Toward Inert Paramagnetic Ni(II)-Based Chemical Exchange Saturation Transfer MRI Agents

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Electronic Supplementary Information(ESI)

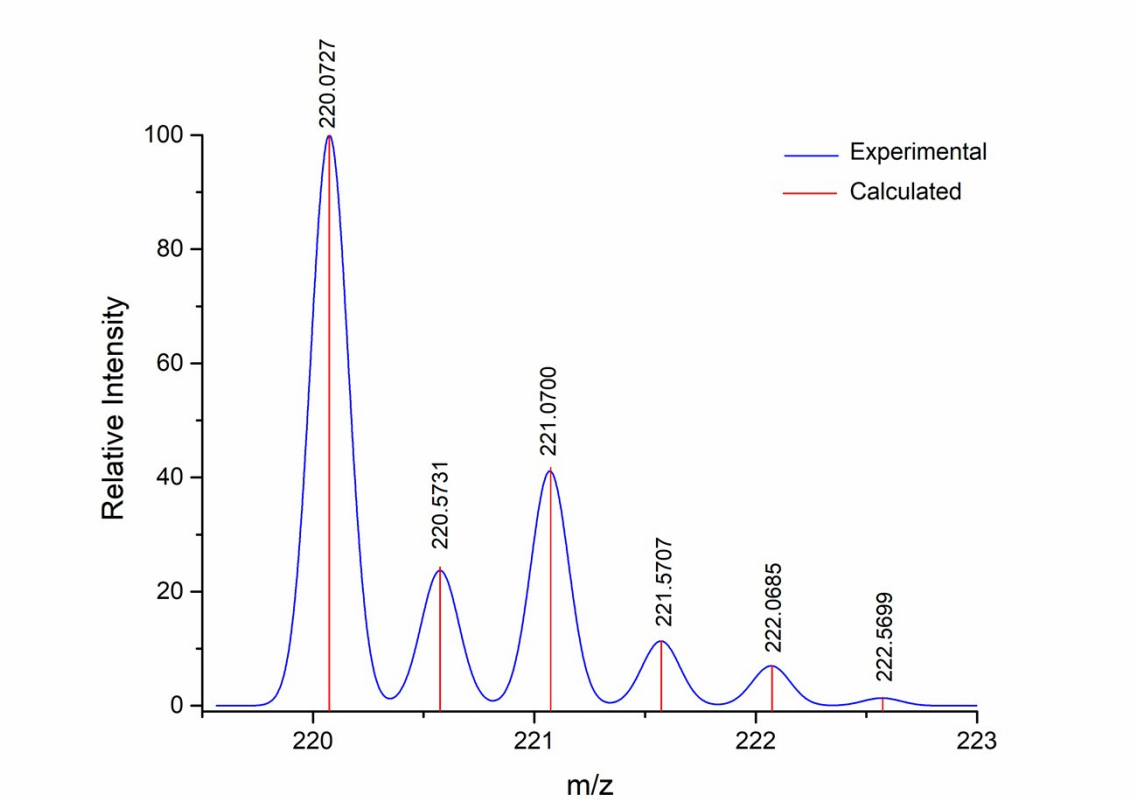

Figure S1. Calculated (red) and observed (blue) mass spectral isotopic distribution for the fragment $[Ni(chxdedpam)]^{2+}$ ($C_{20}H_{26}N_6NiO_2^{2+}$).

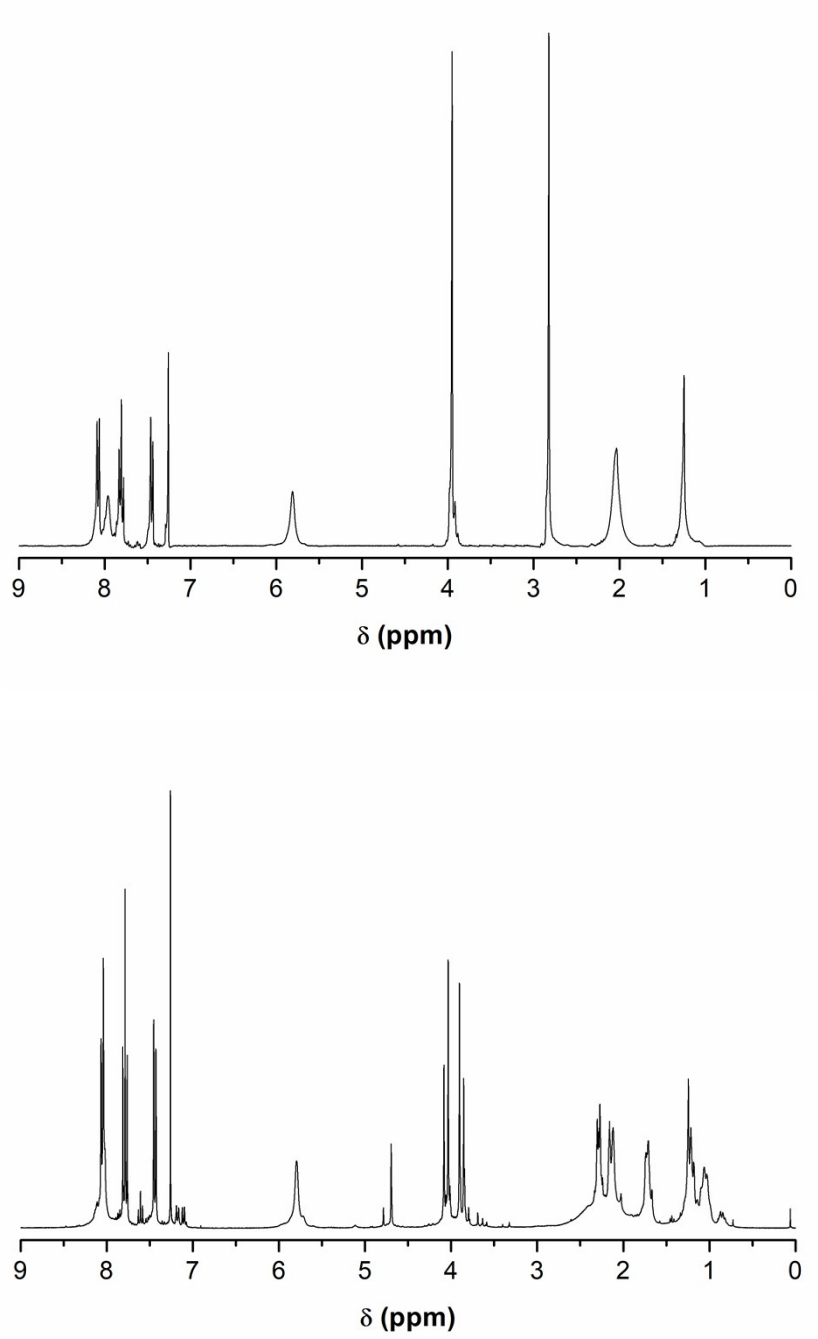

Figure S2. ^{1}H NMR spectra (300 MHz, 25 ^{o}C) of H_2dedpam (top) and chxdedpam (bottom) recorded in $CDCl_3$ solution.

