Supporting Information

Organocatalyzed Asymmetric Tandem Conjugate Addition-Protonation of Isocyanoacetates to 2-Chloroacrylonitrile

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1. X-Ray crystal data of compound 4d

Table 1. Crystal data and structure refinement for **4d** (CCDC 1047215).

Empirical formula	$C_{13}H_{10}BrClN_2O_2$	
Formula weight	341.59	
Temperature	173(2)	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 5.9701(2) Å	α = 90°.
	b = 7.3338(3) Å	β = 90°.
	c = 31.4408(13) Å	γ = 90°.
Volume	1376.59(9) $Å^3$	
Z	4	
Density (calculated)	1.648 mg/m^3	
Absorption coefficient	3.178 mm^{-1}	
F(000)	680	
Crystal size	0.42 x 0.36 x 0.32 mm^3	
Theta range for data collection	2.59 to 25.00°.	
Index ranges	-7<=h<=6, -8<=k<=8, -37<=l<=37	
Reflections collected	15878	
Independent reflections	2422 [R(int) = 0.0361]	
Data / restraints / parameters	2422 / 0 / 172	
Goodness-of-fit on F^2	1.059	
Final R indices [I>2sigma(I)]	R1 = 0.0235, wR2 = 0.0560	
R indices (all data)	R1 = 0.0256, wR2 = 0.0569	
Largest diff. peak and hole	0.336 and -0.194 $e.Å^{-3}$	

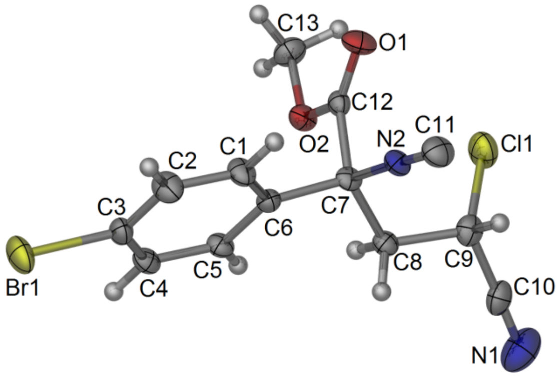
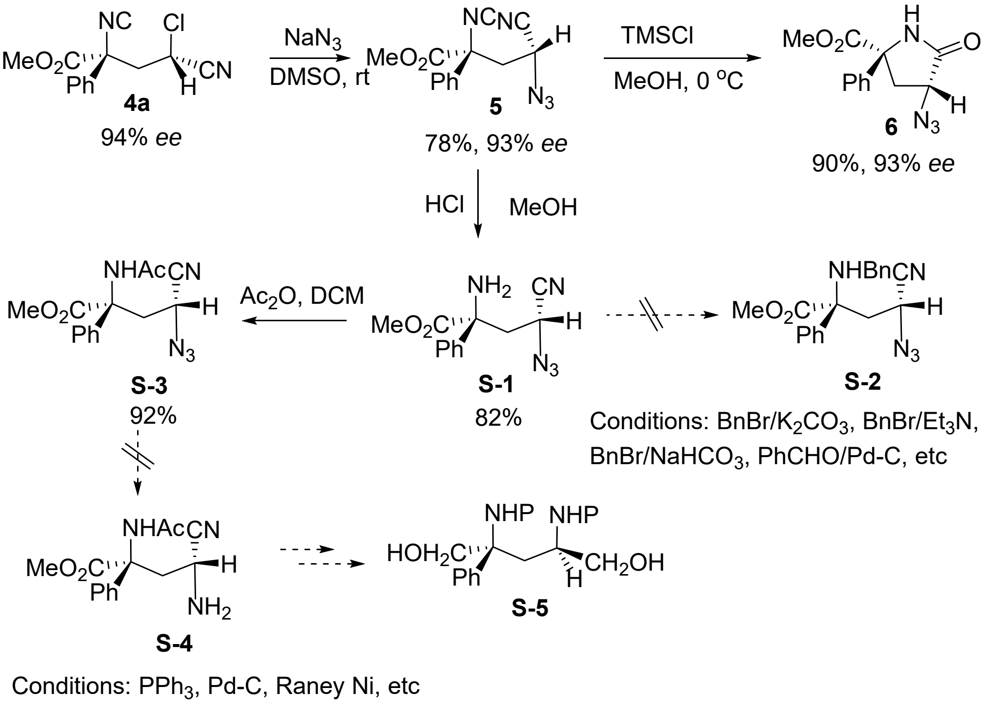


Figure S1. ORTEP plot of the X-ray crystal structure of 4d (displacement ellipsoids are drawn at the 50% probability level)

2. Investigation on the transformation of adduct 4a

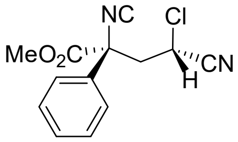
Since treatment of **5** with trimethylsilyl chloride (TMSCl) in methanol, a γ-lactam **6** rather than the expected diester was obtained. To avoid the cyclization during the esterification, we switched the sequence and intended to hydrolyze the isocyano group to amino group first, followed by protection of amino group. The isocyano group in **5** can be easily hydrolyzed into free amino group in HCl/MeOH to give compound **S-1** in 82% yield. Considering that both the N-Bn protecting group and azide can be transformed into free amino group under the catalytic hydrogenation conditions, we tried to synthesize the compound **S-2**. However, to our surprise, the desired **S-2** can't be afforded under the various different N-benzylation or reductive amination conditions, such as $BnBr/K_2CO_3$, $BnBr/Et_3N$, $BnBr/NaHCO_3$, PhCHO/Pd-C, etc. Although N-Ac protected compound **S-3** can be obtained in 92% yield from **S-1**, no desired **S-4** compound were obtained under the various reduction conditions (PPh_3, Pd-C, Raney Ni, etc), either no reaction or complex reaction was observed. The synthetic transformation of compound **S-1** to **S-5** were still undergoing (Scheme S-1).



Scheme S1. Investigation on the synthetic transformation of azide 4a

3. Copies of HPLC analysis spectra of compounds 4-6

4a (Table 3, entry 1)



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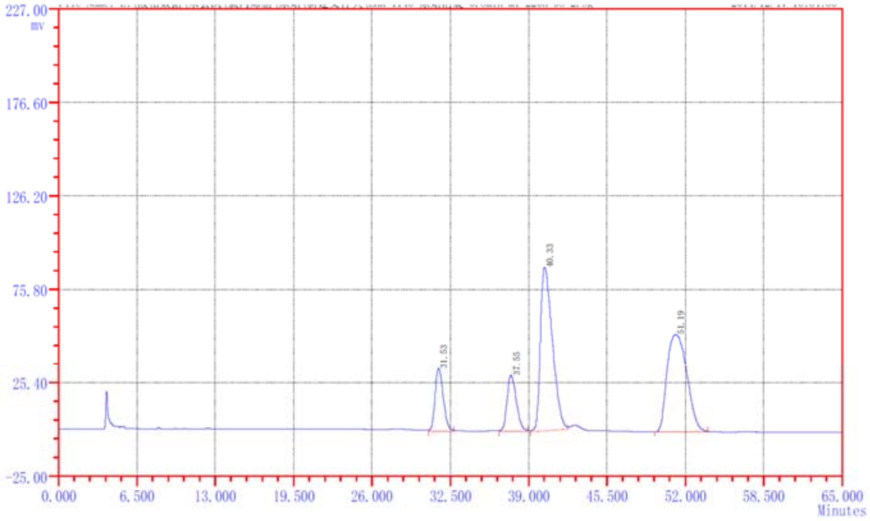

ID	组分名	保留时间	峰高	峰面积	浓度	拖尾因子	理论塔板
1		31.527	33952	1603876.5	10.4701	1.24	8877
2		37.550	30240	1606581.2	10.4878	1.23	9956
3		40.325	88212	6100398.4	39.8235	1.61	6777
4		51.190	52633	6007719.1	39.2185	1.27	4009
	Σ:		205037	15318575.1	100.0000		

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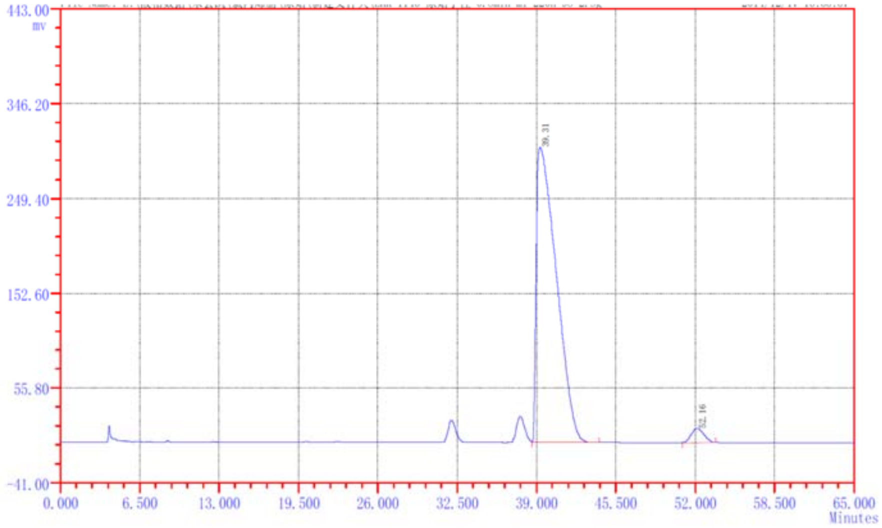
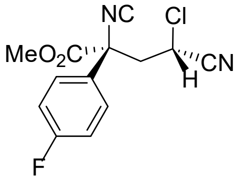


ID	组分名	保留时间	峰高	峰面积	浓度	拖尾因子	理论塔板
1		39.307	301718	34387339.3	96.9768	3.26	2371
2		52.163	14763	1072019.5	3.0232	1.15	10285
	Σ:		316481	35459358.8	100.0000		

4b (Table 3, entry 2)



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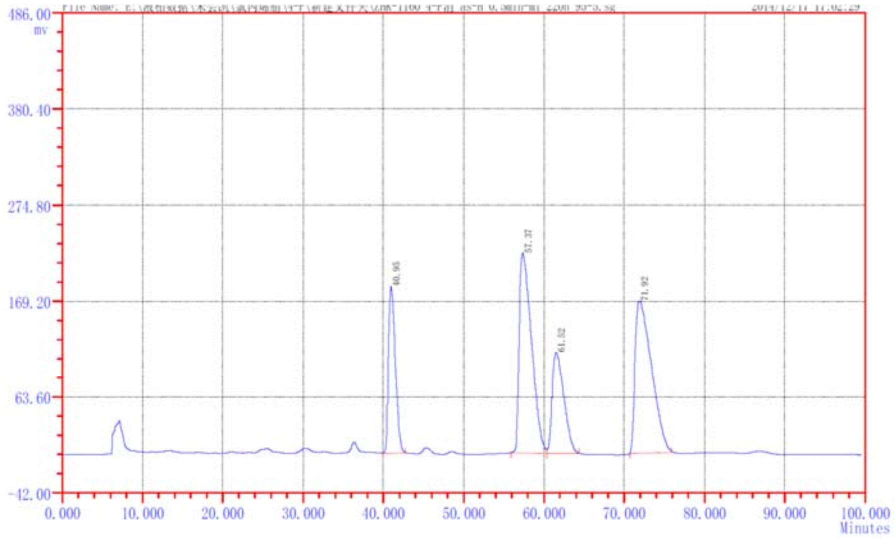

ID	组分名	保留时间	峰高	峰面积	浓度	拖尾因子	理论塔板
1		40.950	184774	10961133.6	15.6528	1.50	9497
2		57.367	220502	23589839.1	33.6870	2.01	5731
3		61.518	111567	11342792.7	16.1979	1.61	7297
4		71.920	168275	24132706.7	34.4623	2.21	5012
	Σ:		685118	70026472.1	100.0000		

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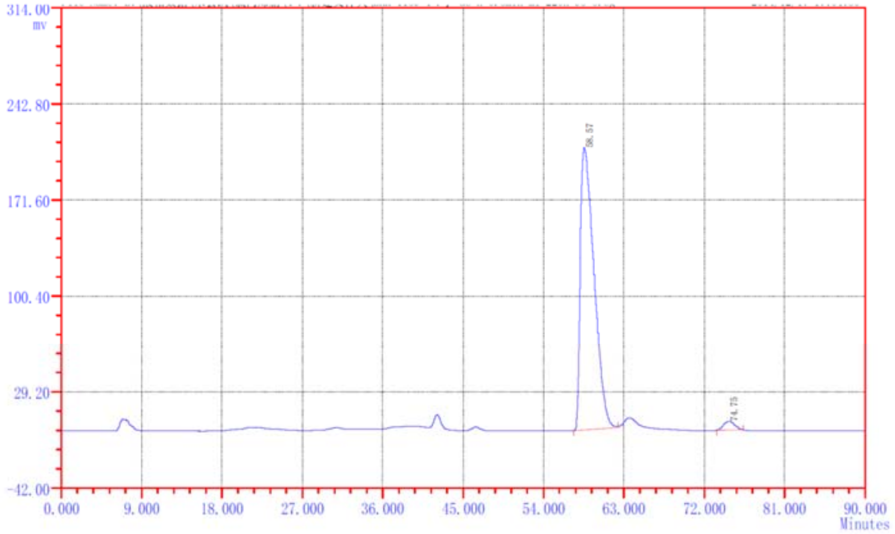
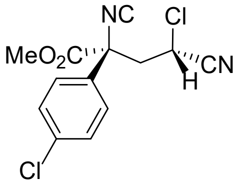


ID	组分名	保留时间	峰高	峰面积	浓度	拖尾因子	理论塔板
1		58.572	209695	22440341.3	97.4050	2.12	5971
2		74.752	6615	597841.0	2.5950	1.16	13635
	Σ:		216310	23038182.3	100.0000		

4c (Table 3, entry 3)



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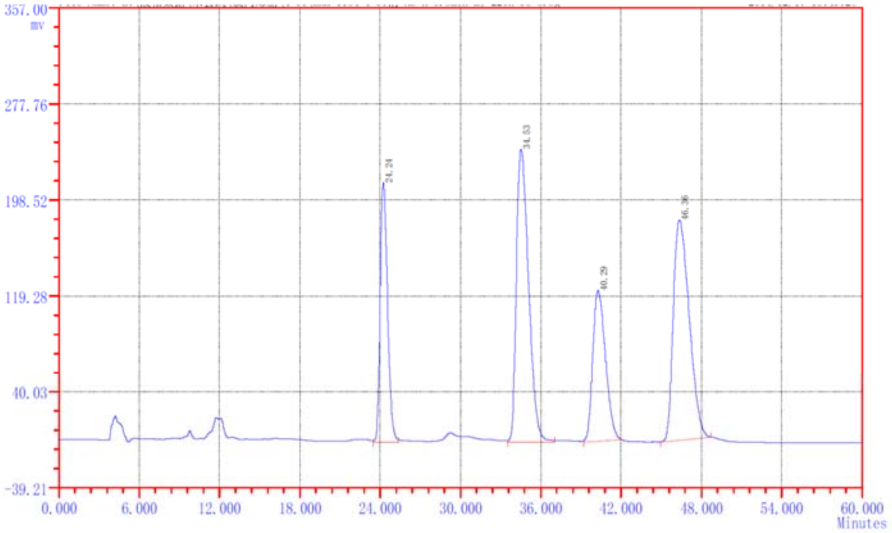

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1		24.240	214396	8170223.6	17.4206	1.27	8064
2		34.530	242186	15370403.4	32.7729	1.47	5900
3		40.290	124637	8248415.2	17.5873	1.31	7387
4		46.363	182139	15110749.1	32.2192	1.48	6225
	Σ:		763358	46899791.2	100.0000		

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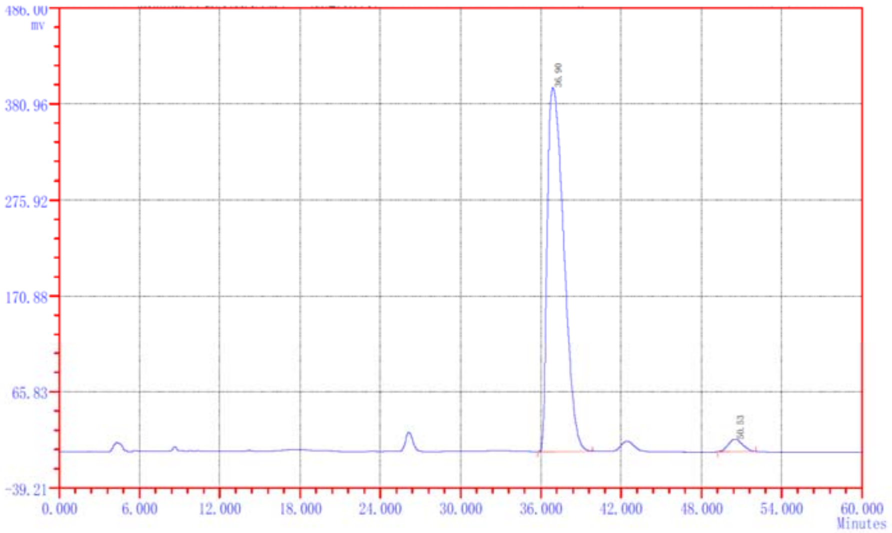
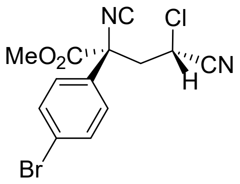


ID	组分名	保留时间	峰高	峰面积	浓度	拖尾因子	理论塔板
1		36.903	398704	34187876.4	97.0475	1.73	3692
2		50.527	13606	1040105.7	2.9525	1.14	8707
	Σ:		412310	35227982.1	100.0000		

4d (Table 3, entry 4)



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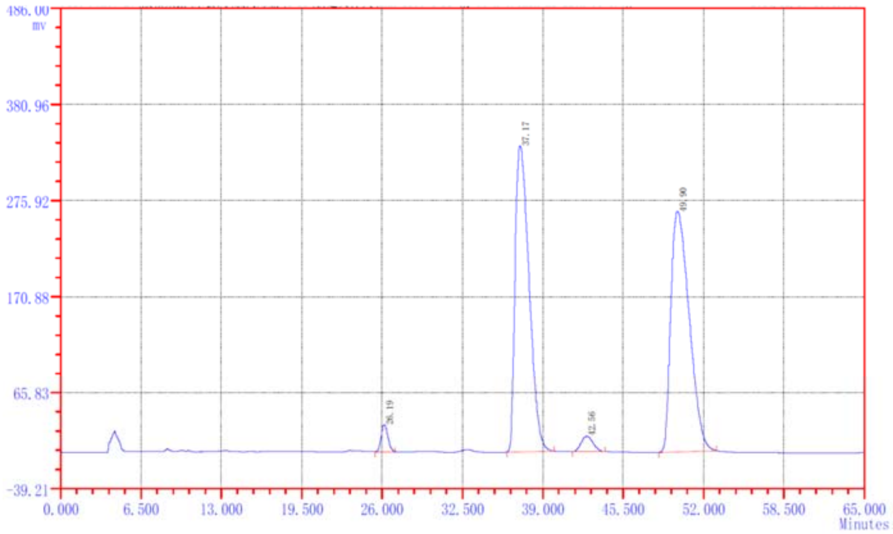

