

**Structural, kinetics and mechanistic studies of asymmetric transfer hydrogenation of
ketones catalyzed by chiral (pyridyl)imine nickel(II) complexes**

Robert T. Kumah, Nokwanda Tsaulwayo, Bheki A. Xulu, Stephen O. Ojwach*

*School of Chemistry and physics, University of KwaZulu-Natal, Pietermaritzburg Campus,
Private Bag X01 Scottsville, 3209, South Africa*

Synthesis and characterization of ligands

(S)-1-phenyl-*N*-(pyridine-2-yl) ethylidene) ethanamine (**L1**)

Compound (*S*)-1-phenyl-*N*-(pyridine-2-yl) ethylidene) ethanamine (**L1**) was synthesized by refluxing 2-acetylpyridine (2.00 g, 16.51mmol), (*S*)-methylbenzylamine (2.00 g, 16.51 mmol), and *p*-TsOH monohydrate (1.0 mol %) toluene (25 mL) for 12 h using Dean Stark apparatus. After 12 h of reaction time, the solvent was removed under vacuum to obtain a brown crude oil. This was dissolved in CH₂Cl₂ (15 mL) and washed with water (3x15 mL). The organic layer was separated followed by drying over anhydrous MgSO₄, filtered and solvent evaporated to obtain **L1** as a brown oil. Yield: 2.67 g (72%). ¹H NMR (CDCl₃, δ, ppm): 1.56 (d, 3H, NCHCH₃, ³J_{HH} = 3.6), 2.24 (s, 3H, CCH₃N), 4.69 (q, 1H, NCH, ³J_{HH} = 4.0), 8.82 (d, 1H, 5H-py, ³J_{HH} = 7.6), 8.86 (d, 1H, 6H-py, ³J_{HH}, = 7.6), 8.23 (dd, 1H, 4H-py, ³J_{HH} = 7.6), 7.98 (dd, 1H, 3H-py, ³J_{HH} = 7.6 Hz); 7.29 (dd, 2H, 3-bz, ³J_{HH},= 8.0Hz); 7.39 (dd, 1H, 4-bz, ³J_{HH} = 8.0 Hz); 7.29 (d, 2H, 2-bz, ³J_{HH} = 8.0 Hz). ¹³C NMR (CDCl₃): δ 24.59 (CH₃), 16.73 (CH₃), 160.48 (C=N), 154.87 (2-Py-C), 149.36 (6-Py-C), 144.63 (o-bz-C), 128.25 (m-bz-C), 127.03 (3-py-C), 121.47 (5-py-c), 69.57 (1C, =N-C). FT-IR (cm⁻¹): (ν_{C=N})_{imine}=1697. ESI- MS: *m/z* (%) 247 [M⁺ + Na⁺, 100]: HRMS-ESI ([M+ Na⁺]): Anal. Calc: 247.1211; Found: 247.1206.

(R)-1-phenyl-*N*-(pyridine-2-yl) ethylidene) ethanamine (**L2**)

(*R*)-1-phenyl-*N*-(pyridine-2-yl) ethylidene) ethanamine (**L2**) was synthesised according to protocol described for **L1** using (*R*)-1- phenyl ethanamine (2.00 g, 16.51mmol), and 2-acetylpyridine (2.00 g, 16.51mmol). Yield = 3.10 g (83 %). ¹H NMR (400 MHz, CDCl₃): δ 2.24 (s, 3H, CCH₃N); 1.6 (d, 3H, NCCH, ³J_{HH} = 3.6 Hz); 4.69 (q, 1H, N-CH, ³J_{HH} = 4.0 Hz), 8.82 (d, 1H, 5H-py, ³J_{HH} = 7.6 Hz); 8.67 (d, 1H, 5H-py, ³J_{HH} = 7.6 Hz); 8.23 (dd, 1H, 4-H-

py, $^3J_{\text{HH}} = 7.6$); 7.98 (dd, 1H, 3-H-py, $^3J_{\text{HH}} = 7.6$ Hz); 7.29 (dd, 2H, 3H-bz, $^3J_{\text{HH}} = 8.0$ Hz); 7.39 (dd, 1H, 4H-bz, $^3J_{\text{HH}} = 8.0$ Hz); 7.29 (d, 2H, 2H-bz, $^3J_{\text{HH}} = 8.0$ Hz). ^{13}C NMR (CDCl_3): δ 24.59 ($\underline{\text{CH}_3}$), 16.73 ($\underline{\text{CH}_3}$), 160.48 ($\underline{\text{C}=\text{N}}$), 154.87 (2-Py-C), 149.36 (6-Py-C), 144.63 (*o*-bz-C), 128.25 (*m*-bz-C), 136.26 (4-py-C), 127.03 (3-py-C), 121.47 (5-py-C), 69.57 (1C, =N-C). FT-IR (cm^{-1}): $\nu(\text{C}=\text{N})_{\text{imine}} = 1687.29$. ESI- MS: m/z (%) 247 [$\text{M}^{++} \text{Na}^+$, 100]. HRMS-ESI ($[\text{M}^+ + \text{Na}^+]$): Anal Calc: 247.1211; Found: 247.1206.

(S)-1-phenyl-*N*-(pyridine-2-yl methylene) ethanamine (**L3**)

To a solution of (*S*)-2-methyl benzylamine (2.15 g, 17.8 mmol) in CH_2Cl_2 (10. mL) was added a solution of 2-pyridine carboxyaldehyde (1.91 g, 17.8 mmol) in CH_2Cl_2 (10. mL) and MgSO_4 (0.50 g) and stirred at room temperature for 12 h. After the reaction period, the crude product was filtered and the solvent was removed under reduced pressure to afford **L2** as a brown oil. Yield = 3.27 g, (87 %). ^1H NMR (400 MHz, CDCl_3): δ 1.6 (d, 3H, NCCH_3 , $^3J_{\text{HH}} = 3.6$); 4.69 (q, 1H, H(a), $^3J_{\text{HH}} = 3.6$), 8.65 (d, 1H, H(d), $^3J_{\text{HH}} = 7.6$); 8.51 (s, 1H, $\underline{\text{HCN}}$); 8.23 (dd, 1H, 3H-py, $^3J_{\text{HH}} = 7.6$); 7.74 (dd, 1H, 4H-py, $^3J_{\text{HH}} = 7.6$); 7.48 (dd, 2H, 5H-py, $^3J_{\text{HH}} = 8.0$ Hz); 7.39 (dd, 1H, 3H-bz, $^3J_{\text{HH}} = 8.0$ Hz); 7.29 (d, 2H, 2H-bz, $^3J_{\text{HH}} = 8.0$ Hz). ^{13}C NMR (CDCl_3): δ 24.59 ($\underline{\text{CH}_3}$), 16.73 ($\underline{\text{CH}_3}$), 160.48 ($\underline{\text{C}=\text{N}}$), 154.87 (5-Py-C), 149.36 (6-Py-C), 144.63 (*o*-bz-C), 128.25 (*m*-bz-C), 127.03 (5-py-C), 121.47 (3-py-c), 69.57 (1C, =N-C). FT-IR (cm^{-1}): $\nu(\text{C}=\text{N})_{\text{imine}} = 1643$, ESI-MS: m/z (%) 233 [$(\text{M}^+ \text{Na}^+)$, 100%]. HRMS-ESI: Anal. Calc: 211.1235; Found: 211.1232.

(R)-1-phenyl-*N*-(pyridine-2-yl methylene) ethanamine (**L4**)

(*S*)-2-methyl benzylamine (2.15 g, 17.8 mmol), 2-pyridine carboxyaldehyde (1.91 g, 17.8 mmol), and $\text{MgSO}_4 \cdot \text{H}_2\text{O}$ (1.00 g). Yield = 3.10 g, (83%). ^1H NMR (400 MHz, CDCl_3): δ 1.6 (d, 3H, NCCH_3 , $^3J_{\text{HH}} = 3.6$); 4.69 (q, 1H, NCH_2 , $^3J_{\text{HH}} = 4.0$), 8.65 (d, 1H, 6H-py, $^3J_{\text{HH}} = 7.6$ Hz); 8.51 (s, 1H, H(c)); 8.23 (dd, 1H, 3H-py, $^3J_{\text{HH}} = 7.6$); 7.98 (dd, 1H, 3H-py, $^3J_{\text{HH}} = 7.6$); 7.48 (dd, 2H, 5H-py, $^3J_{\text{HH}} = 7.29$ Hz); 7.39 (dd, 1H, 3H-bz, $^3J_{\text{HH}} = 8.0$); 7.29 (d, 2H, 4H-bz,

$^3J_{\text{HH}} = 8.0$); 7.28 (dd, 2H, 2H-bz $^3J_{\text{HH}} = 8.0$). ^{13}C NMR (CDCl_3): δ 24.59 (CH_3), 16.73 (CH_3), 160.48 ($\text{C}=\text{N}$), 154.87 (2-Py-C), 149.36 (6-Py-C), 144.63 (*o*-bz-C), 128.25 (*m*-bz-C), 127.03 (5-py-C), 121.47 (3-py-c), 137.25 (4-py-C), 69.57 (1C, =N-C). FT-IR (cm^{-1}): ($\nu_{\text{C}=\text{N}}$)_{imine}=1642, ESI-MS: m/z (%) 233 [(M +Na)⁺, 100%]. HRMS-ESI: Anal. Calc. 211.1235; Found: 211.1233.



Fig S1. ¹H NMR spectrum of L1.

