Electronic Supplementary Information

Catalytic Enantiospecific Deuteration of Complex Aminoacid Mixtures with Ruthenium Nanoparticles

Gabriel Mencia,[a] Pauline Rouan,[b] Pier-Francesco Fazzini,[c] Hanna Kulyk,[b] **Victor Varela-Izquierdo,**[a] *Guy Lippens,[b] Bruno Chaudret[a]*

[a] Laboratoire de Physique et Chimie des Nano-Objets, Université de Toulouse, LPCNO, INSA, UPS, CNRS-UMR5215, 135 Avenue de Rangueil, 31077 Toulouse, France E-mail: chaudret@insa-toulouse.fr

[b] Toulouse Biotechnology Institute (TBI), University of Toulouse, CNRS, INRAE, INSA Toulouse, 135 Avenue de Rangueil, 31400 Toulouse Cedex, France

[c] CEMES-CNRS, Université de Toulouse, CNRS, 29 rue Jeanne Marvig, 31055 Toulouse, France

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1. General procedures and characterization techniques

Reagents

[Ru(COD)(COT)] precursor was purchased from Nanomeps Toulouse, $Ni(COD)_2$ from Alfa-Aesar, tetrahydrofuran from CARLO ERBA, D_2 gas from Air liquid (France), Deuterated solvents from Eurisotop, H_2 from Hydrogen Gas Generator AVANTEC model 40H (water electrolysis). 2,6-diisopropylaniline, formaldehyde, glyoxal, ammonium chloride, acetic acid, propanesultone and potassium tert-butoxide were purchased from Merck. All the reagents were used without further purification.

Transmission Electron Microscopy (TEM)

MNPs were observed by TEM after the deposition of a drop of a solution of the isolated NPs suspended in water over a copper grid coated with amorphous carbon. TEM analyses were performed at Raimond Castaing Microanalysis Centre (UAR 3623) (Toulouse, France) using a JEOL JEM 1400 electron microscope working at 120 kV. The NPs average size approximation was made by manual analysis of the magnified micrographs measuring 200 particles on a given grid using ImageJ software.

High Resolution TEM coupled to Energy Dispersive X-ray Spectroscopy (HR-TEM-EDX)

MNPs were observed by HR-TEM after the deposition of a drop of a solution of the isolated MNPs suspended in THF or water over a holey carbon-coated copper grid. HR-TEM analysis was performed at Raimond Castaing Microanalysis Centre (UAR 3623) (Toulouse, France). TEM and scanning transmission electron microscopy (STEM) studies were performed using a JEOL cold-FEG JEM-ARM200F operated at 200kV equipped with a probe Cs corrector reaching a spatial resolution of 0.078 nm. EDX spectra were recorded on a JEOL CENTURIO SDD detector.

Thermogravimetric analysis (TGA)

TGA analyses were performed in a TGA/DSC 1 STAR System equipped with an ultra-microbalance UMX5, a gas switch GC200 and sensors DTA and DSC. The samples were analyzed through a two steps oxidation/reduction method. First the sample was heated from 25 °C to 500 °C at 20°C/min under air and kept at 500 ºC during 2h. After cooling down, it was heated again from 25 °C to 700 °C at 30 °C/min under a gas mixture Ar/H_2 4% and kept at 700 ºC during 3h.

Inductively coupled plasma atomic emission spectroscopy

Chemical composition of the powder was determined by inductively coupled plasma mass spectrometry (ICP-MS, Pascher laboratory) after digestion in acid media.

Nuclear Magnetic Resonance (NMR)

^{1}H-NMR experiments were recorded in a 500 MHz Bruker Avance spectrometer using deuterated solvents as internal reference.

Catalytic assay

Catalytic assays were carried out, generally, using L-lysine as model substrate. Thus, 0.150 mmol of the substrate, 2 mL of D_2O, and 8 mol% of the corresponding metals (based on TGA, and ICP-MS analysis of the nanocatalysts), were added to a Fischer-Porter flask (100 mL). Reactor was pressurized with 2 bars of D_2 and the reaction was stirred at 55 ºC during 48 h. Then, an aliquot of the reaction was taken for NMR analysis. The deuteration percentage was calculated from the relationship between the integrals from the starting substrate and product.

Example of the calculations for the deuterium incorporation:

$$\%\ no\ deuterated\ (\alpha - Lys): \frac{I(\alpha - Lys^1)}{I(\alpha - Lys^0)} \times 100$$

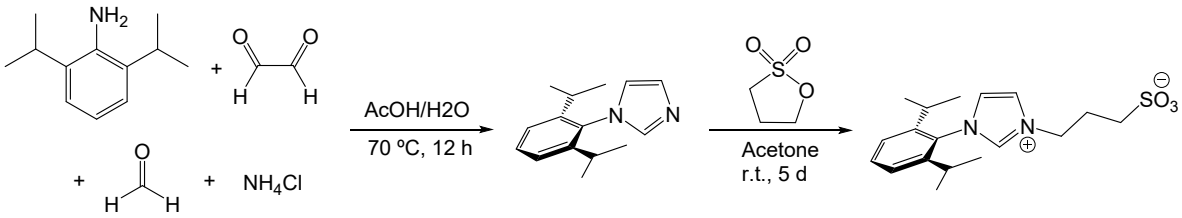
$$\%\ deuterium\ incorporation\ (\alpha - Lys): 100 - \%\ no\ deuterated\ (\alpha - Lys)$$

Being α-Lys^1 the integral for Lys-H$^\alpha$ obtained from the different ^{1}H-NMR experiments.

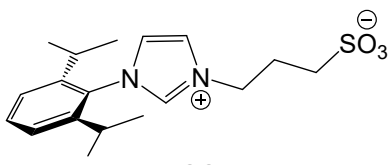
Being α-Lys^0 the maximum integral value for Lys-H$^\alpha$.

2. Synthesis and characterization data for imidazolium salt and free carbene

Imidazolium salt (**IPrPrSO$_3$H**) was synthesized following the method previously described by Shaugnessy and co-workers (Scheme S1).[1]



Scheme S1. Synthesis of imidazolium salt **IPrPrSO$_3$H**.

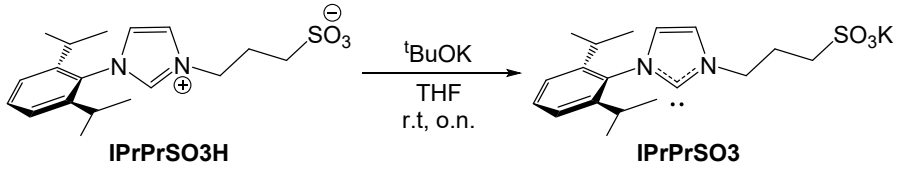


IPrPrSO3H

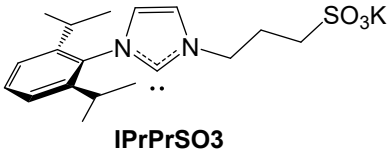
IPrPrSO$_3$H: glacial acetic acid (17.5 mL), formaldehyde (37 % aqueous solution, 5.00 mL, 66.70 mmol) and glyoxal (40 % aqueous solution, 8.20 mL, 71.80 mmol) were added with constant stirring at rt in a two-necked round-bottom flask. Subsequently, ammonium acetate (5.43 g, 70.45 mmol), glacial acetic acid (17.5 mL) and water (1.5 mL) were mixed in an addition funnel, to which 2,6-diisopropylaniline (13.80 mL, 66.05 mmol) was added. The solution containing the aniline was added dropwise into the two-necked round-bottom flask, previously heated to 70 ºC. Then, it was stirred at 70 ºC for 48 hours and allowed to cool to room temperature (r. t.). The solution obtained was added to a saturated $NaHCO_3$ solution, allowing neutralization, and stirred for 1 hour at r. t. Precipitate was filtered using a Büchner funnel and the brown residue was sublimated under vacuum at 80 ºC over night. To form the propylsulfonate chain, 1-(2,6-diisopropylphenyl)-

1*H*-imidazole (2.24 g, 9.81 mmol) was added to acetone in a Schlenk flask with propanesultone in excess (2.39 g, 19.6 mmol) and left to stir at r. t. for 5 days. **IPrPrSO$_3$H** was obtained as a white solid which is filtered and washed with acetone (3.22 g, 93.9%). (^{1}H-NMR D_2O, 500 MHz): δ = 9.15 (t, $^4J_{H,H}$= 1.6 Hz, 1H, CH^2 Im), 7.82 (dd, $^3J_{H,H}$= 1.9 Hz, $^4J_{H,H}$= 1.6 Hz, 1H, CH^5 Im), 7.69 (dd, $^3J_{H,H}$= 1.9 Hz, $^4J_{H,H}$= 1.6 Hz, 1H, CH^4 Im), 7.60 (t, $^4J_{H,H}$= 7.9 Hz, 1H, *p*-CH IPr), 7.43 (t, $^4J_{H,H}$= 7.9 Hz, 2H, *m*-CH IPr), 4.50 (t, $^3J_{H,H}$= 7.0 Hz, 2H, $CH_2CH_2CH_2$), 2.44 (t, $^3J_{H,H}$= 7.0 Hz, 2H, $CH_2CH_2CH_2$), 2.39 (quint, $^3J_{H,H}$= 7.2 Hz, 2H, $CH_2CH_2CH_2$), 2.31 (hept, 2H, $^3J_{H,H}$= 7.0 Hz, *o*-$CH(CH_3)_2$ IPr), 1.12 (d, 6H, $^3J_{H,H}$= 2.5 Hz, *o*-$CH(CH_3)_2$ IPr), 1.11 (d, 6H, $^3J_{H,H}$= 2.2 Hz, *o*-$CH(CH_3)_2$ IPr) ppm.

IPrPrSO$_3$: N-heterocyclic carbene was synthesized *in situ* and their ^{1}H NMR spectrum were recorded from an aliquot extracted before being used as stabilizer for MNPs. The free carbene was generated by the addition of potassium *tert*-butoxide (1.1 eq) to the imidazolium salt (1 eq) solution in THF (30 mL) and allowed to react overnight.



Scheme S2. Synthesis of **IMesPrSO$_3$**.



IPrPrSO$_3$: 0.0561 g (0.160 mmol) of **IPrPrSO$_3$H** and 0.0198 g (0.176 mmol) of potassium *tert*-butoxide were added in a Schlenck tube with 30 mL of THF and allowed to react for 16 h (Scheme S2). Afterwards, an aliquot was taken and evaporated under vacuum before being re-dissolved in THF-d_8 under inert atmosphere. ^{1}H-NMR spectrum was recorded immediately afterwards. (^{1}H-NMR THF-d_8, 500 MHz): 7.13 (d, $^3J_{H,H}$= 7.9 Hz, 2H, *m*-CH IPr), 6.91 (t, $^3J_{H,H}$= 7.6 Hz, 1H, *p*-CH IPr), 3.99 (m, 4H, $CH_2CH_2CH_2$), 1.68 (m, 5H, $CH_2CH_2CH_2$ + *o*-$CH(CH_3)_2$ IPr), 1.18 (s, 6H, *o*-$CH(CH_3)_2$ IPr) ppm.

3. Synthesis and characterization data for Ru and Ru-Ni nanoparticles

All the nanoparticles synthesis were carried out inside the glove box and under inert atmosphere. Ru-based NPs were synthesized using the procedure known as the organometallic approach.

Ru@IPrPrSO3[2] and **Ru@PTA**[3] were synthesized as it was previously described in the literature.

Ru-Ni@IPrPrSO$_3$: **IPrPrSO$_3$** was synthesized before used it as stabilizer, as it was already mentioned (Scheme S2). The free carbene was formed by the addition of 19.8 mg of potassium *tert*-butoxide (0.176 mmol) to 56.1 mg of **IMesPrSO$_3$H** (0.160 mmol) solution in THF (30 mL) and allowed to react overnight. Ru(COD)(COT) and Ni(COD)$_2$ in different molar percentages (1:1, 1:4) (total of 0.8 mmol) were added to a Fischer-Porter under inert atmosphere with THF (30 mL) under inert atmosphere. Subsequently, free carbene solution was added (0.2 eq). 3 bars of H_2 were used to pressurize and allowed to react at r. t. overnight.

Finally, solvent was removed under vacuum (up to 2 mL aprox.) and the Ru-Ni NPs were precipitated and washed with pentane (3 x 30 mL) and dried under vacuum overnight.

RuNi@IPrPrSO$_3$: 0.0561 g (0.160 mmol) of **IMesPrSO$_3$H** and 0.0198 g (0.176 mmol) of potassium *tert*-butoxide were used, along with 0.1254 g (0.4001 mmol) of Ru(COD)(COT) and 0.1100 g (0.3999 mmol) of Ni(COD)$_2$ with the method above described (116.3 mg; 92.2 %). Metal weight percentage of 51.3% (0.196 eq. of NHC) determined by TGA. **Ru:Ni molar ratio:** 53:47, determined by ICP-MS. **TEM:** 1.5 ± 0.3 nm.

RuNi$_4$@IPrPrSO$_3$: 0.0561 g (0.160 mmol) of **IMesPrSO$_3$H** and 0.0198 g (0.176 mmol) of potassium *tert*-butoxide were used, along with 0.0501 g (0.160 mmol) of Ru(COD)(COT) and 0.1760 g (0.6399 mmol) of Ni(COD)$_2$ with the method above described (108.9 mg; 93.9 %). Metal weight percentage of 45.1% (0.211 eq. of NHC) determined by TGA. **Ru:Ni molar ratio:** 22:78, determined by ICP-MS. **TEM:** 1.3 ± 0.2 nm.

Supported Ru NPs: Ru(COD)(COT) and the support, in a weight ratio of 10%, were added to a Fischer-Porter under inert atmosphere with THF (5 mL). The mixture was stirred during 24 h for wet impregnation. Subsequently, 3 bars of H_2 were used to pressurize the reactor and reaction was stirred at r. t. overnight. Finally, solvent was removed under vacuum and the supported Ru NPs were washed with pentane (3 x 30 mL) and dried under vacuum overnight.

Ru/C: 0.3442 g (1.10 mmol) of Ru(COD)(COT) and 1 g of Carbon were used for the method above described (1.087 g; 97.9 %). Metal weight percentage of 9.9 % determined by TGA. **TEM:** 3.0 ± 0.6 nm.

Ru/Cmeso: 0.3442 g (1.10 mmol) of Ru(COD)(COT) and 1 g of Mesoporous Carbon were used for the method above described (1.063 g; 95.7 %). Metal weight percentage of 12.6 % determined by TGA. **TEM:** 2.6 ± 0.5 nm.

4. ICP-MS determination

Table S1. Mass and molar percentages of Ru and Ni in bimetallic NPs determined by ICP-AES.

Entry	MNPs	Ru ppm	Ni ppm	Mass (mg)	Vol (mL)	Ru % mass	Ni % mass	Ru:/Ni mol ratio
1	**RuNi@IMesPrSO$_3$**	66.38	33.42	9.31	50	35.65	17.95	53:47
2	**RuNi$_4$@IMesPrSO$_3$**	26.43	54.84	9.63	50	13.72	28.47	22:78

5. XRD measurements for Ru-Ni NPs and Supported Ru NPs

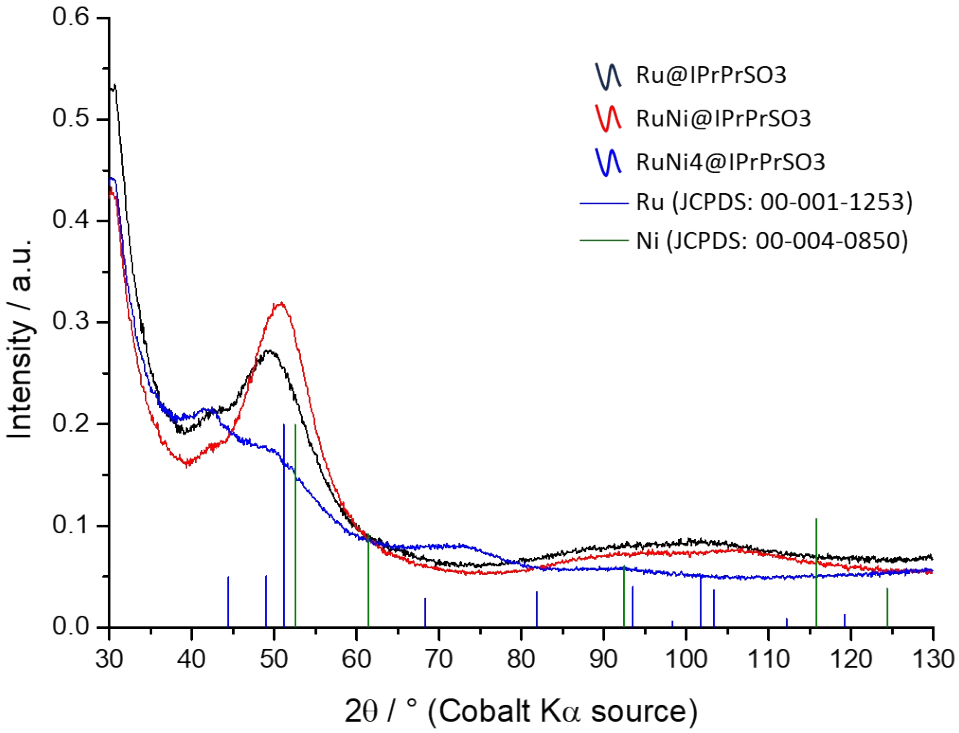


Figure S1. XRD diffractogram for **Ru/Ru-Ni NPs** systems. References: Ru hcp and Ni fcc structures.

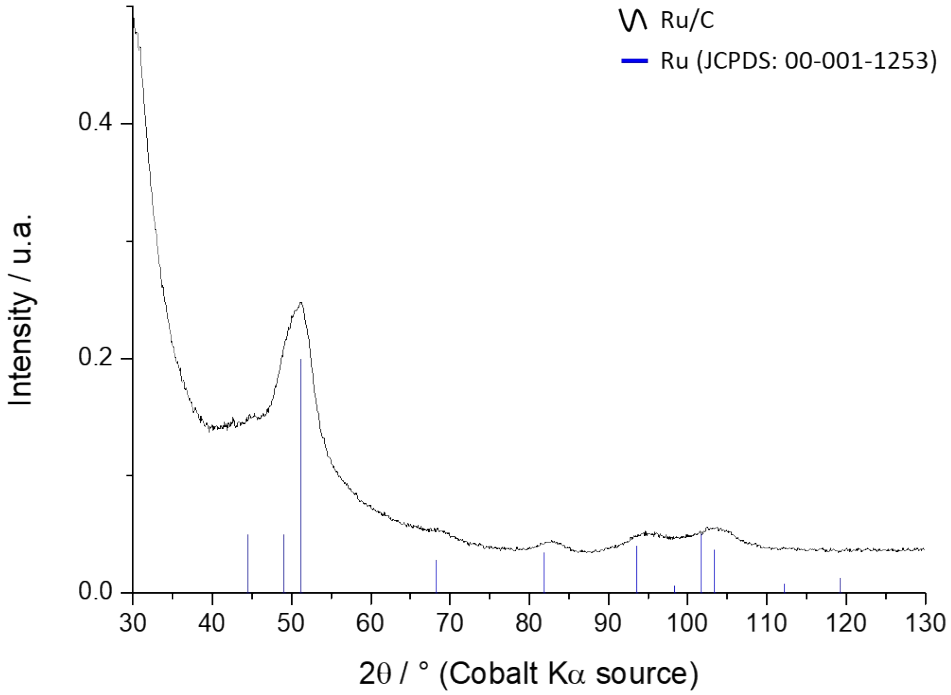


Figure S2. XRD diffractogram for **RuNP/C** system showing an hcp structure.

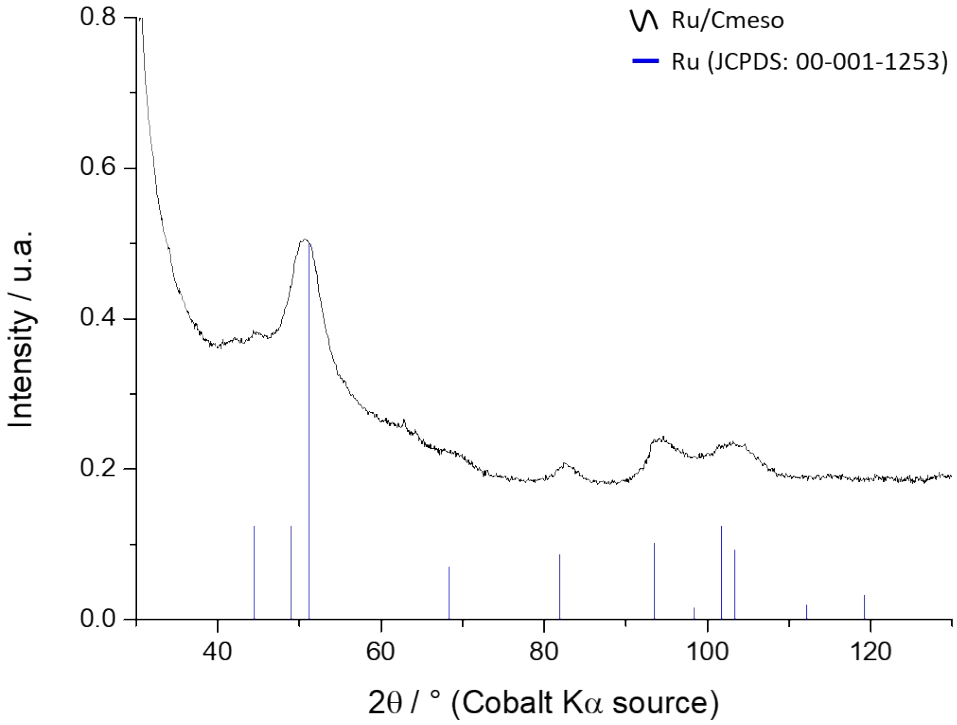


Figure S3. XRD diffractogram for **RuNP/Cmeso** system showing an hcp structure.

6. TEM images for Ru and Ru-Ni NPs

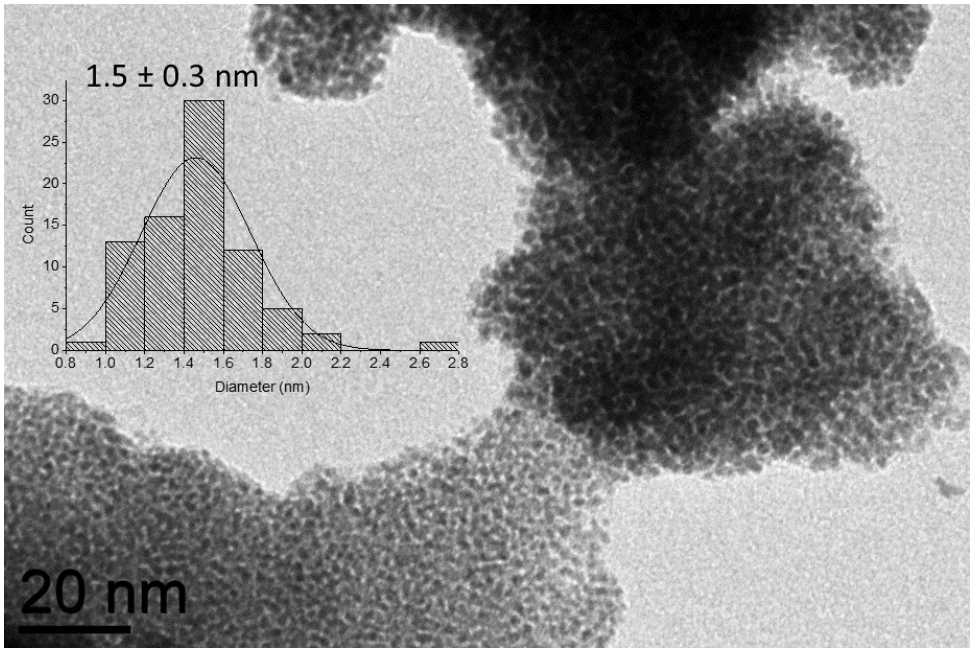


Figure S4. TEM micrograph and size distribution for **Ru@IPrPrSO$_3$** NPs.

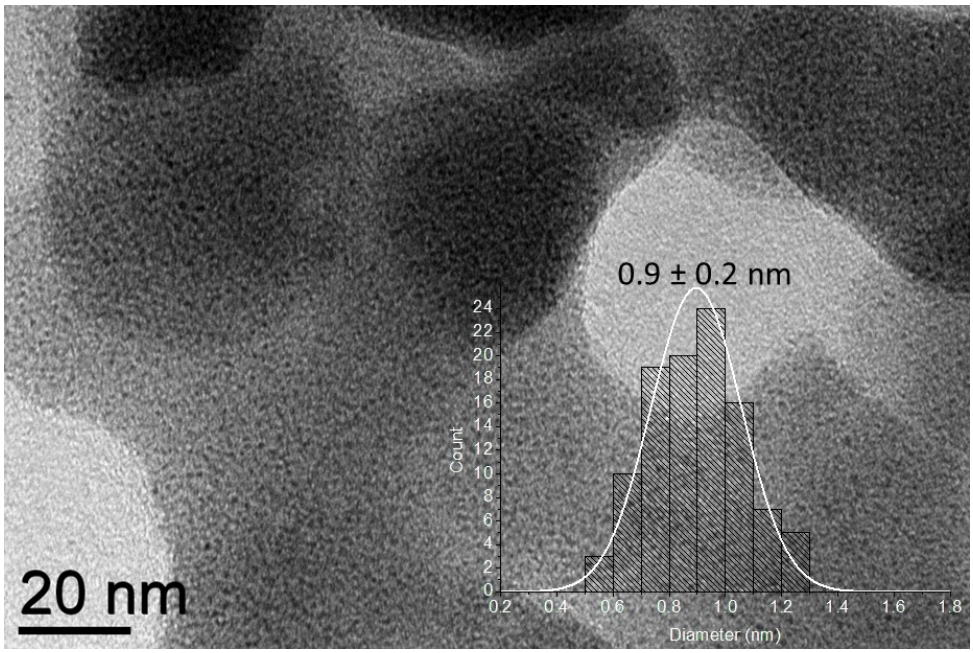


Figure S5. TEM micrograph and size distribution for **Ru@PTA** NPs.

