Supporting information For

Novel indole fused chromene derivatives: Synthesis, cytotoxic properties and key computational insights

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- **Table S1**: Physicochemical properties of compounds **4a-j**
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Table S1: Physicochemical properties of compounds **4a-j**

Molecule	#Heavy atoms	#Aromatic heavy atoms	Fraction Csp3	#Rotatable bonds	#H-bond acceptors	#H-bond donors	MR	TPSA
4a	26	9	0.33	1	3	1	99.35	81.04
4b	27	9	0.36	2	3	1	104.16	81.04
4c	27	9	0.33	1	4	1	99.31	81.04
4d	28	9	0.36	2	4	1	104.11	81.04
4e	29	9	0.33	2	5	1	108.17	126.86
4f	30	9	0.36	3	5	1	112.98	126.86
4g	28	9	0.36	2	4	1	105.84	90.27
4h	29	9	0.39	3	4	1	110.65	90.27
4i	27	9	0.33	1	3	1	107.05	81.04
4j	28	9	0.36	2	3	1	111.86	81.04
CTRL	26	12	0.17	3	4	3	101.36	129.54

Table S2: Lipophilicity and water solubility of compounds **4a-j**

Molecule	iLOGP	XLOGP3	WLOGP	MLOGP	Silicos-IT Log P	Consensus Log P	ESOL Log S	ESOL Solubility (mg/ml)
4a	2.81	2.94	3.63	1.57	3.01	2.79	-4.04	3.20E-02
4b	2.97	3.24	4.11	1.79	3.4	3.1	-4.24	2.10E-02
4c	2.94	3.04	4.19	1.95	3.43	3.11	-4.2	2.30E-02
4d	3.11	3.34	4.67	2.17	3.82	3.42	-4.4	1.50E-02
4e	2.57	2.77	3.54	1.46	0.85	2.24	-4.12	3.01E-02
4f	2.73	3.07	4.02	1.68	1.25	2.55	-4.32	1.95E-02
4g	3.04	2.91	3.64	1.24	3.07	2.78	-4.12	2.87E-02
4h	3.03	3.21	4.12	1.46	3.47	3.06	-4.32	1.87E-02
4i	3.2	3.63	4.39	2.17	3.69	3.42	-4.95	4.78E-03
4j	3.38	3.93	4.87	2.38	4.08	3.73	-5.15	3.10E-03
CTRL	26	12	0.17	3	4	3	101.36	129.54

Table S3: Some other water solubility parameters of compounds **4a-j**

Molecule	ESOL Class	Ali Log S	Ali Solubility (mg/ml)	Ali Solubility (mol/l)	Ali Class	Silicos-IT LogSw	Silicos-IT Solubility (mg/ml)	Silicos-IT Solubility (mol/l)	Silicos-IT class
4a	Moderately soluble	-4.3	1.73E-02	4.97E-05	Moderately soluble	-5.13	2.55E-03	7.35E-06	Moderately soluble
4b	Moderately soluble	-4.62	8.77E-03	2.43E-05	Moderately soluble	-5.53	1.07E-03	2.96E-06	Moderately soluble
4c	Moderately soluble	-4.41	1.43E-02	3.91E-05	Moderately soluble	-5.4	1.45E-03	3.97E-06	Moderately soluble
4d	Moderately soluble	-4.72	7.25E-03	1.91E-05	Moderately soluble	-5.79	6.08E-04	1.60E-06	Moderately soluble
4e	Moderately soluble	-5.09	3.19E-03	8.13E-06	Moderately soluble	-4.48	1.30E-02	3.31E-05	Moderately soluble
4f	Moderately soluble	-5.4	1.61E-03	3.97E-06	Moderately soluble	-4.87	5.44E-03	1.34E-05	Moderately soluble
4g	Moderately soluble	-4.47	1.29E-02	3.42E-05	Moderately soluble	-5.24	2.17E-03	5.75E-06	Moderately soluble
4h	Moderately soluble	-4.78	6.53E-03	1.67E-05	Moderately soluble	-5.63	9.09E-04	2.32E-06	Moderately soluble
4i	Moderately soluble	-5.02	4.07E-03	9.55E-06	Moderately soluble	-5.92	5.10E-04	1.20E-06	Moderately soluble

4j	Moderately soluble	-5.33	2.05E-03	4.66E-06	Moderately soluble	-6.31	2.14E-04	4.86E-07	Poorly soluble
CTRL	Moderately soluble	-4.94	4.81E-03	1.15E-05	Moderately soluble	-5.25	2.36E-03	5.65E-06	Moderately soluble