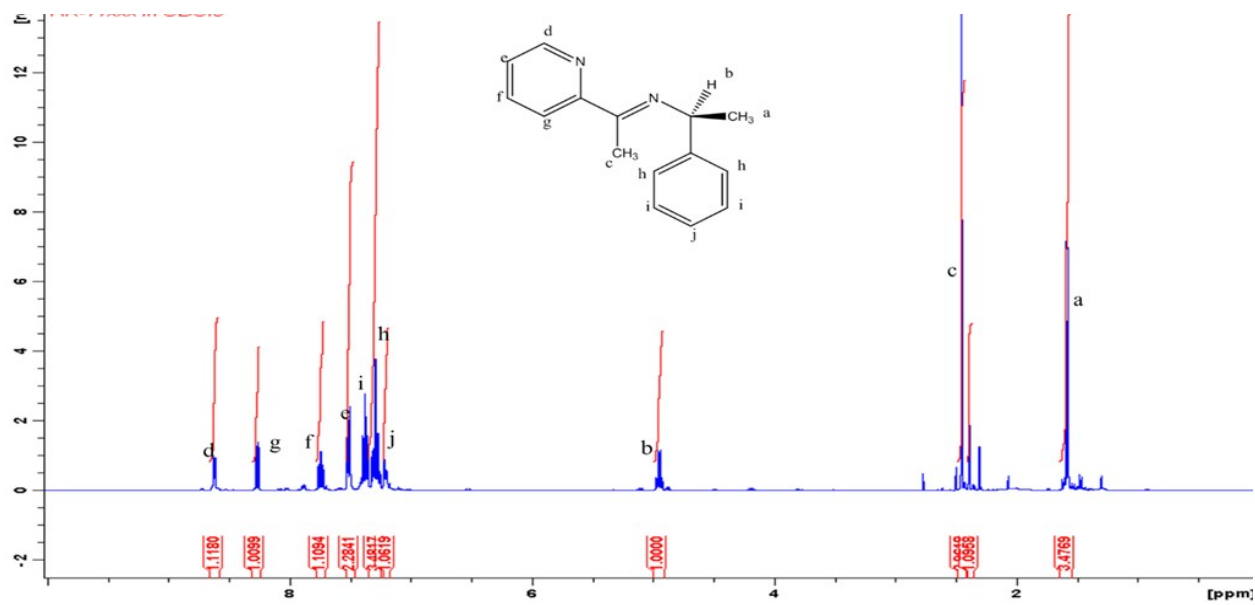


Fig S2. ¹H NMR spectrum of L2.

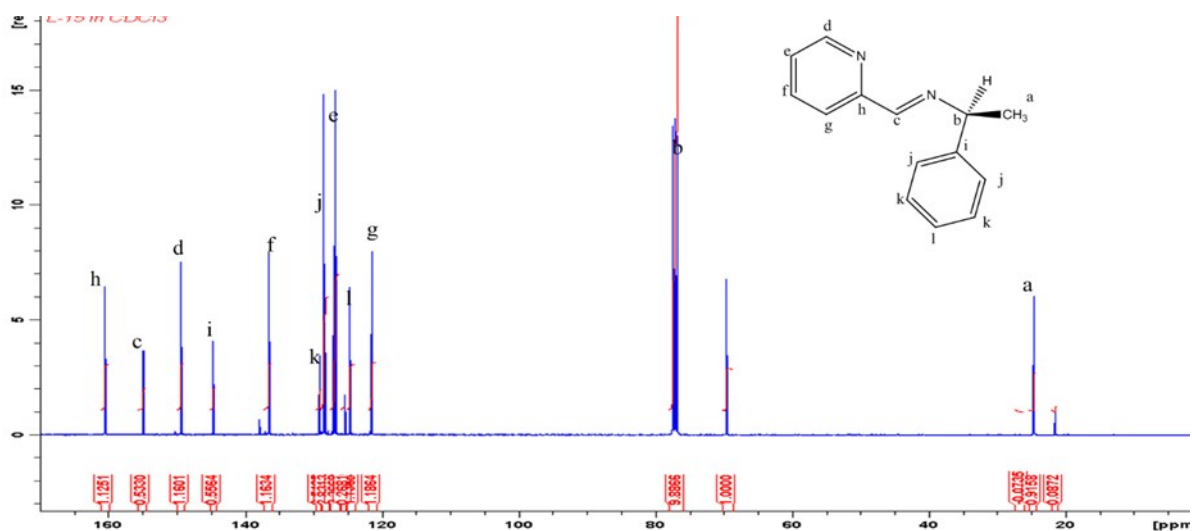


Fig S5. ¹³C NMR spectrum of L3.

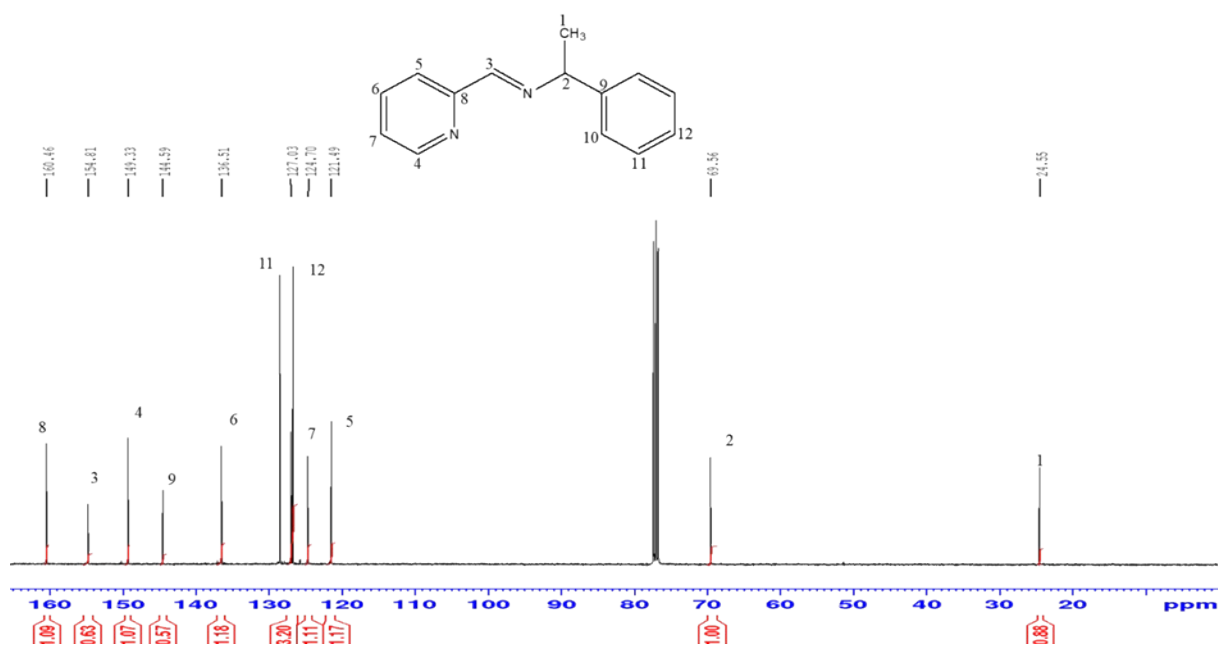


Fig S6. ¹³C NMR spectrum of L4.

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 500.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 2

Monoisotopic Mass, Even Electron Ions

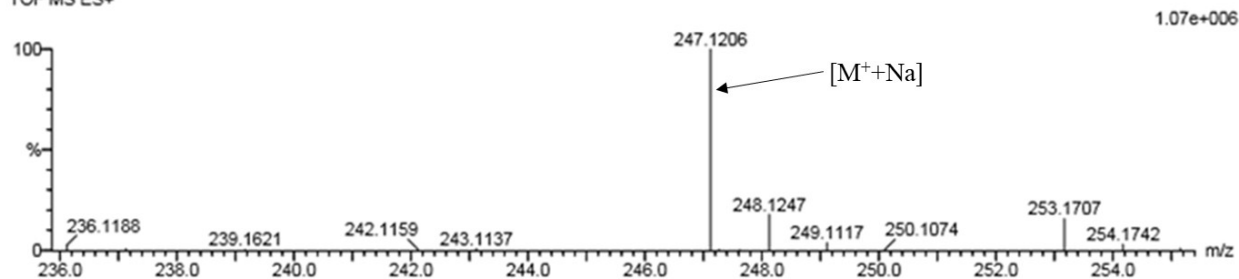
8 formula(e) evaluated with 1 results within limits (up to 20 closest results for each mass)

Elements Used:

C: 15-20 H: 15-20 N: 0-5 Na: 0-1

RK-L1(S) 2 (0.034) Cm (1:61)

TOF MS ES+



Minimum:				-1.5				
Maximum:		5.0	5.0	500.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula	
247.1206	247.1211	-0.5	-2.0	8.5	45.3	0.0	C15 H16 N2 Na	

Fig. S7. HR MS of L1

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 500.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 2

Monoisotopic Mass, Even Electron Ions

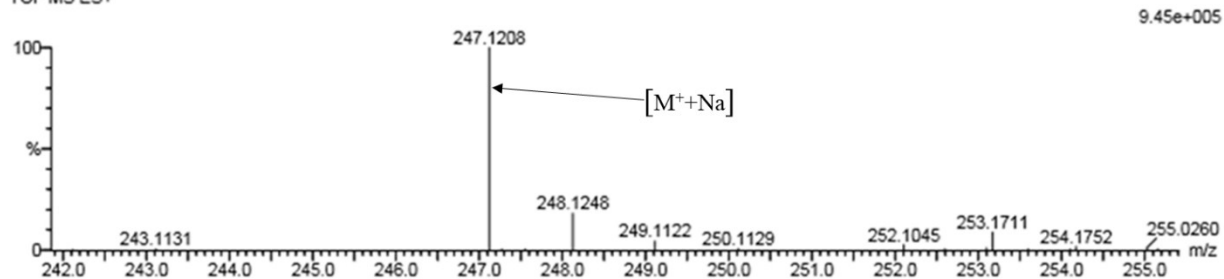
8 formula(e) evaluated with 1 results within limits (up to 20 closest results for each mass)

Elements Used:

C: 15-20 H: 15-20 N: 0-5 Na: 0-1

RK-L3(R) 8 (0.237) Cm (1:61)

TOF MS ES+



Minimum:				-1.5				
Maximum:		5.0	5.0	500.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula	
247.1208	247.1211	-0.3	-1.2	8.5	48.3	0.0	C15 H16 N2 Na	

Fig. S8. HR MS of L2.

