Sequential Michael addition, cross-coupling and [3+2] cycloaddition reactions within the coordination sphere of chiral Ni(II) Schiff base complexes derived from dehydroamino acids: pathways to the asymmetric synthesis of structurally diverse O-substituted serine and threonine analogs

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Contents

Experimental section

Materials

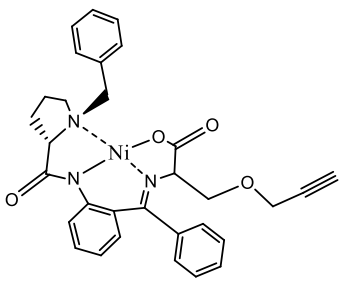
All reagents were obtained from commercial sources and used without further purification. The initial 2 complexes were prepared following literature protocols. TLC analyses were performed on glass plates coated with silica gel 60 F254. Column chromatography was performed on silica gel (60×120 mesh) on a glass column. Melting points (mp) were determined by «Electrothermal». ^{1}H and ^{13}C NMR spectra («Mercury-300 Varian» 300 MHz respectively, Bruker Avance Neo 400 MHz) were recorded using TMS as an internal standard (0 ppm). Elemental analyses were carried out on elemental analyzer EURO EA 3000. The enantiomeric purity of the amino acids was determined by HPLC («Waters Alliance 2695 HPLC System») on the chiral phase column Nautilus-E, 5 μm, 4.6 mm × 250 mm (BioChemMak ST, Moscow, Russia), using a mixture of 20% of MeOH and 80% of 88 mM aqueous solution of KH_2PO_4 as the eluent. The optical rotation was measured on a Perkin Elmer-341 polarimeter. LCMS analysis was performed on Shimadzu LCMS 2020 with Prominence-I LC-2030C 3D. The CD analyses were carried out on Chirascan™ V100.

General Procedures

Complex 3a

A 2 g (3.9 mmol) sample of Ni^{II}-(*S*)-BPB-(*S*)-ΔAla was dissolved in 3.5 ml of CH_3CN in a round-bottomed flask. Then, a solution of 0.156 g (3.9m mol) NaOH in 3.5 ml of propargyl alcohol was added. The reaction mixture was stirred at room temperature. The course of the reaction was monitored by TLC (SiO_2, 3/1 ethyl acetate/chloroform) until the disappearance of the initial complex. Based on TLC data, the reaction took 2.5 hours to complete. After the completion, the mixture was extracted with ethyl acetate and distilled water, dried over $MgSO_4$ to remove trace amounts of water, and filtered through filter paper. The resulting filtrate was evacuated to dryness and the residue was recrystallized from acetone.

Complex 3a



3a

Yield 90% (2.0g), Mp+218 ^{0}C, $[\alpha]_D^{20}$+2625^{0} (c=0.15, CH_3OH). Anal Calc. for: $C_{31}H_{29}N_3NiO_4$ (566.27) C 65.75; H 5.16; N 7.42; Found: C 65.91; H 5.39; N 7.69: MS, *m*/*z*: 565.151:

^{1}H NMR: (CDCl3) δ=1.97-2.15 (2H, m, γ, δ-Ha Pro); 2.41 (1H, t, J=2.4, ≡CH); 2.44-2.58 (1H, m, β-Ha Pro); 2.81-2.92 (1H, m, β-Hb Pro); 3.42 (1H, dd, J=10.9, 6.0, α-H

Pro); 3.48-3.54 (1H, m, δ-Hb Pro); 3.51 (1H, dd, J=9.7, 3.3, OCH2CH) (17a); 3.57 (1H, d, J=12.6, CH2Ph) (8a); 3.78 (1H, dd, J=9.7, 2.9, OCH2CH) (17b); 3.83-3.99 (1H, m, γ-Hb Pro); 4.08 (1H, dd, J=3.3, 2.9, CH) (1); 4.22 (1H, dd, J=15.9, 2.4, OCH2C≡CH) (18a); 4.38 (1H, d, J=12.6, CH2Ph) (8b); 4.42 (1H, dd, J=15.9, 2.4, OCH2C≡CH) (18b); 6.61-6.69 (2H, m, Ar); 6.98-7.04 (1H, m, Ar); 7,15 (1H, ddd, J=8.7, 6.2, 2.5, C6H4) (3); 7.18-7.27 (2H, m, Ar), 7.33-7.40 (2H, m, Ar); 7.42-7.54 (3H, m, Ar); 8.03-8.07 (2H, m, orto-C6H5); 8.15 (1H, b,d J=8.7, C6H4) (2).

^{13}C NMR: (CDCl3) δ= 23.2 (γ-CH2 Pro); 30.9 (β-CH2 Pro); 57.1 (δ-CH2 Pro); 59.0 (OCH2); 62.9 (CH2Ph); 70.6 (α-CH Pro); 70.8 (CH); 71.1 (OCH2C≡CH); 75.4 (C≡CH); 79.1 (C≡CH); 120.7 (CH); 124.0 (CH); 126.9; 127.0 (CH); 128.1 (CH); 128.90 (2CH); 128.93 (CH); 129.04 (CH); 129.05(CH); 129.8 (CH); 131.7 (2CH); 132.2 (CH); 133.26 (CH); 133.33; 134.1; 142.8; 171.2; 177.4; 180.4.

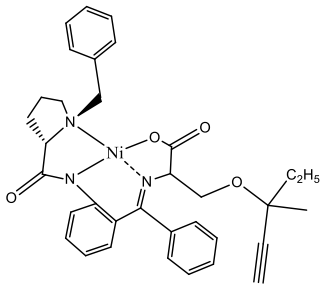
Complex 3b

Based on TLC data, the conversion was around 20%, therefore separation of the product was deemed impractical.

Complex 3c

A 2 g (0.0039 mol) sample of Ni^{II}-(*S*)-BPB-(*S*)-ΔAla was dissolved in 5ml CH_3CN in a round-bottomed flask. Then, 1.15 g (0.011mol) of 3-methylpent-1-yn-3-ol and 0.23 g (0.011 mol) of NaOH were added. The reaction mixture was stirred at room temperature. The course of the reaction was monitored by TLC (SiO_2, 3/1 ethyl acetate/chloroform) until the disappearance of the traces of the initial complex. Based on TLC data, the reaction took 2.5 hours to complete. After the completion, the mixture was extracted with ethyl acetate and distilled water, dried over $MgSO_4$ to remove trace amounts of water, and filtered through filter paper. The resulting filtrate was evacuated to dryness and the residue was purified by column chromatography on silica.

Complex 3c



3c

Yield 82% (1.96g), Mp 133^{0}C, $[\alpha]_D^{20}$ +2143.28^0 (c=0.15, CH_3OH). Anal Calc. for: $C_{34}H_{35}N_3NiO_4$ (608.353) C 67.13; H 5.80; N 6.91; Found: C 67.37; H 6.06; N 7.15: MS, *m*/*z*: 607.198:

Mixture of 2 diastereoisomers 1/1.

^{1}H NMR: (CDCl3) δ=0.99 (1.5H, t, J=7.4) and 1.08 (1.5H, t, J=7.4, CH_3Et); 1.47 (1.5H, s) and 1.56 (1.5H, s, CH_3); 1.76-1.89 (2H, m) and 1.93-2.12 (2H, m, C<u>H</u>$_2$CH$_3$ and γ, δ-H$_a$ Pro); 2.39 (0.5H, s) and 2.40 (0.5H, s, ≡CH); 2.43-2.59 (1H, m) and 2.73-2.88 (1H, m, β-CH_2 Pro); 3.44 (1H, dd, J=10.7, 6.2, α-H Pro); 3.55 (1H, dd, J=9.5, 3.6, OCH_2); 3.61 (0.5H, d, J=12.7,) and 3.61 (0.5H, d, J=12.7, C<u>H</u>$_2$Ph); 3.54-3.62 (1H, m, δ-H$_b$ Pro); 3.67-3.82 (1H, m, γ-H$_b$ Pro); 3.87 (0.5H, dd, J=9.5, 3.6) and 3.89 (0.5H, dd, J=9.5, 3.6, OCH_2); 4.09 (0.5H, t, J=3.6) and 4.10 (0.5H, t, J=3.6, OCH); 4.40 (0.5H, d, J=12.7) and 4.42 (0.5H,, d, J=12.7, CH_2Ph); 6.62-6.69 (2H, m, Ar); 7.00-7.05 (1H, m, Ar); 7.11-7.25 (3H, m, Ar); 7.32-7.38 (2H, m, Ar); 7.45-7.53 (3H, m, Ar); 8.01-8.05 (2H, m, Ar) and 8.22-8.26 (1H, m, Ar).

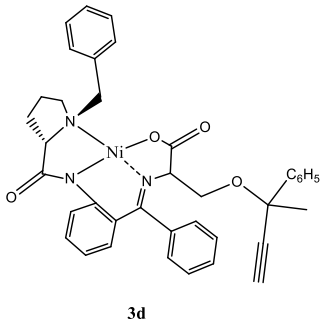
^{13}C NMR: (CDCl3) δ=8.4 and 9.0 (<u>C</u>H$_3$CH$_2$); 23.8 (γ-CH_2 Pro); 25.4 and 26.0 (CH_2); 30.9 and 31.0 (β-CH_2 Pro); 33.0 and 34.5 (CH_3); 57.0 (δ-CH_2 Pro); 62.99 and 63.02 (<u>C</u>H$_2$Ph); 65.7 and 65.8 (OCH_2); 70.4 and 70.5 (CH); 70.95 and 71.00 (α-CH Pro); 73.9 and 74.1 (≡CH); 74.5 and 74.7 (O<u>C</u>CH$_3$); 84.7 and 85.0 (≡C); 120.6-134.3 (Ar); 142.8 and 142.9 (Ar); 171.36 and 171.39 (Ar); 177.8 and 178.0 (Ar); 180.3 (Ar).

Complex 3d

2g (0.0039 mol) sample of Ni^{II}-(*S*)-BPB-(*S*)-ΔAla was dissolved in 5ml CH_3CN in a round-bottomed flask. Then, 1.72g (0.011 mol) 2-phenylbut-3-yn-2-ol and 0.23g (0.011 mol) NaOH was added. The reaction mixture was stirred at room temperature. The course of the reaction was monitored by TLC (SiO_2, 3/1 ethyl acetate/chloroform) until the disappearance of the initial complex. Based on TLC data, the reaction took 2.5 hours to complete.

After the completion, the mixture was extracted with ethyl acetate and distilled water, dried over $MgSO_4$ to remove trace amounts of water, and filtered through filter paper. The resulting filtrate was evacuated to dryness and the residue was purified by column chromatography on silica.

Complex 3d



3d

Yield 78% (2.01g), Mp+97^{0}C, $[\alpha]_D^{20}$+2063.8^0 (c=0.15, CH_3OH). Anal Calc. for: $C_{38}H_{35}N_3NiO_4$ (656.396) C 69.53; H 5.37; N 6.40; Found: C 69.87; H 5.68; N 6.67: MS, *m*/*z*: 655.198:

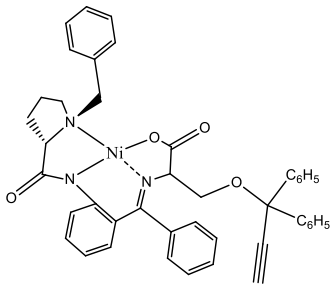
Mixture of 2 diastereoisomers 70/30% (A/B)

^{1}H NMR: ($CDCl_3$) δ=1.94 (1H, s) and 2.05 (2H, s, CH_3); 1.96-2.10 (2H, m, γ, δ-H_a Pro); 2.42-2.64 (1H, m) and 2.73-2.87 (1H, m, β-CH_2 Pro); 2.68 (0.3H, s) and 2.71 (0.7H, s, ≡CH); 2.96 (0.7H, dd, J=10.5, 4.3, OCH (H)); 3.45 (0.3H, dd, J=10.8, 6.1) and 3.49 (0.7H, dd, J=10.8, 6.1 α-H Pro); 3.55-3.67 (3H, m); 3.78-3.96 (2,3H m); 4.37 (0.3H, d, J=12.6) and 4.46 (0.7H, d, J=12.6, C$\underline{H}_2$Ph); 5.48-5.52 (0.7H, m); 6.49 (0.7H, dd, J=8.2, 1.7), 6.63-6.71 (1.3H, m); 6.94-7.01 (1.7H, m); 7.04-7.23 (4.7H, m); 7.28-7.46 (5.3H, m); 7.52-7.57 (0.7H, m); 7.72-7.76 (1.3H, m); 8.02-8.07 (2H, m); 8.29 (0.3H, bd, J=8.6) and 8.43 (0.7H, dd, J=8.6, 1.1).

^{13}C NMR: (CDCl3) δ=23.6(A) and 23.7 (B)- γ-CH_2 Pro; 30.8 (B) and 31.0 (A)-β-CH_2 Pro; 32.9 (A) and 33.0 (B)-CH_3; 57.0 (A) and 57.1 (B)-δ-CH_2 Pro; 63.0 (A) and 63.05 (B)-$\underline{C}H_2$Ph; 66.7 (A) and 67.0 (B)-OCH_2; 70.4, 70.5 and 70.7-α-CH Pro and CH; 76.84 (B) and 76.86 (A)-≡C; 76.92 (B) and 76.95 (A)-≡CH; 82.5 (A,B)-$\underline{C}$Me;120.6 (A) and 120.7 (B) Ar; 123.5 (A) and 123.7 (B) Ar; 126.0 (B) and 126.4 (A) Ar; 126.7 (A) and 126.9 (B) Ar; 127.9-128.9 Ar; 129.5 (A) and 129.7 (B) Ar; 131.6 (B) and 131.7 (A) Ar; 132.3 (B) and 132.4 (A) Ar; 133.2 (A) and 133.3 (B) Ar; 133.4 (A) and 133.6 (B) Ar; 133.9 (A) and 134.2 (B) Ar; 141.4 (B) and 142.5 (A) Ar; 142.8 (B) and 142.9 (A) Ar; 171.4 (A) and 171.6 (B) Ar; 177.5 (B) and 177.8 (A) Ar; 180.4 (B) and 180.6 (A) Ar.

Complex 3e

A 2g (0.0039 mol) sample of Ni^{II}-(*S*)-BPB-(*S*)-ΔAla was dissolved in 5 ml CH_3CN in a round-bottomed flask. Then, 1.72 g (0.011 mol) 1,1-diphenylprop-2-yn-1-ol and 0.23 g (0.011 mol) NaOH was added. The reaction mixture was stirred at room temperature. The course of the reaction was monitored by TLC (SiO_2, 3/1 ethyl acetate/chloroform) until the disappearance of the initial complex. Based on TLC data, the reaction took 2.5 hours to complete. After the completion, the mixture was extracted with ethyl acetate and distilled water, dried over $MgSO_4$ to remove trace amounts of water, and filtered through filter paper. The resulting filtrate was evacuated to dryness and the residue was purified by column chromatography on silica.



3e

Complex 3e

Yield 70% (1.97g), Mp+104^{0}C, $[\alpha]_D^{20}$+1801.86^0 (c=0.15, CH_3OH). Anal Calc. for: $C_{43}H_{37}N_3NiO_4$ (718.465) C 71.88; H 5.19; N 5.85; Found: C 72.04; H 5.47; N 6.17: MS, *m*/*z*: 617.214:

^{1}H NMR: ($CDCl_3$) δ=1.30-1.44 (1H, m, γ-H_a Pro), 1.93-2.02 (1H, δ-H_a Pro); 2.04-2.20 (2H, m); 2.73-2.89 (1H, m, β-H_b Pro); 2.84 (1H, s, ≡CH); 3.35 (1H, dd, J=10.4, 6.6, α-H Pro); 3.38 (1H, dd, J=10.6, 4.6, OCH_2); 3.46-3.52 (1H, m, , δ-H_b Pro); 3.51 (1H, d, J=12.6, C<u>H</u>$_2$Ph); 4.05-4.10 (2H, m, C<u>H</u>C<u>H</u>$_2$O); 4.33 (1H, d, J=12.6, C<u>H</u>$_2$Ph), 5.89-5.93 (1H, m, Ar); 6.52 (1H, dd, J=8.2, 1.7, C_6H_4); 6.65 (1H, ddd, J=8.2, 7.0, 1.2, C_6H_4); 7.05-7.21 (7H, m, Ar); 7.29-7.44 (7H, m, Ar); 7.48-7.53 (2H, Ar); 7.80-7.85 (2H, m, Ar); 8.05-8.09 (2H, m, Ar); 8.34 (1H, dd, J=8.7, 1.2, C_6H_4).

^{13}C NMR: ($CDCl_3$) δ=23.2 (γ-CH_2 Pro); 30.6 (β-CH_2 Pro); 57.5 (δ-CH_2 Pro); 63.3 (<u>C</u>H$_2$Ph); 67.2 (OCH_2); 70.5 (α-CH Pro); 70.8 (CH); 78.9 (≡CH); 81.3 (≡C); 82.6 (<u>C</u>Ph$_2$); 120.5 (Ar); 123.6 (Ar); 126.3 (Ar); 126.7 (Ar); 127.7 (Ar); 128.0 (Ar); 128.1 (Ar); 128.2 (Ar); 128.3 (Ar); 128.7 (Ar); 128.8 (Ar); 129.5 (Ar); 130.1 (Ar); 131.6 (Ar); 132.4 (Ar); 133.4 (Ar); 133.5 (Ar); 134.0 (Ar); 141.4 (Ar); 142.9 (Ar); 143.1 (Ar); 171.6 (Ar); 177.7 (Ar); 180.6 (Ar).

Complex 3f

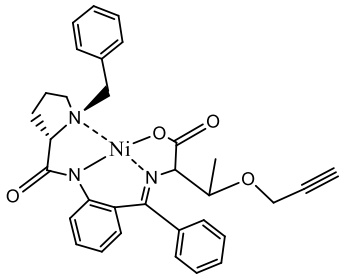
Based on TLC data, the conversion was around 10%, therefore separation of the product was deemed impractical.

Complex 4a

A 10 g (0.0191 mol) sample of Ni^{II}-(*S*)-BPB-(*S*)-(*E*)-Δ-aminobutyric acid was dissolved in a 100 ml solution of a 0.3 M solution of sodium salt of propargyl alcohol in propargyl alcohol. The reaction mixture was stirred at 50-55°C under a nitrogen atmosphere. The course of the reaction was monitored by TLC (SiO_2, 3/1 ethyl acetate/chloroform) until the disappearance of the initial complex. Based on TLC data, the reaction took 5 hours to complete.

After the completion of the reaction, the mixture was neutralized with glacial acetic acid and evaporated to dryness. The product was recrystallized from acetone.

Complex 4a



4a

Yield 90% (9.90 g), Mp+218^{0}C, $[\alpha]_D^{20}$+2393,1^0 (c=0.145, CH_3OH). Anal Calc. for: $C_{32}H_{31}N_3NiO_4$ (580.30) C 66.23; H 5.38; N 7.24; Found: C 66.24; H 5.37; N 7.22: MS, *m*/*z*: 580.100:

^{1}H NMR: ($CDCl_3$),δ=1.07 (3H, d,J=6.5, CH_3); 1.98-2.13 (2H, m, γ, δ-Ha Pro); 2.19 (1H, t, J=2.3, ≡CH); 2.44-2.58 (1H, m, β-Ha Pro);2.84-2.96 (1H, m, β- Hb Pro); 3.42 (1H, dd, J=10.8, 6.2, α-H Pro); 3.44-3.56 (1H, m, γ -Hb Pro); 3.60 (1H, d, J=12.7, C<u>H</u>$_2$Ph) (8a); 3.72 (1H, qd, J=6.5, 2.1, C<u>H</u>CH$_3$) (17); 3.90 (1H, d, J=2.1, C<u>H</u>CHCH$_3$) (1); 4.23 (1H, dd, J=16.5, 2.3, OC<u>H</u>$_2$C≡CH) (19a); 4.46 (1H, d, J=12.7, C<u>H</u>$_2$Ph) (8b); 4.68 (1H, dd, J=16.5, 2.3, OC<u>H</u>$_2$C≡CH) (19b); 6.60-6.70 (2H, m, C_6H_4); 7.00-7.04 (1H, m, Ar); 7.10-7.22 (2H, m, Ar); 7.24-7.37 (3H, m, Ar); 7.42-7.56 (3H, m, Ar); 8.01-8.05 (2H, m, orto-C_6H_5); 8,20 (1H, ddd, J=8.6 1.0, 0.7, C_6H_4).

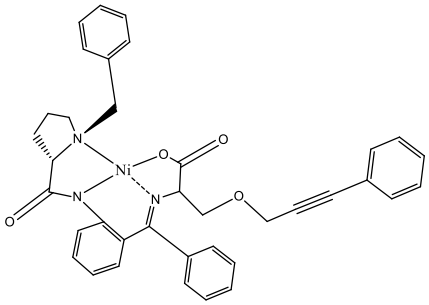
^{13}C NMR: ($CDCl_3$) δ=15.6 (CH_3); 23.0 (γ-CH_2 Pro); 30.8 (β-CH_2 Pro); 56.7 (OCH_2); 57.0 (δ-CH_2 Pro); 62.9 (<u>C</u>H$_2$Ph); 70.4 (α-CH Pro); 74.3 (NCH); 75.0 (≡CH); 77.0 (<u>C</u>HMe); 80.1 (≡C); 120.5 (CH); 123.9 (CH); 126.6 (C); 127.2 (CH); 128.1 (CH); 128.9 (2 CH); 129.0 (CH); 129.1 (CH); 129.8 (2 CH); 131.8 (2 CH); 132.2 (CH); 133.2 (C); 133.3 (C); 134.2 (C); 142.9 (C); 170.9 (C); 176.2 (C); 180.3 (C).

Complex 7

To a mixture of 0.78 ml (7.0 mmol) of Iodobenzene, 5ml of triethylamine, 0.12 g (0.1 mmol) $PdCl_2(PPh_3)_2$ and 0.067 g (0.3 mmol) of copper iodide were added in a pressure tube, supplied with an argon gas flow. Then a solution of 2 g (3.5 mmol) of complex **3a** in 5 ml of 1,4-dioxane was added. The reaction mixture was heated to 60^{0}C with stirring. The course of the reaction was monitored by TLC (SiO_2, 3/1 ethyl acetate/chloroform) until the disappearance of the initial complex. Based on TLC data, the reaction took 6 hours to complete.

After the completion, the mixture was extracted with ethyl acetate and distilled water, dried over $MgSO_4$ to remove trace amounts of water, and filtered through filter paper. The resulting filtrate was evacuated to dryness and the residue was recrystallized from acetone.

Complex 7



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Yield 58% (1.46g), Mp+101^{0}C, $[\alpha]_D^{20}$ +2166.88^0 (c=0.15, CH_3OH). Anal Calc. for:$C_{37}H_{33}N_3NiO_4$(642.369) C 68.31; H 5.38; N 6.50; Found: C 66.05; H 5.34; N 7.68: MS, *m*/*z*: 641.182:

^{1}H NMR: ($CDCl_3$) δ=1.95-2.11 (2H, m, γ, δ-H_a Pro); 2.40-2.54 (1H, m, β-H_a Pro); 2.84-2.95 (1H, m, β-H_b Pro); 3.42 (1H, dd, J=10.8, 6.1, α-H Pro); 3.48-3.55 (1H, m, δ-H_b Pro); 3.59 (1H, d, J=12.6, C<u>H</u>$_2$Ph); 3.60 (1H, dd, J=9.6, 3.4, OC<u>H</u>$_2$CH); 3.79 (1H, dd, J=9.6, 2.7, OC<u>H</u>$_2$CH); 3.87-4.04 (1H, m,γ-H_b Pro); 4.11 (1H, dd, J=3.4, 2.7, CH);4.39 (1H, d, J=12.6, C<u>H</u>$_2$Ph); 4.43 (1H, d, J=15.7; $OCH_2C{\equiv}C$);4.66 (1H, d, J=15.7, $OCH_2C{\equiv}C$); 6.60 (1H, br. dd, J=8.2, 2.1, C_6H_4); 6.64 (1H, ddd, J=8.2, 6.6, 1.1, C_6H_4); 6.95-6.99 (1H, m, Ar); 7.15 (1H, ddd, J=8.6, 6.6, 2.1, C_6H_4); 7.19-7.31 (6H, m, Ar); 7.33-7.52 (6H, m, Ar); 8.03-8.07 (2H,m, Ar); 8.16 (1H, dd, J=8.6, 1.2, C_6H_4).

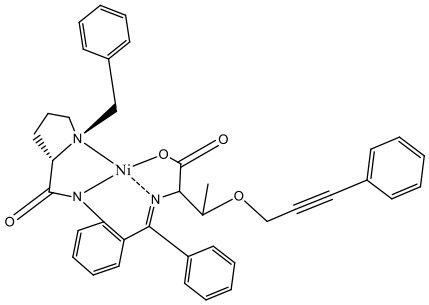
^{13}C NMR: ($CDCl_3$) δ=23.1 (γ-CH_2Pro); 30.9 (β-CH_2 Pro); 57.1 (δ-CH_2 Pro); 59.7 (OCH_2); 62.9 (<u>C</u>H_2Ph); 70.6-70.8 (2CH, OCH_2); 120.7; 122.4; 124.1; 127.0; 128.1; 128.4 (2C); 128.7; 128.91 (2C); 128.94; 129.00; 129.04; 129.8; 131.7 (2C); 131.9 (2C); 132.2; 133.26; 133.31; 134.0; 142.7; 171.1; 177.8; 180.5.

