Rh(III)-catalysed synthesis of cinnolinium and fluoranthenium salts by using C-H activation/annulation reactions: Organelle specific mitochondrial staining application

Sivakalai Mayakrishnan, [a] Masilamani Tamizmani, [b] Chandrasekar Balachandran, [c] Shin Aoki, [c] Narayanan Uma Maheswari [a]*

[a] Organic & Bioorganic Chemistry Laboratory, CSIR-Central Leather Research Institute, Adyar, Chennai-600 020, India.
Corresponding author; 044-24437120, E-mail: umamaheswari@clri.res.in

[b] State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Road, Shanghai, 200032, China

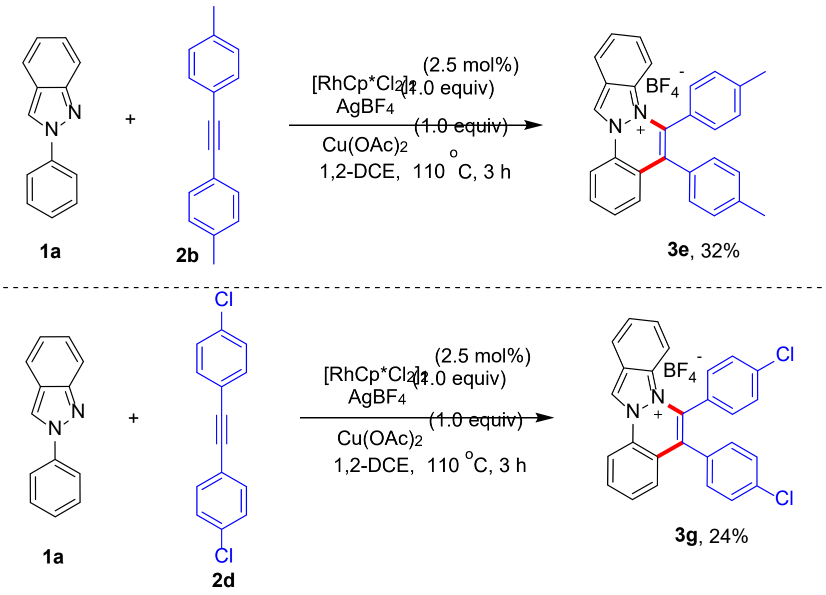
[c] Faculty of Pharmaceutical Sciences, Tokyo University of Science, 2641 Yamazaki, Noda 278-8510, Japan

Electronic Supporting Information

Table of Contents

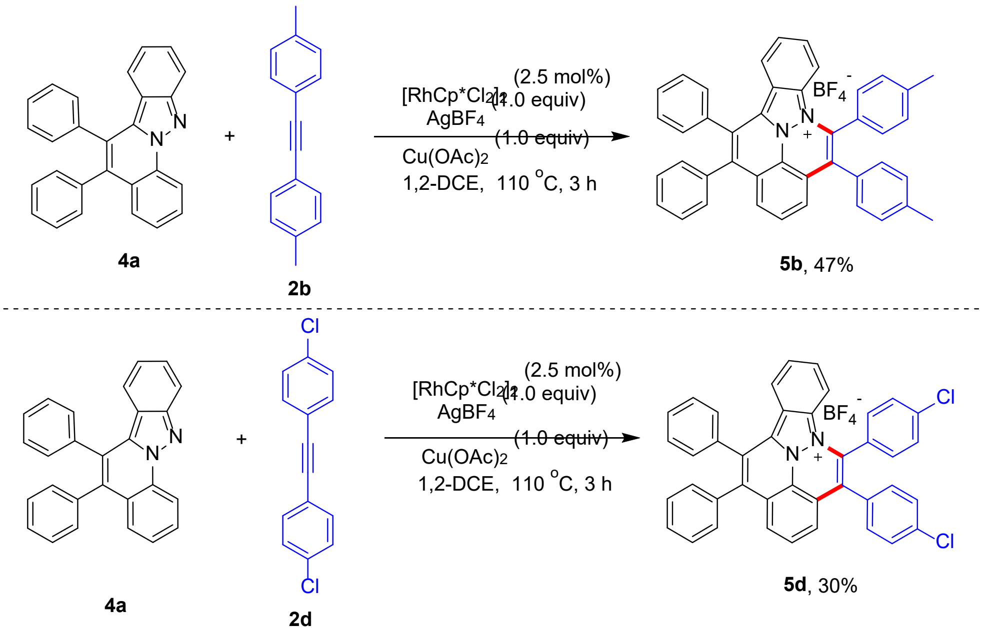
1. **Parallel competitive reaction** 3
2. **H to D exchange experiments** 5
3. **Photoluminescence spectrum** 7
4. **Copy of ^{1}H, ^{13}C and HRMS spectra** 16
5. **DFT Calculations** 56
6. **Reference** 67

1. Parallel competitive reaction



Scheme S1

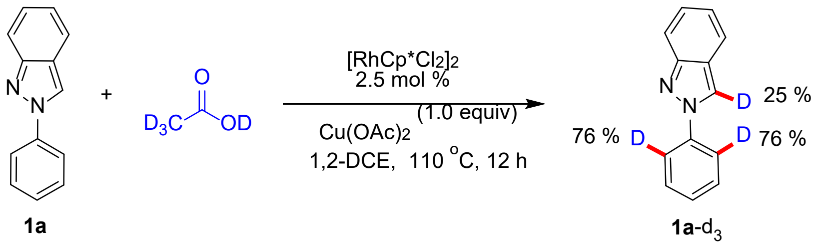
A solution of 2-phenyl-2H-indazole **1a** (58 mg, 0.3 mmol), 1,2-di-p-tolylethyne **2b** (62 mg, 0.3 mmol), $AgBF_4$ (58 mg 0.3 mmol), $[RhCp^*Cl_2]_2$ (9.0 mg, 5.0 mol %), and $Cu(OAc)_2$ (54 mg 0.3 mmol) in 1,2-DCE (3 mL). The tube was sealed with a Teflon-coated screw cap and the reaction solution was heated at 110 °C for 3 hours. At the same time, another solution of 2-phenyl-2H-indazole **1a** (58 mg, 0.3 mmol), 1,2-bis(4-chlorophenyl)ethyne **2d** (74 mg, 0.3 mmol), $AgBF_4$ (58 mg 0.3 mmol), $[RhCp^*Cl_2]_2$ (9.0 mg, 5.0 mol %), and $Cu(OAc)_2$ (54 0.3 mmol) in 1,2-DCE (3 mL). The tube was sealed with a Teflon-coated screw cap and the reaction solution was heated at 110 °C for 3 hours. After cooling ambient temperature, the solvent was removed from both the reaction mixtures under reduced pressure and the residues of the reaction mixtures were separately purified by silica gel (100-200 mesh) column chromatography using Methanol/DCM as the eluant to afford **3e** 32% and **3g** 24% (3e:3g = ~1.3:1).



Scheme S2

A solution of 5,6-diphenylindazolo[2,3-a]quinoline **1a** (111 mg, 0.3 mmol), 1,2-di-p-tolylethyne **2c** (61 mg, 0.3 mmol), $AgBF_4$ 58 mg (0.3 mmol), $[RhCp^*Cl_2]_2$ (9 mg, 5.0 mol %), and $Cu(OAc)_2$ (0.3 mmol) in 1,2-DCE 3.0 mL. The tube was sealed with a Teflon-coated screw cap and the reaction solution was heated at 110 °C for 3 hours. At the same time, another solution of 2-phenyl-2H-indazole **1a** (111 mg, 0.3 mmol), 1,2-bis(4- chlorophenyl)ethyne **2d** (74 mg, 0.3 mmol), $AgBF_4$ 58 mg (0.3 mmol), $[RhCp^*Cl_2]_2$ (9 mg, 5.0 mol %), and $Cu(OAc)_2$ (0.3 mmol) in 1,2-DCE 3 ml. The tube was sealed with a Teflon-coated screw cap and the reaction solution was heated at 110 °C for 3 hours. After cooling ambient temperature, the solvent was removed from both the reaction mixtures under reduced pressure and the residues of the reaction mixtures were separately purified by silica gel (100-200 mesh) column chromatography using Methanol/DCM as the eluant to afford **5b** 30% and **5d** 47% (**5b**:**5d** = ~1.7:1.0)

2. H to D exchange experiments



Scheme S3

To an oven-dried 20 mL reaction tube with septum containing were added 2-phenyl-2H-indazole **1a** 58.2 mg (0.3 mmol, 1.0 equiv), $[RhCp^*Cl_2]2$ (9.18 mg, 0.015 mmol, 0.05 equiv), $Cu(OAc)_2$ 55.6 mg, (0.3 mmol, 1.0 equiv), Acetic acid-*d₄* 0.38 ml (20.0 equiv) and 1,2-DCE 3.0 ml. The reaction mixture was heated at 110 °C for 12 h. After the reaction mixture was cooled to room temperature diluted with CH_2Cl_2, filtered through celite and the filtrate was concentrated under reduced pressure. After that, purification was performed by column chromatography on silica gel using hexane and ethyl acetate (90:10) as eluent. Desired product colourless solid **1a-*d₃*** 52 mg was obtained in 90% of yield. The H/D exchange was found to be 76% at the protons attached to C-2 and C-5 in the recovered 2-phenyl-2H-indazole **1a-*d₃***. Also found H/D exchange 25% at the indazole *2-H* position. These results also clearly reveal that the C-H bond activation as a key intermediate in the reaction as well as it is the reversible process.

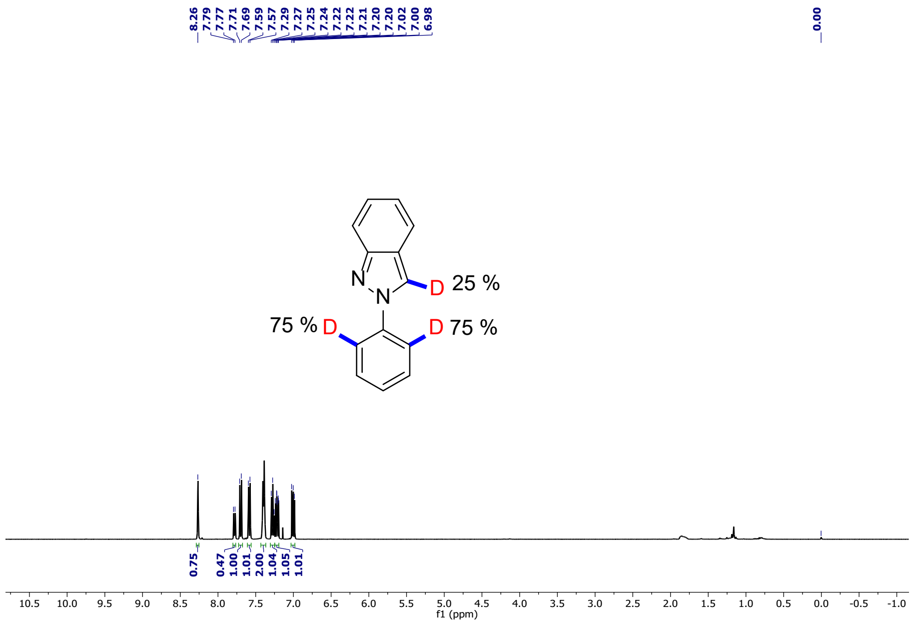
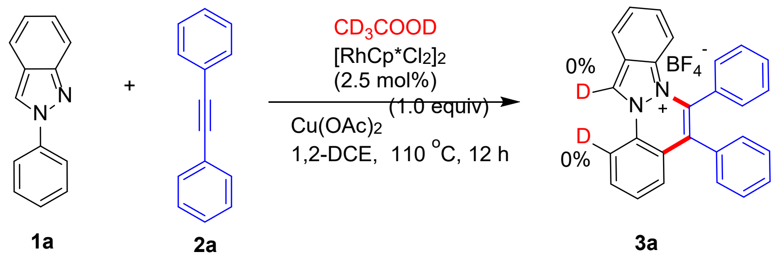


Figure SI1: Preliminary mechanistic study



Scheme S4

To an oven-dried 20 mL reaction tube with septum containing were added 2-phenyl-2H-indazole **1a** 58 mg (0.3 mmol, 1.0 equiv), diphenylacetylene **2a** 52 mg (0.3 mmol), $AgBF_4$ 58 mg (0.3 mmol%), $[RhCp^*Cl_2]_2$ (9 mg, 0.015 mmol, 0.05 equiv), $Cu(OAc)_2$ 56 mg, (0.3 mmol, 1.0 equiv), acetic acid-d_4 0.38 ml (20.0 equiv) and 1,2-DCE 3.0 ml. The reaction mixture was heated at 110 °C for 12 h. After the reaction mixture was cooled to room temperature diluted with CH_2Cl_2, filtered through celite and the filtrate was concentrated under reduced pressure. After that, purification was performed by column chromatography on silica gel using DCM and Methanol (95:5) as eluent. Desired product colourless solid **3a** was obtained in 78% of yield.

3. Photoluminescence spectrum

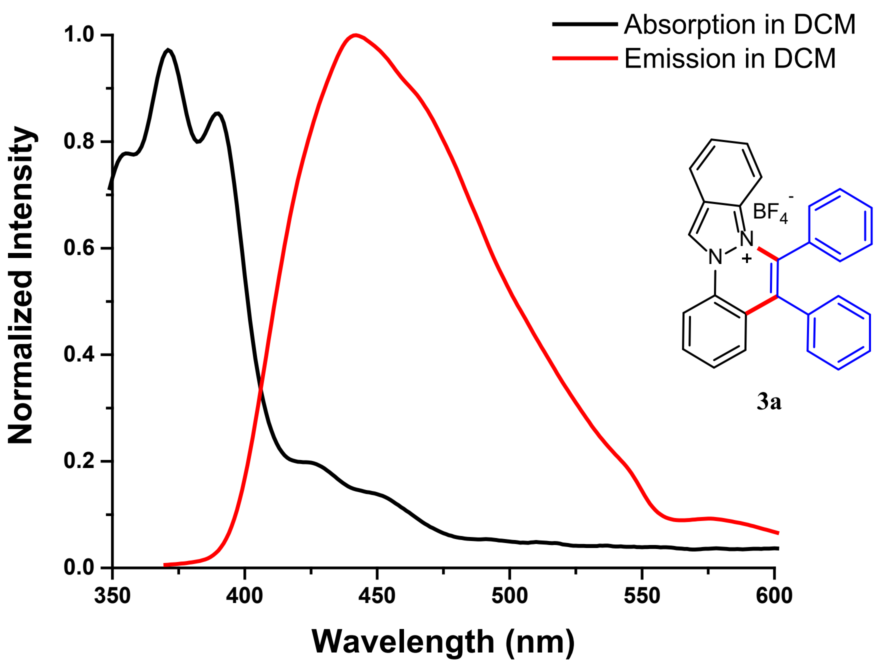


Figure SI2: Normalized absorption (black), Fluorescence in DCM (red) spectra of compound **3a**

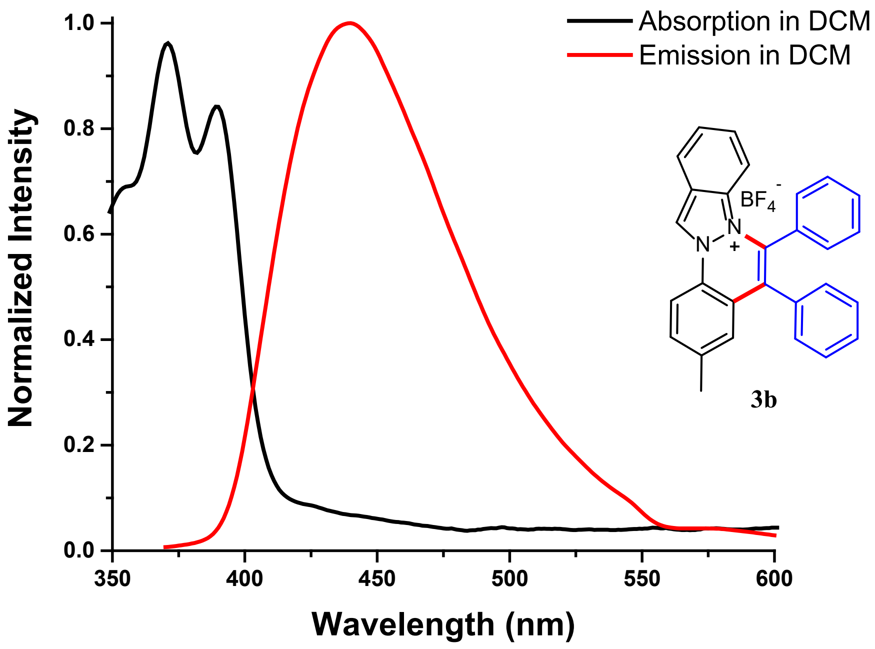


Figure SI3: Normalized absorption (black), Fluorescence in DCM (red) spectra of compound **3b**

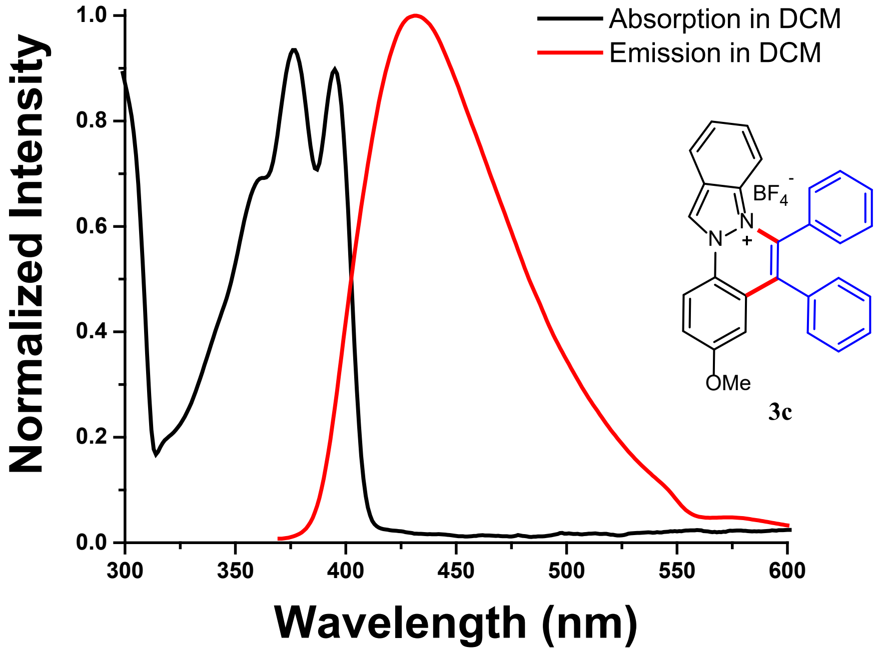


Figure SI4: Normalized absorption (black), Fluorescence in DCM (red) spectra of compound **3c**

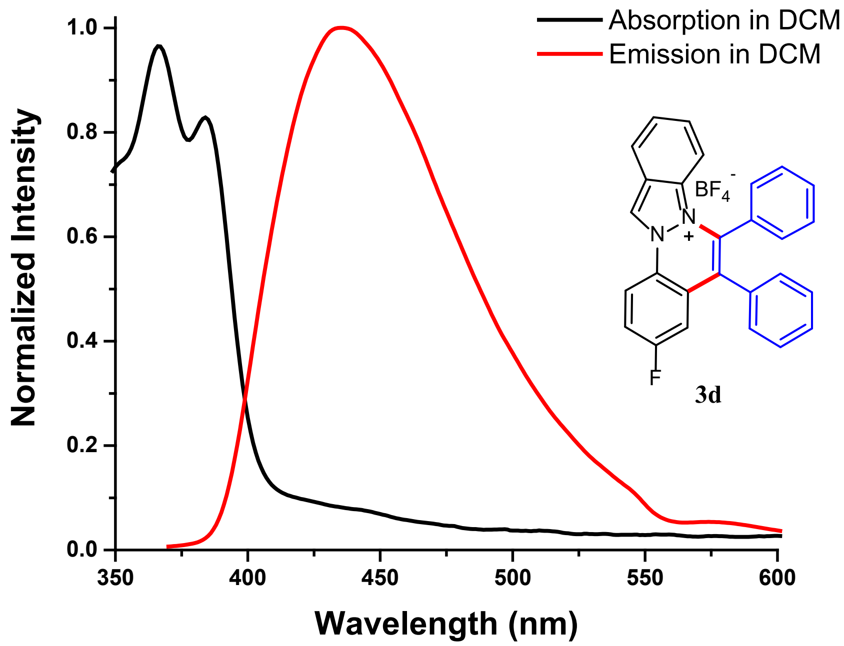


Figure SI5: Normalized absorption (black), Fluorescence in DCM (red) spectra of compound **3d**

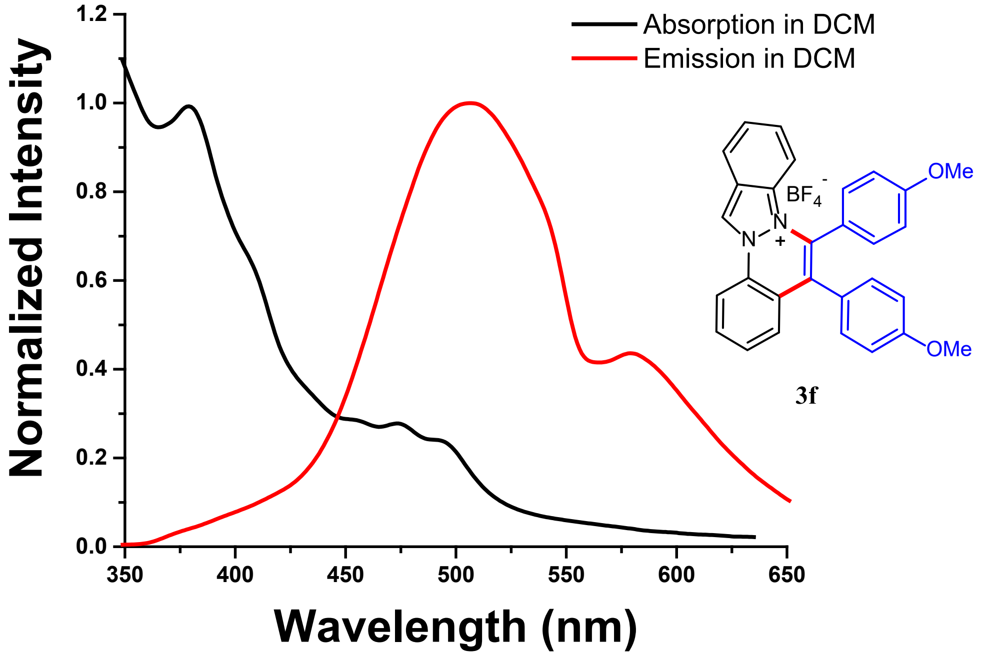


Figure SI6: Normalized absorption (black), Fluorescence in DCM (red) spectra of compound **3f**

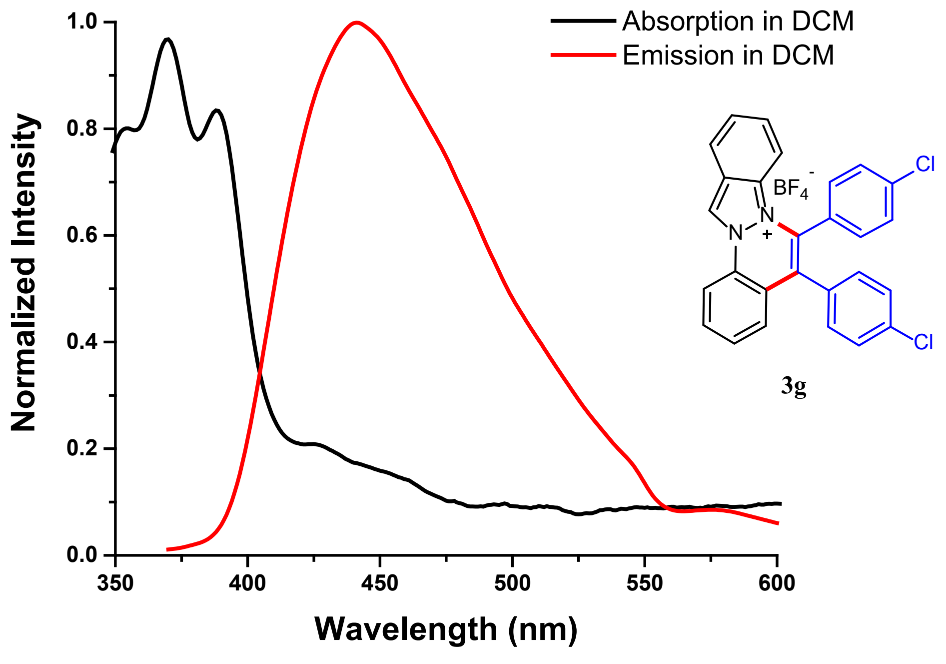


Figure SI7: Normalized absorption (black), Fluorescence in DCM (red) spectra of compound **4g**

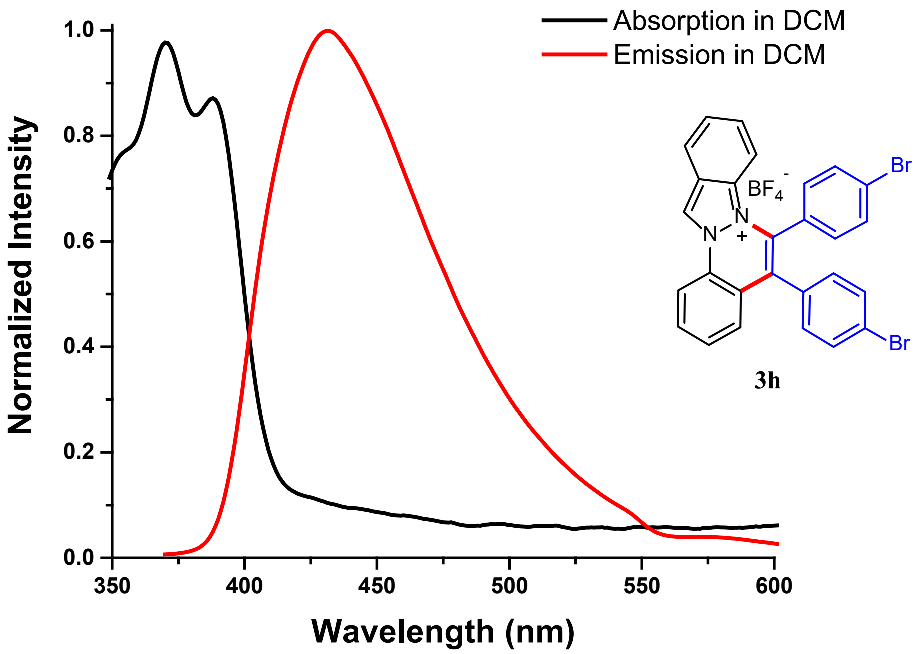


Figure SI8: Normalized absorption (black), Fluorescence in DCM (red) spectra of compound **3h**

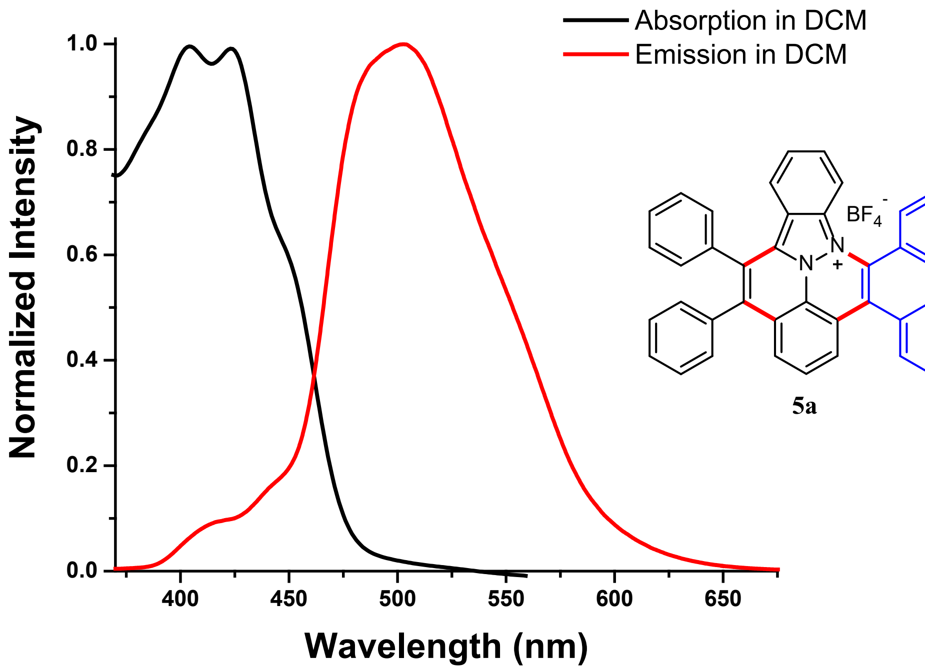


Figure SI9: Normalized absorption (black), Fluorescence in DCM (red) spectra of compound **5a**

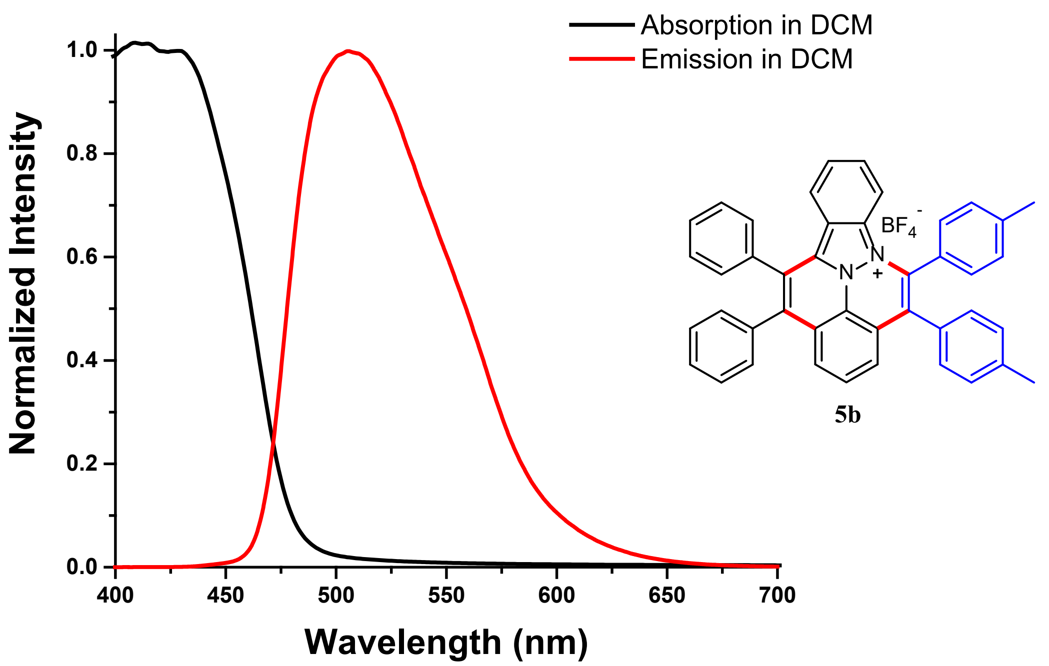


Figure SI10: Normalized absorption (black), Fluorescence in DCM (red) spectra of compound **5b**

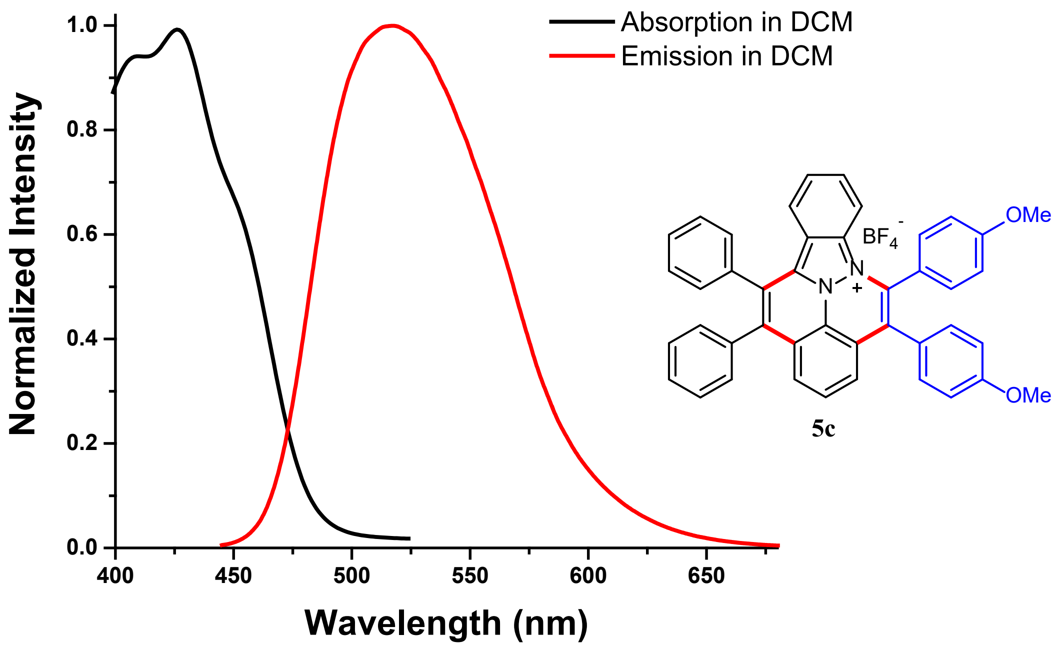


Figure SI11: Normalized absorption (black), Fluorescence in DCM (red) spectra of compound **5c**

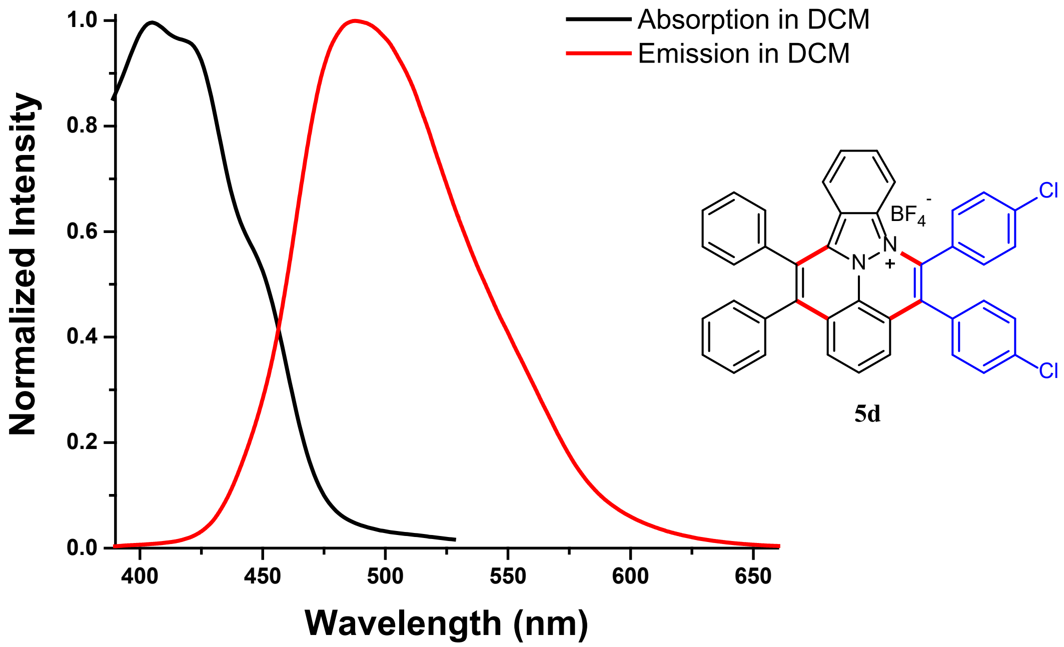


Figure SI12: Normalized absorption (black), Fluorescence in DCM (red) spectra of compound **5d**

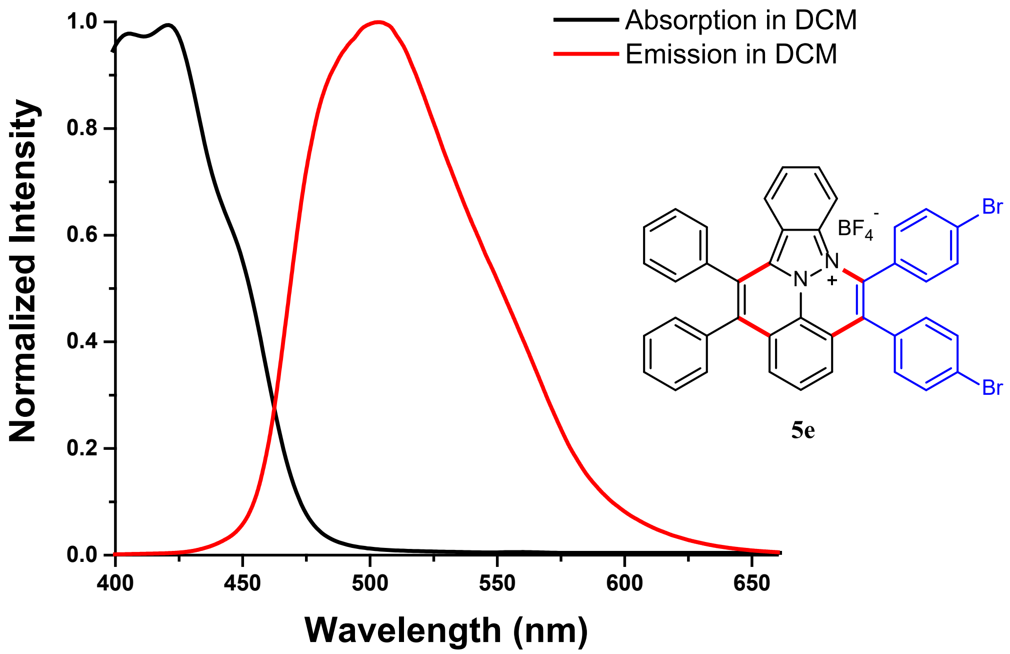


Figure SI13: Normalized absorption (black), Fluorescence in DCM (red) spectra of compound **5e**

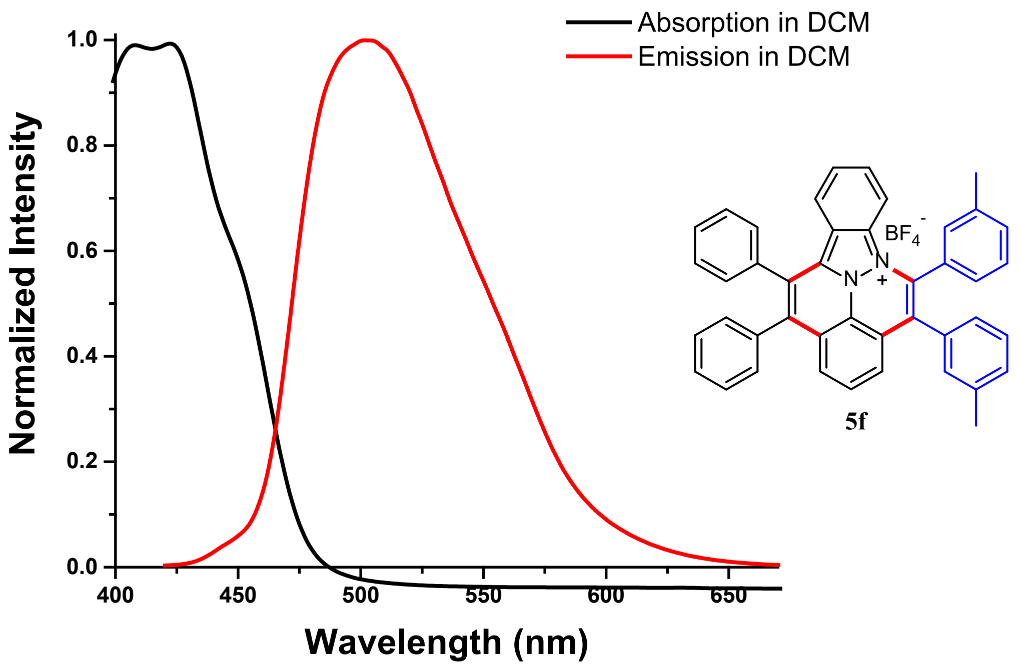


Figure SI14: Normalized absorption (black), Fluorescence in DCM (red) spectra of compound **5f**

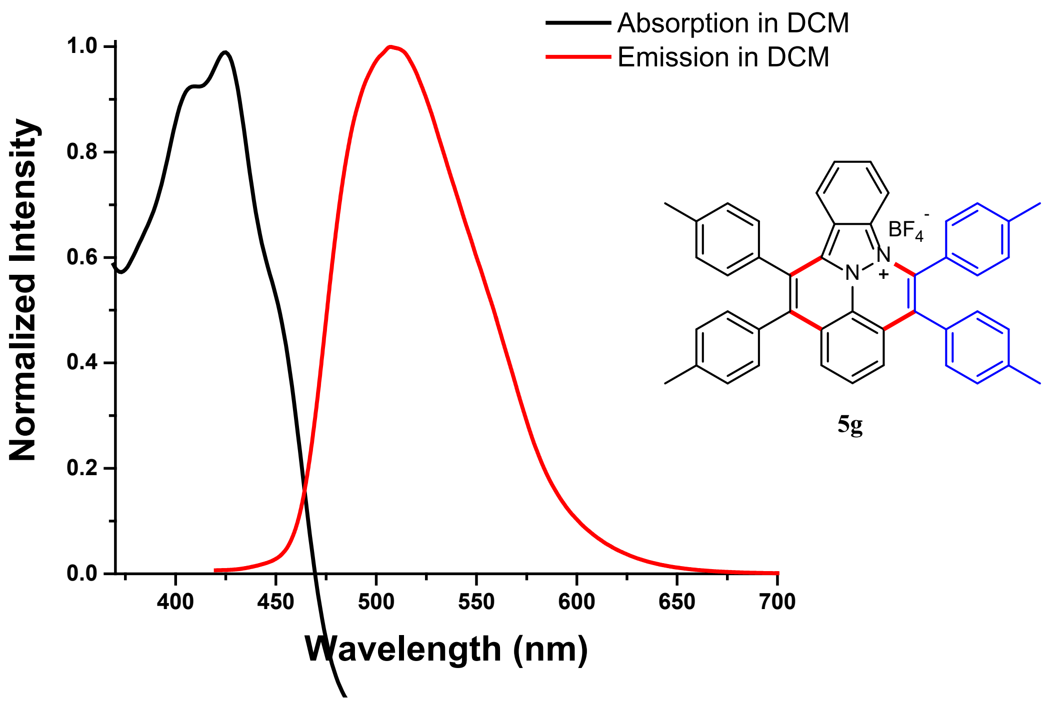


Figure SI15: Normalized absorption (black), Fluorescence in DCM (red) spectra of compound **5g**

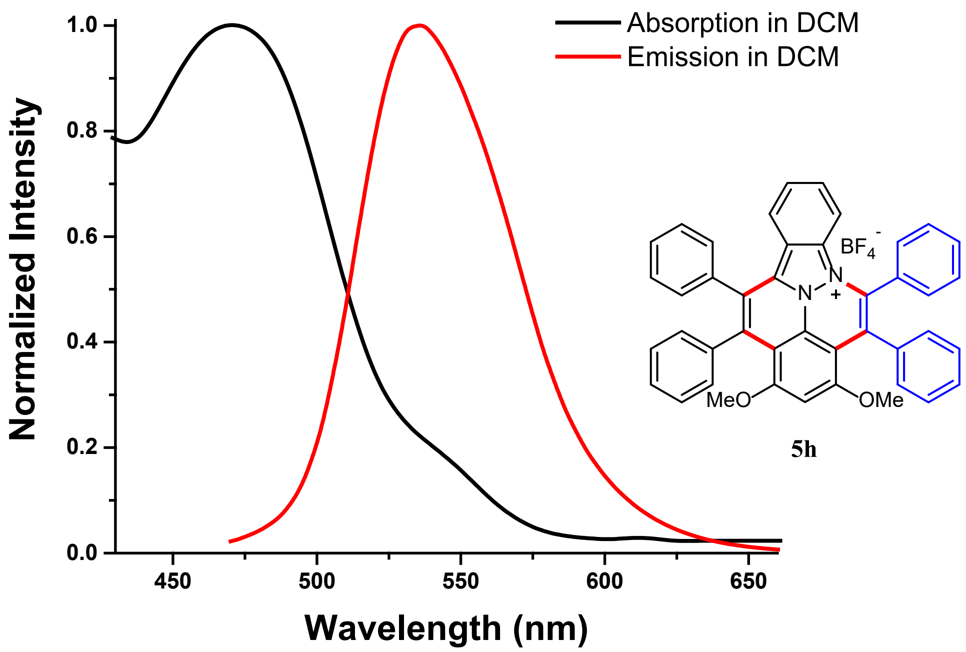


Figure SI16: Normalized absorption (black), Fluorescence in DCM (red) spectra of compound **5h**