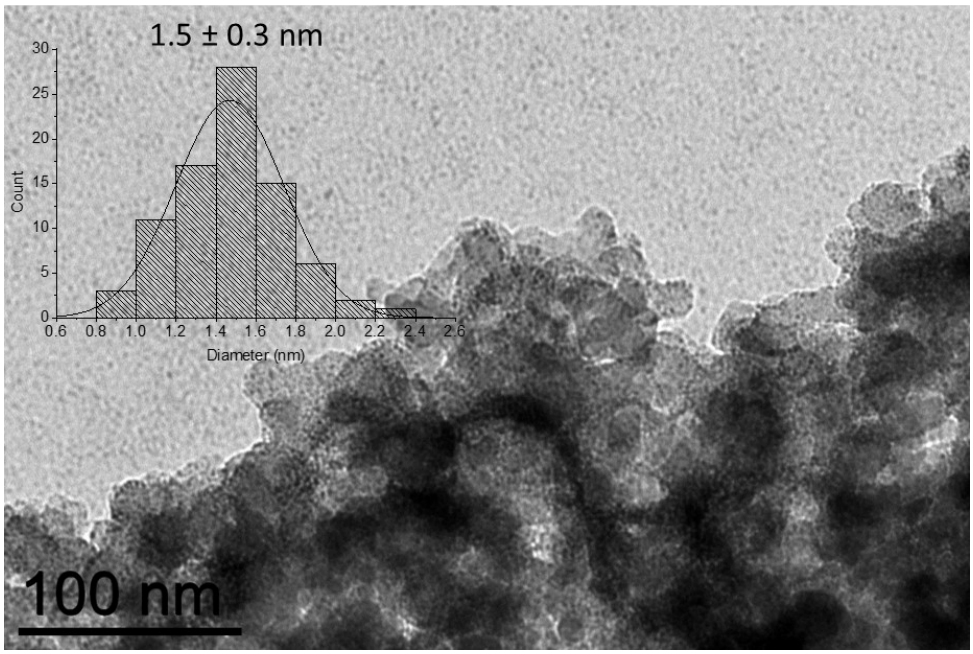


Figure S6. TEM micrograph and size distribution for **RuNi@IPrPrSO$_3$** NPs.

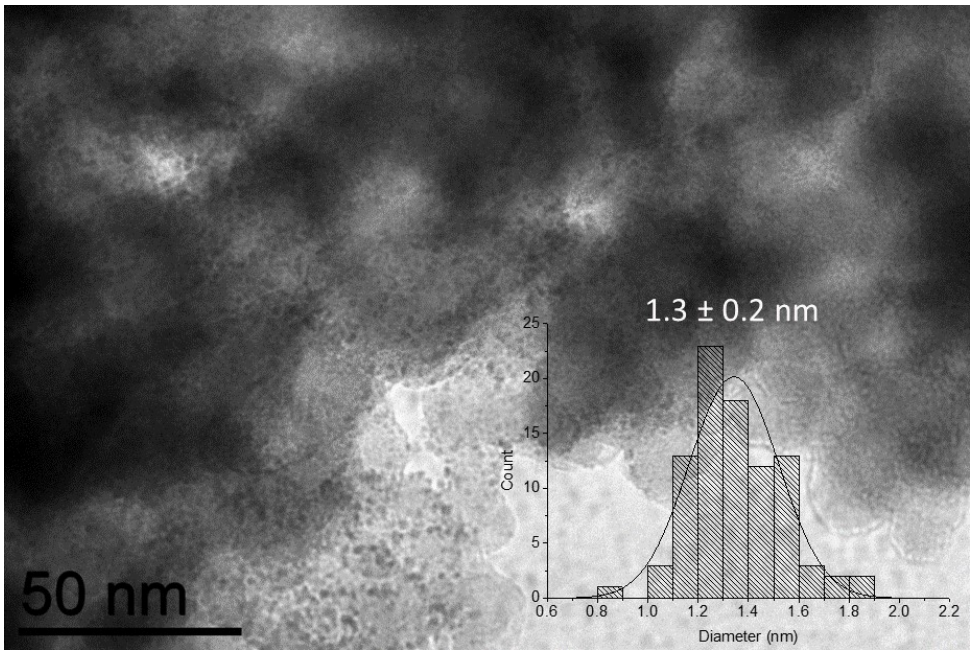


Figure S7. TEM micrograph and size distribution for **RuNi4@IPrPrSO$_3$** NPs.

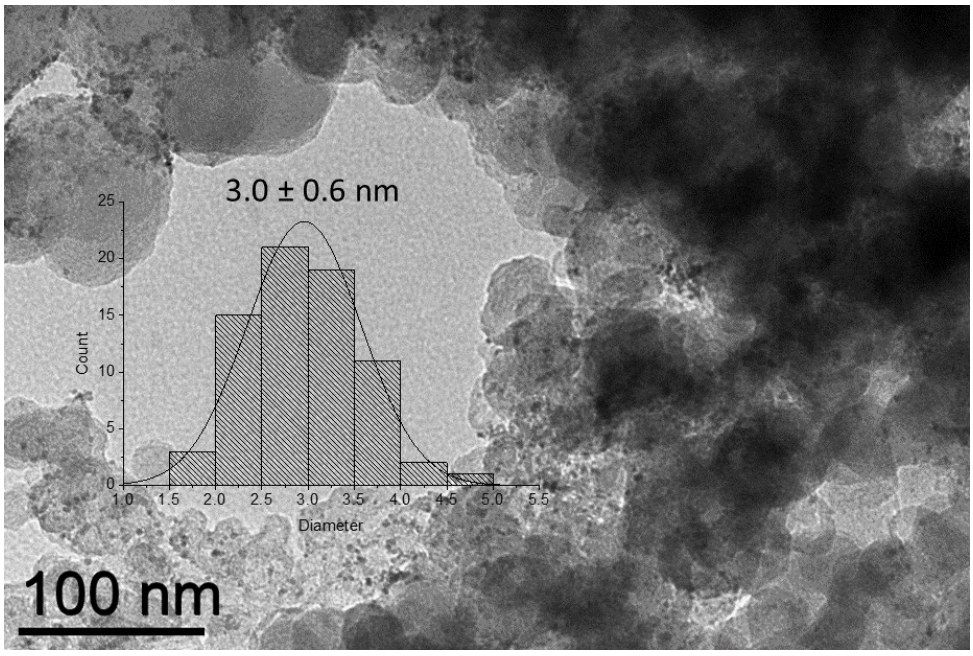


Figure S8. TEM micrograph and size distribution for **RuNP/C** NPs.

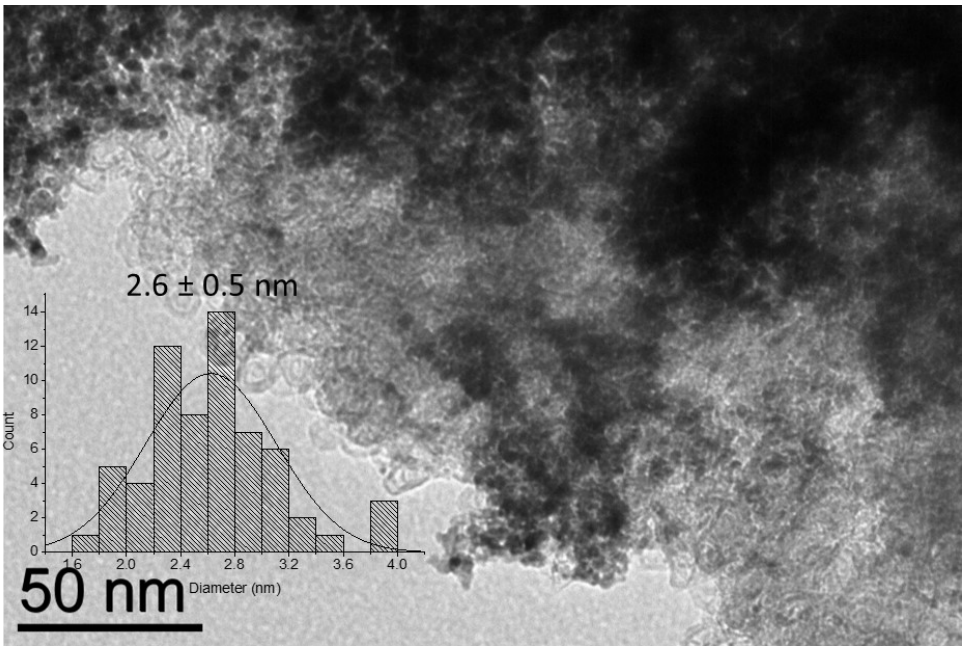


Figure S9. TEM micrograph and size distribution for **RuNP/Cmeso** NPs.

Table S2. Sizes of NPs obtained.

Entry	MNPs	Size (nm)
1	**Ru@IPrPrSO$_3$**	1.5 ± 0.3
2	**Ru@PTA**	0.9 ± 0.2
3	**RuNi@IPrPrSO$_3$**	1.5 ± 0.3
4	**RuNi4@IPrPrSO$_3$**	1.3 ± 0.2
5	**Ru/C**	3.0 ± 0.6
6	**Ru/Cmeso**	2.6 ± 0.5

7. HR-TEM images for Ru and Ru-Ni NPs

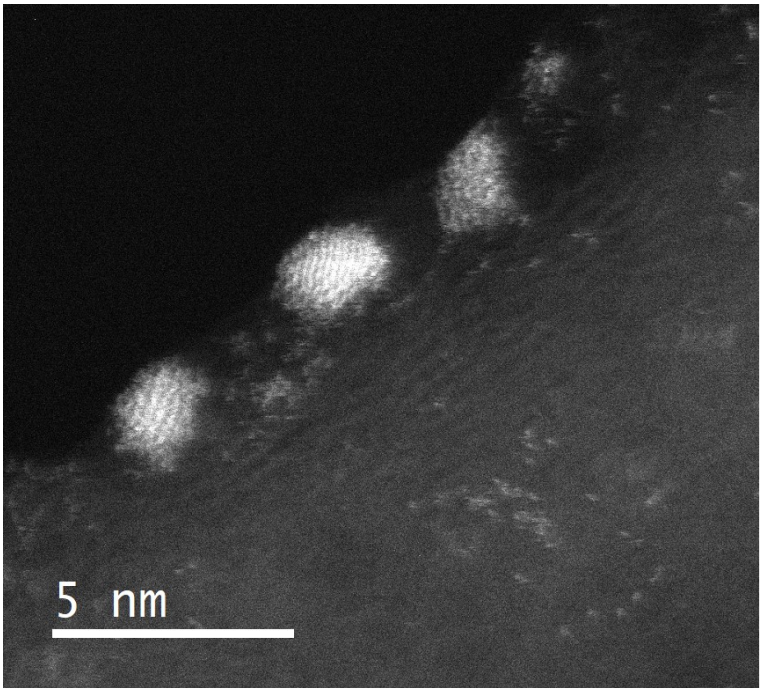


Figure S10. STEM-HAADF micrograph for **Ru@IPrPrSO$_3$** NPs.

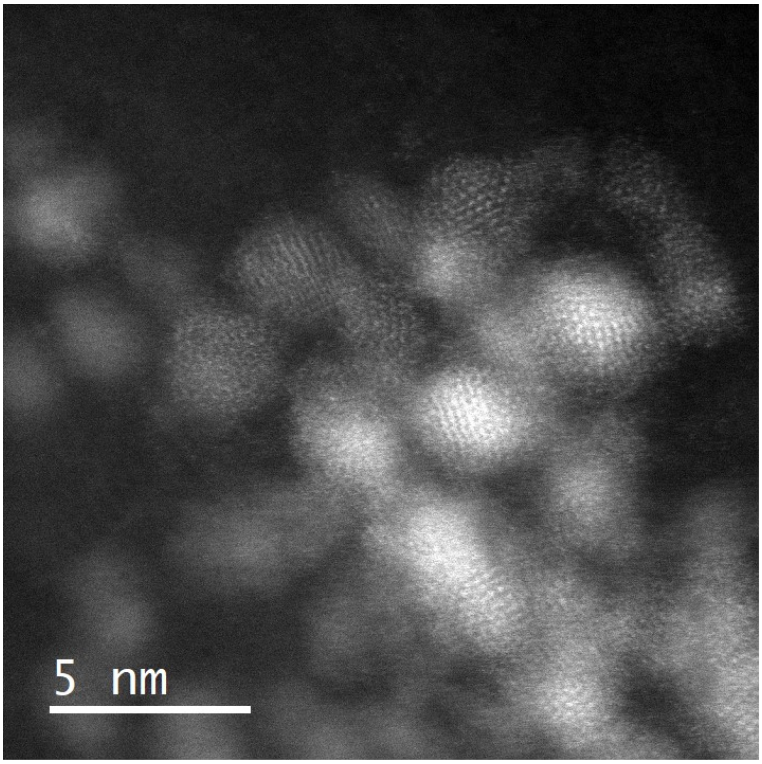


Figure S11. STEM-HAADF micrograph for **RuNi@IPrPrSO$_3$** NPs.

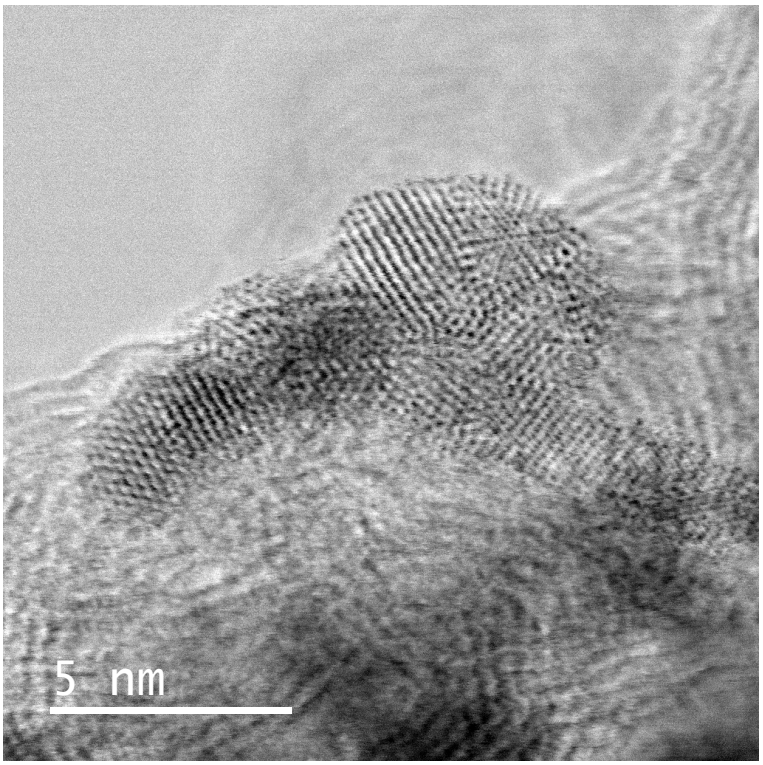


Figure S12. STEM-BF micrograph for **RuNP/Cmeso** NPs

8. EDX spectra for Ru-based NPs

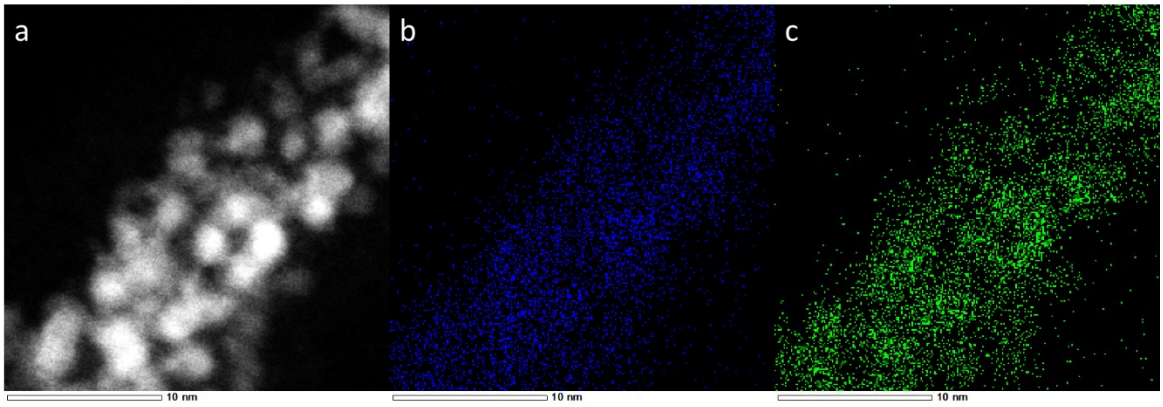


Figure S13. HR-STEM-HAADF image of **RuNi@IPrPrSO$_3$** NPs (a). Elemental mapping of Ru (b) and Ni (c).

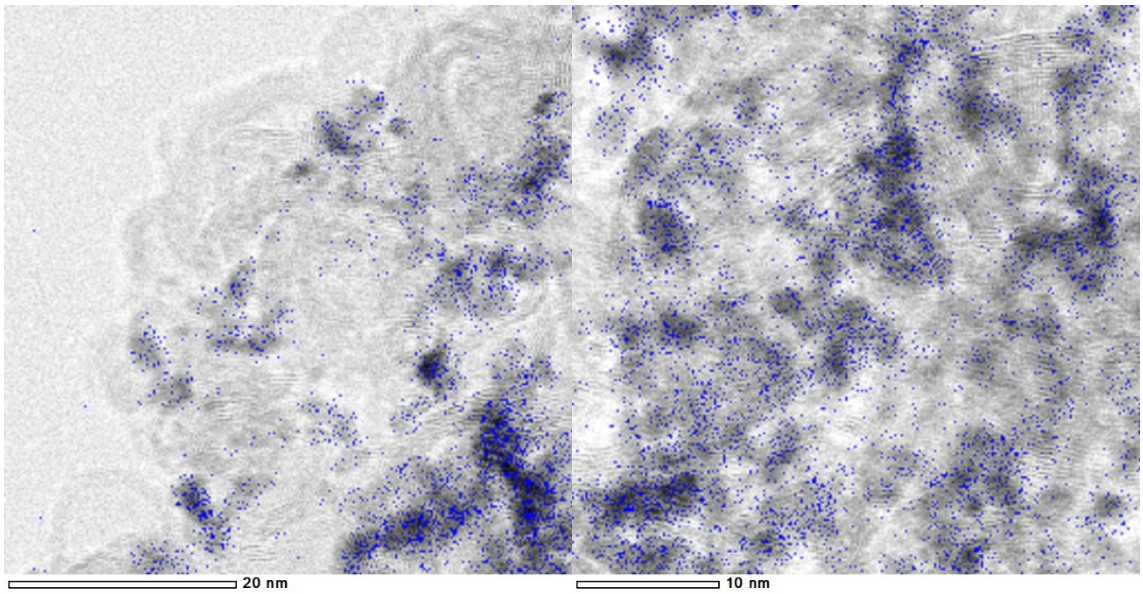


Figure S14. HR-STEM-EDX image of **RuNP/Cmeso**.

9. SEM images for supported Ru NPs

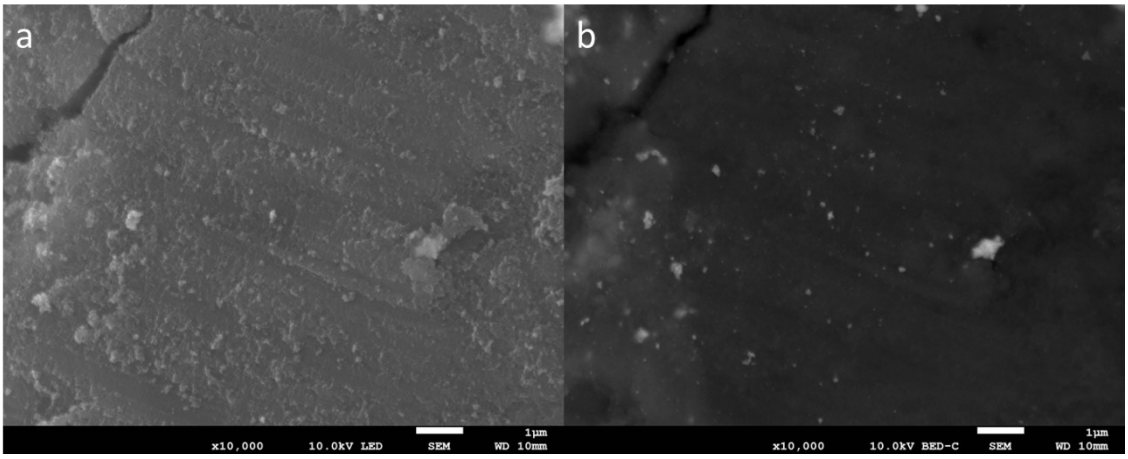


Figure S15. SEM (a) and SEM-BSE (b) images for RuNP/C.

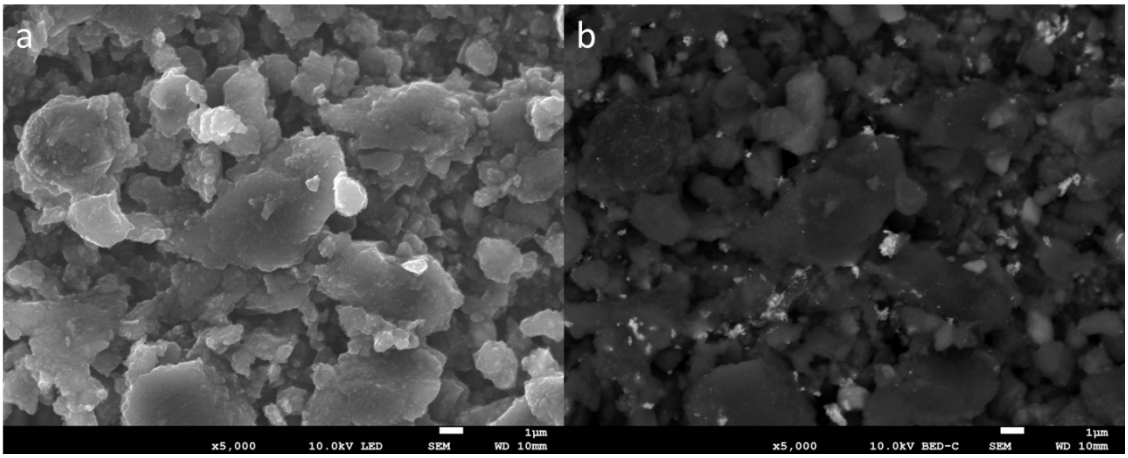
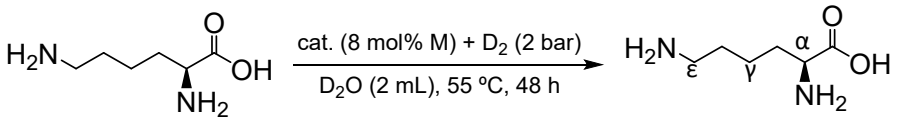


Figure S16. SEM (a) and SEM-BSE (b) images for RuNP/Cmeso.

10. H/D exchange of mixture of amino acids

Table S3. HIE reaction of L-lysine using mono and bimetallic NPs. Conditions: 2 bars of D_2, 55 °C and stirred for 48h.



L-Lysine

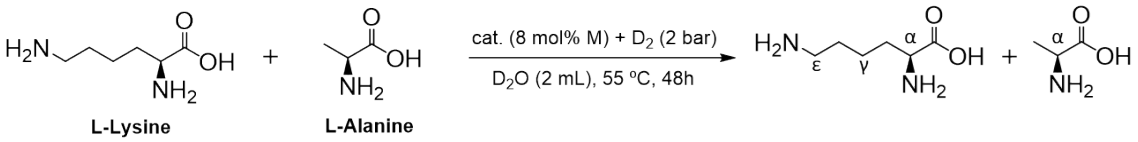
		Deuterium incorporation (%)[a]		
Entry	Catalyst	α	γ	ε
1	**Ru@IPrPrSO3**	99	30	99
2	**Ru@PTA**	98	0	73
3	**RuNi@IPrPrSO3**	98	24	98
4	**RuNi4@IPrPrSO3**	98	15	97
5	**Ru/C[b]**	99	12	99
6	**Ru/Cmeso[c]**	99	26	99

[a]Determined by ^{1}H-NMR spectroscopy. [b]Reaction conditions: 4 bars of D_2, 120 °C and stirred for 5h. [c]Reaction conditions: 4 bars of D_2, 120 °C and stirred for 30 min.

Table S4. Control experiments performed with Ru/Cmeso at different pHs and temperatures with and without catalyst and D_2 pressure. General conditions: 34 mM L-Lys, 12.1 mg of Ru/Cmeso (1.21 mg Ru 8 mol %), 2h.

Entry	Catalyst	Solvent	pH	D_2 pressure (bar)	Temperature (°C)	Deuterium incorporation (%)	
						α-Lys	ε-Lys
1	**Ru/C_{meso}**	D_2O	9	2	55	52	32
2	-	D_2O	9	2	55	3	<1
3	**Ru/C_{meso}**	D_2O	9	-	55	<1	<1
4	**Ru/C_{meso}**	D_2O	9	2	80	97	92
5	-	D_2O	9	2	80	12	4
6	**Ru/C_{meso}**	D_2O	9	-	80	<1	<1
7	**Ru/C_{meso}**	D_2O	7	2	55	<1	<1
8	-	D_2O	7	2	55	<1	<1
9	**Ru/C_{meso}**	D_2O	7	-	55	<1	<1

Table S5. Deuterium incorporation over a mixture of L-alanine and L-lysine with different MNPs as catalysts. General conditions: 8 mol% of metal, 55 °C, 2 bar D_2, 48h.



L-Lysine L-Alanine

Entry	Catalyst	[Ala] (mM)	[Lys] (mM)	pH	Deuterium incorporation (%)[a]		
					α-Ala	α-Lys	ε-Lys
1	**Ru@IPrPrSO3**	34	34	6	15	91	78
2	**Ru@IPrPrSO3**	68	68	6	5	59	56
3	**Ru@IPrPrSO3**	34	34	7.5	39	95	95
4	**Ru@IPrPrSO3**	34	34	9	14	82	55
5	**Ru@IPrPrSO3**	68	68	9	35	99	99
6	**Ru@IPrPrSO3**	34	34	7.5 (PBS 100 mM)	35	90	90
7	**Ru@IPrPrSO3**	34	34	7.5 (PBS 100 mM + 25 mM NaCl)	56	99	90
8	**Ru@IPrPrSO3**	68	68	7.5 (PBS 100 mM + 25 mM NaCl)	69	86	83
9	**Ru@IPrPrSO3**[b]	68	68	9	80	99	99
10	**Ru@PTA**	68	68	9	46	99	99
11	**Ru@PTA**	34	34	7.5 (PBS 100 mM)	10	90	28
12	**Ru@PTA**	34	34	7.5 (PBS 100 mM + 25 mM NaCl)	7	22	24
13	**Ru@PTA**	68	68	7.5 (PBS 100 mM + 25 mM NaCl)	7	26	20
14	**RuNi@IPrPrSO3**	34	34	7.5	7	30	10
15	**RuNi@IPrPrSO3**	34	34	9	15	90	90
16	**RuNi4@IPrPrSO3**	34	34	9	1	31	21
17	**Ru/Cmeso**[b]	68	68	7.5	98	98	98
18	**Ru/Cmeso**[b]	68	68	9	98	98	98

[a]Determined by 1D ^{1}H-NMR and/or 2D J-resolved ^{1}H-NMR spectroscopy. [b]Reaction conditions: 8 mol% of metal, 120 °C, 4 bar D_2, 1h.

