Electronic Supplementary Information

Metal-free Oxoammonium Salt-Mediated Oxidative Ugi-Azide Multicomponent Reaction

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1. General Information and Materials

All reactions were carried out under argon inert gas atmosphere with Schlenk technique. *N*-Aryl tetrahydroisoquinolines **1** were synthesized according to literature known procedures.[1,2] The TEMPO salt, $T^{+}BF_4^{-}$, was prepared according to a previous publication.[3] The following technical grade solvents were distilled prior to use: Ethylacetate (EtOAc), pentane (PE) and dichloromethane (DCM). Acetonitrile (MeCN) was purified and dried by a solvent-purification system (SPS) and stored under argon over molecular sieves. All other chemicals, whose syntheses are not described in the experimental part, were commercial acquired and used without further purification.

NMR spectra were measured at 300 K on a Bruker Avance II 300 (^{1}H: 300 MHz, ^{13}C: 75 MHz), Bruker Avance II 400 (^{1}H: 400 MHz, ^{13}C: 100 MHz, ^{19}F: 375 MHz, ^{31}P: 243 MHz) or an Agilent DD2 600 (^{1}H: 600 MHz, ^{13}C: 150 MHz). Chemical shifts δ in ^{1}H- and ^{13}C-NMR spectra are noted in ppm and calibrated based on residual solvent signals. The NMR data was analyzed using the MestReNova software from Mestrelab Research S.L. The following NMR assignment abbreviations were used: singlet (s), doublet (d), triplet (t) and multiplet (m).

High resolution mass spectra were recorded on a Bruker MicrOTof, or a Thermo Fischer Scientific Orbitrap LTQ XL using electrospray ionization (ESI) in positive mode (ESI^+).

Silica type 60 F_{254} coated aluminum plates (500 cm x 200 cm) from the company Merck were used for analytical thin layer chromatography (TLC). Visualization of the compounds was achieved by UV light (254 nm) or an appropriate staining solution (potassium permanganate or phosphomolybdic acid) followed by heating.

Flash column chromatography was performed with Merck Geduran Si 60 (0.063 nm – 0.0200 mm).

2. Electrochemical Oxidation Screening

Typical Procedure (entry 5): TEMPO (4.69 mg, 0.03 mmol, 20 mol%), THIQ **1a** (30.3 mg, 0.15 mmol, 1.0 equiv.), NaN_3 (10.7 mg, 0.165 mmol, 1.1 equiv.) and CyNC (18.2 g, 20.7 µL, 0.165 mmol, 1.1 equiv.) were dissolved in dry, degassed MeCN (≤0.7% H_2O, 3 mL) in a 5 mL cell. The cell was equipped with a graphite plate as anode and a nickel plate as cathode. The reaction was performed with the IKA ElectraSyn 2.0 at a constant current of 16.8 mA (~ 5 mA/cm²) for 40 min (2.7 F) at r.t.. After the indicated reaction time, the mixture was transferred to a round bottom flask, the solvent removed under reduced pressure, CH_2Br_2 (10.07 µL, 0.15 mmol, 1.0 equiv.) added as an internal standard to the crude product and the yield determined by ^{1}H-NMR spectroscopy.

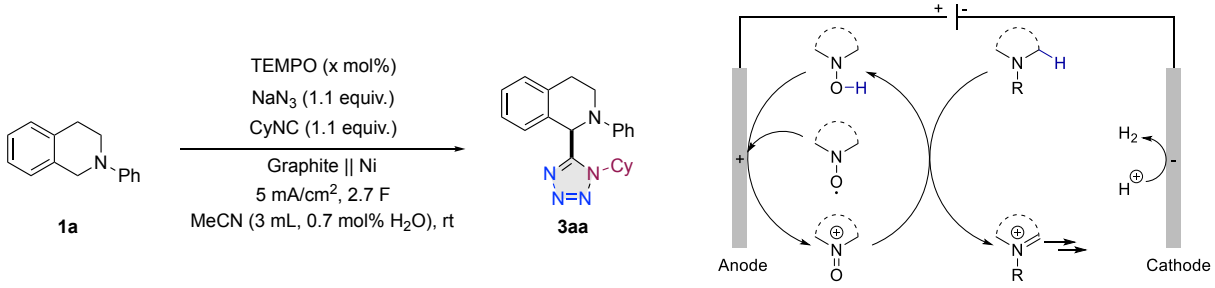


Table S1. Screening conditions for the electrochemical oxidation for the model reaction with **1a**.[a]

entry	TEMPO (mol%)	Electrolyte (equiv.)	Concentration (M)	Comment / differing conditions	t (min)	Conversion (%)[b]	**3aa** Yield (%)[c]
1	5	-	0.05	I_{real} = 3-6 mA	60	31	8
2	5	-	0.1	I_{real} = 3-6 mA	75	57	23
3	10	-	0.05	I_{real} = 3-6 mA	40	65	20
4	10	-	0.1	I_{real} = 3-6 mA	80	50	27
5	20	-	0.05	I_{real} = 3-6 mA	40	77	34
6	20	-	0.1	I_{real} = 3-6 mA	80	45	13
7	5	$Bu_4N^+BF_4^-$ (1)	0.05	--	45	70	2
8	5	$Bu_4N^+N_3^-$ (1.1)	0.05	--	40	90	2
9	5	$Et_4N^+BF_4^+$ (1)	0.05	0.3-0.8 mA, 1.5 V	24h	99	32
10	0.1	$Et_4N^+BF_4^+$ (1)	0.05	V_{real} = 2.7 V	6.5h	72	19
11	20	-	0.1	Pt || Pt, 0.21 mA/cm² (1.5 mA) + 3.5 eq. HCl (Et_2O, 1M)	12h	80	12
12	20	$Et_4N^+BF_4^+$ (1)	0.1	Pt || Pt, 0.27 mA/cm² + 3.5 eq. TFE	12h	72	18

[a] Conditions: **1a** (1.0 equiv.), CyNC (1.1 equiv.), NaN_3 (1.1 equiv.), TEMPO and electrolyte were dissolved in MeCN (3 mL) in a 5 mL cell. The cell was equipped with a graphite anode and Ni-cathode and the reaction performed at r.t. under constant current or voltage conditions (2.7 F). [b] Conversion of the substrate **1a** determined by ^{1}H-NMR. [c] Yield of the product **3aa** determined by ^{1}H-NMR with CH_2Br_2 as internal standard.

Cyclic Voltammetry: The cyclic voltammograms were taken on a Metrohm Autolab PGSTAT204 potentiostat using a silver wire counter electrode and a glassy carbon working electrode. The pH was not adjusted and the voltammogram was taken at r.t. in a 0.1 M MeCN solution of Bu_4NPF_6 containing the designated substrate in a 5 mM concentration. The scan rate was 50 mV/s.

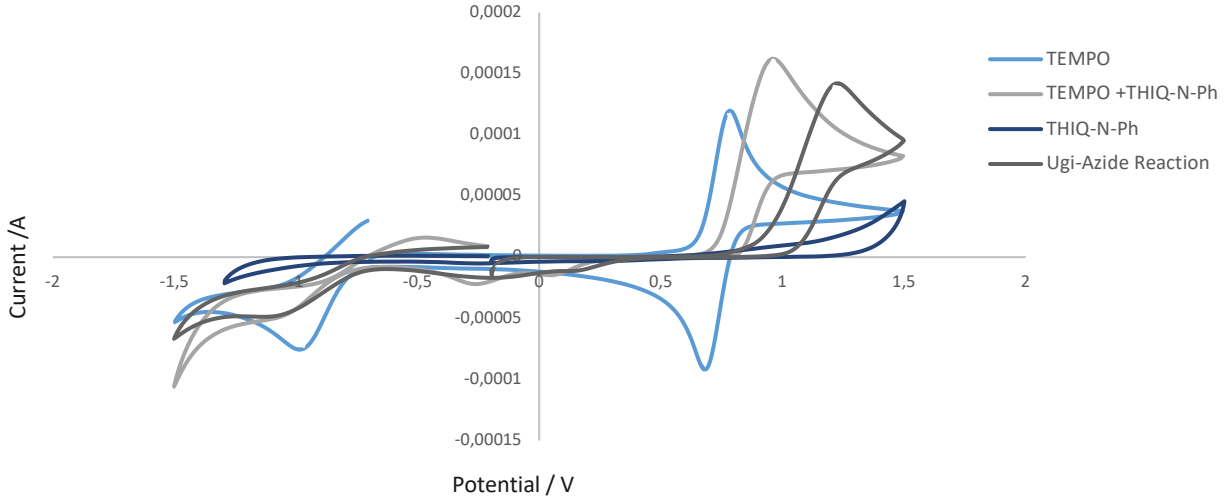


Figure S1. CV measurements of TEMPO (light blue), THIQ **1a** (light grey), the mixture of both (blue) and the full reaction (grey) using a substrate concentration of 5 mM and 0.1 M of electrolyte ($Bu_4N^+PF_6^-$) in dry, degassed acetonitrile at r.t.

3. Computational Studies

Geometries and energies were both obtained using density functional theory at B3LYP[4]-GD3BJ[5]-SMD[6](MeCN)/6-311++G(d,p)[7] level of theory. Calculations were performed with Gaussian16 program.[8] The connections between minima and transition states on the Gibbs energy surfaces were assured by intrinsic reaction coordinate calculations and verified by the analysis of the eigenvalues of the Hessian. Therefore, for energy profiles constructions we considered three molecules: singly charged model substrate *N*-methyl tetrahydroisoquinolinium (**THIQ$^+$**, **I**) formed from the corresponding THIQ **1** upon a first oxidation with $T^+BF_4^-$, methyl isocynide (**CH_3NC**) and azide ion (**N_3^-**). Notice that in the calculations we neglected the oxidation step and the effect of the counter ions (BF_4^- and Na^+).

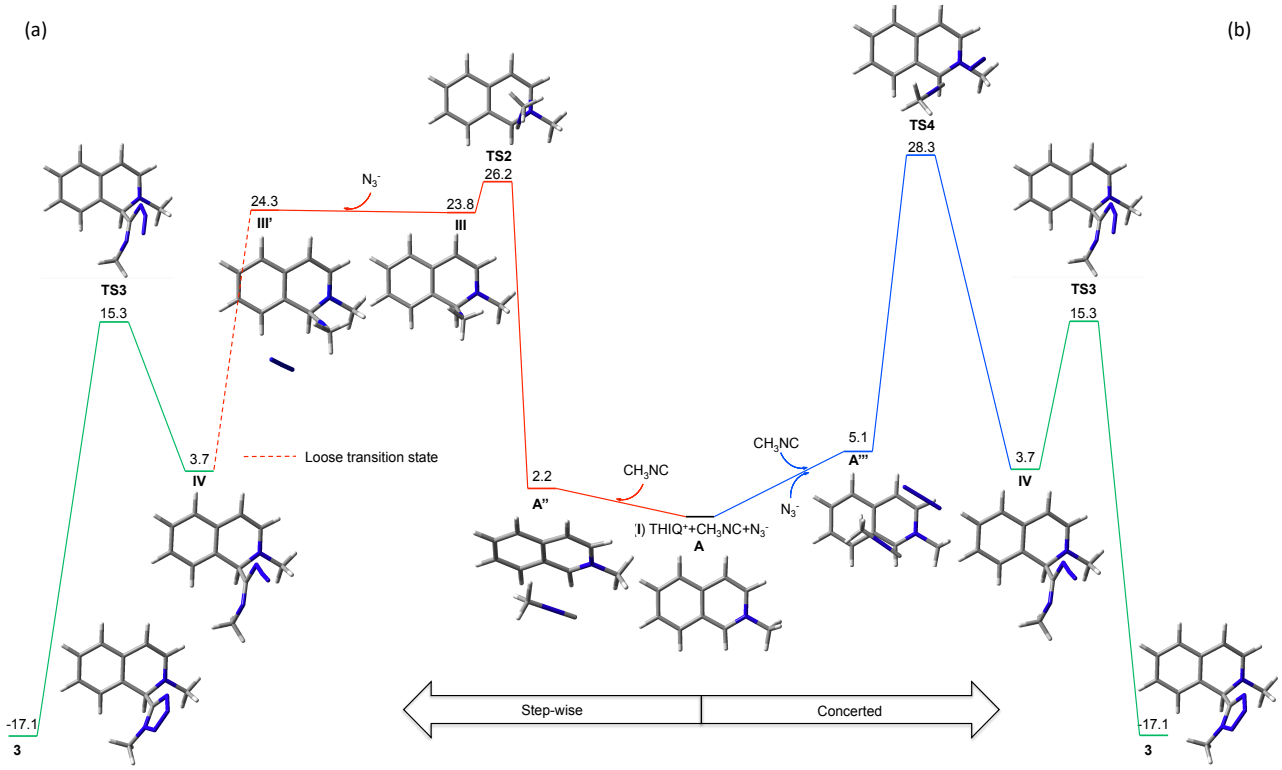


Figure S2. Complete free reaction profiles ((a) step-wise isocyanide-azide additions in red (left), and (b) concerted pathway in blue (right) followed by cyclization in green) computed using DFT-B3LYP/6-311++G(d,p)-GD3BJ-SMD(MeCN) level of theory.

Figure S2 shows the free energy surfaces were built (at r.t.) starting from three above-mentioned molecules: $THIQ^+$ (**I**), CH_3NC and N_3^- (**A**). Initially, we explored a possible concerted mechanism, in which the three molecules directly interact (via **A'''**) to form the intermediate **IV** (via transition state **TS4**). The transition state of this one-step reaction is rather high, comprising a 28.3 kcal mol^{-1} energetic barrier. Therefore, the reactivity of **THIQ$^+$ (I)** towards the nucleophilic attack of either the azide ion (N_3^- – **A'**) or the methyl isocynide (CH_3NC – **A''**) in a step-wise manner was next investigated.

The step-wise mechanism starts with the attack of the isocyanide nucleophile and formation of a weakly bounded complex **A''** that is only 0.7 kcal mol^{-1} less stable than **A'**. However, the formation of the nitrilium intermediate **III** (via **TS2**) involves a significant amount of energy (24 kcal mol^{-1}) and this species is quite unstable (23.8 kcal mol^{-1}). The relative stabilities are most probably overestimated due to the way of building of the free energy surfaces (neglecting the counter ions). The next step is the N_3^- attack, building a weakly bonded **III'** that evolves with a loose transition state (see the scan of the corresponding C-N bond in Figure S3) to the stable intermediate **IV**. The final cyclization of **IV** involves a relatively small energy barrier (**TS3**) and leads to the stable product **3** (-17.1 kcal mol^{-1}).

In summary, the step-wise mechanism is more probable, with the **TS2** barrier 2.1 kcal mol^{-1} lower than the reaction-determining step for the concerted reaction (**TS4**)

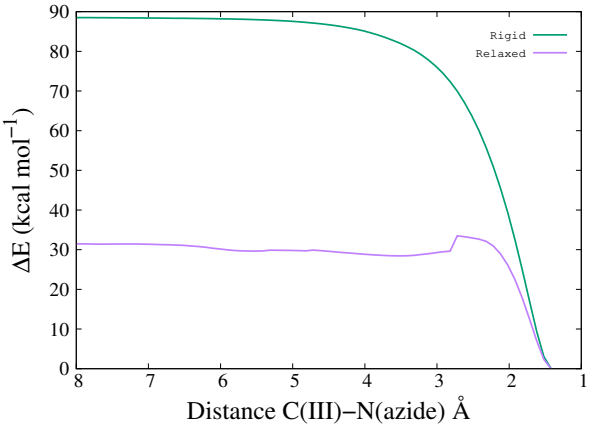


Figure S3. Rigid (green) and relaxed (purple) scans along the newly formed C-N bond of compound **III'** (see dashed line in Figure S2), computed at DFT-B3LYP/6-311++G(d,p)-GD3BJ-SMD(MeCN) level of theory.

Alternatively, the azide nucleophilic attack reaction is a non-productive pathway towards the desired product **3**, leading to the organic azide **II** (Figure S4). Although the azidation of THIQ under similar oxidative conditions (TEMPO$^+$BF$_4^-$, TMSN$_3$, MeCN, r.t.) is known,[9] the product **II** was not observed in the reaction mixture with any of the employed azide sources. However, this step is kinetically the most probable, i.e. the relative height of the barrier of TS1 vs. TS2 or TS4 is the lowest. Indeed, azide **II** is thermodynamically less stable than the initial mixture **A** and the barrier for the reversible reaction **II** to **A** is very small (**TS1** - 0.1 kcal mol^{-1}). Thus, this equilibrium is strongly shifted towards **THIQ$^+$ (I)**.

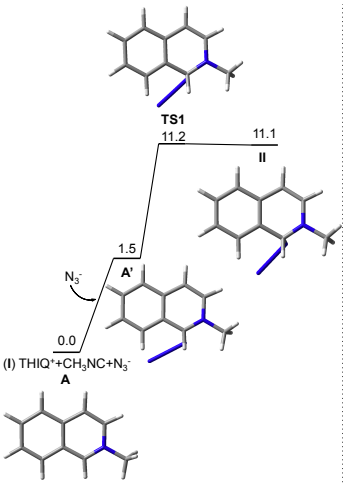


Figure S4. Azide attack pathway.

XYZ coordinates of the key saddle points in Å:

THIQ$^+$ (I)

6	-0.328553	-0.599267	-0.000017
6	-0.583368	0.805858	0.000015
6	0.533493	1.679383	0.000024
6	1.798864	1.178372	0.000005
1	-1.196791	-2.581649	-0.000060
6	-1.407903	-1.518925	-0.000034
6	-1.921745	1.257892	0.000034
1	0.387222	2.751721	0.000043
1	2.685969	1.794317	0.000010
6	-2.952481	0.345419	0.000020
6	-2.697458	-1.047342	-0.000015
1	-2.119319	2.323121	0.000060
1	-3.978518	0.694036	0.000036
1	-3.529666	-1.740744	-0.000027
6	3.413526	-0.657631	0.000012
1	3.911658	-0.280232	0.892255
1	3.417963	-1.744210	-0.000202
1	3.911820	-0.279879	-0.891988
7	2.016098	-0.180282	-0.000020
6	1.003503	-1.040521	-0.000032
1	1.249712	-2.093935	-0.000055

II

6	0.511460	-0.008338	-0.406168
6	0.968051	1.108940	0.327476
6	-0.007550	2.070996	0.785852
6	-1.288043	1.973130	0.356353
1	1.049513	-1.769210	-1.514679
6	1.418480	-0.923435	-0.944640
6	2.352007	1.263627	0.521297
1	0.298165	2.915286	1.389338
1	-2.033084	2.724005	0.586015
6	3.247137	0.341236	-0.005362
6	2.785946	-0.751536	-0.748121
1	2.714290	2.119940	1.079971
1	4.311568	0.474835	0.152978
1	3.488517	-1.462588	-1.166494
6	-3.136388	0.843875	-0.790978
1	-3.244905	0.296777	-1.728625
1	-3.694389	0.319429	-0.007686
1	-3.549461	1.844192	-0.917032
7	-1.718793	0.947868	-0.457850
7	-1.414319	-1.129300	0.753200
7	-1.009702	-2.275361	0.710202
7	-0.637770	-3.354722	0.702610
6	-0.958103	-0.241883	-0.505549
1	-1.234107	-0.841734	-1.371876

III

6	0.799711	-0.001193	-0.547243
6	1.244858	-0.527222	0.681236
6	0.353988	-1.394465	1.430618
6	-0.757886	-1.880517	0.834878
1	1.260037	1.162883	-2.291377
6	1.632971	0.766744	-1.353275
6	2.561749	-0.248248	1.079782
1	0.638565	-1.745491	2.413292
1	-1.385142	-2.630800	1.299554
6	3.394304	0.526101	0.278299
6	2.938754	1.030575	-0.942796
1	2.926895	-0.652382	2.017498
1	4.407883	0.733797	0.602320
1	3.592585	1.628668	-1.566089
6	-2.407785	-1.968714	-0.990881
1	-2.579405	-2.994507	-0.667046
1	-3.246196	-1.343992	-0.657034
1	-2.360553	-1.946156	-2.080598
7	-1.133109	-1.509290	-0.446249
6	-0.653108	-0.232995	-0.912748
1	-0.812025	-0.137855	-1.988763
6	-2.812797	2.702388	0.913977
1	-2.137204	3.222579	1.592719
1	-3.622921	2.226260	1.465685
1	-3.207829	3.384200	0.161336
7	-2.071732	1.682572	0.246382
6	-1.468226	0.874184	-0.288916

IV

6	-1.119124	0.179374	0.447271
6	-1.862716	-0.710329	-0.356976
6	-1.358732	-2.051538	-0.576078
6	-0.261402	-2.466144	0.101220
1	-1.031571	2.115902	1.363879
6	-1.615147	1.446927	0.740235
6	-3.098093	-0.272954	-0.865922
1	-1.900842	-2.742295	-1.207691
1	0.098796	-3.485812	0.031183
6	-3.579856	1.001281	-0.583621
6	-2.843603	1.866688	0.227998
1	-3.680560	-0.950471	-1.481659
1	-4.534070	1.318274	-0.990086
1	-3.218364	2.857377	0.457460
6	1.662446	-2.150237	1.586503
1	2.555133	-1.898406	0.999332
1	1.764952	-1.703452	2.578576
1	1.610023	-3.233352	1.695356
7	0.442178	-1.667236	0.960525
6	0.263388	-0.218265	0.944380
1	0.387558	0.139144	1.966549
6	1.994207	2.182613	1.634265
1	1.514291	1.628477	2.445171

1	1.452752	3.123060	1.491019
1	3.011047	2.439922	1.939635
7	2.061718	1.479599	0.365098
6	1.341501	0.475911	0.097319
7	1.458013	-0.167033	-1.177578
7	2.284684	0.322579	-1.950787
7	3.015358	0.702329	-2.721299

3

6	-1.087866	-0.158467	-0.439354
6	-1.876525	0.569035	0.478450
6	-1.455823	1.903834.	0.854360
6	-0.452416	2.496893	0.163367
1	-0.923414	-1.914744	-1.659890
6	-1.530181	-1.380569	-0.937547
6	-3.087746	0.002349.	0.911645
1	-2.016523	2.467233	1.588068
1	-0.190083	3.537243	0.314683
6	-3.507740	-1.235203	0.435402
6	-2.738161	-1.927188	-0.502431
1	-3.704110	0.552903	1.614611
1	-4.444424	-1.655885	0.784390
1	-3.071395	-2.883622	-0.887973
6	1.375133	2.521941	-1.471705
1	2.317167	2.373506	-0.929753
1	1.489853	2.129975	-2.484834
1	1.169367	3.590400	-1.533753
7	0.256549	1.854967	-0.820938
6	0.278802	0.398942	-0.818963
1	0.535431	0.062744	-1.825405
6	1.913219	-2.351913	-0.999790
1	1.717203	-1.907653	-1.973975
1	1.105098	-3.031777	-0.731366
1	2.861243	-2.884584	-1.020316
7	2.019692	-1.290653	-0.004175
6	1.357877	-0.122487	0.118634
7	1.812264	0.489262	1.202874
7	2.747987	-0.329563	1.737168
7	2.881100	-1.400977	1.026944

TS1

6	0.487966	-0.034792	0.427772
6	0.914559	-1.165528	-0.307889
6	-0.085185	-2.097317	-0.761299
6	-1.369599	-1.945430	-0.362459
1	1.082192	1.718674	1.525595
6	1.425344	0.865641	0.951684
6	2.292793	-1.352642	-0.518299
1	0.196844	-2.954827	-1.357732
1	-2.144856	-2.659580	-0.604547
6	3.210935	-0.448616	-0.005751
6	2.781696	0.659482	0.738354
1	2.628320	-2.217966	-1.079241
1	4.270560	-0.605153	-0.174007
1	3.506768	1.354095	1.145546
6	-3.186715	-0.736443	0.758183
1	-3.279723	-0.168105	1.683391
1	-3.713855	-0.208830	-0.042020
1	-3.630141	-1.721290	0.898089
7	-1.769808	-0.889060	0.430256
7	-1.394954	1.273260	-0.824919
7	-0.874083	2.355573	-0.728560
7	-0.362022	3.382751	-0.631534
6	-0.949149	0.210671	0.566038
1	-1.245905	0.875173	1.370215

TS2

6	0.757705	-0.309821	-0.584647
6	1.069698	-0.469882	0.782957
6	0.050665	-0.978642	1.665236
6	-1.110609	-1.442678	1.150090
1	1.454516	0.270299	-2.535505
6	1.720297	0.143396	-1.491933
6	2.375429	-0.168669	1.212995
1	0.240641	-1.060741	2.726992
1	-1.875512	-1.914622	1.751369
6	3.325650	0.275701	0.307851
6	3.003368	0.429439	-1.049338
1	2.627920	-0.292865	2.260001
1	4.328311	0.505033	0.650126
1	3.754691	0.774167	-1.749579
6	-2.672893	-1.833231	-0.711891
1	-3.059593	-2.622944	-0.070860
1	-3.377845	-0.992944	-0.720587
1	-2.554993	-2.212629	-1.726638
7	-1.373313	-1.395016	-0.207654
6	-0.632958	-0.548029	-1.016806
1	-0.773811	-0.733246	-2.073864
6	-2.017990	3.003038	0.726553
1	-1.148605	3.258546	1.332825
1	-2.849026	2.700087	1.363351
1	-2.307134	3.849512	0.103263
7	-1.672262	1.909068	-0.117896
6	-1.391786	1.045042	-0.829742

TS3

6	-1.098757	-0.190393	-0.437865
6	-1.939832	0.591758	0.382344
6	-1.558025	1.956181	0.681404
6	-0.486571	2.496656	0.053760
1	-0.829132	-2.058595	-1.458351
6	-1.481892	-1.474048	-0.819634
6	-3.152125	0.030104	0.821293
1	-2.172707	2.566012	1.329665
1	-0.219231	3.539331	0.176726
6	-3.518364	-1.259659	0.453226
6	-2.688339	-2.016243	-0.377616
1	-3.808163	0.623952	1.449115
1	-4.456229	-1.674365	0.806113
1	-2.975053	-3.018046	-0.675440
6	1.485476	2.416701	-1.399533
1	2.380735	2.230578	-0.792873
1	1.654512	2.013696	-2.401039
1	1.330947	3.492490	-1.477605
7	0.301489	1.799092	-0.822335
6	0.260012	0.349039	-0.849341
1	0.483838	0.027140	-1.868127
6	2.116426	-2.092941	-1.421643
1	1.620082	-1.615745	-2.272213
1	1.627792	-3.050428	-1.222962
1	3.156319	-2.295328	-1.684651
7	2.084504	-1.282345	-0.227133
6	1.362003	-0.285285	0.034255
7	1.513076	0.371748	1.297474
7	2.439785	-0.273274	1.907098
7	3.147748	-1.174065	1.754574

TS4

6	-1.408539	-0.125247	0.522155
6	-1.744615	-0.622520	-0.757029
6	-0.970980	-1.710643	-1.290765
6	-0.046715	-2.320944	-0.511319
1	-1.872331	1.276082	2.088597
6	-2.156707	0.902359	1.110994
6	-2.849666	-0.060244	-1.426153
1	-1.172656	-2.088894	-2.283948
1	0.505188	-3.193754	-0.830670
6	-3.583227	0.955007	-0.836373
6	-3.243028	1.437860	0.438535
1	-3.118747	-0.435509	-2.407156
1	-4.430645	1.380855	-1.361641
1	-3.826992	2.229742	0.892098
6	1.266368	-2.529592	1.565854
1	2.179460	-1.929694	1.501832
1	0.943795	-2.599529	2.605318
1	1.459022	-3.527845	1.178220
7	0.215140	-1.897576	0.773584
6	-0.211196	-0.656762	1.181701
1	-0.153836	-0.507848	2.254782
6	1.479715	3.144191	0.491068
1	0.704541	3.653144	1.066256
1	1.402944	3.408101	-0.562562
1	2.465969	3.411600	0.867922
7	1.293144	1.736793	0.627080
6	1.065594	0.610330	0.766394
7	2.858962	-0.783316	-0.774915
7	3.285492	0.275988	-1.073147
7	3.680443	1.351079	-1.343947

4. References

[1] C. R. Johnson, M. I. Ansari and A. Coop, *ACS omega* 2018, **3**, 10886–10890.

[2] T. Zhang, W. Liang, Y. Huang, X. Li, Y. Liu, B. Yang, C. He, X. Zhou and J. Zhang, *Chem. Commun.* 2017, **53**, 12536–12539.

[3] H. Richter and O. García Mancheño, *Eur. J. Org. Chem.* 2010, 4460-4467.

[4] A. D. Becke, *J. Chem. Phys.* 1993, **98**, 5648–5652.

[5] S. Grimme, S. Ehrlich and L. Goerigk, *J. Comput. Chem.* 2011, **32**, 1456–1465.

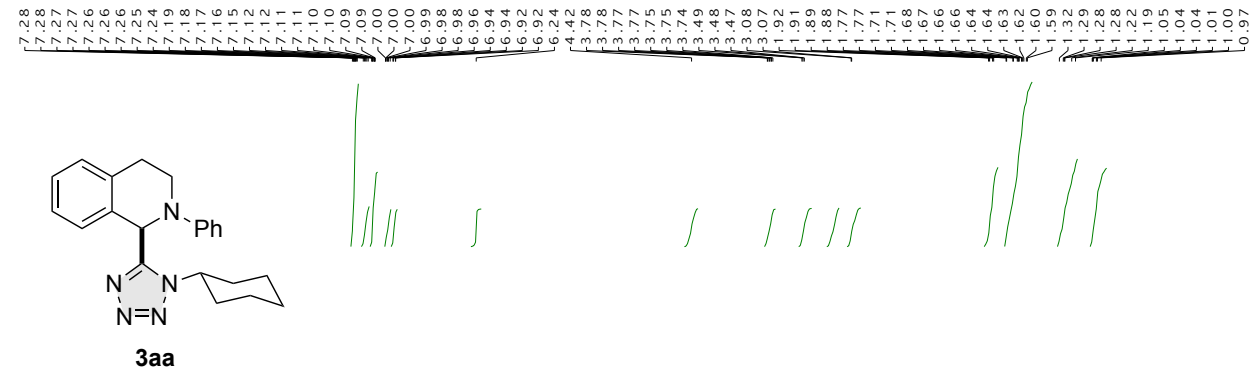
[6] A. V. Marenich, C. J. Cramer and D. G. Truhlar, *J. Phys. Chem. B*, 2009, **113**, 6378–6396.

[7] (a) W. J. Hehre, R. Ditchfield and J. A. Pople, *J. Chem. Phys.* 1972, **56**, 2257–2261; (b) A. D. McLean and G. S. Chandler, *J. Chem. Phys.* 1980, **72**, 5639–5648; (c) K. Raghavachari, J. S. Binkley, R. Seeger and J. A. Pople, *J. Chem. Phys.* 1980, **72**, 650–654; (d) M. J. Frisch, J. A. Pople and J. S. Binkley, *J. Chem. Phys.* 1984, **80**, 3265–3269; (e) T. Clark, J. Chandrasekhar, G. W. Spitznagel and P. v. R. Schleyer, *J. Comp. Chem.* 1983, **4**, 294–301.