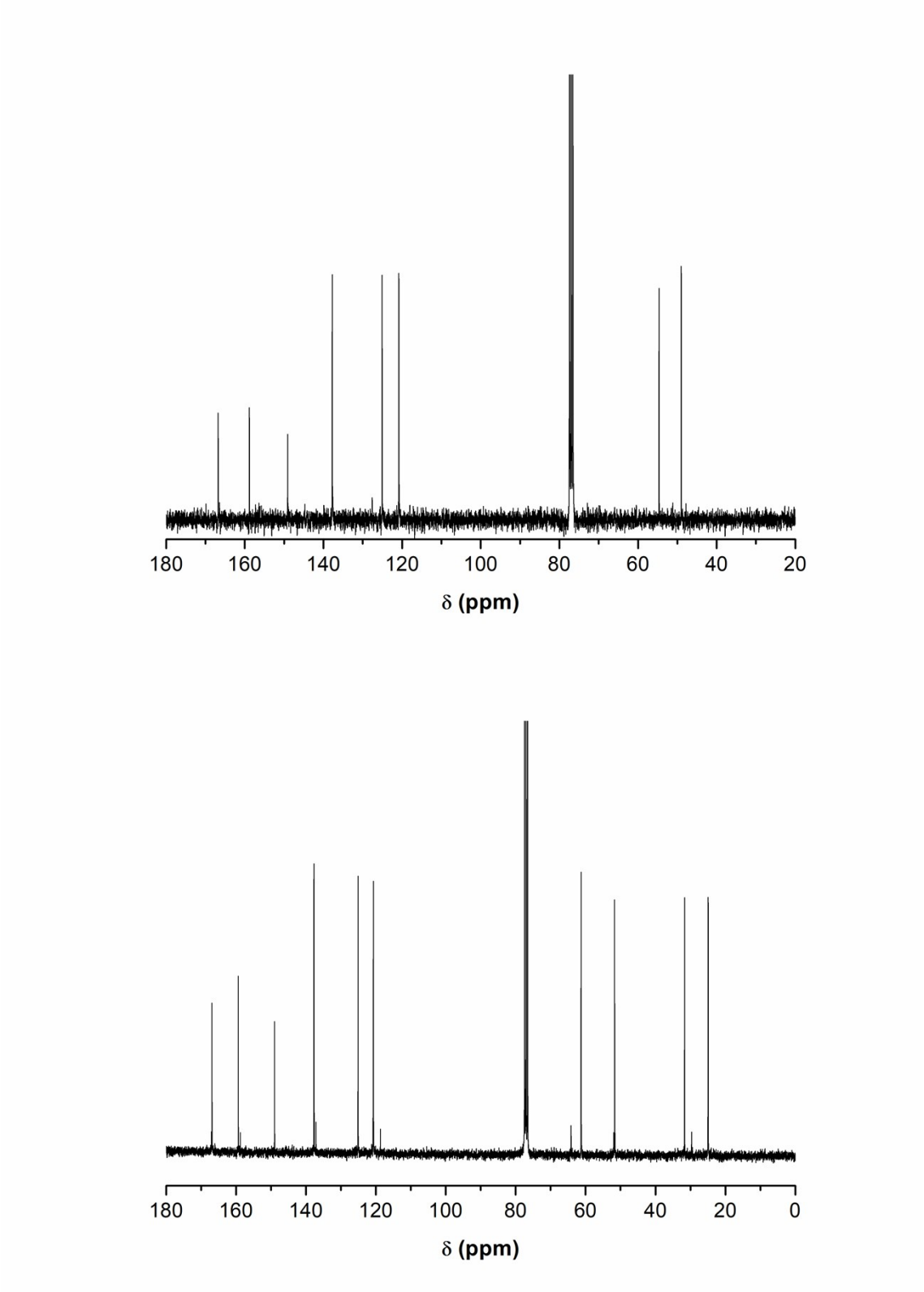

Figure S3. ^{13}C NMR spectra (75.5 MHz, 25 ^{o}C) of dedpam (top) and chxdedpam (bottom) recorded in $CDCl_3$ solution.

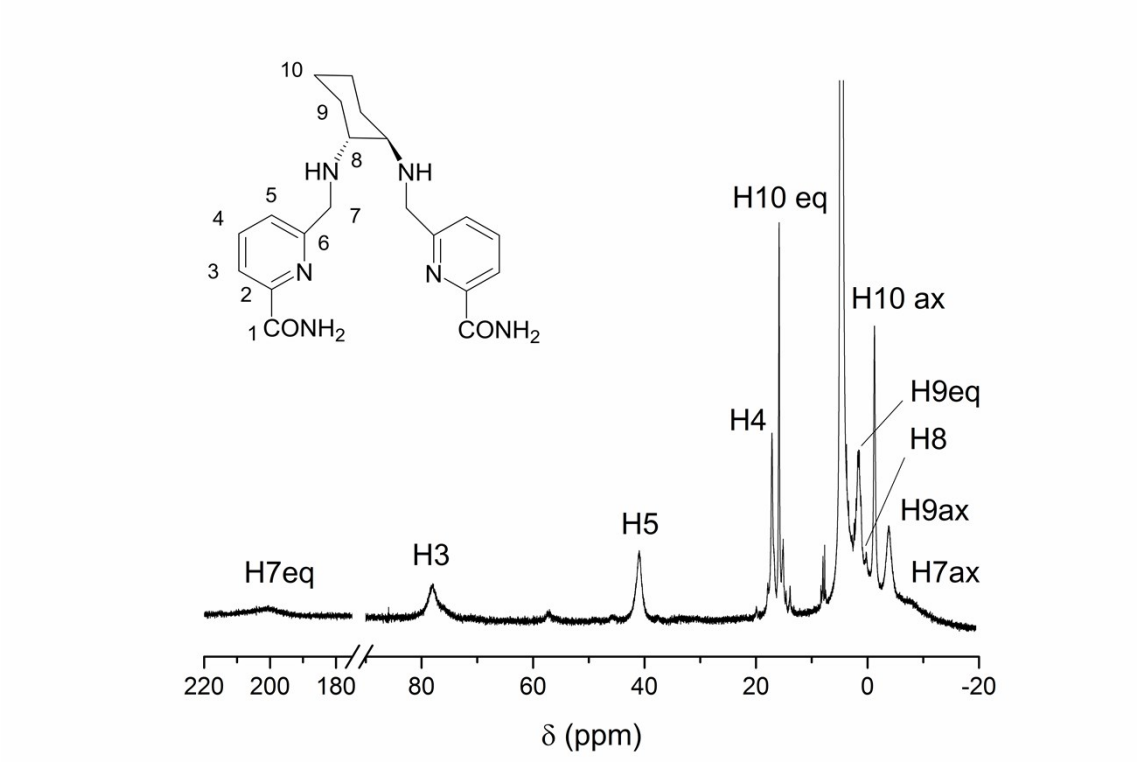

Figure S4. ^{1}H NMR spectrum of $[Ni(chxdedpam)]^{2+}$ and numbering scheme of ligand proton nuclei.