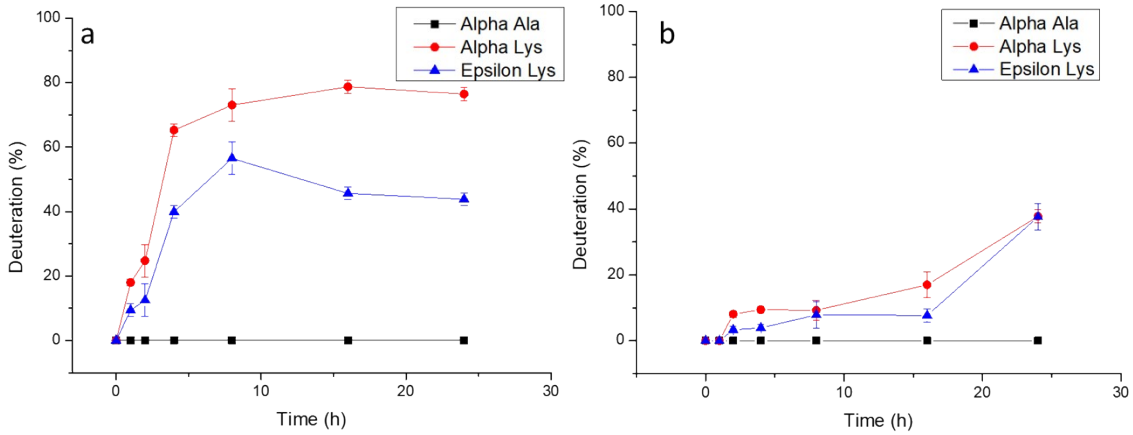


Figure S17. Deuteration Profiles of the mixture alanine/lysine at 30 °C (2 bar D_2) using Ru@IPrPrSO$_3$ (a) and RuNi@IPrPrSO$_3$ (b) as catalysts.

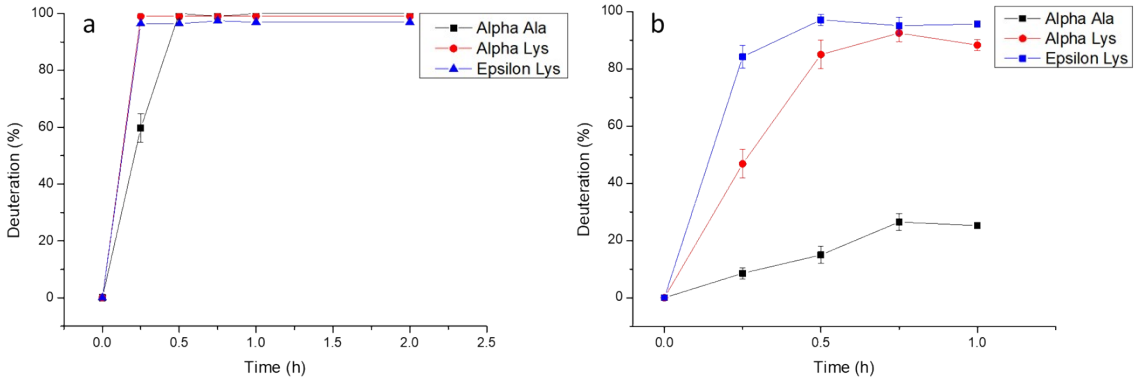


Figure S18. Deuteration Profiles of the mixture alanine/lysine at 120 °C (2 bar D_2) using Ru@IPrPrSO$_3$ (a) and RuNi@IPrPrSO$_3$ (b) as catalysts.

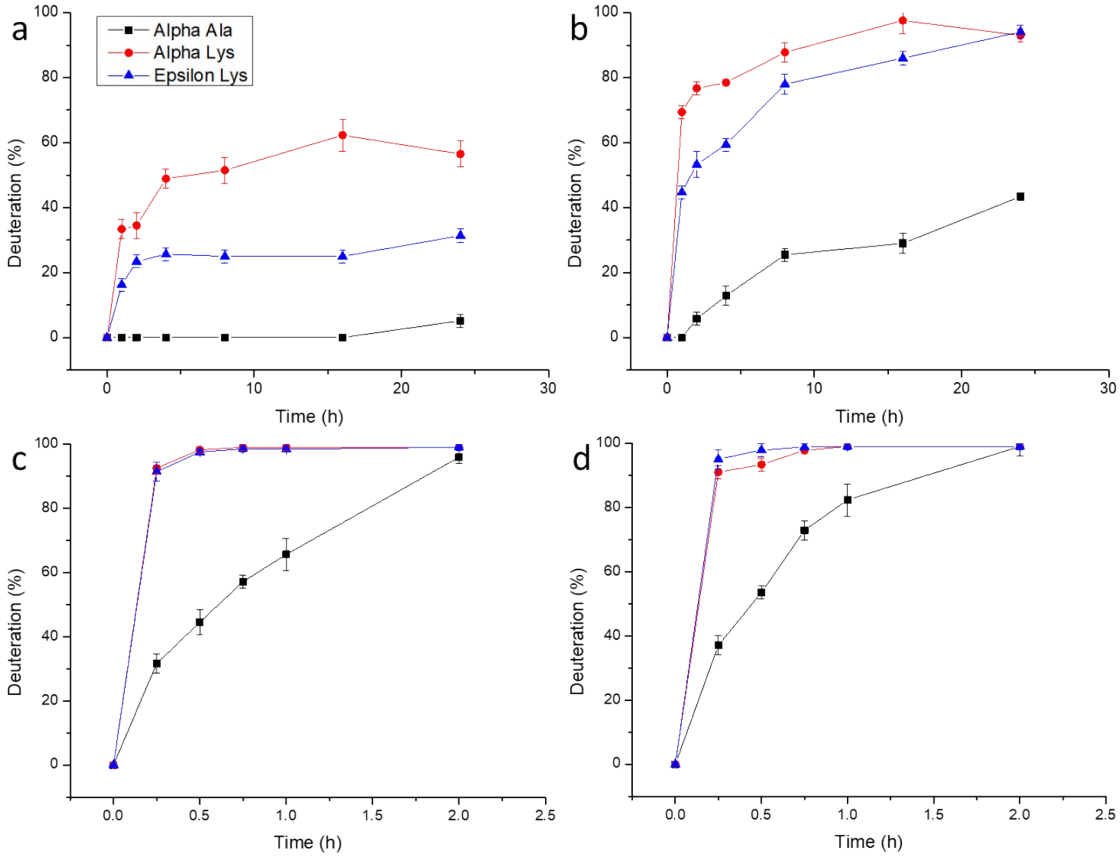


Figure S19. Deuteration Profiles of the mixture alanine/lysine using Ru/Cmeso and 2 bar of D_2 pressure at 30 ˚C (a), 55 ˚C (b), 120 ˚C (c), and under 4 bar of D_2 pressure at 120 ˚C (d).

11. NMR spectra

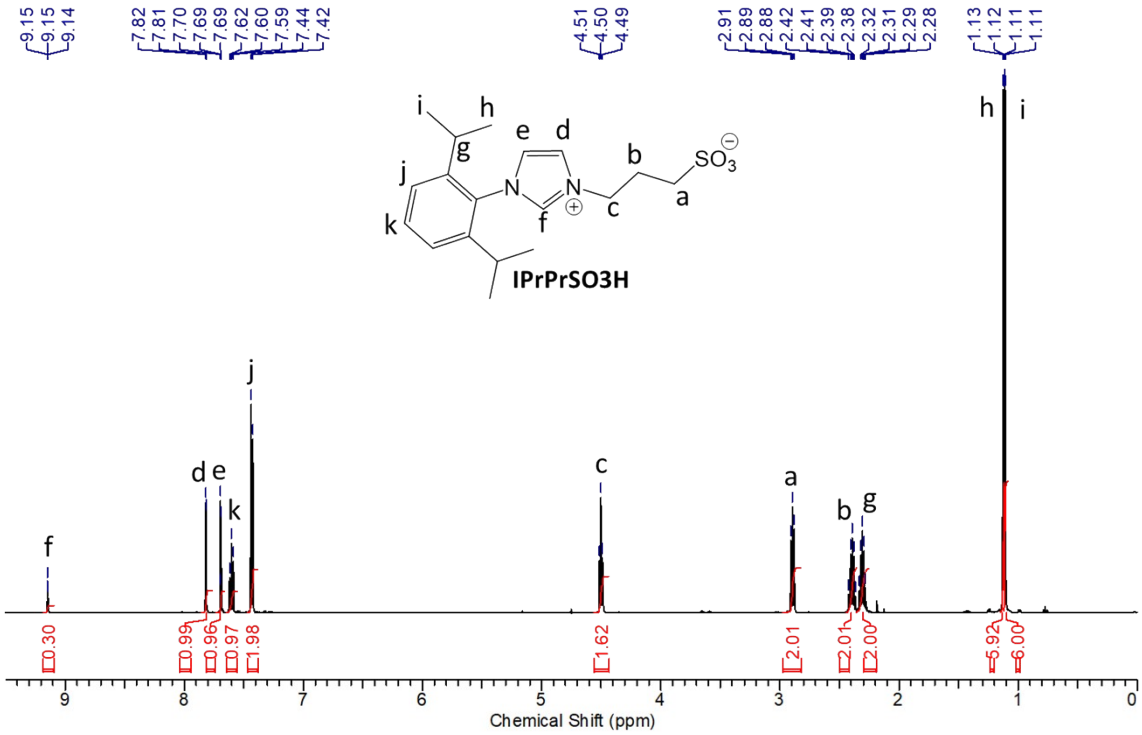


Figure S20. ^{1}H-NMR spectrum of **IPrPrSO$_3$H** in D_2O.

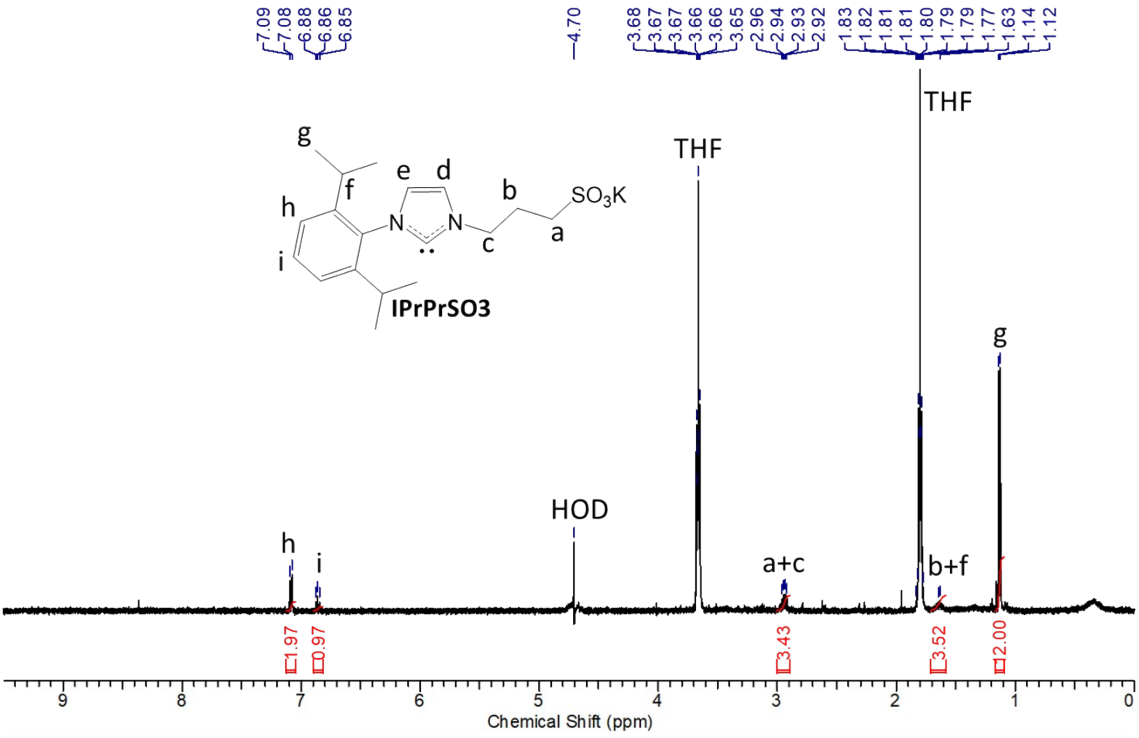


Figure S21. *In situ* ^{1}H-NMR spectrum of IPrPrSO$_3$ in THF-d_8.

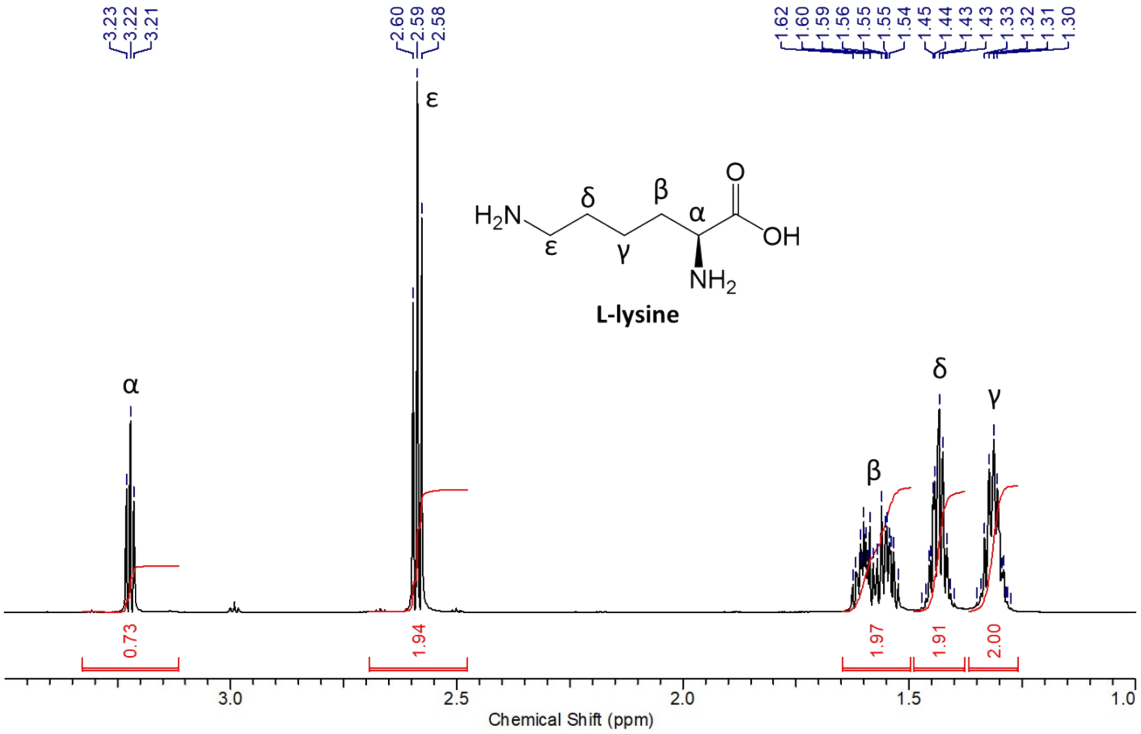


Figure S22. [1]H-NMR spectrum of L-lysine in D_2O.

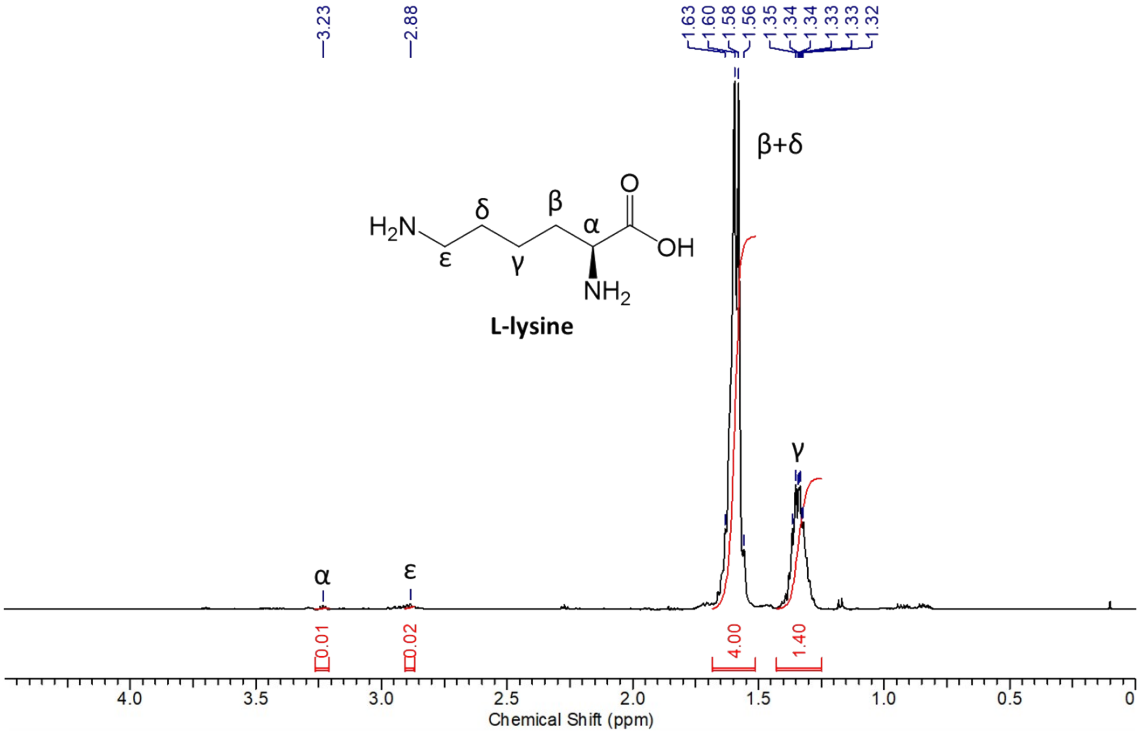


Figure S23. [1]H-NMR spectrum of L-lysine in D_2O after reacting with **Ru@IPrPrSO3** (8 mol% of metal, 55 °C, 2 bars D_2 during 48 h) (Table S3, entry 1).

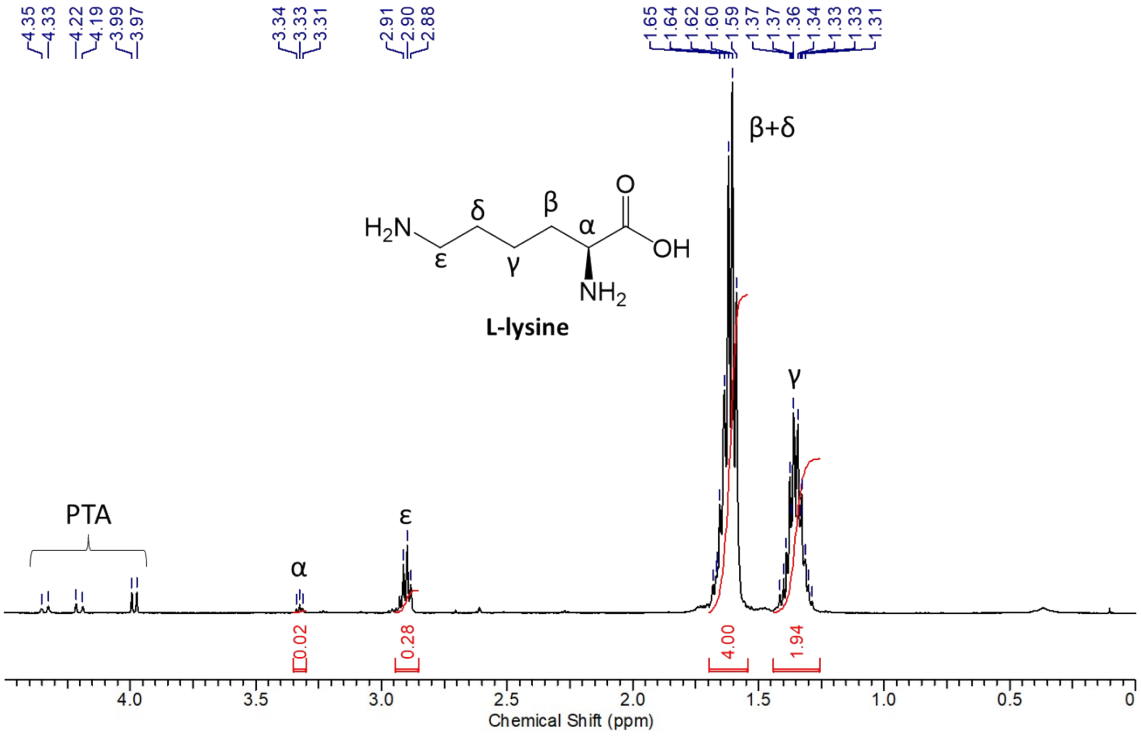


Figure S24. ^{1}H-NMR spectrum of L-lysine in D_2O after reacting with **Ru@PTA** (8 mol% of metal, 55 °C, 2 bars D_2 during 48 h) (Table S3, entry 2).

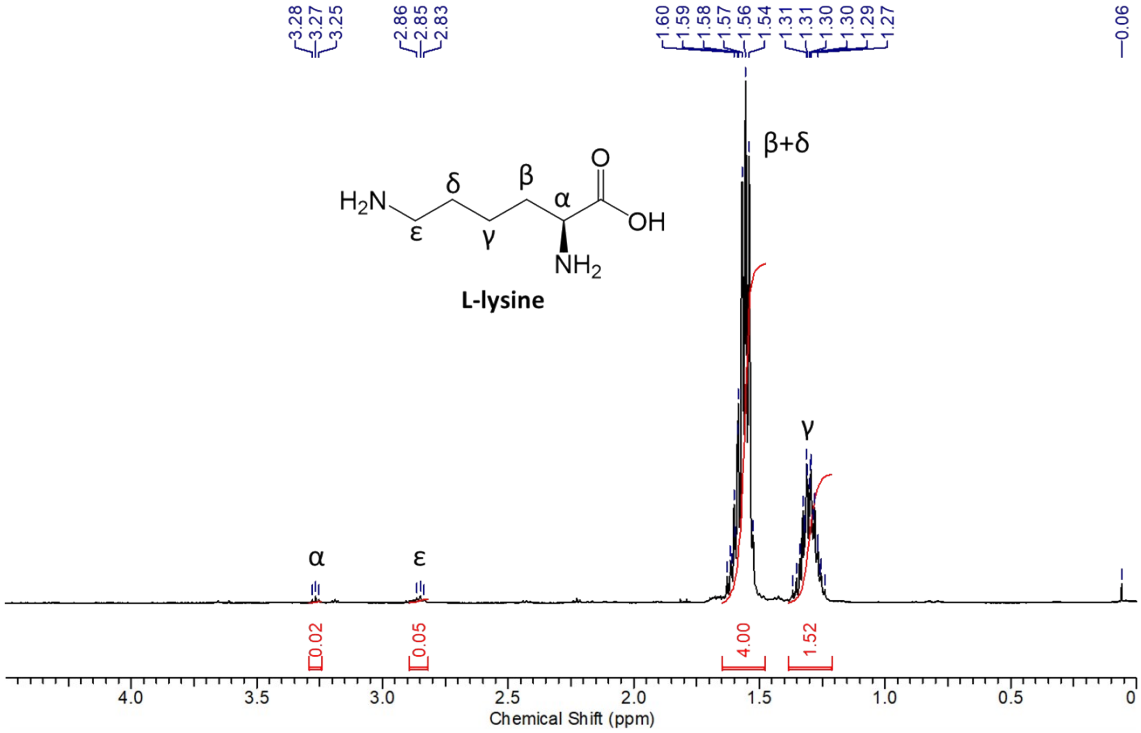


Figure S25. ^{1}H-NMR spectrum of L-lysine in D_2O after reacting with **RuNi@IPrPrSO3** (8 mol% of metal, 55 °C, 2 bars D_2 during 48 h) (Table S3, entry 3).

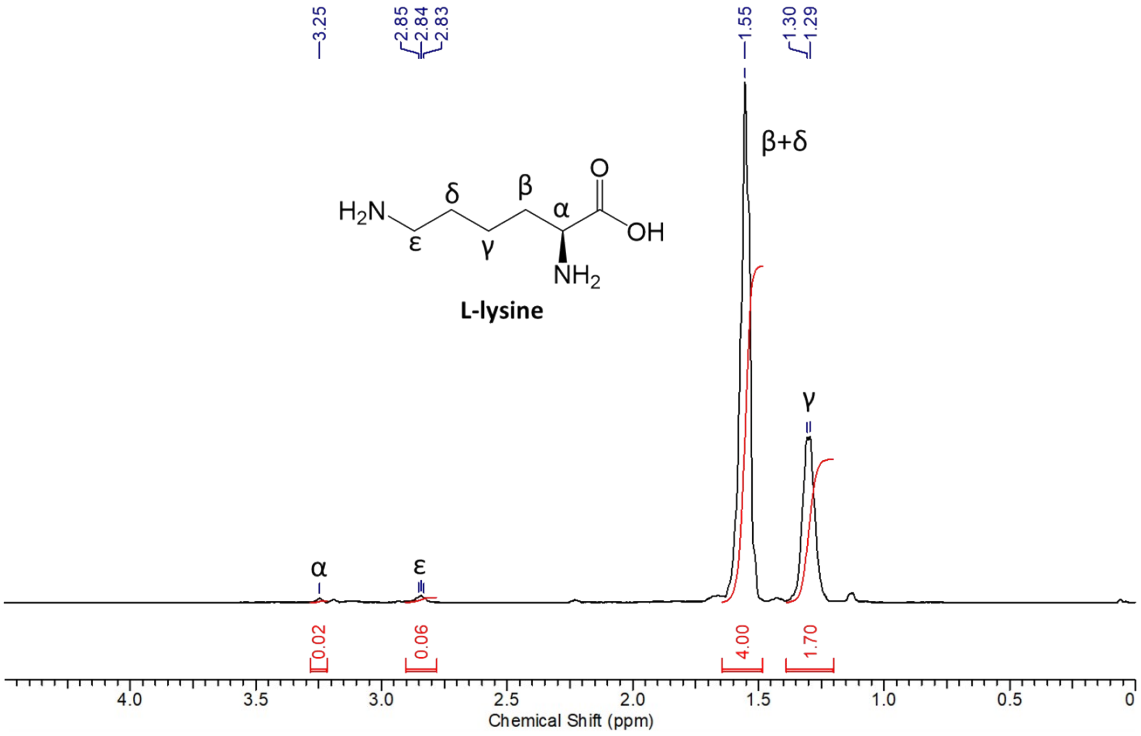


Figure S26. ^{1}H-NMR spectrum of L-lysine in D_2O after reacting with **RuNi4@IPrPrSO3** (8 mol% of metal, 55 °C, 2 bars D_2 during 48 h) (Table S3, entry 4).