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1		26.185	29920	1131028.2	2.0236	1.14	9563
2		37.168	334826	26405491.2	47.2435	1.62	4427
3		42.557	17081	1132885.8	2.0269	1.12	8206
4		49.903	263039	27222868.4	48.7060	1.57	4634
	Σ:		644866	55892273.7	100.0000		

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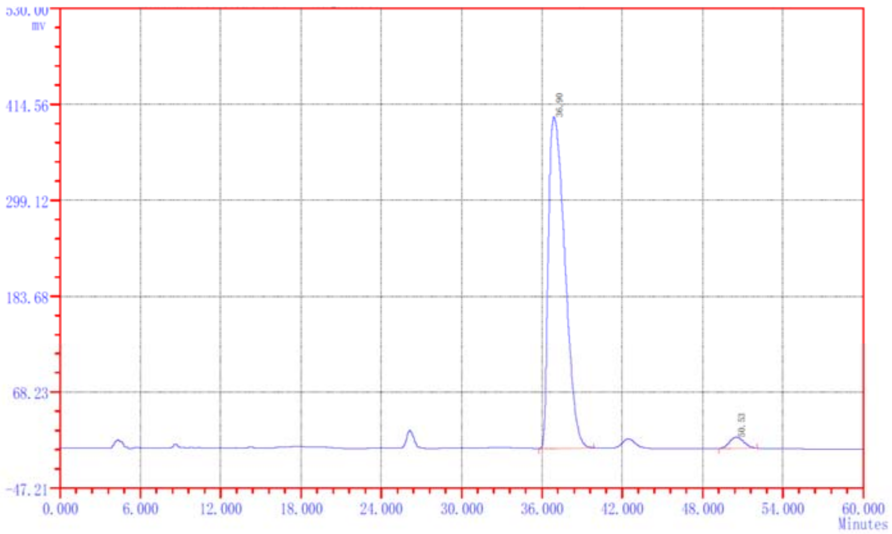

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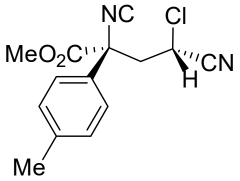
1		36.903	398704	34187876.4	97.0475	1.73	3692
2		50.527	13606	1040105.7	2.9525	1.14	8707
	Σ:		412310	35227982.1	100.0000		

4e (Table 3, entry 5)



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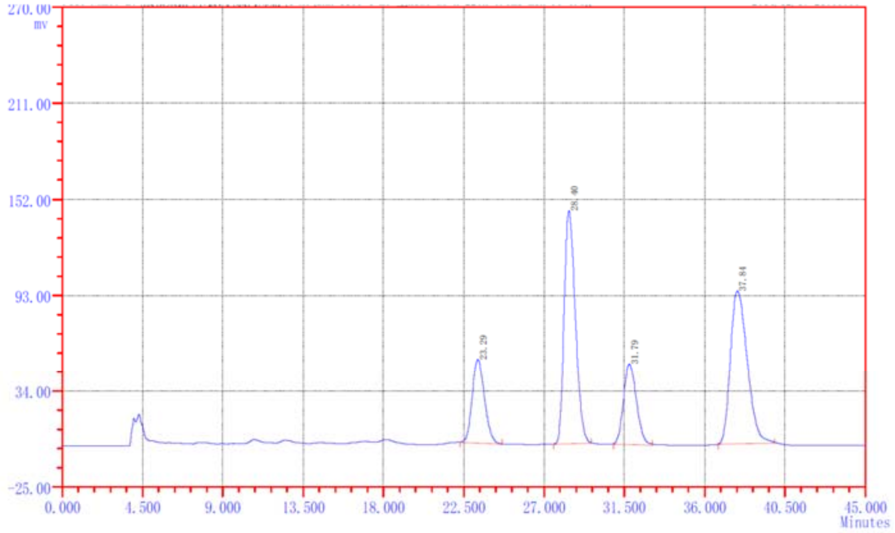

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1		23.287	51740	2482798.7	14.1909	1.13	4694
2		28.395	143559	6290989.3	35.9574	1.29	8368
3		31.788	49657	2501927.9	14.3003	1.13	7934
4		37.845	94478	6219969.9	35.5514	1.32	6586
	Σ:		339434	17495685.8	100.0000		

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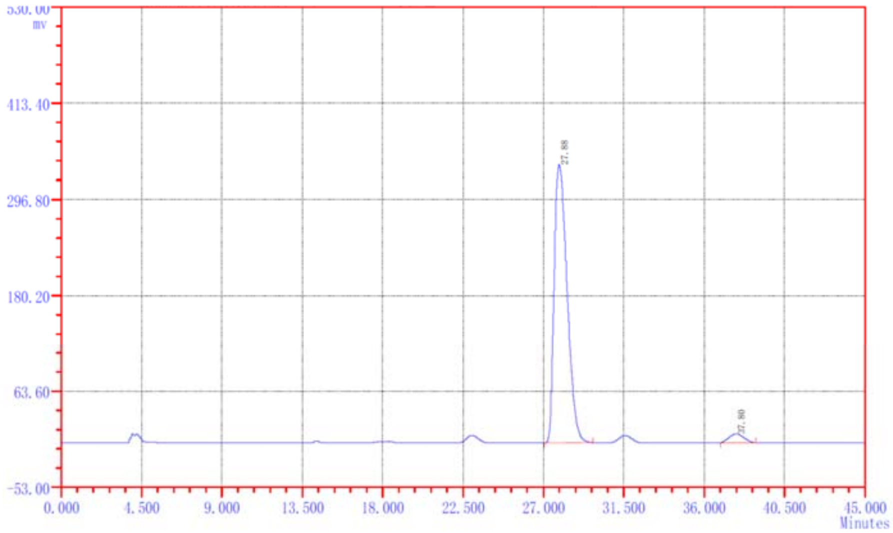

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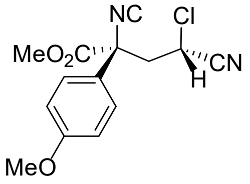
1		27.880	337873	17070900.5	96.4568	1.50	6069
2		37.795	10950	627083.6	3.5432	1.08	8681
	Σ:		348823	17697984.1	100.0000		

4f (Table 3, entry 6)



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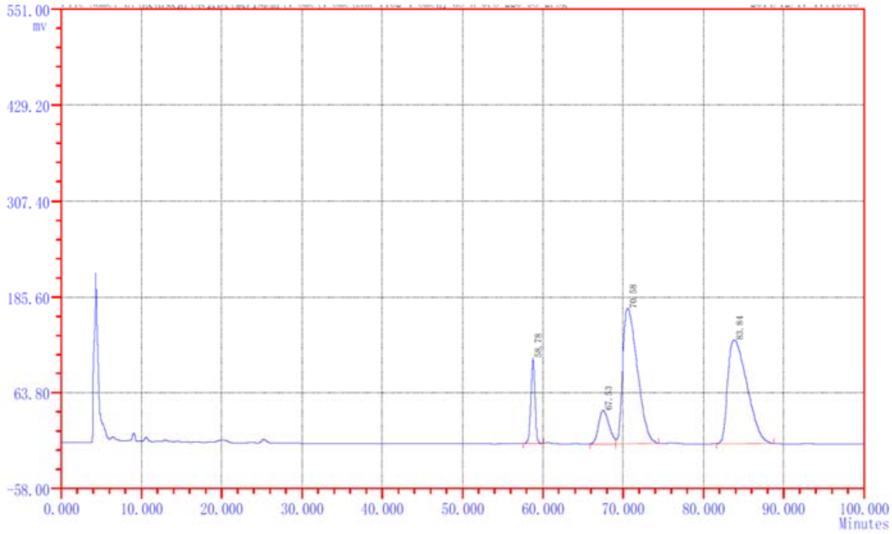

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1		58.780	109907	3834718.6	7.4166	0.95	56568
2		67.525	42468	3836657.1	7.4203	1.14	11135
3		70.577	172451	21864485.6	42.2871	1.65	6176
4		83.843	132836	22168983.0	42.8760	1.71	5030
	Σ:		457662	51704844.3	100.0000		

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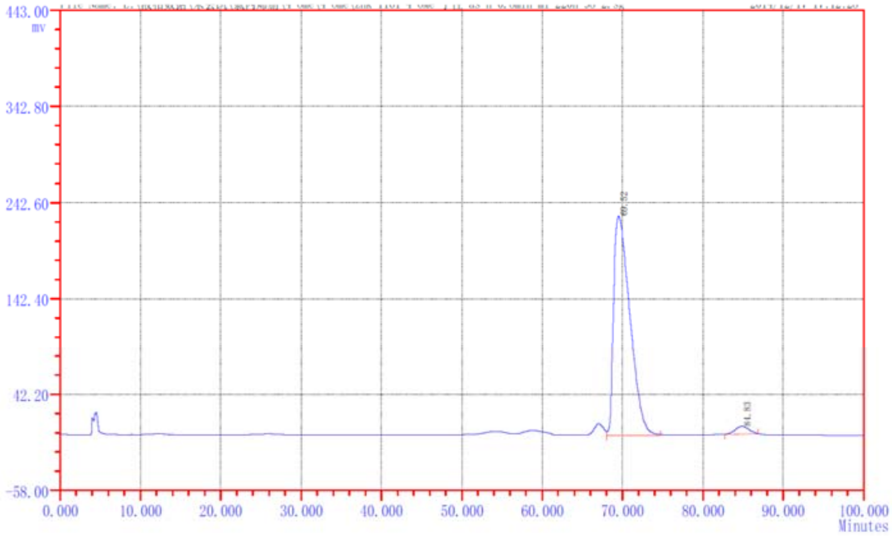

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1		69.517	229648	32304574.4	96.9119	1.96	4867
2		84.830	8409	1029386.8	3.0881	1.05	9571
	Σ:		238057	33333961.3	100.0000		

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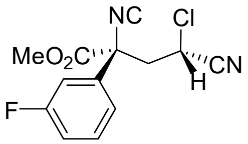

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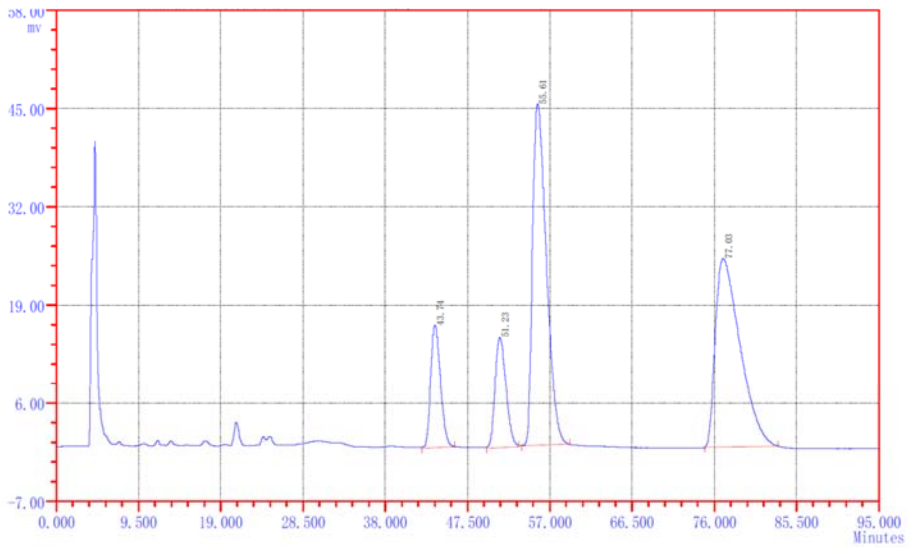

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1		43.737	16241	1277840.5	10.1792	1.27	6159
2		51.228	14649	1277701.4	10.1781	1.27	6875
3		55.612	45178	5005093.7	39.8704	1.58	5022
4		77.028	24995	4992778.2	39.7723	1.95	2964
	Σ:		101063	12553413.9	100.0000		

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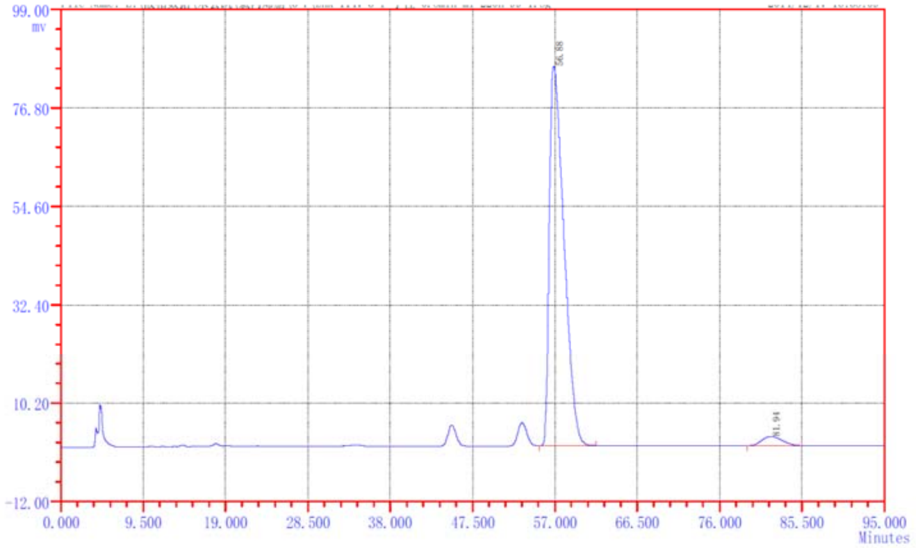

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1		56.875	85698	10014062.5	96.5333	1.87	4722
2		81.943	2144	359622.8	3.4667	0.00	4757
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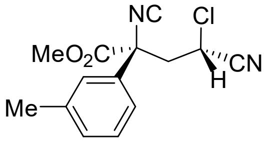
4h (Table 3, entry 8)



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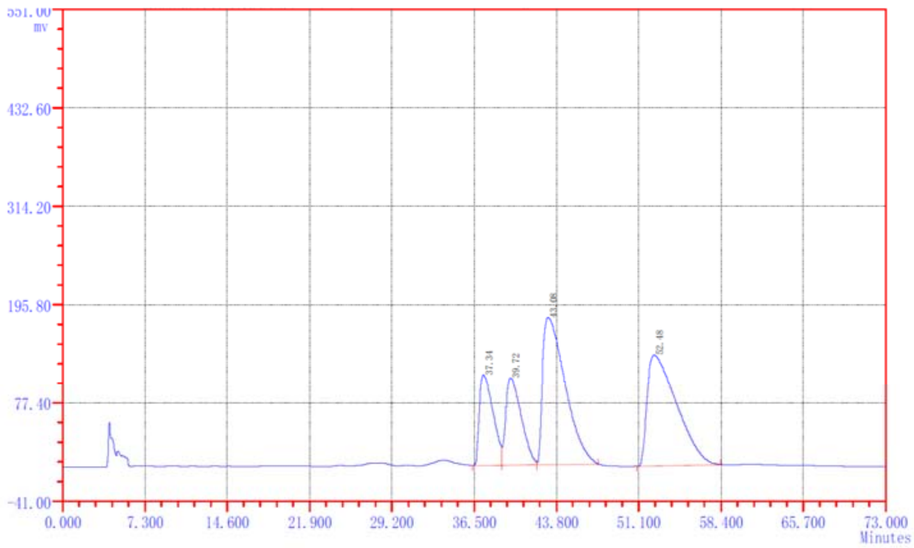

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1		37.337	109326	9246965.0	13.4863	1.69	3884
2		39.723	105522	10059312.0	14.6711	1.93	3461
3		43.075	177827	24865931.3	36.2660	2.70	1891
4		52.485	133997	24393221.8	35.5766	2.58	1657
	Σ:		526672	68565430.1	100.0000		

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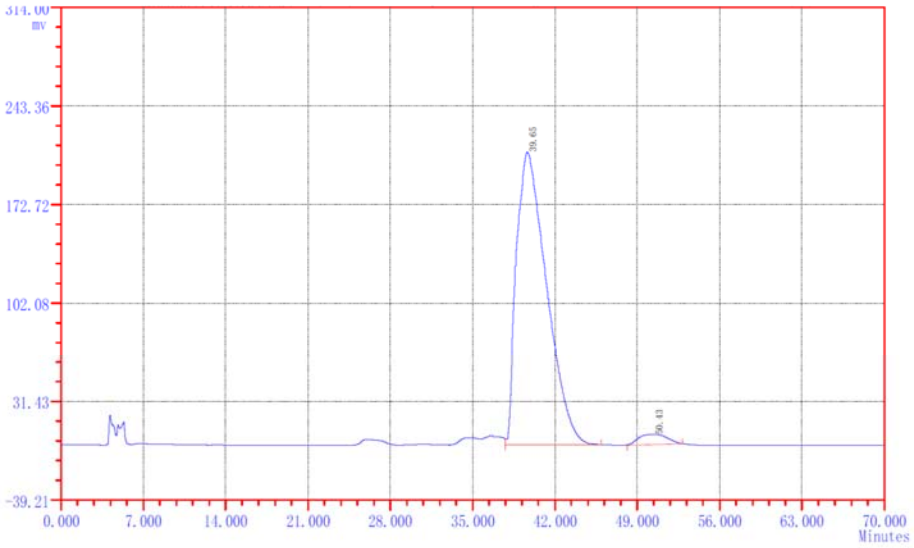

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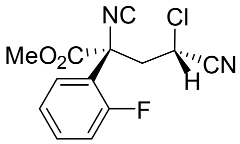
1		39.653	210298	37563838.8	96.7951	1.77	982
2		50.427	7376	1243734.5	3.2049	1.09	1783
	Σ:		217674	38807573.3	100.0000		

4i (Table 3, entry 9)



