Supplementary Information for the paper

Design, synthesis, characterization, *in vitro* screening, molecular docking, 3D-QSAR, and ADME-Tox investigations of novel pyrazole derivatives as antimicrobial agents

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Table S1 Physical and spectroscopic characterization data of the synthesized compounds.

N°	R	Time (h)	Formula (M.)	M.p[b] (°C)	Yield[c] (%)	NMR-^{1}H (ppm)		^{13}C-NMR (ppm)	IR(cm^{-1})	HRMS *(m/z)* $[M+H]^+$
						R_1/ R_2	NH	R_1 and R_2	NH	
4a	H	4	$C_{30}H_{25}N_3O$ (443.1998)	160-162	92	$C\underline{H}_2$ (3.26) $C\underline{H}_3$ (1.32)	8.72	$\underline{C}H_2$ (37.2) $\underline{C}H_3$ (14.4)	3316	444.2088
4b	OCH_3	5	$C_{31}H_{27}N_3O_2$ (473.2103)	146-148	84	$C\underline{H}_2$ (3.26) $C\underline{H}_3$ (1.32)	8.73	$\underline{C}H_2$ (37.2) $\underline{C}H_3$ (14.4)	3314	474.2180
5a	H	10	$C_{35}H_{27}N_3O$ (505.2154)	170-172	70	$C\underline{H}_2$ (4.51)	9.24	$\underline{C}H_2$ (46.4)	3312	506.2228
5b	OCH_3	8	$C_{36}H_{29}N_3O_2$ (535.2260)	188-190	88	$C\underline{H}_2$ (4.51)	9.25	$\underline{C}H_2$ (46.4)	3327	536.2342
5c	Cl	7	$C_{35}H_{26}ClN_3O$ (539.1764)	138-140	65	$C\underline{H}_2$ (4.52)	9.25	$\underline{C}H_2$ (46.4)	3335	540.1845
5d	CH_3	9	$C_{36}H_{29}N_3O$ (519.2311)	152-154	76	$C\underline{H}_2$ (4.51)	9.24	$\underline{C}H_2$ (46.4)	3300	520.2394
6a	H	11	$C_{31}H_{25}N_3O$ (455.1998)	148-140	66	$C\underline{H}_2$ (3.91) $\underline{H}C{=}C$ (5.93) $C{=}C\underline{H}_2$ (5.21)	8.96	$\underline{C}H_2$ (44.7)	3292	456.2081
6b	OCH_3	10	$C_{32}H_{27}N_3O_2$ (485.2103)	146-148	73	$C\underline{H}_2$ (3.9) $\underline{H}C{=}C$ (5.94) $C{=}C\underline{H}_2$ (5.2)	8.96	$\underline{C}H_2$ (44.7)	3346	486.2181
6c	Cl	8	$C_{31}H_{24}ClN_3O$ (489.1608)	130-132	69	$C\underline{H}_2$ (3.92) $\underline{H}C{=}C$ 5.94) $C{=}C\underline{H}_2$ (5.23)	8.97	$\underline{C}H_2$ (44.7)	3352	490.1697
7a	H	9	$C_{31}H_{23}N_3O$ (453.1841)	178-180	57	$C\underline{H}_2$ (4.03) $C{\equiv}C\underline{H}$ (2.26)	8.85	$\underline{C}H_2$ (32.2) $\underline{C}{\equiv}C$ (79.5) $C{\equiv}\underline{C}H$ (71.5)	3329	454.1925
7b	OCH_3	5	$C_{32}H_{25}N_3O_2$ (483.1947)	170-172	68	$C\underline{H}_2$ (4.03) $C{\equiv}C\underline{H}$ (2.26)	8.86	$\underline{C}H_2$ (32.2) $\underline{C}{\equiv}C$ (79.6) $C{\equiv}\underline{C}H$ (71.5)	3323	484.2022
8a	H	2	$C_{29}H_{23}N_3O$ (429,1841)	200-202	83	$C\underline{H}_3$ (2.92)	8.80	$\underline{C}H_3$ (29.3)	3316	430.1931
8b	OCH_3	2.30	$C_{30}H_{25}N_3O_2$ (459,1947)	176-178	89	$C\underline{H}_3$ (2.92)	8.79	$\underline{C}H_3$ (29.3)	3309	460.2040
8c	Cl	3	$C_{29}H_{22}ClN_3O$ (463,1451)	174-176	76	$C\underline{H}_3$ (2.93)	8.81	$\underline{C}H_3$ (29.3)	3350	464.1540
8d	CH_3	1	$C_{30}H_{25}N_3O$ (443,1998)	172-174	91	$C\underline{H}_3$ (2.92)	8.81	$\underline{C}H_3$ (29.3)	3318	444.2092
9a[c]	H	14	$C_{30}H_{25}N_3O$ (443,1998)	180-182	55	$2C\underline{H}_3$ (2.67)	-	$2\underline{C}H_3$ (43.9)	-	444.2069
9b[c]	OCH_3	13	$C_{31}H_{27}N_3O_2$ (473,2103)	134-136	67	$2C\underline{H}_3$ (2.67)	-	$2\underline{C}H_3$ (44.0)	-	474.2189
9c[c]	Cl	17	$C_{30}H_{24}ClN_3O$ (477,1608)	164-166	59	$2C\underline{H}_3$ (2.67)	-	$2\underline{C}H_3$ (44.1)	-	478.1701
9d[c]	CH_3	12	$C_{31}H_{27}N_3O$ (457,2154)	158-160	74	$2C\underline{H}_3$ (2.68)	-	$2\underline{C}H_3$ (44.0)	-	458.2250

[a] Reagents and conditions: **3a-d** (1 equiv), R-X (1 equiv), DMF (20 mL), BTBA (0,5 equiv.), NaH (1 equiv), rt.
[b] Isolated yield.
[c] Conditions: **3a-d** (1 equiv), CH_3I (2 equiv), NaH (2 equiv).

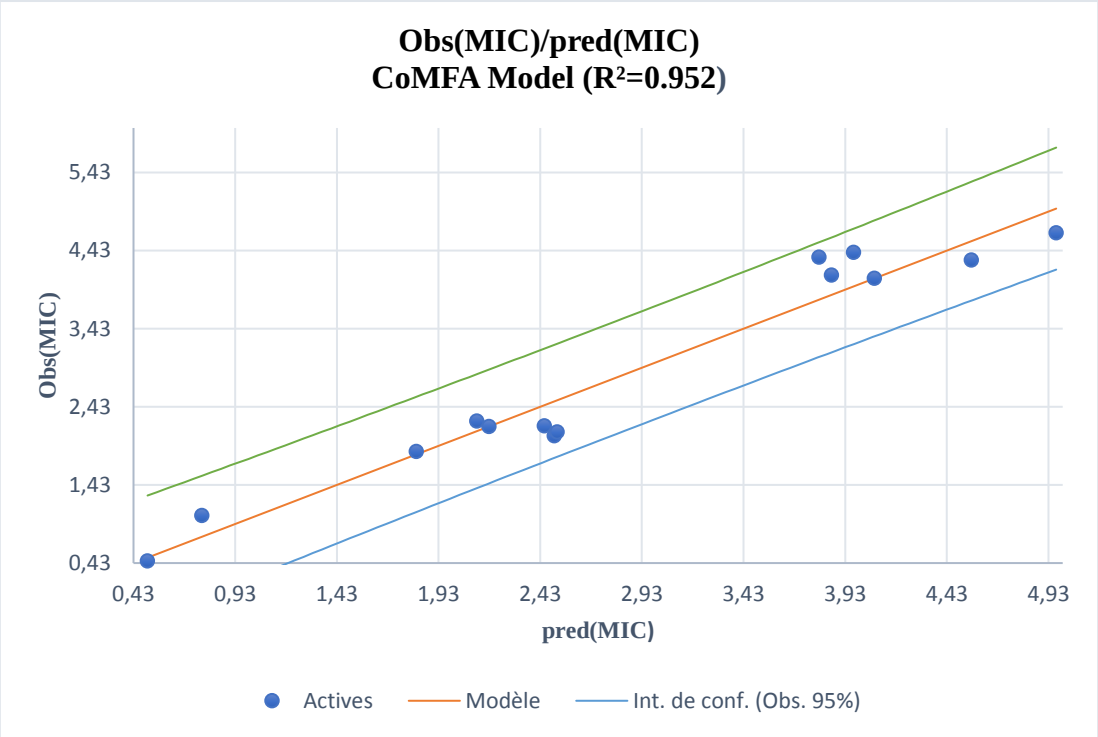


Figure S1. Plots of experimental and predicted MIC values for the 14 pyrazoles used in CoMFA model

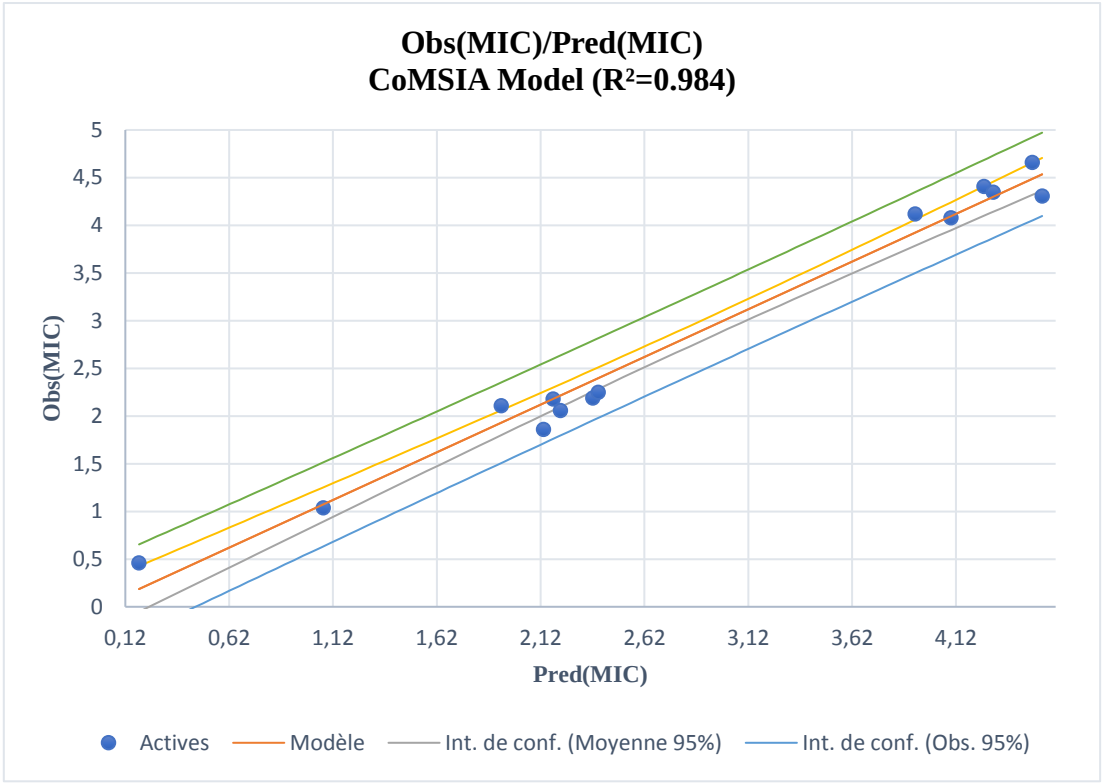


Figure S2. Plots of experimental and predicted MIC values for the 14 pyrazoles used in CoMSIA model

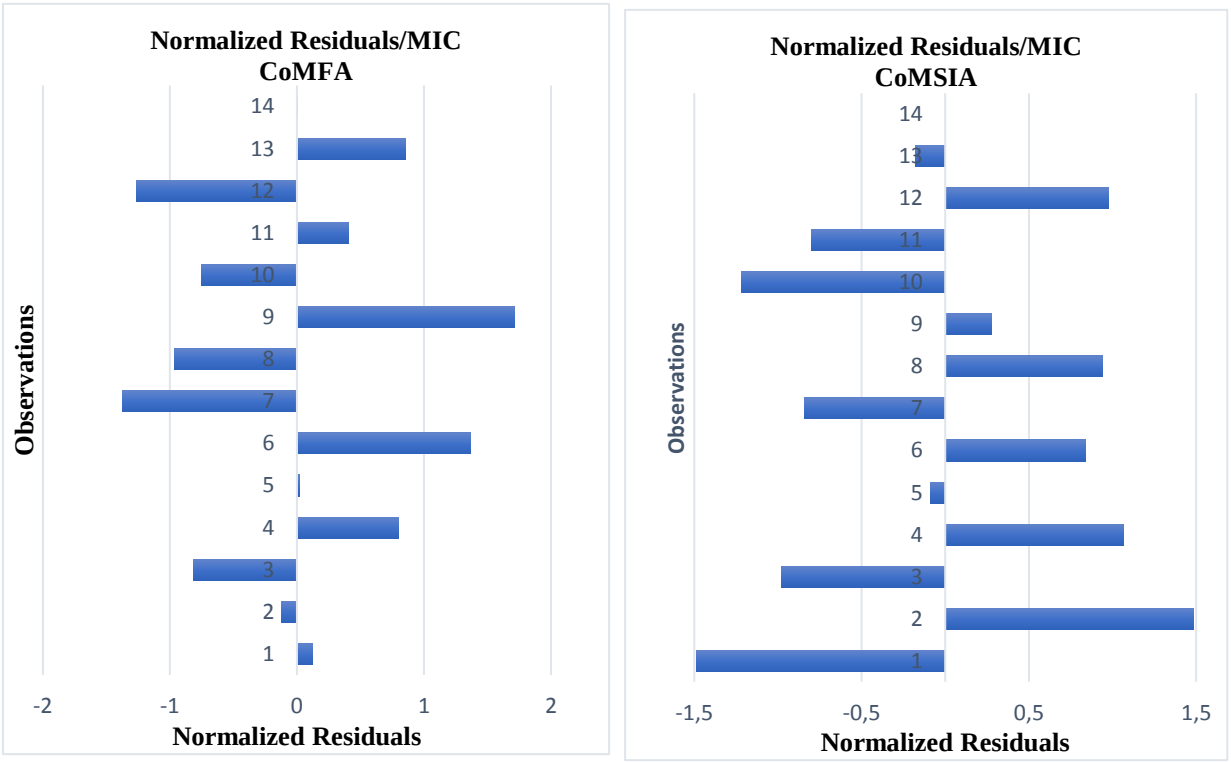
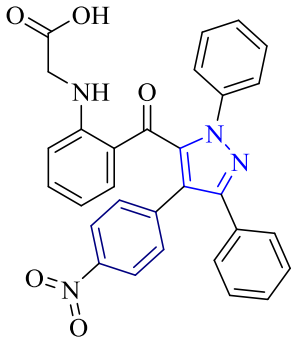
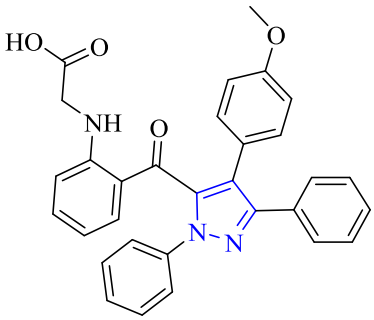
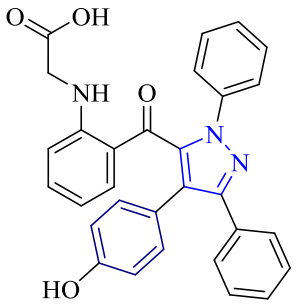
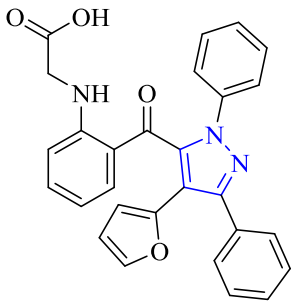
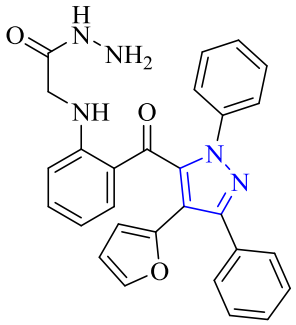
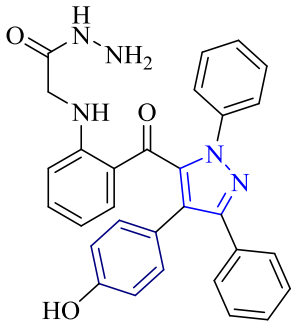
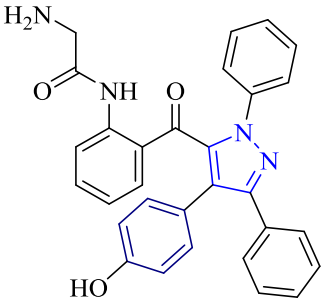
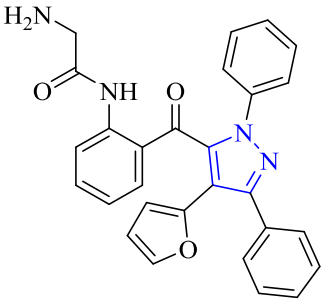
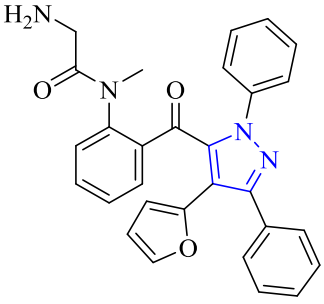
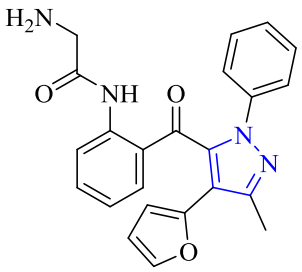
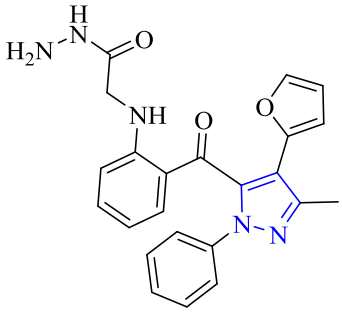
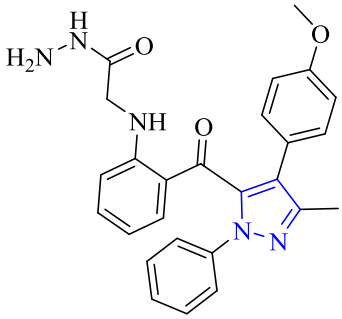
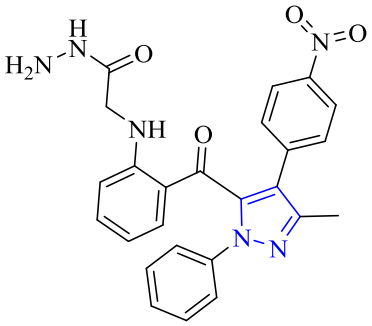
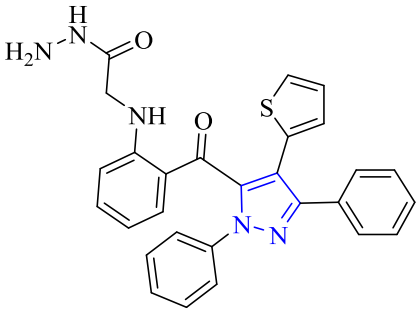