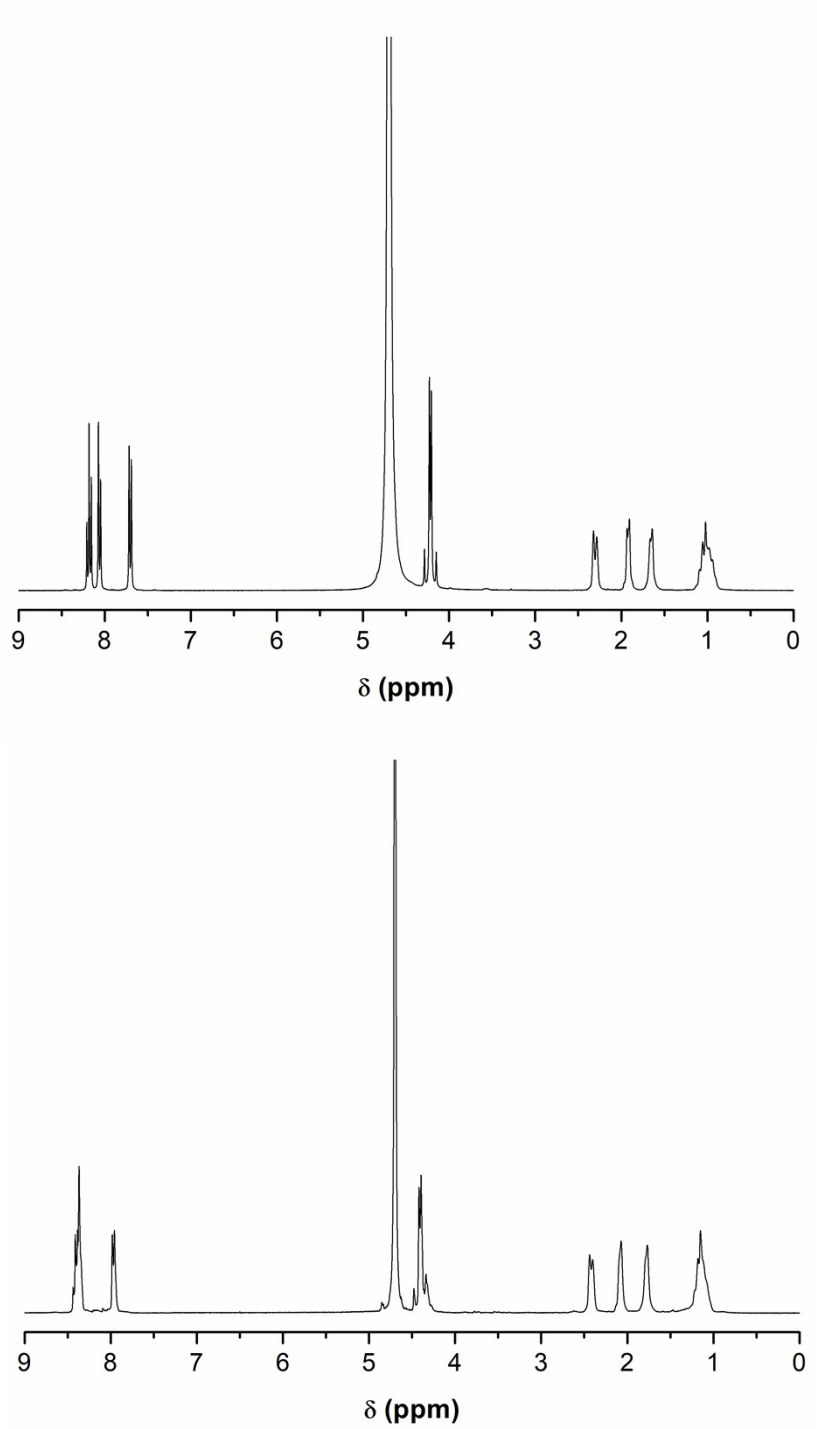

Figure S5. ^{1}H NMR spectra (300 MHz, 25 ^{o}C, pD 7.0) of [Zn(chxdedpa)] (top) and $[Zn(chxdedpam)]^{2+}$ (bottom) recorded in D_2O solution.