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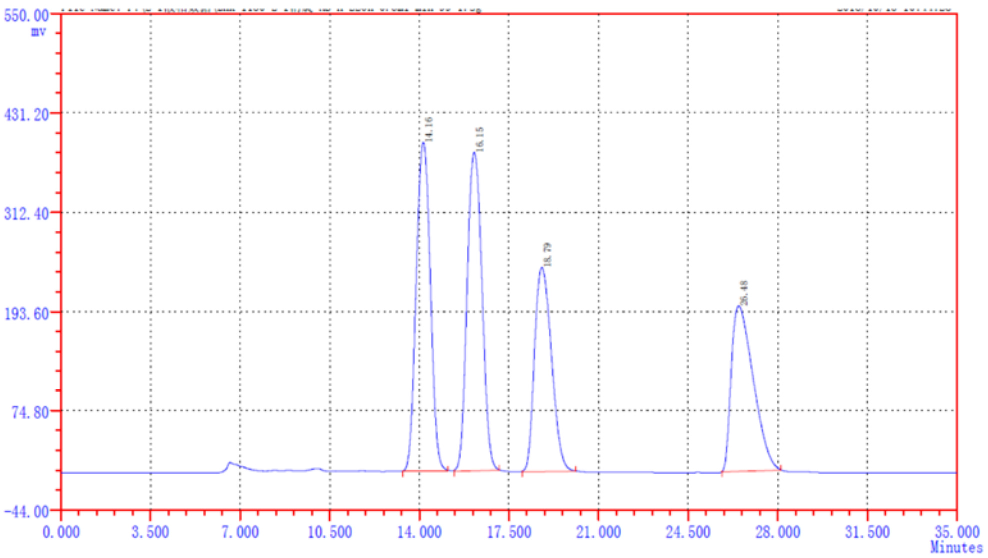

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1		14.157	393780	15156940.7	28.2799	1.03	2696
2		16.147	381025	15328222.1	28.5995	1.09	3211
3		18.787	244594	11281149.7	21.0484	1.26	3307
4		26.477	198267	11829896.2	22.0723	1.77	3925
	Σ:		1217666	53596208.6	100.0000		

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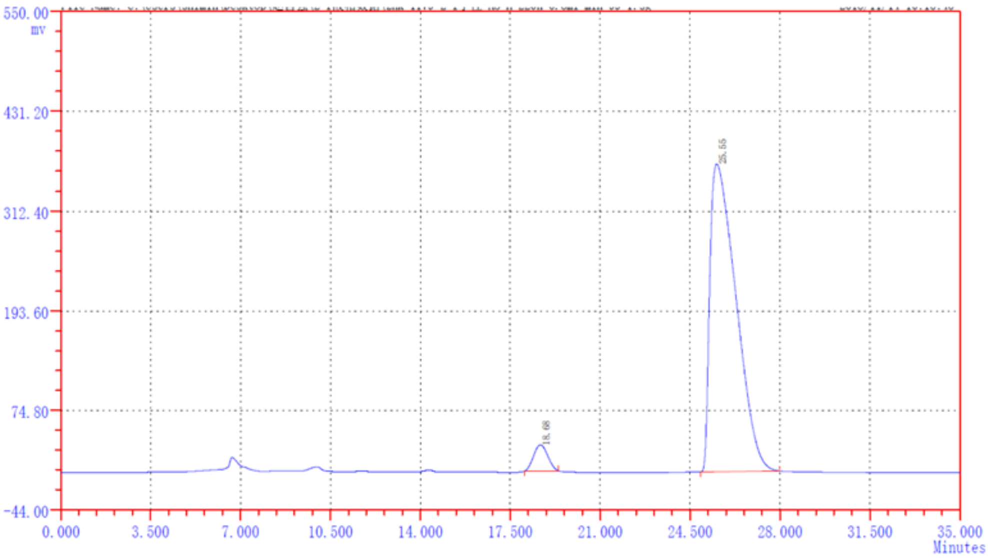

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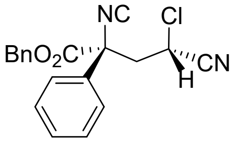
1		18.683	31126	1180834.7	4.3590	1.06	4834
2		25.547	366959	25908983.3	95.6410	2.32	2609
	Σ:		398085	27089818.0	100.0000		

4k (Table 3, entry 11)



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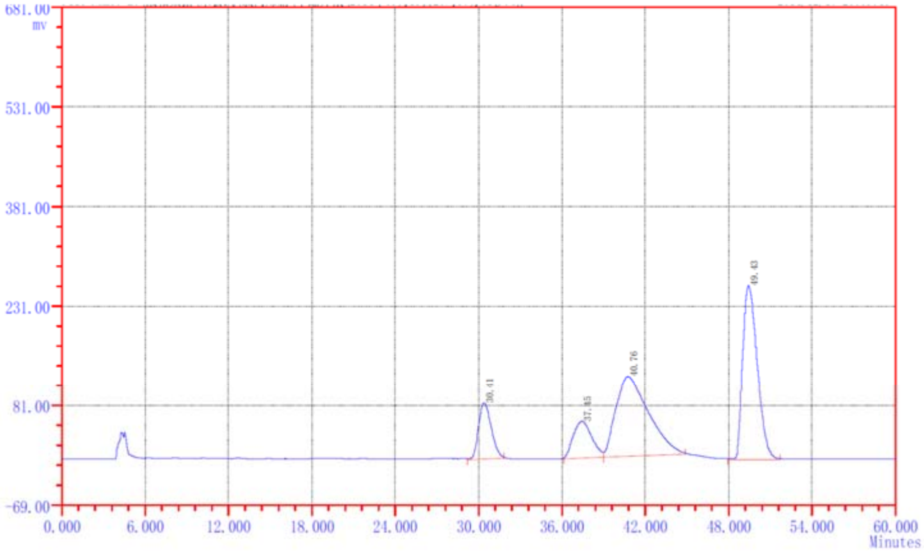

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1		30.407	84165	5390229.7	10.8421	1.28	4493
2		37.450	55280	5183689.8	10.4266	1.15	3179
3		40.760	120796	19812726.8	39.8520	1.62	1231
4		49.432	262915	19329159.1	38.8793	1.45	9010
	Σ:		523156	49715805.4	100.0000		

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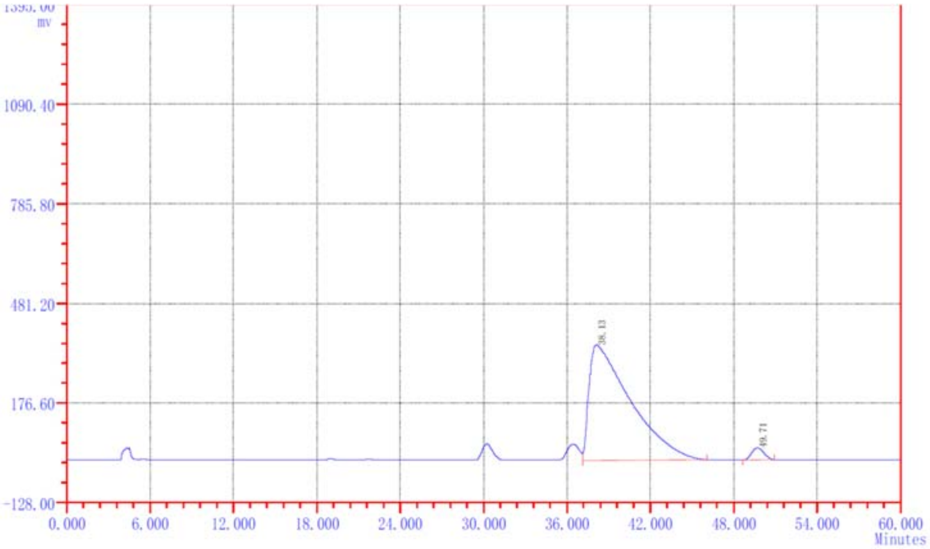

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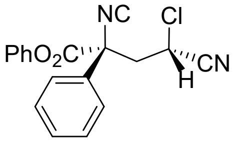
1		38.125	354200	73409485.0	96.9655	3.73	674
2		49.712	37288	2297303.2	3.0345	1.13	12976
	Σ:		391488	75706788.2	100.0000		

4l (Table 3, entry 12)



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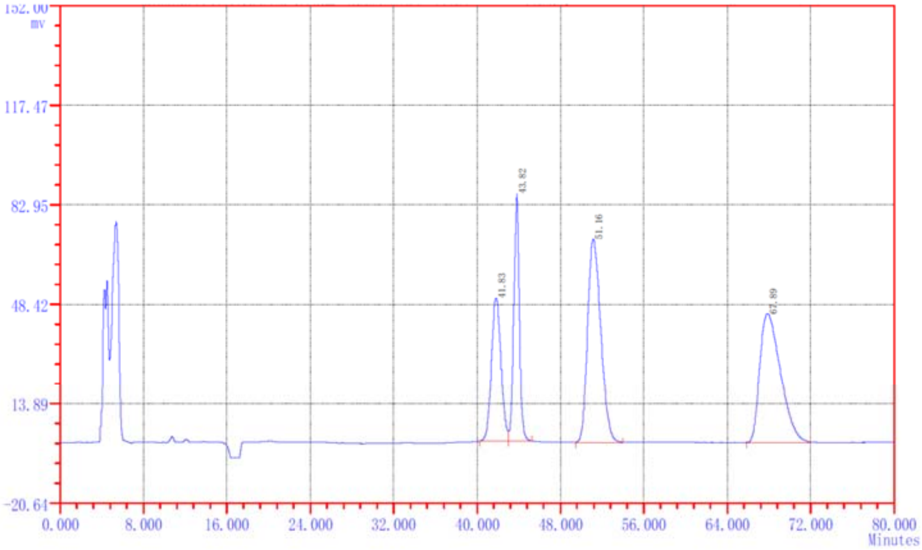

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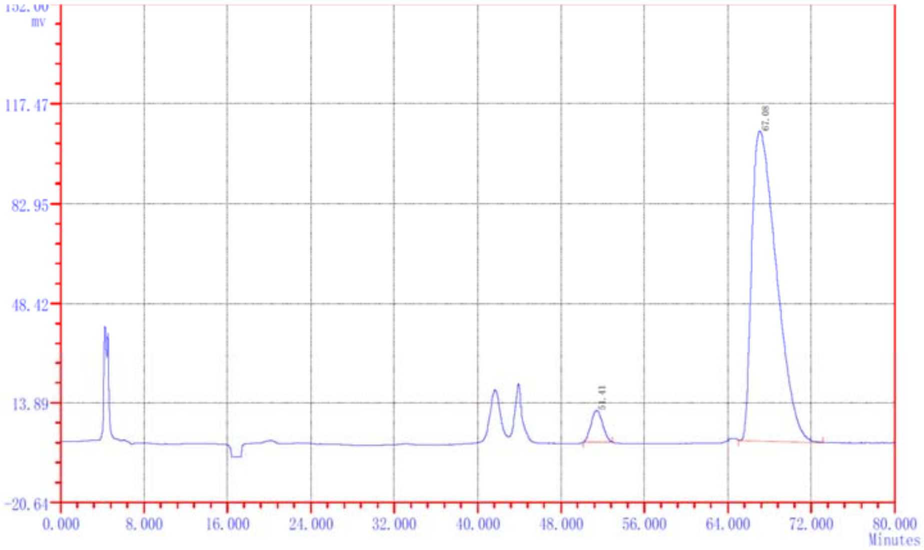
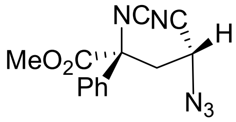
2		43.818	86087	3191099.1	16.8617	0.98	27850
3		51.157	70712	6268916.8	33.1248	1.24	6636
4		67.888	44920	6266655.1	33.1128	1.52	4720
	Σ:		251550	18925156.4	100.0000		

Enantioenriched

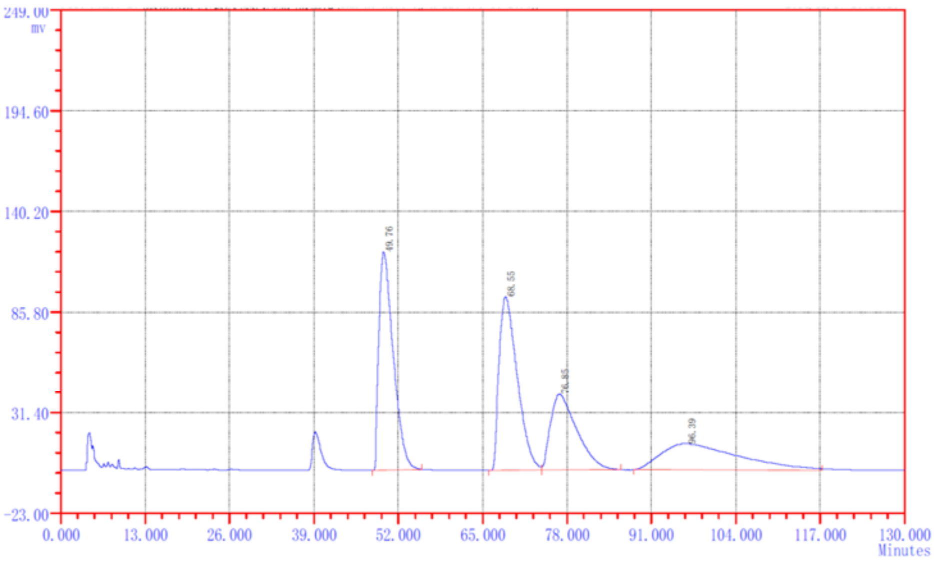


ID	组分名	保留时间	峰高	峰面积	浓度	拖尾因子	理论塔板
1		51.415	11029	859657.3	4.6043	1.08	8672
2		67.080	107364	17811180.4	95.3957	1.82	3259
	Σ:		118393	18670837.7	100.0000		

5 (Scheme 3)

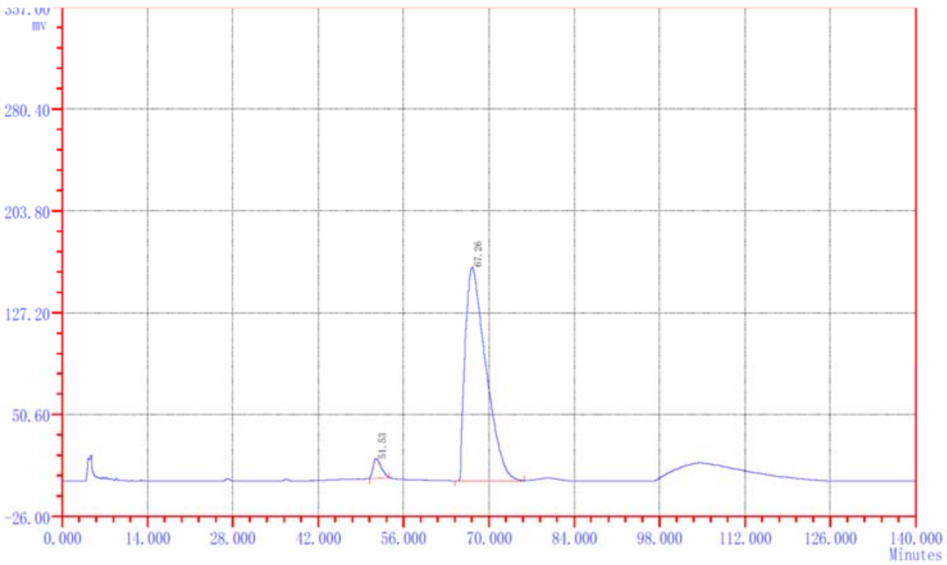


Racemic



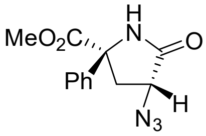
ID	组分名	保留时间	峰高	峰面积	浓度	拖尾因子	理论塔板
1		49. 757	118311	18199294. 5	30. 3634	1. 94	2085
2		68. 552	94036	18367845. 0	30. 6446	1. 76	2455
3		76. 852	41146	11533089. 7	19. 2416	1. 81	1498
4		96. 388	14159	11837993. 8	19. 7503	1. 90	265
	Σ:		267652	59938223. 0	100. 0000		

Enantioenriched

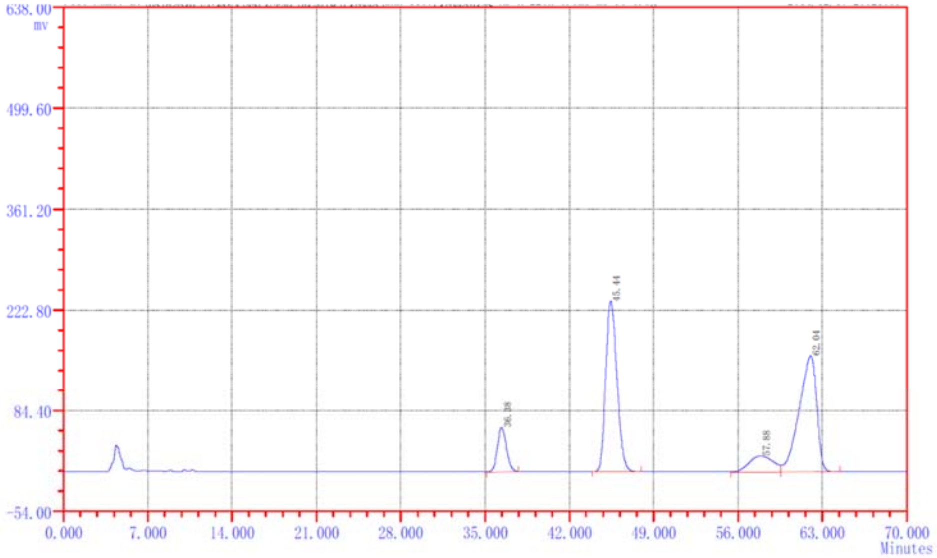


ID	组分名	保留时间	峰高	峰面积	浓度	拖尾因子	理论塔板
1		51. 533	14868	1399926. 9	3. 5490	1. 58	5970
2		67. 263	161067	38045408. 1	96. 4510	1. 96	1616
	Σ:		175935	39445335. 0	100. 0000		

6 (Scheme 3)

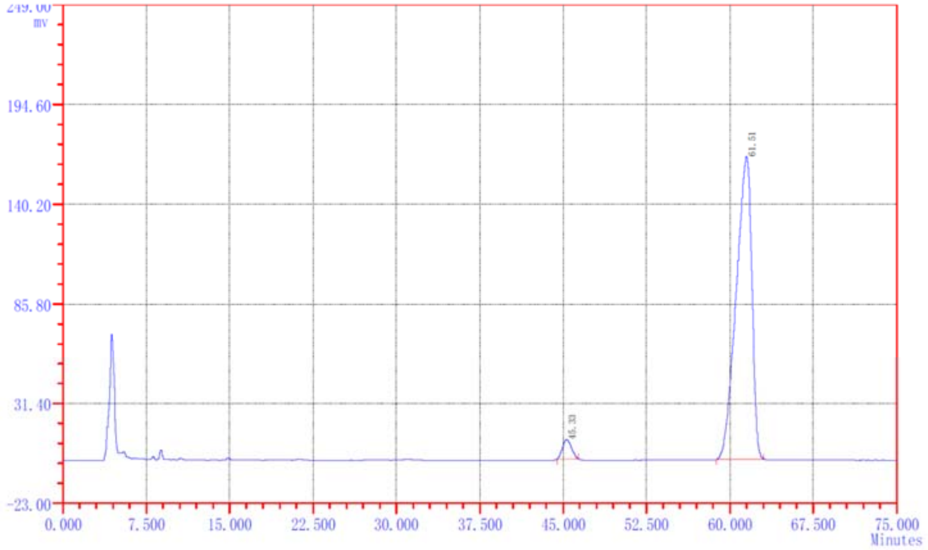


Racemic



ID	组分名	保留时间	峰高	峰面积	浓度	拖尾因子	理论塔板
1		36.380	62003	3304521.6	8.7410	1.14	9287
2		45.440	234709	15297019.3	40.4633	1.19	9688
3		57.883	22348	3102893.9	8.2077	0.92	3464
4		62.037	159947	16100273.6	42.5880	0.72	7570
	Σ:		479007	37804708.4	100.0000		

