

Supplementary Information

Novel Adamantanyl Based Thiadiazolyl-Pyrazoles Targeting EGFR in Triple Negative Breast Cancer

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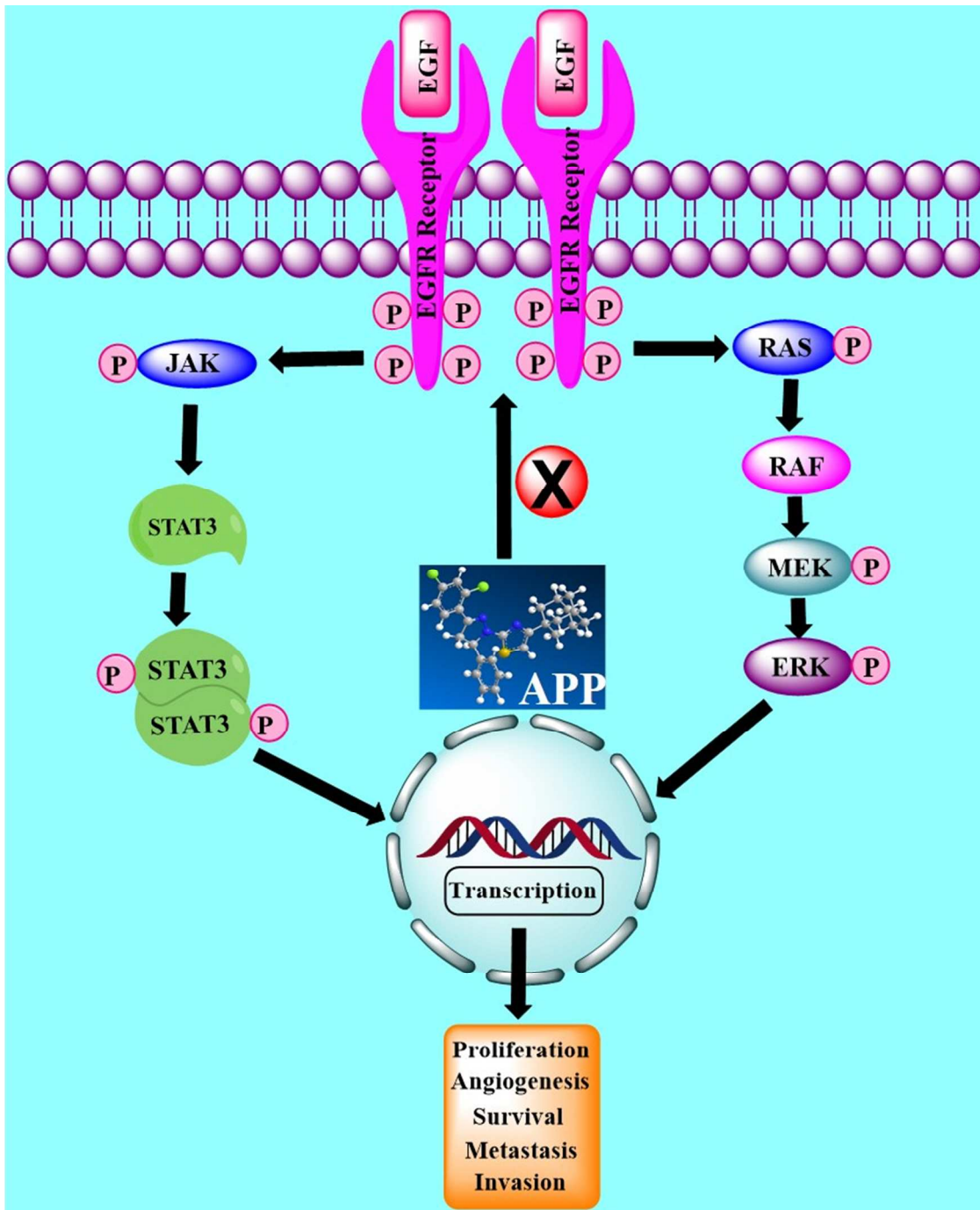
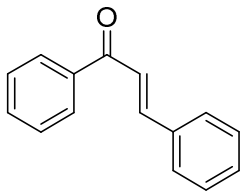
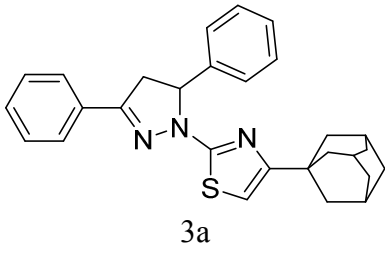
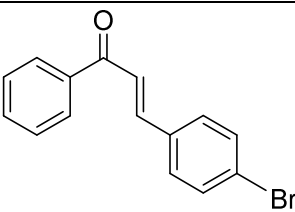
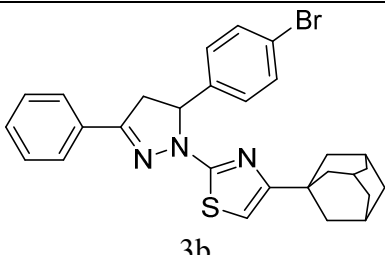
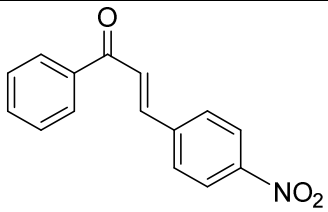
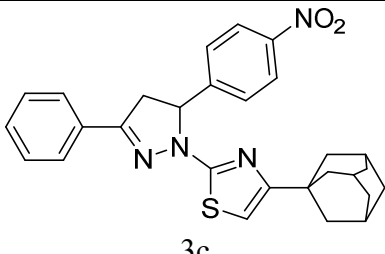
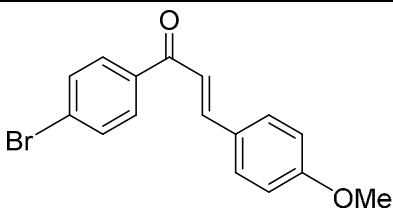
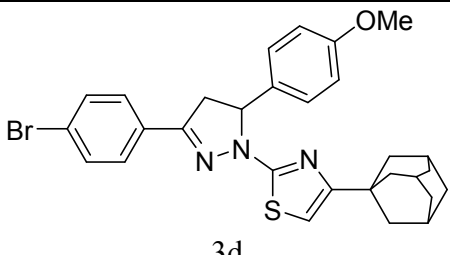
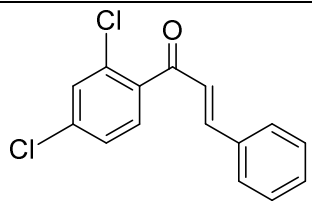
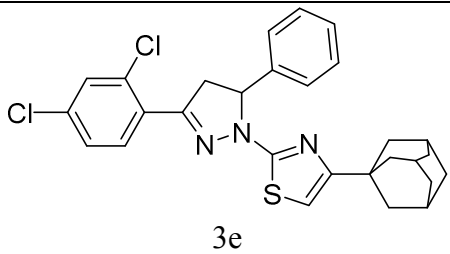
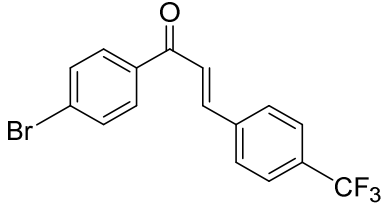
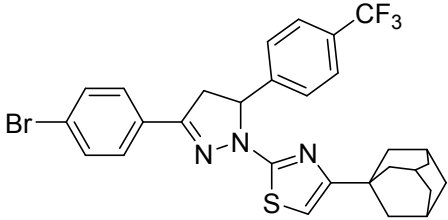
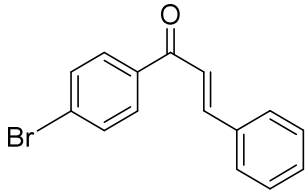
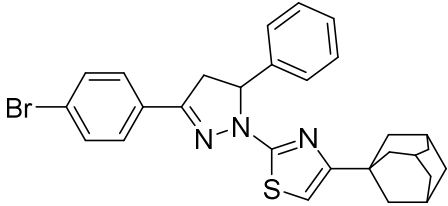
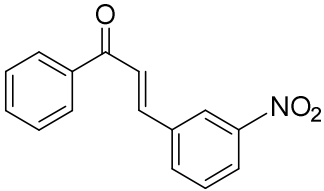
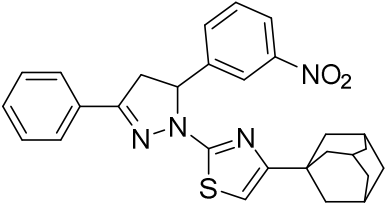
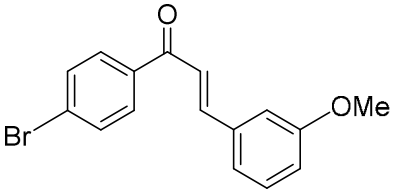
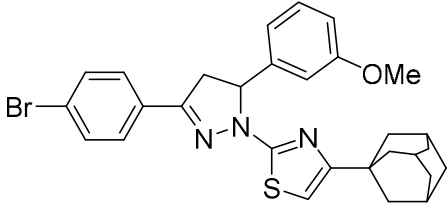
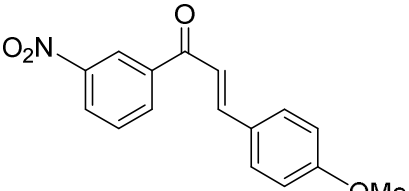
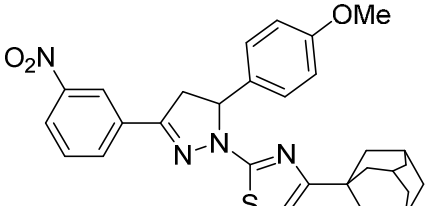
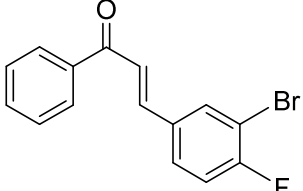
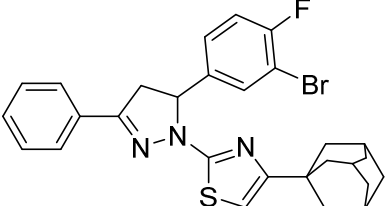
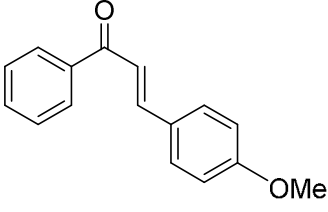
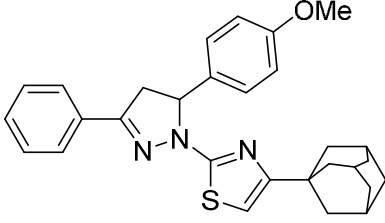


Figure S1: Overview of EGFR signaling and mechanism of action of the lead molecule (APP)

Table S1: Physical parameters for the newly synthesized compounds 3(a-l).