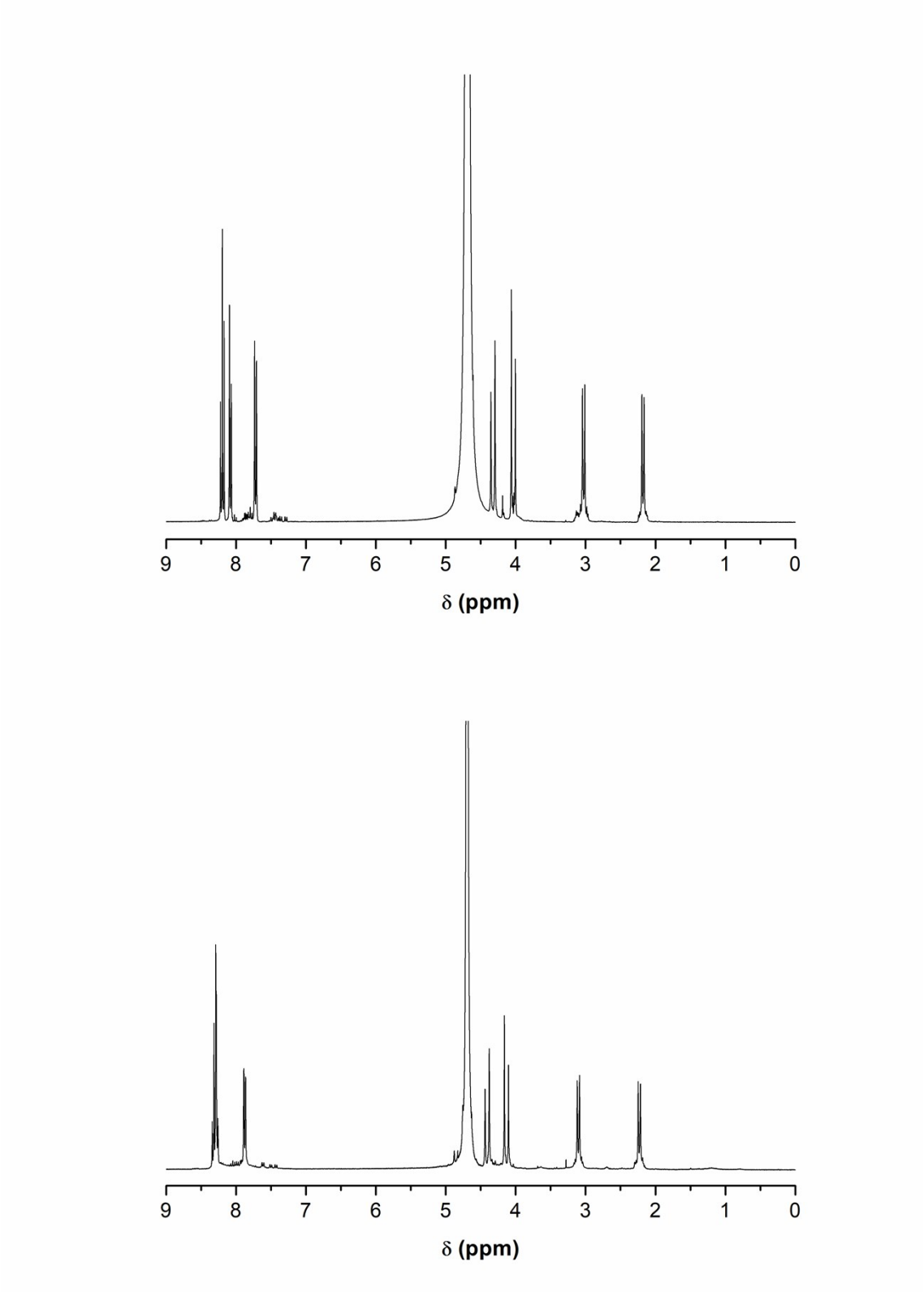

Figure S6. ^{1}H NMR spectra (300 MHz, 25 ^{o}C, pD 7.0) of [Zn(dedpa)] (top) and $[Zn(dedpam)]^{2+}$ (bottom) recorded in D_2O solution.

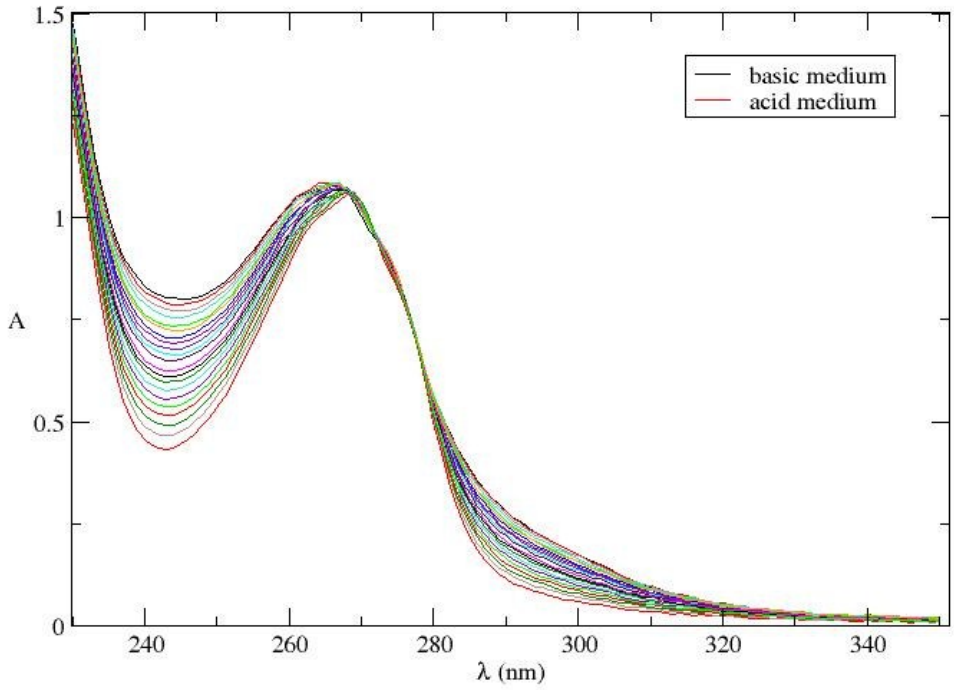

Figure S7. UV absorption spectra of an equimolar mixture (1.2×10^{-4} M) of $dedpa^{2-}$ and Ni^{2+} recorded from basic pH ($[OH^-]=7.4\ 10^{-5}$ M , upper curve, bold black, in this media 100% of the ligand is forming the complex) to acidic pH (HCl 0.14 M lower curve, bold red, where 24% is [Ni(dedpa)], 73.5% H_4dedpa^{2+}, and 2.5% is H_3dedpa^{+}).

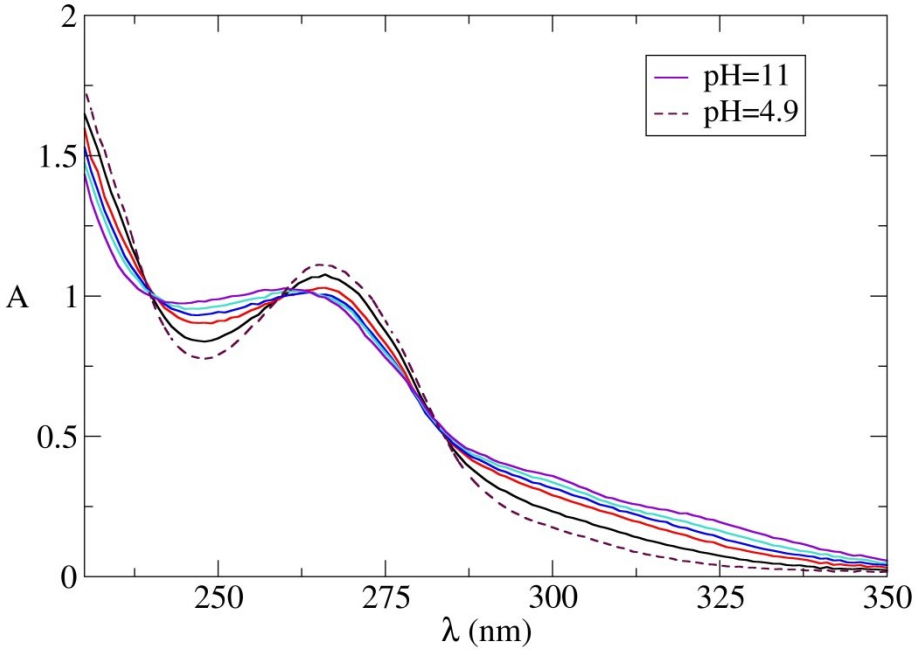

Figure S8. UV absorption spectra of an equimolar mixture of dedpam and Ni^{2+} recorded at different pH values (8.6×10^{-5} M) in the pH range 4.9-11. At pH 5 the main species in solution is $[Ni(dedpam)]^{2+}$, while at pH 11 the deprotonated $[Ni(H_{-2}dedpam)]$ species predominates.

