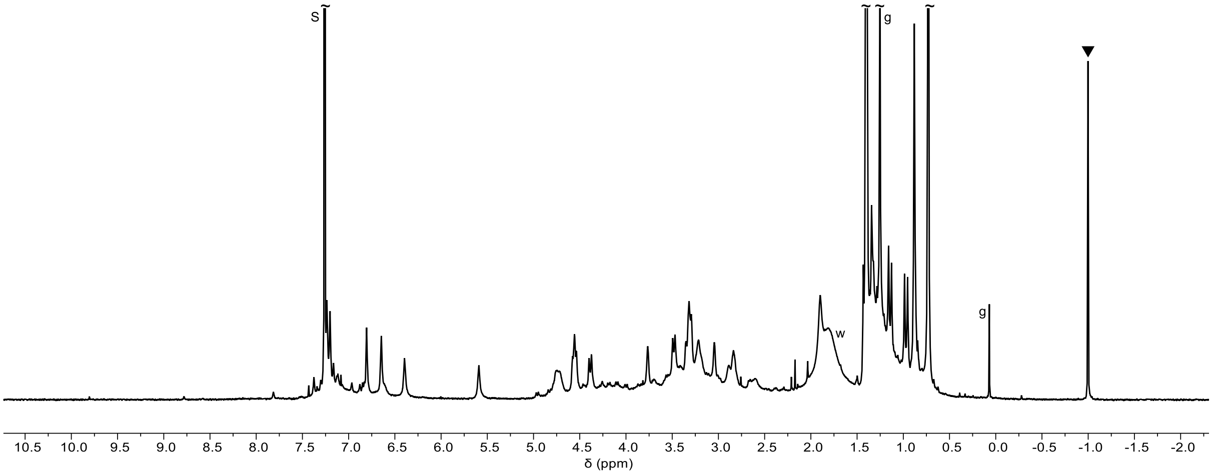

*Figure S 19: ^{1}H NMR spectrum (CDCl$_3$, 600 MHz, 298 K, C ≈ 2.10^{-3} M) of complex **[2.Zn⊃CH$_3$COO$^-$]$^{+}$**; ▼: CH$_3$COO$^-$$_{in}$, S: solvent, w: water, g: grease.*