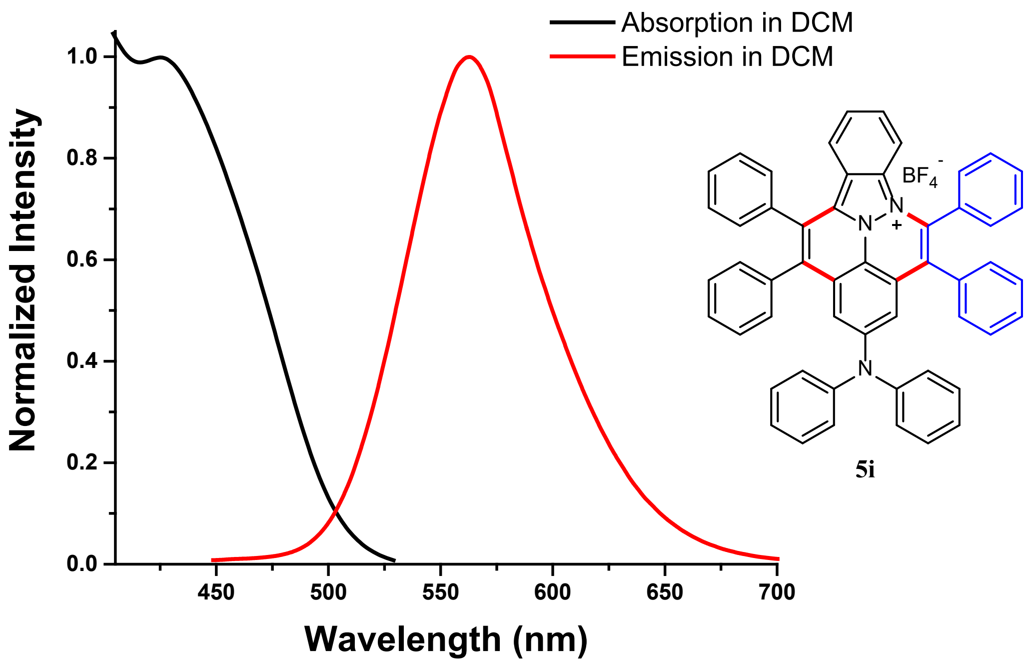


Figure SI17: Normalized absorption (black), Fluorescence in DCM (red) spectra of compound **5i**

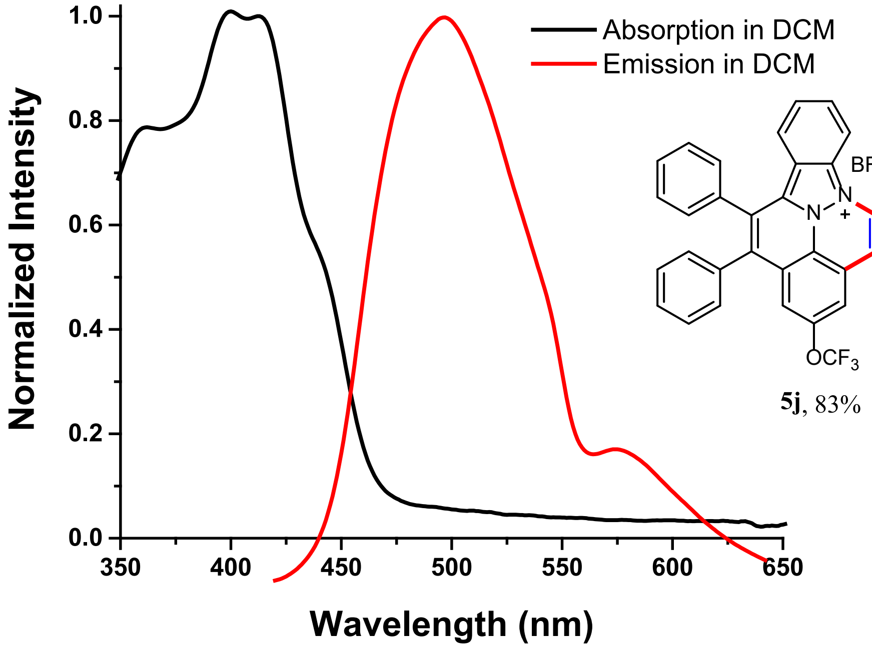


Figure SI18: Normalized absorption (black), Fluorescence in DCM (red) spectra of compound **5j**

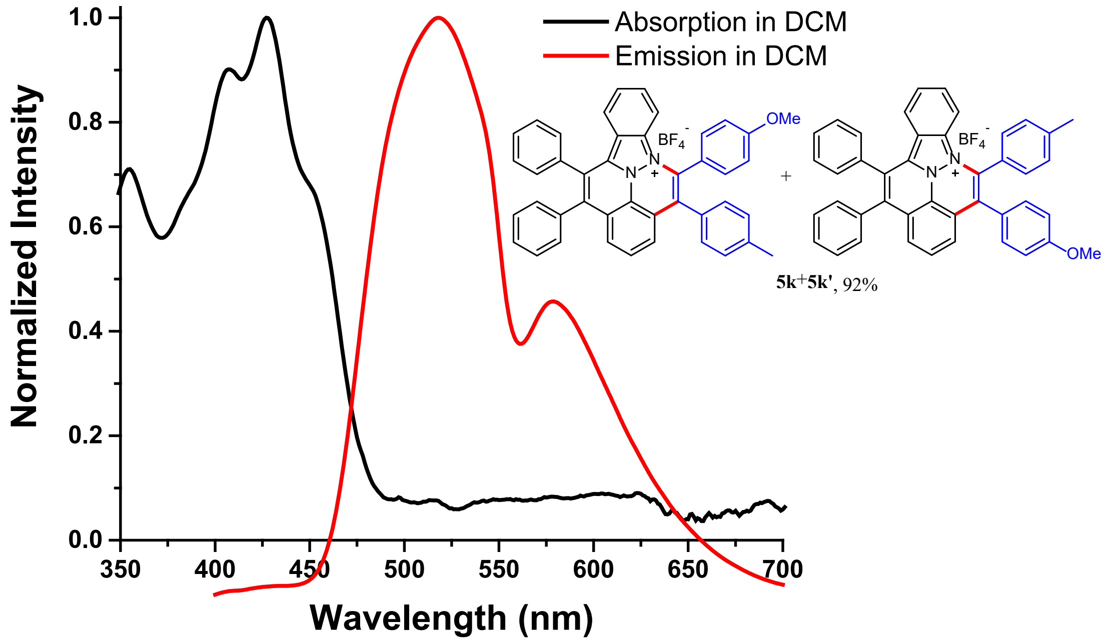


Figure SI19: Normalized absorption (black), Fluorescence in DCM (red) spectra of compound **5k**

