

Supporting Information for

**Chemical Dynamic Thermodynamic Resolution and S/R
Interconversion of Unprotected Unnatural Tailor-Made α -Amino
Acids**

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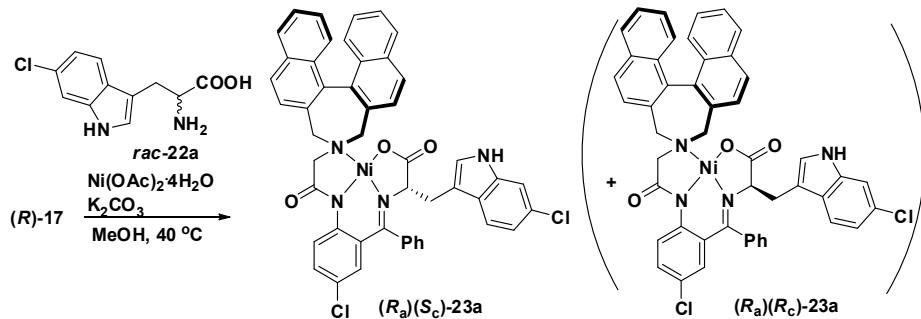
Email: hliu@simm.ac.cn and vadym.soloshonok@ehu.es

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(A) Details of reactions of ligand (*R*)-17 with *rac*-6-Cl-tryptophan 22a; progress and stereochemical outcome over time.

Table S1. Reaction of ligand (*R*)-17 with *rac*-6-Cl-tryptophan 22a; progress and stereochemical outcome over time.



Time (h)	Ratio by HPLC		
	$(R_a,S_c)\text{-}23\text{a}$	$(R_a,R_c)\text{-}23\text{a}$	$(R)\text{-}17$
0.5	30.7527	8.8456	60.4018
1.0	54.2235	11.8130	33.9636
1.5	64.6929	12.0382	23.2689
2.0	74.5682	9.1660	16.2658
4.0	86.8404	4.5592	8.6004
8.0	94.2181	1.0049	4.7770
48.0	97.5975	0.4493	1.9533

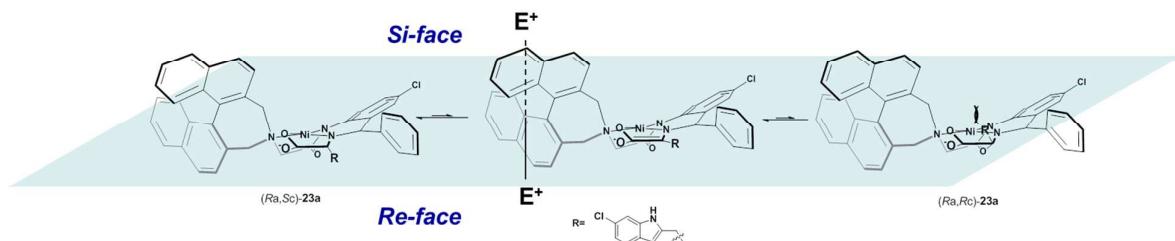
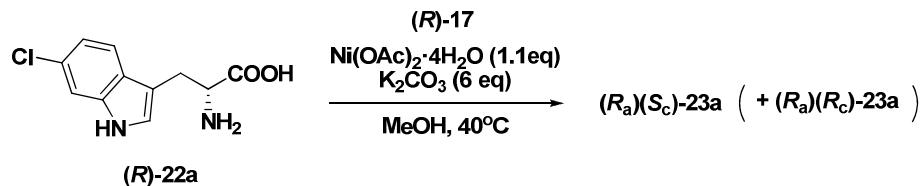


Figure S1. The transformation process between $(R_a,S_c)\text{-}23\text{a}$ and $(R_a,R_c)\text{-}23\text{a}$ via the corresponding intermediate enolate.

(B) Details of reactions of ligand (*R*)-17 with (*R*)-6-Cl-tryptophan 22a; progress and stereochemical outcome over time.

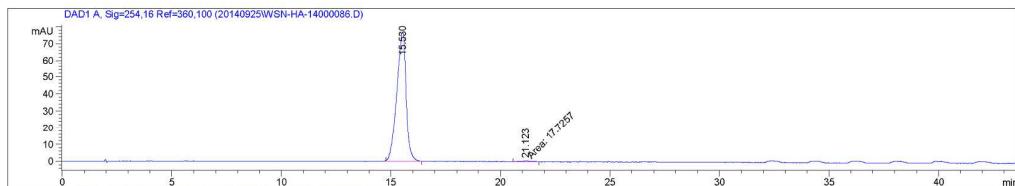
Table S2. Reaction of ligand (*R*)-17 with (*R*)-6-Cl-tryptophan 22a; progress and stereochemical outcome over time.



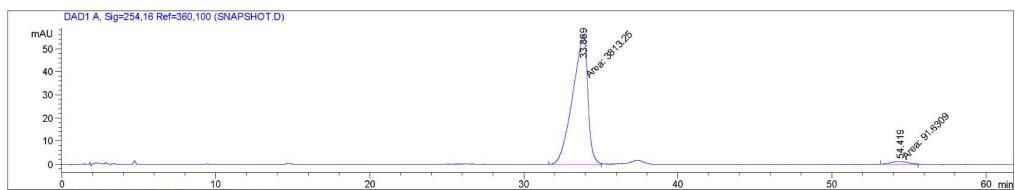
Time (h)	Ratio by HPLC		
	(<i>R_a,S_c</i>)-23a	(<i>R_a,R_c</i>)-23a	(<i>R</i>)-17
0.5	3.6379	23.2229	73.1393
1.0	12.8239	31.1949	55.9812
1.5	20.4547	30.5085	49.0368
2.0	31.1162	26.9836	41.9003
2.5	46.1306	20.9944	32.875
3.0	54.3759	17.315	28.3091
3.5	59.9312	14.9301	25.1387
4.0	68.3273	11.3497	20.323
5.0	74.0484	8.573	17.3786
6.0	76.8959	6.8861	16.218
7.0	82.9946	4.3519	12.653
8.0	88.6183	2.417	8.9648
9.0	89.1251	2.045	8.8299
12.0	92.2041	0.9924	6.8035
24.0	94.5354	0.4237	5.0409
33.0	95.6723	0.3578	3.9699

(C) Determination of the diastereomeric ratio (dr) of specific Ni(II) complexes by LC/MS analysis.

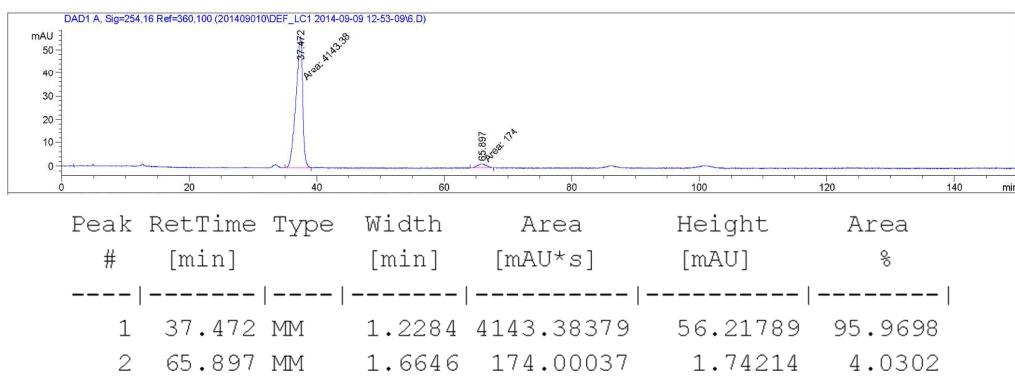
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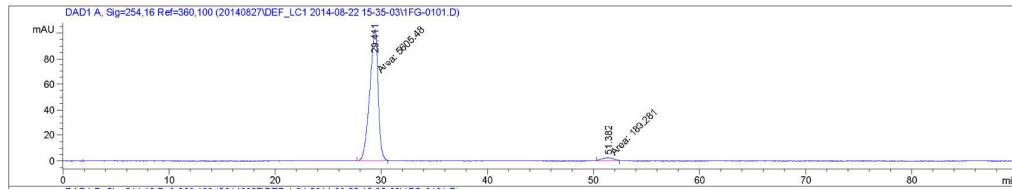
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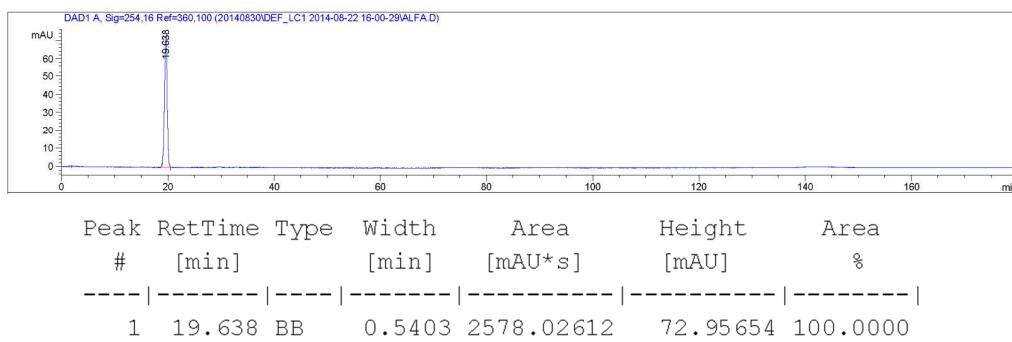
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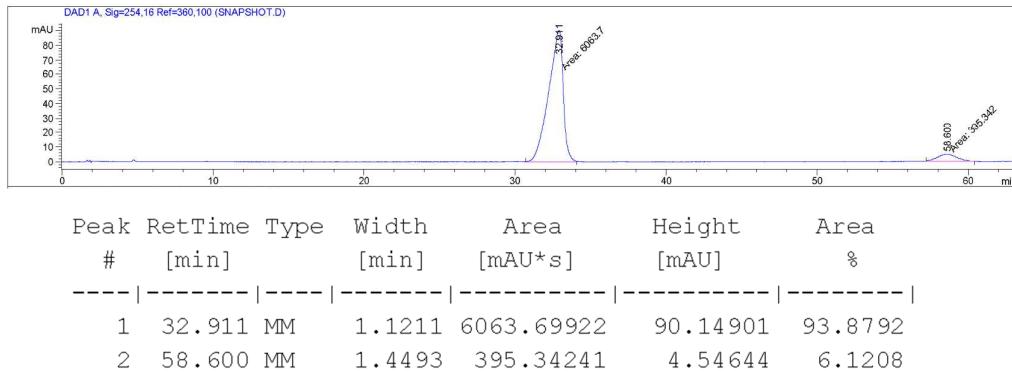
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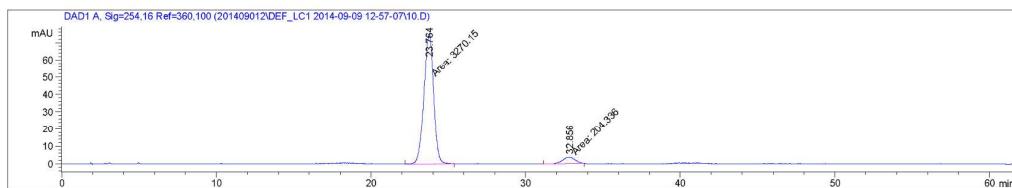
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23f

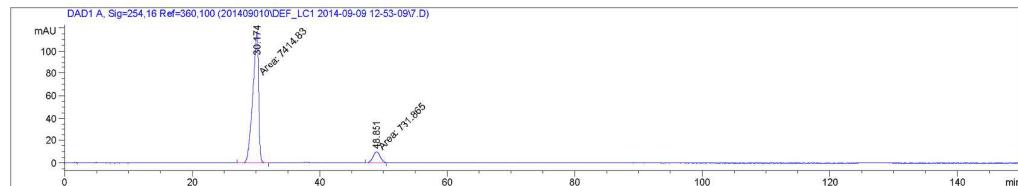


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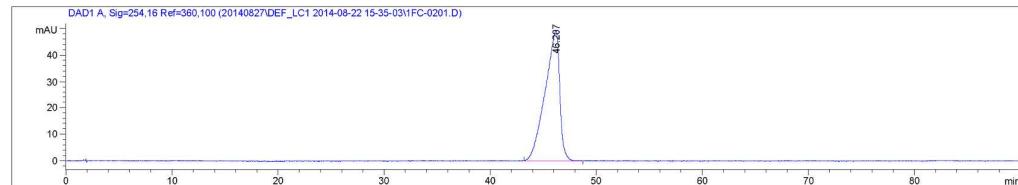
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.764	MM	0.7243	3270.15039	75.25347	94.1190
2	32.856	MM	0.9331	204.33572	3.64960	5.8810

23h



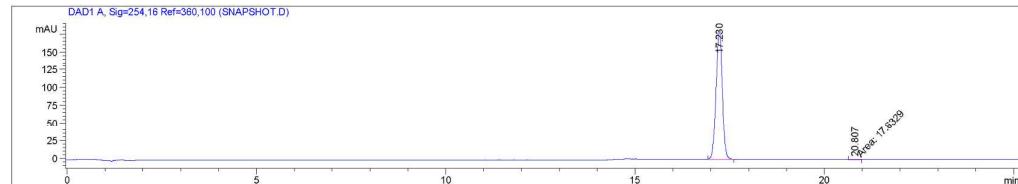
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.174	MM	1.0572	7414.82959	116.89558	91.0164
2	48.851	MM	1.2949	731.86523	9.42018	8.9836

23i



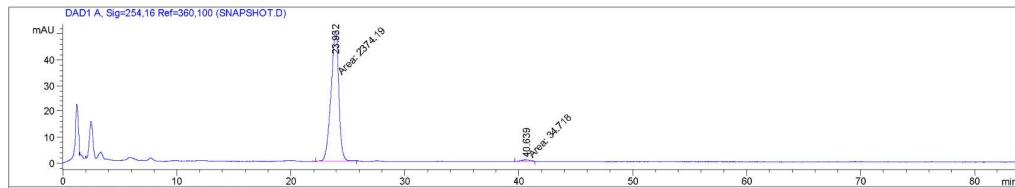
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	46.207	BB	1.2664	4725.81445	49.20817	100.0000

23j



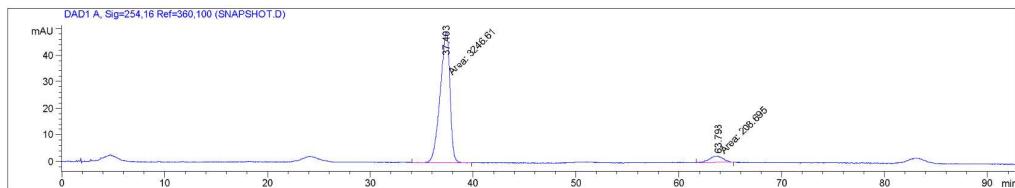
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.230	BB	0.1735	2052.79932	182.13216	99.1483
2	20.807	MM	0.2909	17.63292	1.01017	0.8517

23k



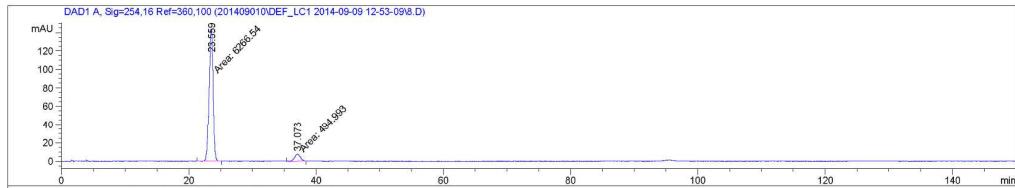
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.932	MM	0.7864	2374.19092	50.31991	98.5588
2	40.639	MM	0.9651	34.71802	5.99537e-1	1.4412

23l



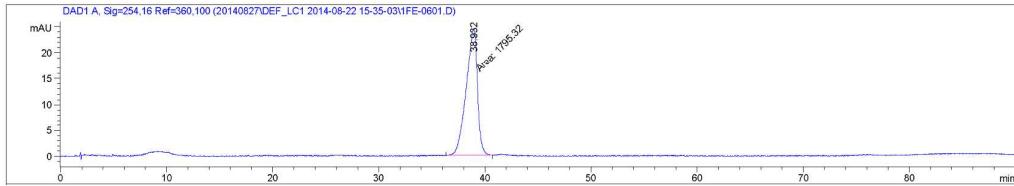
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1	37.403	MM	1.0973	3246.60767	49.31196	93.9602
2	63.798	MM	1.4894	208.69505	2.33535	6.0398

23m



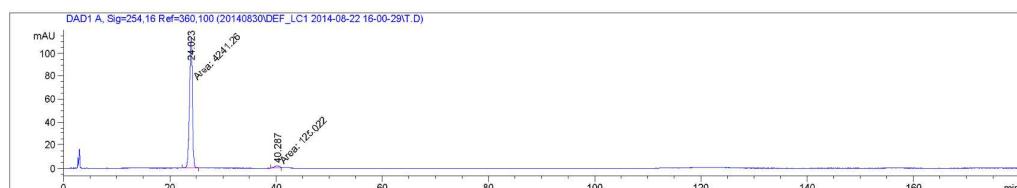
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.559	MM	0.7281	6266.54297	143.43860	92.6793
2	37.073	MM	1.0911	494.99252	7.56138	7.3207

23n



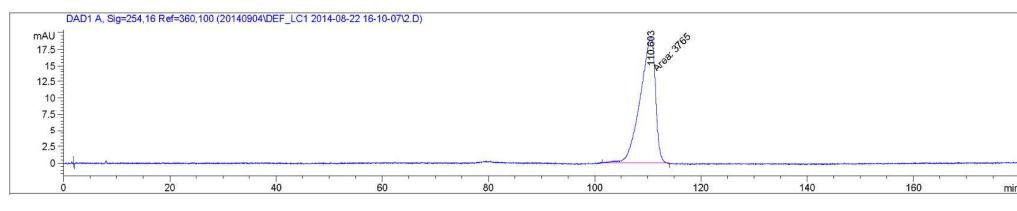
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	38.932	MM	1.2281	1795.31738	24.36415	100.0000

23o



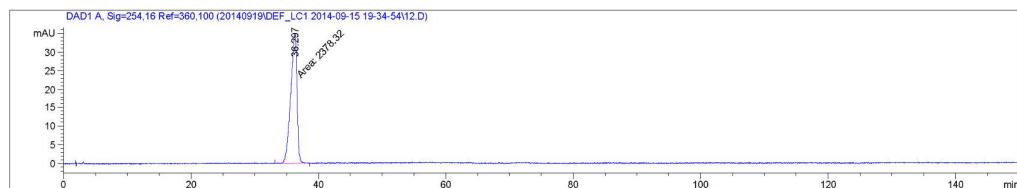
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.023	MM	0.6216	4241.26172	113.72540	97.1366
2	40.287	MM	1.1851	125.02213	1.75831	2.8634

23p



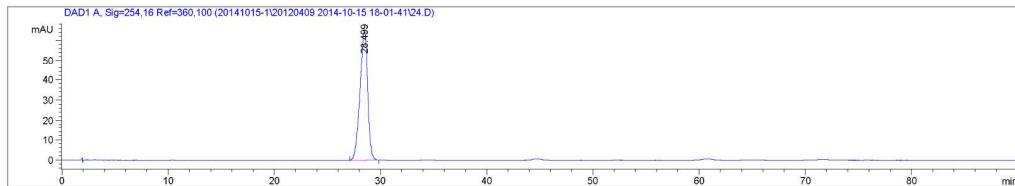
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	110.603	MM	3.2583	3765.00244	19.25861	100.0000

23q

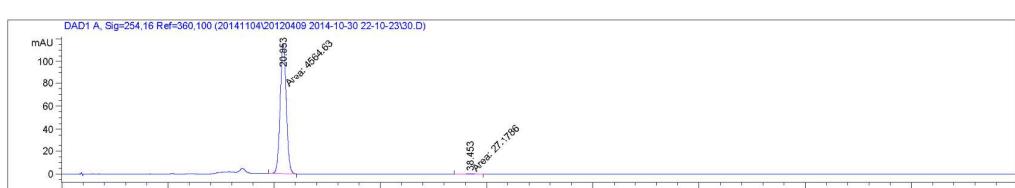


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	36.297	MM	1.1400	2378.32397	34.77060	100.0000

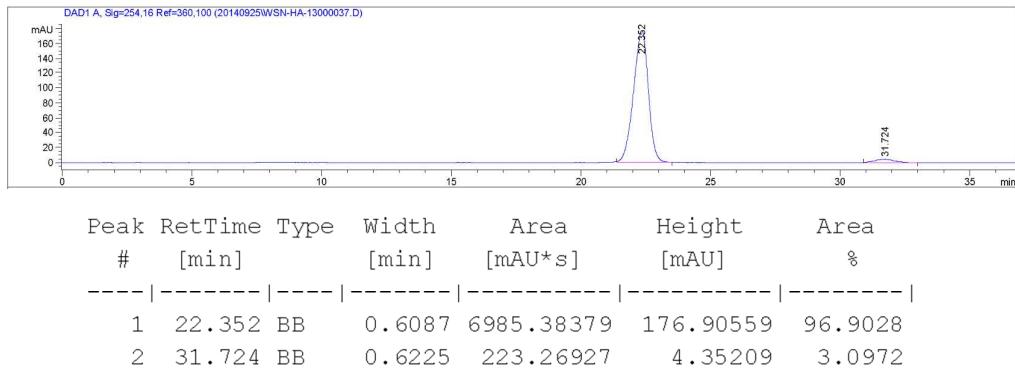
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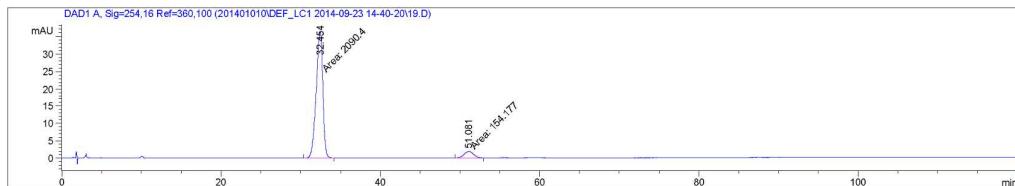
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23t