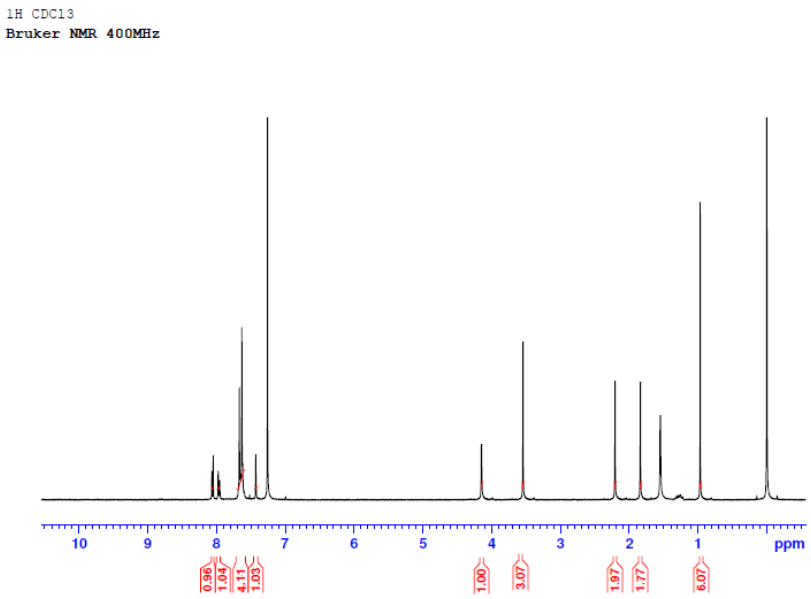
Table S4: Pharmacokinetics parameters of compounds **4a-j**

Molecule	GI absorption	BBB permeant	Pgp substrate	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor	log Kp (cm/s)
4a	High	No	Yes	Yes	Yes	Yes	No	Yes	-6.33
4b	High	No	Yes	Yes	Yes	Yes	No	Yes	-6.2
4c	High	No	Yes	Yes	Yes	Yes	No	Yes	-6.37
4d	High	No	Yes	No	Yes	Yes	No	Yes	-6.24
4e	High	No	Yes	No	Yes	Yes	No	Yes	-6.73
4f	Low	No	Yes	No	Yes	Yes	No	Yes	-6.6
4g	High	No	Yes	No	Yes	Yes	No	Yes	-6.54
4h	High	No	Yes	No	Yes	Yes	No	Yes	-6.41
4i	High	No	Yes	Yes	Yes	Yes	No	Yes	-6.32
4j	High	No	Yes	No	Yes	Yes	No	Yes	-6.2
CTRL	High	No	Yes	Yes	Yes	Yes	Yes	Yes	-7.02

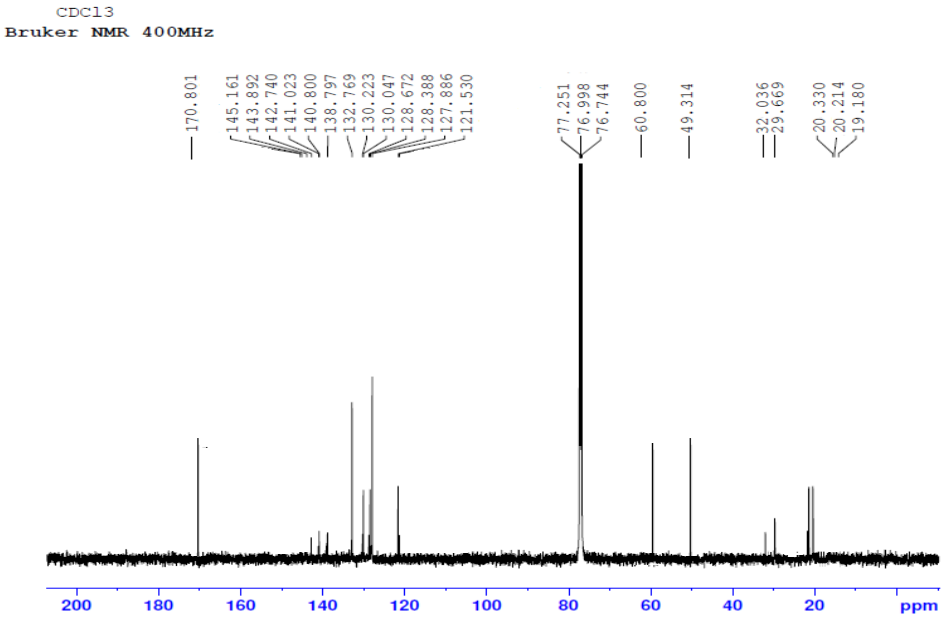
Table S5: Drug likeness and medicinal chemistry of compounds **4a-j**

Molecule	Lipinski #violations	Ghose #violations	Veber #violations	Egan #violations	Muegge #violations	Bioavailability Score	PAINS #alerts	Brenk #alerts	Leadlikeness #violations	Synthetic accesibility
4a	0	0	0	0	0	0.56	0	0	0	4.19
4b	0	0	0	0	0	0.56	0	0	1	4.29
4c	0	0	0	0	0	0.56	0	0	1	4.18
4d	0	0	0	0	0	0.56	0	0	1	4.3
4e	0	0	0	0	0	0.56	0	2	1	4.29
4f	0	0	0	0	0	0.56	0	2	1	4.39
4g	0	0	0	0	0	0.56	0	0	1	4.27
4h	0	0	0	0	0	0.56	0	0	1	4.38
4i	0	0	0	0	0	0.56	0	0	2	4.19
4j	0	0	0	0	0	0.56	0	0	2	4.29
CTRL	0	0	0	0	0	0.55	0	1	1	4.14