Figure S3. The plot of residuals for the training sets obtained from the CoMFA and CoMSIA models

Table S2 Structures and their predicted MIC of newly designed inhibitors based on 3D-QSAR models.

References	Structure	(Pred MIC) CoMFA	(Pred MIC) CoMSIA
C1		**1.424**	**2.434**
C2		**2.488**	**2.412**
C3		**1.636**	**2.172**
C4		**2.267**	**3.286**

C5		**1.011**	**2.244**
C6		**0.293**	**1.082**
C7		**0.816**	**1.092**
C8		**1.658**	**2.082**
C9		**0.110**	**1.031**

C10		**1.641**	**2.136**
C11		**2.143**	**1.151**
C12		**1.630**	**1.158**
C13		**1.231**	**1.396**
C14		**1.956**	**1.048**

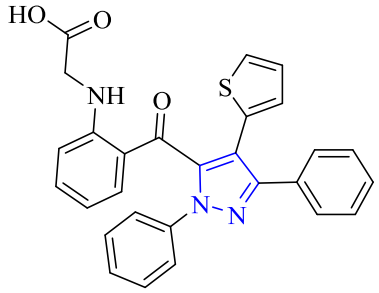
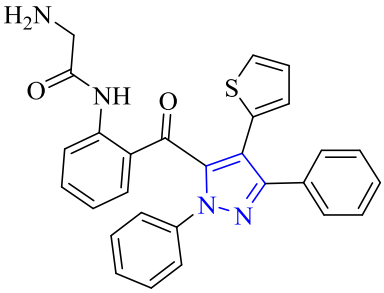
C15		**2.801**	**2.341**
C16		**1.388**	**2.044**

Table S3 Prediction of drug-likeness for the synthesized 14 compounds and 16 designed ones.

	MW(Da)	LogP	n-OHNH acceptors	n-OHNH donors	Lipinski's violations	Drug-Like	n-ROTB	TPSA(A²)	Flexibility	S.A
Rule	**<500**	**≤5**	**<10**	**≤5**	**<2**	**Yes/No**	**≤10**	**<140**	**Yes/No**	**0<S.A<10**
Synthesized molecules										
5b	535.647	**4.55**	**3**	**1**	**1**	**No**	**9**	**46.92**	**Yes**	
5c	540.066	**4.78**	**2**	**1**	**1**	**No**	**8**	**56.15**	**Yes**	
6a	455.561	**3.85**	**2**	**1**	**0**	**Yes**	**8**	**46.92**	**Yes**	
6b	485.587	**4.77**	**3**	**1**	**0**	**Yes**	**9**	**56.15**	**Yes**	
6c	490.006	**4.24**	**2**	**1**	**0**	**Yes**	**8**	**46.92**	**Yes**	
7a	453.545	**4.16**	**2**	**1**	**0**	**Yes**	**7**	**46.92**	**Yes**	
7b	483.571	**4.06**	**3**	**1**	**0**	**Yes**	**8**	**46.92**	**Yes**	
8a	429.523	**4.11**	**2**	**1**	**0**	**Yes**	**6**	**56.15**	**Yes**	
8b	459.549	**4.28**	**3**	**1**	**0**	**Yes**	**7**	**46.92**	**Yes**	
8c	463.968	**3.86**	**2**	**1**	**0**	**Yes**	**6**	**46.92**	**Yes**	
9a	443.550	**3.87**	**2**	**0**	**0**	**Yes**	**6**	**56.15**	**Yes**	
9b	473.576	**3.92**	**3**	**0**	**0**	**Yes**	**7**	**46.92**	**Yes**	
9c	477.995	**4.11**	**2**	**0**	**0**	**Yes**	**6**	**56.15**	**Yes**	
9d	457.577	**4.00**	**2**	**0**	**0**	**Yes**	**6**	**46.92**	**Yes**	
Designed molecules										
C1	518.52	**2.72**	**6**	**2**	**1**	**Yes**	**9**	**130.04**	**Yes**	**4.15**
C2	**503.55**	**3.71**	**5**	**2**	**1**	**Yes**	**9**	**93.45**	**Yes**	**3.89**
C3	**489.52**	**3.04**	**5**	**3**	**0**	**Yes**	**8**	**104.45**	**Yes**	**3.80**
C4	**463.48**	**3.27**	**5**	**2**	**0**	**Yes**	**8**	**97.36**	**Yes**	**3.89**
C5	**477.51**	**3.23**	**5**	**3**	**0**	**Yes**	**9**	**115.18**	**Yes**	**4.02**
C6	**503.55**	**2.80**	**5**	**4**	**1**	**Yes**	**9**	**122.27**	**Yes**	**3.95**
C7	**488.54**	**2.97**	**5**	**3**	**0**	**Yes**	**8**	**110.24**	**Yes**	**3.82**
C8	**462.50**	**3.30**	**5**	**2**	**0**	**Yes**	**8**	**103.15**	**Yes**	**3.90**
C9	**476.53**	**3.49**	**5**	**1**	**0**	**Yes**	**8**	**94.36**	**Yes**	**4.02**
C10	**400.43**	**2.77**	**5**	**2**	**0**	**Yes**	**7**	**103.15**	**Yes**	**3.49**

C11	**415.44**	**2.80**	**5**	**3**	**0**	**Yes**	**8**	**115.18**	**Yes**	**3.63**
C12	**455.51**	**3.10**	**5**	**3**	**0**	**Yes**	**9**	**111.27**	**Yes**	**3.63**
C13	**470.48**	**2.42**	**6**	**3**	**0**	**Yes**	**9**	**147.86**	**No**	**3.63**
C14	**493.58**	**3.29**	**4**	**3**	**0**	**Yes**	**9**	**130.28**	**Yes**	**3.95**
C15	**479.55**	**2.68**	**4**	**2**	**0**	**Yes**	**8**	**112.46**	**Yes**	**3.82**
C16	**478.56**	**3.33**	**4**	**2**	**0**	**Yes**	**8**	**118.25**	**Yes**	**3.83**

MW: Molecular Weight**, MLog P:** logarithm of partition coefficient of compound between n-octanol and water**, n-OHNH acceptors:** Number of hydrogen bond acceptors**, n-OHNH donors:** Number of hydrogen bonds donors**, n-ROTB**: Number of Rotatable Bonds**, S.A**: Synthetic accessibility**, TPSA:** Topological Polar Surface Area**.**

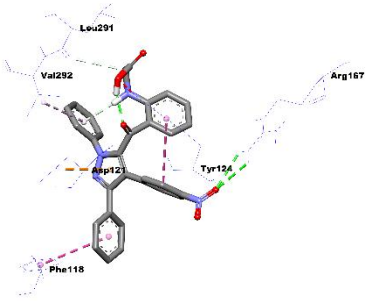
Table S4 ADMET properties

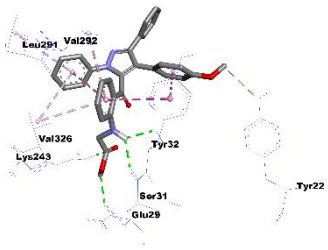
	Properties															
	Absorption		Distribution			Metabolism							Excretion	Toxicity		
models	Intestinal absorption (human)	P-Gp substrate	VDss (human)	BBB permeability	CNS permeability	CYP							Total clearance	AMES toxicity	Skin Sensitisation	Oral Rat Acute Toxicity (LD_{50})
						Substrate		Inhibitor								
						2D6	3A4	1A2	2C19	2C9	2D6	3A4				
Unity	Numeric (%absorbed)	Categorical (yes/no)	Numeric (Log L kg^{-1})	Numeric (Log BB)	Numeric (Log PS)	Categorical (Yes/No)							Numeric (log mL min^{-1} kg^{-1})	Categorical (Yes/No)	Categorical (Yes/No)	Numeric (mol/kg)
Predicted values of synthesized molecules																
5b	96.432	No	-0.848	0.272	-1.373	No	**Yes**	Yes	No	No	No	No	0.600	**No**	No	**2.917**
5c	93.336	Yes	-0.744	0.422	-0.030	No	**Yes**	Yes	No	No	No	No	0.040	**No**	No	**3.107**
6a	99.870	No	-0.755	0.099	-0.549	No	**Yes**	No	**Yes**	**Yes**	No	No	0.685	**No**	No	**3.881**
6b	96.278	No	-0.985	0.171	-1.646	No	**Yes**	No	**Yes**	**Yes**	No	**Yes**	0.669	**No**	No	**4.148**
6c	94.430	No	-0.918	0.299	-0.599	No	**Yes**	No	**Yes**	**Yes**	No	**Yes**	0.204	**No**	No	**4.006**
7a	100	Yes	-0.788	-0.146	-0.141	No	**Yes**	No	**Yes**	**Yes**	No	No	0.563	**No**	No	**3.89**
7b	97.554	No	-1.009	0.195	-1.662	No	**Yes**	No	**Yes**	**Yes**	No	No	0.615	**No**	No	**4.16**
8a	99.723	No	-0.758	0.163	-0.508	No	**Yes**	No	**Yes**	**Yes**	No	**Yes**	0.625	**No**	No	**2.932**
8b	100	No	-0.820	-0.236	-0.236	No	**Yes**	No	**Yes**	**Yes**	No	No	0.657	**No**	No	**2.747**
8c	98.176	Yes	-0.756	0.132	-0.506	No	**Yes**	No	**Yes**	**Yes**	No	No	0.150	**No**	No	**3.047**
9a	100	No	-0.766	0.283	-0.796	No	**Yes**	No	**Yes**	**Yes**	No	**Yes**	0.694	**No**	No	**2.885**
9b	99.089	No	-0.752	0.307	-0.801	No	**Yes**	No	**Yes**	**Yes**	No	No	0.734	**No**	No	**2.648**
9c	100	No	-0.769	0.224	-0.845	No	**Yes**	No	**Yes**	**Yes**	No	No	0.209	**No**	No	**3.034**
9d	100	No	-0.772	0.237	-0.845	No	**Yes**	No	**Yes**	**Yes**	No	No	0.697	**No**	No	**3.028**
Predicted values of designed molecules																
Unity	Numeric (%absorbed)	Categorical (yes/no)	Numeric (Log L kg^{-1})	Numeric (Log BB)	Numeric (Log PS)	Categorical (Yes/No)							Numeric (log mL min^{-1} kg^{-1})	Categorical (Yes/No)	Categorical (Yes/No)	Numeric (mol/kg)
C1	100	No	-1.300	-1.407	-2.215	No	Yes	Yes	No	No	No	No	0.748	No	No	2.565

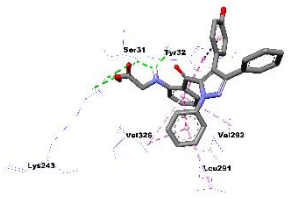
C2	82	Yes	-1.348	-1.128	-2.117	No	Yes	No	No	Yes	No	No	0.383	No	No	2.840
C3	77.581	Yes	-1.387	-1.417	-2.148	No	Yes	Yes	No	Yes	No	No	0.328	No	No	2.509
C4	82	Yes	-0.911	-1.062	-1.962	Yes	Yes	Yes	No	Yes	No	No	0.373	No	No	2.506
C5	92	Yes	-0.68	-1.396	-2.304	Yes	Yes	No	Yes	Yes	No	No	0.312	No	No	2.560
C6	87	Yes	-1.305	-1.403	-2.489	No	Yes	No	Yes	Yes	No	No	0.178	No	No	2.567
C7	94	Yes	1.303	-1.199	-2.144	No	Yes	Yes	No	Ye	No	No	0.315	No	No	2.644
C8	99	Yes	-0.595	-1.028	-1.958	No	Yes	Yes	Yes	No	Yes	No	0.514	No	No	2.537
C9	100	Yes	-0.261	-1.018	-1.893	No	Yes	No	Yes	No	No	No	0.433	No	No	2.262
C10	92	Yes	0.318	-0.945	-2.25	No	Yes	Yes	No	No	No	Yes	0.671	No	No	2.666
C11	86	Yes	-0.298	-1.361	-2.595	Yes	Yes	Yes	Yes	Yes	No	Yes	0.291	Yes	No	2.271
C12	88	Yes	-0.96	-1.362	-2.738	No	Yes	No	Yes	Yes	No	Yes	0.281	Yes	No	2.774
C13	83	Yes	-1.273	-1.372	-2.733	No	Yes	No	Yes	Yes	No	Yes	0.359	Yes	No	2.575
C14	94	Yes	-1.111	-1.349	-2.306	Yes	Yes	No	Yes	Yes	No	No	0.027	No	No	2.554
C15	96	Yes	-1.253	-1.06	-1.965	No	Yes	No	No	Yes	No	No	0.184	No	No	2.504
C16	97	Yes	-1.086	-1.024	-1.961	No	Yes	No	Yes	No	Yes	No	0.562	No	No	2.265

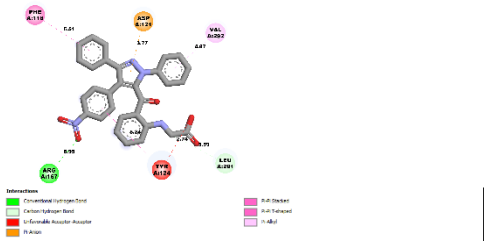
Table S5 Summary of molecular docking results