[8] M. J. Frisch, *et al.* Gaussian16 Revision B.01. 2016; Gaussian Inc. Wallingford CT.

[9] J. Dong, Q. Xia, C. Yan, H. Song, Y. Liu and Q. Wang, *J. Org. Chem.* 2018, **83**, 4516–4524.

5. NMR Collection



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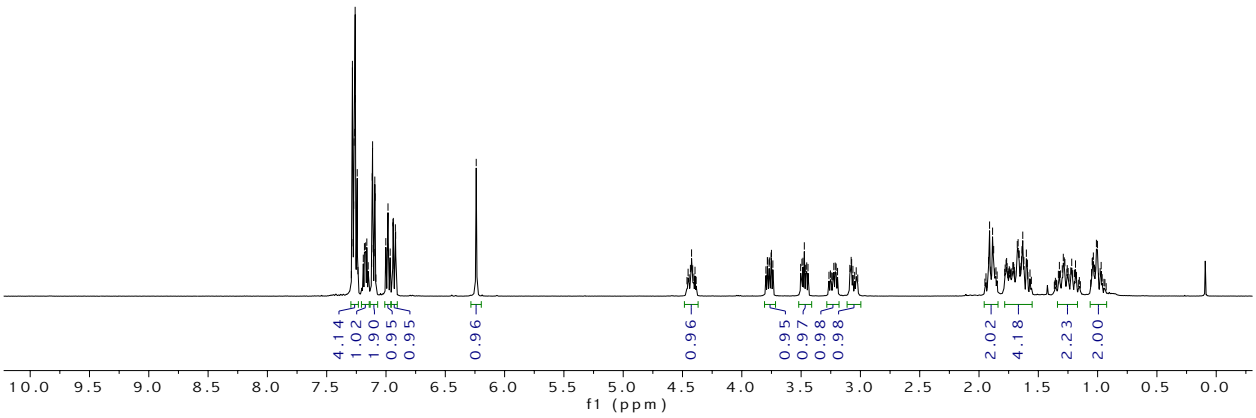

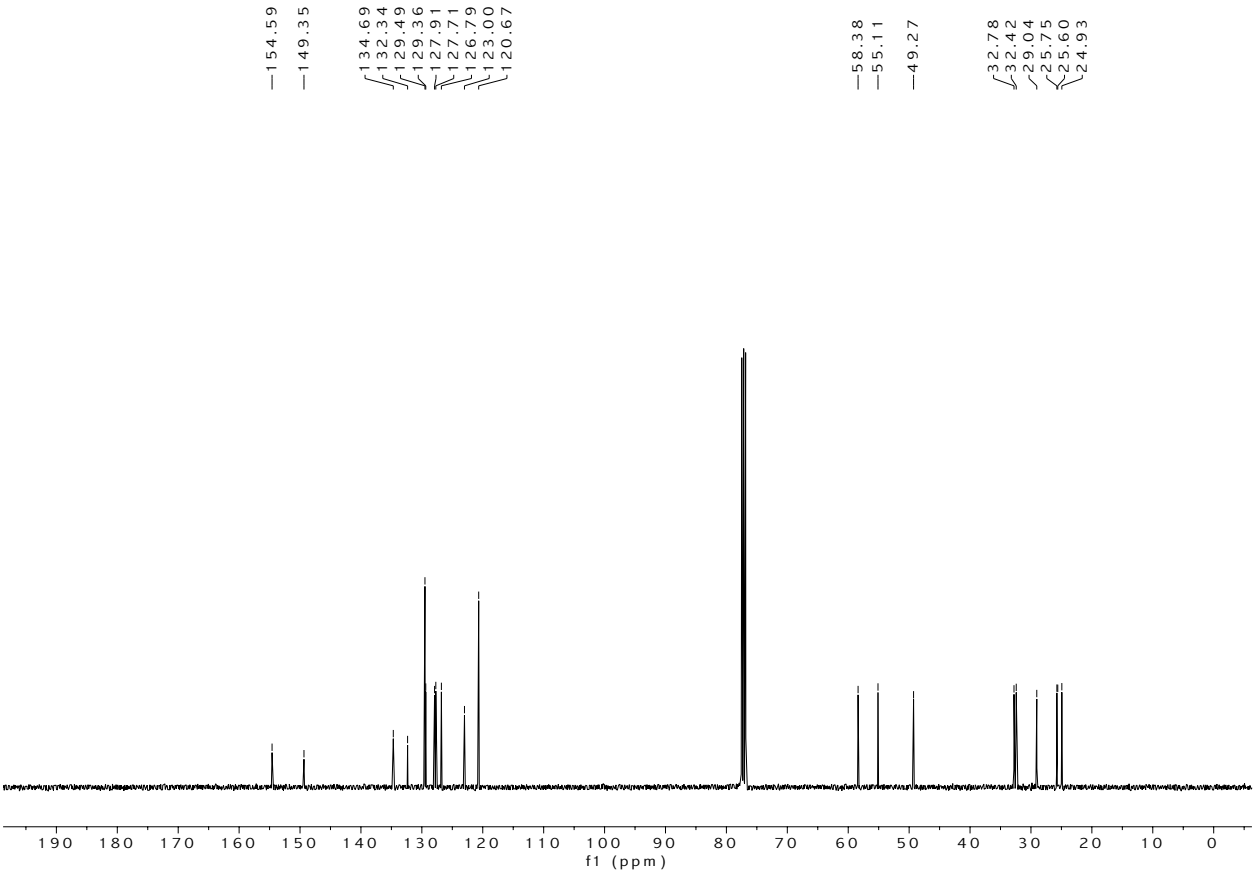

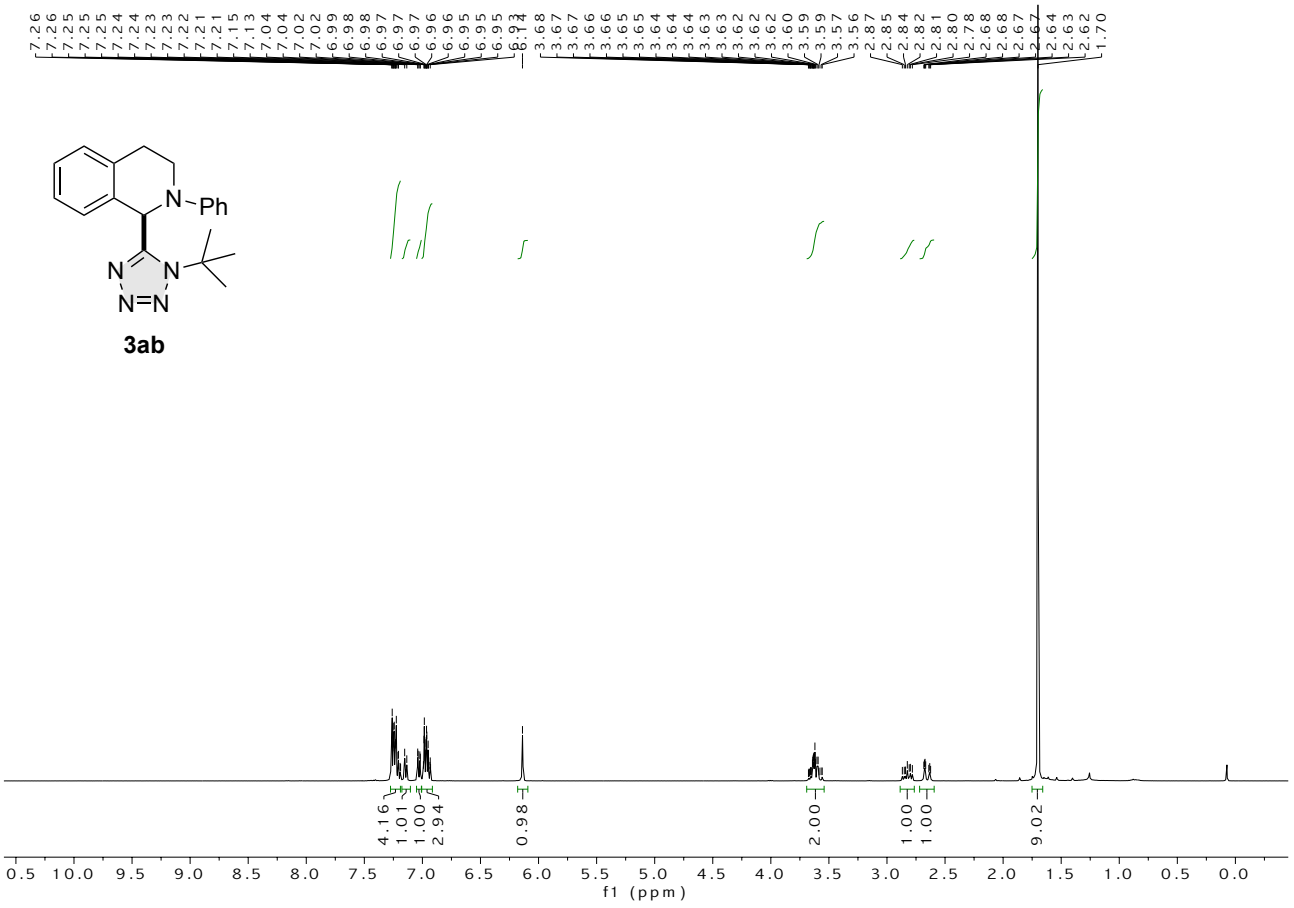
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3.68 3.67 3.67 3.66 3.66 3.65 3.65 3.64 3.64 3.64 3.63 3.63 3.62 3.62 3.62 3.60 3.59 3.59 3.57 3.56
2.87 2.85 2.84 2.82 2.81 2.80 2.78 2.68 2.68 2.67 2.67 2.64 2.63 2.62 1.70
N-Ph
N
N
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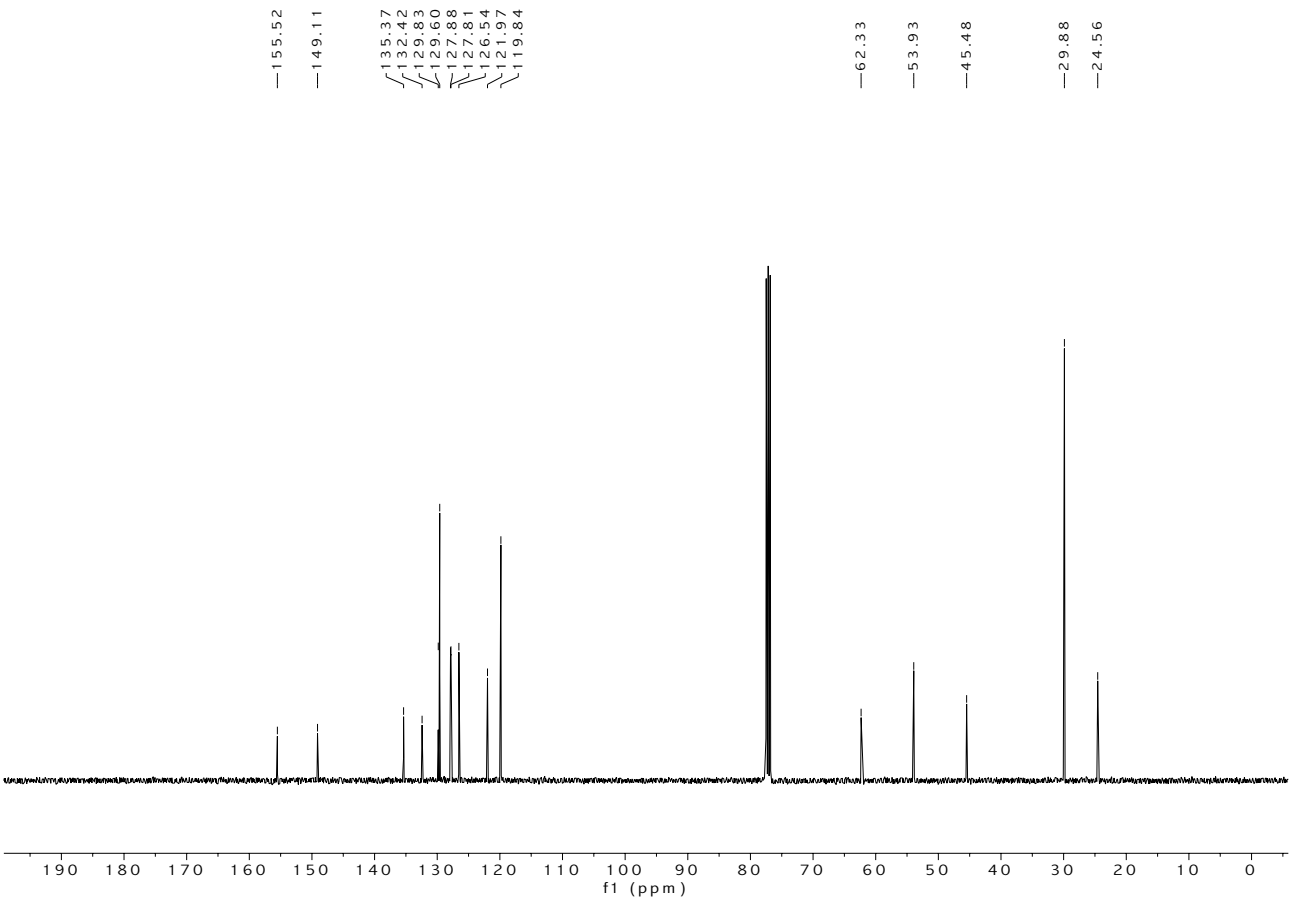
1.00
2.94
0.98
2.00
1.00
1.00
9.02
f1 (ppm)

3ab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149.11
135.37
132.42
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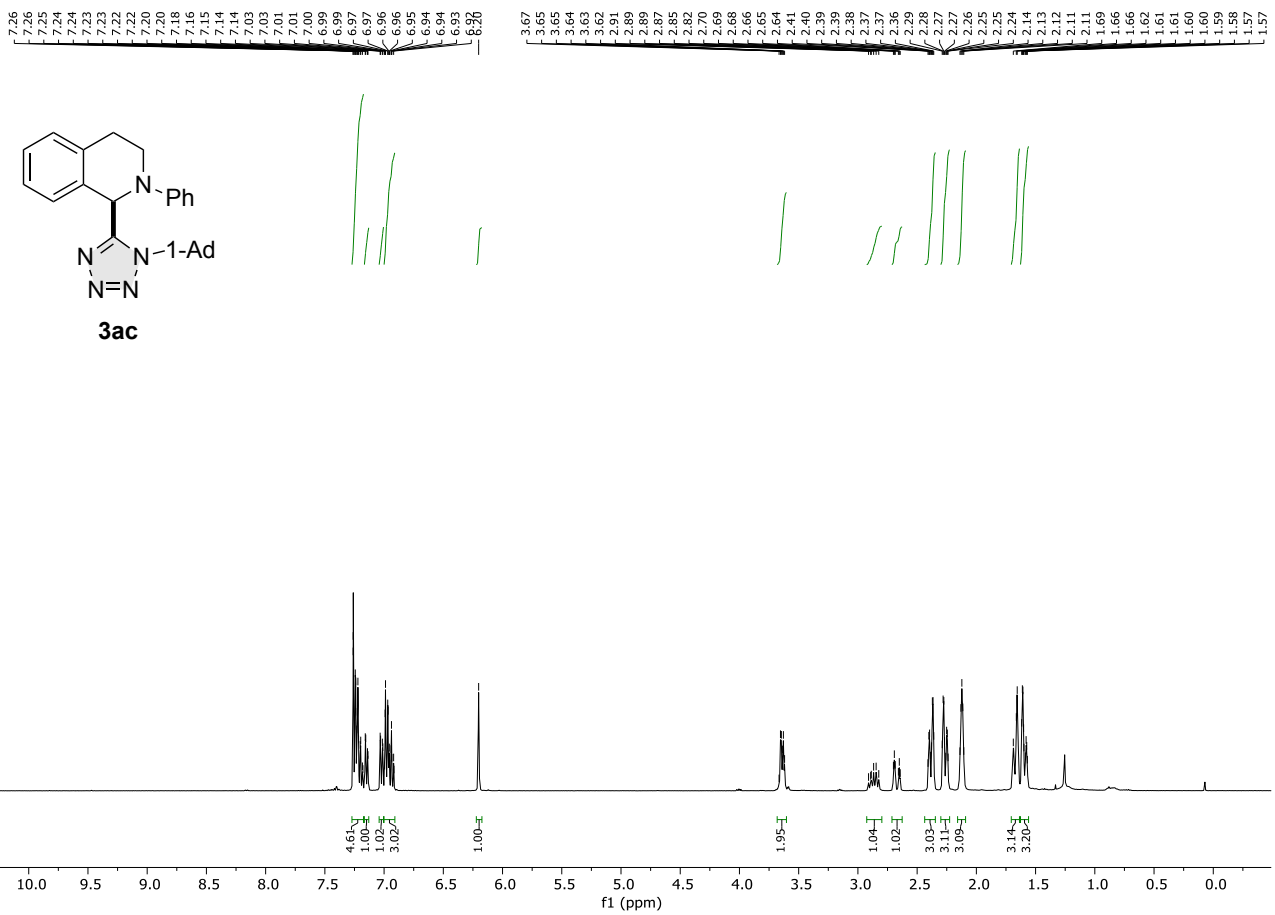
119.84
62.33
53.93
45.48
29.88
24.56
f1 (ppm)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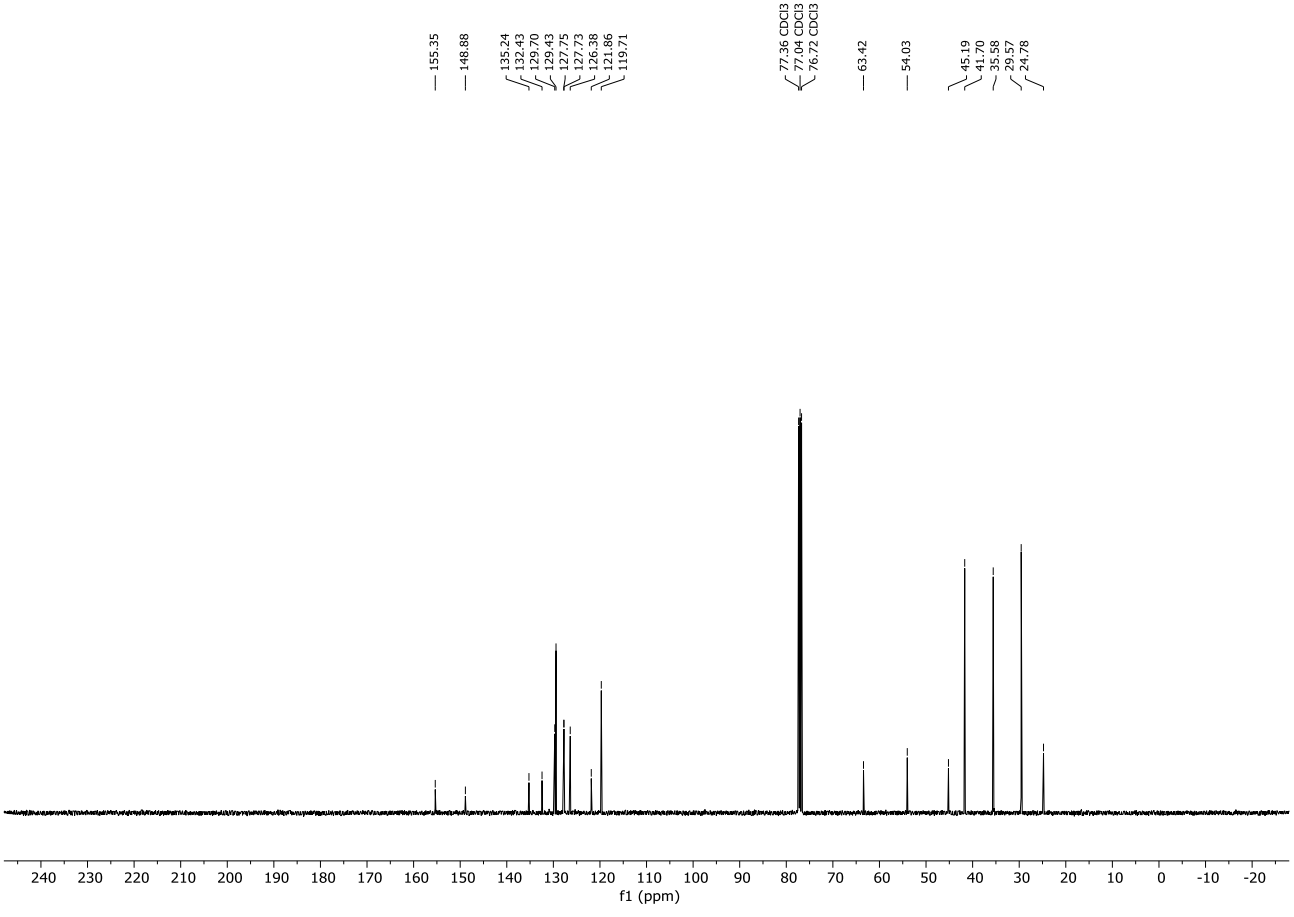
3.67 3.65 3.65 3.64 3.64 3.63 3.62 2.91 2.89 2.89 2.87 2.85 2.82 2.70 2.69 2.68 2.66 2.65 2.64 2.41 2.40 2.39 2.39 2.38 2.37 2.37 2.36 2.29 2.28 2.27 2.27 2.26 2.25 2.25 2.24 2.14 2.13 2.12 2.11 2.11 1.69 1.66 1.66 1.62 1.61 1.61 1.60 1.60 1.59 1.58 1.57 1.57
N
Ph
N
N
1-Ad
N=N
4.61
1.00
1.02
3.02
1.00
1.95
1.04
1.02
3.03
3.11
3.09
3.14
3.20
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

3ac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76.72 CDCl3
63.42
54.03
45.19
41.70
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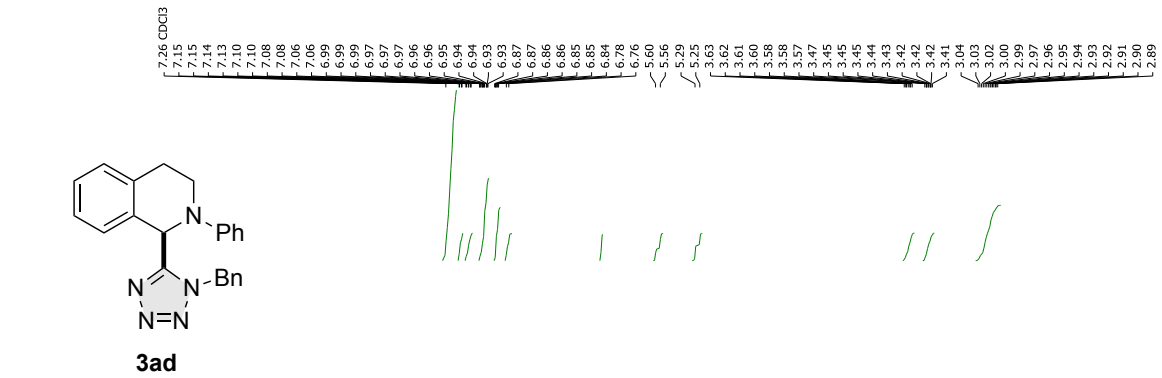
29.57
24.78
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)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7.08
7.06
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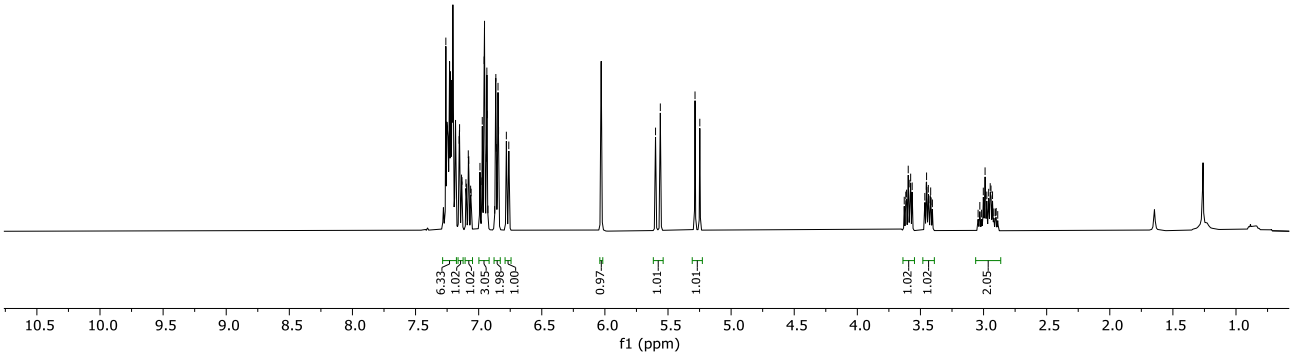
6.99
6.99
6.97
6.97
6.97
6.96
6.96
6.95
6.94
6.94
6.93
6.93
6.87
6.87
6.86
6.86
6.85
6.84
6.78
6.76
5.60
5.56
5.29
5.25
3.63
3.62
3.61
3.60
3.58
3.58
3.57
3.47
3.45
3.45
3.45
3.44
3.43
3.42
3.42
3.42
3.41
3.04
3.03
3.02
3.00
2.99
2.97
2.96
2.95
2.94
2.93
2.92
2.91
2.90
2.89
N
Ph
N
N
Bn
N=N

3ad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1.02
1.02
2.05
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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4.5
4.0
3.5
3.0
2.5
2.0
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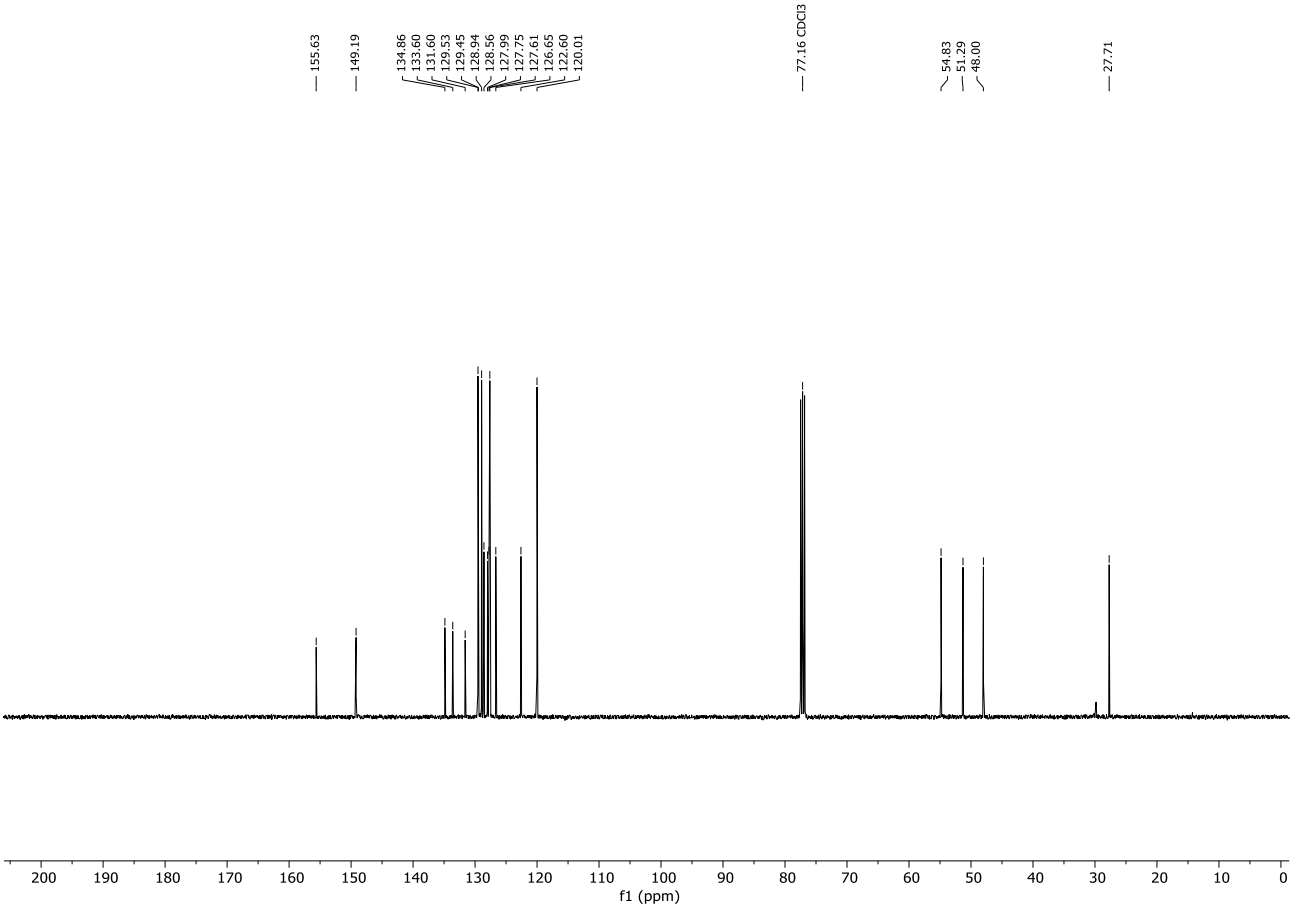
1.0
f1 (ppm)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127.99
127.75
127.61
126.65
122.60
120.01
77.16 CDCl3
54.83
51.29
48.00
27.71
200
190
180
170
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150
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130
120
110
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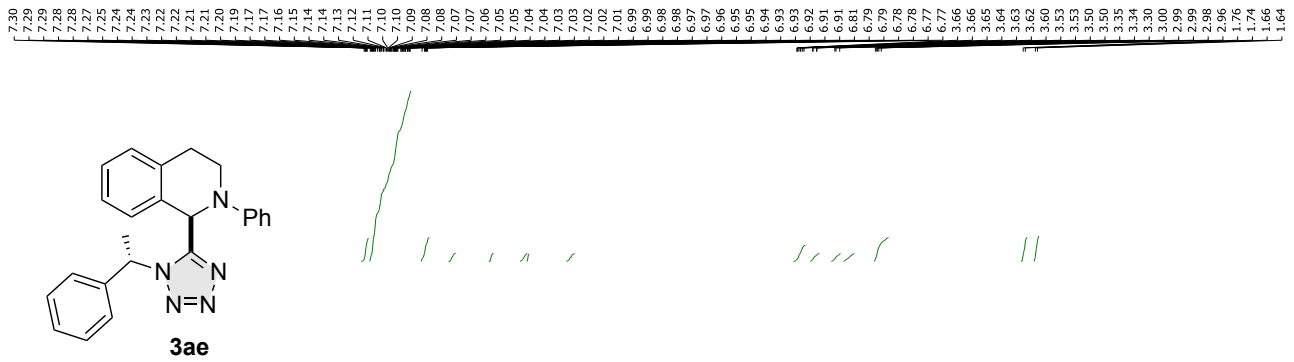
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