Complex 8

To a mixture of 0.77 ml (6.8 mmol) of Iodobenzene, 5 ml of triethylamine, 0.12 g (0.1 mmol) of $PdCl_2(PPh_3)_2$ and 0.065 g (3.4 mmol) of copper iodide were added in a pressure tube, supplied with an argon gas flow. Then a solution of 2 g (3.4 mmol) of complex **4a** in 5 ml of 1,4-dioxane was added. The reaction mixture was heated to 60^{0}C with stirring. The course of the reaction was monitored by TLC (SiO_2, 3/1 ethyl acetate/chloroform) until the disappearance of the initial complex. Based on TLC data, the reaction took 6 hours to complete.

After the completion, the mixture was extracted with ethyl acetate and distilled water, dried over $MgSO_4$ to remove trace amounts of water, and filtered through filter paper. The resulting filtrate was evacuated to dryness and the residue was recrystallized from acetone.

Complex 8



10

Yield 56% (1.40g), Mp +252^{0}C, $[\alpha]_D^{20}$ +1427.6^0 (c=0.15, CH_3OH). Anal Calc. for:$C_{38}H_{35}N_3NiO_4$(656.40) C 69.53; H 5.37; N 6.40; Found: C 69.84; H 5.63; N 6.69: MS, *m*/*z*: 655.20:

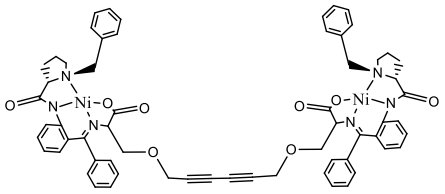
^{1}H NMR: ($CDCl_3$) δ=1.13 (3H, d, J=6.4, CH_3); 1.96-2.13 (2H, m, γ, δ-H_a Pro); 2.46-2.60 (1H, m) and 2.92-3.04 (1H, m, β-CH_2 Pro); 3.39 (1H, dd, J=10.5, 6.5, α-H Pro); 3.48-3.57 (1H, m, γ-H_b Pro); 3.63 (1H, d, J=12.7, C<u>H</u>$_2$Ph); 3.87 (1H, qd, J=6.4, 2.2, C<u>H</u>CH_3); 3.91 (1H, d, J=2.2, NC<u>H</u>$CHCH_3$); 3.82-3.97 (1H, m, δ-H_b Pro); 4.48 (1H, d, J=12.7, C<u>H</u>$_2$Ph); 4.52 (1H, d, J=16.3) and 4.89 (1H, d, J=16.3, OCH_2); 6.50-6.59 (2H, m, C_6H_4); 6.84-6.89 (1H, m, Ar); 7.03-7.25 (8H, m, Ar); 7.29-7.37 (3H, m, Ar); 7.41-7.52 (2H, m, Ar); 7.98-8.04 (2H, m, Ar) and 8.29 (1H, dd, J=8.7, 0.9, C_6H_4).

^{13}C NMR: ($CDCl_3$) δ=15.3 (CH_3); 22.8 (γ-CH_2 Pro); 31.1 (β-CH_2 Pro); 56.8 (OCH_2); 57.1 (δ-CH_2Pro); 62.6 (<u>C</u>H_2Ph); 70.5 (α-CH Pro); 74.4 (CH); 75.9 (CH); 85.0 (<u>C</u>≡C); 86.9 (C≡<u>C</u>); 120.4 (Ar); 121.8 (Ar); 123.9 (Ar); 126.5 (Ar); 127.2 (Ar); 128.1 (Ar); 128.2 (2CH, Ar); 128.5; 128.8 (2CH, Ar); 128.9 (Ar); 129.0 (Ar); 129.6 (Ar); 131.7 (2CH, Ar); 131.8 (2CH, Ar); 132.0 (Ar); 133.1 (Ar); 133.2 (Ar); 134.2 (Ar); 143.2 (Ar); 170.7 (Ar); 176.3 (Ar); 180.4 (Ar).

Complex 9

To a mixture of 5 ml of 1,4-dioxane and 5 ml of triethylamine, 0.67 g (3.5 mmol) of copper iodide and 2 g (3.5 mmol) of complex **3a** were added. The reaction mixture was stirred at room temperature. The course of the reaction was monitored by TLC (SiO_2, 3/1 chloroform/acetone) until the disappearance of the initial complex. Based on TLC data, the reaction took 96 hours to complete. After the completion, the mixture was extracted with ethyl acetate and distilled water, dried over $MgSO_4$ to remove trace amounts of water, and filtered through filter paper. The resulting filtrate was evacuated to dryness and the residue was recrystallized from acetone.

Complex 9



7

Yield 66% (2.63g), Mp+143 ^{0}C, $[\alpha]_D^{20}$ +2572^{0} (c=0.15, CH_3OH). Anal Calc. for: $C_{62}H_{56}N_6Ni_2O_8$ (1130.530) C 65.87; H 4.99; N 7.43; Found: C 66.05; H 5.34; N 7.68: MS, *m*/*z*: 1128.287:

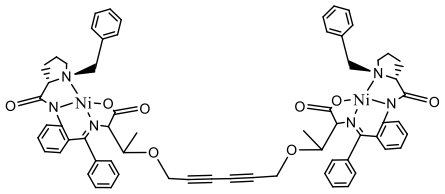
^{1}H NMR: ($CDCl_3$) δ=1.88-2.09 (2H, m, γ, δ-H_a Pro); 2.43-2.57 (1H, m, β-H_a Pro); 2.76-2.87 (1H, m, β-H_b Pro); 3.40 (1H, dd, J=10.8; 6.0, α-H Pro); 3.40-3.49 (1H, m, δ-H_e Pro); 3.46 (1H, dd, J=9.6; 3.3, OC<u>H</u>$_2$CH); 3.50 (1H, d, J=12.6, CH_2Ph), 3.70 (1H, dd, J=9.6; 2.8, OCH_2CH), 3.76-3.93 (1H, m, γ-H_b Pro); 4.05 (1H, dd, J=3.3; 2.8, OCH_2C<u>H</u>), 4.22 (1H, d, J=16.0, OCH_2C≡); 4.31 (1H, d, J=12.6, C<u>H</u>$_2$Ph); 4.44 (1H, d, J=16.0; OCH_2C≡); 6.59-6.66 (2H, m, Ar); 6.94-7.00 (1H, m, Ar); 7.11 (1H, ddd, J=8.8; 5.5; 3.2 Ar); 7.16-7.25 (2H, m, Ar); 7.31-7.39 (2H, m, Ar); 7.41-7.51 (3H, m, Ar); 8.06-8.13 (3H, m, Ar).

^{13}C NMR: ($CDCl_3$) δ=23.2 (γ-CH_2 Pro); 30.9 (β-CH_2 Pro); 57.2 (δ-CH_2 Pro); 59.5 (OCH_2); 63.0 (<u>C</u>H_2Ph); 70.57 (<u>C</u>HCH_2); 70.61 (α-CH Pro); 71.0 (<u>C</u>≡CH); 71.3 (O<u>C</u>H_2C≡); 75.2 (C≡<u>C</u>); 120.6 (CH, Ar); 124.0 (CH, Ar); 126.7; 126.9 (CH, Ar); 127.9 (CH, Ar); 128.9 (2CH, Ar); 129.0(CH, Ar); 129.2 (CH, Ar); 129.9 (CH, Ar); 131.6 (2CH, Ar); 132.1 (CH, Ar); 133.2(CH, Ar); 133.5; 133.9; 142.9; 171.2; 177.3; 180.5.

Complex 10

To a mixture of 5 ml of 1,4-dioxane and 5 ml of triethylamine, 0.67 g (3.5 mmol) of copper iodide and 2.03 g (3.5 mmol) of complex **4a** were added. The reaction mixture was stirred at room temperature. The course of the reaction was monitored by TLC (SiO_2, 3/1 chloroform/acetone) until the disappearance of the initial complex. Based on TLC data, the reaction took 96 hours to complete. After the completion, the mixture was extracted with ethyl acetate and distilled water, dried over $MgSO_4$ to remove trace amounts of water, and filtered through filter paper. The resulting filtrate was evacuated to dryness and the residue was recrystallized from acetone.

Complex 10



8

Yield 70% (1.42 g), Mp+190 ^{0}C, $[\alpha]_D^{20}$+1851,25^0 (c=0.526, CH_3OH). Anal Calc. for: $C_{64}H_{60}N_6Ni_2O_8$ (1158.58) C 66.35; H 5.22; N 7.25; Found: C 66.31; H 5.25; N 7.29: MS, *m*/*z*: 1159.21:

^{1}H NMR: ($CDCl_3$) δ=0.99 (3H, d,J=6.4, CH_3); 1.90-2.08 (2H, m, γ, δ-Ha Pro); 2.51 (1H, m, β-Ha Pro);2.80 (1H, m, β- Hb Pro); 3.30-3.56 (3H, m, J=10.8, 6.2, α, γ, δ-Hb Pro); 3.53 (1H, d, J=12.6, C<u>H</u>$_2$Ph); 3.76 (1H, m, J=6.5, 2.1, C<u>H</u>CH$_3$) (17); 3.82 (1H, d, J=1.8, NC<u>H</u>) (1); 3.98 (1H, d, J=16.9, OC<u>H</u>$_2$) (19a); 4.41 (1H, d, J=12.6, C<u>H</u>$_2$Ph); 4.47 (1H, d, J=16.9, OC<u>H</u>$_2$); 6.59-6.66 (2H, m, C_6H_4); 6.87-6.92 (1H, m, Ar); 7.04-7.10 (1H, m, Ar); 7.13-7.25 (2H, m, Ar); 7.29-7.40 (3H, m, Ar); 7.43-7.54 (2H, m, orto-C_6H_5); 8,00-8.05 (2H, m, Ar), 8.26 (1H, b.d, J=8.6, Ar).

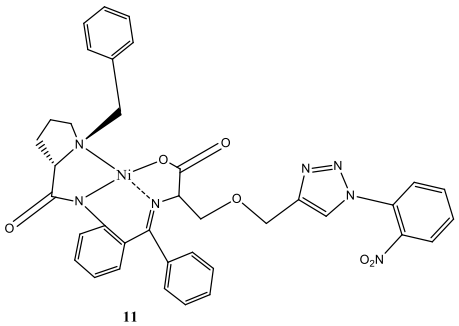
^{13}C NMR: ($CDCl_3$) δ=15.7 (CH_3); 23.0 (γ-CH_2 Pro); 30.8 (β-CH_2 Pro); 57.0 (OCH_2); 57.3 (δ-CH_2 Pro); 62.8 (<u>C</u>H$_2$Ph); 69.9 (α-CH Pro); 70.5 (b., NCH); 74.2 (b.); 75.8 and 77.1 (<u>C</u>≡C); 120.2 (CH); 123.8 (CH); 126.5 (C); 127.2 (CH); 128.0 (CH); 128.8 (3 CH); 128.9 (CH); 129.1 (CH); 129.7 (2 CH); 131.7 (2 CH); 131.9 (CH); 133.3 (C); 134.2 (C); 143.5 (C); 170.8 (C); 176.0 (C); 180.5 (C).

Complex 11

1.16 g (7.0 mmol) of 1-azido-2-nitrobenzene was dissolved in 5 ml of 1,4-dioxane in a round-bottomed flask, supplied with an argon gas flow, at room temperature. Then, 0.067 g (0.3 mmol) of CuI was added and the mixture was stirred for 5 min followed by addition of 0.738 ml (5.2 mmol) of Et_3N. After 30 min, 2 g (3.5 mmol) of complex **3a** was added and the reaction mixture was heated to 60^{0}C with stirring. The course of the reaction was monitored by TLC (SiO_2, 3/1 ethyl acetate/chloroform) until the disappearance of the initial complex. Based on TLC data, the reaction took 40 min to complete.

After the completion, the mixture was extracted with ethyl acetate and distilled water, dried over $MgSO_4$ to remove trace amounts of water, and filtered through filter paper. The resulting filtrate was evacuated to dryness and the residue was recrystallized from acetone.

Complex 11



11

Yield 83% (2.37g), Mp+231^{0}C, $[\alpha]_D^{20}$ +1884.82^0 (c=0.15, CH_3OH). Anal Calc. for: $C_{37}H_{33}N_7NiO_6$(730.39) C 60.84; H 4.55; N 13.42; Found: C 61.08; H 4.93; N 13.78: MS, *m*/*z*: 729.18:

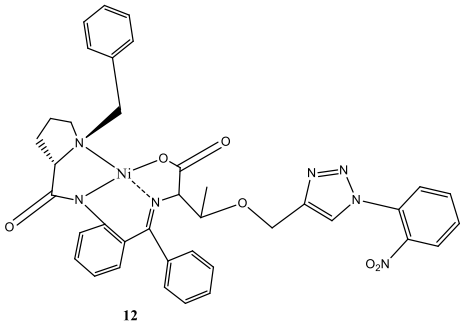
^{1}H NMR: ($CDCl_3$) δ=1.97-2.13 (2H, m, γ, δ-H_a Pro); 2.43-2.58 (1H, m, β-H_a Pro); 2.67-2.79 (1H, m, β-H_b Pro); 3.43 (1H, dd, J=10.9, 5.9, α-H Pro); 3.49 (1H, dd, J=9.6; 3.2; OC$\underline{H}_2$CH); 3.56 (1H, d, J=12.6, C$\underline{H}_2$Ph); 3.46-3.55 (1H, m, γ-H_b Pro); 3.81-3.96 (1H, m, δ-H_b Pro); 3.86 (1H, dd, J=9.6, 2.6, OC$\underline{H}_2$CH); 4.04 (1H, dd, J=3.2, 2.6, CH); 4.35 (1H, d, J=12.6, CH_2Ph); 4.98 (1H, d, J=13.9) and 5.06 (1H, d, J=13.9, OCH_2); 6.58-6.64 (2H, m, Ar); 6.70-6.74 (1H, m, Ar); 7.07 (1H, ddd, J=8.8, 7.1, 3.0, Ar); 7.16-7.22 (2H, m, Ar); 7.26-7.29 (1H, m, Ar); 7.32-7.38 (2H, m, Ar); 7.41-7.51 (3H, m, Ar); 7.56-7.65 (2H, m, Ar); 7.91 (1H, s, =CHN); 7.95-8.01 (1H, m, Ar); 8.05-8.10 (3H, m, Ar).

^{13}C NMR: ($CDCl_3$) δ=22.9 (γ-CH_2 Pro); 30.9 (β-CH_2 Pro); 57.2 (δ-CH_2 Pro); 63.1 ($\underline{C}H_2$Ph); 64.7 (OCH_2); 70.5 (CH); 71.0 (α-CH Pro); 71.1 (OCH_2); 120.7 (CH); 123.9 (CH); 124.0 (CH); 125.5 (CH); 126.5; 126.8 (CH); 127.7 (CH); 127.8 (CH); 128.88 (2CH); 128.91 (CH); 129.1 (CH); 129.4 (CH); 129.8; 129.9 (CH); 130.5 (CH); 131.6 (2CH); 132.1 (CH); 133.3 (CH); 133.4; 133.6; 133.9 (CH); 142.5; 144.3; 145.8; 171.2; 177.5; 180.4.

Complex 12

1.13 g (6.9 mmol) of 1-azido-2-nitrobenzene was dissolved in 5 ml 1,4-dioxane in a round-bottomed flask, supplied with an argon gas flow, at room temperature. Then, 0.065 g (0.3 mmol) of CuI was added and the mixture was stirred for 5 min followed by the addition of 0.720 ml (5.2 mmol) of Et_3N. After 30 min, 2 g (3.4 mmol) of complex **4a** was added and the reaction mixture was heated to 60^{0}C with stirring. The course of the reaction was monitored by TLC (SiO_2, 3/1 ethyl acetate/chloroform) until the disappearance of the initial complex. Based on TLC data, the reaction took 40 min to complete. After the completion, the mixture was extracted with ethyl acetate and distilled water, dried over $MgSO_4$ to remove trace amounts of water, and filtered through filter paper. The resulting filtrate was evacuated to dryness and the residue was recrystallized from acetone.

Complex 12



12

Yield 80% (2.27g), Mp +246^{0}C, $[\alpha]_D^{20}$ +2124.5^0 (c=0.15, CH_3OH). Anal Calc. for: $C_{38}H_{35}N_7NiO_6$ (744.42) C 61.31; H 4.74; N 13.17; Found: C 61.55; H 5.12; N 13.51: MS, *m*/*z*: 743.20:

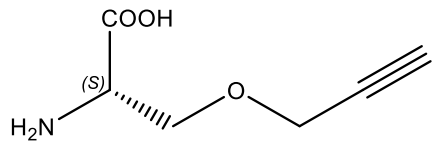
^{1}H NMR: ($CDCl_3$) δ=1.19 (3H, d, J=6.3, CH_3); 2.00-2.18 (2H, m, γ, δ-H_a Pro); 2.40-2.70 (2H, m, β-H_a Pro and β-H_b Pro); 3.45 (1H, dd, J=10.9, 5.9, α-H Pro); 3.51 (1H, d, J=12.6, C<u>H</u>$_2$Ph); 3.53-3.59 (1H, m, δ-H_b Pro); 3.65 (1H, qd, J=6.3, 2.7, C<u>H</u>CH$_3$); 3.79 (1H, d, J=2.7, C<u>H</u>CHCH$_3$); 3.81-3.98 (1H, m, γ-H_b Pro); 4.42 (1H, d, J=12.6, C<u>H</u>$_2$Ph); 5.00 (1H, d, J=14.4) and 5.34 (1H, d, J=14.4, OC<u>H</u>$_2$); 6.45-6.53 (3H, m, Ar); 6.83-6.86 (1H, m, Ar); 6.87-6.96 (1H, m, Ar); 7.09-7.18 (2H, m, Ar); 7.26-7.32 (2H, m, Ar); 7.37-7.52 (5H, m, Ar); 7.86-7.89 (1H, m, Ar); 7.90 (1H, s, =CHN, Ar); 7.94 (1H, dt, J=8.6, 0.8, Ar); 8.03-8.08 (2H, m, Ar).

^{13}C NMR: ($CDCl_3$) δ=14.8 (CH_3); 23.1 (γ-CH_2 Pro); 30.9 (β-CH_2 Pro);57.3 (δ-CH_2 Pro);61.4 (OCH_2);63.2 (<u>C</u>H$_2$-Ph); 70.2 (α-CH Pro); 74.4 (CH); 75.4 (CH); 126.6(Ar); 123.8(Ar); 123.9 (Ar); 125.3 (Ar); 126.1 (Ar); 126.9 (Ar); 127.6(Ar); 127.7 (Ar); 128.9 (3C, Ar); 129.0 (Ar); 129.3 (Ar); 129.4 (Ar); 129.9 (Ar); 130.2 (Ar); 131.6 (2C, Ar); 131.8 (Ar); 133.4 (Ar); 133.5 (Ar); 133.8(Ar); 142.2 (Ar); 143.9 (Ar); 146.2(Ar); 170.8 (Ar); 175.9 (Ar); 180.3(Ar).

General procedure for isolation of amino acids

A suspension of the complex in CH_3OH was slowly added to a vigorously stirred 2 M aqueous HCI solution at 50-60^{O}C. After the complexes were decomposed (10-20 min), the free amino acids were purified using a cation-exchange column (Dowex-50 (H^+ form)).

(S)-2-amino-3-(O-propargyl)propionic acid 5a



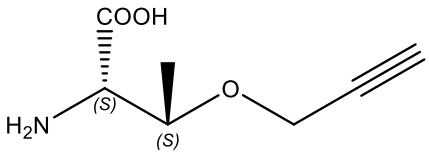
5a

Yield 72% (0.4 g), Mp 190^{0}C, $[\alpha]_D^{20}$ +15.5^0 (c=0.10, CH_3OH). Anal Calc. for: $C_6H_9NO_3$ (143.141) C 50.35; H 6.34; N 9.79; Found: C 50.63; H 6.62; N 10.03: MS,m/z: 143.058:

^{1}H NMR: (DMSO/CF_3COOD) δ=3.52 (1H, t, J=2.4, ≡CH); 3.79 (1H; dd; J=10.5; 3.2, OC<u>H</u>$_2$CH); 3.88 (1H, dd, J=10.5; 4.5, OCH_2CH); 4.22 (1H, dd, J=16.0; 2.4, OC<u>H</u>$_2$C≡CH); 4.23 (1H, dd, J=16.0; 2.4, OC<u>H</u>$_2$C≡CH); 4.24 (1H, br, CH); 8.37 (2H, br, NH_2).

^{13}C NMR: (DMSO/CF_3COOD) δ=52.1 (CH); 58.1 (CH_2); 67.0 (CH_2); 78.1 (≡CH); 79.3 (≡C); 168.8 (CO).

(2*S*,3*S*)-2-amino-3-(O-propargyl)butanoic acid 6a



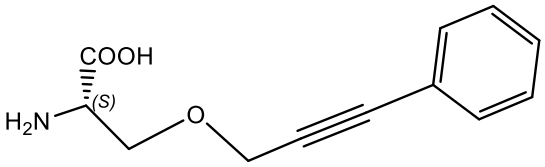
6a

Yield 67% (0.9 g), Mp185°C.$[\alpha]_D^{20}$ = +26.5° (c= 0.2,6N HCl).Anal Calc. for: $C_7H_{11}NO_3$ (157.17) C, 53.89; H, 7.14; N, 8.88; Found: C, 53.49; H, 7.05; N, 8.91: MS, *m*/*z*: 158.00

^{1}H NMR: (CDOD), δ=1.22 (3H, d,J=6.6, CH_3); 2.91 (1H, t, J=2.4, ≡CH);3.91 (1H, d, J=3.7, NCH); 4.27 (1H, dd, J=16.2, 2.4, OCH_2); 4.31 (1H, dd, J=16.2, 2.4, OCH_2); 4.32 (1H, qd, J=6.6, 3.7, C<u>H</u>CH_3).

^{13}C NMR: (CDOD) δ= 14.2 (CH_3); 56.9 (OCH_2); 59.0 (NCH); 73.8 (OCH); 76.2 (≡CH); 80.5 (≡C); 171.5 (CO).

(S)-2-amino-3-((3-phenylprop-2-yn-1-yl)oxy)propanoic acid 13



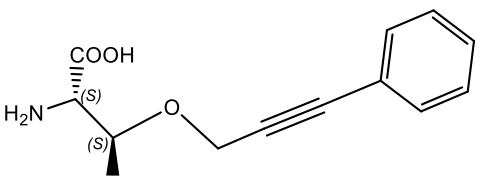
13

Yield 47% (0.36 g), Mp +175.8^{0}C, $[\alpha]_D^{20}$ +21^0 (c=0.2, 6N HCl). Anal Calc. for: $C_{12}H_{13}NO_3$ (219.24) C 65.74; H 5.98; N 6.39; Found: C 66.02; H 6.27; N 6.74: MS, *m*/*z*: 219.09:

^{1}H NMR: (D_2O) δ=3.88-3.99 (3H, m, C<u>H</u>$_2$C<u>H</u>); 4.42 (2H, s, OC<u>H</u>$_2$C≡CPh); 7.32-7.42 (3H, m) and 7.45-7.50 (2H, m, C_6H_5).

^{13}C NMR: (D_2O) δ=55.9 (CH); 60.3 (CH_2); 69.2 (CH_2); 86.2 (C≡C); 88.4 (C≡C); 123.1; 130.2 (2CH); 130.7 (2CH); 133.2 (2CH); 172.4 (CO).

(S)-2-amino-3-((3-phenylprop-2-yn-1-yl)oxy)butanoic acid 14



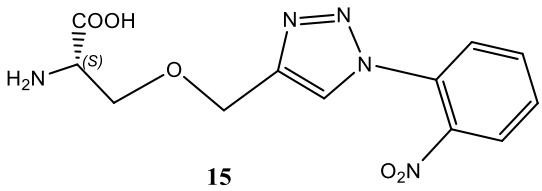
14

Yield 43% (0.31 g), Mp +189^{0}C, $[\alpha]_D^{20}$ +21^0 (c=0.2, 6N HCl). Anal Calc. for: $C_{13}H_{15}NO_3$ (233.26) C 66.94 H 6.48; N 6.00; Found: C 67.22; H 6.84; N 6.26: MS, *m*/*z*: 233.11:

^{1}H NMR: (CD_3OD) δ=1.26 (3H, d, J=6.6, CH_3); 3.96 (1H, d, J=3.7, NCH); 4.41 (1H, qd, J=6.6, 3.7, C<u>H</u>CH_3); 4.50 (1H, d, J=16.2, CH_2); 4.54 (1H, d, J=16.2, CH_2); 7.31-7.39 (3H, m, C_6H_5); 7.43-7.49 (2H, m, C_6H_5).