Ligands	Binding energy (kcal/mol)	Hydrogen-Bonding Interaction	Electrostatic Interaction	Hydrophobic Interaction
5c	**-9.2**	**SER31** and **TYR32**	**LYS243**	**LEU291**, **VAL292**, **VAL36**, **TYR22**, **PHE118**
C1	-8.8	ARG167, LEU291 and TY124	ASP121	PHE118, VAL292 and TYR124
C2	-8.9	TYR32, SER31, GLU29, LYS243 and TYR22	-	LEU291, VAL326 and VAL292
C3	-8.9	TYR32, SER31 and LYS243	-	LEU291, VAL326 and VAL292
C4	-9.0	TYR32, SER31 and LYS243	-	LEU291, VAL326, TYR32 and VAL292
C5	**-9.2**	TYR32, SER31 and LYS243	-	LEU291, VAL326 and VAL292
C6	**-9.2**	TYR32, SER31, GLU29 and LYS243	-	LEU291, VAL326, TYR32 and VAL292
C7	**-9.2**	TYR32 and SER31	-	LEU291, VAL326, TYR32 and VAL292
C8	**-9.2**	TYR32, SER31 and **GLY327**	-	LEU291, VAL326, TYR32 and VAL292
C9	-8.3	LEU291	-	TYR32, VAL326, ILE318, VAL292 and PRO239
C10	-8.2	TYR32 and **GLY327**	ASP121	VAL292, VAL326, LEU291 and TYR32
C14	**-9.2**	LYS243, SER31 and TYR32	-	TYR32, VAL292, VAL326 and LEU291
C15	-8.8	SER31, **LYS243** and TYR32	-	TYR32, **VAL292**, VAL326 and LEU291
C16	-9.0	TYR32, **SER31** and **GLY327**	-	LEU291, VAL326, TYR32 and **VAL292**
Ampicillin	-7.6	**SER31**, **GLY327**, **LYS243**, **THR241**	-	**TYR124** and **Val292**
Streptomycin	-9.1	ALA123, ASP113, PRO116, LEU115, **GLU117**, GLU119, GLU33 and ARG132	-	TYR40

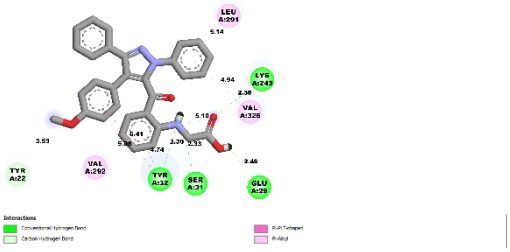




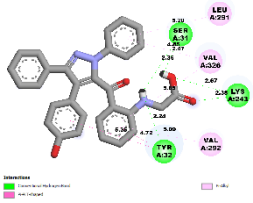




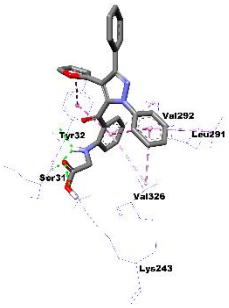
C1-protein

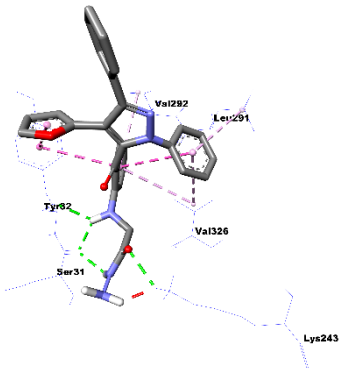


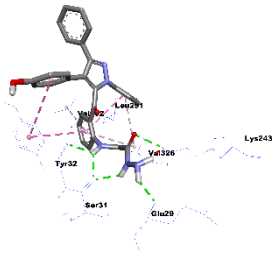
C2-protein

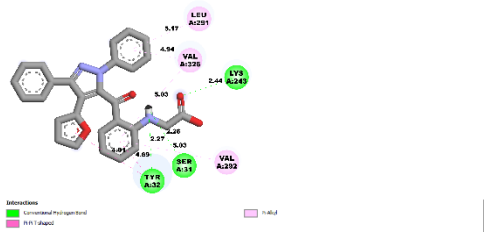


C3-protein

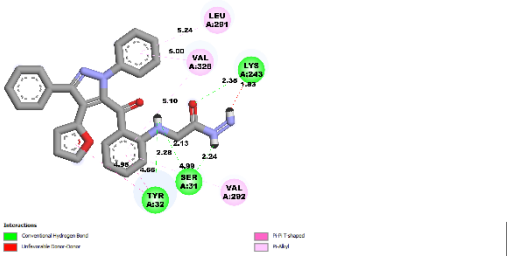




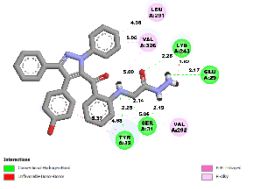




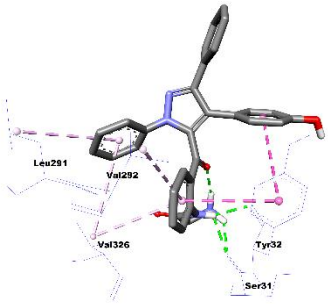
C4-protein

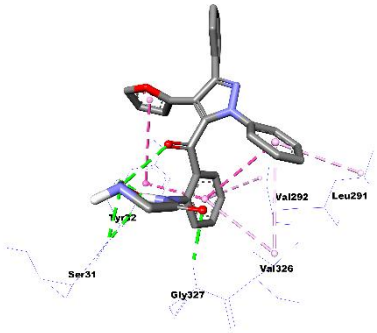


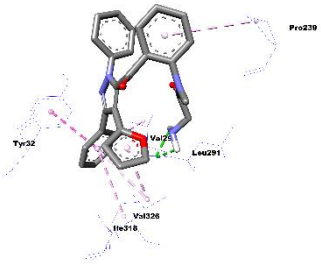
C5-protein

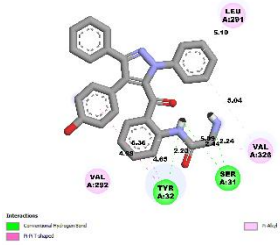


C6-protein









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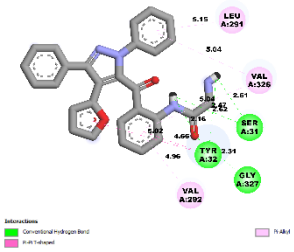
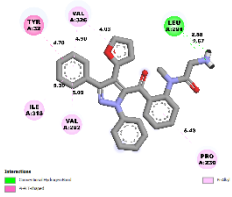
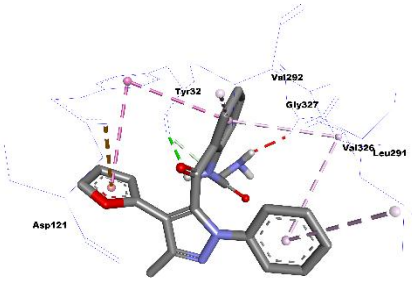
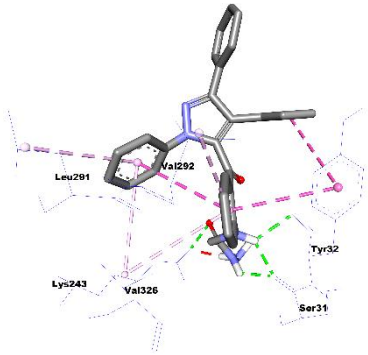


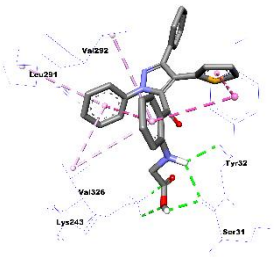
C8-protein

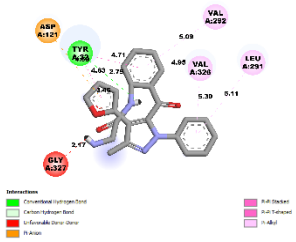


C9-protein

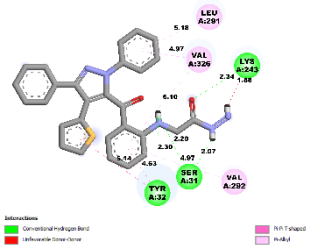




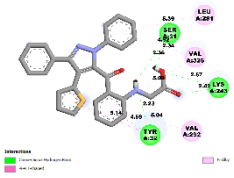




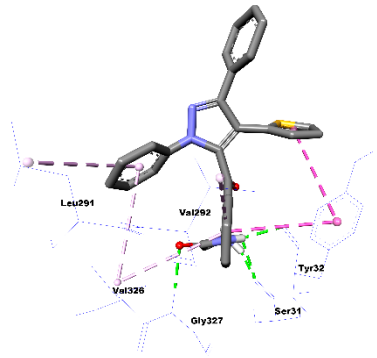
C10-protein

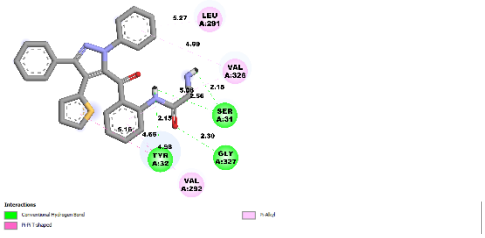


C14-protein



C15-protein





C16--protein

Figure S4. Visualization's 3D and 2D of docking results of the ligands designed.

1. Chemical reagents and instruments

All chemicals used were of analytical grade and were used without further purification and were purchased from commercial suppliers. The progress of the reactions was monitored by TLC (Merck, silica gel 60 F254), and spots were visualized under UV light (VILBER LOURMAT, VL-215.LC). Column chromatography was performed using Merck silica gel (70-230 mesh) and n-hexane / diethyl ether mixture as eluent. The melting points were determined with an uncertainty of ± 2 °C using a KOFLER BENCH. The IR spectra were recorded in the range of 450–4000 cm^{-1} on a BRUKER VERTEX 70 FT-IR Spectrometer, and wavenumbers are given in cm^{-1}. The NMR spectra (^{1}H and ^{13}C) were recorded at room temperature on a BRUKER AVANCE II 300 Ultra-Shield (300 MHz for ^{1}H and 75 MHz for ^{13}C) spectrometer using $CDCl_3$ as solvent. For the ^{13}C NMR spectra, the APT experiment was used, which provide information on the multiplicity of the ^{13}C signals (CH_3, CH_2, CH and C_q). In these spectra, the negative signals correspond to the CH_3 and CH carbons and the positive signals correspond to the CH_2 and quaternary C carbons. The chemical displacements are expressed in ppm and the coupling constants *J* are expressed in Hertz (Hz). The spin multiplicities are reported as singlet (s), doublet (d), triplet (t), multiplet (m), doublet of doublets (dd), doublet of triplets (dt) and broad (br). High-resolution mass spectra were recorded on a Waters/Vion IMS-QTOF: Spectrometer–, equipped with an electrospray ionization (ESI), source operating in either positive and negative ion mode.

2. Characterization data of all synthesized pyrazoles (4-9)

a) 5-(2-ethylaminobenzoyl)-1,3,4-triphenyl-1H pyrazole (4a)

Yield (92 %); m.p.: 160-162 °C; FT-IR (υ_{max}, cm^{-1}): 3316 (N-H), 3075, 3054 and 3032 (C-H aromatic), 2958, 2920 and 2866 (C-H aliphatic), 1613 (>C=O), 1575 (>C=N, pyrazole ring), 1515, 1499 (>C=C<, aromatic ring), 1455, 1427 (C-N<); ^{1}H NMR (300 MHz, $CDCl_3$) (δ/ppm): 1.32 (t, 3H, –C**H**$_3$, *J* = 7.2 Hz), 3.22-3.31 (m, 2H, –C**H**$_2$–), 6.27-6.33 (m, 1H, Ar–**H**), 6.61 (d, 1H, Ar–**H**, *J* = 8.7 Hz), 7.19-7.39 (m, 13H, Ar–**H**), 7.53-7.59 (m, 4H, Ar–**H**), 8.72 (t, 1H, N–**H**, *J* = 4.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) (δ/ppm): 14.4 (**C**H_3), 37.2 (**C**H_2), 111.3, 114.1, 117.5, 122.1, 123.6, 127.0, 127.5, 127.9, 128.2, 128.4, 129.1, 129.9, 131.9, 132.5, 134.7, 136.0, 139.8, 139.9 (>**C**–N<), 149.8 (>**C**=N–), 151.7 (>**C**–NH–), 190.3 (>**C**=O); ESI-QTOF-MS **(**m/z): mass calculated for $[C_{30}H_{25}N_3O+H]^+$: 444.20855, found: 444.20888.

b) 5-(2-ethylaminobenzoyl)-4-(4-methoxyphenyl)-1,3-diphenyl-1H-pyrazole (4b)

Yield (84 %); m.p.: 146-148 °C; FT-IR (υ_{max}, cm^{-1}): 3314 (N-H), 3060 (C-H aromatic), 2969, 2936, 2873 and 2836 (C-H aliphatic), 1618 (>C=O), 1568 (>C=N, pyrazole ring), 1498 (>C=C<, aromatic ring), 1458 and 1426 (C-N<), 1245 (C-O); ^{1}H NMR (300 MHz, $CDCl_3$) (δ/ppm): 1.33 (t, 3H, –C**H**$_3$, J = 7.2 Hz), 3.22-3.31 (m, 2H, –C**H**$_2$–), 3.76 (s, 3H, –OC**H**$_3$), 6.29-6.34 (m, 1H, Ar–**H**), 6.61 (d, 1H, Ar–**H**, J = 8.7 Hz), 6.76 (d, 2H, Ar–**H**, J = 8.7 Hz), 7.13-7.20 (m, 2H, Ar–**H**), 7.22-7.38 (m, 8H, Ar–**H**), 7.52-7.60 (m, 4H, Ar–**H**), 8.73 (t, 1H, N–**H**, J = 4.8Hz); ^{13}C NMR (75 MHz, $CDCl_3$) (δ/ppm): 14.4 (**C**H_3), 37.2 (**C**H_2), 55.1 (–O**C**H_3), 111.3, 113.7, 114.1, 117.5, 121.8, 123.5, 124.1, 127.5, 127.8, 128.2, 128.4, 129.1, 131.0, 132.7, 134.7, 136.0, 139.8, 139.9 (>**C**–N<), 149.8 (>**C**=N–), 151.7 (>**C**–NH–), 158.6 (>**C**–OCH_3), 190.5 (>C=O); ESI-QTOF-MS (m/z): mass calculated for $[C_{31}H_{27}N_3O_2+ H]^+$: 474.21785, found: 474.21800.

c) 5-(2-benzylaminobenzoyl)-1,3,4-triphenyl-1H-pyrazole (5a)

Yield (70 %); m.p.: 170-172 °C; FT-IR (υ_{max}, cm^{-1}): 3312 (N-H), 3083, 3056 and 3031 (C-H aromatic), 2916 and 2852 (C-H aliphatic), 1613 (>C=O), 1569 (>C=N, pyrazole ring), 1515 and 1496 (>C=C<, aromatic ring), 1428 (C-N<); ^{1}H NMR (300 MHz, $CDCl_3$) (δ/ppm): 4.51 (d, 2H, –C**H**$_2$–, J = 5.7 Hz), 6.31-6.36 (m, 1H, Ar–**H**), 6.55 (d, 1H, Ar–**H**, J = 8.7 Hz), 7.14-7.41 (m, 18H, Ar–**H**), 7.56-7.61 (m, 4H, Ar–**H**), 9.24 (t, 1H, N-**H**, J = 5.7 Hz, exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$) (δ/ppm): 46.4 (**C**H_2), 112.0, 114.9, 118.2, 122.3, 123.7, 126.8, 127.2, 127.3, 127.8, 128.0, 128.4, 128.5, 128.7, 129.2, 129.9, 131.8, 132.5, 134.6, 136.1, 136.4, 138.2, 139.8, 140.0 (>**C**–N<), 149.9 (>**C**=N–),151.5 (>**C**–NH–), 190.7 (>**C**=O); ESI-QTOF-MS (m/z): mass calculated for $[C_{35}H_{27}N_3O+ H]^+$: 506.22281, found: 506.22288.

d) 5-(2-benzylaminobenzoyl)-4-(4-methoxyphenyl)-1,3-diphenyl-1H-pyrazole (5b)