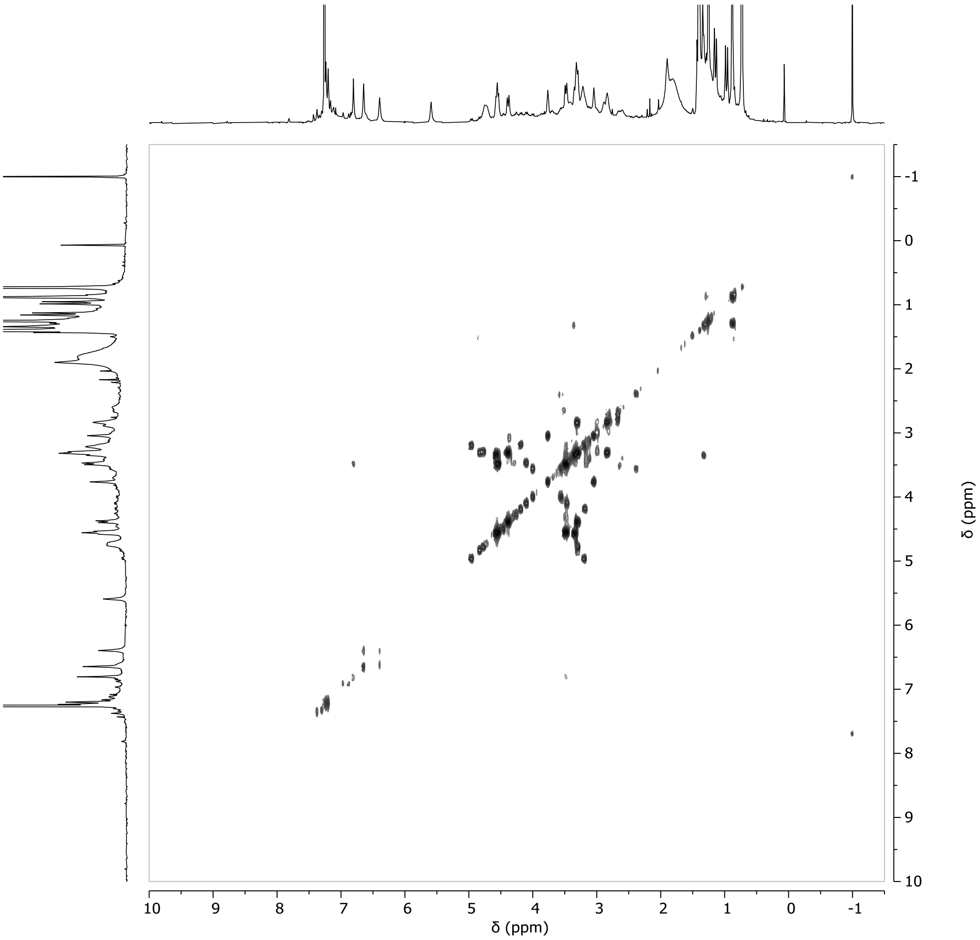

Figure S 20: gDQCOSY NMR spectrum ($CDCl_3$, 600 MHz, 298 K) of complex ***$[2.Zn\supset CH_3COO^-]^+$***.

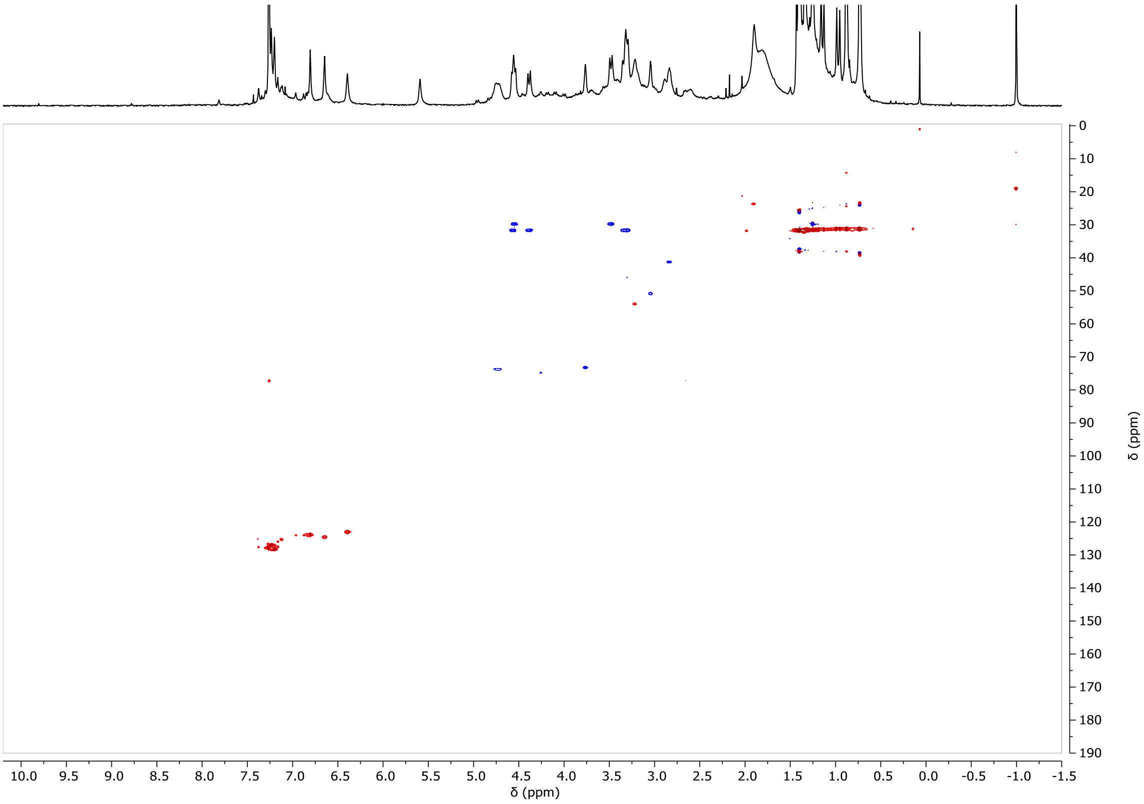

Figure S 21: Edited-gHSQCAD NMR spectrum ($CDCl_3$, 600 MHz, 298 K) of complex ***$[2.Zn\supset CH_3COO^-]^+$***.