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 500.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 2

Monoisotopic Mass, Even Electron Ions

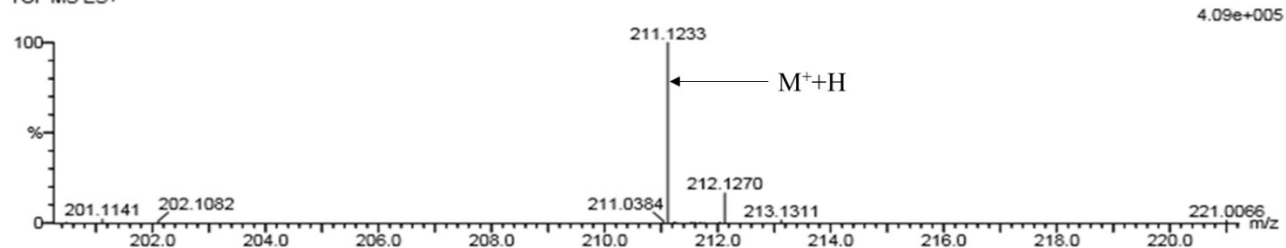
3 formula(e) evaluated with 1 results within limits (up to 20 closest results for each mass)

Elements Used:

C: 10-15 H: 10-15 N: 0-5

RK-L4(R) 3 (0.068) Cm (1:61)

TOF MS ES+



Minimum:				-1.5				
Maximum:		5.0	5.0	500.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula	
211.1233	211.1235	-0.2	-0.9	8.5	111.9	0.0	C14 H15 N2	

Fig. S9. HR MS of L3.

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 500.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 2

Monoisotopic Mass, Even Electron Ions

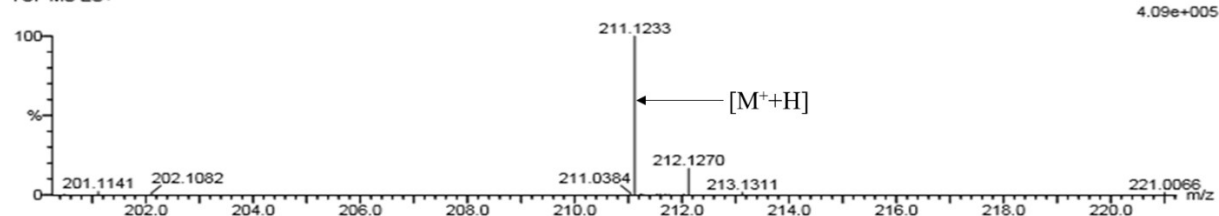
3 formula(e) evaluated with 1 results within limits (up to 20 closest results for each mass)

Elements Used:

C: 10-15 H: 10-15 N: 0-5

RK-L4(R) 3 (0.068) Cm (1:61)

TOF MS ES+



Minimum:				-1.5				
Maximum:		5.0	5.0	500.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula	
211.1233	211.1235	-0.2	-0.9	8.5	111.9	0.0	C14 H15 N2	

Fig. S10. HR-MS of L4.

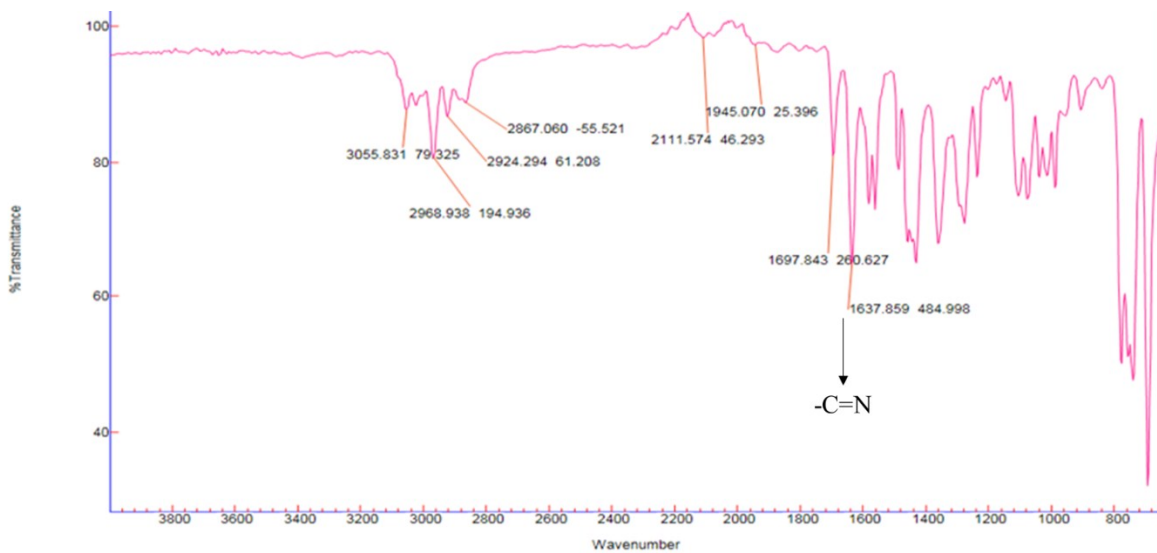


Fig. S11. FT-IR spectrum of L1.

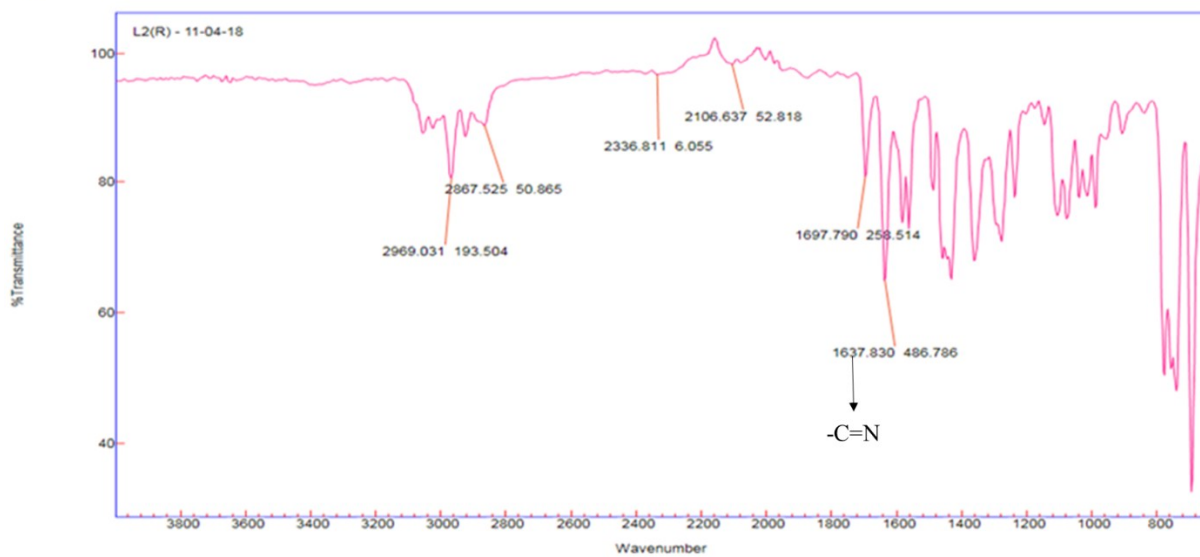


Fig. S12. FT-IR spectrum of L2.

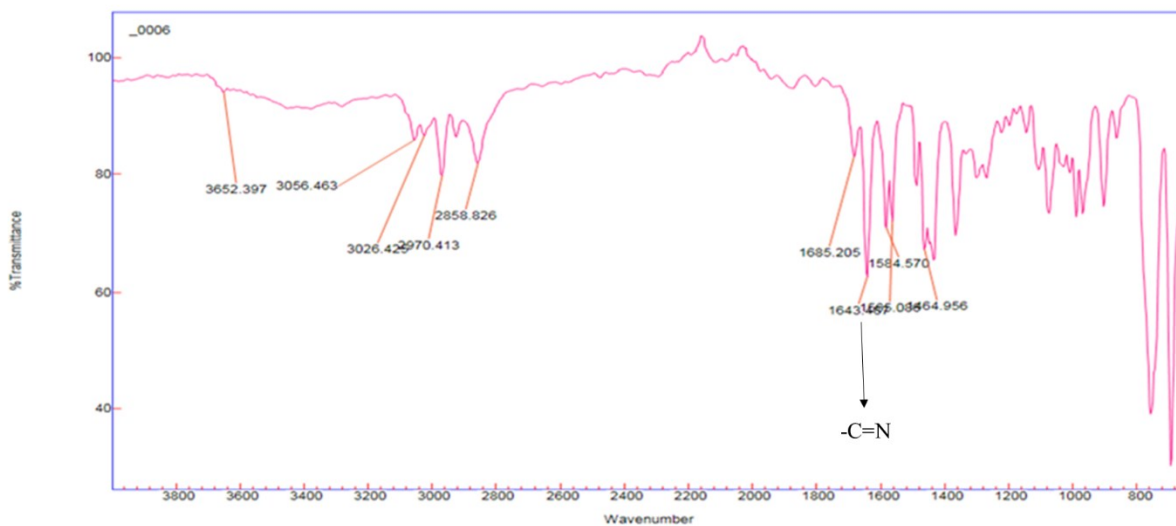


Fig. S13. FT-IR spectrum of L3.