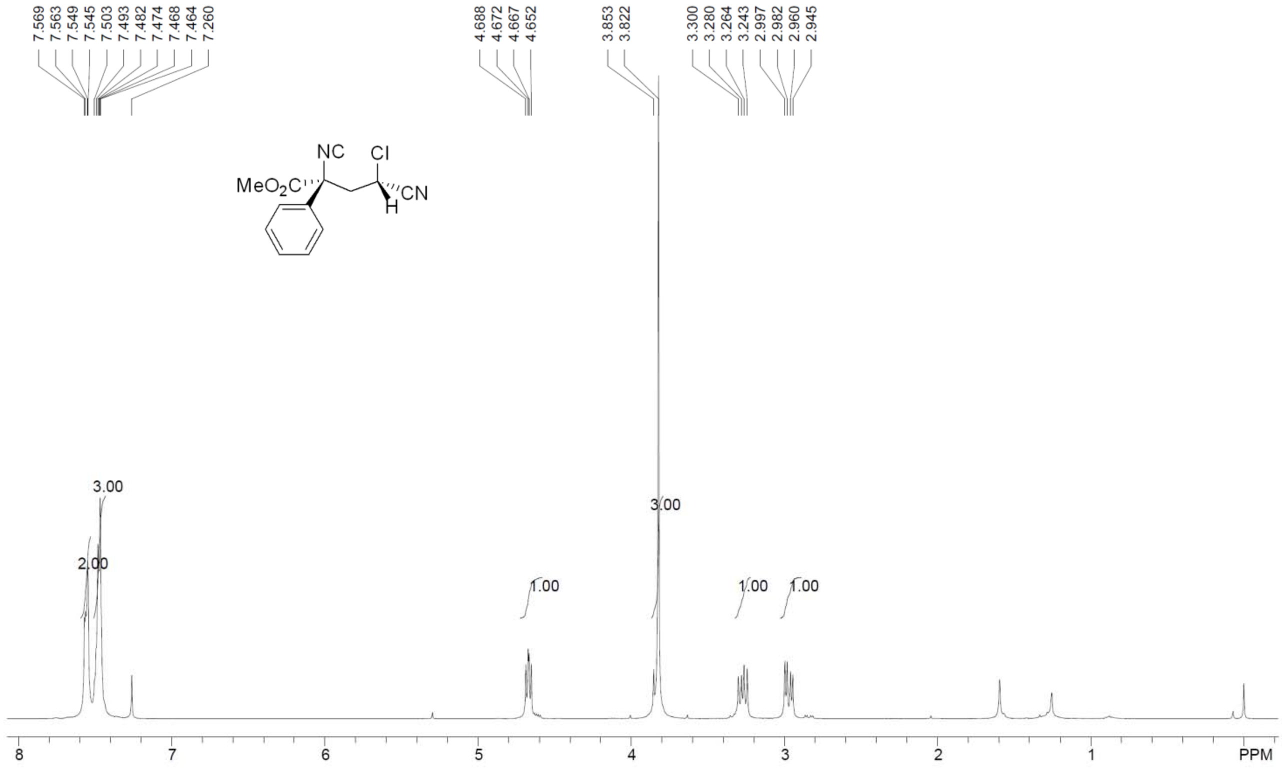
Enantioenriched



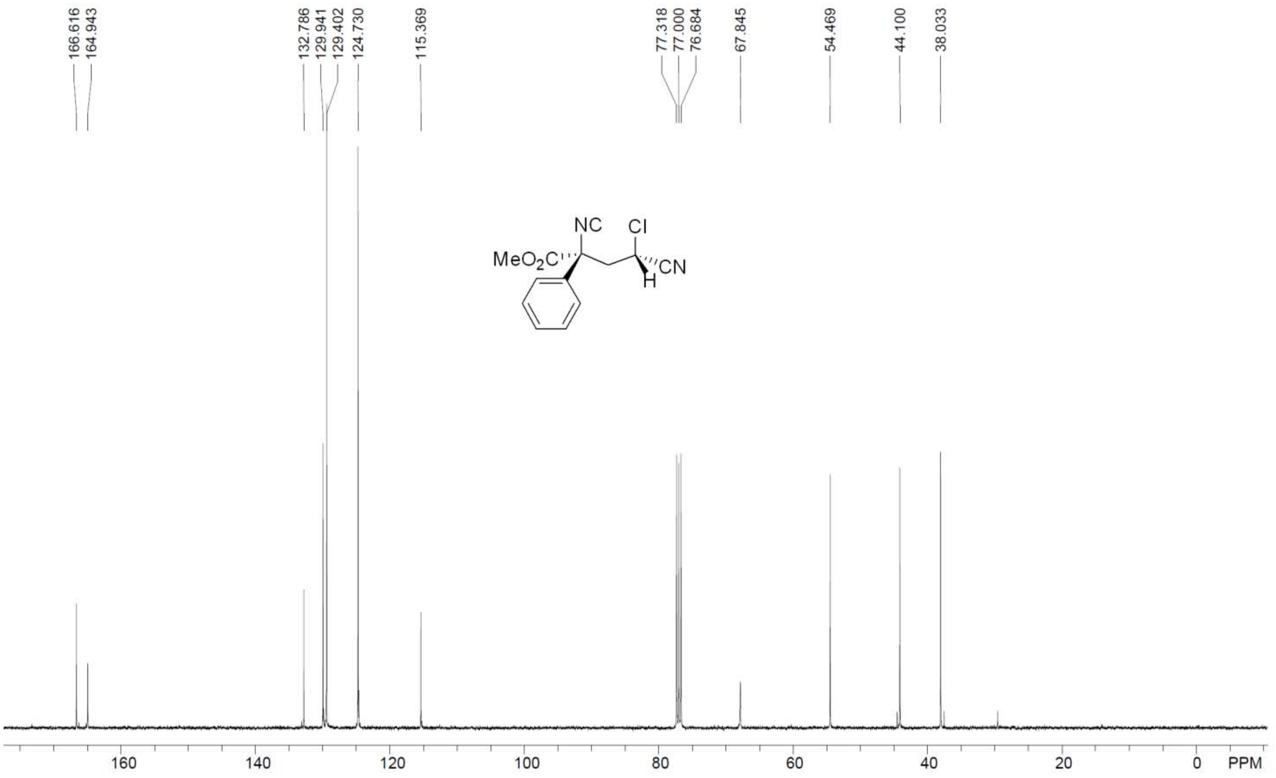
ID	组分名	保留时间	峰高	峰面积	浓度	拖尾因子	理论塔板
1		45.325	10660	599429.8	3.5622	1.10	12949
2		61.508	165485	16228276.9	96.4378	0.75	7841
	Σ:		176145	16827706.7	100.0000		