Yield (88 %); m.p.: 188-190 °C; FT-IR (υ_{max}, cm^{-1}): 3313 (N-H), 3059, 3027 (C-H aromatic), 2931 and 2834 (C-H aliphatic), 1621 (>C=O), 1563 (>C=N, pyrazole ring), 1492 (>C=C<, aromatic ring), 1446 (C-N<), 1236 (C-O); ^{1}H NMR (300 MHz, $CDCl_3$) (δ/ppm): 3.77 (s, 3H, –OC**H**$_3$), 4.51 (d, 2H, –C**H**$_2$–, J = 6 Hz), 6.32-6.38 (m, 1H, Ar–**H**), 6.62-6.65 (m, 2H, Ar–**H**), 7.08-7.28 (m, 9H, Ar–**H**), 7.30-7.40 (m, 12H, Ar–**H**), 9.25 (t, 1H, N**H**, J = 5.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) (δ/ppm): 46.4 (CH_2), 55.0 (–O**C**H_3), 111.9, 114.8, 118.2, 123.6, 125.5, 126.8, 127.2, 128.2, 128.3, 128.4, 128.7, 128.7, 129.1, 131.0, 131.9, 136.5, 138.2, 139.8, 140.0, 140.1 (>**C**–N<), 149.9 (>**C**=N–), 151.5 (>**C**–NH–), 158.7 (>**C**–OCH_3), 190.0 (>**C**=O); ESI-QTOF-MS (m/z): mass calculated for $[C_{31}H_{27}N_3O_2H]^+$: 536.2335, found: 536.2342.

e) 5-(2-benzylaminobenzoyl)-4-(4-chlorophenyl)-1,3-diphenyl-1H-pyrazole (5c)

Yield (65 %); m.p.: 138-140 °C; FT-IR (υ_{max}, cm^{-1}): 3335 (N-H), 3027 (C-H aromatic), 2915 and 2855 (C-H aliphatic), 1619 (>C=O), 1572 (>C=N, pyrazole ring), 1512 and 1494 (>C=C<, aromatic ring), 1428 (C-N<), 757 (C-Cl); ^{1}H NMR (300 MHz, $CDCl_3$) (δ/ppm): 4.52 (d, 2H, –C**H**$_2$–, J = 6 Hz), 6.33-6.39 (m, 1H, Ar–**H**), 6.59 (d, 1H, Ar–**H**, J = 8.4 Hz), 7.16-7.29 (m, 5H, Ar–**H**), 7.31-7.41 (m, 12H, Ar–**H**), 7.55-7.60 (m, 4H, Ar–**H**), 9.25 (t, 1H, N-**H**, J = 5.7 Hz, exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$) (δ/ppm): 46.4 (**C**H_2), 112.1, 114.9, 118.1, 120.9, 123.6, 126.8, 127.3, 127.8, 128.1, 128.4, 128.4, 128.6, 128.7, 129.1, 131.1, 132.2, 133.1, 134.4, 136.2, 138.1, 139.7, 140.0 (>**C**–N<), 149.8 (>**C**=N–),151.6 (>**C**–NH–), 190.5 (>**C**=O); ESI-QTOF-MS (m/z): mass calculated for $[C_{35}H_{26}ClN_3O+ H]^+$: 540.18507, found: 540.18457.

f) 5-(2-benzylaminobenzoyl)-1,3-diphenyl-4-(p-tolyl)-1H-pyrazole (5d)

Yield (76 %); m.p.: 152-154 °C; FT-IR (υ_{max}, cm^{-1}): 3300 (N-H), 3061 and 3028 (C-H aromatic), 2917 and 2859 (C-H aliphatic), 1617 (>C=O), 1573 (>C=N, pyrazole ring), 1519 and 1496 (>C=C<, aromatic ring), 1428 (C-N<); ^{1}H NMR (300 MHz, $CDCl_3$) (δ/ppm): 2.31 (s, 3H, –C**H**$_3$), 4.51 (d, 2H, –C**H**$_2$–, J = 6 Hz), 6.34-6.35 (m, 1H, Ar–**H**), 6.55 (d, 1H, Ar–**H**, J = 8.4 Hz), 6.80-6.90 (m, 2H, Ar–**H**), 7.02-7.08 (m, 2H, Ar–**H**), 7.12-7.15 (m, 3H, Ar–**H**), 7.20-7.29 (m, 2H, Ar–**H**), 7.30-7.39 (m, 5H, Ar–**H**), 7.54-7.62 (m, 6H, Ar–**H**), 9.24 (t, 1H, N-**H**, J = 5.7 Hz, exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$) (δ/ppm): 21.2 (**C**H_3), 46.3 (**C**H_2), 111.8, 114.8, 118.3, 122.2, 123.6, 126.8, 127.2, 127.6, 127.8, 128.1, 128.2, 128.4, 128.6, 129.0, 129.1, 129.6, 132.6, 134.6, 135.9, 136.5, 136.7, 138.2, 139.9 (>**C**–N<), 149.8 (>**C**=N–),151.4 (>**C**–NH–), 190.9 (>**C**=O); ESI-QTOF-MS (m/z): mass calculated for $[C_{36}H_{29}N_3O+ H]^+$: 520.23963, found: 520.23941.

g) 5-(2-allylaminobenzoyl)-1,3,4-triphenyl-1H-pyrazole 6a

Yield (66 %); m.p.: 148-150 °C; FT-IR (υ_{max}, cm^{-1}): 3292 (N-H), 3061 and 3026 (=CH vinylic and C-H aromatic), 2985, 2913 and 2854 (C-H aliphatic), 1616 (>C=O), 1568 (>C=N, pyrazole ring), 1515 and 1497 (>C=C<, aromatic ring), 1429 (C-N<); ^{1}H NMR (300 MHz, $CDCl_3$) (δ/ppm): 3.89-3.94 (m, 2H, –C**H**$_2$–), 5.18-5.25 (m, 2H, =C**H**$_2$ allylic), 5.89-5.99 (m, 1H, –C**H**= allylic), 6.31-6.36 (m, 1H, Ar–**H**), 6.58 (d, 1H, Ar–**H**, J = 8.4 Hz), 7.18-7.39 (m, 13H, Ar–**H**), 7.53-7.60 (m, 4H, Ar–**H**), 8.96 (t, 1H, N-**H**, J = 5.7 Hz, exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$) (δ/ppm): 44.7 (–**C**H_2–), 111.7, 114.5, 116.1 (=**C**H_2 allylic), 117.9, 123.6, 127.1, 127.8, 127.9, 128.3, 128.4, 128.6, 129.1, 129.9, 131.8, 132.5, 133.8, 134.6, 135.9 (–**C**H= allylic), 138.1, 139.8, 139.9 (>**C**–N<), 149.8 (>**C**=N–),151.6 (>**C**–NH–), 190.6 (>**C**=O); ESI-QTOF-MS (m/z): mass calculated for $[C_{31}H_{25}N_3O+ H]^+$: 456.20782, found: 456.20812.

h) 5-(2-allylaminobenzoyl)-4-(4-methoxyphenyl)-1,3-diphenyl-1H-pyrazole 6b

Yield (73 %); m.p.: 146-148 °C; FT-IR (υ_{max}, cm^{-1}): 3346 (N-H), 3060 and 3026 (=CH vinylic and C-H aromatic), 2985, 2954 and 2835 (C-H aliphatic), 1614 (>C=O), 1567 (>C=N, pyrazole ring), 1497 (>C=C<, aromatic ring), 1424 (C-N<), 1242 (C-O); ^{1}H NMR (300 MHz, $CDCl_3$) (δ/ppm): 3.77 (s, 3H, –OC**H**$_3$), 3.89-3.93 (m, 2H, –C**H**$_2$–), 5.17-5.26 (m, 2H, =C**H**$_2$ allylic), 5.87-5.99 (m, 1H, –C**H**= allylic), 6.31-6.37 (m, 1H, Ar–**H**), 6.59 (d, 1H, Ar–**H**, J = 8.4 Hz), 6.74-6.78 (m, 2H, Ar–**H**), 7.13-7.38 (m, 10H, Ar–**H**), 7.52-7.61 (m, 4H, Ar–**H**), 8.96 (t, 1H, N-**H**, J = 5.7 Hz, exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$) (δ/ppm): 44.7 (–**C**H_2–), 55.1 (–O**C**H_3), 111.7, 113.8, 114.5, 116.1 (=**C**H_2 allylic), 117.9, 121.1, 121.8, 123.5, 124.0, 127.5, 127.8, 128.2, 128.4, 128.6, 129.1, 131.0, 132.6, 133.8, 134.6, 135.9 (–**C**H= allylic), 139.8, 139.8 (>**C**–N<), 149.8 (>**C**=N–),151.6 (>**C**–NH–),158.6 (>**C**–OCH_3), 190.8 (>**C**=O); ESI-QTOF-MS (m/z): mass calculated for $[C_{32}H_{27}N_3O_2+H]^+$: 486.21761, found: 486.21814.

i) 5-(2-allylaminobenzoyl)-4-(4-chlorophenyl)-1,3-diphenyl-1H-pyrazole 6c

Yield (69 %); m.p.: 130-132 °C; FT-IR (υ_{max}, cm^{-1}): 3352 (N-H), 3081, 3062 and 3015 (=CH vinylic and C-H aromatic), 2982, 2983 and 2839 (C-H aliphatic), 1613 (>C=O), 1566 (>C=N, pyrazole ring), 1496 (>C=C<, aromatic ring), 1421 (C-N<), 726 (C-Cl); ^{1}H NMR (300 MHz, $CDCl_3$) (δ/ppm): 3.90-3.95 (m, 2H, –C**H**$_2$–), 5.19-5.27 (m, 2H, =C**H**$_2$ allylic), 5.87-6.00 (m, 1H, –C**H**= allylic), 6.31-6.36 (m, 1H, Ar–**H**), 6.61 (d, 1H, Ar–**H**, J = 8.7 Hz), 7.14-7.39 (m, 12H, Ar–**H**), 7.52-7.57 (m, 4H, Ar–**H**), 8.96 (t, 1H, N-**H**, J = 5.7 Hz, exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$) (δ/ppm): 44.7 (–**C**H_2–), 111.8, 114.6, 116.2 (=**C**H_2 allylic), 117.7, 120.8, 123.6, 127.7, 128.1, 128.4, 128.6, 129.1, 130.4, 131.1, 132.2, 133.1, 133.7, 134.4, 136.2 (–**C**H= allylic), 139.7, 140.0 (>**C**–N<), 149.8 (>**C**=N–),151.7 (>**C**–NH–), 190.3 (>**C**=O); ESI-QTOF-MS (m/z): mass calculated for $[C_{31}H_{24}ClN_3O+H]^+$: 490.16939, found: 490.16973.

j) 5-(2-propargylaminobenzoyl)-1,3,4-triphenyl-1H-pyrazole 7a

Yield (57 %); m.p.: 178-180 °C; FT-IR (υ_{max}, cm^{-1}): 3329 (N-H), 3282 (≡CH propargylic), 3060 (C-H aromatic), 2910 and 2853 (C-H aliphatic), 1616 (>C=O), 1562 (>C=N, pyrazole ring), 1496 (>C=C<, aromatic ring), 1426 (C-N<); ^{1}H NMR (300 MHz, $CDCl_3$) (δ/ppm): 2.26 (t, 1H, –C≡C**H**, J = 2.4Hz), 4.04 (dd, 2H, –C**H**$_2$–, J = 2.4, 5.7Hz), 6.38-6.44 (m, 1H, Ar–**H**), 6.72 (d, 1H, Ar–**H**, J = 8.1Hz), 7.21-7.41 (m, 13H, Ar–**H**), 7.50-7.59 (m, 4H, Ar–**H**), 8.85 (t, 1H, N-**H**, J = 5.7Hz, exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$) (δ/ppm): 32.2 (–**C**H_2–), 71.5 (–C≡**C**H), 79.7 (–**C**≡CH), 111.5, 115.5, 118.6, 122.4, 123.7, 127.1, 127.7, 127.9, 128.2, 128.3, 128.4, 129.1, 129.9, 130.8, 131.7, 132.4, 134.6, 136.0, 139.7, 139.7 (>**C**–N<), 149.8 (>**C**=N–

),150.5 (>**C**–NH–), 190.8 (>**C**=O); ESI-QTOF-MS (m/z): mass calculated for $[C_{31}H_{23}N_3O+H]^+$: 454.19237, found: 454.19251.

k) 4-(4-methoxyphenyl)-1,3-diphenyl-5-(2-propargylaminobenzoyl)- 1H-pyrazole 7b

Yield (68 %); m.p.: 170-172 °C; FT-IR (υ_{max}, cm^{-1}): 3323 (N-H), 3247 (≡CH propargylic), 3042 (C-H aromatic), 2956, 2914 and 2834 (C-H aliphatic), 1617 (>C=O), 1566 (>C=N, pyrazole ring), 1496 (>C=C<, aromatic ring), 1427 (C-N<), 1245 (C-O); ^{1}H NMR (300 MHz, $CDCl_3$) (δ/ppm): 2.26 (t, 1H, –C≡C**H**, *J* = 2.4Hz), 3.76 (s, 3H, –OC**H**$_3$), 4.04 (dd, 2H, –C**H**$_2$–, *J* = 2.4, 5.7Hz), 6.04-6.45 (m, 1H, Ar–**H**), 6.71-6.78 (m, 3H, Ar–H), 7.12-7.16 (m, 2H, Ar–**H**), 7.25-7.41 (m, 8H, Ar–**H**), 7.51-7.57 (m, 2H, Ar–**H**), 7.58-7.61 (m, 2H, Ar–**H**), 8.86 (t, 1H, N-**H**, *J* = 5.7Hz, exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$) (δ/ppm): 32.2 (–**C**H_2–), 55.1 (–O**C**H_3), 71.5 (–C≡**C**H), 79.7 (–**C**≡CH), 111.6, 113.8, 115.5, 118.6, 122.1, 123.6, 123.9, 127.6, 127.7, 127.8, 128.2, 128.4, 129.1, 131.0, 132.6, 134.7, 136.0, 139.8(>**C**–N<), 149.8 (>**C**=N–), 150.5 (>**C**–NH–), 158.7 (>**C**–OCH_3), 190.0 (>**C**=O); ESI-QTOF-MS (m/z): mass calculated for $[C_{32}H_{25}N_3O_2+H]^+$: 484.20195, found: 484.20220.

l) 5-(2-methylaminobenzoyl)-1,3,4-triphenyl-1H-pyrazole (8a)

Yield (83 %); m.p.: 200-202 °C; FT-IR (υ_{max}, cm^{-1}): 3316 (N-H), 3051 (C-H aromatic), 2984, 2900, 2868 and 2817 (C-H aliphatic), 1618 (>C=O), 1569 (>C=N, pyrazole ring), 1522 and 1499 (>C=C<, aromatic ring), 1424 (C-N<); ^{1}H NMR (300 MHz, $CDCl_3$) (δ/ppm): 2.92 (d, 3H, –C**H**$_3$, *J* = 5.1 Hz), 6.30-6.35 (m, 1H, Ar–**H**), 6.60 (d, 1H, Ar–**H**, *J* = 8.4 Hz), 7.20-7.39 (m, 13H, Ar–**H**), 7.53-7.55 (m, 4H, Ar–**H**), 8.81 (q, 1H, N–**H**, , *J* = 4.8 Hz, exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$) (δ/ppm): 29.3(**C**H_3), 110.9, 114.2, 117.5, 123.7, 127.1, 127.6, 127.9, 128.3, 128.5, 129.1, 129.9, 131.8, 132.5, 134.7, 136.1, 139.8, 139.9 (>**C**–N<), 149.8 (>**C**=N–), 152.7 (>**C**–NH–), 190.4 (>**C**=O); ESI-QTOF-MS (m/z): mass calculated for $[C_{29}H_{23}N_3O+H]^+$: 430.19312, found: 430.19316.

m)4-(4-methoxyphenyl)-5-(2-methylaminobenzoyl)-1,3-diphenyl-1H-pyrazole (8b)

Yield (89 %); m.p.: 176-178 °C; FT-IR (υ_{max}, cm^{-1}): 3309 (N-H), 3052, 3005 (C-H aromatic), 2933, 2905 and 2834 (C-H aliphatic), 1617 (>C=O), 1570 (>C=N, pyrazole ring), 1519 and 1497 (>C=C<, aromatic ring), 1427 (C-N<), 1286 (C-O); ^{1}H NMR (300 MHz, $CDCl_3$) (δ/ppm): 2.92 (d, 3H, –CH_3, *J* = 5.1Hz), 3.77 (s, 3H, OCH_3), 6.34-6.37 (m, 1H, Ar–H), 6.61 (d, 1H, Ar–H, *J* = 8.4 Hz), 6.76-6.79 (m, 2H, Ar–H), 7.12-7.16 (m, 2H, Ar–H), 7.27-7.38 (m, 8H, Ar–H), 7.51-7.55 (m, 4H, Ar–H), 8.80 (q, 1H, N–H, , *J* = 5.4Hz); ^{13}C NMR (75 MHz, $CDCl_3$) (δ/ppm):