4. Copy of ^{1}H, ^{13}C and HRMS spectra

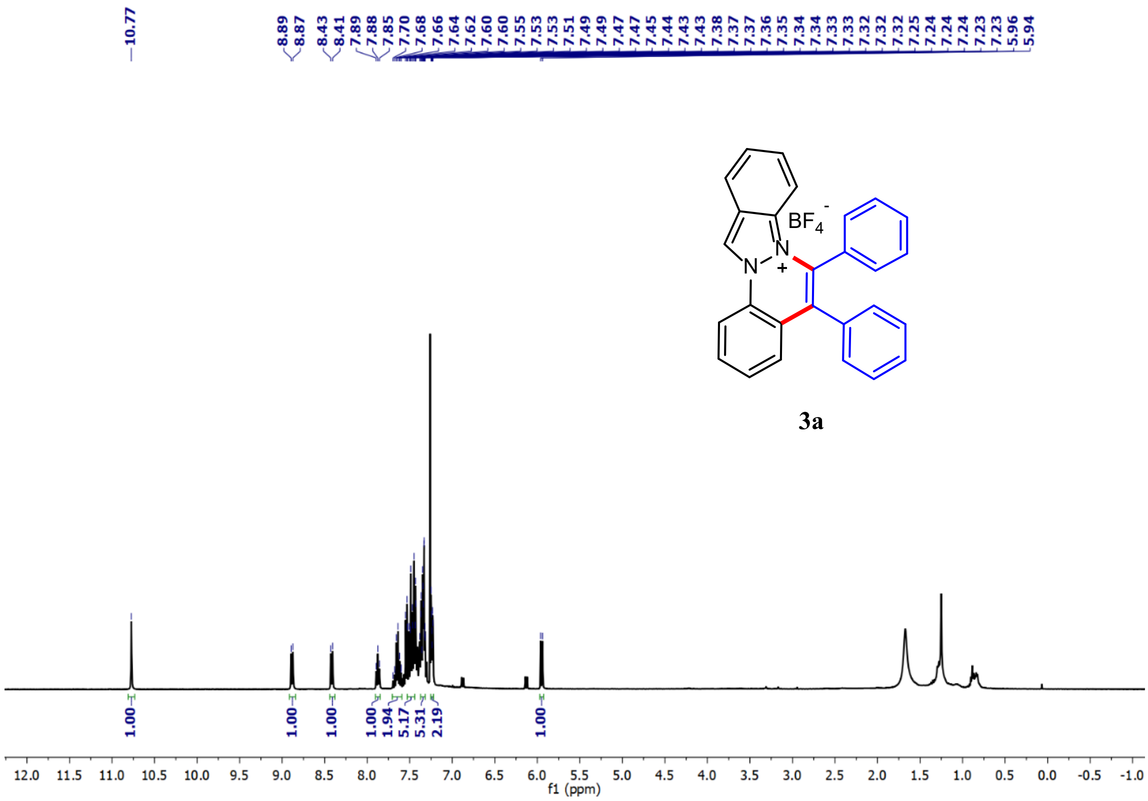


Figure S20: ^{1}H NMR spectrum of compound **3a** in $CDCl_3$

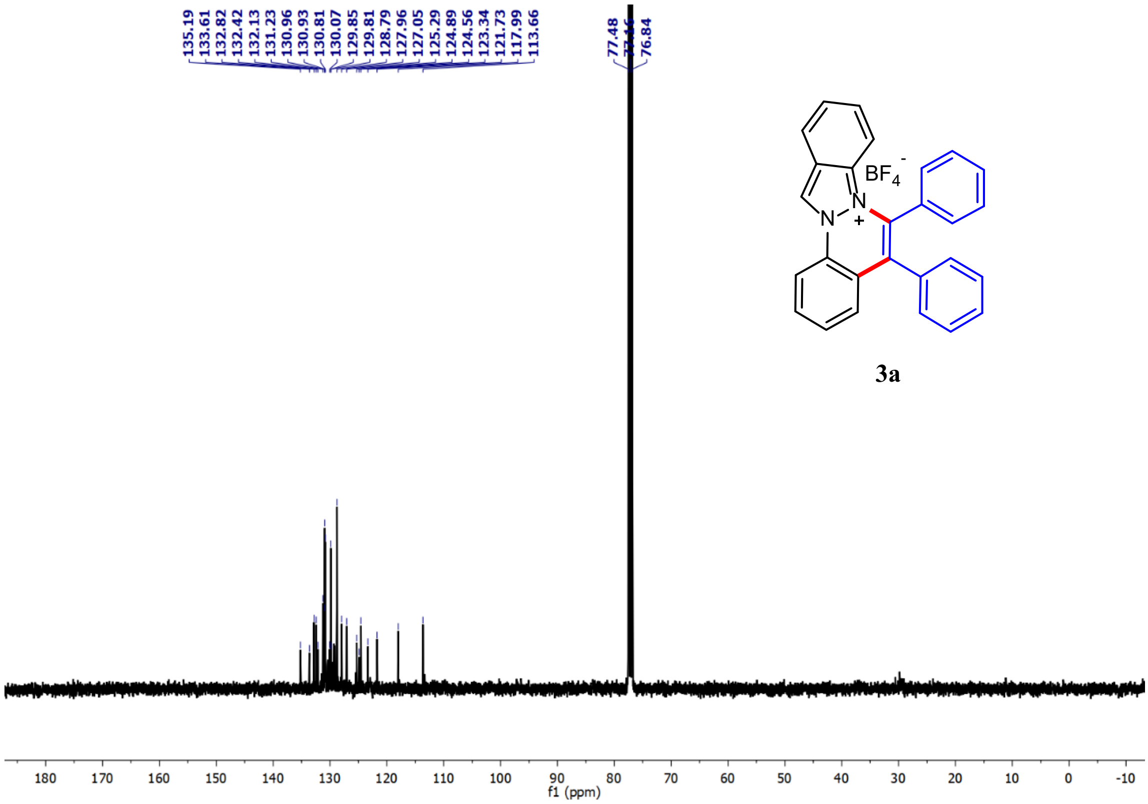


Figure S21: ^{13}C NMR spectrum of compound **3a** in $CDCl_3$

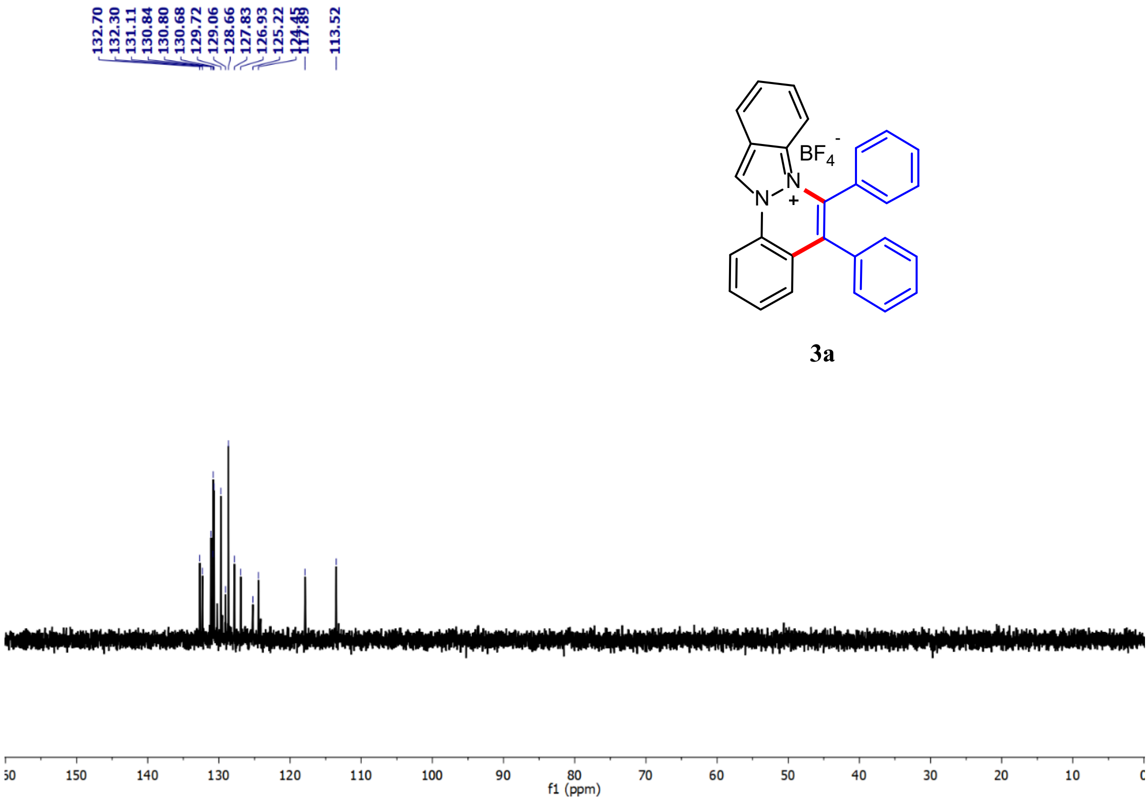


Figure S22:DEPT-135 NMR spectrum of compound **3a** in $CDCl_3$

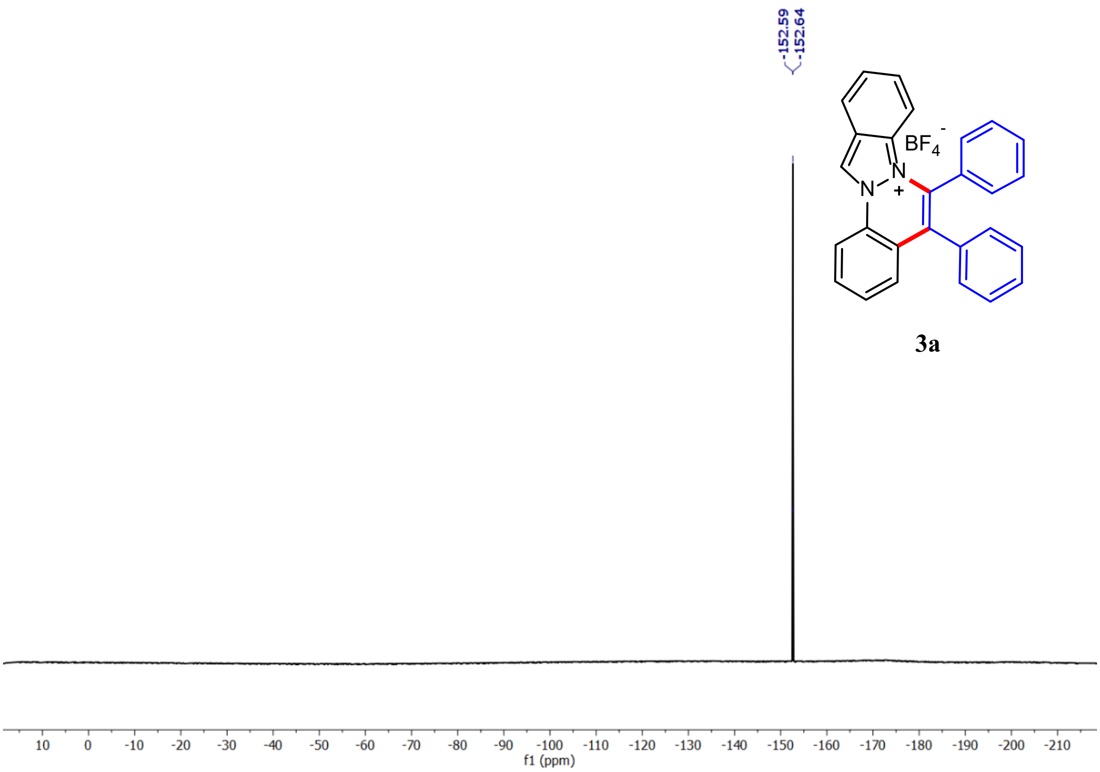


Figure S23: ^{19}F spectrum of compound **3a**

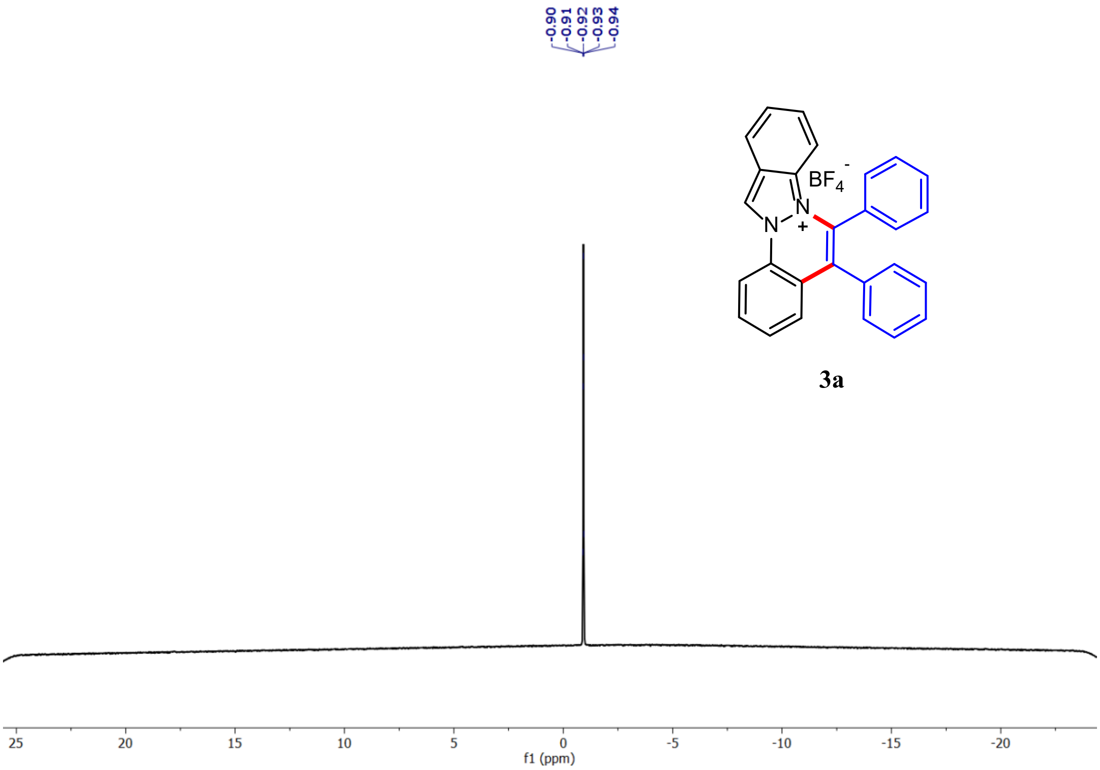


Figure S24: ^{11}B spectrum of compound **3a**

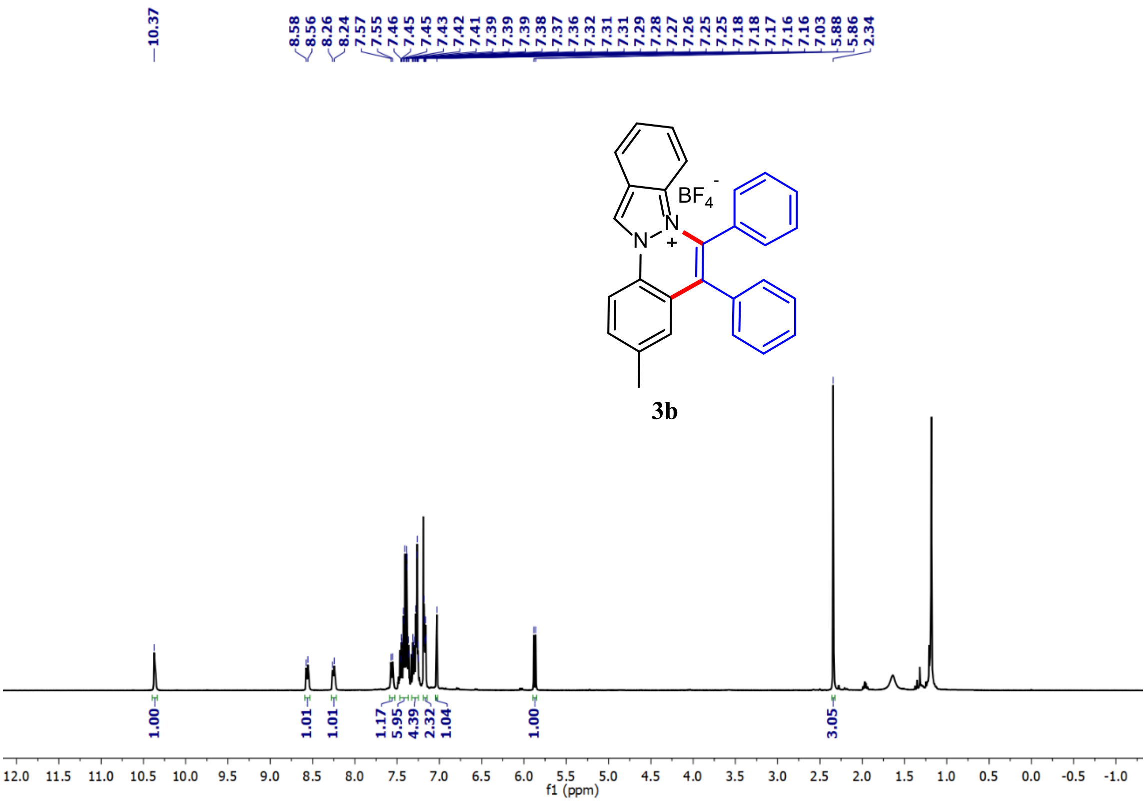


Figure S25: ^{1}H NMR spectrum of compound **3b** in $CDCl_3$

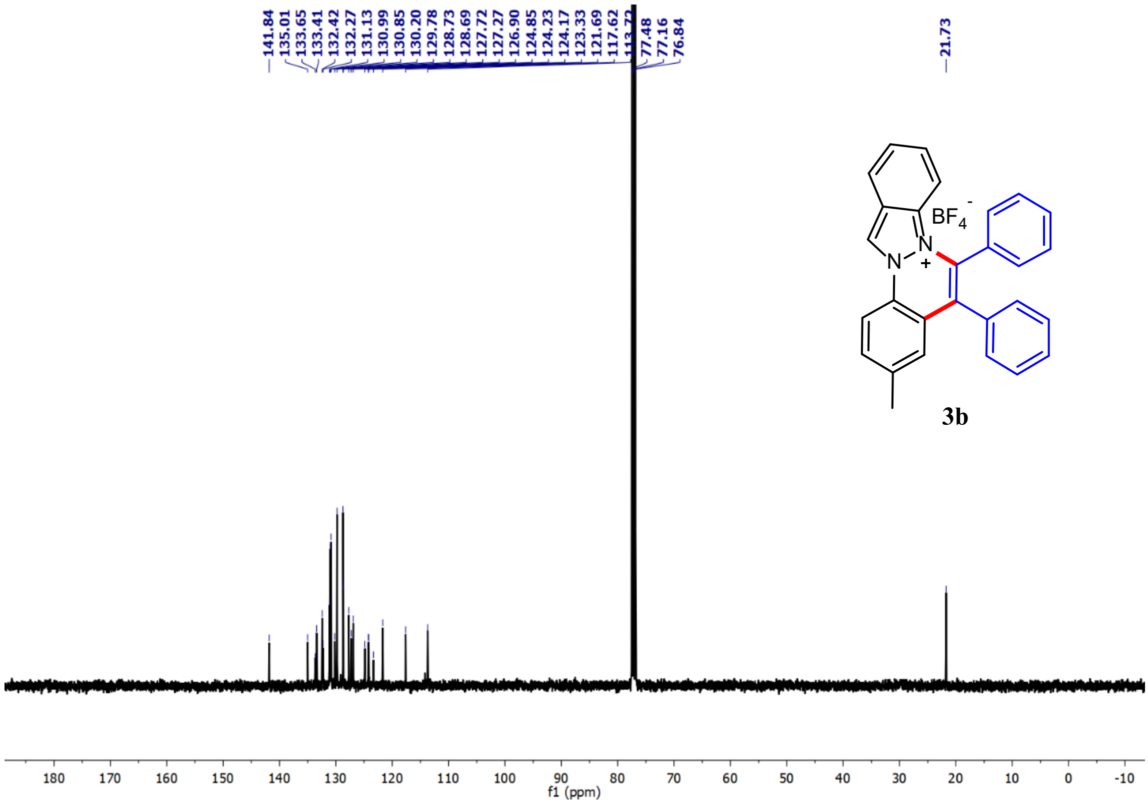


Figure S26: ^{13}C NMR spectrum of compound **3b** in $CDCl_3$

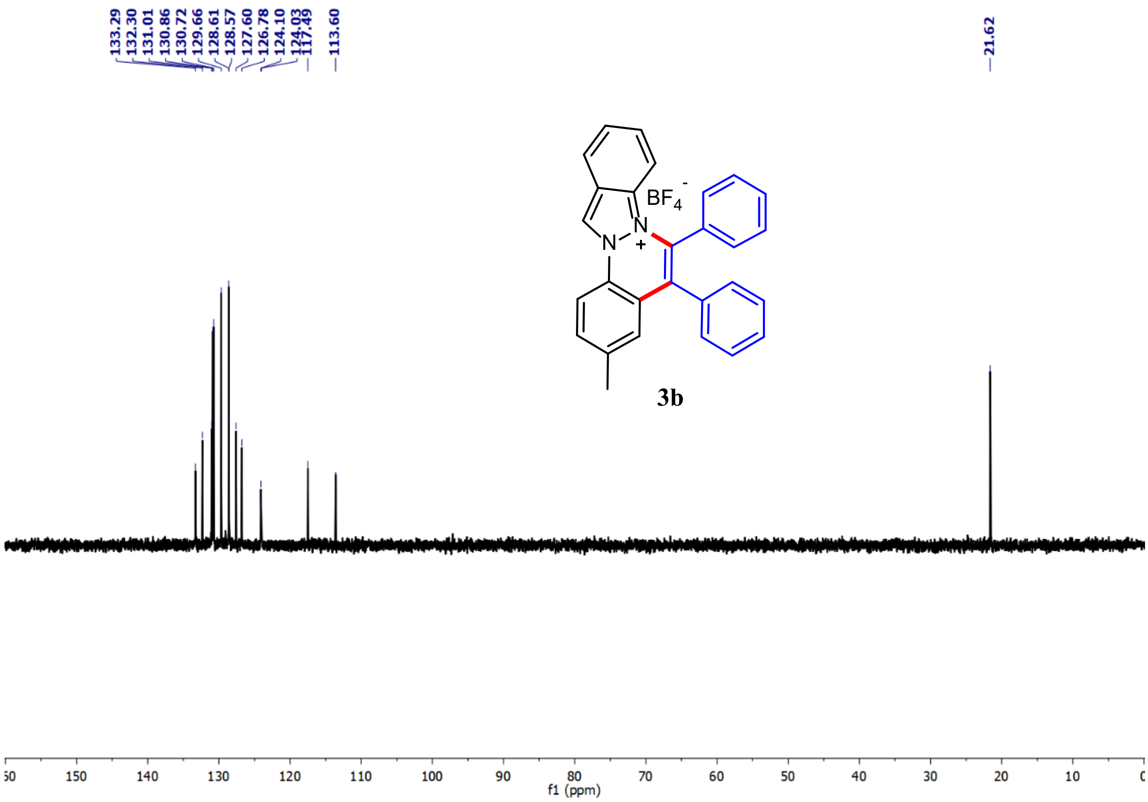


Figure S27: DEPT-135 NMR spectrum of compound 3**b** in $CDCl_3$

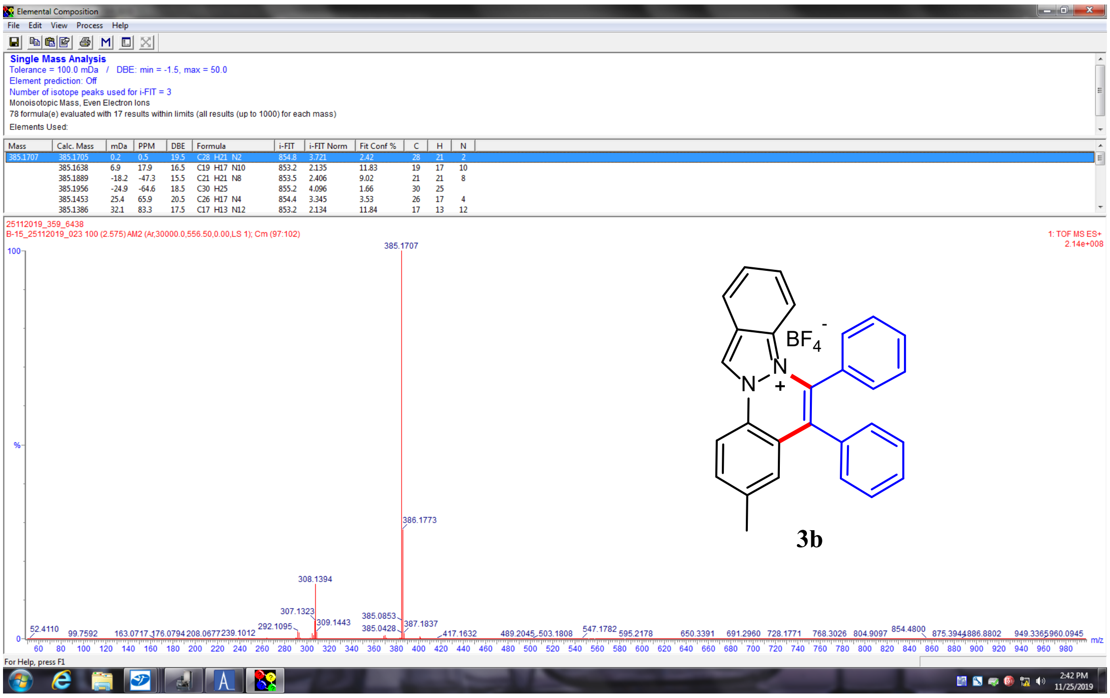


Figure S28: HRMS spectrum of compound **3b**

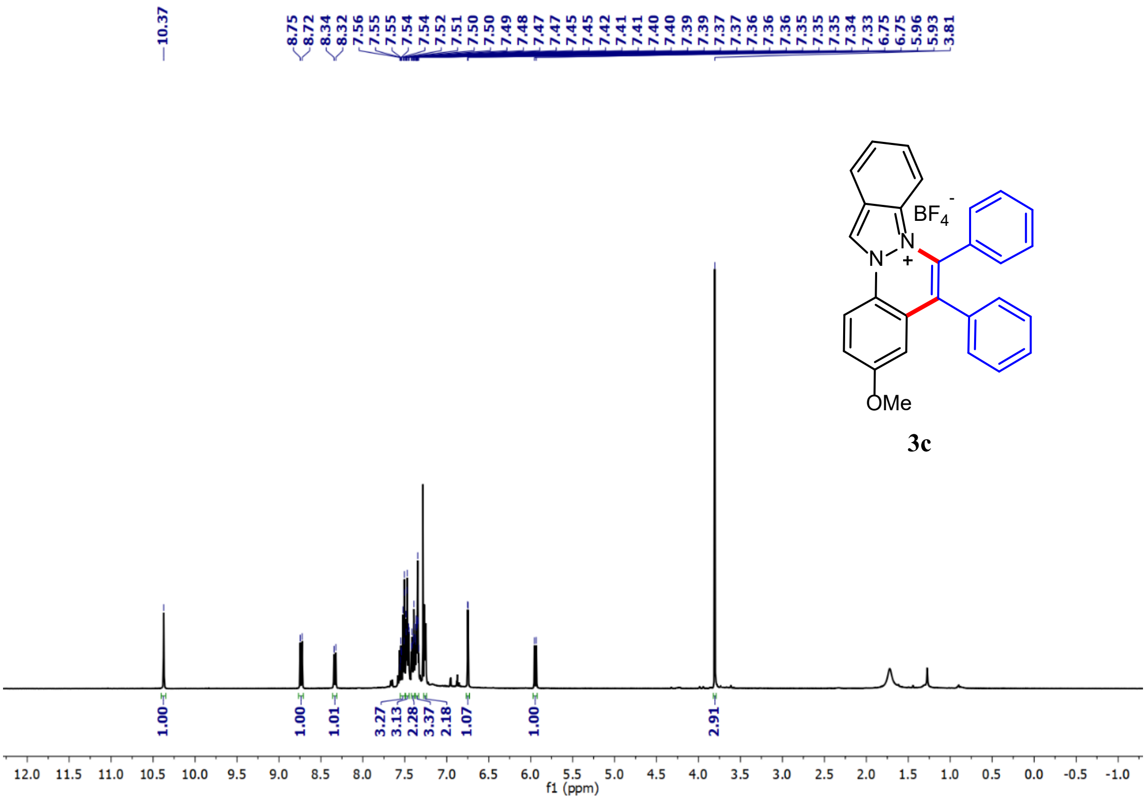


Figure S29: ^{1}H NMR spectrum of compound **3c** in $CDCl_3$

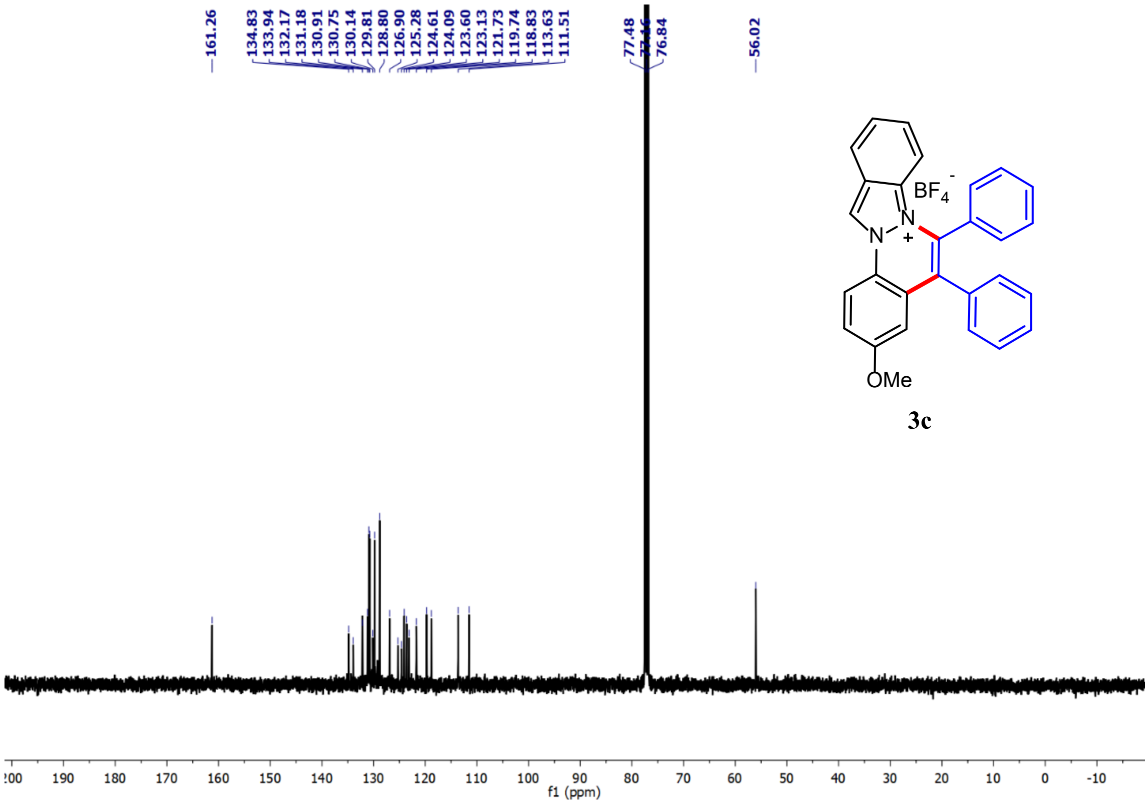


Figure S30: ^{13}C NMR spectrum of compound **3c** in $CDCl_3$

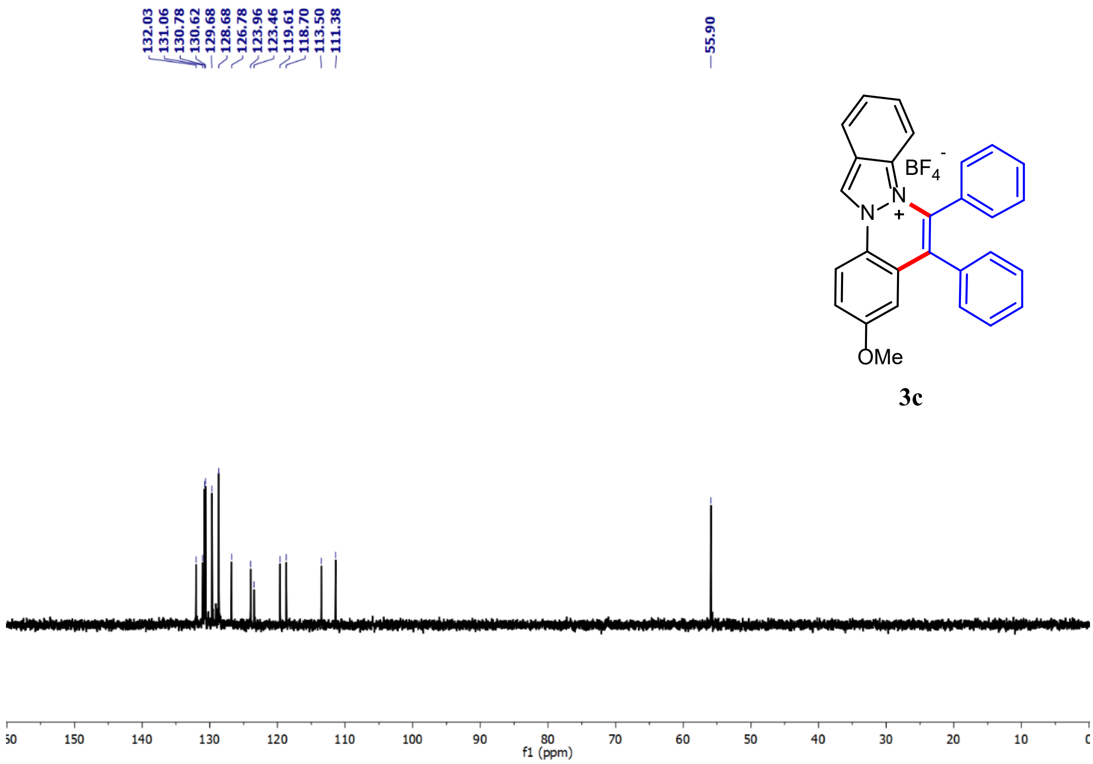


Figure S31: DEPT-135 NMR spectrum of compound **3c** in $CDCl_3$

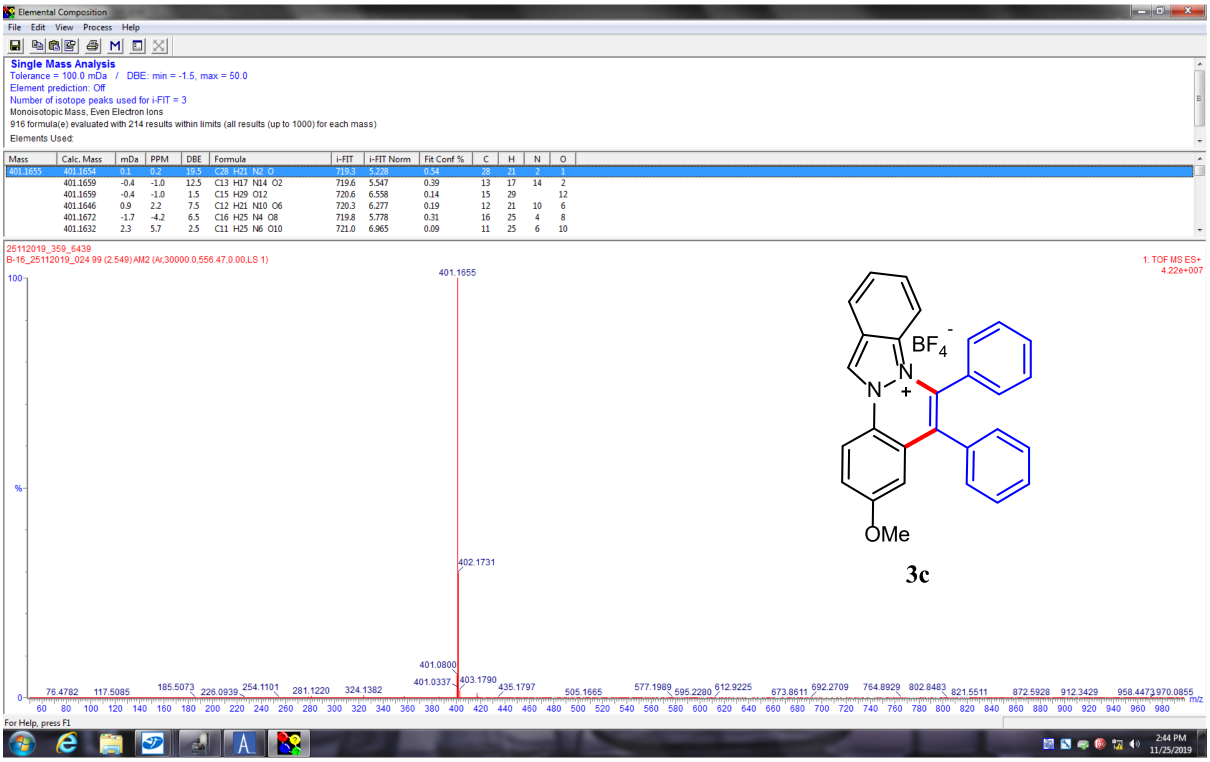


Figure S32: HRMS spectrum of compound **3c**

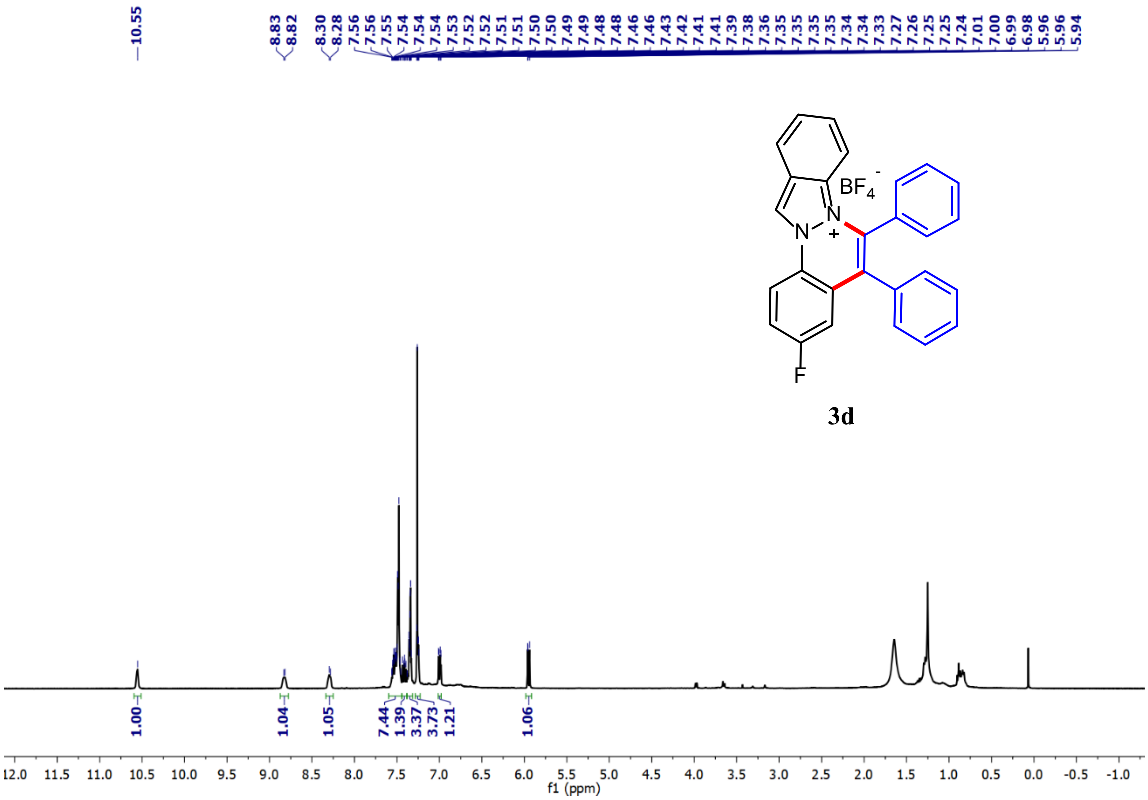


Figure S33: ^{1}H NMR spectrum of compound **3d** in $CDCl_3$

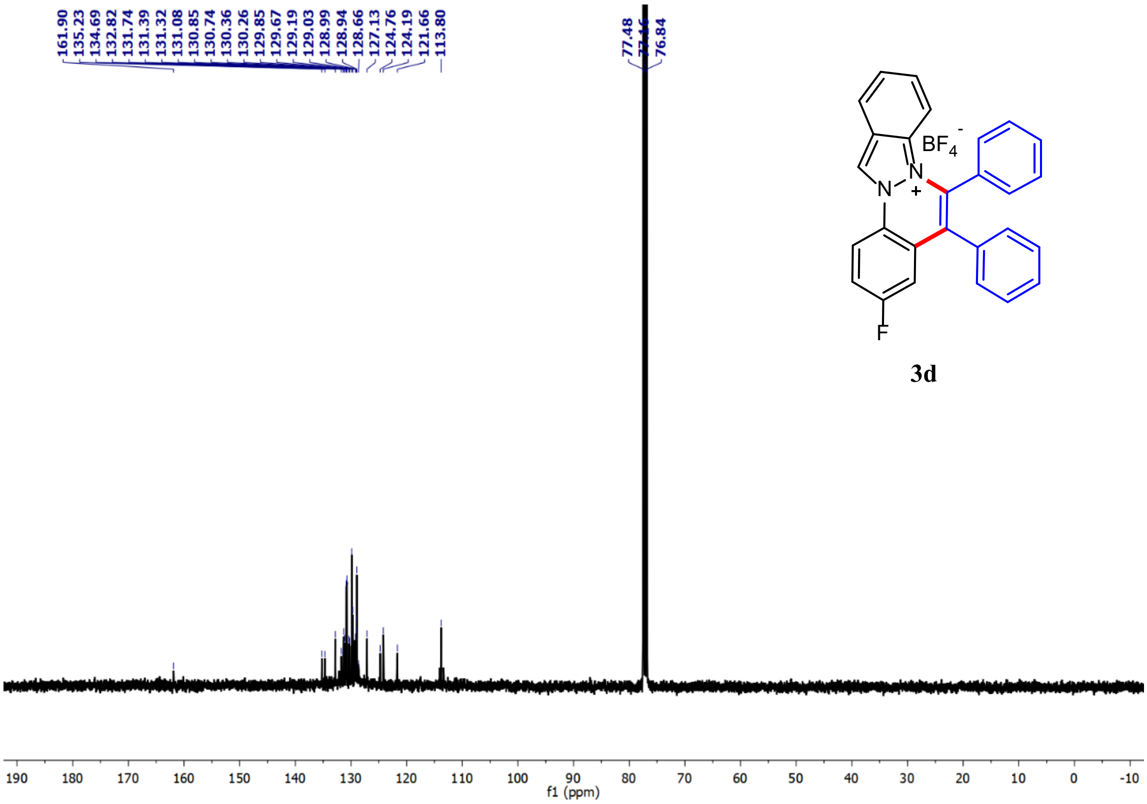
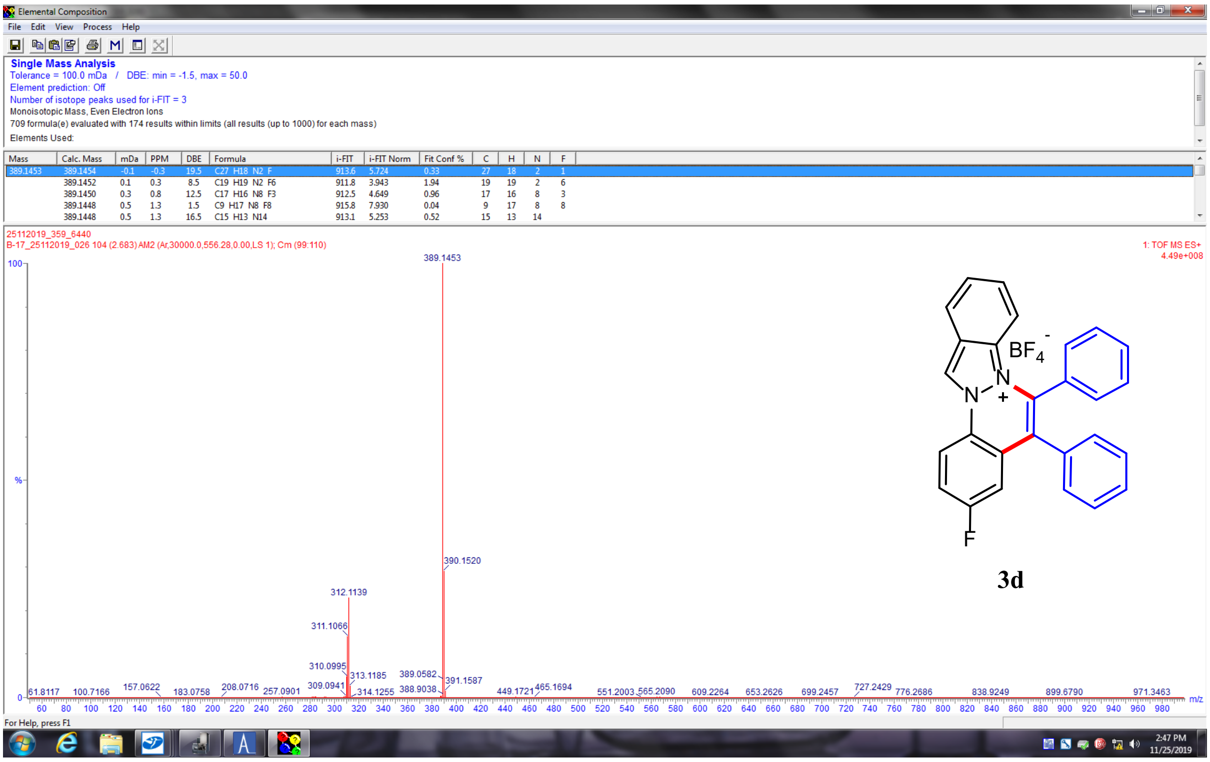


Figure S34: ^{13}C NMR spectrum of compound **3d** in $CDCl_3$



Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	F
389.1453	389.1454	-0.1	-0.3	19.5	C27 H18 N2 F	913.6	5.724	0.33	27	18	2	1
	389.1452	0.1	0.3	8.5	C19 H19 N2 F6	911.8	3.943	1.94	19	19	2	6
	389.1450	0.3	0.8	12.5	C17 H16 N8 F3	912.5	4.649	0.96	17	16	8	3
	389.1448	0.5	1.3	1.5	C9 H17 N8 F8	915.8	7.930	0.04	9	17	8	8
	389.1448	0.5	1.3	16.5	C15 H13 N14	913.1	5.253	0.52	15	13	14	