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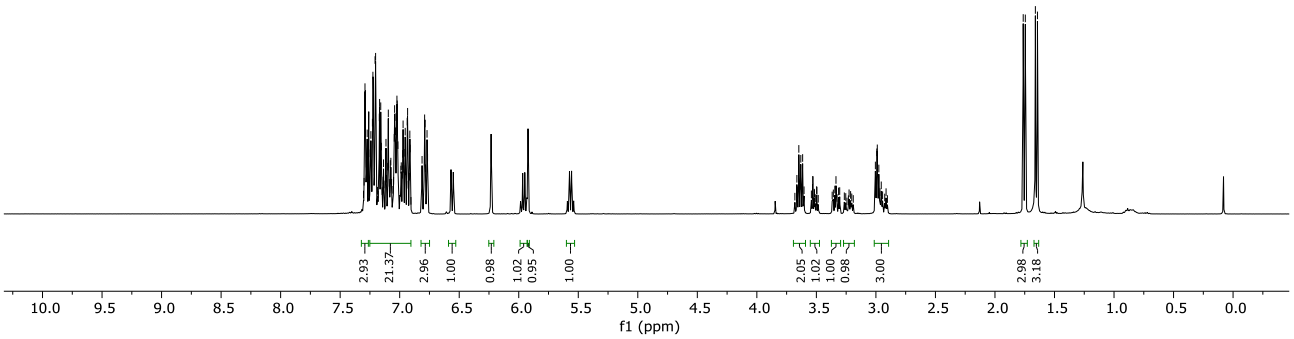

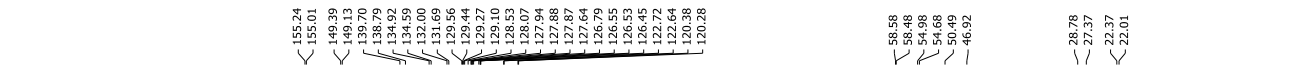

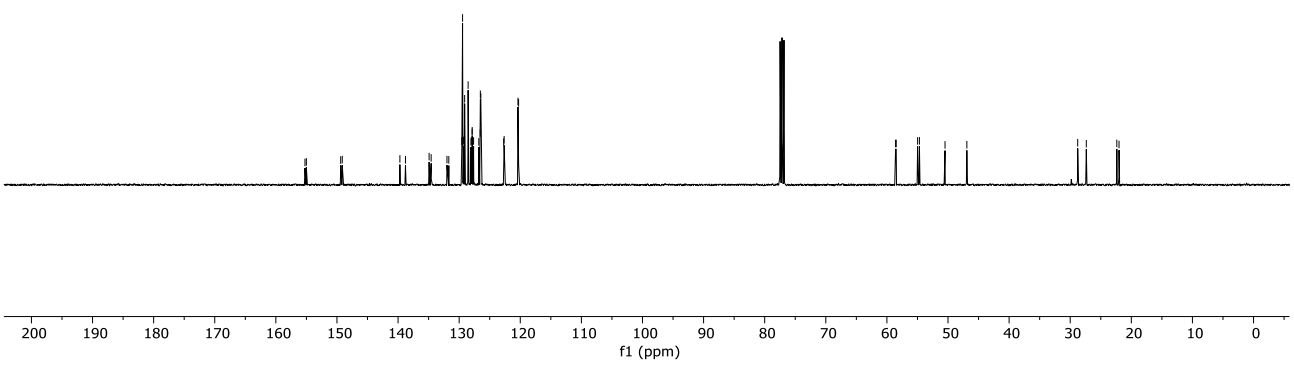


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7.45
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7.43
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7.29
7.17
7.16
7.16
7.15
7.09
7.08
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7.07
7.06
7.05
7.04
7.03
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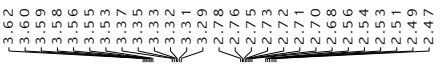
6.73
6.70
6.14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3.33
3.32
3.31
3.29
2.78
2.76
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2.72
2.71
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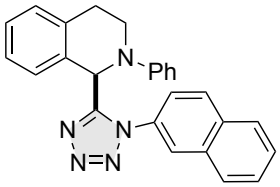
2.54
2.53
2.51
2.49
2.47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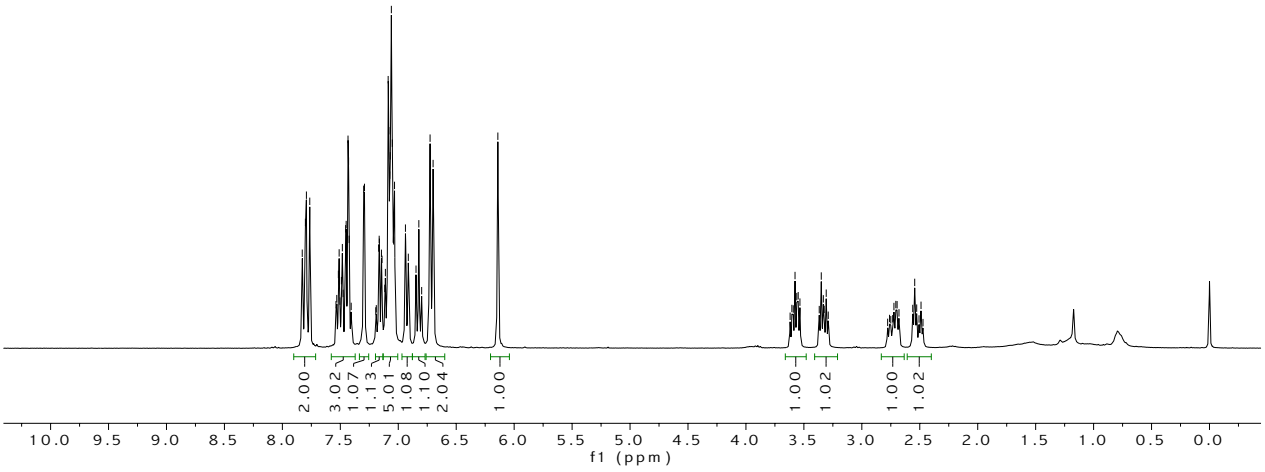
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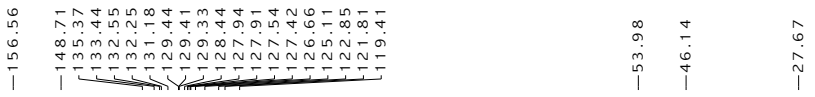
5.01
1.08
1.10
2.04
1.00
1.00
1.02
1.00
1.02
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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128.44
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127.42
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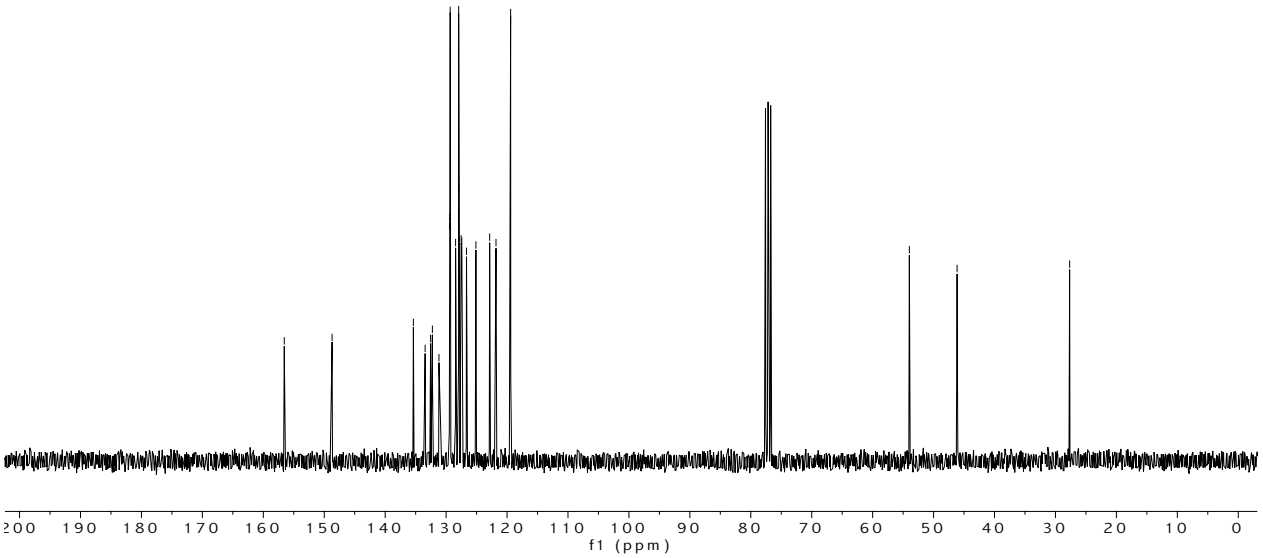
121.81
119.41
53.98
46.14
27.67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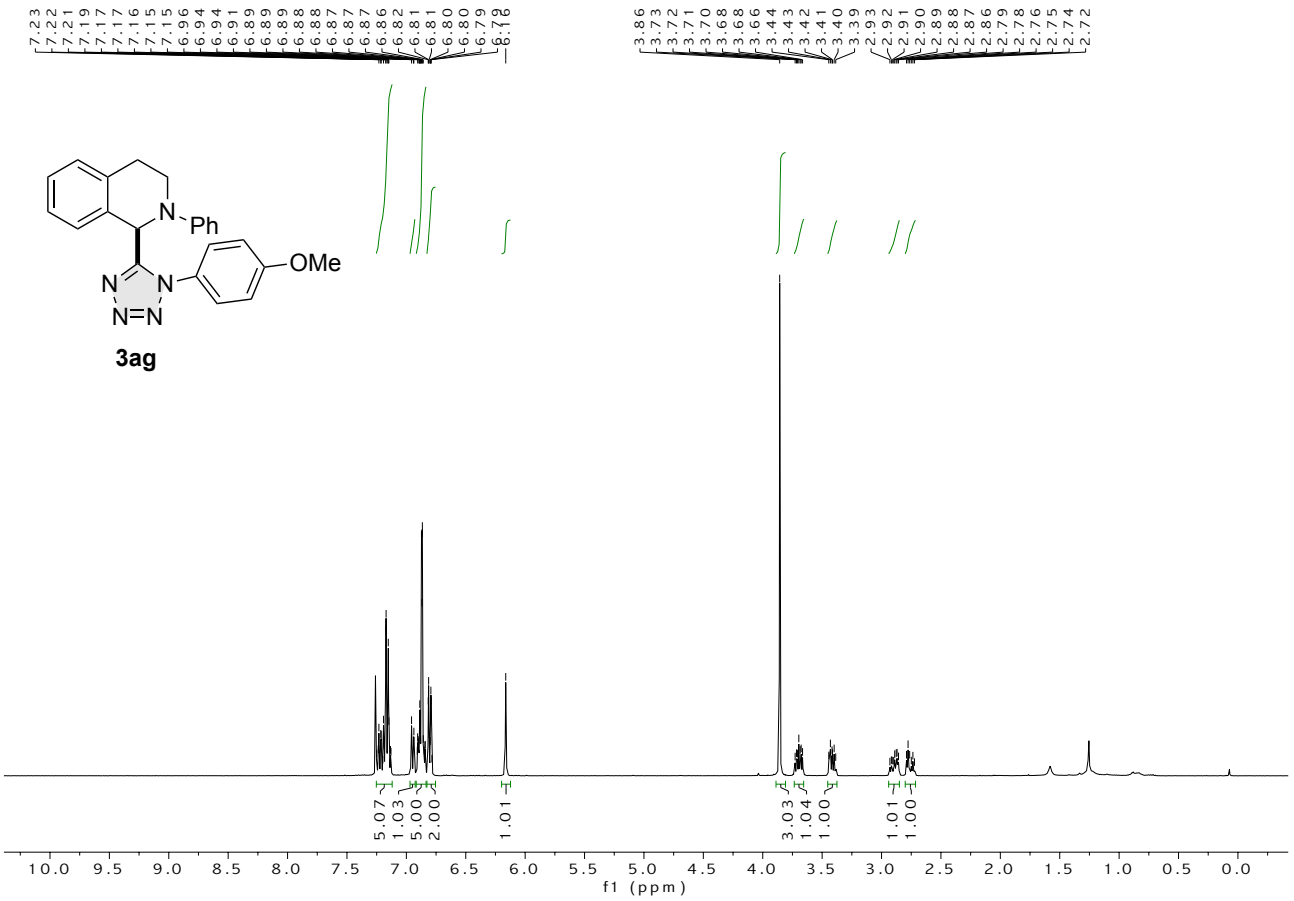
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7.19
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7.17
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7.15
7.15
6.96
6.94
6.94
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6.89
6.89
6.89
6.88
6.88
6.87
6.87
6.87
6.86
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6.81
6.81
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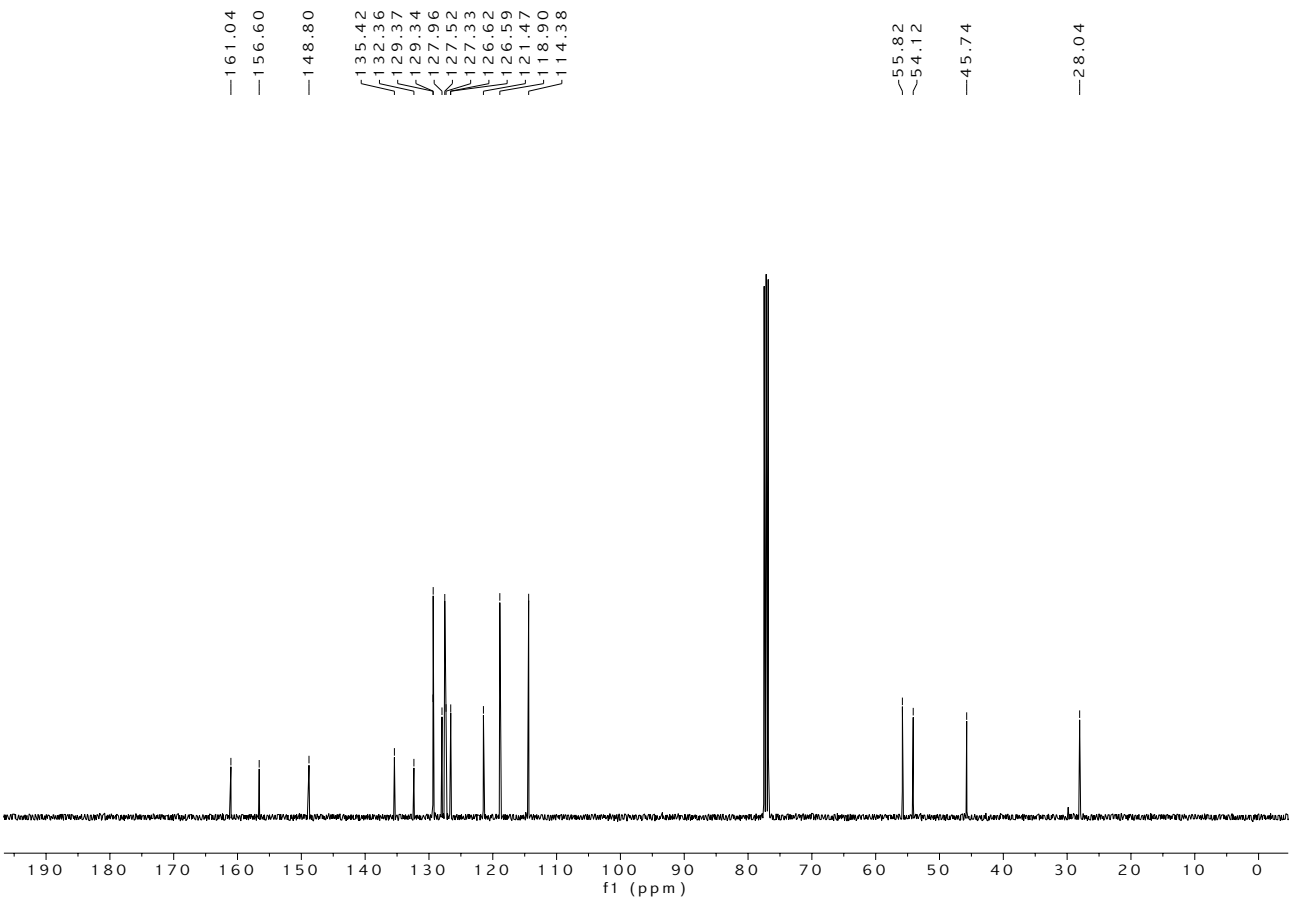
6.79
6.79
6.76
3.86
3.73
3.72
3.71
3.70
3.68
3.68
3.66
3.44
3.43
3.42
3.41
3.40
3.39
2.93
2.92
2.91
2.90
2.89
2.88
2.87
2.86
2.79
2.78
2.76
2.75
2.74
2.72
N
Ph
N
N
N=N
OMe
3ag
5.07
1.03
5.00
2.00
1.01
3.03
1.04
1.00
1.01
1.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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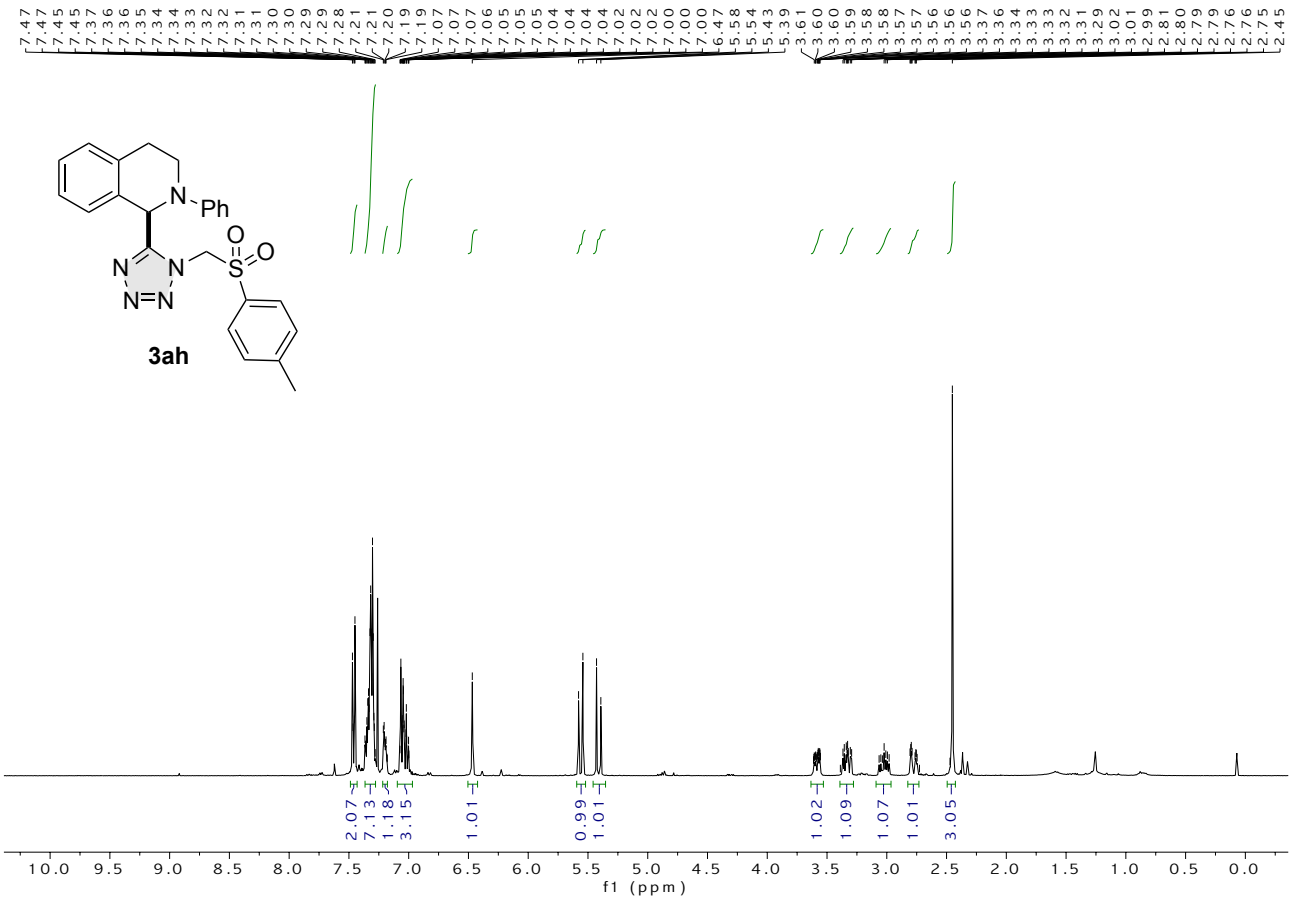
129.37
129.34
127.96
127.52
127.33
126.62
126.59
121.47
118.90
114.38
55.82
54.12
45.74
28.04
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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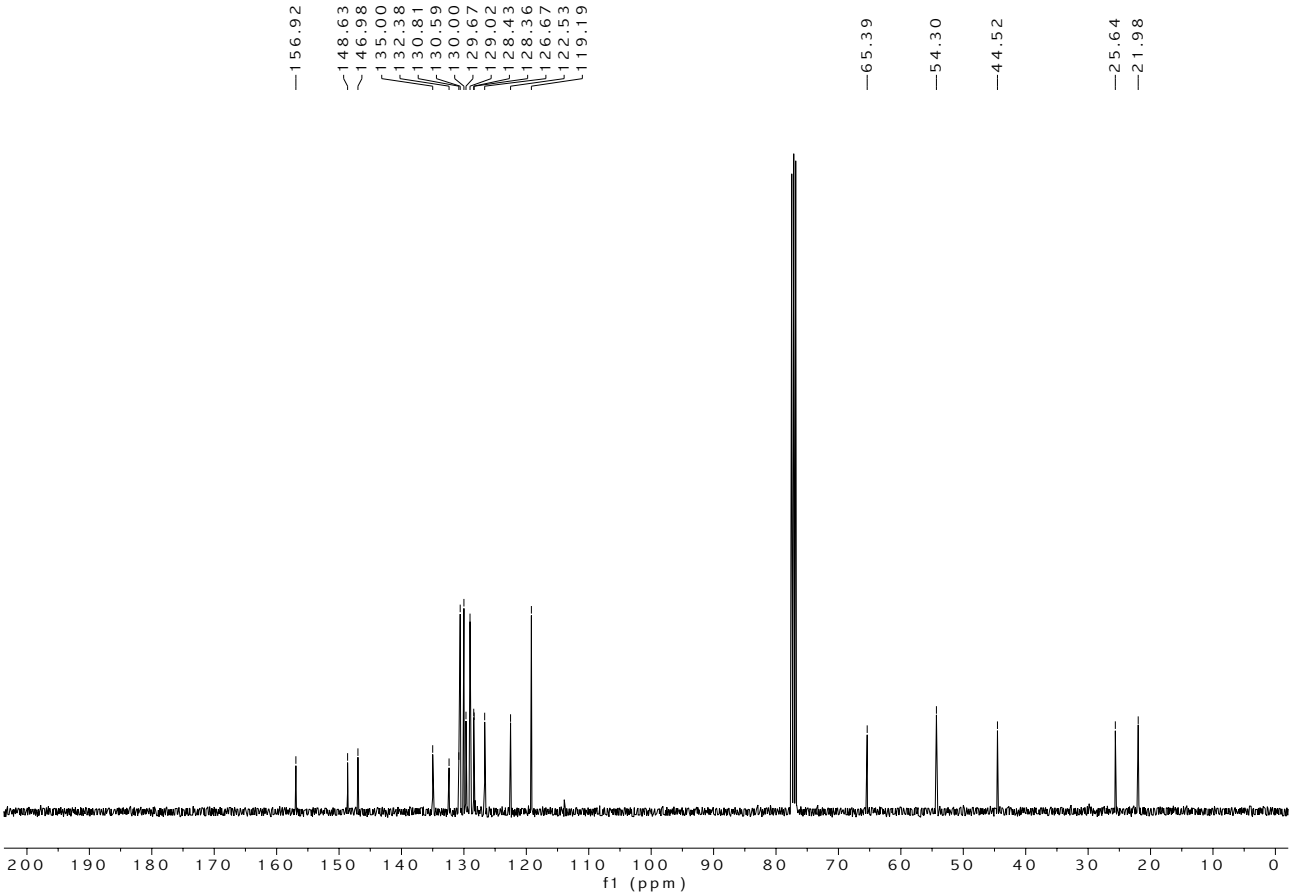
3.61 3.60 3.60 3.59 3.58 3.58 3.57 3.57 3.56 3.56 3.56 3.37 3.36 3.34 3.33 3.33 3.32 3.31 3.29 3.02 3.01 2.99 2.81 2.80 2.79 2.79 2.76 2.76 2.75 2.45
N
Ph
O
O
S
N
N
N=N
3ah
2.07 7.13 1.18 3.15 1.01 0.99 1.01 1.02 1.09 1.07 1.01 3.05
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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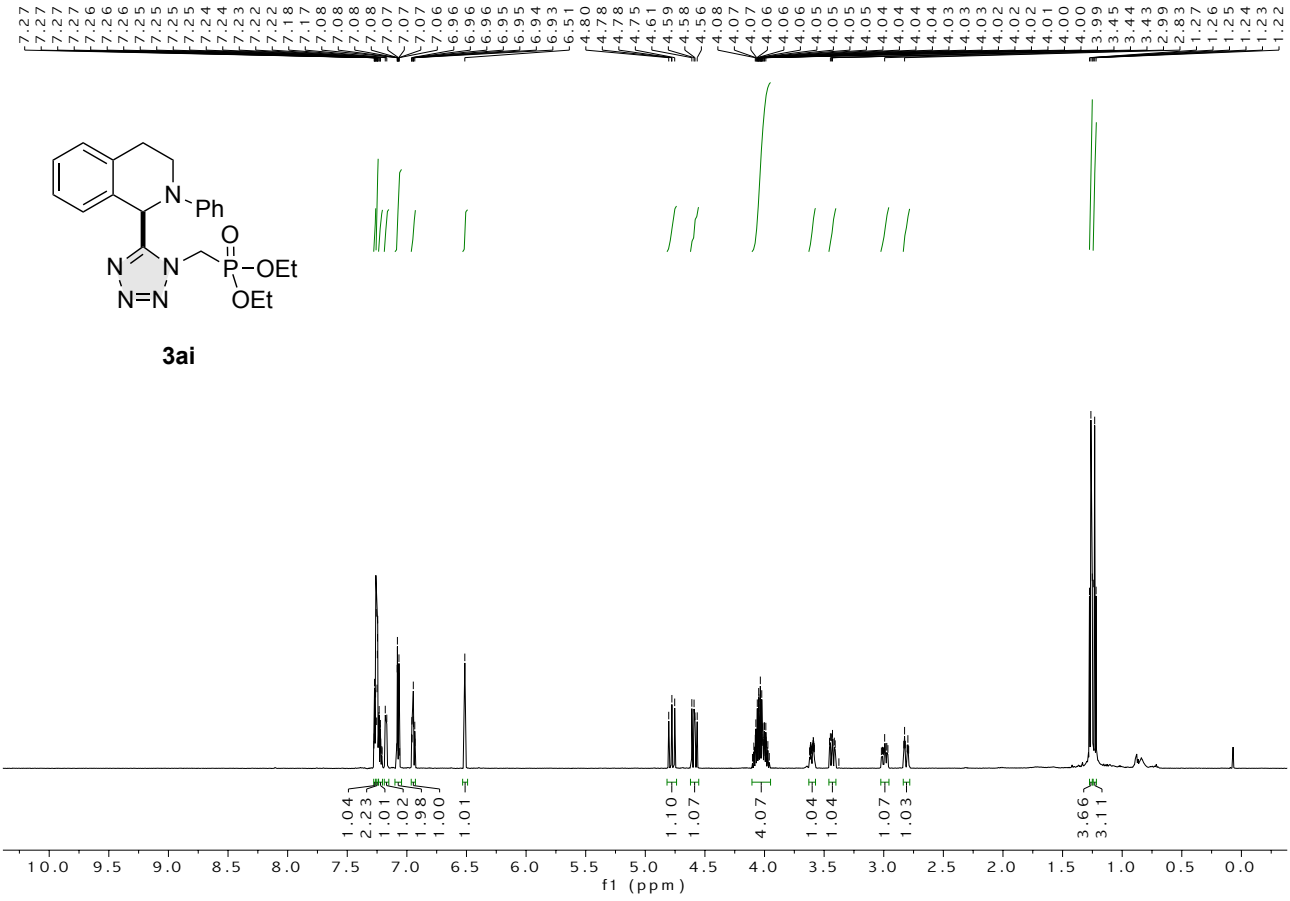
130.00
129.67
129.02
128.43
128.36
126.67
122.53
119.19
65.39
54.30
44.52
25.64
21.98
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


N
Ph
O
N
N
P
OEt
N=N
OEt

3ai

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2.23
1.01
1.02
1.98
1.00
1.01
1.10
1.07
4.07
1.04
1.04
1.07
1.03
3.66
3.11
f1 (ppm)


156.33
156.32
148.89
135.00
131.22
129.71
129.55
128.29
128.15
126.59
122.03
119.02
77.16 CDCl3
63.86
63.81
63.69
63.65
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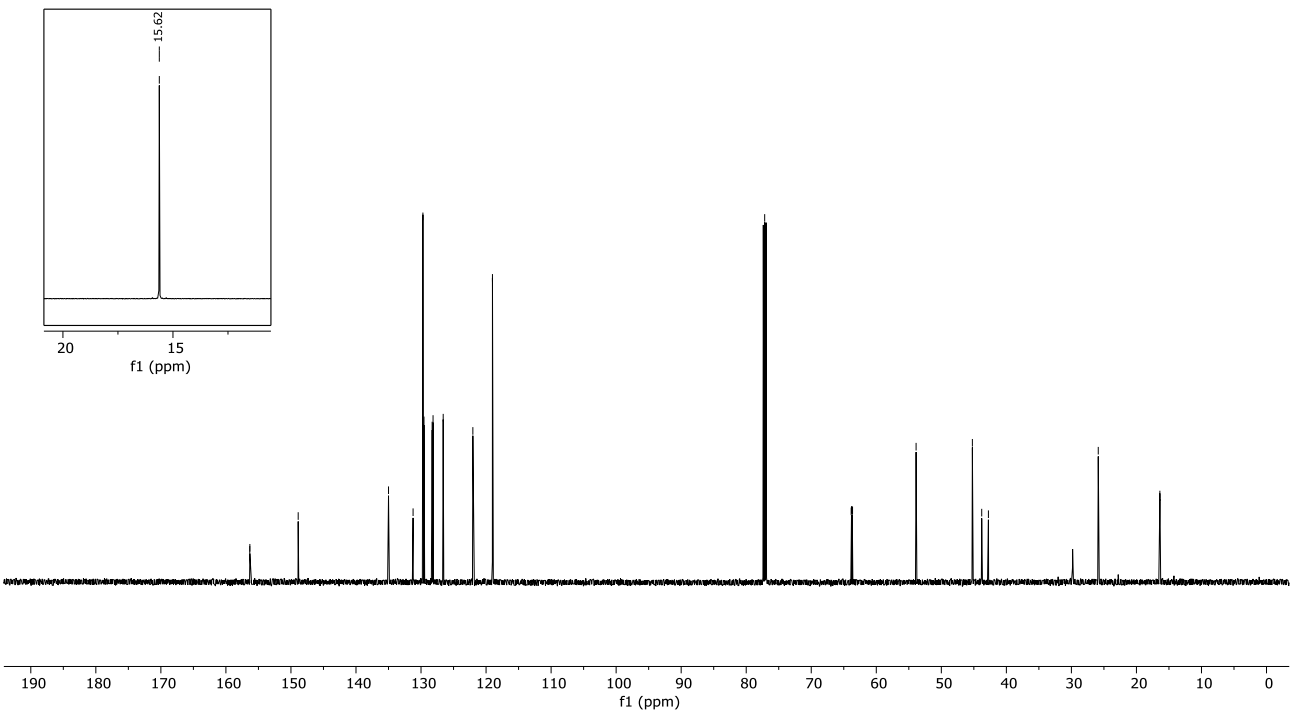
45.23
43.79
42.76
25.87
16.44
16.41
16.40
16.38