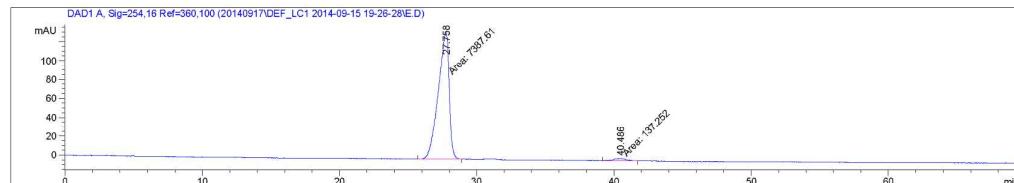


23u



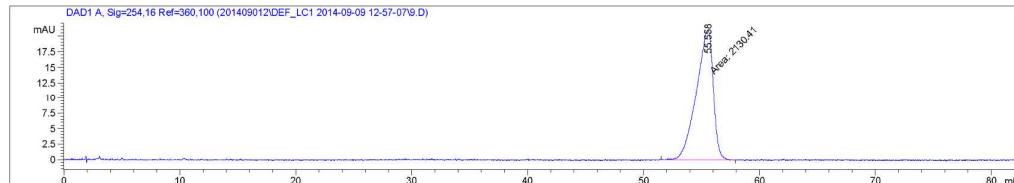
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1	32.454	MM	0.9608	2090.40112	36.25967	93.1311
2	51.081	MM	1.3658	154.17676	1.88134	6.8689

23v



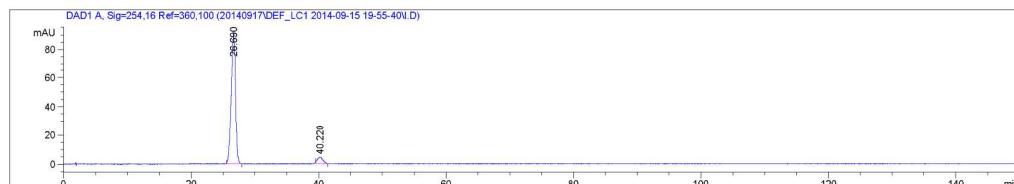
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.758	MM	0.9121	7387.61133	134.98888	98.1760
2	40.486	MM	1.0287	137.25177	2.22379	1.8240

23w



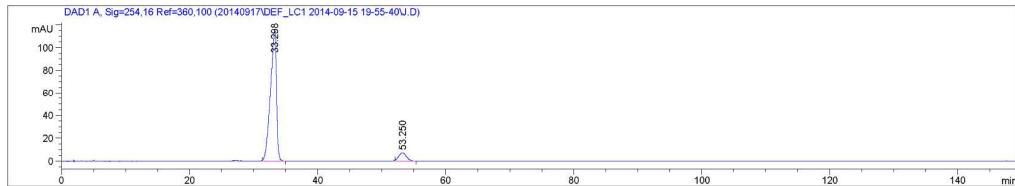
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	55.558	MM	1.6900	2130.40527	21.00991	100.0000

23x

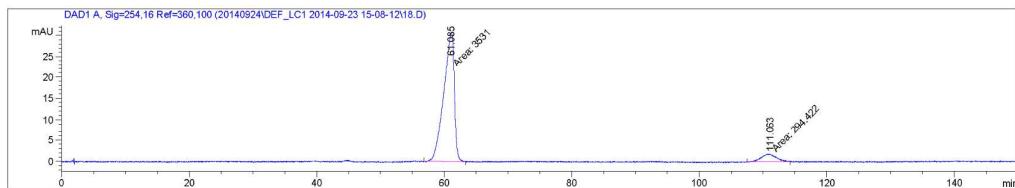


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.690	BB	0.6945	4236.40967	90.76275	94.2364
2	40.220	BB	0.6982	259.10394	4.36716	5.7636

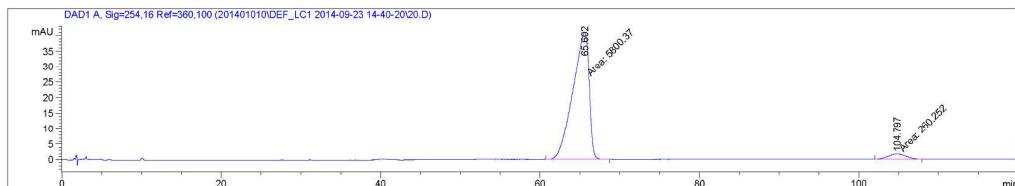
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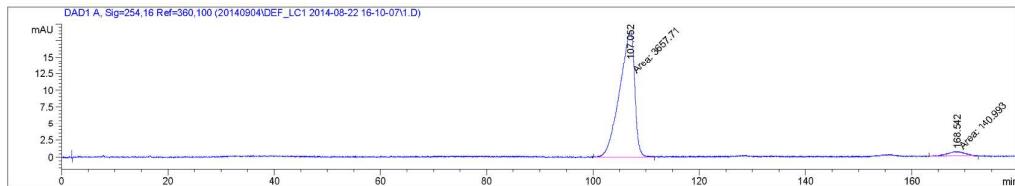
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23aa

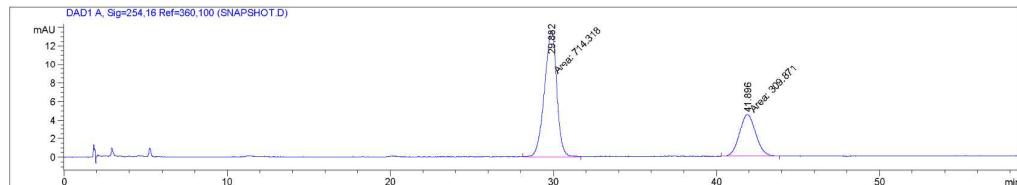


23bb



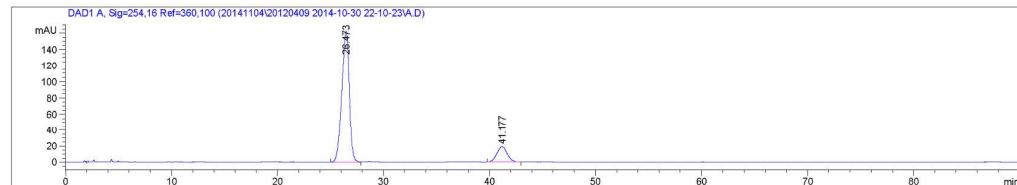
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1	107.052	MM	3.2193	3657.70752	18.93632	96.2884
2	168.542	MM	3.5636	140.99297	6.59411e-1	3.7116

23cc



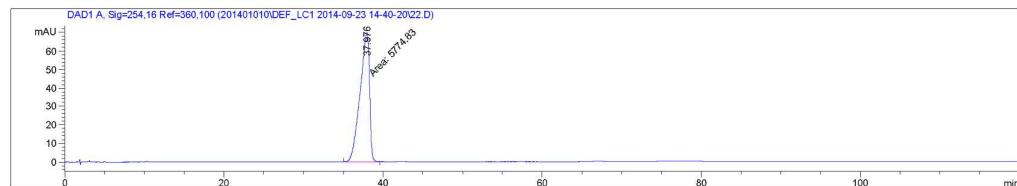
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1	29.882	MM	0.8737	714.31793	13.62668	69.7447
2	41.896	MM	1.1468	309.87115	4.50357	30.2553

23dd



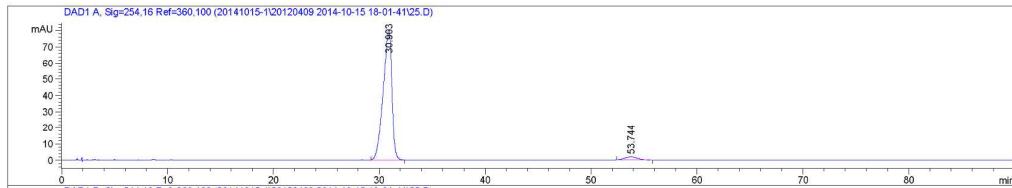
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1	26.473	BB	0.7558	7965.83203	162.52586	86.3204
2	41.177	BB	1.0194	1262.38269	18.89685	13.6796

23ee

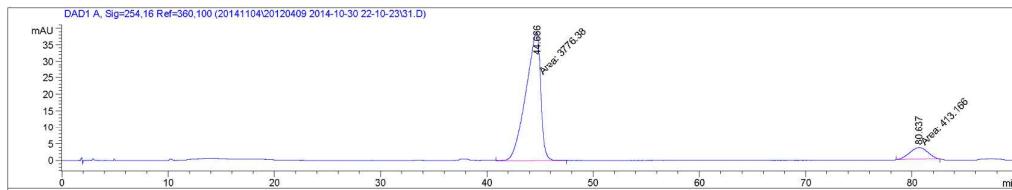


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	37.976	MM	1.3776	5774.83057	69.86739	100.0000

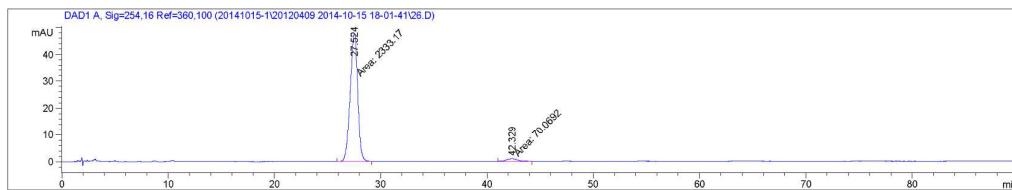
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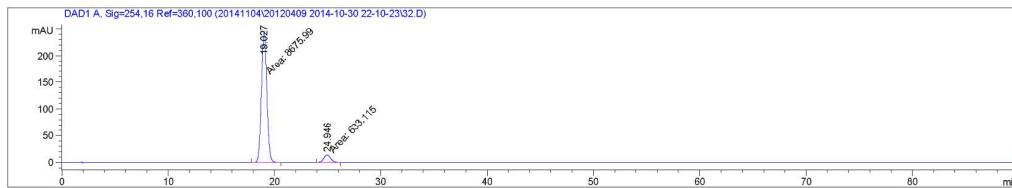
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23hh



23ii

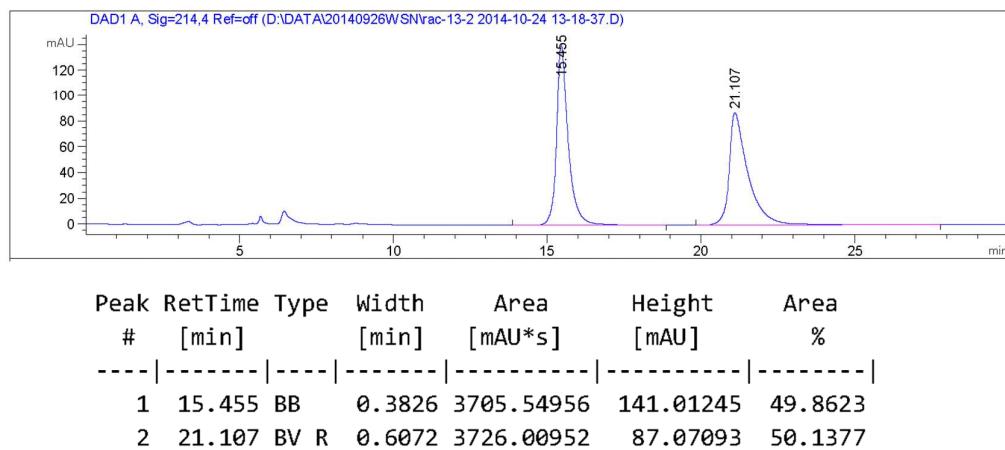


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.027	MM	0.5881	8675.98828	245.86617	93.1990
2	24.946	MM	0.7601	633.11469	13.88181	6.8010

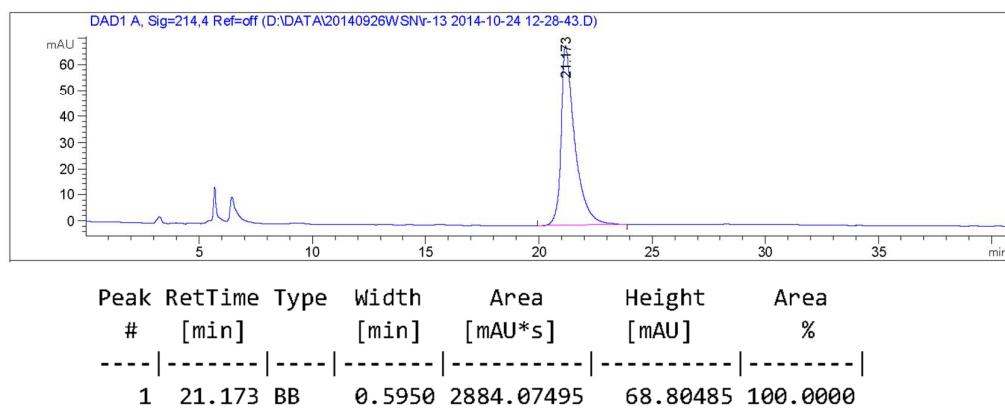
(D) Determination of the enantiomeric excess (ee) of specific chiral amino acids or Cbz-derivatives by HPLC or UFLC analysis.

Racemic amino acids and racemic Cbz-derivatives were purchased and measured for RetTime as contrast to determinate the ee value of corresponding chiral amino acids hydrolyzed from Ni(II) complexes.

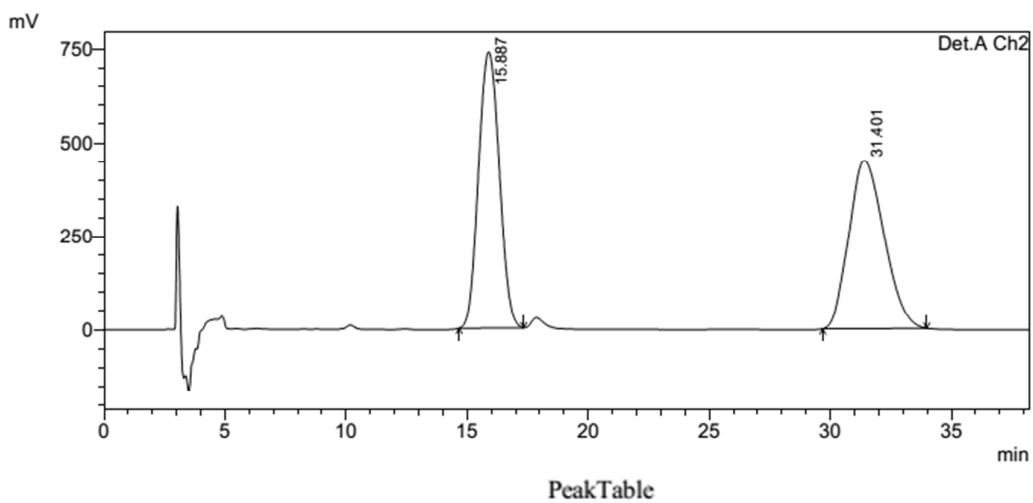
Rac-4-Chlorophenylalanine 22j



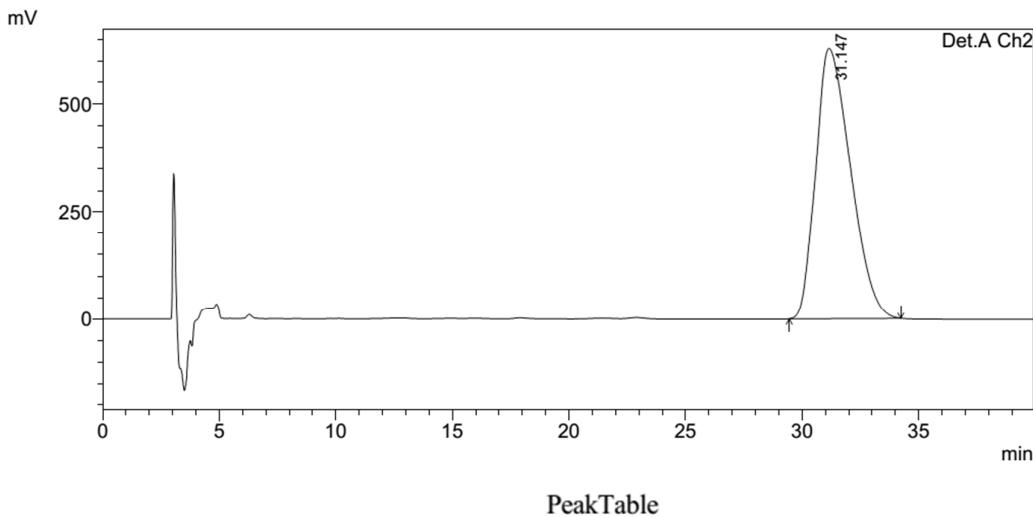
(R)-4-Chlorophenylalanine 22j



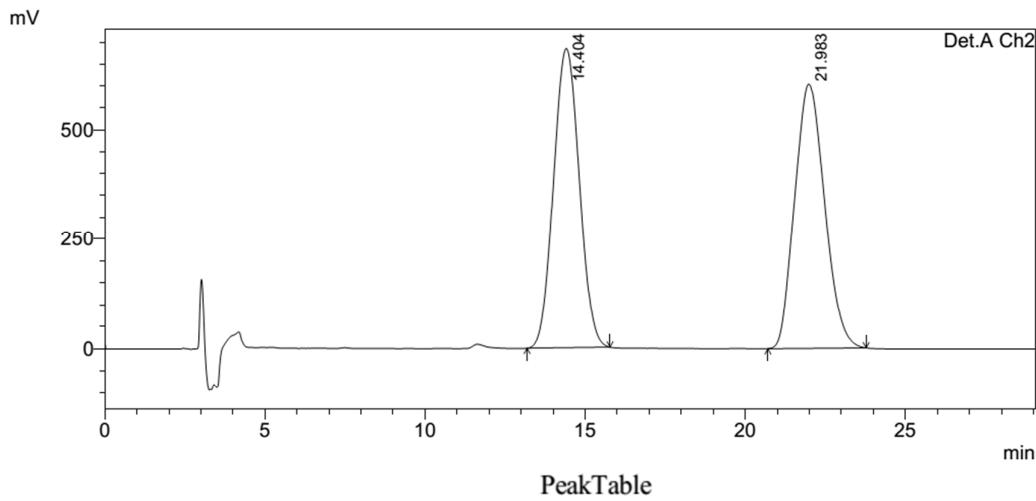
(Rac)-N-Cbz-n-Butylglycine 24y



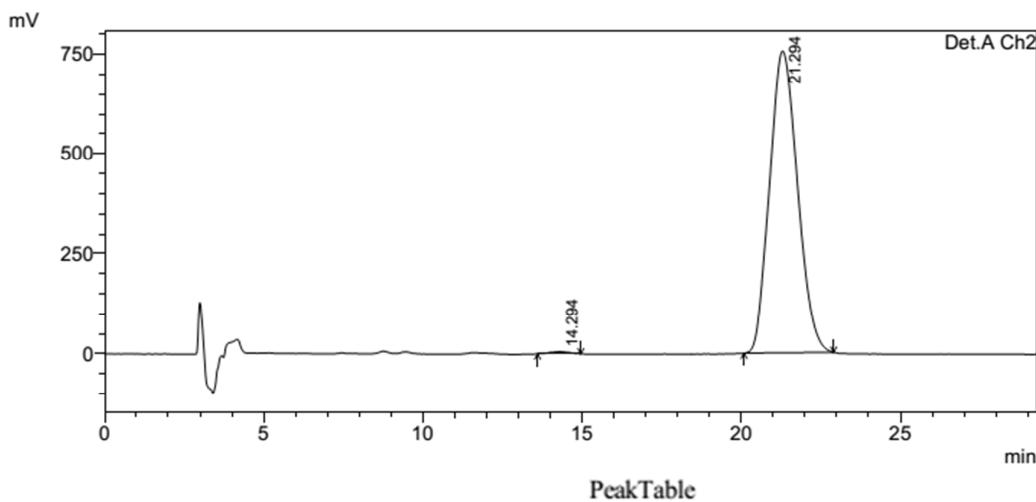
(R)-N-Cbz-n-Butylglycine 24y



(Rac)-N-Cbz-c-Butylglycine 24bb

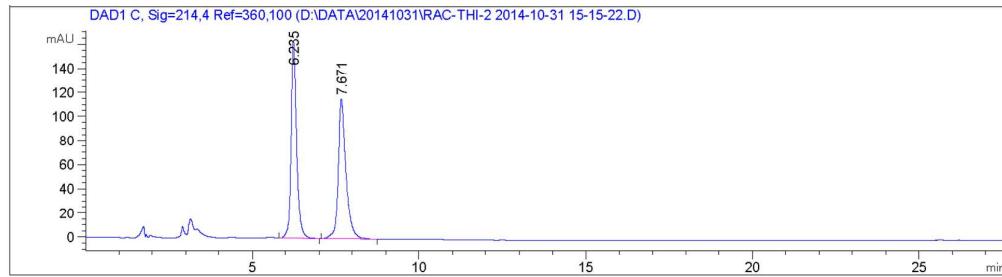


(R)-N-Cbz-c-Butylglycine 24bb



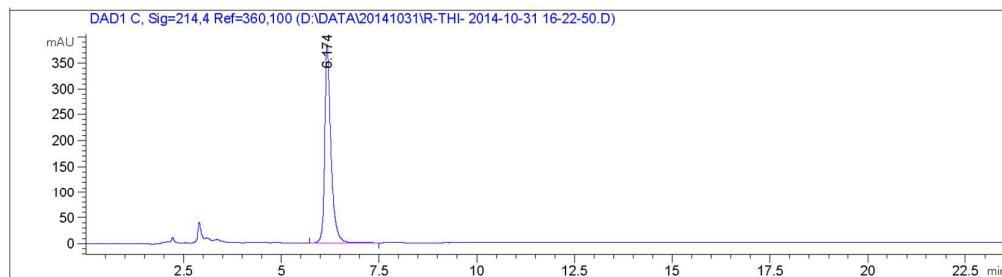
Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.294	223380	5121	0.482	0.674
2	21.294	46074009	755246	99.518	99.326
Total		46297388	760367	100.000	100.000