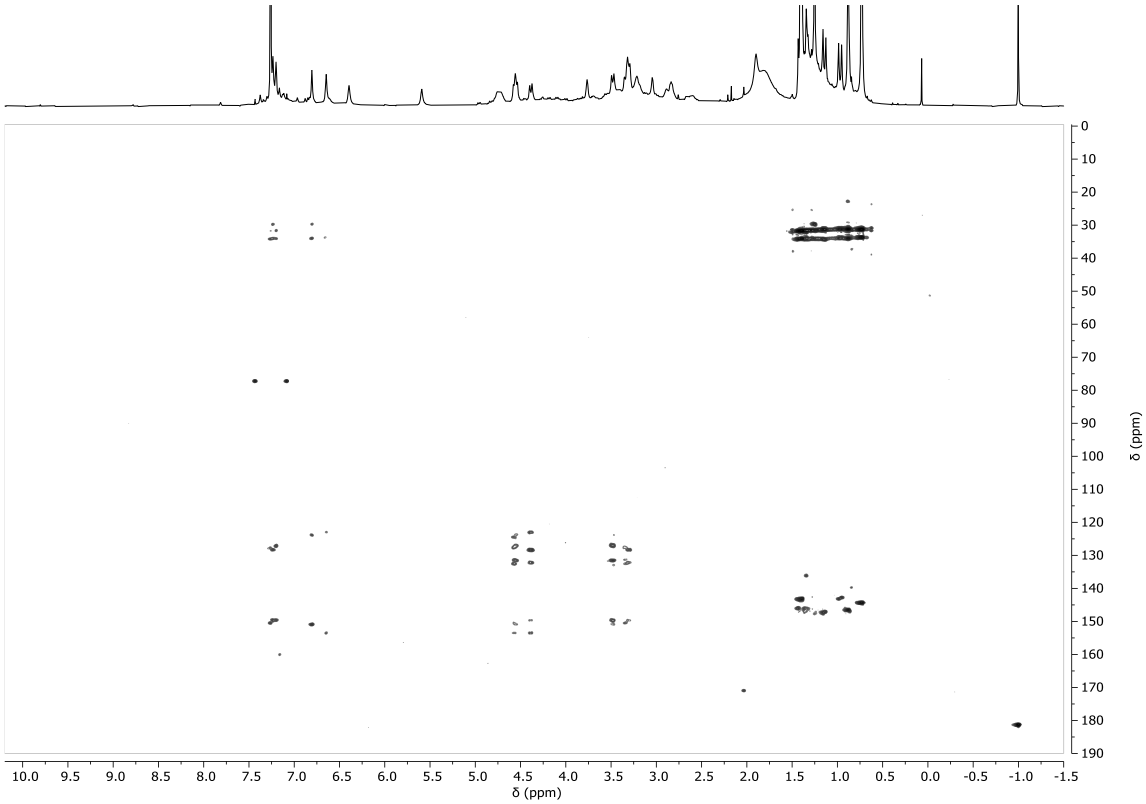

Figure S 22: gHMBCAD NMR spectrum (CDCl$_3$, 600 MHz, 298 K) of complex ***[2.Zn⊃CH$_3$COO$^-$]$^+$****.*