Figure S35: HRMS spectrum of compound **3d**

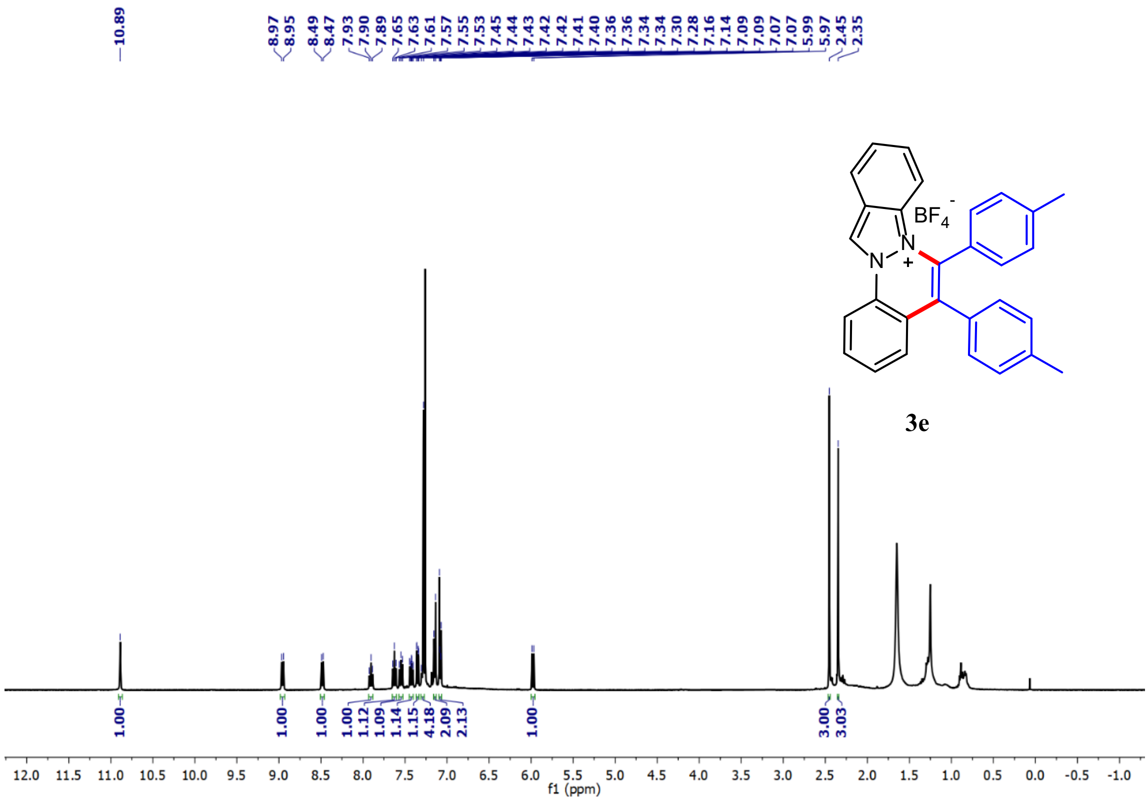


Figure S36: ^{1}H NMR spectrum of compound **3e** in $CDCl_3$

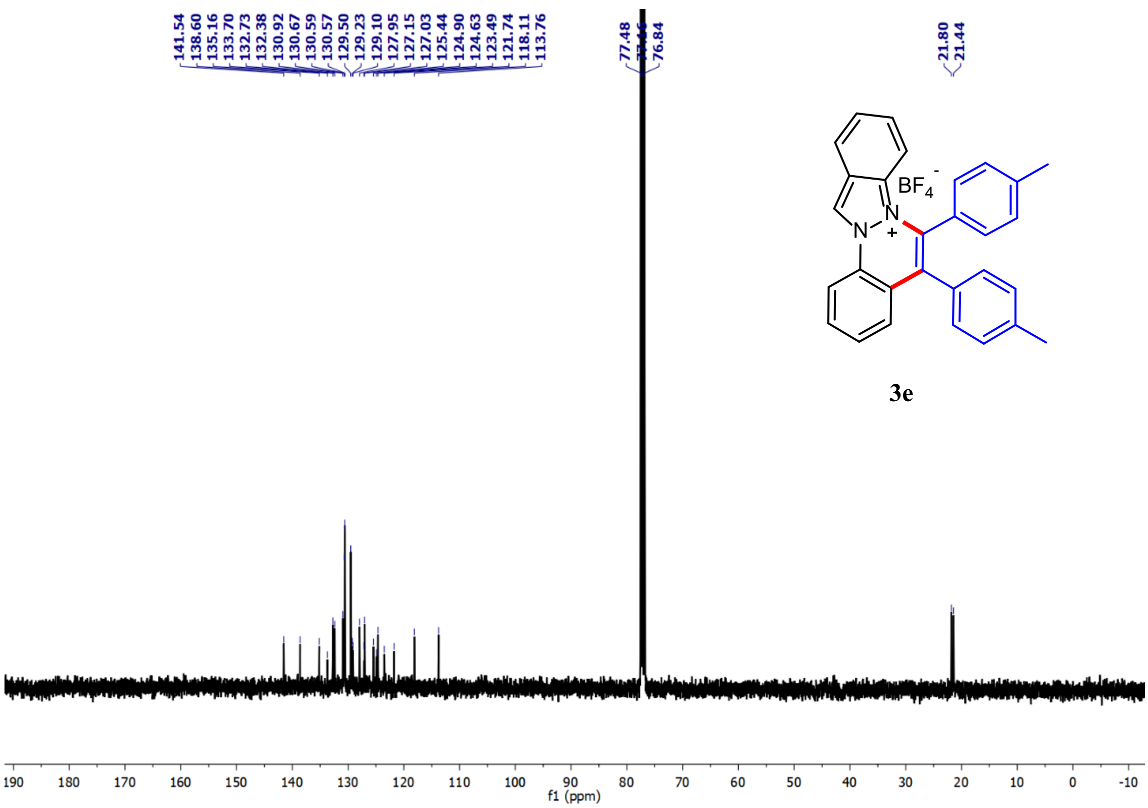


Figure S37: ^{13}C NMR spectrum of compound **3e** in $CDCl_3$

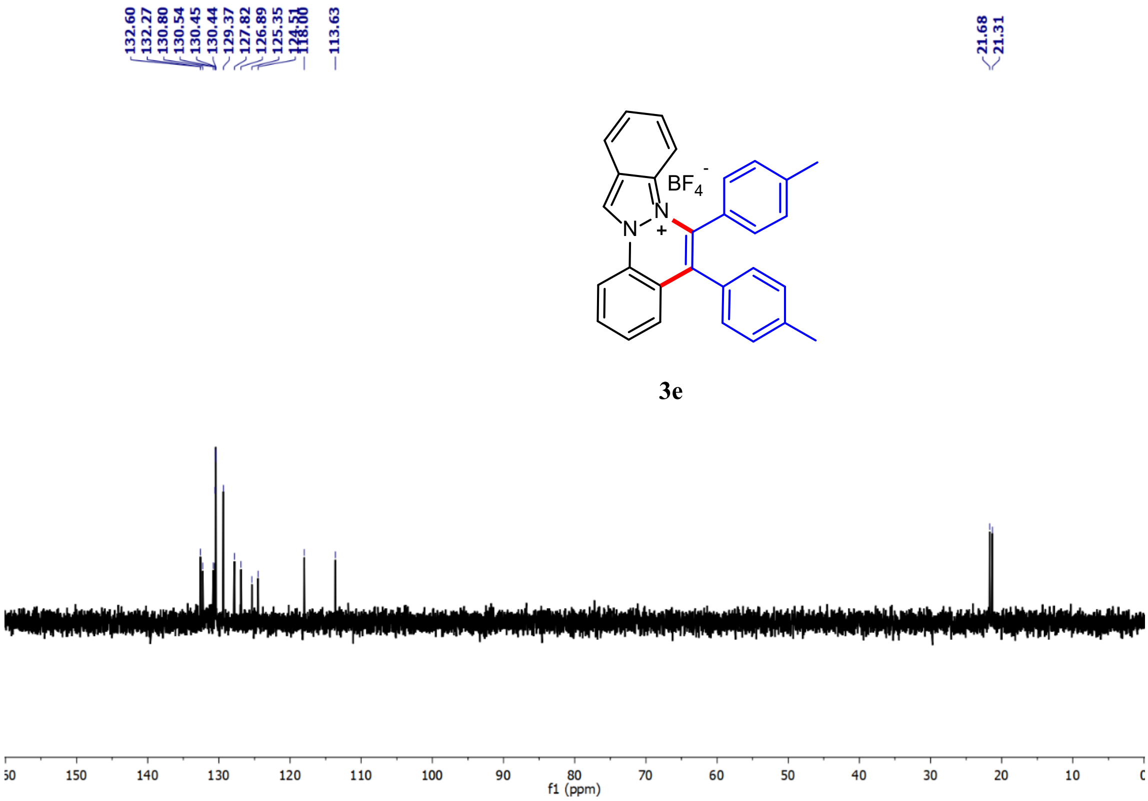


Figure S38: DEPT-135 NMR spectrum of compound **3e** in $CDCl_3$

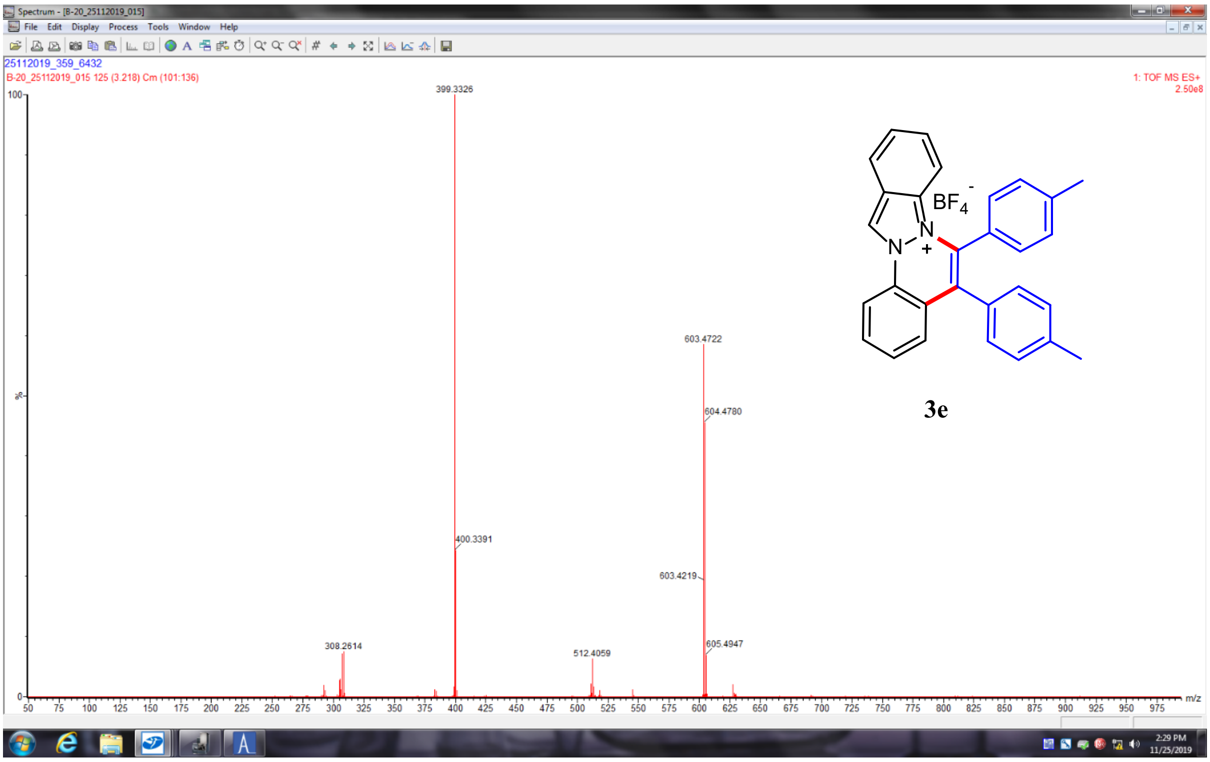


Figure S39: HRMS spectrum of compound **3e**

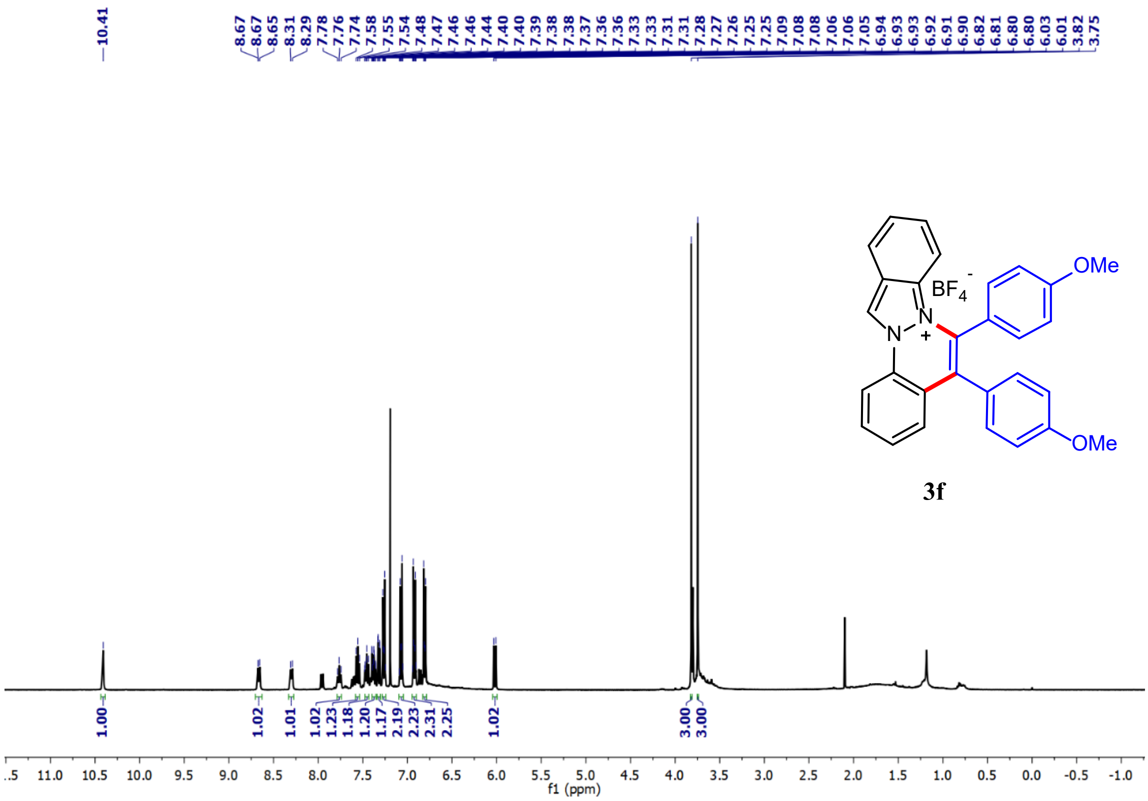


Figure S40: [1]H NMR spectrum of compound **3f** in $CDCl_3$

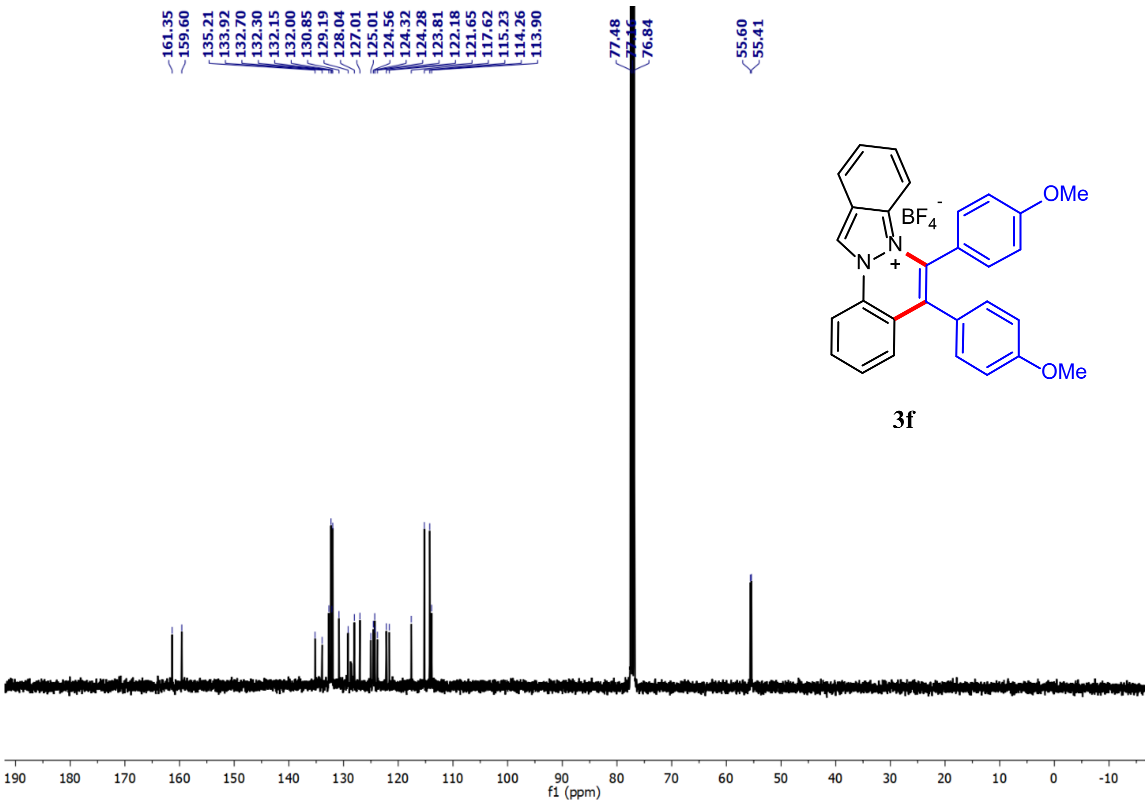


Figure S41: [13]C NMR spectrum of compound **3f** in $CDCl_3$

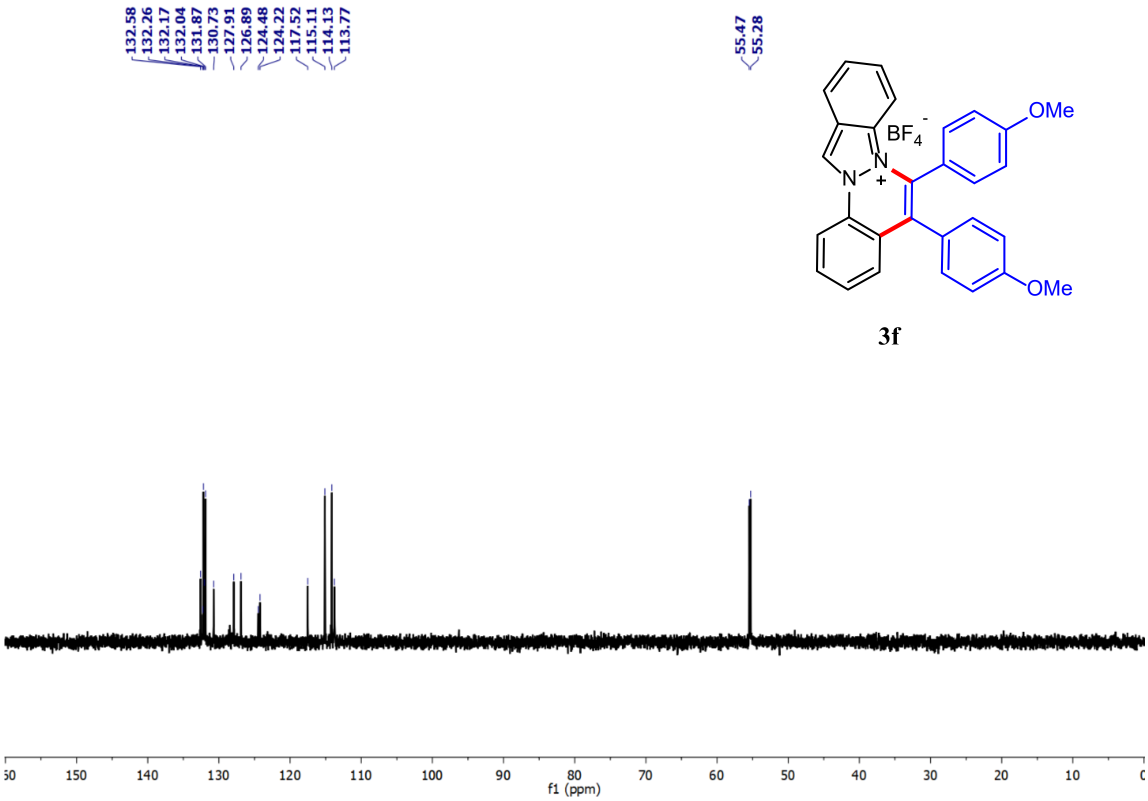


Figure S42: DEPT-135 NMR spectrum of compound **3f** in $CDCl_3$

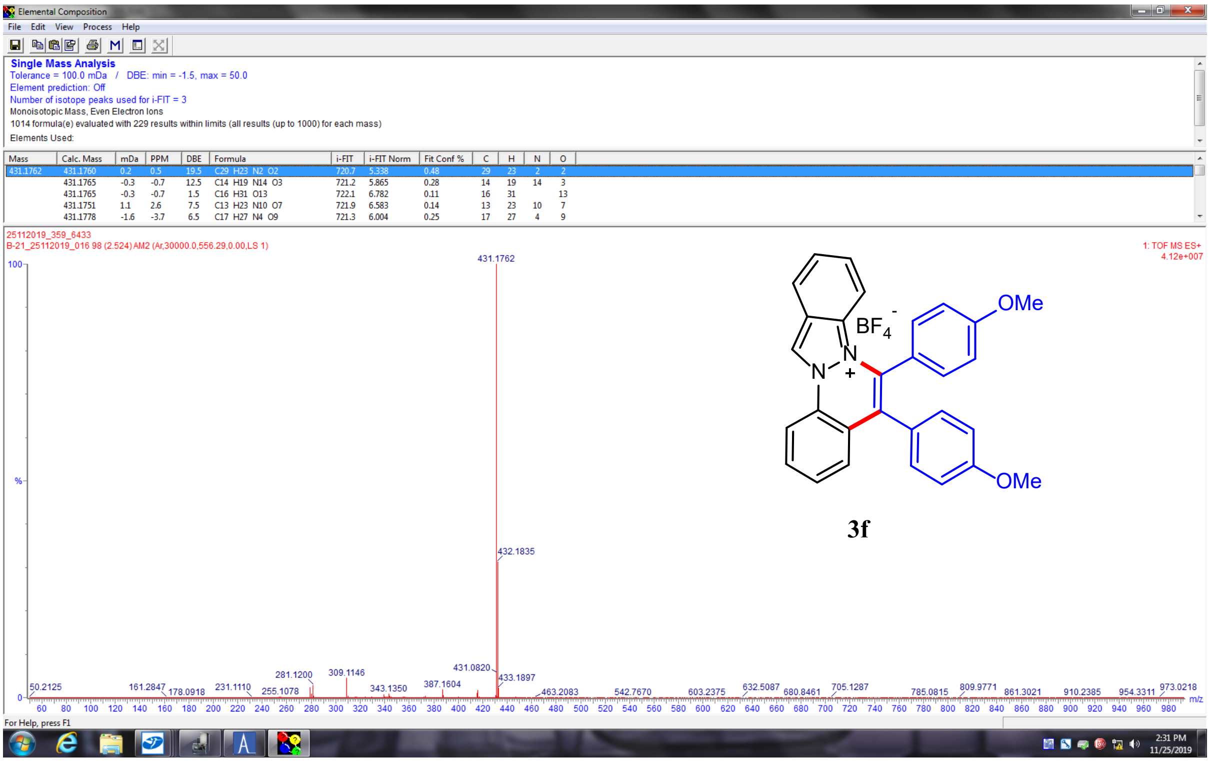


Figure S43: HRMS spectrum of compound **3f**

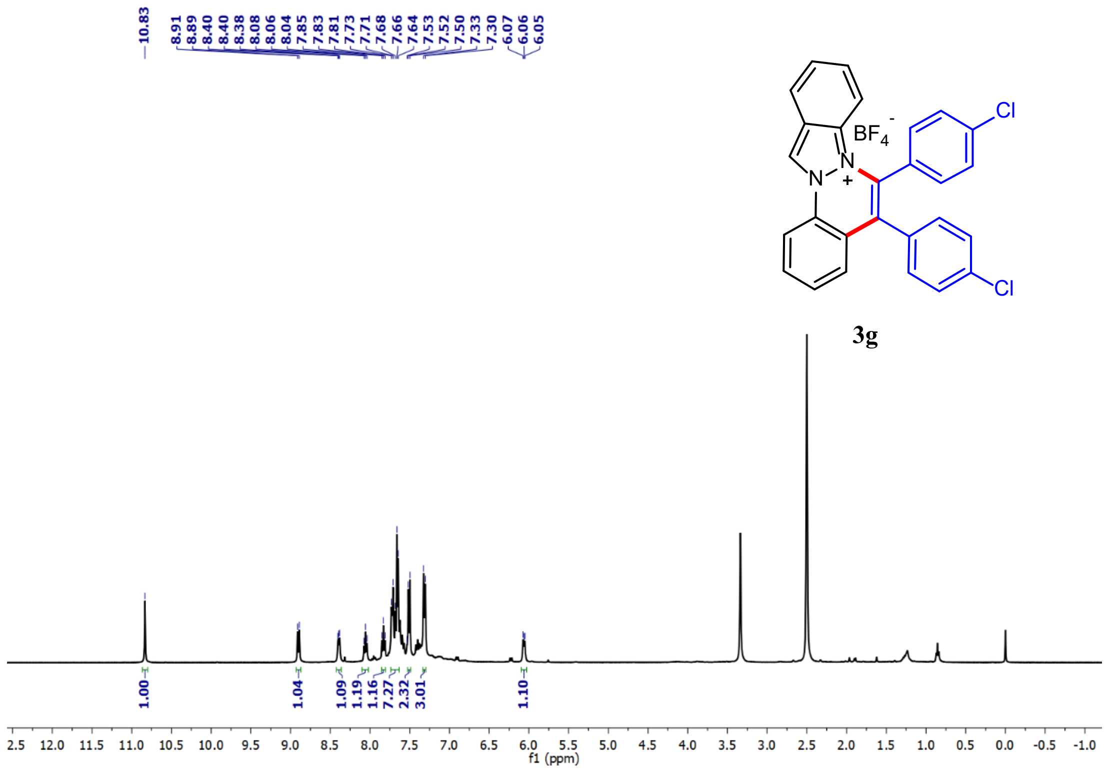


Figure S44: ^{1}H NMR spectrum of compound **3g** in DMSO-d$_6$

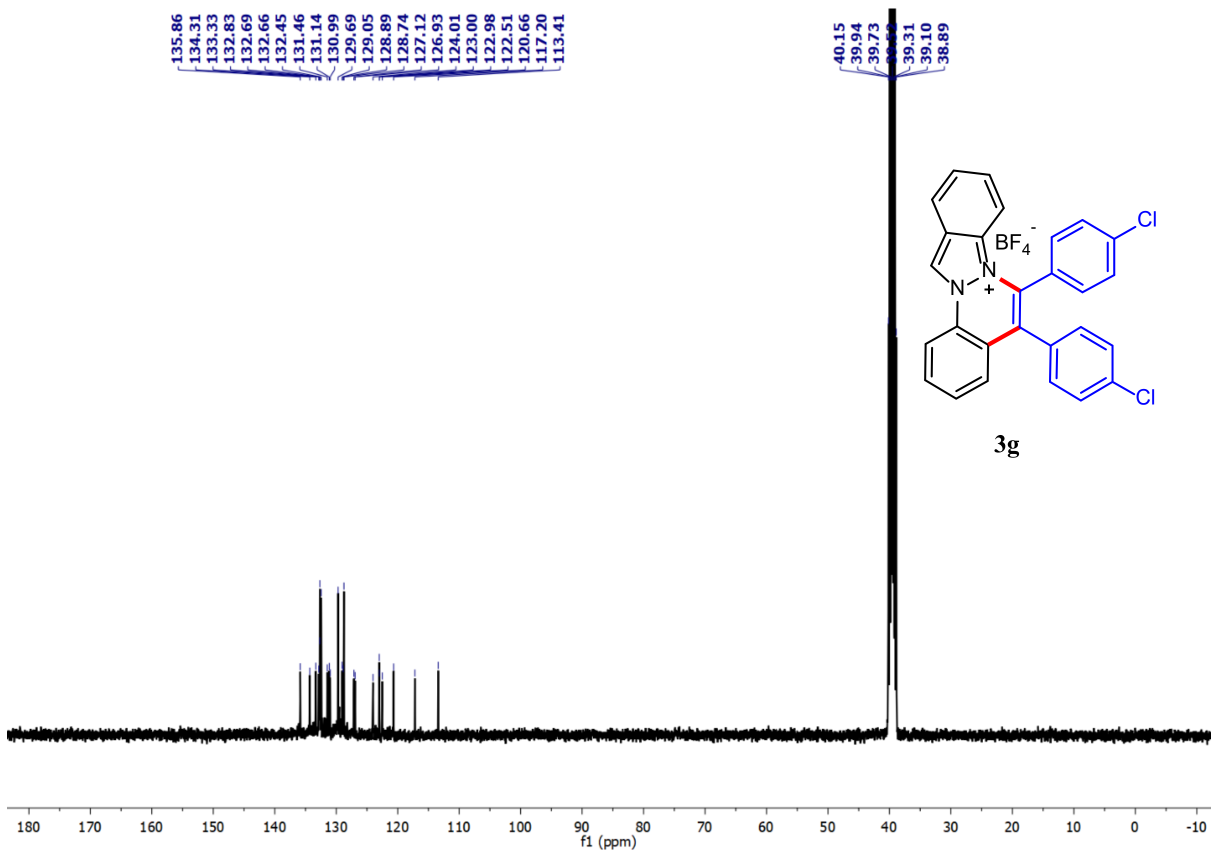


Figure S45: ^{13}C NMR spectrum of compound **3g** in DMSO-d$_6$

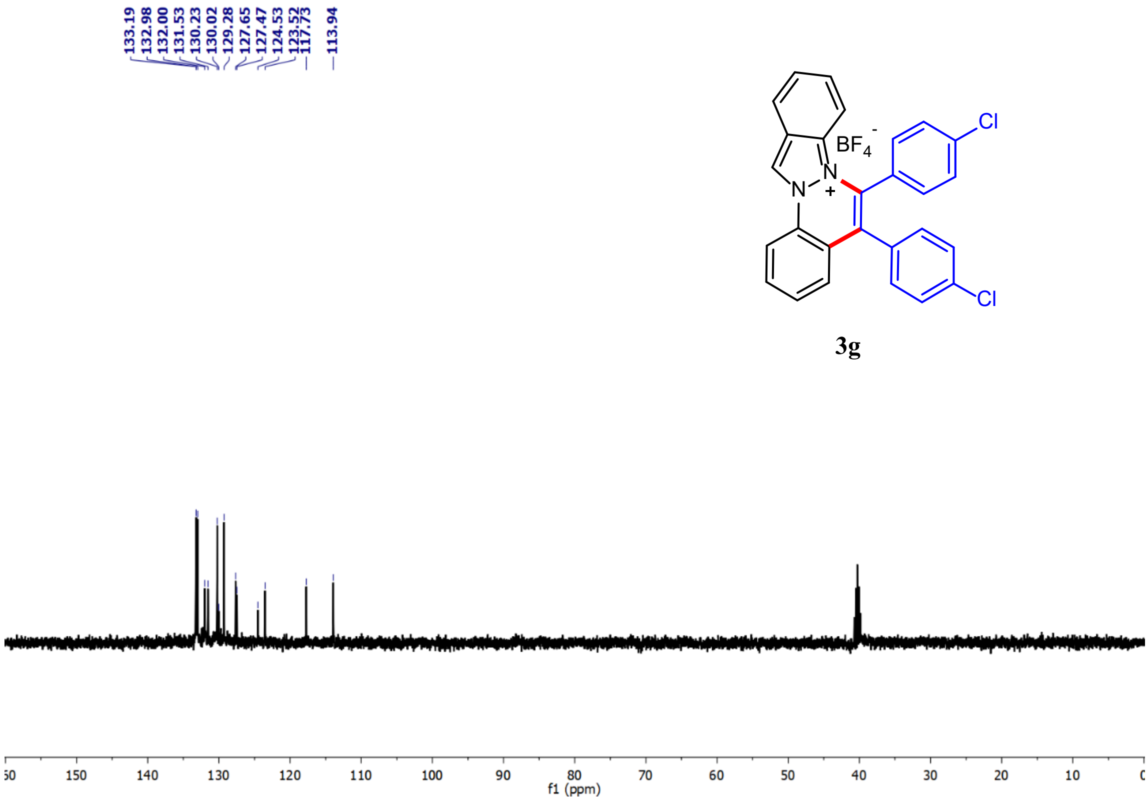


Figure S46: DEPT-135 NMR spectrum of compound **3g** in DMSO-d_6

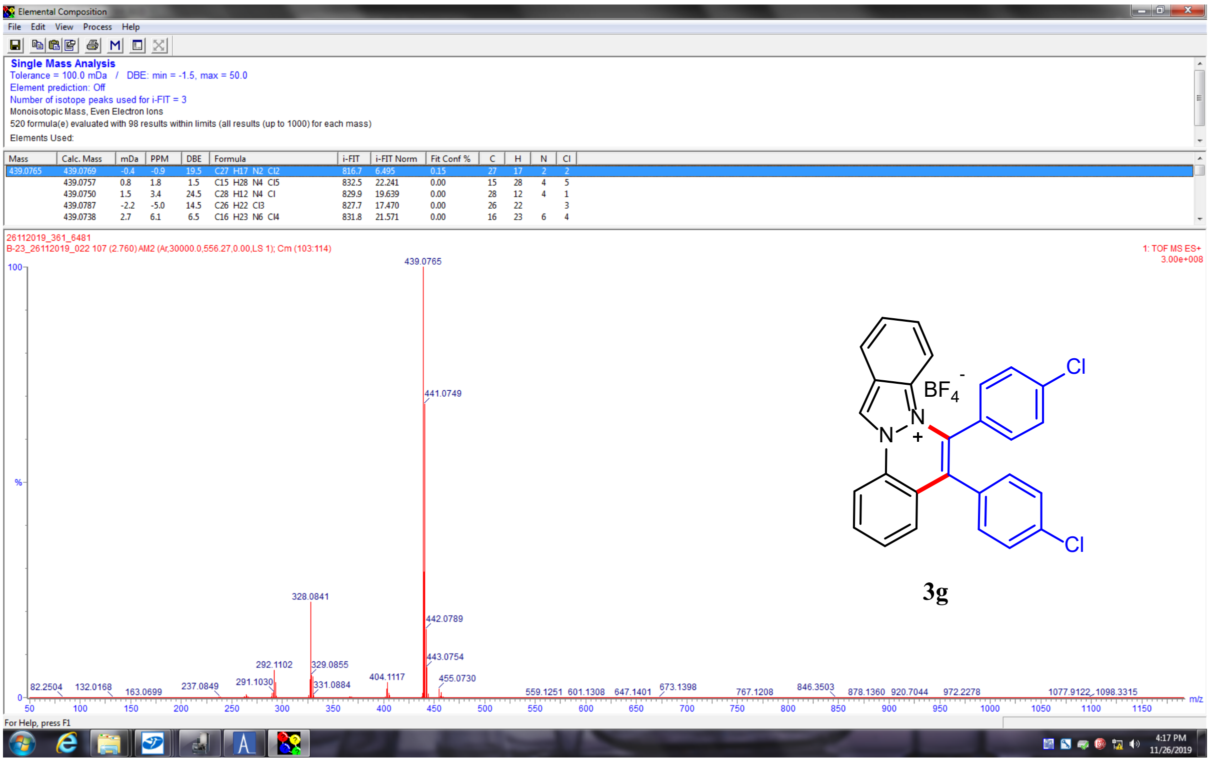


Figure S47: HRMS spectrum of compound **3g**

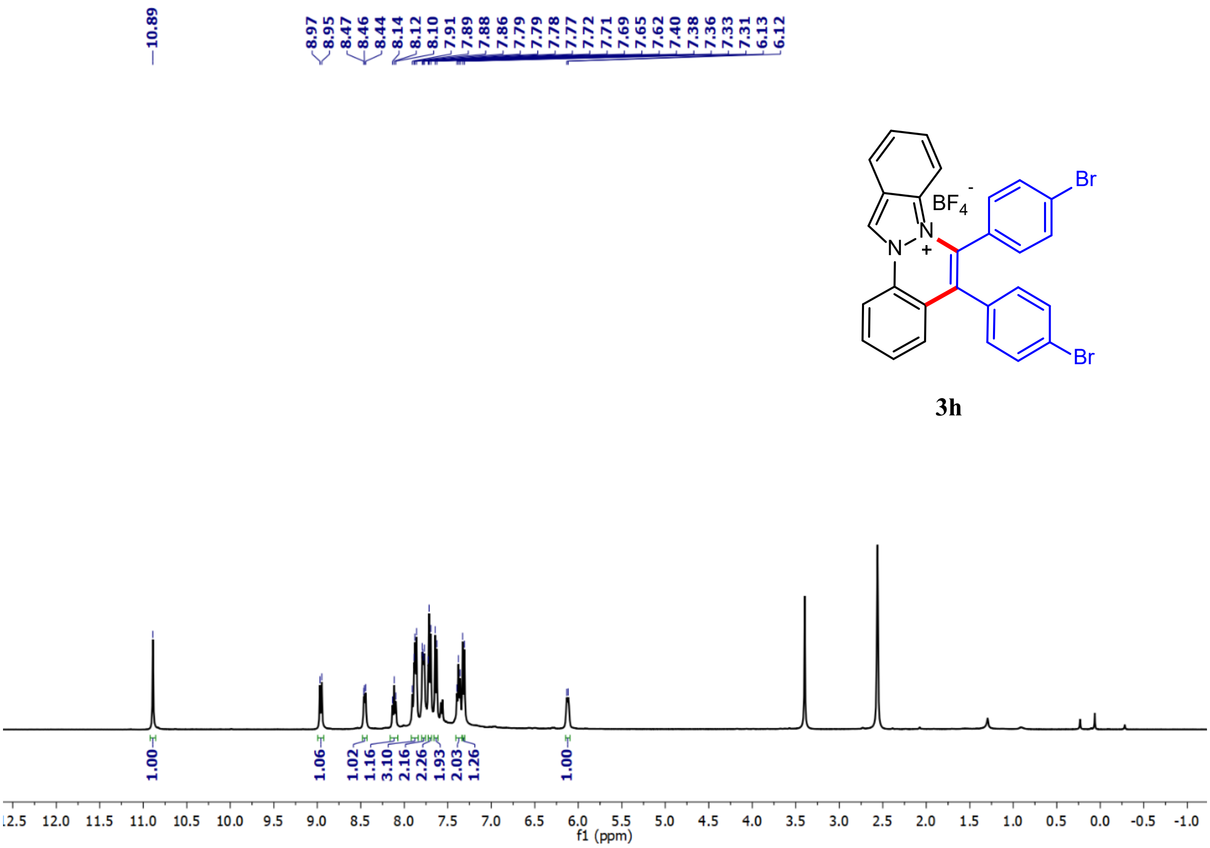


Figure S48: ^{1}H NMR spectrum of compound **3h** in DMSO-d$_6$

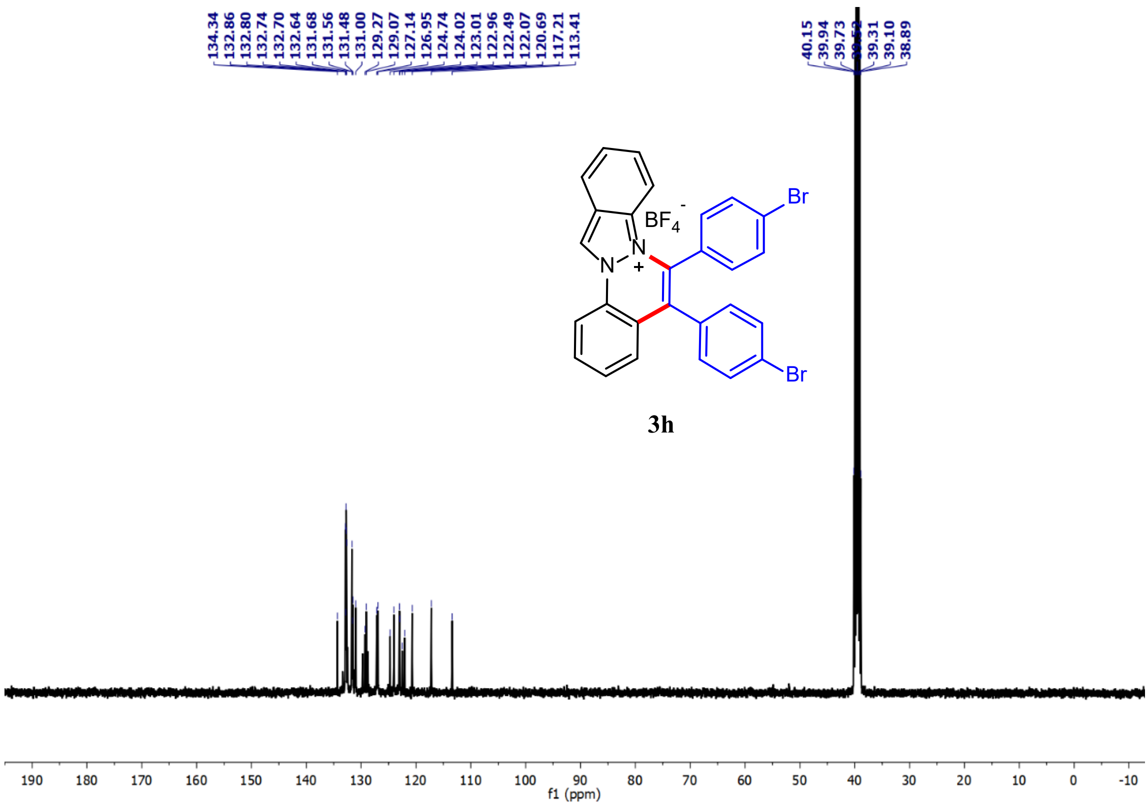


Figure S49: ^{13}C NMR spectrum of compound **3h** in DMSO-d$_6$

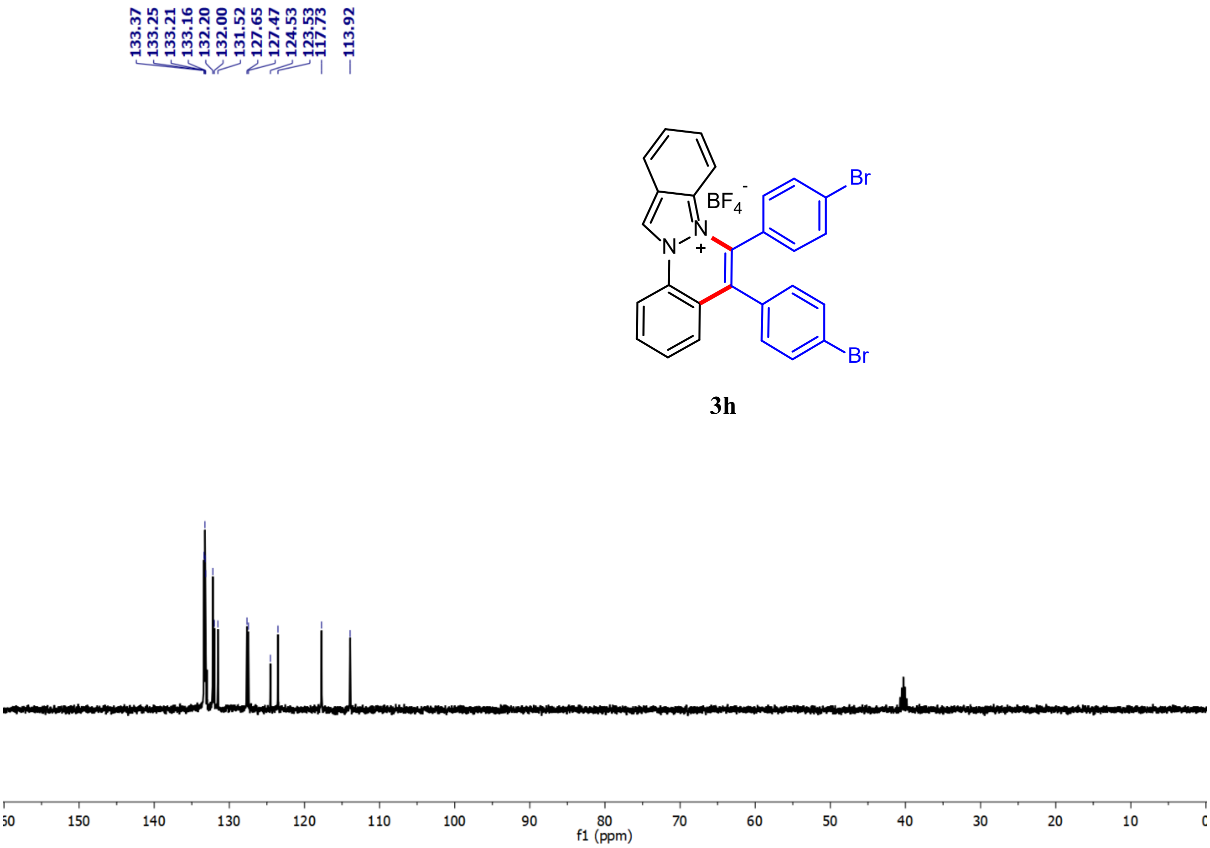


Figure S50: DEPT-135 NMR spectrum of compound **3h** in DMSO-d_6

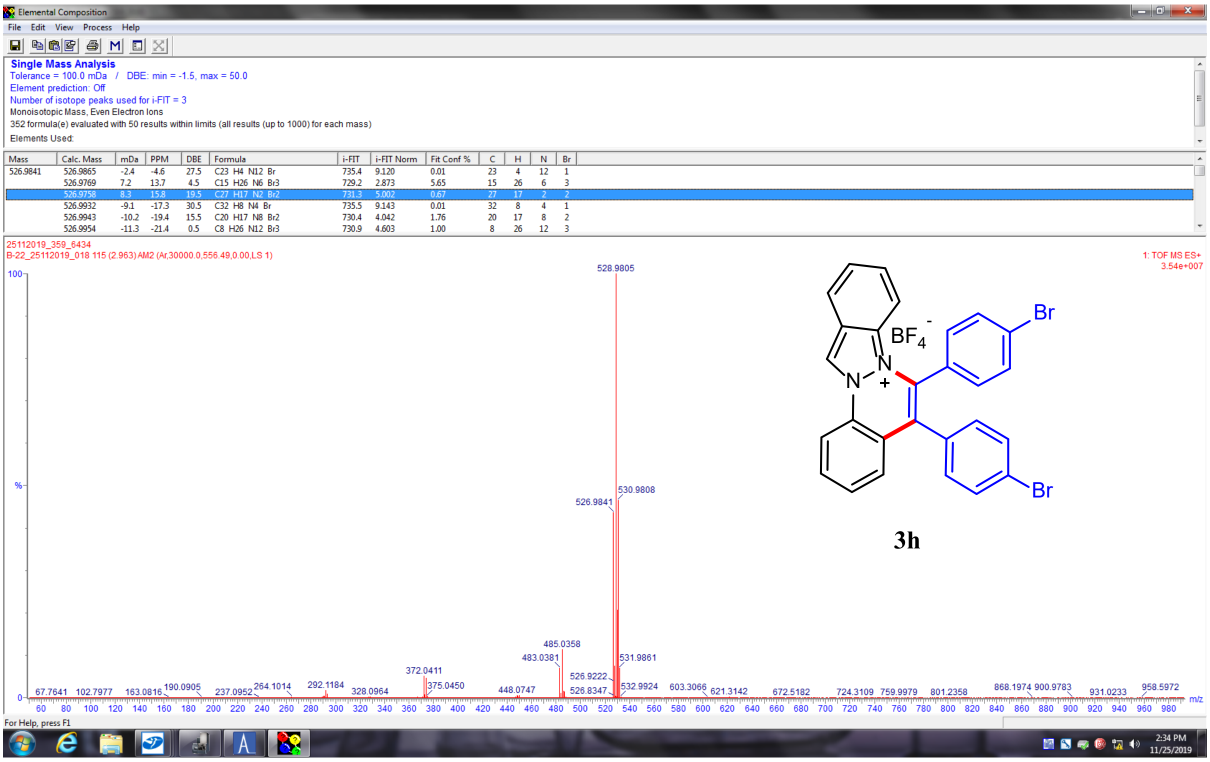


Figure S51: HRMS spectrum of compound **3h**

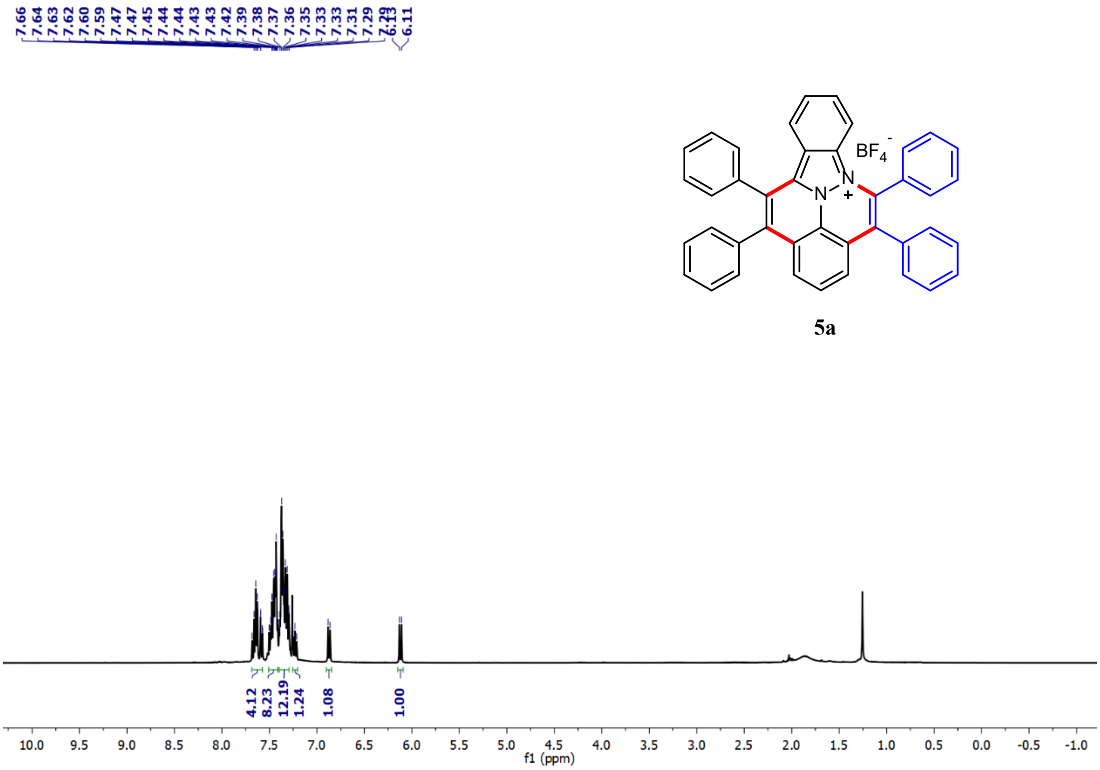


Figure S52: ^{1}H NMR spectrum of compound **5a** in $CDCl_3$

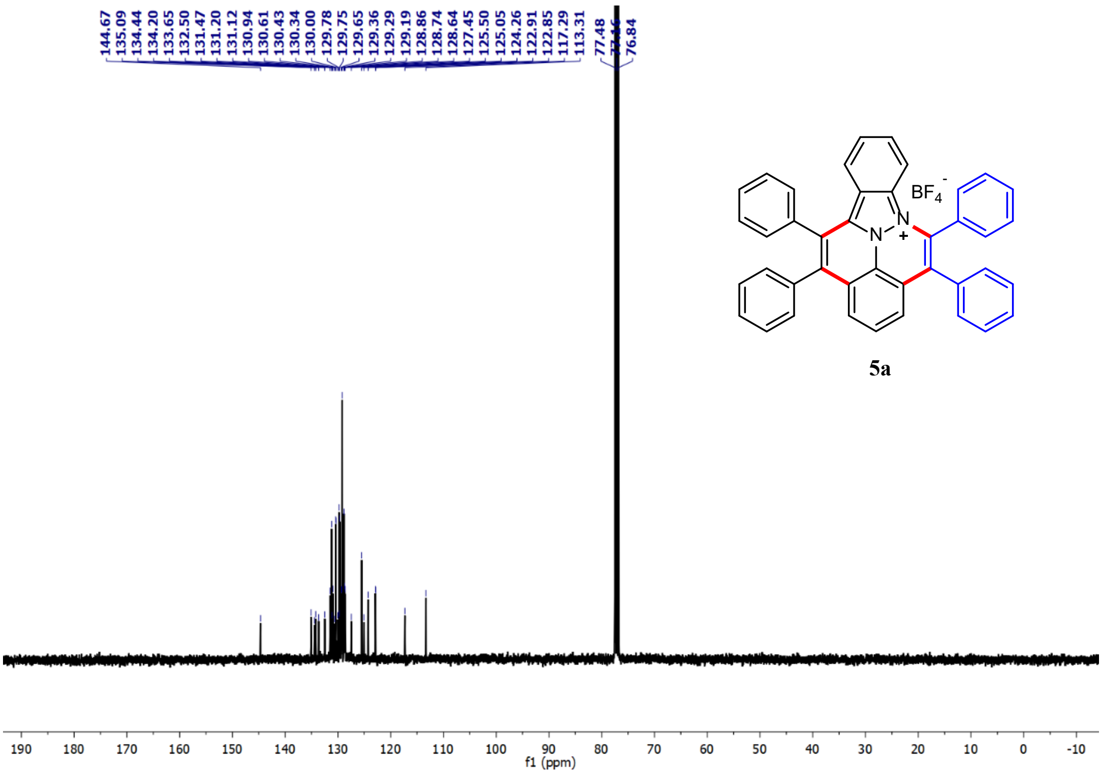


Figure S53: ^{13}C NMR spectrum of compound **5a** in $CDCl_3$

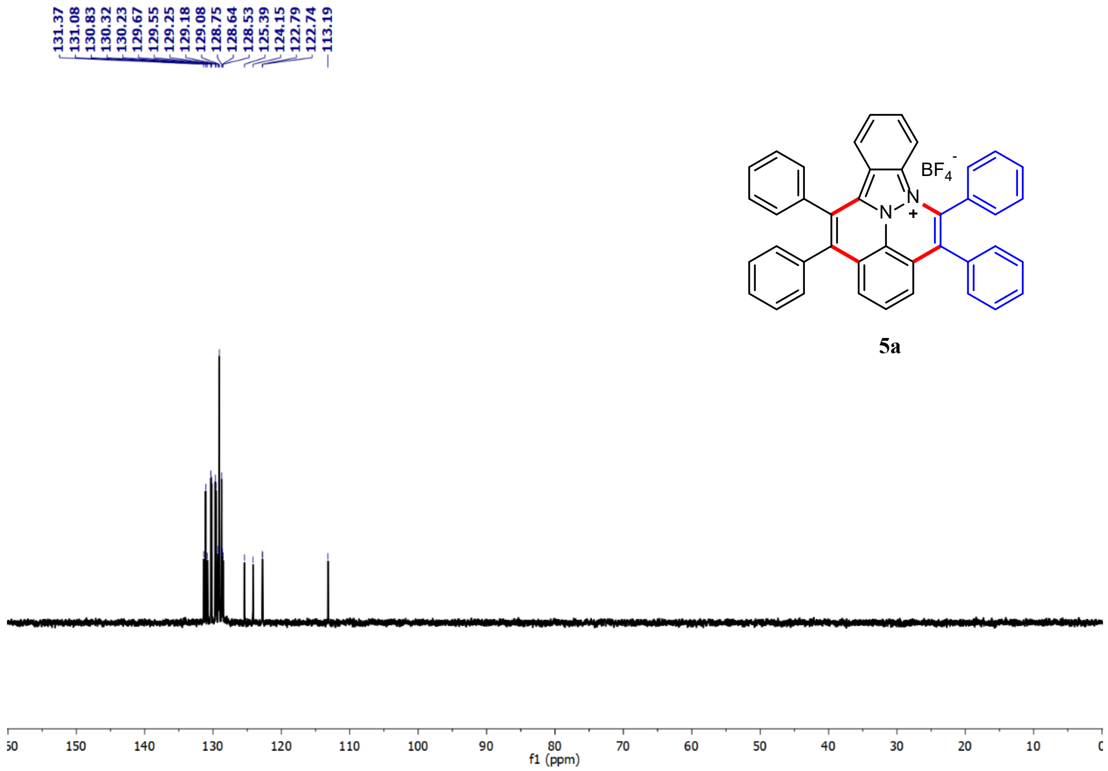
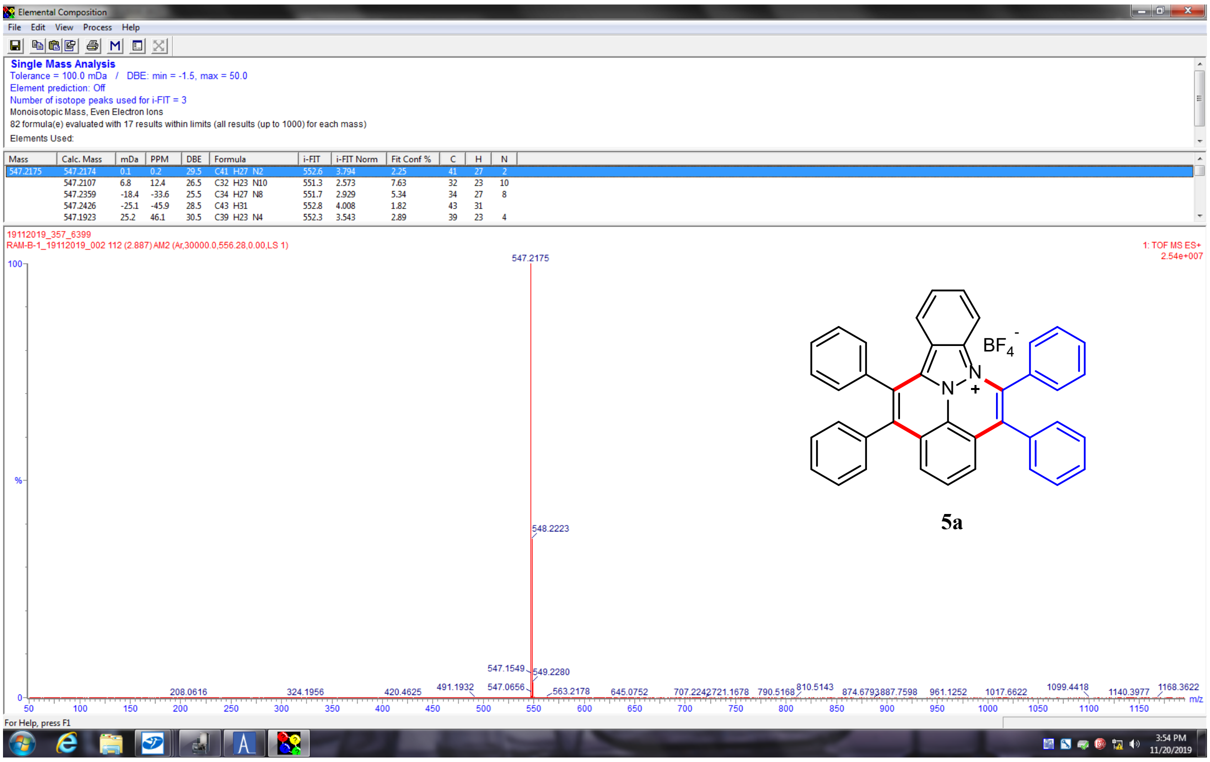


Figure S54: DEPT-135 NMR spectrum of compound **5a** in $CDCl_3$



Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N
547.2175	547.2174	0.1	0.2	29.5	C41 H27 N2	552.6	3.794	2.25	41	27	2
	547.2107	6.8	12.4	26.5	C32 H23 N10	551.3	2.573	7.63	32	23	10
	547.2359	-18.4	-33.6	25.5	C34 H27 N8	551.7	2.929	5.34	34	27	8
	547.2426	-25.1	-45.9	28.5	C43 H31	552.8	4.008	1.82	43	31	
	547.1923	25.2	46.1	30.5	C39 H23 N4	552.3	3.543	2.89	39	23	4