Fig. S14. FT-IR spectrum of Ni1.

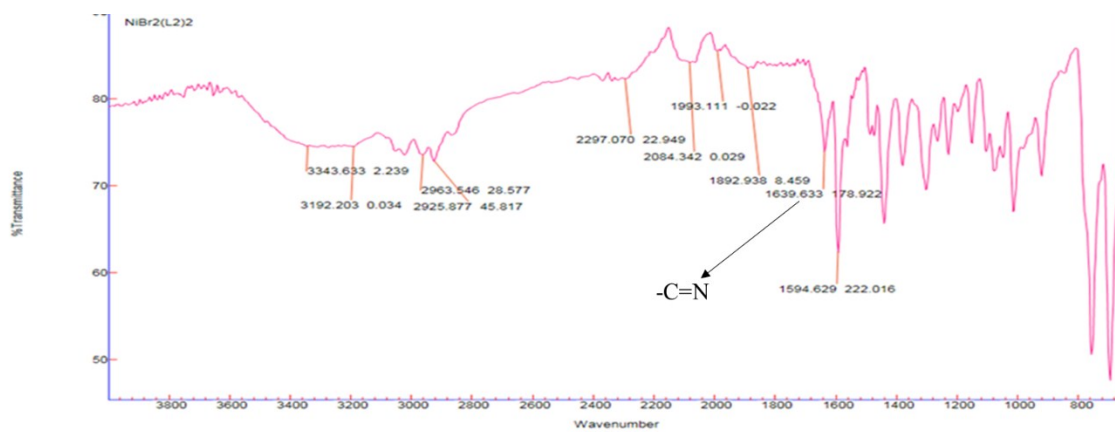


Fig. S15. FT-IR spectrum of Ni2.

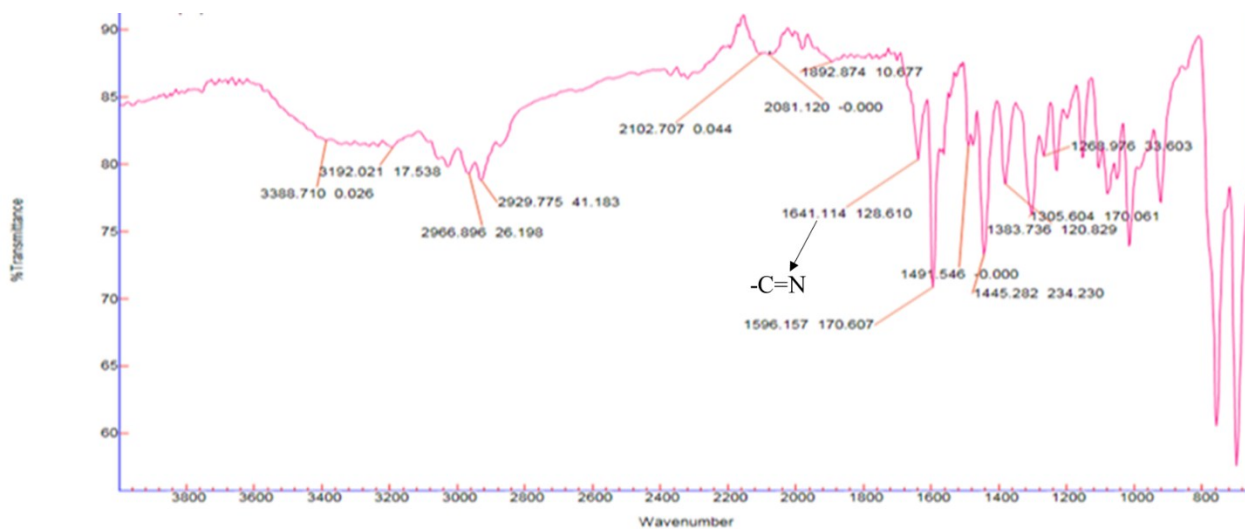


Fig. S16. FT-IR spectrum of Ni3.

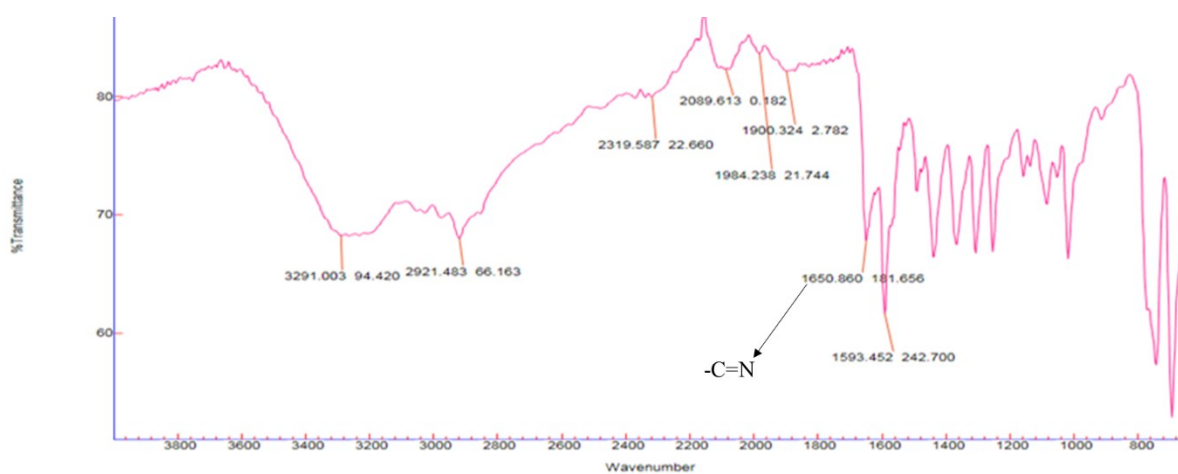


Fig. S17. FT-IR spectrum of Ni4.

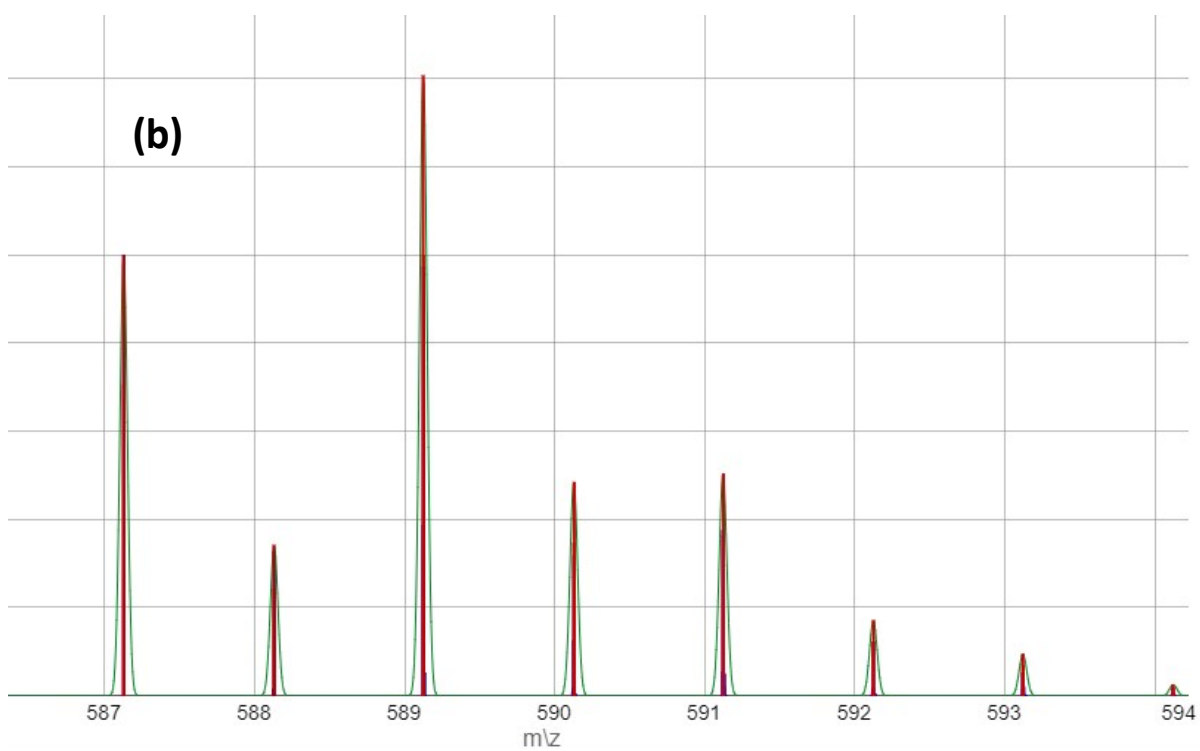
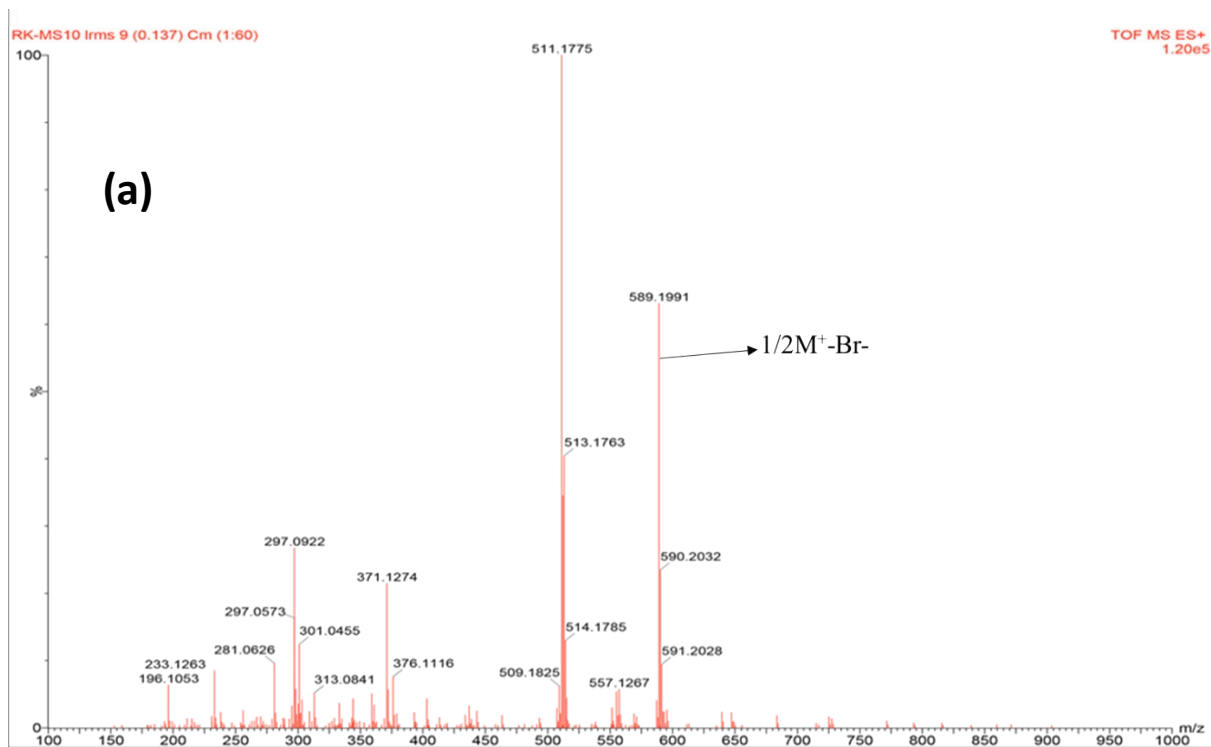