Sl. No	Chalcone (1a-l)	Product ^a (3a-l)	Yield ^b (%)
1		 3a	93
2		 3b	87
3		 3c	85
4		 3d	87
5		 3e	90

6		 3f	93
7		 3g	89
8		 3h	84
9		 3i	89
10		 3j	89
11		 3k	91

12		 <p style="text-align: center;">31</p>	86
<p>^a Reaction conditions; chalcone (1eq) in [BMIM][BF₄] (5ml), thiosemicarbazide (1.2eq), piperidine (2-3 drops) and 2-(adamantan-1-yl)acetyl bromide (1eq), 6 h at 80 °C. ^bProduct yield after recrystallisation from ethanol.</p>			

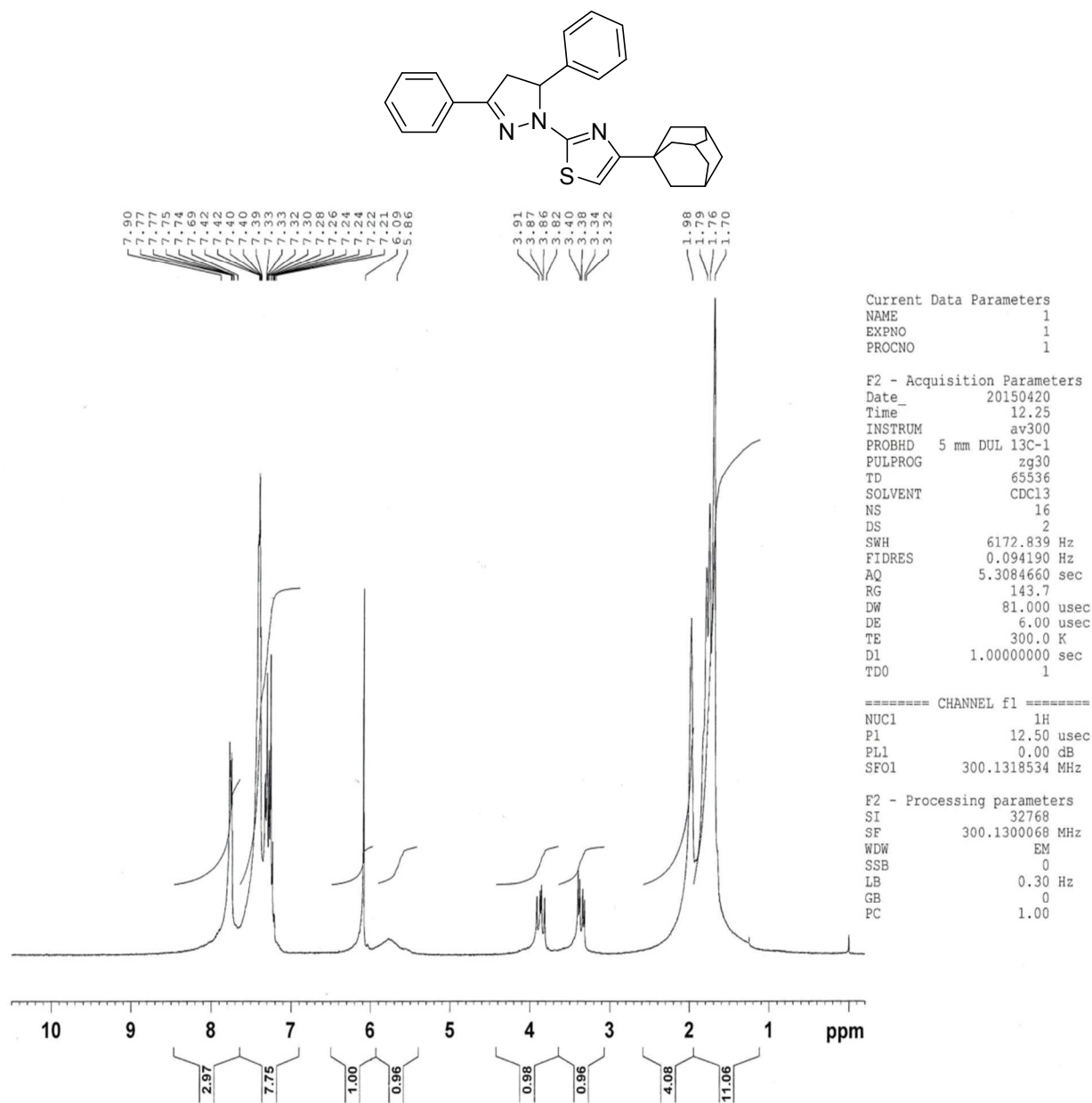


Figure S2: ^1H NMR spectrum of the compound 3a

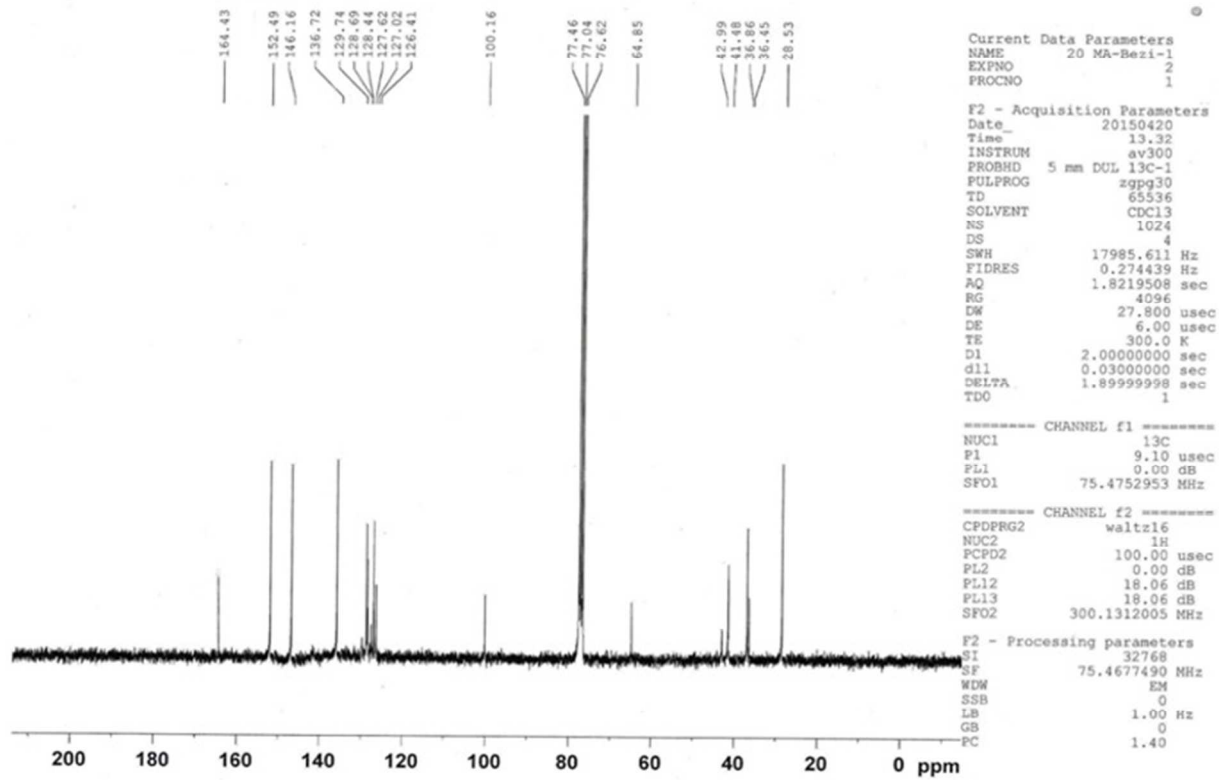


Figure S3: ^{13}C NMR spectrum of the compound 3a

Comment 1
Comment 2

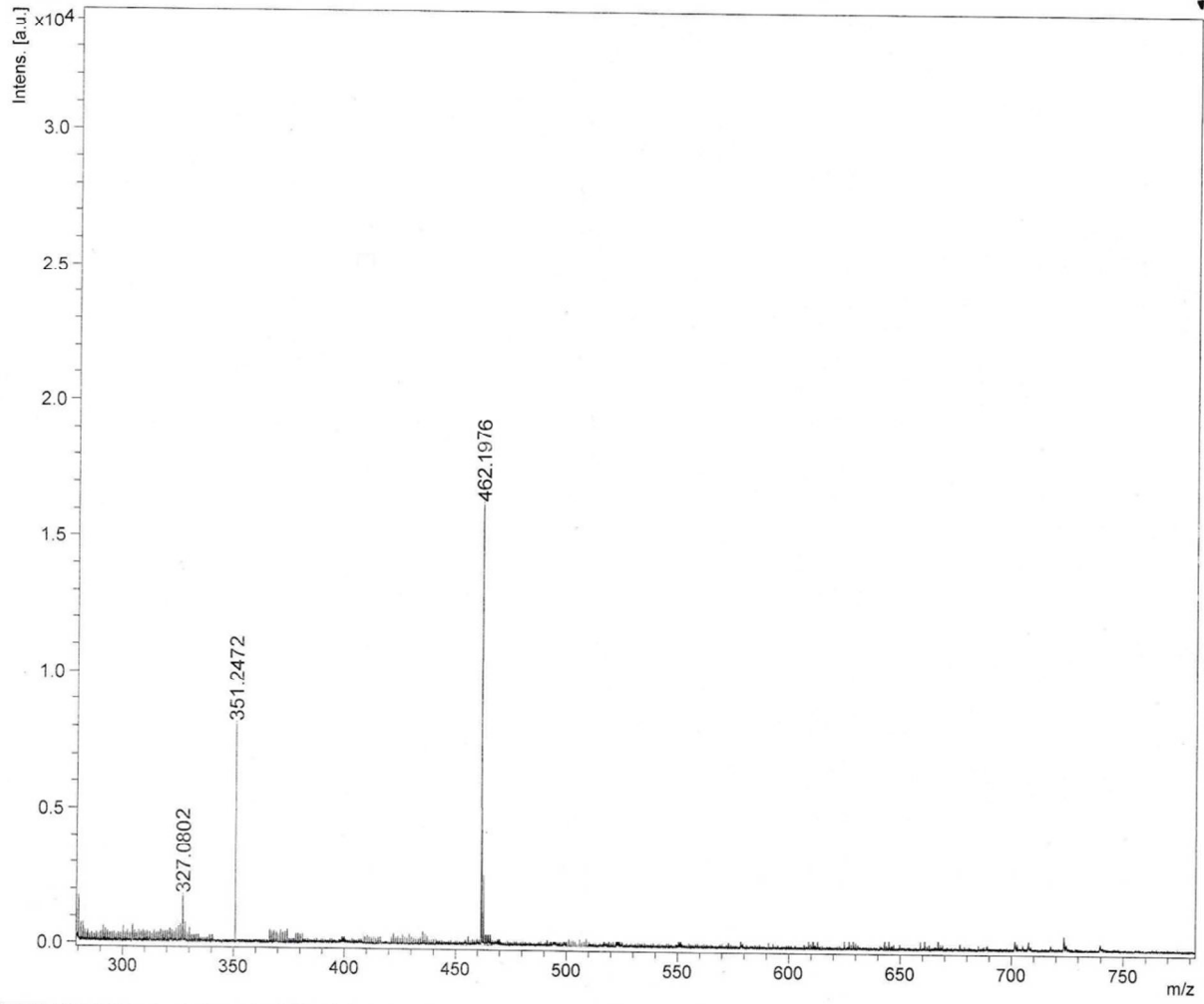


Figure S4: Mass spectra of spectrum of the compound 3a

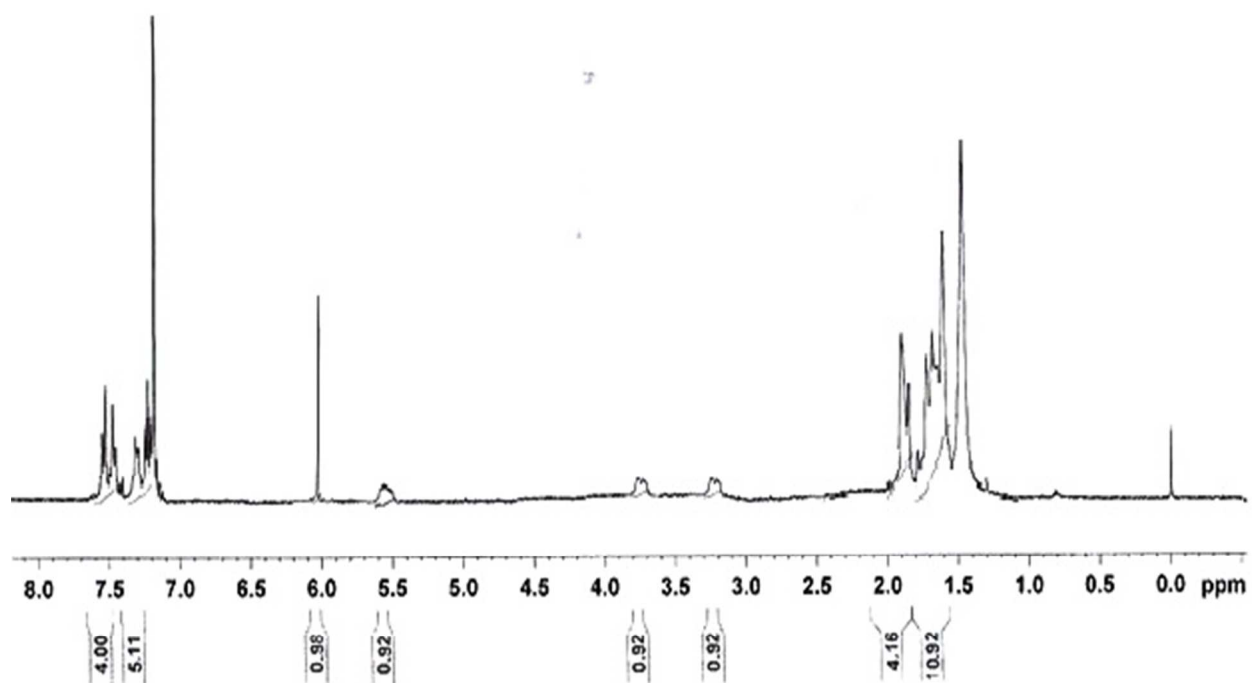
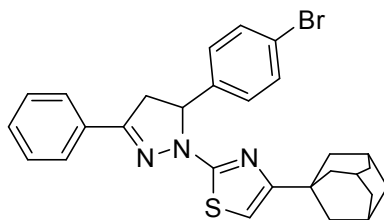