3. Copies of NMR spectra for the compounds 4-6.

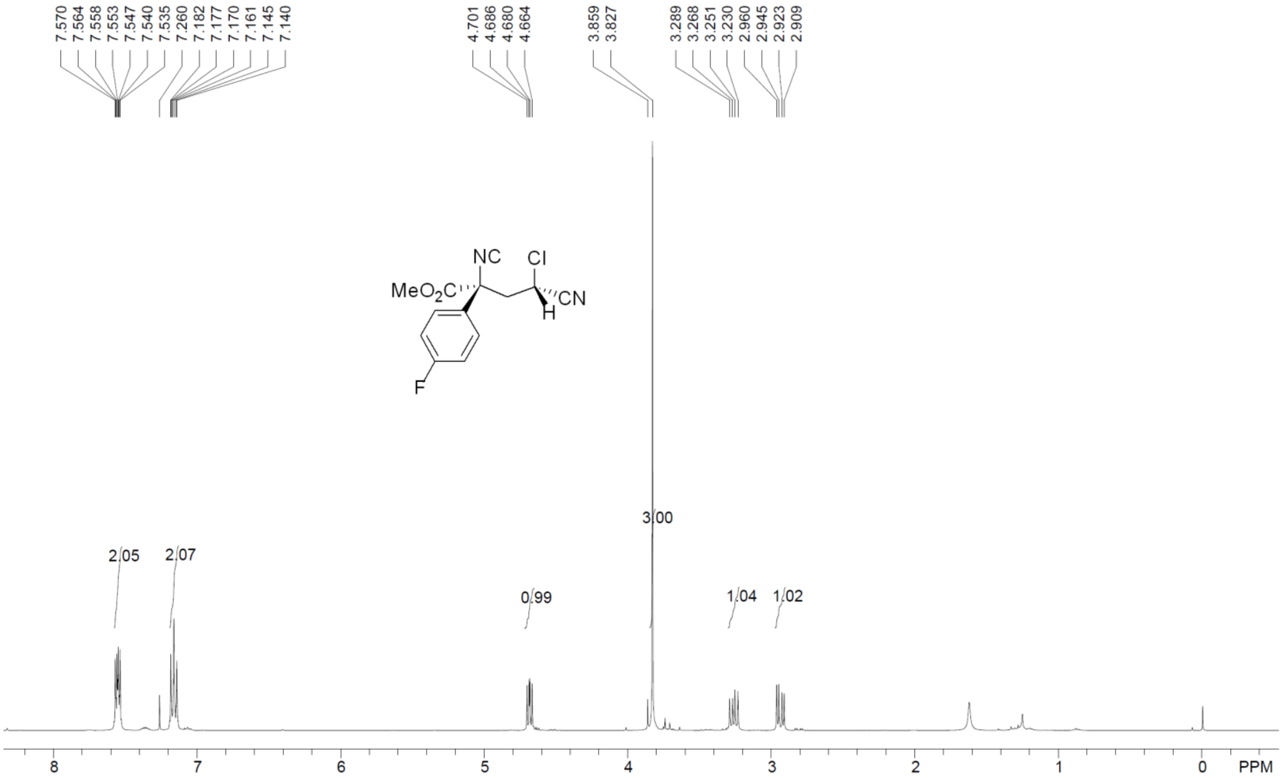
^{1}H NMR of **4a**



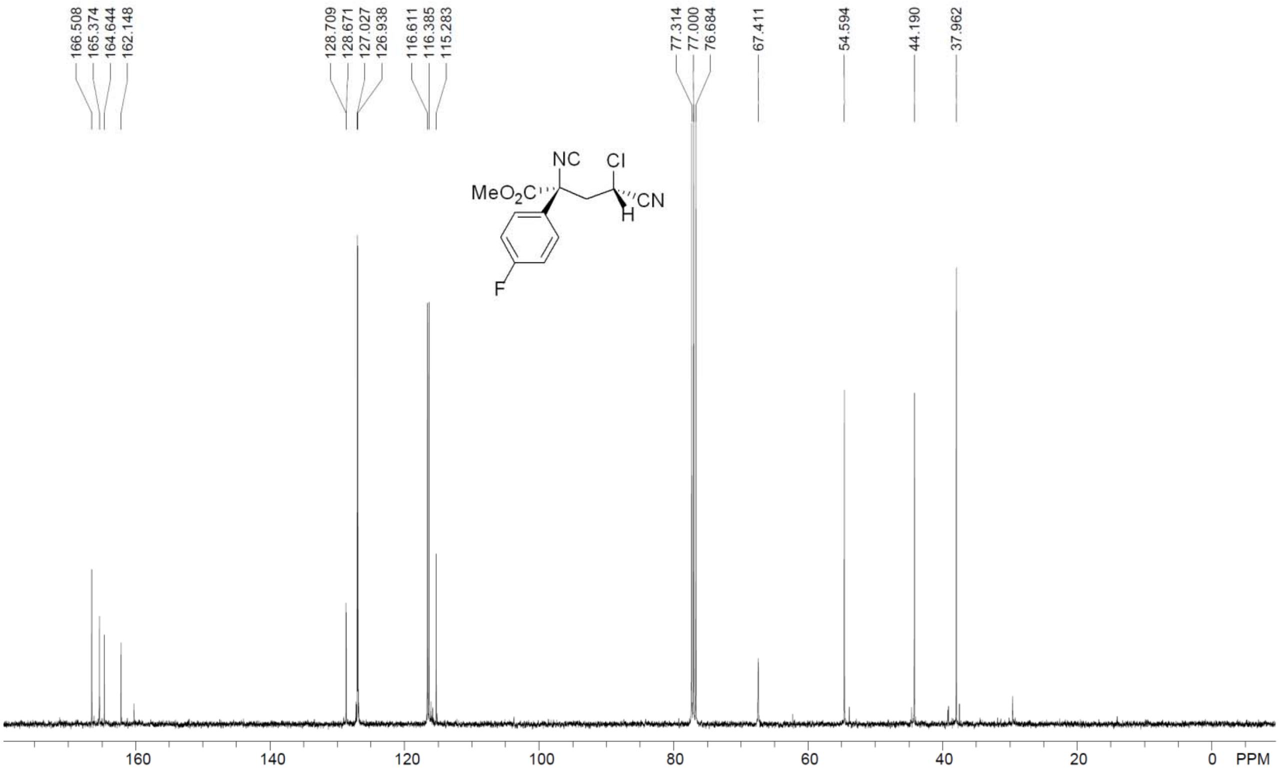
^{13}C NMR of **4a**



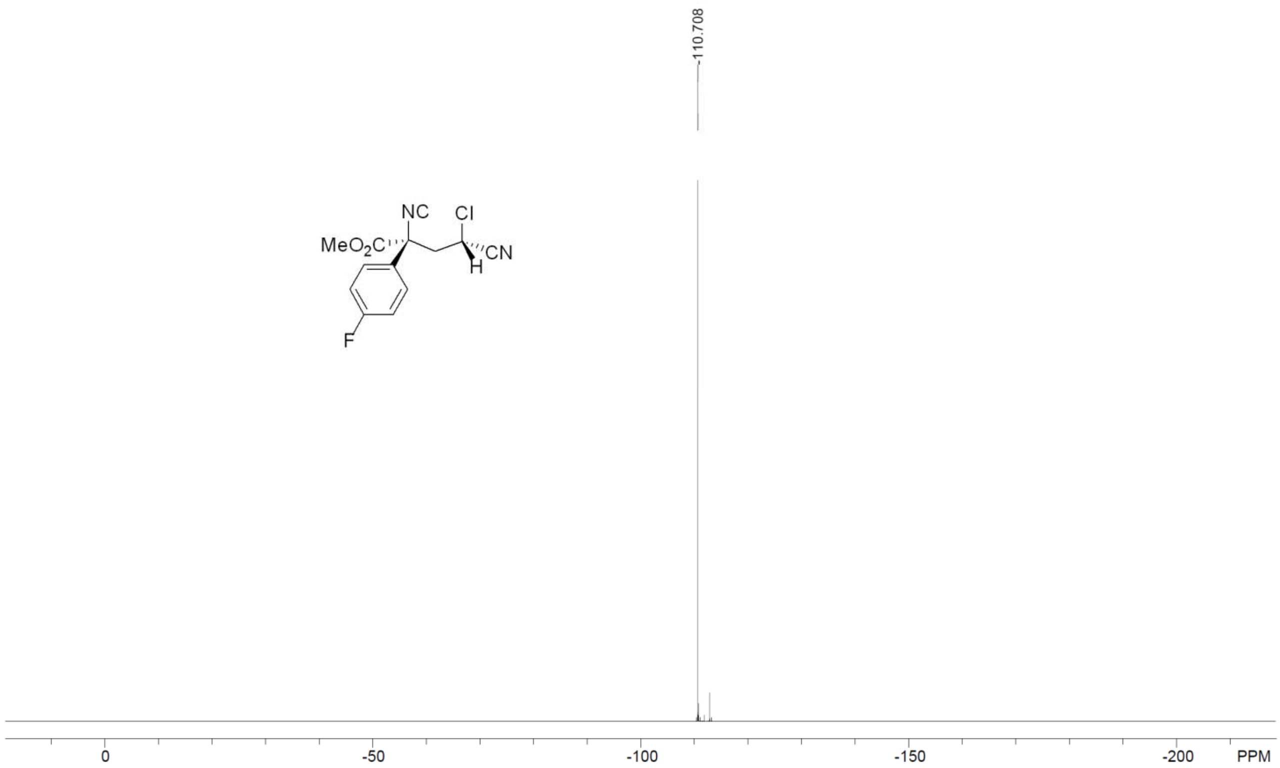
^{1}H NMR of **4b**



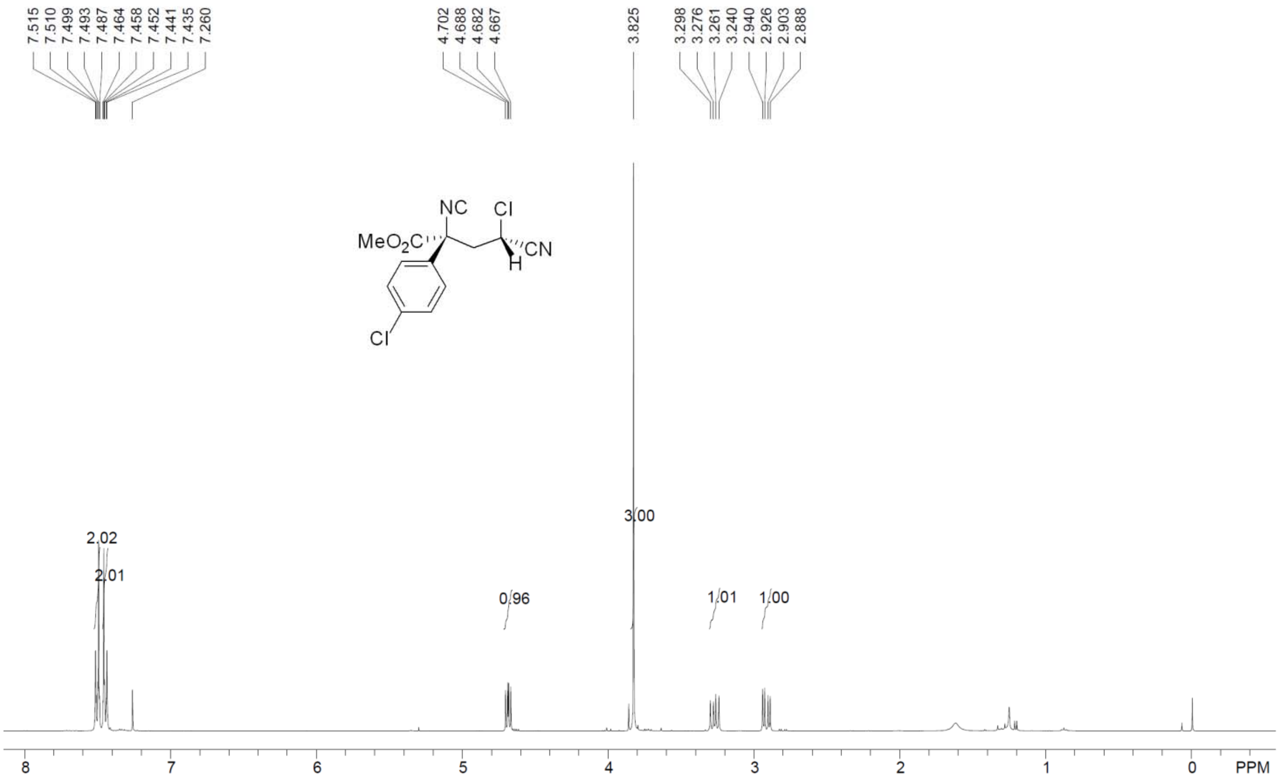
^{13}C NMR of **4b**



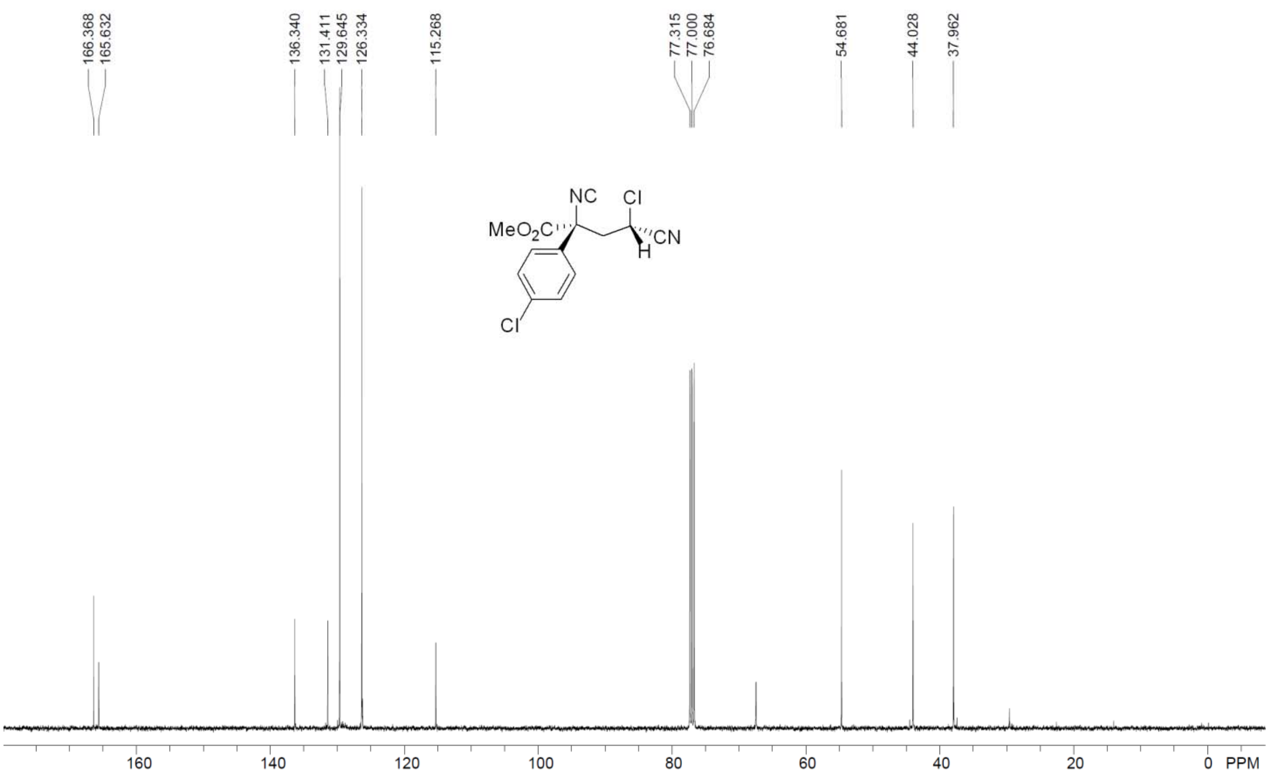
^{19}F NMR of **4b**



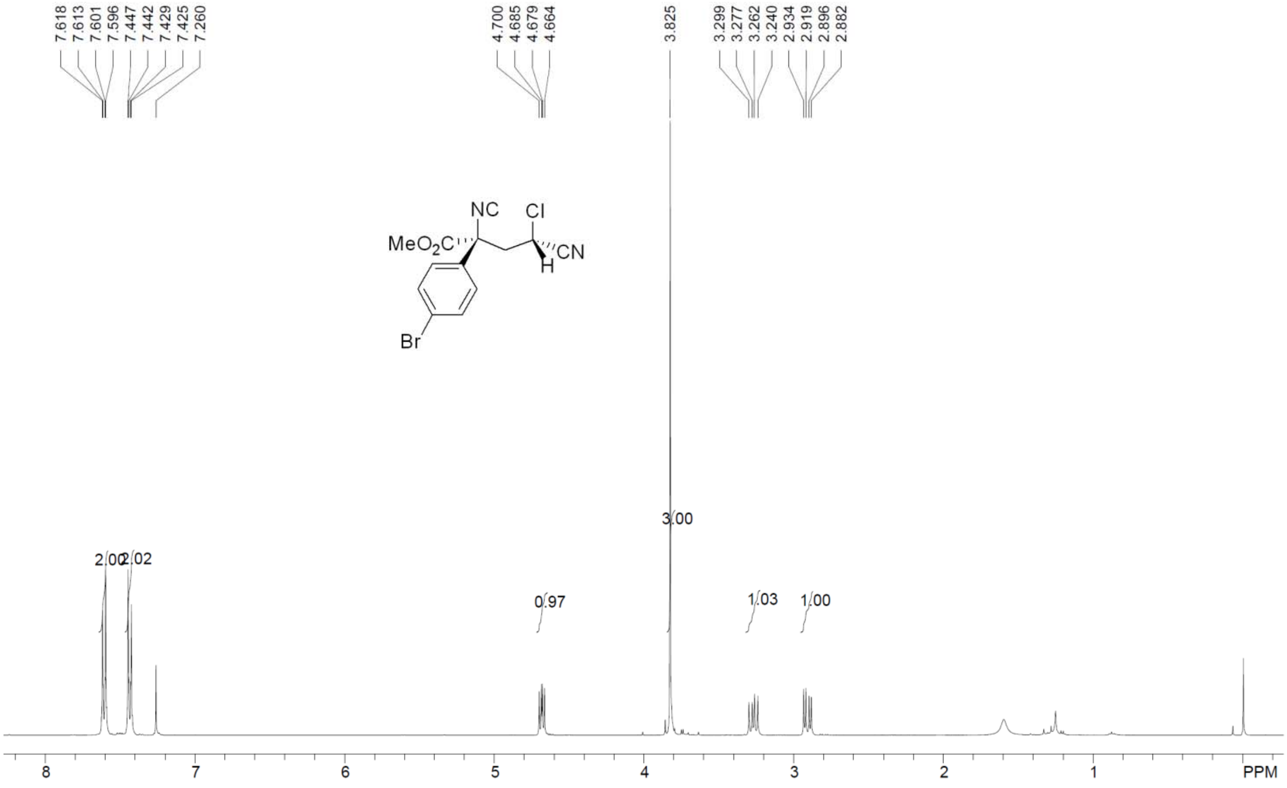
^{1}H NMR of **4c**



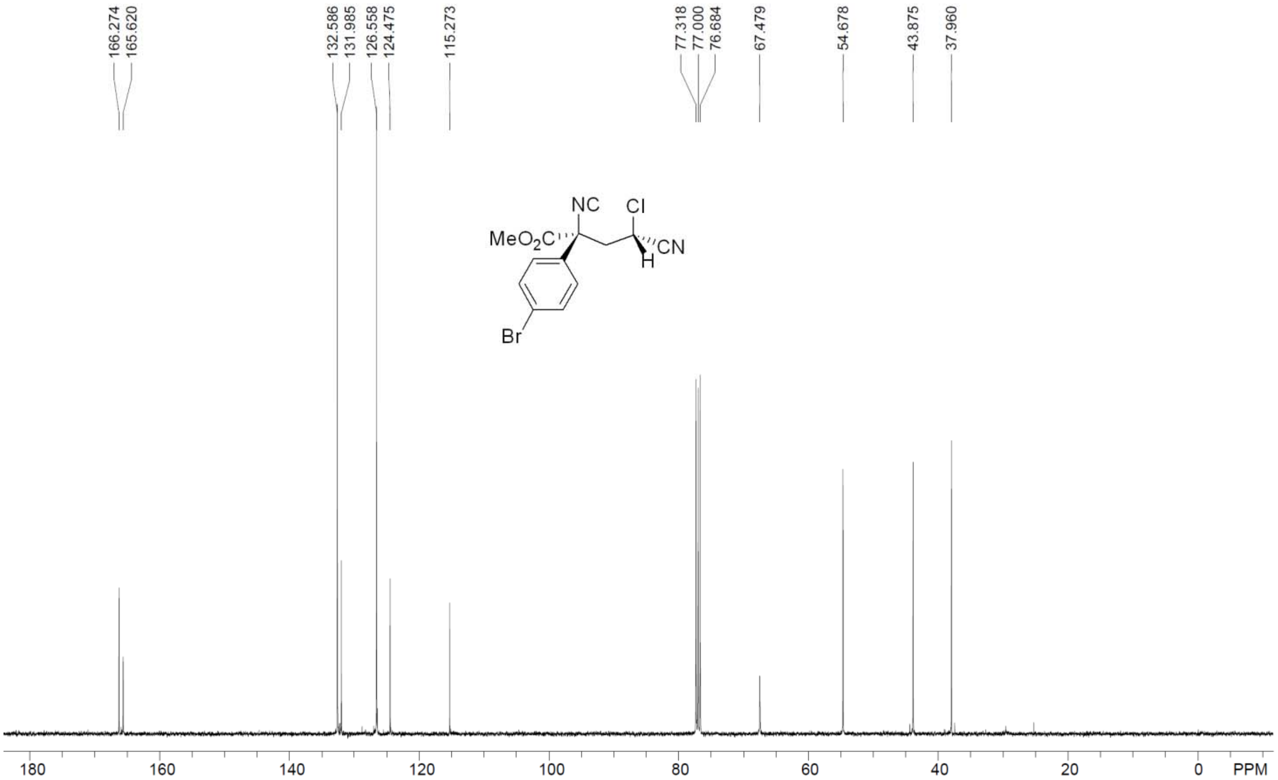
^{13}C NMR of **4c**