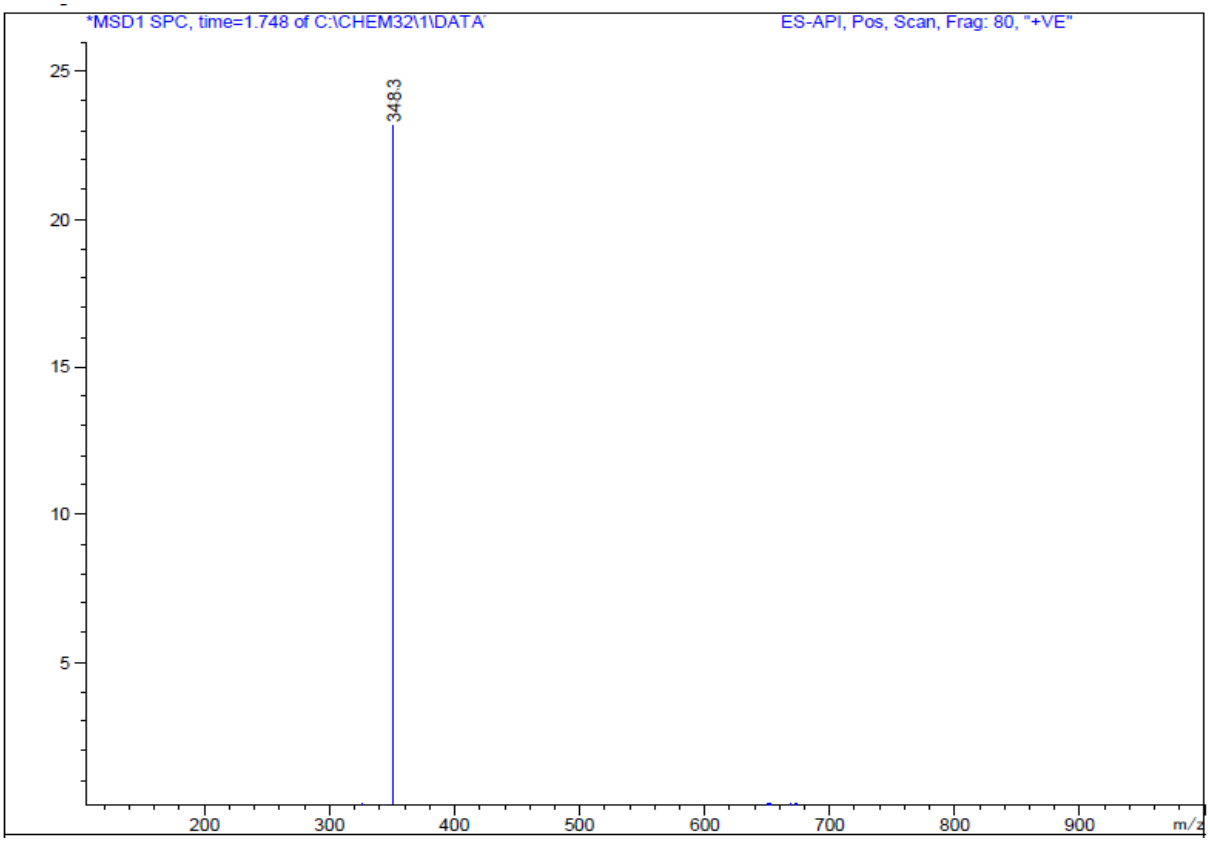
Spectroscopic Characterization of the Synthesized Compounds