Figure S5: ¹H NMR spectrum of the compound 3b

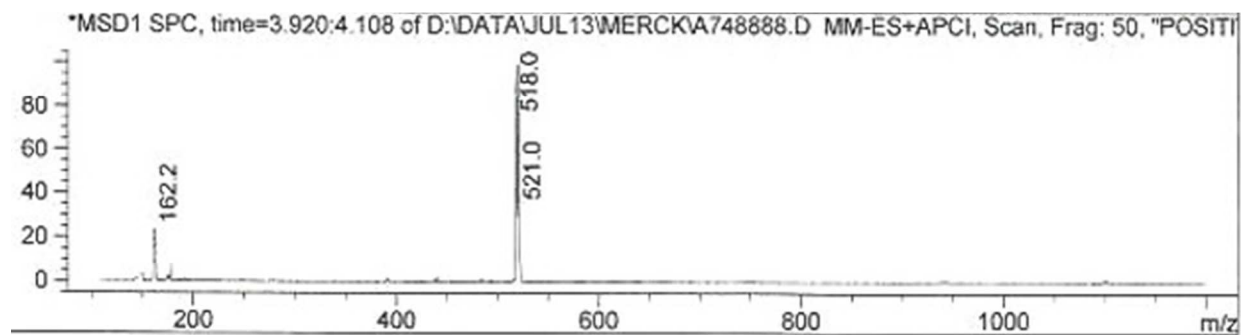


Figure S6: Mass spectra of spectrum of the compound 3b

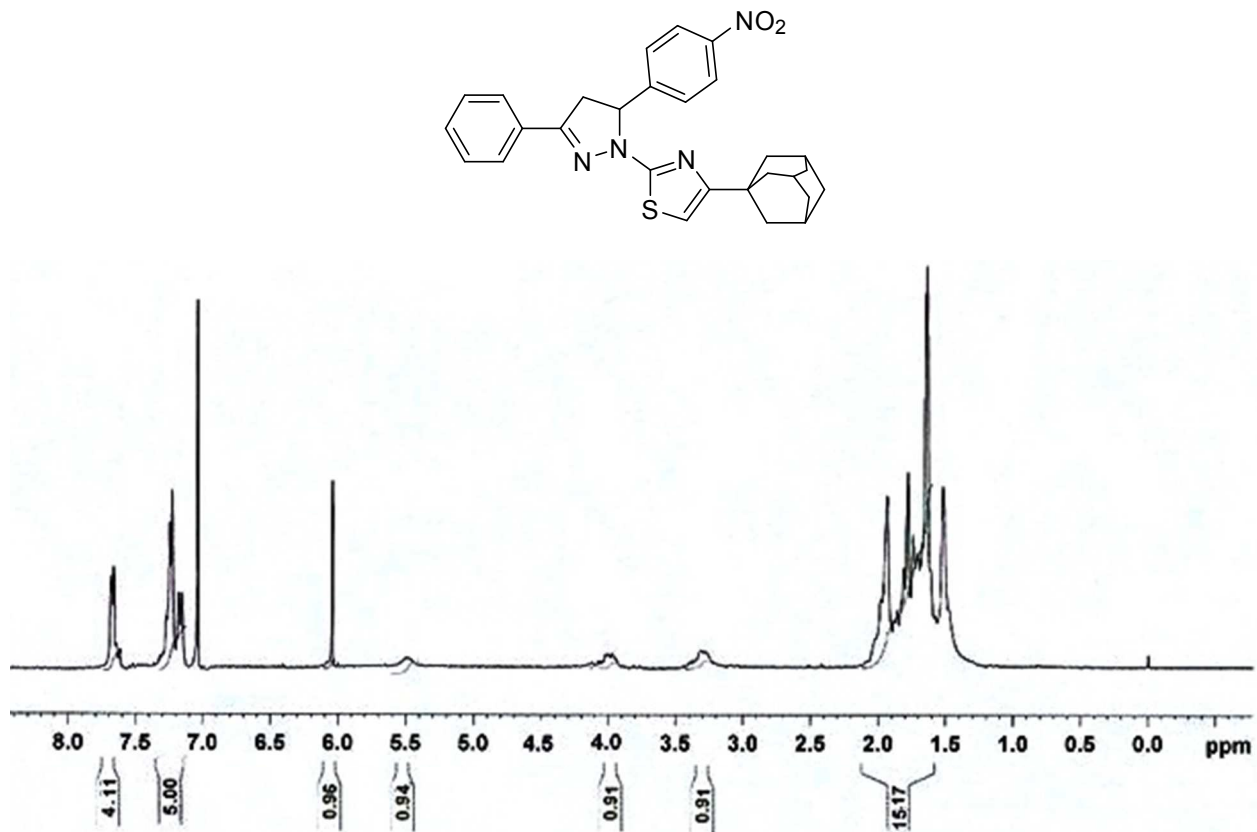


Figure S7: ¹H NMR spectrum of the compound 3c

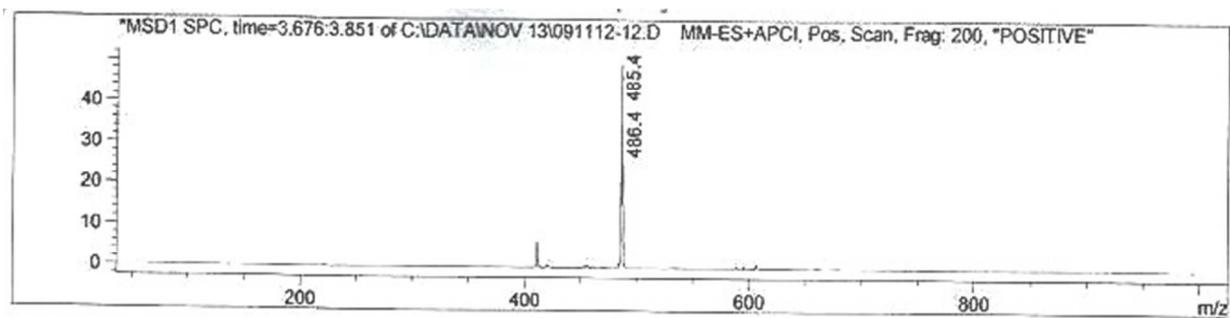


Figure S8: Mass spectra of spectrum of the compound 3c

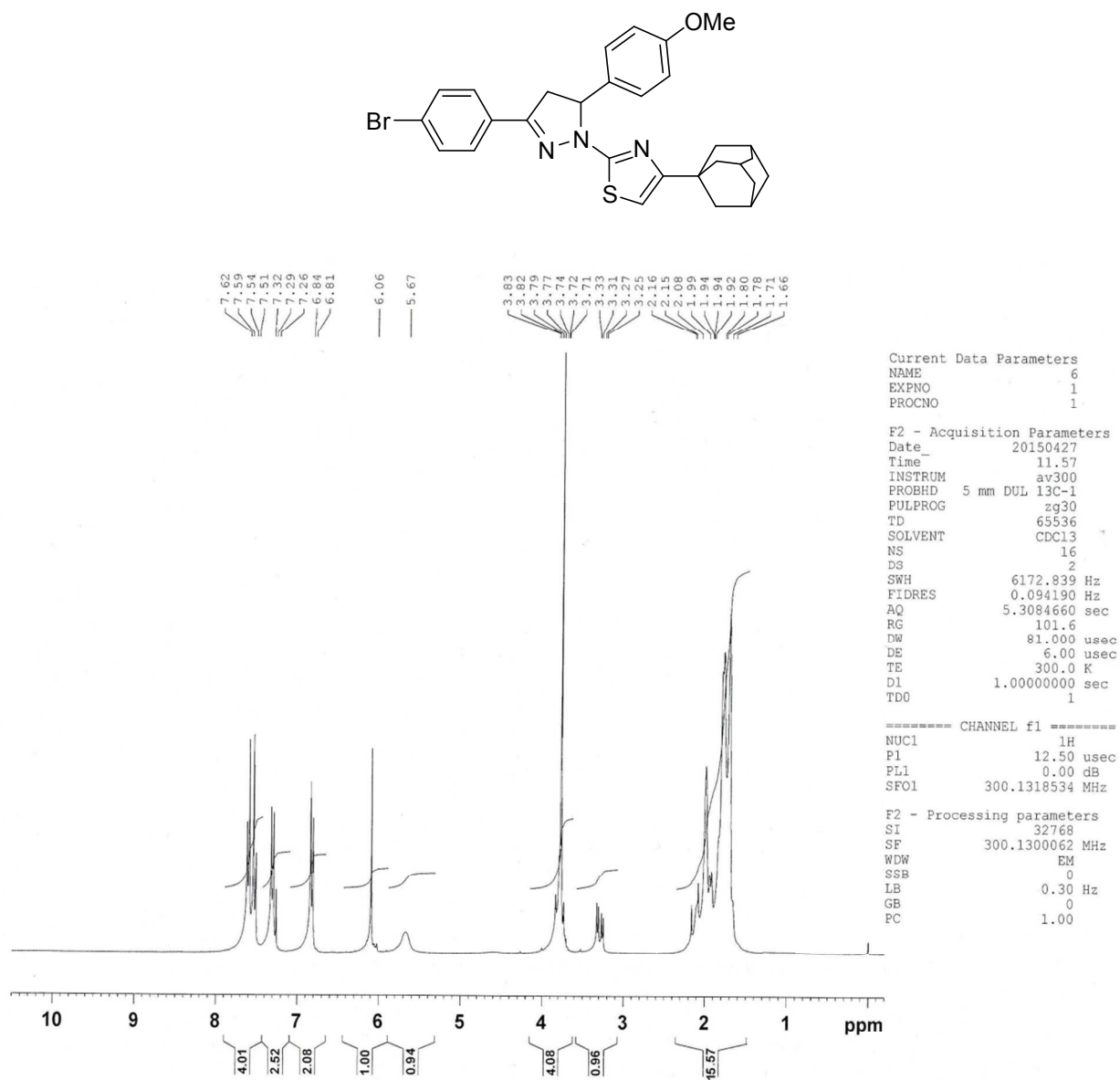