^{31}P NMR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20
15
f1 (ppm)
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180
170
160
150
140
130
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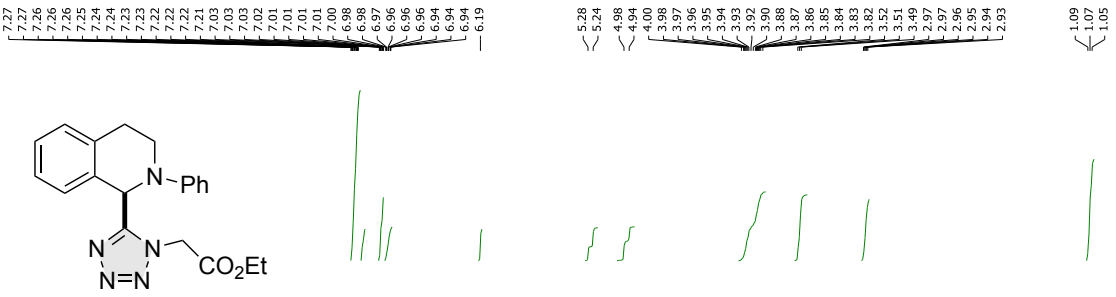
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



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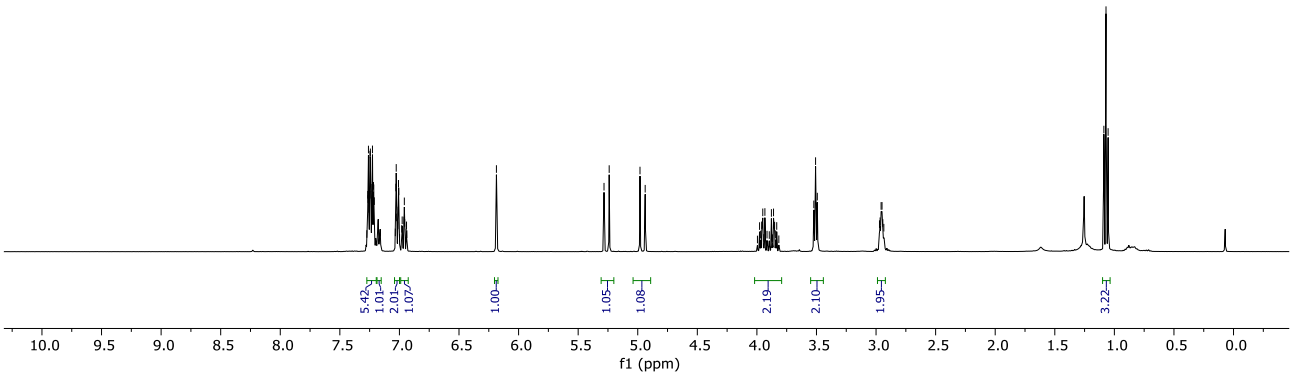
Ph
N
N
N=N
CO2Et

3aj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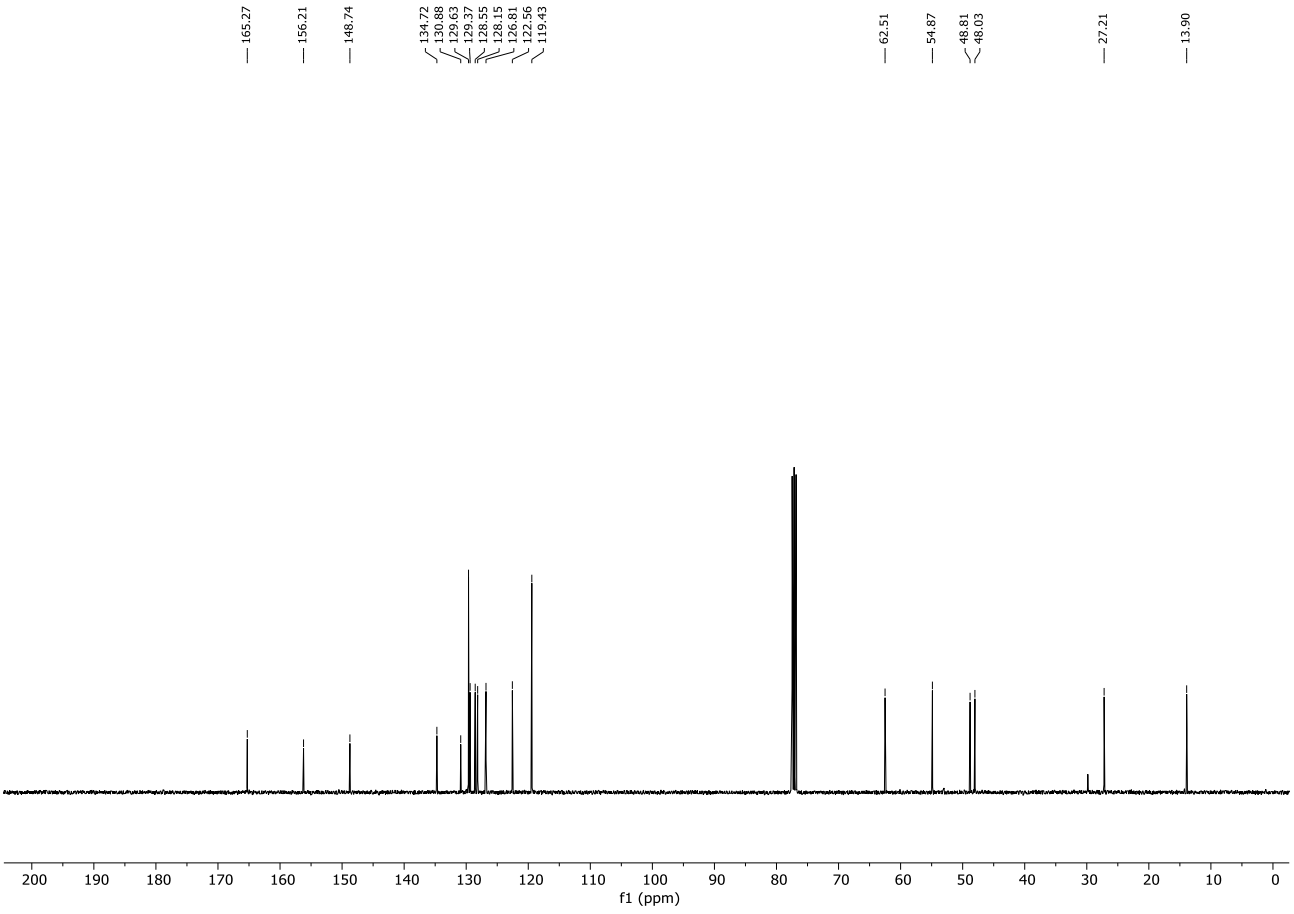
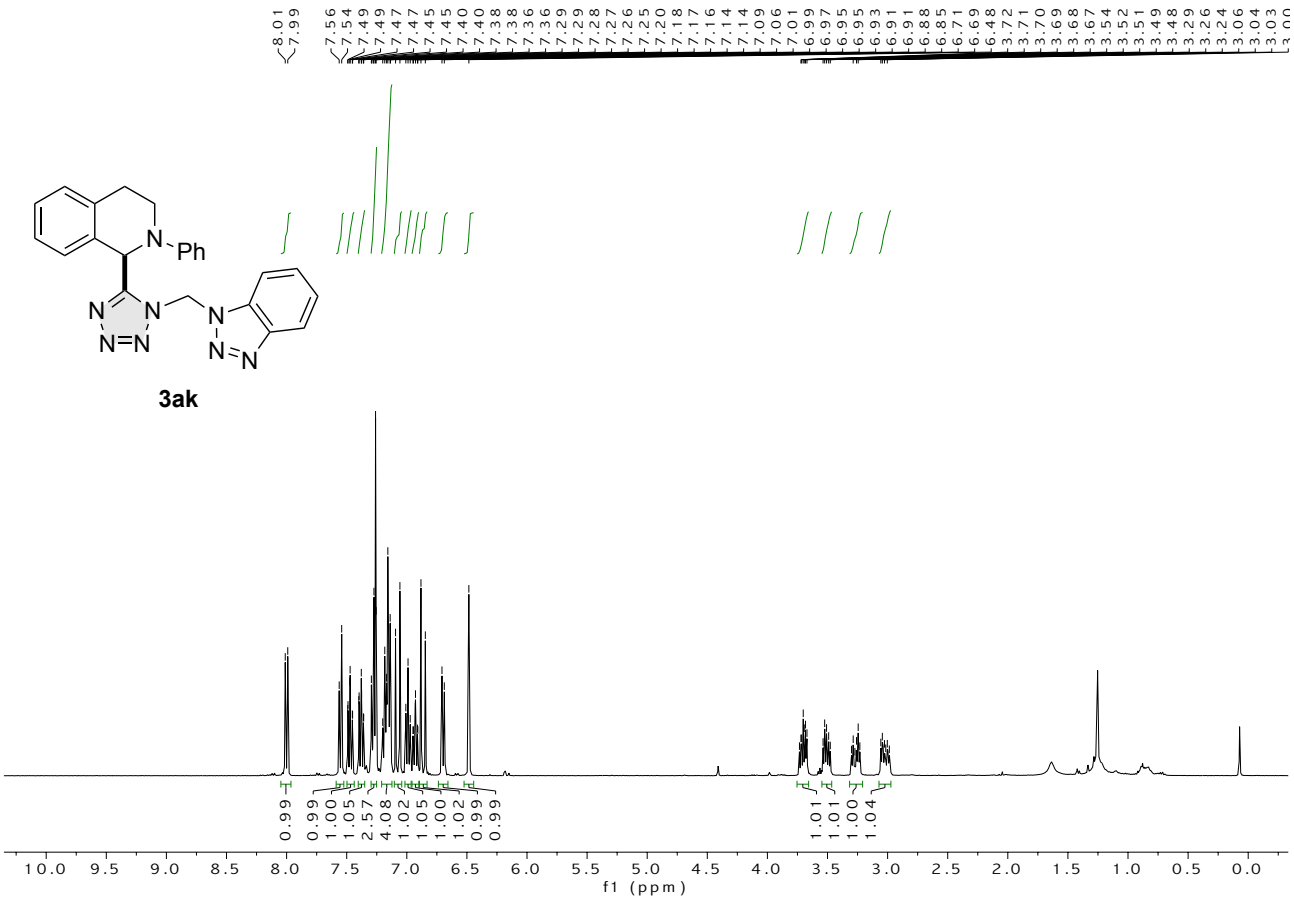
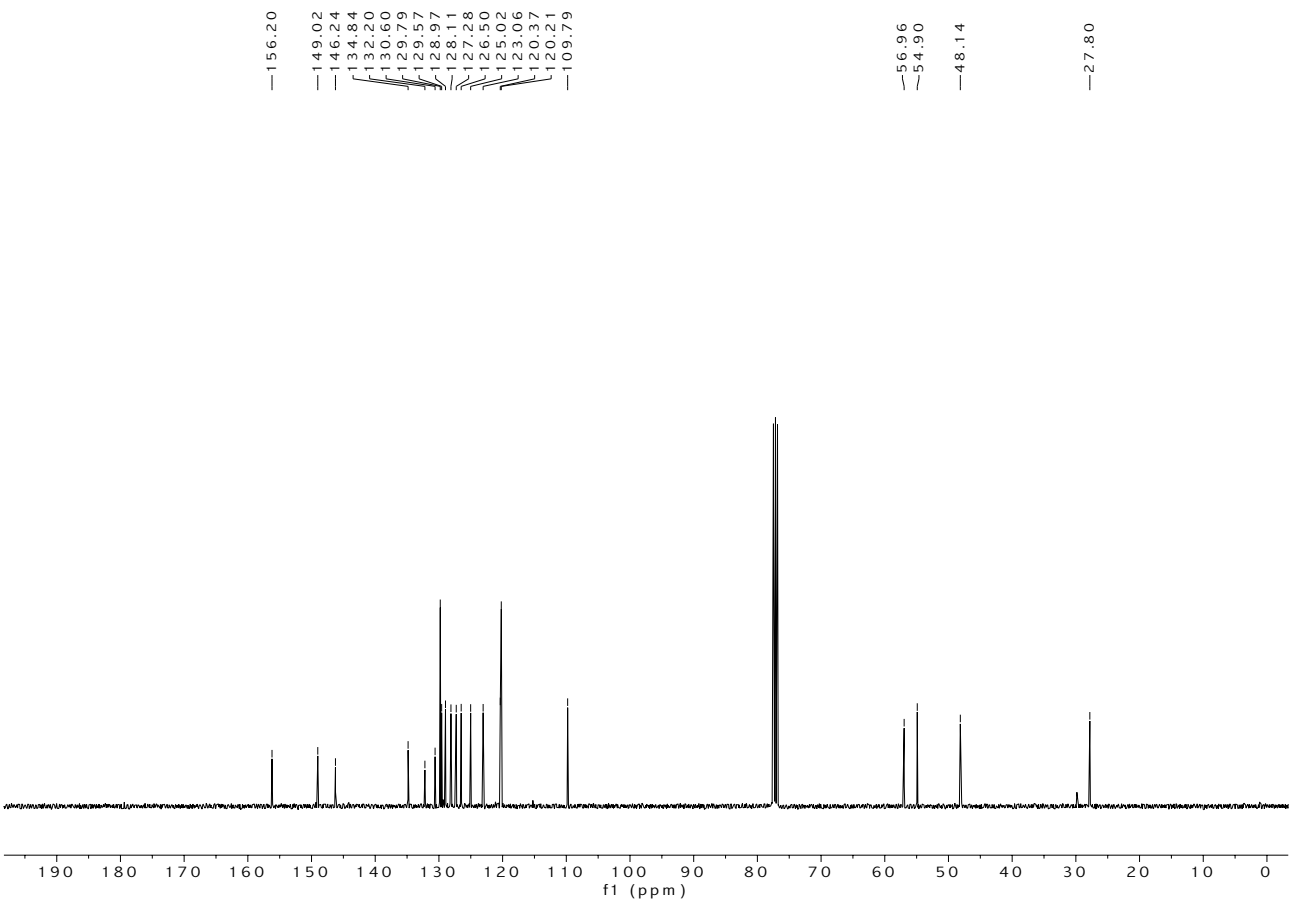
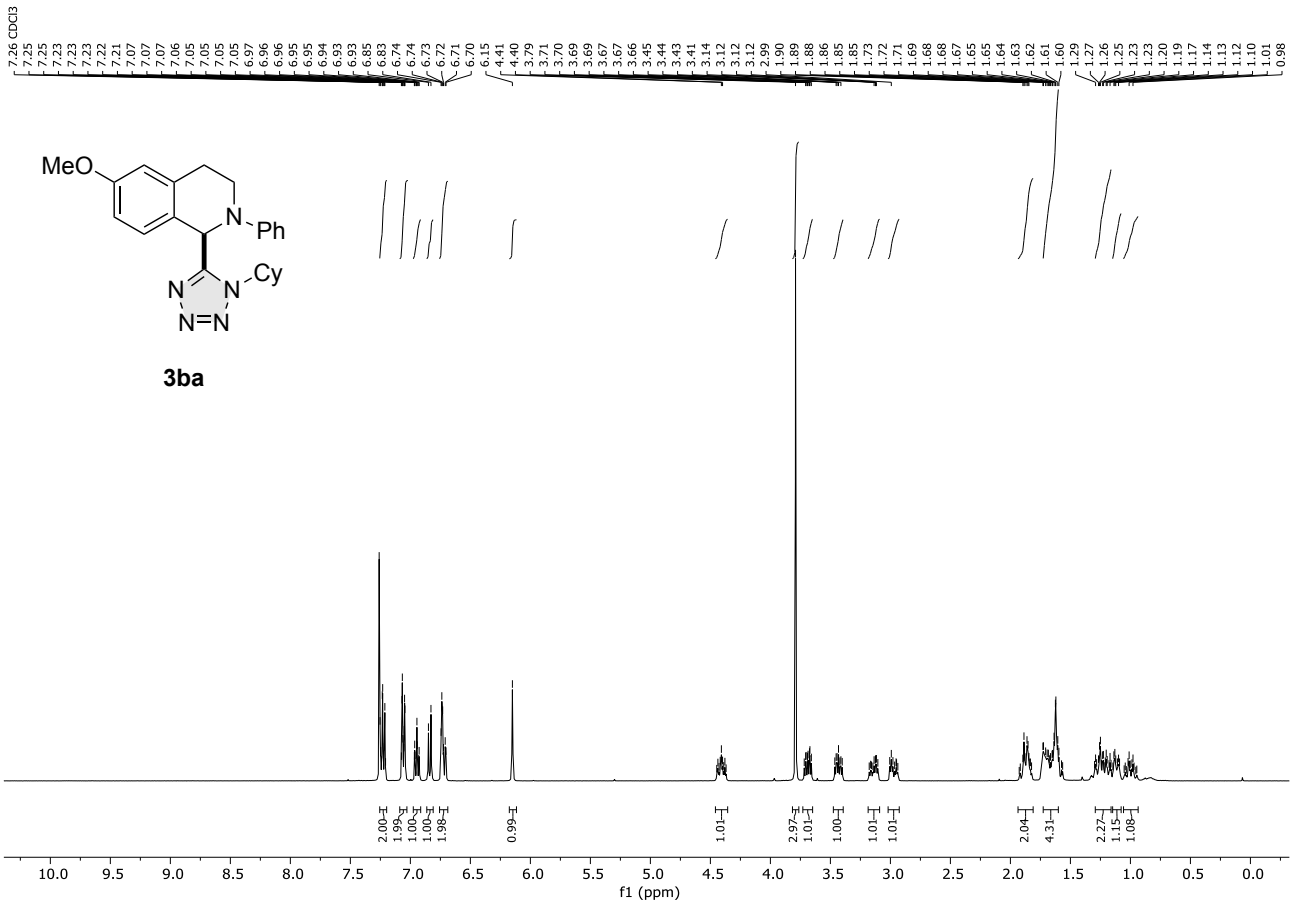
2.01
1.07
1.00
1.05
1.08
2.19
2.10
1.95
3.22
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


165.27
156.21
148.74
134.72
130.88
129.63
129.37
128.55
128.15
126.81
122.56
119.43
62.51
54.87
48.81
48.03
27.21
13.90
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

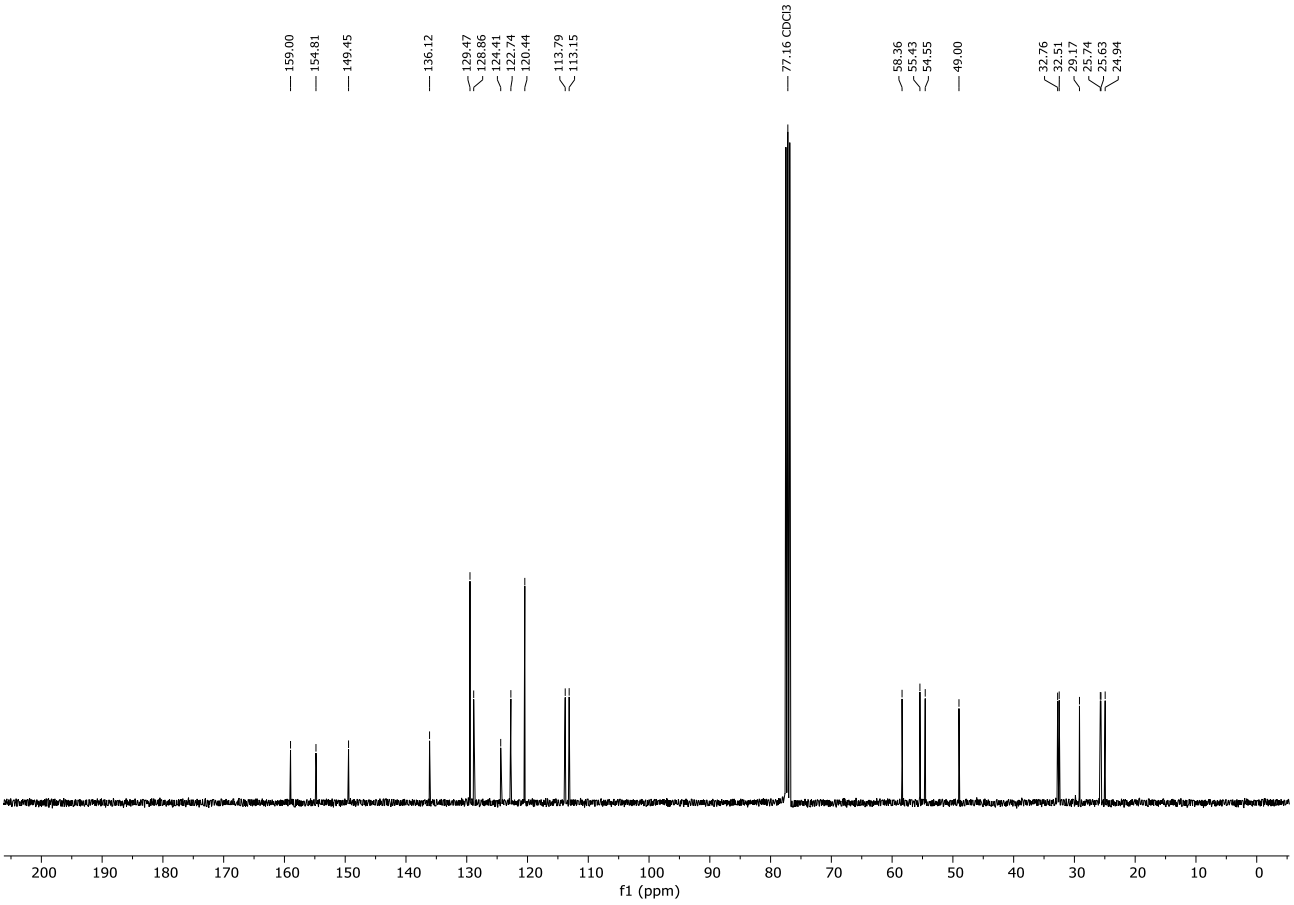

8.01
7.99
7.56
7.54
7.49
7.49
7.47
7.47
7.45
7.45
7.40
7.38
7.36
7.36
7.29
7.29
7.28
7.27
7.26
7.25
7.20
7.18
7.17
7.16
7.14
7.14
7.09
7.06
7.01
6.99
6.97
6.95
6.95
6.93
6.91
6.91
6.88
6.85
6.71
6.69
6.48
3.72
3.71
3.70
3.69
3.68
3.67
3.54
3.52
3.51
3.49
3.48
3.29
3.26
3.24
3.06
3.04
3.03
N
Ph
N
N
N=N
N
N
N=N
0.99
0.99
1.00
1.05
2.57
4.08
1.02
1.05
1.00
1.02
0.99
0.99
1.01
1.01
1.00
1.04
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

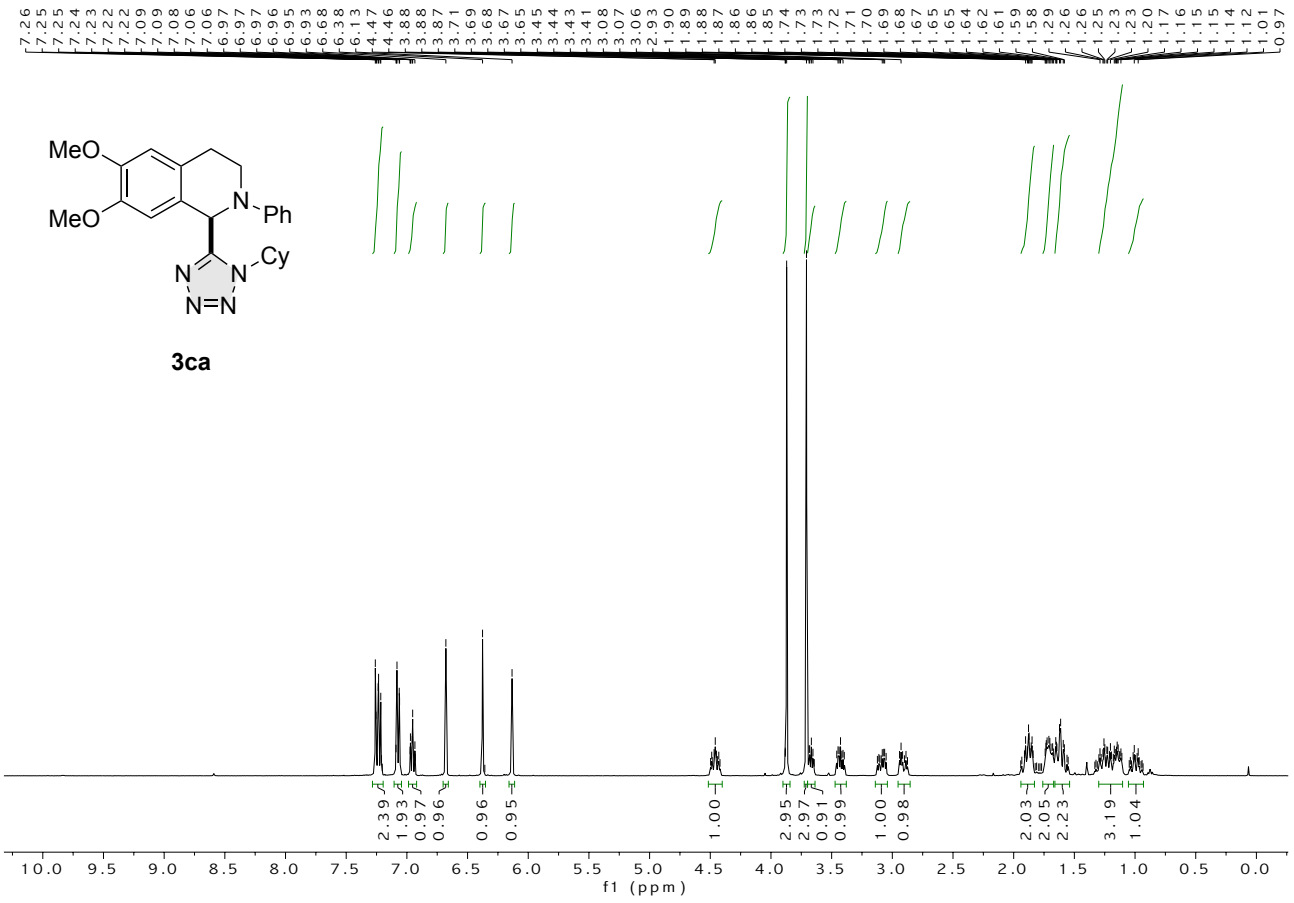
3ak


156.20
149.02
146.24
134.84
132.20
130.60
129.79
129.57
128.97
128.11
127.28
126.50
125.02
123.06
120.37
120.21
109.79
56.96
54.90
48.14
27.80
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