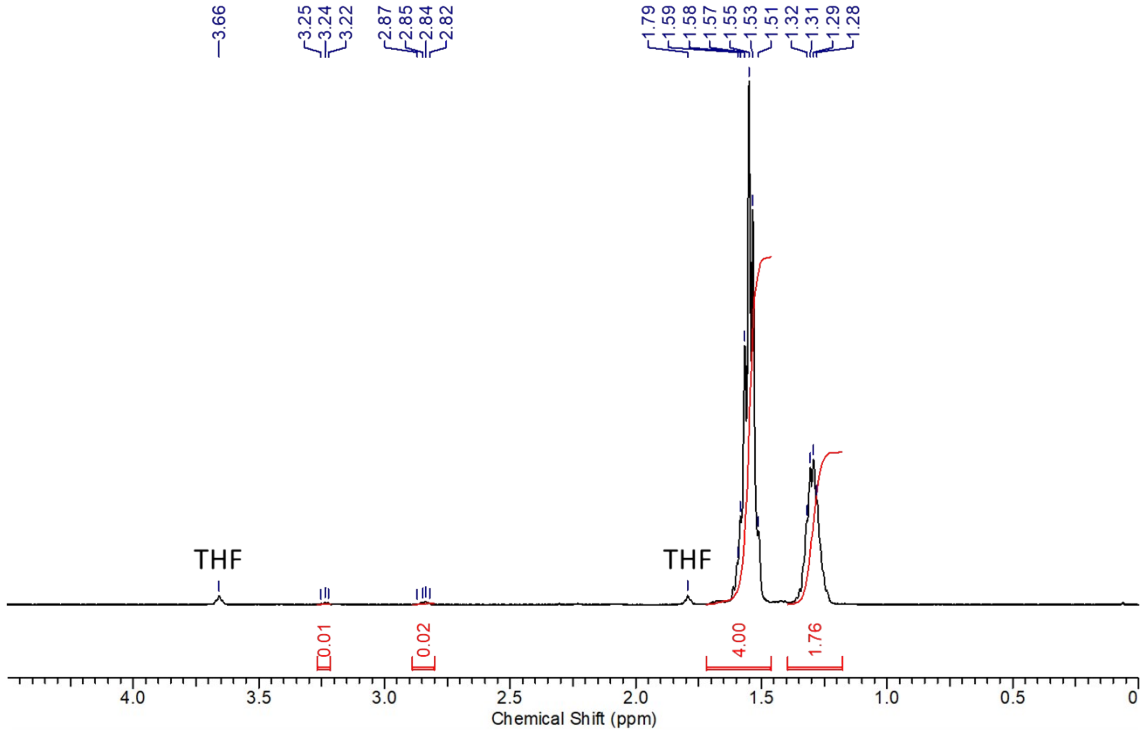


Figure S27. ^{1}H-NMR spectrum of L-lysine in D_2O after reacting with **RuNP/C** (8 mol% of metal, 120 °C, 4 bars D_2 during 5 h) (Table S3, entry 5).

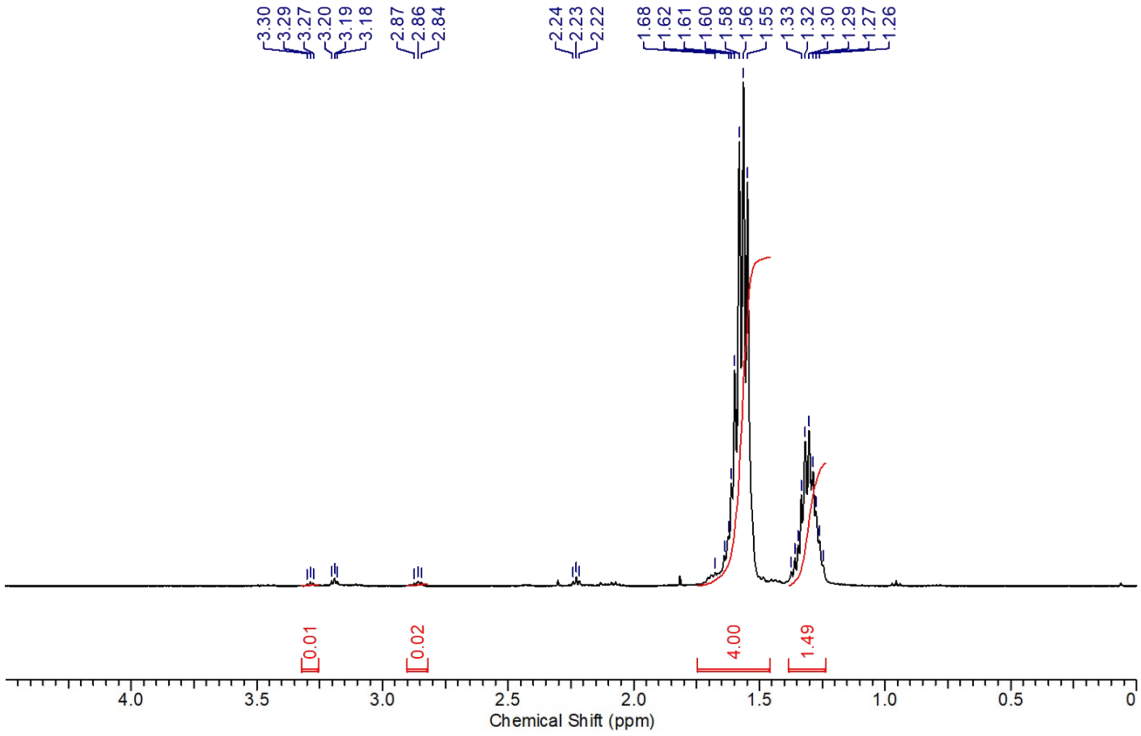


Figure S28. ^{1}H-NMR spectrum of L-lysine in D_2O after reacting with **RuNP/Cmeso** (8 mol% of metal, 120 °C, 4 bars D_2 during 30 min) (Table S3, entry 6).

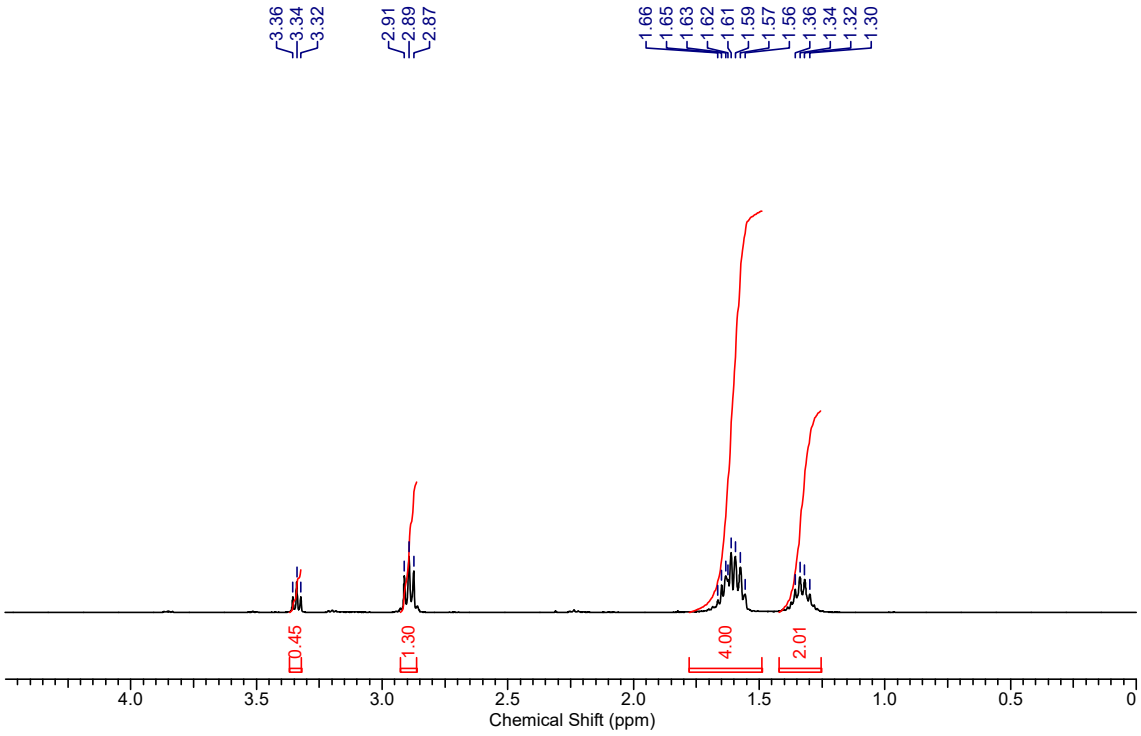


Figure S29. ^{1}H-NMR spectrum of L-lysine in D_2O after reacting with **RuNP/Cmeso** (8 mol% of metal, 55 °C, 2 bars D_2 during 2 h at pH 9) (Table S4, entry 1).

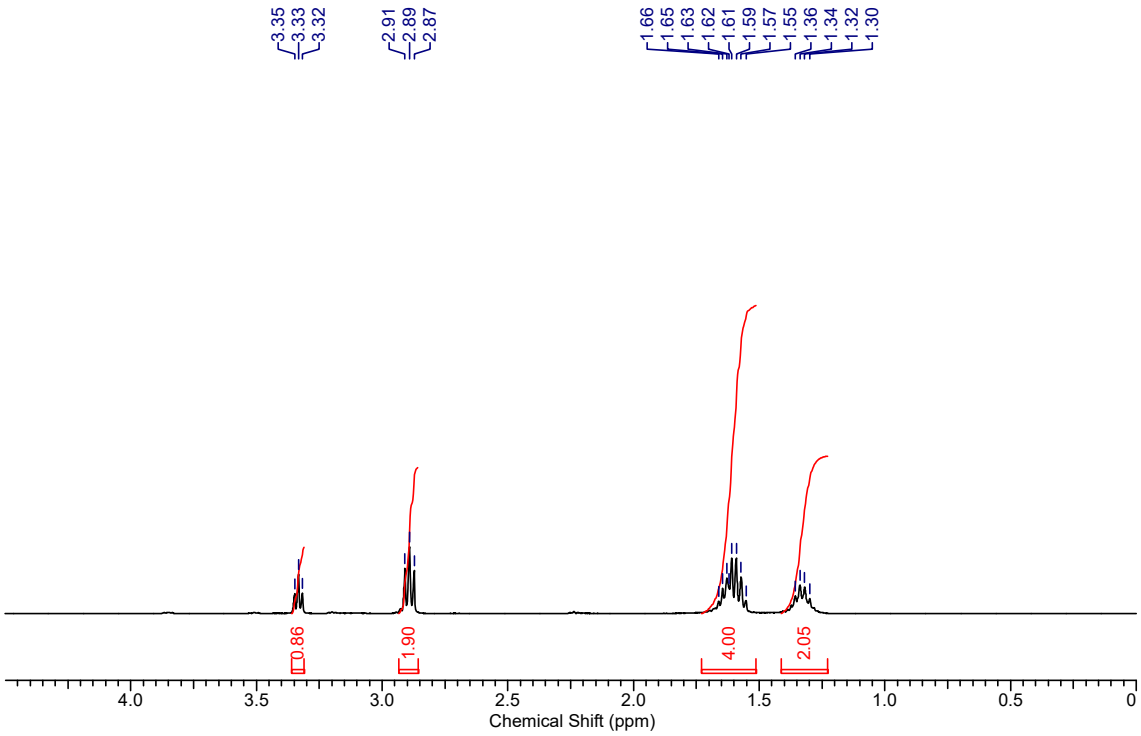


Figure S30. ^{1}H-NMR spectrum of L-lysine in D_2O after reacting without catalyst (55 °C, 2 bars D_2 during 2 h at pH 9) (Table S4, entry 2).

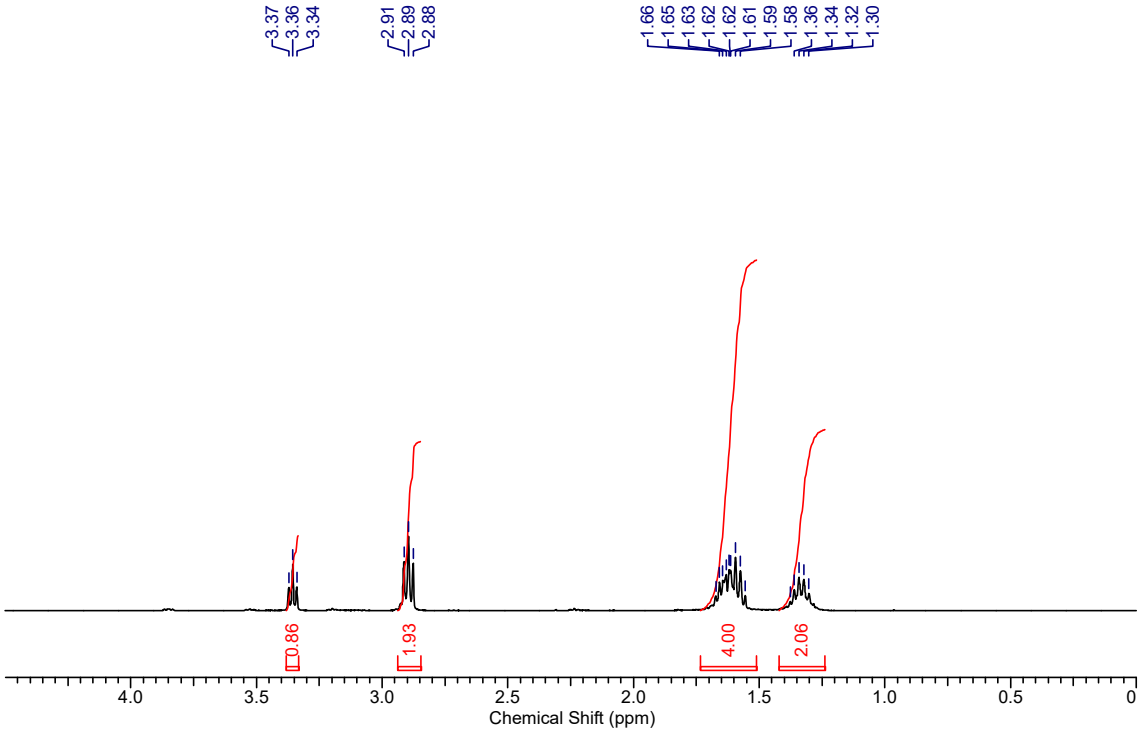


Figure S31. ^{1}H-NMR spectrum of L-lysine in D_2O after reacting with **RuNP/Cmeso** without D_2 (8 mol% of metal, 55 °C, during 2 h at pH 9) (Table S4, entry 3).

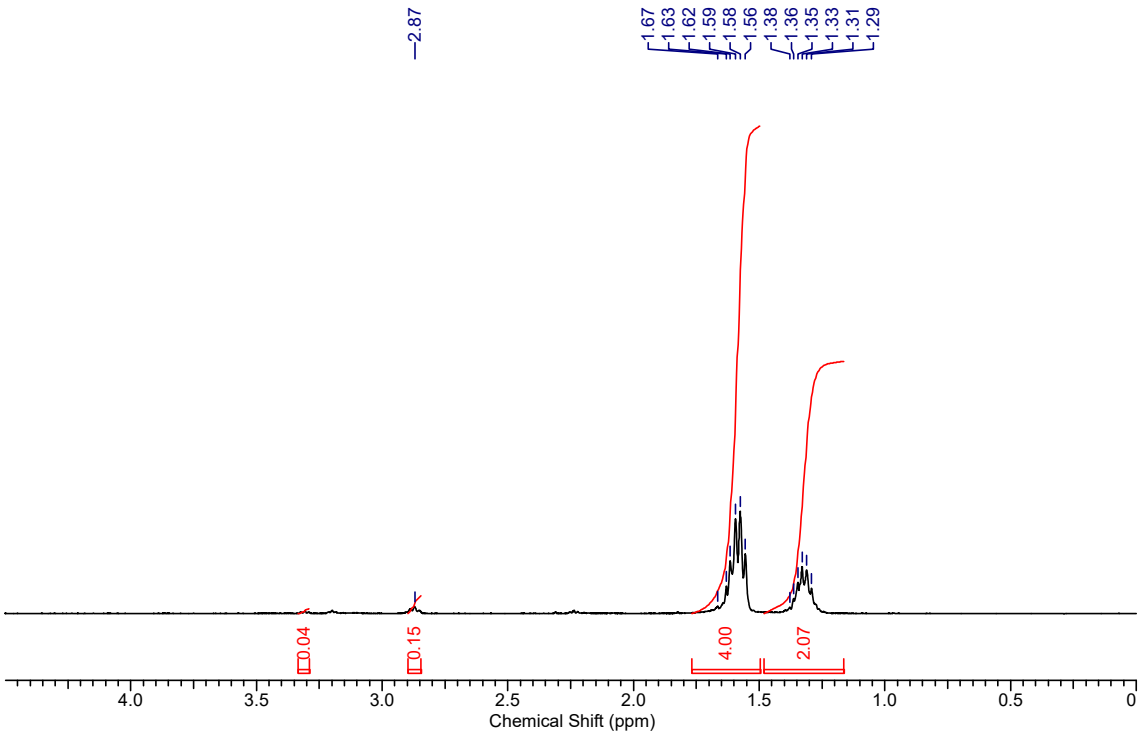


Figure S32. ^{1}H-NMR spectrum of L-lysine in D_2O after reacting with **RuNP/Cmeso** (8 mol% of metal, 80 °C, 2 bars D_2 during 2 h at pH 9) (Table S4, entry 4).

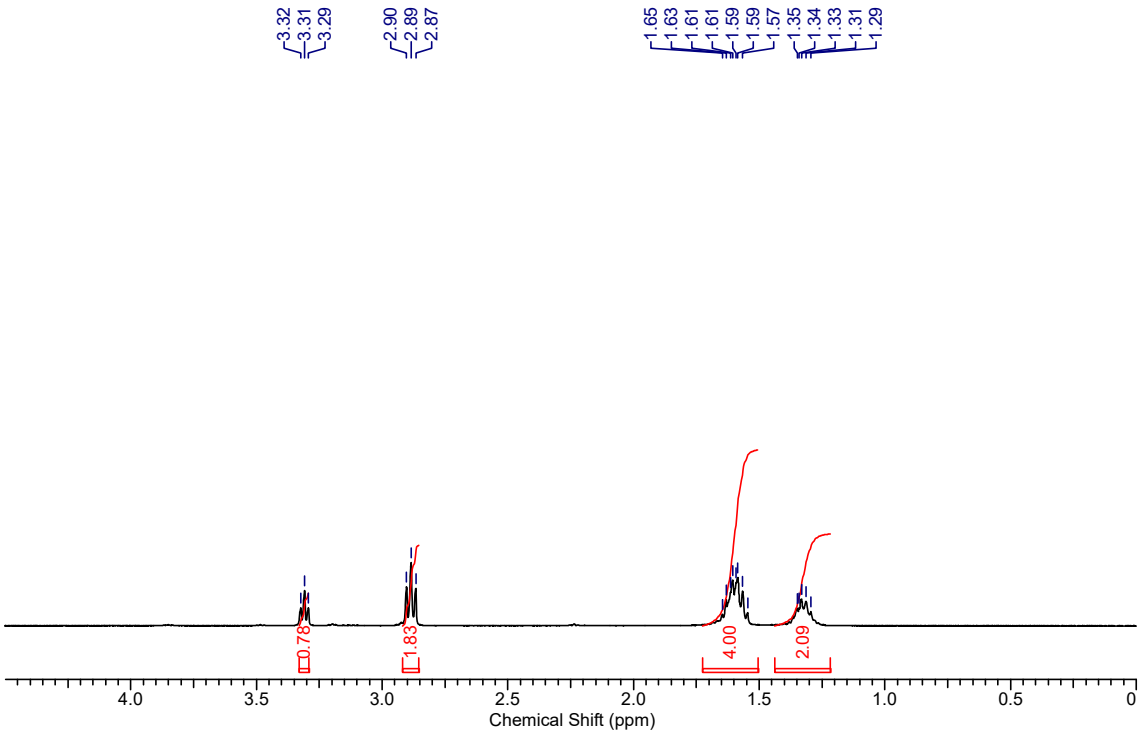


Figure S33. ^{1}H-NMR spectrum of L-lysine in D_2O after reacting without catalyst (80 °C, 2 bars D_2 during 2 h at pH 9) (Table S4, entry 5).

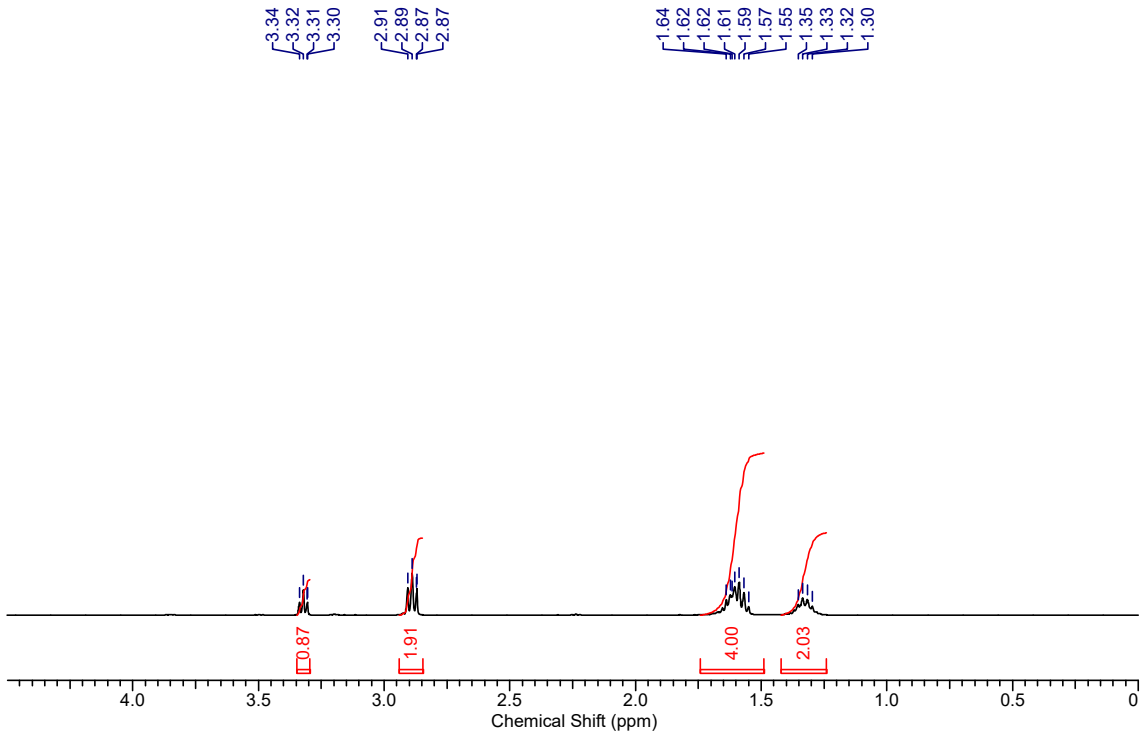


Figure S34. ^{1}H-NMR spectrum of L-lysine in D_2O after reacting with **RuNP/Cmeso** without D_2 (8 mol% of metal, 80 °C, during 2 h at pH 9) (Table S4, entry 6).

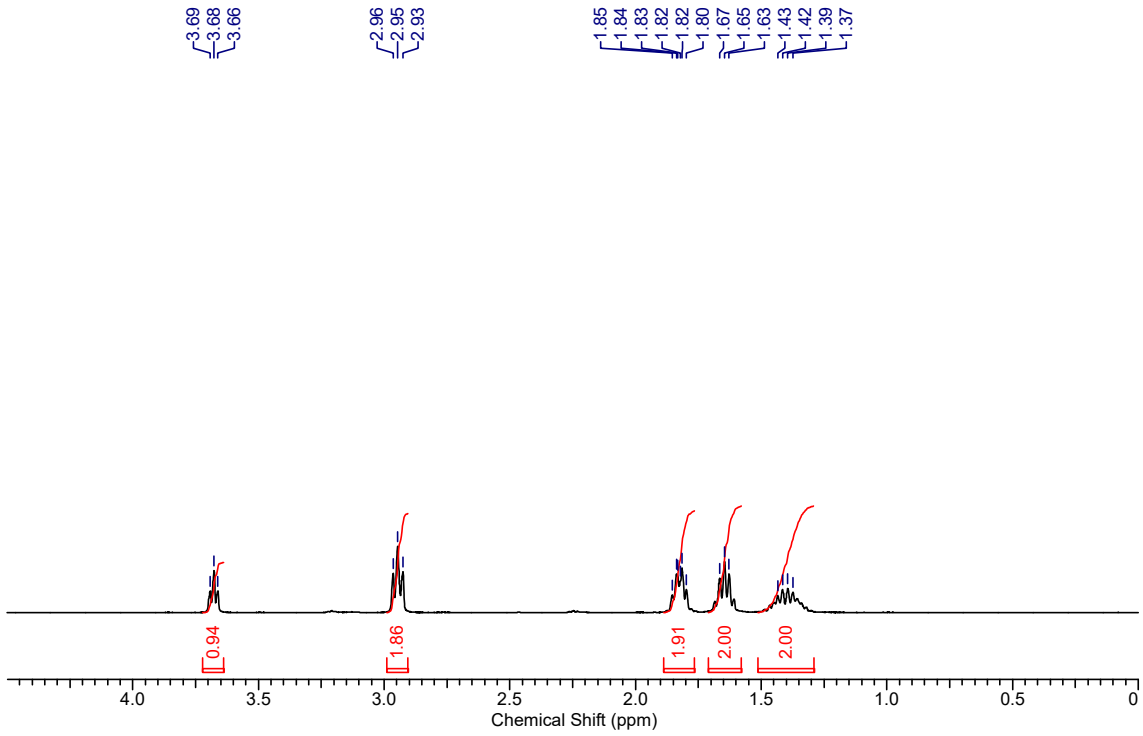


Figure S35. ^{1}H-NMR spectrum of L-lysine in D_2O after reacting with **RuNP/Cmeso** (8 mol% of metal, 55 °C, 2 bars D_2 during 2 h at pH 7) (Table S4, entry 7).