Rac-3-(2-Thienyl)alanine 22hh



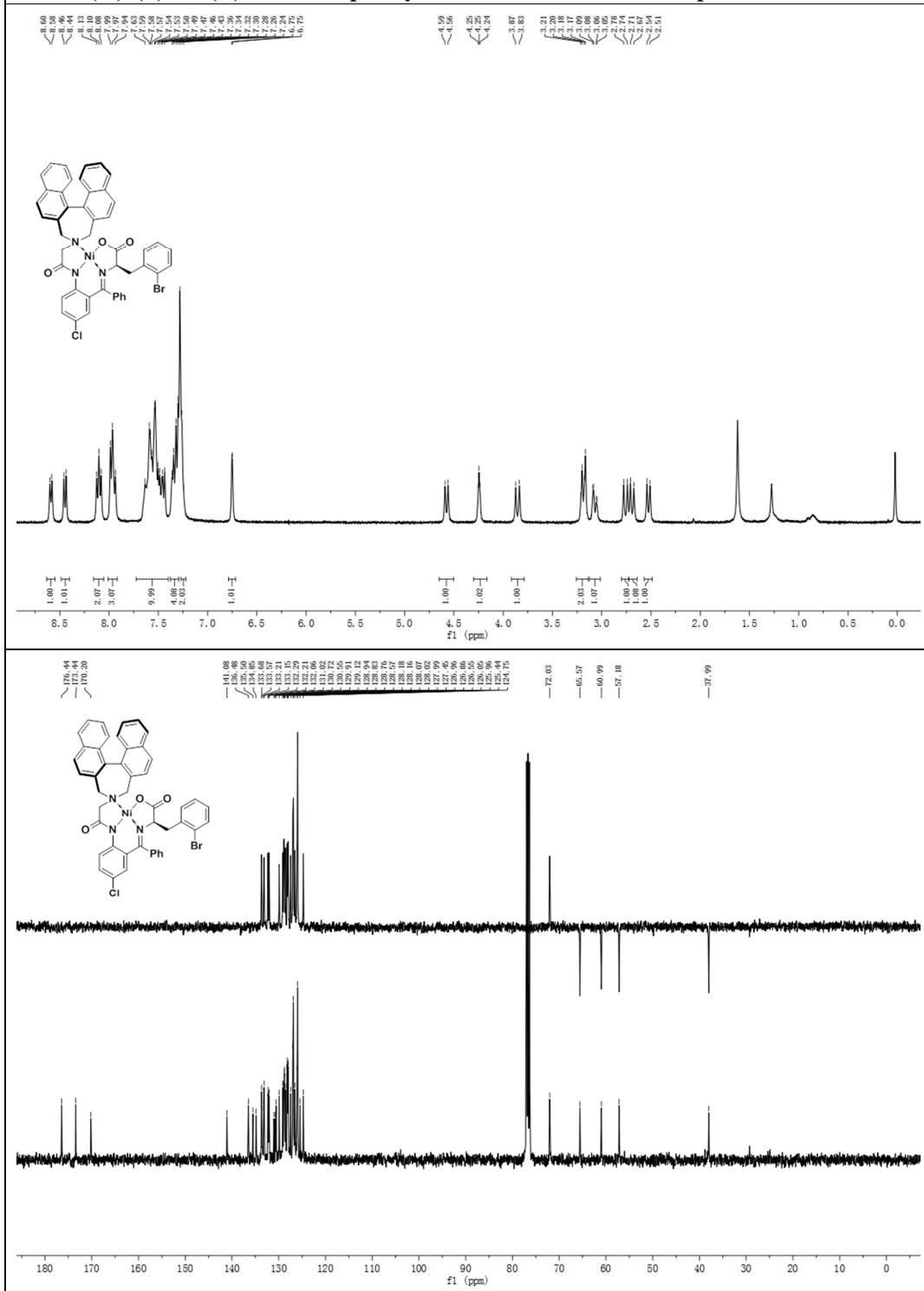
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.235	BB	0.1683	1855.70605	163.66466	49.9619
2	7.671	BB	0.2323	1858.53589	115.75990	50.0381

(S)-3-(2-Thienyl)alanine 22hh

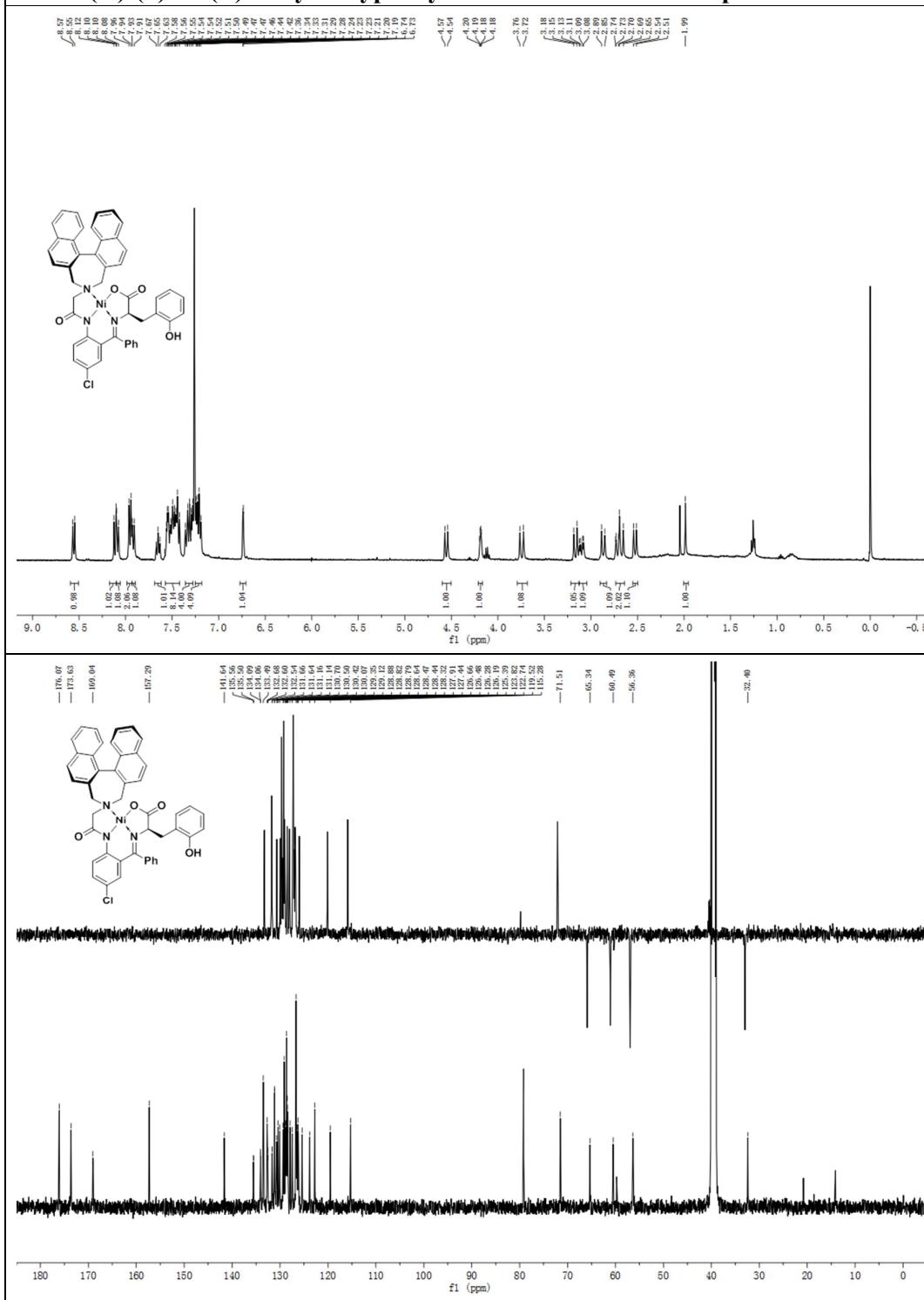


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.174	BB	0.1613	4240.68604	385.61395	100.0000

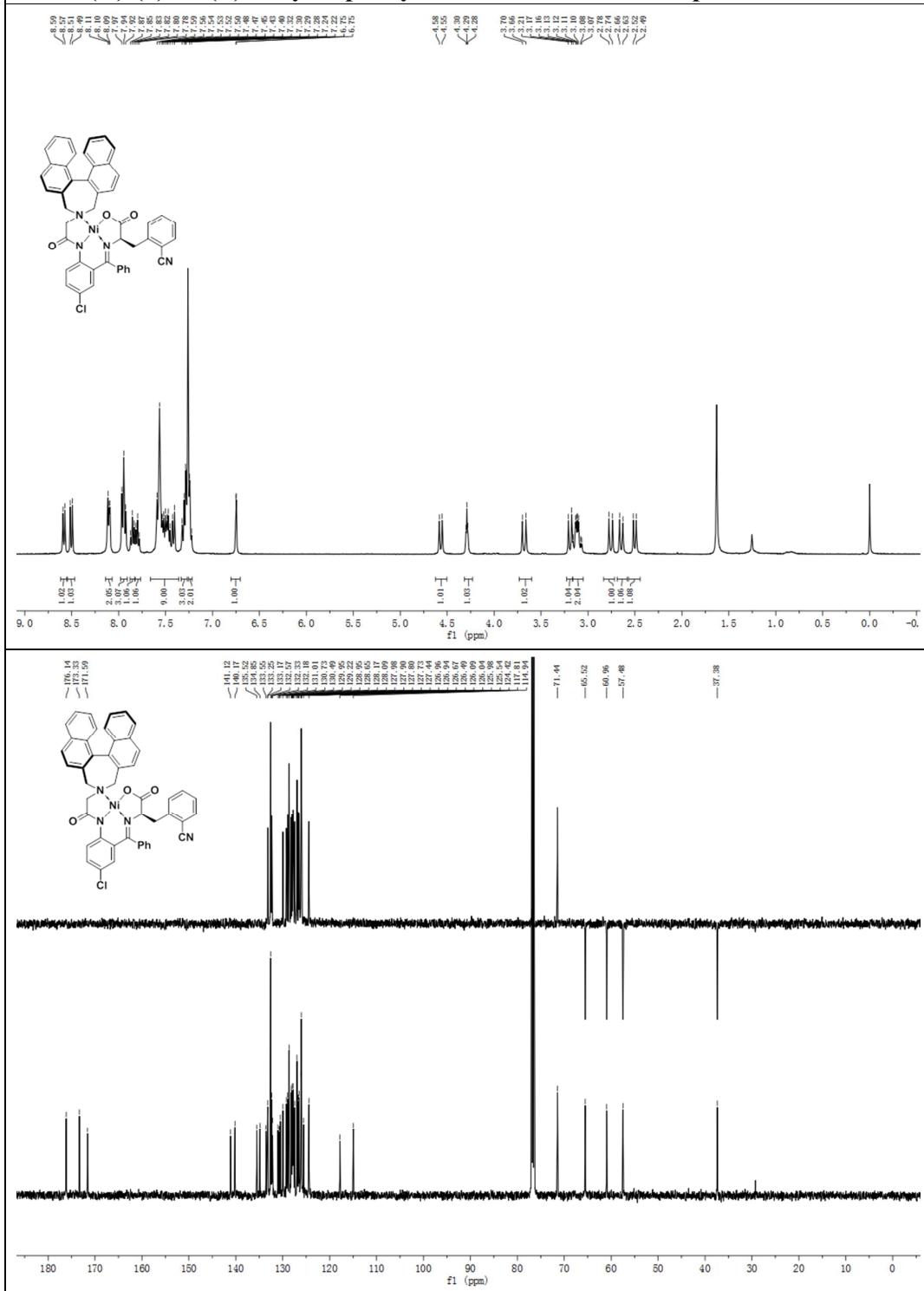
Nickel(II)-(S)-17/(R)-2-Bromophenylalanine Schiff Base Complex 23b



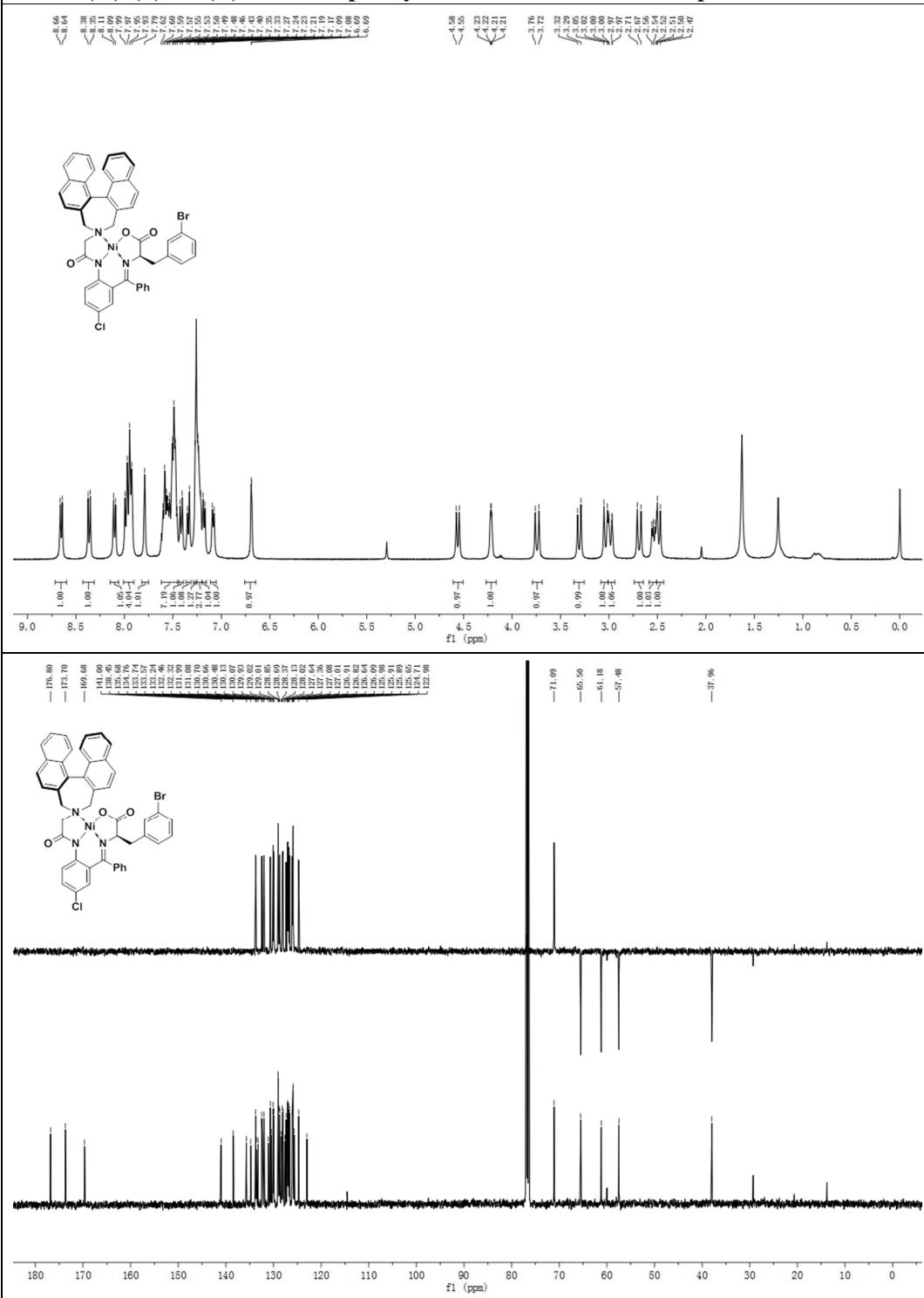
Nickel(II)-(S)-17/(R)-2-Hydroxyphenylalanine Schiff Base Complex 23d



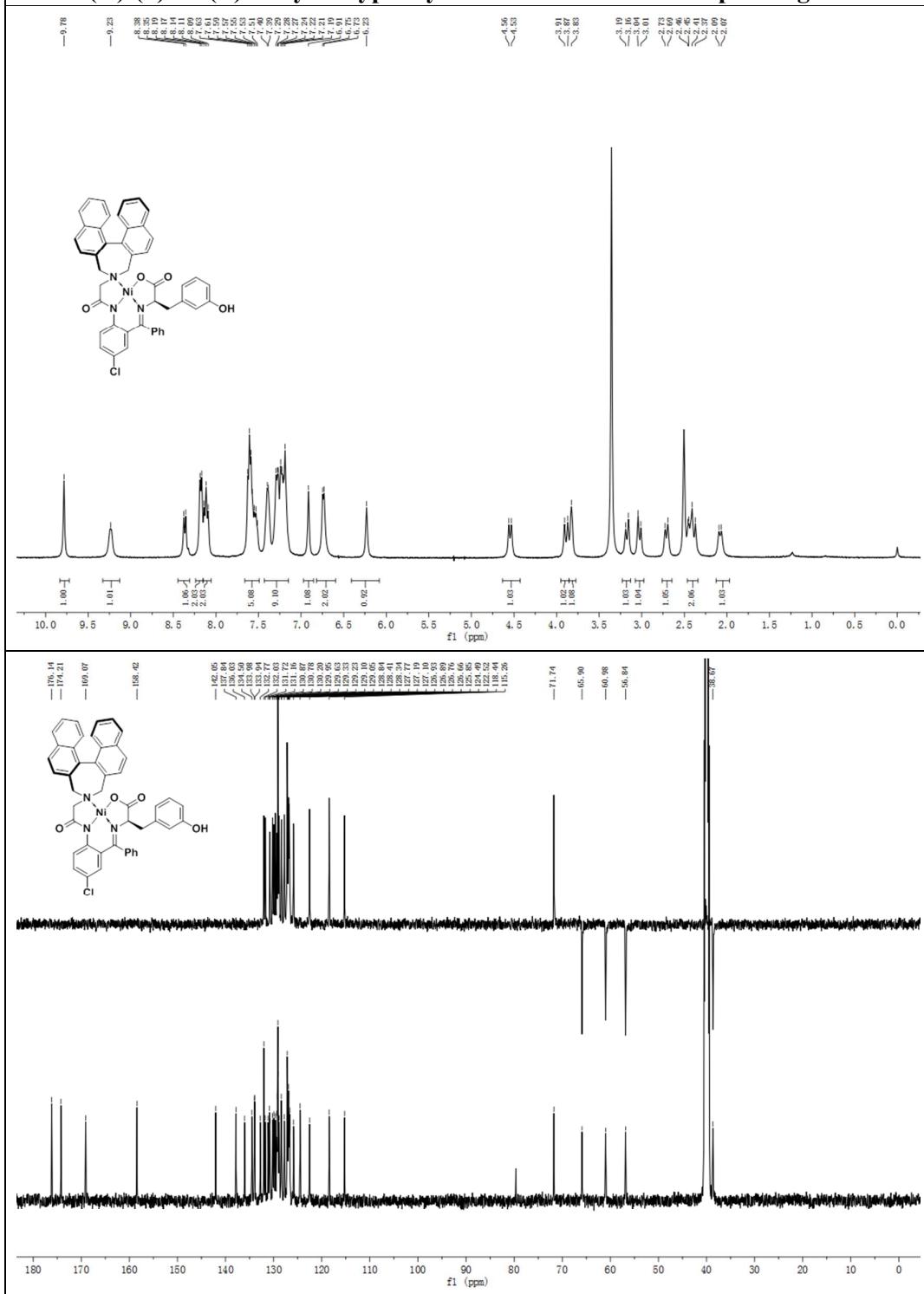
Nickel(II)-(S)-17/(R)-2-Cyanophenylalanine Schiff Base Complex 23e



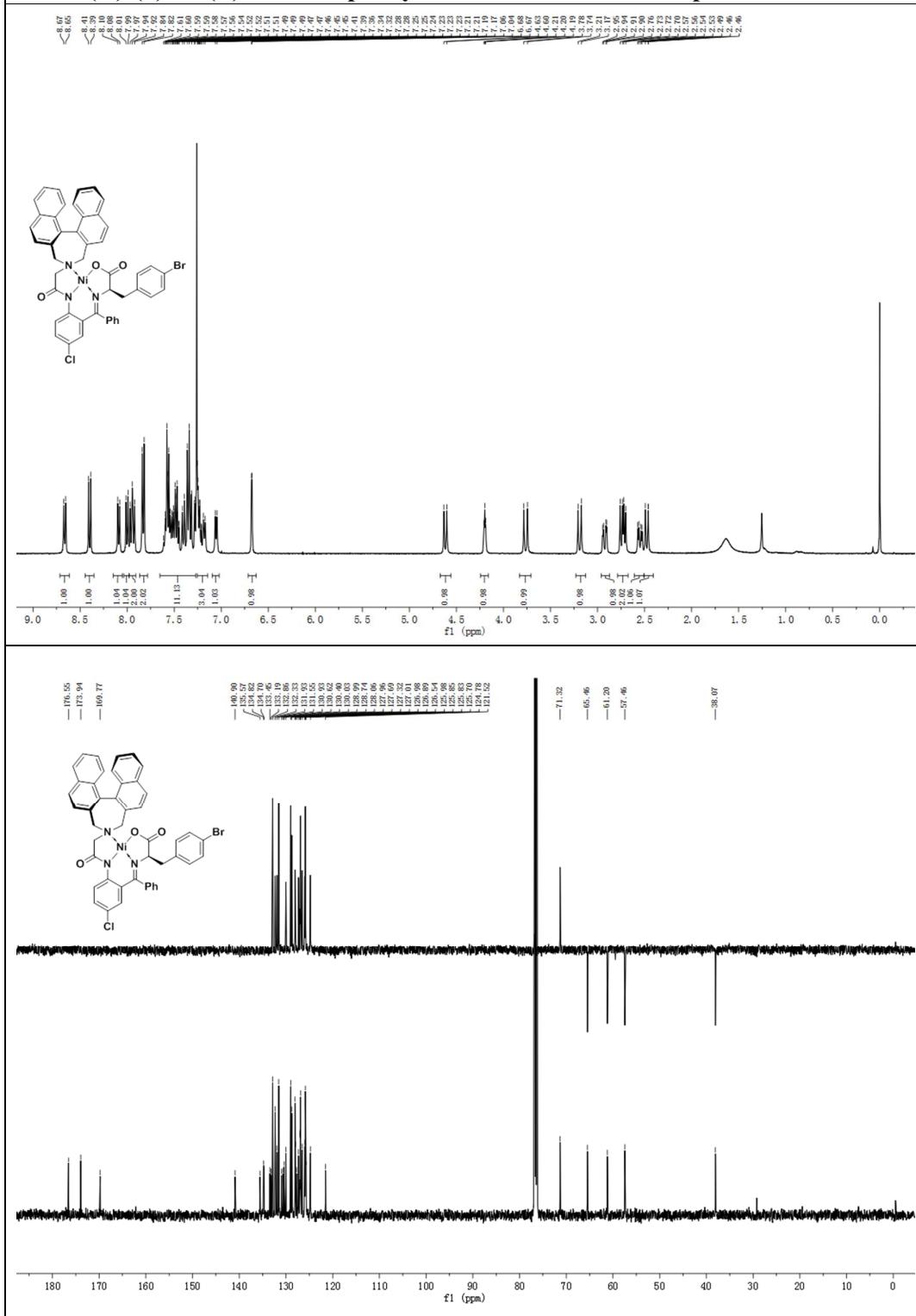
Nickel(II)-(S)-17/(R)-3-Bromophenylalanine Schiff Base Complex 23f