Fig. S18: (a) ESI-MS (Low resolution) spectra of complex Ni1. (b) Experimental (green) and simulated (red) spectrum for signal at $m/z = 589.1991(1/2M^+ - Br)$ in complex Ni1.

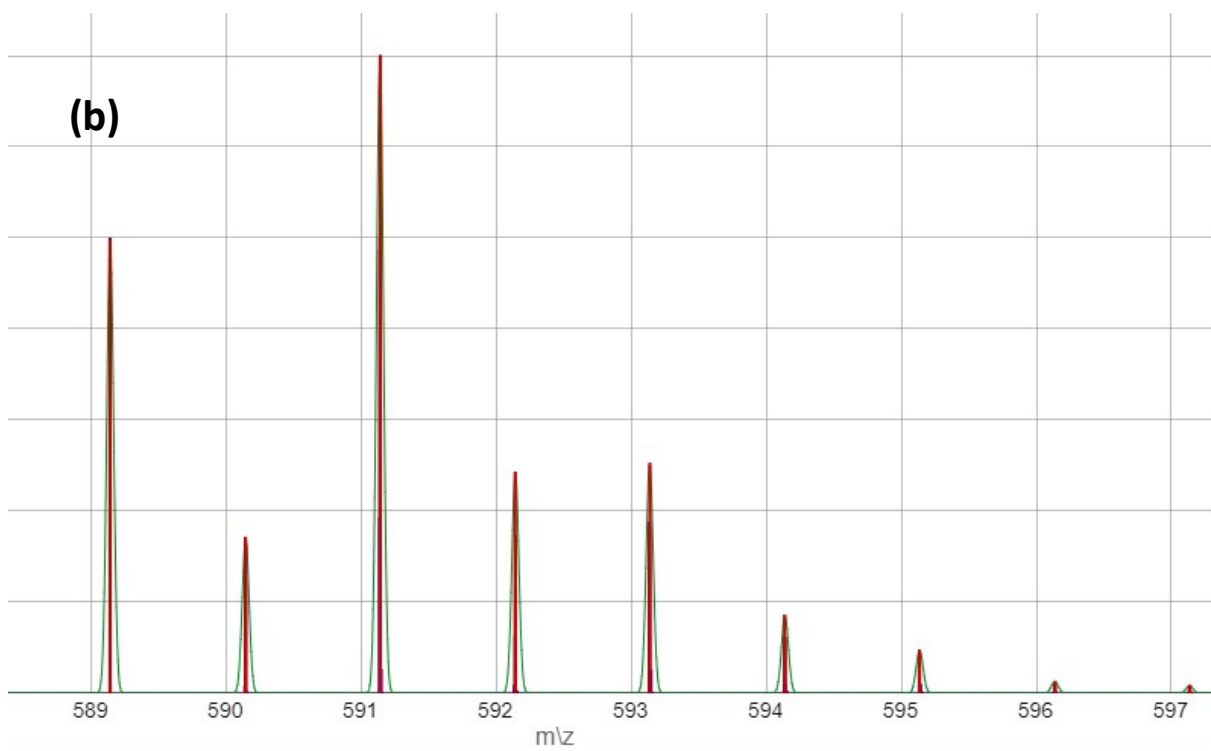
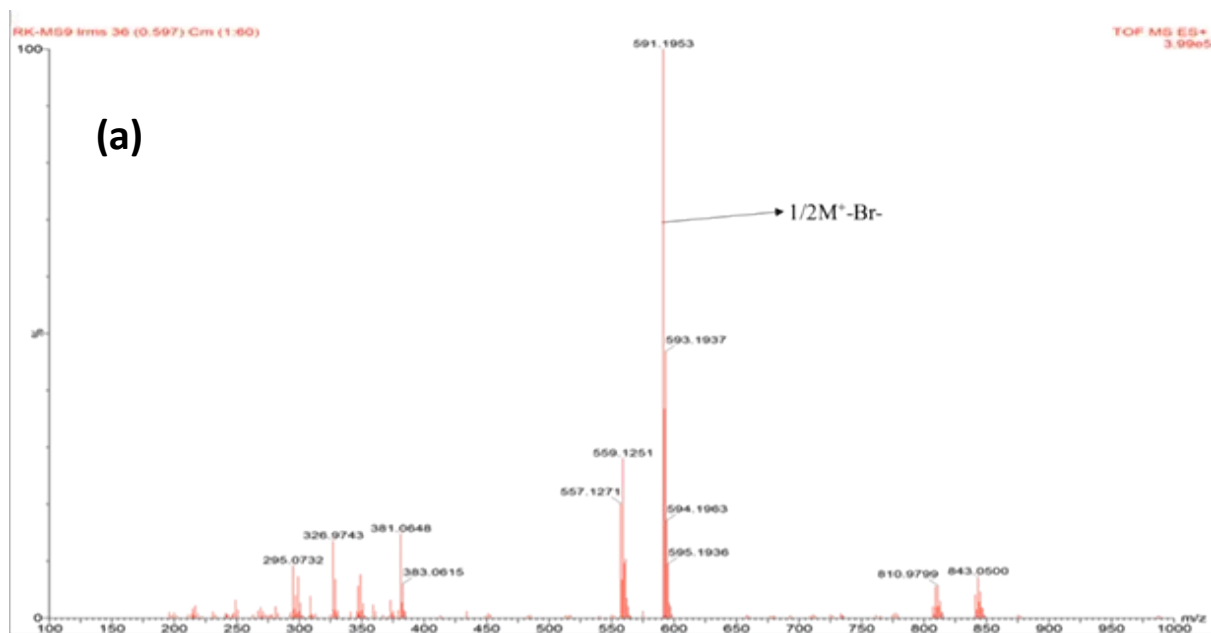


Fig. S19 (a) ESI-MS (Low resolution) spectrum of **Ni2**. **(b)** Experimental (green) and simulated (red) spectrum for molecular ion at $m/z = 591.1953$ in Complex **Ni2**