29.2 (CH$_3$), 55.1 (–OCH$_3$), 110.9, 113.9, 114.2, 117.5, 123.5, 123.7, 127.6, 128.2, 128.5, 129.1, 129.6, 131.0, 131.2, 133.7, 134.6, 136.2, 139.8, 140.0 (>C–N<), 148.7 (>C=N–), 152.7 (>C–NH–),158.8 (>C–OCH$_3$), 190.4 (>C=O); ESI-QTOF-MS (m/z): mass calculated for [$C_{30}H_{25}N_3O_2$+ H]$^+$: 460.20398, found: 460.20405.

n) 4-(4-chlorophenyl)-5-(2-methylaminobenzoyl)-1,3-diphenyl-1H-pyrazole (8c)

Yield (76 %); m.p.: 174-176 °C; FT-IR (υ_{max}, cm^{-1}): 3350 (N-H), 3073, 3056, 3027 (C-H aromatic), 2920, 2906 and 2881 (C-H aliphatic), 1619 (>C=O), 1566 (>C=N, pyrazole ring), 1518 and 1497 (>C=C<, aromatic ring), 1424 (C-N<), 725 (C-Cl); ^{1}H NMR (300 MHz, $CDCl_3$) (δ/ppm): 2.93 (d, 3H, –C**H$_3$**, *J* = 5.1Hz), 6.32-6.37 (m, 1H, Ar–**H**), 6.63 (d, 1H, Ar–**H**, *J* = 8.4 Hz), 7.14-7.21 (m, 4H, Ar–**H**), 7.25-7.39 (m, 7H, Ar–**H**), 7.53-7.58 (m, 4H, Ar–**H**), 8.81 (q, 1H, N–**H**, , *J* = 5.7Hz, exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$) (δ/ppm): 29.3 (**C**H$_3$), 111.1, 114.3, 117.4, 120.7, 123.6, 127.7, 128.1, 128.4, 128.4, 128.6, 129.1, 130.4, 131.1, 132.3, 133.1, 134.5, 136.3, 139.7, 140.0 (>**C**–N<), 149.8 (>**C**=N–), 152.8 (>**C**–NH–),190.1 (>**C**=O); ESI-QTOF-MS (m/z): mass calculated for [$C_{29}H_{22}ClN_3O$+ H]$^+$: 464.15393, found: 464.15401.

o) 5-(2-methylaminobenzoyl)-1,3-diphenyl-4-(p-tolyl)-1H-pyrazole (8d)

Yield (91 %); m.p.: 172-174 °C; FT-IR (υ_{max}, cm^{-1}): 3318 (N-H), 3058, 3023 (C-H aromatic), 2977, 2918, 2868 and 2816 (C-H aliphatic), 1618 (>C=O), 1568 (>C=N, pyrazole ring), 1518 and 1498 (>C=C<, aromatic ring), 1423 (C-N<); ^{1}H NMR (300 MHz, $CDCl_3$) (δ/ppm): 2.29 (s, 3H, –C**H$_3$**), 2.92 (d, 3H, –C**H$_3$**, *J* = 5.1Hz), 6.31-6.37 (m, 1H, Ar–**H**), 6.61 (d, 1H, Ar–**H**, *J* = 8.4 Hz), 7.02 (d, 2H, Ar–**H**, *J* = 7.8 Hz), 7.12 (d, 2H, Ar–**H**, *J* = 8.1 Hz), 7.23-7.38 (m, 8H, Ar–**H**), 7.52-7.61 (m, 4H, Ar–**H**), 8.82 (q, 1H, N–**H**, *J* = 6Hz, exchangeable with D_2O); ^{13}C NMR (75 MHz, $CDCl_3$) (δ/ppm): 21.2 (**C**H$_3$), 29.3 (**C**H$_3$), 110.9, 114.2, 117.6, 122.0, 123.6, 127.5, 127.8, 128.2, 128.4, 128.7, 129.0, 129.1, 129.7, 132.7, 134.7, 136.1, 136.7, 139.8, 139.9 (>**C**–N<), 149.9 (>**C**=N–), 152.7 (>**C**–NH–),190.6 (>**C**=O); ESI-QTOF-MS (m/z): mass calculated for [$C_{30}H_{25}N_3O$+ H]$^+$: 444.20926, found: 444.20927.

p) 5-(2-dimethylaminobenzoyl)-1,3,4-triphenyl-1H-pyrazole (9a)

Yield (55 %); m.p.: 180-182 °C; FT-IR (υ_{max}, cm-1): 3057 (C-H aromatic), 2995, 2926, 2880 and 2808 (C-H aliphatic), 1624 (>C=O), 1596 (>C=N, pyrazole ring), 1544 and 1496 (>C=C<, aromatic ring), 1409 (C-N<); ^{1}H NMR (300 MHz, $CDCl_3$) (δ/ppm): 2.67 (s, 6H, C**H$_3$**), 6.66-6.74 (m, 2H, Ar–**H**), 7.18-7.37 (m, 12H, Ar–**H**), 7.49-7.59 (m, 5H, Ar–**H**); ^{13}C NMR (75 MHz, $CDCl_3$) (δ/ppm): 43.9 (2 **C**H$_3$), 116.3, 118.1, 123.3, 124.8, 126.8, 127.3, 127.7, 127.8, 127.9,

128.1, 128.2, 128.7, 130.7, 132.0, 132.5, 133.5,133.9, 139.8, 140.5 (>**C**–N<), 149.8 (>**C**=N–), 152.4 (>**C**–$N(CH_3)_2$),186.7 (>**C**=O); ESI-QTOF-MS (m/z): mass calculated for $[C_{30}H_{25}N_3O+ H]^+$: 4744.20704, found: 444.20696.

q) 4-(4-methoxyphenyl)-5-(2-dimethylaminobenzoyl)-1,3-diphenyl-1H-pyrazole (9b)

Yield (67 %); m.p.: 134-136 °C; FT-IR (υ_{max}, cm^{-1}): 3062, 3000 (C-H aromatic), 2961 and 2836 (C-H aliphatic), 1629 (>C=O), 1597 (>C=N, pyrazole ring), 1544 and 1497 (>C=C<, aromatic ring), 1420 (C-N<), 1243 (C-O); ^{1}H NMR (300 MHz, $CDCl_3$) (δ/ppm): 2.67 (s, 6H, –C**H**$_3$),3.78 (s, 3H, –OC**H**$_3$), 6.67-6.77 (m, 4H, Ar–**H**), 7.15-7.24 (m, 2H, Ar–**H**), 7.26-7.35 (m, 7H, Ar–**H**), 7.46-7.58 (m, 5H, Ar–**H**); ^{13}C NMR (75 MHz, $CDCl_3$) (δ/ppm): 44.0 (2 –**C**H_3), 55.1 (–O-**C**H_3), 113.4, 116.3, 118.2, 124.8, 127.7, 127.7, 128.1, 128.2, 128.7, 131.9, 133.4, 133.8, 140.0, 140.5 (>**C**–N<), 149.9 (>**C**=N–), 152.4 (>**C**–$N(CH_3)_2$), 158.7 (>**C**–OCH_3), 186.9 (>**C**=O); ESI-QTOF-MS (m/z): mass calculated for $[C_{31}H_{27}N_3O_2+ H]^+$:474.21868, found: 474.21889.

r) 4-(4-chlorophenyl)-5-(2-dimethylaminobenzoyl)-1,3-diphenyl-1H-pyrazole (9c)

Yield (59 %); m.p.: 164-166 °C; FT-IR (υ_{max}, cm^{-1}): 3062 (C-H aromatic), 2960, 2925 and 2810 (C-H aliphatic), 1626 (>C=O), 1595 (>C=N, pyrazole ring), 1544 and 1497 (>C=C<, aromatic ring), 1414 (C-N<), 729 (C-Cl); ^{1}H NMR (300 MHz, $CDCl_3$) (δ/ppm): 2.67 (s, 6H, –C**H**$_3$), 6.67-6.76 (m, 2H, Ar–**H**), 7.20-7.24 (m, 4H, Ar–**H**), 7.25-7.34 (m, 1H, Ar–**H**), 7.36-7.37 (m, 6H, Ar–**H**), 7.48-7.53 (m, 5H, Ar–**H**); ^{13}C NMR (75 MHz, $CDCl_3$) (δ/ppm): 44.1 (2 –**C**H_3), 116.5, 118.5, 122.1, 124.9, 126.9, 128.0, 128.0, 128.2, 128.3, 128.7, 130.6, 132.0, 132.2, 133.3,133.6, 133.6, 139.8, 140.5 (>**C**–N<), 149.8 (>**C**=N–), 152.5 (>**C**–$N(CH_3)_2$), 186.5 (>**C**=O); ESI-QTOF-MS (m/z): mass calculated for $[C_{30}H_{24}ClN_3O+ H]^+$: 478.16992, found: 478.17013.

s) 5-(2-dimethylaminobenzoyl)-1,3-diphenyl-4-(p-tolyl)-1H-pyrazole (9d)

Yield (67 %); m.p.: 158-160 °C; FT-IR (υ_{max}, cm^{-1}): 3060 (C-H aromatic), 2923 and 2808 (C-H aliphatic), 1625 (>C=O), 1595 (>C=N, pyrazole ring), 1545 and 1496 (>C=C<, aromatic ring), 1419 (C-N<); ^{1}H NMR (300 MHz, $CDCl_3$) (δ/ppm): 2.3 (s, 3H, –C**H**$_3$),2.68 (s, 6H, –C**H**$_3$), 6.67-6.74 (m, 2H, Ar–**H**), 7.01 (d, 2H, Ar–**H**, J = 7.8Hz), 7.12-7.15 (m, 2H, Ar–**H**), 7.21-7.34 (m, 7H, Ar–**H**), 7.47-7.59 (m, 5H, Ar–**H**); ^{13}C NMR (75 MHz, $CDCl_3$) (δ/ppm): 21.2 (–**C**H_3), 44.0 (2 –**C**H_3), 116.2, 118.1, 123.4, 124.8, 126.8, 127.7, 127.7, 128.1, 128.1, 128.7, 128.9, 130.5, 132.6, 133.4, 134.0, 136.9, 139.9, 140.5 (>**C**–N<), 149.8 (>**C**=N–), 152.4 (>**C**–$N(CH_3)_2$), 186.8 (>**C**=O); ESI-QTOF-MS (m/z): mass calculated for $[C_{31}H_{27}N_3O_2+ H]^+$: 458.22451, found: 458.22503.

3. Antimicrobial Activity

The antimicrobial activity of the synthesized compounds was studied against *Listeria innocua CECT 4030, Staphylococcus aureus CECT 976, Escherichia coli K12* as positive and negative bacterial strains. *Candida albicans* ATCC 10231 was used to evaluate the antifungal activity [S1]. The fungi strain was cultured in malt extract (15g in 1liter) [S2], and the used bacterial strains were cultivated in Luria-Bertani (LB) medium (10g Tryptone, 5g Yeast extract, 10g NaCl in 1liter). The fungi strain and all pathogens bacteria were incubated at 37°C for 48h.

The tested compounds were dissolved in the dimethyl sulfoxide (DMSO) and mixed with sterile LB medium. The *in vitro* screening of the compounds against bacterial and fungi strains was carried out using the broth microdilution method in 96-well plates, according to the previously described methods [S3,S4], and following guidelines of the Clinical and Laboratory Standards Institute (CLSI, approved Standard M7-A8 and M27-A3) [S5,S6]. From a stock solution of the tested compounds and reference drugs dissolved in DMSO, the required concentrations of 2000, 1000, 500, 250, 125, 62.5, 31.25, 15.62, 7.81 and 3.90 µg/mL were prepared by the successive dilution ½. Each well was inoculated by 100µL of Luria Bertani medium liquid culture medium (LB) for bacteria and Malt Extract (ME) liquid culture medium for fungi, more than 50µL of the tested compounds; every well was then inoculated with 50µL of the microbial concentration. Negative controls (bacteria and fungi without drugs) and positive controls (fungi and bacteria plus a serially diluted antibiotic) were included on every plate. The fluconazole and Streptomycin were used as positives controls for fungi and bacteria, respectively. After incubation at appropriate temperature and period, the activity assay and viability of microbial cell were evaluated with 2,3,5-triphenyl-2H-tetrazolium chloride (TTC) indicator (0.04 mg/mL), 10µL of TTC was added to each well. Results were recorded visually in terms of Minimum inhibitory concentration (MIC, µmol/mL). The Minimum Inhibitory Concentration (MIC) was the lowest concentration of synthesized compounds that completely inhibit microbial strains.

The minimum fungicidal concentrations (MFCs) and the minimum bactericidal concentrations (MBCs) was determined by sub-culturing negative wells that showed no microbial growth. Bacterial strains were subculture onto the surface of LB agar medium and fungal strain on EM agar medium. The MFC and MBC were defined as the lowest concentrations of compounds resulting no microbial growth of strains on the LB and EM agar media [S7].

4. FT-IR, ^{1}H, ^{13}C NMR and HRMS spectra of synthesized compounds

a) 5-(2-ethylaminobenzoyl)-1,3,4-triphenyl-1H pyrazole (4a)

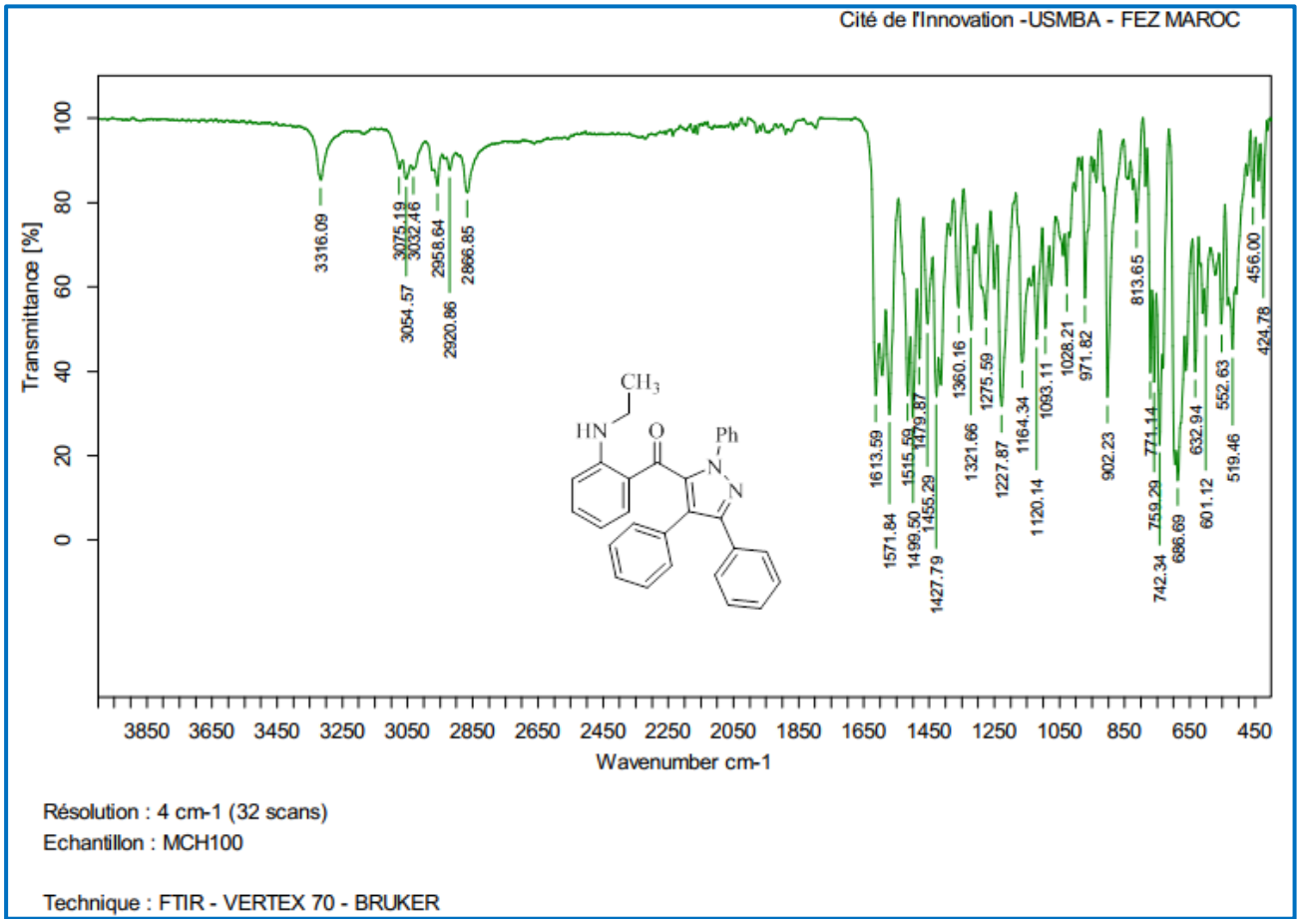


Figure S5. IR spectrum of compound (**4a**)