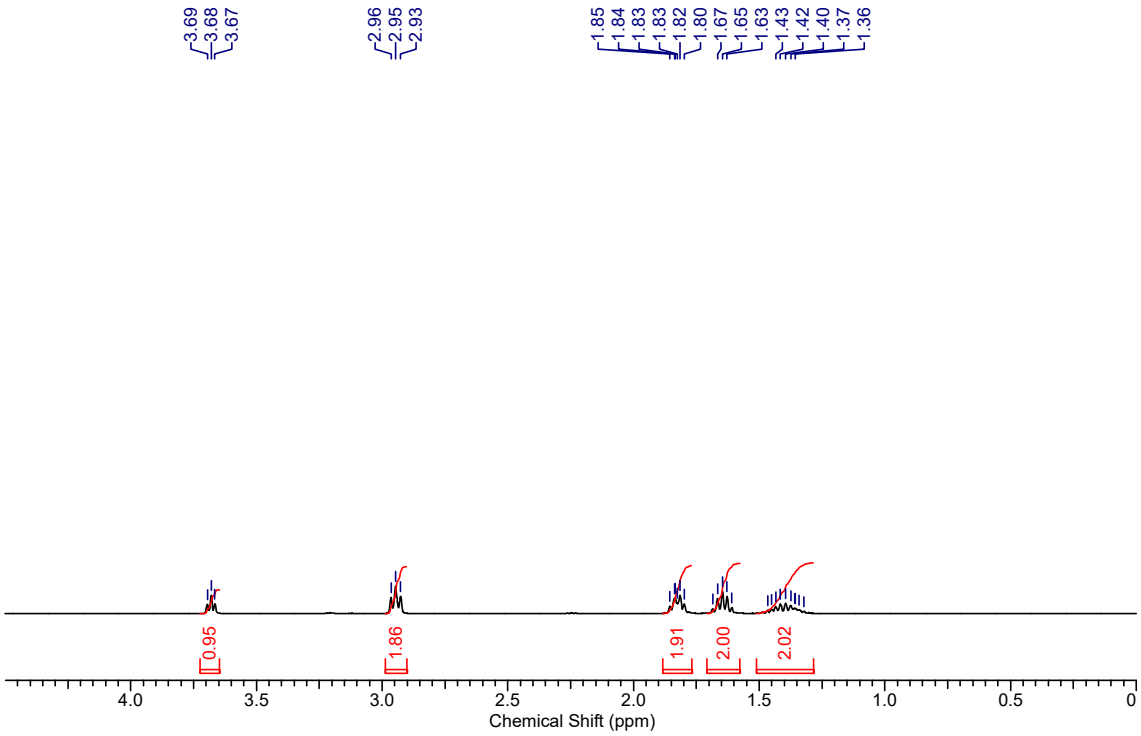


Figure S36. ^{1}H-NMR spectrum of L-lysine in D_2O after reacting without catalyst (55 °C, 2 bars D_2 during 2 h at pH 7) (Table S4, entry 8).

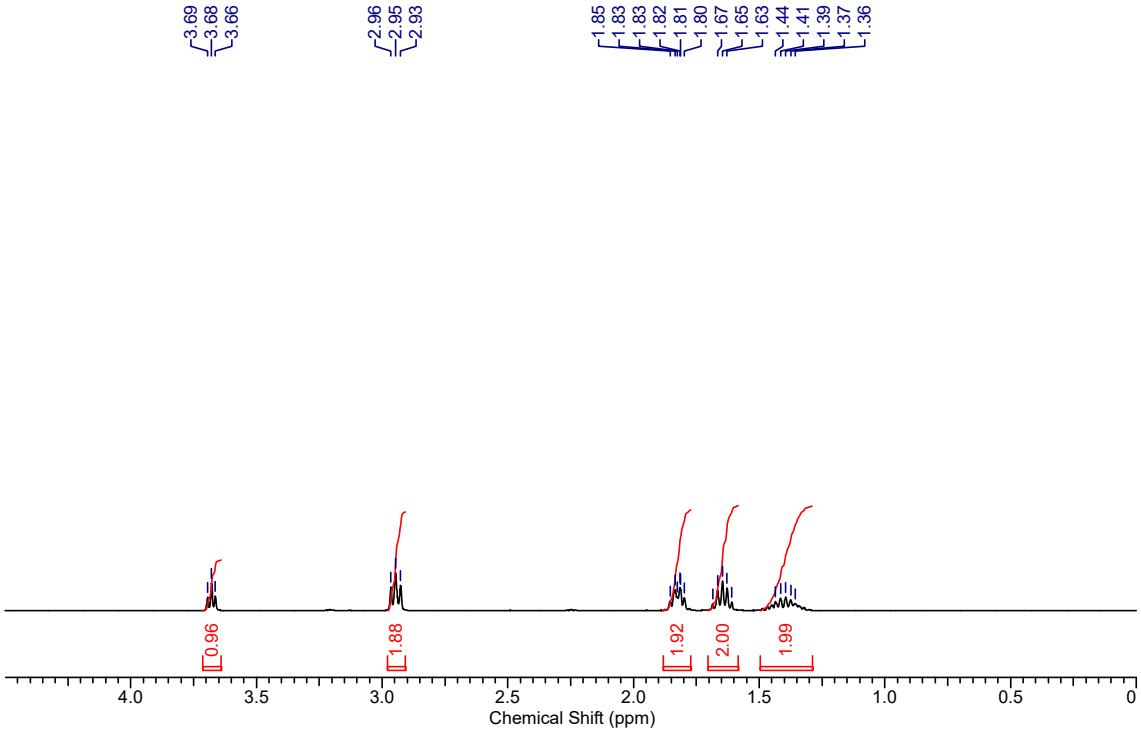


Figure S37. ^{1}H-NMR spectrum of L-lysine in D_2O after reacting with **RuNP/Cmeso** without D_2 (8 mol% of metal, 55 °C, during 2 h at pH 7) (Table S4, entry 9).

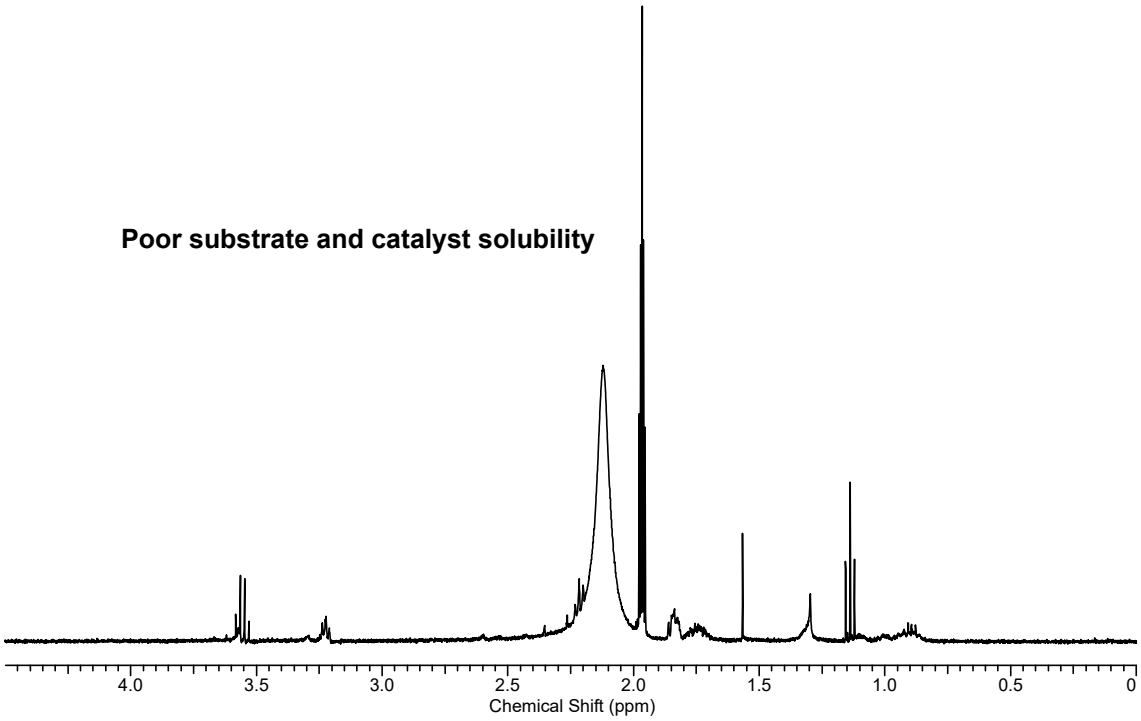


Figure S38. [1]H-NMR spectrum of L-lysine in acetonitrile-d_3 after reacting with **RuNP/Cmeso** (8 mol% of metal, 55 °C, 2 bars D_2 during 2 h) (Table S4, entry 10).

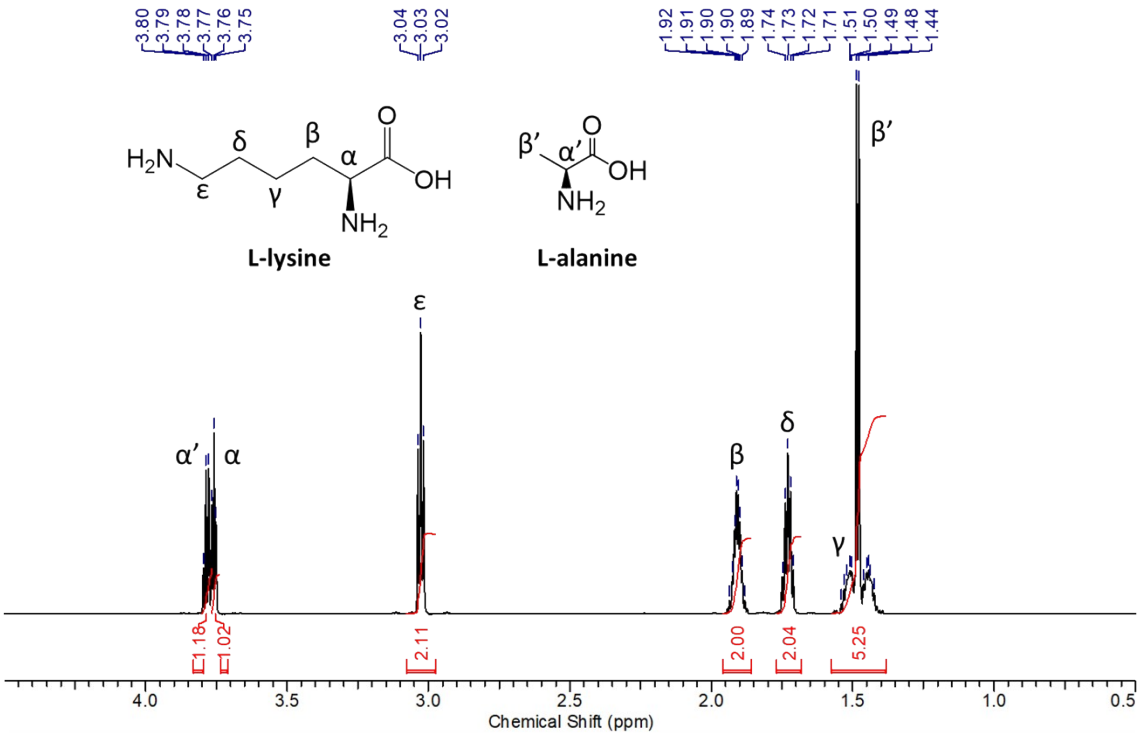


Figure S39. [1]H-NMR spectrum of a mixture of L-Alanine and L-lysine in D_2O.

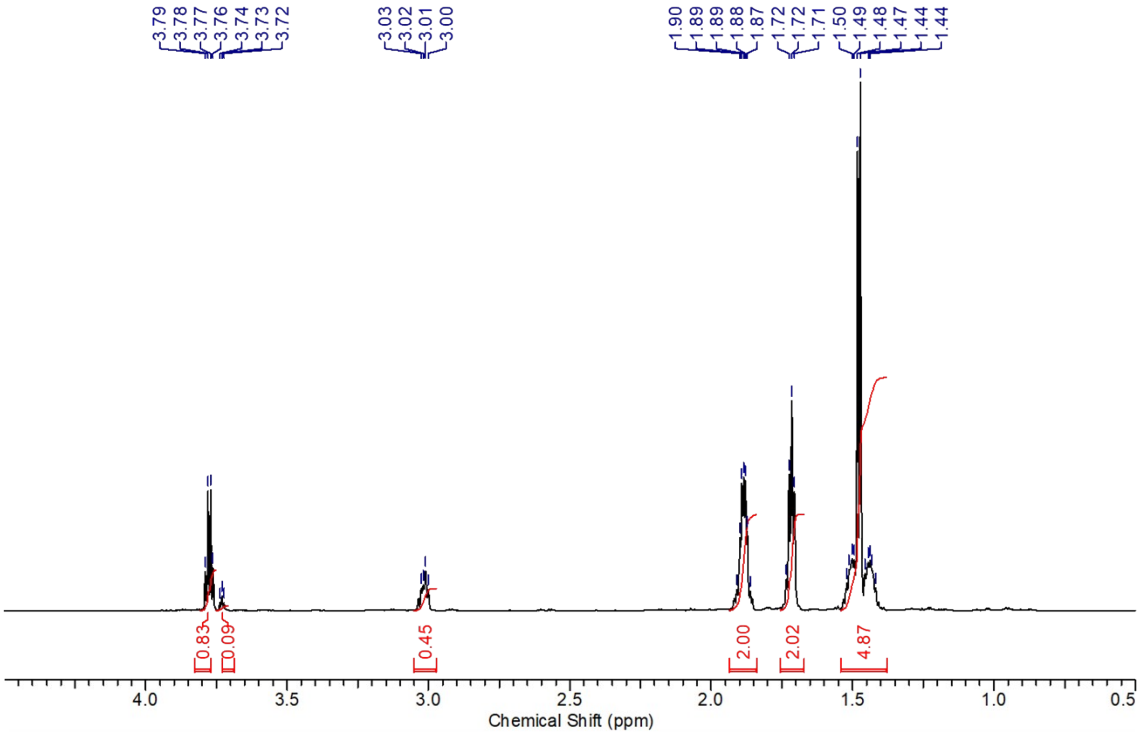


Figure S40. ^{1}H-NMR spectrum of L-alanine/L-lysine (34 mM each) in D_2O after reacting with **Ru@IPrPrSO3** (8 mol% of metal, 55 °C, 2 bars D_2, pH 6, during 48 h) (Table S5, entry 1).

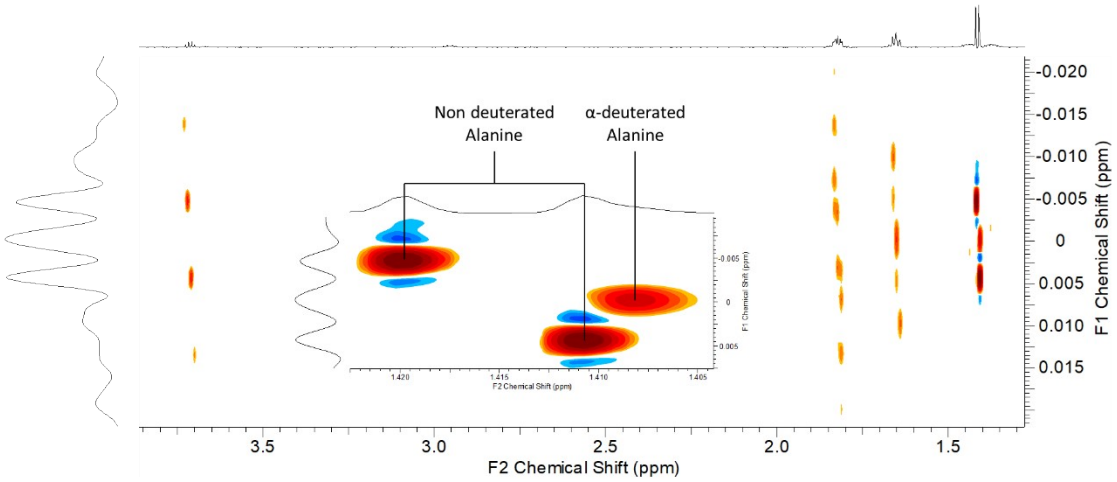


Figure S41. 2D J-resolved ^{1}H-NMR spectrum of L-alanine/L-lysine (34 mM each) in D_2O after reacting with **Ru@IPrPrSO3** (8 mol% of metal, 55 °C, 2 bars D_2, pH 6, during 48 h) (Table S5, entry 1).

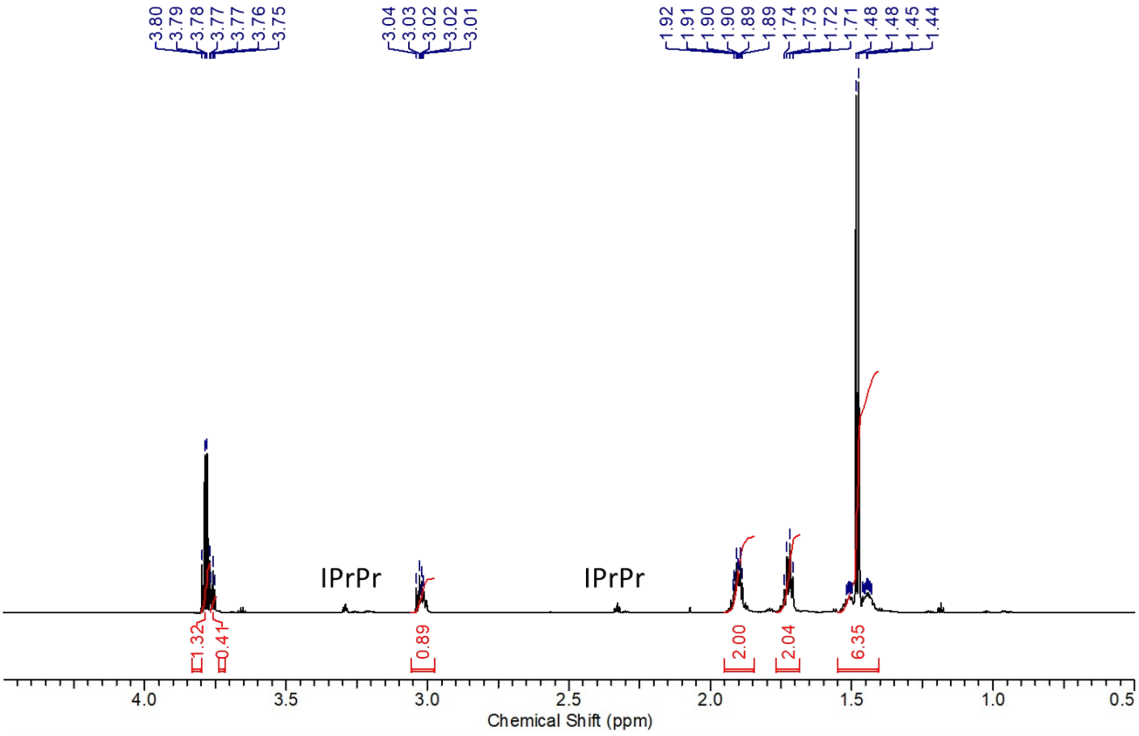


Figure S42. ^{1}H-NMR spectrum of L-alanine/L-lysine (68 mM each) in D_2O after reacting with **Ru@IPrPrSO3** (8 mol% of metal, 55 °C, 2 bars D_2, pH 6, during 48 h) (Table S5, entry 2).

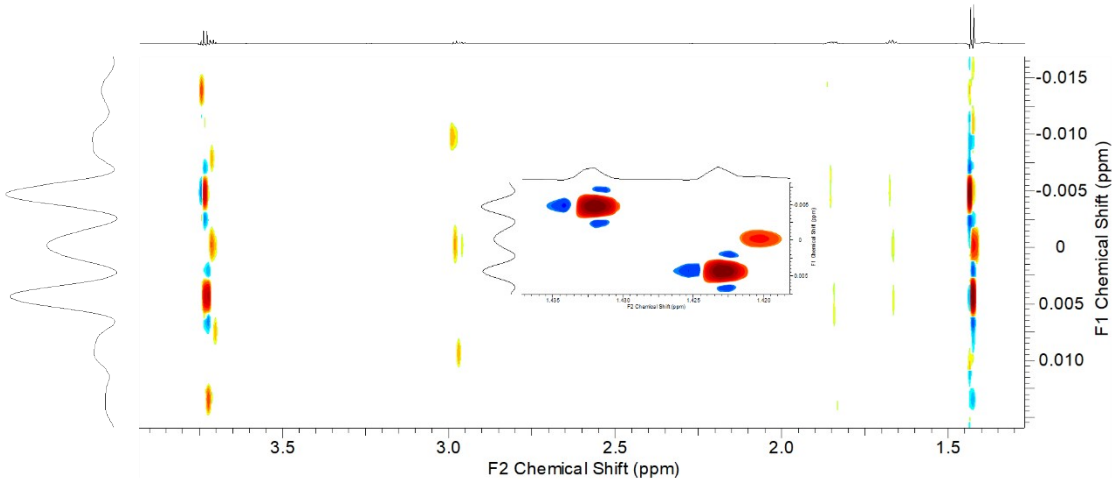


Figure S43.2D J-resolved ^{1}H-NMR spectrum of L-alanine/L-lysine (68 mM each) in D_2O after reacting with **Ru@IPrPrSO3** (8 mol% of metal, 55 °C, 2 bars D_2, pH 6, during 48 h) (Table S5, entry 2).

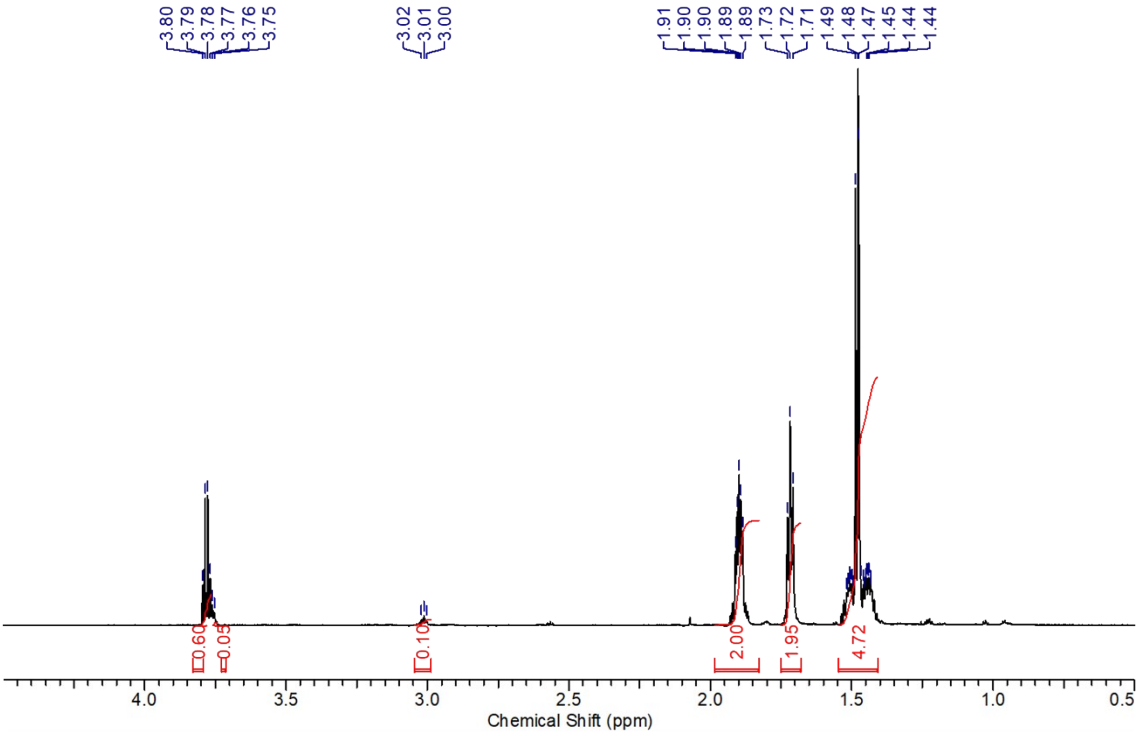


Figure S44. ^{1}H-NMR spectrum of L-alanine/L-lysine (34 mM each) in D_2O after reacting with **Ru@IPrPrSO3** (8 mol% of metal, 55 °C, 2 bars D_2, pH 7.5, during 48 h) (Table S5, entry 3).

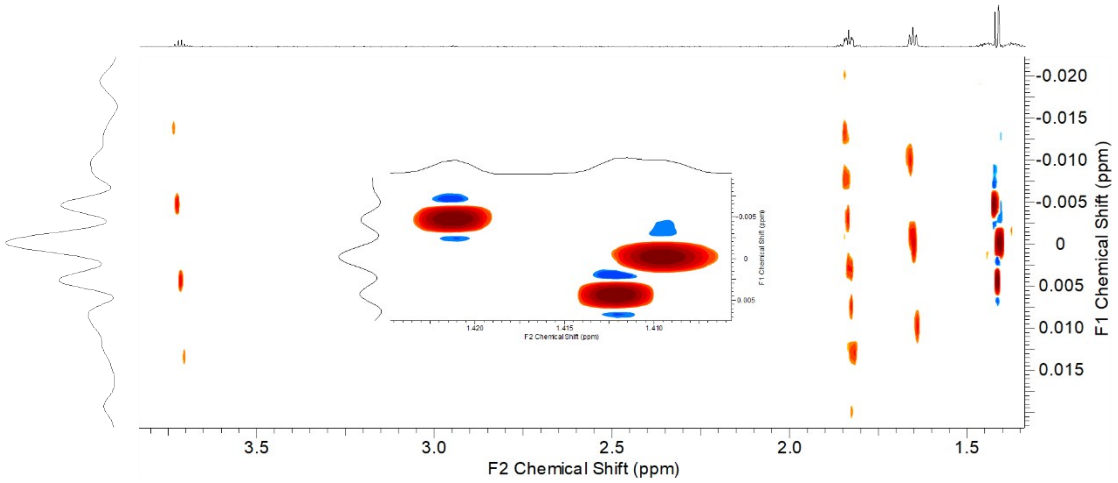


Figure S45. 2D J-resolved ^{1}H-NMR spectrum of L-alanine/L-lysine (34 mM each) in D_2O after reacting with **Ru@IPrPrSO3** (8 mol% of metal, 55 °C, 2 bars D_2, pH 7.5, during 48 h) (Table S5, entry 3).