Figure S9: ^1H NMR spectrum of the compound 3d

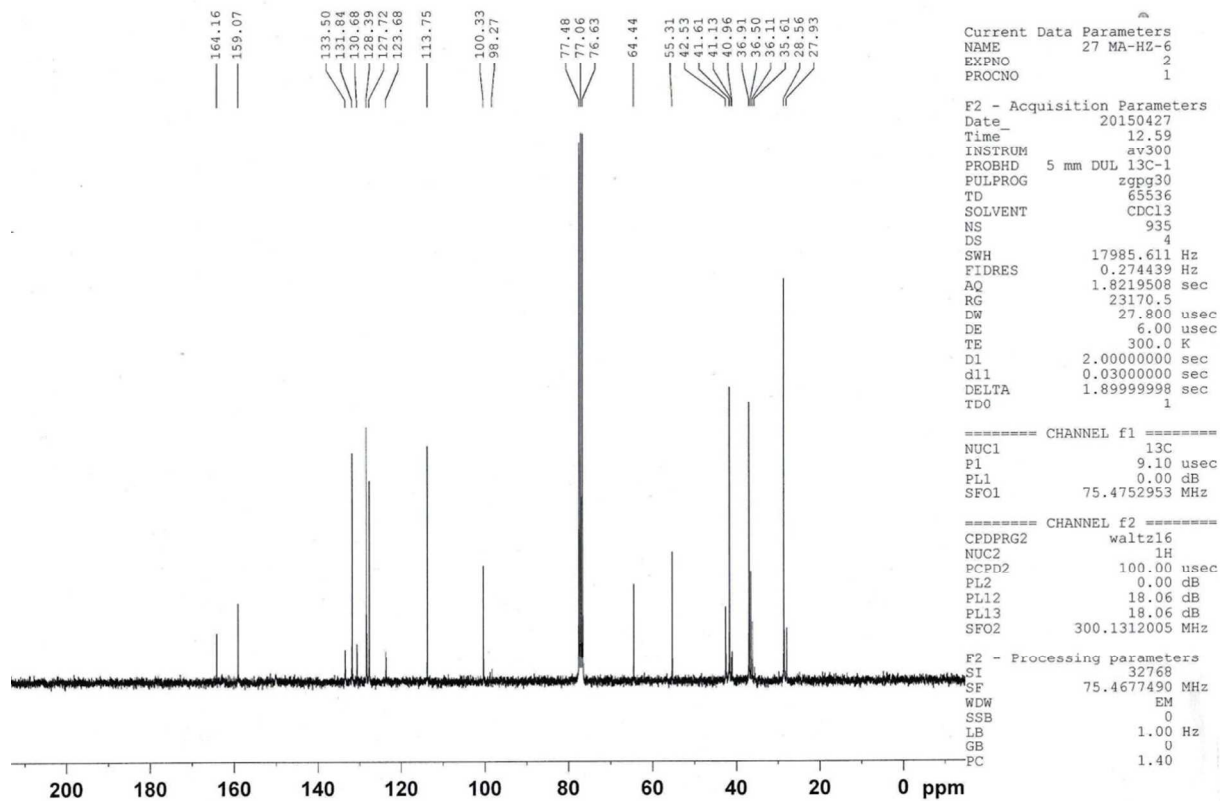


Figure S10: ¹³C of spectrum of the compound 3d

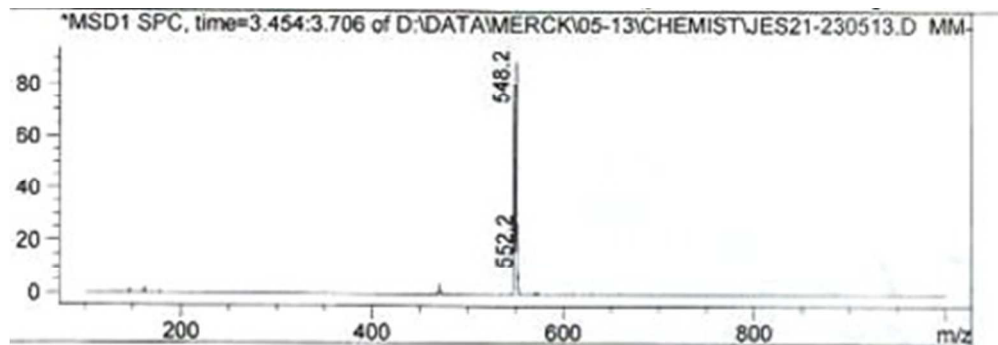


Figure S11: Mass spectrum of the compound 3d

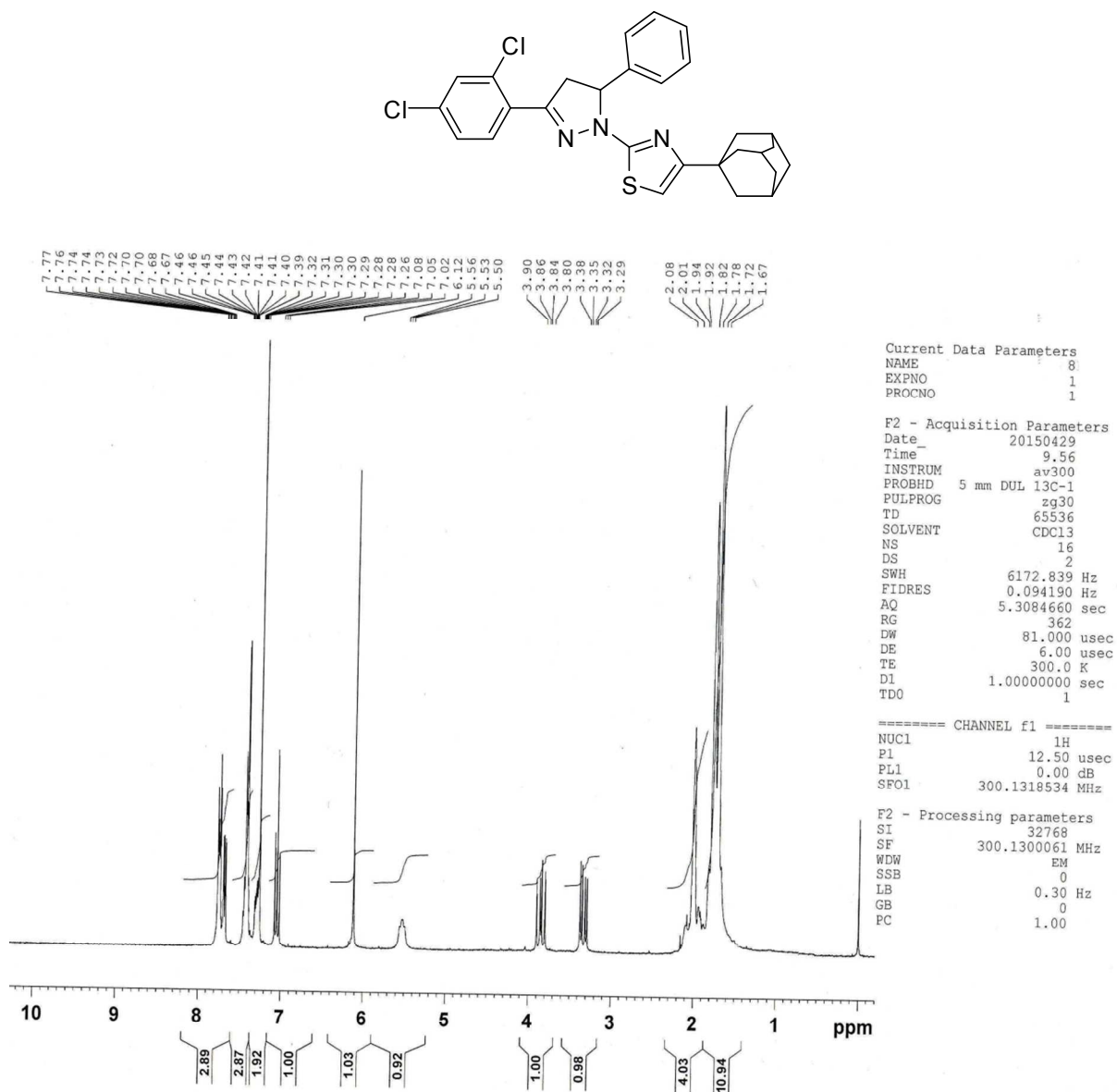


Figure S12: ¹H Spectrum of compound 3e (APP)

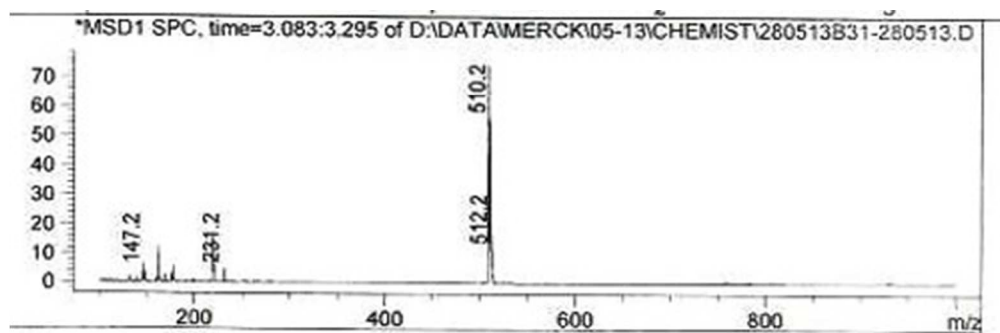


Figure S13: Mass spectrum of compound 3e (APP)