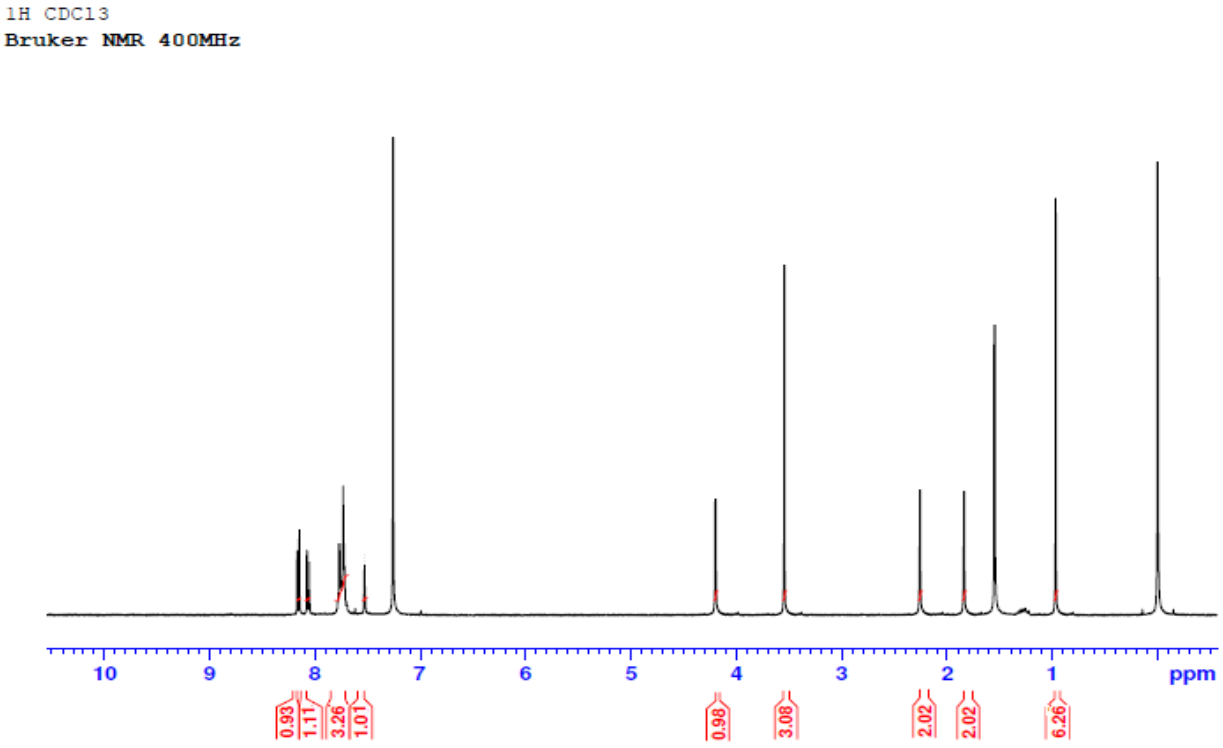
^{1}H NMR spectrum of compound **4a**



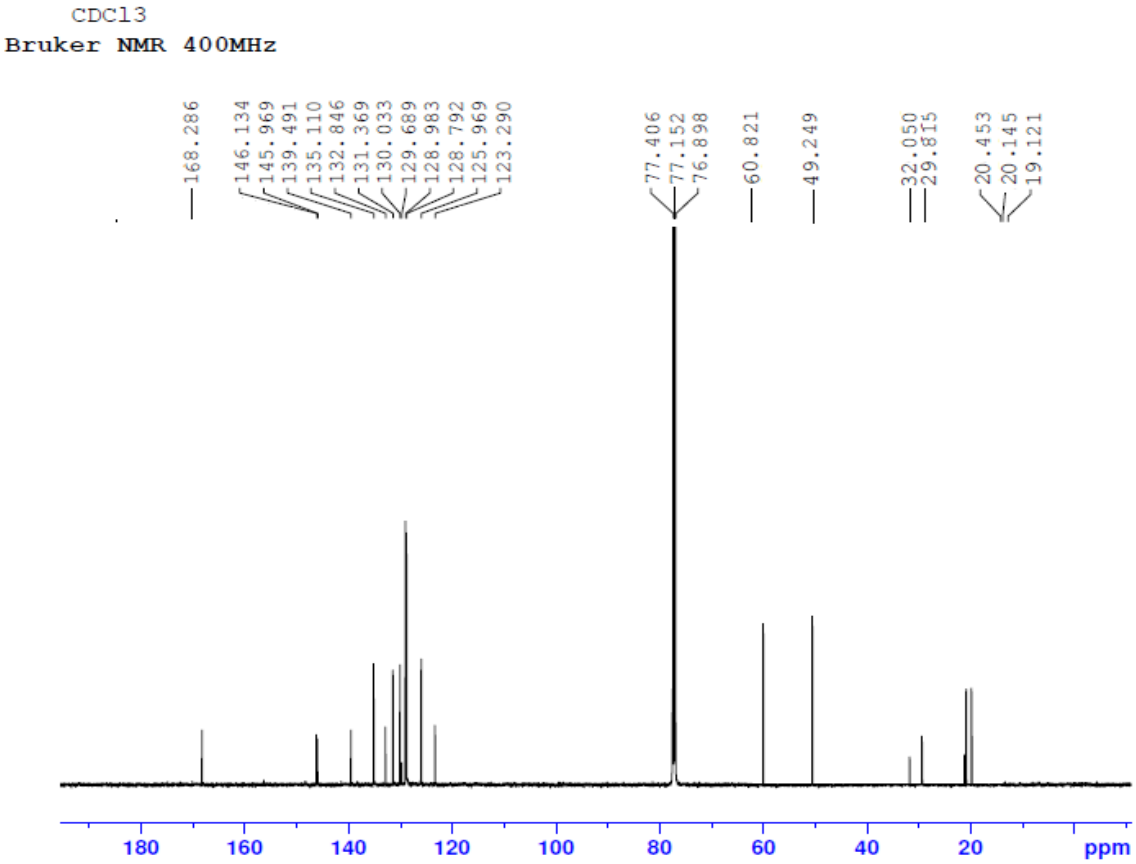
^{13}C NMR spectrum of compound **4a**