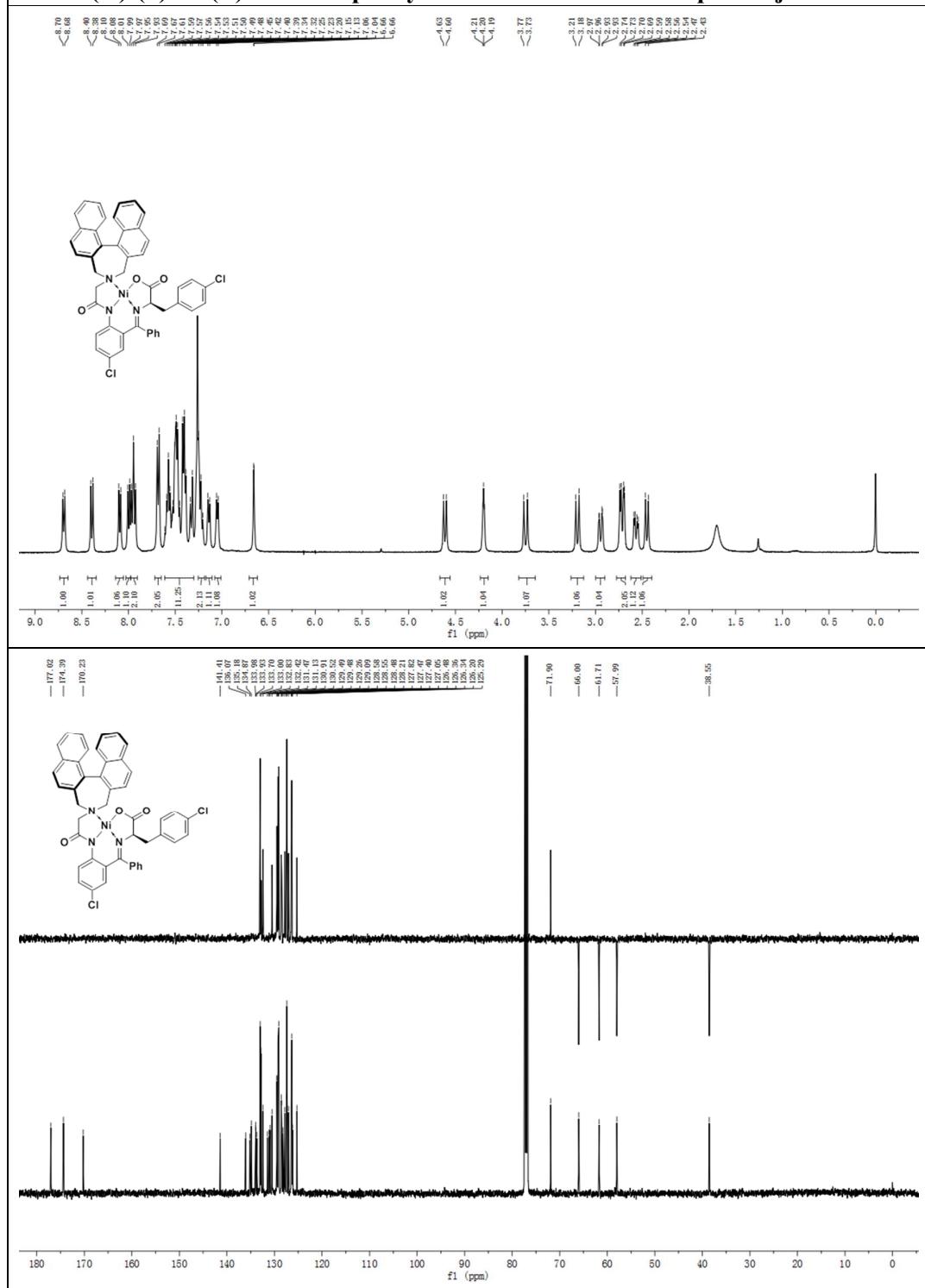
Nickel(II)-(S)-17/(R)-3-Hydroxyphenylalanine Schiff Base Complex 23g



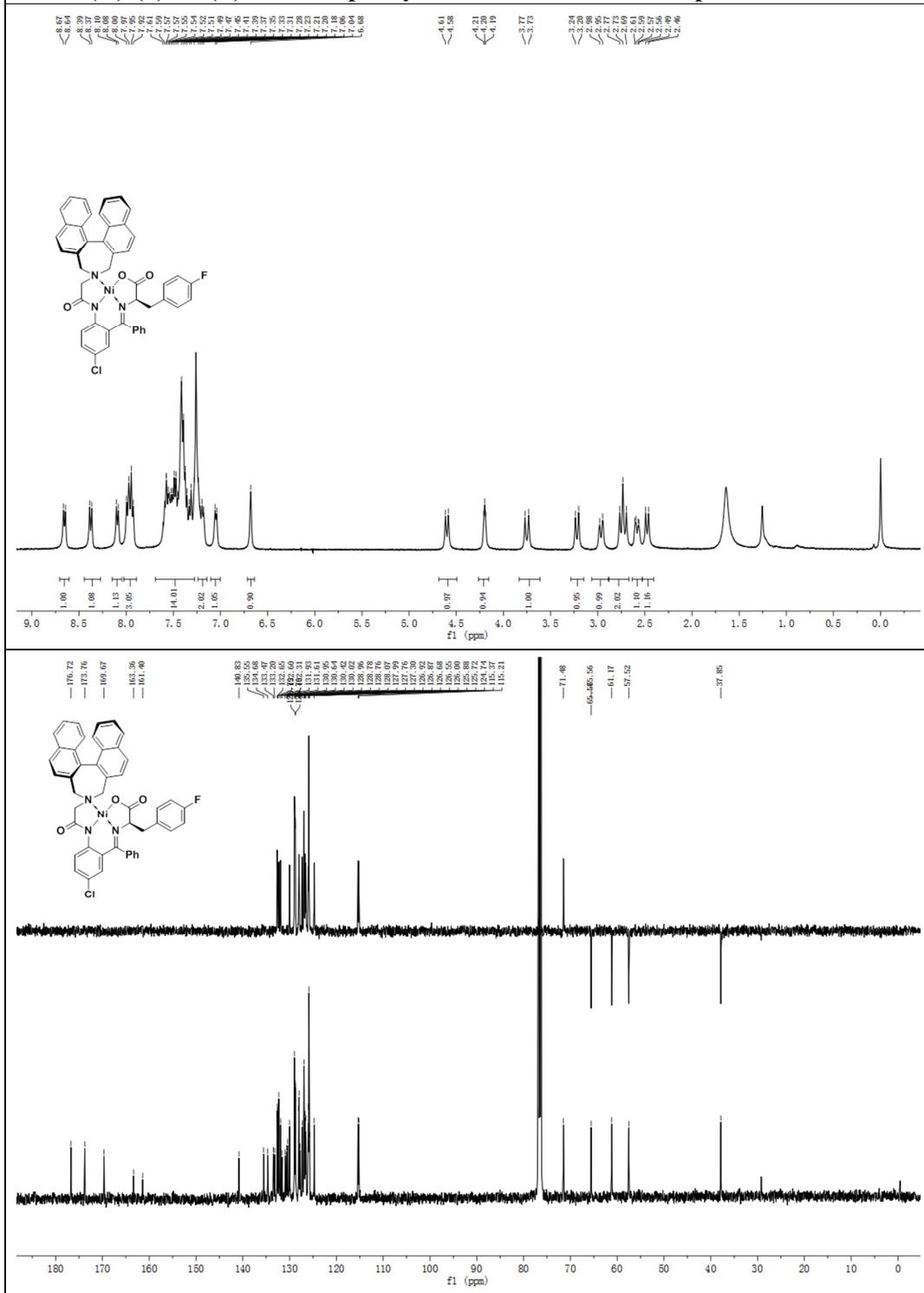
Nickel(II)-(S)-17/(R)-4-Bromophenylalanine Schiff Base Complex 23i



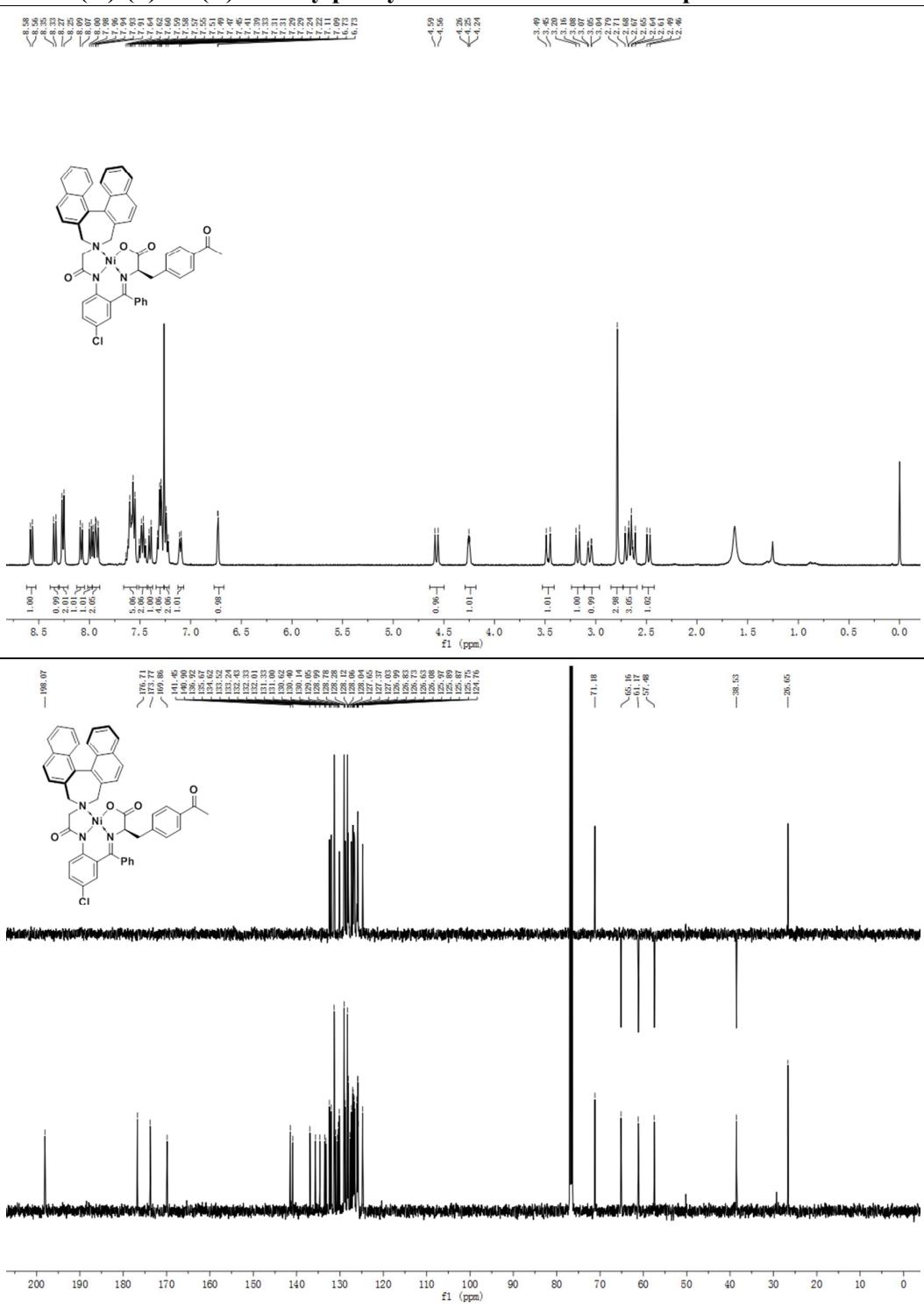
Nickel(II)-(S)-17/(R)-4-Chlorophenylalanine Schiff Base Complex 23j



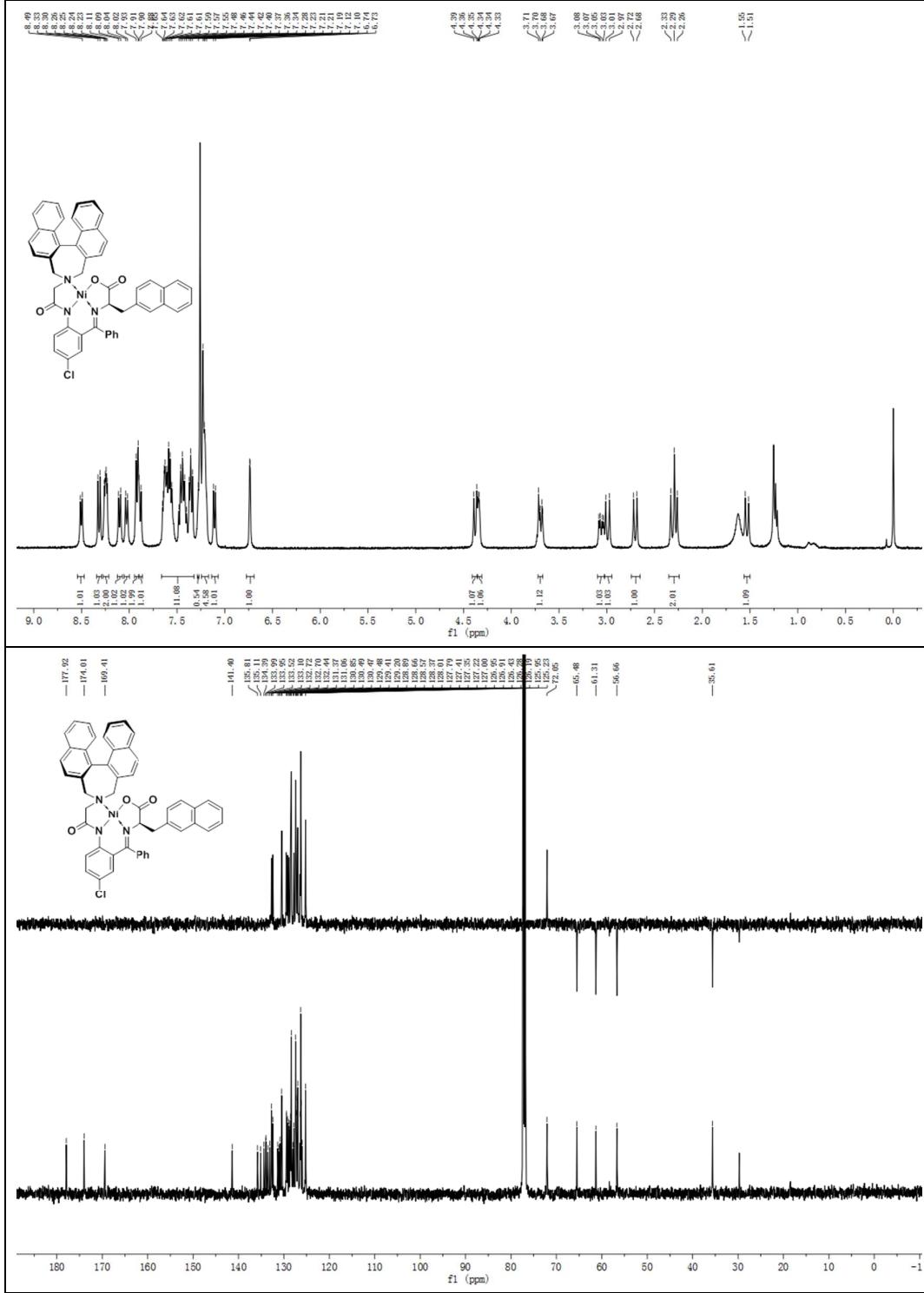
Nickel(II)-(S)-17/(R)-4-Fluorophenylalanine Schiff Base Complex 23k



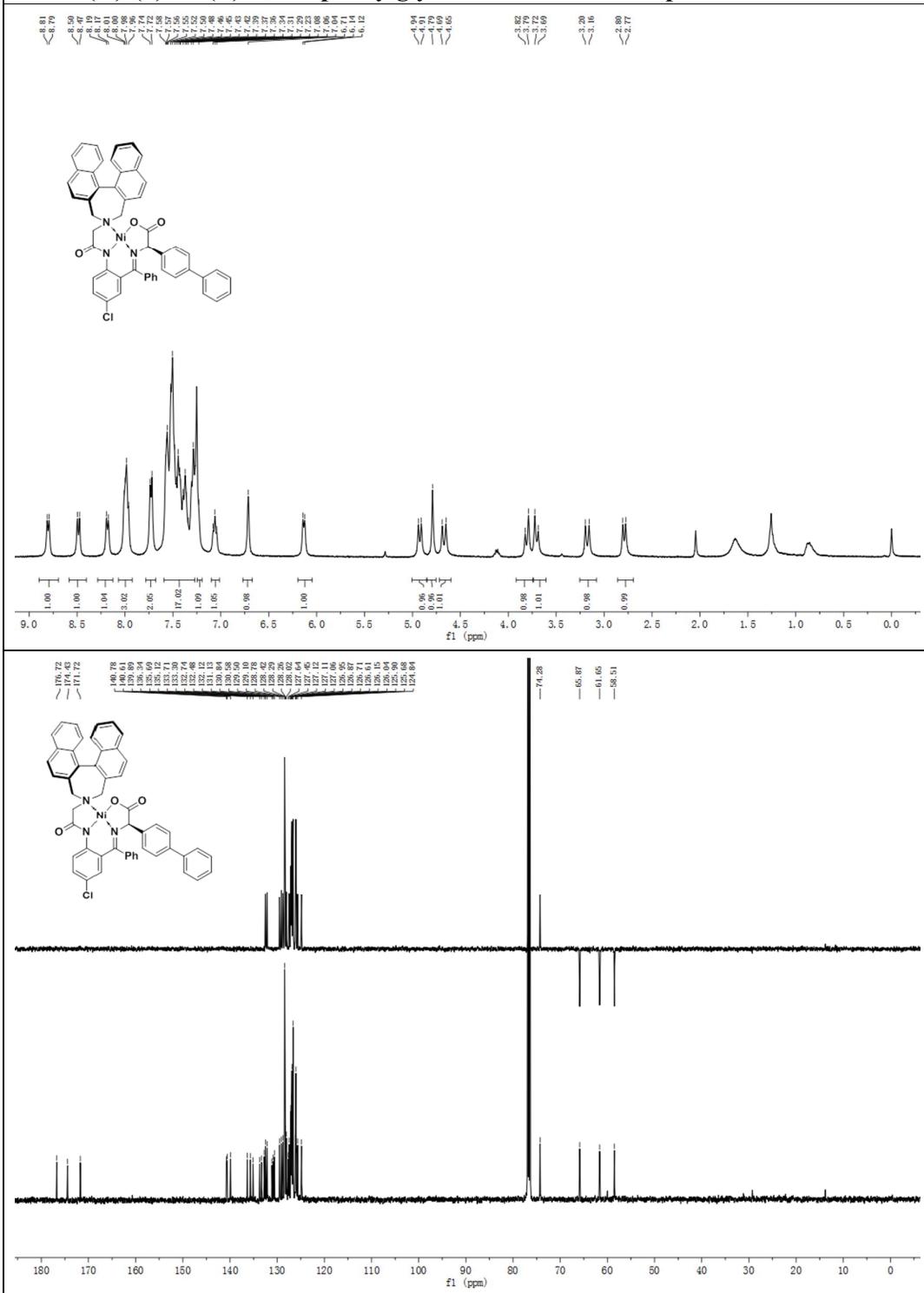
Nickel(II)-(S)-17/(R)-4-acetylphenylalanine Schiff Base Complex 23m



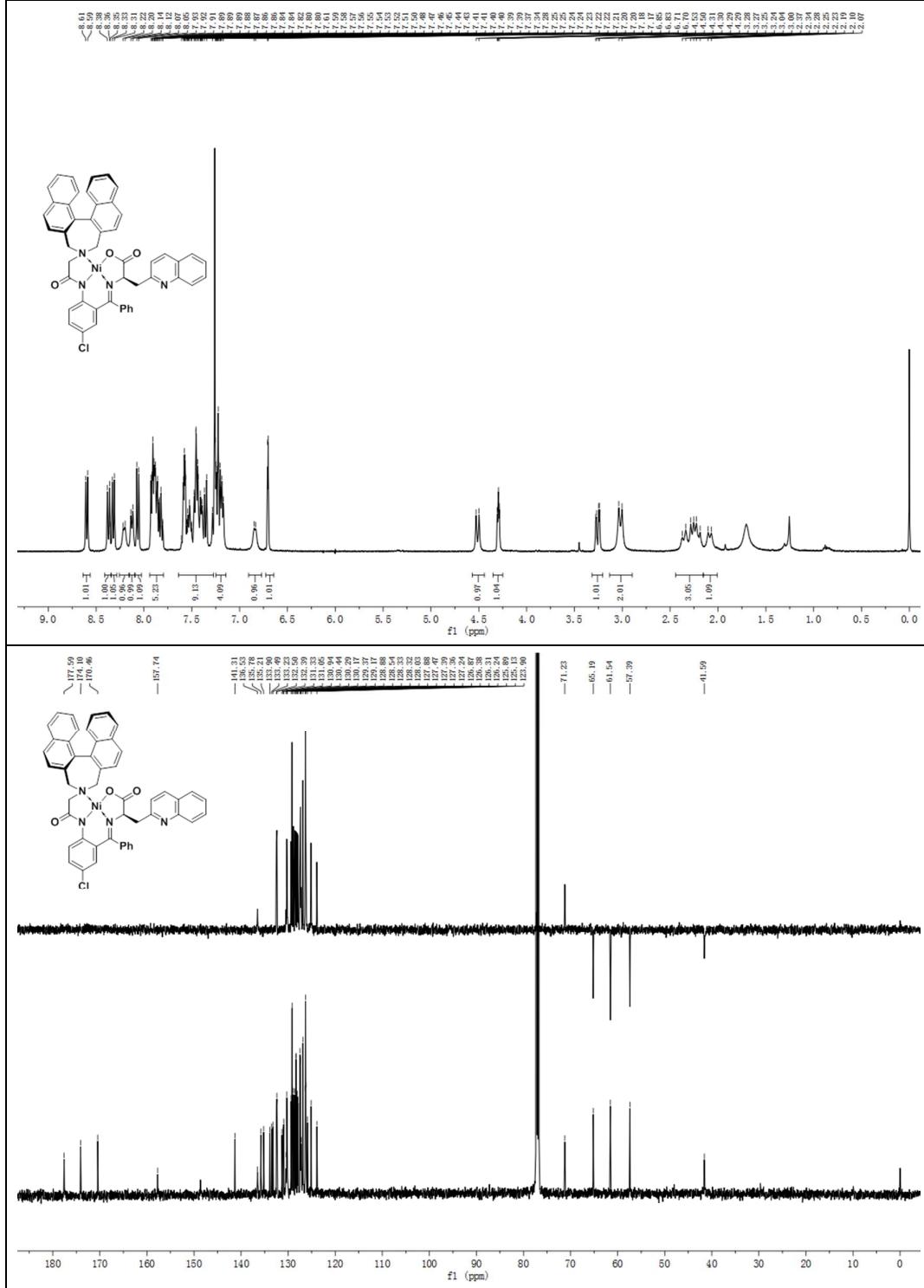
Nickel(II)-(S)-17/(R)-3-(2-Naphthyl)alanine Schiff Base Complex 23n