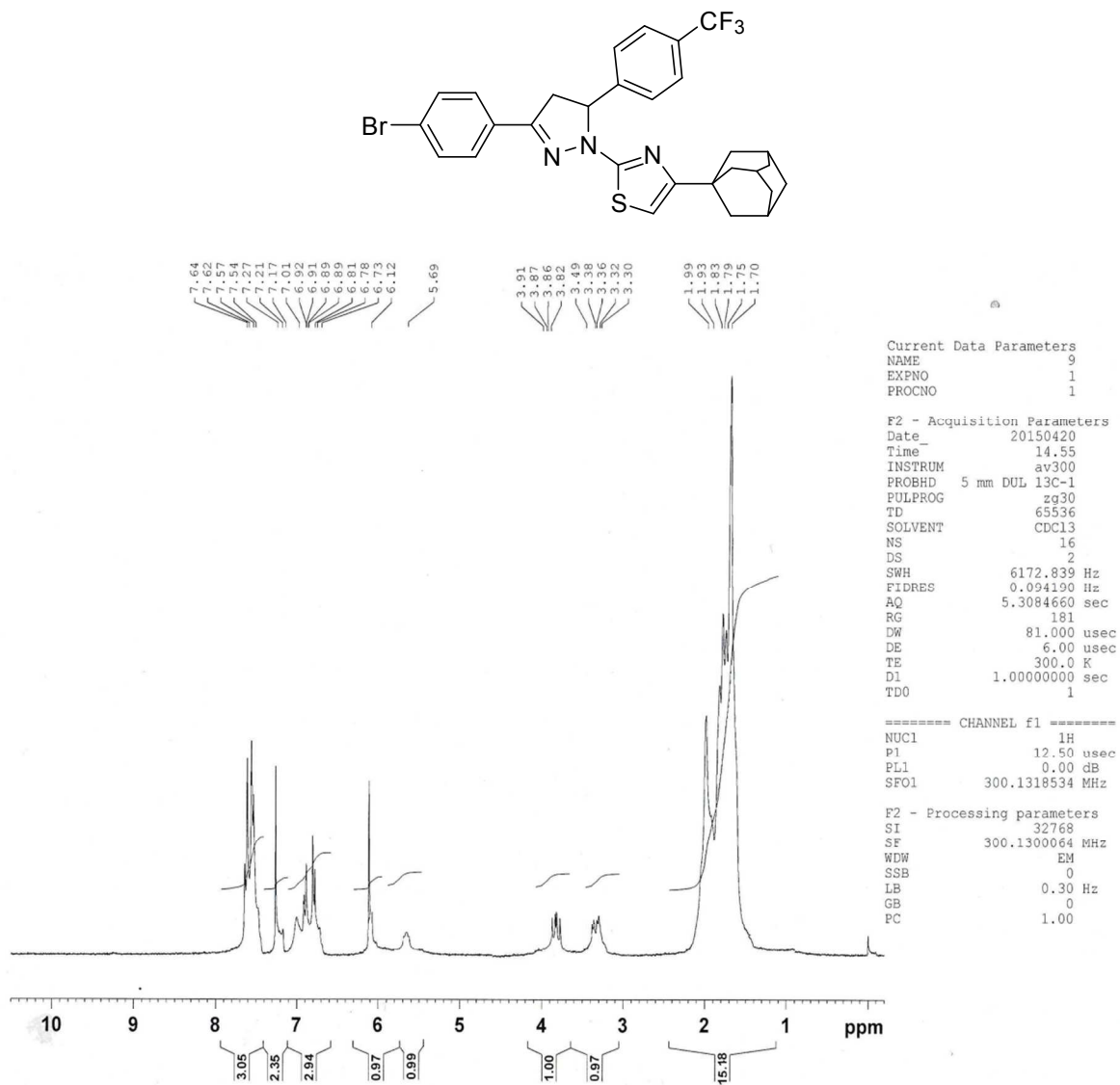


Figure S14: ¹H Spectrum of compound 3f

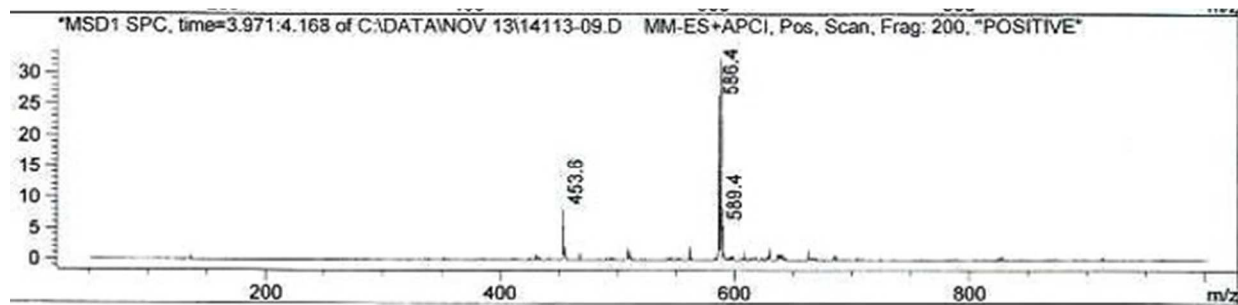


Figure S15: Mass Spectrum of compound 3f

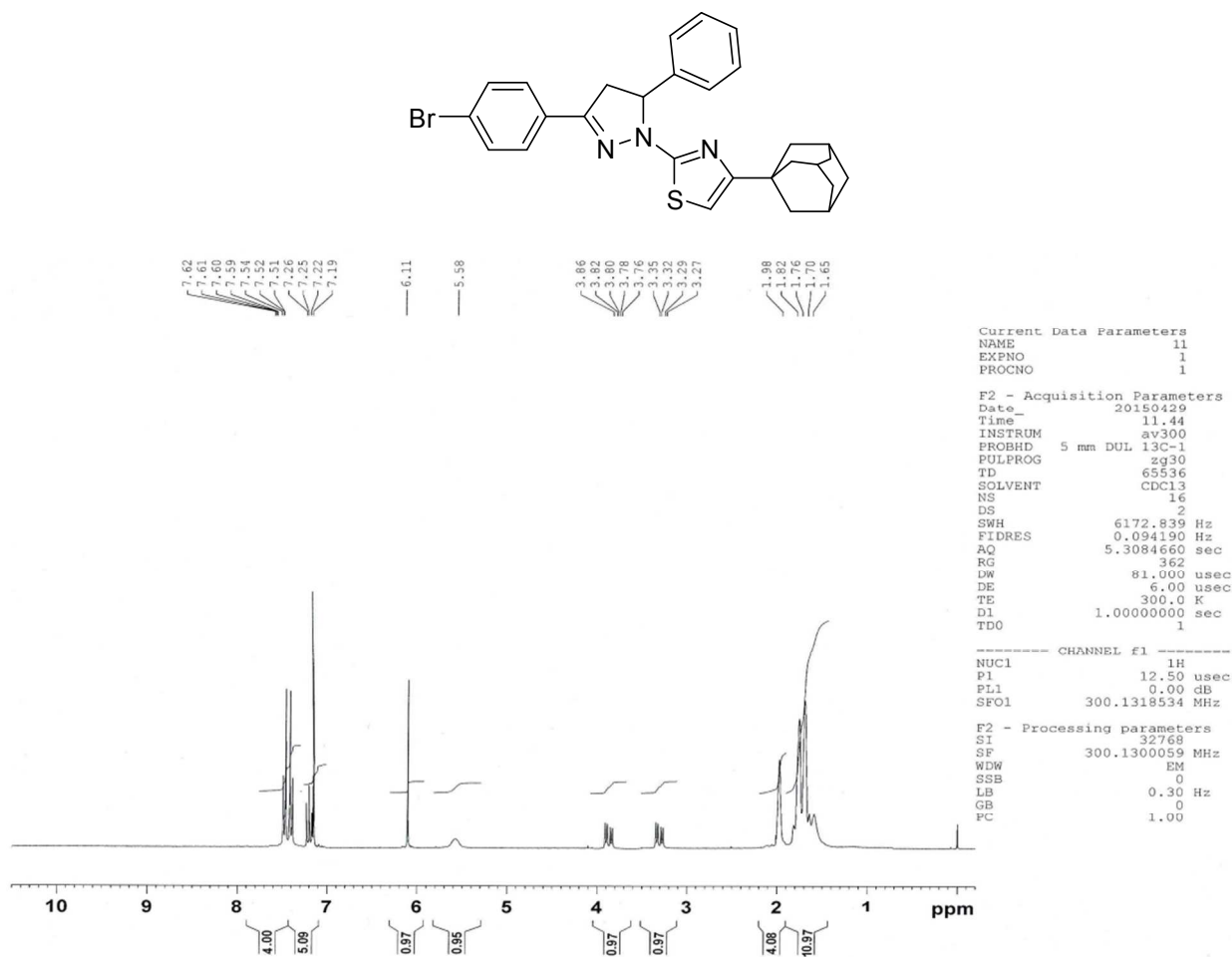


Figure S16: ^1H Spectrum of compound 3g

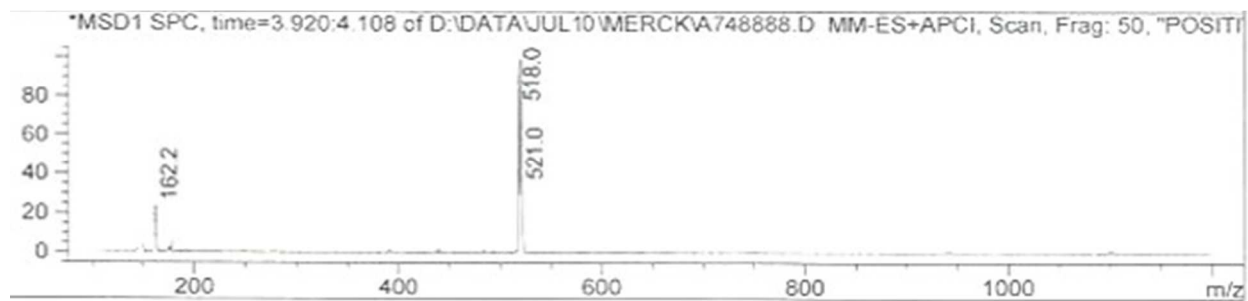