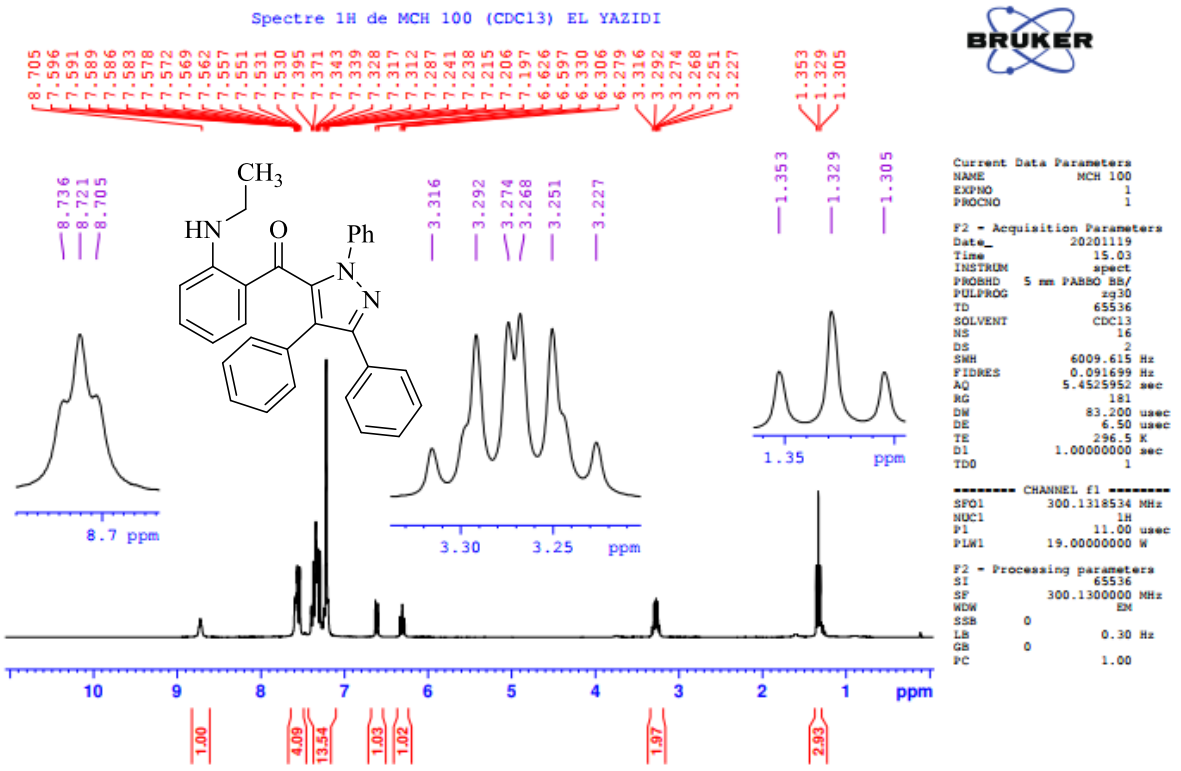


Figure S6. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound (**4a**)

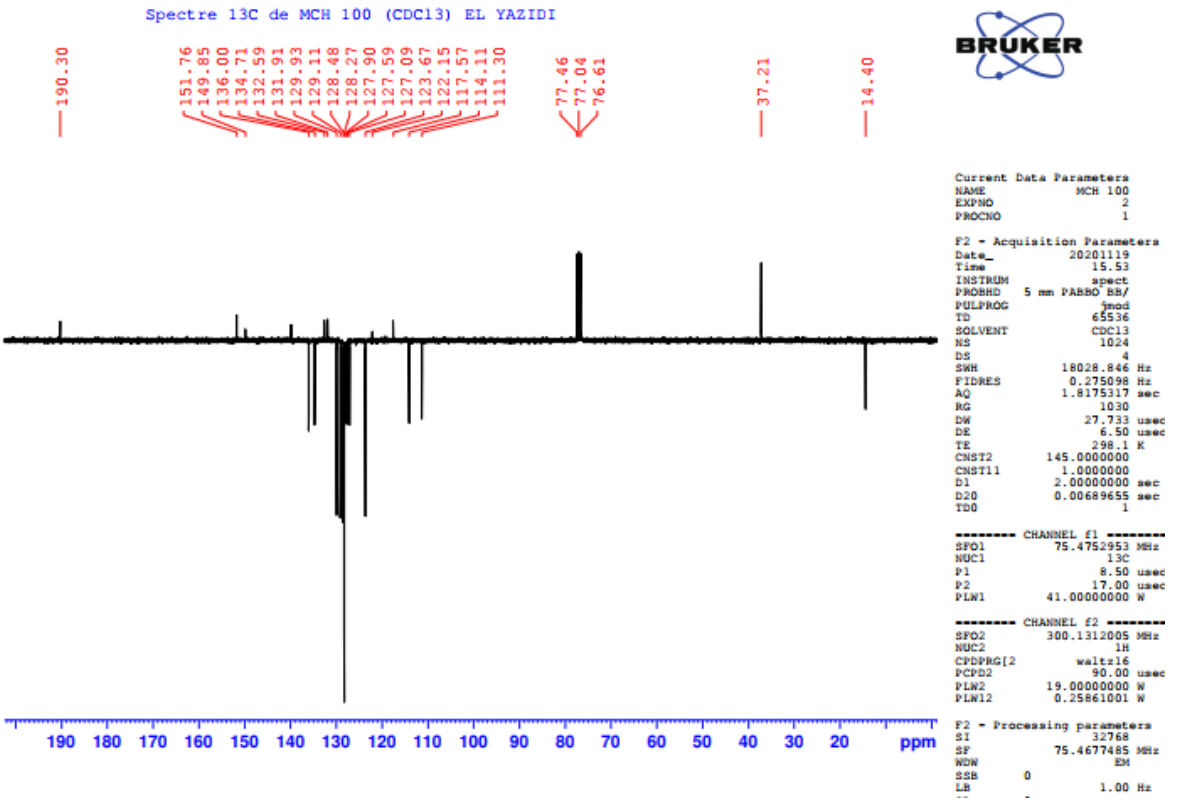


Figure S7. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound (**4a**)

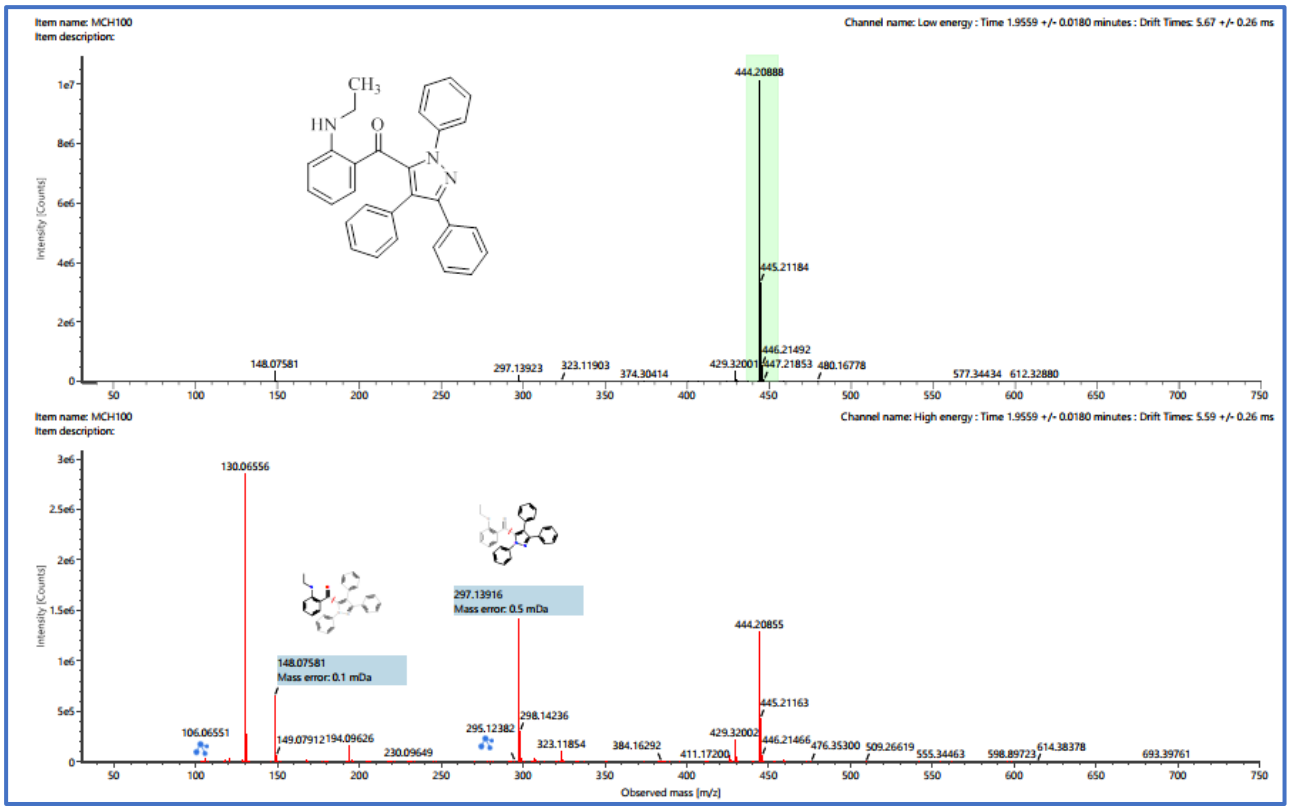


Figure S8. Mass spectrum of compound (**4a**)

b) 5-(2-ethylaminobenzoyl)-4-(4-methoxyphenyl)-1,3-diphenyl-1H-pyrazole (4b)

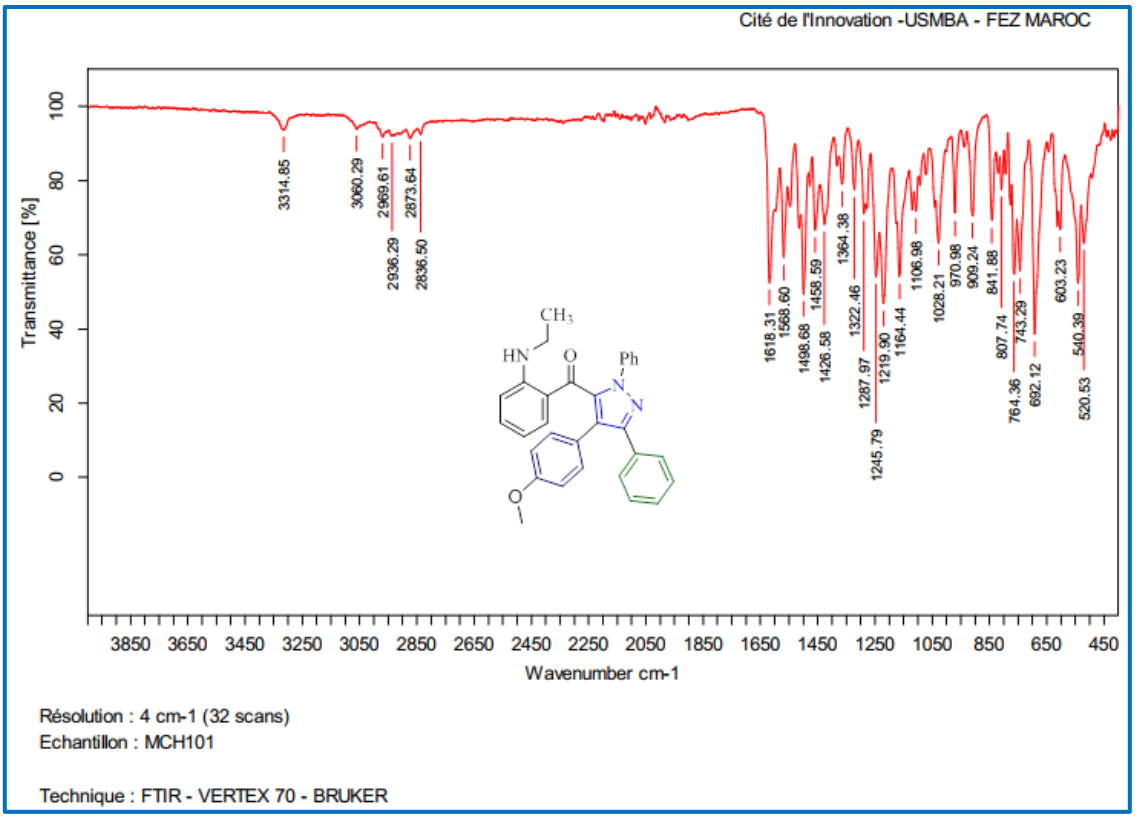


Figure S9. IR spectrum of compound (**4b**)

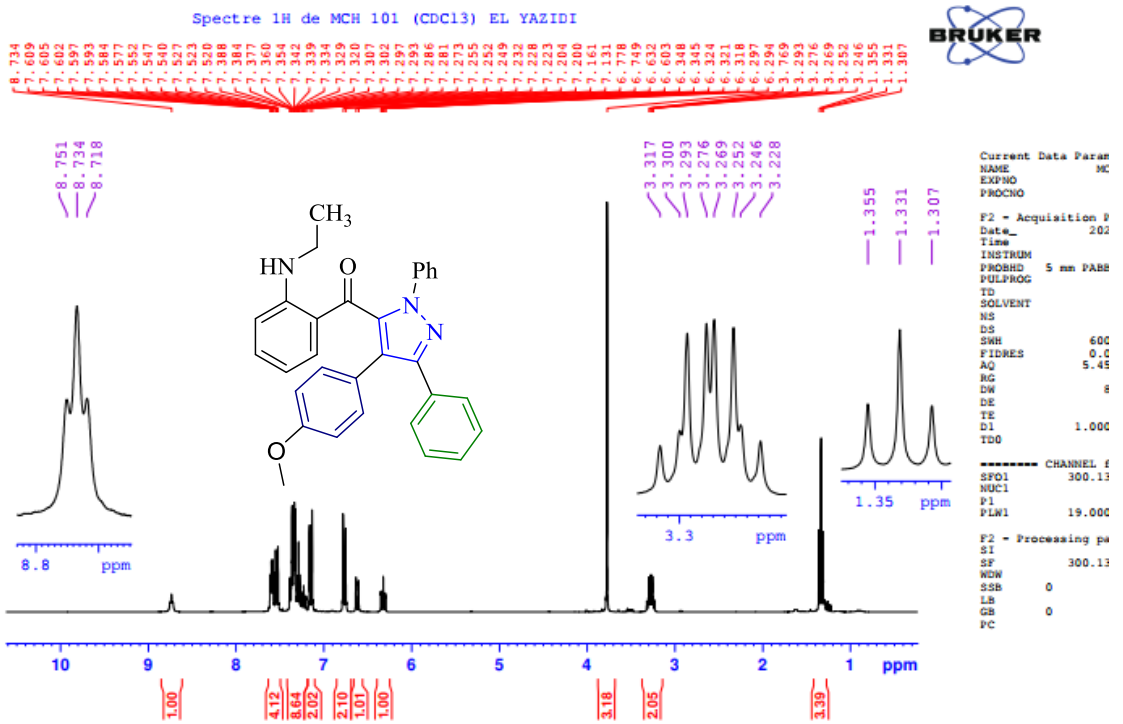


Figure S10. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound (**4b**)