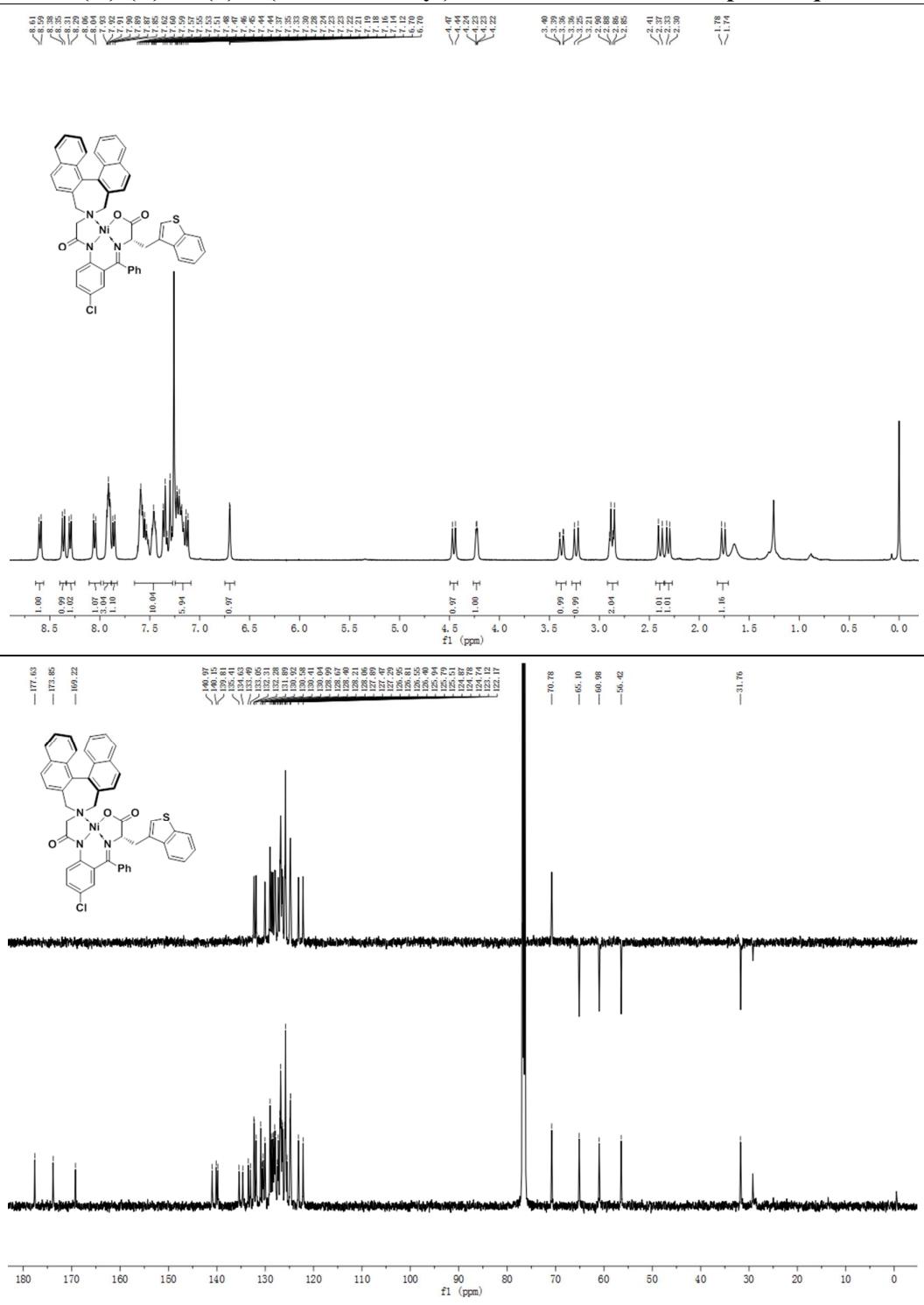
Nickel(II)-(S)-17/(R)-1,1'-biphenylglycine Schiff Base Complex 23o



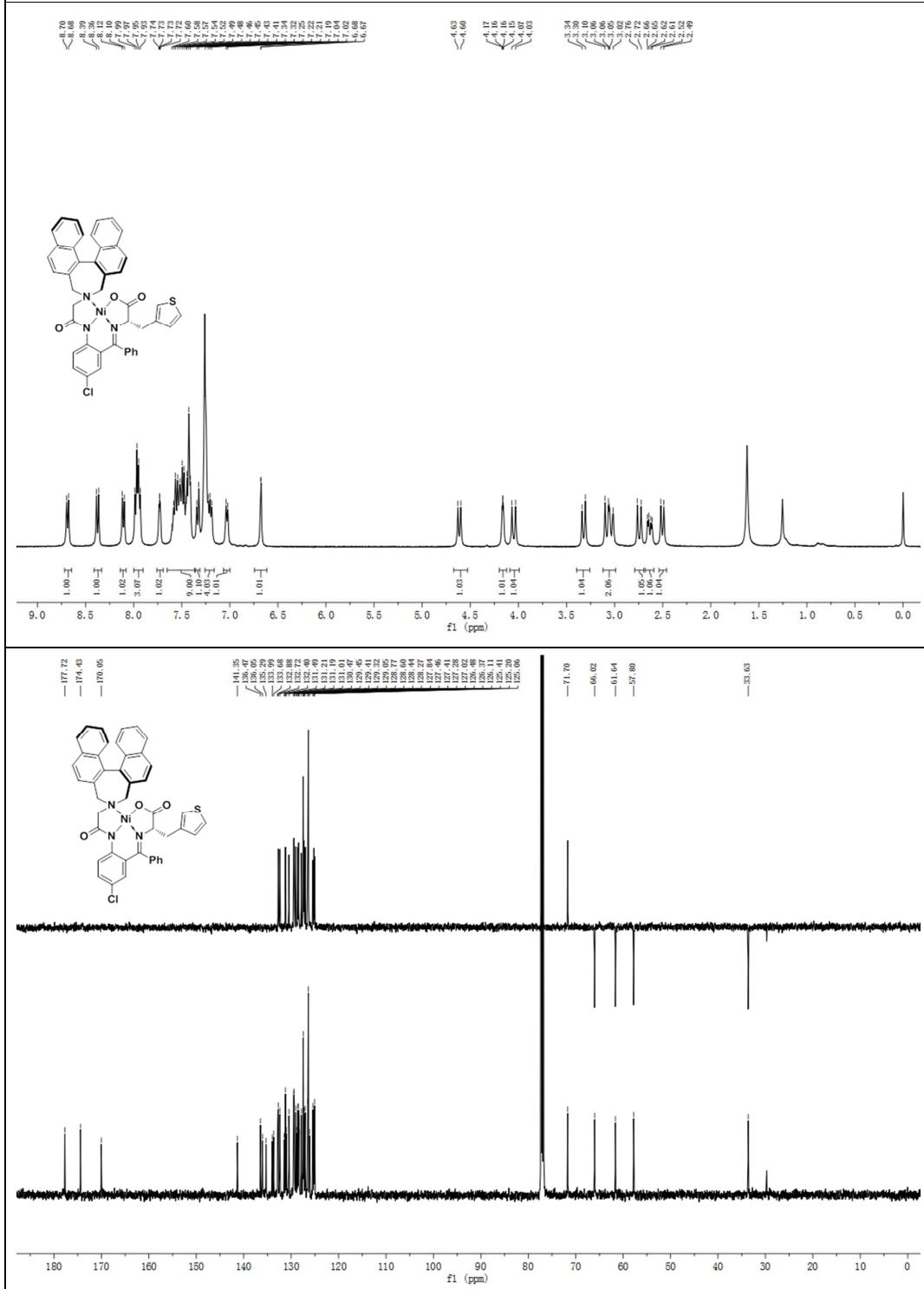
Nickel(II)-(S)-17-(R)-3-(2-Quinolyl)alanine Schiff Base Complex 23p



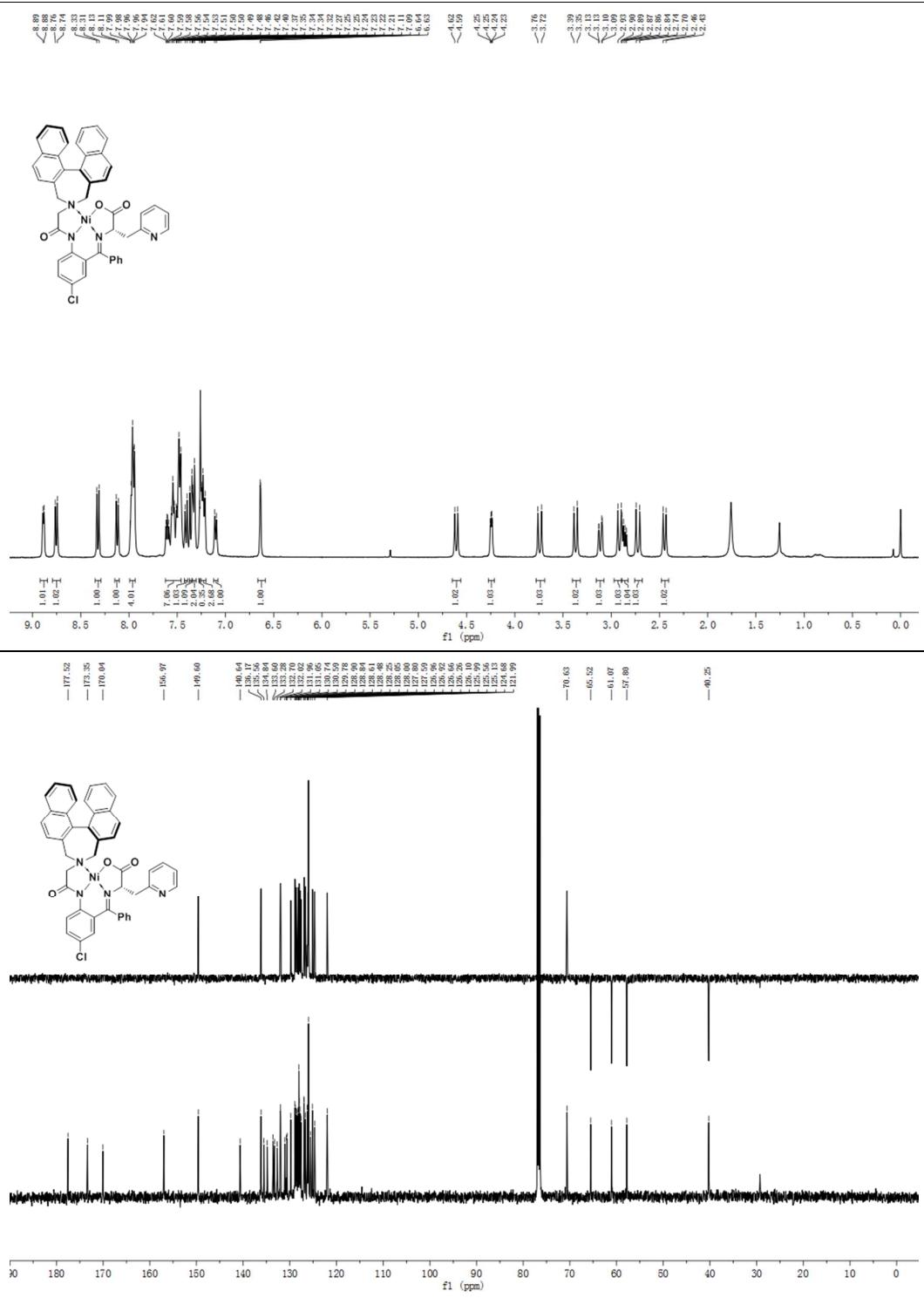
Nickel(II)-(R)-17/(S)-3-(3-Benzothienyl)alanine Schiff Base Complex 23q



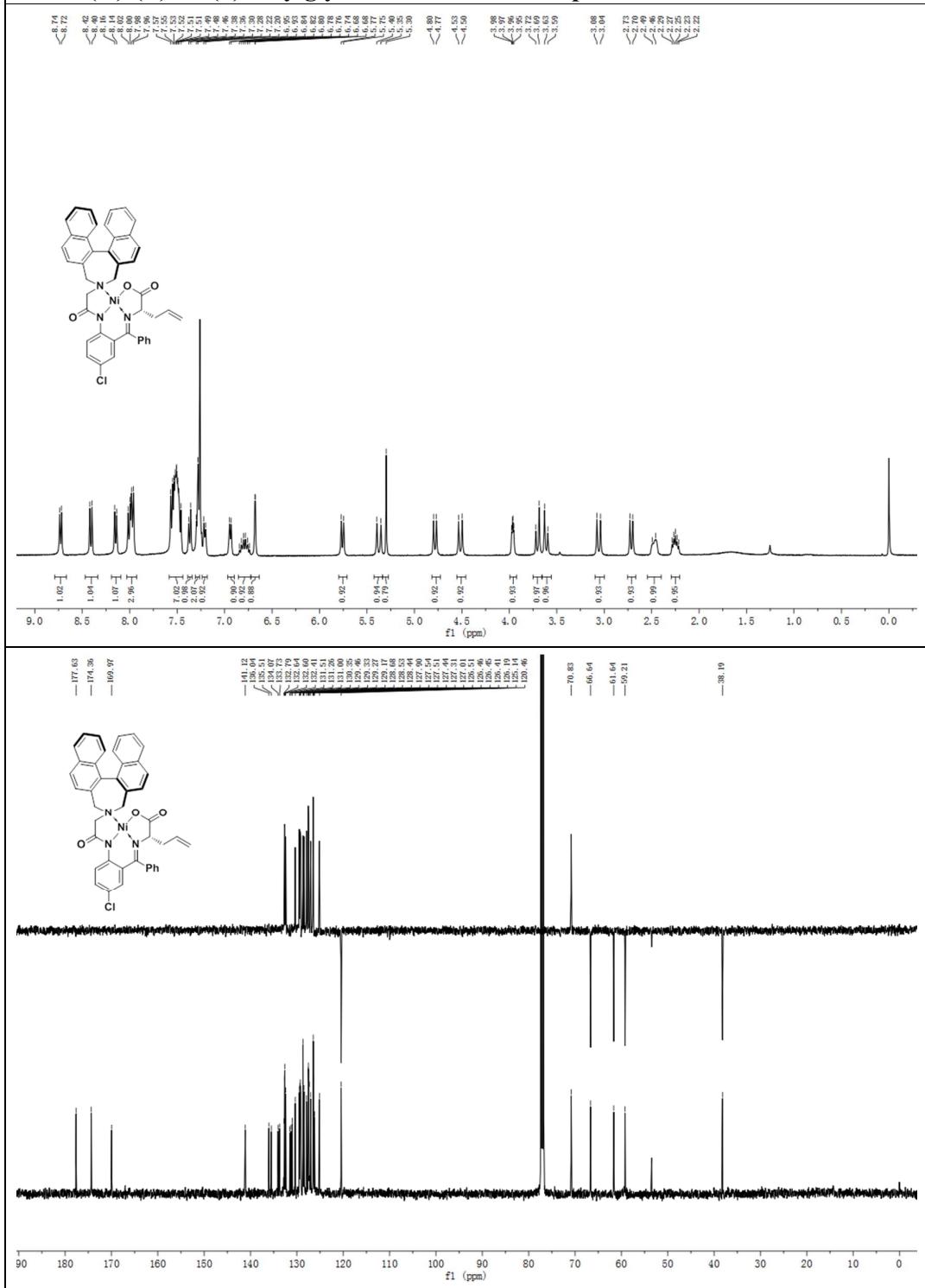
Nickel(II)-(R)-17/(S)-3-(3-Thienyl)alanine Schiff Base Complex 23r



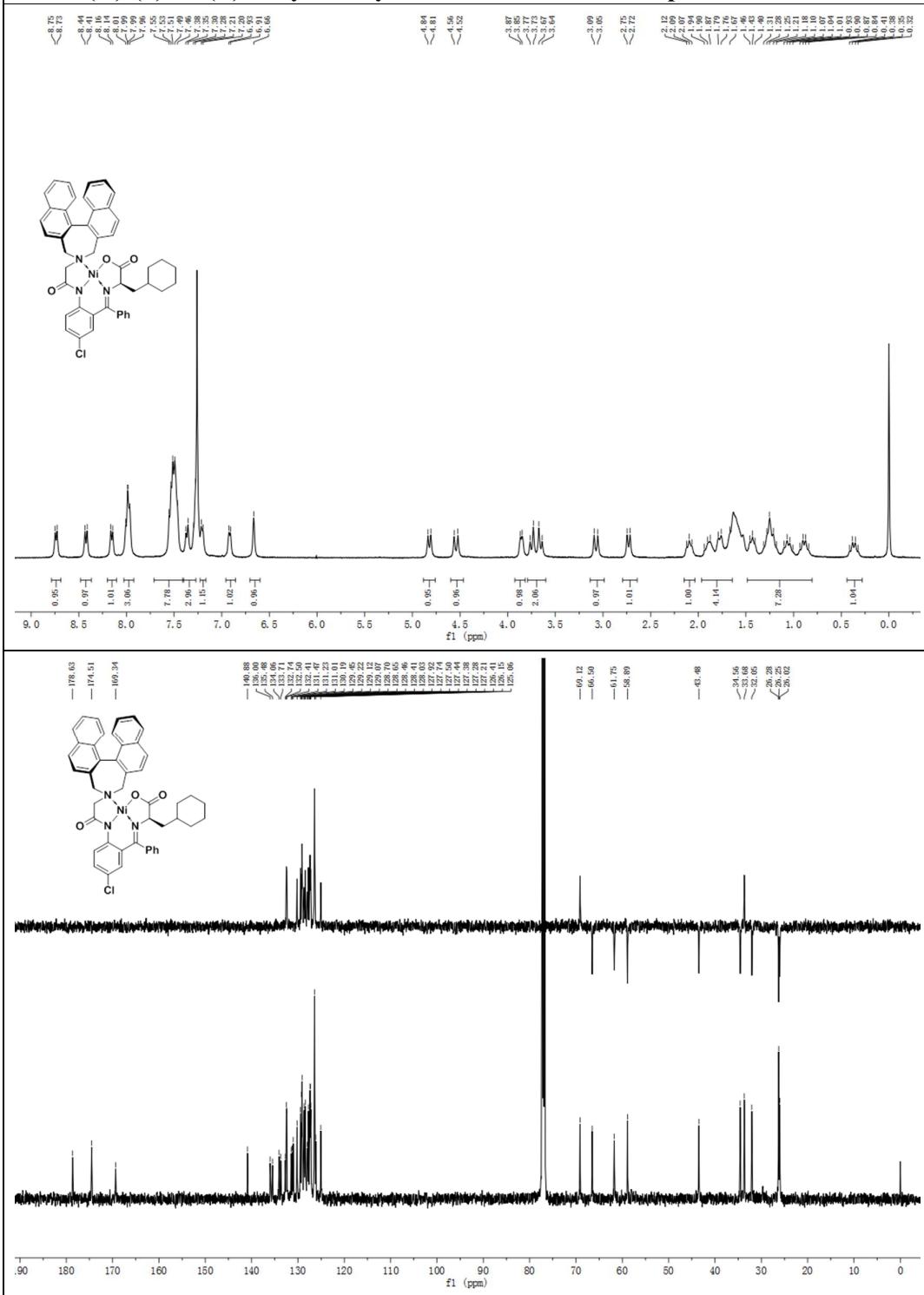
Nickel(II)-(R)-17/(S)-3-(2-Pyridyl)alanine Schiff Base Complex 23s



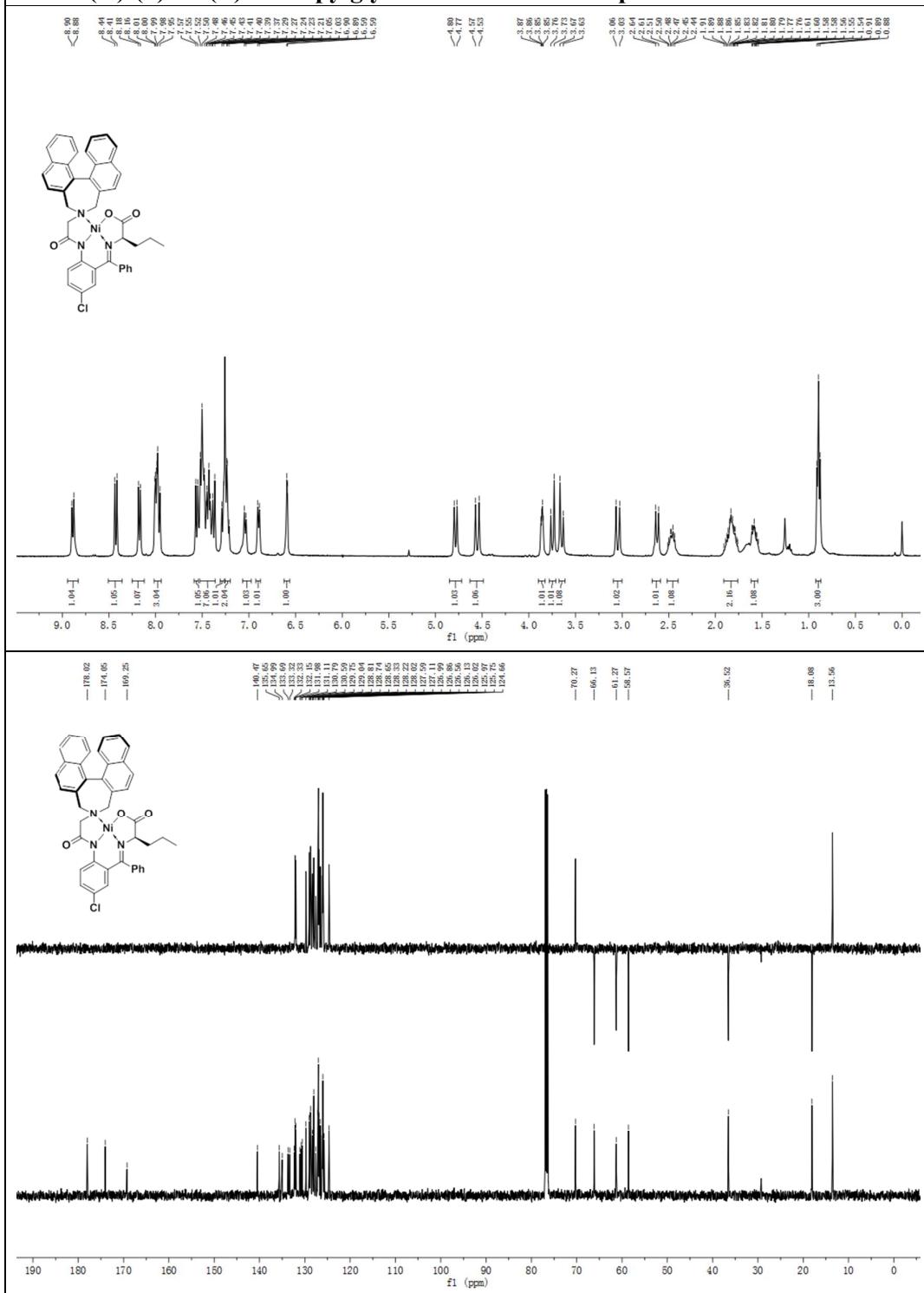
Nickel(II)-(R)-17/(S)-Allylglycine Schiff Base Complex 23t