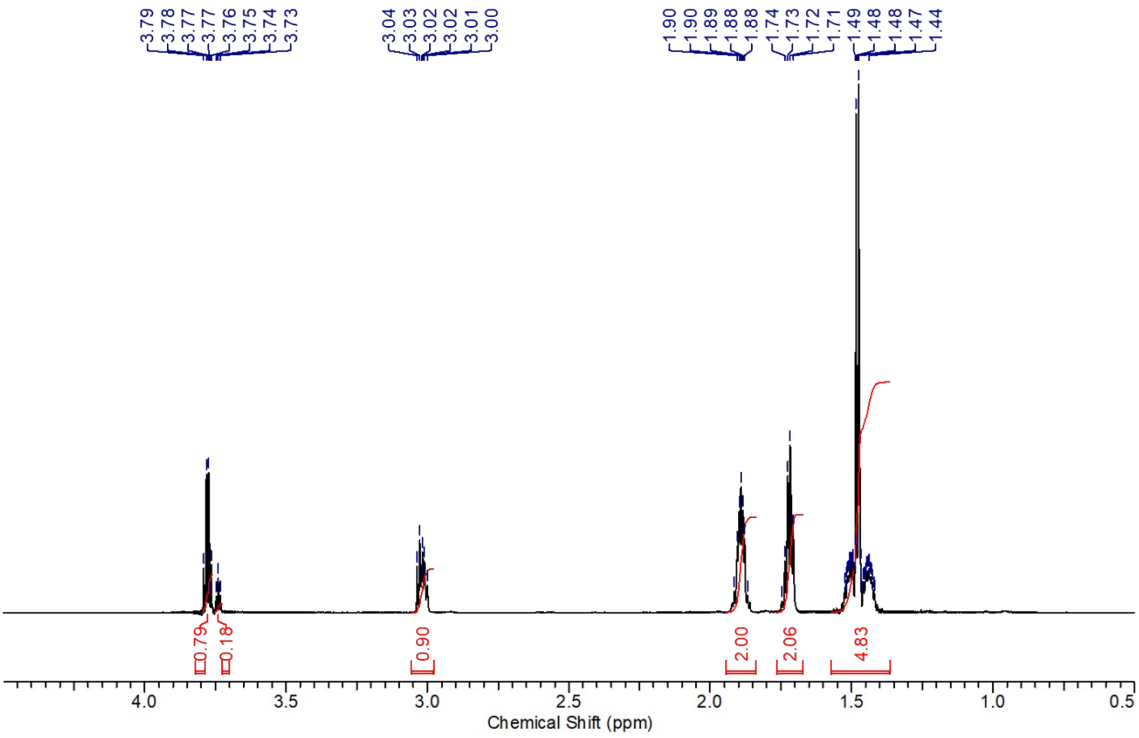


Figure S46. ^{1}H-NMR spectrum of L-alanine/L-lysine (34 mM each) in D_2O after reacting with **Ru@IPrPrSO3** (8 mol% of metal, 55 °C, 2 bars D_2, pH 9, during 48 h) (Table S5, entry 4).

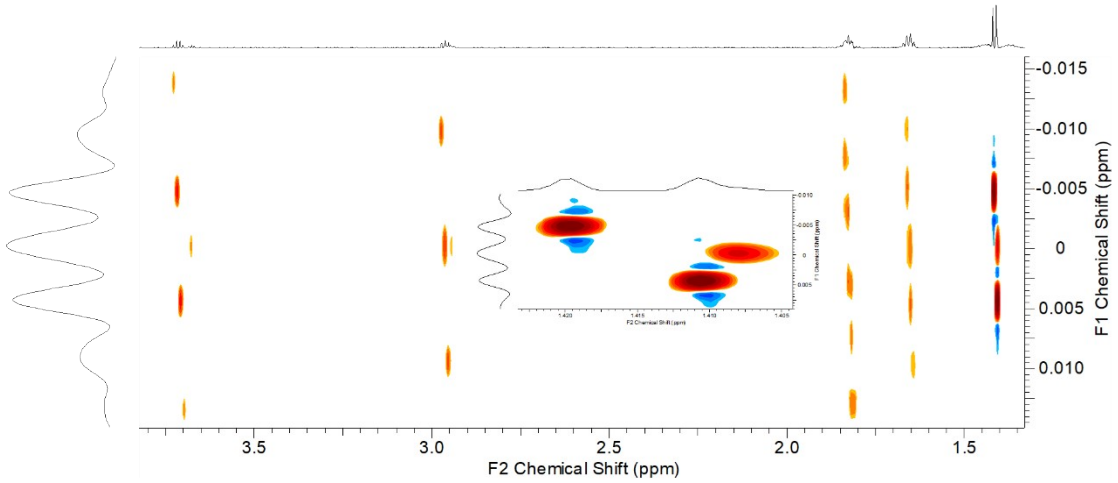


Figure S47. 2D J-resolved ^{1}H-NMR spectrum of L-alanine/L-lysine (34 mM each) in D_2O after reacting with **Ru@IPrPrSO3** (8 mol% of metal, 55 °C, 2 bars D_2, pH 9, during 48 h) (Table S5, entry 4).

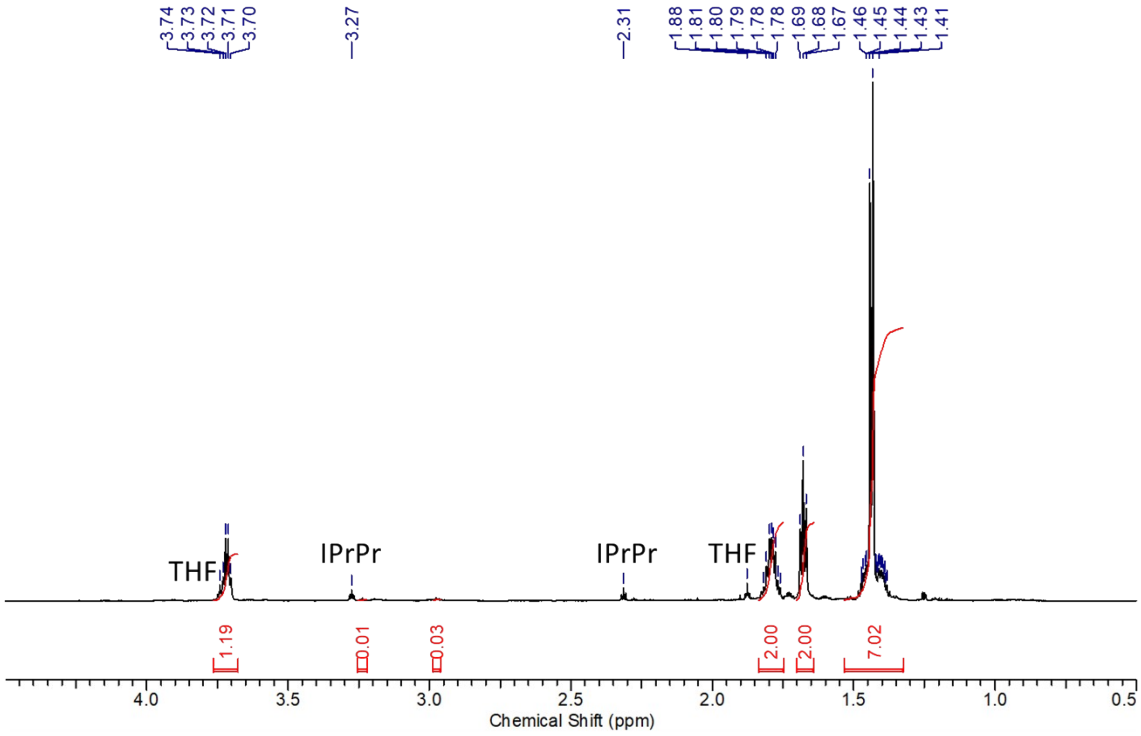


Figure S48. ^{1}H-NMR spectrum of L-alanine/L-lysine (68 mM each) in D_2O after reacting with **Ru@IPrPrSO3** (8 mol% of metal, 55 °C, 2 bars D_2, pH 9, during 48 h) (Table S5, entry 5).

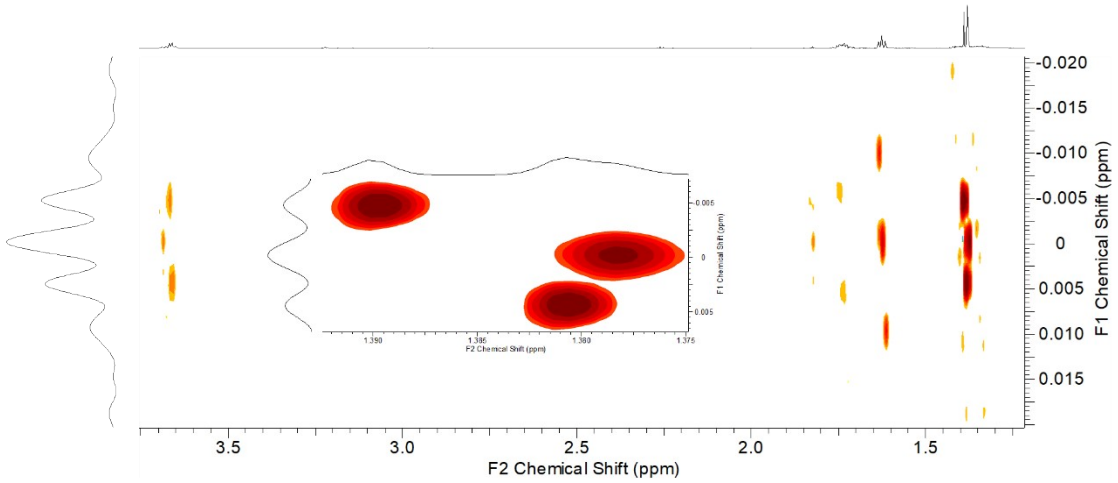


Figure S49. 2D J-resolved ^{1}H-NMR spectrum of L-alanine/L-lysine (68 mM each) in D_2O after reacting with **Ru@IPrPrSO3** (8 mol% of metal, 55 °C, 2 bars D_2, pH 9, during 48 h) (Table S5, entry 5).

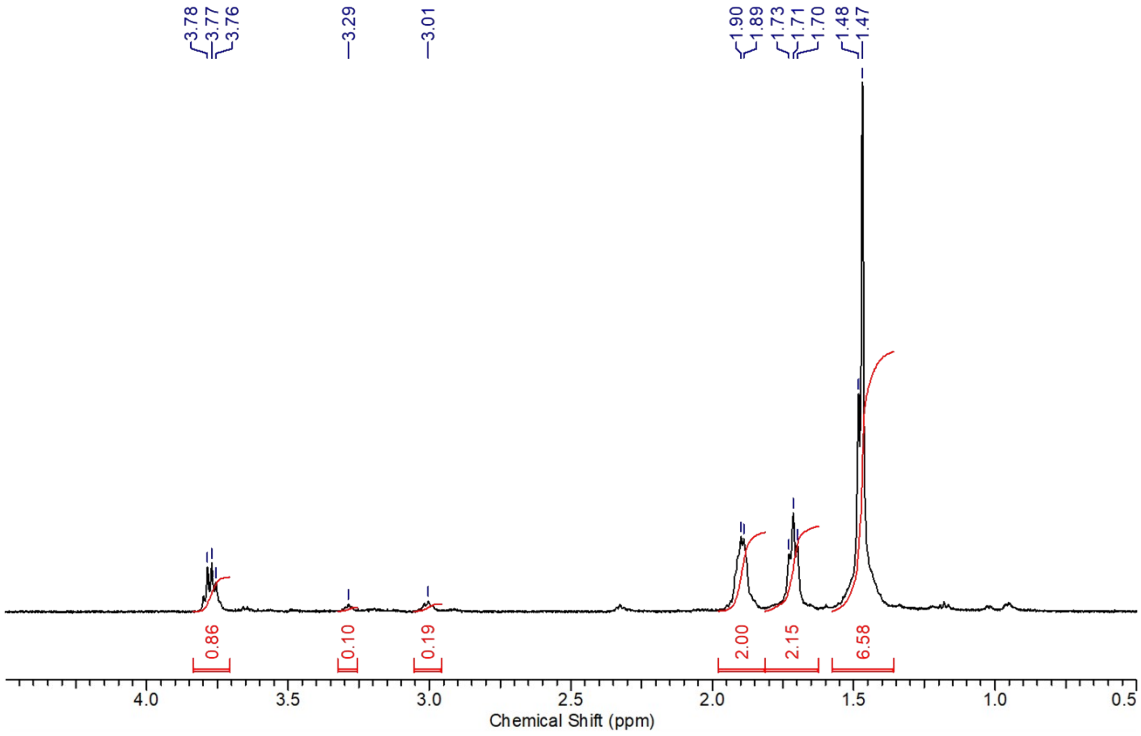


Figure S50. ^{1}H-NMR spectrum of L-alanine/L-lysine (34 mM each) in D_2O after reacting with **Ru@IPrPrSO3** (8 mol% of metal, 55 °C, 2 bars D_2, pH 7.5 + 100 mM PBS, during 48 h) (Table S5, entry 6).

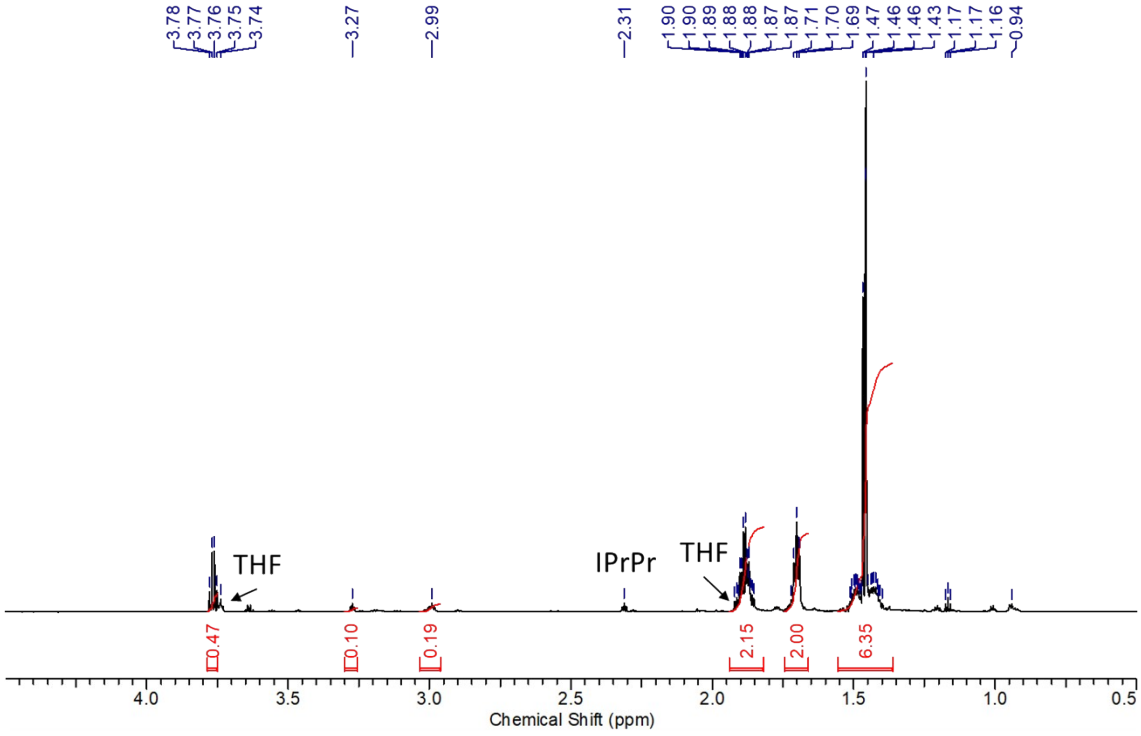


Figure S51. ^{1}H-NMR spectrum of L-alanine/L-lysine (34 mM each) in D_2O after reacting with **Ru@IPrPrSO3** (8 mol% of metal, 55 °C, 2 bars D_2, pH 7.5 + 100 mM PBS + 25 mM NaCl, during 48 h) (Table S5, entry 7).

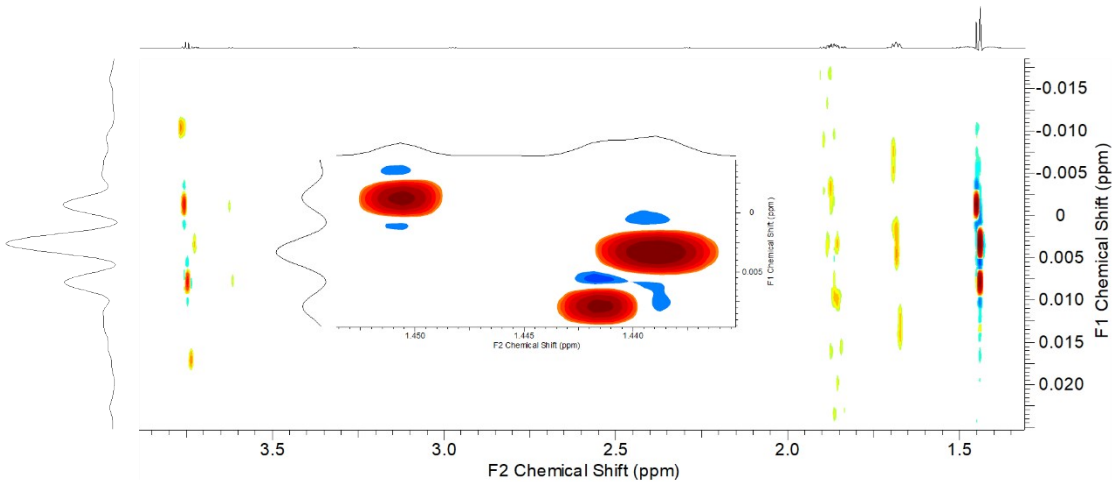


Figure S52. 2D J-resolved ^{1}H-NMR spectrum of L-alanine/L-lysine (34 mM each) in D_2O after reacting with **Ru@IPrPrSO3** (8 mol% of metal, 55 °C, 2 bars D_2, pH 7.5 + 100 mM PBS + 25 mM NaCl, during 48 h) (Table S5, entry 7).

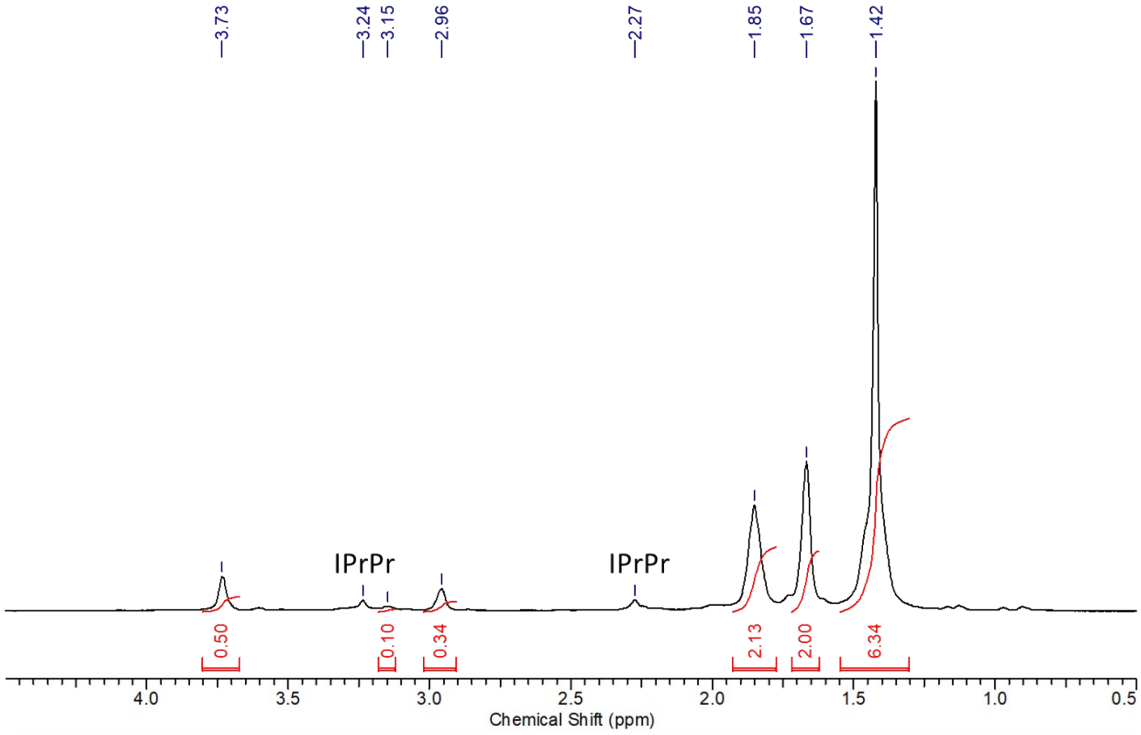


Figure S53. ^{1}H-NMR spectrum of L-alanine/L-lysine (68 mM each) in D_2O after reacting with **Ru@IPrPrSO3** (8 mol% of metal, 55 °C, 2 bars D_2, pH 7.5 + 100 mM PBS + 25 mM NaCl, during 48 h) (Table S5, entry 8).

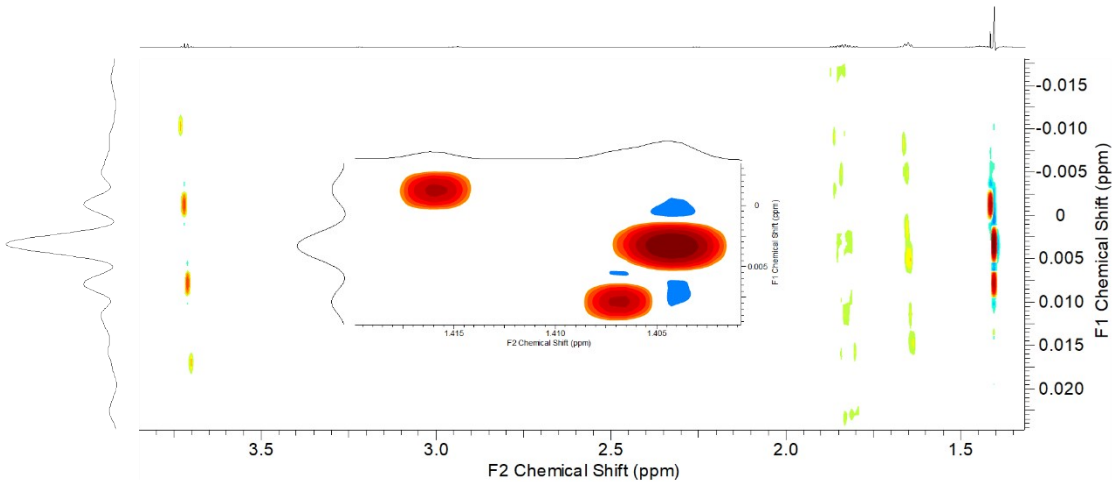


Figure S54. 2D J-resolved ^{1}H-NMR spectrum of L-alanine/L-lysine (68 mM each) in D_2O after reacting with **Ru@IPrPrSO3** (8 mol% of metal, 55 °C, 2 bars D_2, pH 7.5 + 100 mM PBS + 25 mM NaCl, during 48 h) (Table S5, entry 8).

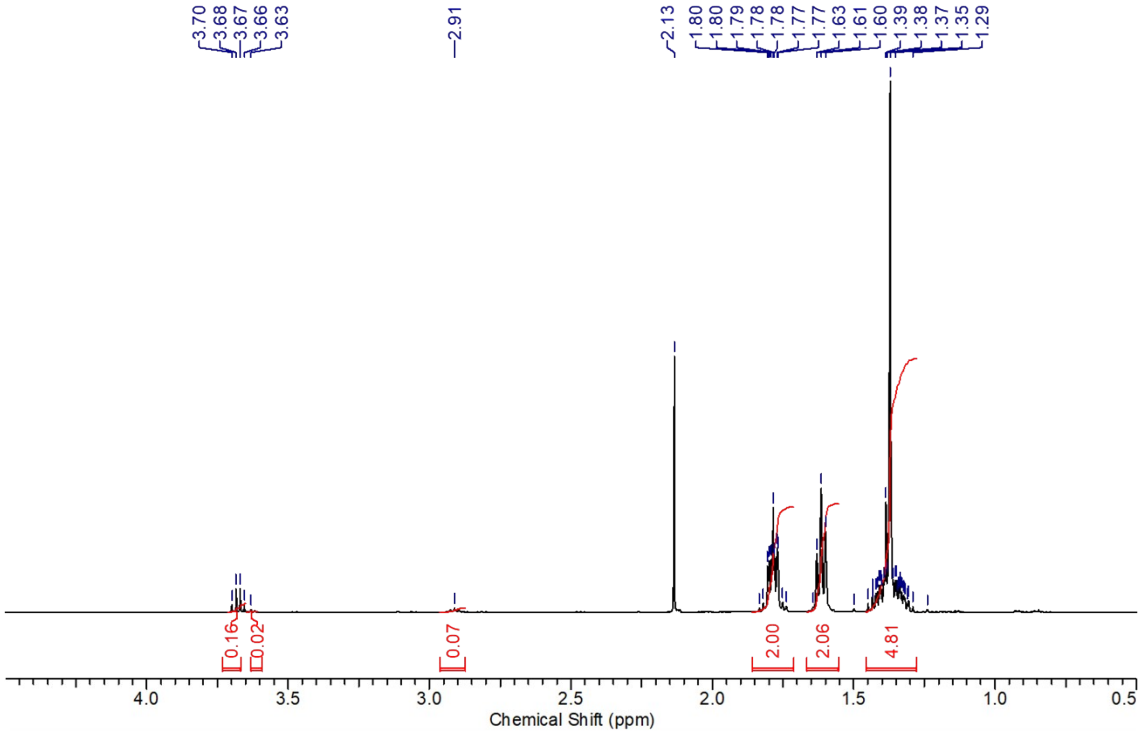


Figure S55. ^{1}H-NMR spectrum of L-alanine/L-lysine (68 mM each) in D_2O after reacting with **Ru@IPrPrSO3** (8 mol% of metal, 120 °C, 4 bars D_2, pH 9, during 1 h) (Table S5, entry 9).