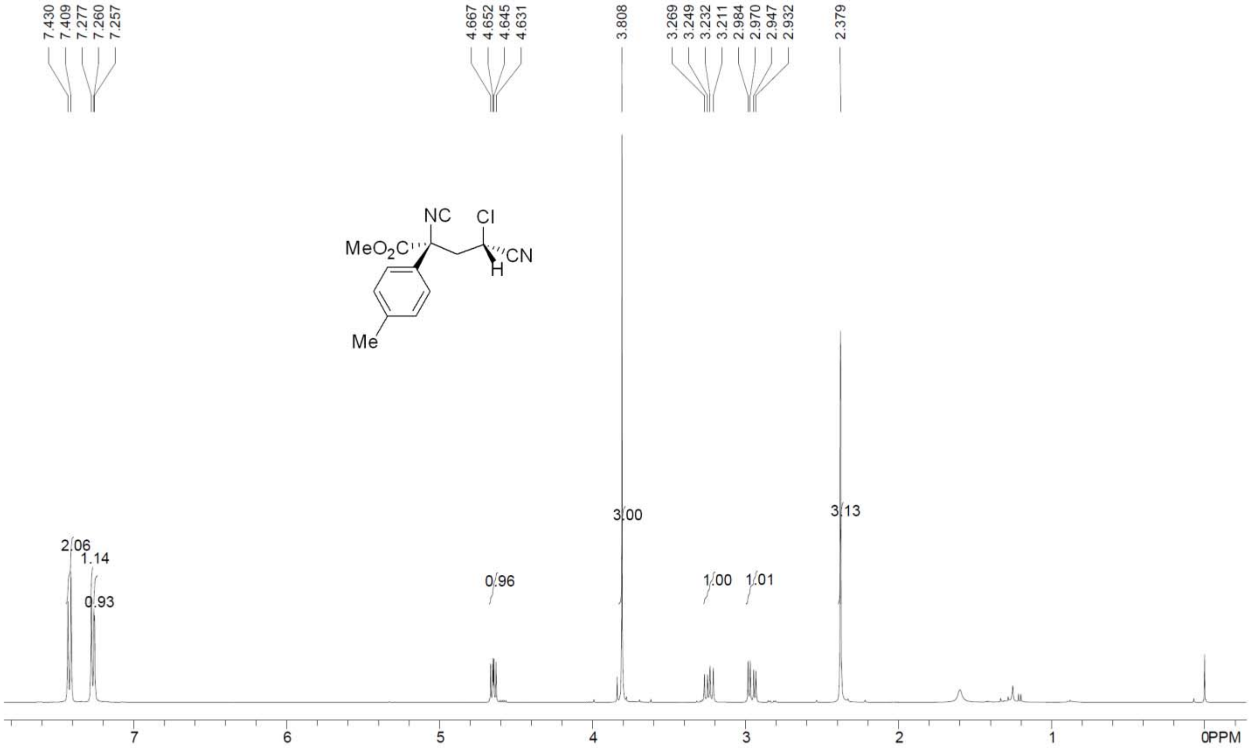
^{1}H NMR of **4d**



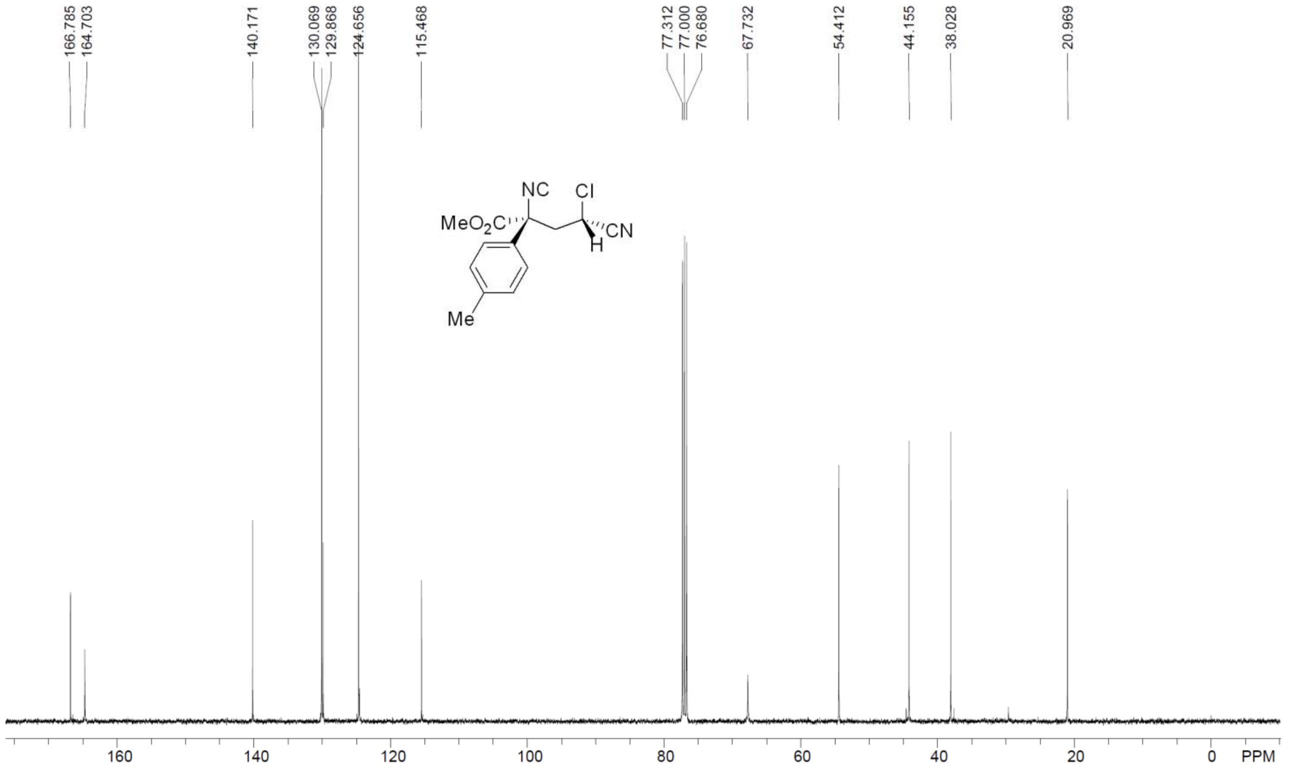
^{13}C NMR of **4d**



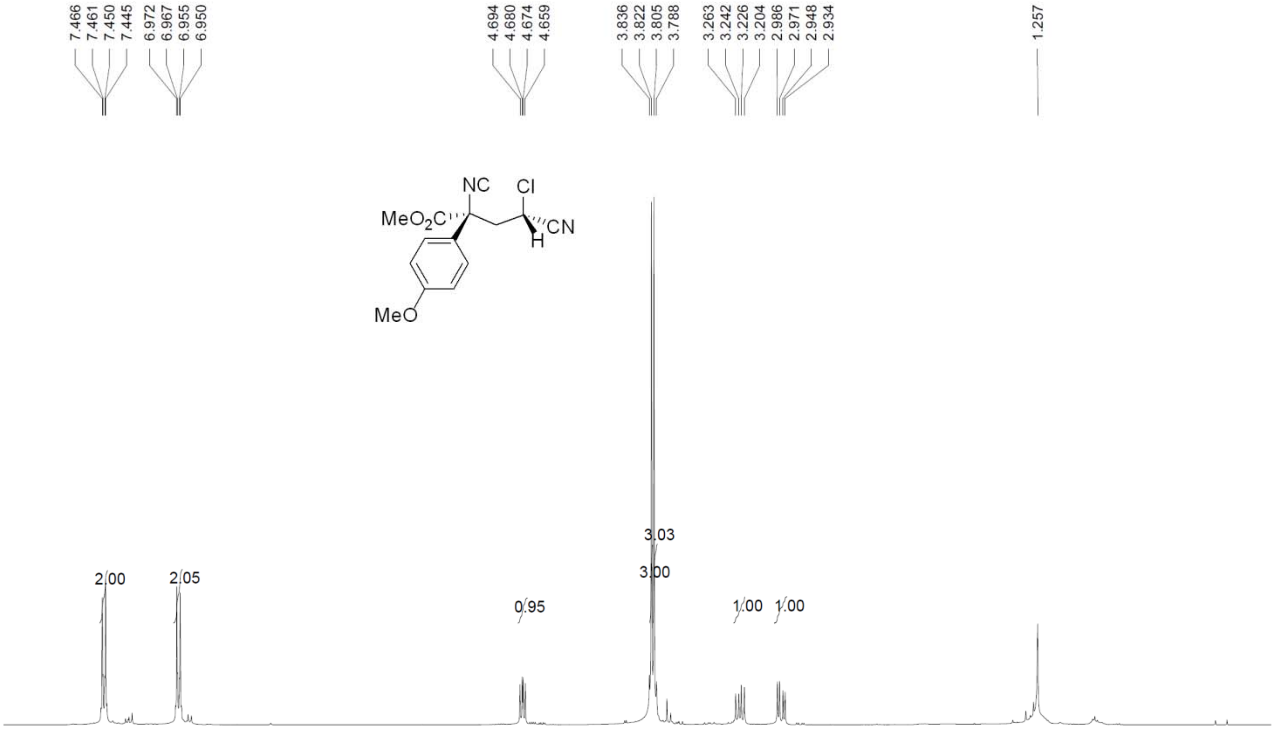
^{1}H NMR of **4e**



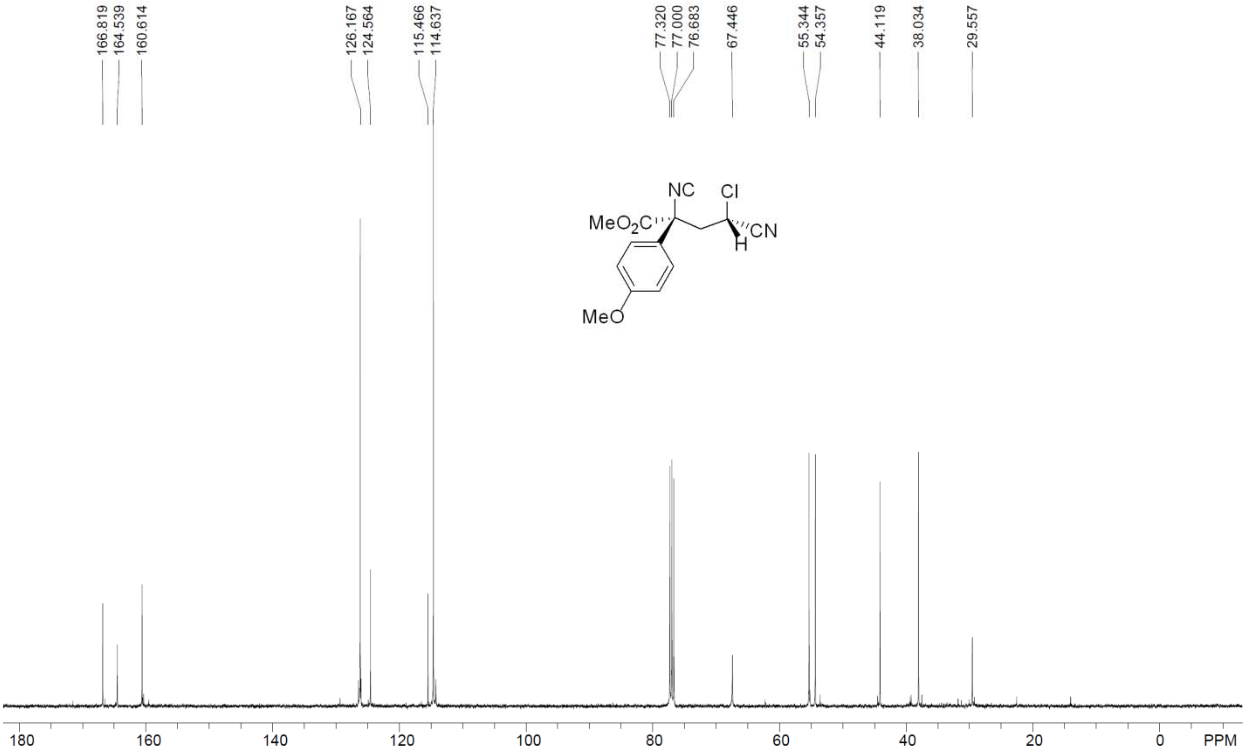
^{13}C NMR of **4e**



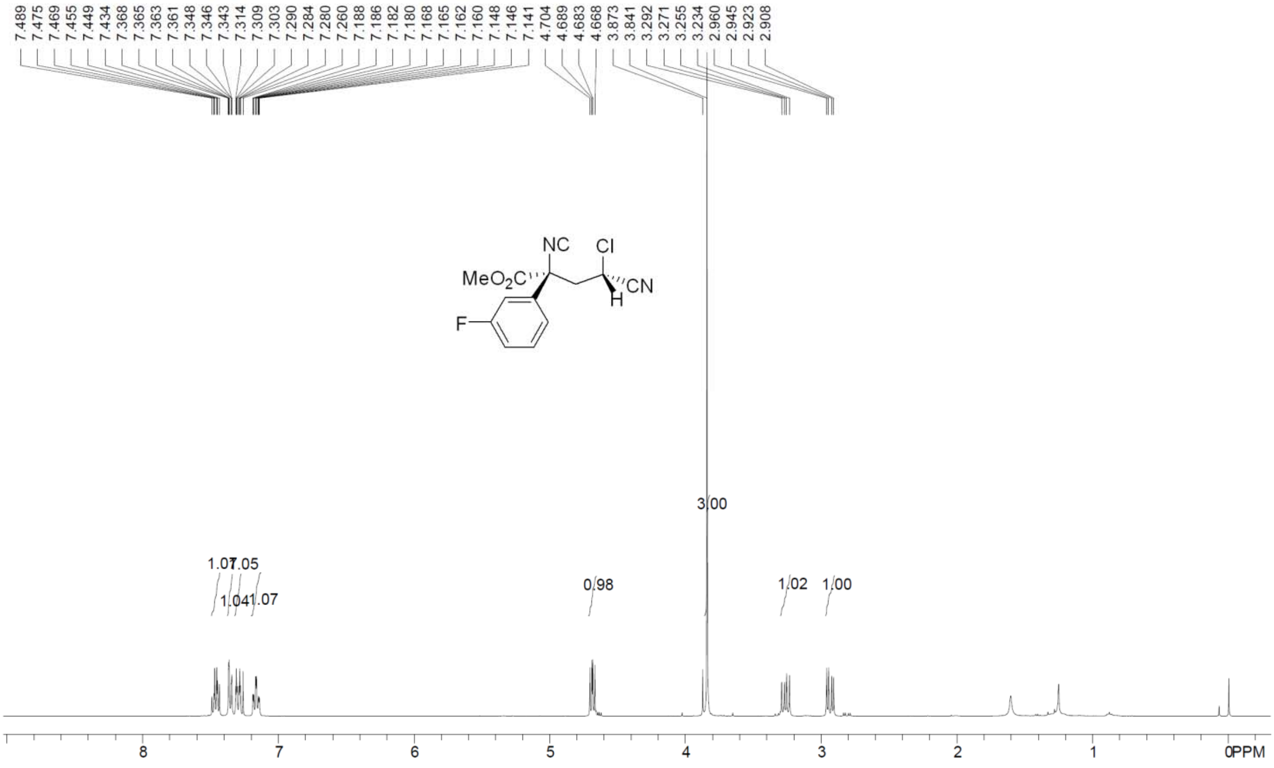
^{1}H NMR of **4f**



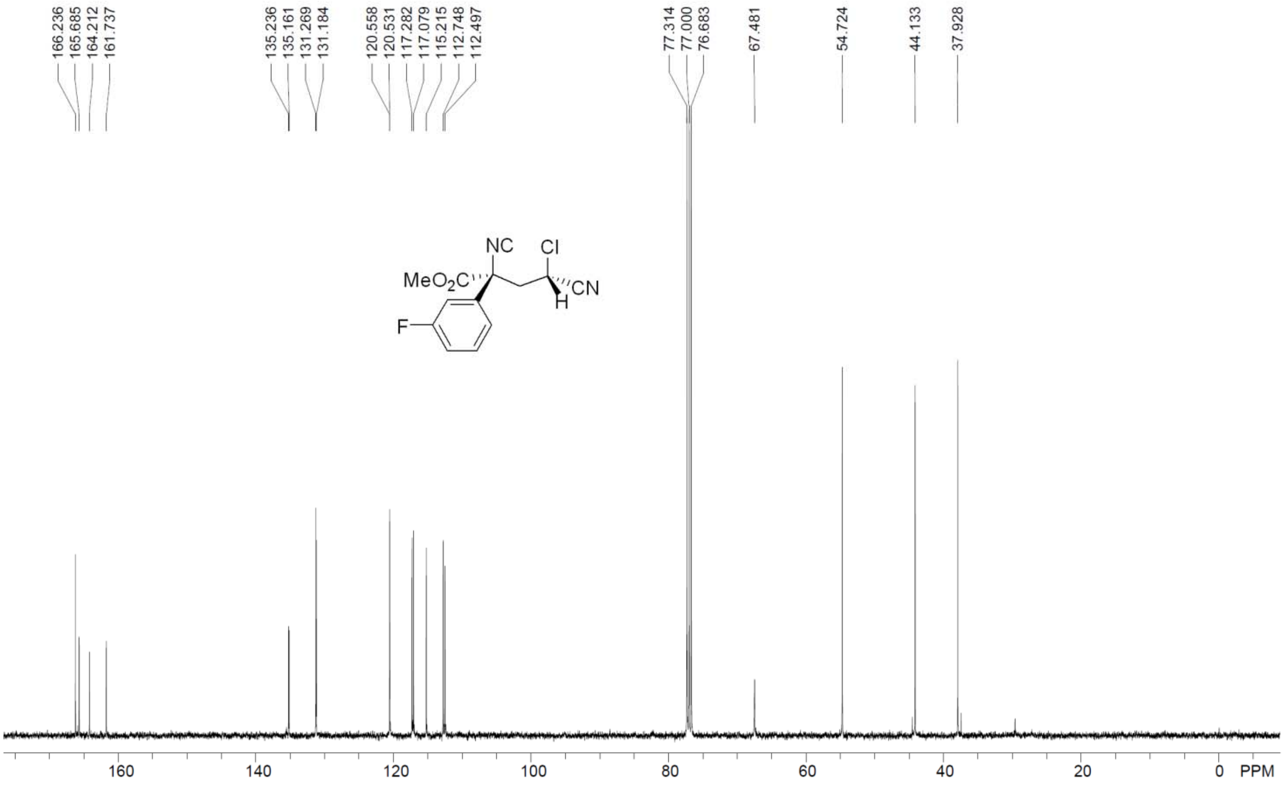
^{13}C NMR of **4f**



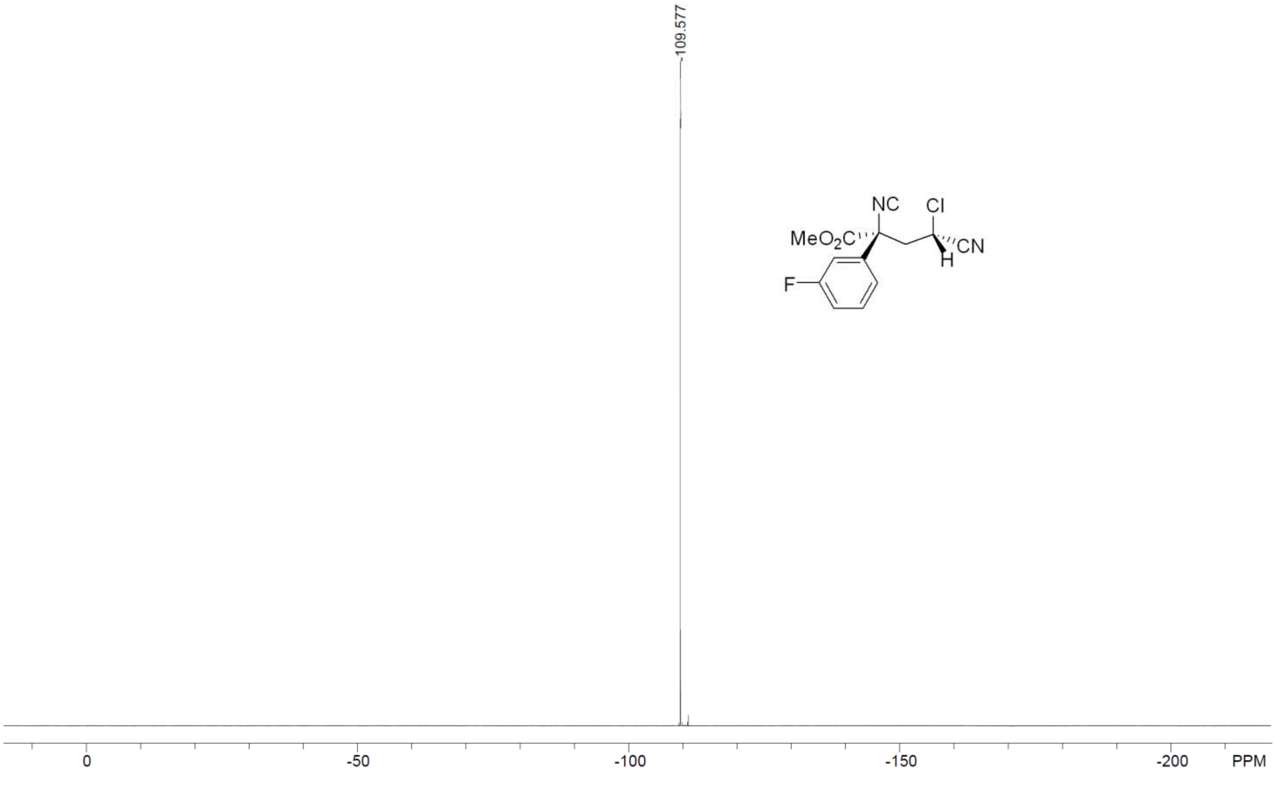
^{1}H NMR of **4g**



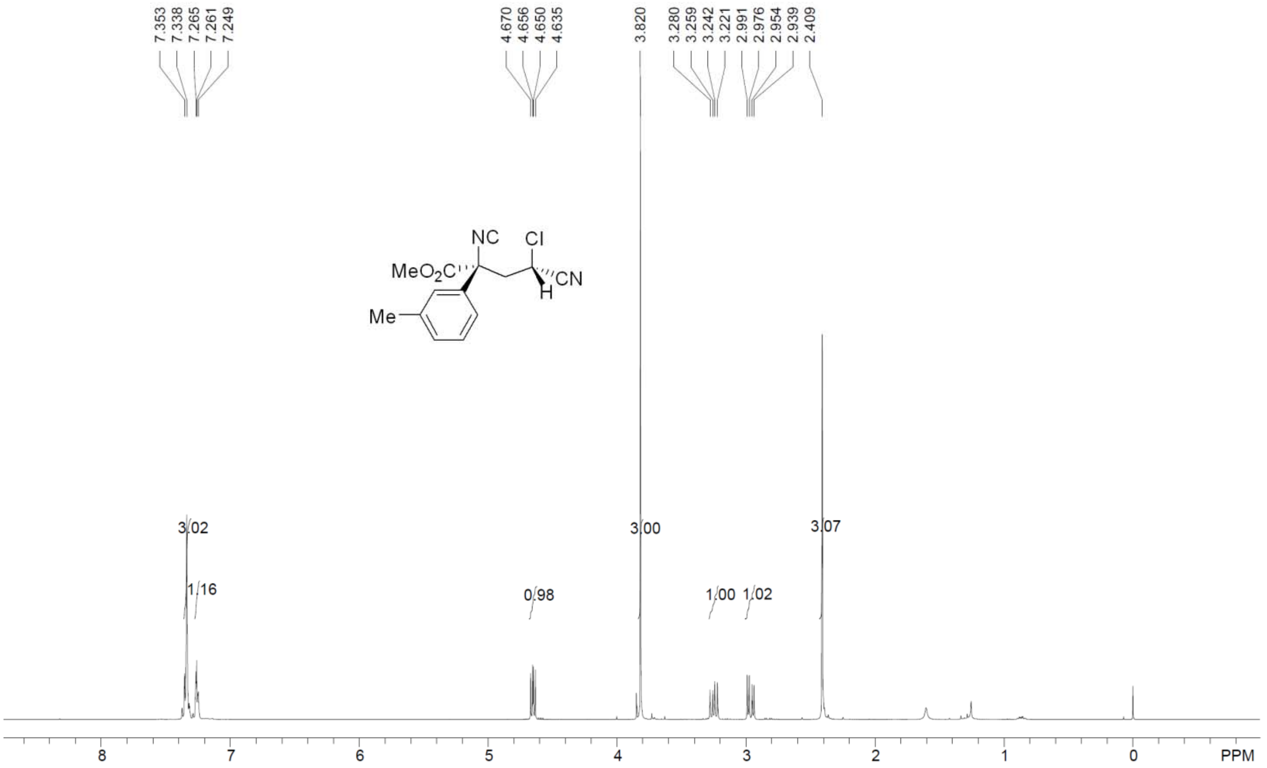
^{13}C NMR of **4g**