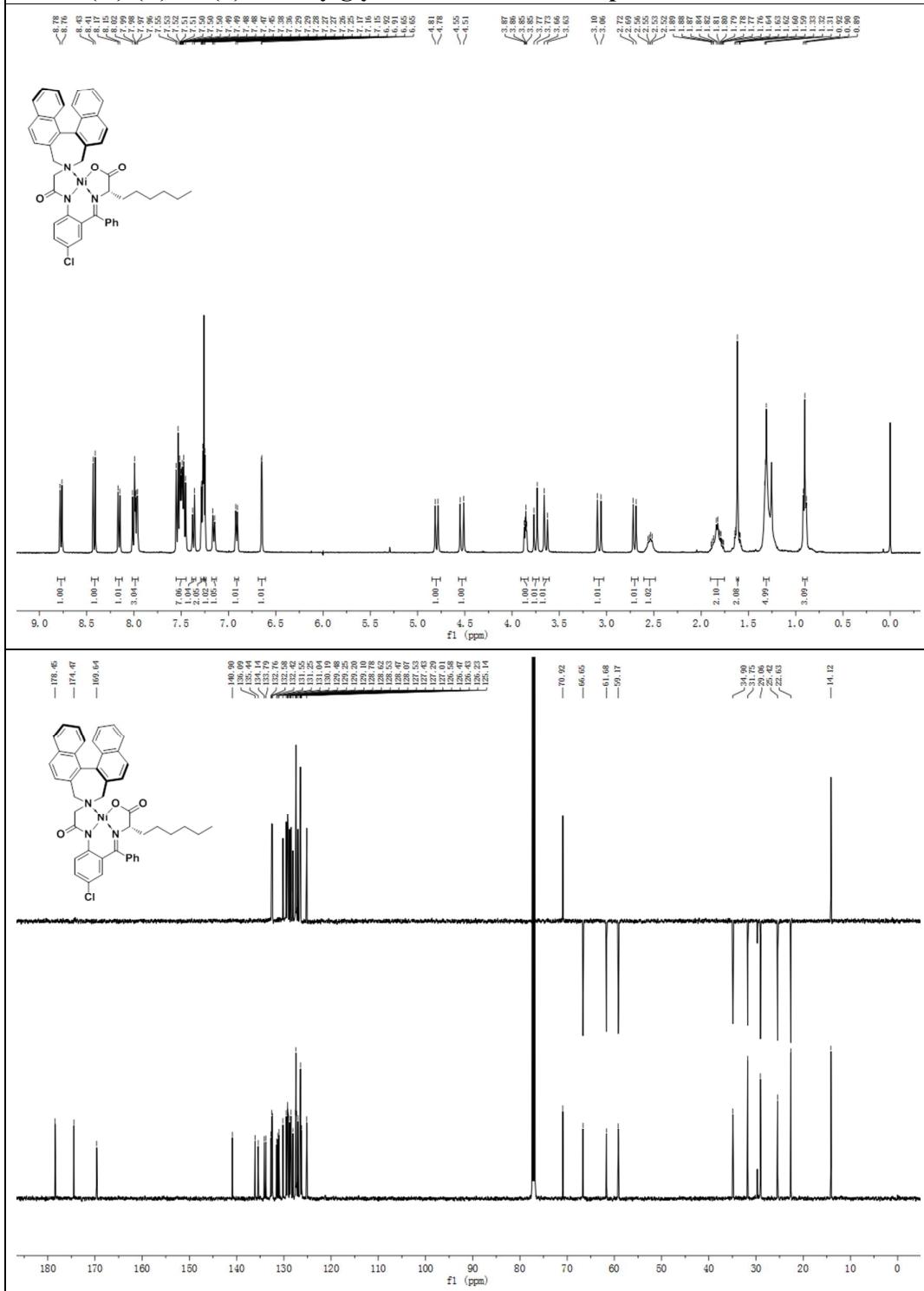
Nickel(II)-(S)-17/(R)-3-Cyclohexylalanine Schiff Base Complex 23w



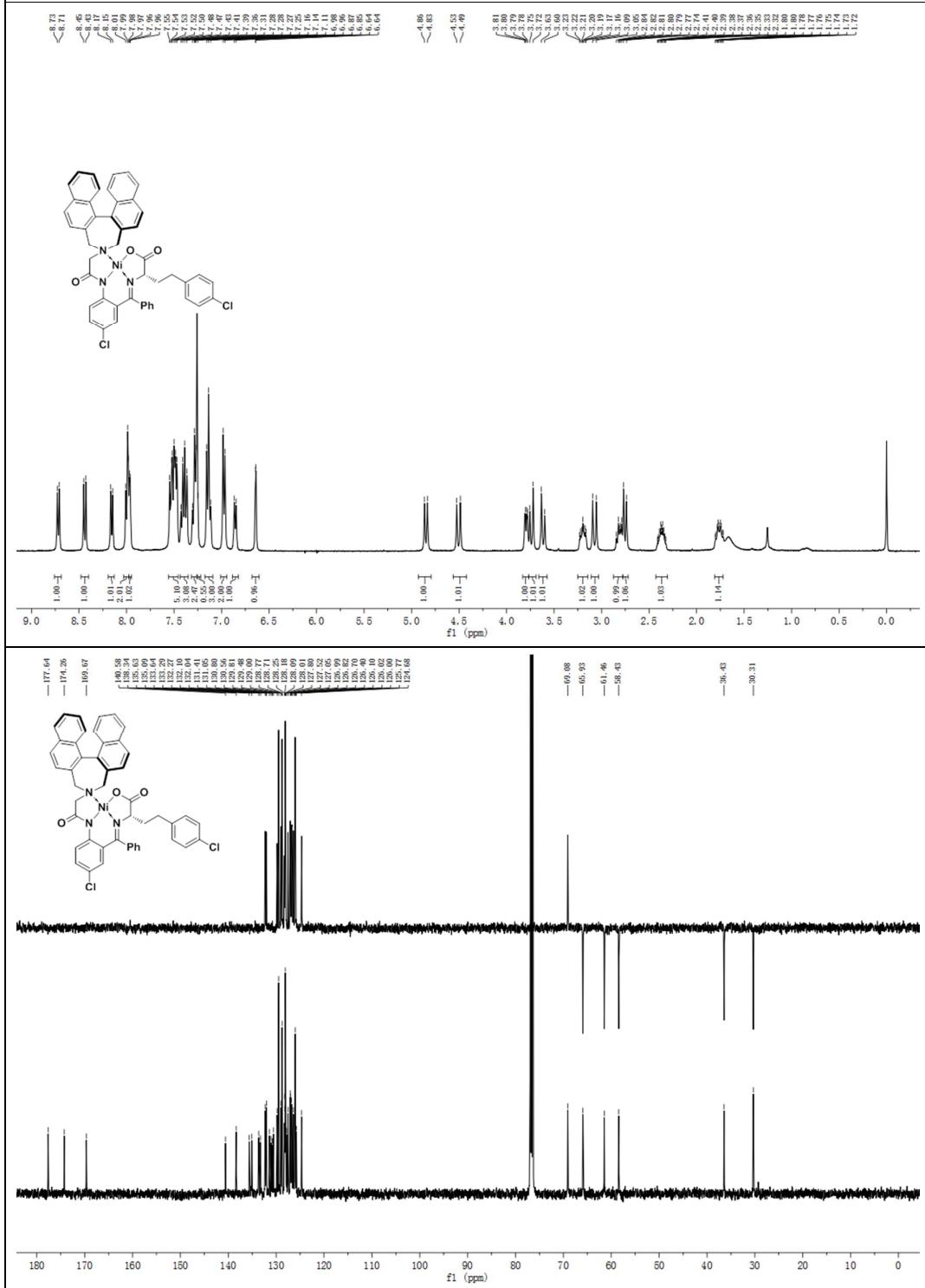
Nickel(II)-(S)-17/(R)-n-Propylglycine Schiff Base Complex 23x

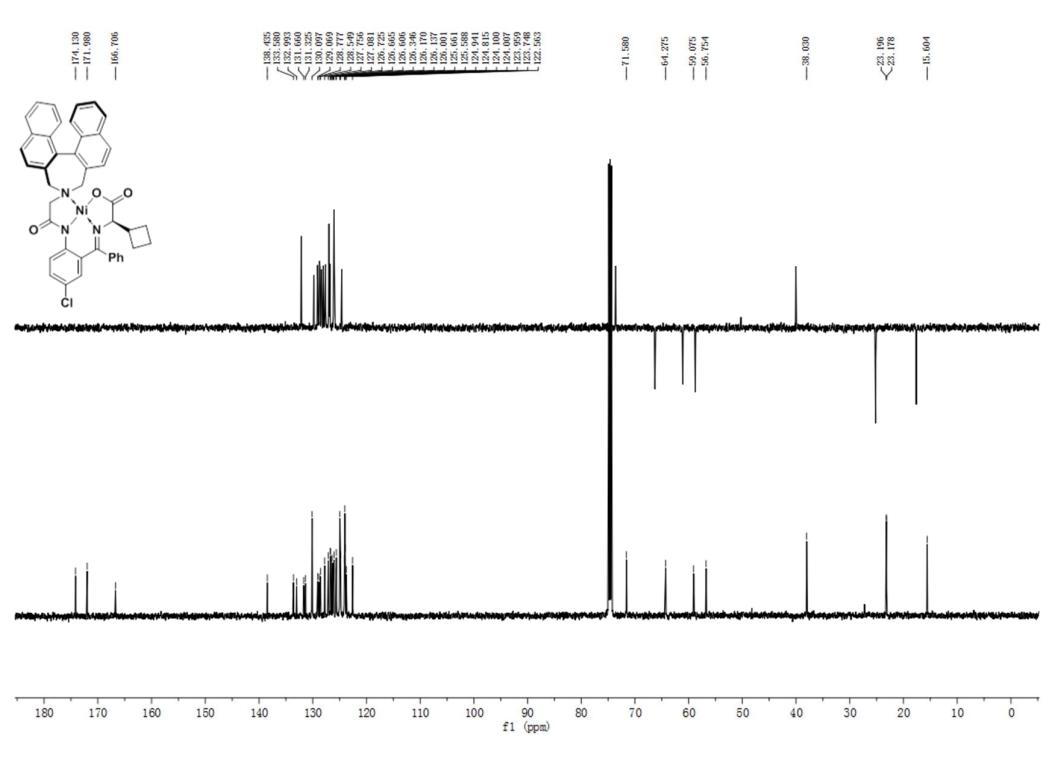
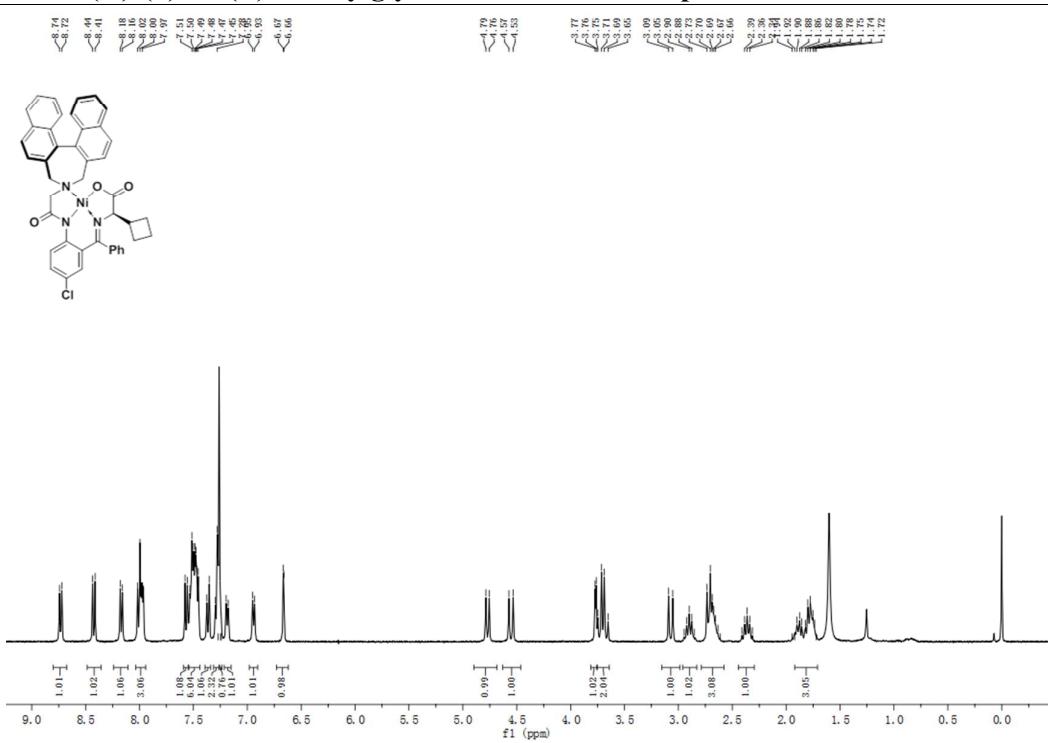