^{13}C NMR: (CD_3OD) δ=14.2 (CH_3); 57.6 (CH); 59.1 (NCH); 73.8 (OCH_2); 85.8 (C≡C); 87.3 (C≡C); 123.8, 129.5 (2CH); 129.7 (CH); 132.7 (CH); 171.5 (CO).

(S)-2-amino-3-((1-(2-nitrophenyl)-1H-1,2,3-triazol-4-yl)methoxy)propanoic acid 15



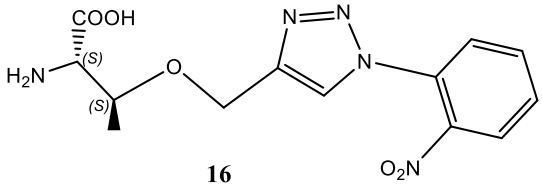
15

Yield 44% (0.47 g), Mp +114^{0}C, $[\alpha]_D^{20}$ +9.36^0 (c=0.2, 6N HCl). Anal Calc. for: $C_{12}H_{13}N_5O_5$ (307.26) C 46.91; H 4.26; N 22.79; Found: C 47.16; H 4.63; N 23.08: MS, *m*/*z*: 307.09:

^{1}H NMR: (DMSO) δ=3.44 (1H, dd, J=7.7, 3.3, CH); 3.72 (1H, dd, J=10.3, 7.7, C$\underline{H}_2$CH); 3.89 (1H, dd, J=10.3, 3.3, C$\underline{H}_2$CH); 4.68 (2H, s, OCH_2); 7.81-7.99 (3H, m) and 8.21 (1H, dd, J=8.0, 1.2, C_6H_4); 8.73 (1H, s, =CHN).

^{13}C NMR: (DMSO) δ=54.2 (CH); 63.5 (CH_2); 69.6 (CH_2); 125.2; 125.5; 127.3; 129.0; 131.1; 134.3; 144.0; 144.8; 167.3.

(S)-2-amino-3-((1-(2-nitrophenyl)-1H-1,2,3-triazol-4-yl)methoxy)butanoic acid 16



16

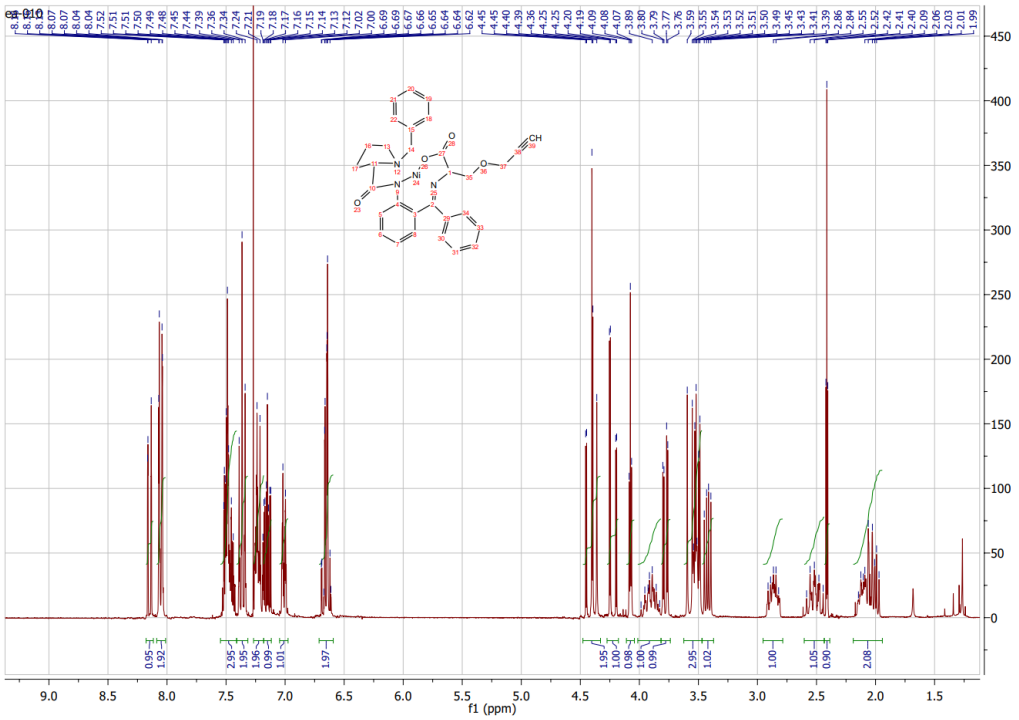
Yield 45% (0.38 g), Mp +214^{0}C, $[\alpha]_D^{20}$ +23^0 (c=0.2, 6N HCl). Anal Calc. for: $C_{13}H_{15}N_5O_5$ (321.29) C 48.60; H 4.71; N 21.80; Found: C 48.86; H 5.07; N 22.09: MS, *m*/*z*: 321.11:

^{1}H NMR: (DMSO-d_6) δ=1.09 (3H, d, J=6.5, CH_3); 3.56 (1H, d, J=3.5, NCH); 4.11 (1H, qd, J=6.5, 3.5, C$\underline{H}$CH$_3$); 4.67 (1H, dd, J=12.6, 0.5, CH_2); 4.70 (1H, dd, J=12.6, 0.5, CH_2); 7.49 (2H, b, NH_2); 7.81-7.88 (2H, m), 7.93-7.99 (1H, m) and 8.21 (1H, dd, J=8.1, 1.5, C_6H_4); 8.69 (1H, t, J=0.5, =CHN).

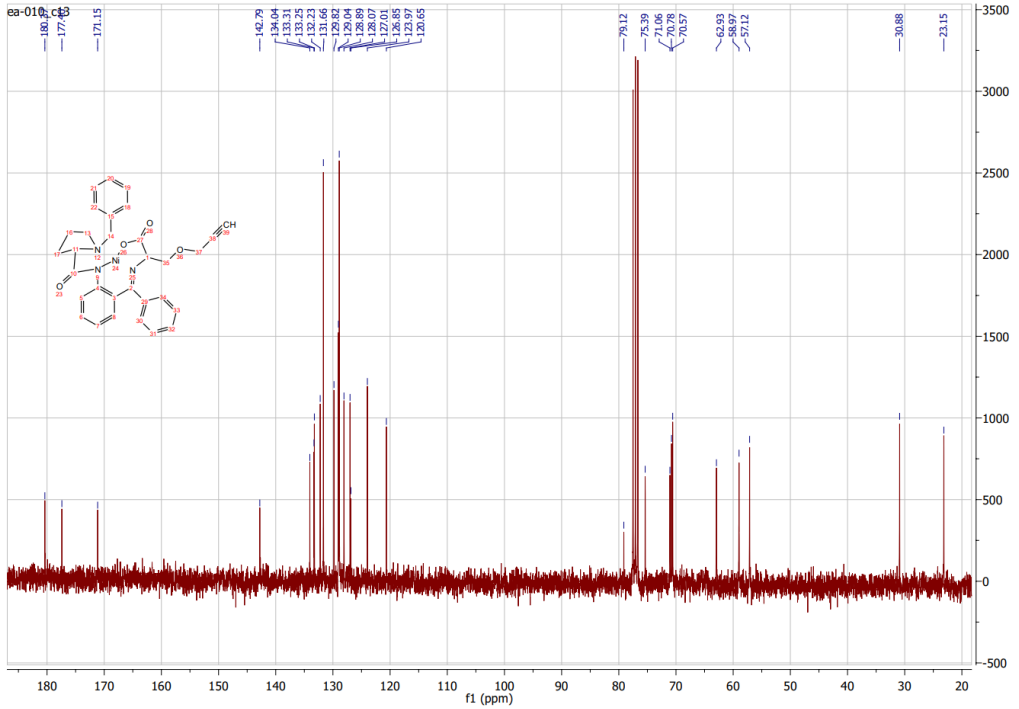
^{13}C NMR: (DMSO-d_6) δ=14.1 (CH_3); 56.7 (CH); 61.0 (NCH); 73.7 (OCH_2); 125.1 (CH); 125.4 (CH); 127.4 (CH); 129.0 (CH); 131.1 (CH); 134.3 (CH); 144.0 (CH); 145.2 (CH); 166.9 (CO).