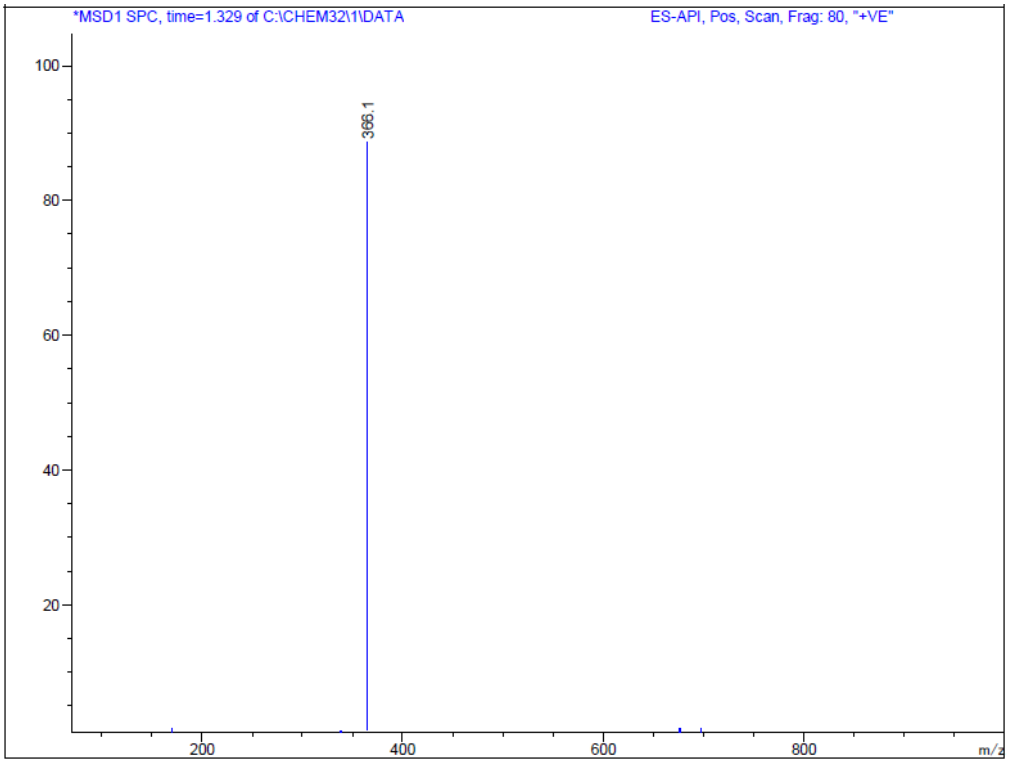
Mass spectrum of compound **4a**



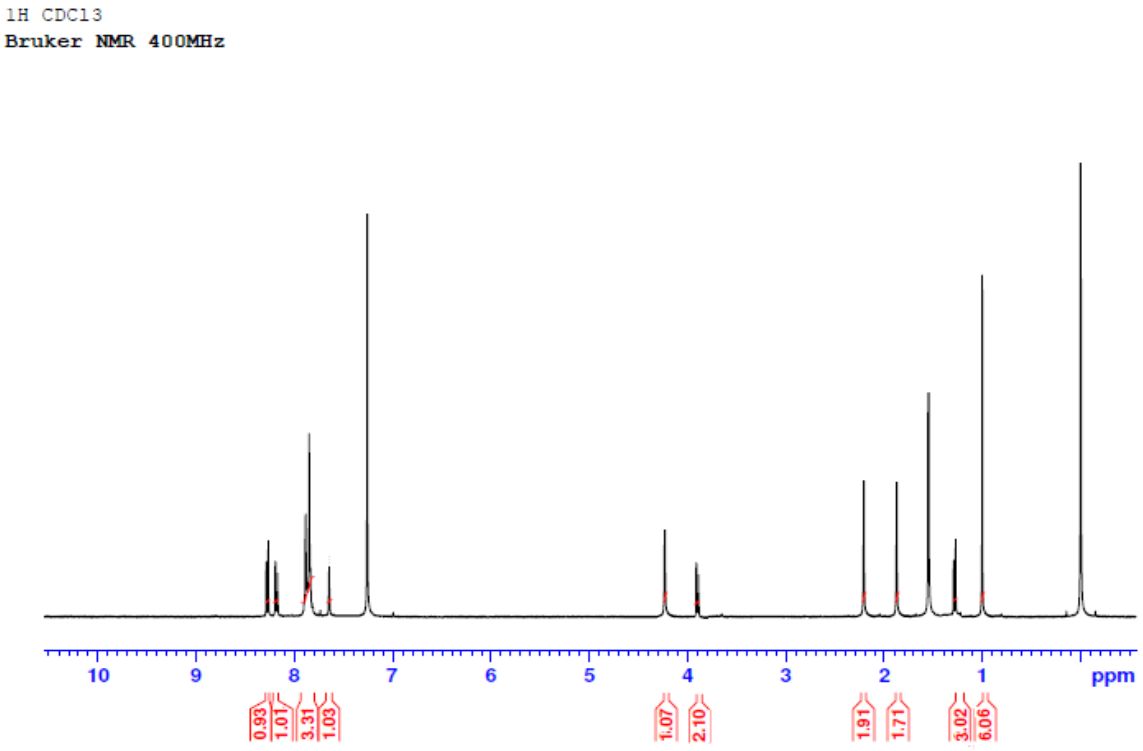