Nickel(II)-(R)-17/(S)-n-Hexylglycine Schiff Base Complex 23z

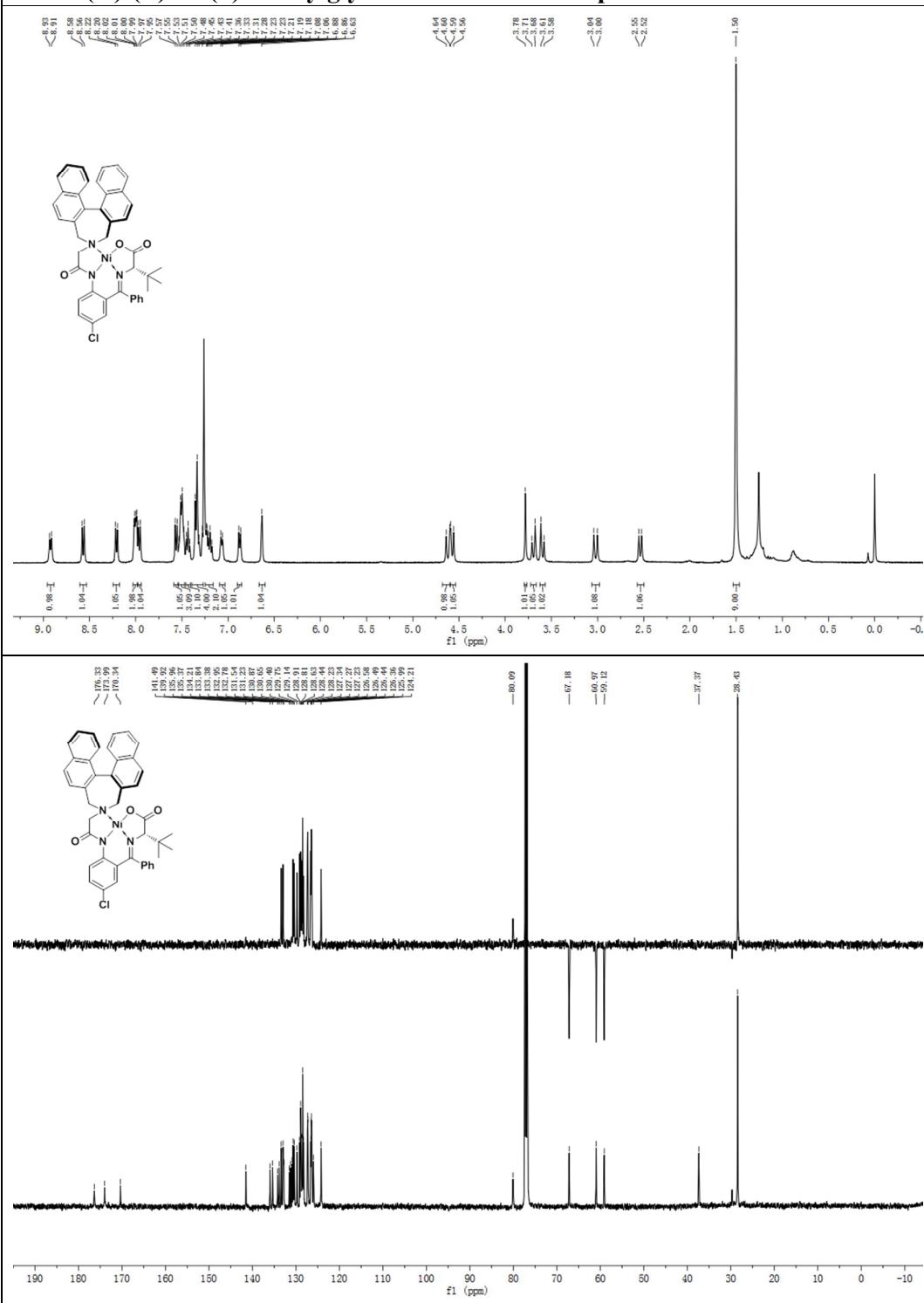


Nickel(II)-(R)-17/(S)-4-Chlorohomophenylalanine Schiff Base Complex 23aa

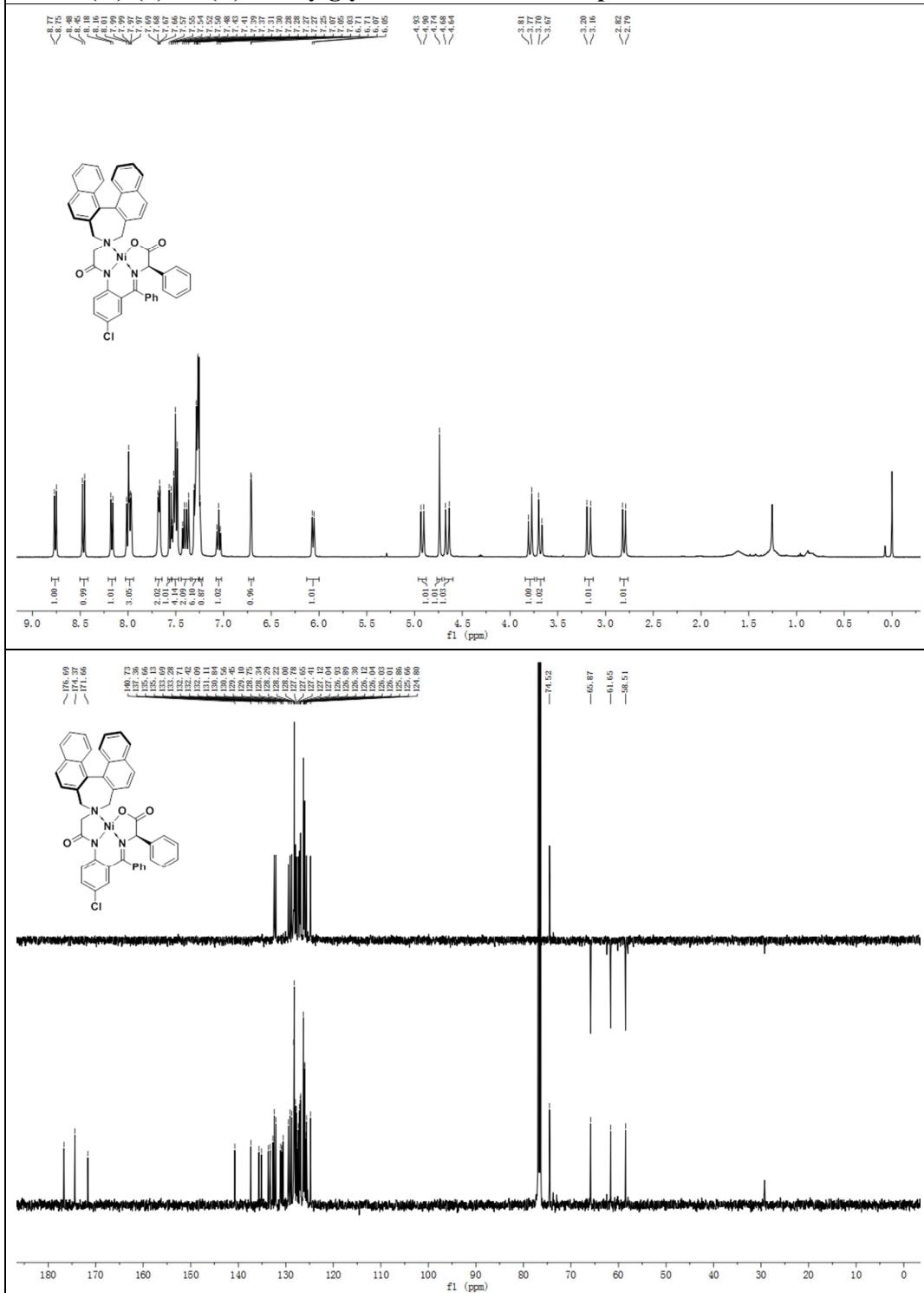


Nickel(II)-(S)-17/(R)-c-Butylglycine Schiff Base Complex 23bb

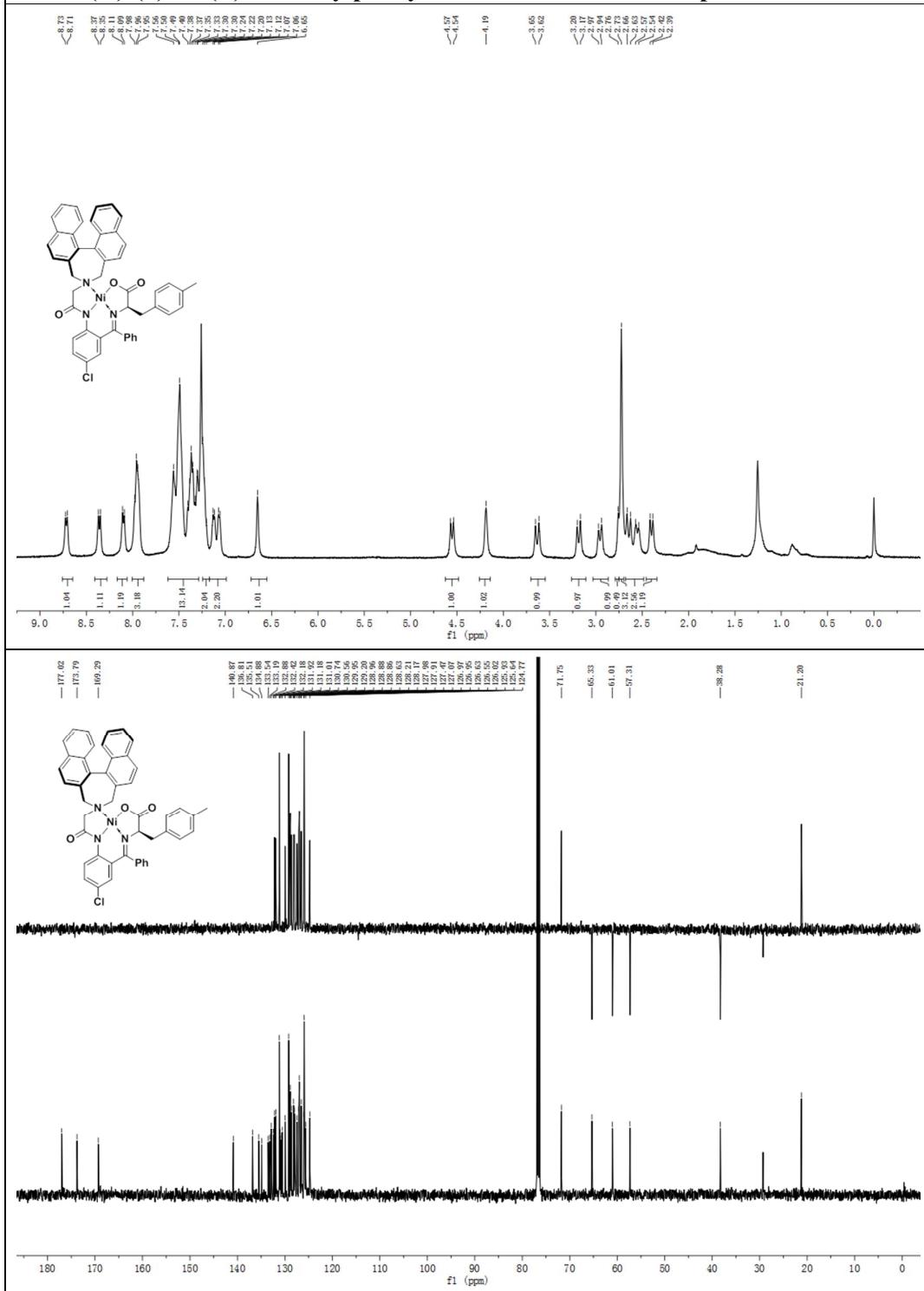
Nickel(II)-(R)-17/(S)-*t*-Butylglycine Schiff Base Complex 23cc



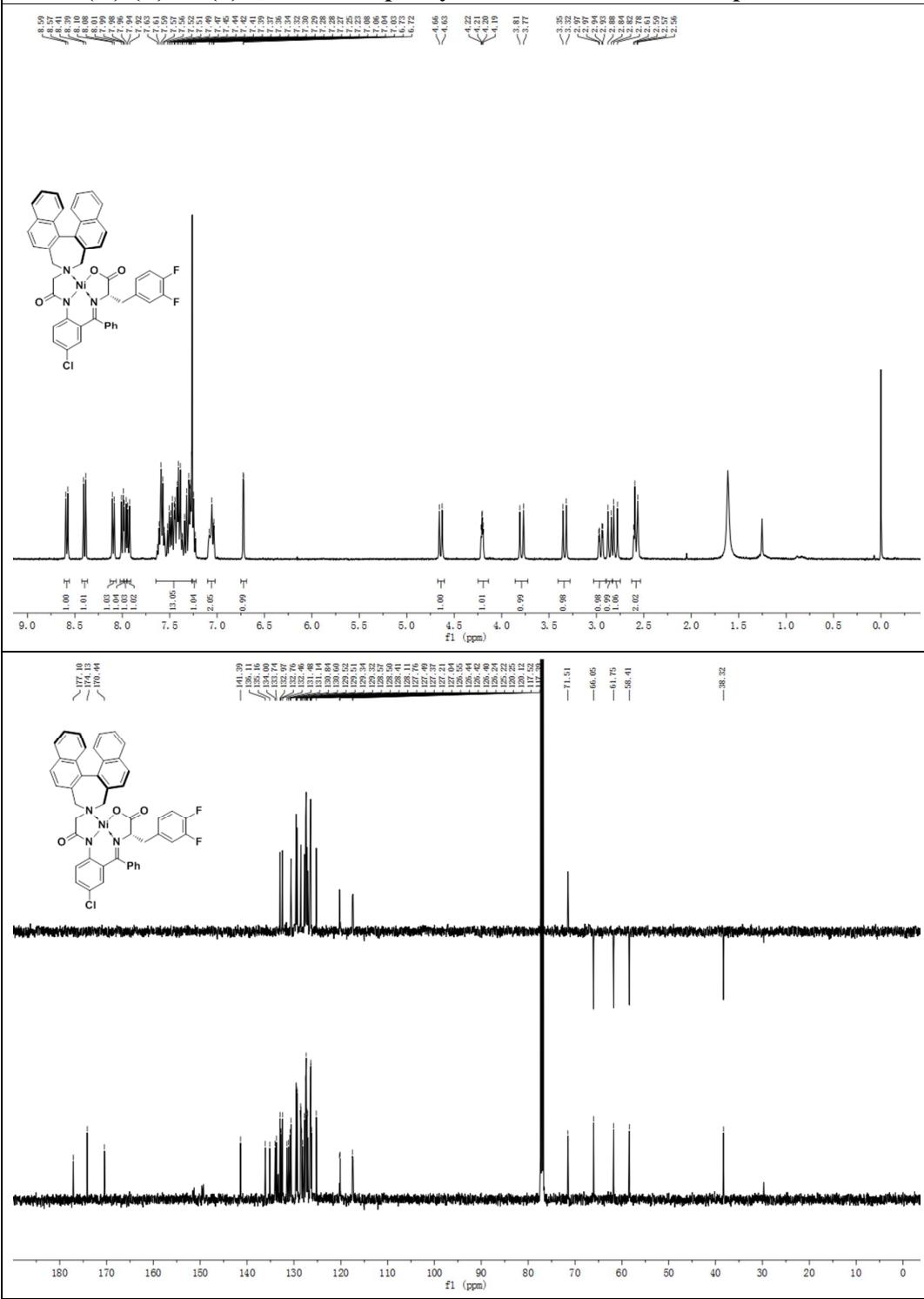
Nickel(II)-(S)-17/(R)-Phenylglycine Schiff Base Complex 23dd



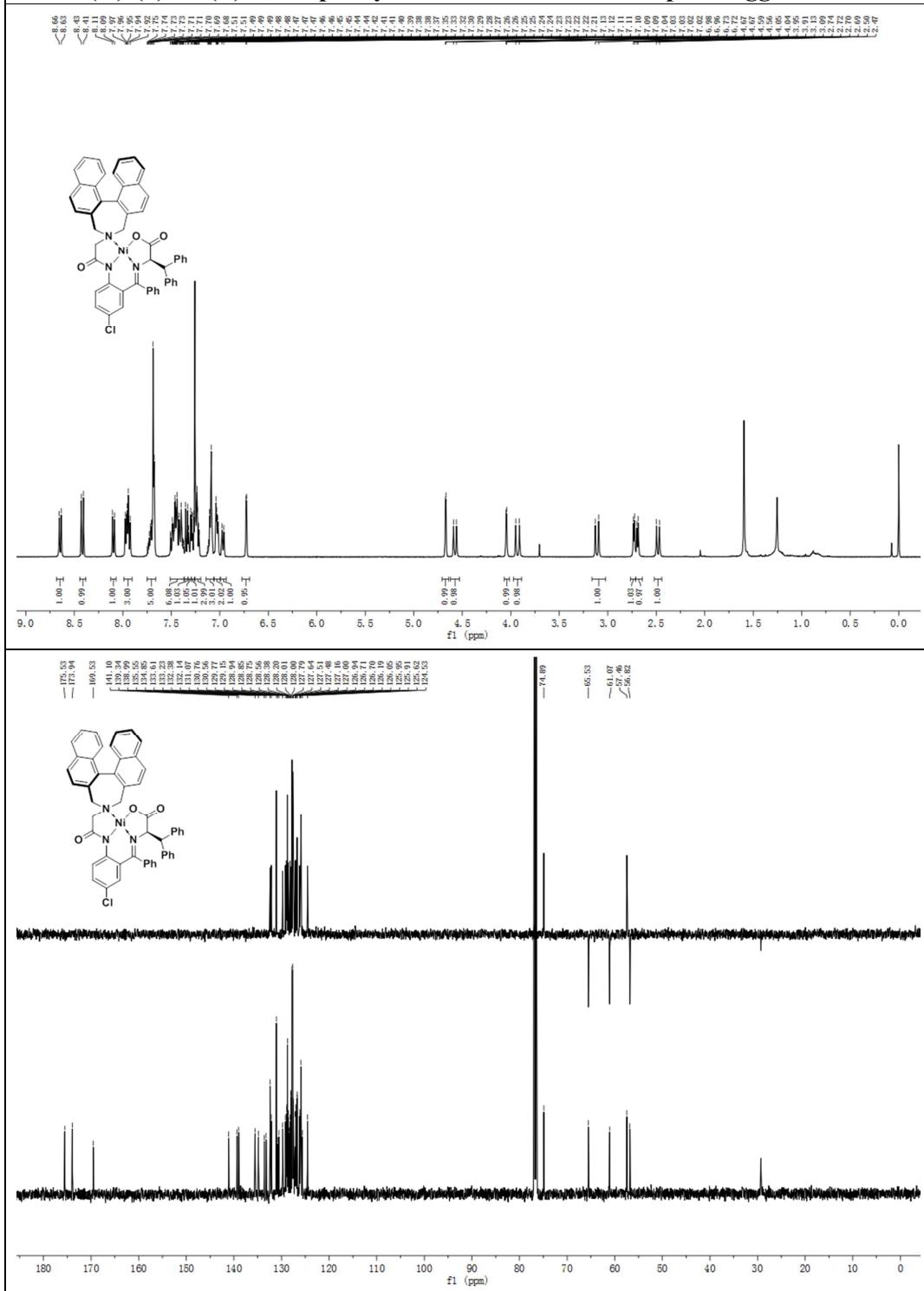
Nickel(II)-(S)-17/(R)-4-Methylphenylalanine Schiff Base Complex 23ee



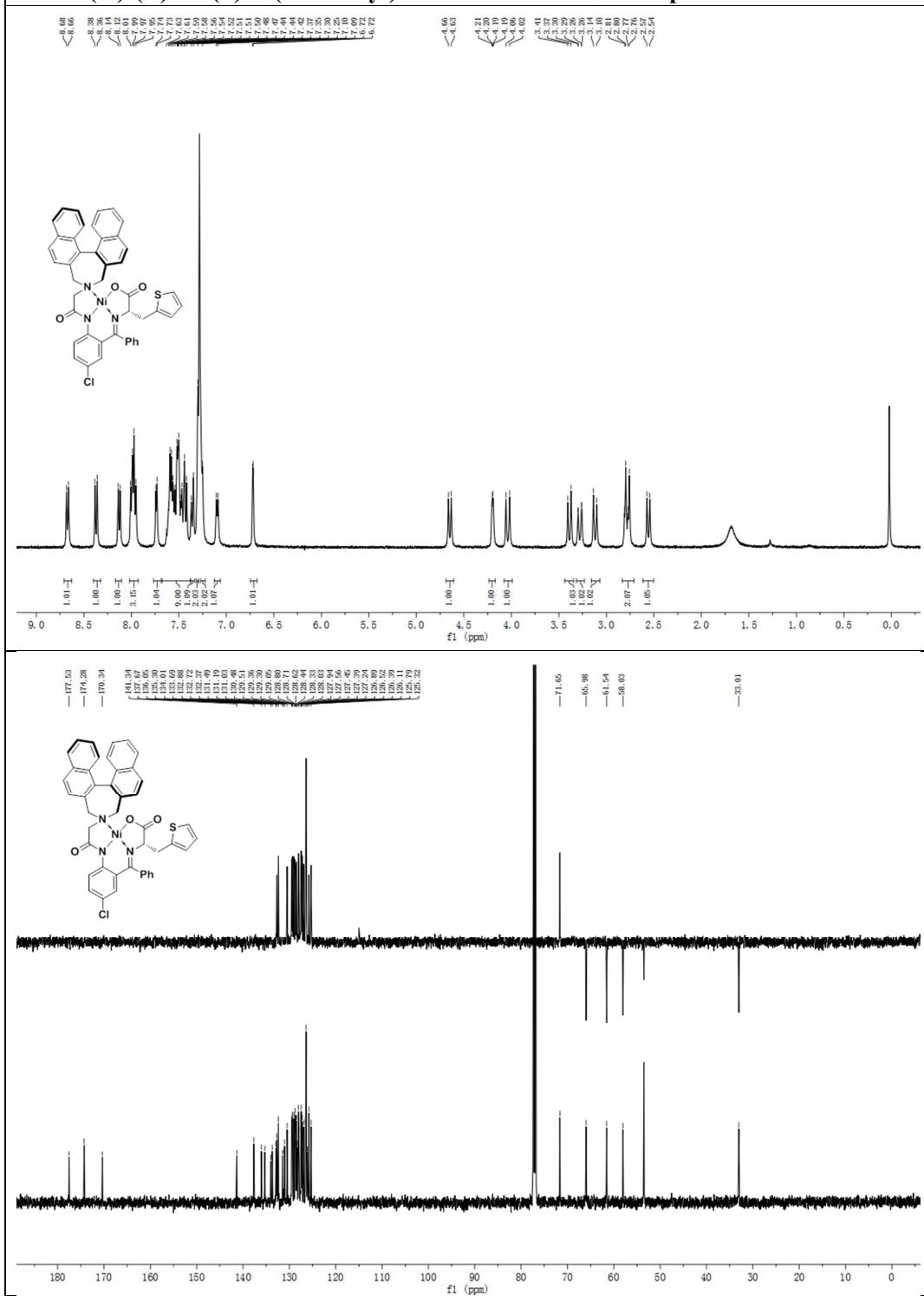
Nickel(II)-(R)-17/(S)-3,4-Difluorophenylalanine Schiff Base Complex 23ff



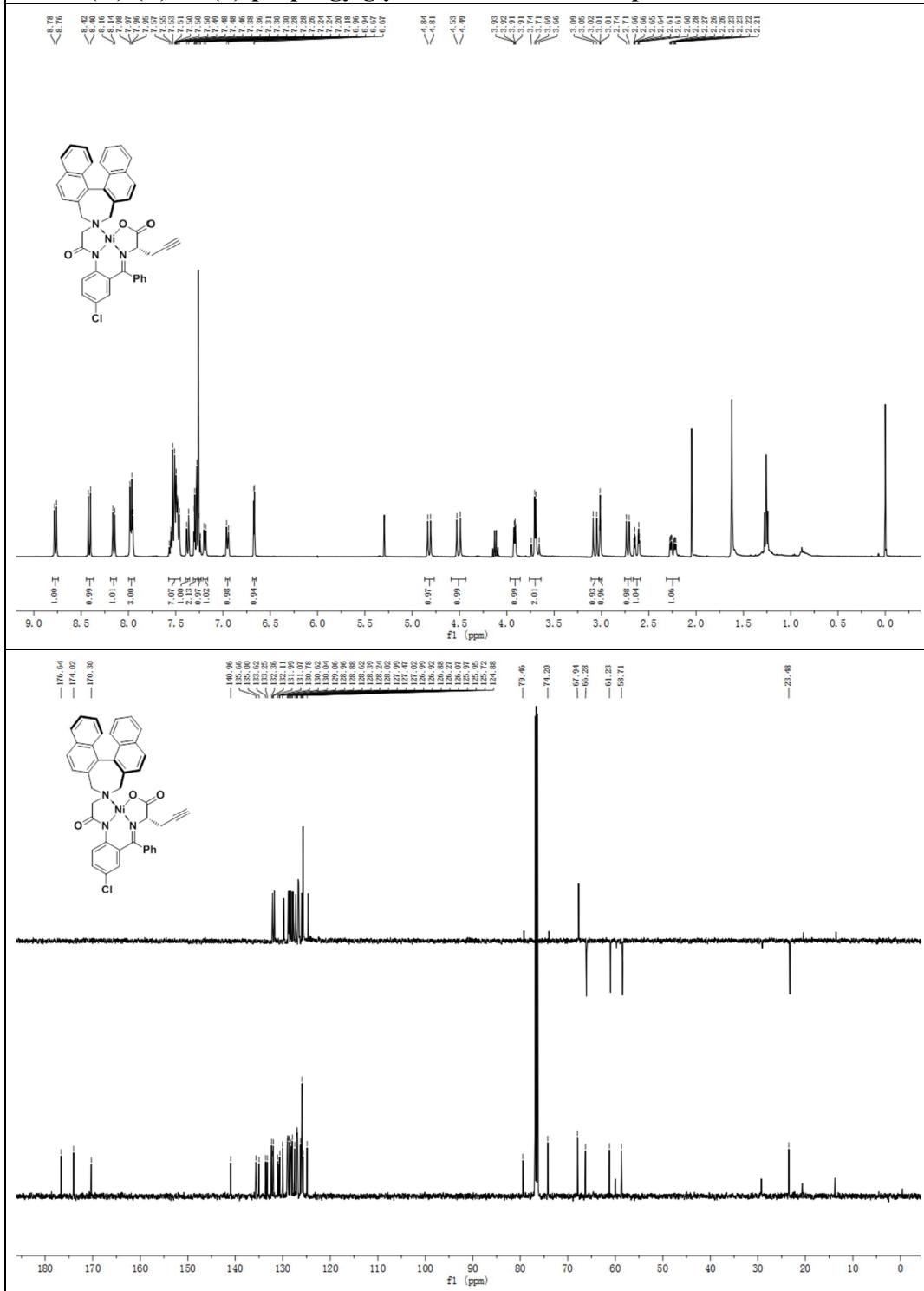
Nickel(II)-(S)-17/(R)-3,3-Diphenylalanine Schiff Base Complex 23gg



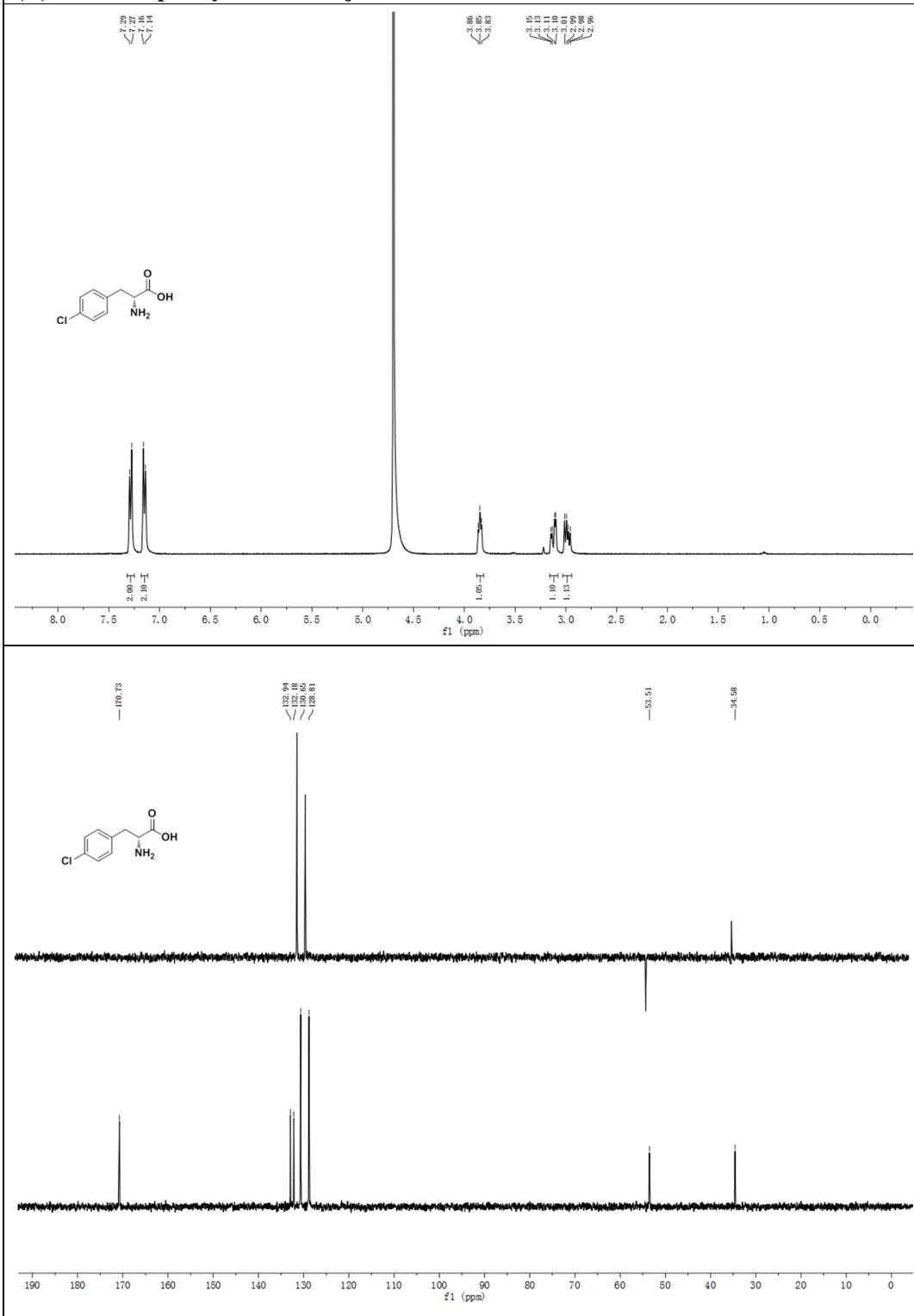
Nickel(II)-(R)-17/(S)-3-(2-Thienyl)alanine Schiff Base Complex 23hh