NMR spectra

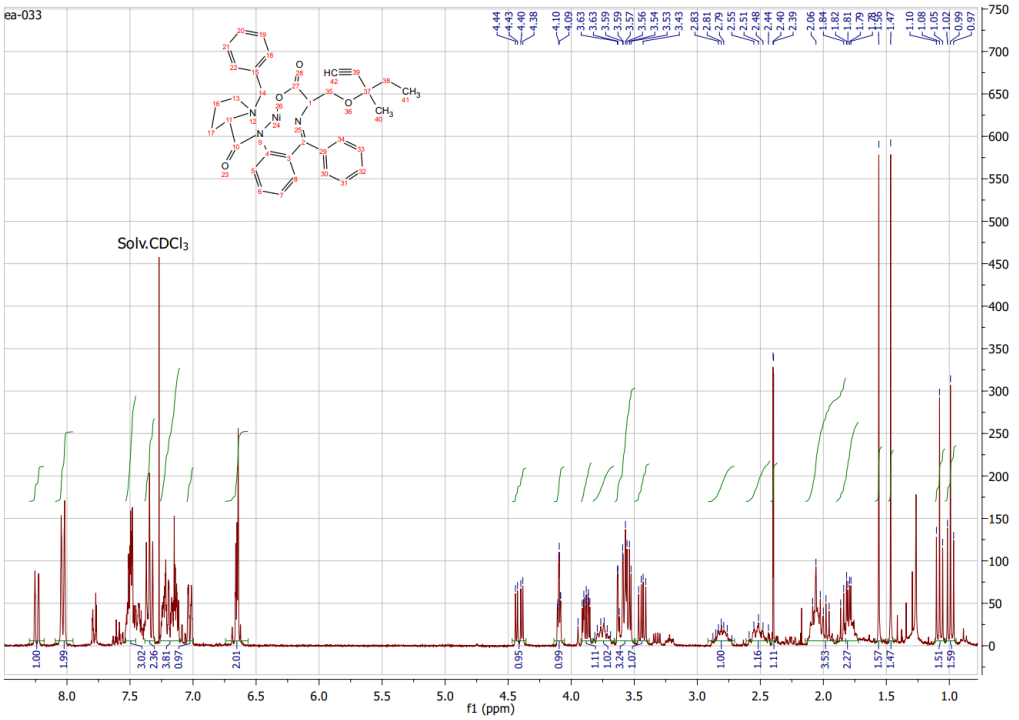
^{1}H NMR Complex 3a



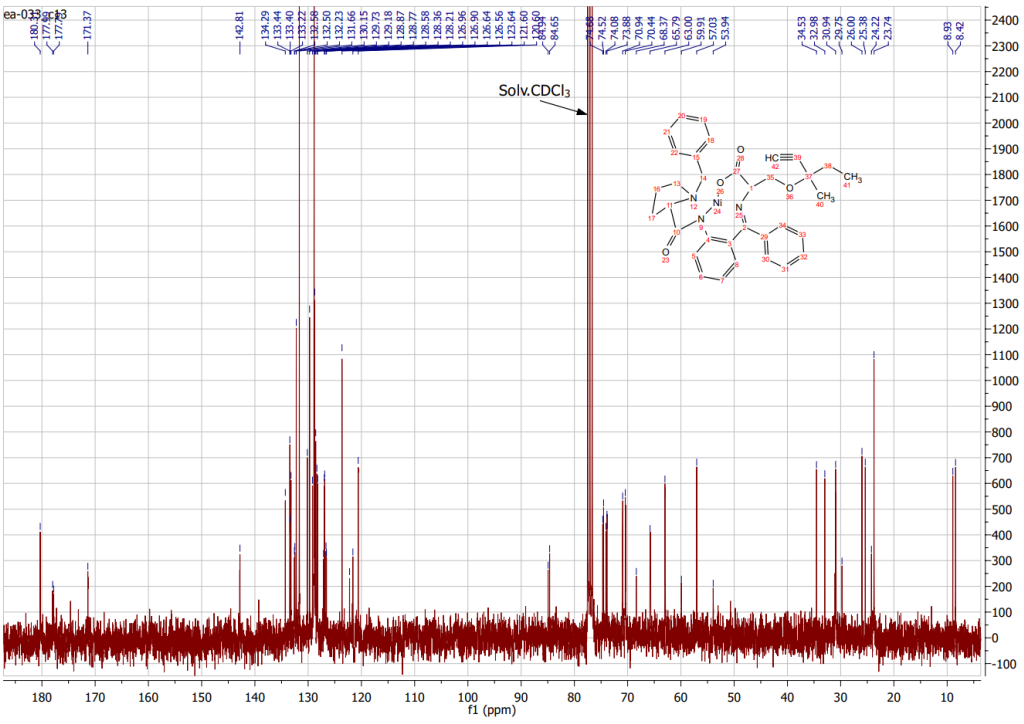
^{13}C NMR Complex 3a



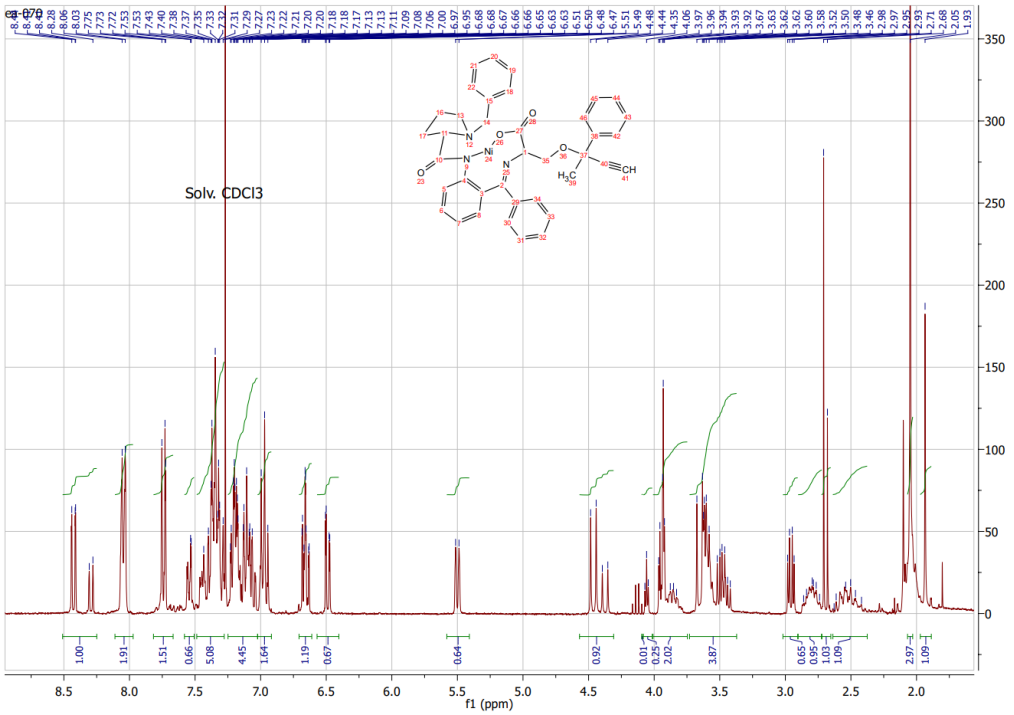
^{1}H NMR Complex 3c



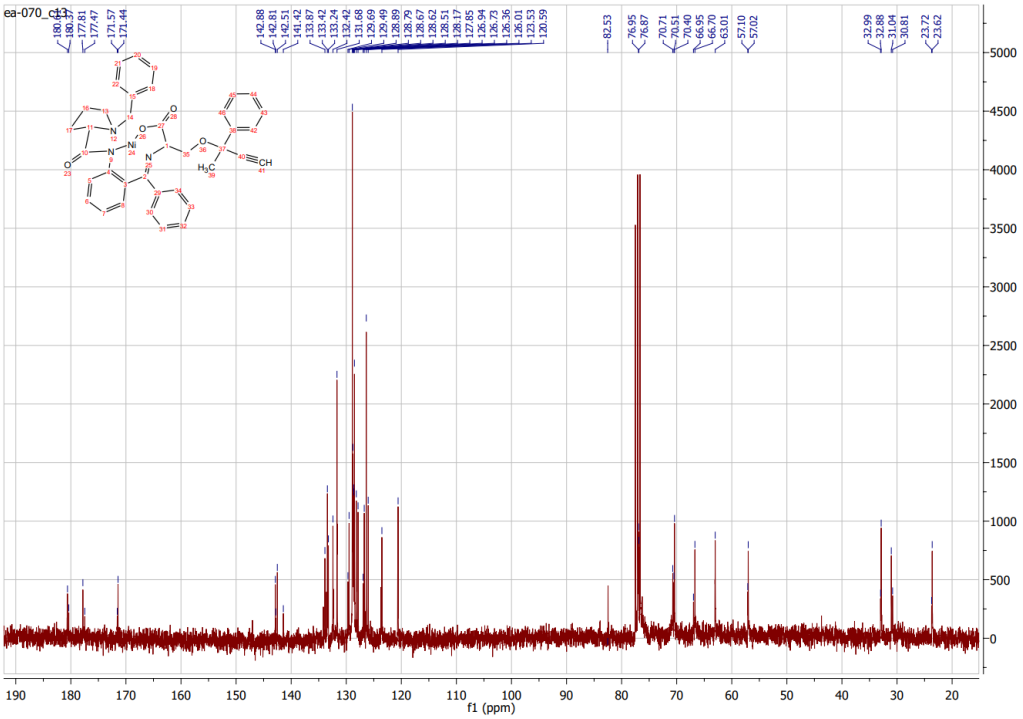
^{13}C NMR Complex 3c



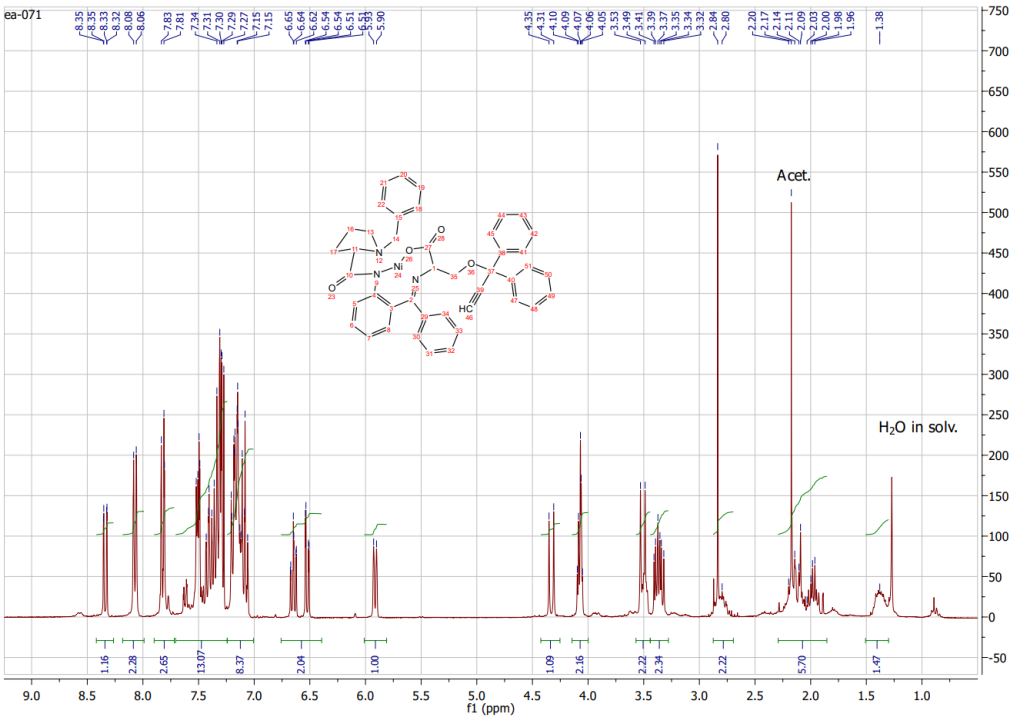
^{1}H NMR Complex 3d



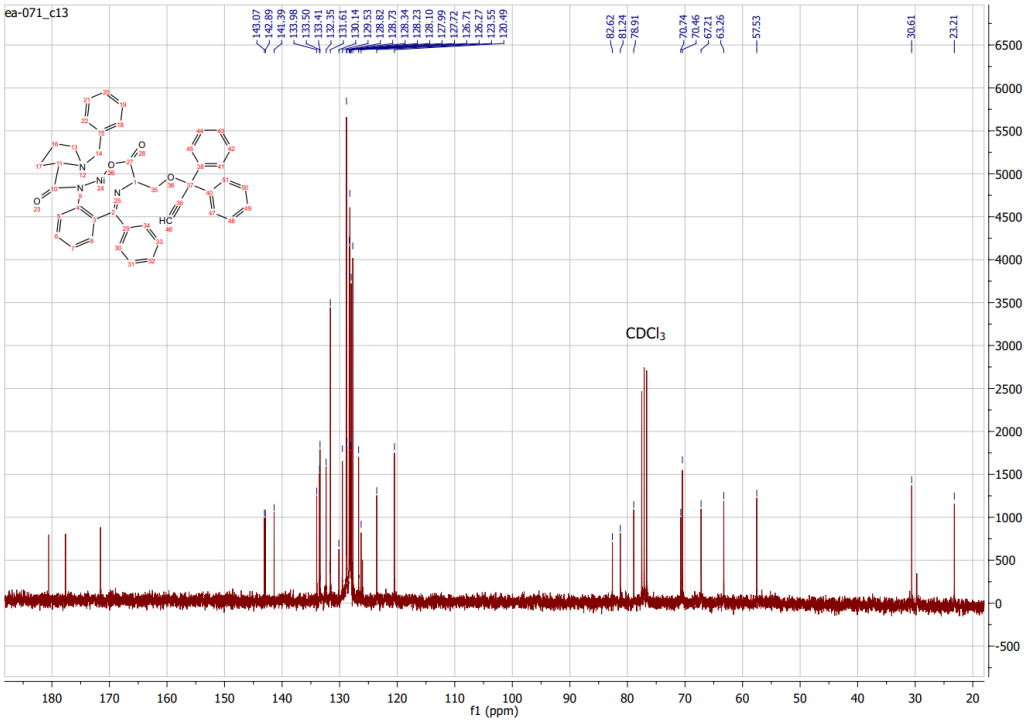
^{13}C NMR Complex 3d



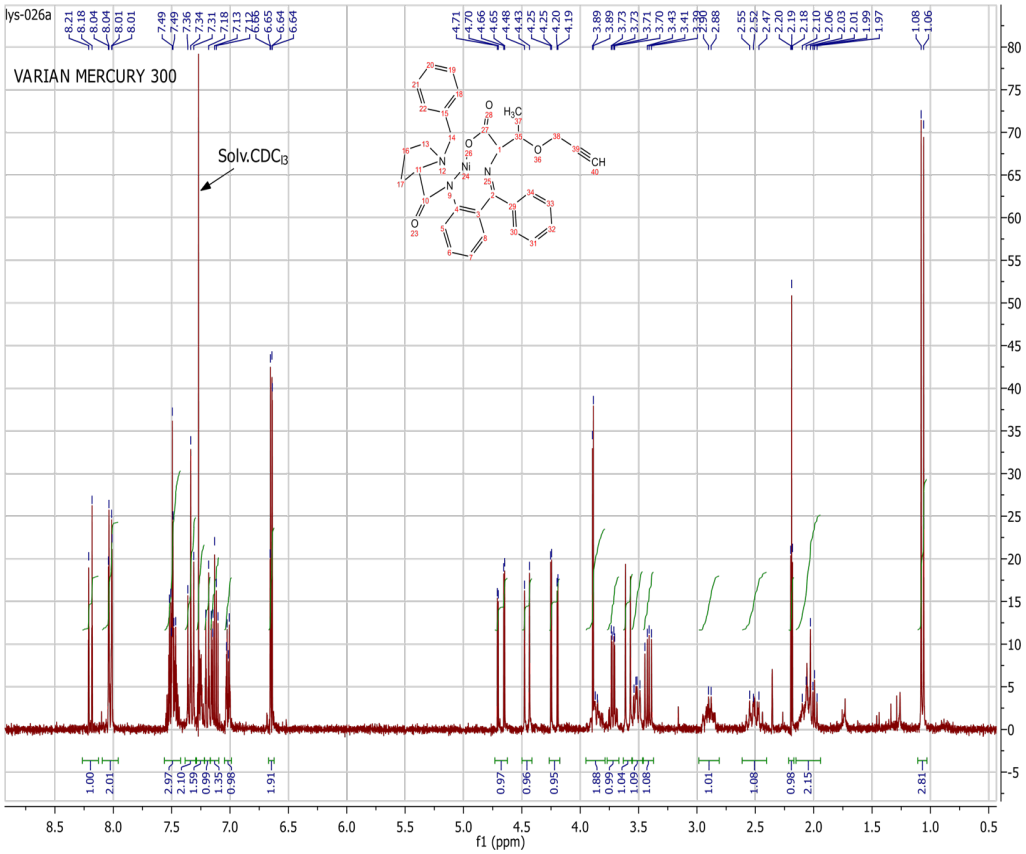
^{1}H NMR Complex 3e



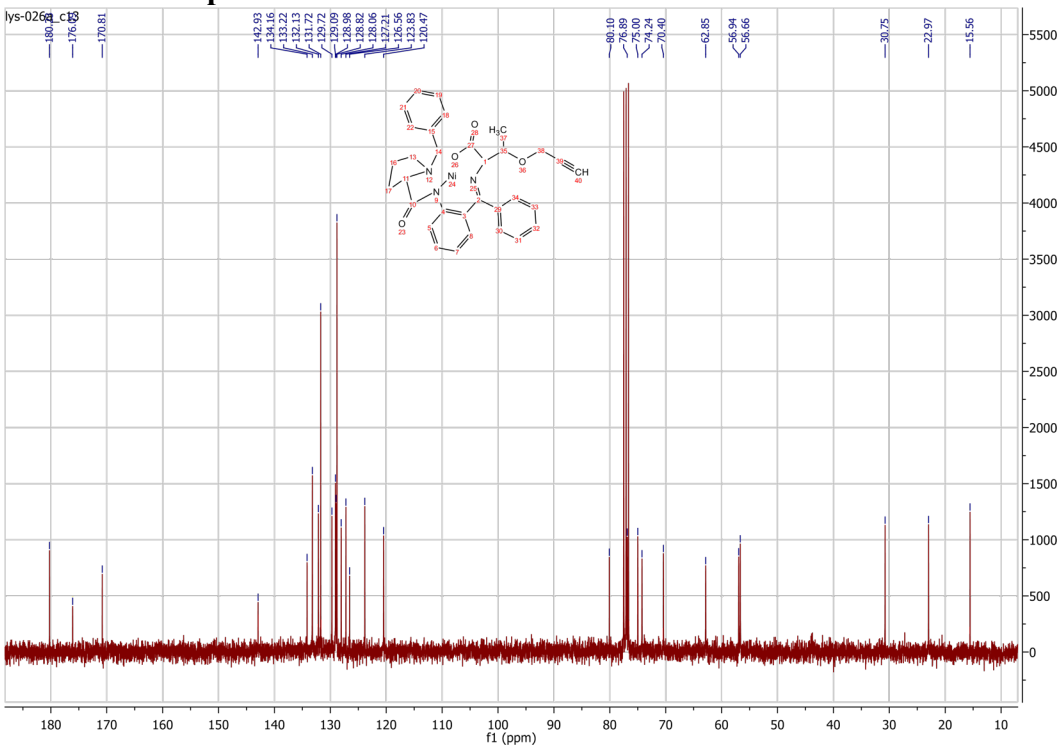
^{13}C NMR Complex 3e



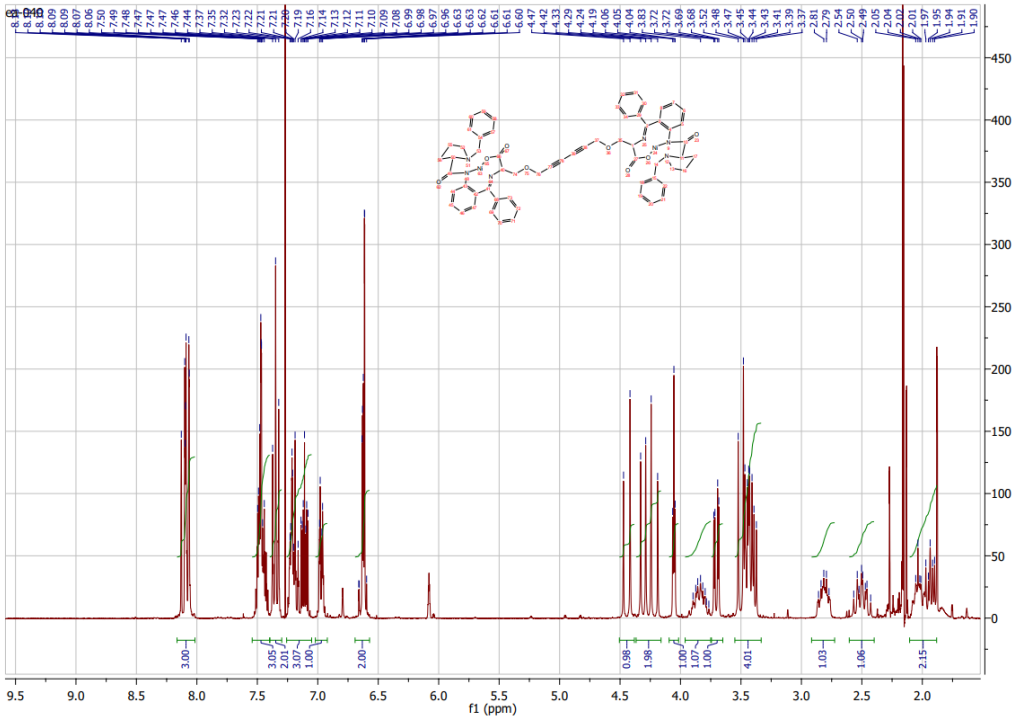
^{1}H NMR Complex 4a



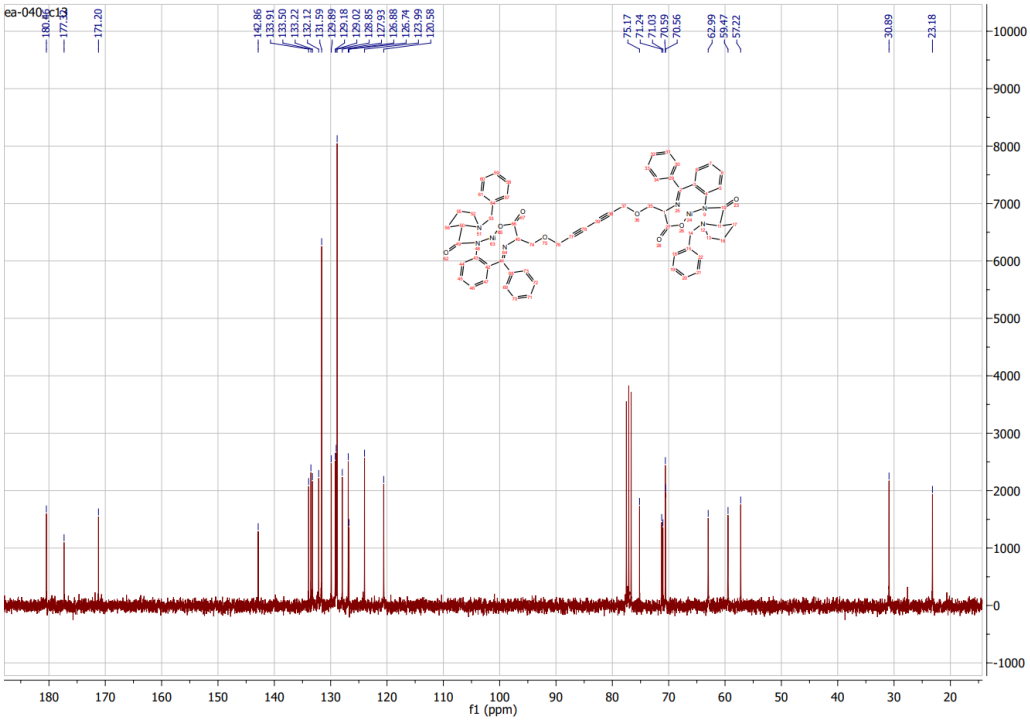
^{13}C NMR Complex 4a



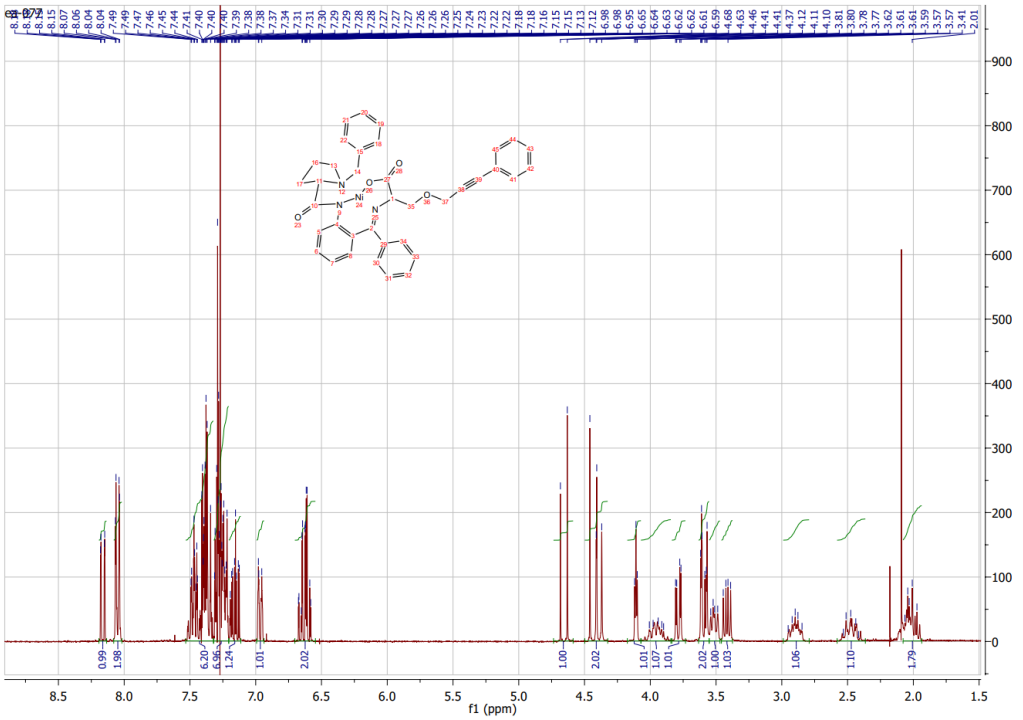
^{1}H NMR Complex 7



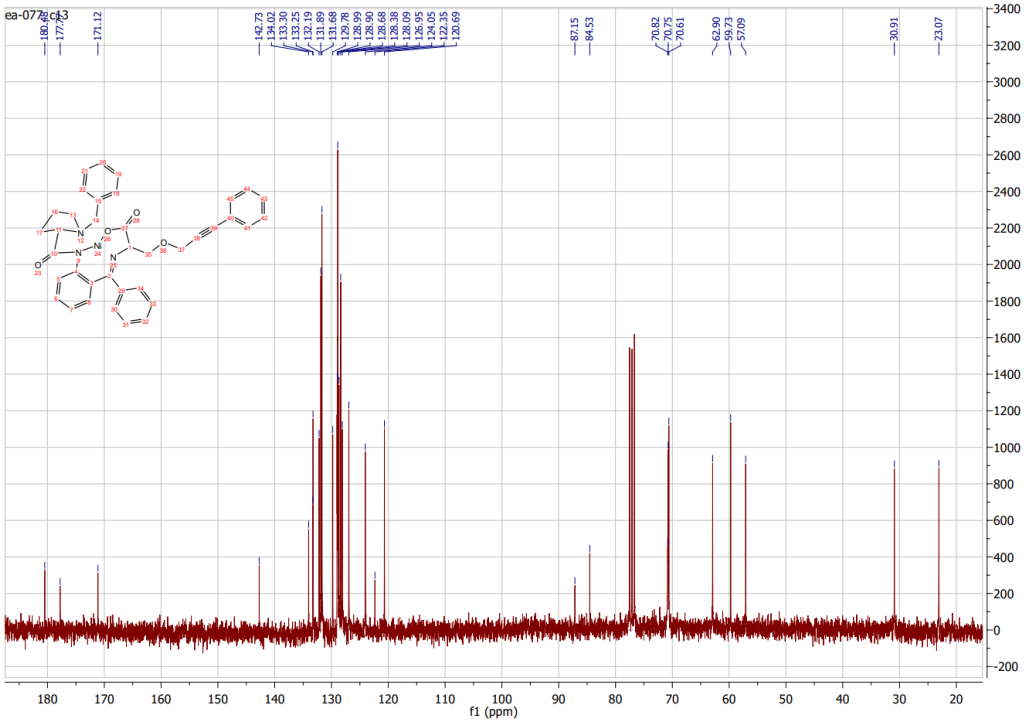
^{13}C NMR Complex 7



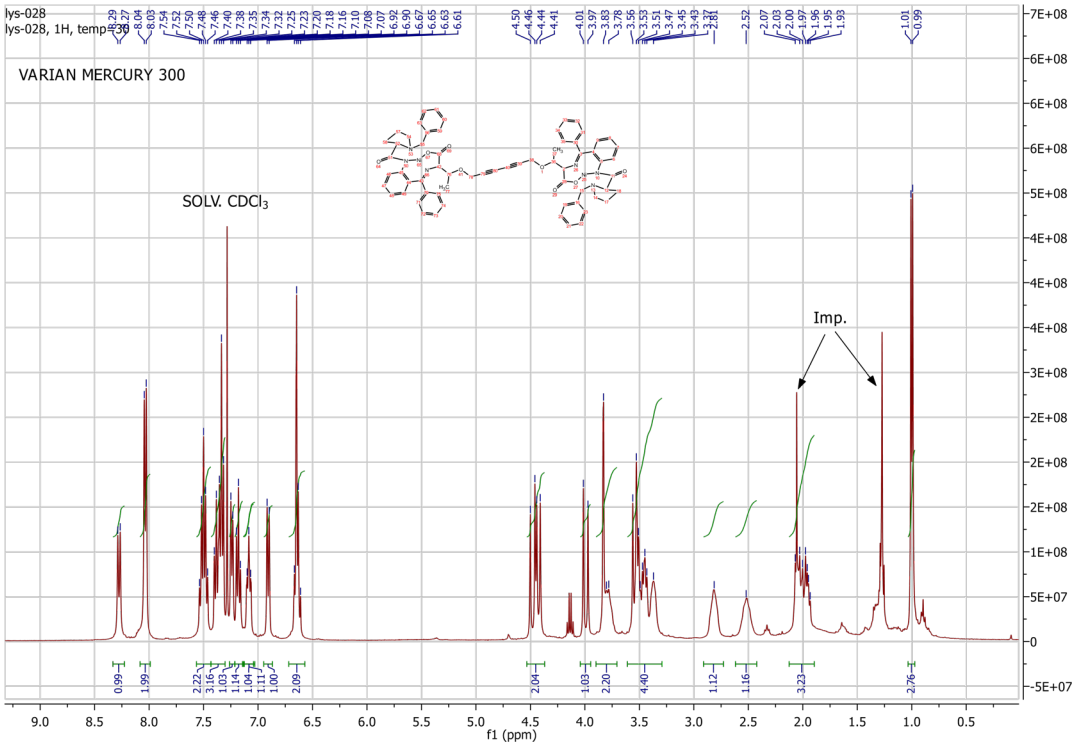
^{1}H NMR Complex 7



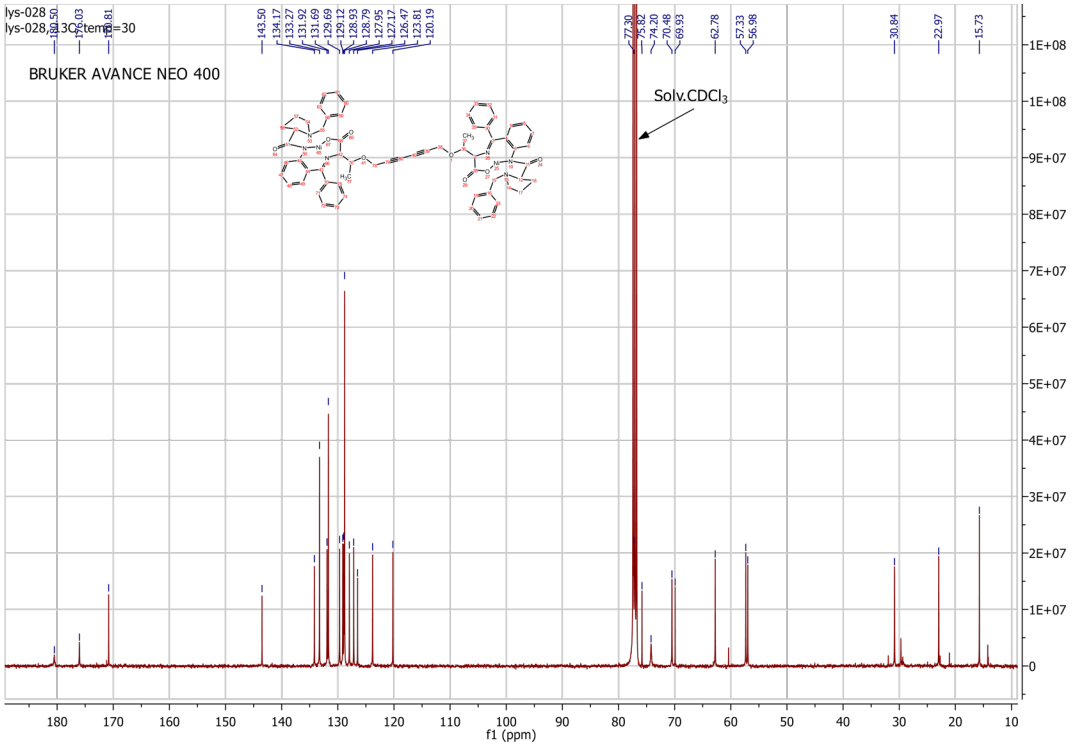
^{13}C NMR Complex 8



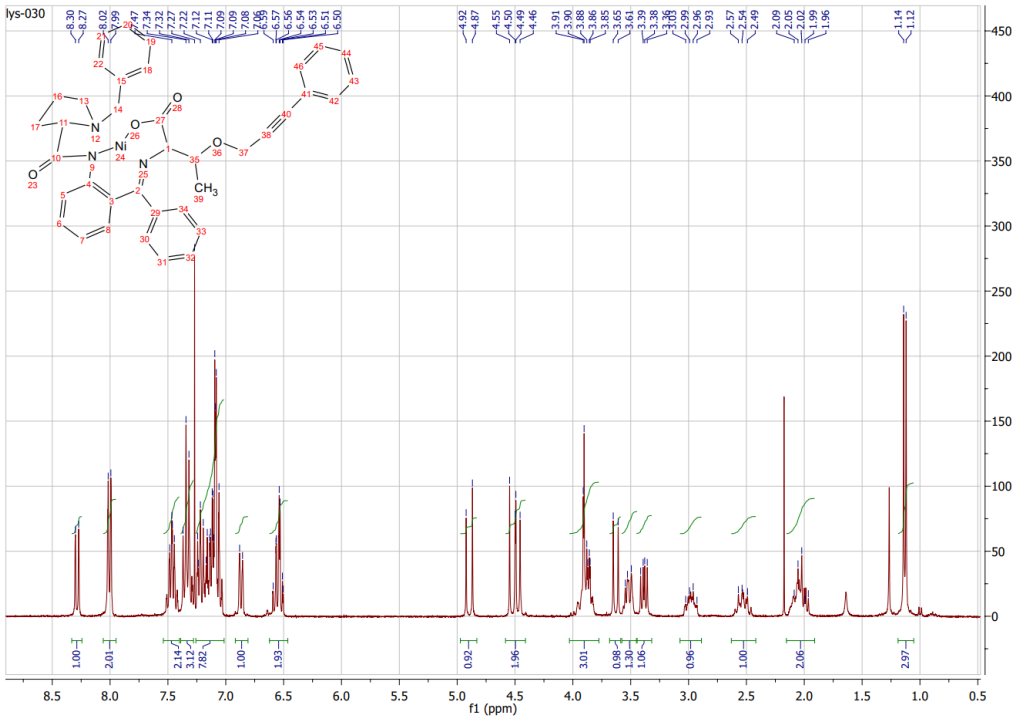
^{1}H NMR Complex 9