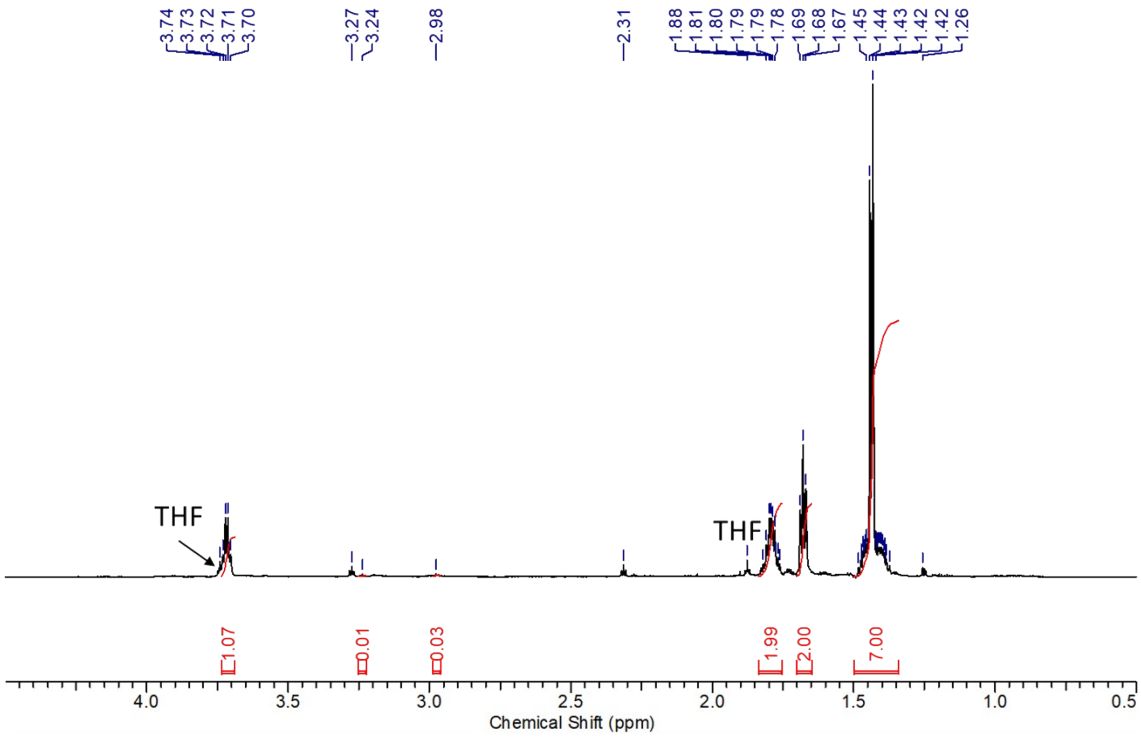


Figure S56. ^{1}H-NMR spectrum of L-alanine/L-lysine (68 mM each) in D_2O after reacting with **Ru@PTA** (8 mol% of metal, 55 °C, 2 bars D_2, pH 9, during 48 h) (Table S5, entry 10).

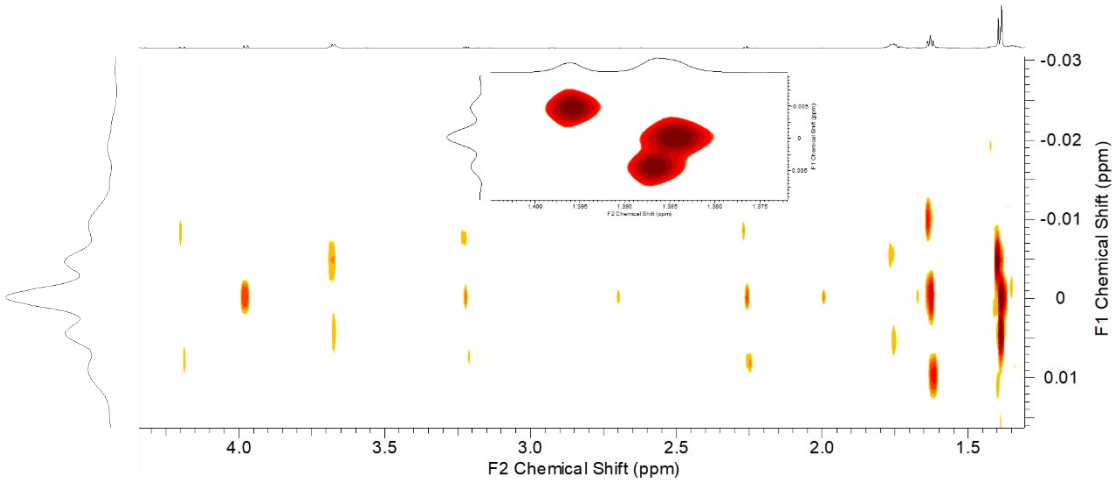


Figure S57. 2D J-resolved ^{1}H-NMR spectrum of L-alanine/L-lysine (68 mM each) in D_2O after reacting with **Ru@PTA** (8 mol% of metal, 55 °C, 2 bars D_2, pH 9, during 48 h) (Table S5, entry 10).

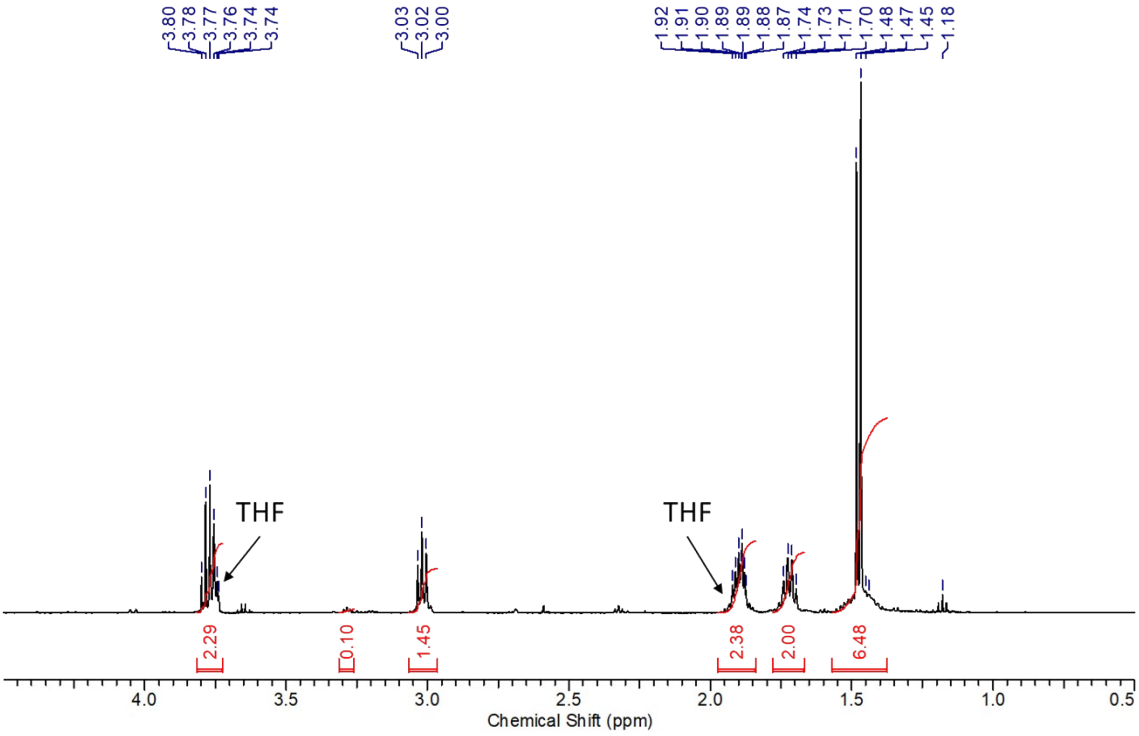


Figure S58. ^{1}H-NMR spectrum of L-alanine/L-lysine (34 mM each) in D_2O after reacting with **Ru@PTA** (8 mol% of metal, 55 °C, 2 bars D_2, pH 7 + 100 mM PBS, during 48 h) (Table S5, entry 11).

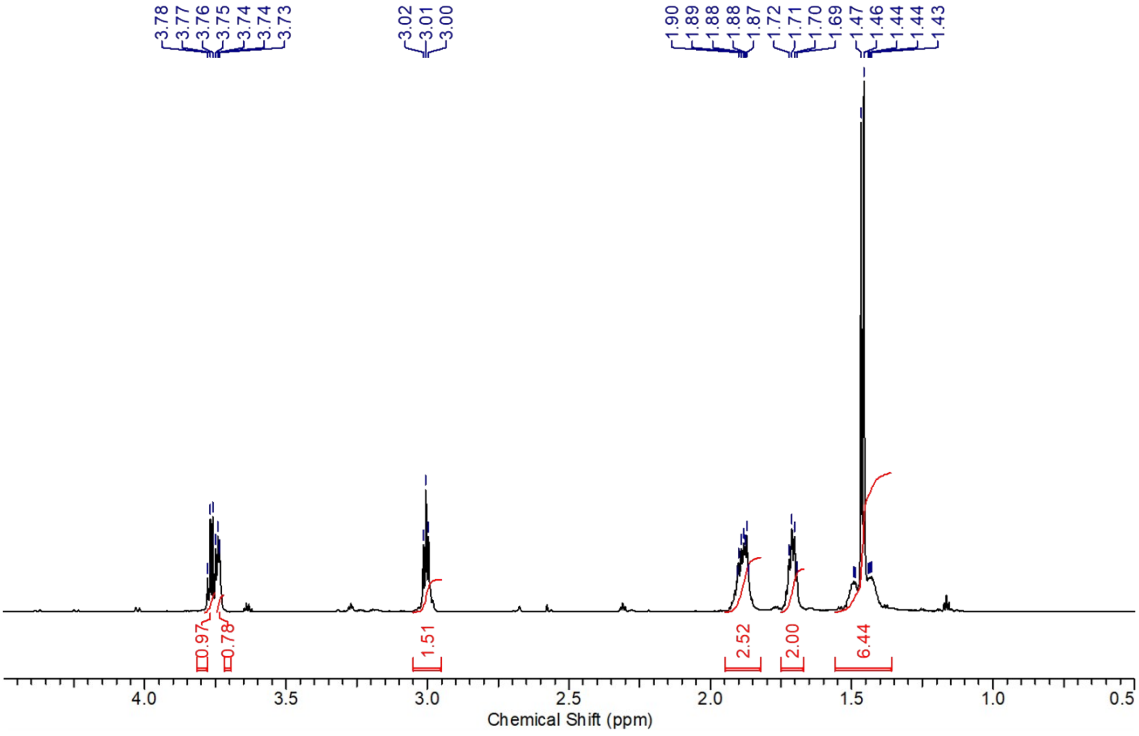


Figure S59. ^{1}H-NMR spectrum of L-alanine/L-lysine (34 mM each) in D_2O after reacting with **Ru@PTA** (8 mol% of metal, 55 °C, 2 bars D_2, pH 7 + 100 mM PBS + 25 mM NaCl, during 48 h) (Table S5, entry 12).

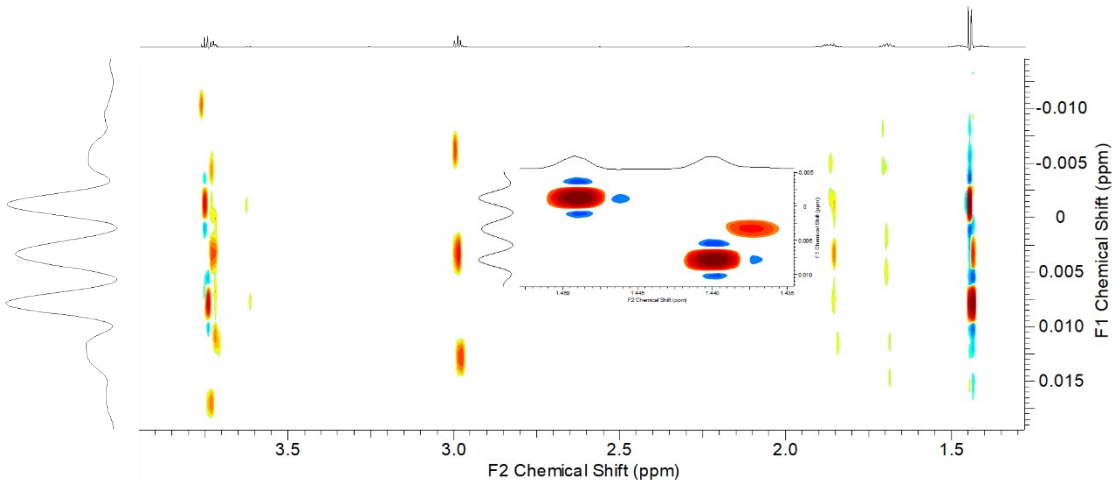


Figure S60. 2D J-resolved ^{1}H-NMR spectrum of L-alanine/L-lysine (34 mM each) in D_2O after reacting with **Ru@PTA** (8 mol% of metal, 55 °C, 2 bars D_2, pH 7 + 100 mM PBS + 25 mM NaCl, during 48 h) (Table S5, entry 12).

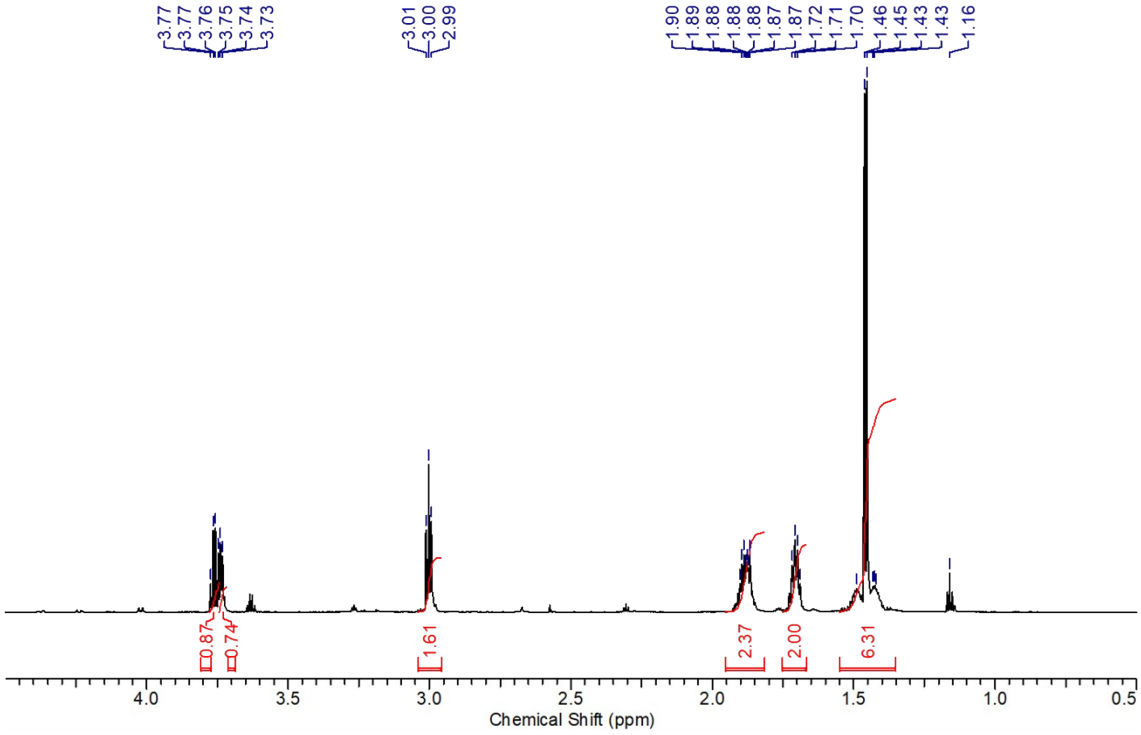


Figure S61. ^{1}H-NMR spectrum of L-alanine/L-lysine (68 mM each) in D_2O after reacting with **Ru@PTA** (8 mol% of metal, 55 °C, 2 bars D_2, pH 7.5 + 100 mM PBS + 25 mM NaCl, during 48 h) (Table S5, entry 13).

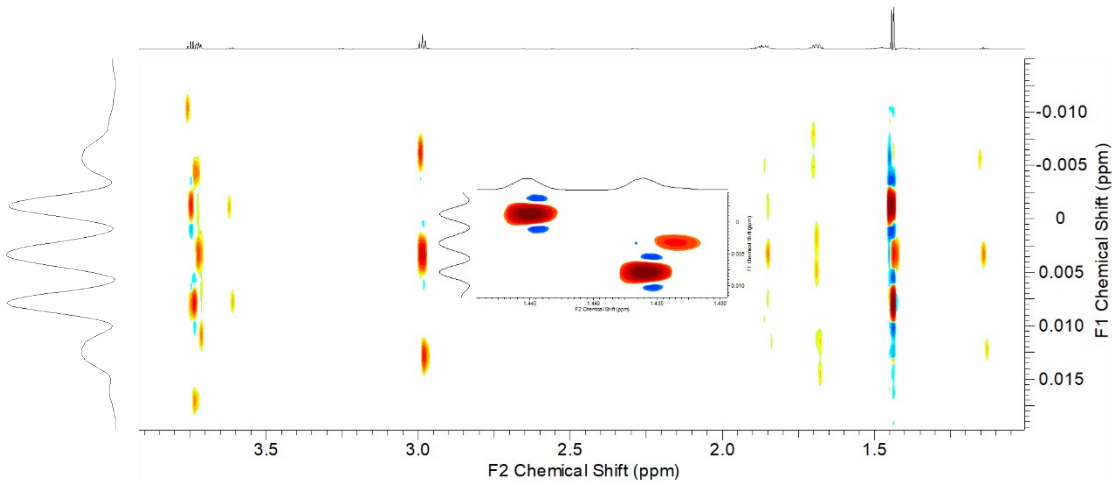


Figure S62. 2D J-resolved ^{1}H-NMR spectrum of L-alanine/L-lysine (68 mM each) in D_2O after reacting with **Ru@PTA** (8 mol% of metal, 55 °C, 2 bars D_2, pH 7.5 + 100 mM PBS + 25 mM NaCl, during 48 h) (Table S5, entry 13).

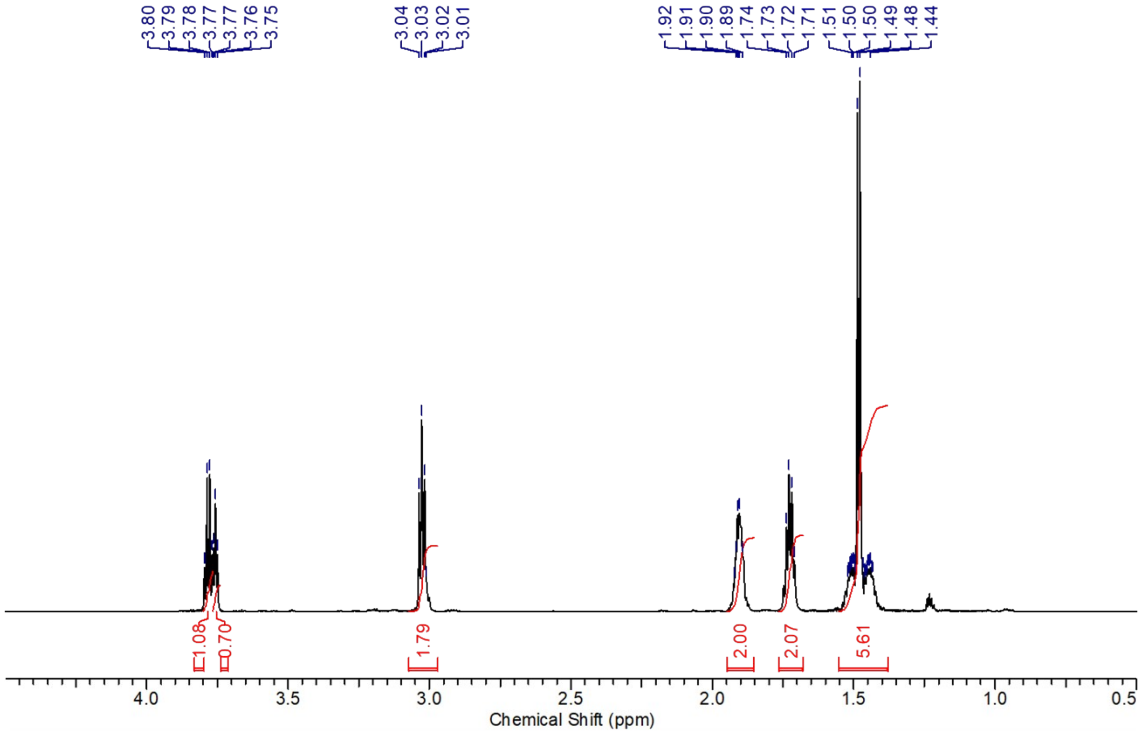


Figure S63. ^{1}H-NMR spectrum of L-alanine/L-lysine (34 mM each) in D_2O after reacting with **RuNi@IPrPrSO3** (8 mol% of metal, 55 °C, 2 bars D_2, pH 7.5, during 48 h) (Table S5, entry 14).

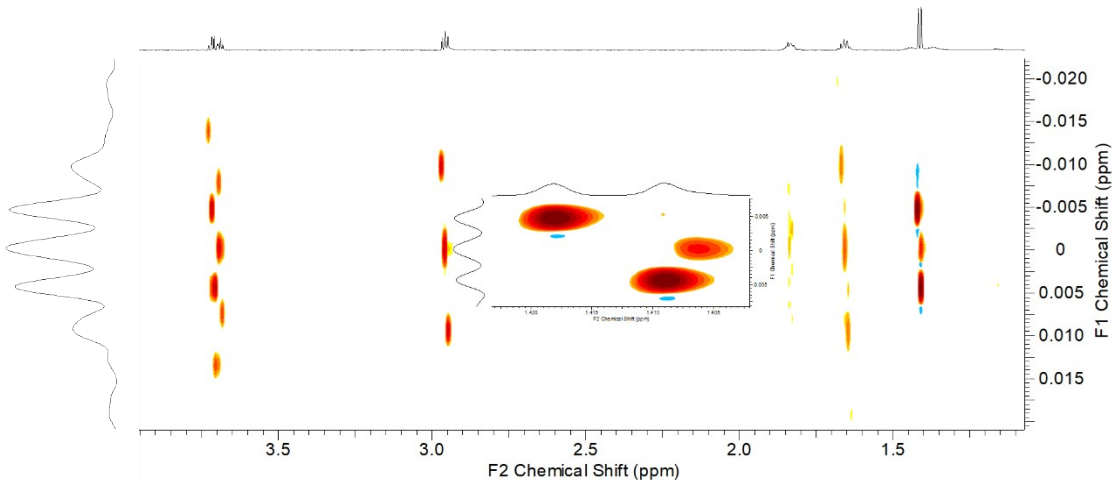


Figure S64. 2D J-resolved ^{1}H-NMR spectrum of L-alanine/L-lysine (34 mM each) in D_2O after reacting with **RuNi@IPrPrSO3** (8 mol% of metal, 55 °C, 2 bars D_2, pH 7.5, during 48 h) (Table S5, entry 14).

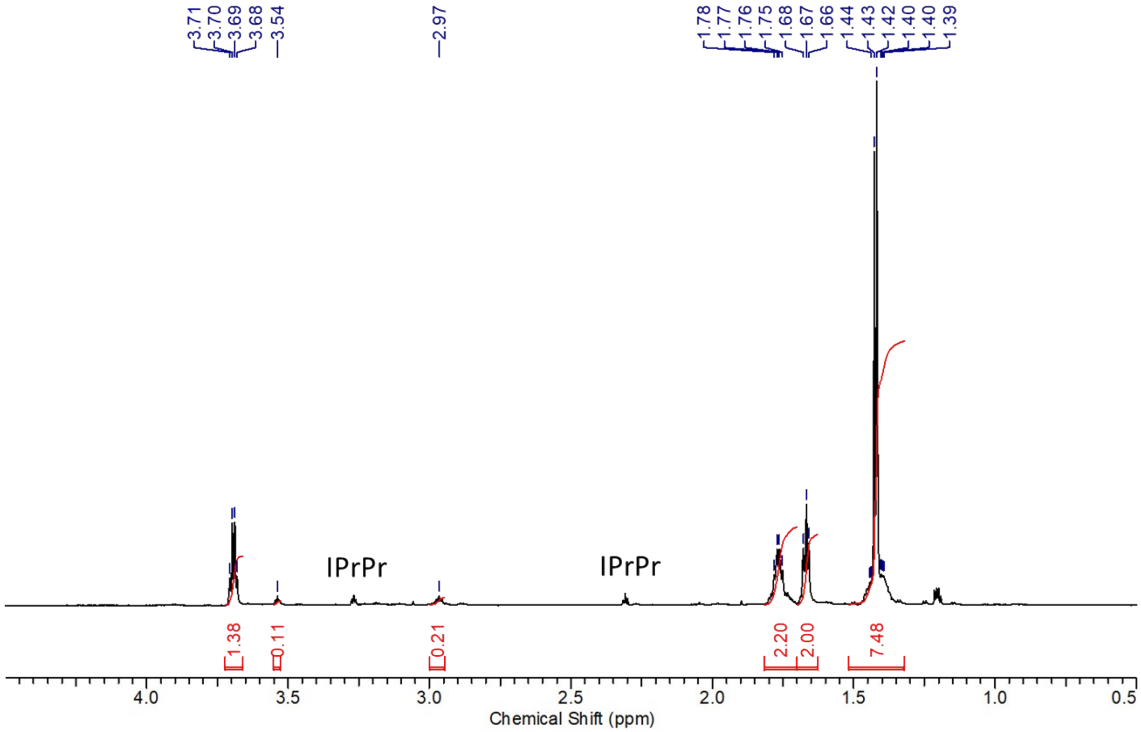


Figure S65. ^{1}H-NMR spectrum of L-alanine/L-lysine (34 mM each) in D_2O after reacting with **RuNi@IPrPrSO3** (8 mol% of metal, 55 °C, 2 bars D_2, pH 9, during 48 h) (Table S5, entry 15).

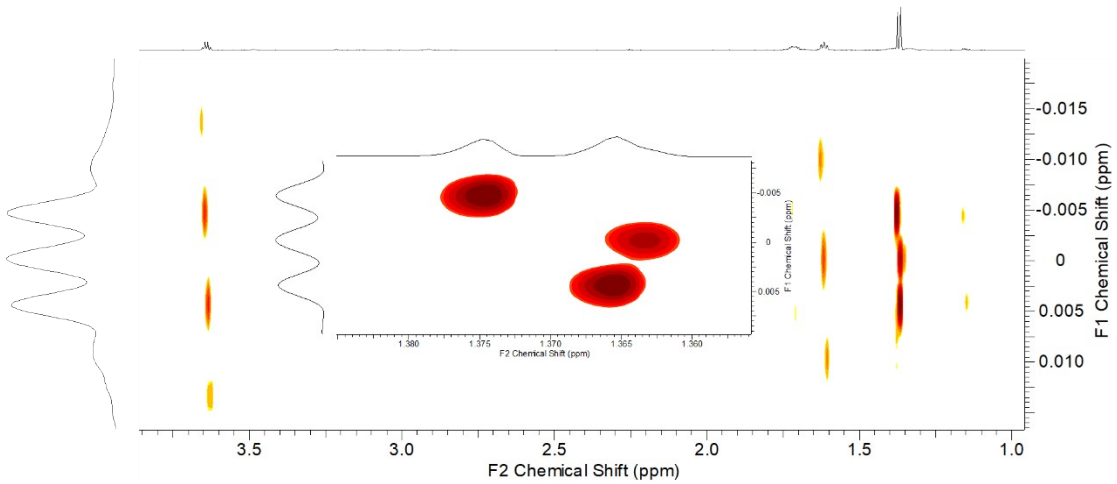


Figure S66. 2D J-resolved ^{1}H-NMR spectrum of L-alanine/L-lysine (34 mM each) in D_2O after reacting with **RuNi@IPrPrSO3** (8 mol% of metal, 55 °C, 2 bars D_2, pH 9, during 48 h) (Table S5, entry 15).