Figure S55: HRMS spectrum of compound **5a**

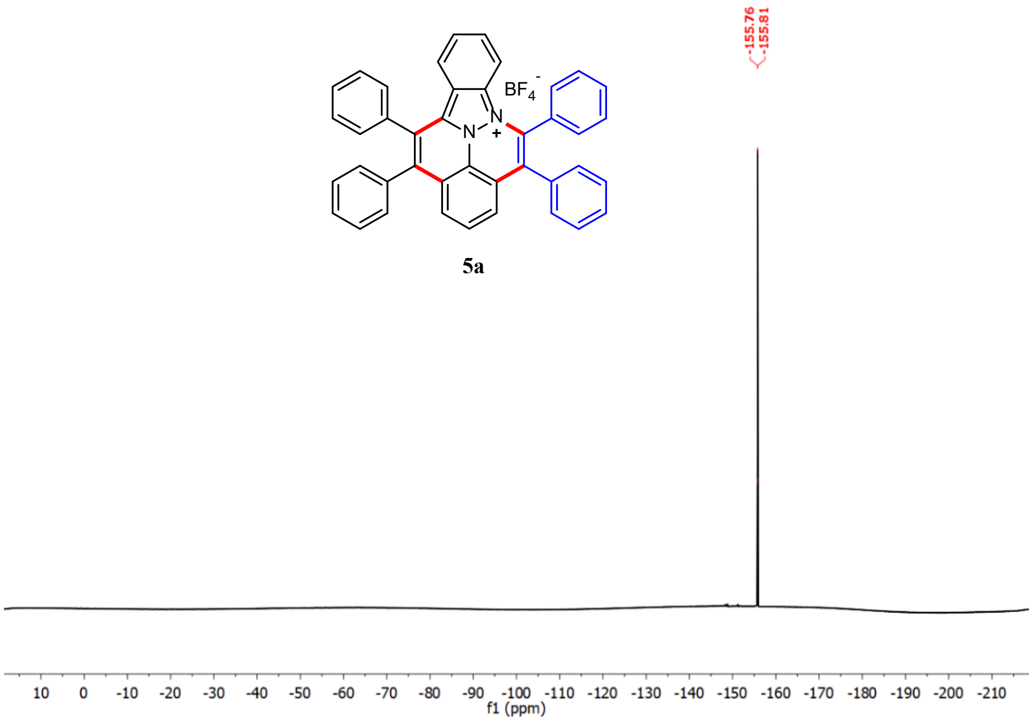


Figure S56: ^{19}F spectrum of compound **5a**

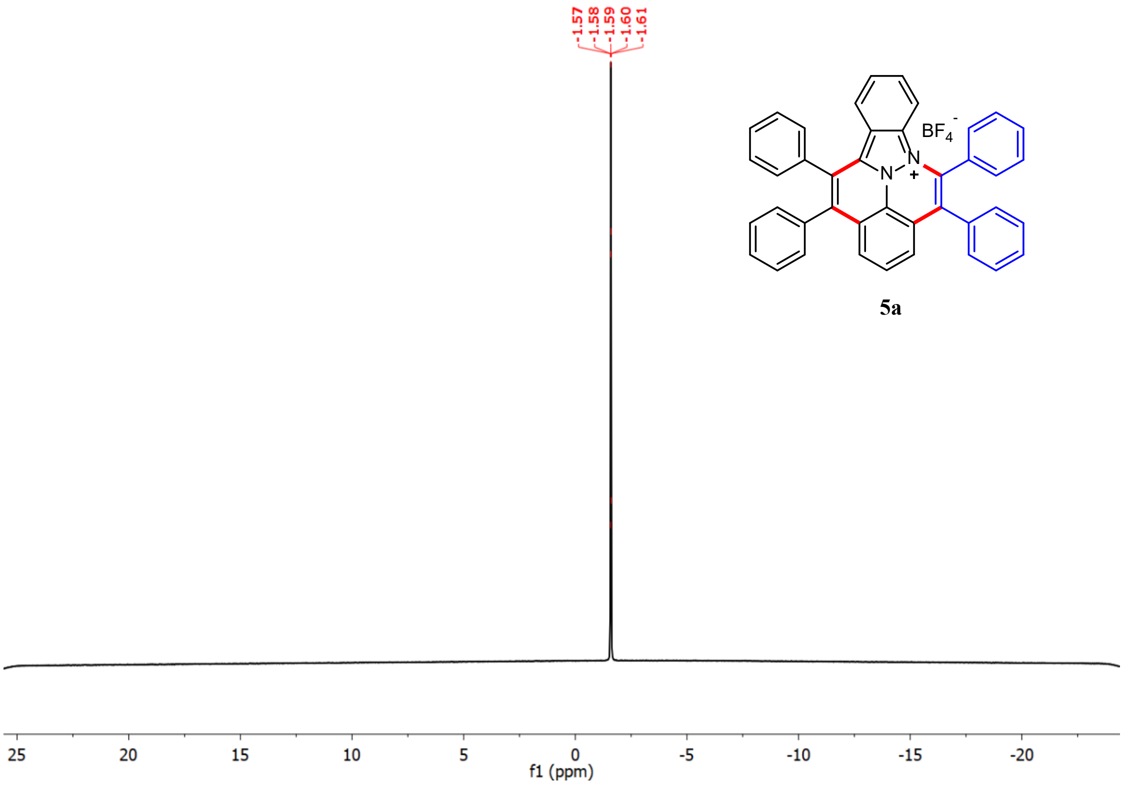


Figure S57: ^{11}B spectrum of compound **5a**

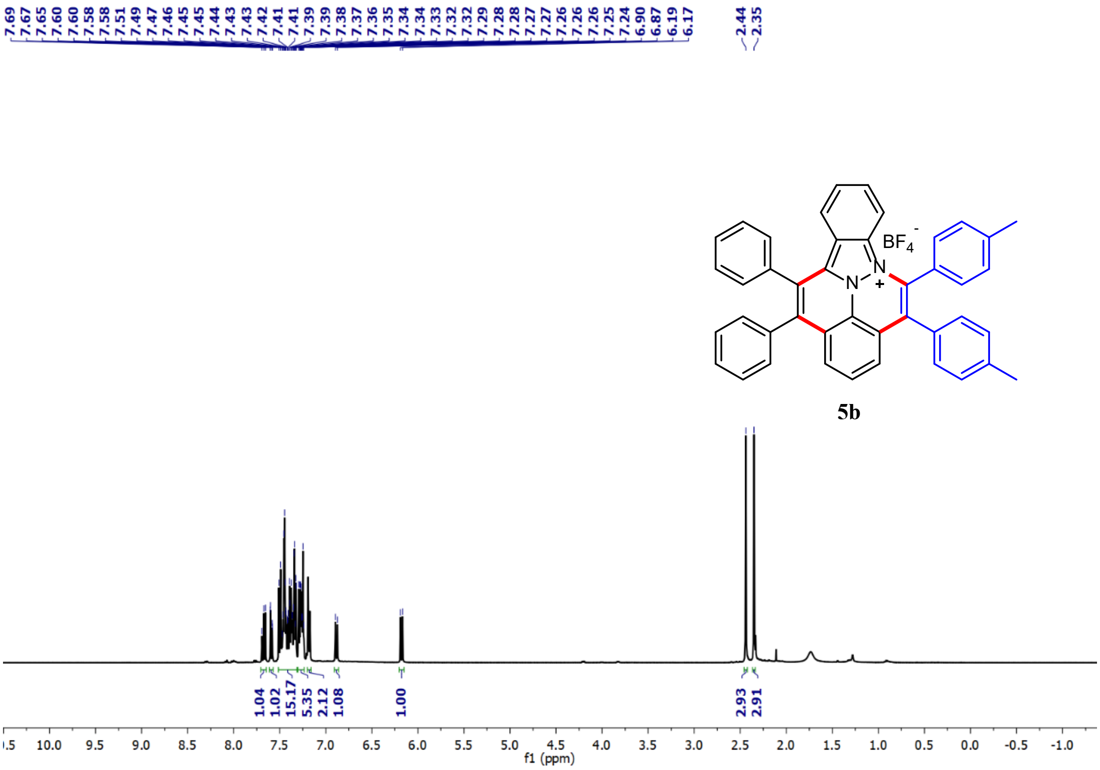


Figure S58: ^{1}H NMR spectrum of compound **5b** in $CDCl_3$

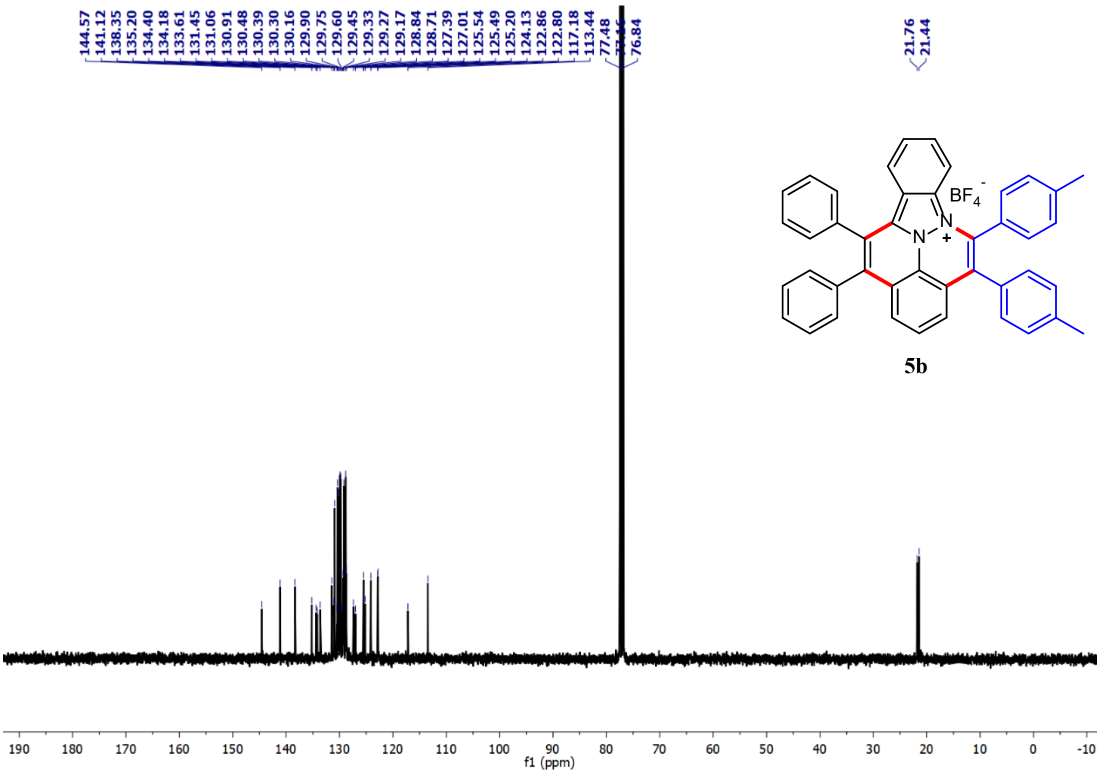


Figure S59: ^{13}C NMR spectrum of compound **5b** in $CDCl_3$

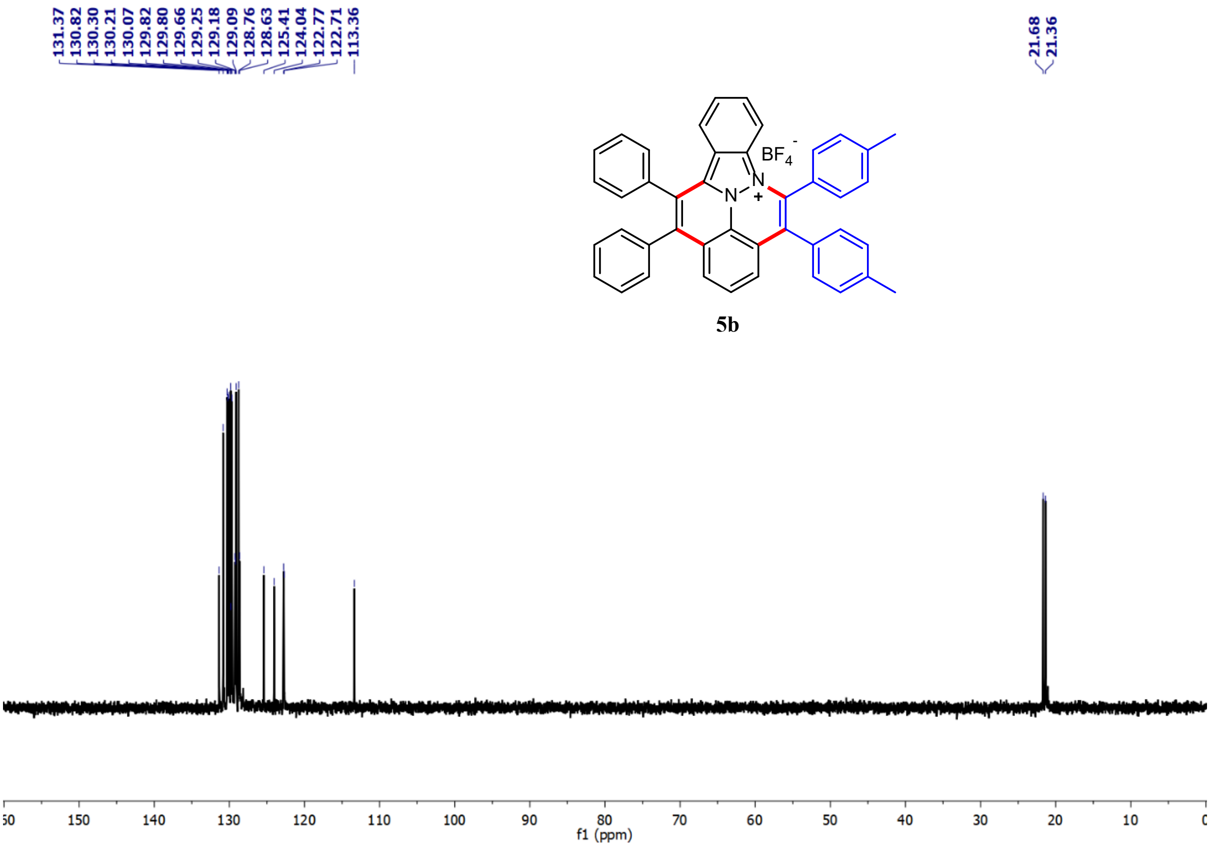


Figure S60: DEPT-135 NMR spectrum of compound **5b** in $CDCl_3$

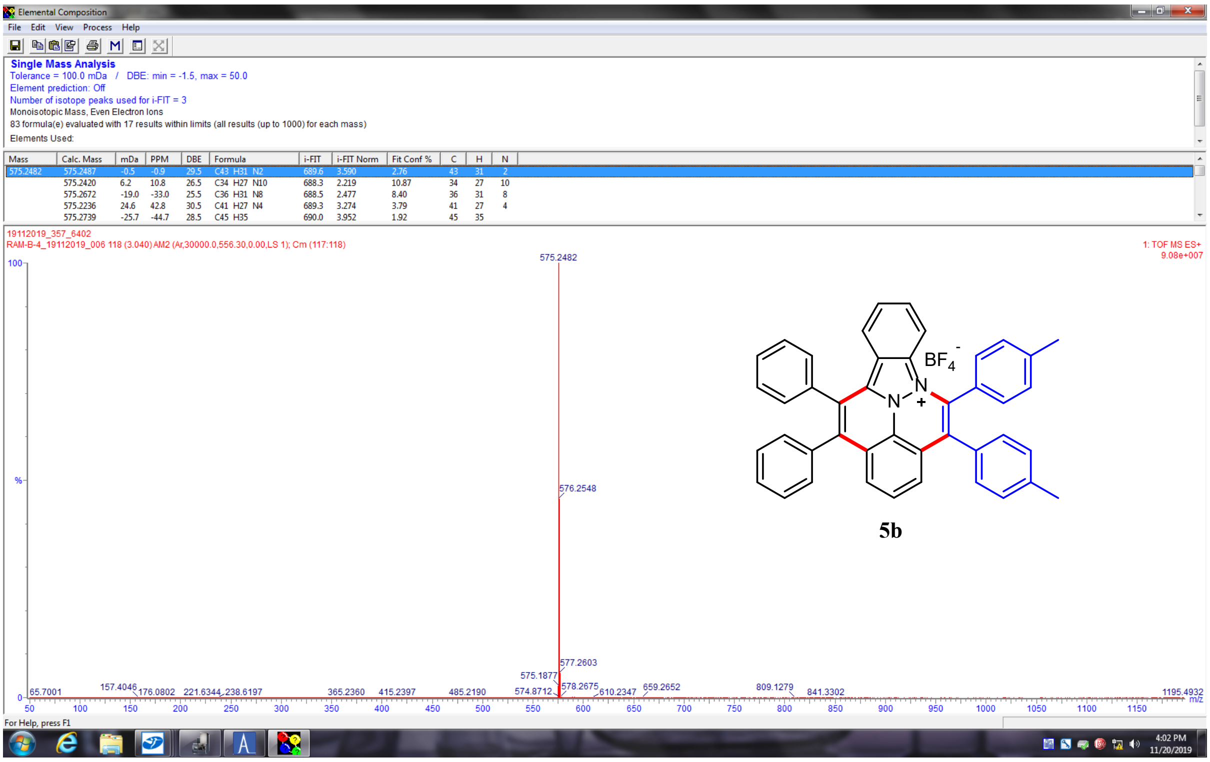


Figure S61: HRMS spectrum of compound **5b**

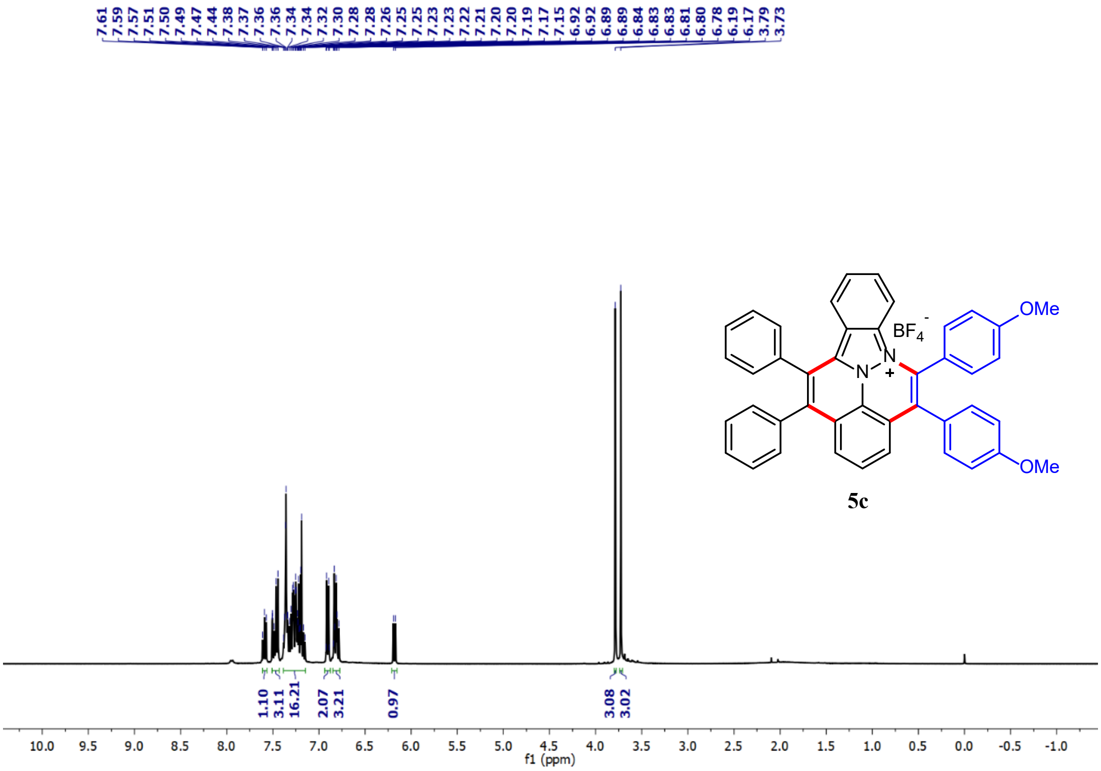


Figure S62: ^{1}H NMR spectrum of compound **5c** in $CDCl_3$

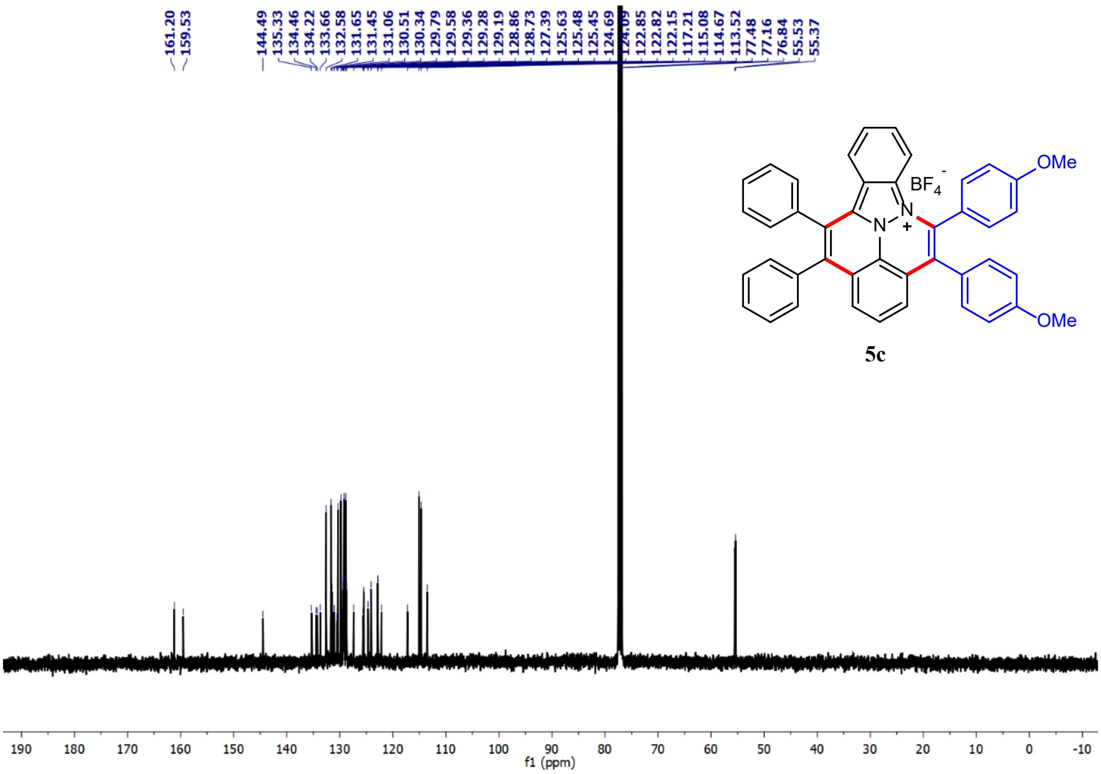


Figure S63: ^{13}C NMR spectrum of compound **5c** in $CDCl_3$

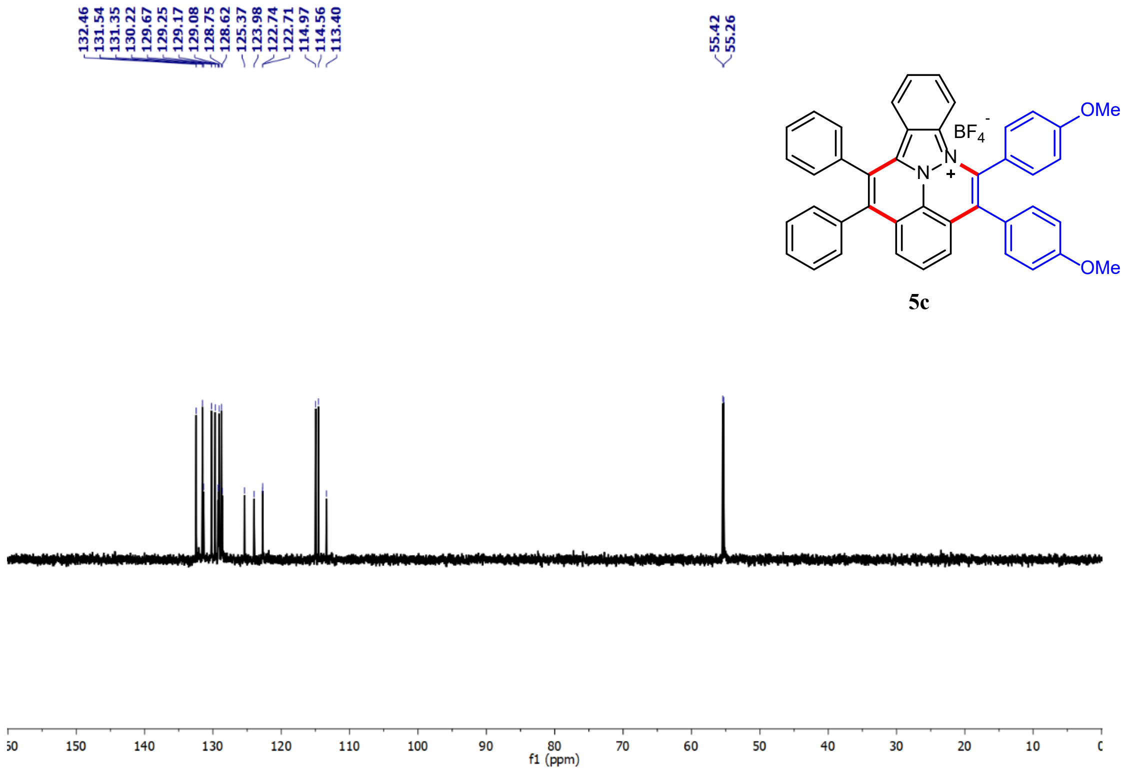


Figure S64: DEPT-135 NMR spectrum of compound **5c** in $CDCl_3$

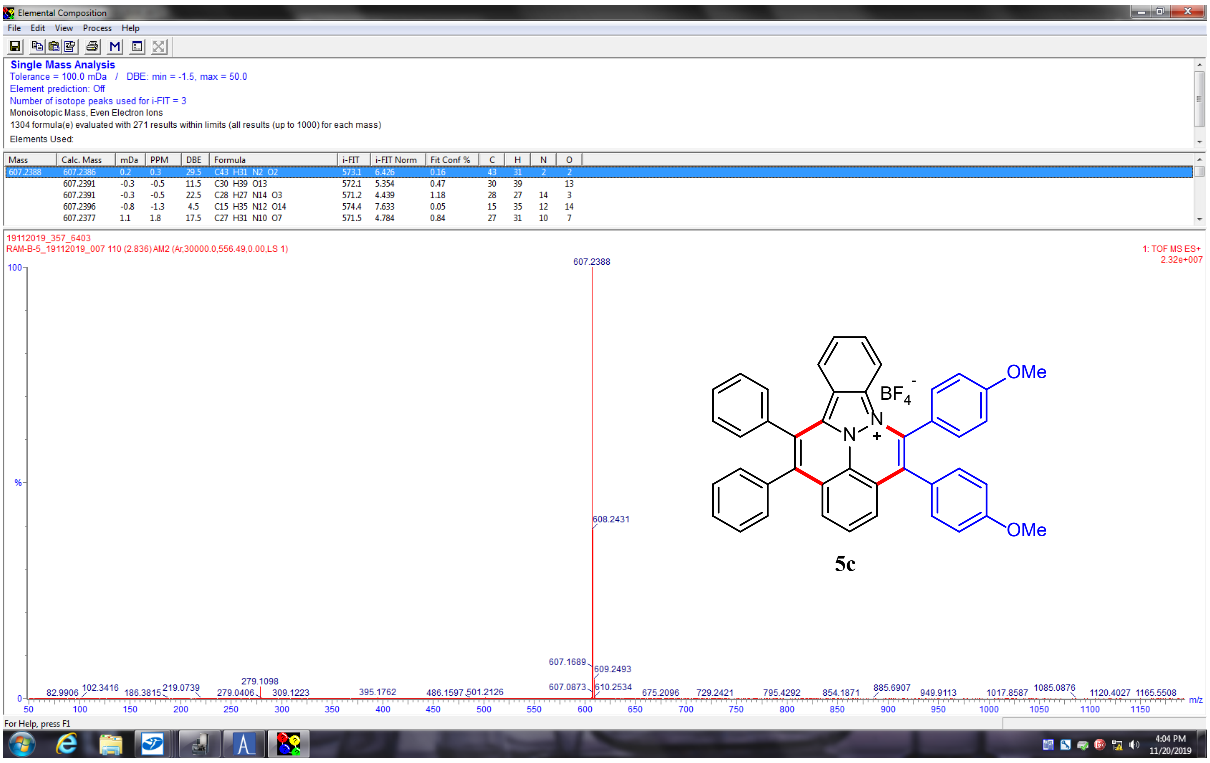


Figure S65: HRMS spectrum of compound **5c**

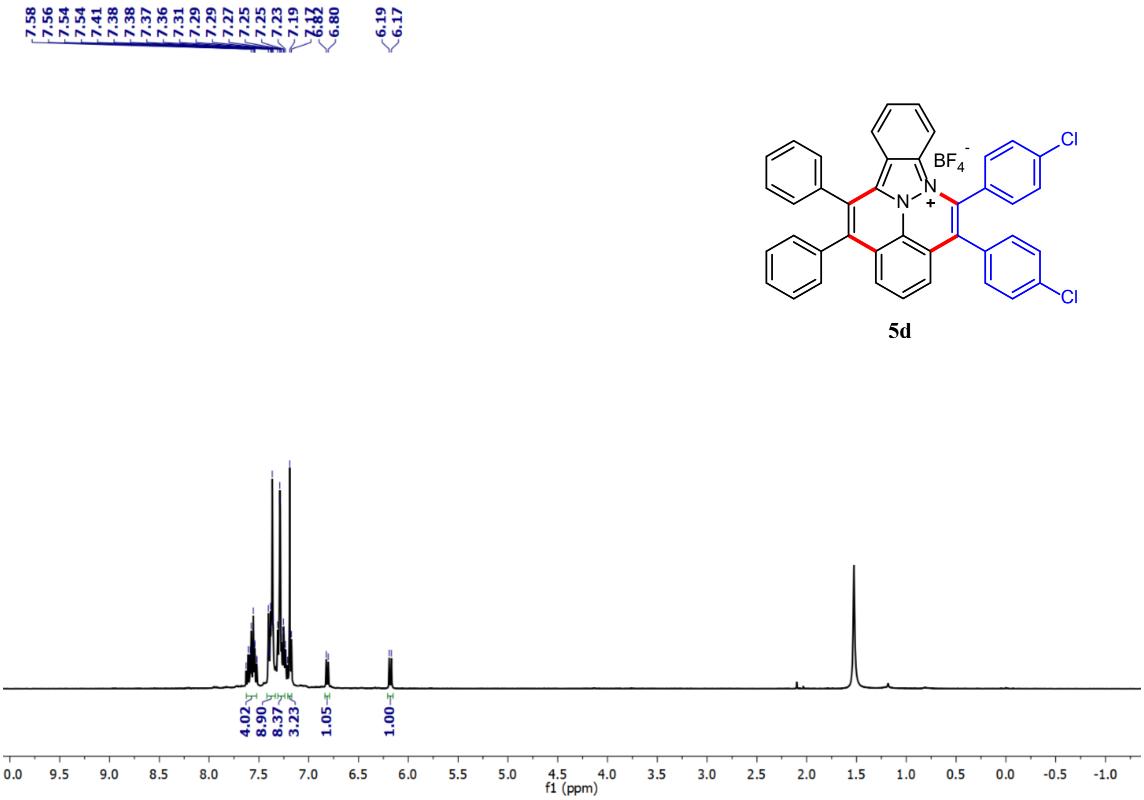


Figure S66: ^{1}H NMR spectrum of compound **5d** in $CDCl_3$

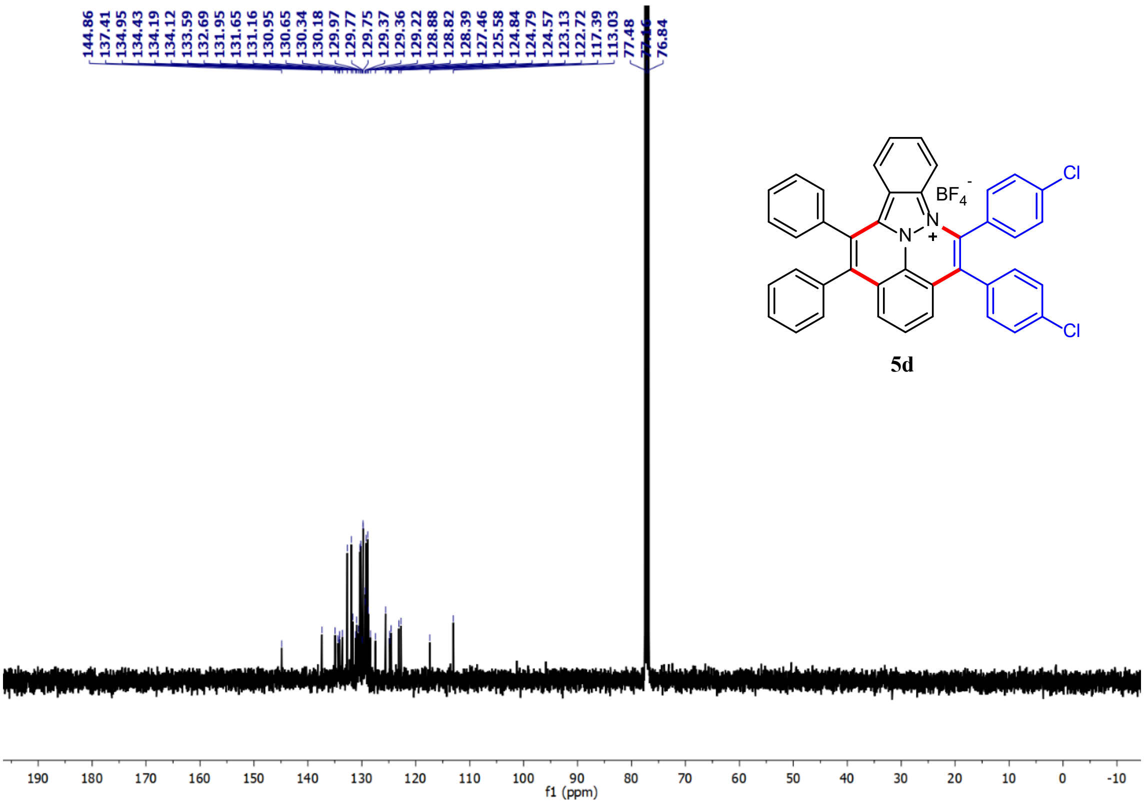


Figure S67: ^{13}C NMR spectrum of compound **5d** in $CDCl_3$

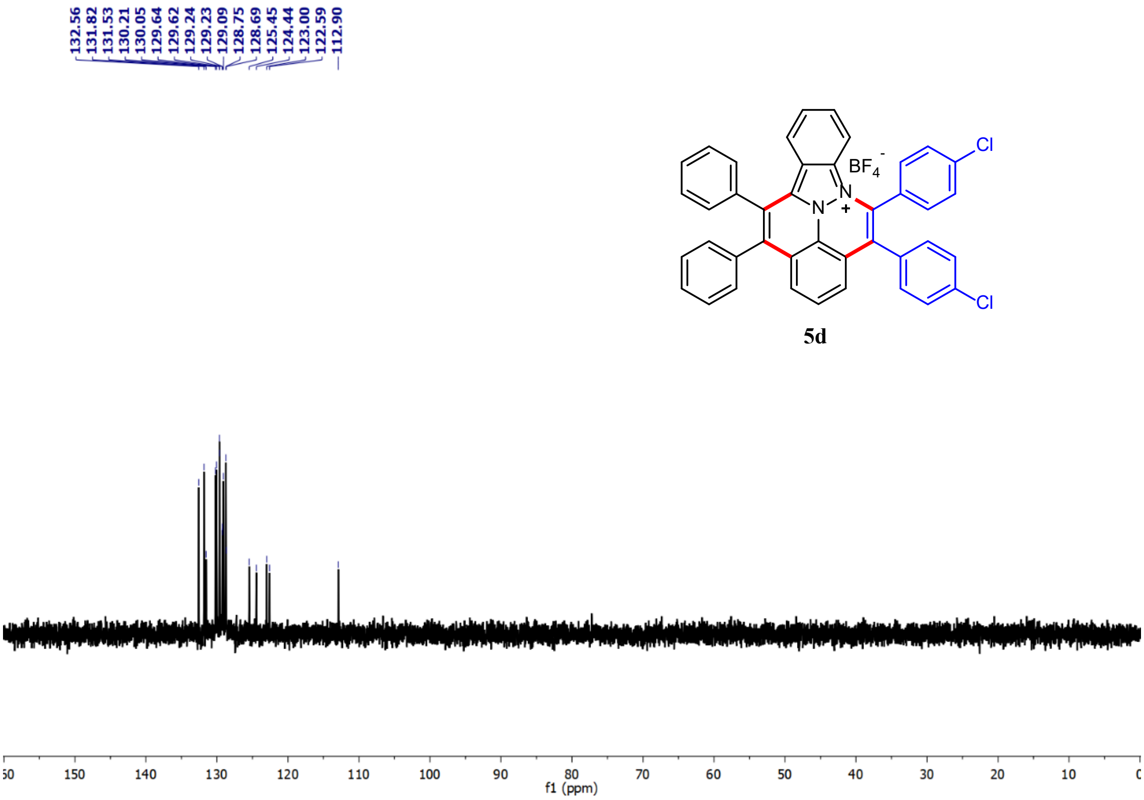


Figure S68: DEPT-135 NMR spectrum of compound **5d** in $CDCl_3$

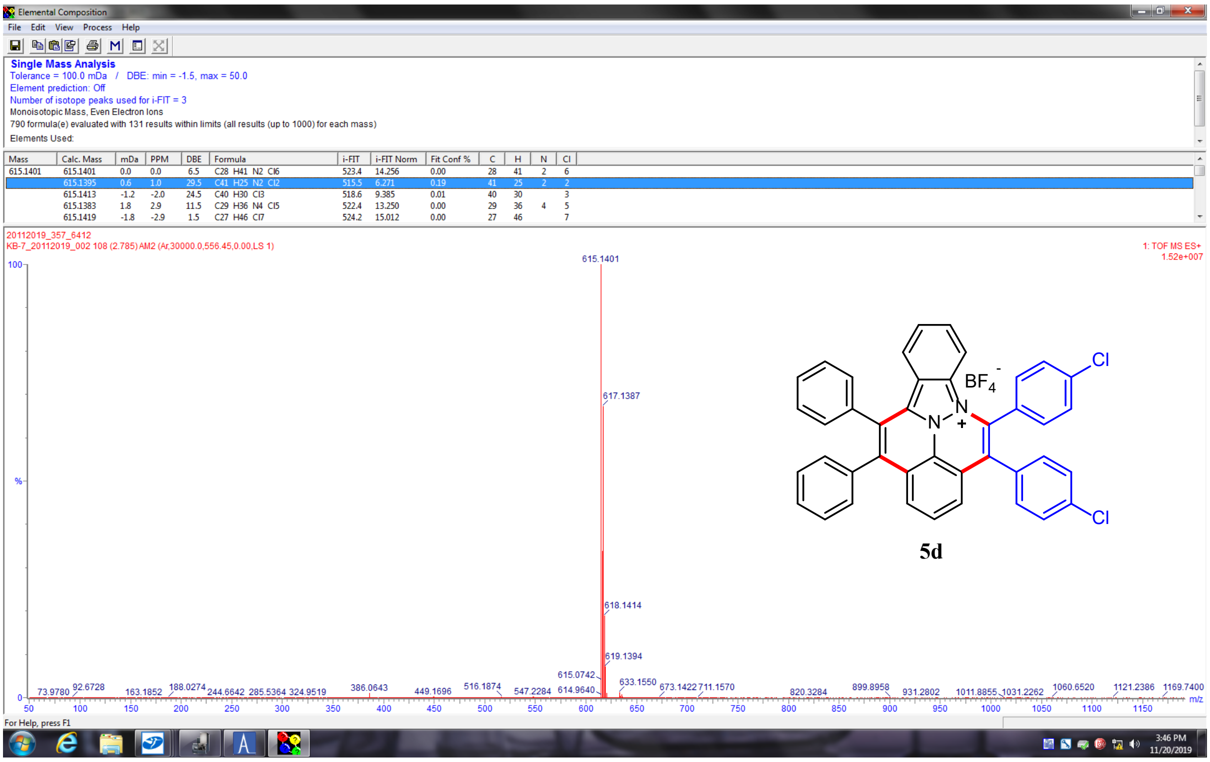


Figure S69: HRMS spectrum of compound **5d**

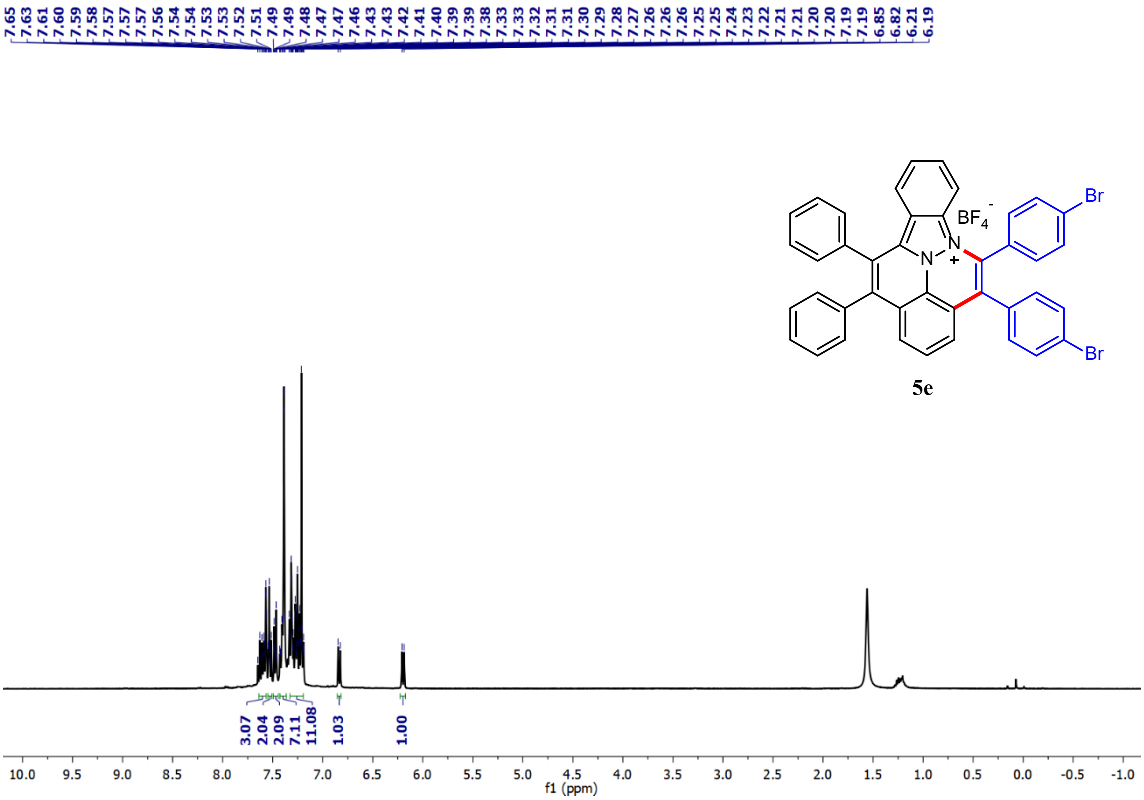


Figure S70: ^{1}H NMR spectrum of compound **5e** in $CDCl_3$

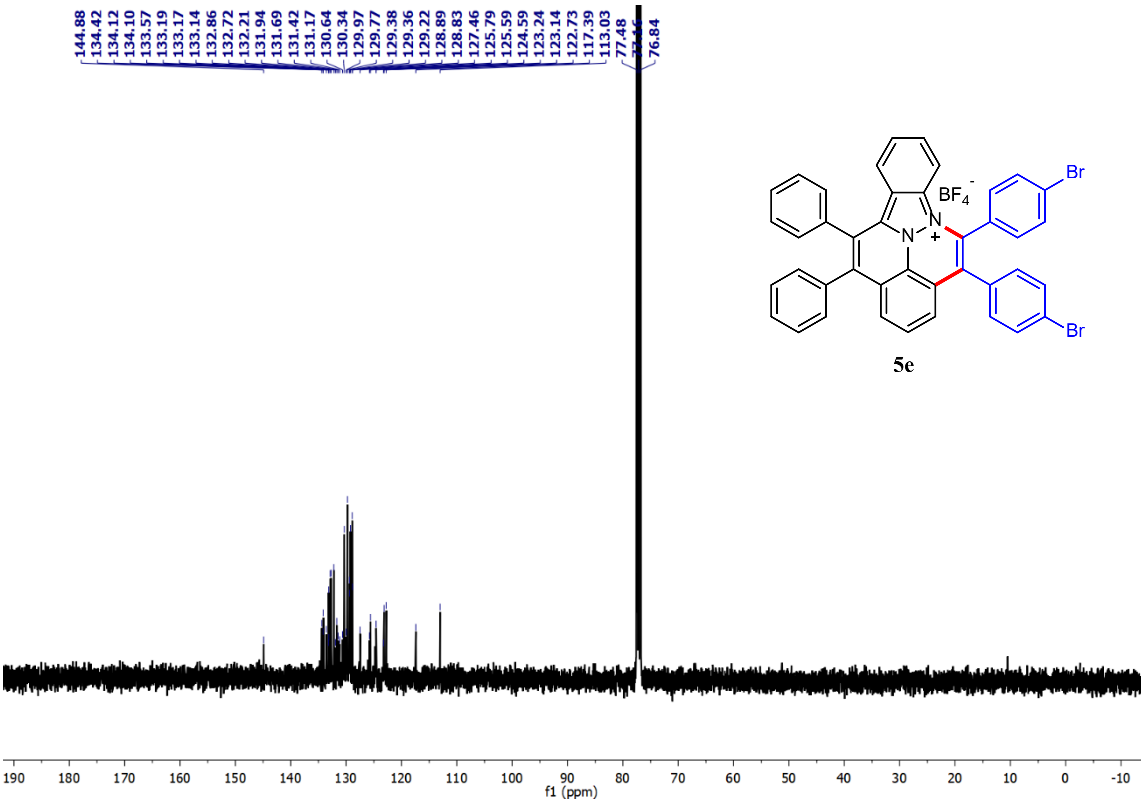


Figure S71: ^{13}C NMR spectrum of compound **5e** in $CDCl_3$

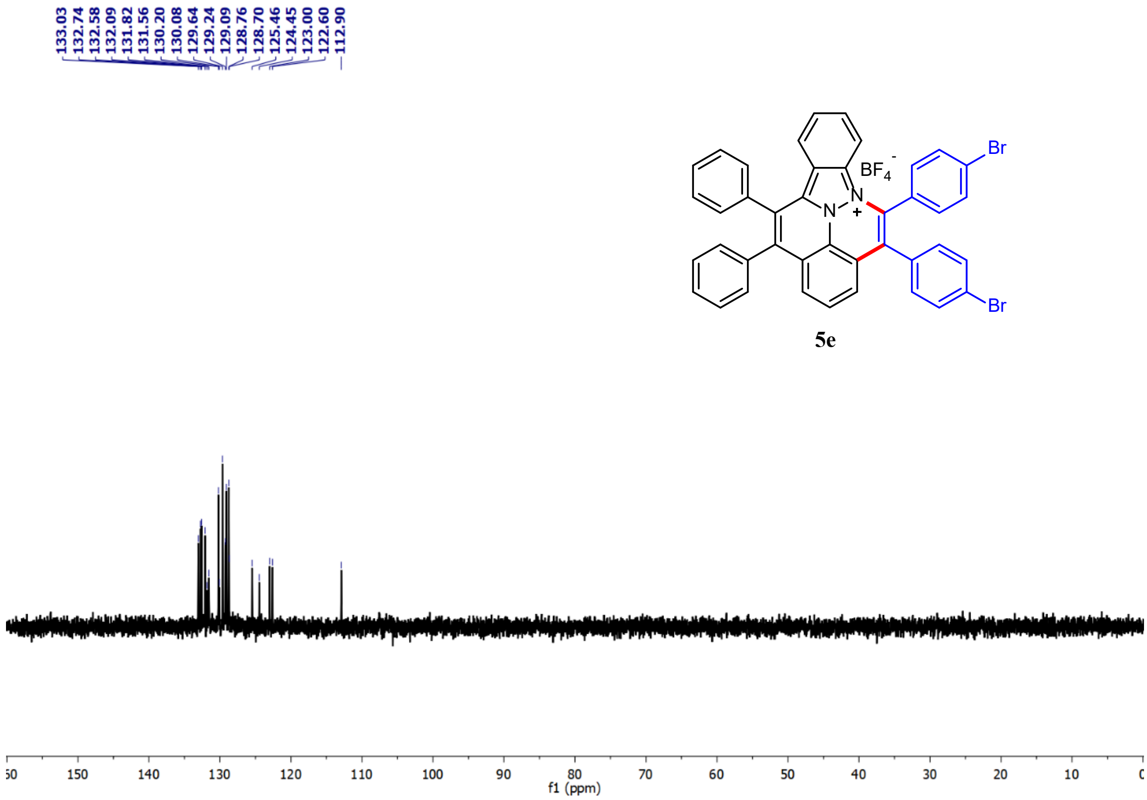
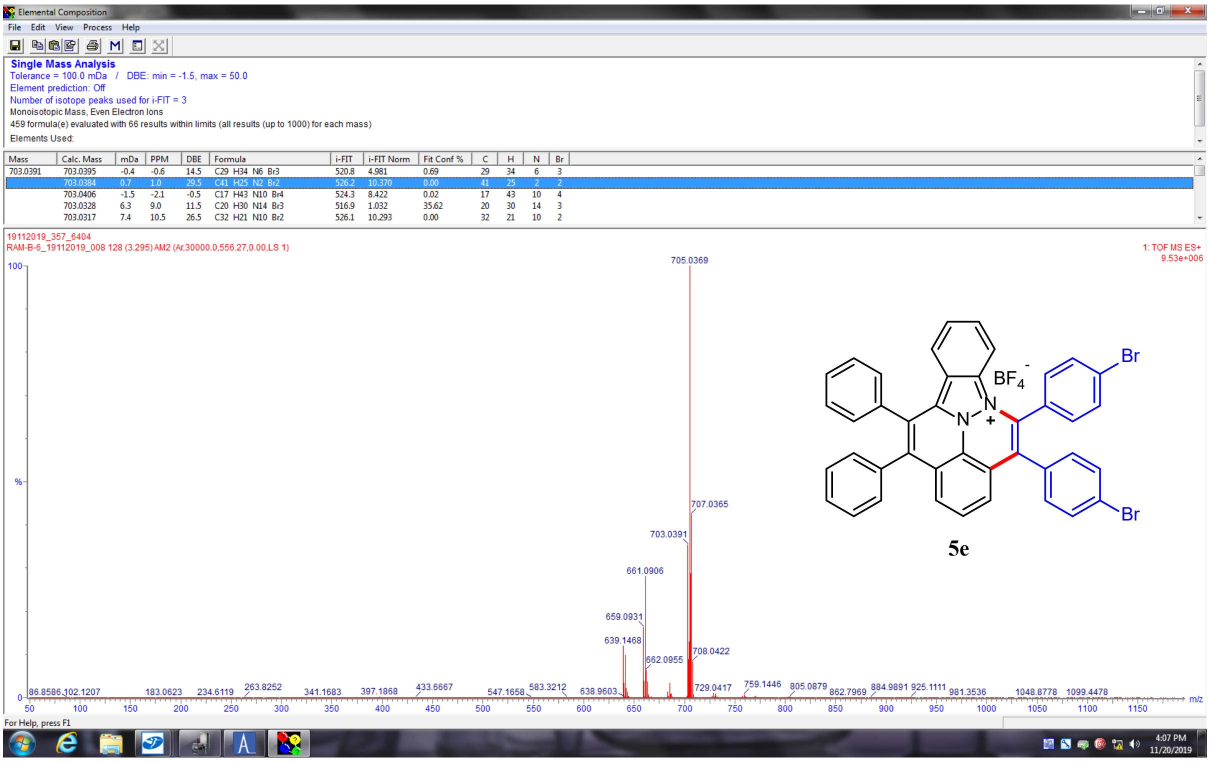


Figure S72: DEPT-135 NMR spectrum of compound **5e** in $CDCl_3$



Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	Br
703.0391	703.0395	-0.4	-0.6	14.5	C29 H34 N6 Br3	520.8	4.981	0.69	29	34	6	3
	703.0384	0.7	1.0	29.5	C41 H25 N2 Br2	526.2	10.370	0.00	41	25	2	2
	703.0406	-1.5	-2.1	-0.5	C17 H43 N10 Br4	524.3	8.422	0.02	17	43	10	4
	703.0328	6.3	9.0	11.5	C20 H30 N14 Br3	516.9	1.032	35.62	20	30	14	3
	703.0317	7.4	10.5	26.5	C32 H21 N10 Br2	526.1	10.293	0.00	32	21	10	2