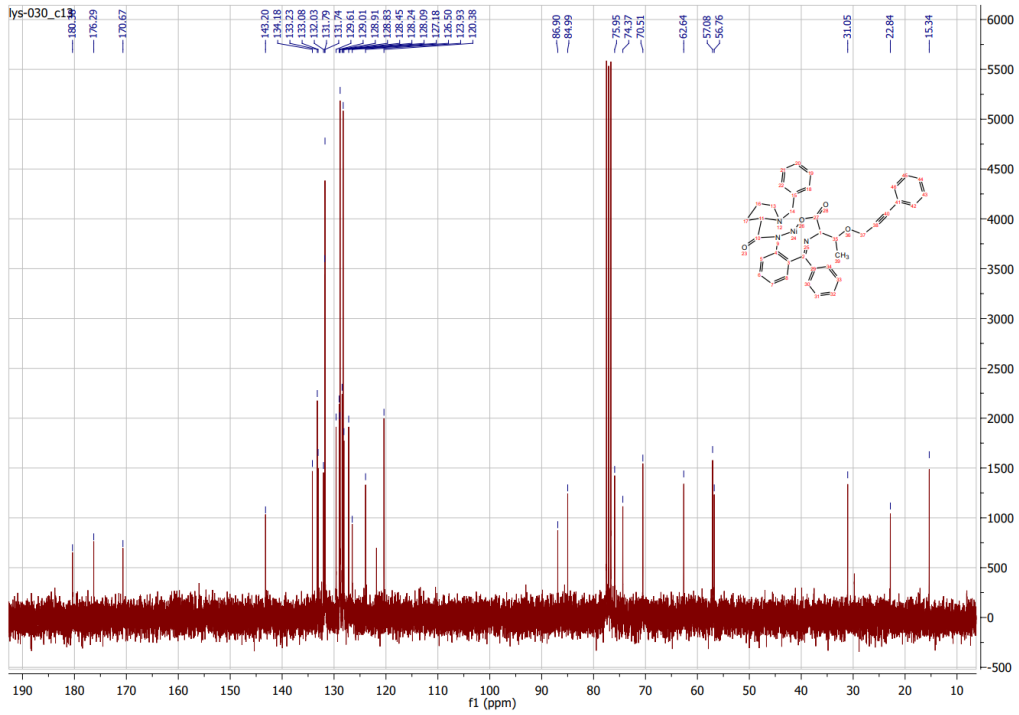
^{13}C NMR Complex ~~10~~



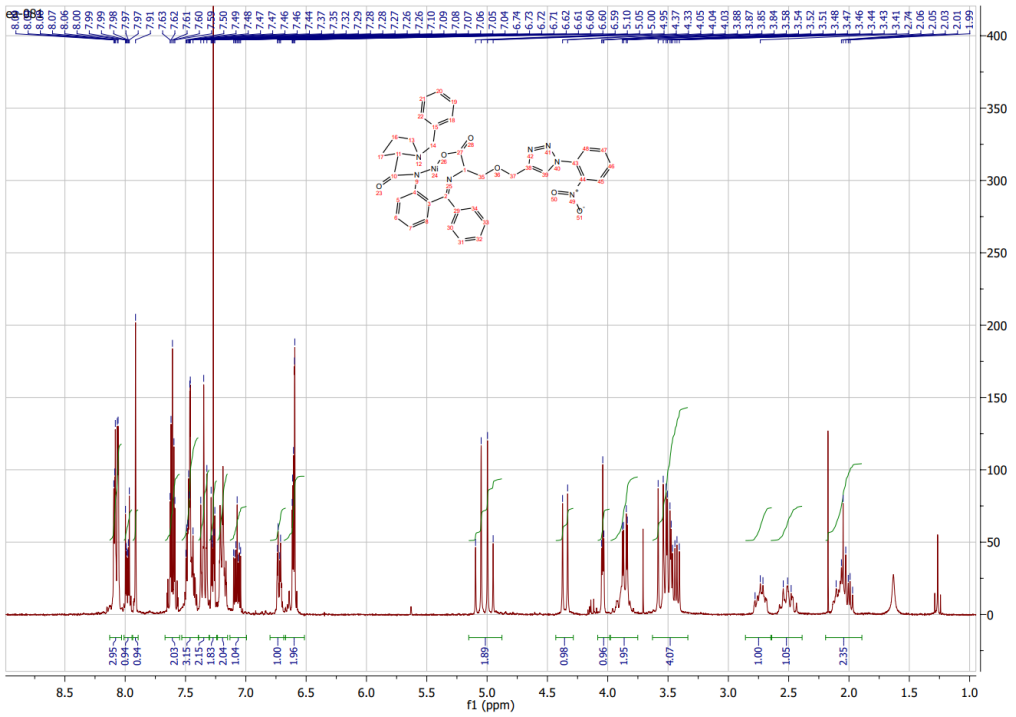
^{1}H NMR Complex 10



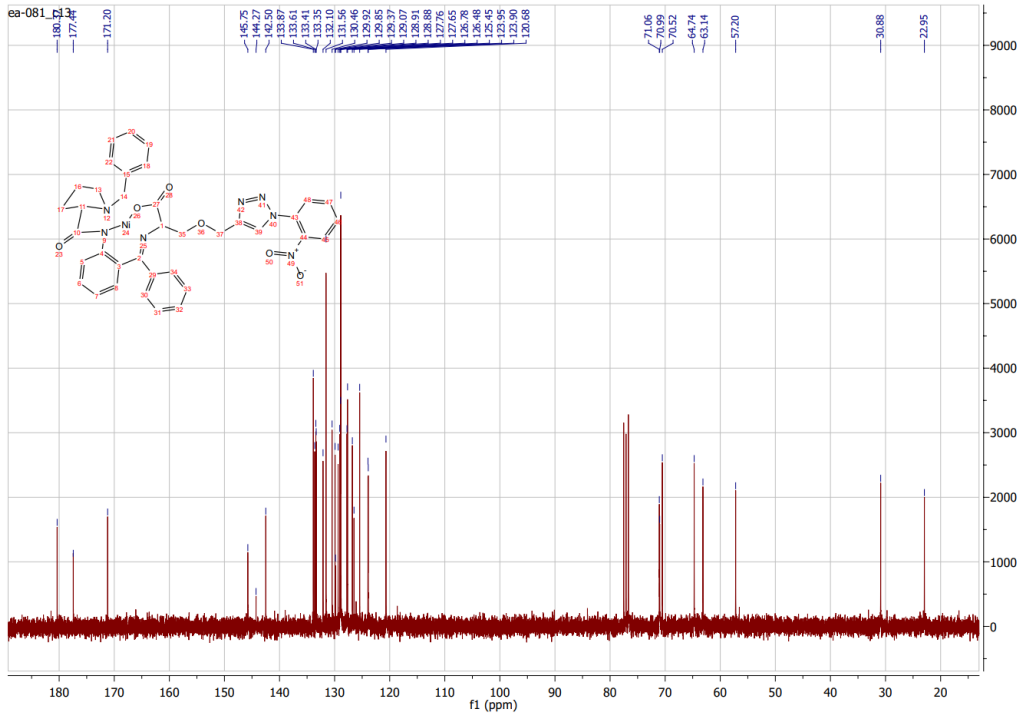
^{13}C NMR Complex 10



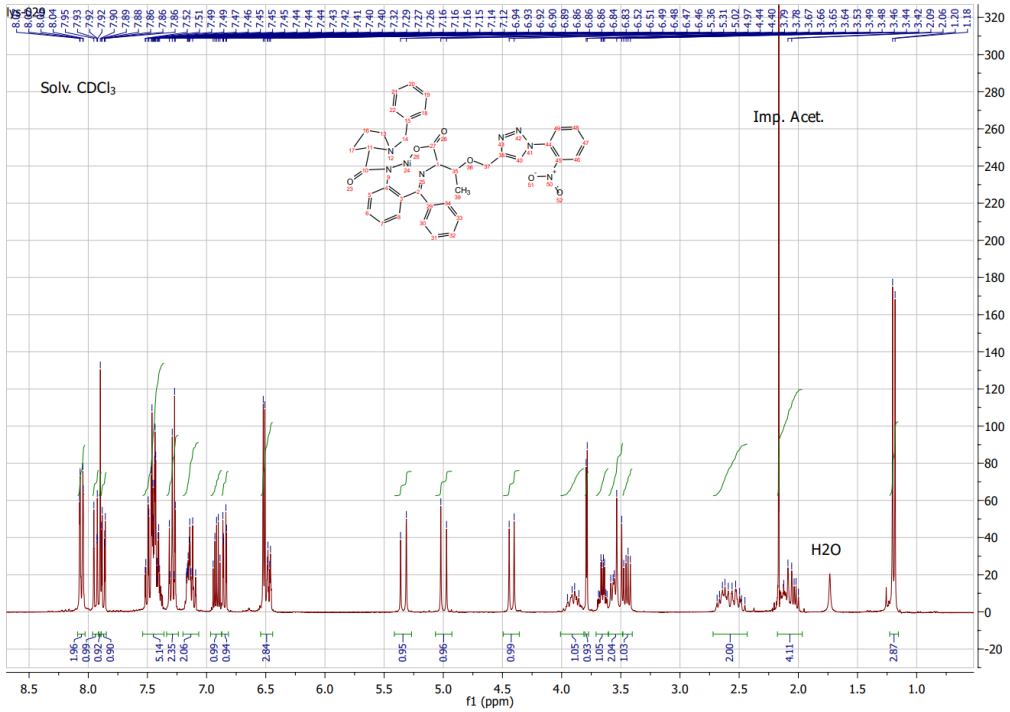
^{1}H NMR Complex 11



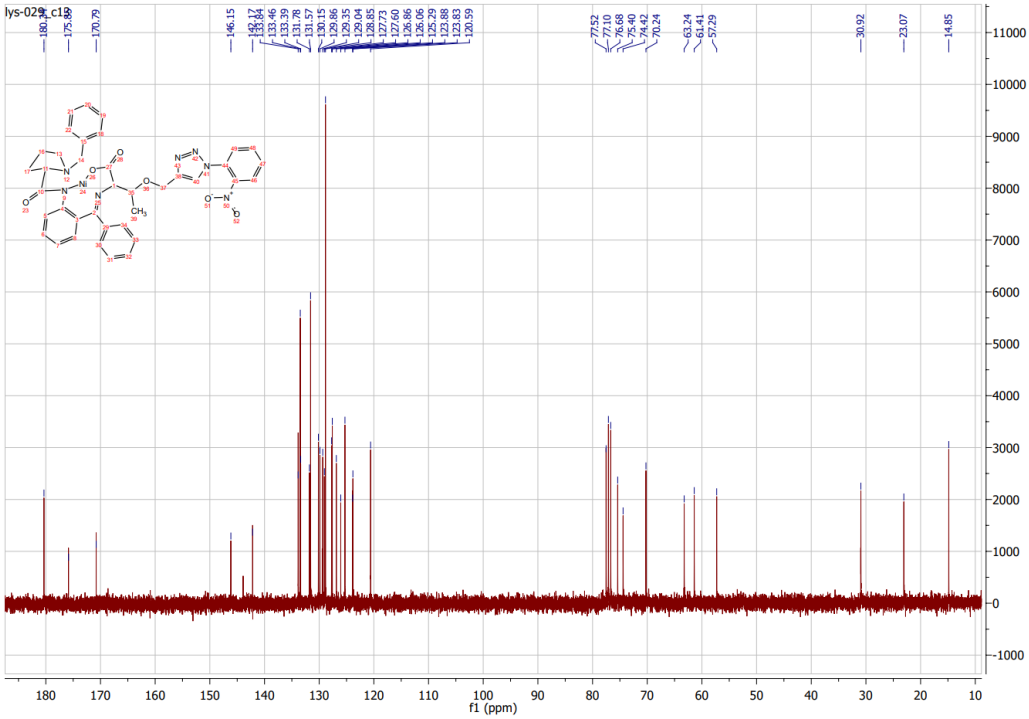
^{13}C NMR Complex 11



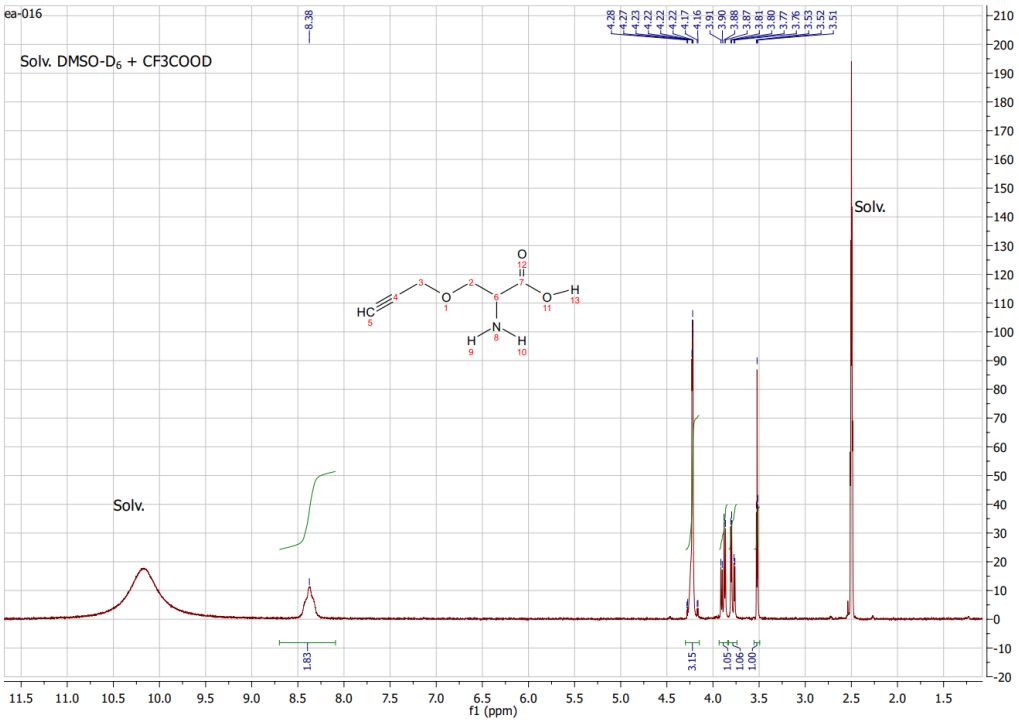
^{1}H NMR Complex 12



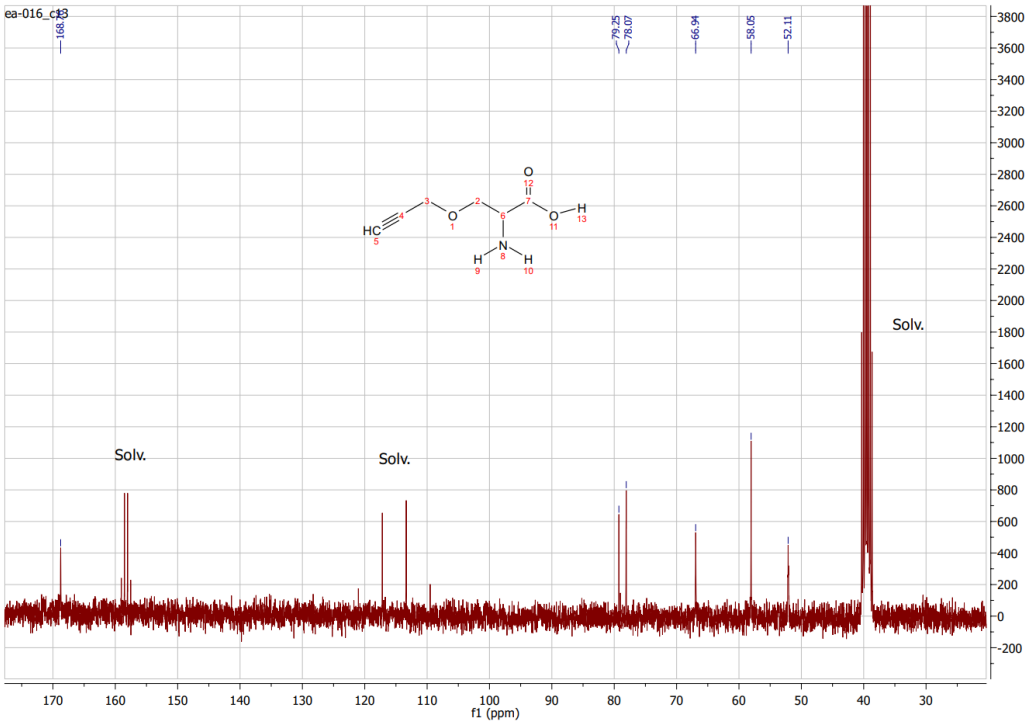
^{13}C NMR Complex 12



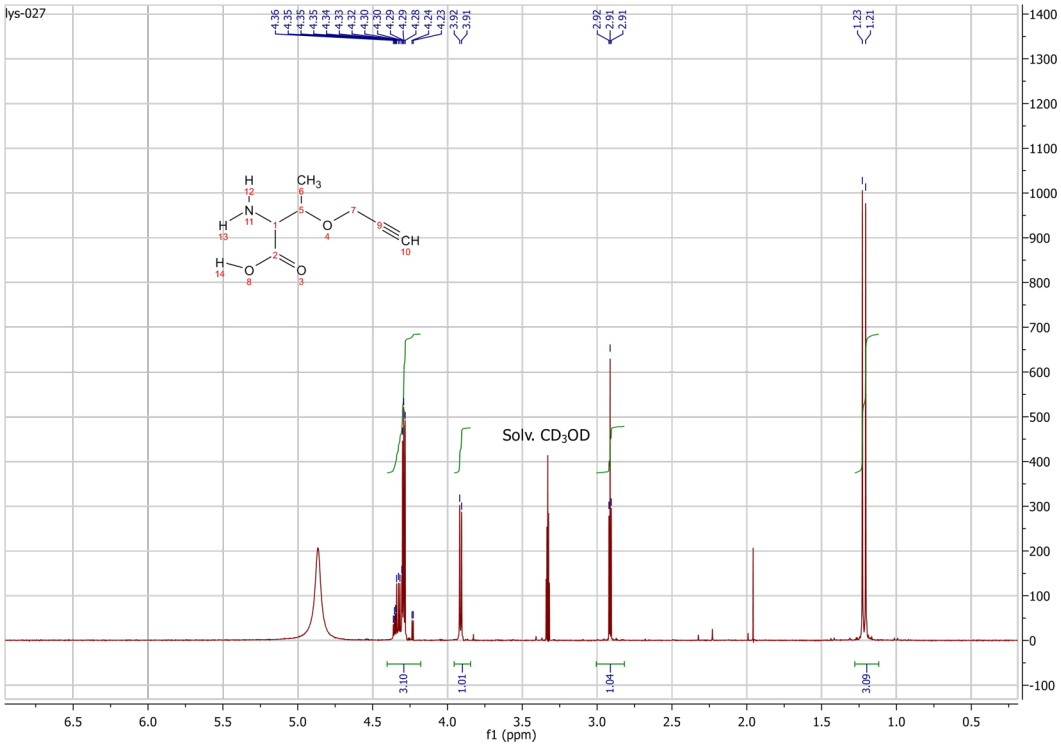
^{1}H NMR (S)-2-amino-3-(O-propargyl)propionic acid, 5a



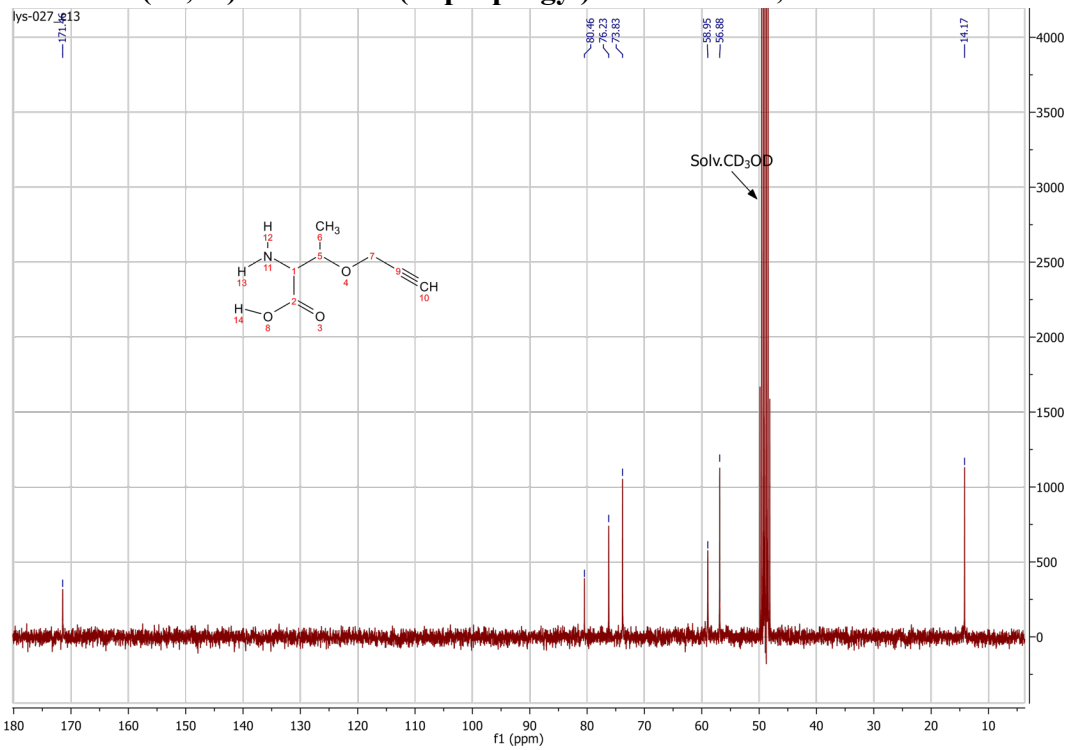
^{13}C NMR (S)-2-amino-3-(O-propargyl)propionic acid, 5a



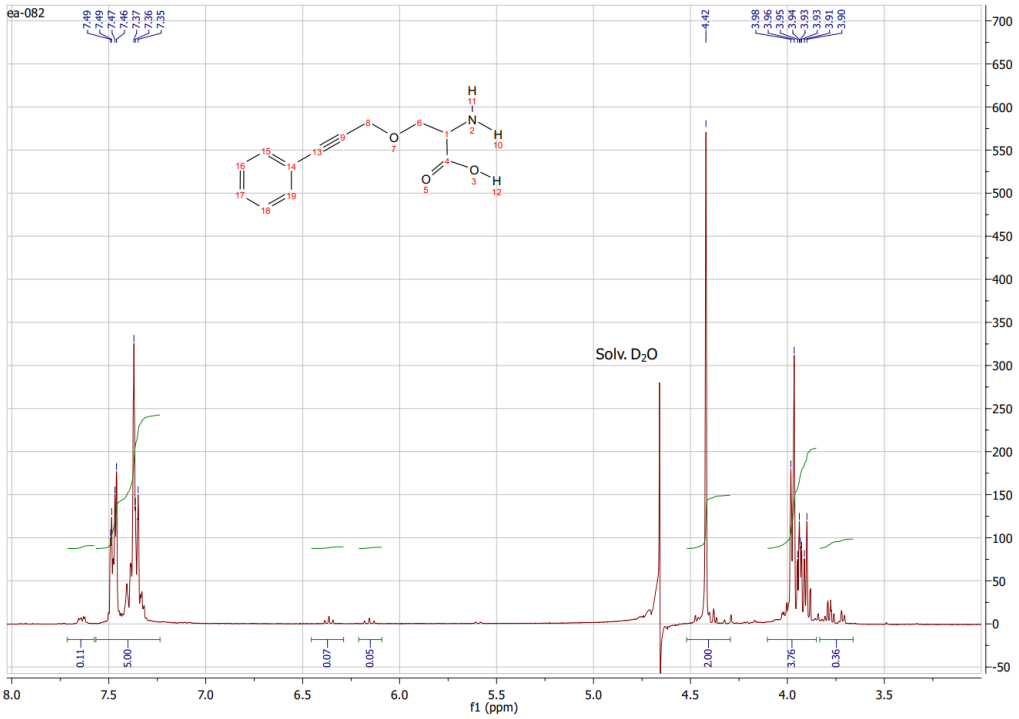
^{1}H NMR (2*S*,3*S*)-2-amino-3-(O-propargyl)butanoic acid, 6a



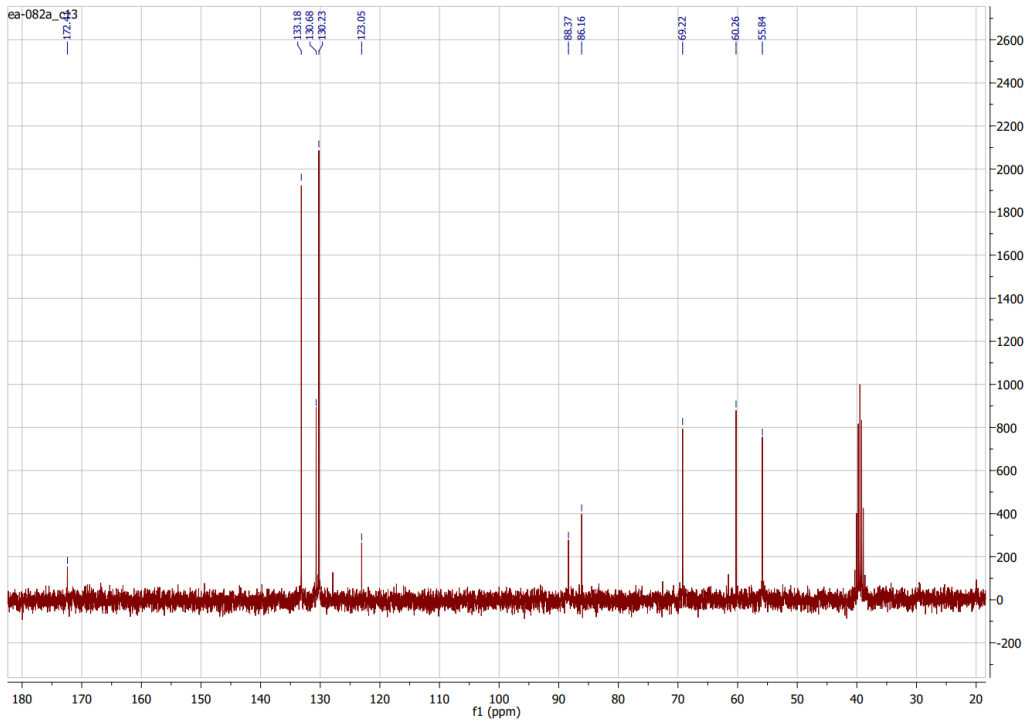
^{13}C NMR (2*S*,3*S*)-2-amino-3-(O-propargyl)butanoic acid, 6a



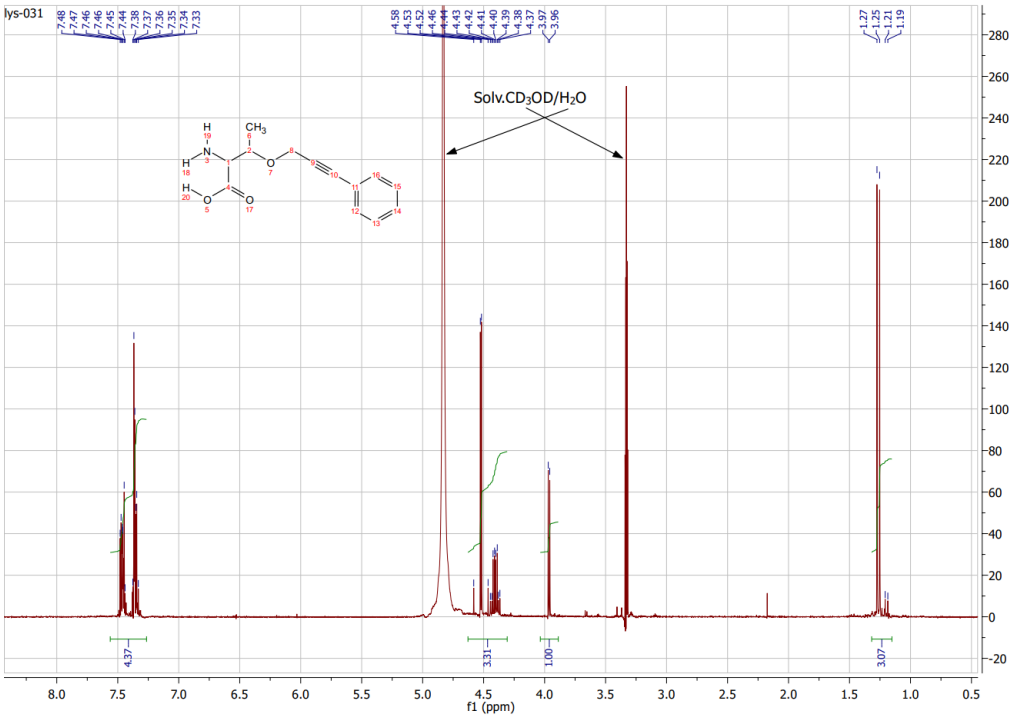
^{1}H NMR (S)-2-amino-3-((3-phenylprop-2-yn-1-yl)oxy)propanoic acid13