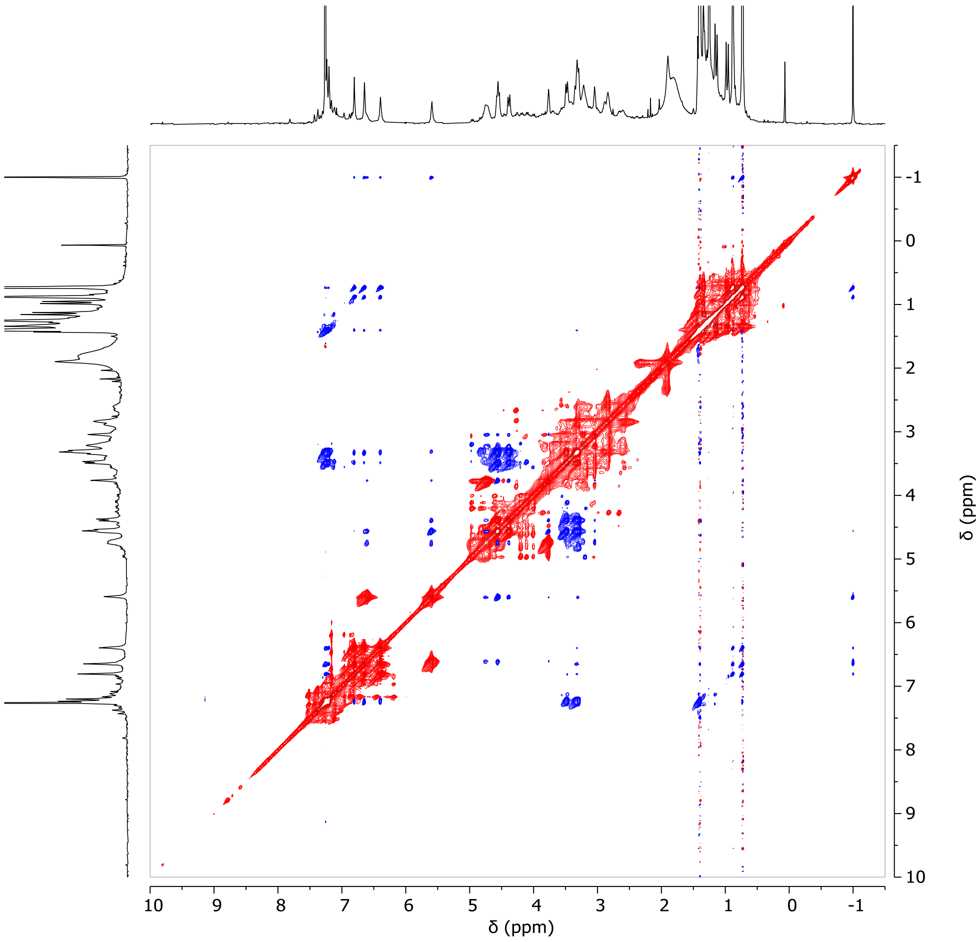

Figure S 23: ROESYAD NMR spectrum (CDCl$_3$, 600 MHz, 298 K, mixing time = 200 ms) of complex ***[2.Zn⊃CH$_3$COO$^-$]$^+$****.*