Figure S73: HRMS spectrum of compound **5e**

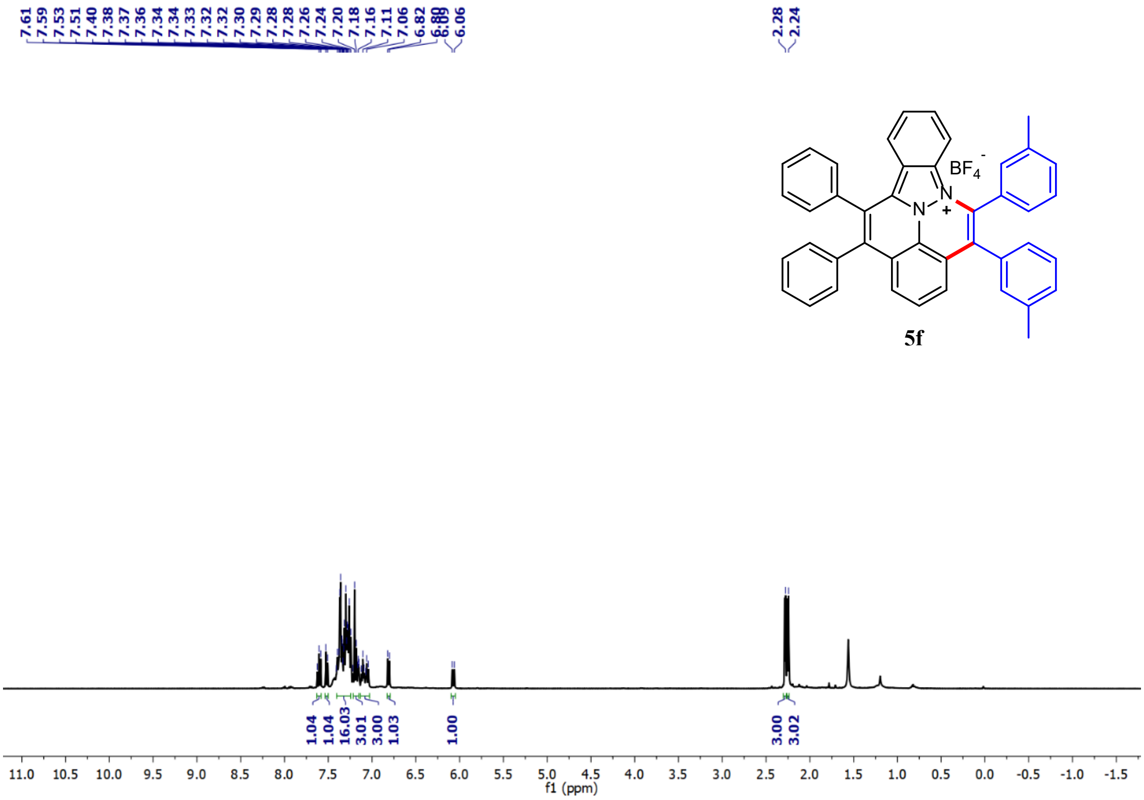


Figure S74: ^{1}H NMR spectrum of compound **5f** in $CDCl_3$

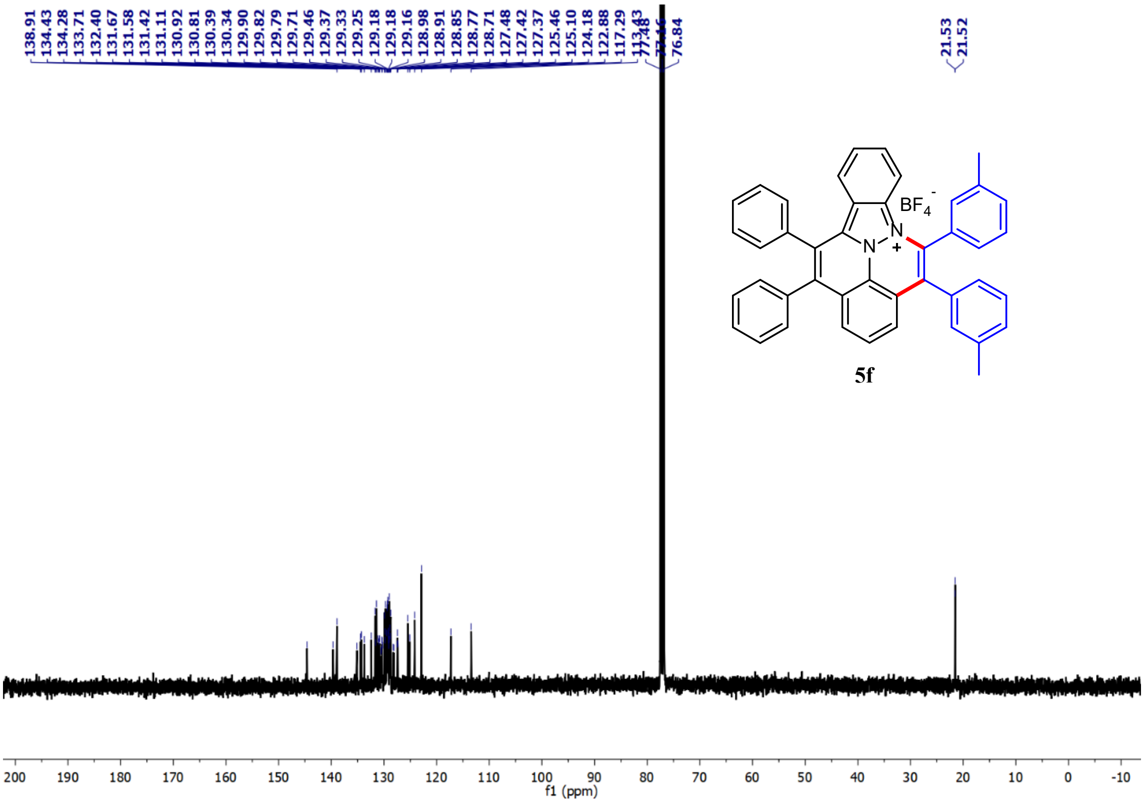


Figure S74: ^{13}C NMR spectrum of compound **5f** in $CDCl_3$

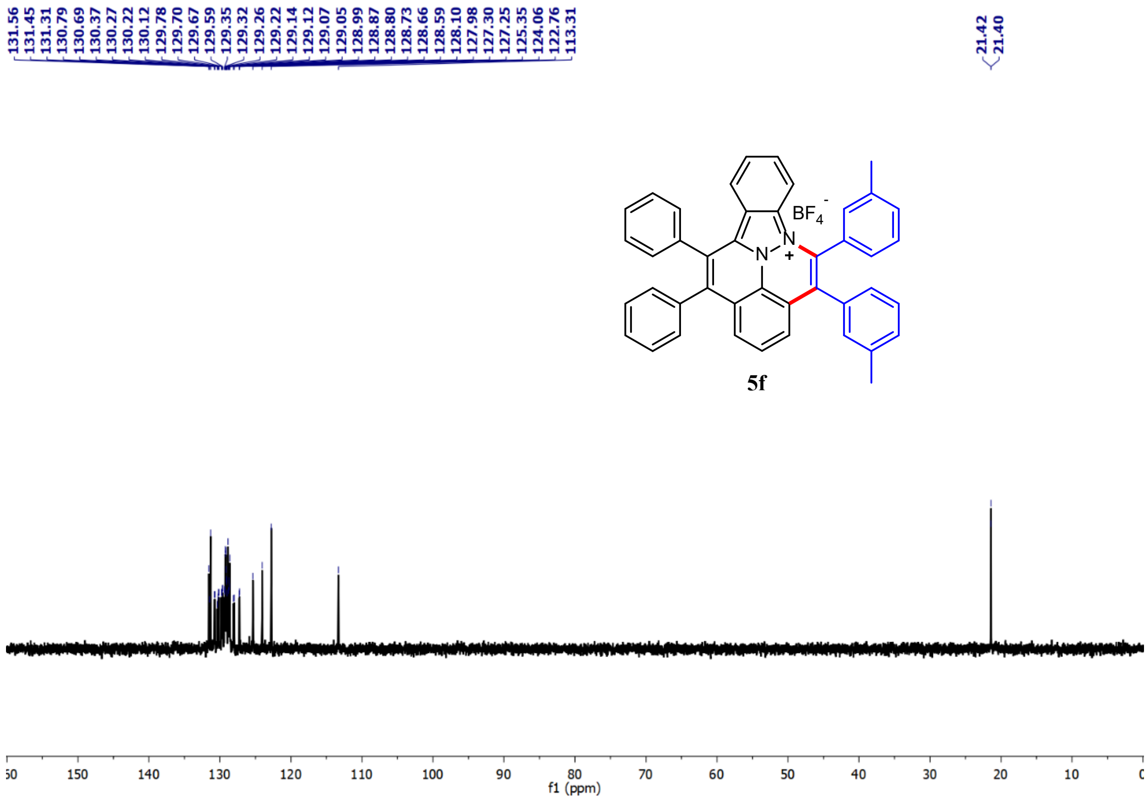


Figure S75: DEPT-135 NMR spectrum of compound **5f** in $CDCl_3$

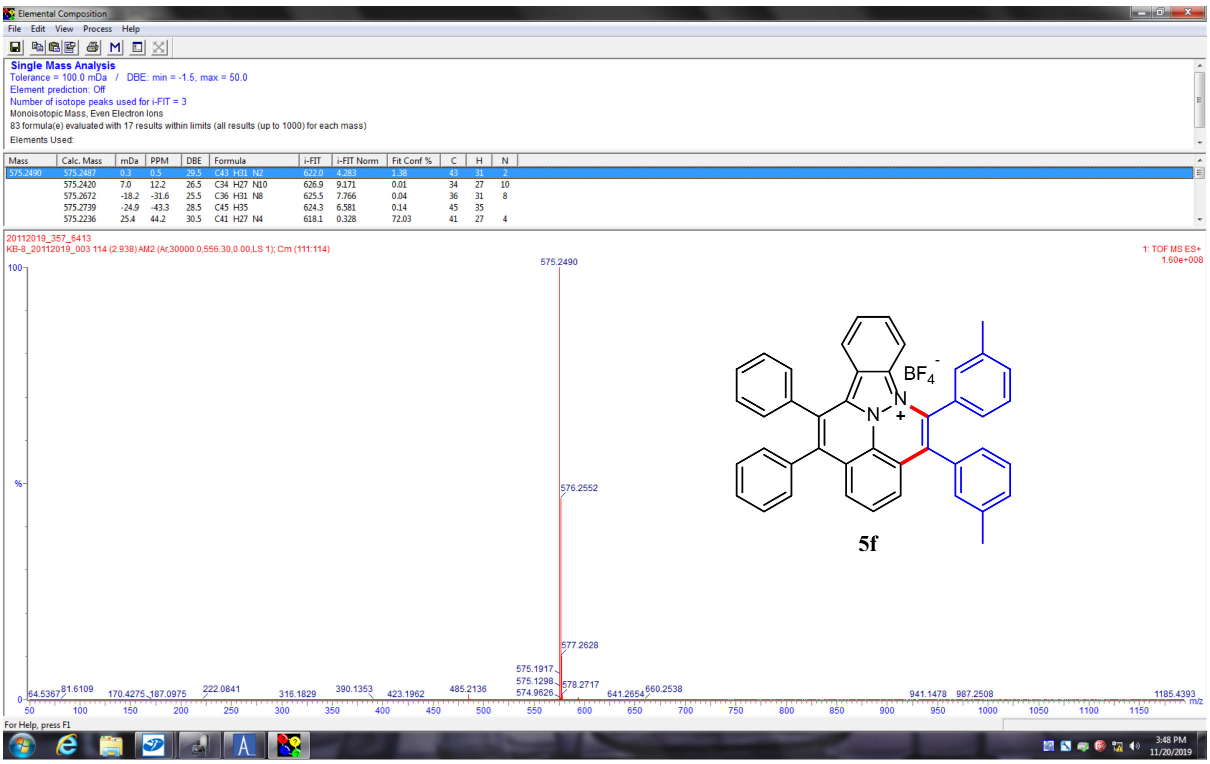


Figure S76: HRMS spectrum of compound **5f**

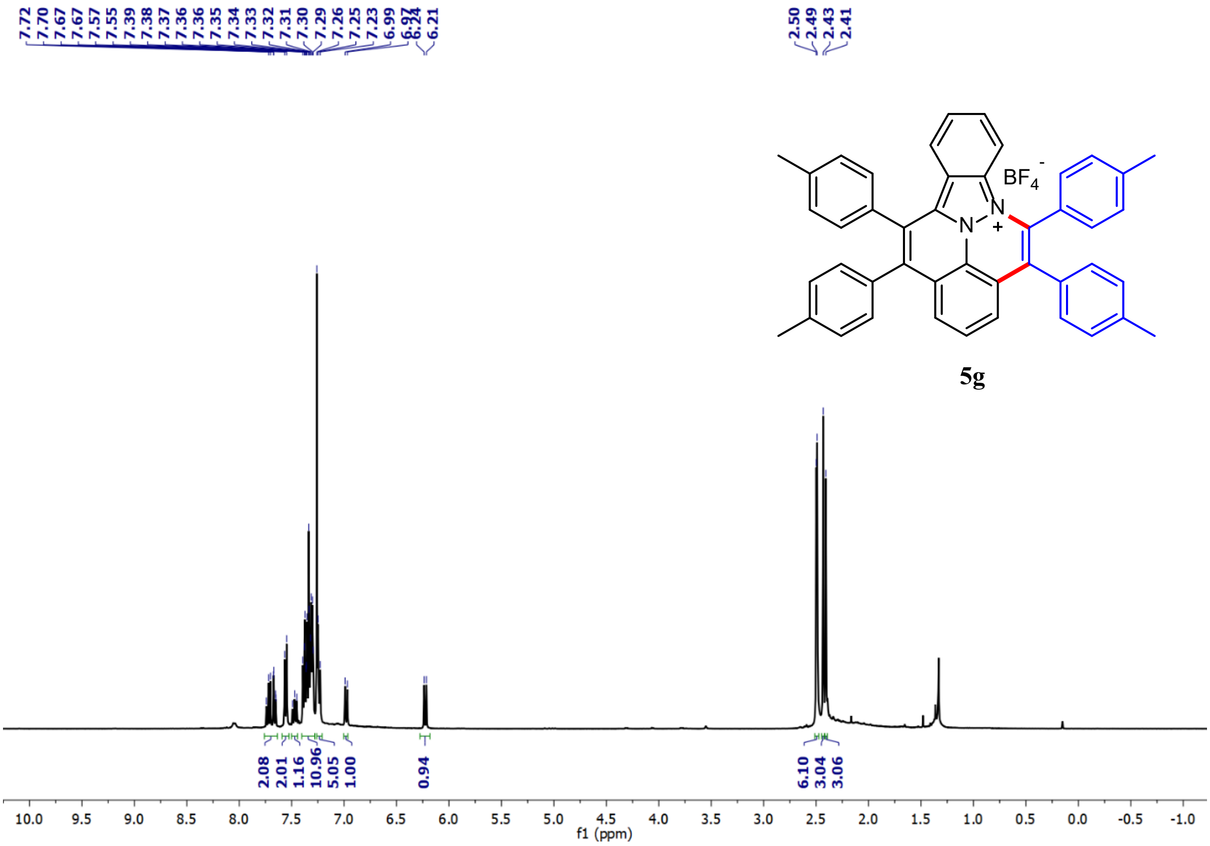


Figure S77: ^{1}H NMR spectrum of compound **5g** in $CDCl_3$

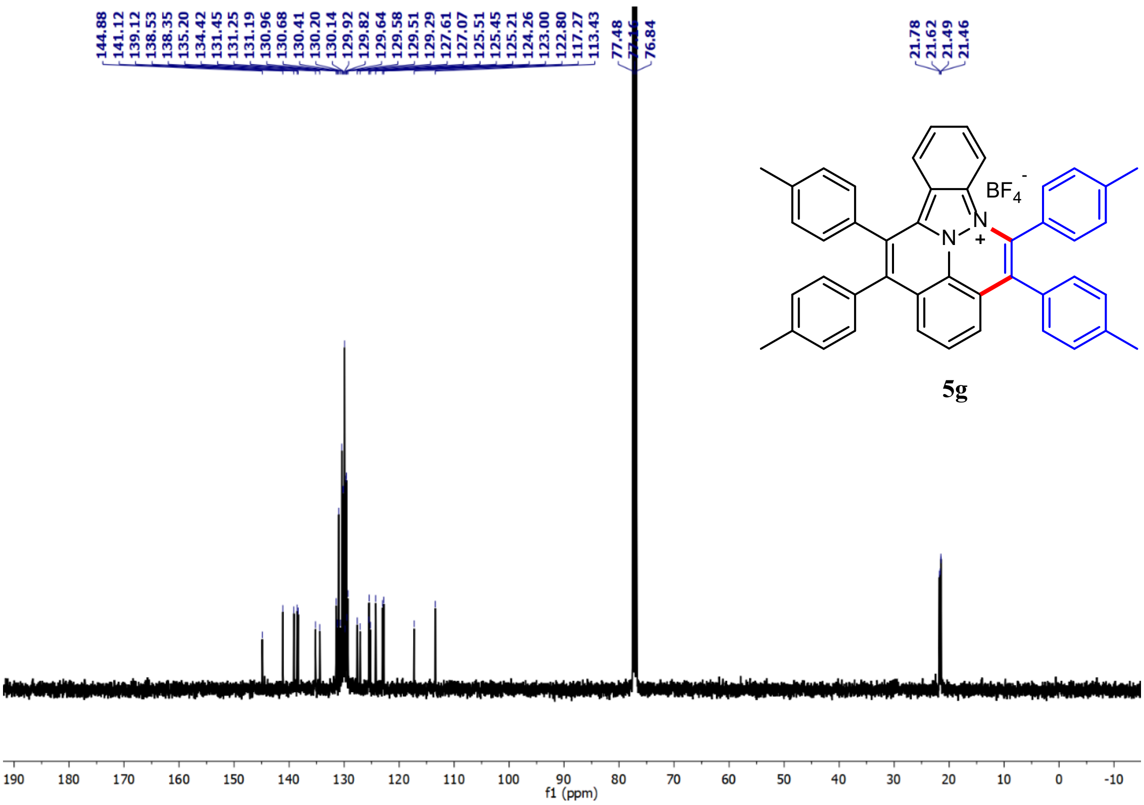


Figure S78: ^{13}C NMR spectrum of compound **5g** in $CDCl_3$

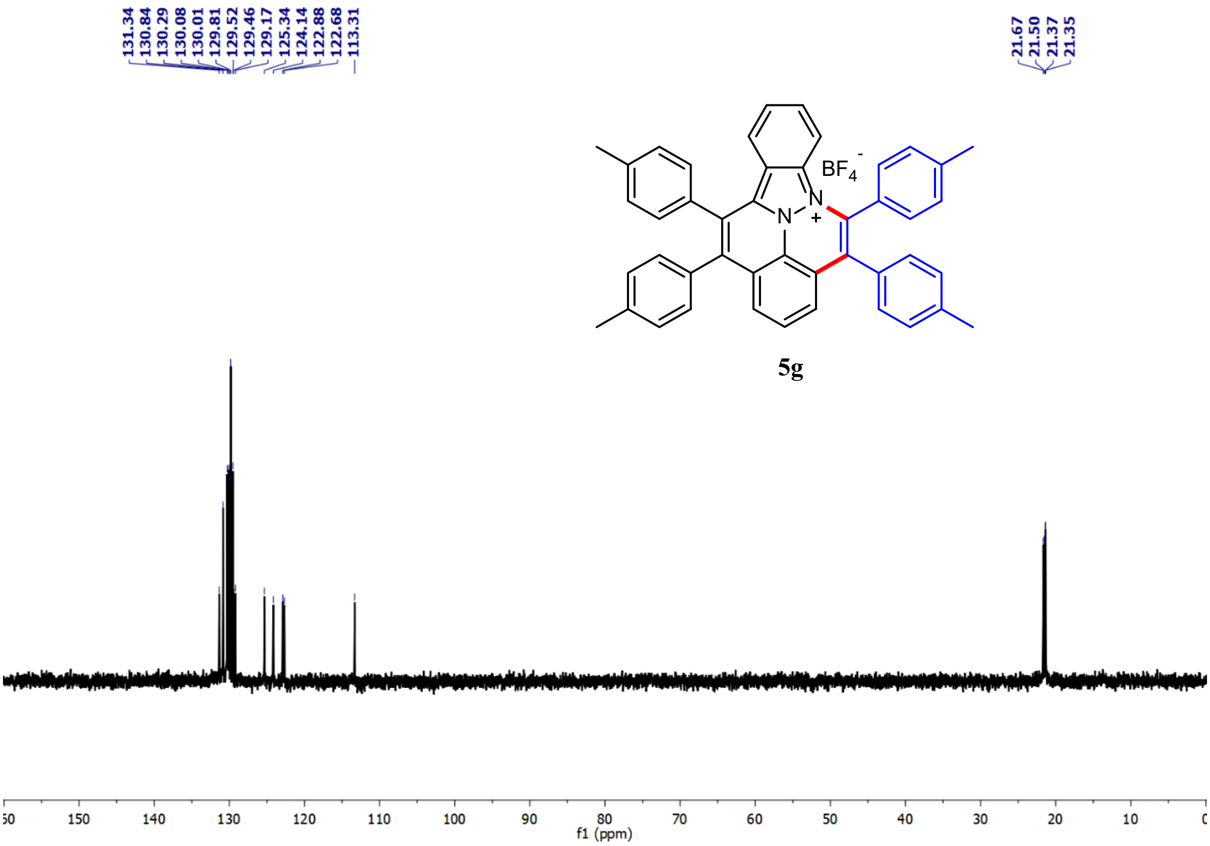
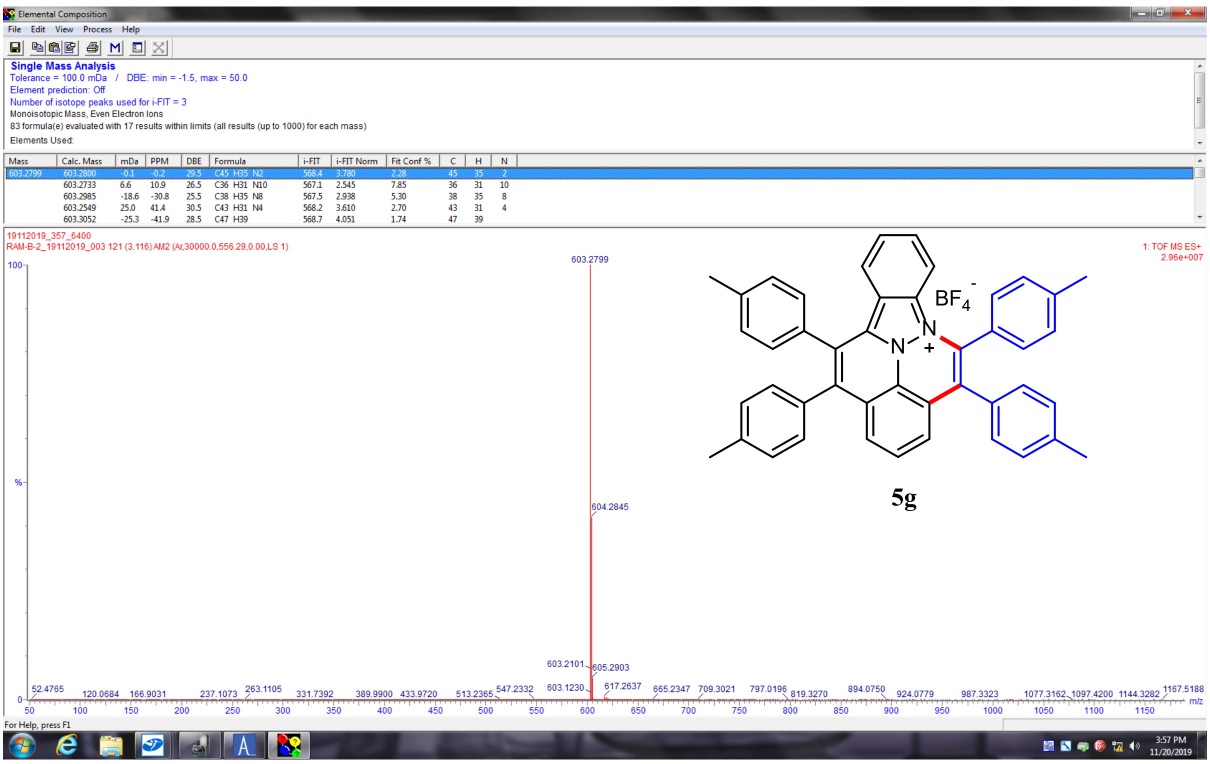


Figure S79: DEPT-135 NMR spectrum of compound **5g** in $CDCl_3$



Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N
603.2799	603.2800	-0.1	-0.2	29.5	C45 H35 N2	568.4	3.780	2.28	45	35	2
	603.2733	6.6	10.9	26.5	C36 H31 N10	567.1	2.545	7.85	36	31	10
	603.2985	-18.6	-30.8	25.5	C38 H35 N8	567.5	2.938	5.30	38	35	8
	603.2549	25.0	41.4	30.5	C43 H31 N4	568.2	3.610	2.70	43	31	4
	603.3052	-25.3	-41.9	28.5	C47 H39	568.7	4.051	1.74	47	39	