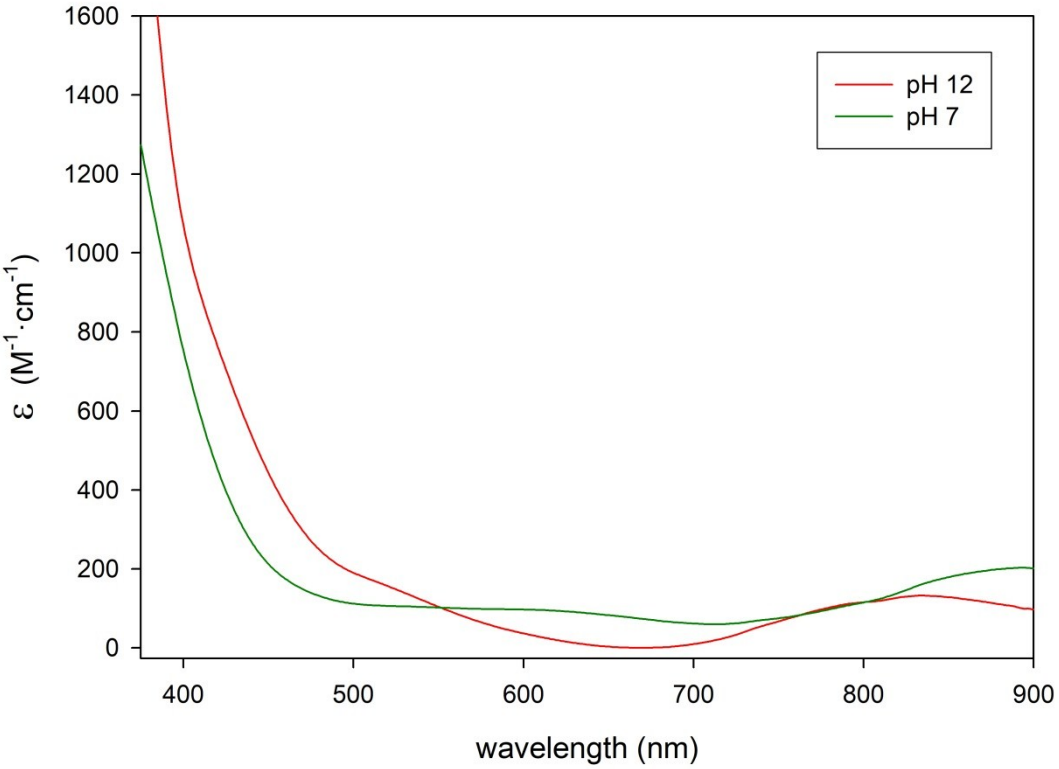

Figure S9. UV absorption spectra of an equimolar mixture of chxdedpam and Ni^{2+} recorded at pH 7 and pH 12 (7.5×10^{-3} M). At pH 7 the main species in solution is $[Ni(chxdedpam)]^{2+}$, while at pH 11 the deprotonated $[Ni(H_{-2}chxdedpam)]$ species predominates.

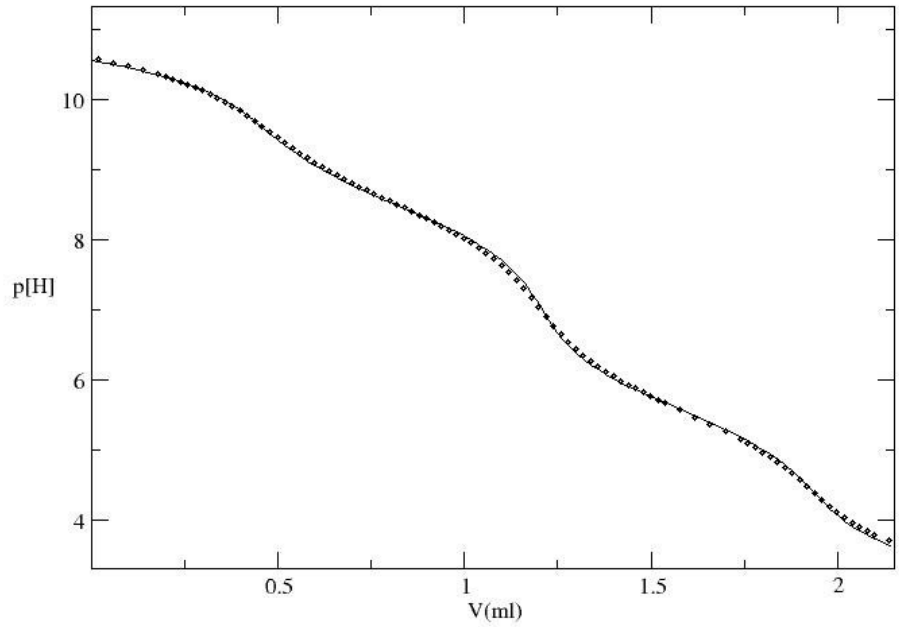

Figure S10. Potentiometric titration of dedpam (0.96 mM) in basic media titrated with HCl (0.02 M). The solid line corresponds to the least-squares fit of the data to obtain the ligand protonation constants.

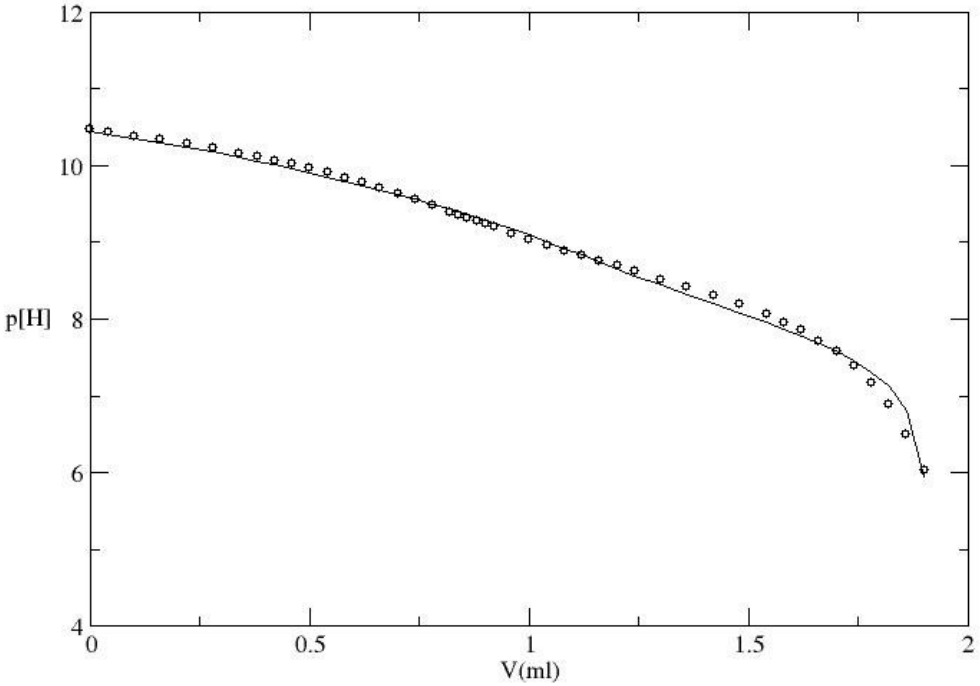

Figure S11. Potentiometric titration of dedpam and Ni^{2+} (both 0.79 mM) in basic medium titrated with HCl (0.02 M).