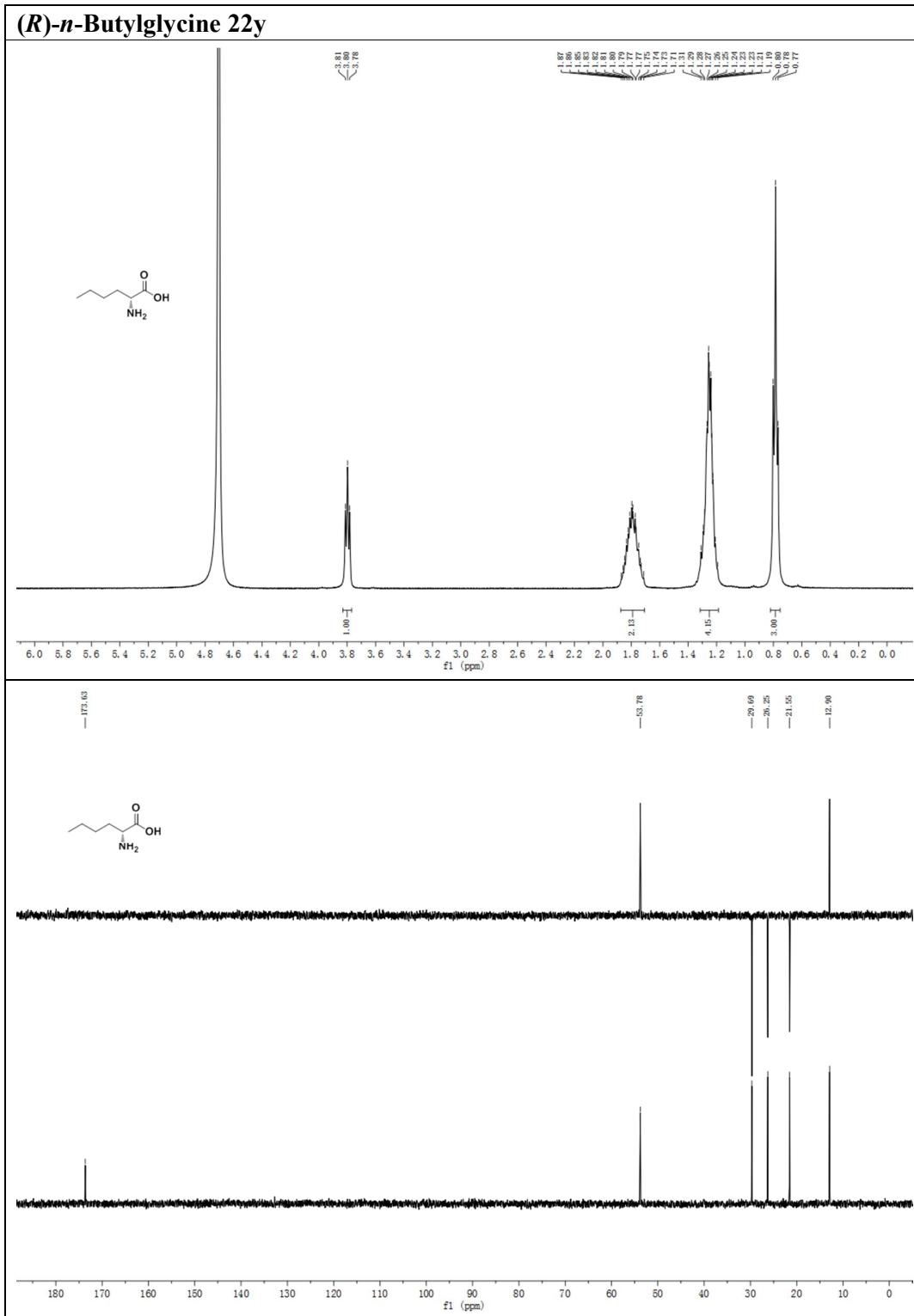
Nickel(II)-(R)-17/(S)-propargylglycine Schiff Base Complex 23ii



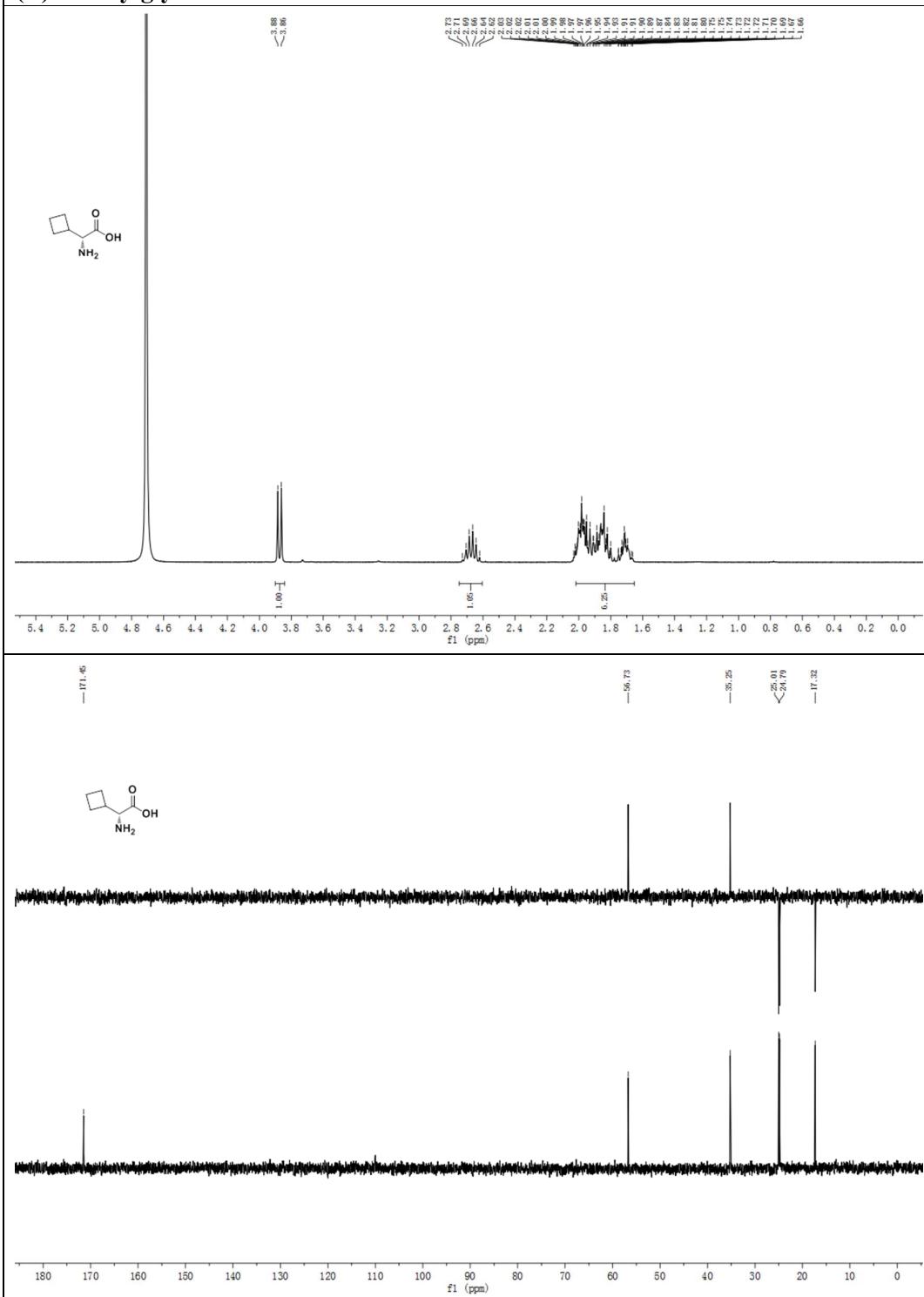
(R)-4-Chlorophenylalanine 22j



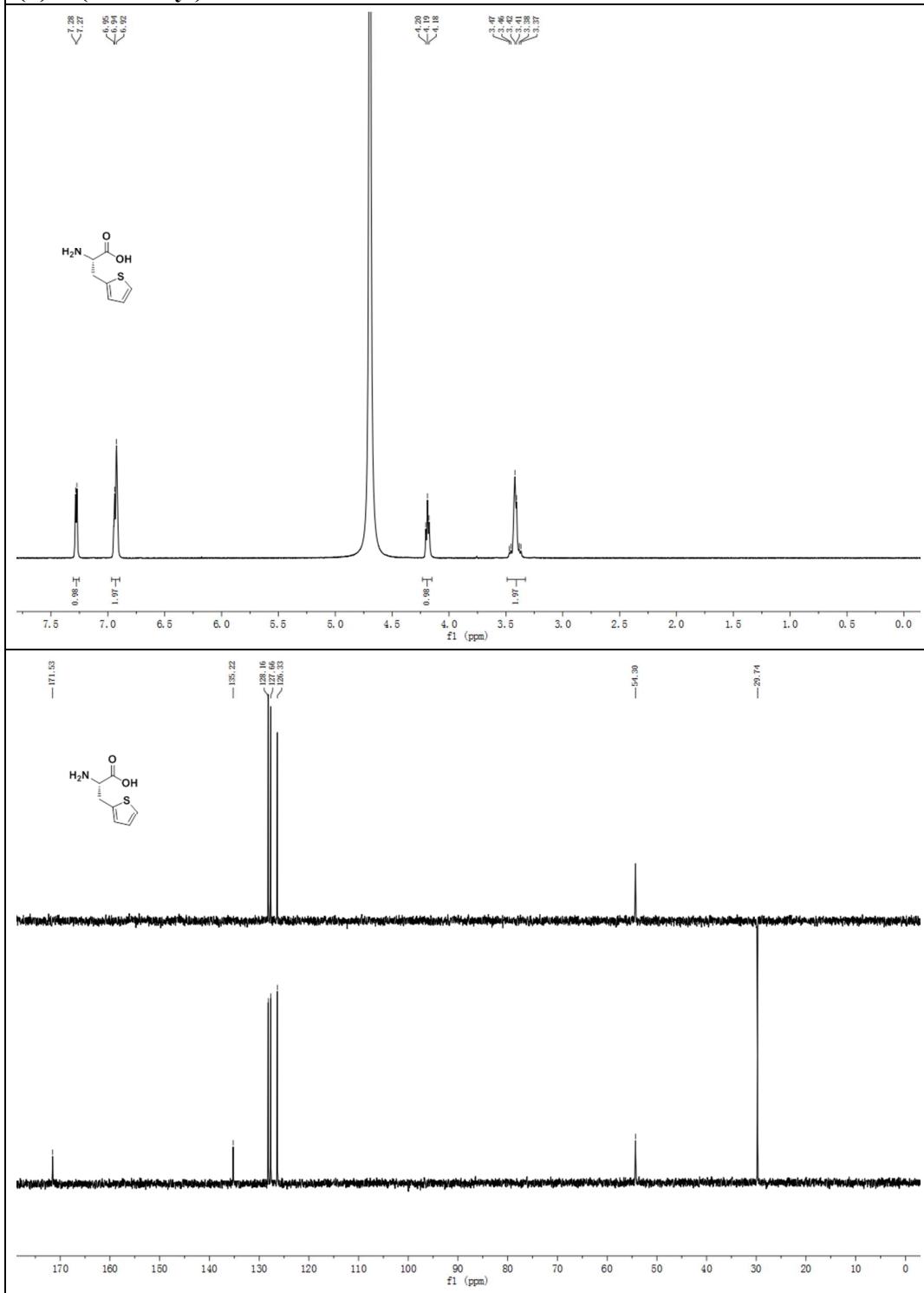
(R)-n-Butylglycine 22y



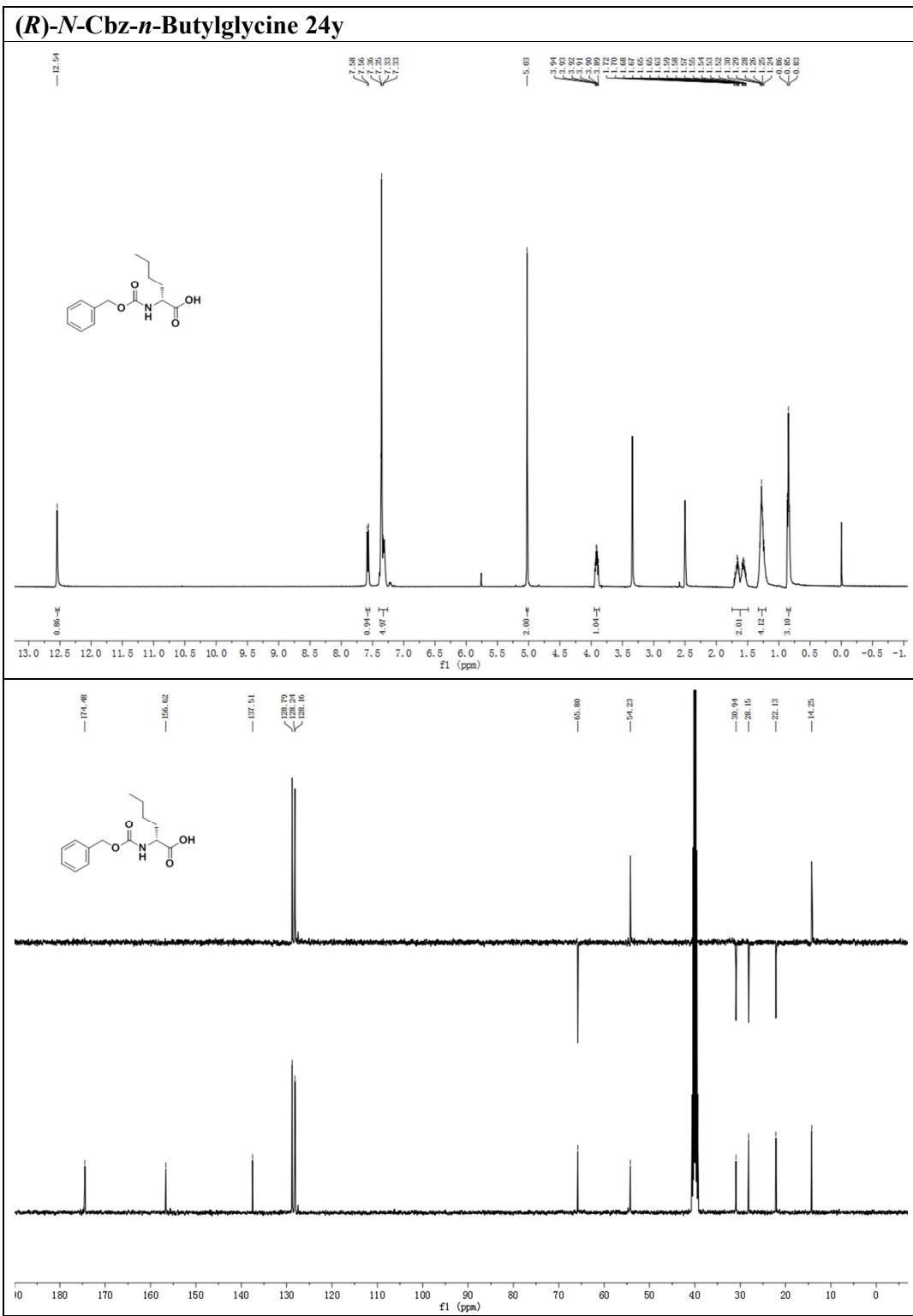
(R)-c-Butylglycine 22bb



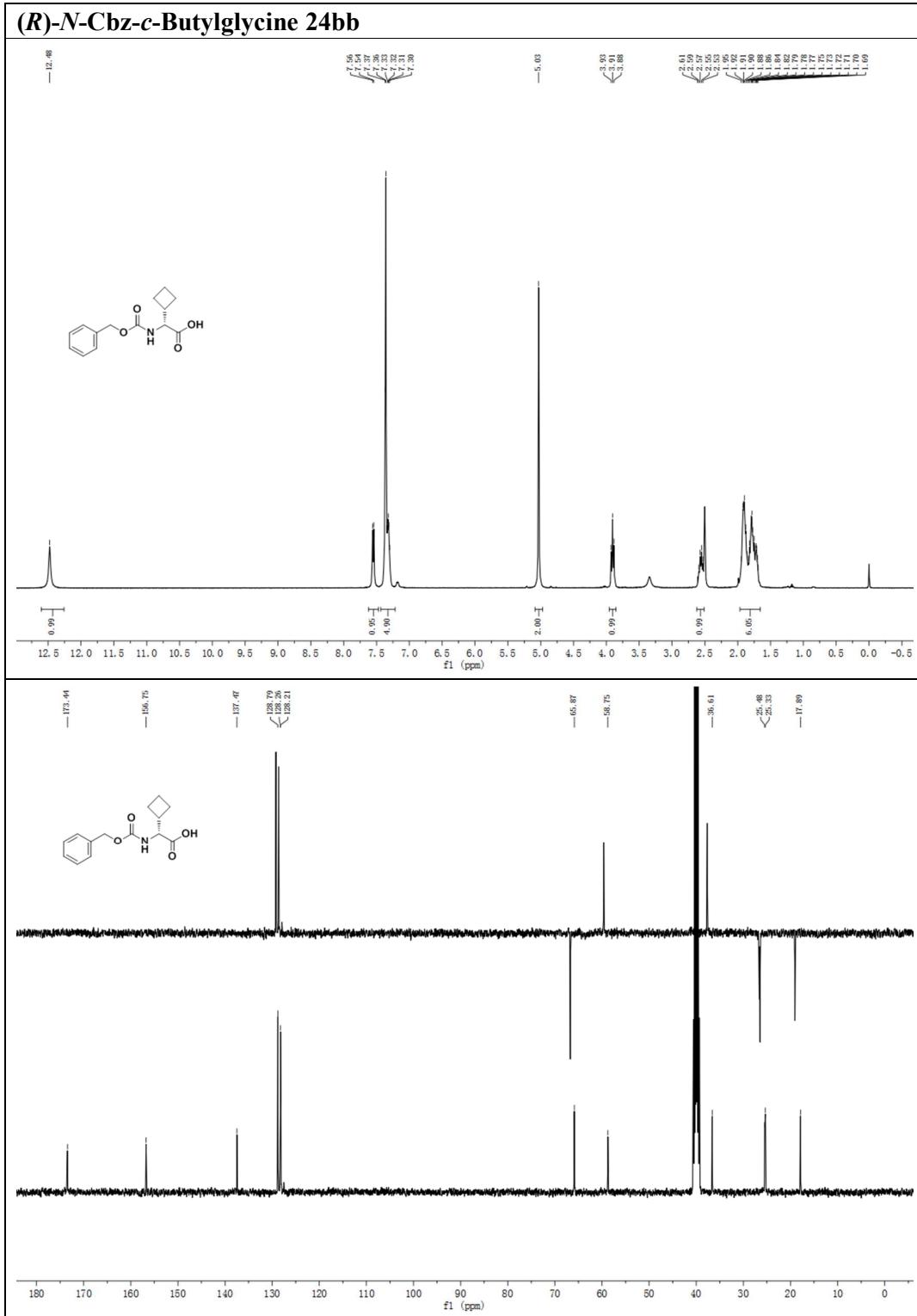
(S)-3-(2-Thienyl)alanine 22hh



(R)-N-Cbz-n-Butylglycine 24y



(R)-N-Cbz-*c*-Butylglycine 24bb



(F) The absolute configuration of (S_a)(R_c)-23j.

X-ray Single Crystal Structure Analysis of (S_a)(R_c)-23j

X-ray crystallographic data of (S_a)(R_c)-23j were solutions at T = 130 K: C₉₃H₇₄Cl₄

N₆Ni₂O₉, M_r = 1678.80, orthorhombic. Space group: P 21 21 21, a = 16.1326(13) Å, b = 19.4409(15) Å, c = 26.943(2) Å, α = 90°, β = 90°, γ = 90°, V = 8450.1(12) Å³, Z = 4. Displacement ellipsoids are drawn at the 50% probability level.

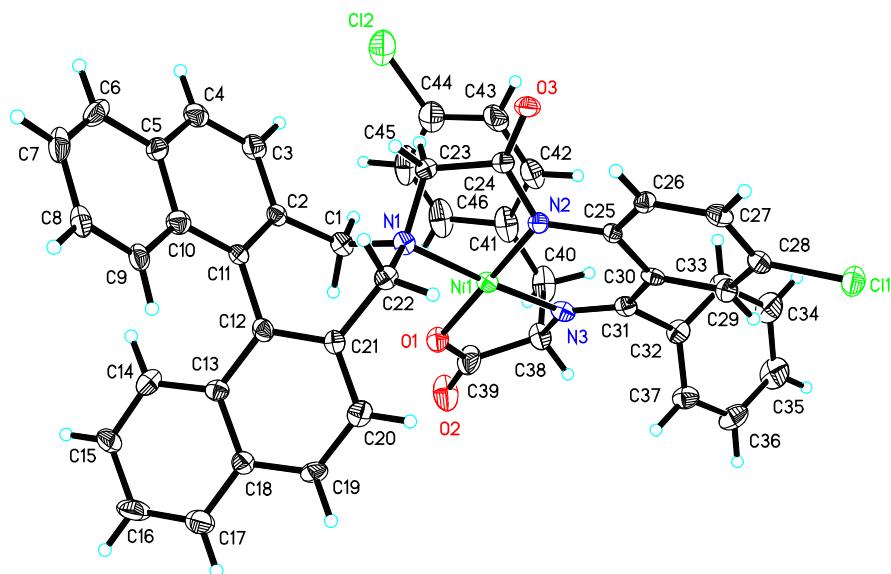


Figure S2. The crystal structure of (S_a)(R_c)-23j by X-ray analysis.

These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif, the CCDC number is 1033608.