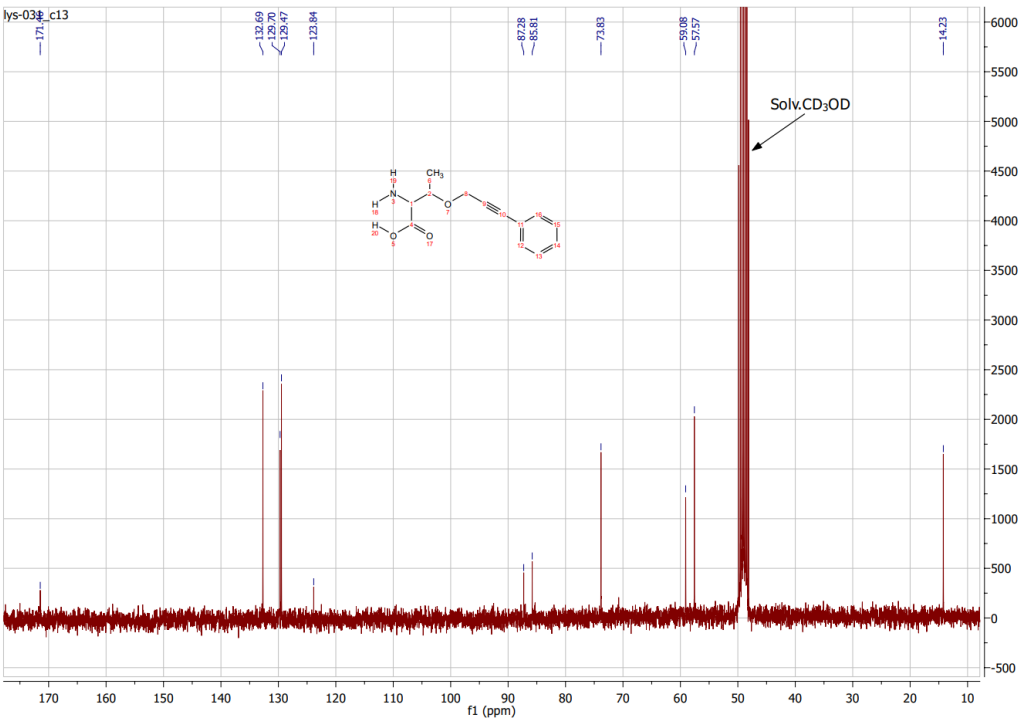
^{13}C NMR (S)-2-amino-3-((3-phenylprop-2-yn-1-yl)oxy)propanoic acid13



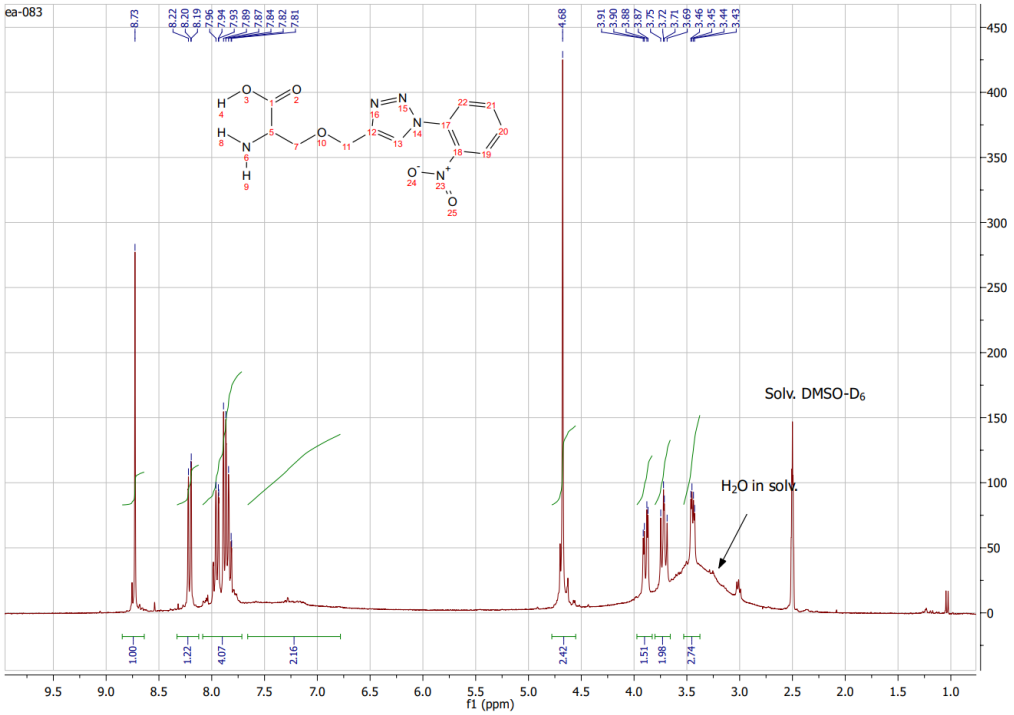
^{1}H NMR (S)-2-amino-3-((3-phenylprop-2-yn-1-yl)oxy)butanoic acid 14



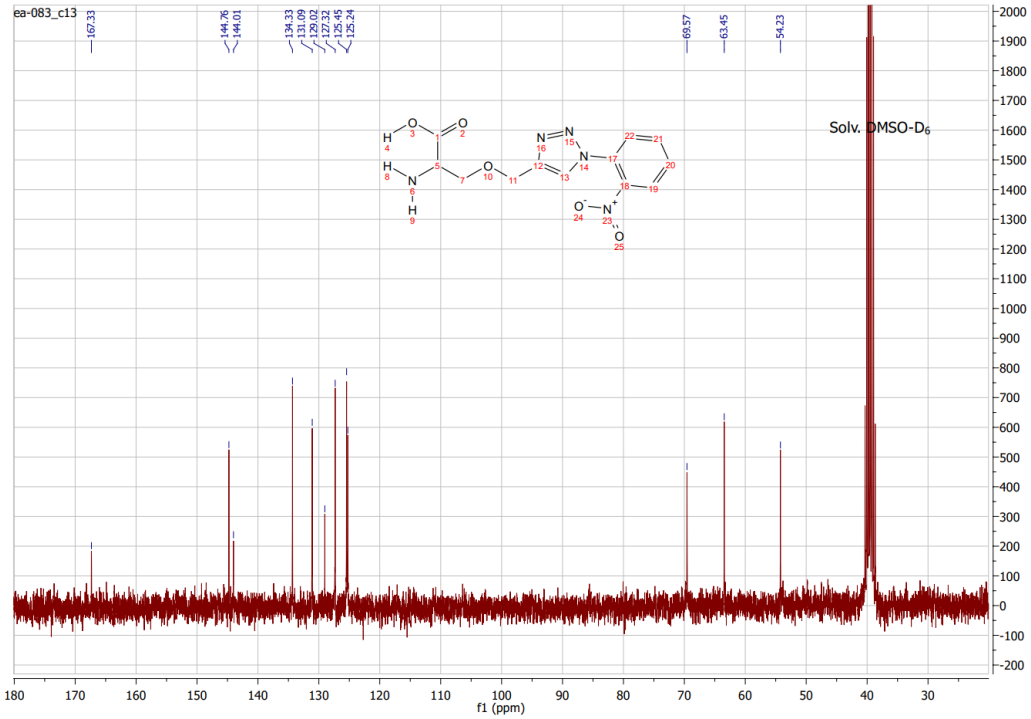
^{13}C NMR (S)-2-amino-3-((3-phenylprop-2-yn-1-yl)oxy)butanoic acid 14



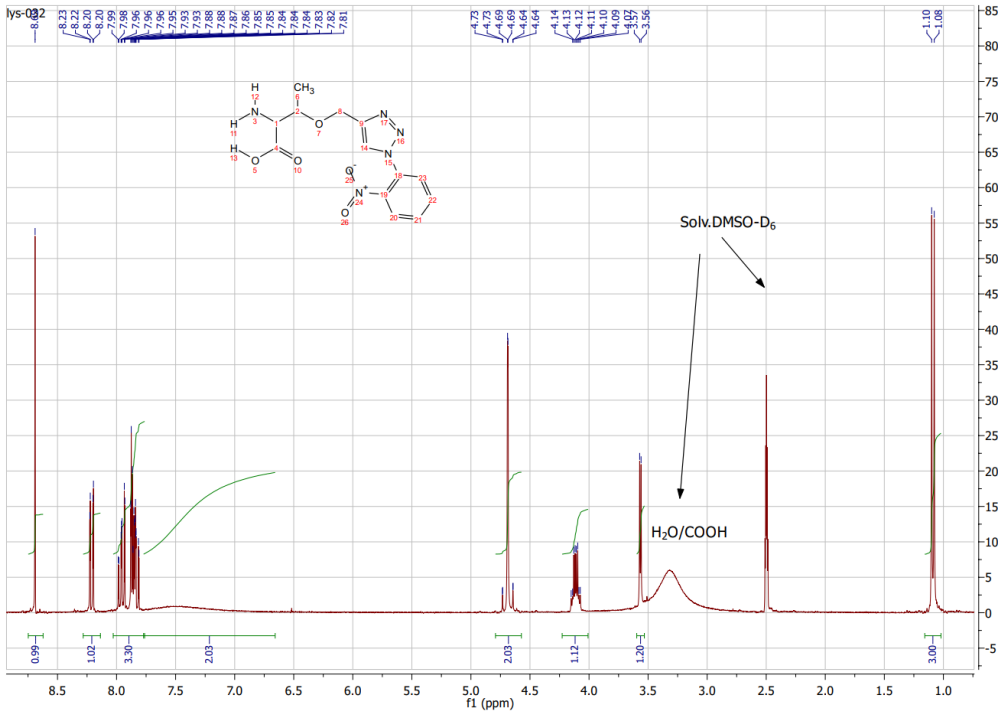
^{1}H NMR (S)-2-amino-3-((1-(2-nitrophenyl)-1H-1,2,3-triazol-4-yl)methoxy)propanoic acid15



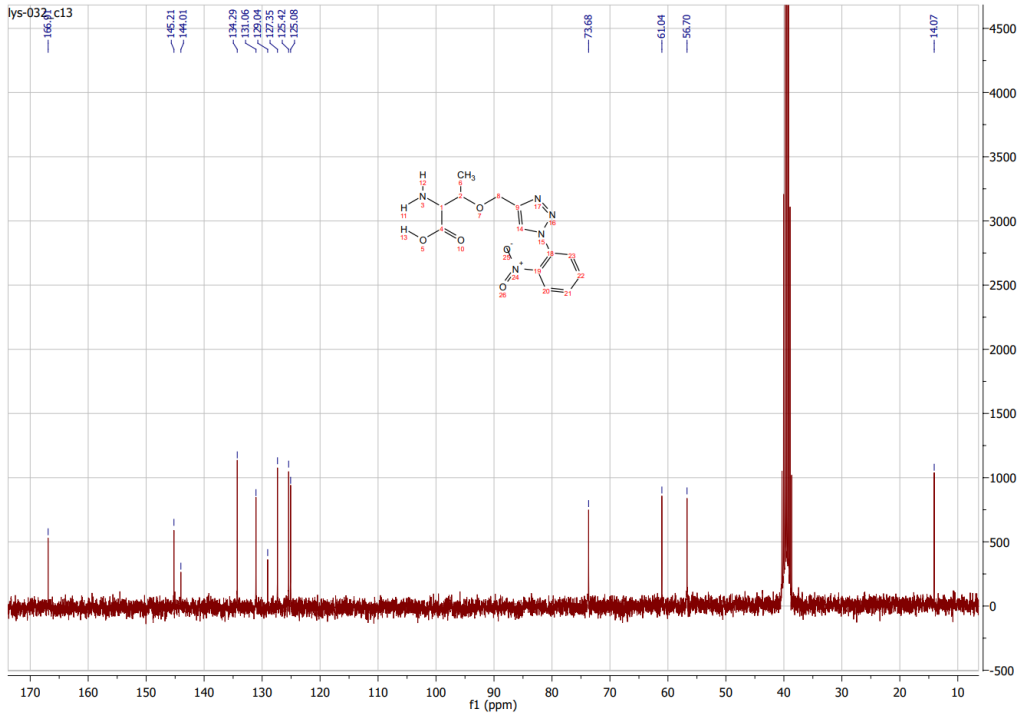
^{13}C NMR (S)-2-amino-3-((1-(2-nitrophenyl)-1H-1,2,3-triazol-4-yl)methoxy)propanoic acid15



^{1}H NMR(S)-2-amino-3-((1-(2-nitrophenyl)-1H-1,2,3-triazol-4-yl)methoxy)butanoic acid16



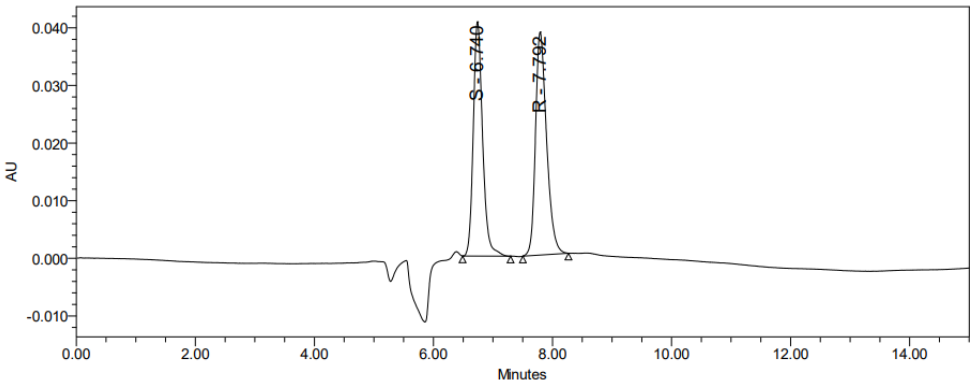
^{13}C NMR(S)-2-amino-3-((1-(2-nitrophenyl)-1H-1,2,3-triazol-4-yl)methoxy)butanoic acid16



HPLC analysis

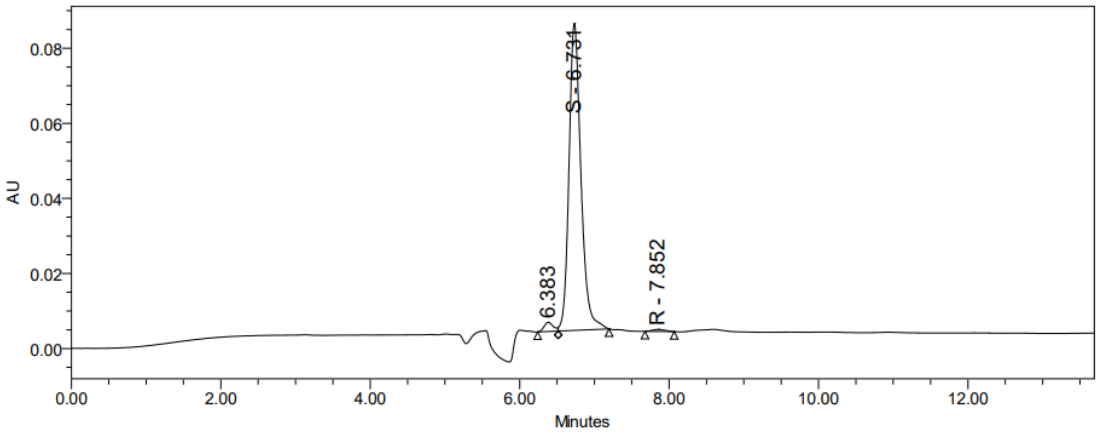
The analysis of non-proteinogenic amino acid samples was performed using a Waters Alliance 2695e Separation Module HPLC system equipped with a PDA detector (Waters Corporation, Milford, MA, USA). The analysis was conducted on a Nautilus-E column, 5 µm, 4.6 mm × 250 mm (BioChemMak ST, Moscow, Russia). The mobile phase consisted of 20% of methanol and 80% of buffer (88 mM potassium dihydrogen phosphate). The separation was carried out at a flow rate of 0.5 mL/min, with the column temperature maintained at 30°C. The PDA detector was set to 200 nm for detection. The injection volume was 10 µL.

HPLC analysis of (*S*, *R*) **-5a**



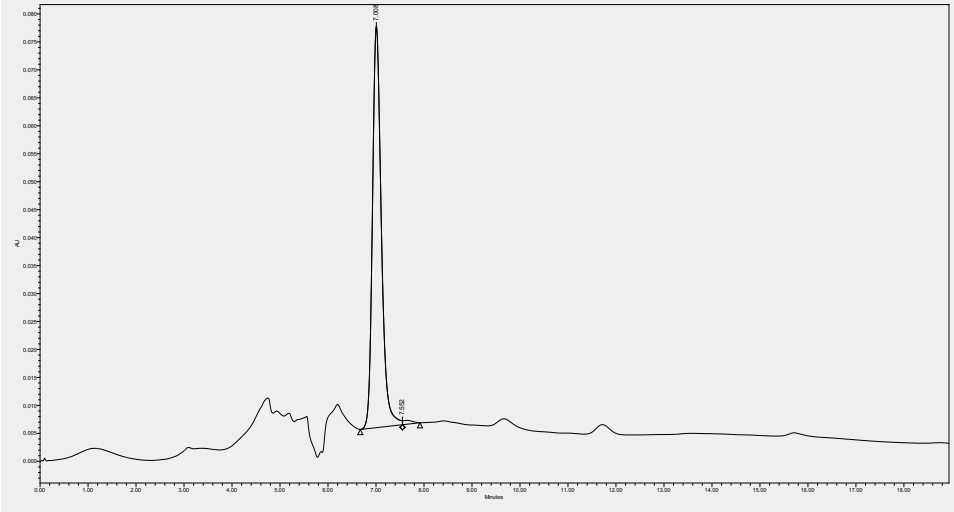
	Name	Retention Time	Area	% Area	Height
1	(*S*)-**5a**	6.740	443874	47.04	40665
2	(*R*)-**5a**	7.792	499762	52.96	38686

HPLC analysis of **5a**



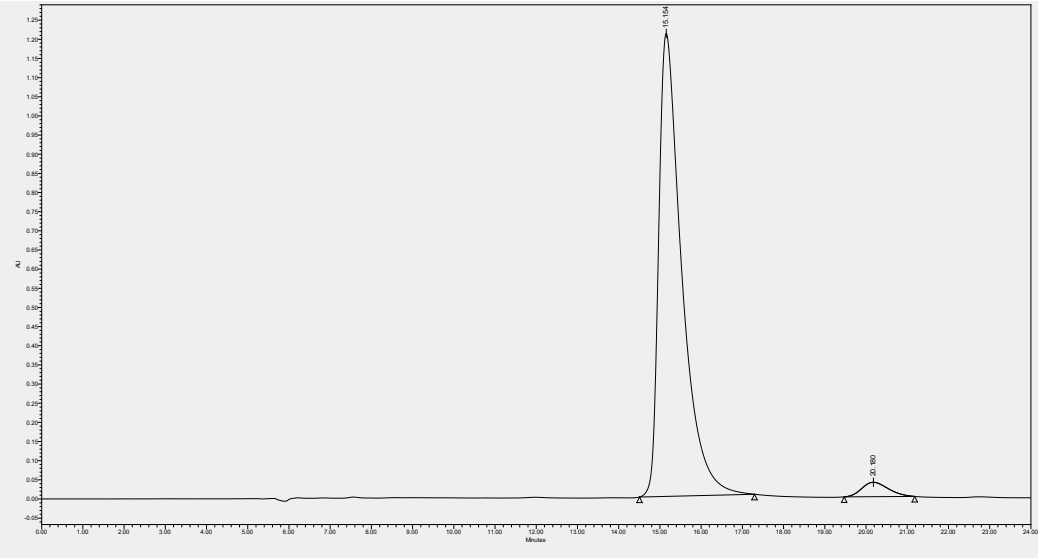
	Name	Retention Time	Area	% Area	Height
1	(*S*)-**5a**	6.731	905877	97.05	81759
2	(*R*)-**5a**	7.852	6543	0.70	545

HPLC analysis of **6a**



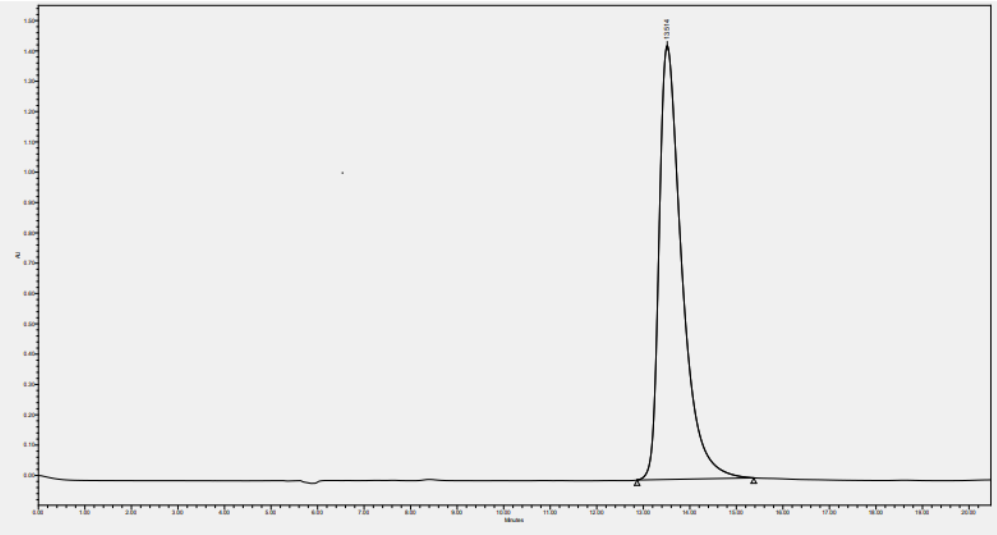
	Name	Retention Time	Area	% Area	Height
1	(*S*)-**6a**	7.008	924711	99.00	71768
2	(*R*)-**6a**	7.552	9374	1.00	708

HPLC analysis of **13**



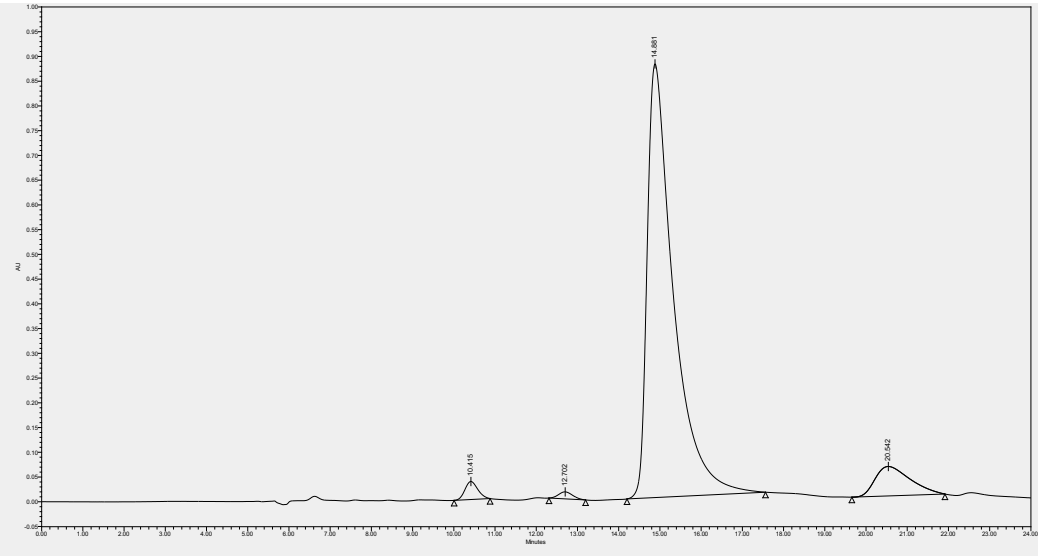
	Name	Retention Time	Area	% Area	Height
1	(*S*)-**13**	15.154	46931083	96.53	1208663
2	(*R*)-**13**	20.180	1686989	3.47	37670

HPLC analysis of **14**



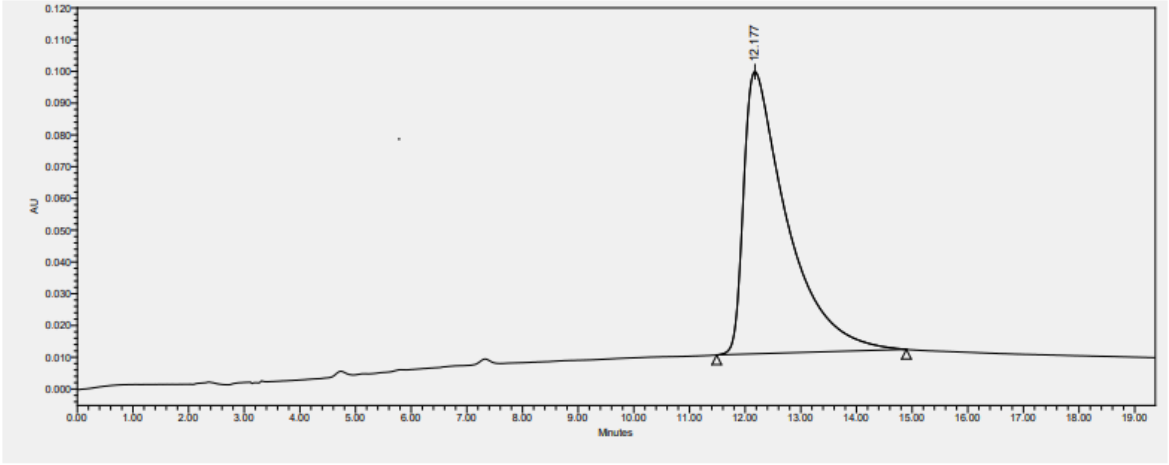
	Name	Retention Time	Area	% Area	Height
1	(*S*)-**14**	13.514	48584532	100.00	1430659
2	(*R*)-**14**				

HPLC analysis of **15**



	Name	Retention Time	Area	% Area	Height
1	(*S*)-**15**	14.881	38735680	89.30	876517
2	(*R*)-**15**	20.542	3518290	8.11	59553

HPLC analysis of **16**

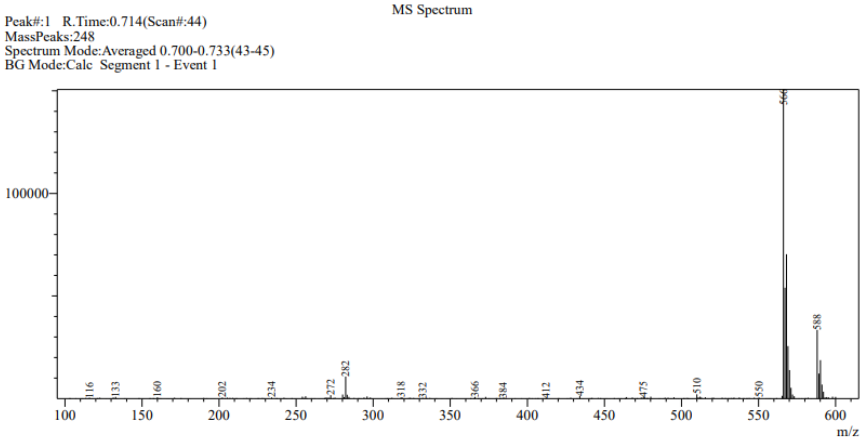


	Name	Retention Time	Area	% Area	Height
1	(*S*)-**16**	12.177	4807855	100.00	88828
2	(*R*)-**16**				

MS spectra

LC-MS: Compounds were analyzed using a Prominence I LC-2030C 3D Plus (Shimadzu Corporation, Kyoto, Japan) LC system connected to a simple quadrupole MS system (LC-MS-2020, Shimadzu Corporation, Kyoto, Japan) equipped with electrospray ionization (ESI) source. The mobile phase contained 0.1 % formic acid in water and 0.1 % formic acid in methanol (20/80 v/v) at a flow rate of 0.2 mL/min. The mass spectrometer was operated in the positive electrospray ionization mode. The interface settings were as follows. Nebulizing-gas flow rate: 1.5 L/min; drying-gas flow rate: 15.0 L/min; interface temperature: 350 °C; heat block temperature: 200 °C, DL temperature: 250 °C. All the peak analyses for the LC-MS were performed using LabSolutions ver. 5.99 SP2 (Shimadzu, Japan).