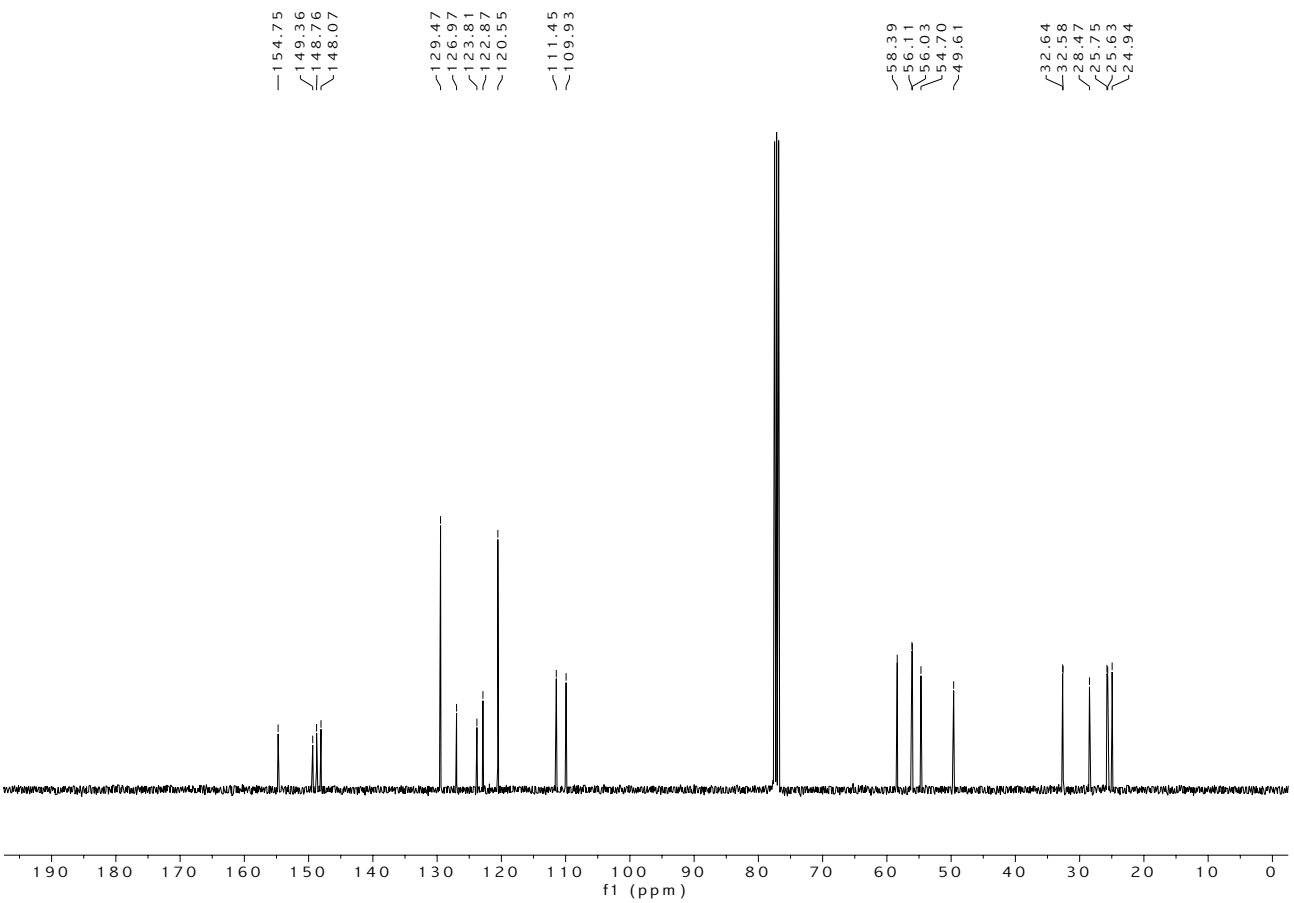


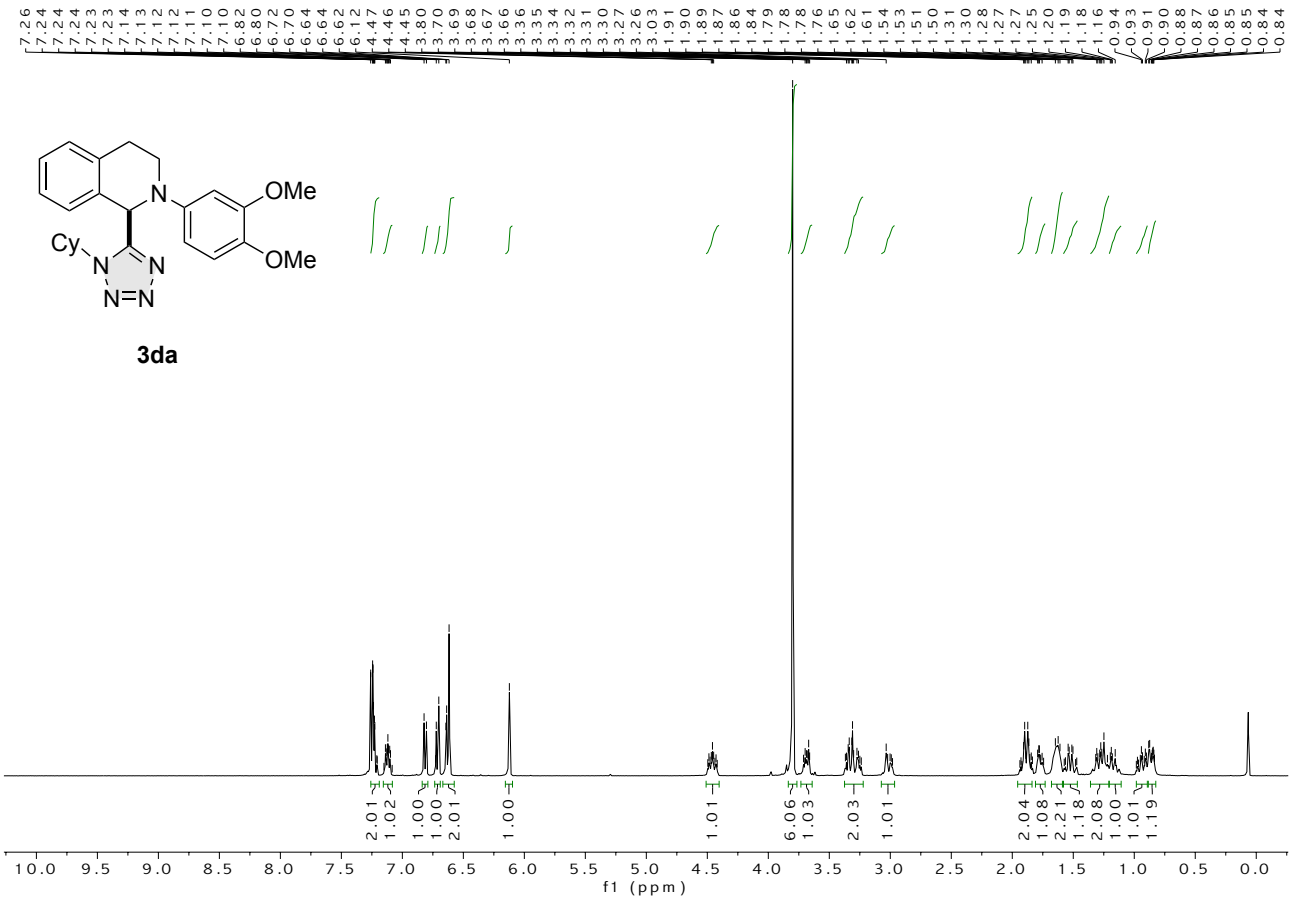
3ba



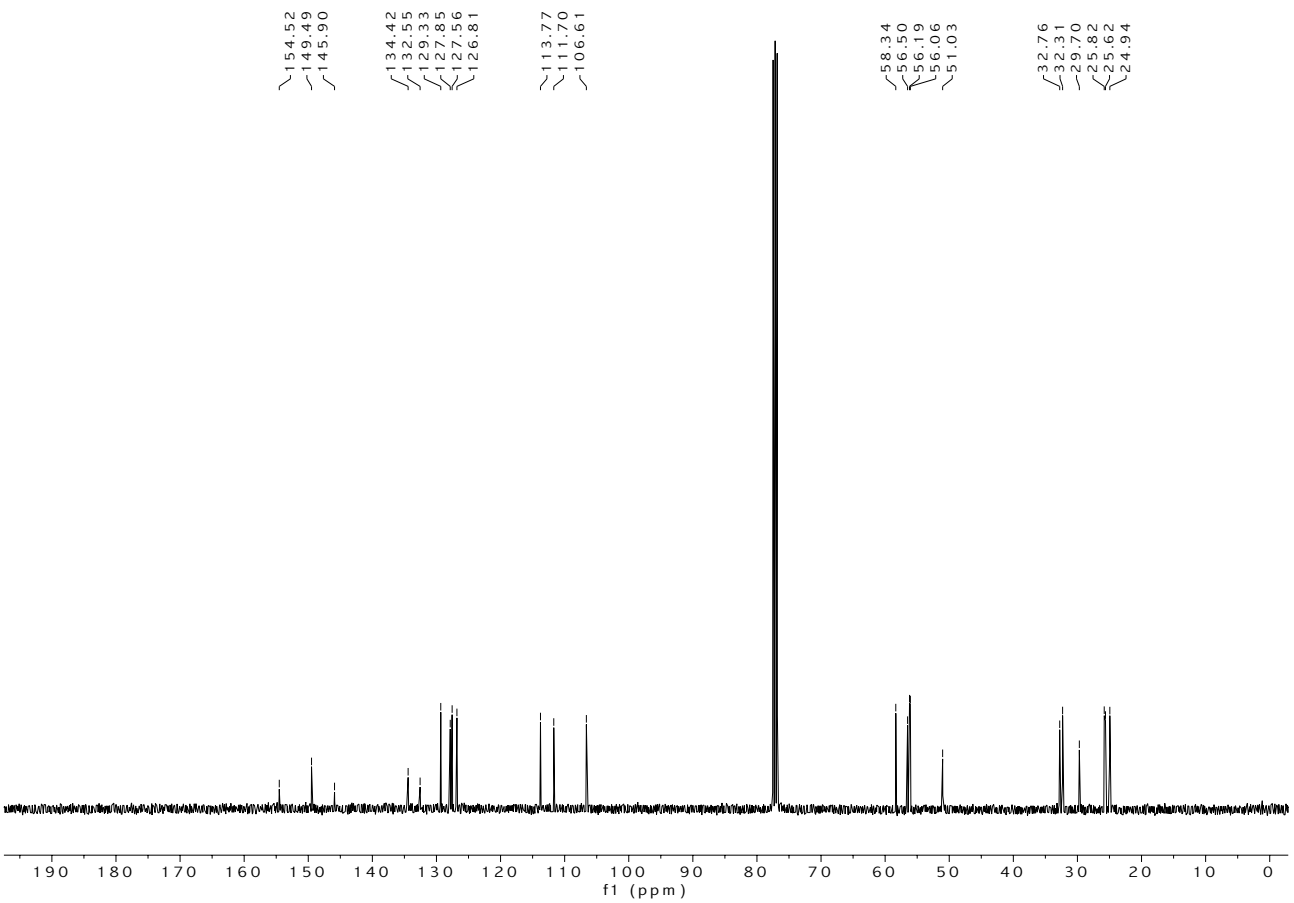


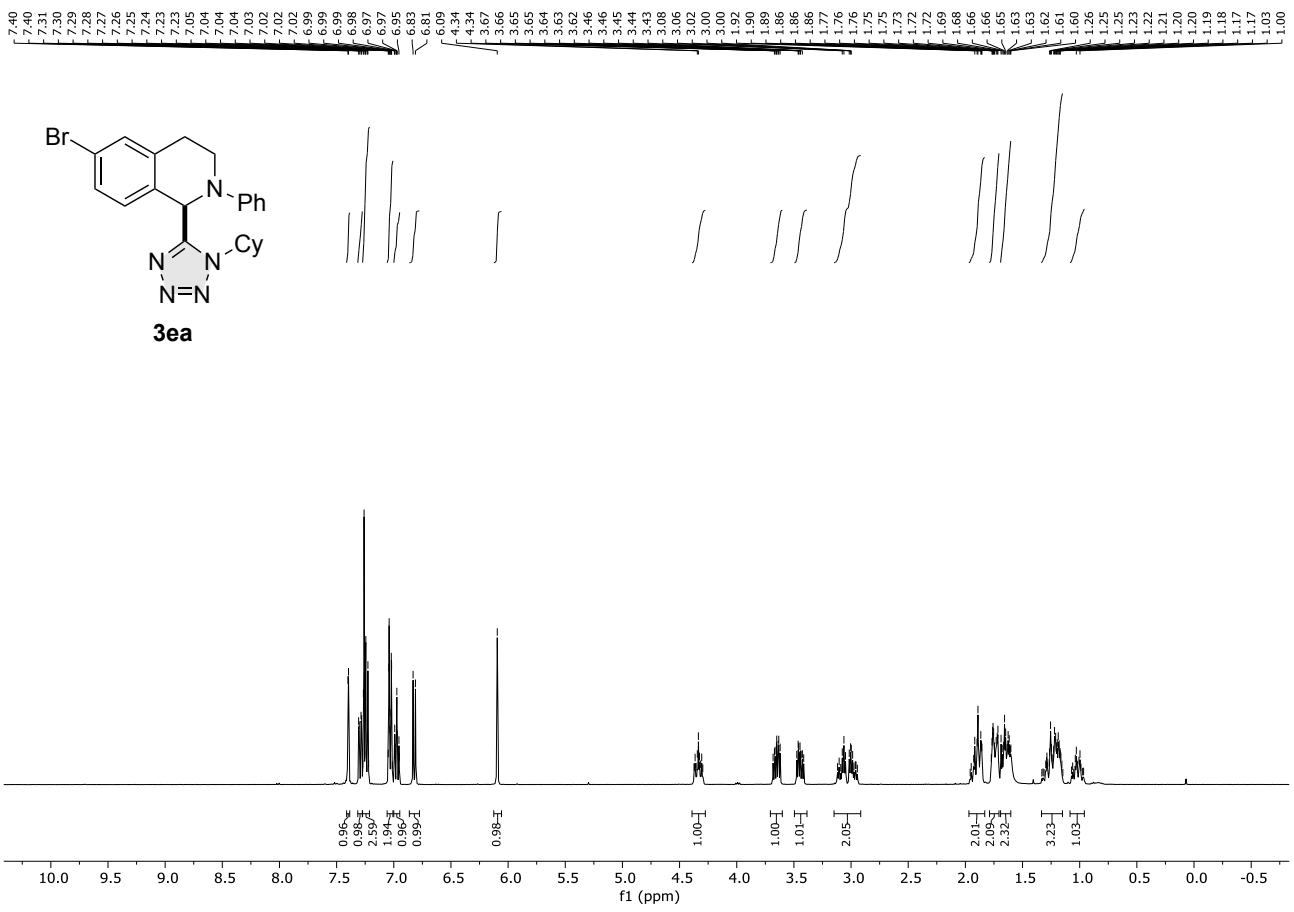
3ca

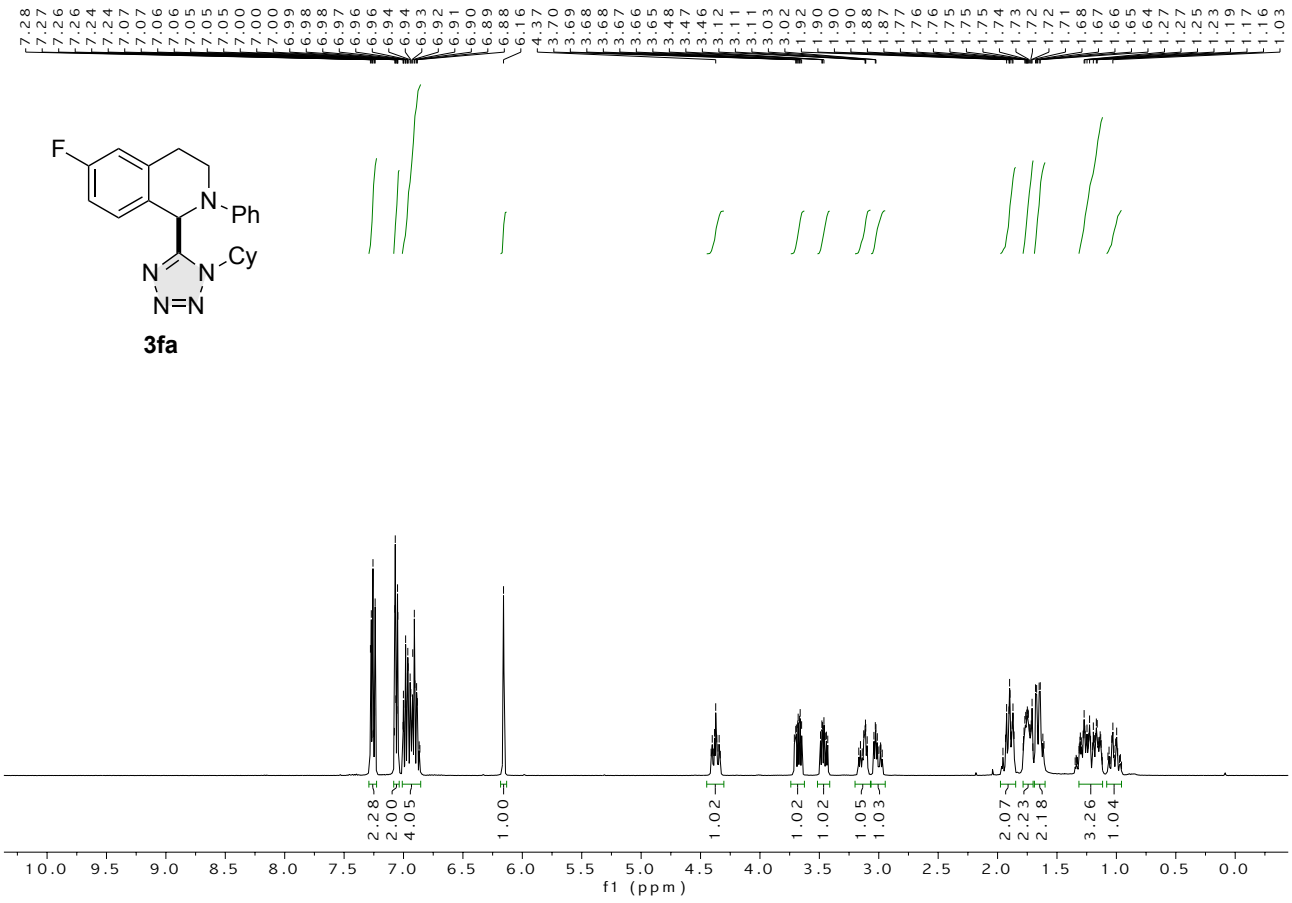


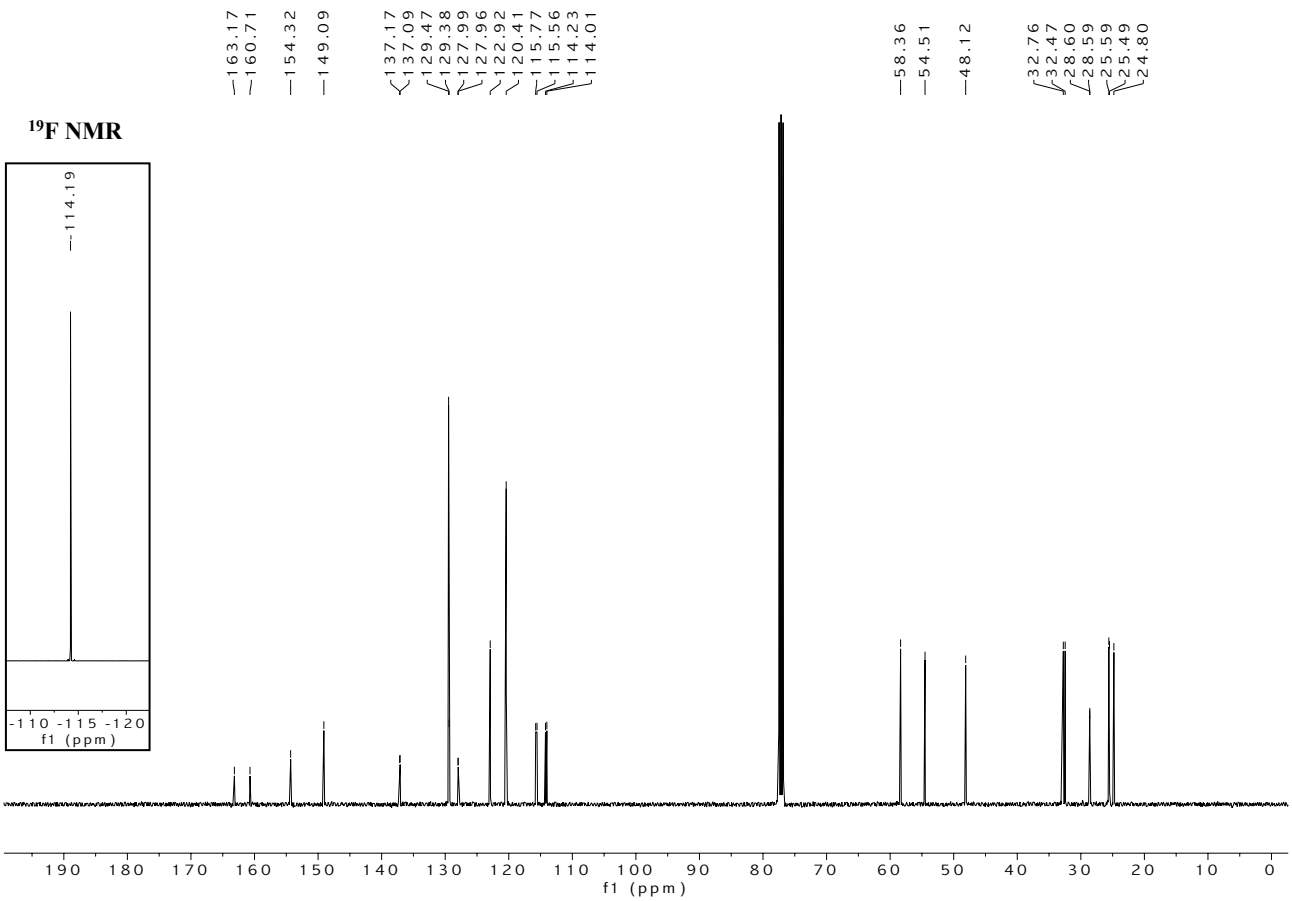


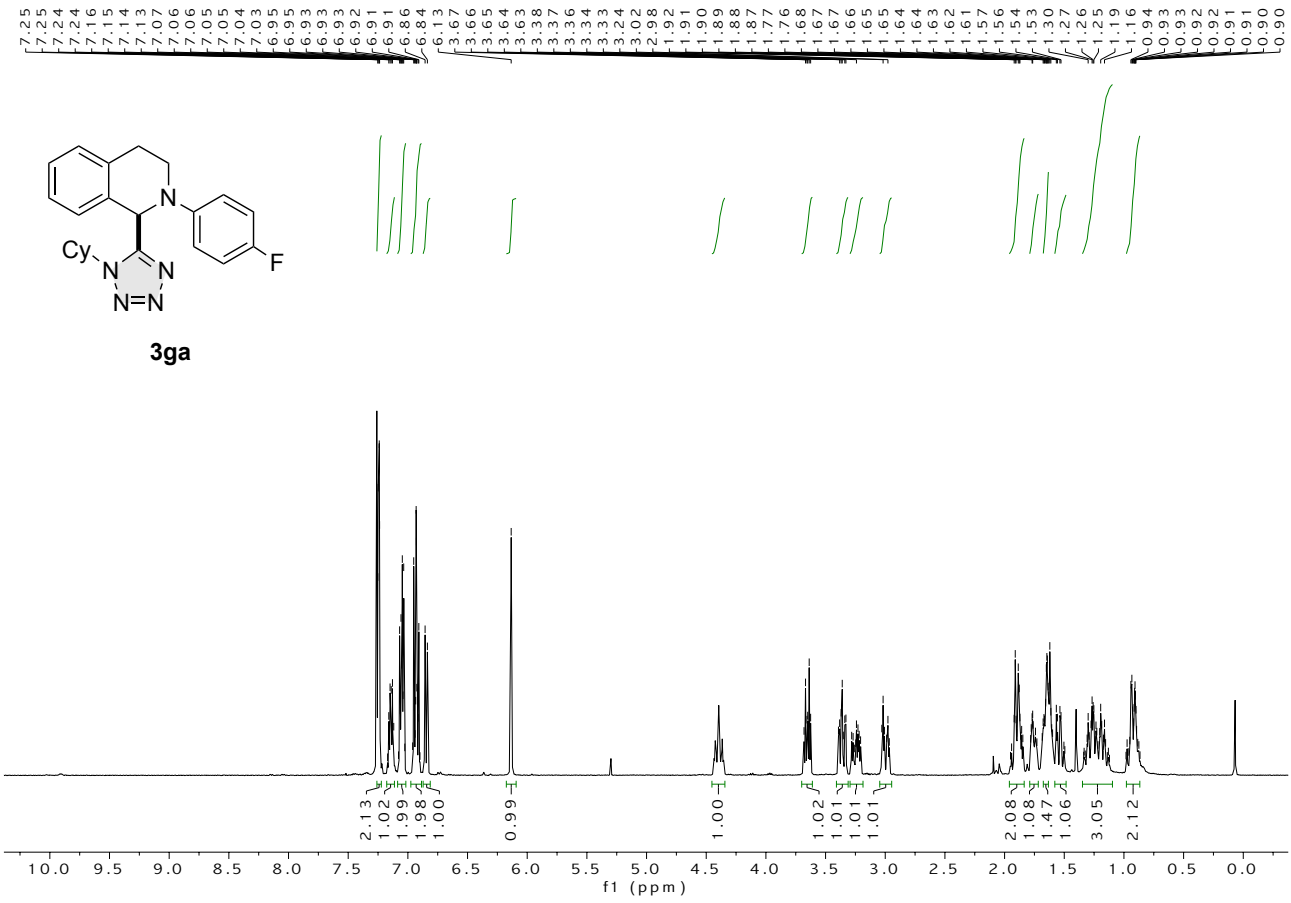
3da



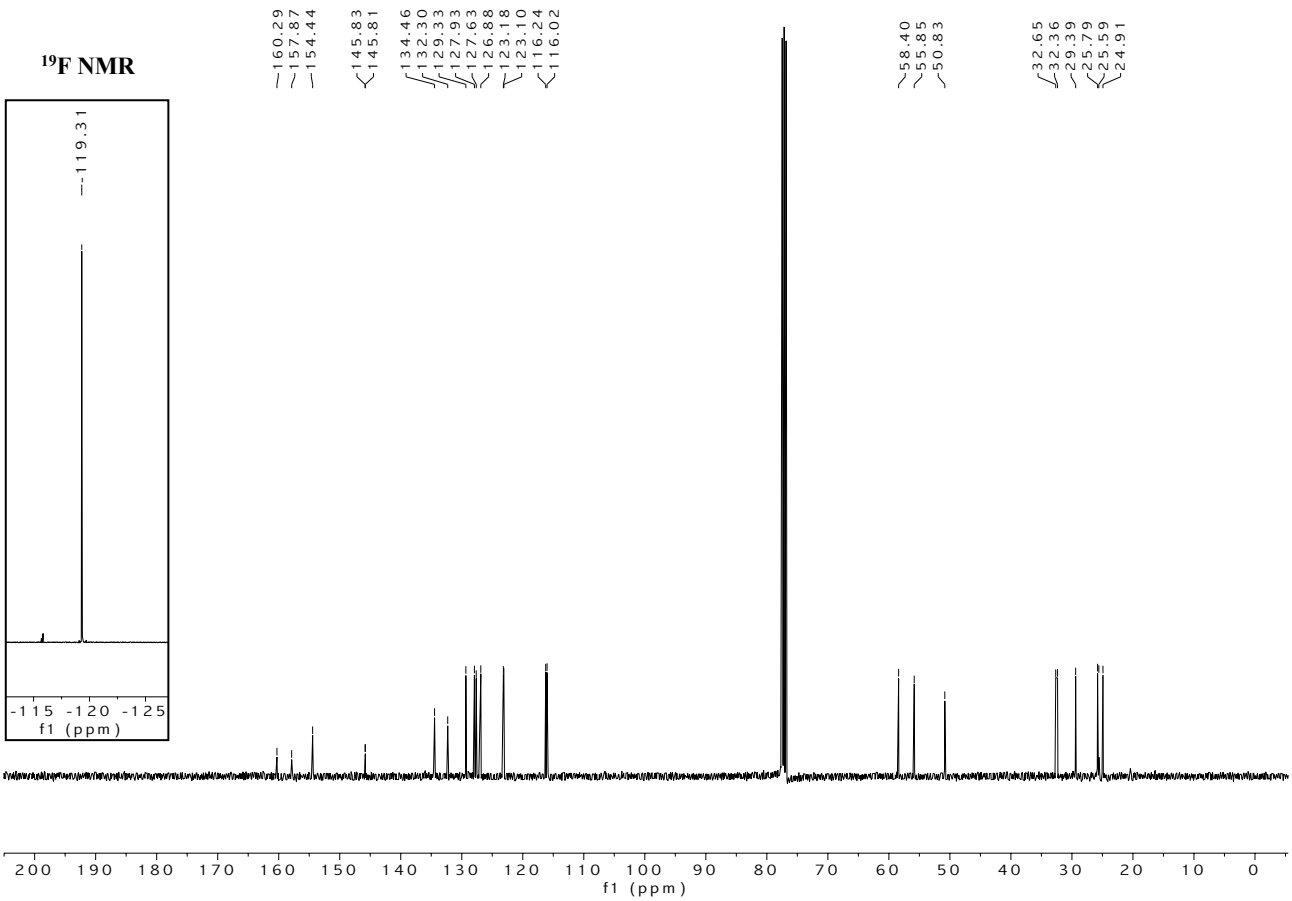

Br
N
Ph
Cy
N
N
N=N
3ea
f1 (ppm)
f1 (ppm)

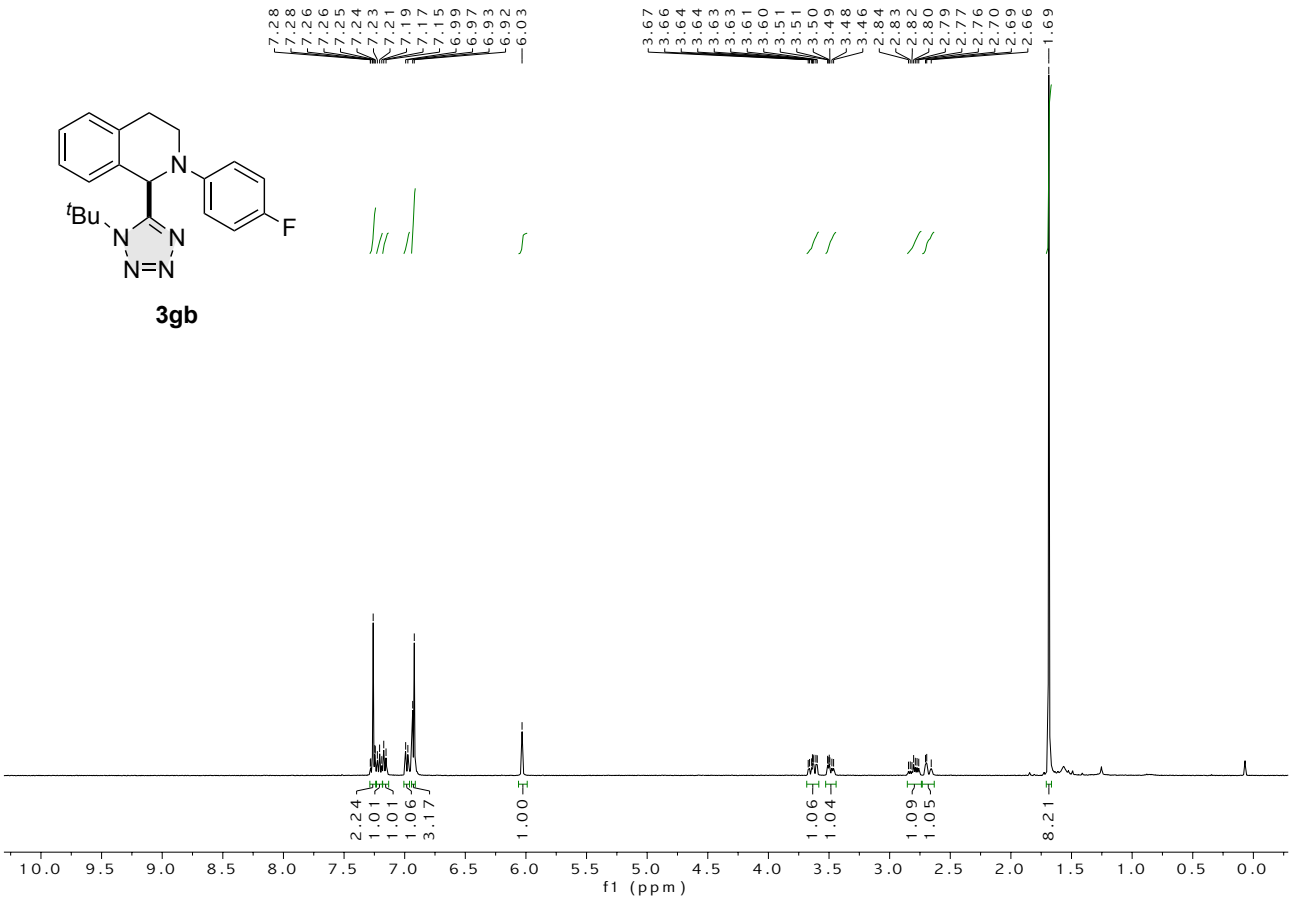

F
N
Ph
N
N
Cy
N=N
3fa
f1 (ppm)