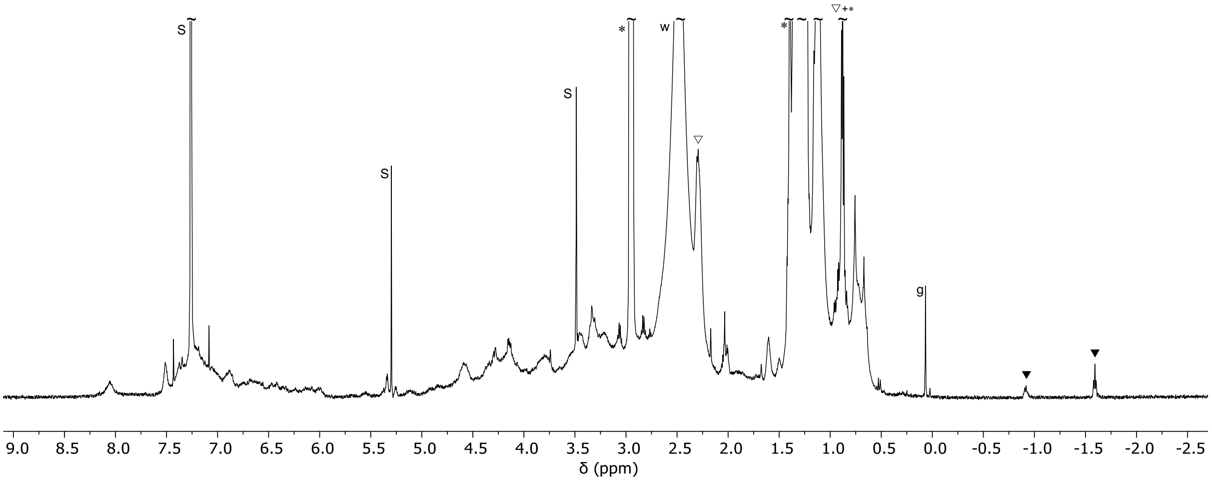

Figure S 24: ^{1}H NMR spectrum (CDCl$_3$, 600 MHz, 298 K, *$C \approx 2.10^{-3}$ M*) of complex **[2.Zn⊃$\mathbf{CH_3CH_2COO^-}$]$^+$** ; ▼: *$CH_3CH_2COO^-_{in}$*, ▽: *$CH_3CH_2COO(H)_{out}$*, * : *Et$_3$N, S: solvent, w: water, g: grease.*

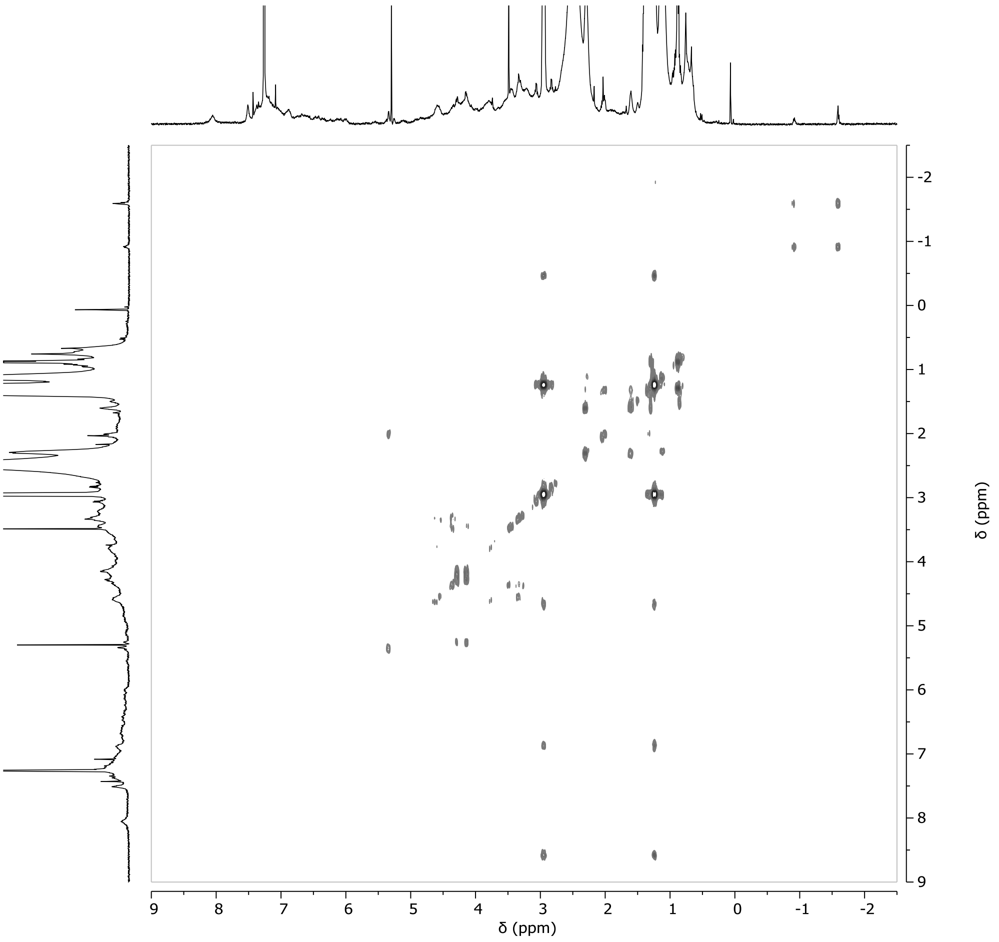

Figure S 25: gDQCOSY NMR spectrum (CDCl$_3$, 600 MHz, 298 K) of complex ***[2.Zn⊃$\mathbf{CH_3CH_2COO^-}$]$^+$.***