^{1}H NMR spectrum of compound **4c**



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



Mass spectrum of compound **4c**



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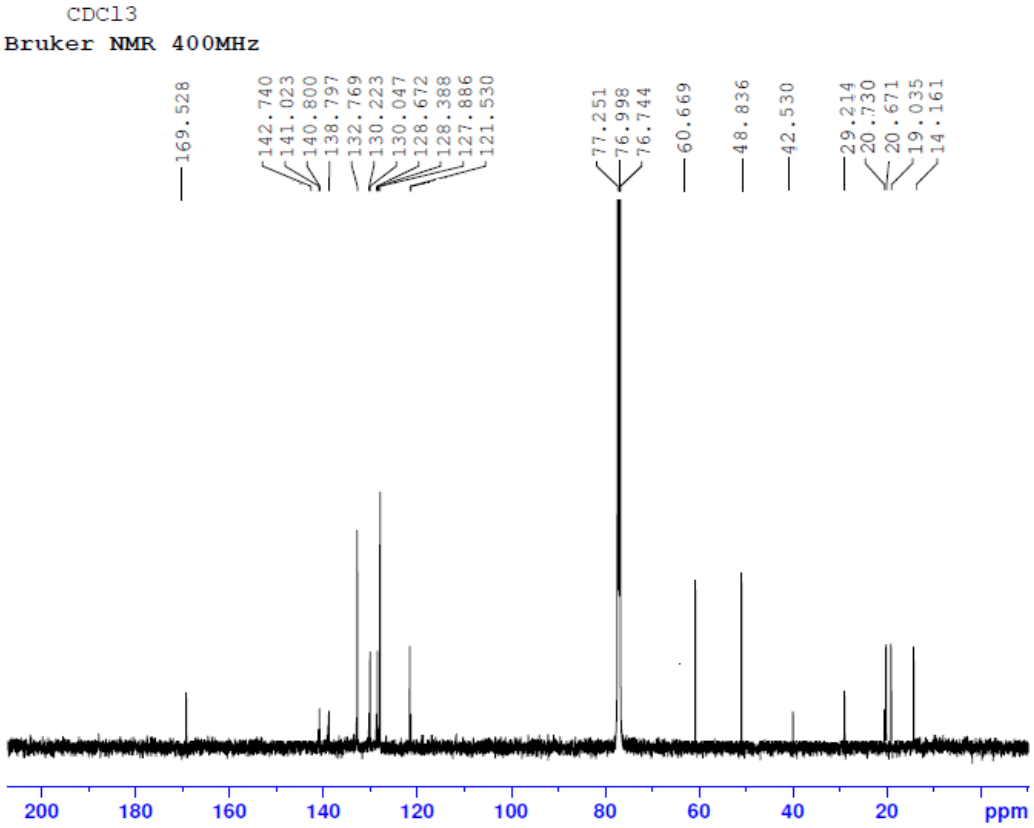
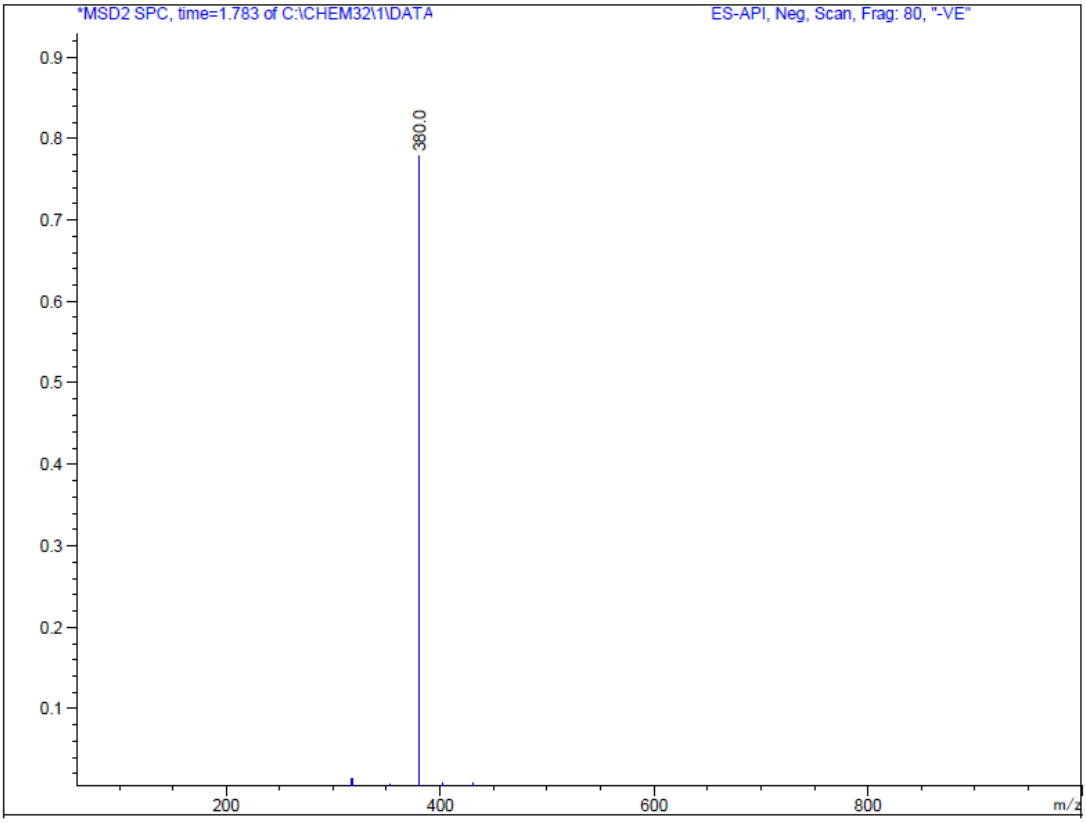
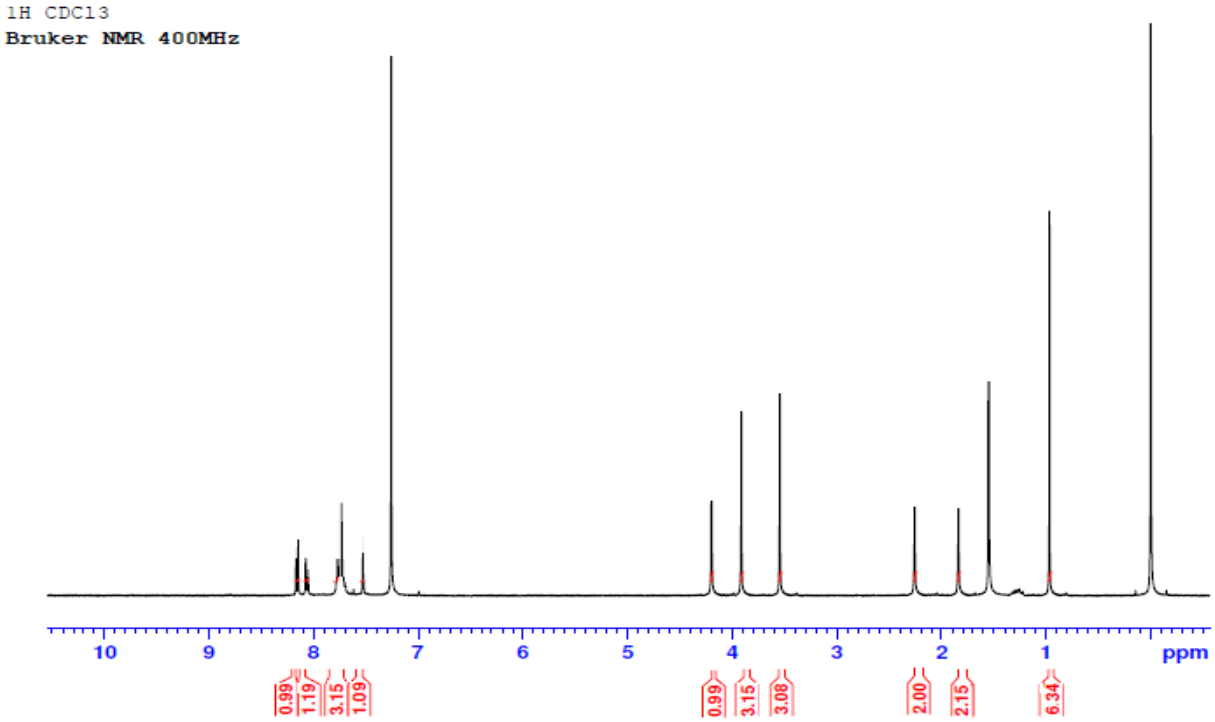