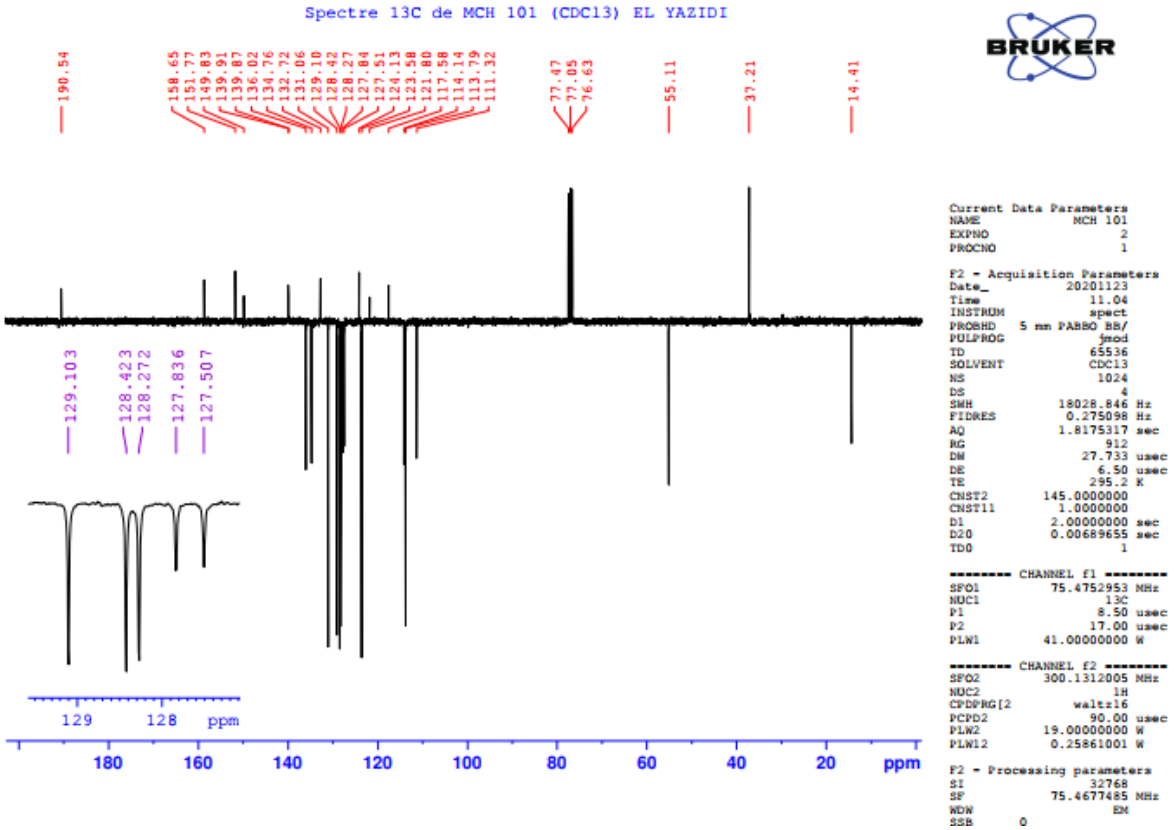


Figure S11. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound (**4b**)

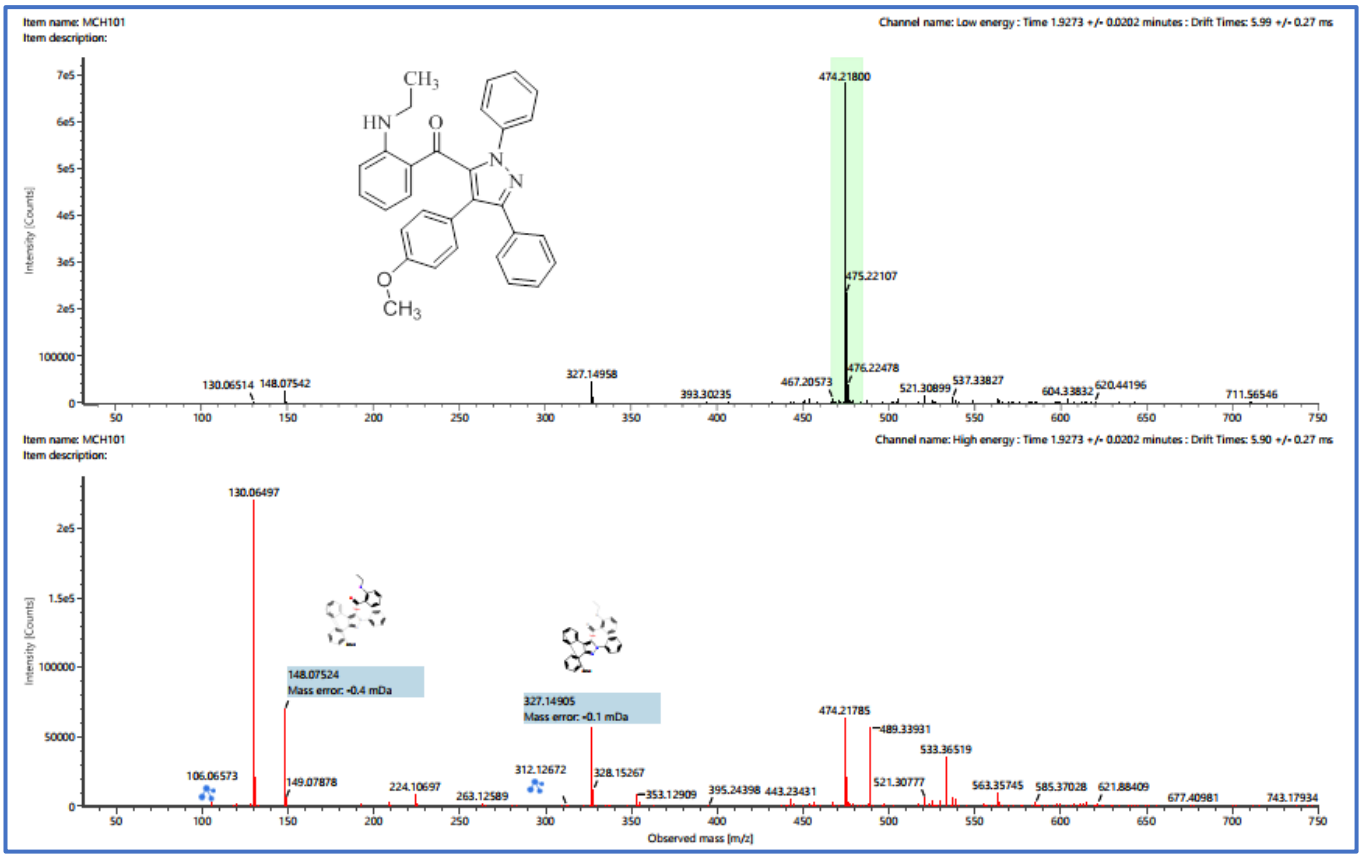


Figure S12. Mass spectrum of compound (**4b**)

c) 5-(2-benzylaminobenzoyl)-1,3,4-triphenyl-1H-pyrazole (5a)

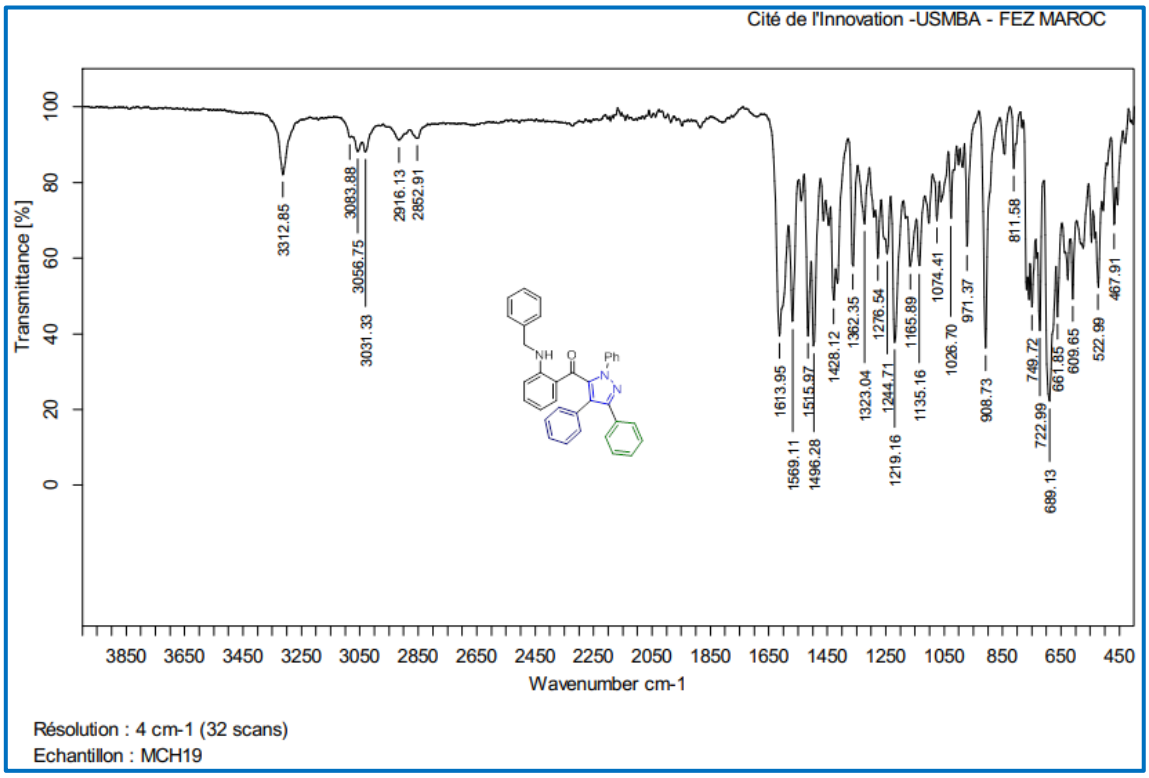


Figure S13. IR spectrum of compound (**5a**)

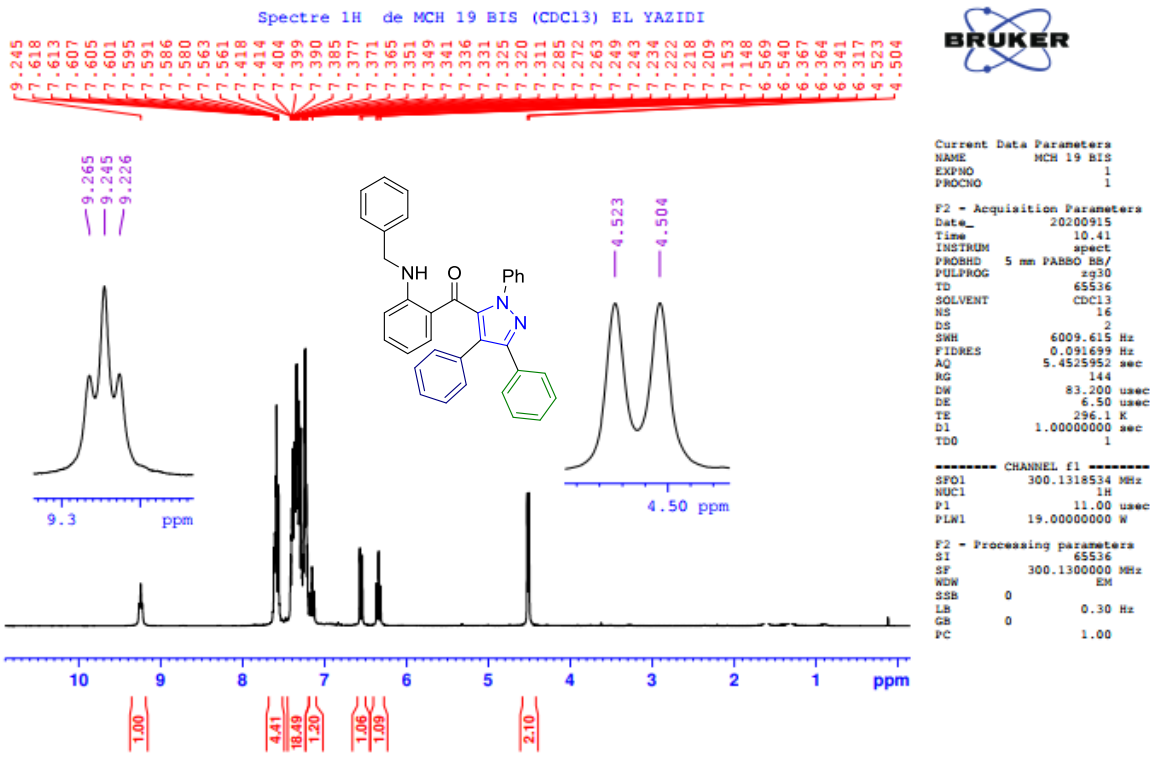


Figure S14. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound (**5a**)

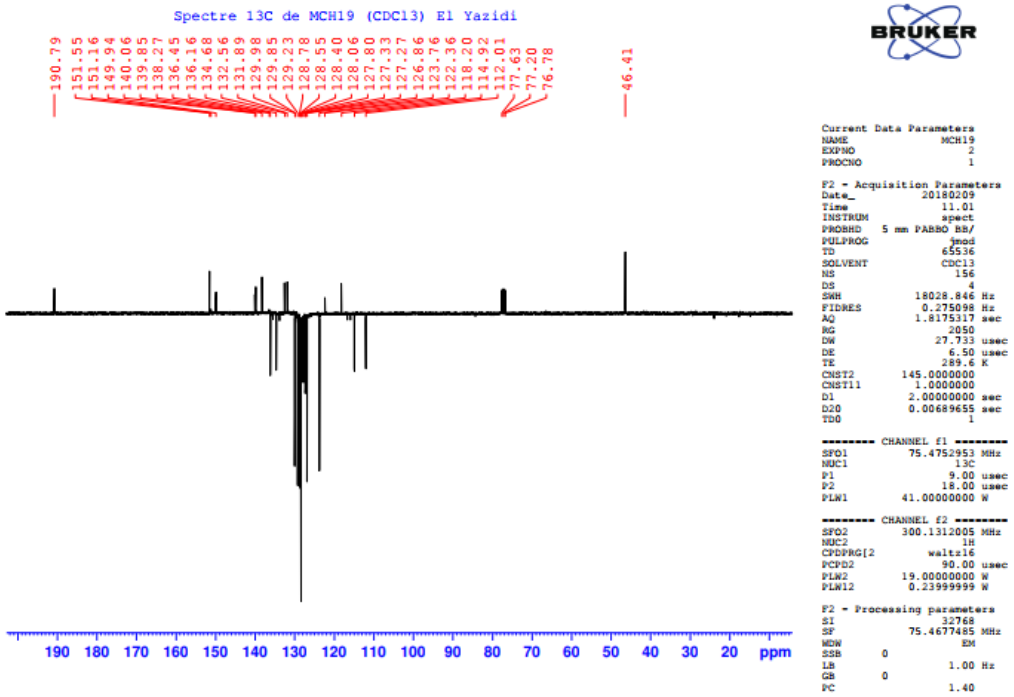


Figure S15. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound (**5a**)

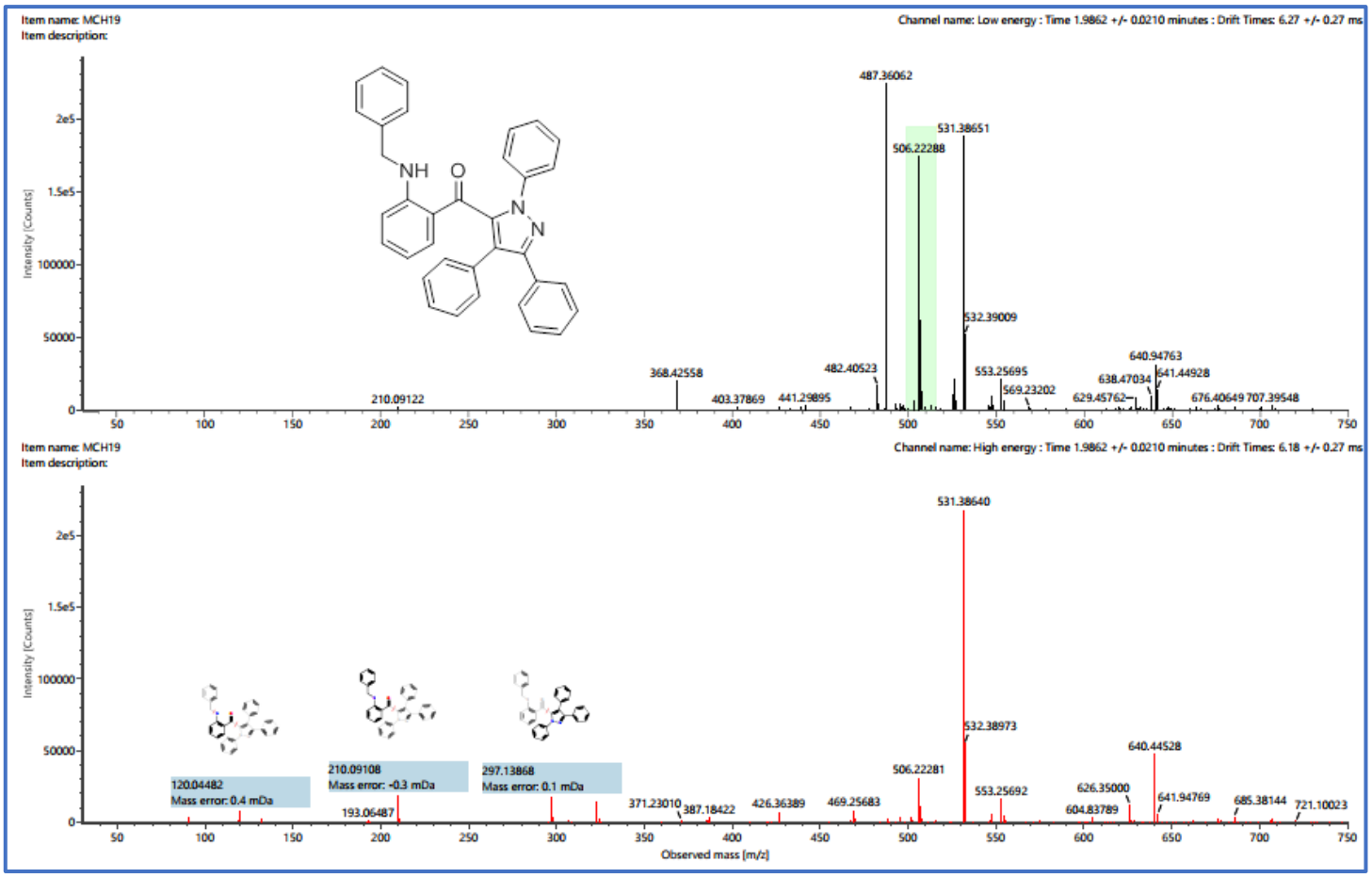


Figure S16. Mass spectrum of compound (**5a**)

d) 5-(2-benzylaminobenzoyl)-4-(4-methoxyphenyl)-1,3-diphenyl-1H-pyrazole (5b)