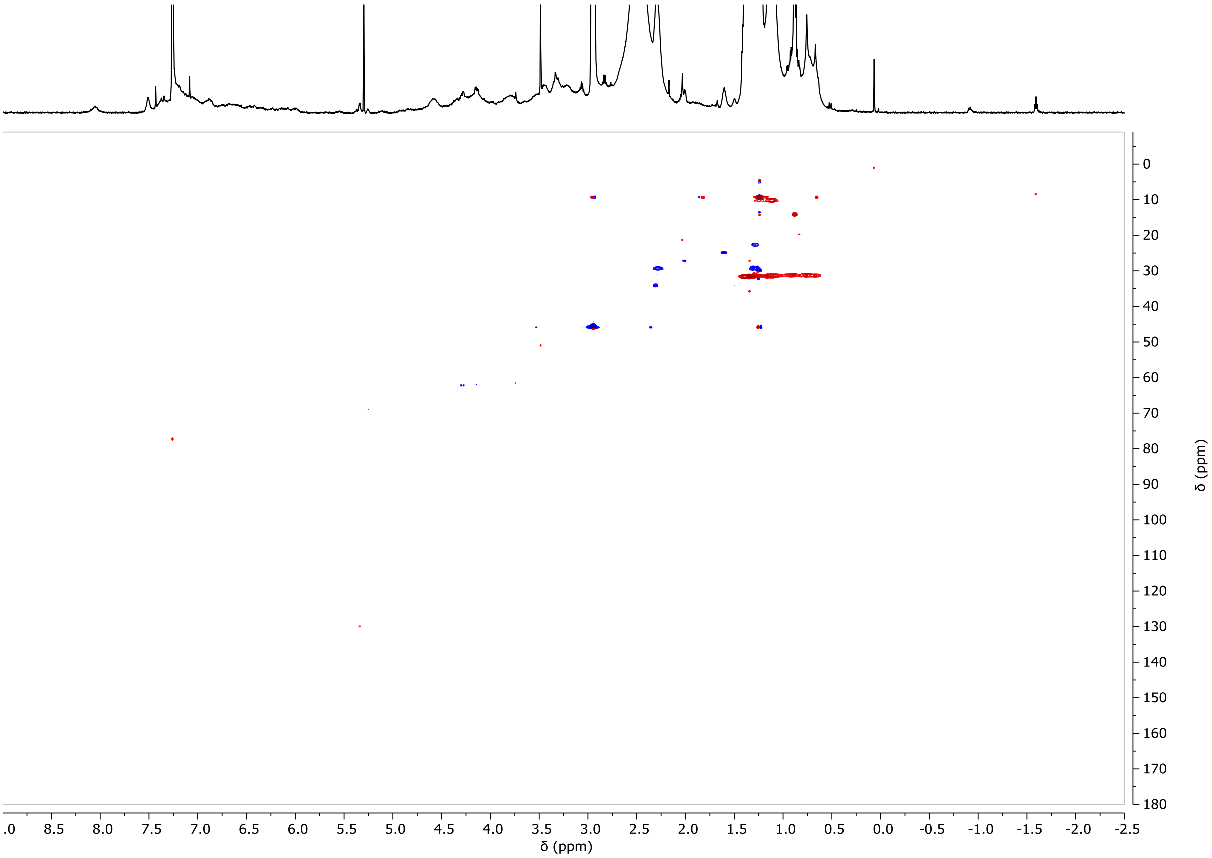

Figure S 26: Edited-gHSQCAD NMR spectrum ($CDCl_3$, 600 MHz, 298 K) of complex ***[2.Zn$\supset CH_3CH_2COO^-$]$^+$**.*

Bibliography

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[1] G. Chang, W. C. Guida and W. C. Still, *J. Am. Chem. Soc.*, 1989, **111**, 4379-4386.

[2] J. L. Banks, H. S. Beard, Y. Cao, A. E. Cho, W. Damm, R. Farid, A. K. Felts, T. A. Halgren, D. T. Mainz, J. R. Maple, R. Murphy, D. M. Philipp, M. P. Repasky, L. Y. Zhang, B. J. Berne, R. A. Friesner, E. Gallicchio and R. M. Levy, *J. Comput. Chem.*, 2005, **26**, 1752-1780.