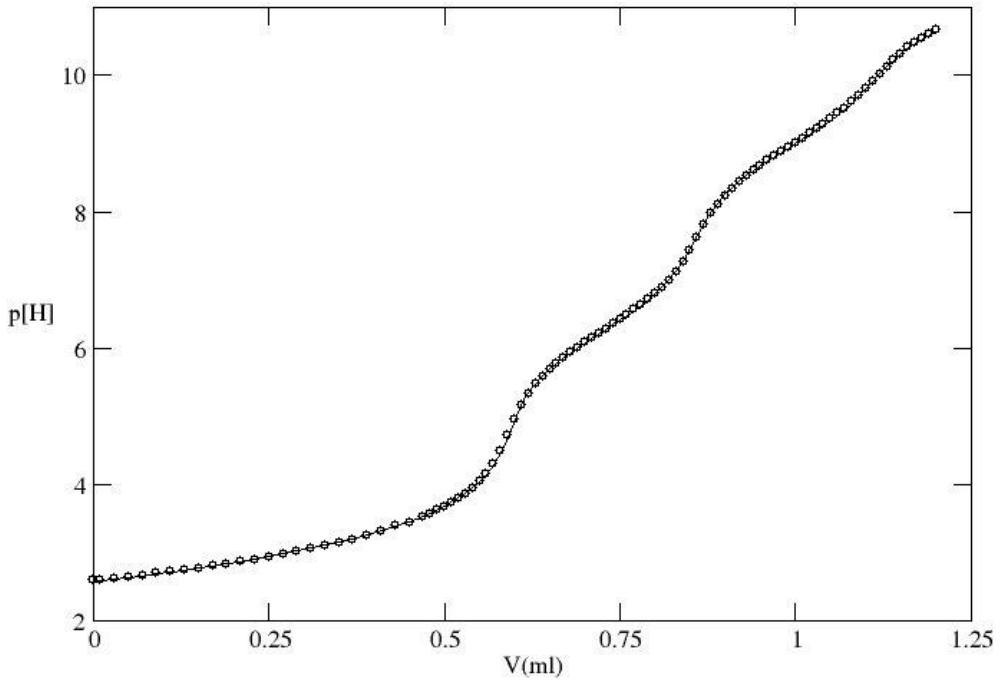

Figure S12. Potentiometric titration of dedpa (2.4 mM) in acid medium titrated with NaOH (0.0925 M). The solid line corresponds to the least-squares fit of the data to obtain the ligand protonation constants.

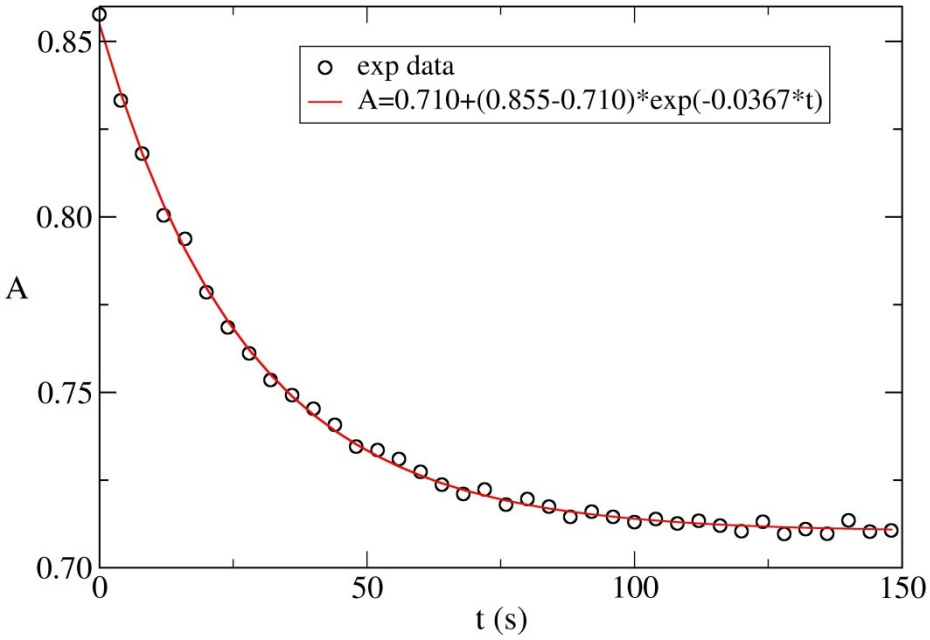

Figure S13. Acid-catalysed dissociation of $[Ni(dedpam)]^{2+}$ in 1 M HCl at 25 ºC. A represents the absorbance of the solution at 265 nm. The red line corresponds to the fit of the data to eq (7) in the main manuscript.

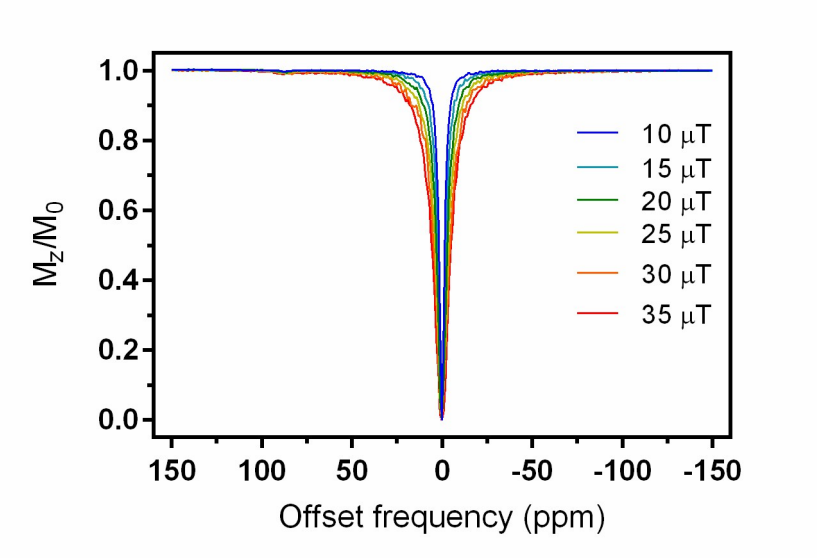

Figure S14. Z-spectra of $[Ni(chxdedpam)]^{2+}$ (15 mM) in H_2O:D_2O (9:1, v/v) at pH 5.9, saturation time 10 s and varying saturation power and temperature.