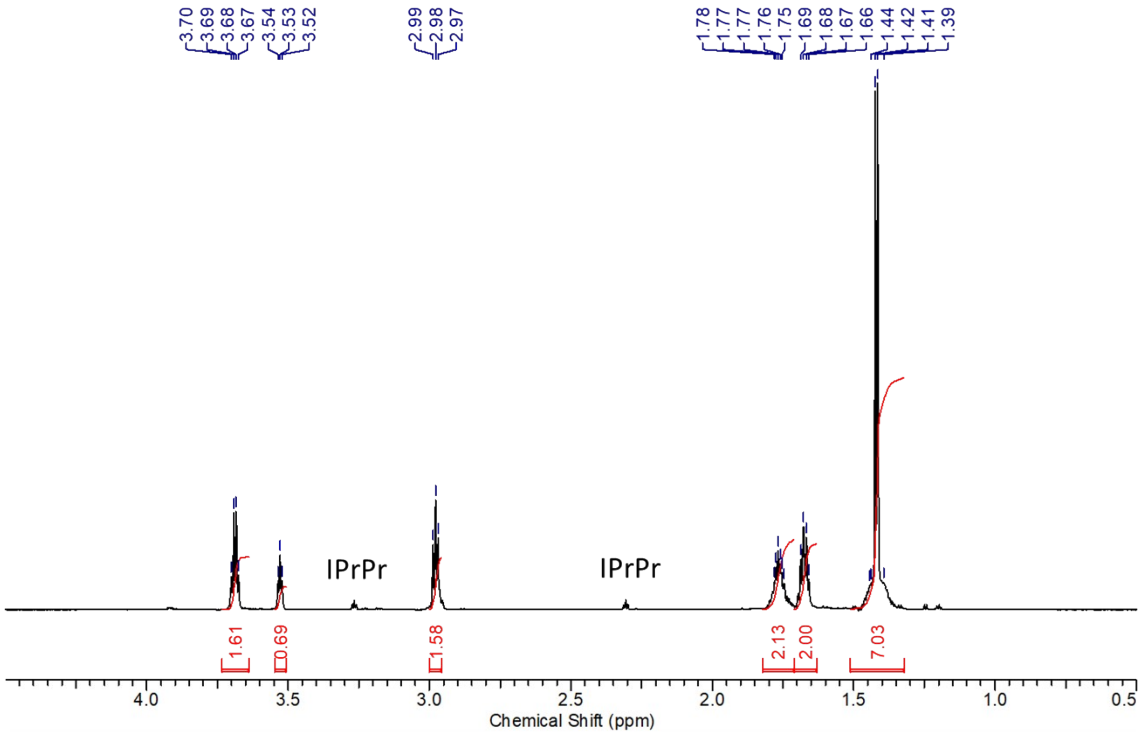


Figure S67. ^{1}H-NMR spectrum of L-alanine/L-lysine (34 mM each) in D_2O after reacting with **RuNi4@IPrPrSO3** (8 mol% of metal, 55 °C, 2 bars D_2, pH 9, during 48 h) (Table S5, entry 16).

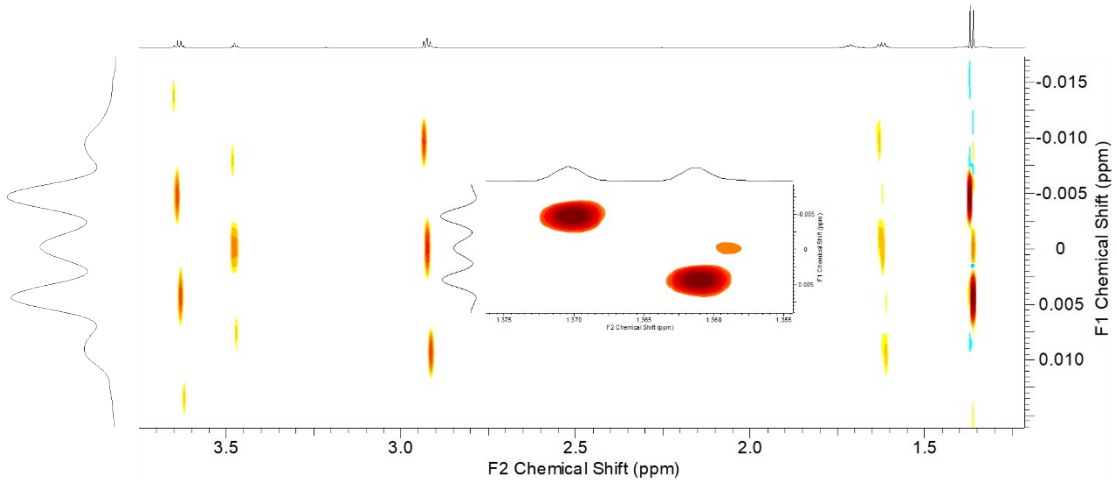


Figure S68. 2D J-resolved ^{1}H-NMR spectrum of L-alanine/L-lysine (34 mM each) in D_2O after reacting with **RuNi4@IPrPrSO3** (8 mol% of metal, 55 °C, 2 bars D_2, pH 9, during 48 h) (Table S5, entry 16).

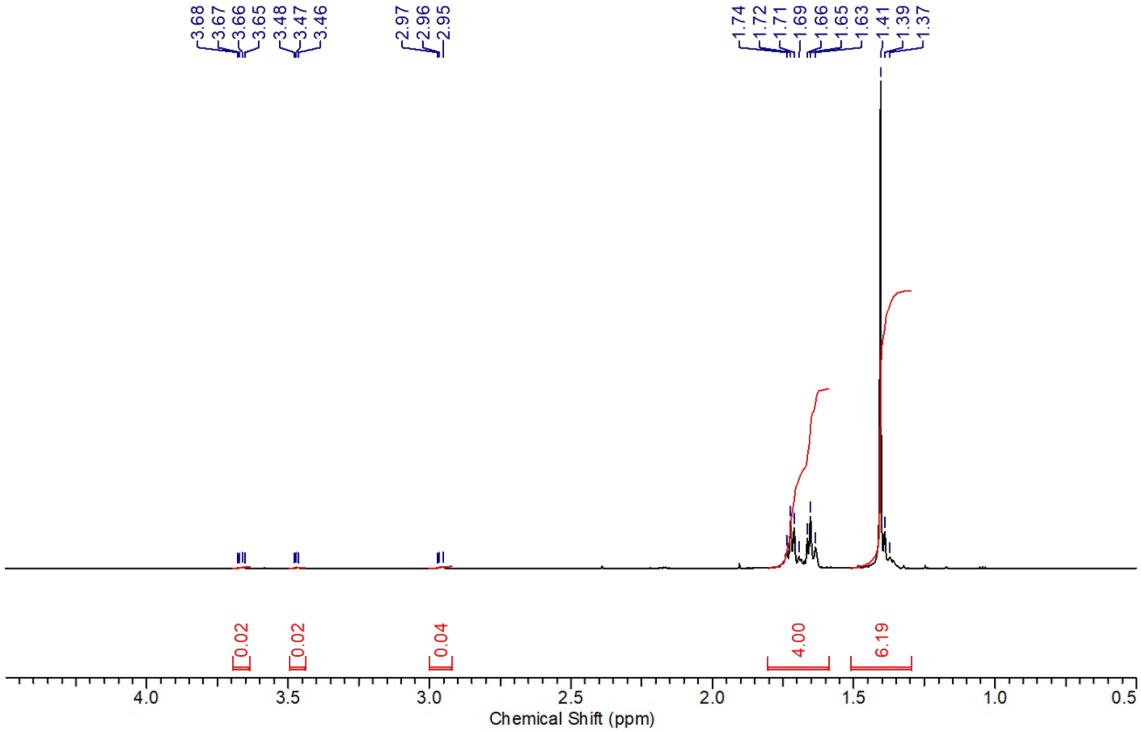


Figure S69. ^{1}H-NMR spectrum of L-alanine/L-lysine (68 mM each) in D_2O after reacting with **RuNP/Cmeso** (8 mol% of metal, 120 °C, 4 bars D_2, pH 7.5, during 1 h) (Table S5, entry 17).

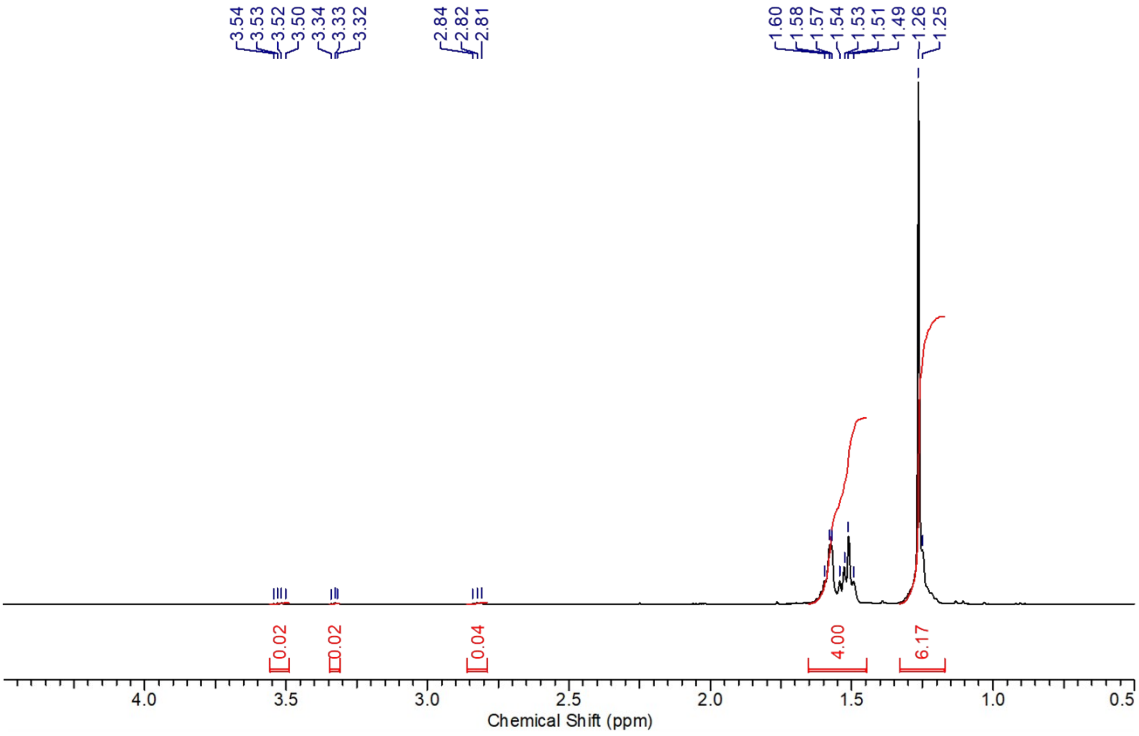


Figure S70. ^{1}H-NMR spectrum of L-alanine/L-lysine (68 mM each) in D_2O after reacting with **RuNP/Cmeso** (8 mol% of metal, 120 °C, 4 bars D_2, pH 9, during 1 h) (Table S5, entry 18).

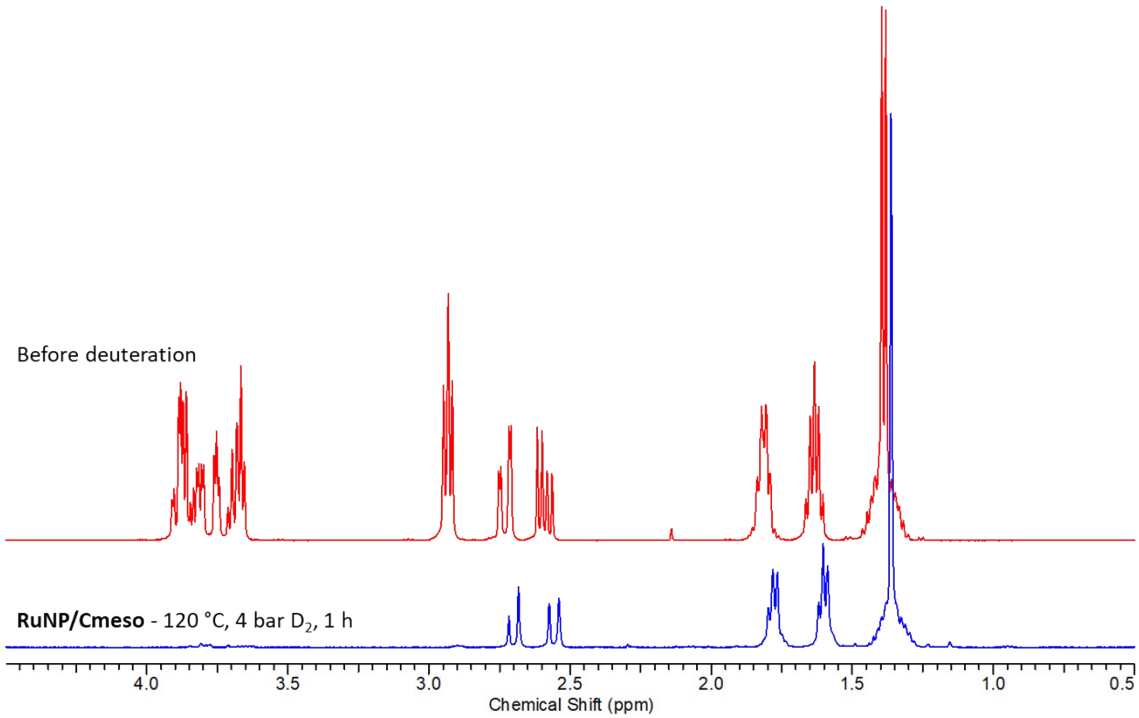


Figure S71. ^{1}H-NMR spectrum of a mixture of L-alanine, L-lysine, L-aspartate and L-serine (34 mM each) in D_2O before (red) and after (blue) reacting with **RuNP/Cmeso** (8 mol% of metal, 120 °C, 4 bars D_2, pH 7, during 1 h).

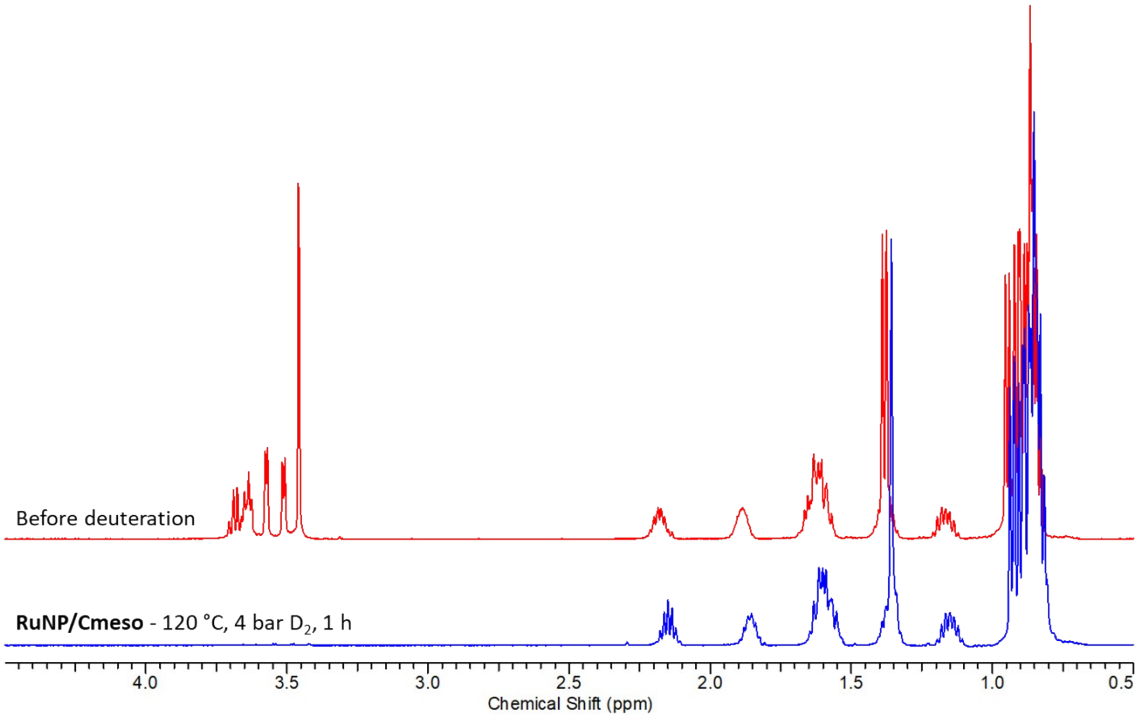


Figure S72. ^{1}H-NMR spectrum of a mixture of L-alanine, L-leucine, L-isoleucine and L-valine and glycine (34 mM each) in D_2O before (red) and after (blue) reacting with **RuNP/Cmeso** (8 mol% of metal, 120 °C, 4 bars D_2, pH 7, during 1 h).

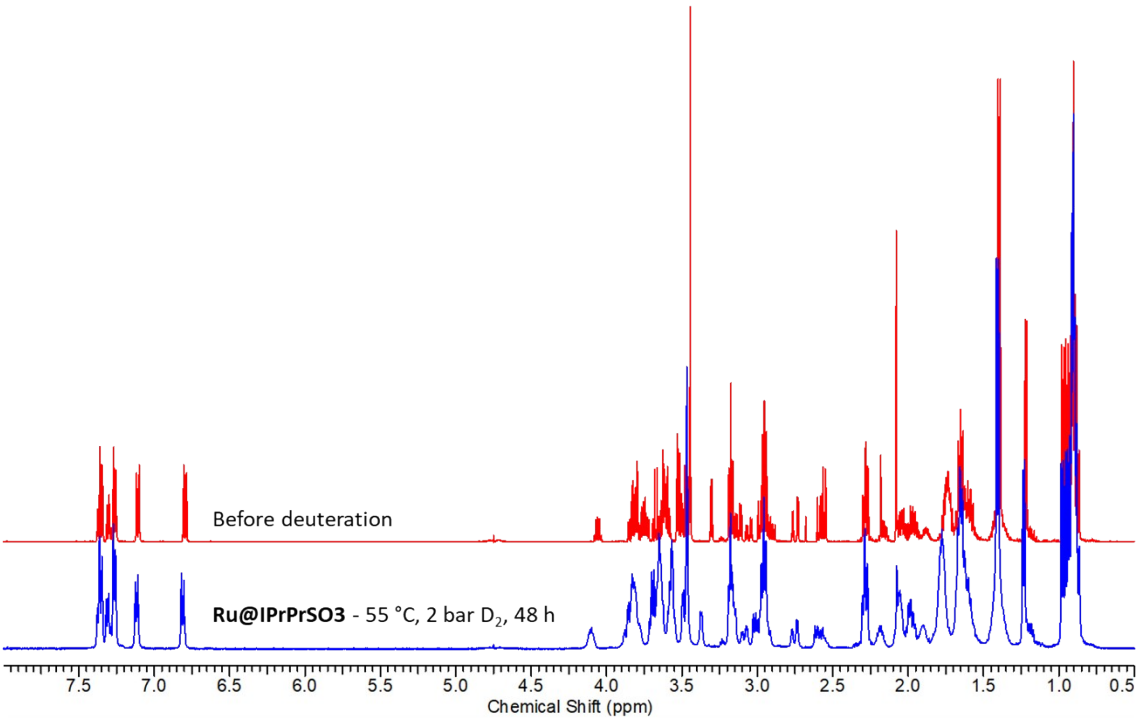


Figure S73. ^{1}H-NMR spectrum of a mixture of 13 amino acids (Ala, Arg, Asp, Gln, Gly, Ile, Leu, Lys, Phe, Ser, Thr, Tyr and Val) (total amino acid concentration:136 mM) in D_2O before (red) and after (blue) reacting with **Ru@IPrPrSO3** (8 mol% of metal, 55 °C, 2 bars D_2, pH 7, during 48 h).

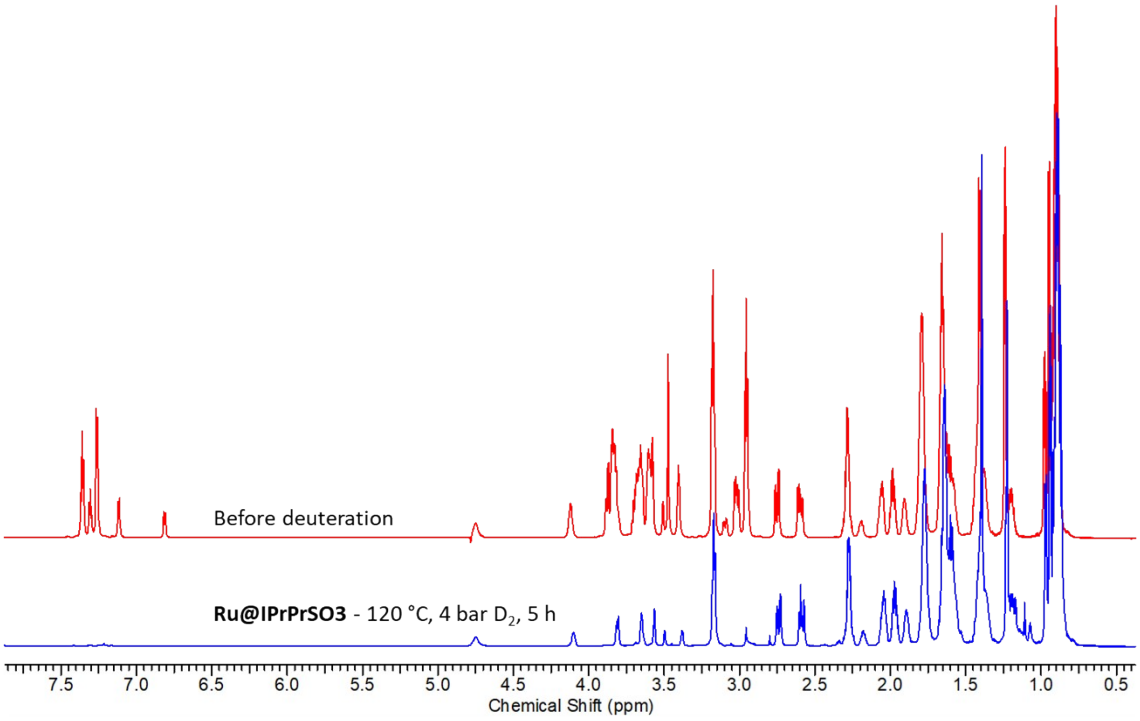


Figure S74. ^{1}H-NMR spectrum of a mixture of 13 amino acids (Ala, Arg, Asp, Gln, Gly, Ile, Leu, Lys, Phe, Ser, Thr, Tyr and Val) (total amino acid concentration:136 mM) in D_2O before (red) and after (blue) reacting with **Ru@IPrPrSO3** (8 mol% of metal, 120 °C, 4 bars D_2, pH 7, during 5 h).

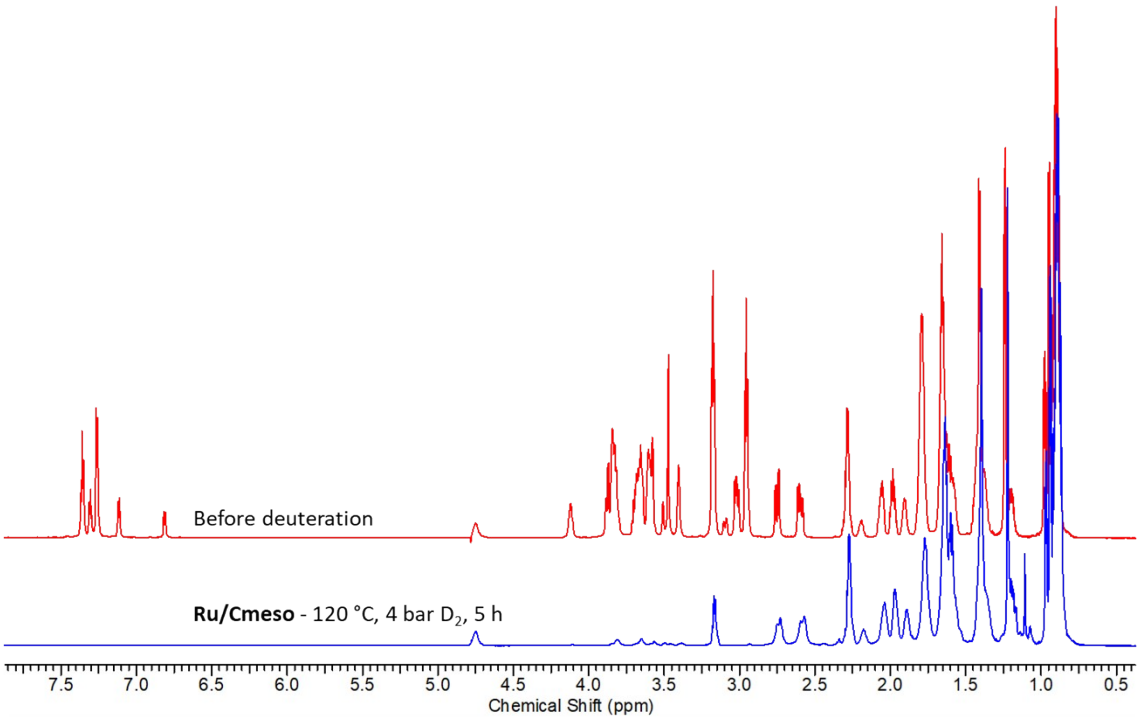


Figure S75. ^{1}H-NMR spectrum of a mixture of 13 amino acids (Ala, Arg, Asp, Glu, Gly, Ile, Leu, Lys, Phe, Ser, Thr, Tyr and Val) (total amino acid concentration:136 mM) in D_2O before (red) and after (blue) reacting with **Ru/Cmeso** (8 mol% of metal, 120 °C, 4 bars D_2, pH 7, during 5 h).

12. References

1. L. R. Moore, S. M. Cooks, M. S. Anderson, H.-J. Schanz, S. T. Griffin, R. D. Rogers, M. C. Kirk and K. H. Shaughnessy, *Organometallics*, 2006, **25**, 5151-5158.
2. L. M. Martínez-Prieto, E. A. Baquero, G. Pieters, J. C. Flores, E. de Jesús, C. Nayral, F. Delpech, P. W. N. M. van Leeuwen, G. Lippens and B. Chaudret, *Chemical Communications*, 2017, **53**, 5850-5853.
3. P.-J. Debouttière, V. Martinez, K. Philippot and B. Chaudret, *Dalton Transactions*, 2009, 10172-10174.