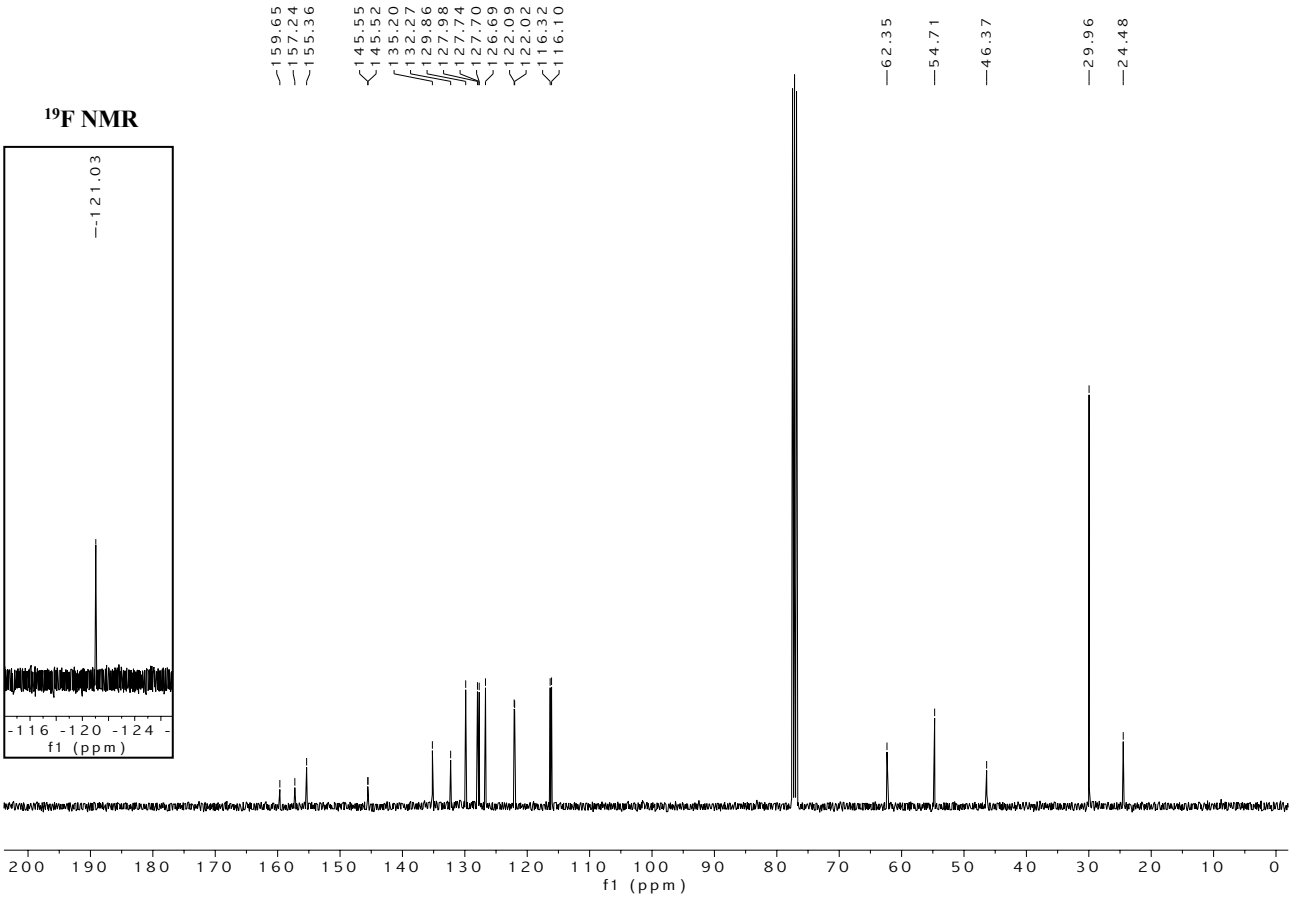

19F NMR
-114.19
-110 -115 -120
f1 (ppm)
f1 (ppm)

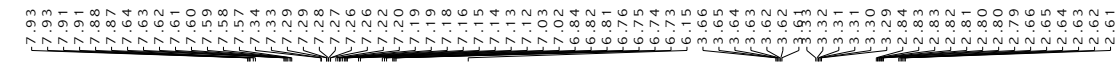


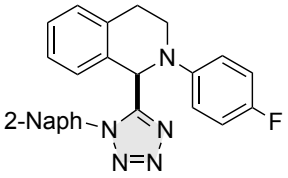
3ga



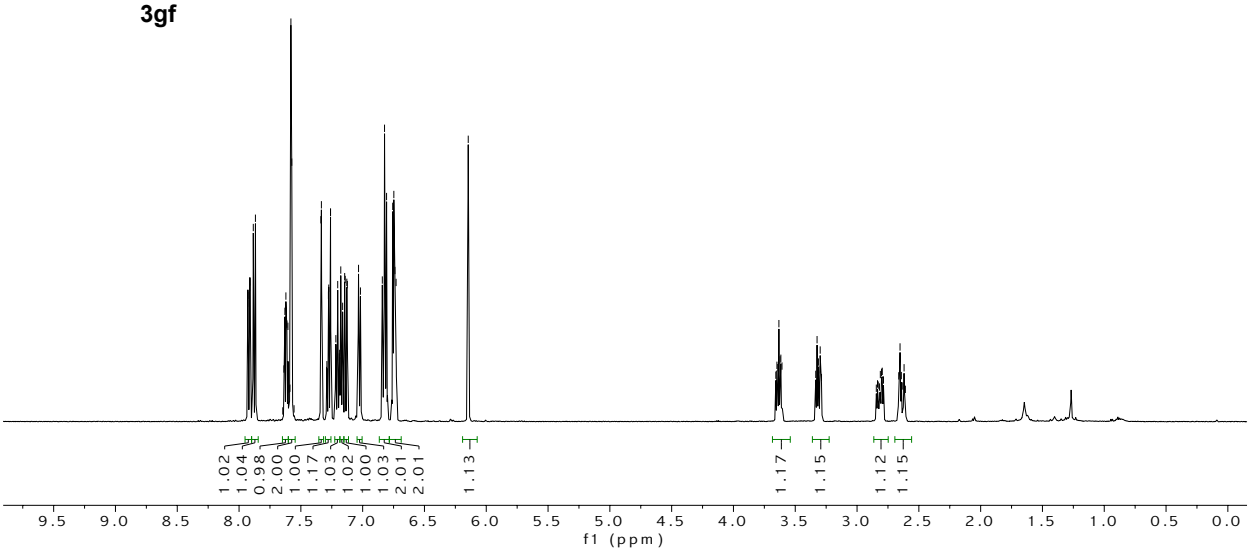

7.28
7.28
7.26
7.26
7.25
7.24
7.23
7.21
7.19
7.17
7.15
6.99
6.97
6.93
6.92
6.03
3.67
3.66
3.64
3.64
3.63
3.63
3.61
3.60
3.51
3.51
3.50
3.49
3.48
3.46
2.84
2.83
2.82
2.80
2.79
2.77
2.76
2.70
2.69
2.66
1.69
tBu
N
N
N
N=N
F
3gb
2.24
1.01
1.01
1.06
3.17
1.00
1.06
1.04
1.09
1.05
8.21
f1 (ppm)

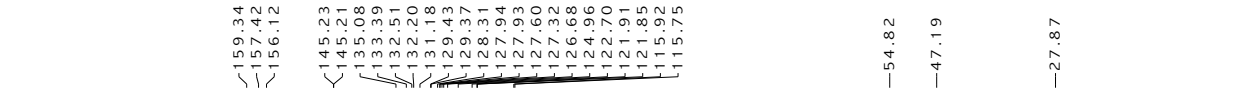

159.65
157.24
155.36
145.55
145.52
135.20
132.27
129.86
127.98
127.74
127.70
126.69
122.09
122.02
116.32
116.10
62.35
54.71
46.37
29.96
24.48
19F NMR
-121.03
-116 -120 -124
f1 (ppm)
f1 (ppm)



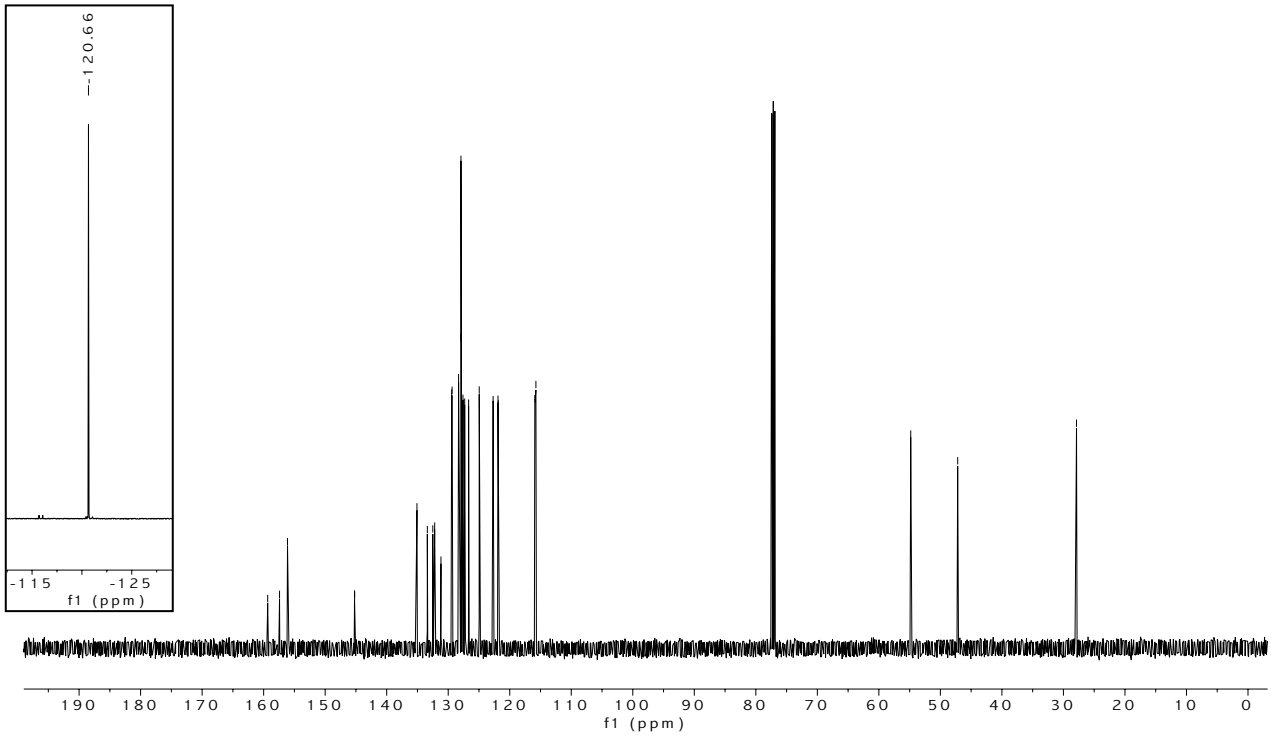

2-Naph
N
N
N
N
F

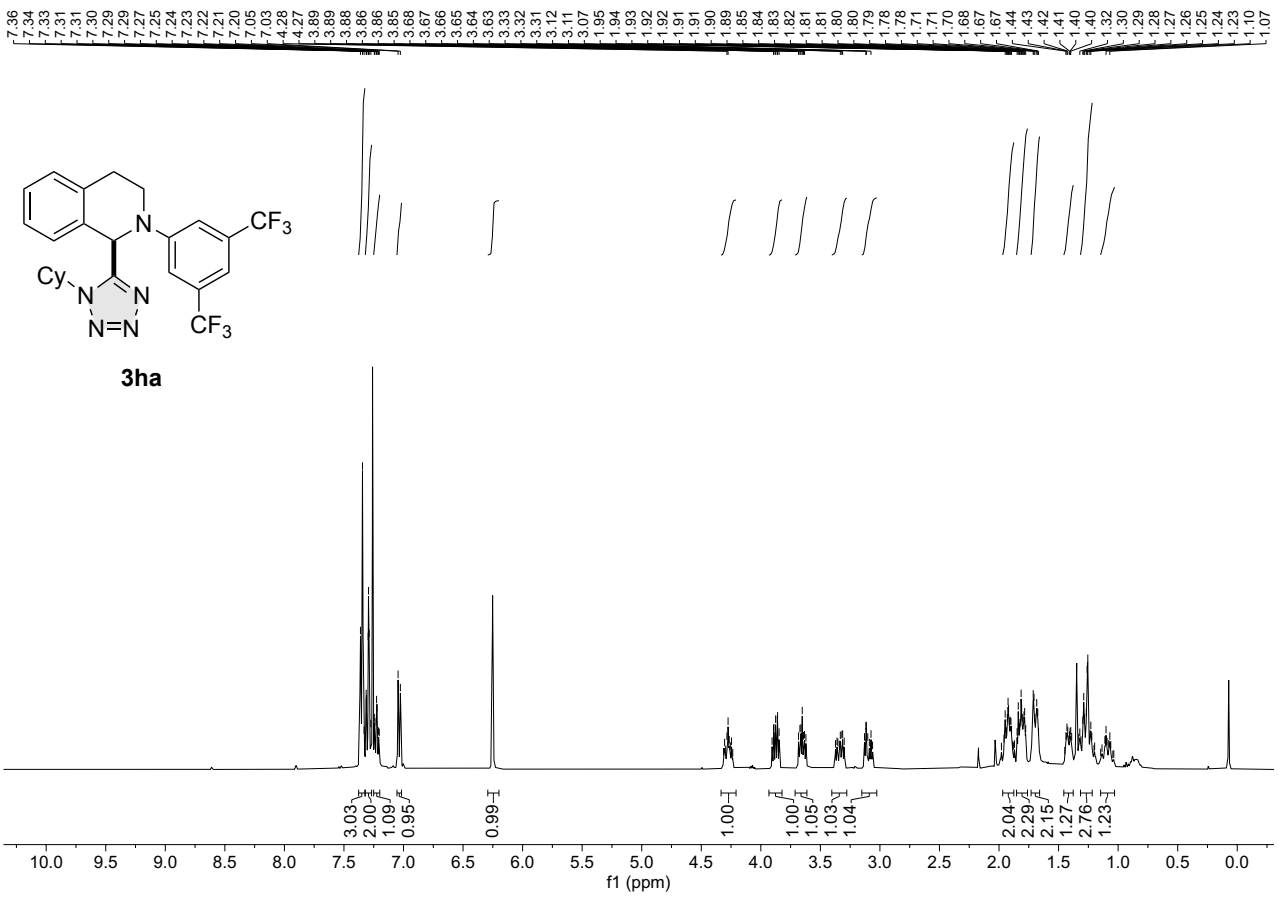
3gf

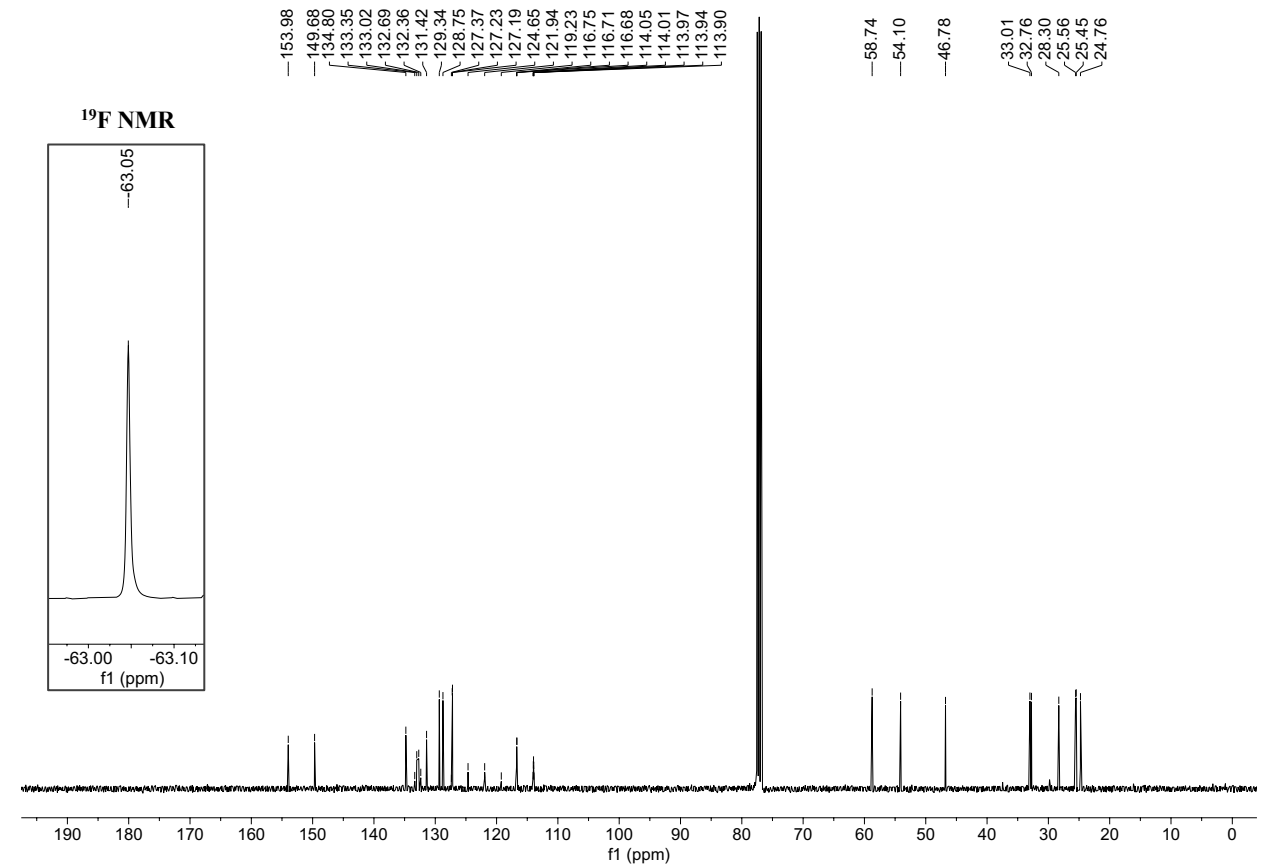

1.02
1.04
0.98
2.00
1.00
1.17
1.03
1.02
1.00
1.03
2.01
2.01
1.13
1.17
1.15
1.12
1.15
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

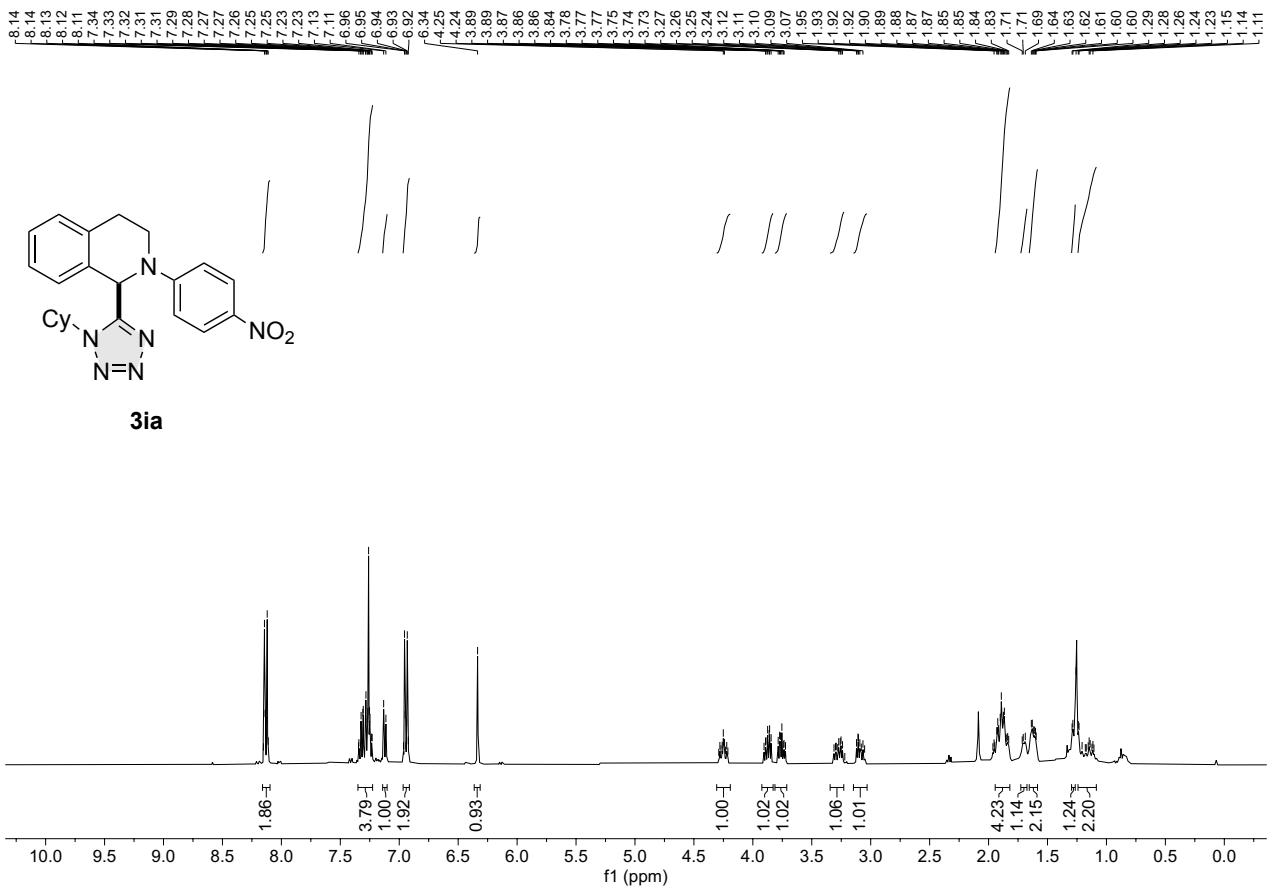


^{19}F NMR

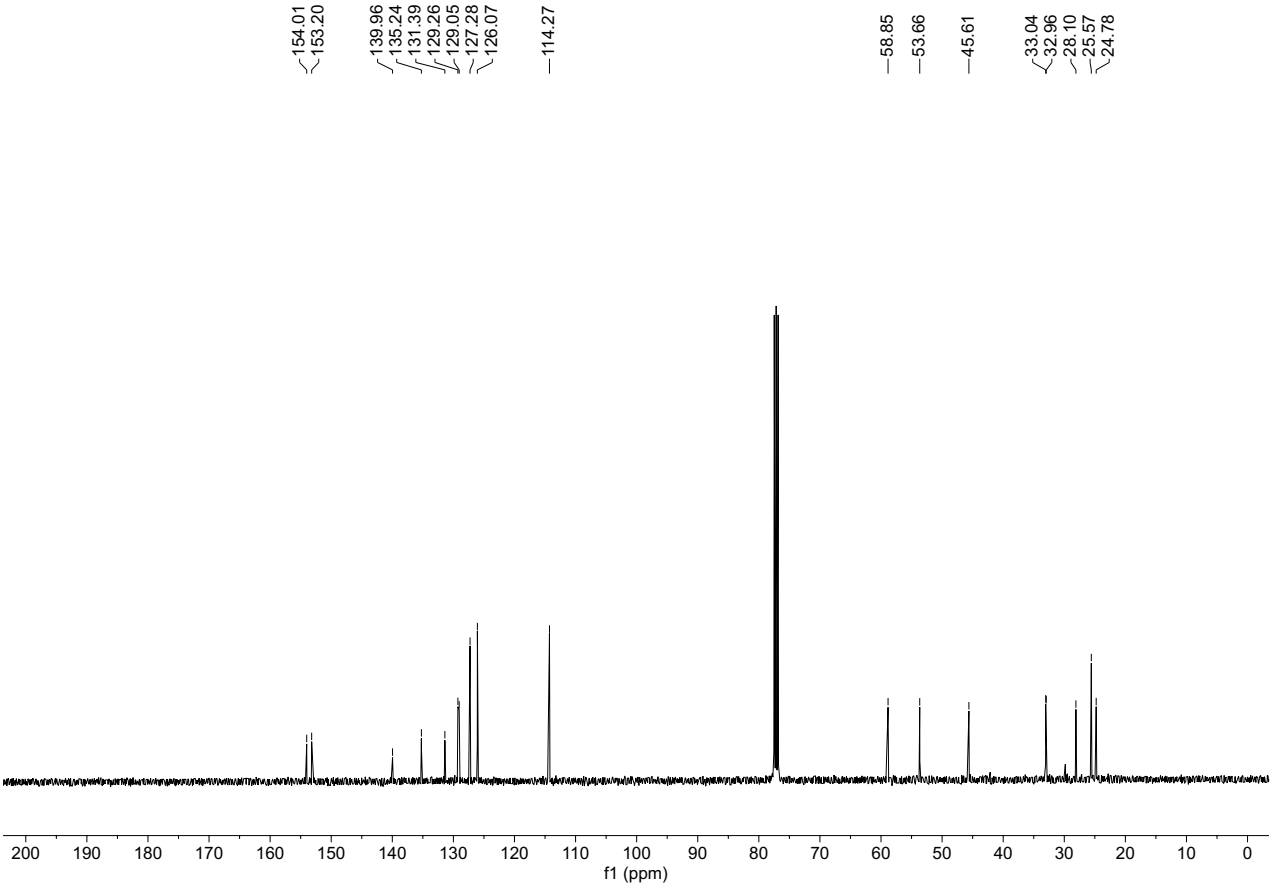

-120.66
-115
-125
f1 (ppm)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

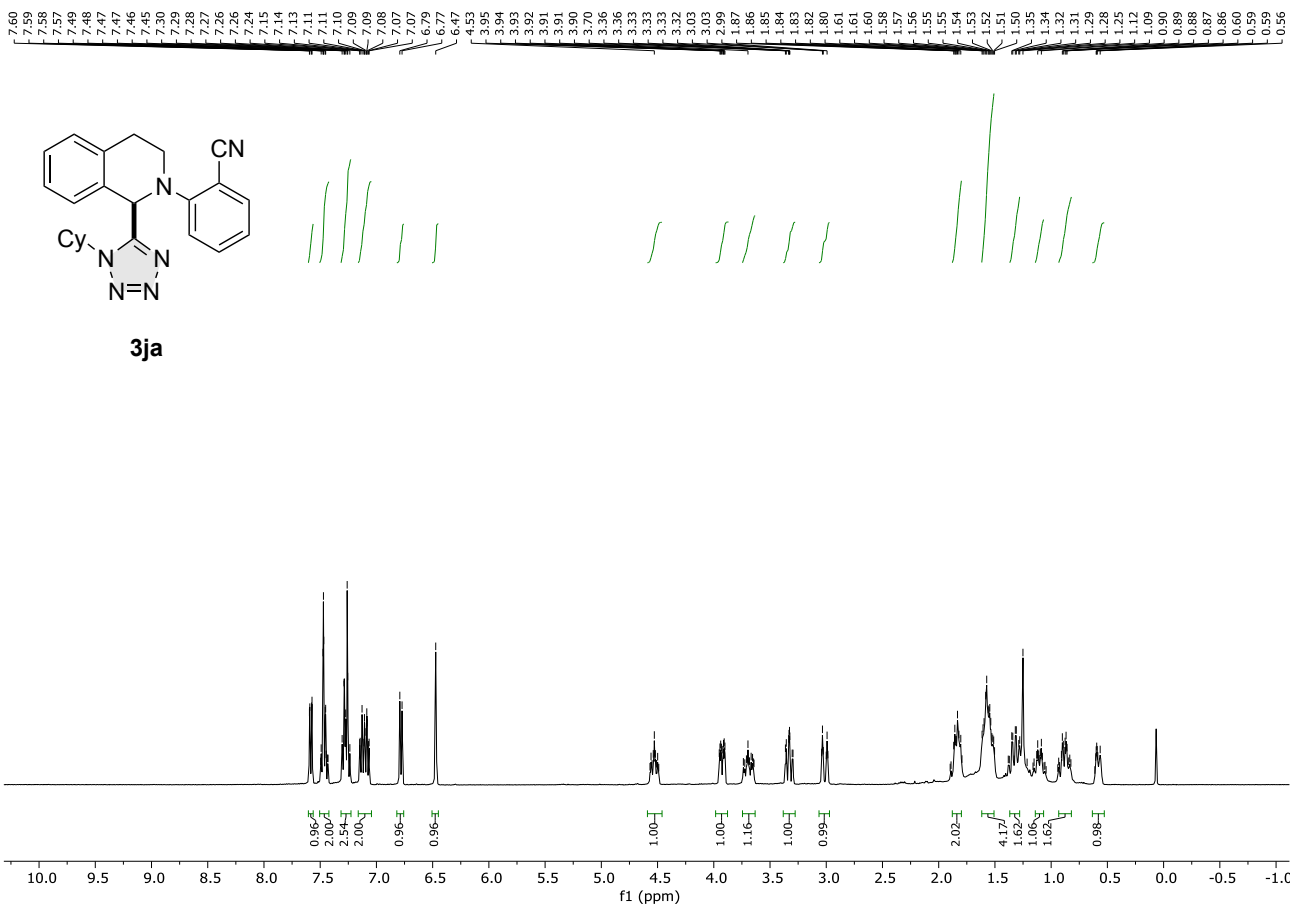

Cy
N
N
N=N
CF3
CF3
3ha
f1 (ppm)


19F NMR
-63.05
-63.00
-63.10
f1 (ppm)
f1 (ppm)

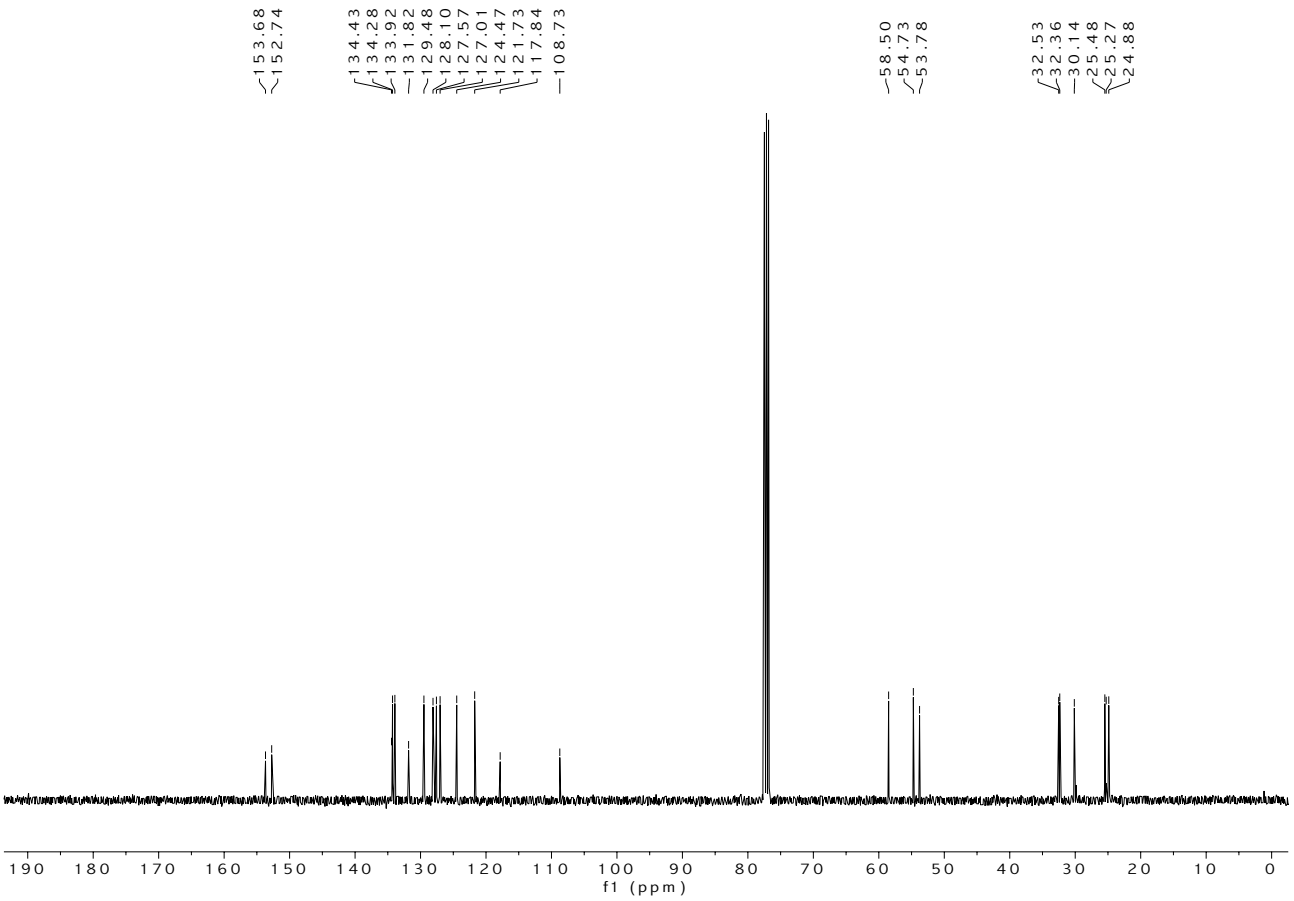

8.14
8.14
8.13
8.12
8.11
7.34
7.33
7.32
7.31
7.31
7.29
7.28
7.27
7.27
7.26
7.25
7.25
7.23
7.23
7.13
7.11
6.96
6.95
6.94
6.93
6.92
6.34
4.25
4.24
3.89
3.89
3.87
3.86
3.86
3.84
3.78
3.77
3.77
3.75
3.74
3.73
3.27
3.26
3.25
3.24
3.12
3.11
3.10
3.09
3.07
1.95
1.93
1.92
1.92
1.90
1.89
1.88
1.87
1.87
1.85
1.84
1.83
1.71
1.71
1.69
1.64
1.63
1.62
1.61
1.60
1.60
1.29
1.28
1.26
1.24
1.23
1.15
1.14
1.11
Cy
N
N
N
N=N
NO2
1.86
3.79
1.00
1.92
0.93
1.00
1.02
1.02
1.06
1.01
4.23
1.14
2.15
1.24
2.20
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