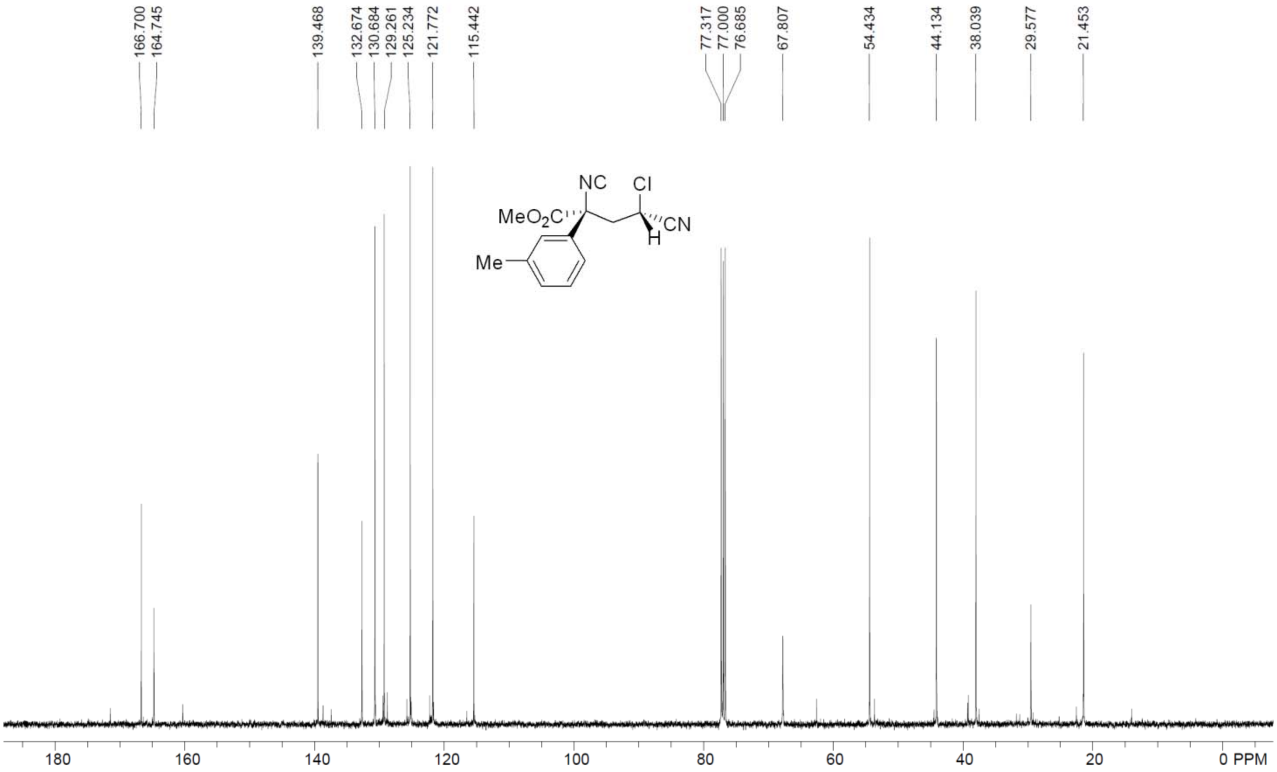
^{19}F NMR of **4g**



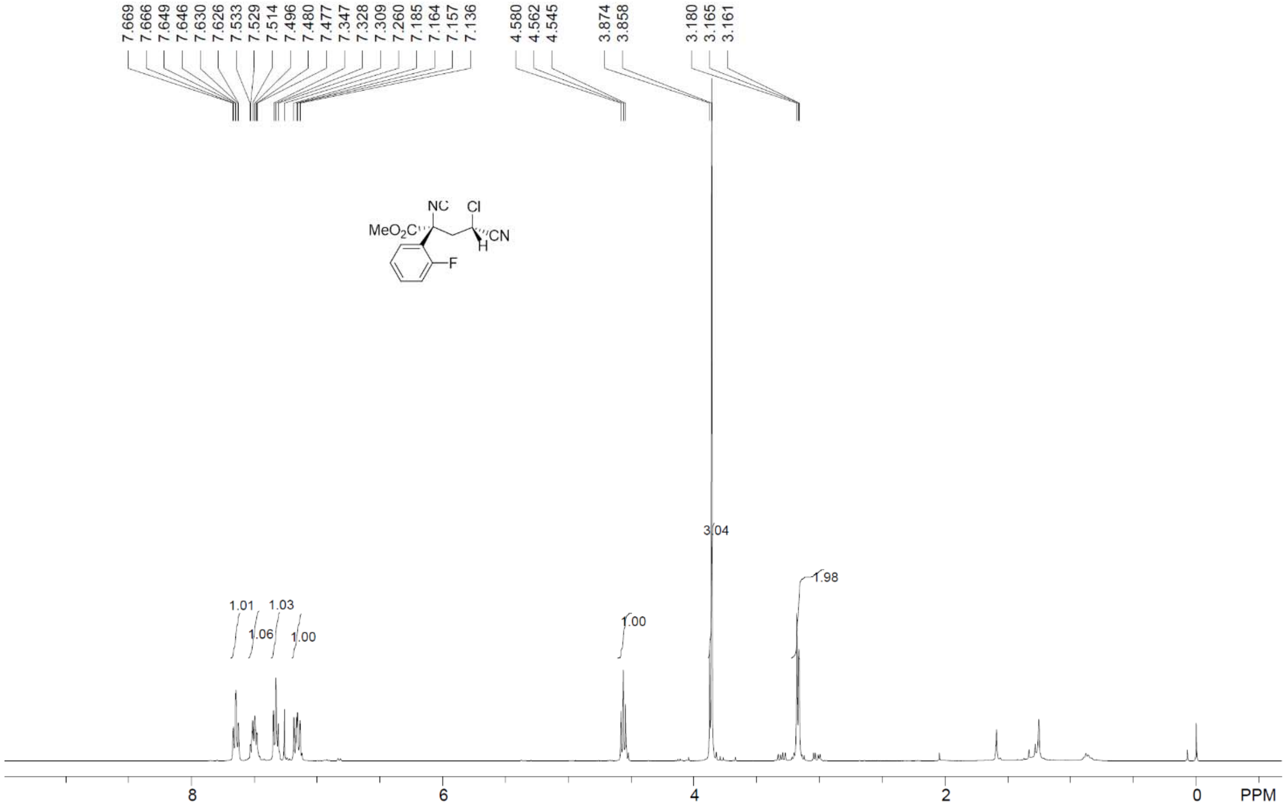
^{1}H NMR of **4h**



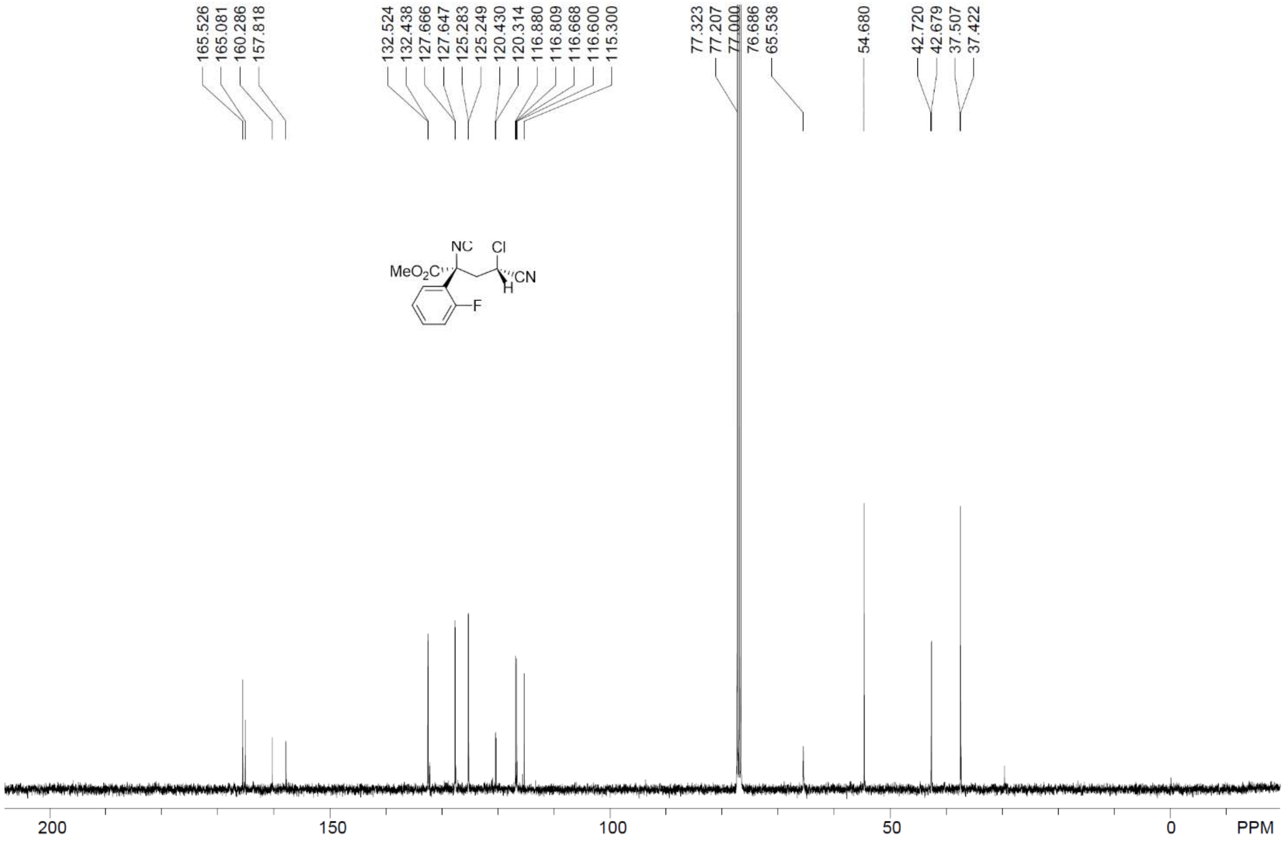
^{13}C NMR of **4h**



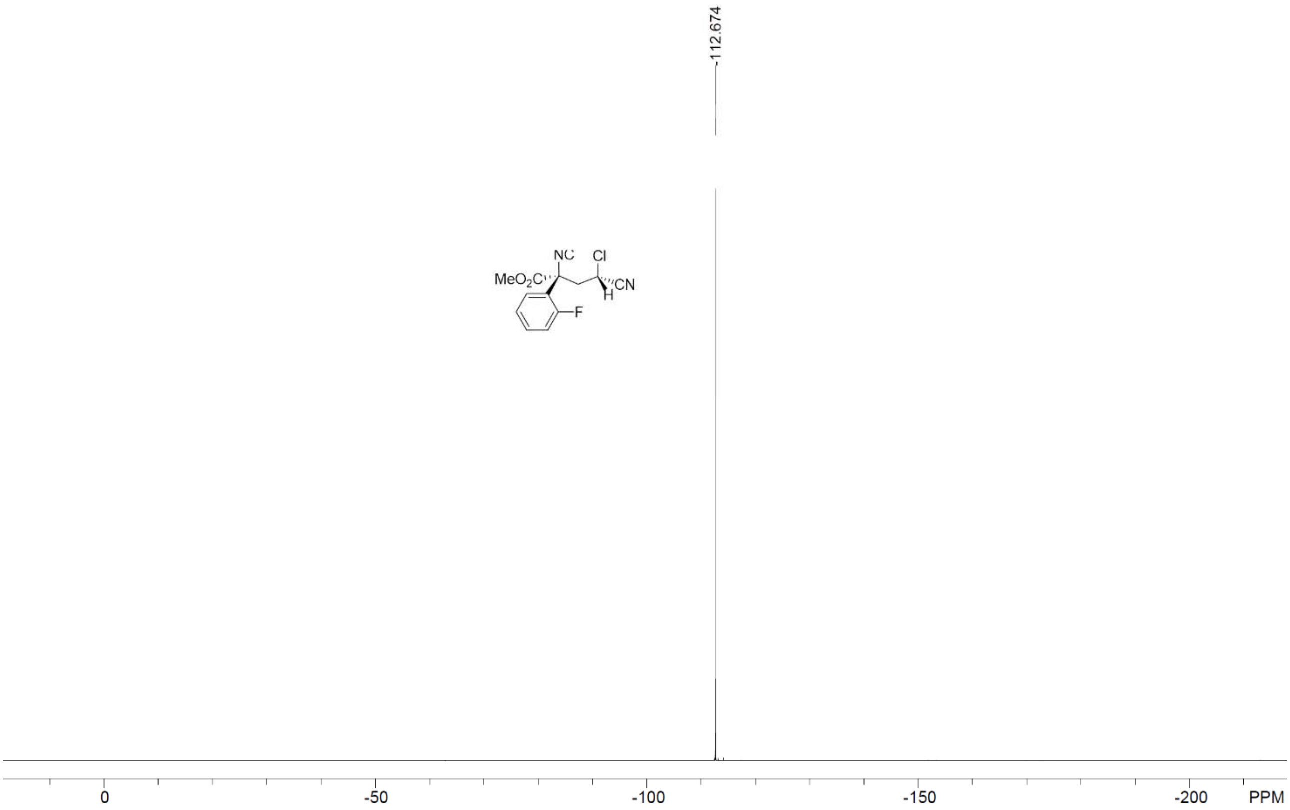
^{1}H NMR of **4i**



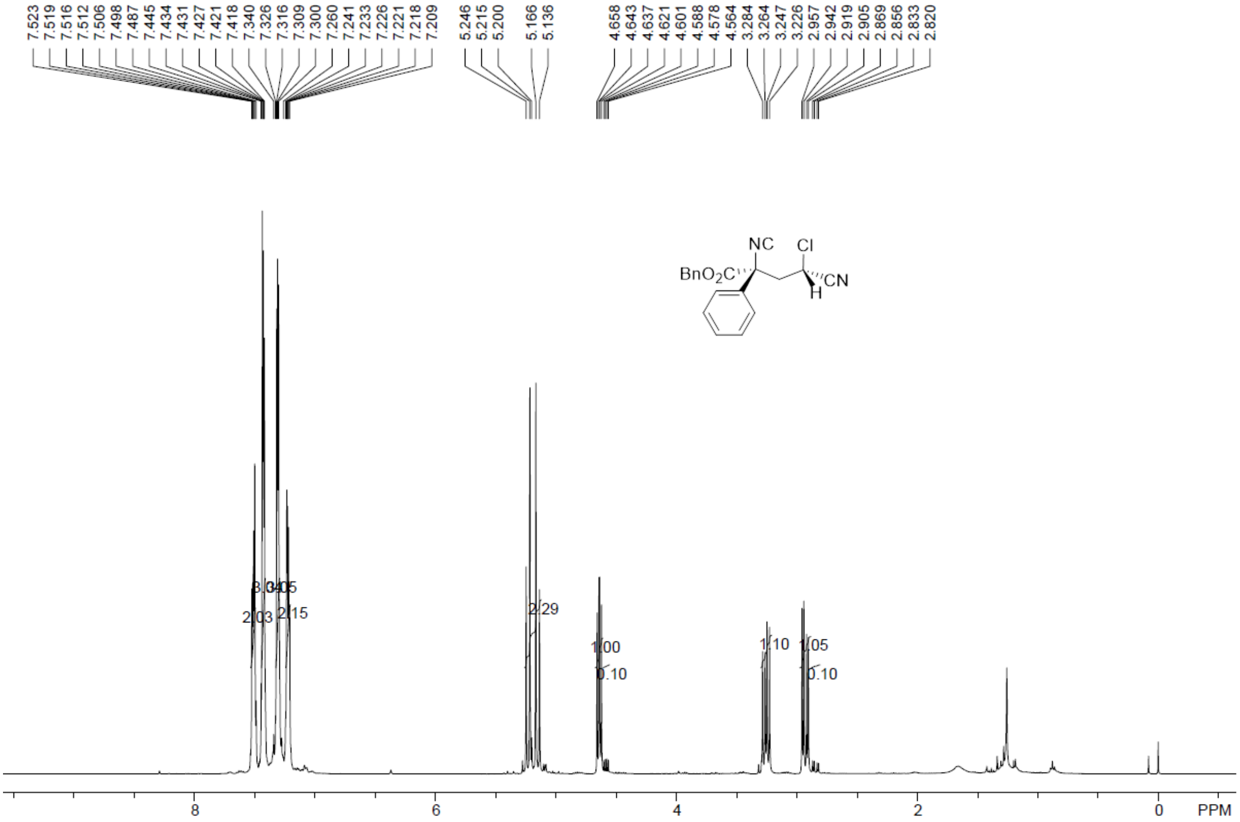
^{13}C NMR of **4i**



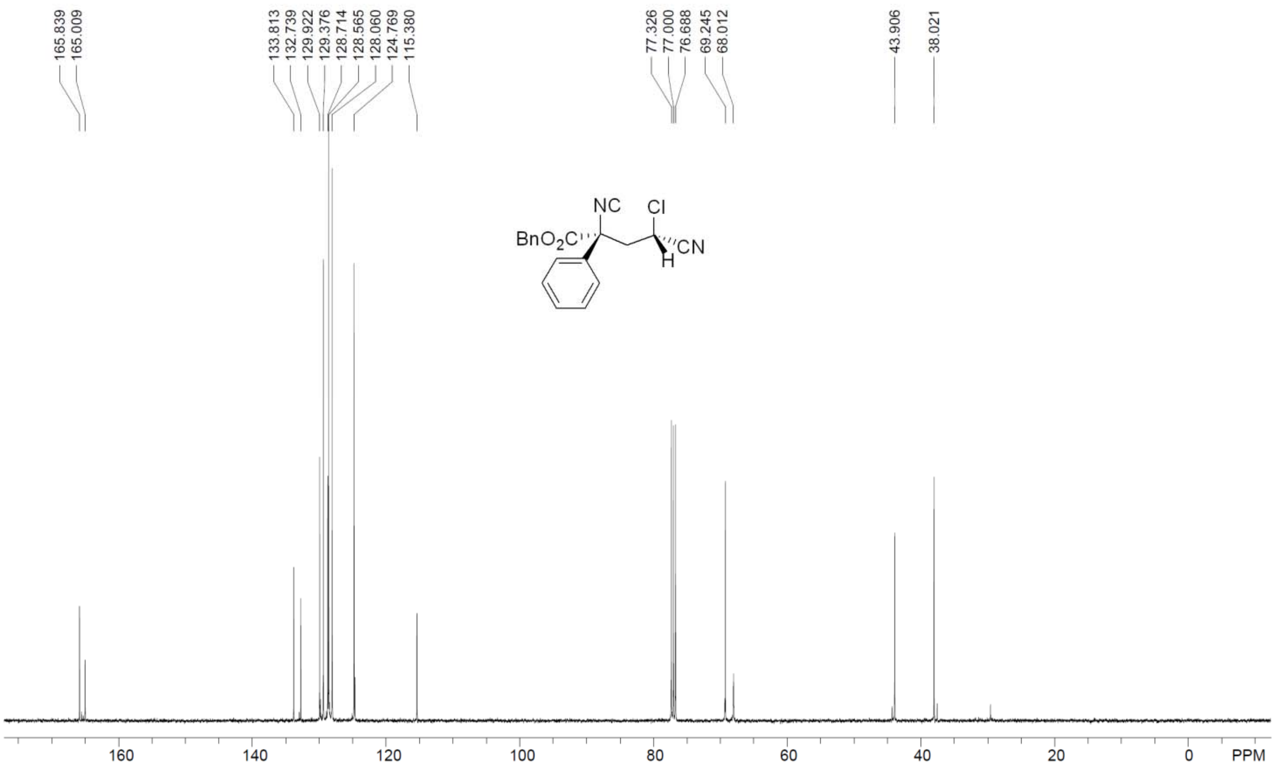
^{19}F NMR of **4i**



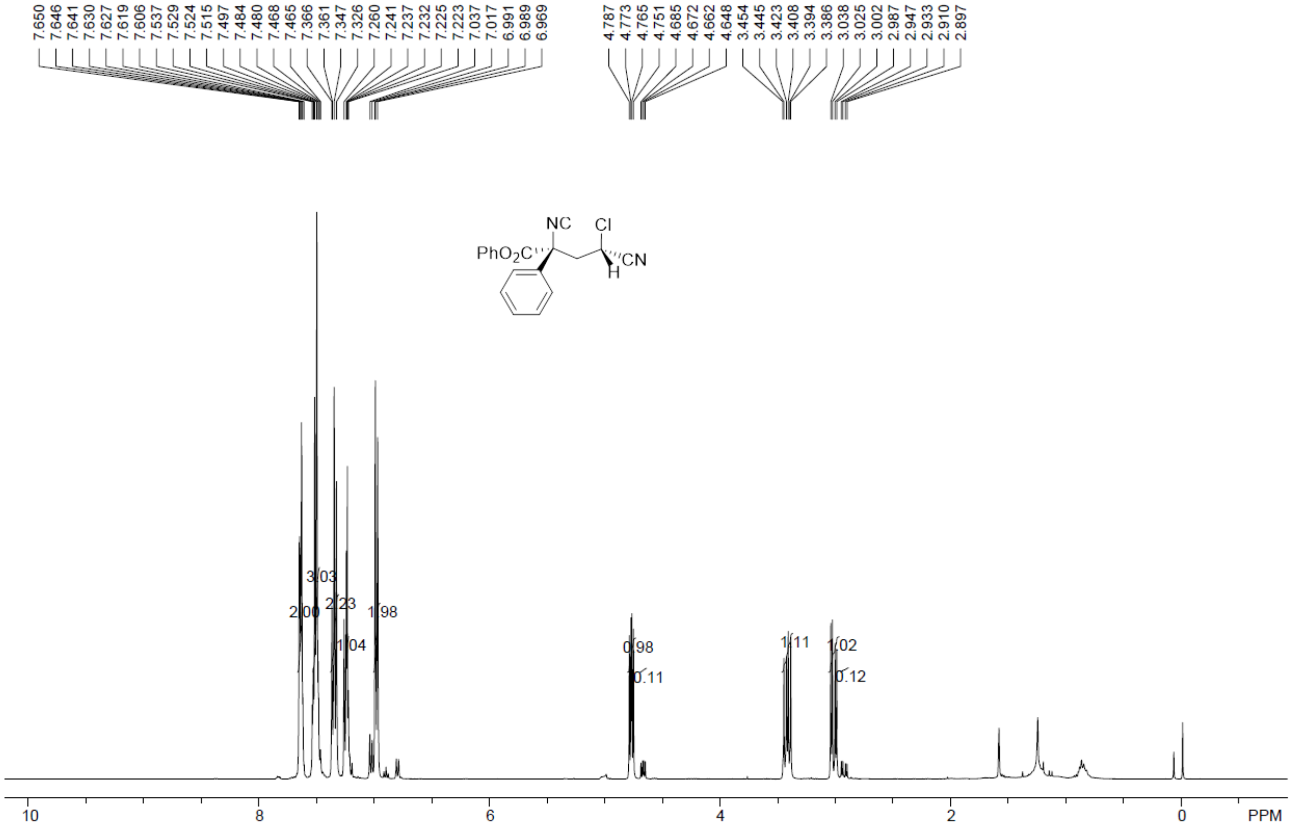
^{1}H NMR of **4k**



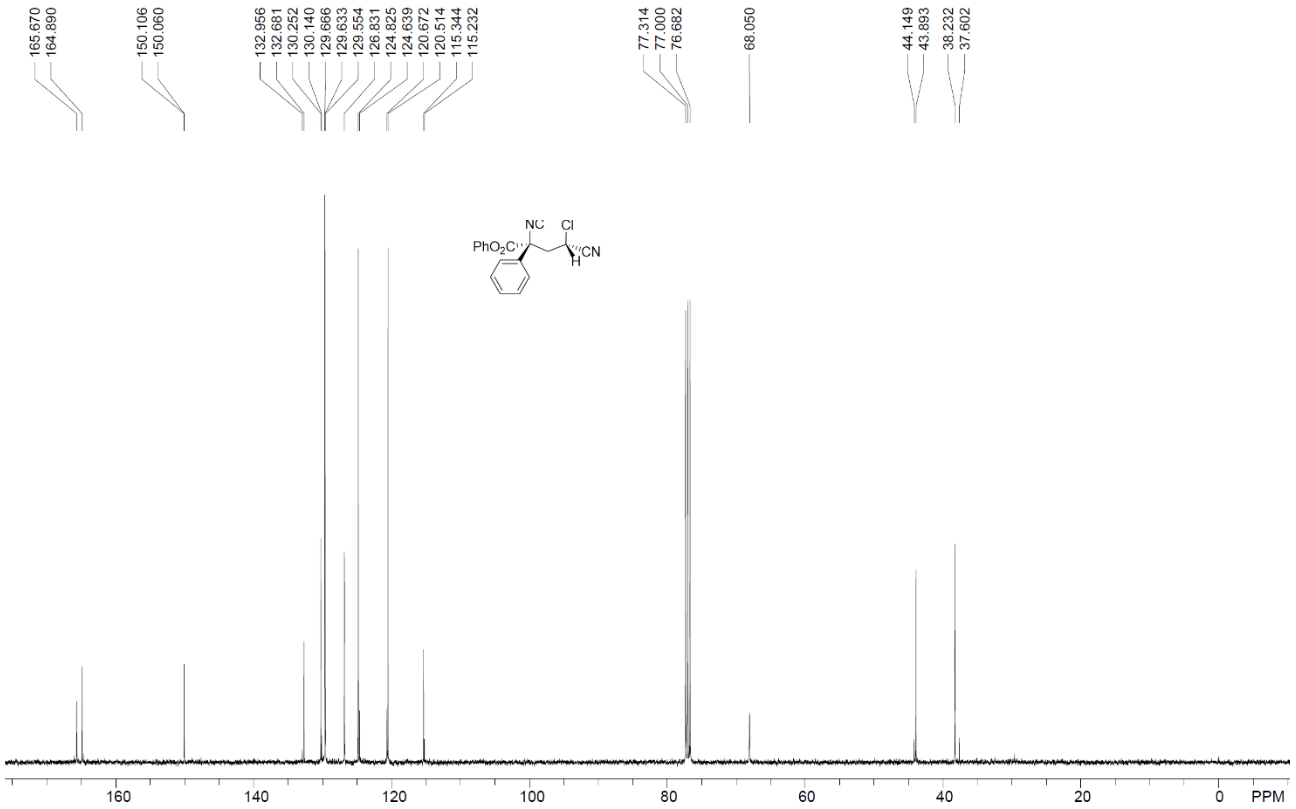