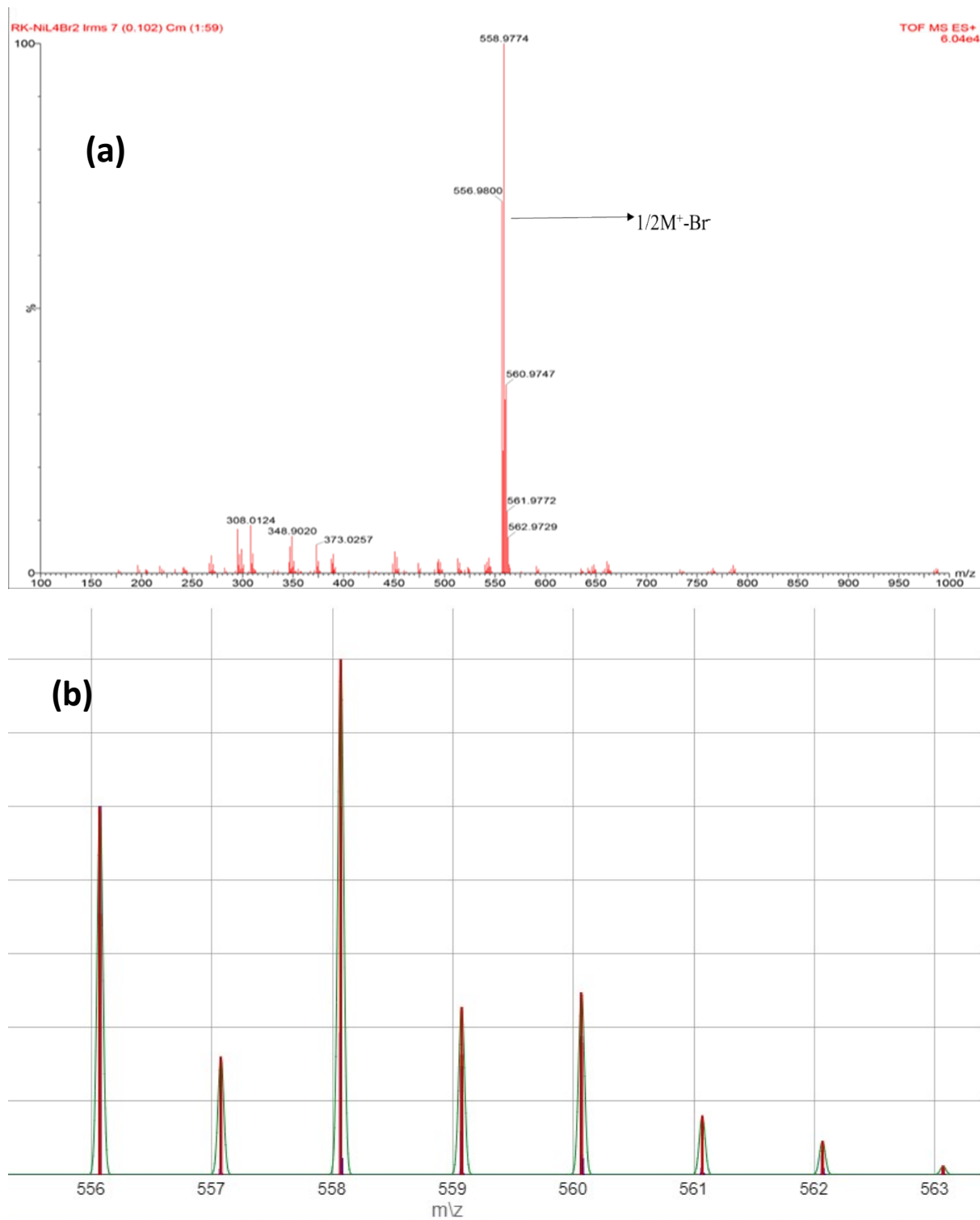


Fig. S20 (a) ESI-MS (low resolution) spectrum of Ni3. **(b)** Experimental (green) and simulated (red) spectrum for molecular ion at $m/z = 558.9774$ in Complex Ni3

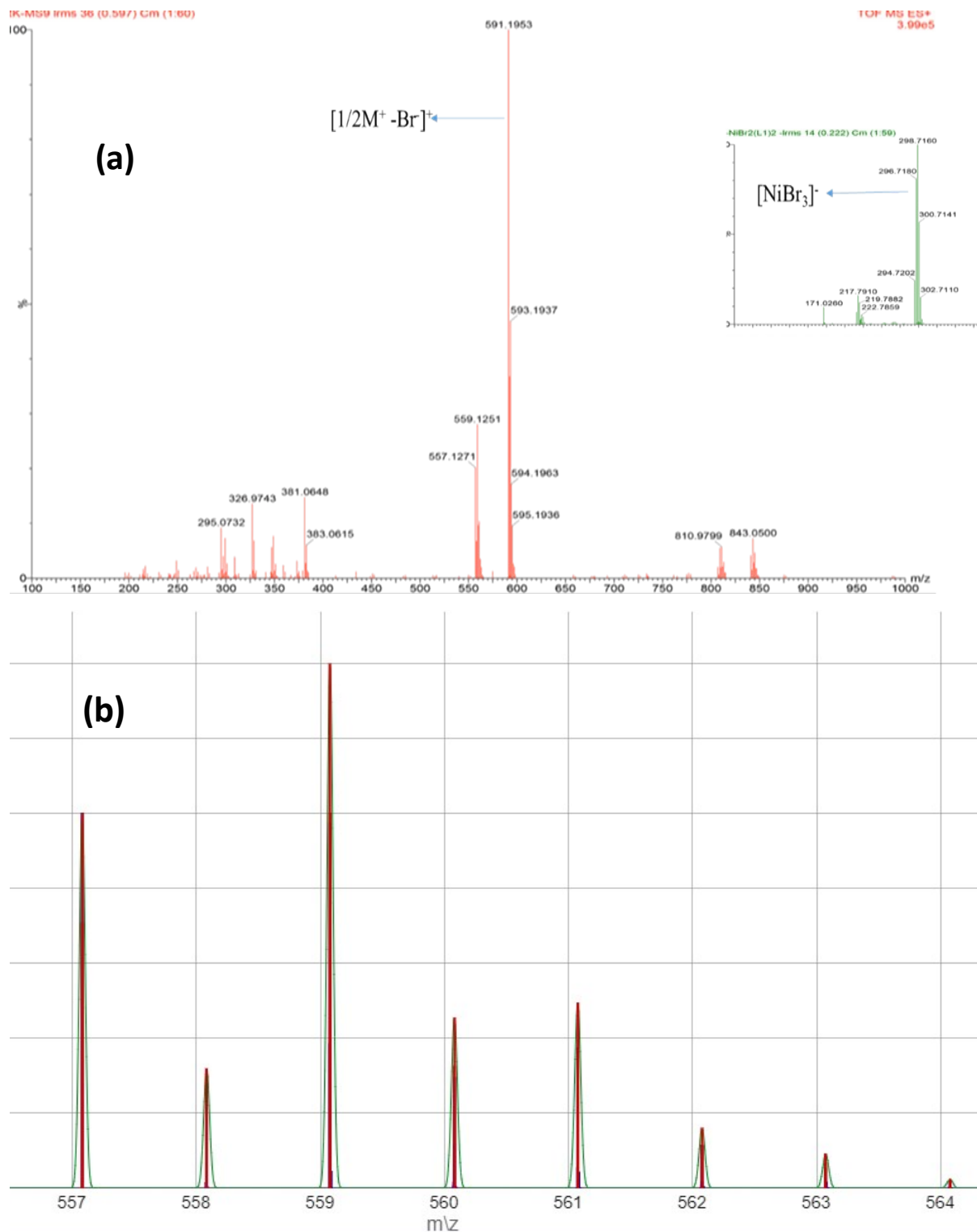


Fig. S21 (a) ESI-MS (low resolution) spectrum of Ni4. Inset shows the mass spectrum acquired in negative mode of the $[NiBr_4]^{2-}$ ($m/z = 373$ amu) counterion. **(b)** Experimental (green) and simulated (red) spectrum for molecular ion at $m/z = 559.1251$ in Complex Ni4.

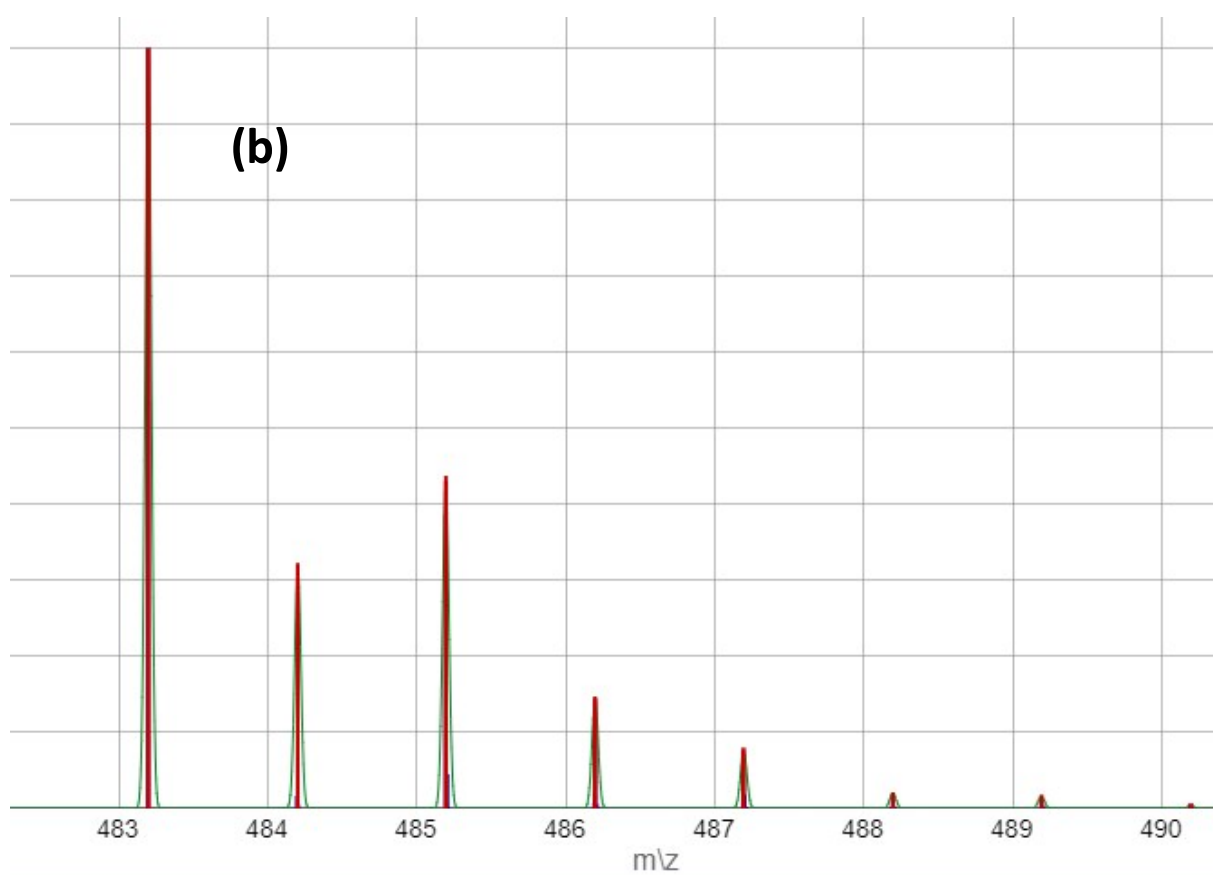
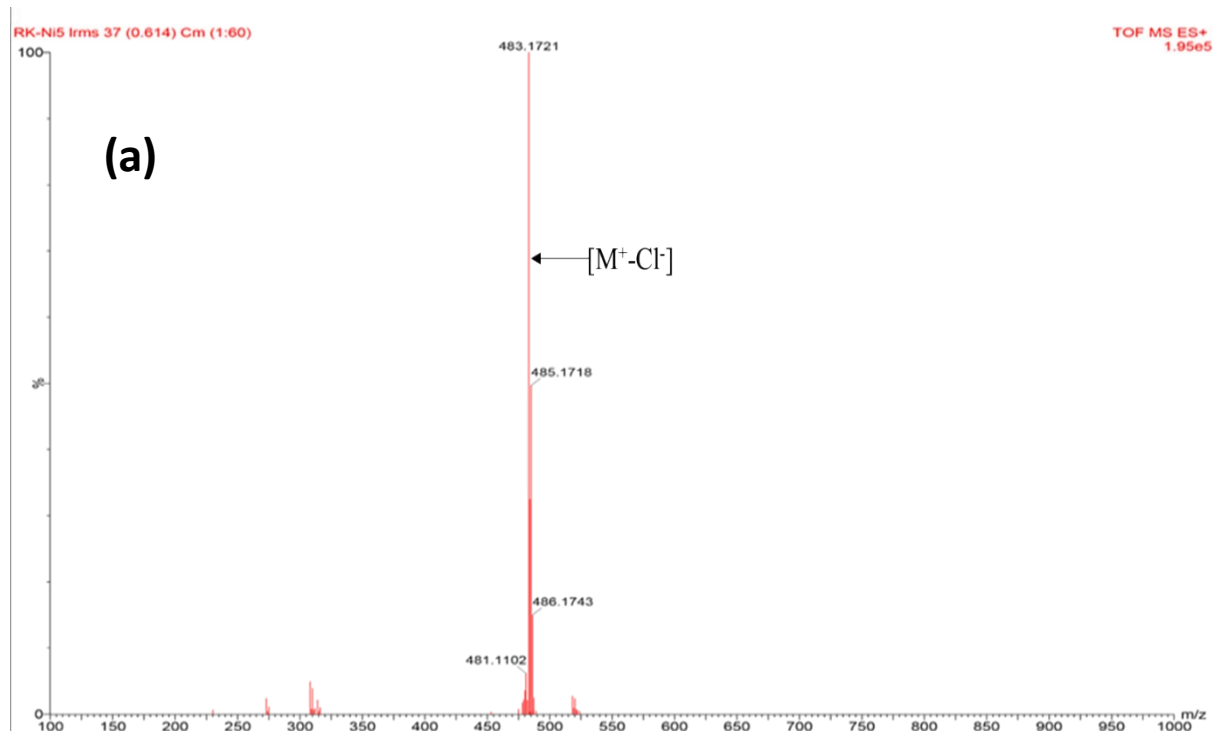