Figure S17: Mass Spectrum of compound 3g

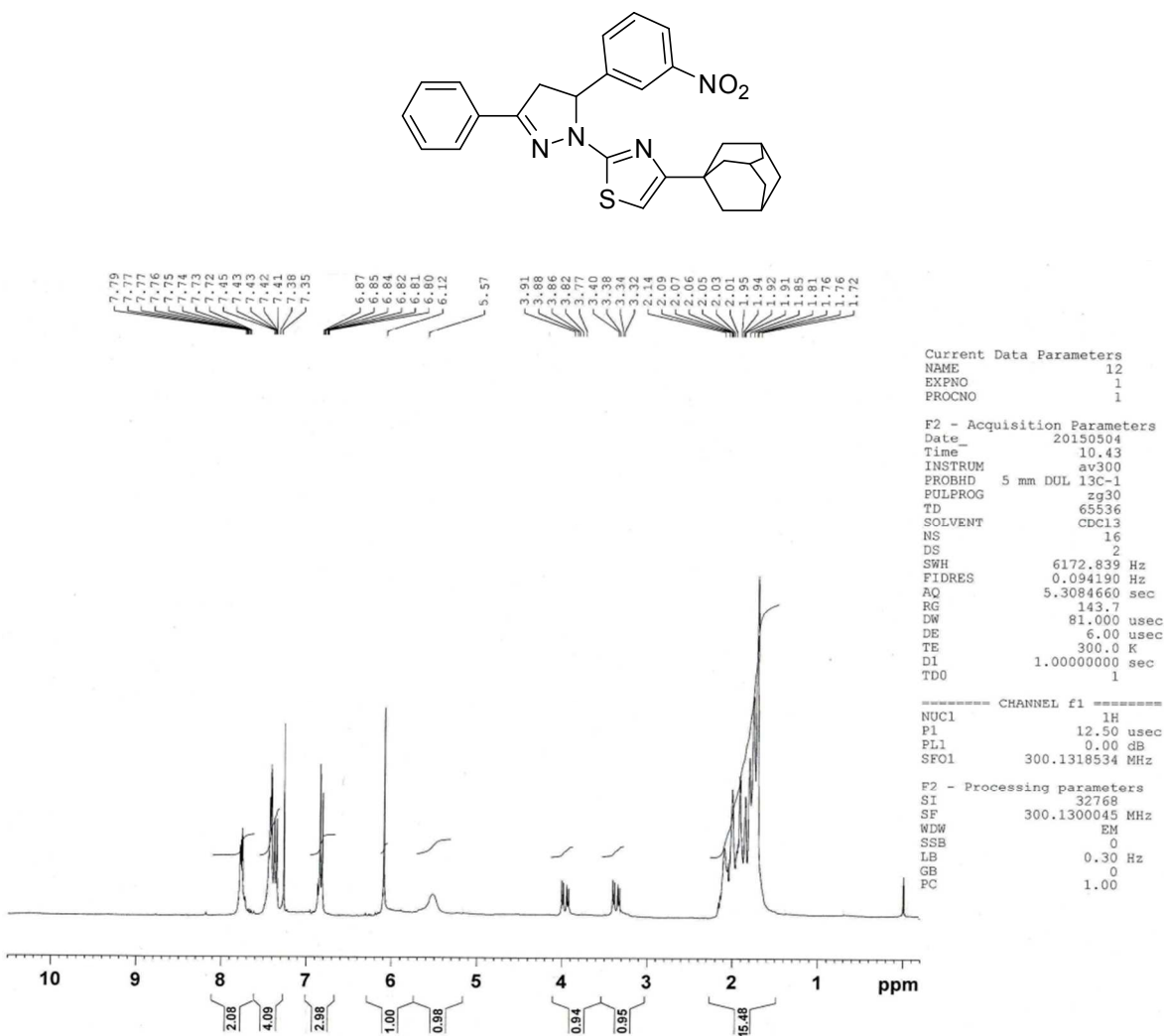


Figure S18: ¹H Spectrum of compound 3h

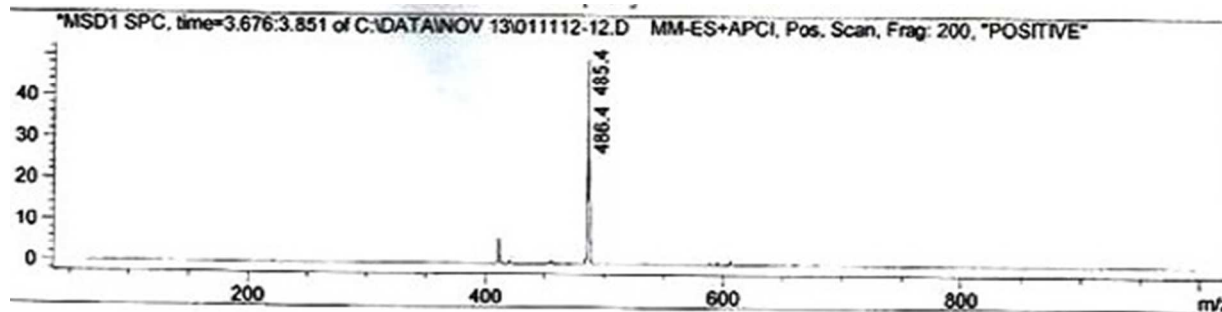


Figure S19: Mass Spectrum of compound 3h

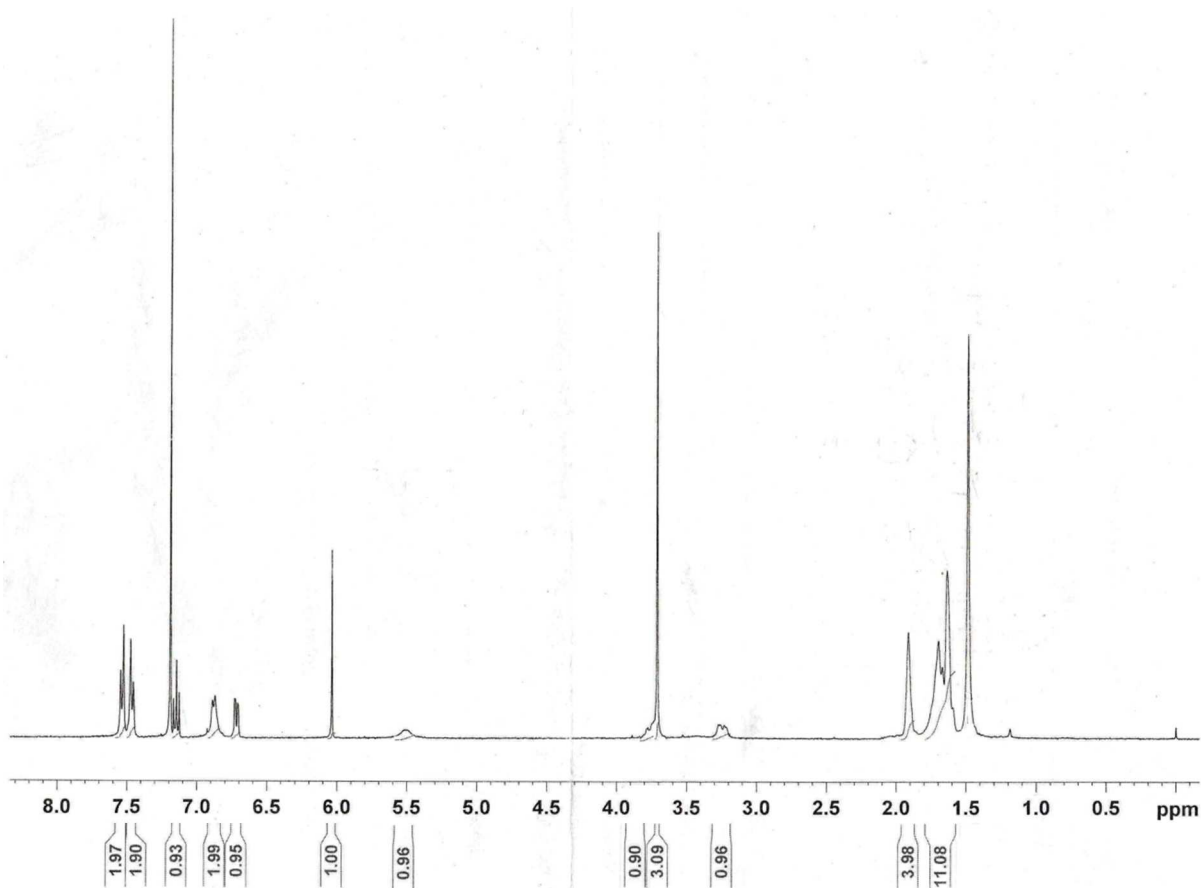
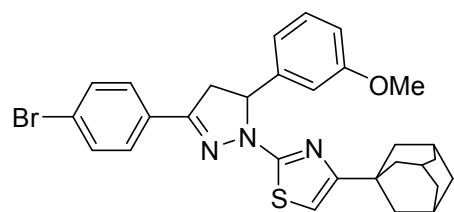