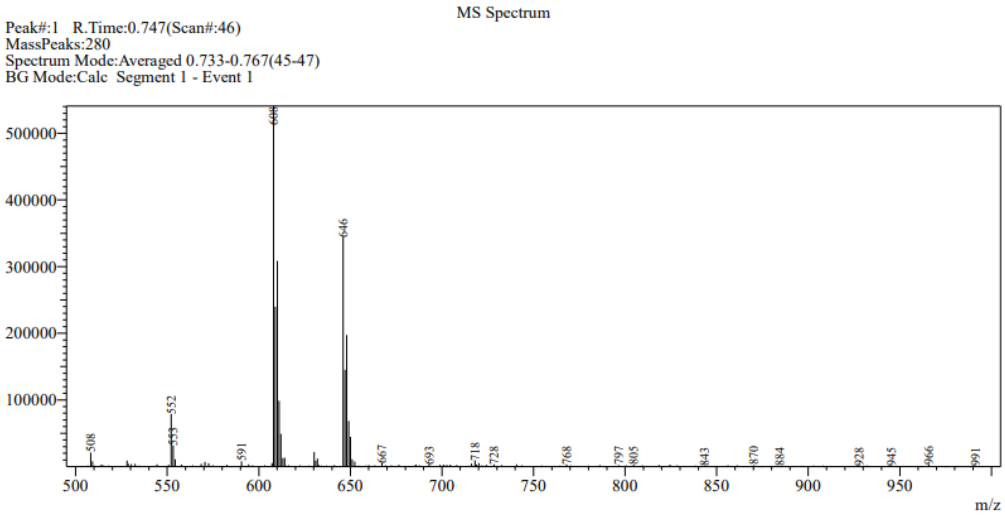
Complex 3a



MASS Peak Table TIC

Peak#	Ret. Time	Area	Base Peak m/z
1	0.714	6401659	566.15
Total		6401659	

Complex 3c



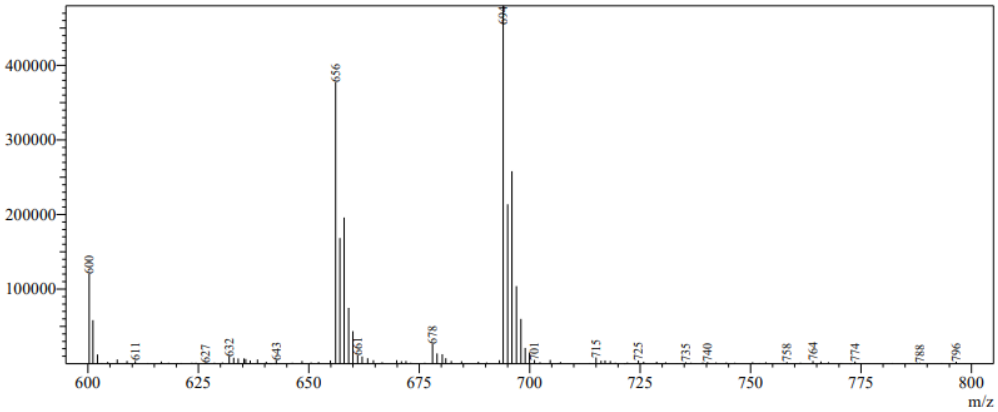
MASS Peak Table TIC

Peak#	Ret. Time	Area	Base Peak m/z
1	0.747	58677846	608.10
Total		58677846	

Complex 3d

MS Spectrum

Peak#:1 R.Time:0.750(Scan#:46)
MassPeaks:130
Spectrum Mode:Averaged 0.733-0.767(45-47)
BG Mode:Calc Segment 1 - Event 1



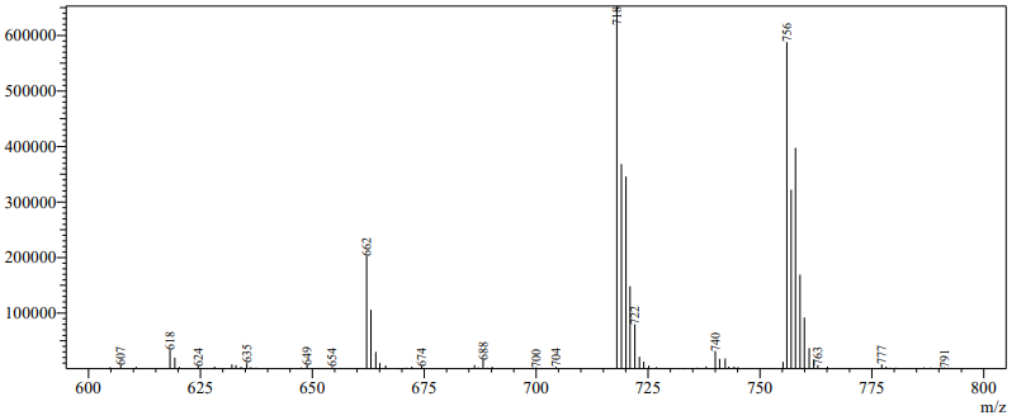
MASS Peak Table TIC

Peak#	Ret. Time	Area	Base Peak m/z
1	0.750	65568332	694.00
Total		65568332	

Complex 3e

MS Spectrum

Peak#:1 R.Time:0.755(Scan#:46)
MassPeaks:123
Spectrum Mode:Averaged 0.733-0.767(45-47)
BG Mode:Calc Segment 1 - Event 1



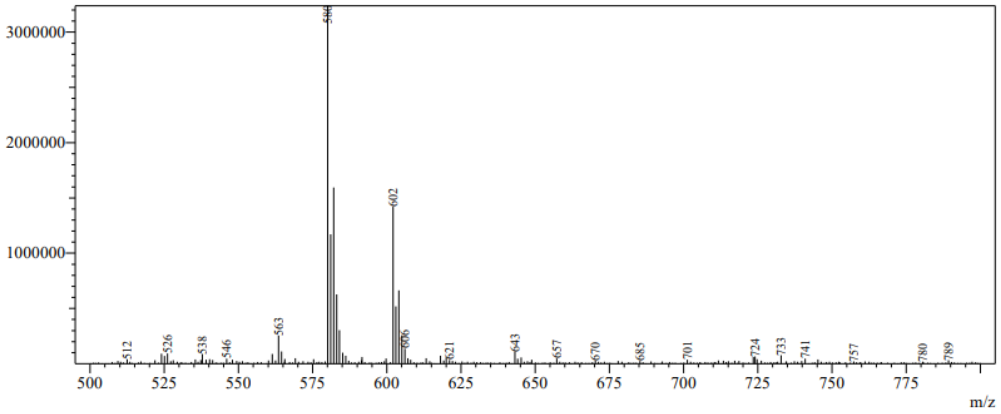
MASS Peak Table TIC

Peak#	Ret. Time	Area	Base Peak m/z
1	0.755	107364113	718.05
Total		107364113	

Complex 4a

MS Spectrum

Peak#:1 R.Time:0.765(Scan#:47)
MassPeaks:301
Spectrum Mode:Averaged 0.750-0.783(46-48)
BG Mode:Calc Segment 1 - Event 1



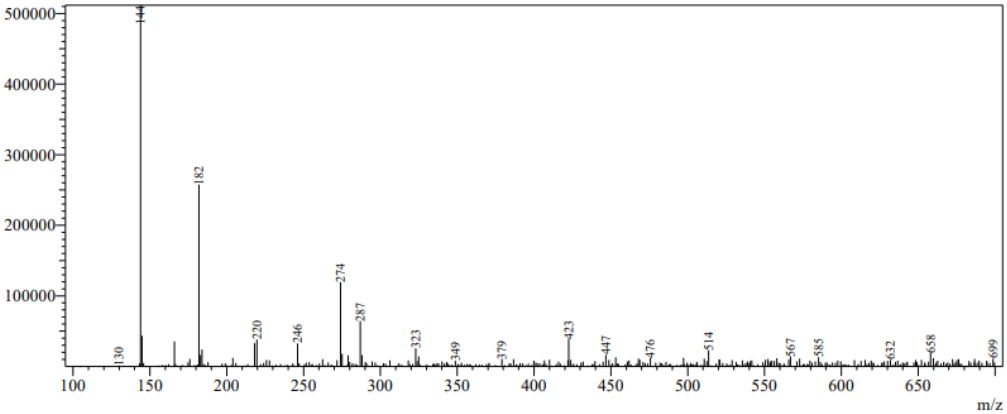
MASS Peak Table TIC

Peak#	Ret. Time	Area	Base Peak m/z
1	0.765	351196910	580.10
Total		351196910	

(S)-2-amino-3-(O-propargyl)propionic acid, 5a.

MS Spectrum

Peak#:1 R.Time:0.750(Scan#:46)
MassPeaks:439
Spectrum Mode:Averaged 0.733-0.767(45-47)
BG Mode:Calc Segment 1 - Event 1



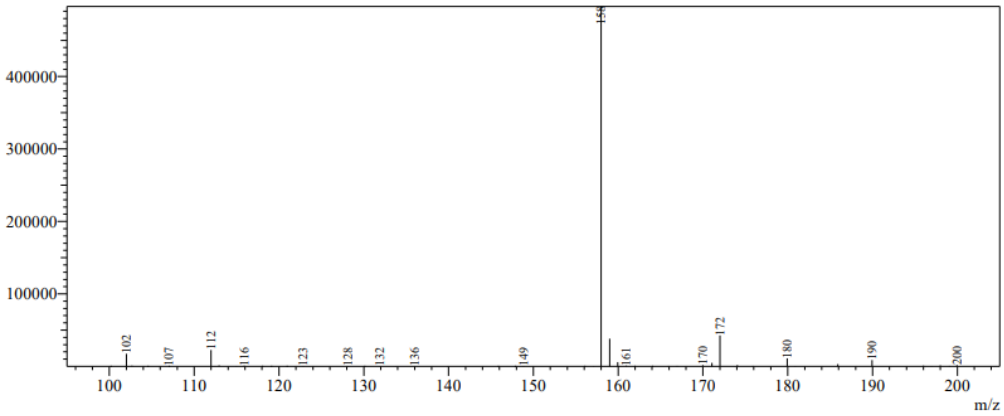
MASS Peak Table TIC

Peak#	Ret. Time	Area	Base Peak m/z
1	0.750	51607782	143.90
Total		51607782	

(2*S*,3*S*)-2-amino-3-(O-propargyl)butanoic acid, 6a

MS Spectrum

Peak#:1 R.Time:0.758(Scan#:92)
MassPeaks:46
Spectrum Mode:Averaged 0.750-0.767(91-93)
BG Mode:Calc Segment 1 - Event 1



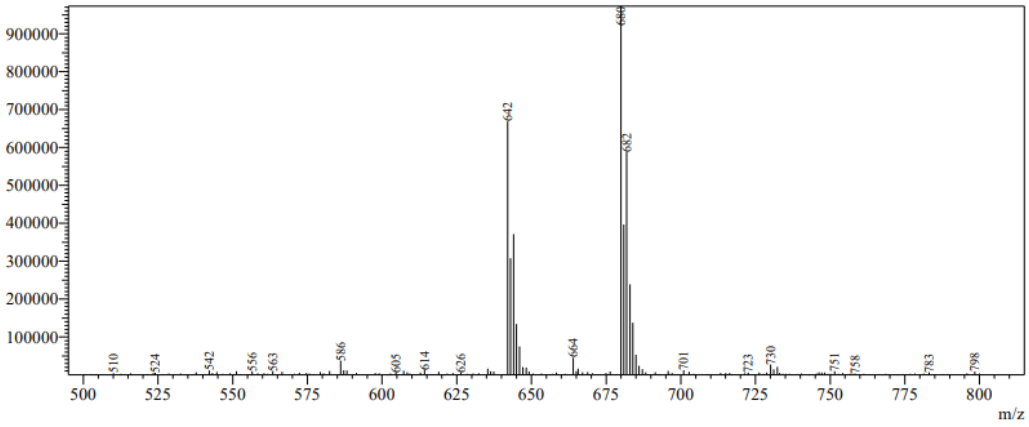
MASS Peak Table TIC

Peak#	Ret. Time	Area	Base Peak m/z
1	0.758	10531747	158.00
Total		10531747	

Complex 7

MS Spectrum

Peak#:1 R.Time:0.735(Scan#:45)
MassPeaks:195
Spectrum Mode:Averaged 0.717-0.750(44-46)
BG Mode:Calc Segment 1 - Event 1



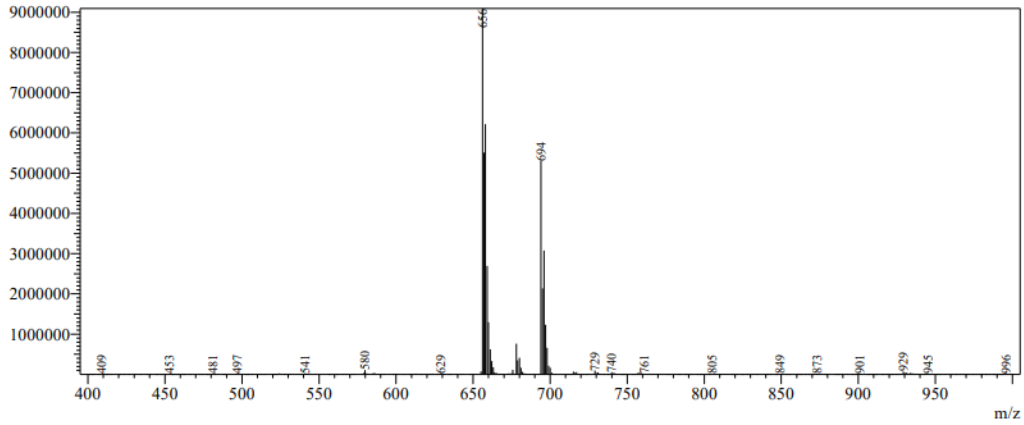
MASS Peak Table TIC

Peak#	Ret. Time	Area	Base Peak m/z
1	0.735	111188434	679.95
Total		111188434	

Complex 8

MS Spectrum

Peak#:1 R.Time:0.834(Scan#:51)
MassPeaks:394
Spectrum Mode:Averaged 0.817-0.850(50-52)
BG Mode:Calc Segment 1 - Event 1



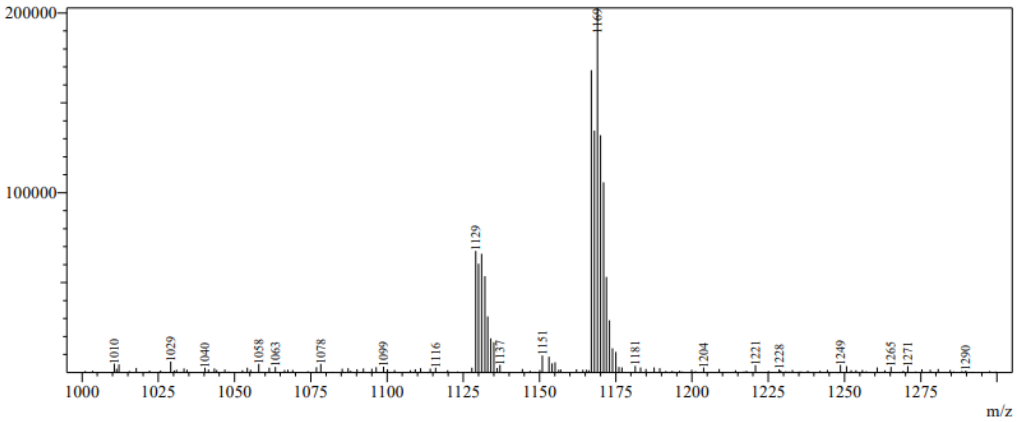
MASS Peak Table TIC

Peak#	Ret. Time	Area	Base Peak m/z
1	0.834	1880388197	656.05
Total		1880388197	

Complex 9

MS Spectrum

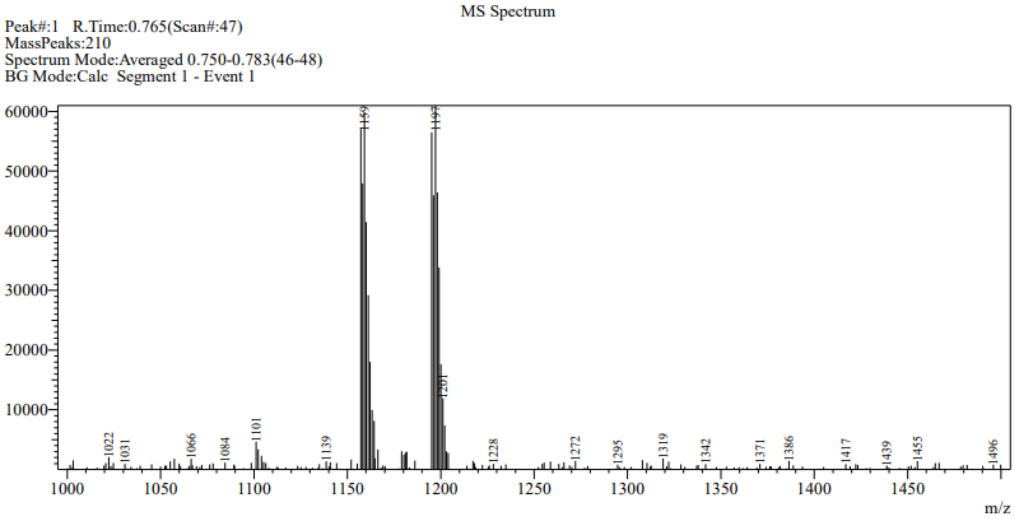
Peak#:1 R.Time:0.739(Scan#:45)
MassPeaks:160
Spectrum Mode:Averaged 0.717-0.750(44-46)
BG Mode:Calc Segment 1 - Event 1



MASS Peak Table TIC

Peak#	Ret. Time	Area	Base Peak m/z
1	0.739	29868945	1169.00
Total		29868945	

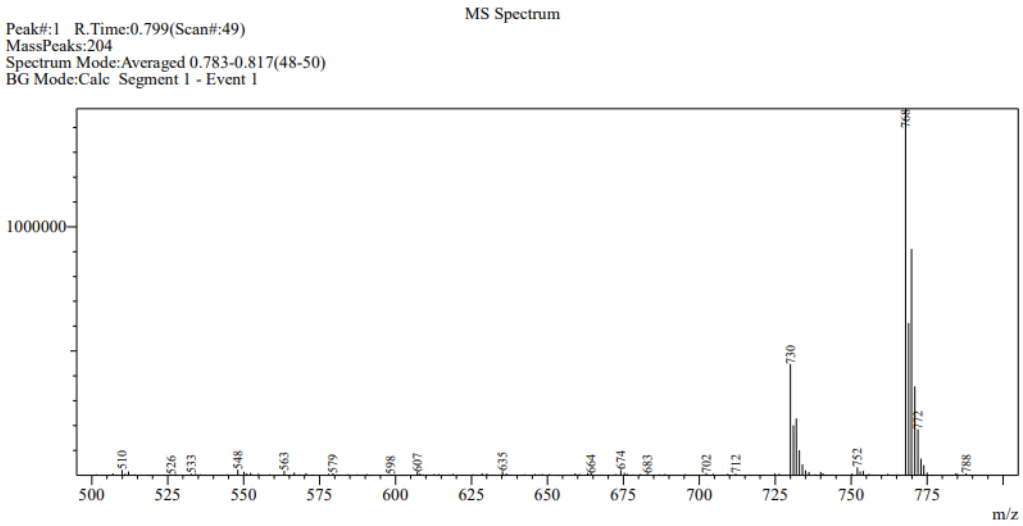
Complex 10



MASS Peak Table TIC

Peak#	Ret. Time	Area	Base Peak m/z
1	0.765	12720011	1197.15
Total		12720011	

Complex11



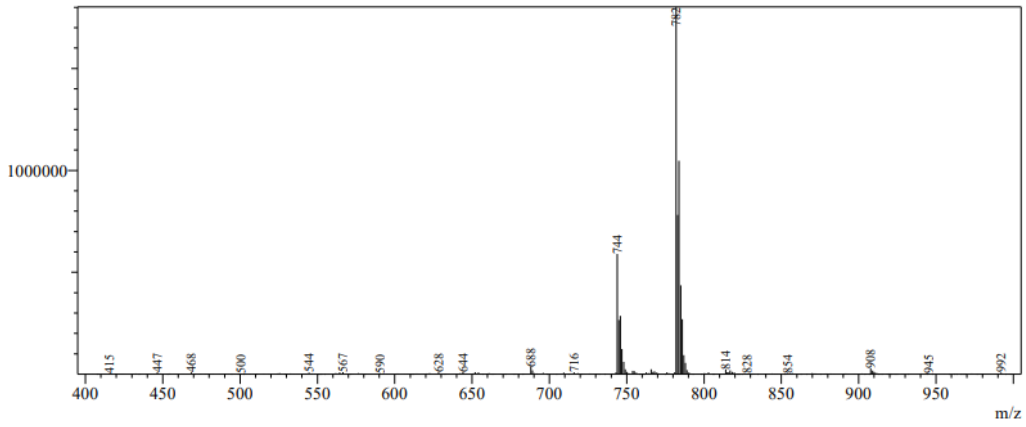
MASS Peak Table TIC

Peak#	Ret. Time	Area	Base Peak m/z
1	0.799	130998021	767.95
Total		130998021	

Complex 12

MS Spectrum

Peak#:1 R.Time:0.802(Scan#:49)
MassPeaks:340
Spectrum Mode:Averaged 0.783-0.817(48-50)
BG Mode:Calc Segment 1 - Event 1