^{13}C NMR of **4k**



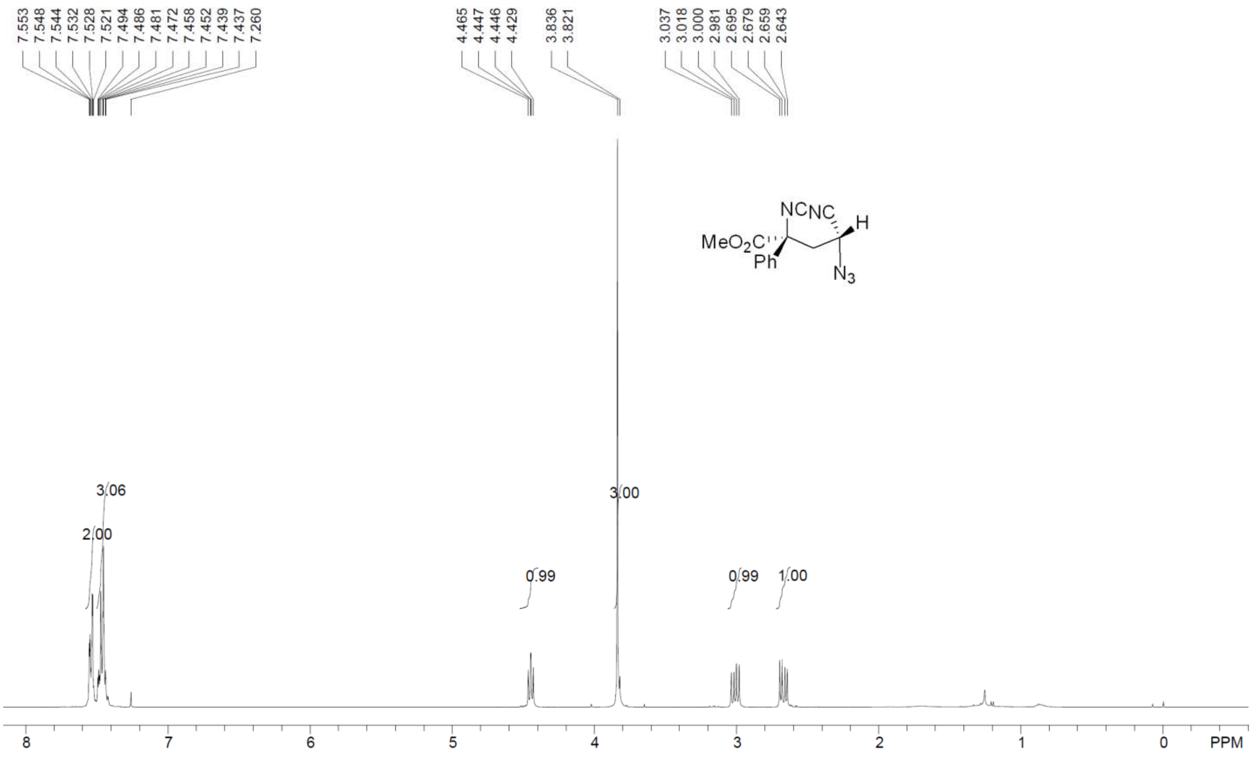
^{1}H NMR of **4l**



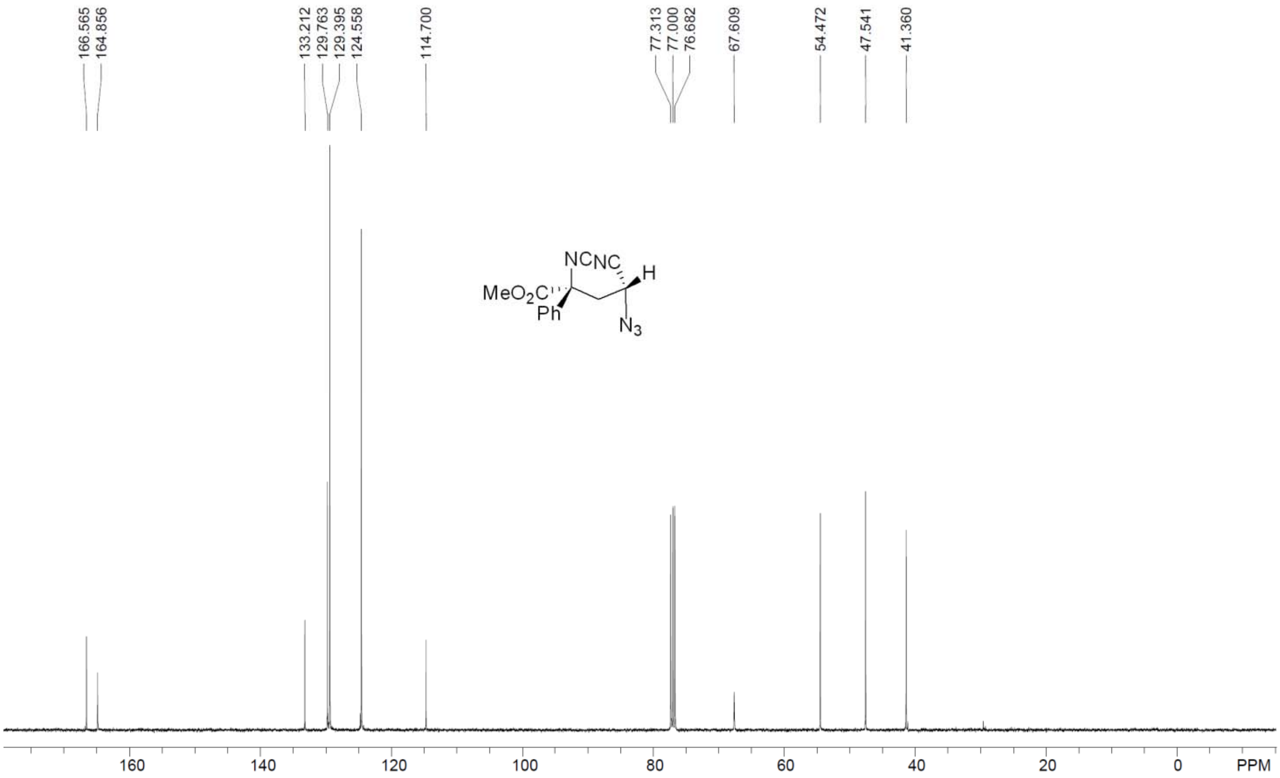
^{13}C NMR of **4l**



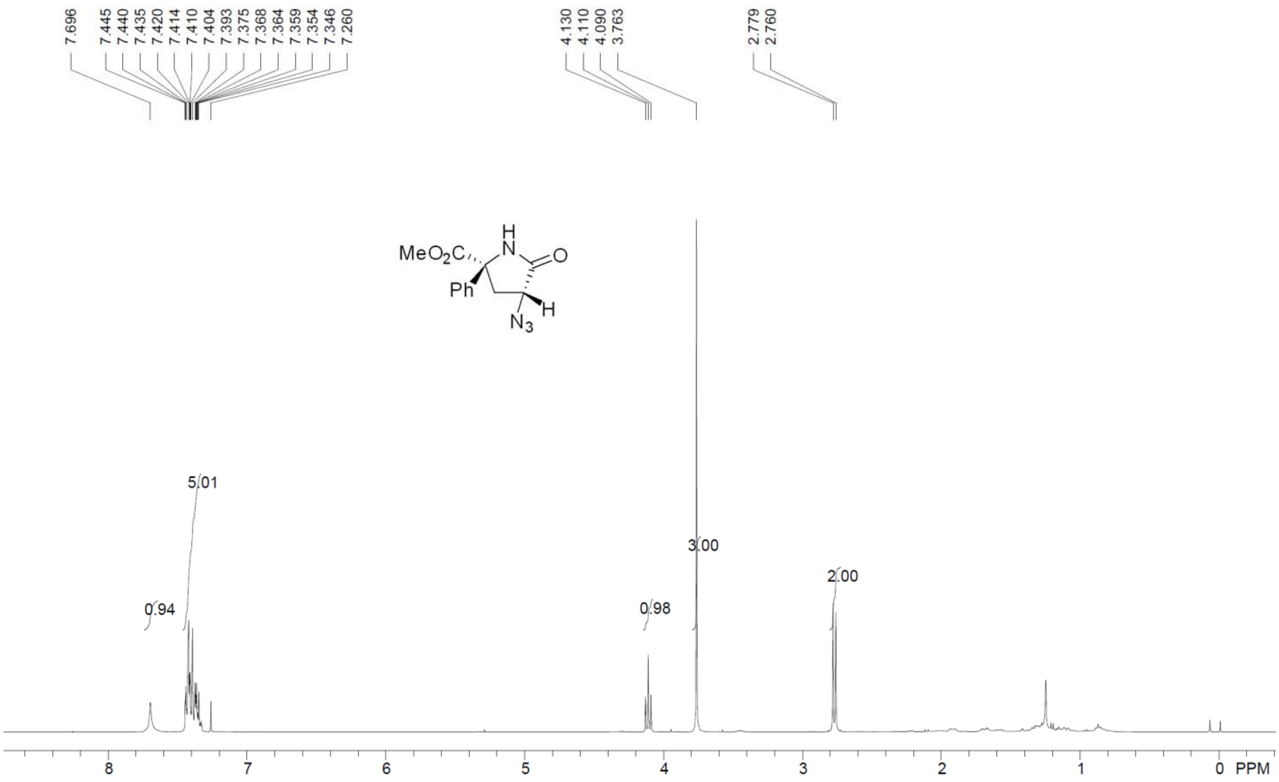
^{1}H NMR of **5**



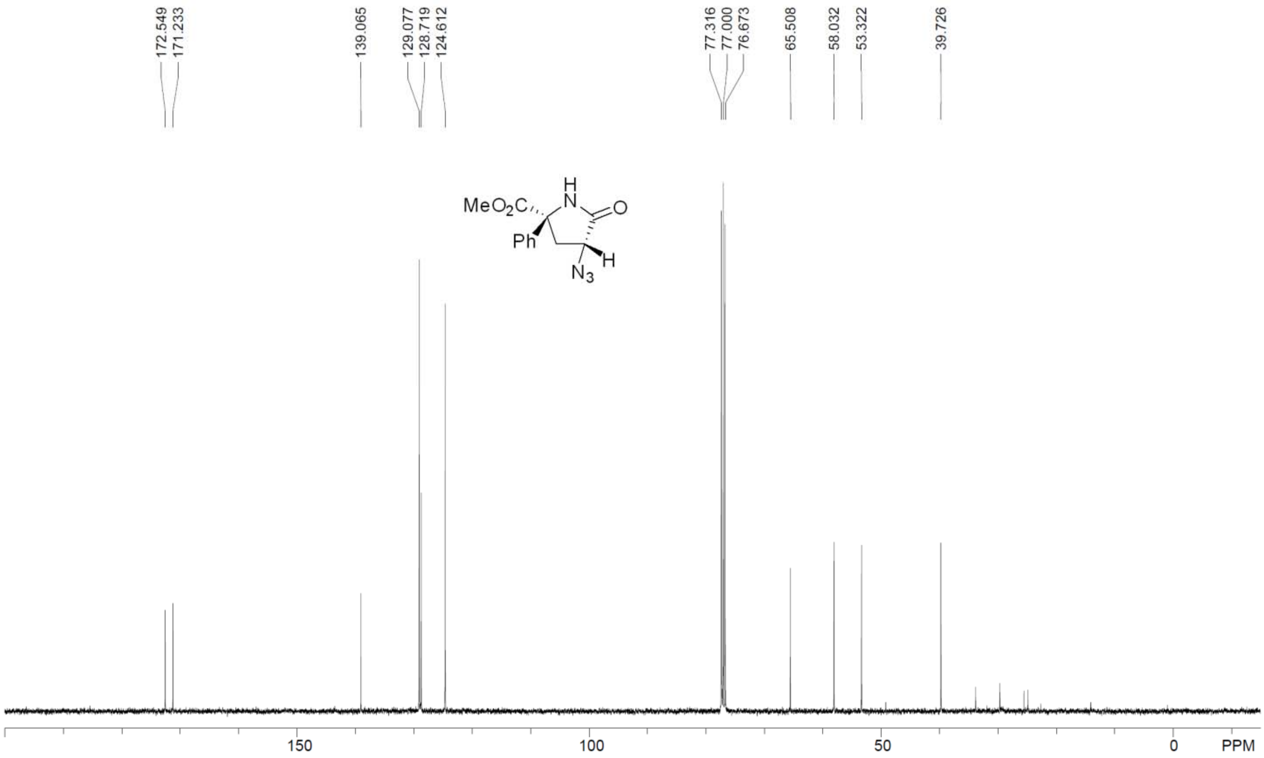
^{13}C NMR of **5**



^{1}H NMR of **6**



^{13}C NMR of **6**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77.000
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H
N
O
Ph
H
N3
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PPM