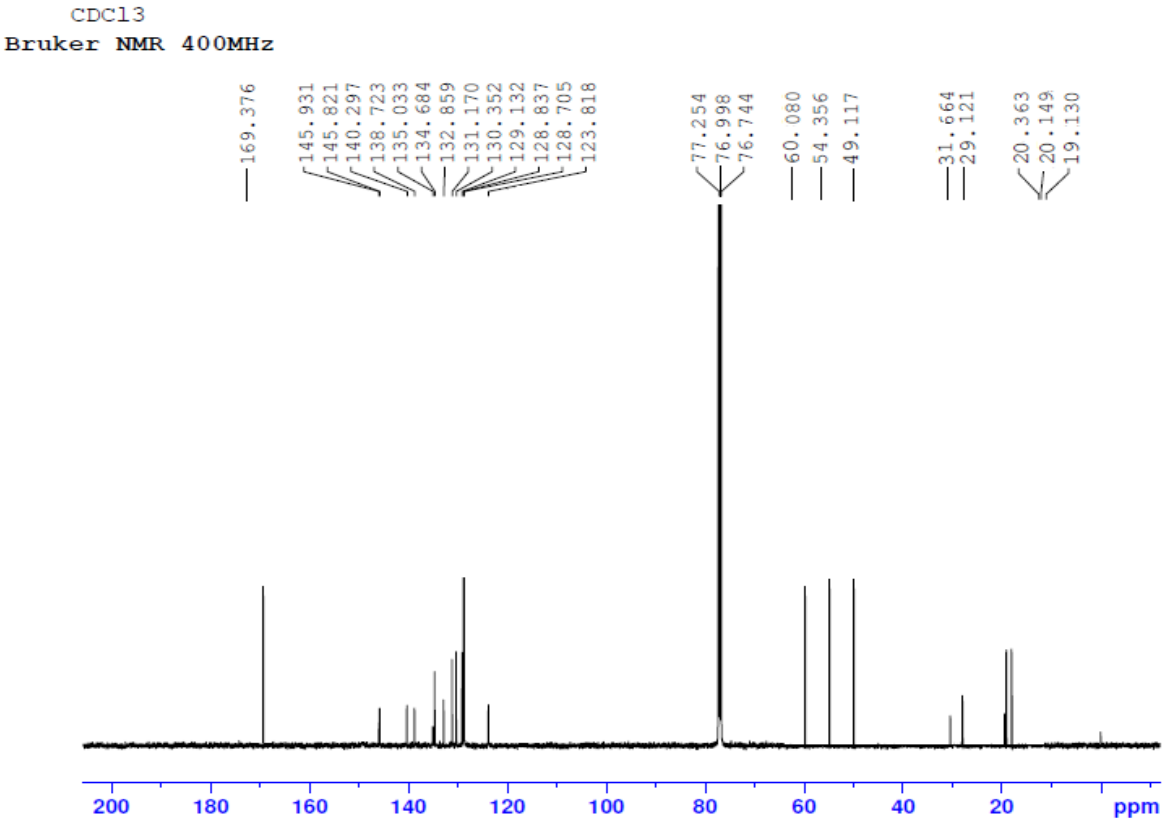
^{13}C NMR spectrum of compound **4d**



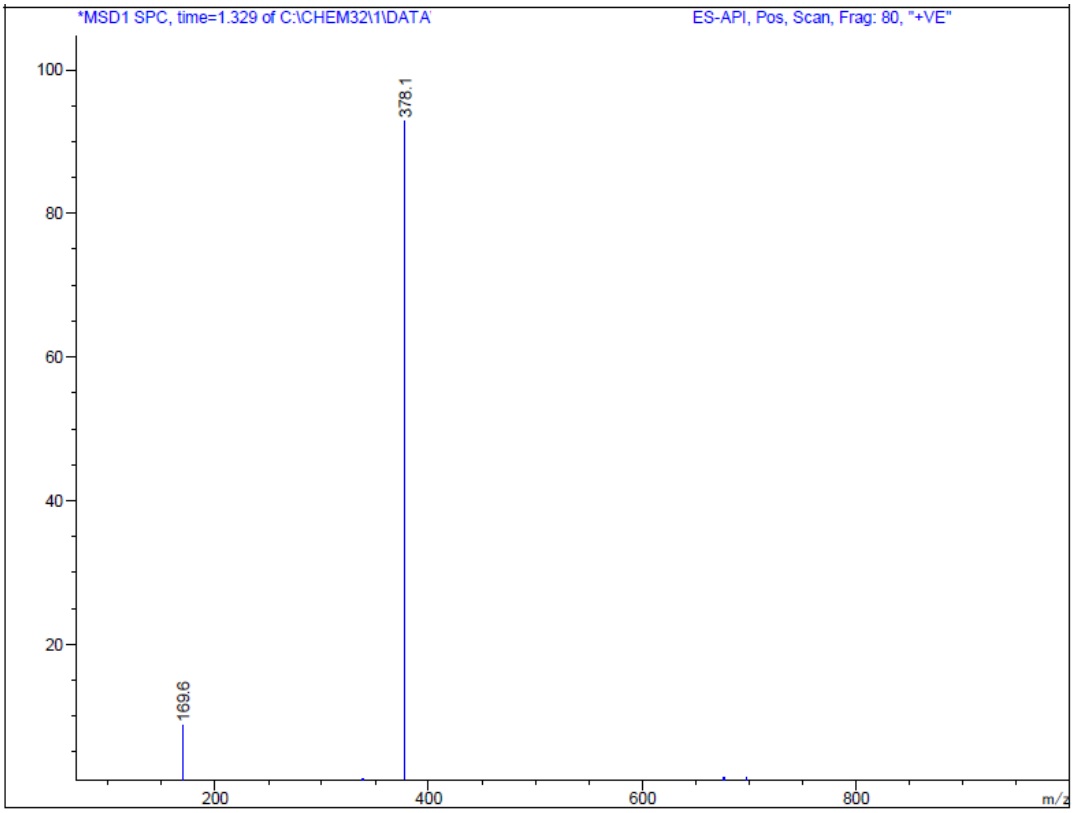
Mass spectrum of compound **4d**



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



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



Mass spectrum of compound **4g**