Figure S20: ¹H Spectrum of compound 3i

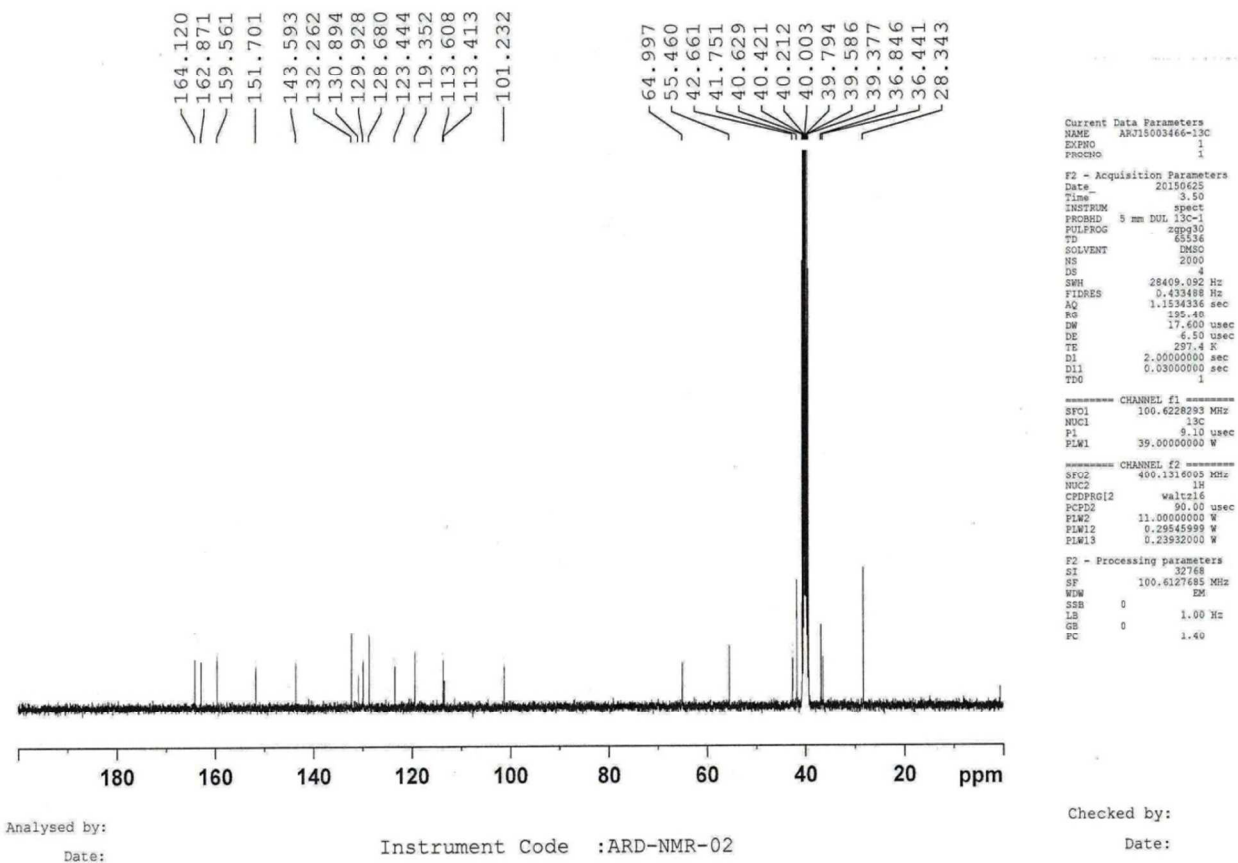


Figure S21: ¹³C Spectrum of compound 3i

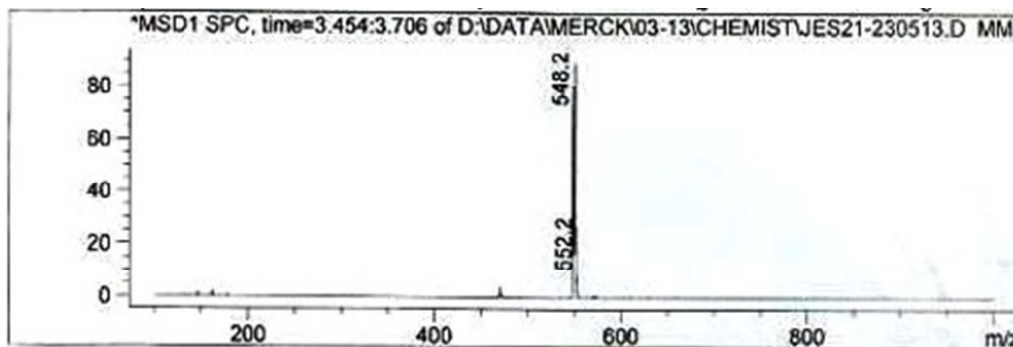


Figure S22: Mass Spectrum of compound 3i

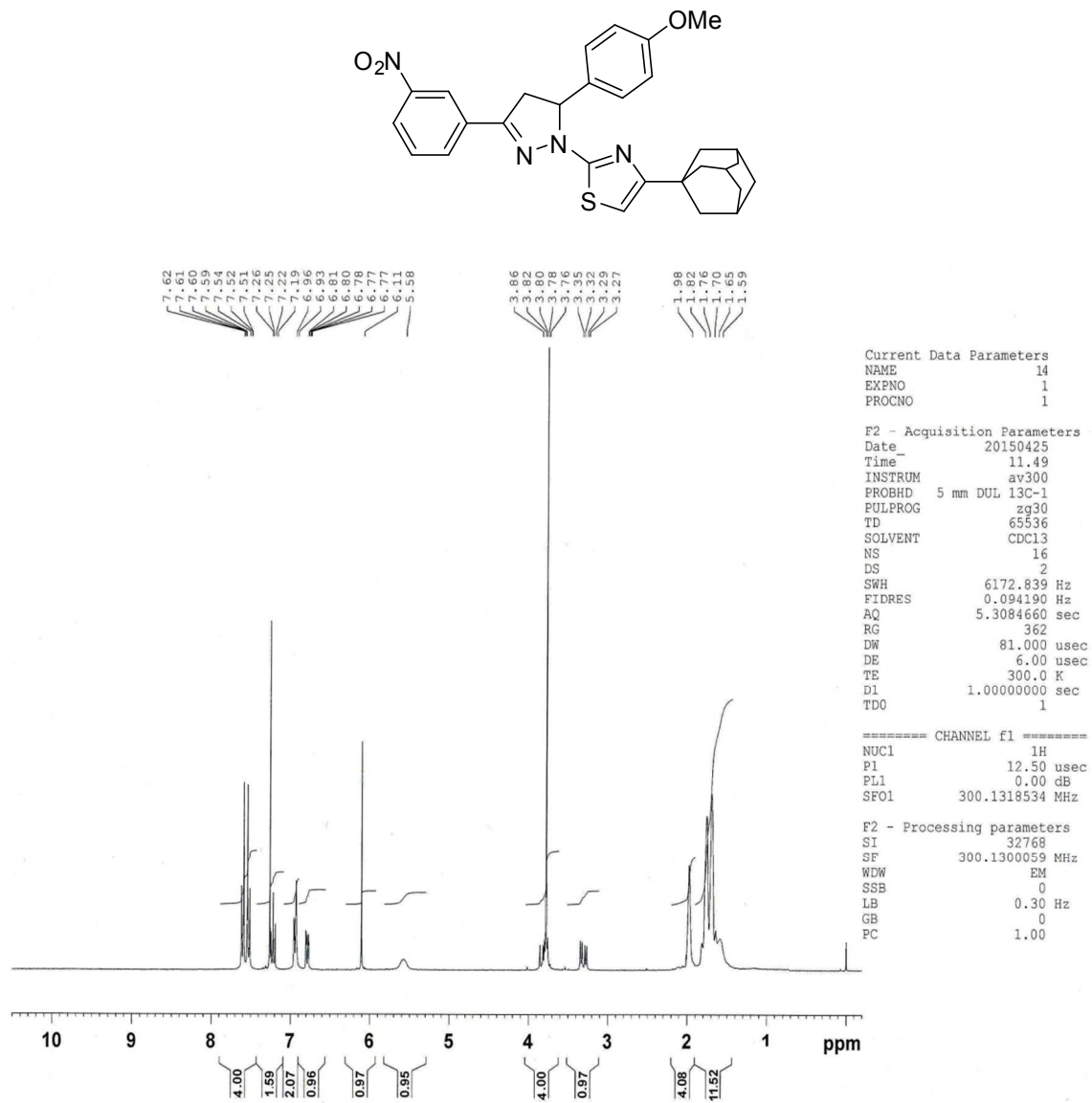


Figure S23: ¹H Spectrum of compound 3j

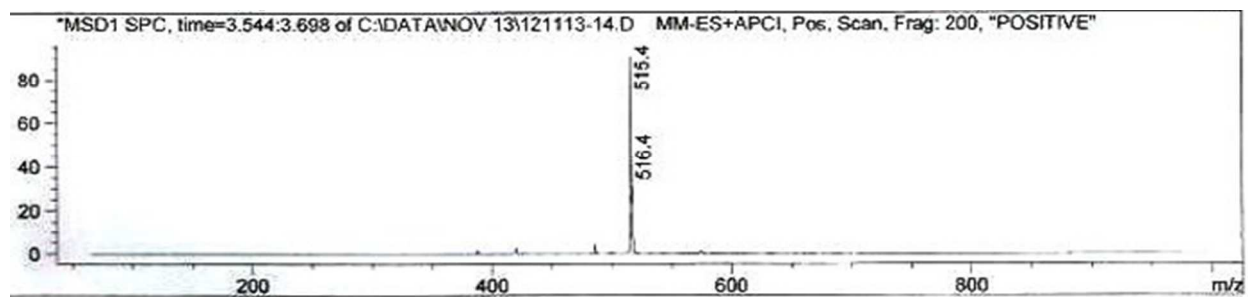


Figure S24: Mass Spectrum of compound 3j

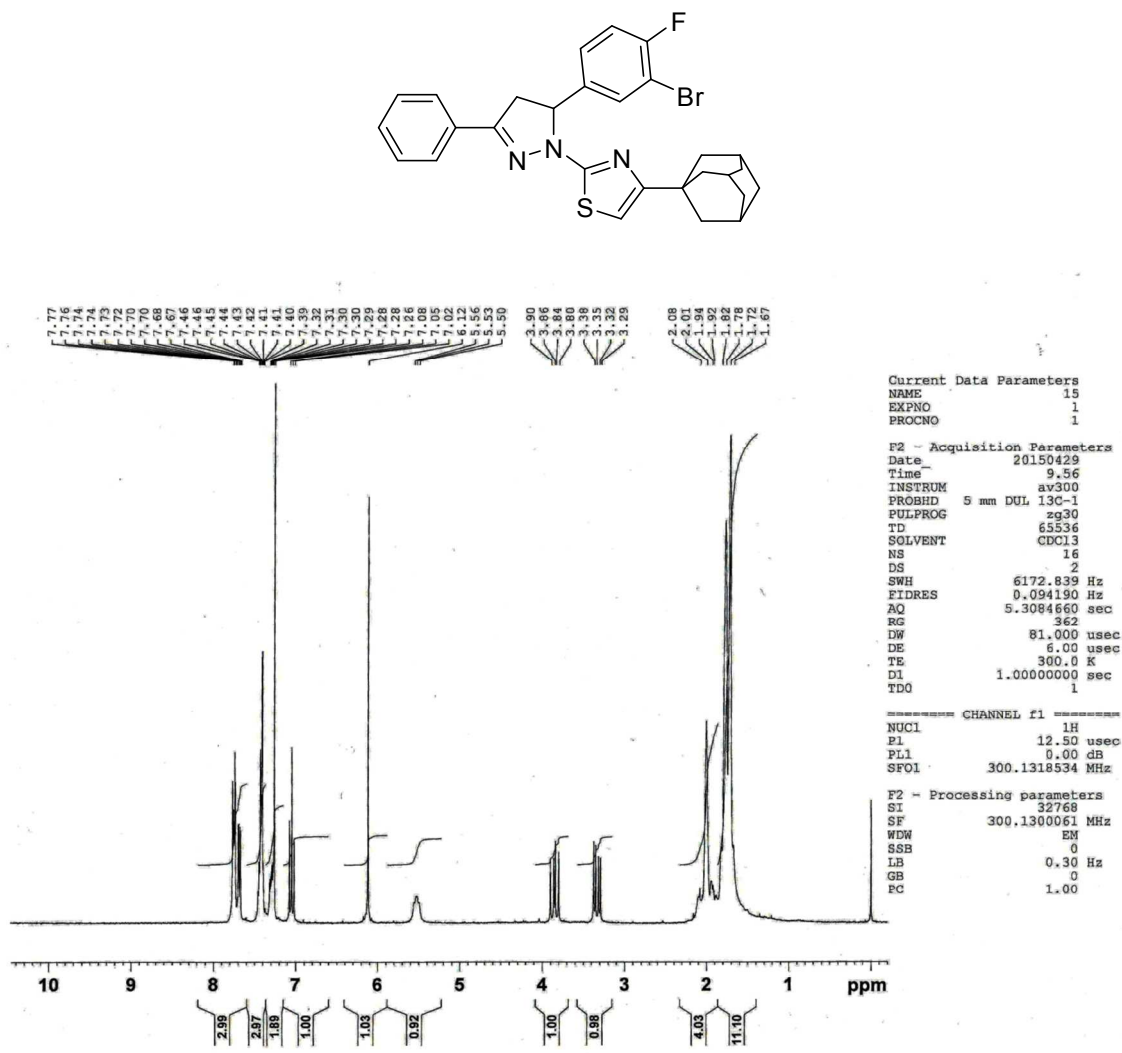


Figure S25: ^1H Spectrum of compound 3k

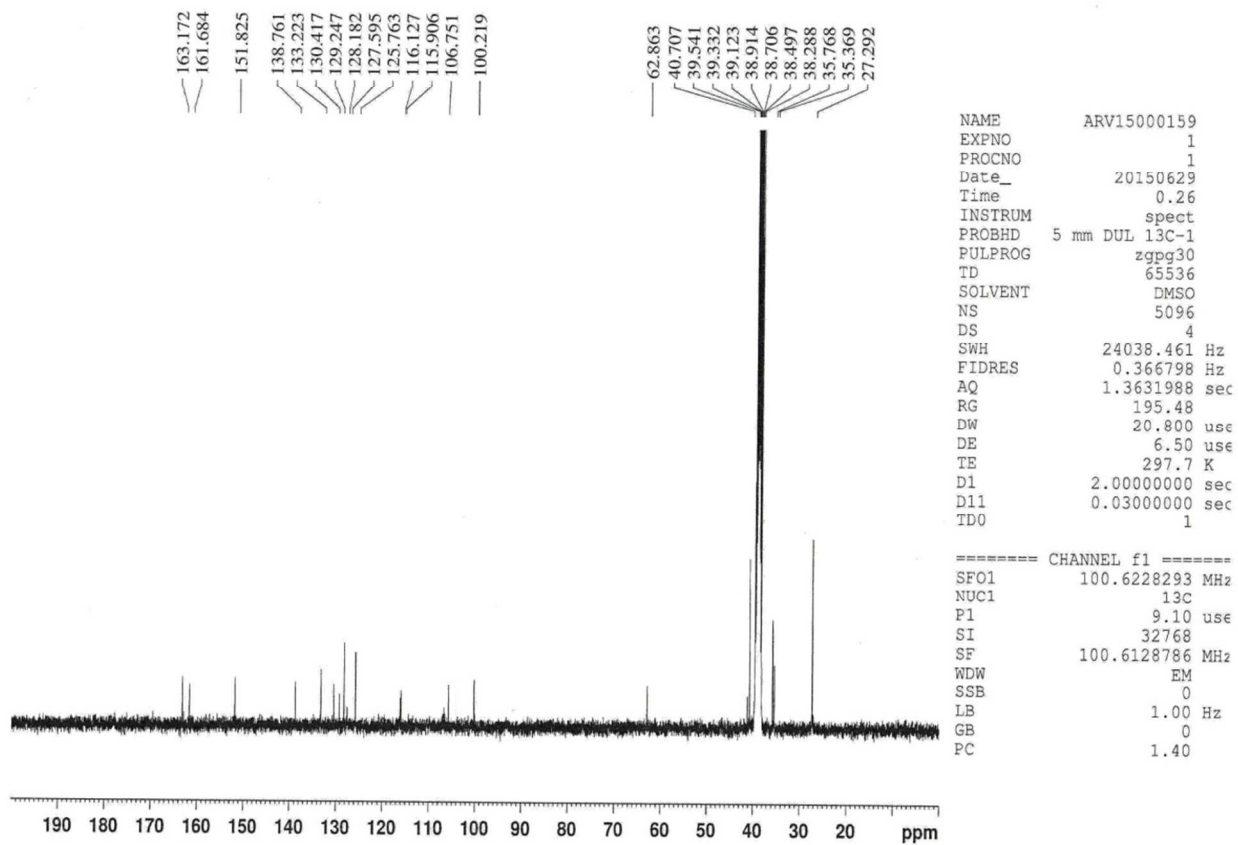


Figure S26: ¹³C Spectrum of compound 3k

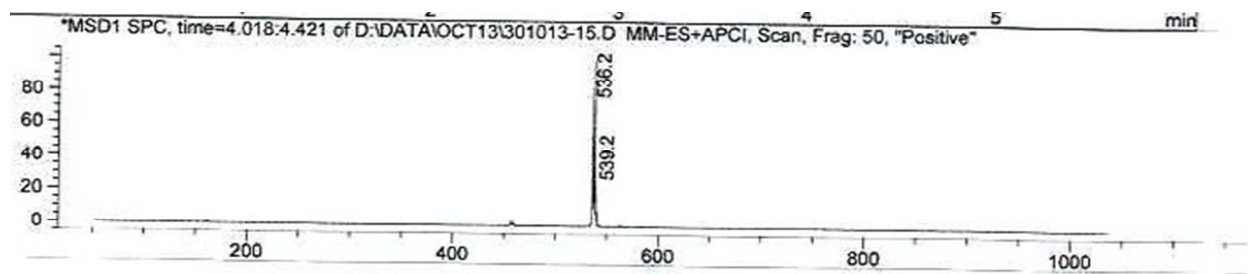


Figure S27: Mass Spectrum of compound 3k

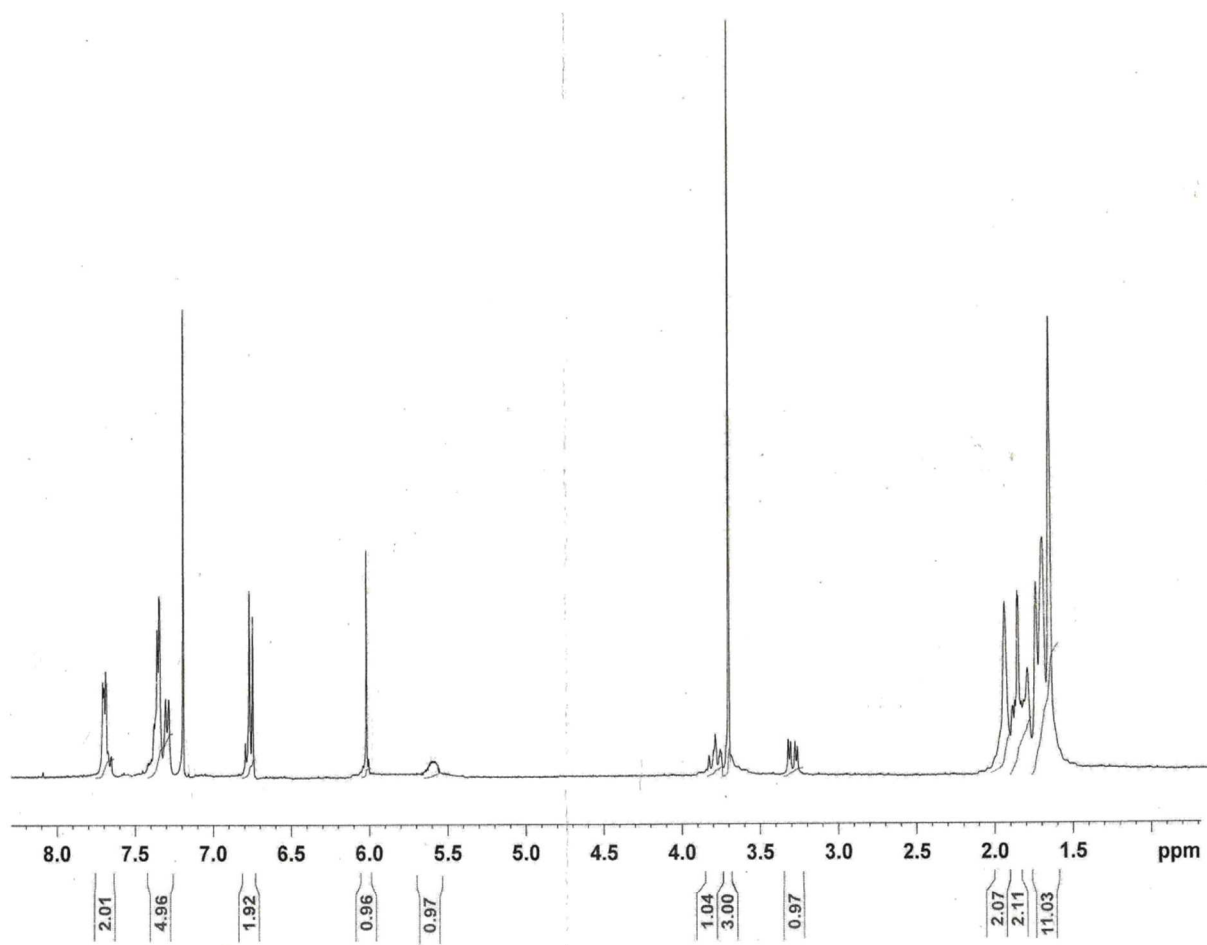
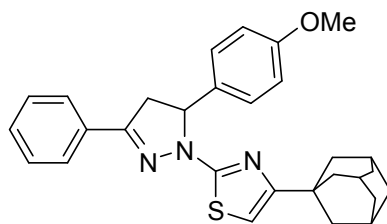


Figure S28: ¹H Spectrum of compound 31

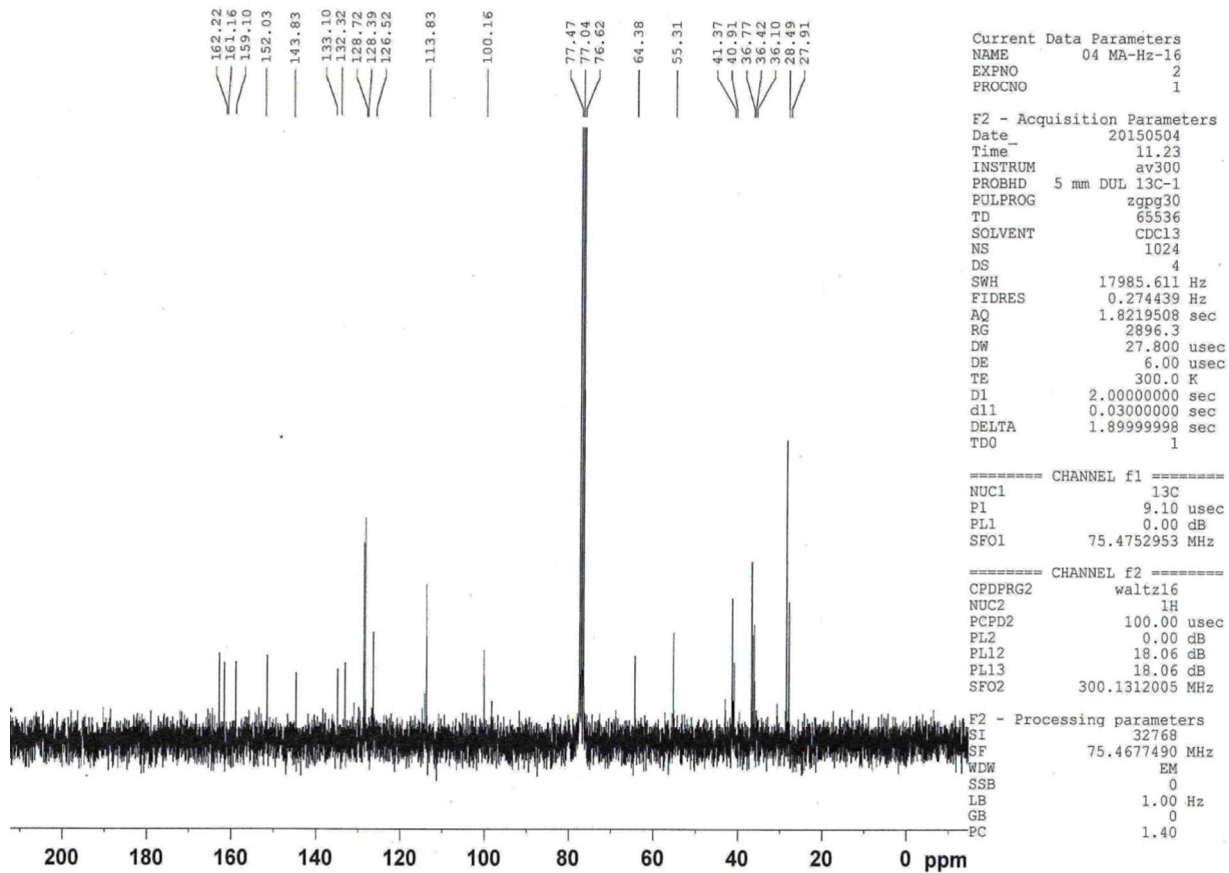


Figure S29: ¹³C Spectrum of compound 31

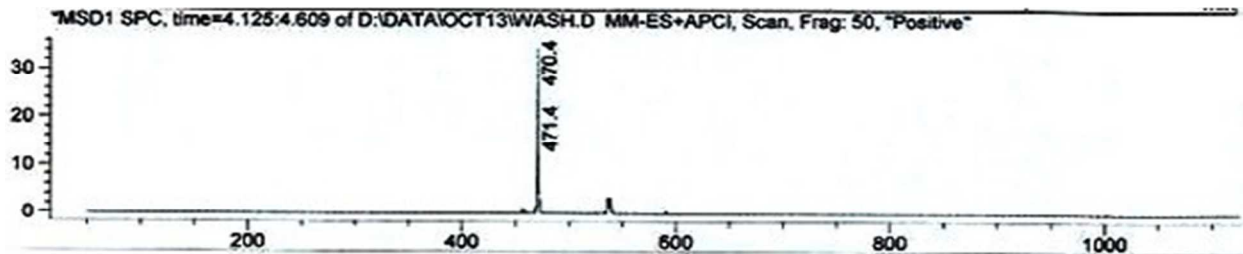


Figure S30: Mass Spectrum of compound 31

Table S2: *In silico* prediction of human targets for the title compounds based on the Parzen-Rosenblatt

Window classifier.

Entry	Predicted targets (with corresponding probabilities)							
3a	Amine oxidase [flavin-containing] A	0.10	Epidermal growth factor receptor	0.09	Cocaine esterase	0.06		
3b	Epidermal growth factor receptor	0.75						
3c	Epidermal growth factor receptor	0.69						
3d	Epidermal growth factor receptor	0.69						
3e	Epidermal growth factor receptor	0.64						
3f	G-protein coupled receptor 55	0.26	Amine oxidase [flavin- containing] B	0.08	Epidermal growth factor receptor	0.07	Cocaine esterase	0.05
3g	Epidermal growth factor receptor	0.42						
3h	G-protein coupled receptor 55	0.86						
3i	Epidermal growth factor receptor	0.08	Amine oxidase [flavin- containing] A	0.06				
3j	G-protein coupled receptor 55	0.27	Amine oxidase [flavin- containing] B	0.08	Epidermal growth factor receptor	0.07	Cocaine esterase	0.05
3k	G-protein coupled receptor 55	0.07	Epidermal growth factor receptor	0.07	Cocaine esterase	0.06		
3l	Epidermal growth factor receptor	0.16	Cocaine esterase	0.06	Liver carboxylesterase 1	0.05		