Fig. S22 (a) ESI-MS (low resolution) spectrum of Ni5. **(b)** Experimental (green) and simulated (red) spectrum for molecular ion at $m/z = 483.1721$ in Complex Ni5

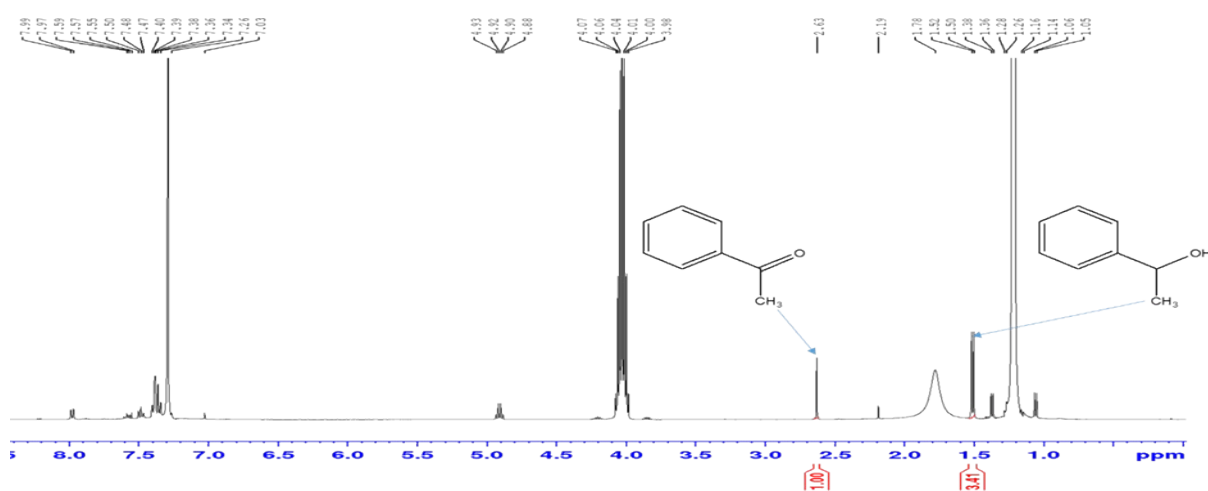


Fig. S23. Typical ^1H NMR spectrum of crude product from ATH reaction of acetophenone using complex **4** after 24 h indicating the intensity of methyl groups of 1-phenylethanol and acetophenone respectively used for calculating percentage conversions.

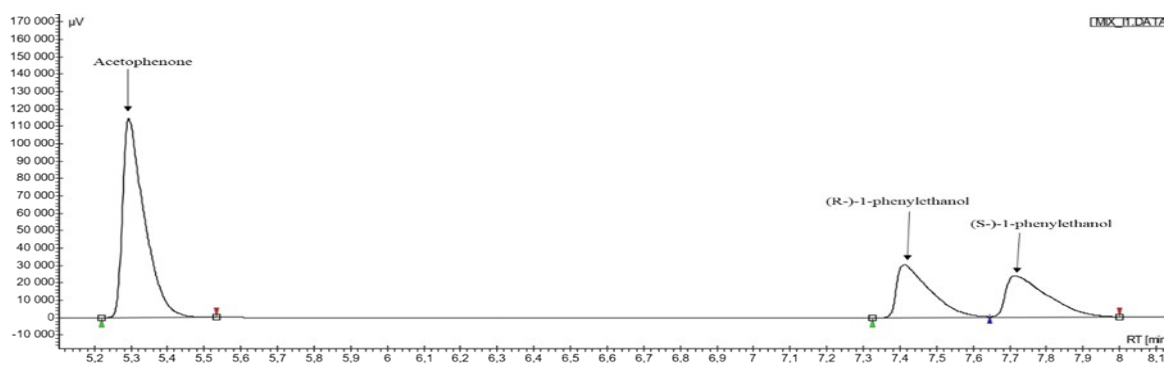


Fig. S24. Typical GC spectrum of crude sampled from ATH reaction of acetophenone after 24 h indicating the intensity of (R-) and (S)-1-phenylethanol and acetophenone.

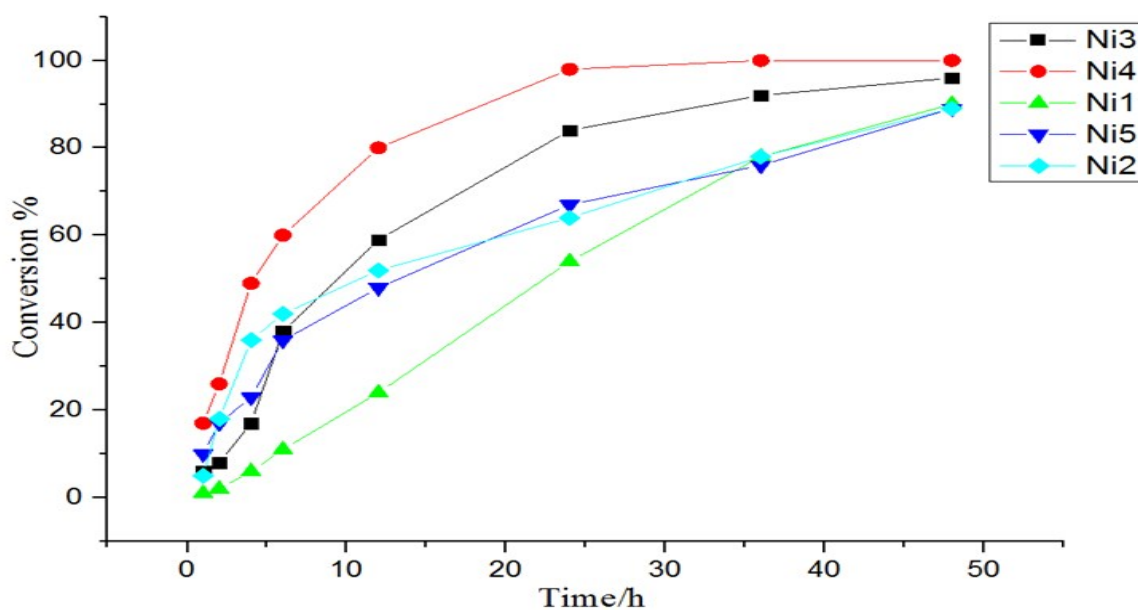


Fig. S25. Time dependence transfer hydrogenation (TH) of acetophenone by the Ni(II)-complexes Ni1- Ni5.