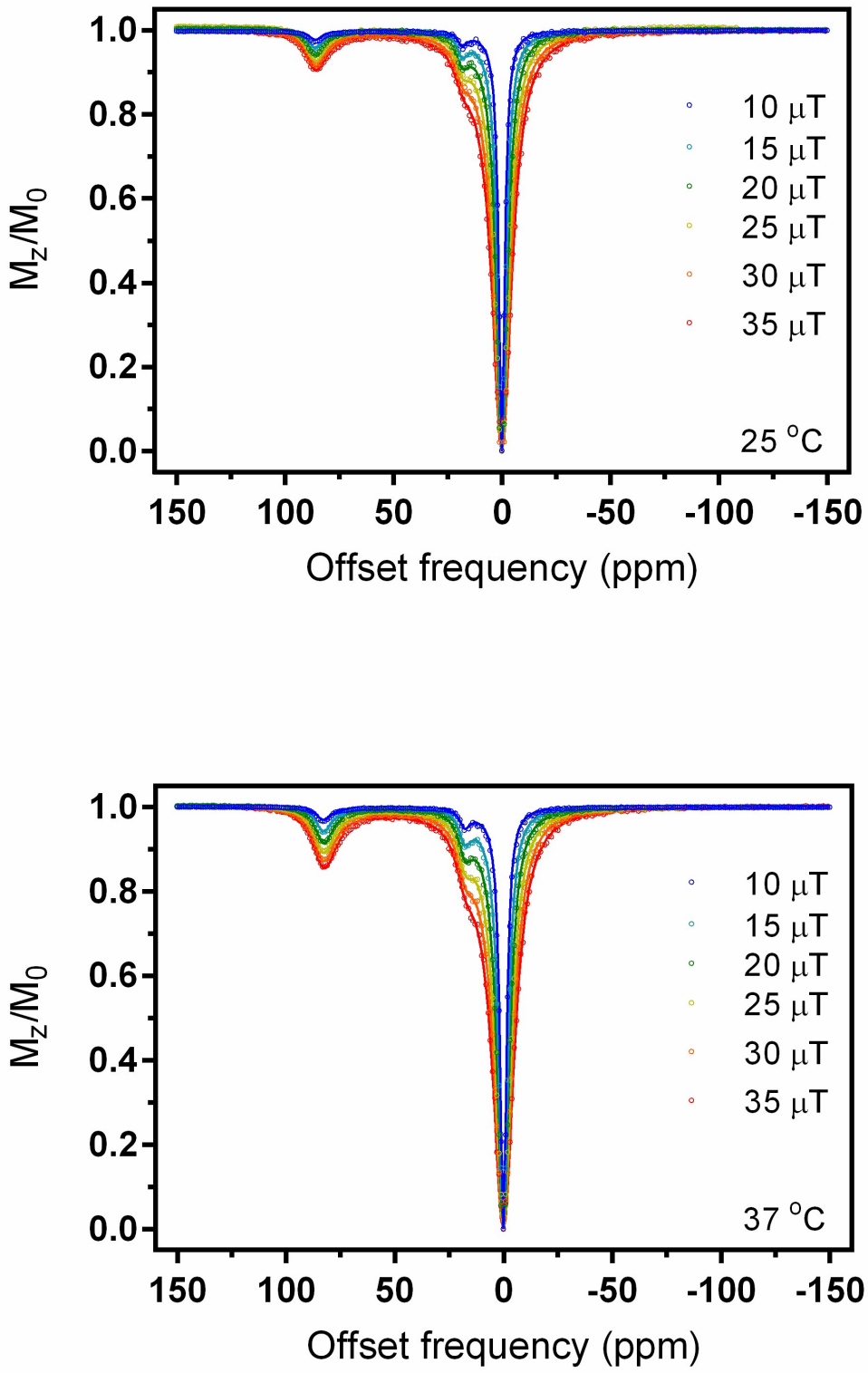

Figure S15. Z-spectra of $[Ni(chxdedpam)]^{2+}$ (15 mM) in H_2O:D_2O (9:1, v/v) at pH 7.2, saturation time 10 s and varying saturation power and temperature.

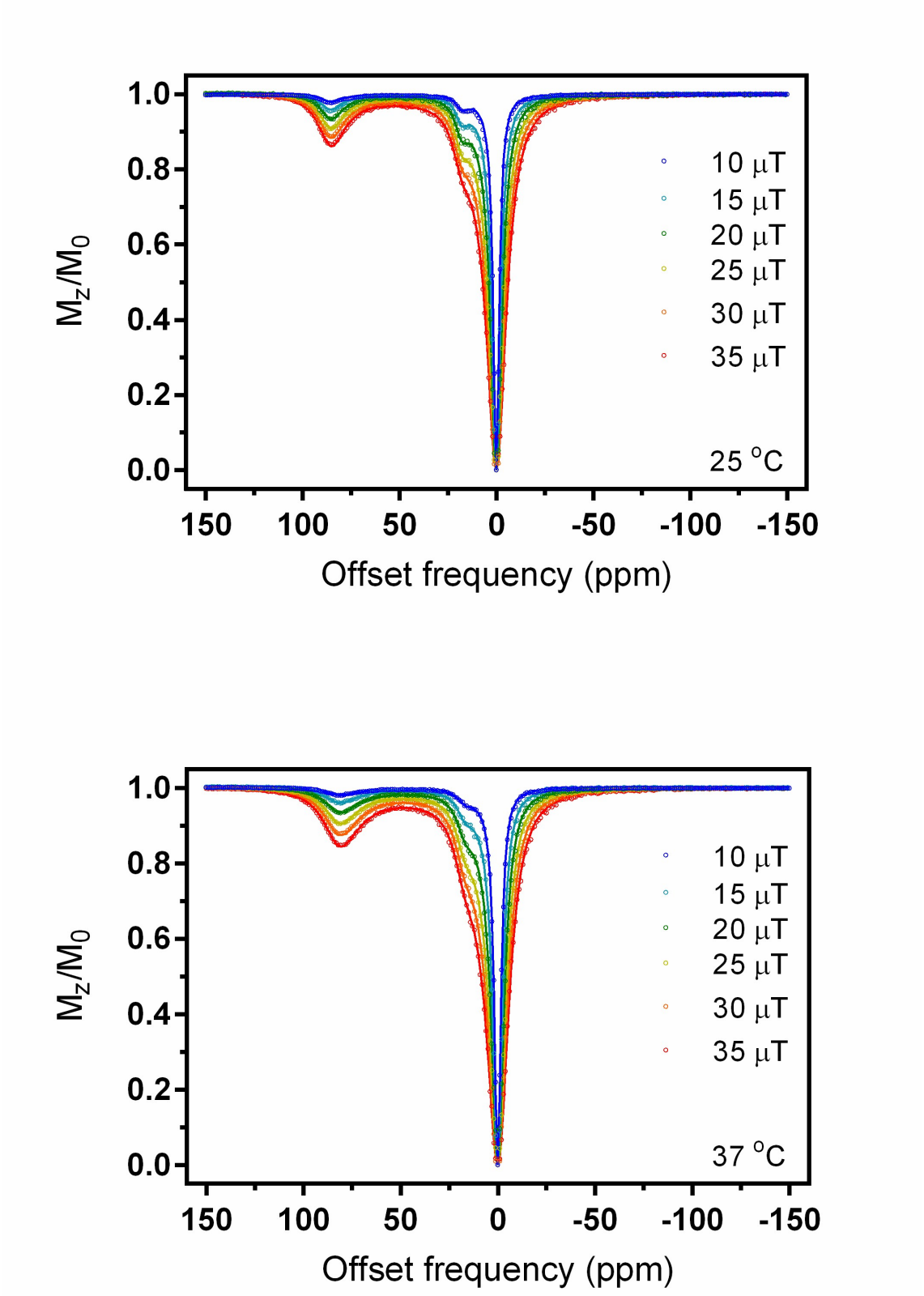

Figure S16. Z-spectra of $[Ni(chxdedpam)]^{2+}$ (15 mM) in H_2O:D_2O (9:1, v/v) at pH 8.0, saturation time 10 s and varying saturation power and temperature.