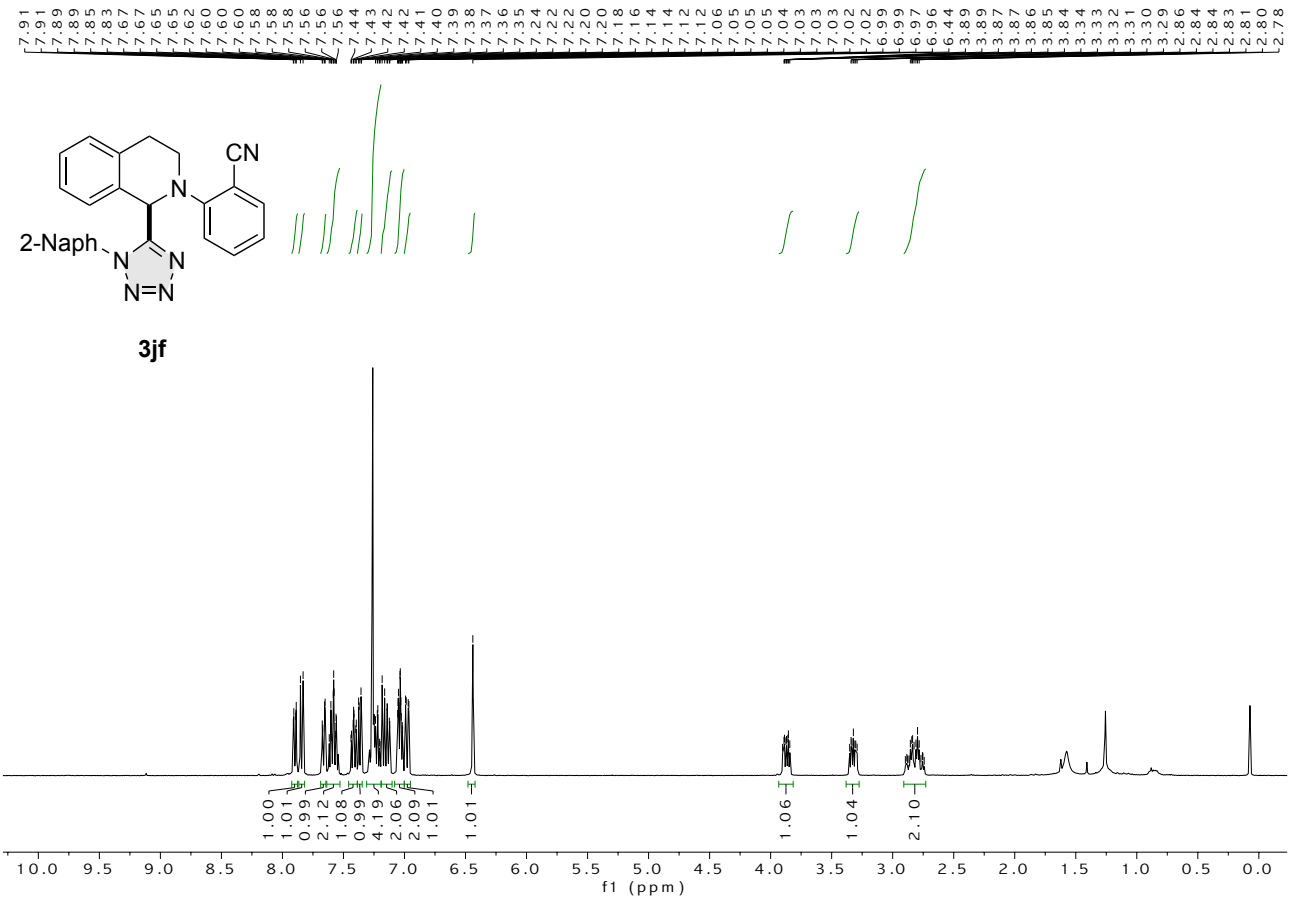
3ia


154.01
153.20
139.96
135.24
131.39
129.26
129.05
127.28
126.07
114.27
58.85
53.66
45.61
33.04
32.96
28.10
25.57
24.78
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



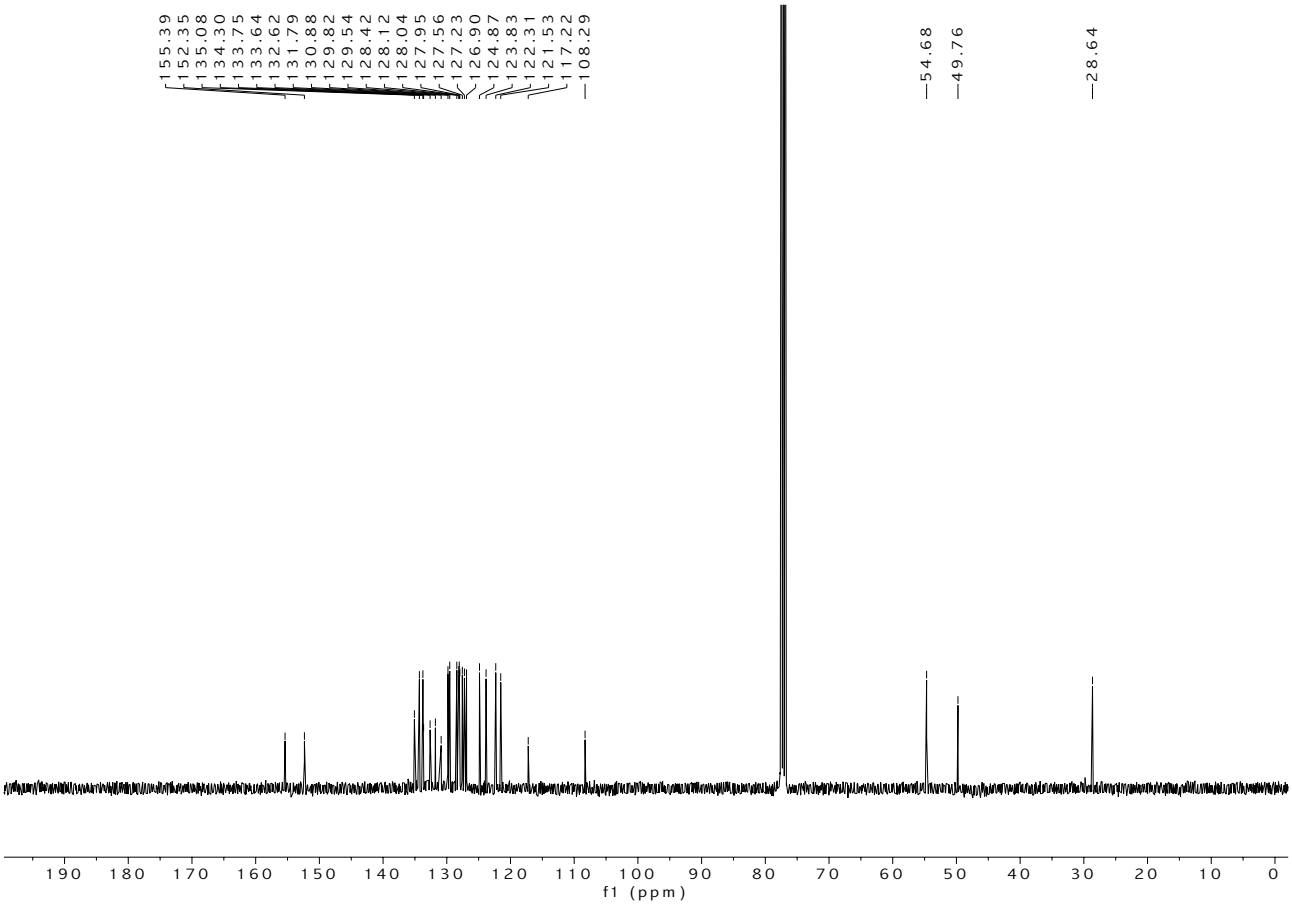
3ja

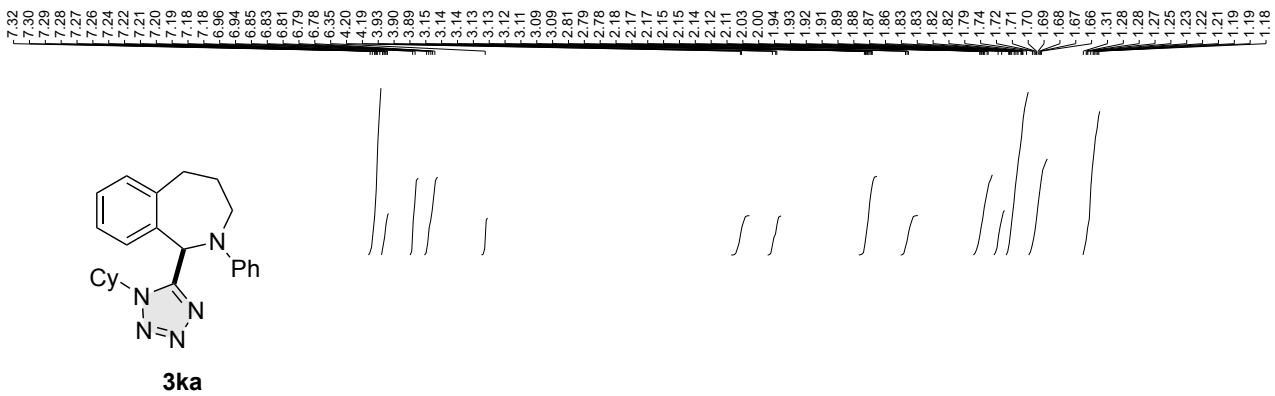



CN
2-Naph
N
N
N=N

3jf

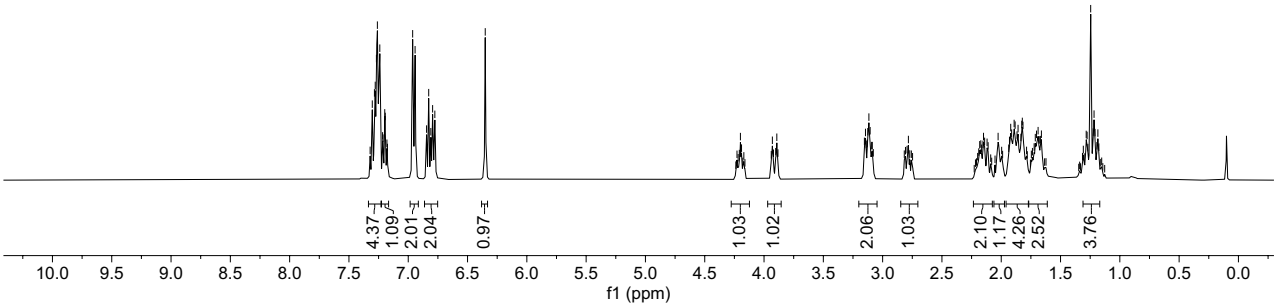
1.00
1.01
0.99
2.12
1.08
0.99
4.19
2.06
2.09
1.01
1.01
1.06
1.04
2.10
f1 (ppm)

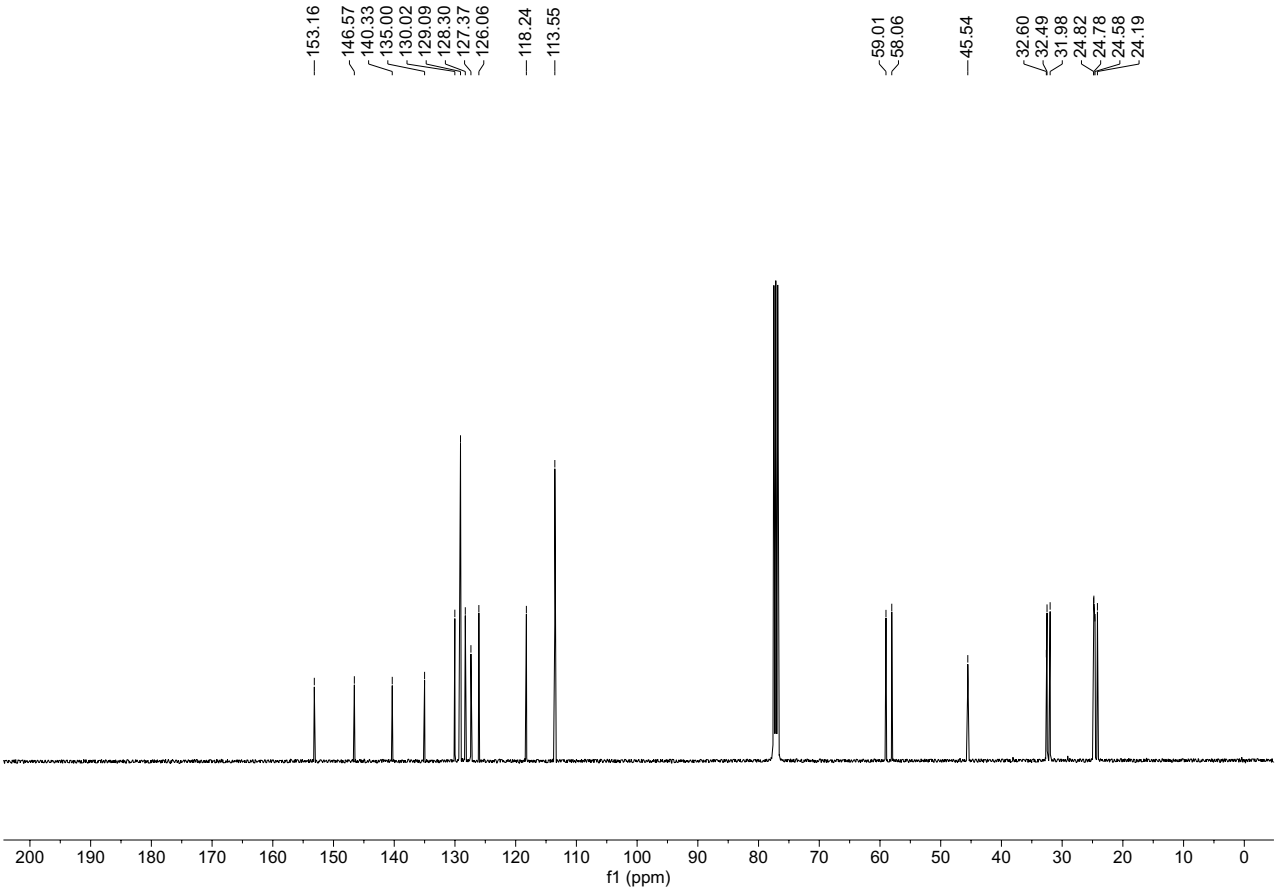

155.39
152.35
135.08
134.30
133.75
133.64
132.62
131.79
130.88
129.82
129.54
128.42
128.12
128.04
127.95
127.56
127.23
126.90
124.87
123.83
122.31
121.53
117.22
108.29
54.68
49.76
28.64
f1 (ppm)

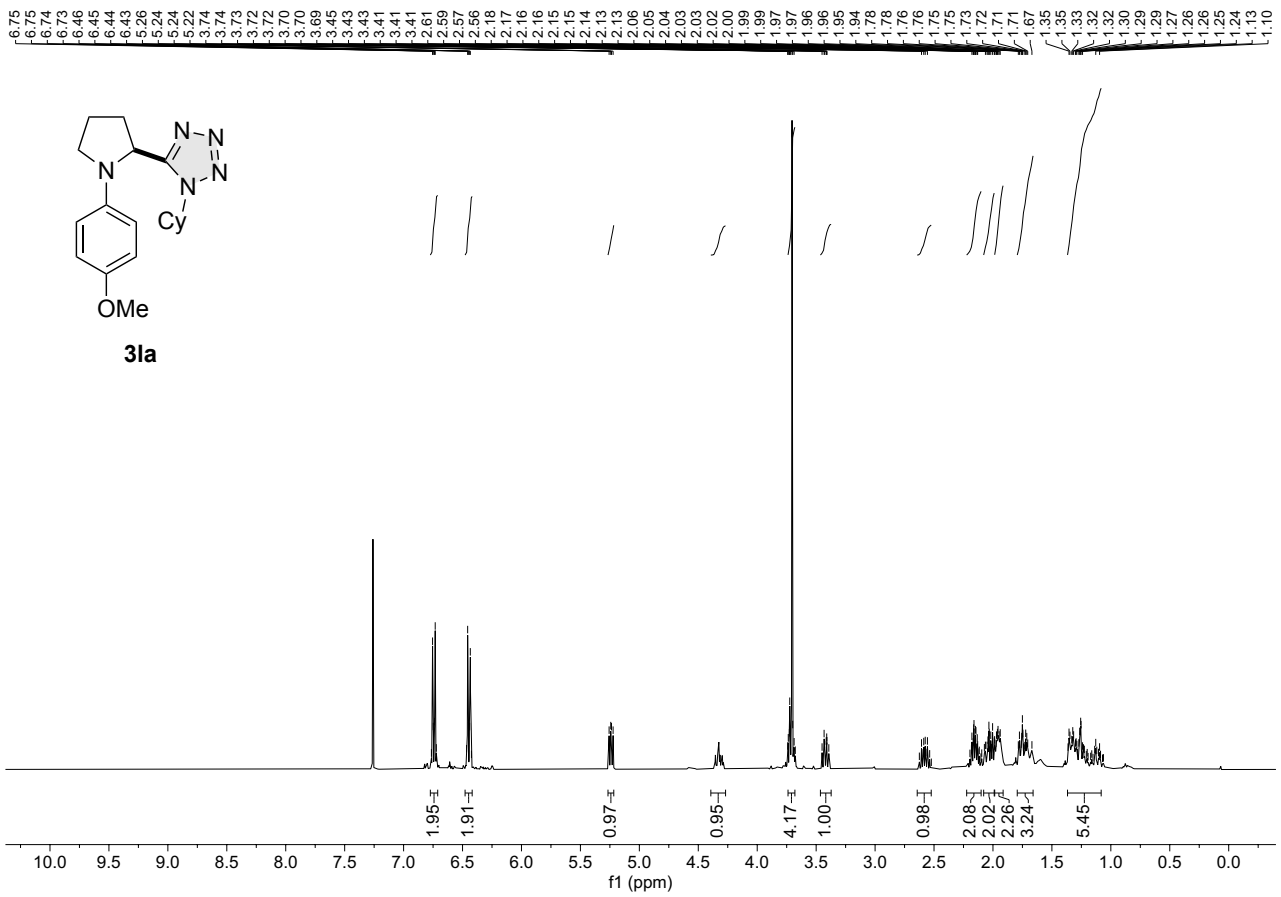

7.32 7.30 7.29 7.28 7.27 7.26 7.24 7.22 7.21 7.20 7.19 7.18 7.18 6.96 6.94 6.85 6.83 6.81 6.79 6.78 6.35 4.20 4.19 3.93 3.90 3.89 3.15 3.14 3.14 3.13 3.13 3.12 3.11 3.09 3.09 2.81 2.79 2.78 2.18 2.17 2.17 2.15 2.15 2.14 2.12 2.11 2.03 2.00 1.94 1.93 1.92 1.91 1.89 1.88 1.87 1.86 1.83 1.83 1.82 1.82 1.79 1.74 1.72 1.71 1.70 1.69 1.68 1.67 1.66 1.31 1.28 1.28 1.27 1.25 1.23 1.22 1.21 1.19 1.19 1.18

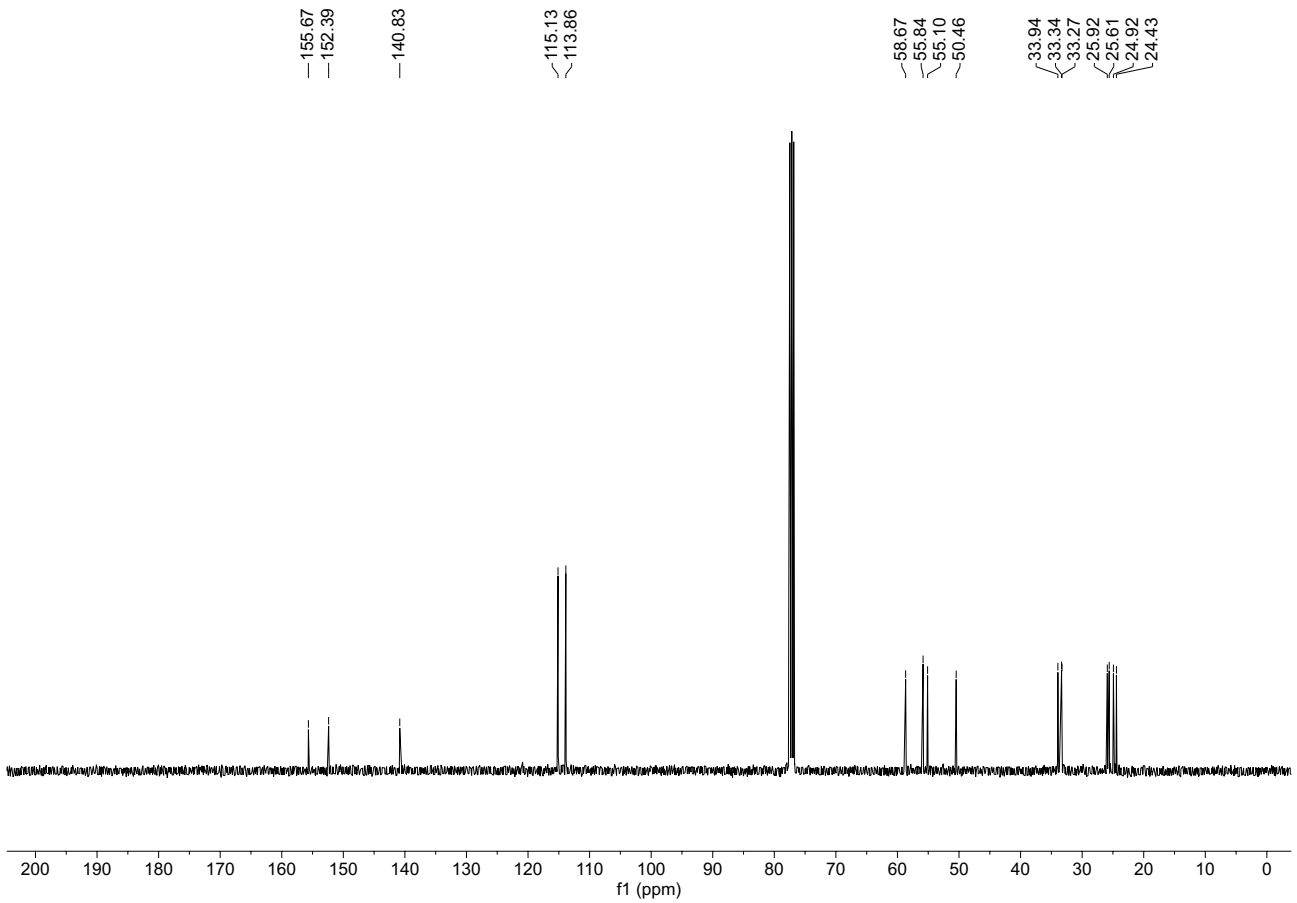
Cy
N
N
N
N
N
Ph

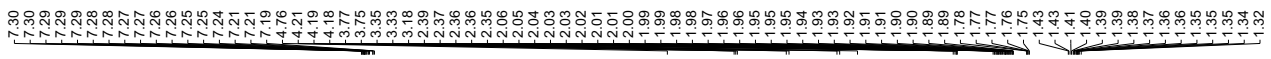
3ka

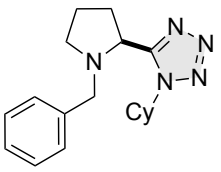

4.37
1.09
2.01
2.04
0.97
1.03
1.02
2.06
1.03
2.10
1.17
4.26
2.52
3.76
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


153.16
146.57
140.33
135.00
130.02
129.09
128.30
127.37
126.06
118.24
113.55
59.01
58.06
45.54
32.60
32.49
31.98
24.82
24.78
24.58
24.19
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

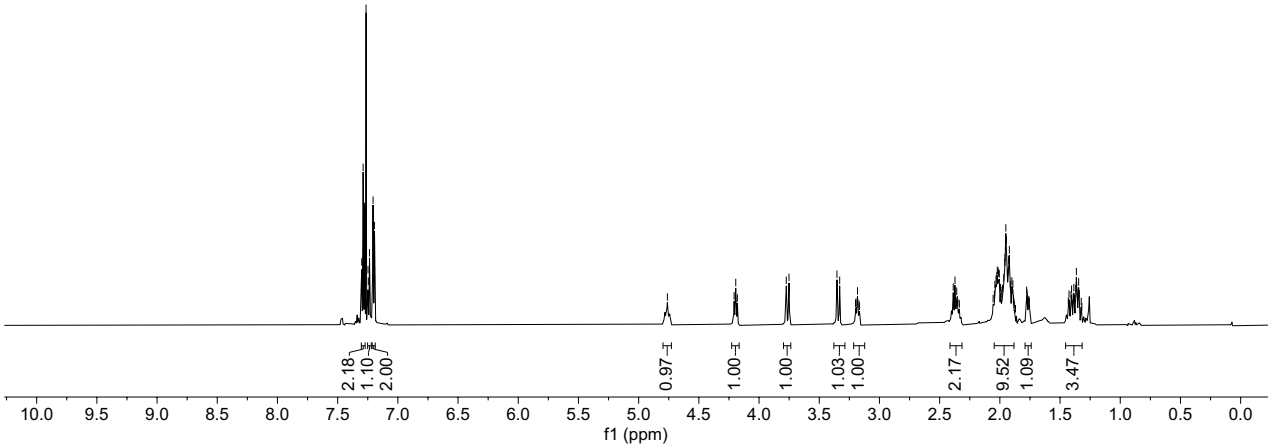

6.75 6.75 6.74 6.73 6.46 6.45 6.44 6.43 5.26 5.24 5.24 5.22 3.74 3.74 3.73 3.72 3.72 3.70 3.70 3.69 3.45 3.43 3.43 3.41 3.41 3.41 2.61 2.59 2.57 2.56 2.18 2.17 2.16 2.16 2.15 2.15 2.14 2.13 2.13 2.06 2.05 2.04 2.03 2.03 2.02 2.00 1.99 1.99 1.97 1.97 1.96 1.96 1.95 1.94 1.78 1.78 1.76 1.76 1.75 1.75 1.73 1.72 1.71 1.71 1.67 1.35 1.35 1.33 1.32 1.32 1.30 1.29 1.29 1.27 1.26 1.26 1.25 1.24 1.13 1.10
N
N
N
N
Cy
OMe
3Ia
1.95 1.91 0.97 0.95 4.17 1.00 0.98 2.08 2.02 2.26 3.24 5.45
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

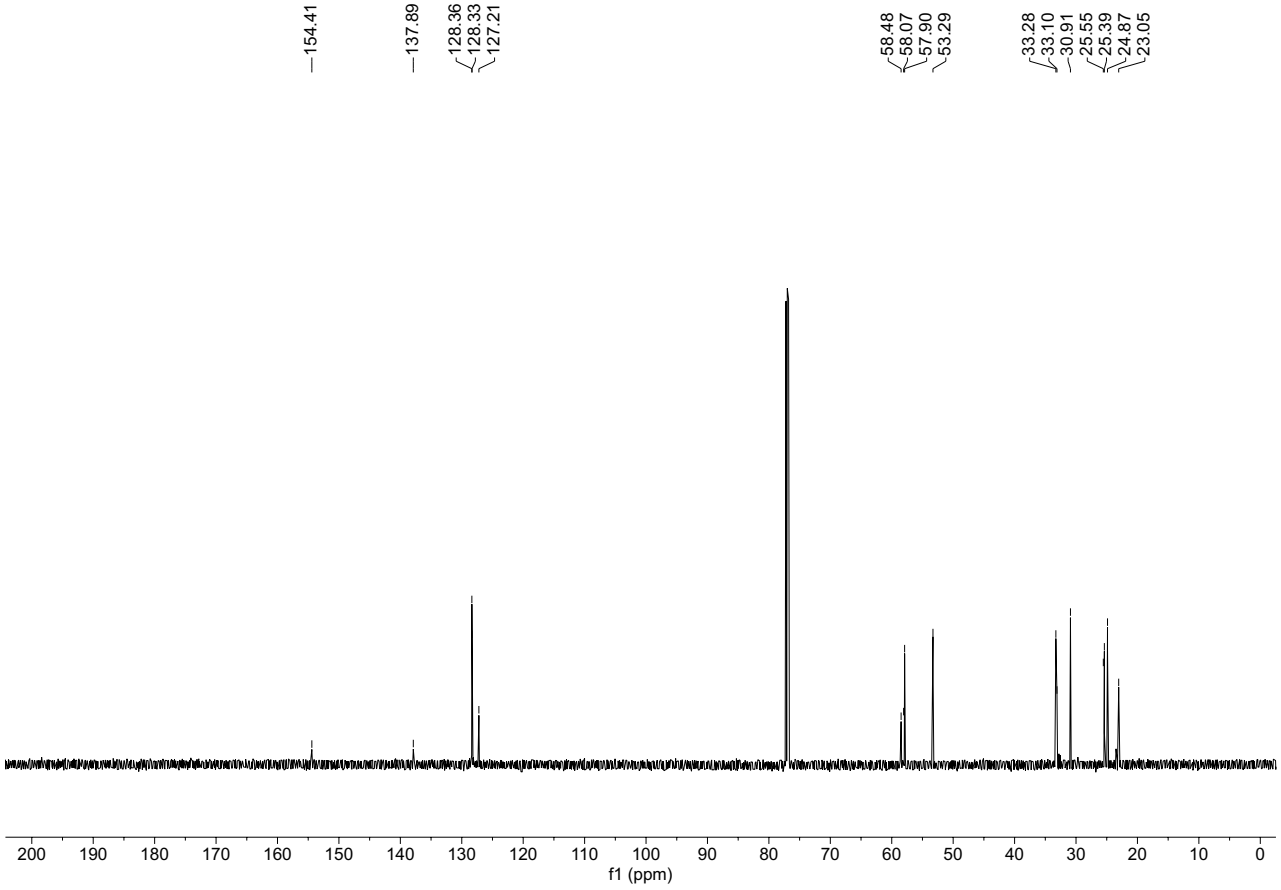

155.67 152.39 140.83 115.13 113.86 58.67 55.84 55.10 50.46 33.94 33.34 33.27 25.92 25.61 24.92 24.43
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