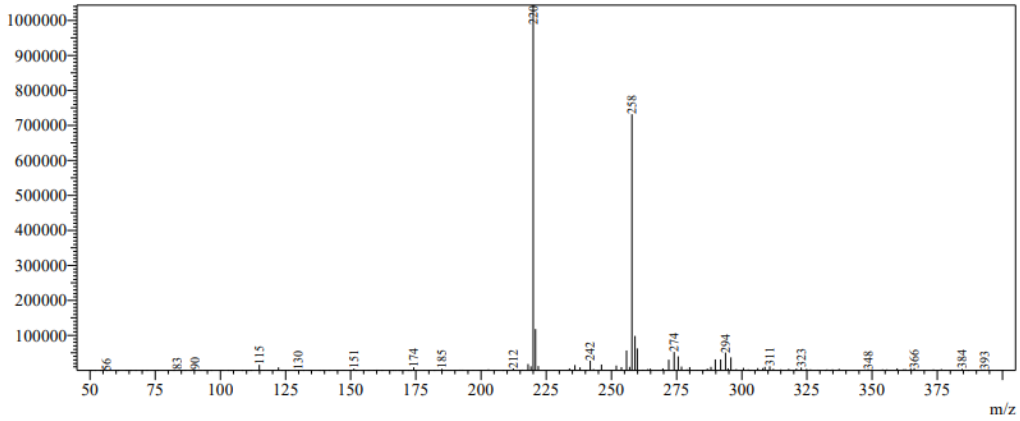
MASS Peak Table TIC

Peak#	Ret. Time	Area	Base Peak m/z
1	0.802	160489526	781.90
Total		160489526	

(S)-2-amino-3-((3-phenylprop-2-yn-1-yl)oxy)propanoic acid 13

MS Spectrum

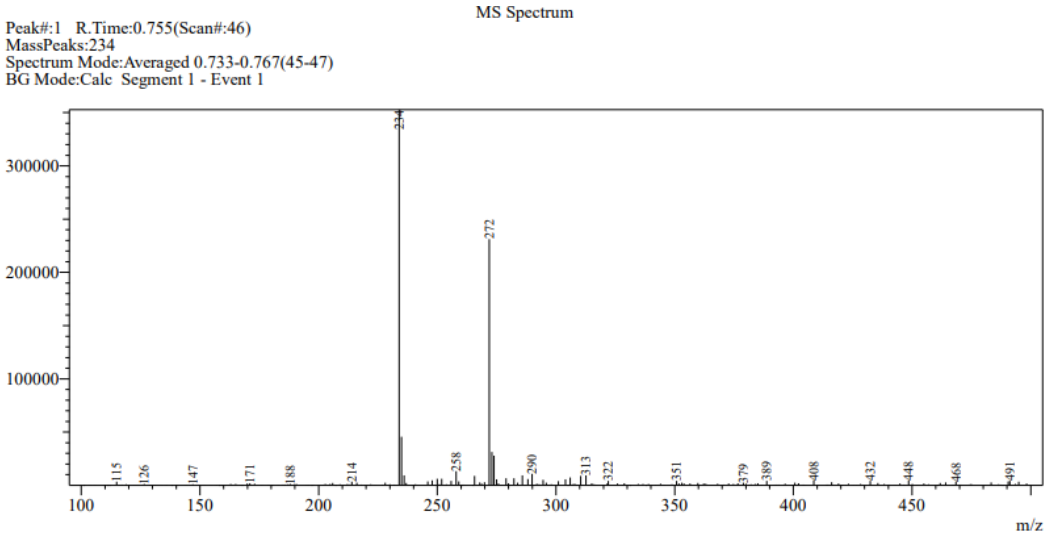
Peak#:1 R.Time:0.734(Scan#:45)
MassPeaks:214
Spectrum Mode:Averaged 0.717-0.750(44-46)
BG Mode:Calc Segment 1 - Event 1



MASS Peak Table TIC

Peak#	Ret. Time	Area	Base Peak m/z
1	0.734	58125051	219.95
Total		58125051	

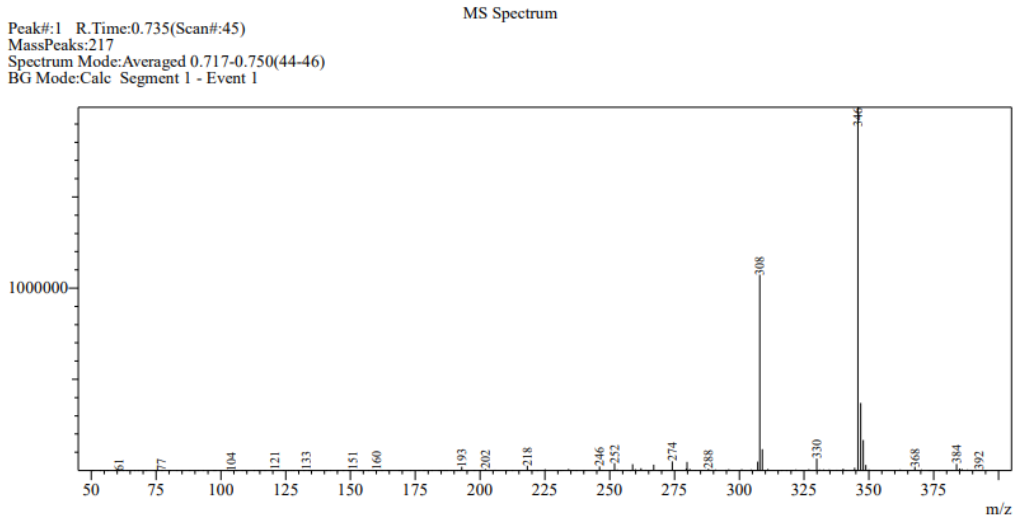
(S)-2-amino-3-((3-phenylprop-2-yn-1-yl)oxy)butanoic acid 14



MASS Peak Table TIC

Peak#	Ret. Time	Area	Base Peak m/z
1	0.755	17594209	233.95
Total		17594209	

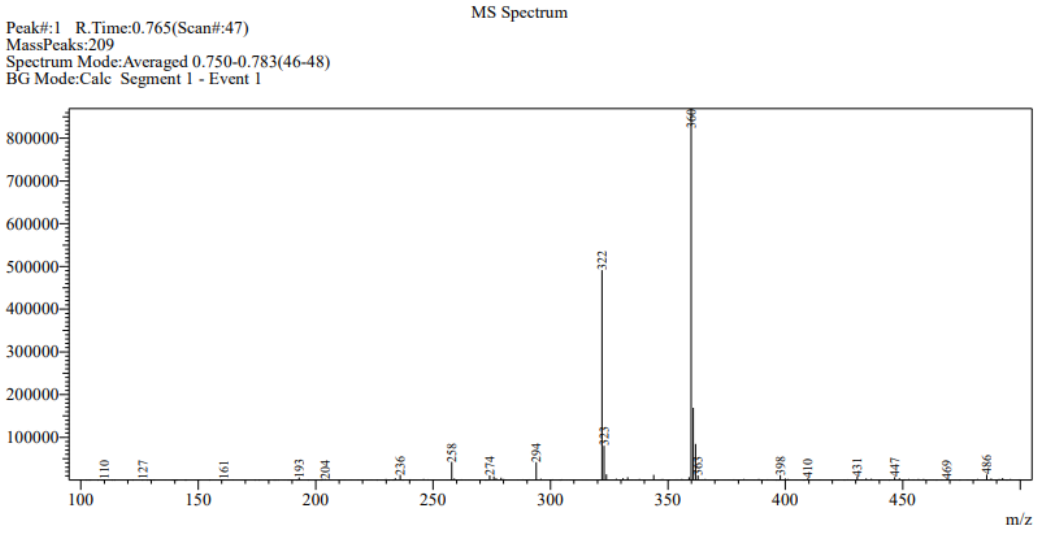
(S)-2-amino-3-((1-(2-nitrophenyl)-1H-1,2,3-triazol-4-yl)methoxy)propanoic acid15



MASS Peak Table TIC

Peak#	Ret. Time	Area	Base Peak m/z
1	0.735	107483483	345.80
Total		107483483	

(S)-2-amino-3-((1-(2-nitrophenyl)-1H-1,2,3-triazol-4-yl)methoxy)butanoic acid 16



MASS Peak Table TIC

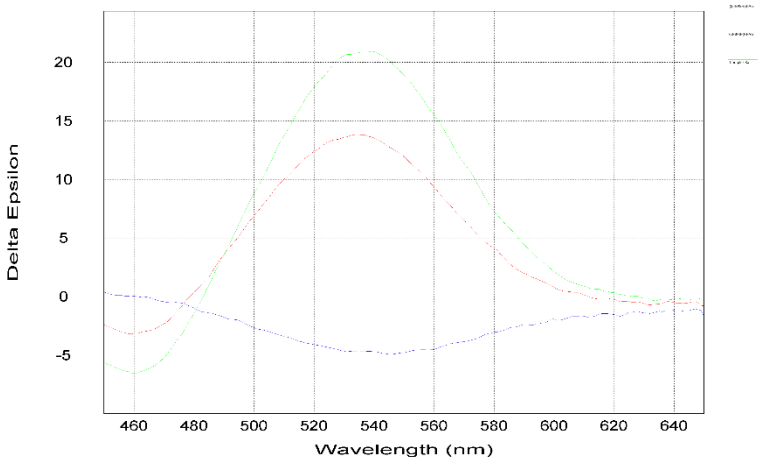
Peak#	Ret. Time	Area	Base Peak m/z
1	0.765	45092673	359.85
Total		45092673	

Circular Dichroism

The CD analyzes was performed on Chirascan™ V100. As a standard, CD curves of (*S*,*S*)- and (*S*,*R*)-diastereomers were produced using the (*S*,*R*)-diastereomer of the alanine complex as the initial alkyne substrate, following a similar procedure[i,ii].

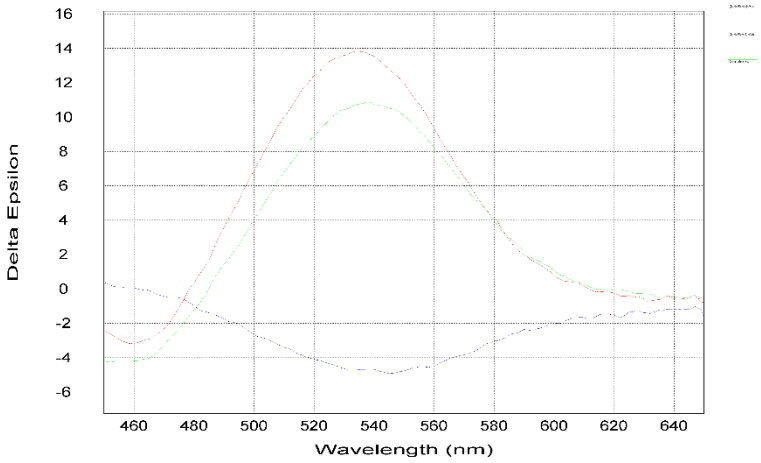
Complex 3a

C:0.2mg/ml. $\Delta\varepsilon_{max}(\lambda_{max})$: -6.56 (461); +20.92(539).



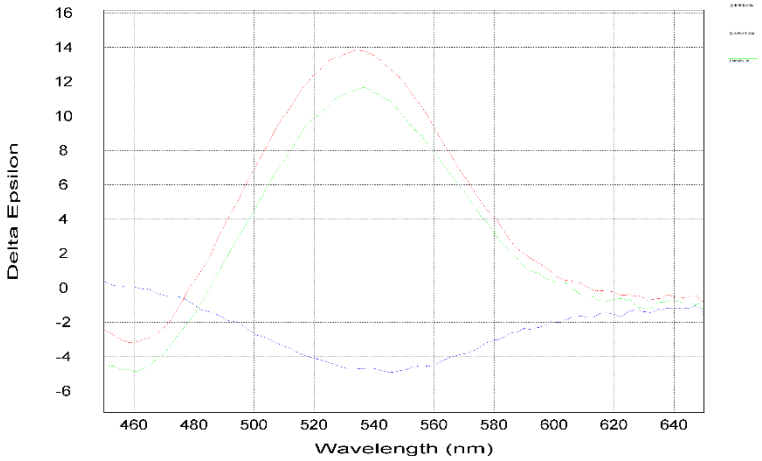
Complex 3c

C:0.2mg/ml. $\Delta\varepsilon_{max}(\lambda_{max})$: -6.56 (461); +10.87 (538).



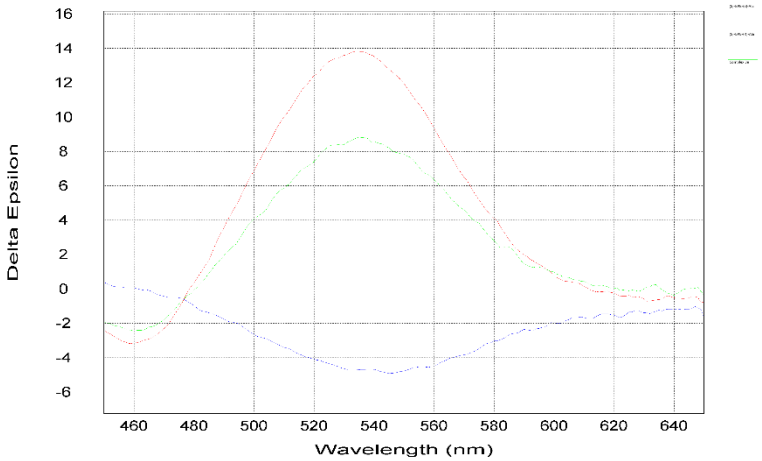
Complex 3d

C:0.2mg/ml. $\Delta\varepsilon_{max}(\lambda_{max})$: -4.87 (460); +11.66 (537).



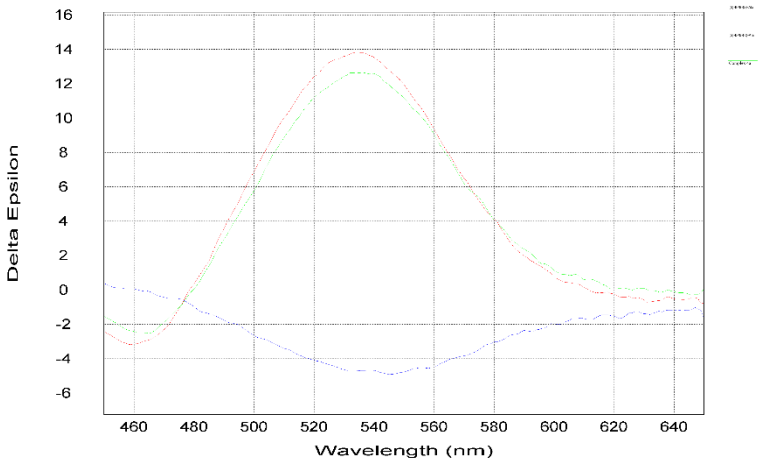
Complex 3e

C:0.2mg/ml. $\Delta\varepsilon_{max}(\lambda_{max})$: -2.44 (460);+8.81 (535).



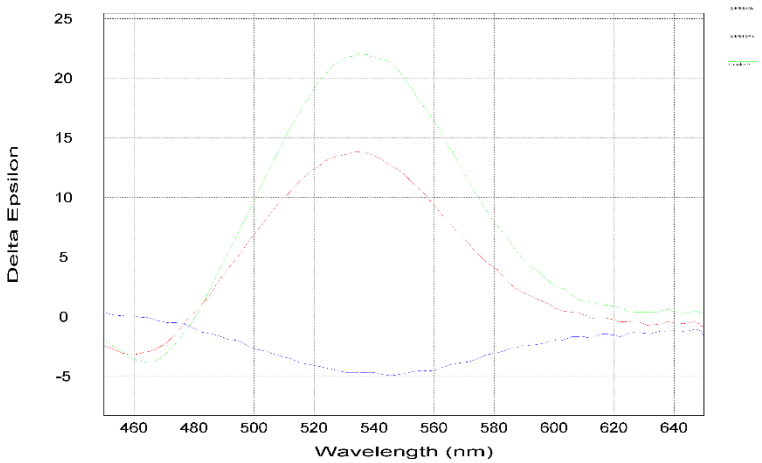
Complex 4a

C:0.2mg/ml. $\Delta\varepsilon_{max}(\lambda_{max})$: -1.60 (465); +7.94 (537).



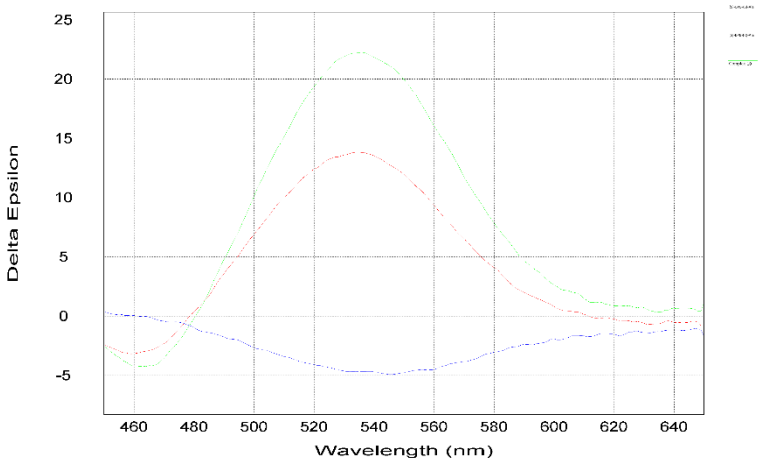
Complex 7

C:0.2mg/ml. $\Delta\varepsilon_{max}(\lambda_{max})$: -3.85 (466); +22.08 (536).



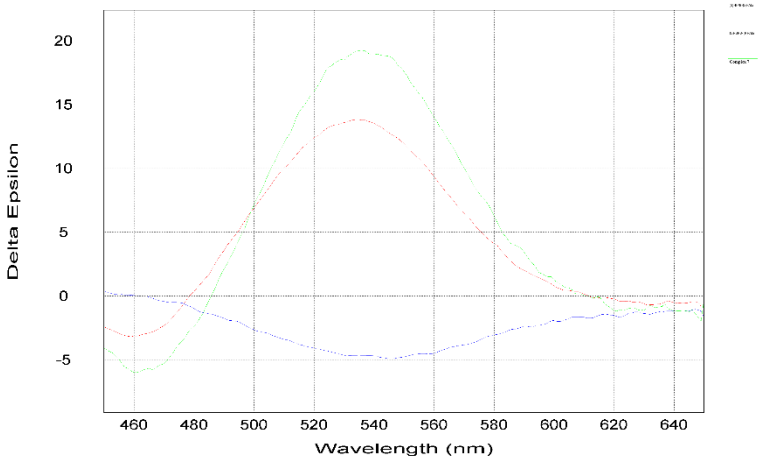
Complex 8

C:0.2mg/ml. $\Delta\varepsilon_{max}(\lambda_{max})$: -4.25 (464); +22.23 (536).



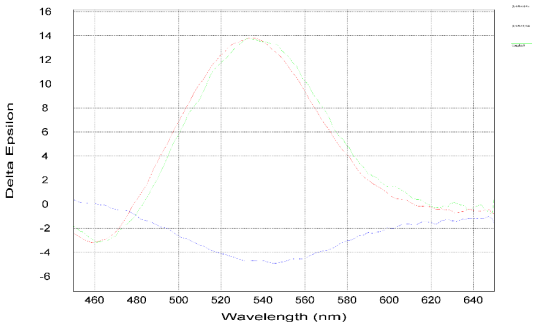
Complex 9

C:0.2mg/ml. $\Delta\varepsilon_{max}(\lambda_{max})$: -5.99 (461); +19.23 (536).



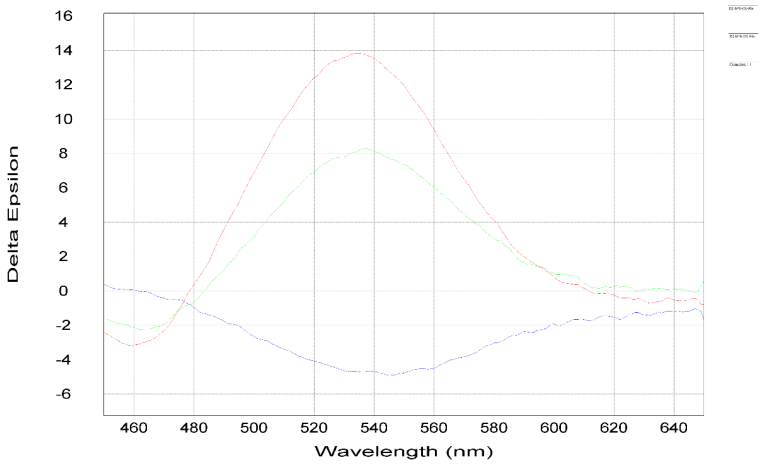
Complex 10

C:0.2mg/ml. $\Delta\varepsilon_{max}(\lambda_{max})$: -3.19 (461); +13.75 (534).



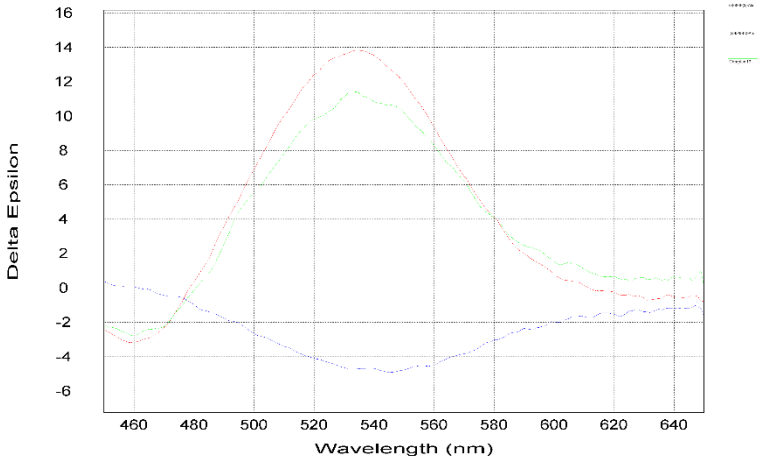
Complex11

C:0.2mg/ml. $\Delta\varepsilon_{max}(\lambda_{max})$: -2.25 (462); +8.29 (537).



Complex 12

C:0.2mg/ml. $\Delta\varepsilon_{max}(\lambda_{max})$: -2.76 (459); +11.41 (533).

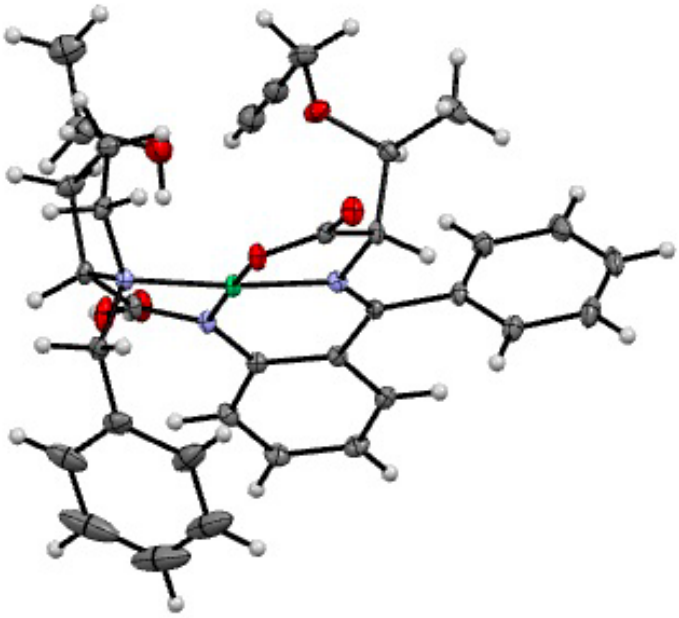


X-ray 4a

The diffraction measurements of crystal of compound **4a** were carried out at a temperature of 100K on a XtaLAB Synergy-S diffractometer using Mo-Kα radiation, ω-scans rotation. A multi-scan absorption correction for all samples was performed using CrysAlisPro 1.171.43.92a (Rigaku Oxford Diffraction, 2023) using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm. The structures were solved by direct method and refined using the software package SHELXTL[iii]. All hydrogen atoms were positioned geometrically and refined using riding model. All non-hydrogen atoms were refined anisotropically by full-matrix least squares methods. Crystallographic and experimental data are listed in Table 1. The full crystallographic data in CIF format are available at: https://www.ccdc.cam.ac.uk/structures/? (free of charge), deposition number is CCDC 2395037.

Table 1. Crystallographic and experimental data

Crystal Data	
Compound	**4a**
Formula	$C_{32}H_{31}N_3O_4Ni$, C_2H_6O, H_2O
Formula Weight	644.39
Crystal System	monoclinic
Space group	$P2_1$
a, b, c [Å]	9.4105(1), 11.8727(1), 14.0699(2)
α, β, γ [deg]	90, 95.565(1), 90
V [Å^3]	1564.59(3)
Z	2
D(calc) [g/cm^3]	1.368
μ(MoKα) [mm^{-1}]	0.670
F(000)	680
Crystal Size [mm]	0.42×0.40×0.22
Data Collection	
Temperature (K)	100
Radiation [Å]	MoKα 0.71073
θ_{min}, θ_{max} [Deg]	2.2, 31.1
Dataset	-13≤h≤12; -16≤k≤15; -19≤l≤18
Tot., Uniq. Data, R(int)	46938, 8379, 0.026
Observed data [I > 2.0 σ(I)]	8256
Refinement	
Nref, Npar	8379, 406
R, wR2, S	0.0226, 0.0583, 1.04



[i]Belokon, Y. N., Sagyan, A. S., Djamgaryan, S. A., Bakhmutov, V. I., Vitt, S. V., Batsanov, A. S., Struchkov, Y. T., &Belikov, V. M. (1990). General method for the asymmetric synthesis of anti-diastereoisomers of β-substitutedL-2-aminobutanoic acids via chiral nickel(II) Schiff's base complexes of dehydroaminobutanoic acid. X-Ray crystal and molecular structure of the nickel(II) complex of the Schiff's base from [(benzylprolyl)amino]benzophenone and dehydroaminobutanoic acid. *Journal of the Chemical Society. Perkin Transactions I/Journal of the Chemical Society. Perkin Transactions. I*, *8*, 2301–2310. https://doi.org/10.1039/p19900002301

[ii]Saghyan AS, Langer P. *Asymmetric Synthesis of Non-Proteinogenic Amino Acids*. John Wiley & Sons; 2016.

[iii] G.M. Sheldrick (2015) "Crystal structure refinement with SHELXL", Acta Cryst., C71, 3-8.