Table S1. [Ni(chxdedpam)]$^{2+}$, TPSSh/TZVP, aqueous solution (0 Imaginary Frequencies)

Atom	Coordinates (Angstroms) X	Y	Z
O	-0.45084600	-1.95469100	1.56084200
O	0.44962200	-1.95489500	-1.56075800
N	-1.98690000	-0.71997200	-0.11119100
N	1.98645700	-0.72114300	0.11127900
N	0.44653700	1.02714100	1.35102800
H	-0.27026600	1.14813500	2.06382800
C	2.62549900	-0.07436000	1.08532800
C	-2.62549800	-0.07293000	-1.08535400
N	-0.44589400	1.02734800	-1.35096300
H	0.27102500	1.14788400	-2.06372500
C	-1.67548600	-2.15534300	1.71647100
C	-2.63588300	-1.50951300	0.75770100
C	4.01030900	-1.67591500	-0.68440200
H	4.55002100	-2.31641600	-1.36909800
C	-4.01070200	-0.17691800	-1.21038500
H	-4.53221200	0.35816500	-1.99384200
C	1.67412900	-2.15636300	-1.71636600
C	-1.72442200	0.69133600	-2.02799800
H	-1.49374100	0.04843400	-2.88089200
H	-2.23222900	1.57929200	-2.41192200
C	-4.01130000	-1.67383200	0.68418500
H	-4.55137600	-2.31413100	1.36878600
C	2.63494900	-1.51099300	-0.75770800
C	1.72490700	0.69042700	2.02801600
H	1.49390000	0.04764600	2.88091100
H	2.23323000	1.57810100	2.41192200
C	4.01066400	-0.17901300	1.21018100
H	4.53253300	0.35584100	1.99355200
C	-0.54200900	2.28020400	-0.54026100
H	-1.51840300	2.24672800	-0.04425500
C	-4.70095300	-0.98415600	-0.31476700
H	-5.77622500	-1.08524100	-0.39282600
C	0.54335000	2.27990600	0.54025400
H	1.51969600	2.24580300	0.04420800
C	4.70041300	-0.98656700	0.31446300
H	5.77565200	-1.08813000	0.39236000
C	0.44936500	3.54601600	1.40002400
H	1.24088000	3.54146800	2.15387900
H	-0.50797700	3.53313900	1.93535400
C	-0.44719400	3.54621900	-1.40008600
H	0.51016900	3.53273100	-1.93536500
H	-1.23867800	3.54217300	-2.15397800
C	0.53887900	4.81420100	0.54456300
H	1.53075100	4.87262000	0.08186400
H	0.43396200	5.69369200	1.18531300
C	-0.53594900	4.81448600	-0.54468300
H	-0.43052200	5.69389000	-1.18546500
H	-1.52777800	4.87350400	-0.08197800

Ni	-0.00017900	-0.55344600	0.00009600
N	2.14504900	-2.92373700	-2.69557500
N	-2.14693600	-2.92225000	2.69578900
H	1.49676000	-3.36304700	-3.33405700
H	3.12976900	-3.07614300	-2.84780400
H	-3.13176400	-3.07404800	2.84793300
H	-1.49896300	-3.36197900	3.33430300

E(UTPSSh) = =-2765.4871973 Hartree
Zero-point correction = 0.458272
Thermal correction to Energy = 0.484051
Thermal correction to Enthalpy = 0.484995
Thermal correction to Gibbs Free Energy = 0.402981
Sum of electronic and zero-point Energies = -2765.028925
Sum of electronic and thermal Energies = -2765.003147
Sum of electronic and thermal Enthalpies = -2765.002202
Sum of electronic and thermal Free Energies = -2765.084217

Table S2. [Ni(chxdedpa)], TPSSh/TZVP, aqueous solution (0 Imaginary Frequencies)

Atom	Coordinates (Angstroms)		
	X	Y	Z
O	-0.43392000	-2.00120700	1.56128900
O	0.43548400	-2.00152200	-1.56161500
O	-2.17026300	-2.94983000	2.64265000
N	-1.98389100	-0.75586600	-0.10908500
N	1.98443400	-0.75456500	0.10916800
N	0.45328000	0.98995100	1.35292800
H	-0.26250400	1.10732700	2.06661400
O	2.17285100	-2.94906900	-2.64216200
C	2.63738400	-0.08643300	1.06208000
C	-2.63731400	-0.08840300	-1.06215600
N	-0.45407200	0.98971900	-1.35335400
H	0.26153900	1.10773500	-2.06711000
C	-1.68033700	-2.22836200	1.75940300
C	-2.61706600	-1.52554200	0.78416100
C	4.00143100	-1.64312000	-0.76072700
H	4.50055800	-2.26793100	-1.48956700
C	-4.02603500	-0.15457800	-1.14004900
H	-4.56047200	0.39449000	-1.90559500
C	1.68215000	-2.22773100	-1.75924400
C	-1.73568500	0.65535400	-2.02267200
H	-1.50701200	-0.00243300	-2.86473000
H	-2.24067500	1.53992700	-2.42060400
C	-4.00023100	-1.64581500	0.76094900
H	-4.49887700	-2.27088900	1.48989200
C	2.61816800	-1.52393400	-0.78397700
C	1.73511500	0.65676800	2.02241600
H	1.50691200	-0.00107600	2.86456100
H	2.23935500	1.54181500	2.42024100
C	4.02614900	-0.15154000	1.14000500

H	4.56017400	0.39803800	1.90547200
C	-0.54512400	2.23554500	-0.53977700
H	-1.51908500	2.20060600	-0.03826500
C	-4.70732700	-0.94247900	-0.21406600
H	-5.78827900	-1.00857000	-0.25514100
C	0.54335200	2.23591000	0.53945200
H	1.51732200	2.20173800	0.03791300
C	4.70801600	-0.93909500	0.21416200
H	5.78901500	-1.00440500	0.25525900
C	0.45397100	3.50619600	1.39525200
H	1.24775900	3.50162400	2.14708700
H	-0.50149100	3.49374100	1.93460400
C	-0.45667100	3.50597600	-1.39545200
H	0.49882700	3.49430300	-1.93476100
H	-1.25042400	3.50091500	-2.14732300
C	0.53905300	4.77514200	0.54116600
H	1.52767700	4.83272200	0.07088700
H	0.43950700	5.65567100	1.18191400
C	-0.54273100	4.77477500	-0.54124900
H	-0.44386200	5.65545600	-1.18189200
H	-1.53139400	4.83154200	-0.07096000
Ni	0.00022700	-0.64663600	0.00016200

E(RTPSSh) = -2804.3388168 Hartree
Zero-point correction = 0.407795
Thermal correction to Energy = 0.432332
Thermal correction to Enthalpy = 0.433276
Thermal correction to Gibbs Free Energy = 0.353332
Sum of electronic and zero-point Energies = -2803.931021
Sum of electronic and thermal Energies = -2803.906485
Sum of electronic and thermal Enthalpies = -2803.905541
Sum of electronic and thermal Free Energies = -2803.985484