Figure S80: HRMS spectrum of compound **5g**

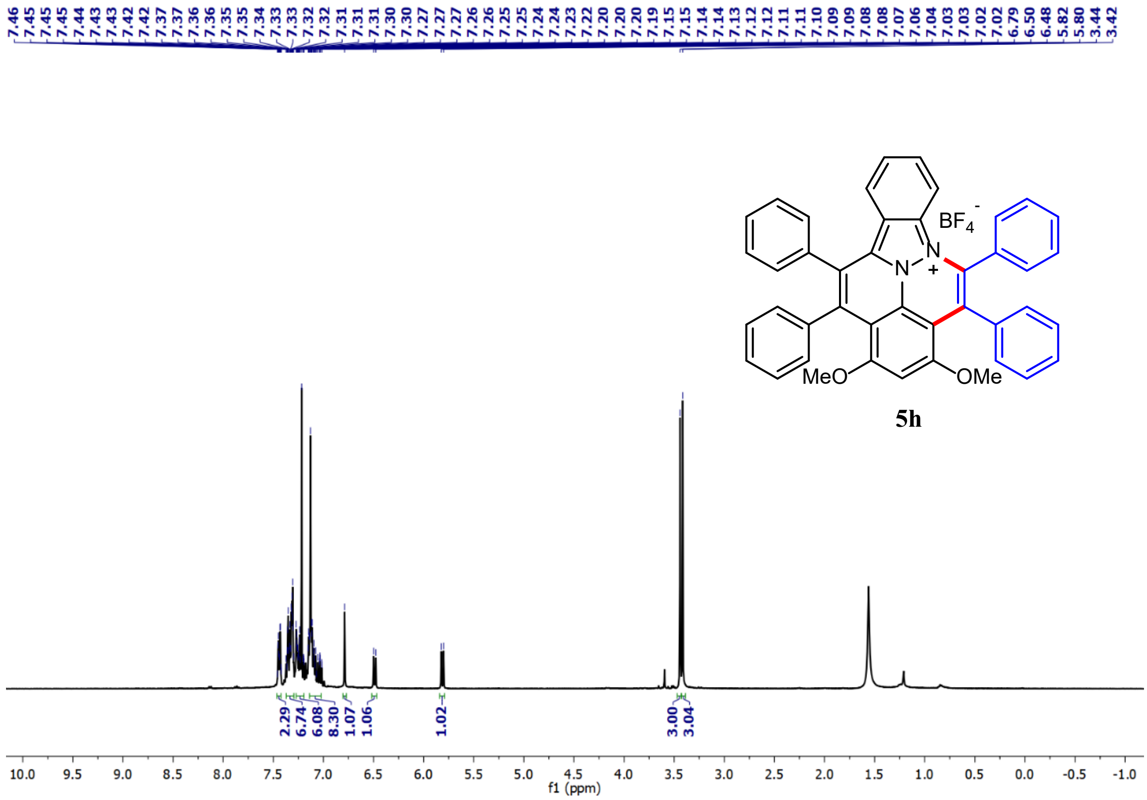


Figure S81: ^{1}H NMR spectrum of compound **5h** in $CDCl_3$

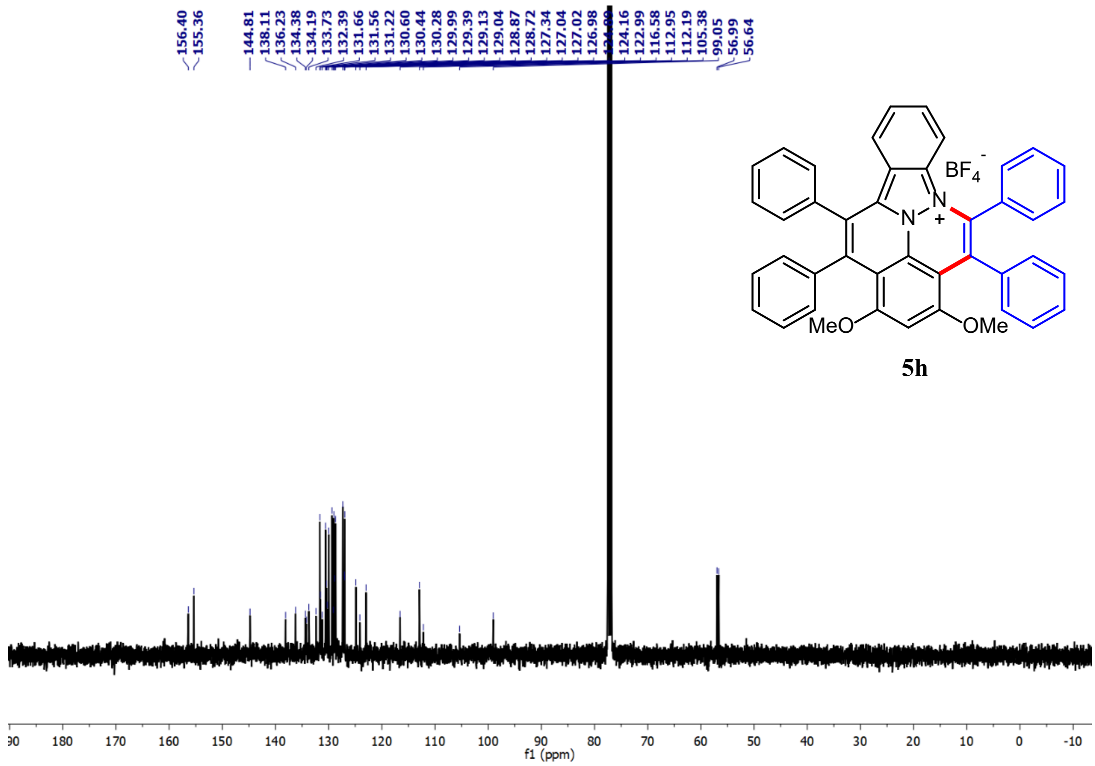


Figure S82: ^{13}C NMR spectrum of compound **5h** in $CDCl_3$

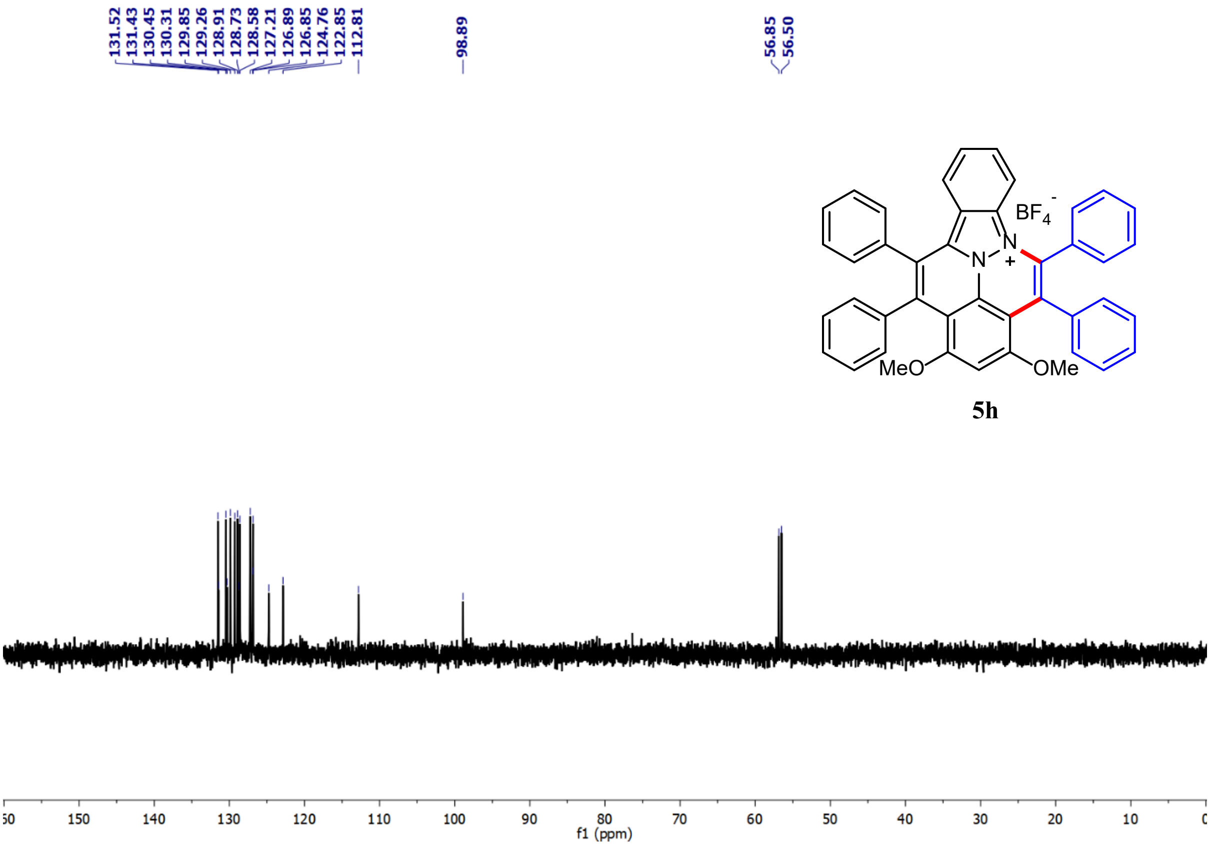


Figure S83: DEPT-135 NMR spectrum of compound **5h** in $CDCl_3$

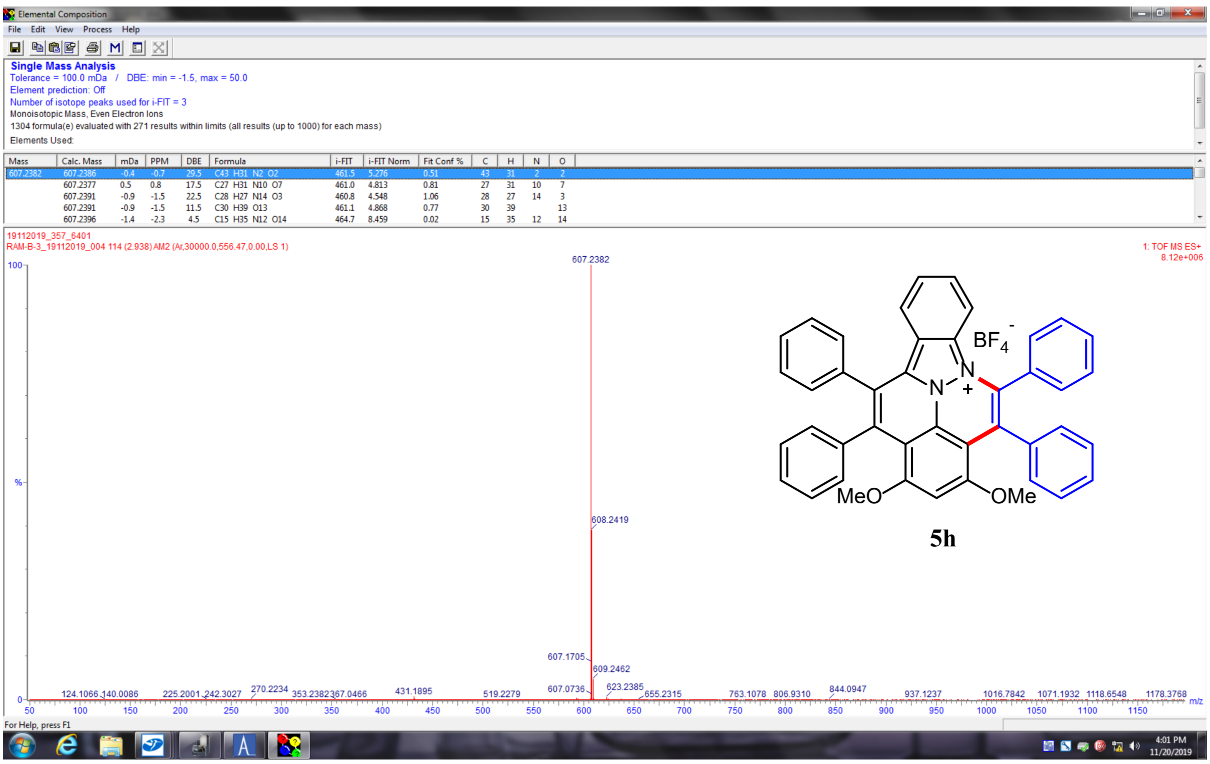


Figure S84: HRMS spectrum of compound **5h**

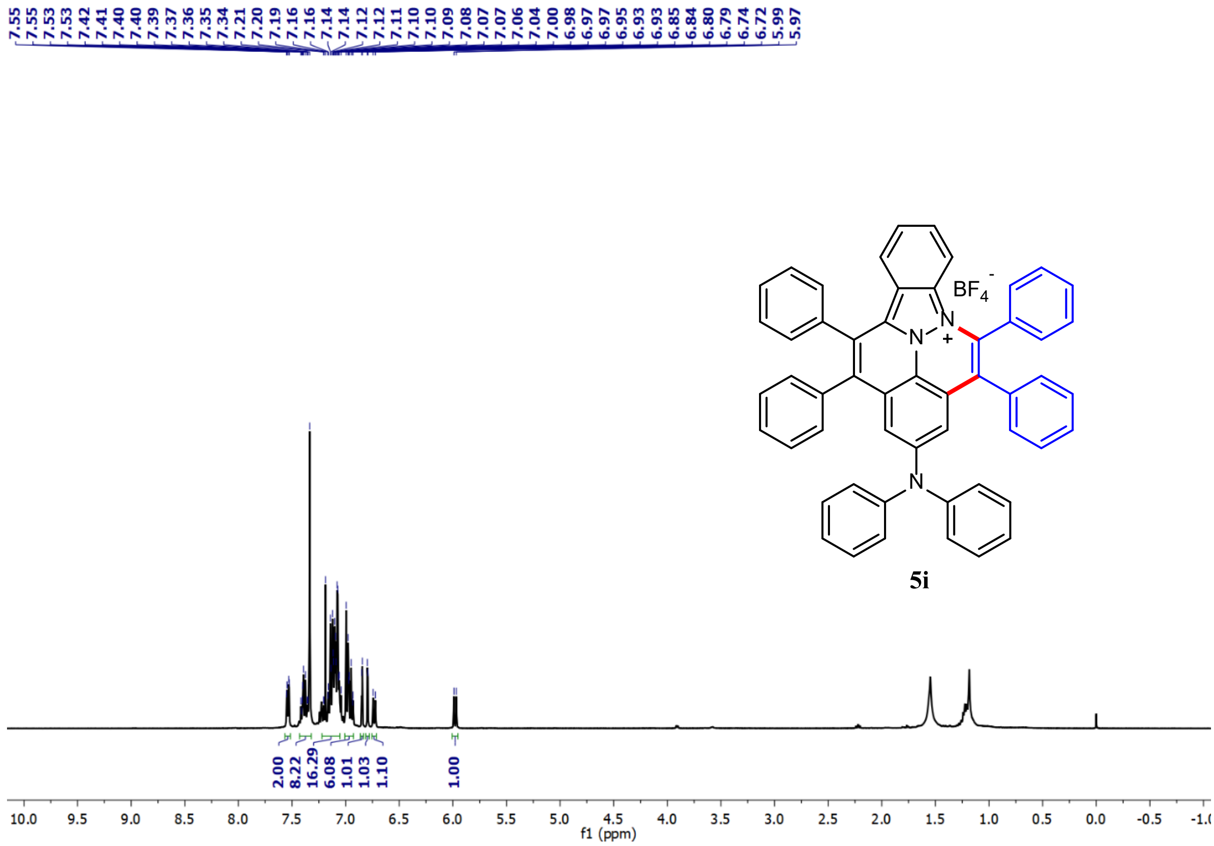


Figure S85: ^{1}H NMR spectrum of compound **5i** in $CDCl_3$

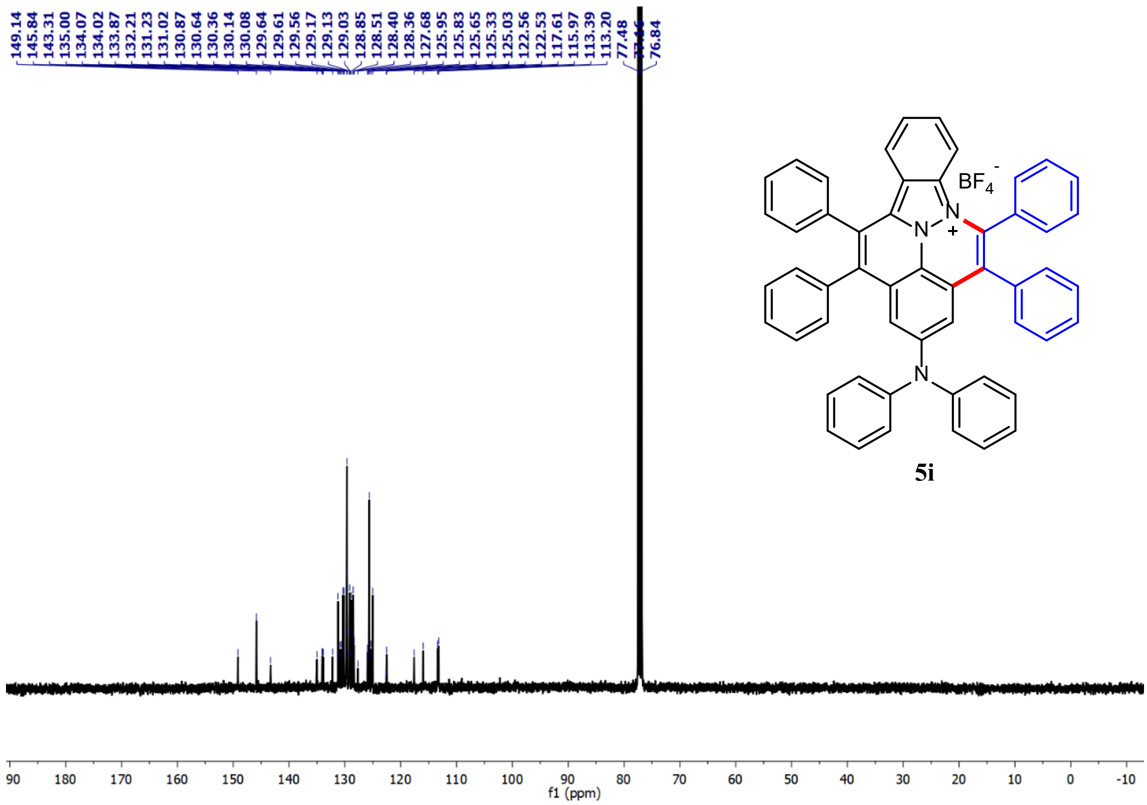


Figure S86: ^{13}C NMR spectrum of compound **5i** in $CDCl_3$

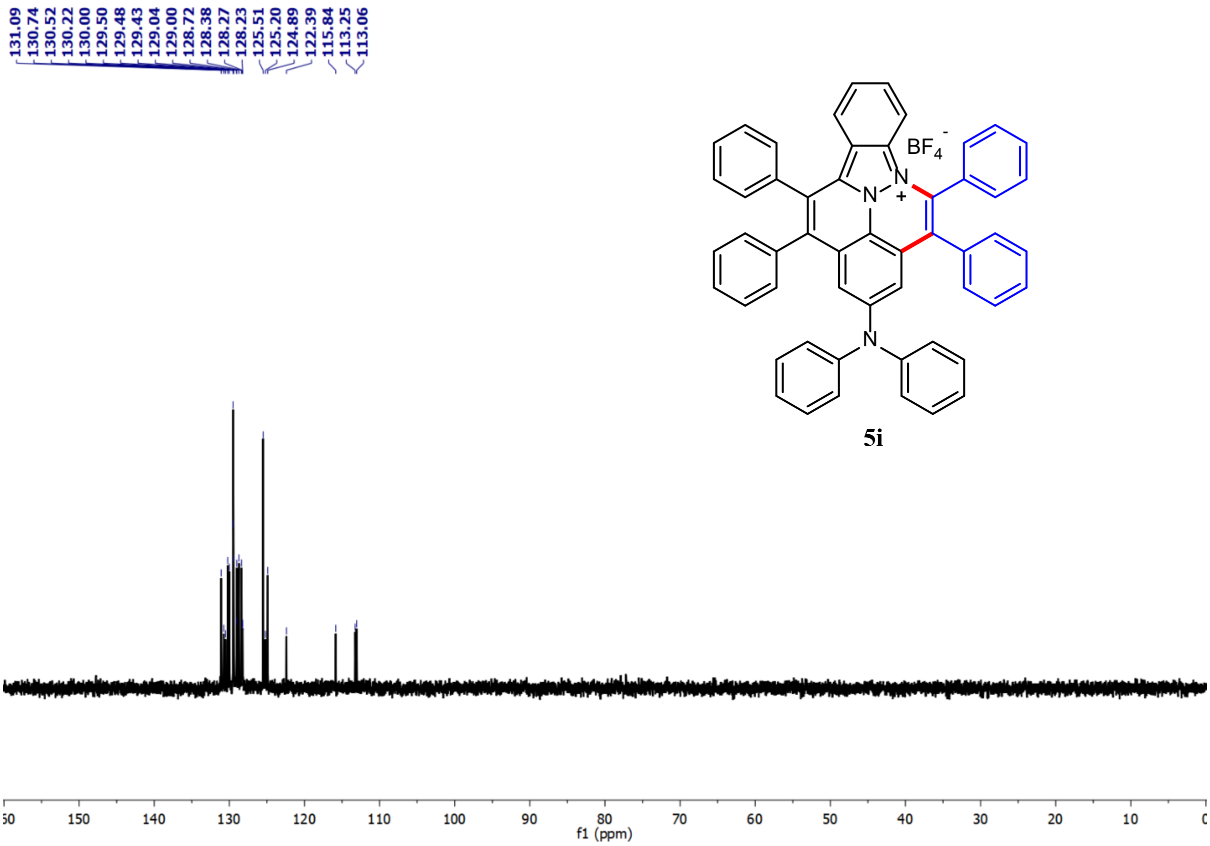


Figure S87: DEPT-135 NMR spectrum of compound **5i** in $CDCl_3$

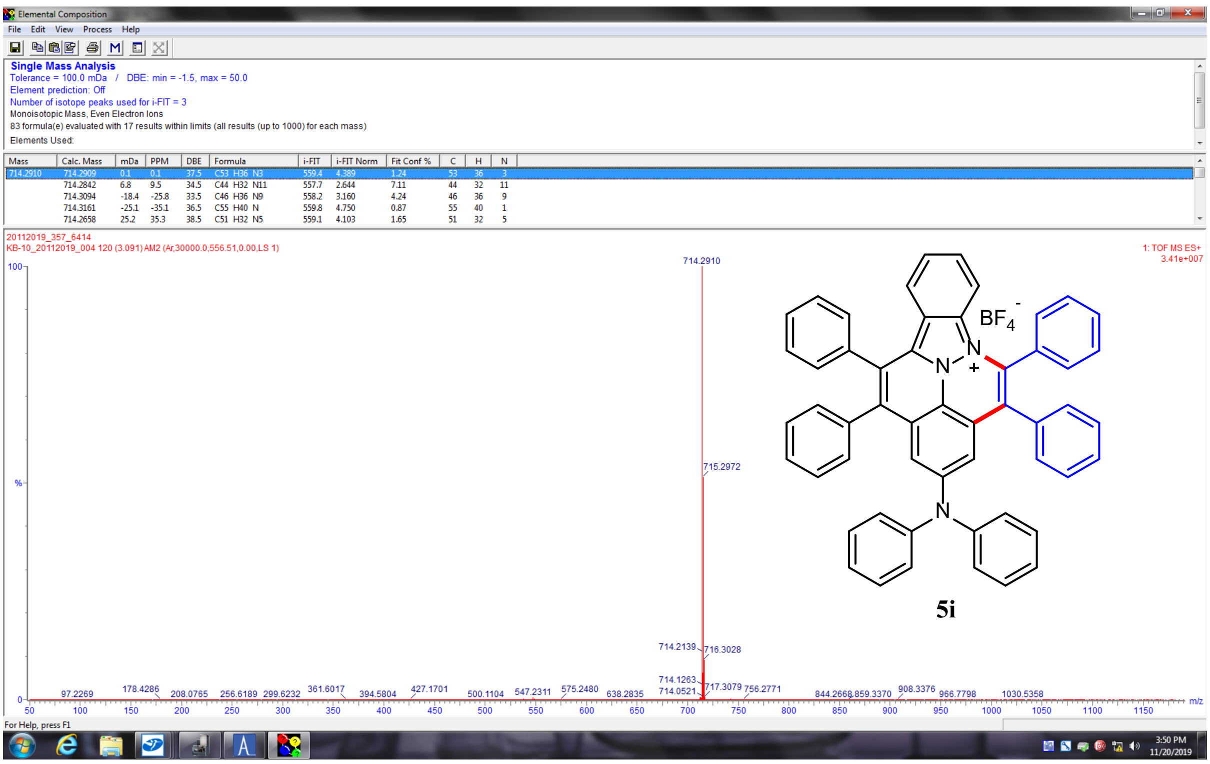


Figure S88: HRMS spectrum of compound **5i**

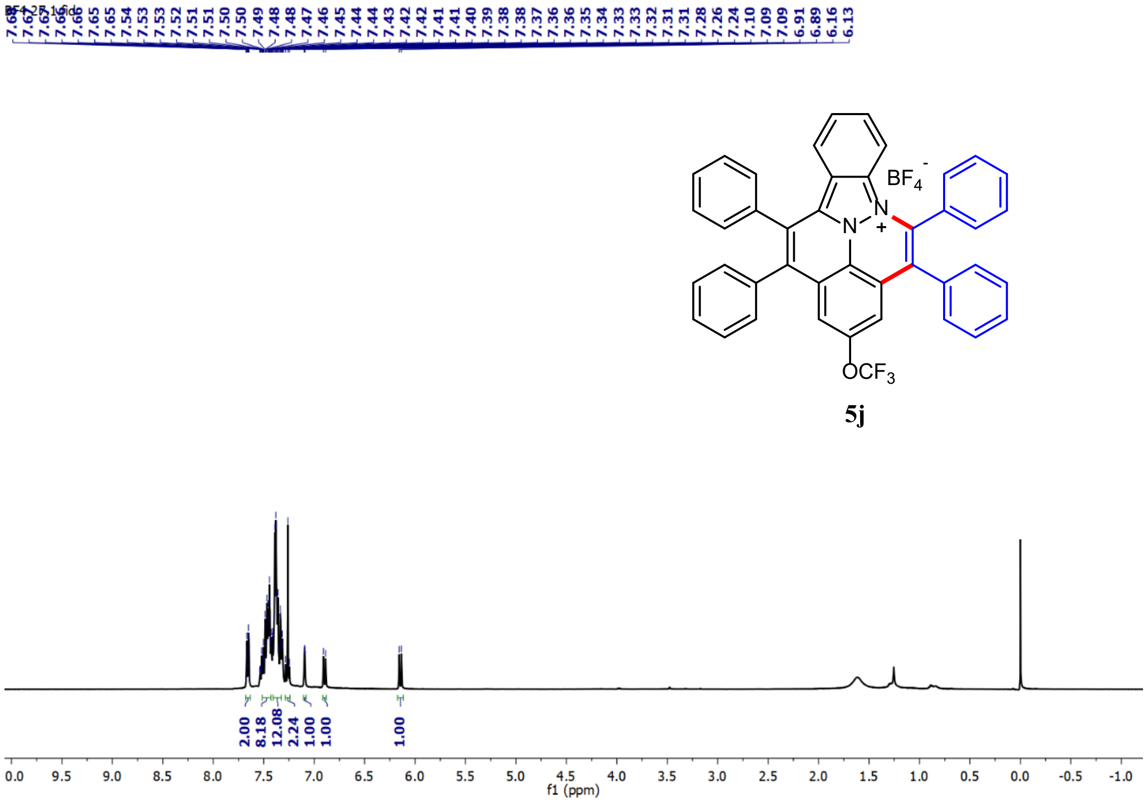


Figure S89: ^{1}H NMR spectrum of compound **5j** in $CDCl_3$

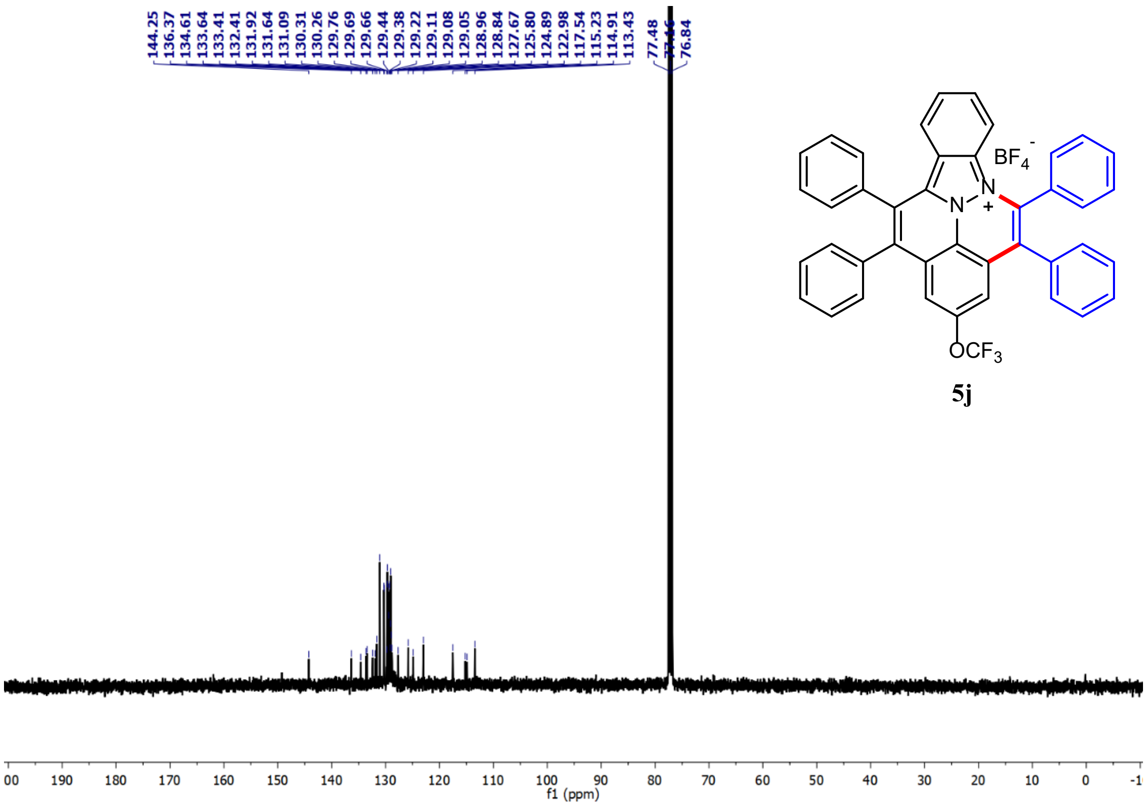


Figure S90: ^{13}C NMR spectrum of compound **5j** in $CDCl_3$

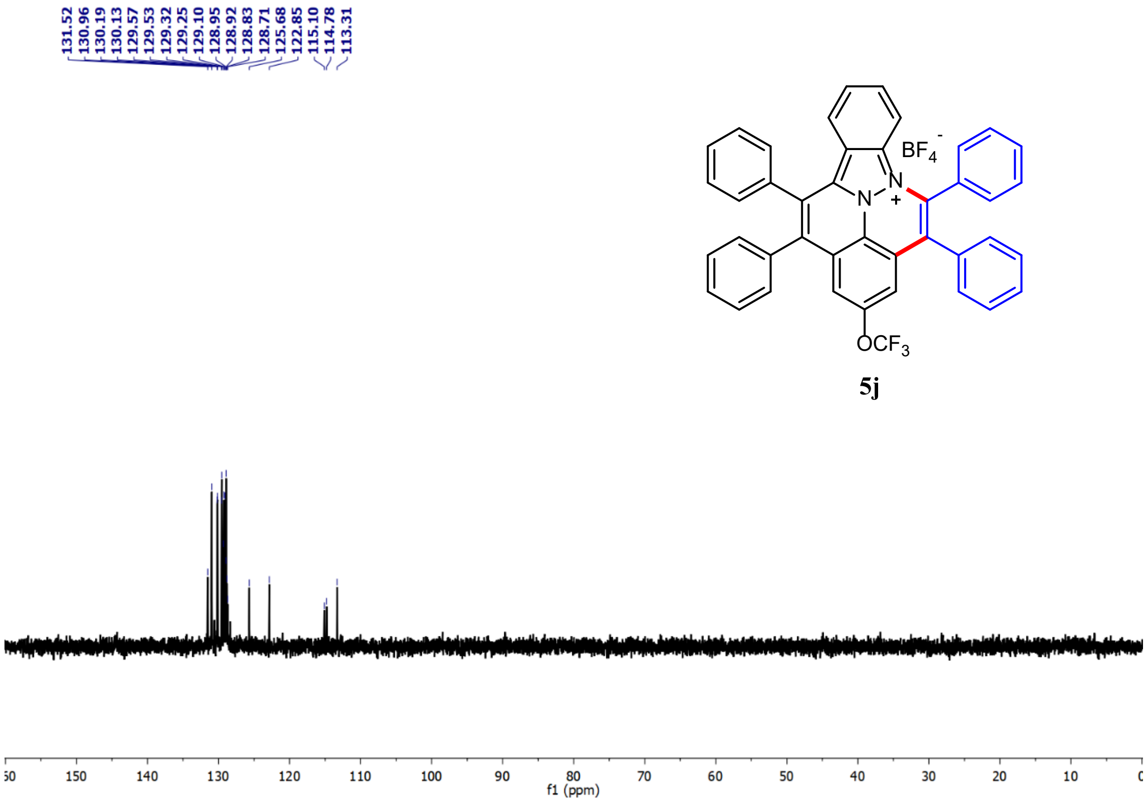


Figure S91: DEPT-135 NMR spectrum of compound **5j** in $CDCl_3$

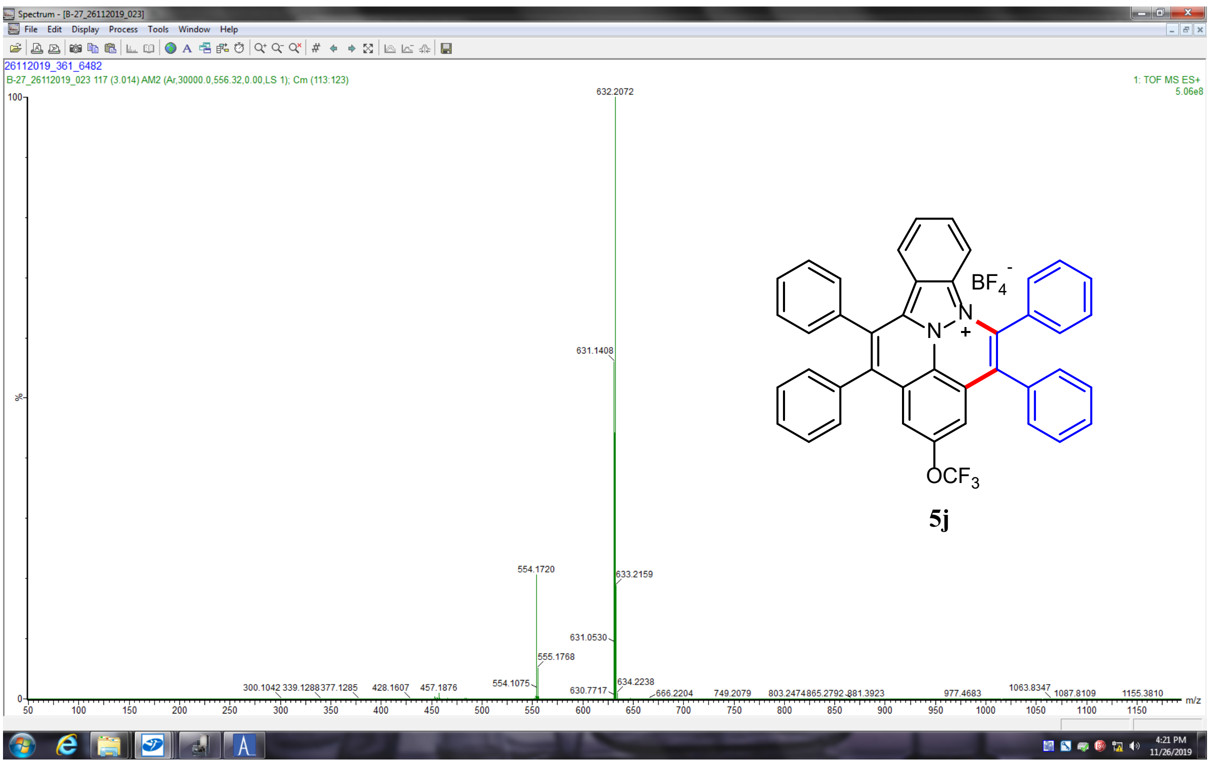


Figure S92: HRMS spectrum of compound **5j**

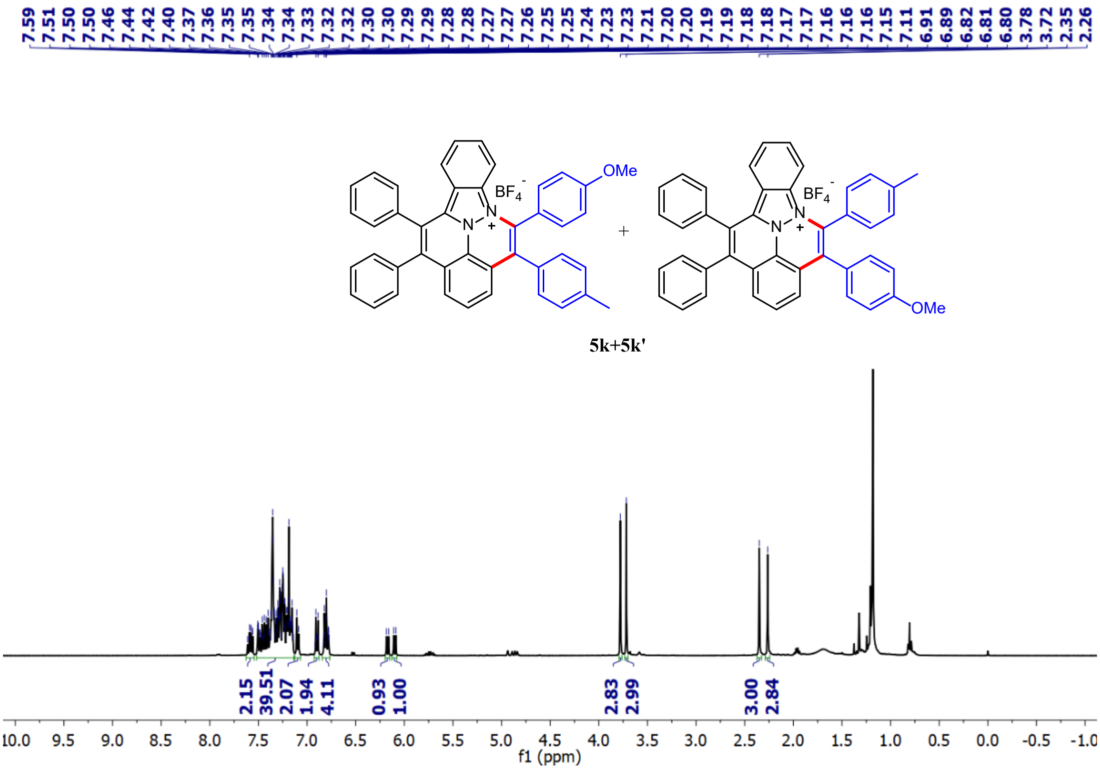


Figure S93: ^{1}H NMR spectrum of compound **5k** in $CDCl_3$

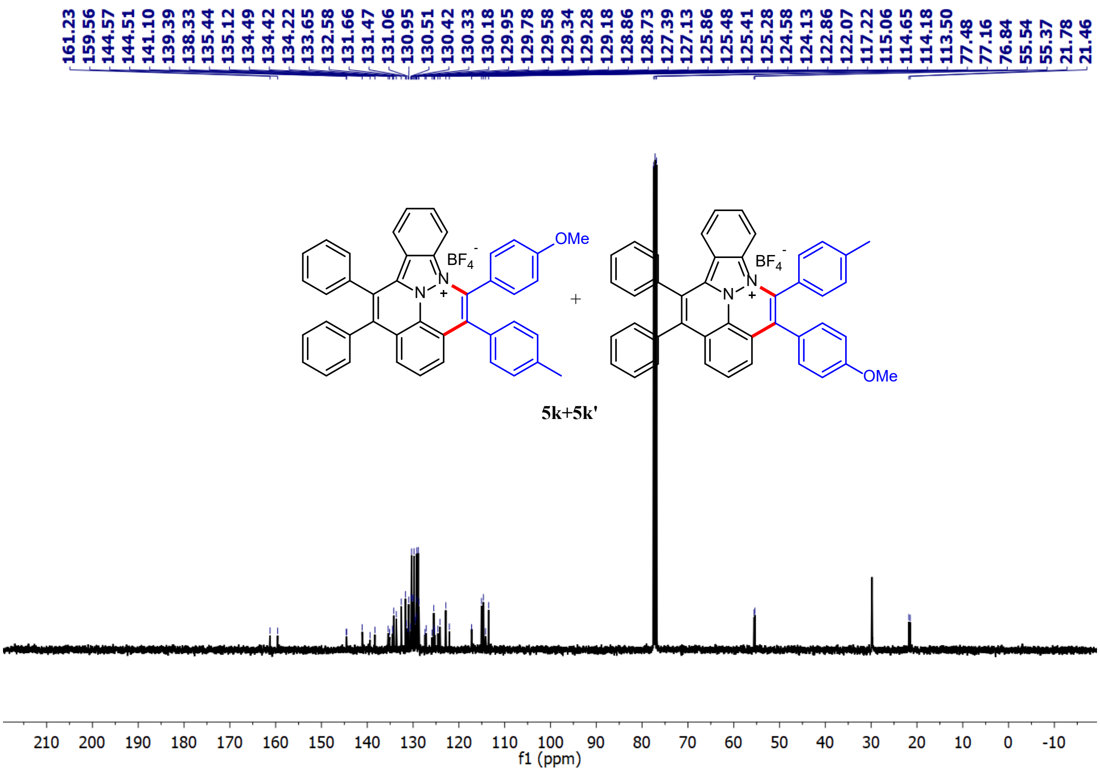


Figure S94: ^{13}C NMR spectrum of compound **5k** in $CDCl_3$

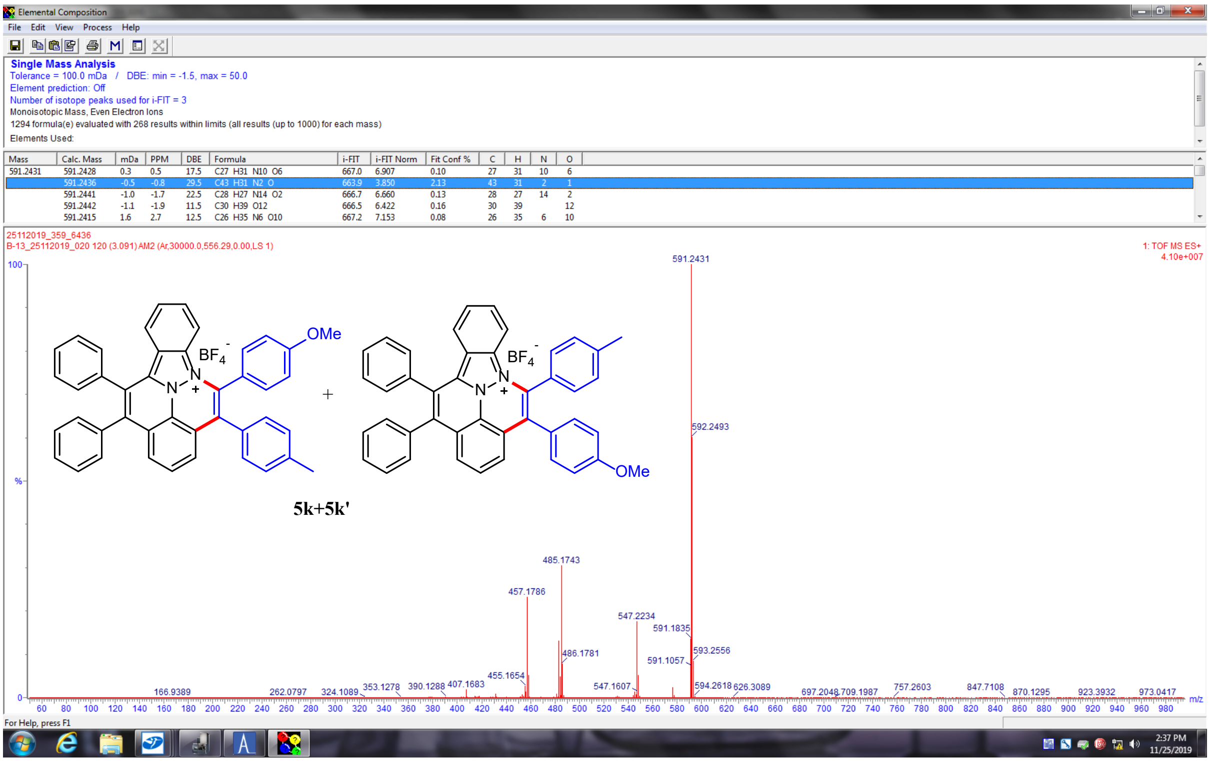


Figure S95: HRMS spectrum of compound **5k+5k'**

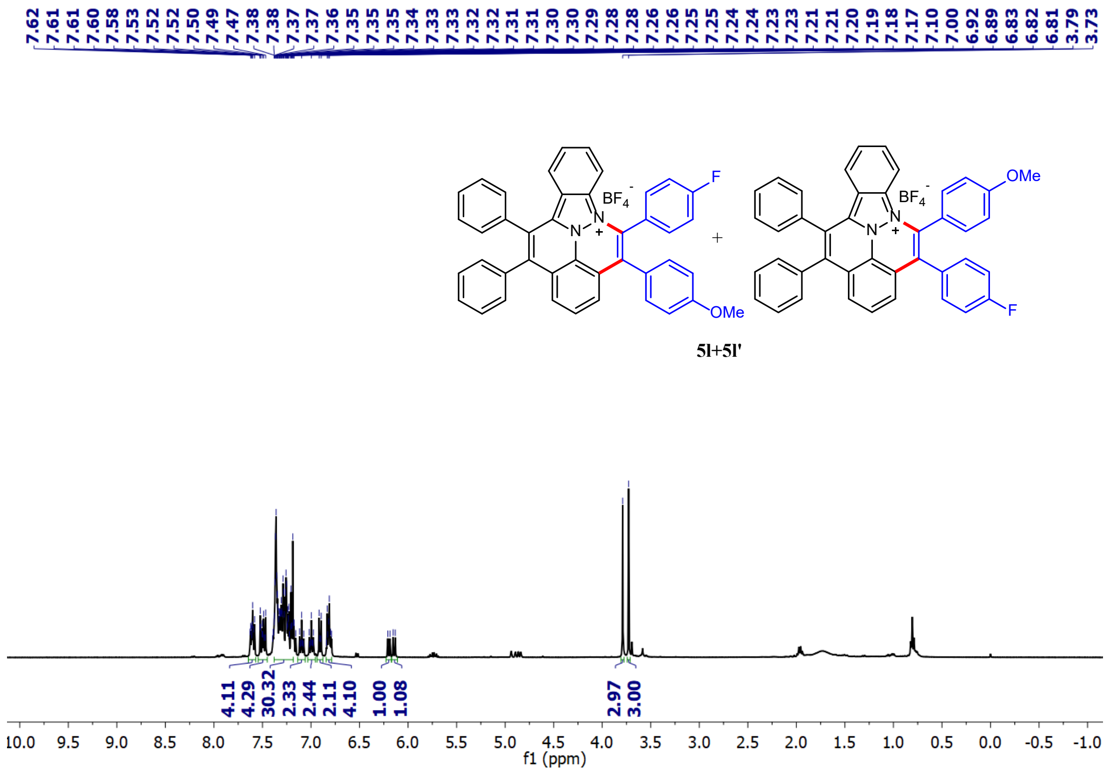


Figure S96: ^{1}H NMR spectrum of compound **5l** in $CDCl_3$

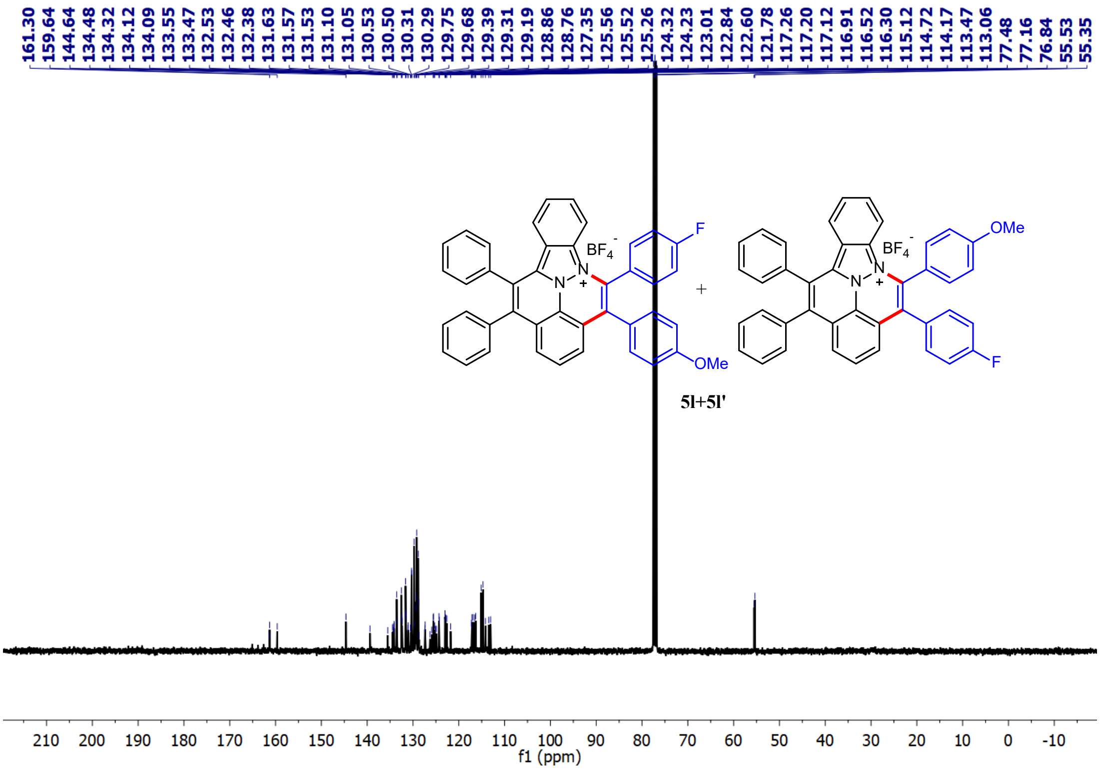


Figure S97: ^{13}C NMR spectrum of compound **5l** in $CDCl_3$

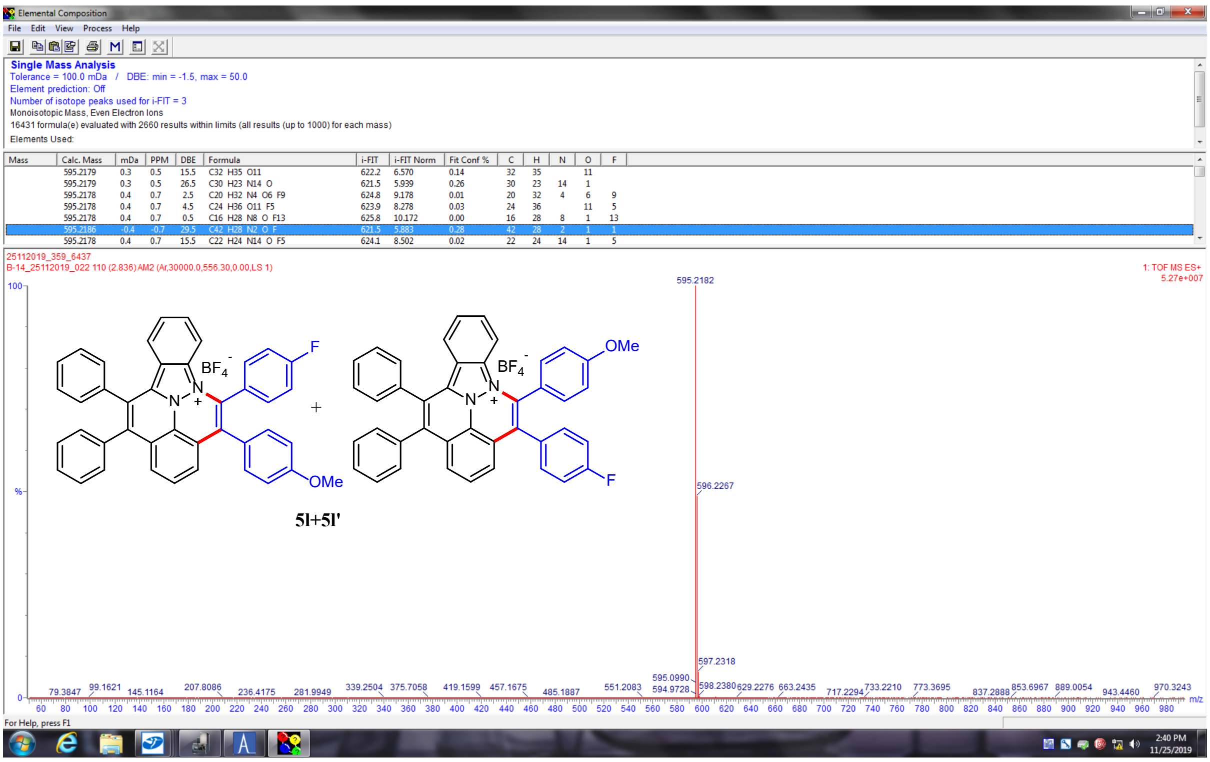


Figure S98: HRMS spectrum of compound **5l+5l'**

5. DFT Calculations

Table 2. Data of DFT studies[1]

Method	**B3LYP/6-311G***		
Compound	**LUMO** (eV)	**HOMO** (eV)	**Gap** (eV)
3a	-5.6346	-9.2603	3.6257
3b	-5.6934	-9.1038	3.4104
3c	-5.6850	-9.0847	3.3997
3d	-5.7168	-9.3781	3.6613
3e	-5.7206	-9.0012	3.2806
3f	-5.8308	-9.1160	3.2852
3g	-5.7962	-9.3231	3.5269
3h	-5.7775	-9.1544	3.3769
5a	-5.1511	-8.5408	3.3897
5b	-5.1040	-8.4167	3.3127
5c	-5.0251	-8.1794	3.1543
5d	-5.3217	-8.6695	3.3478
5e	-5.3013	-8.6377	3.3364
5f	-5.0958	-8.4758	3.38
5g	-5.0039	-8.3479	3.344
5h	-5.0814	-8.1149	3.0335
5i	-4.605	-7.466	2.86
5j	-5.31873	-8.6741	3.3553
5k	-5.0436	-8.3190	3.2754
5k'	-5.12689	-8.48288	3.3559
5l	-5.2531	-8.5745	3.3214
5l'	-5.2466	-8.5773	3.3307