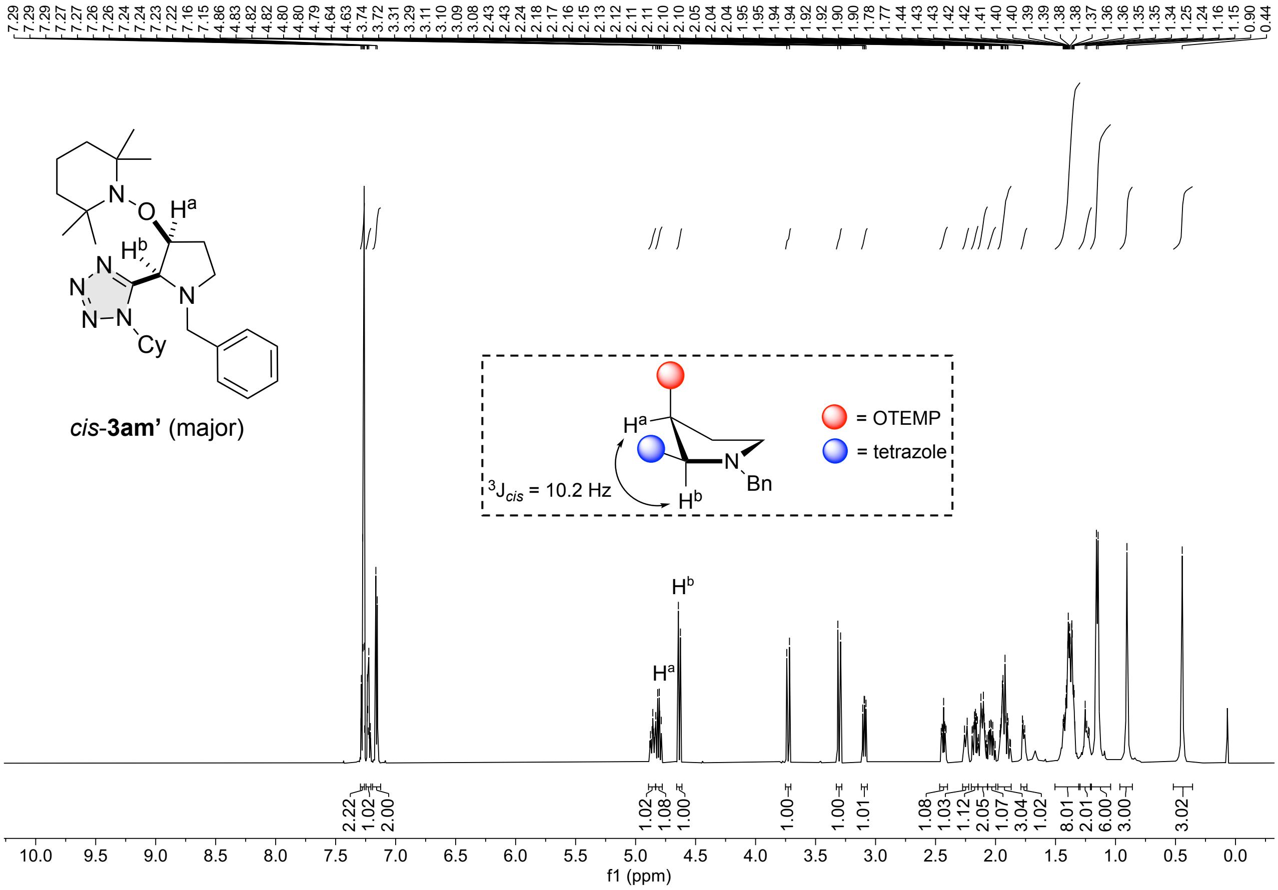


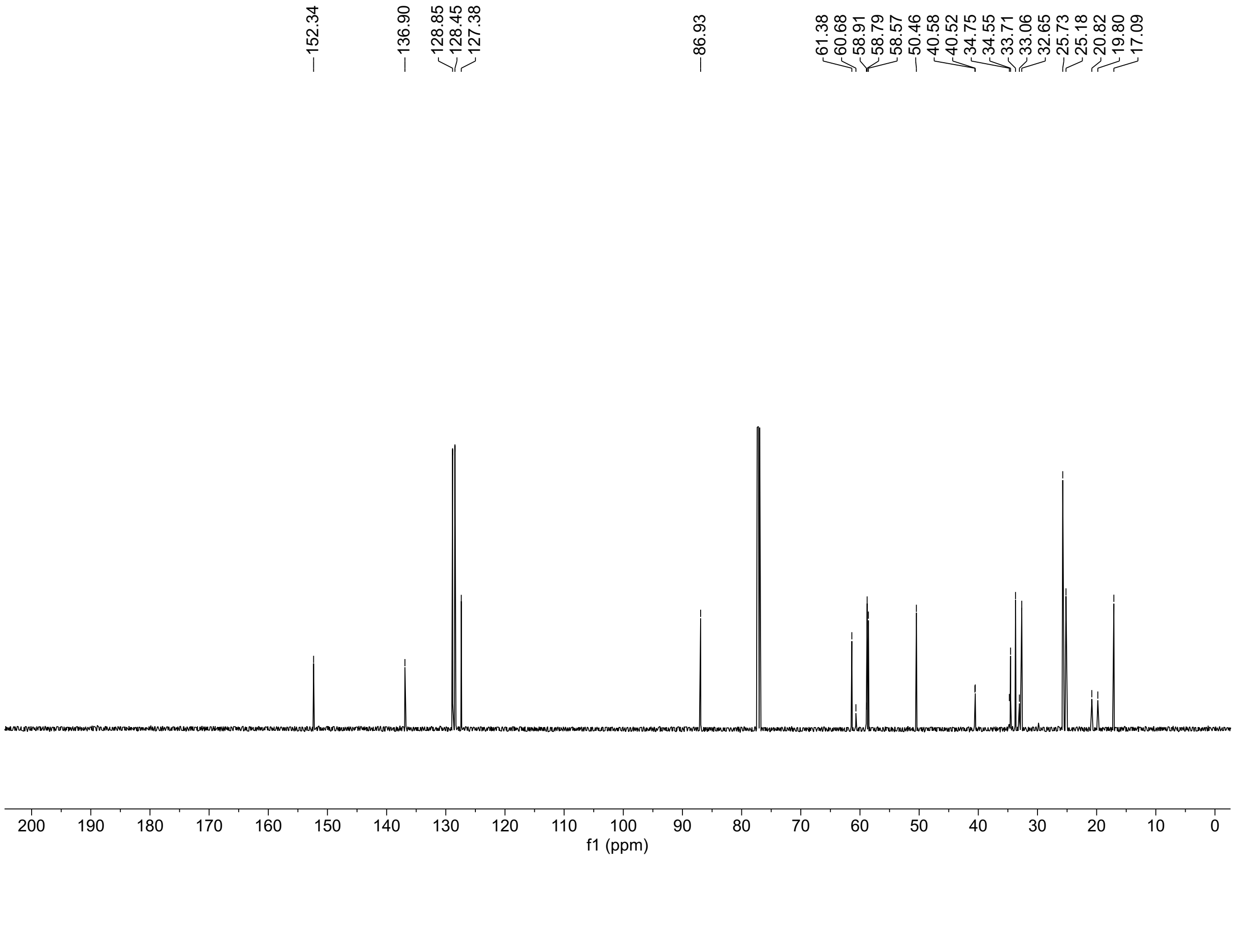


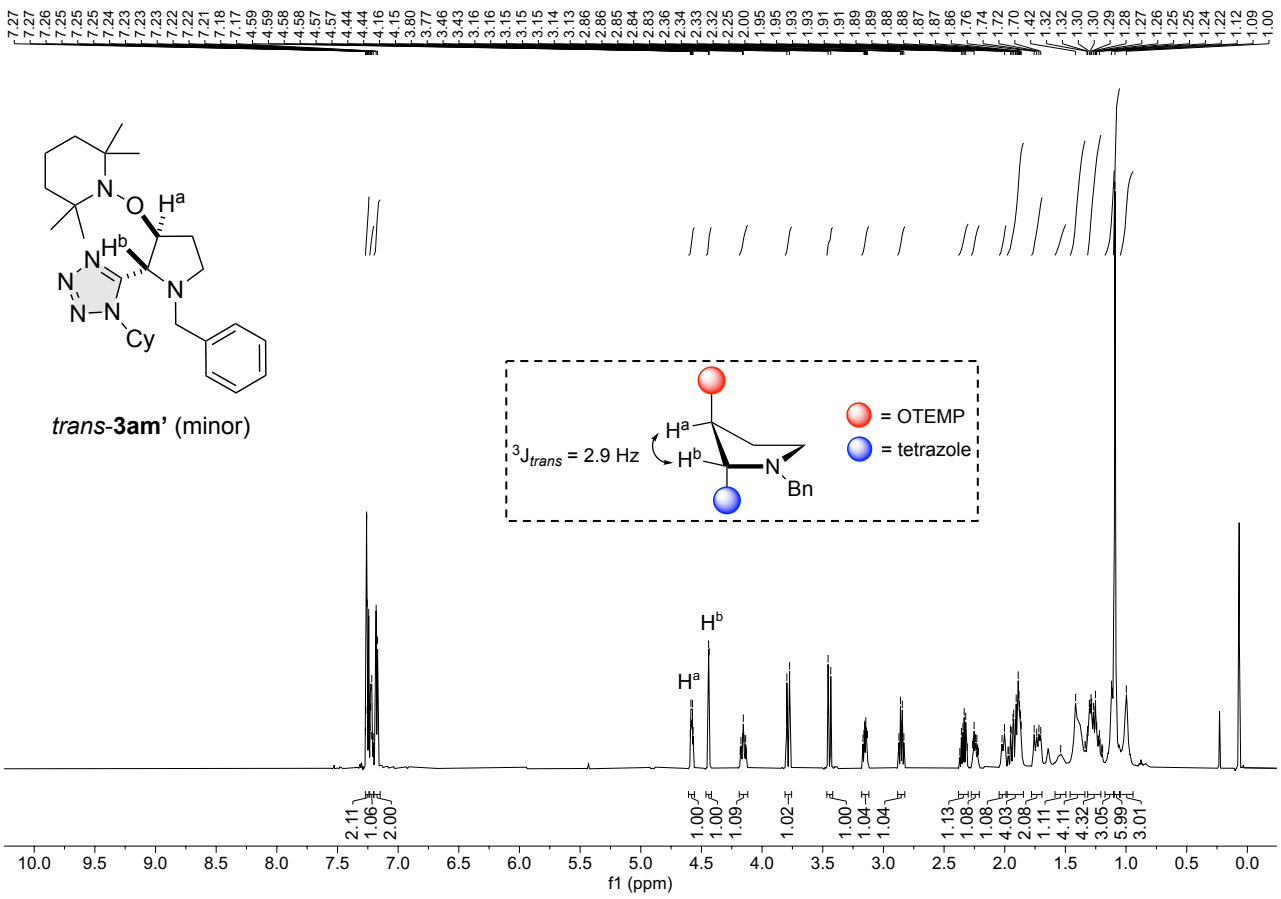
3ma

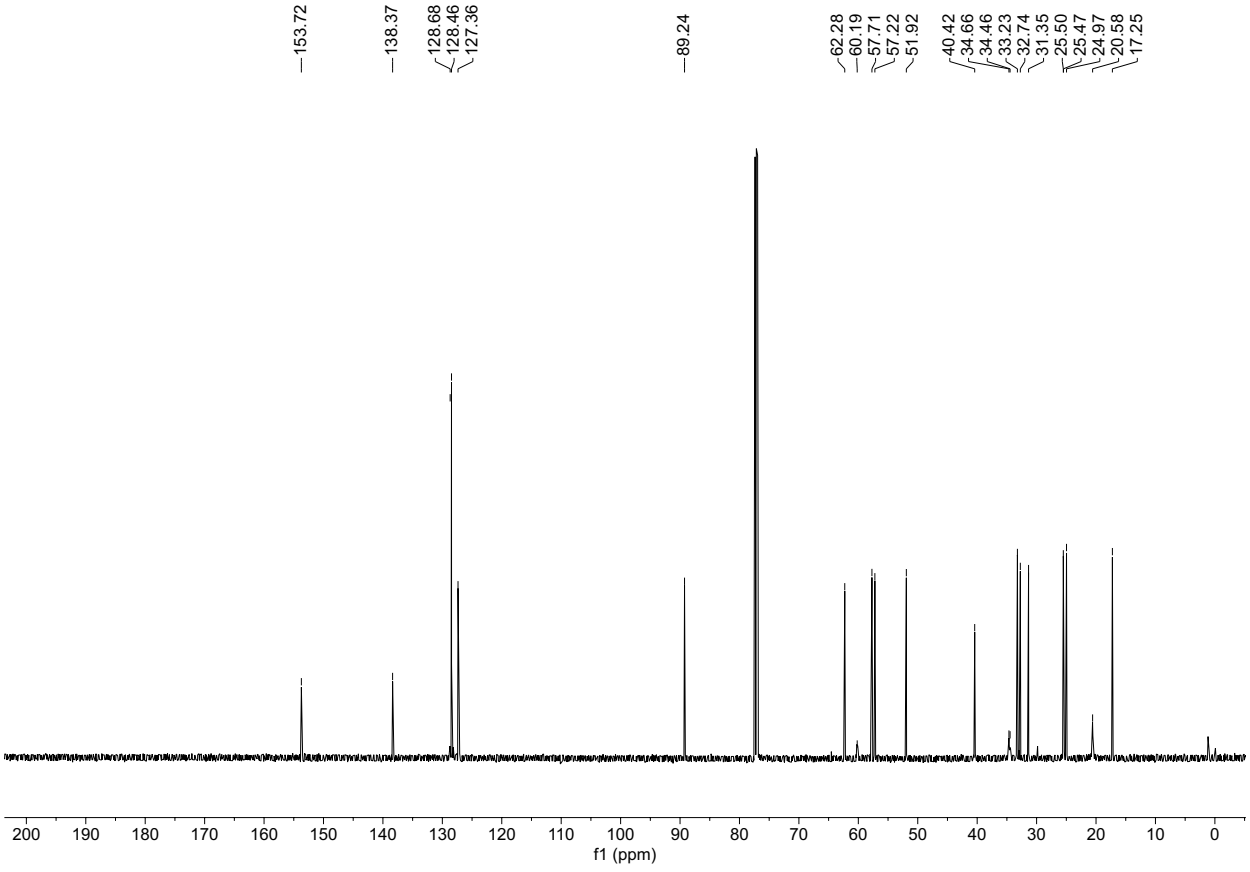


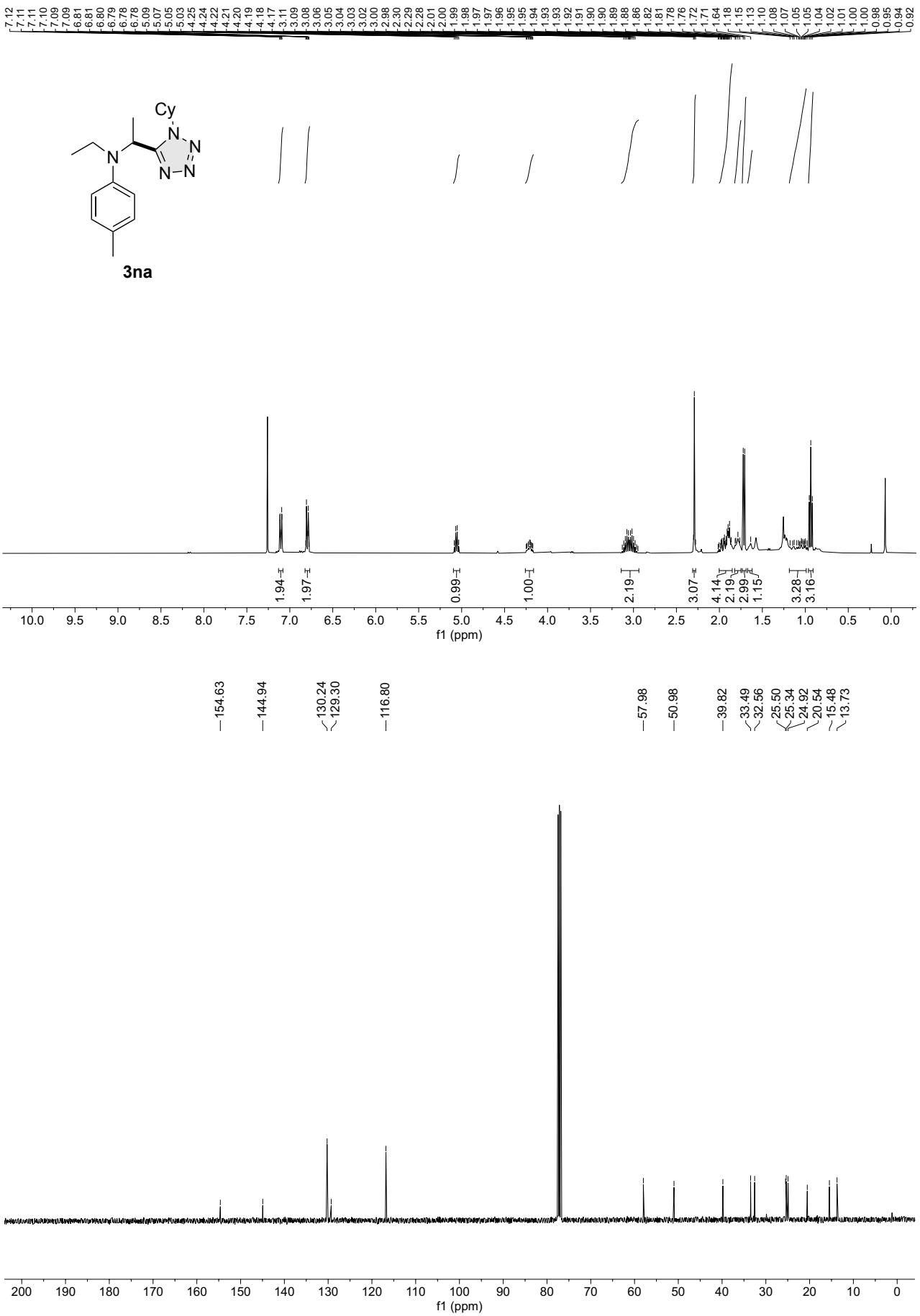


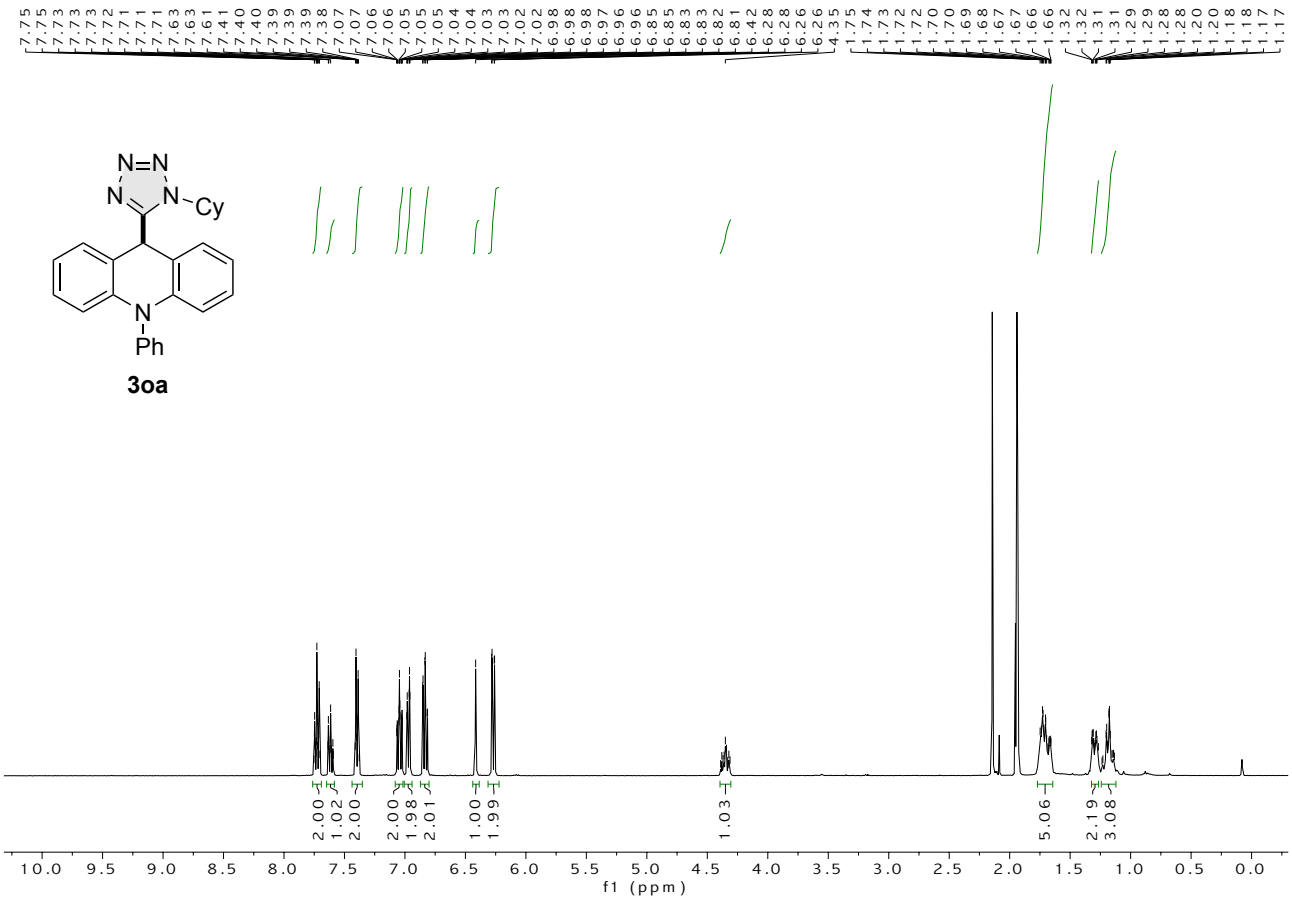

7.29 7.29 7.27 7.26 7.26 7.24 7.24 7.23 7.22 7.16 7.15 4.86 4.83 4.82 4.82 4.80 4.79 4.64 4.63 3.74 3.72 3.31 3.29 3.11 3.10 3.09 3.08 2.43 2.43 2.24 2.18 2.17 2.16 2.15 2.13 2.12 2.11 2.11 2.10 2.10 2.05 2.04 2.04 1.95 1.95 1.94 1.94 1.92 1.92 1.90 1.90 1.78 1.77 1.44 1.43 1.43 1.42 1.42 1.41 1.40 1.40 1.39 1.39 1.38 1.38 1.37 1.36 1.36 1.35 1.35 1.34 1.25 1.24 1.16 1.15 0.90 0.44
cis-**3am'** (major)
= OTEMP
= tetrazole
$^3J_{cis}$ = 10.2 Hz
Bn
Ha
Hb
2.22 1.02 2.00 1.02 1.08 1.00 1.00 1.00 1.01 1.08 1.03 1.12 2.05 1.07 3.04 1.02 8.01 2.01 6.00 3.00 3.02
f1 (ppm)

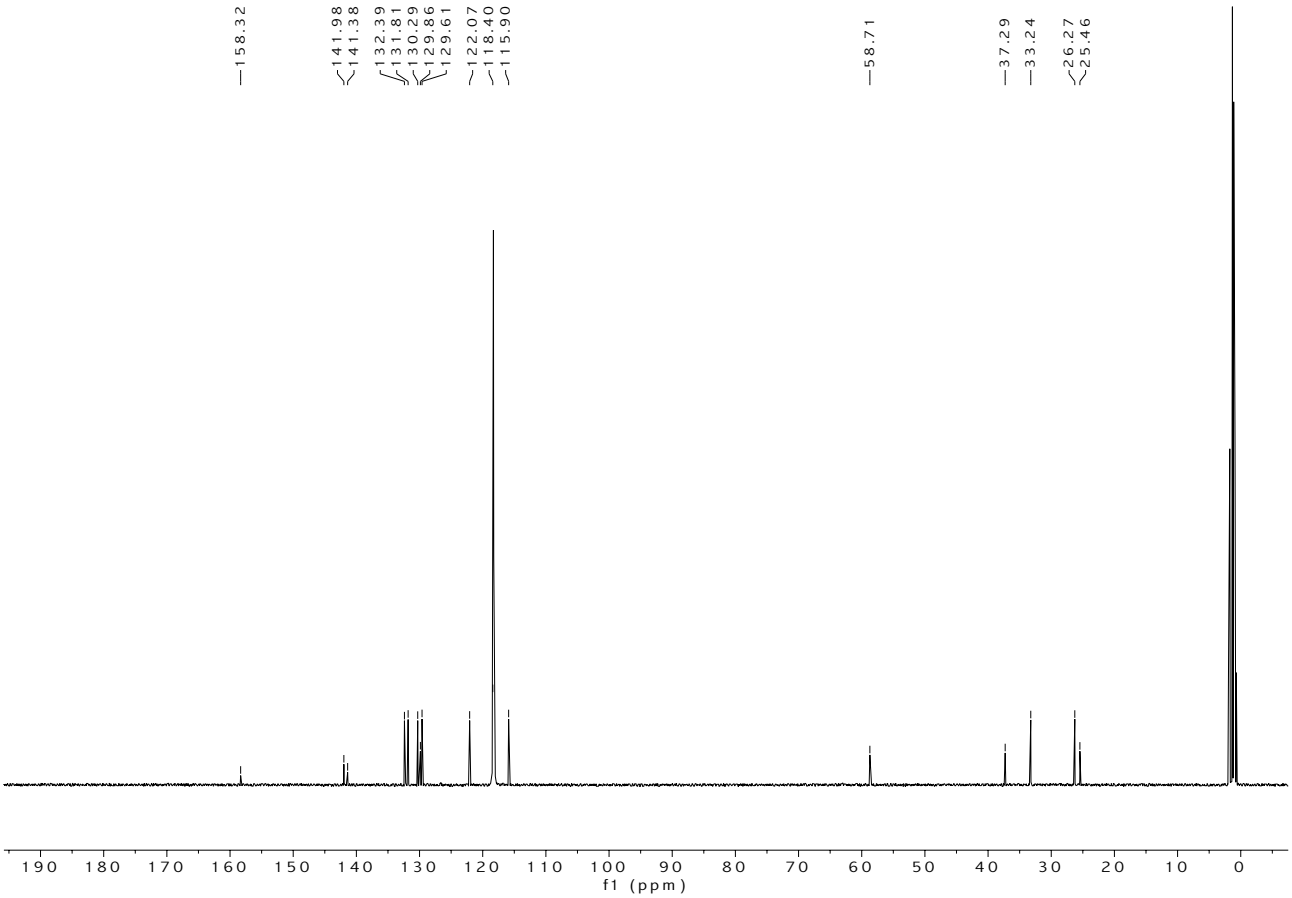

152.34 136.90 128.85 128.45 127.38 86.93 61.38 60.68 58.91 58.79 58.57 50.46 40.58 40.52 34.75 34.55 33.71 33.06 32.65 25.73 25.18 20.82 19.80 17.09
f1 (ppm)


7.27 7.27 7.26 7.25 7.25 7.25 7.24 7.23 7.23 7.22 7.22 7.21 7.18 7.17 4.59 4.59 4.58 4.58 4.57 4.44 4.44 4.16 4.15 3.80 3.77 3.46 3.43 3.16 3.16 3.15 3.15 3.15 3.14 3.13 2.86 2.86 2.85 2.84 2.83 2.36 2.34 2.33 2.32 2.25 2.00 1.95 1.95 1.93 1.93 1.91 1.91 1.89 1.89 1.88 1.88 1.87 1.87 1.86 1.76 1.74 1.72 1.70 1.42 1.32 1.32 1.30 1.30 1.29 1.28 1.27 1.26 1.25 1.25 1.24 1.22 1.12 1.09 1.00
trans-3am' (minor)
$^3J_{trans}$ = 2.9 Hz
= OTEMP
= tetrazole
Bn
Cy
2.11 1.06 2.00 1.00 1.00 1.09 1.02 1.00 1.04 1.04 1.13 1.08 1.08 4.03 2.08 1.11 4.11 4.32 3.05 5.99 3.01
f1 (ppm)


153.72 138.37 128.68 128.46 127.36 89.24 62.28 60.19 57.71 57.22 51.92 40.42 34.66 34.46 33.23 32.74 31.35 25.50 25.47 24.97 20.58 17.25
f1 (ppm)


7.12 7.11 7.11 7.10 7.09 7.09 6.81 6.81 6.80 6.79 6.78 6.78 5.09 5.07 5.05 5.03 4.25 4.24 4.22 4.21 4.20 4.19 4.18 4.17 3.11 3.09 3.08 3.06 3.05 3.04 3.03 3.02 3.00 2.98 2.30 2.29 2.28 2.01 2.00 1.99 1.98 1.97 1.97 1.96 1.95 1.95 1.94 1.93 1.93 1.92 1.91 1.90 1.90 1.89 1.88 1.86 1.82 1.81 1.78 1.76 1.72 1.71 1.64 1.18 1.15 1.13 1.10 1.08 1.07 1.05 1.05 1.04 1.02 1.01 1.00 1.00 0.98 0.95 0.94 0.92
Cy
N
N
N
N
N
3na
1.94 1.97 0.99 1.00 2.19 3.07 4.14 2.19 2.99 1.15 3.28 3.16
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
154.63 144.94 130.24 129.30 116.80 57.98 50.98 39.82 33.49 32.56 25.50 25.34 24.92 20.54 15.48 13.73
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


N=N
N
N
Cy
N
Ph
3oa
f1 (ppm)


158.32
141.98
141.38
132.39
131.81
130.29
129.86
129.61
122.07
118.40
115.90
58.71
37.29
33.24
26.27
25.46
f1 (ppm)