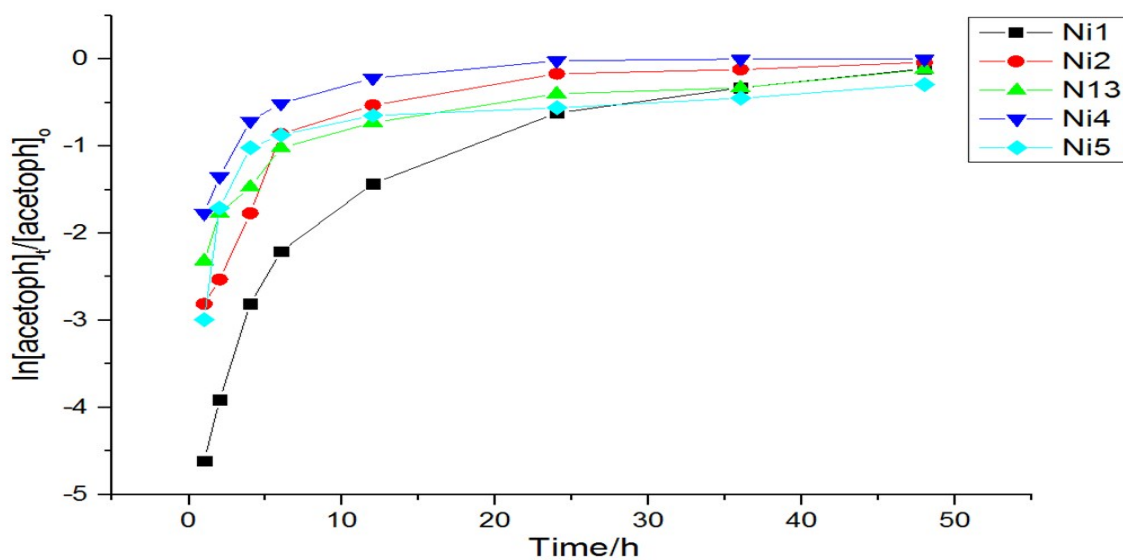


Fig. S26. Graphs showing pseudo-first order/first-order exponential fits of kinetics for complexes Ni1-Ni5. The linear section (0-10 mins) of the plots was used in calculating the order of the ATH reactions with respect to acetophenone substrate.

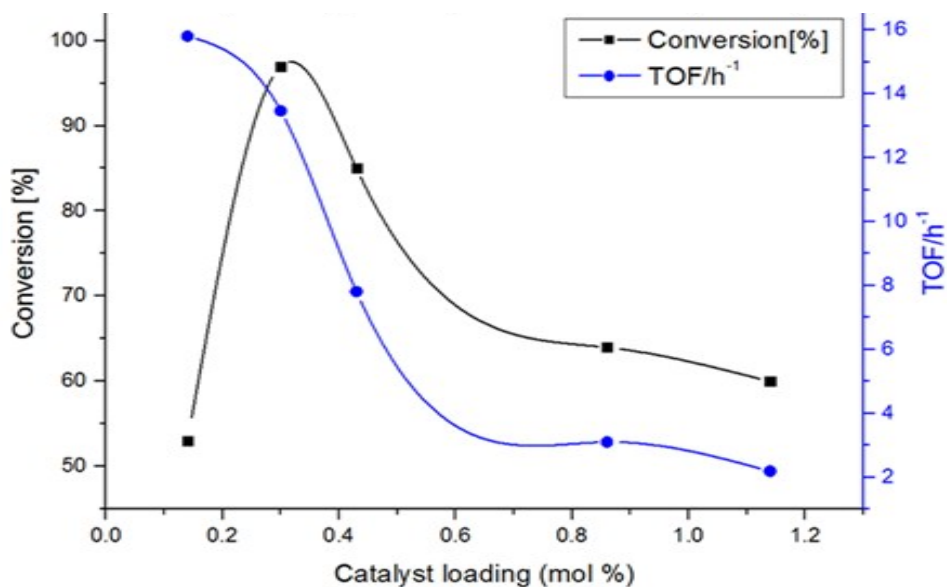


Fig. S27. Plots of catalytic activity versus catalyst loading for complexes Ni4.

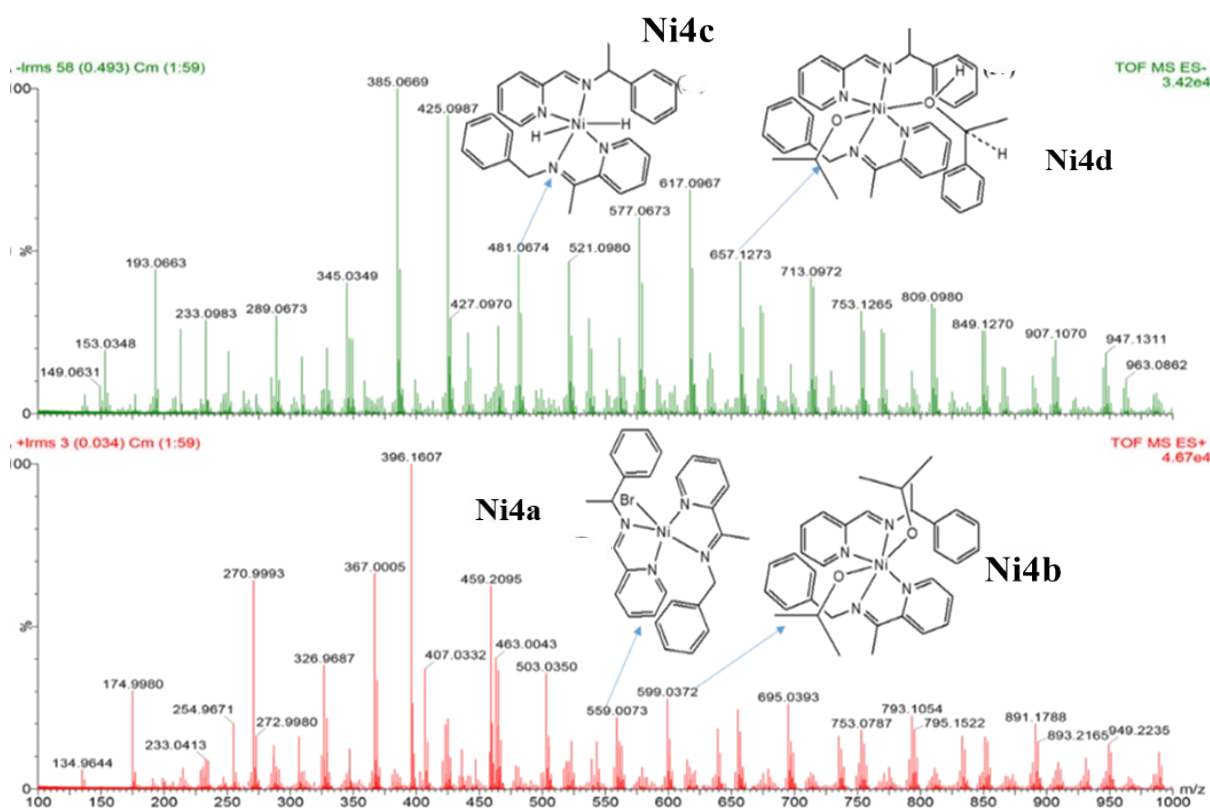


Fig. S28. ESI-MS (low resolution) showing molecular mass corresponding to fragments of reactive intermediates present in reacting mixture sampled after 12 h of ATH of acetophenone.

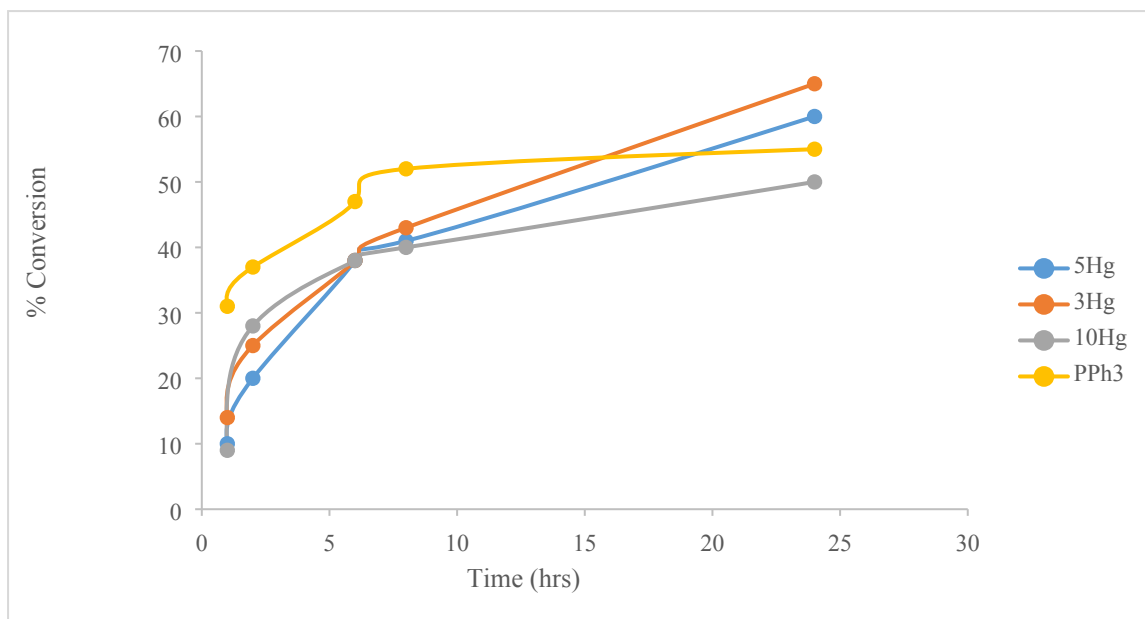


Fig. S29. Mercury (3, 5, and 10 drops) and PPh₃ (100 mol%) poisoning tests. The observed catalytic activities of Ni₄ in the presence of excess mercury and 100% PPh₃ (55%) poison agents support that presence of largely homogeneous active species in the transfer hydrogenation reactions.