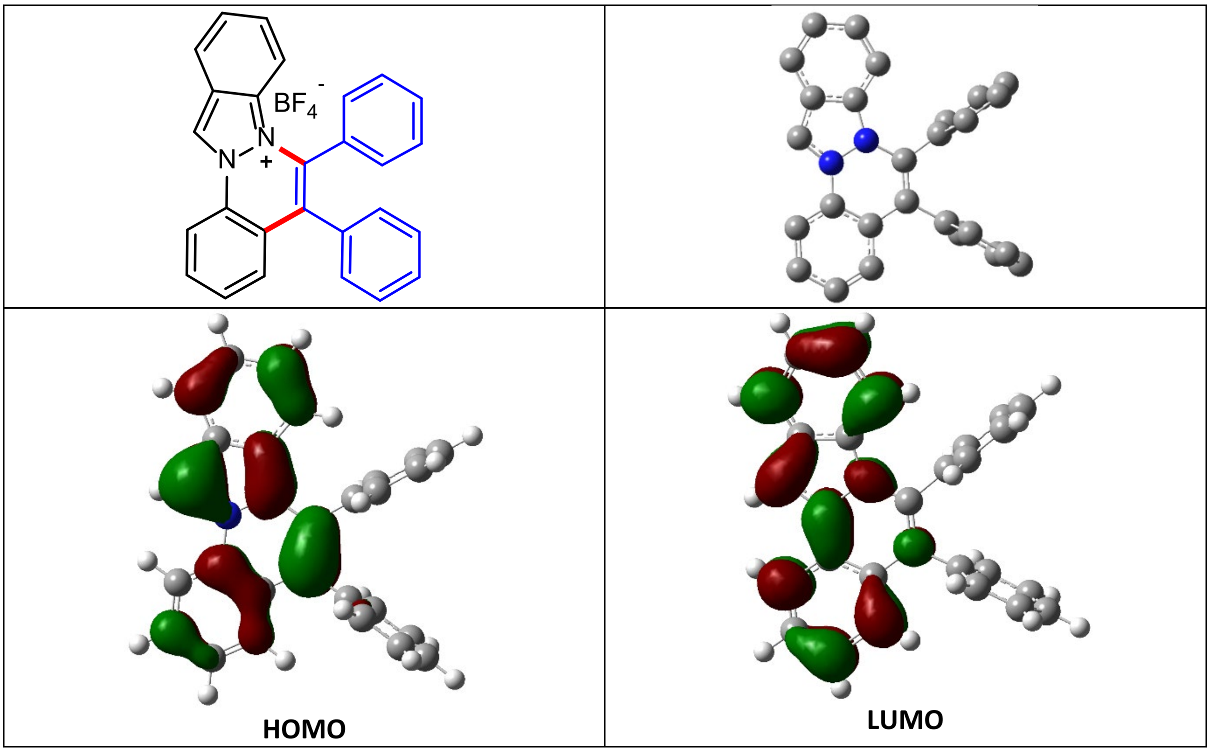


Figure S99: HOMO-LUMO of the compound **3a**

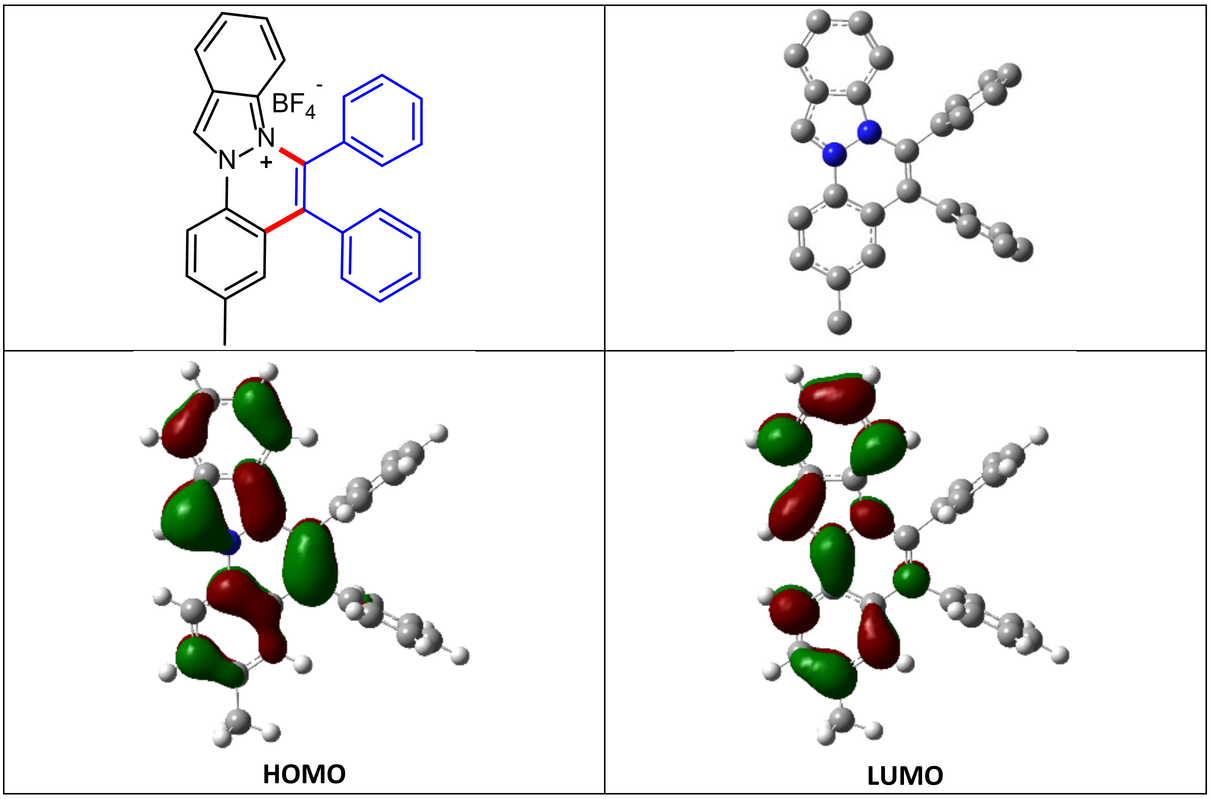


Figure S100: HOMO-LUMO of the compound **3b**

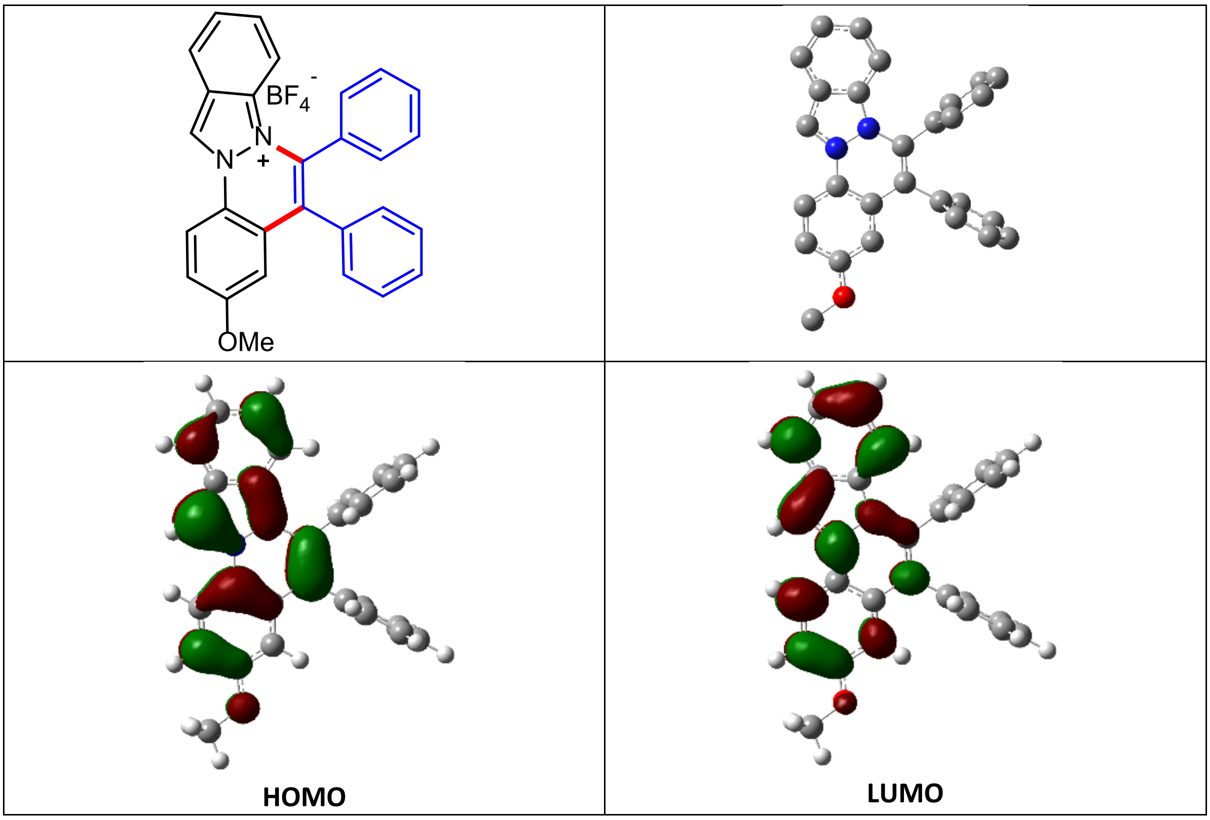


Figure S101: HOMO-LUMO of the compound **3c**

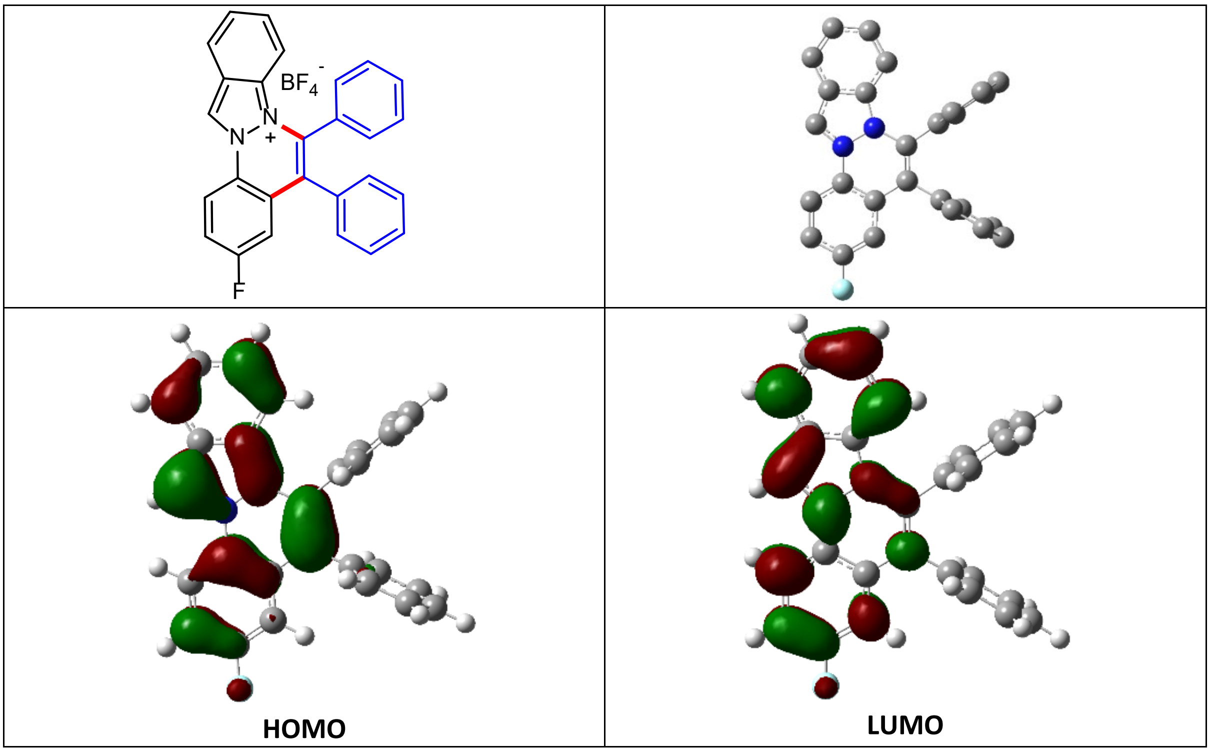


Figure S102: HOMO-LUMO of the compound **3d**

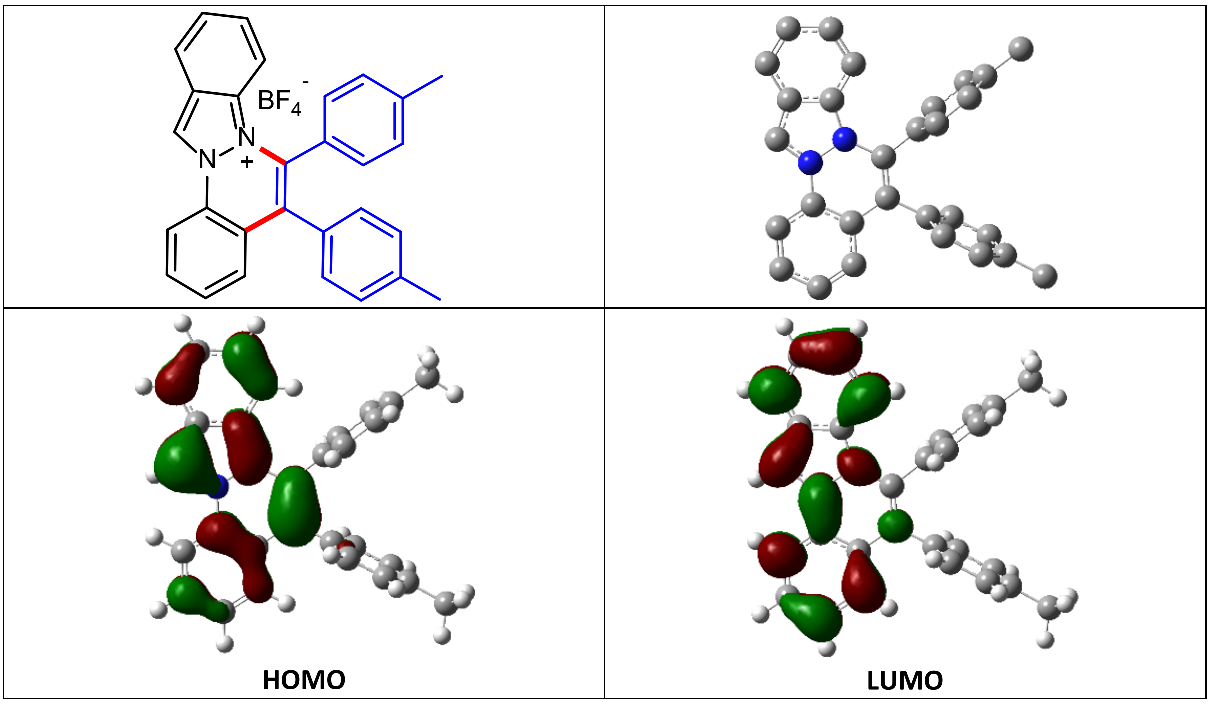


Figure S103: HOMO-LUMO of the compound **3e**

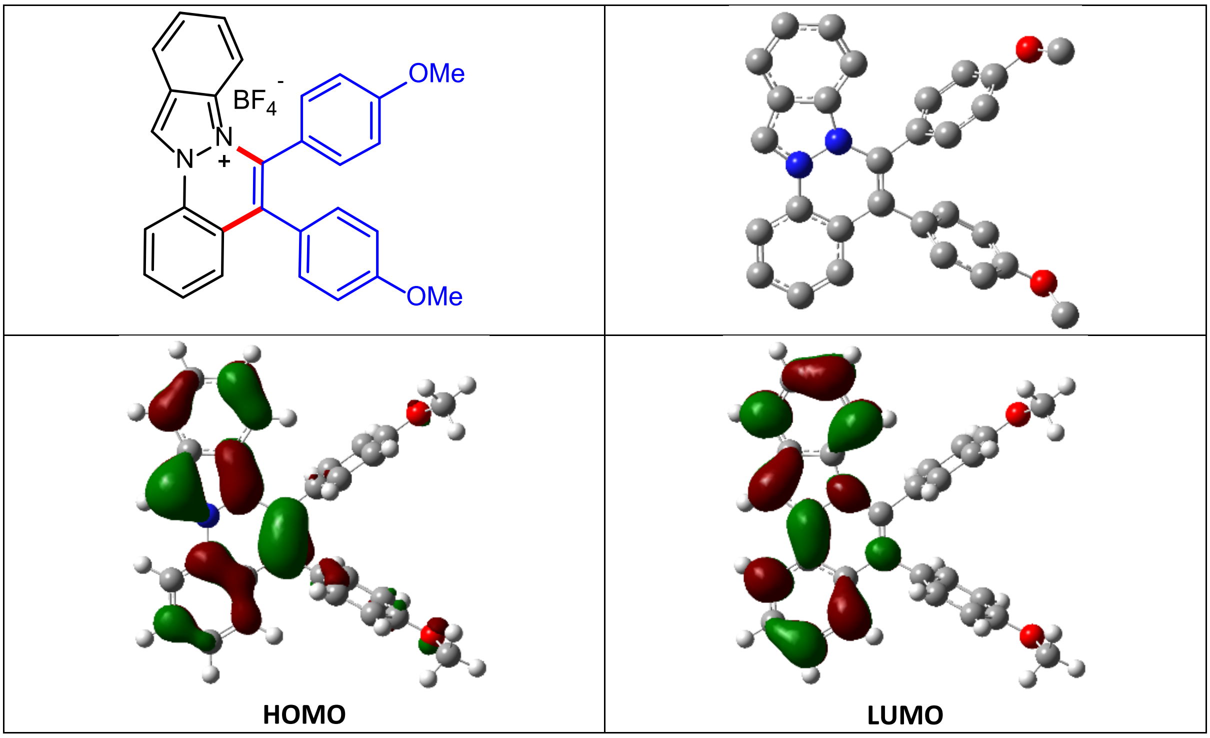


Figure S104: HOMO-LUMO of the compound **3f**

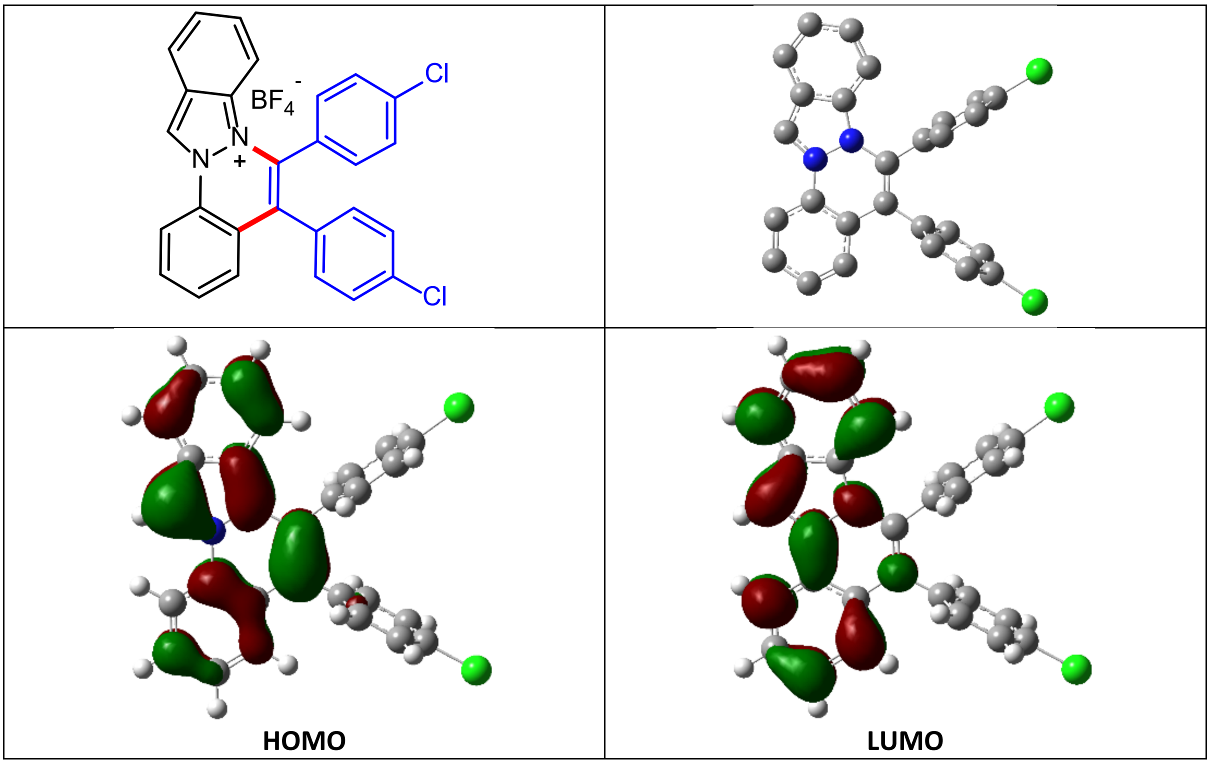


Figure S105: HOMO-LUMO of the compound **3g**

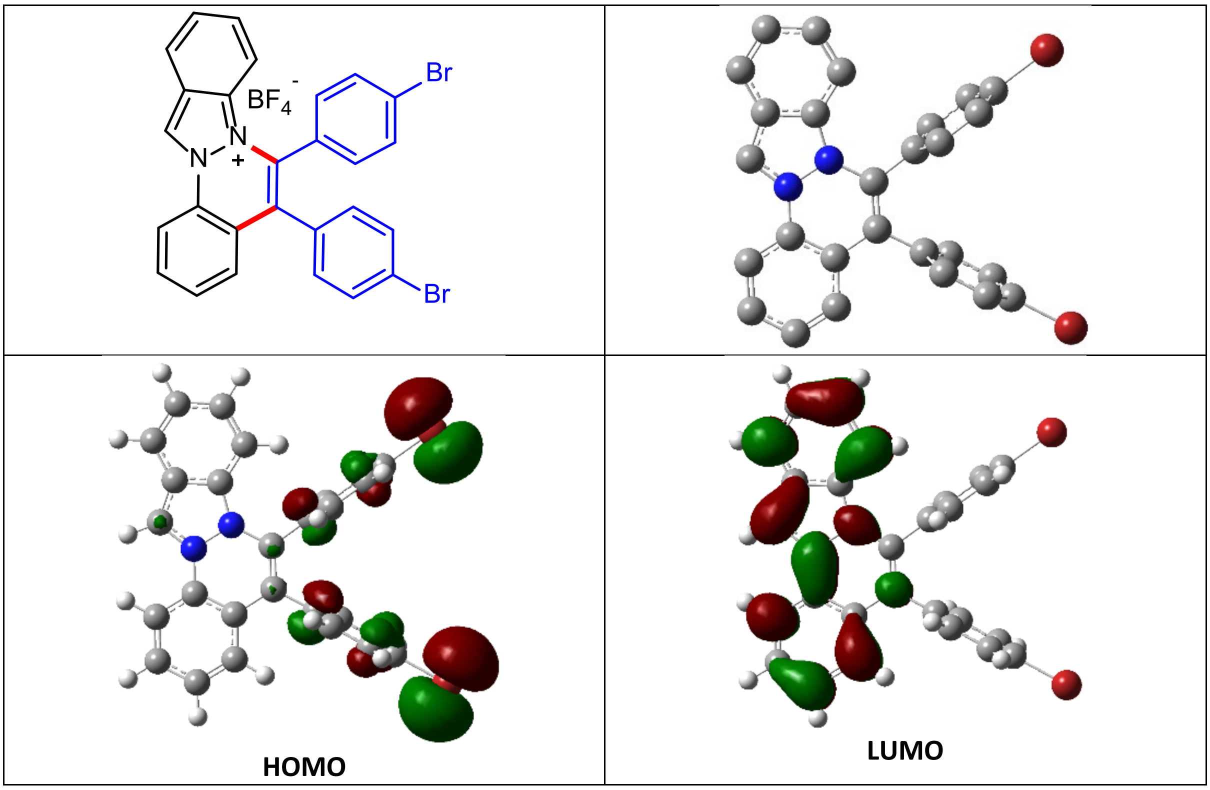


Figure S106: HOMO-LUMO of the compound **3h**

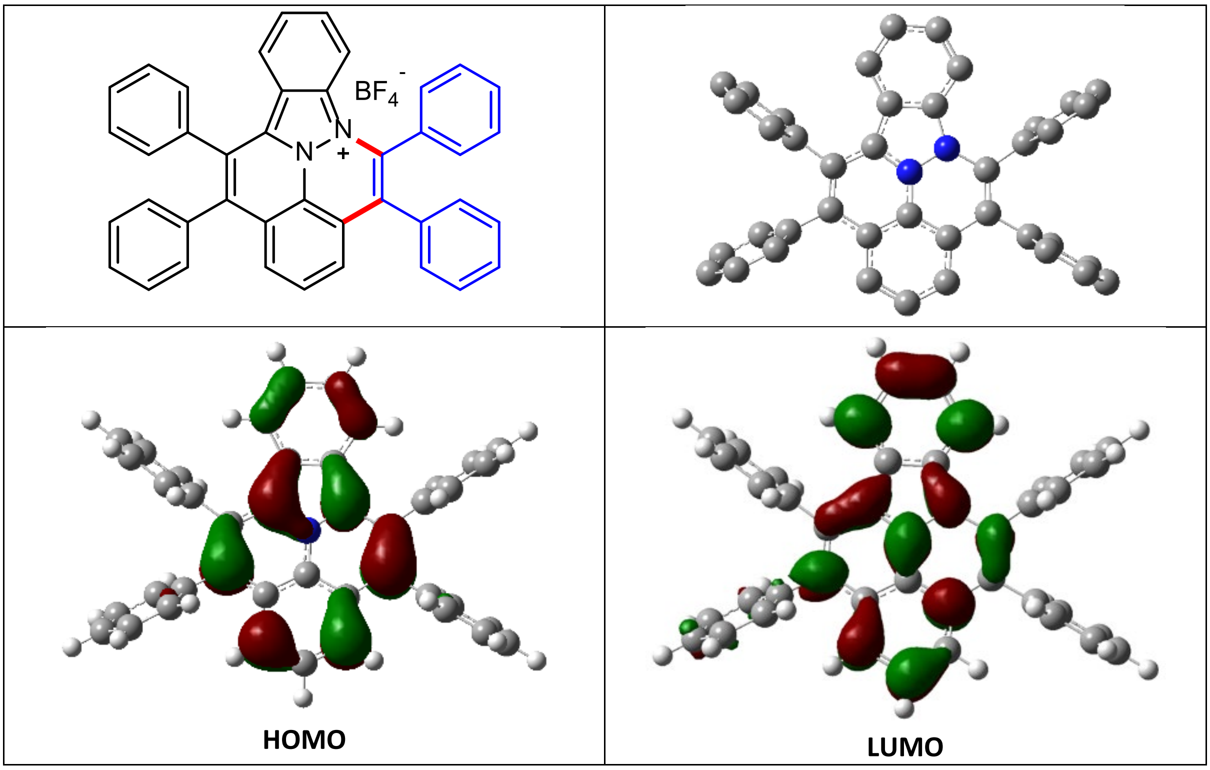


Figure S107: HOMO-LUMO of the compound **5a**

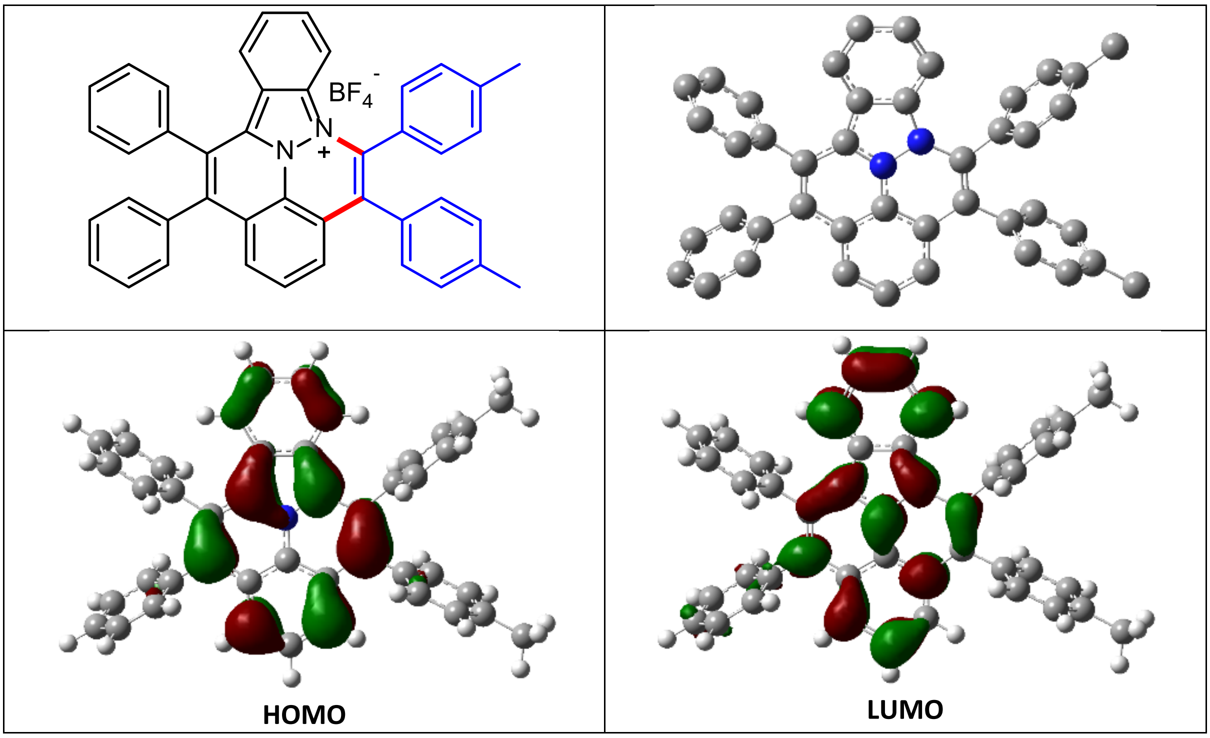


Figure S108: HOMO-LUMO of the compound **5b**

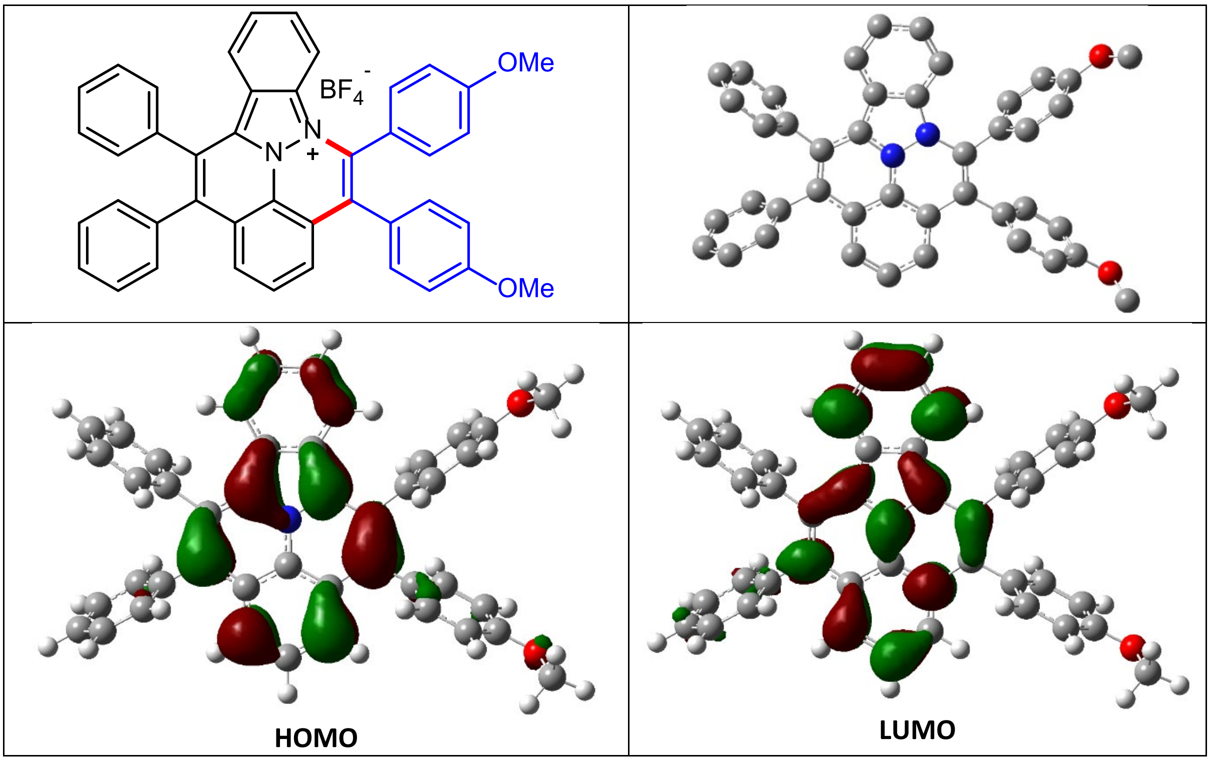


Figure S109: HOMO-LUMO of the compound **5c**

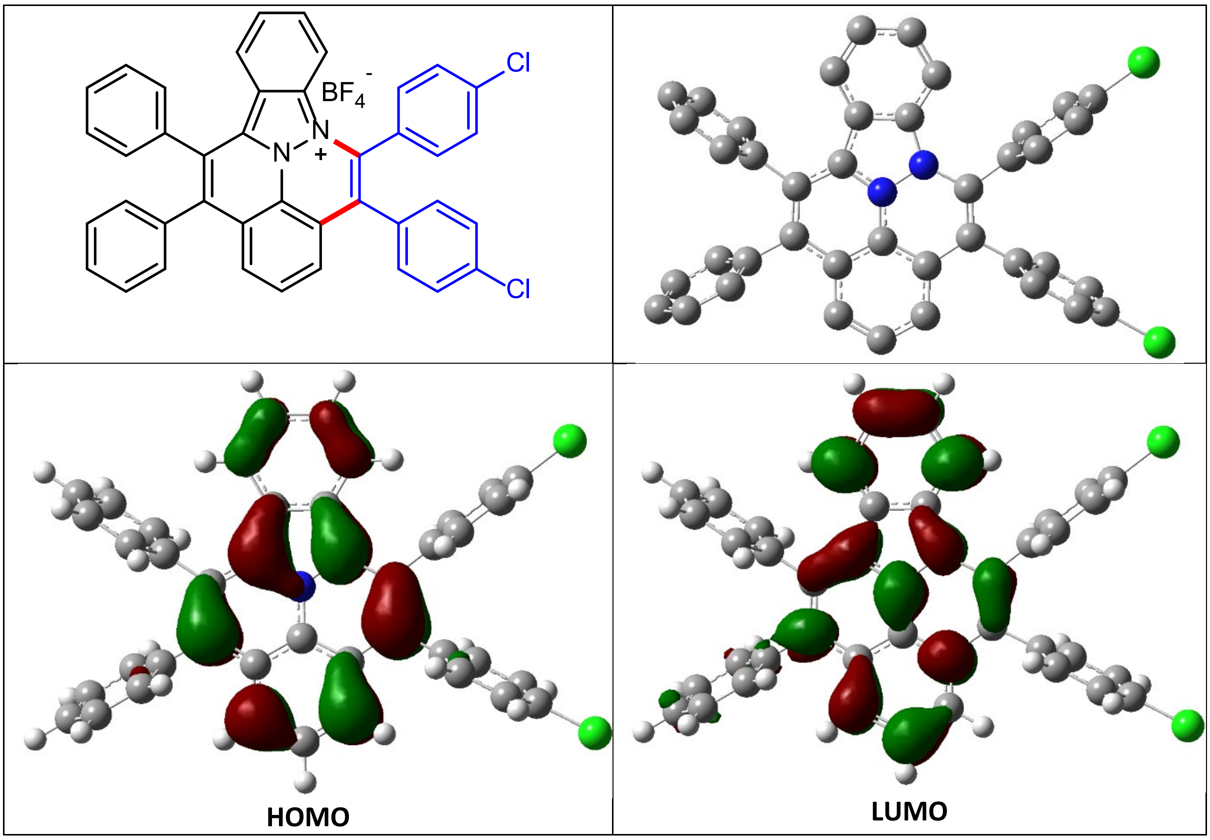


Figure S110: HOMO-LUMO of the compound **5d**

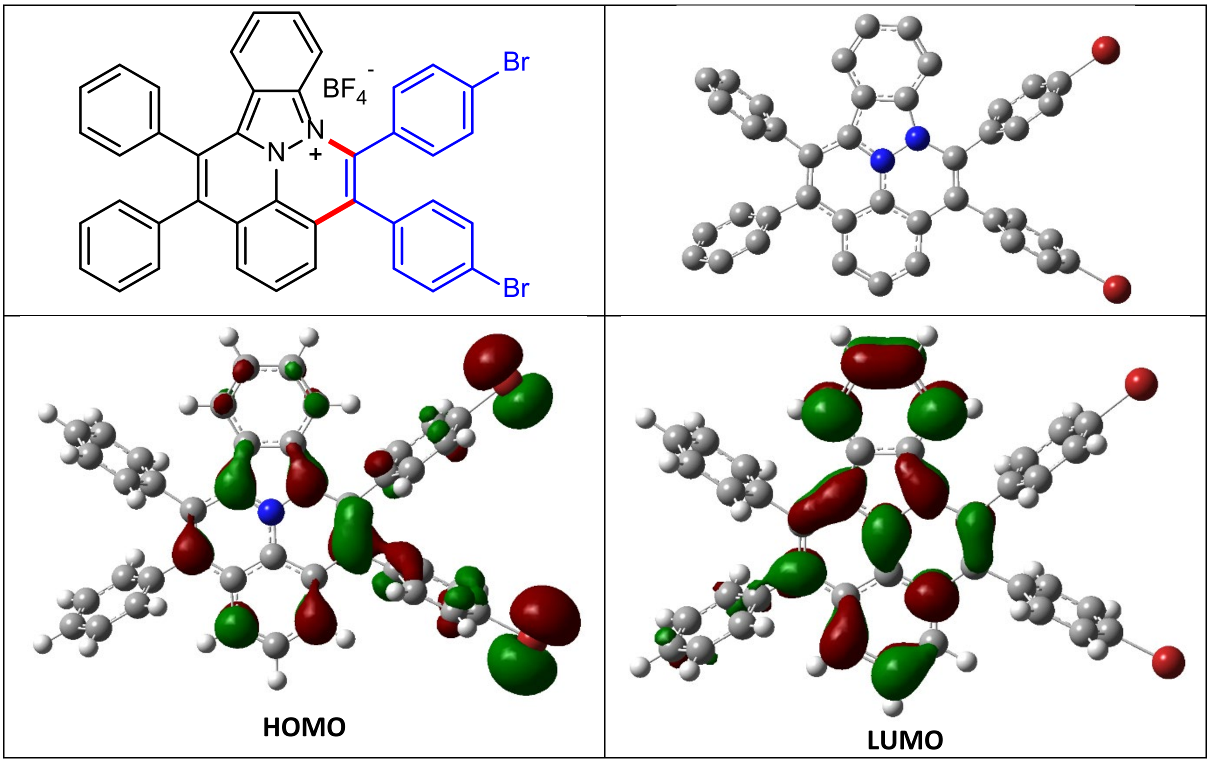


Figure S111: HOMO-LUMO of the compound **5e**

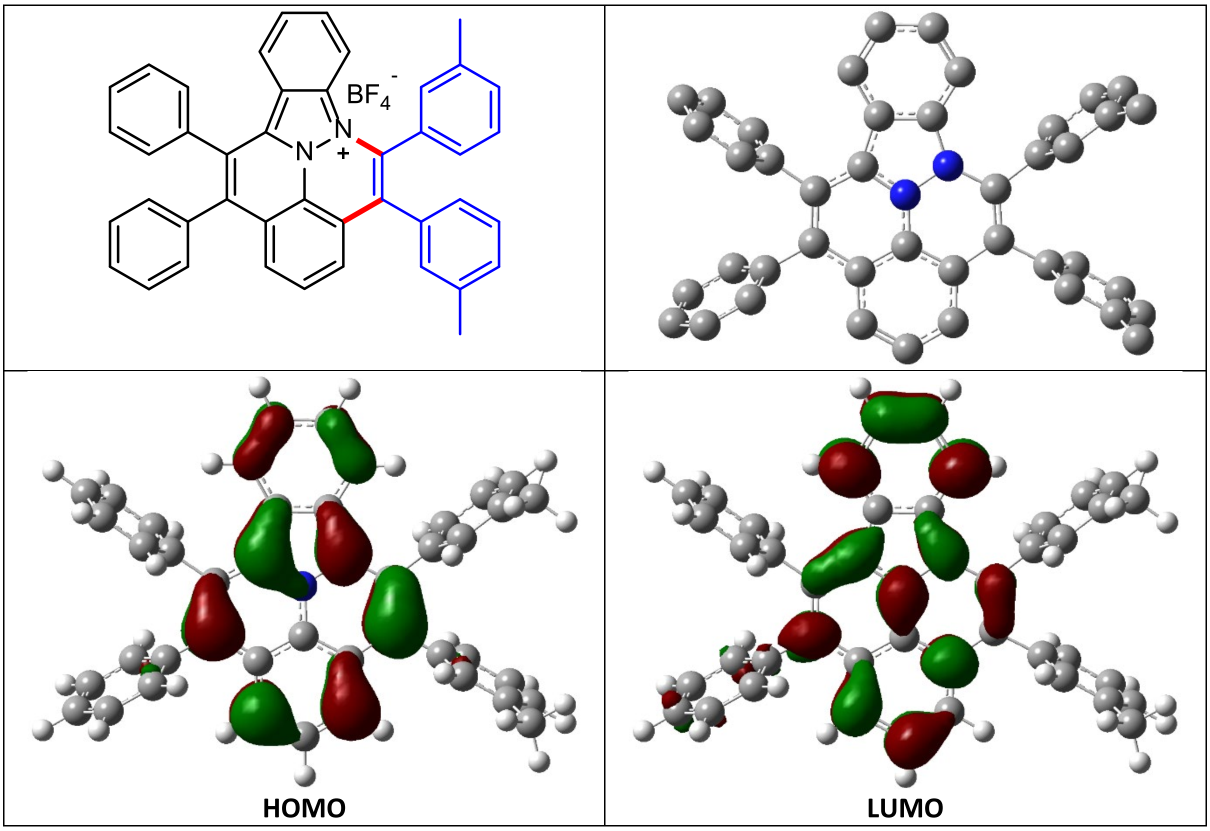


Figure S112: HOMO-LUMO of the compound **5f**

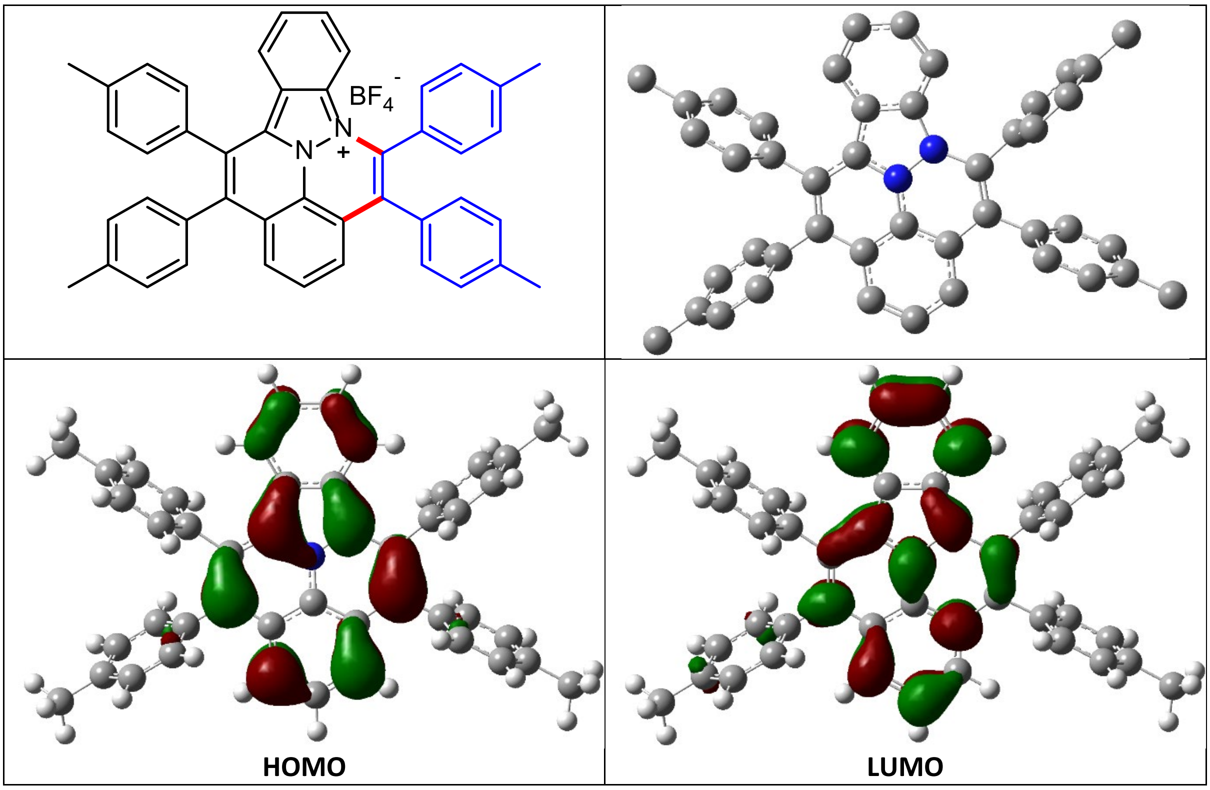


Figure S113: HOMO-LUMO of the compound **5g**

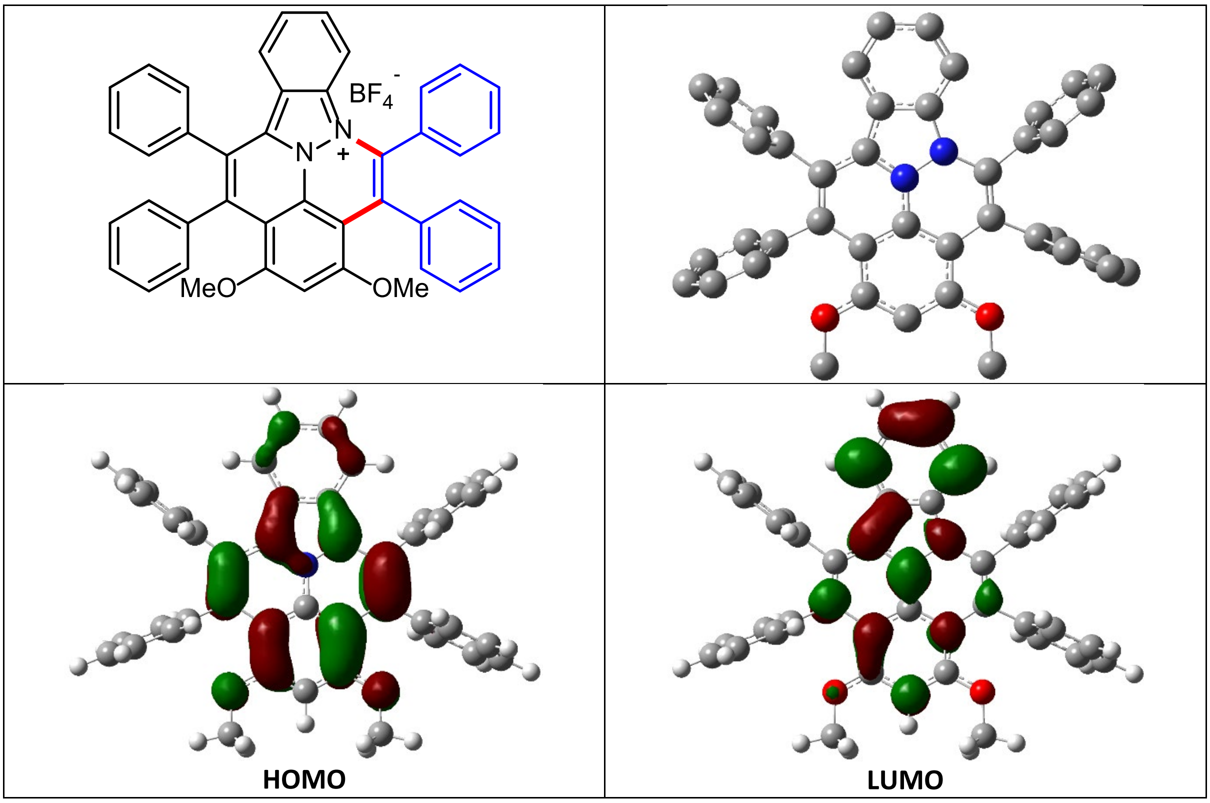


Figure S114: HOMO-LUMO of the compound **5h**

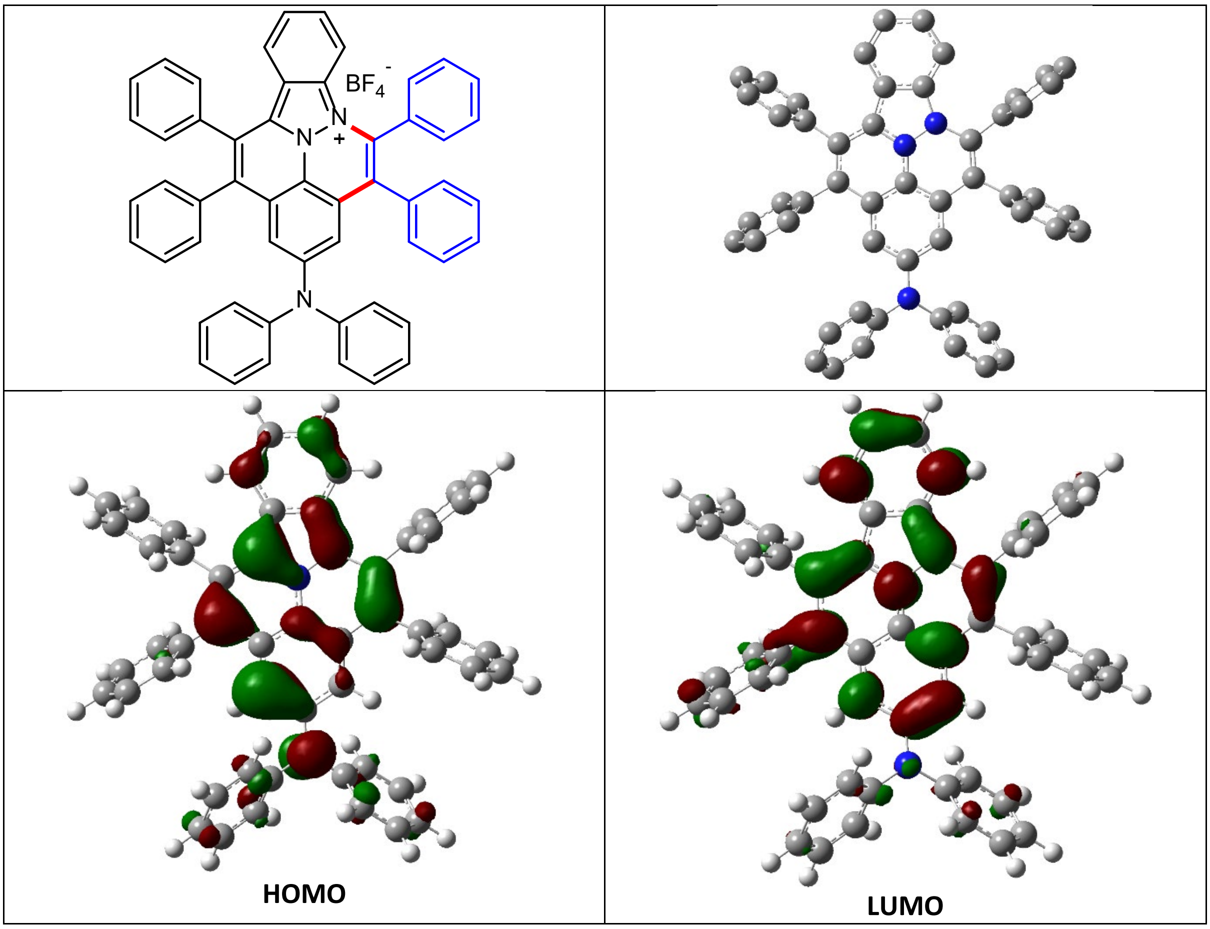


Figure S115: HOMO-LUMO of the compound **5i**

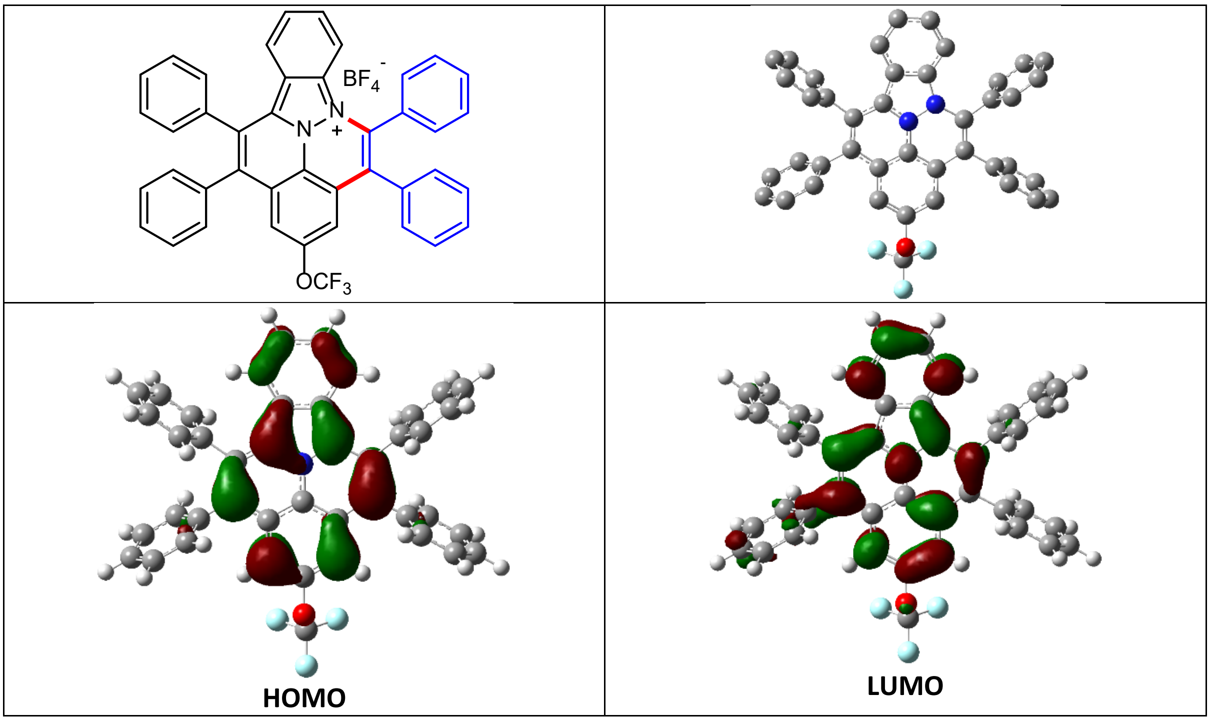


Figure S116: HOMO-LUMO of the compound **5j**

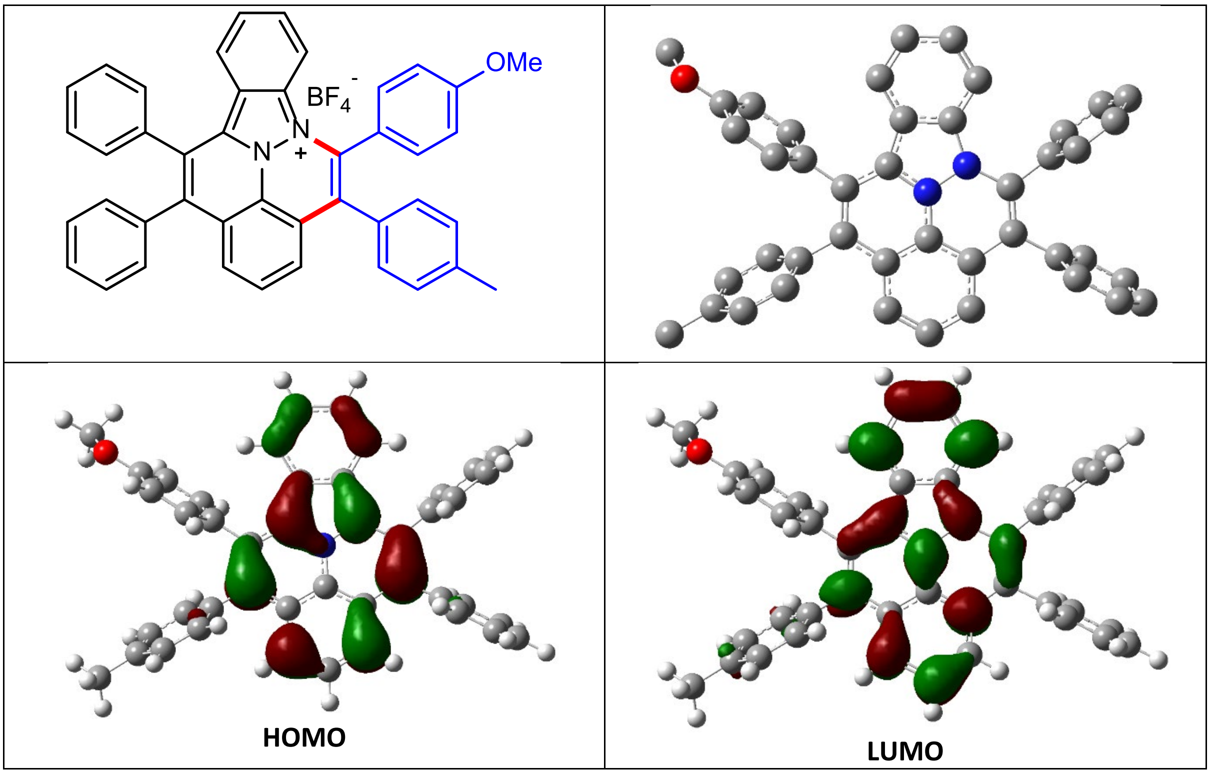


Figure S117: HOMO-LUMO of the compound **5k**

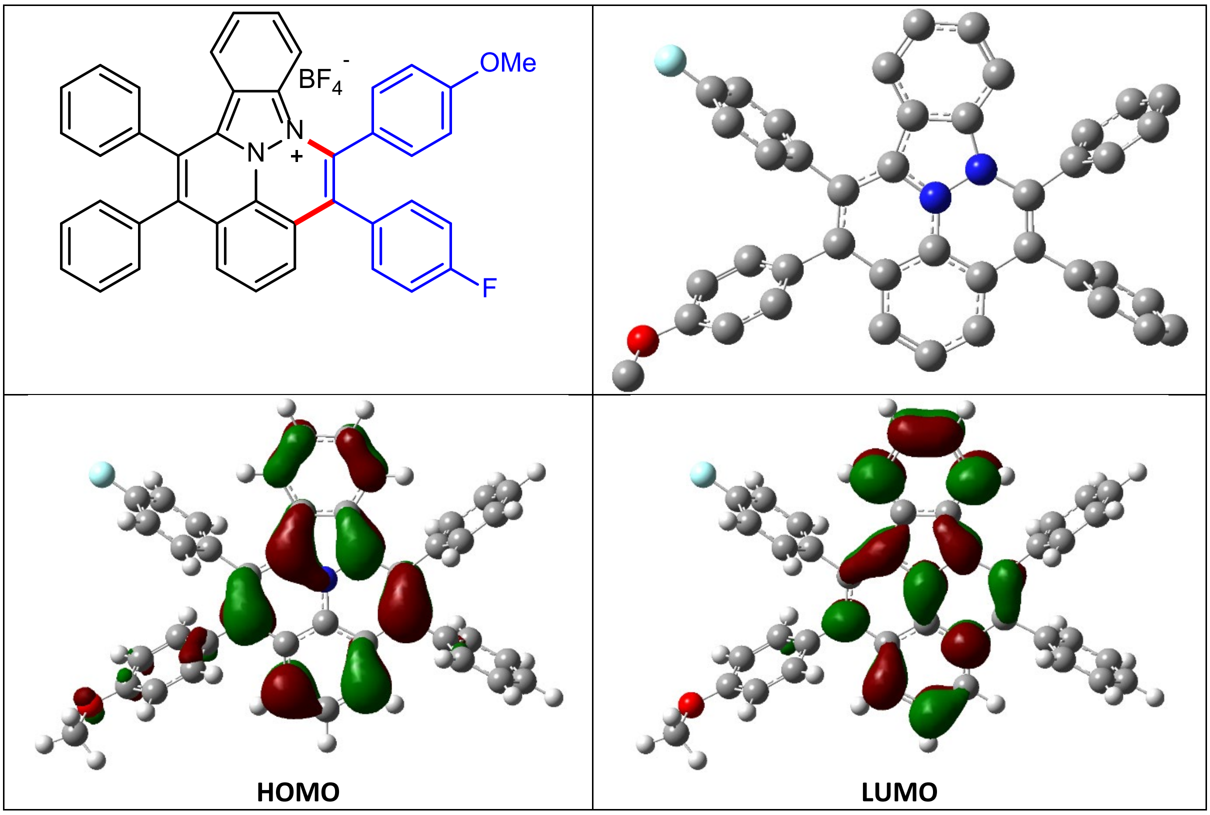


Figure S118: HOMO-LUMO of the compound **5l**

6. Reference

1. Gaussian 16, Revision C.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, and D. J. Fox, Gaussian, Inc., Wallingford CT, **2016**.