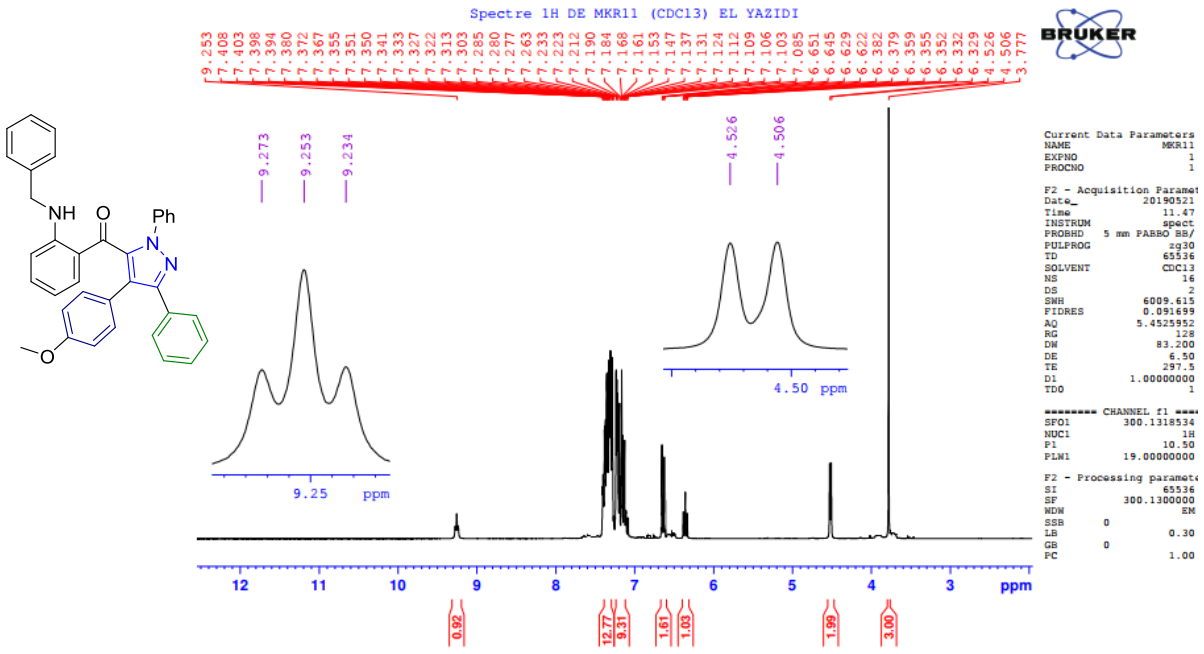


Figure S17. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound (**5b**)

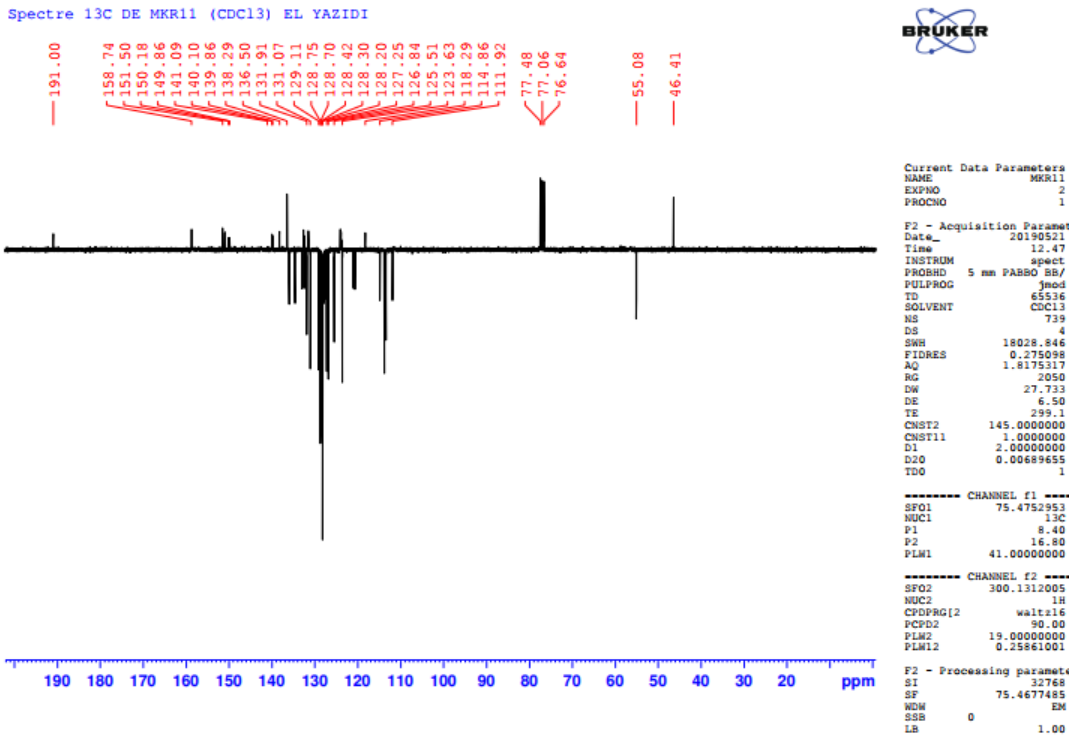


Figure S18. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound (**5b**)

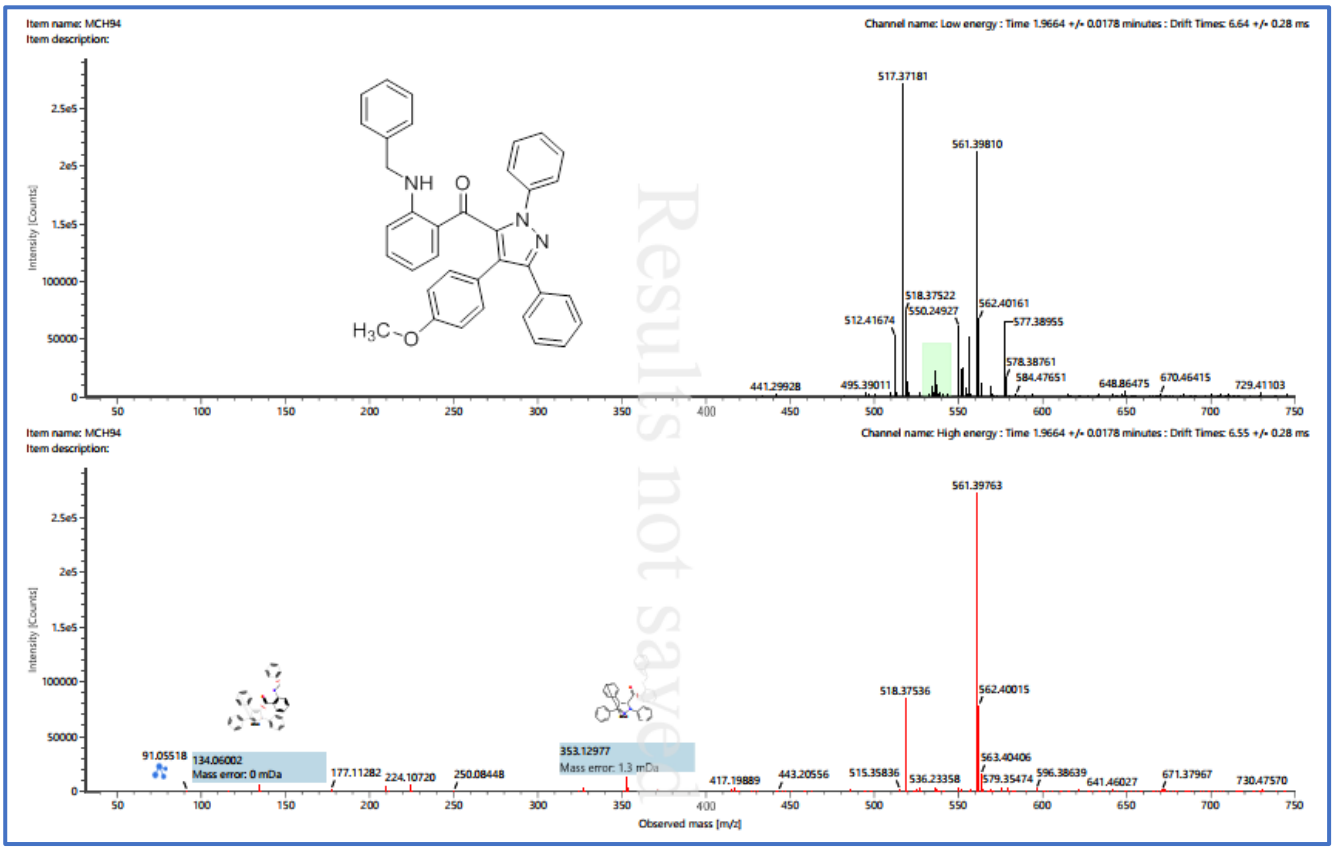


Figure S 19. Mass spectrum of compound (**5b**)

e) 5-(2-benzylaminobenzoyl)-4-(4-chlorophenyl)-1,3-diphenyl-1H-pyrazole (5c)

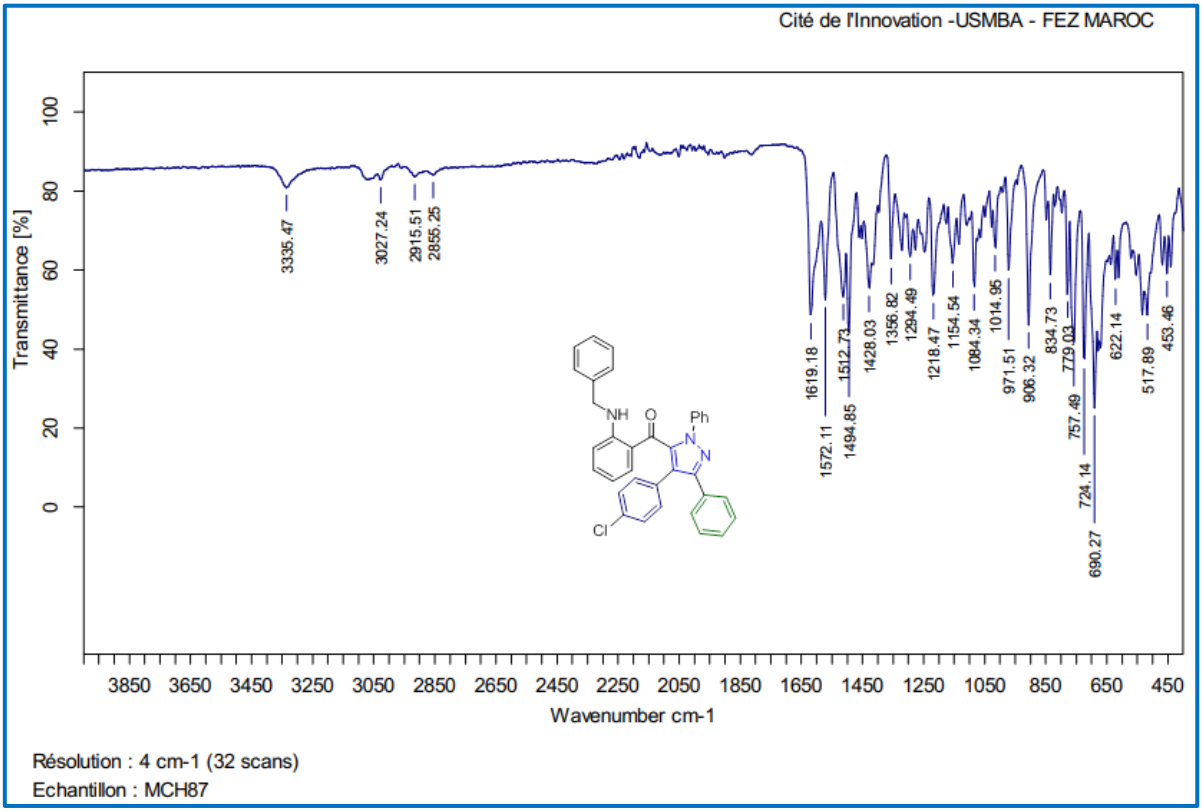


Figure S20. IR spectrum of compound (**5c**)

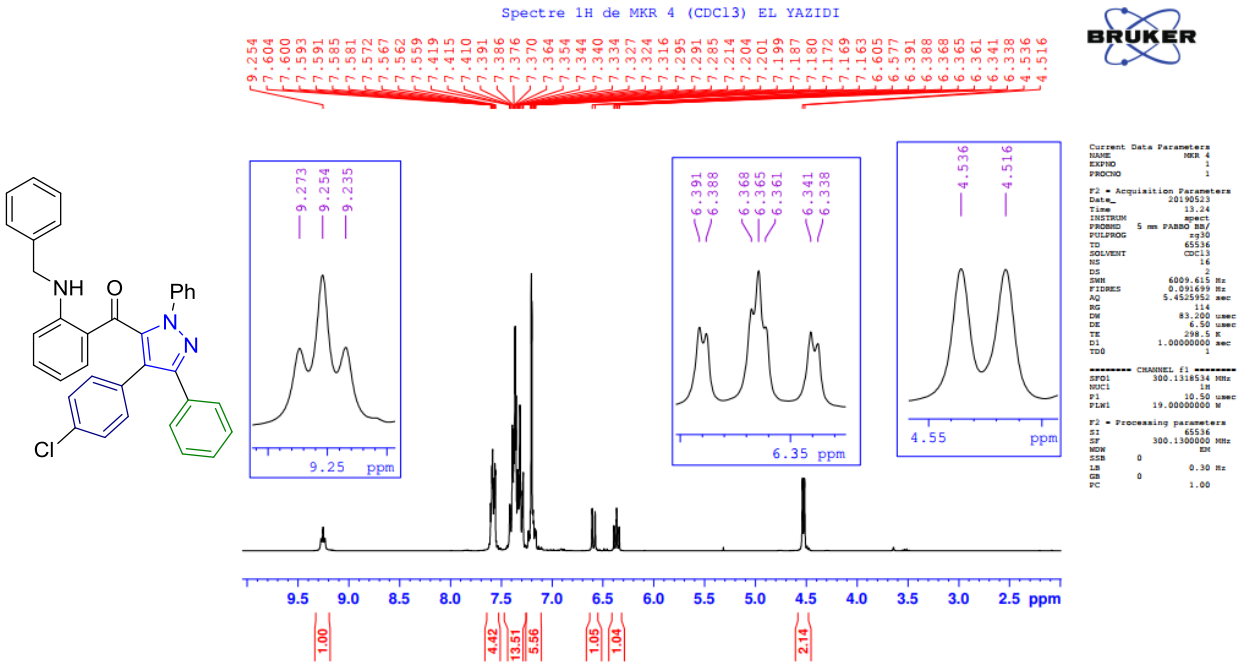


Figure S21. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound (**5c**)

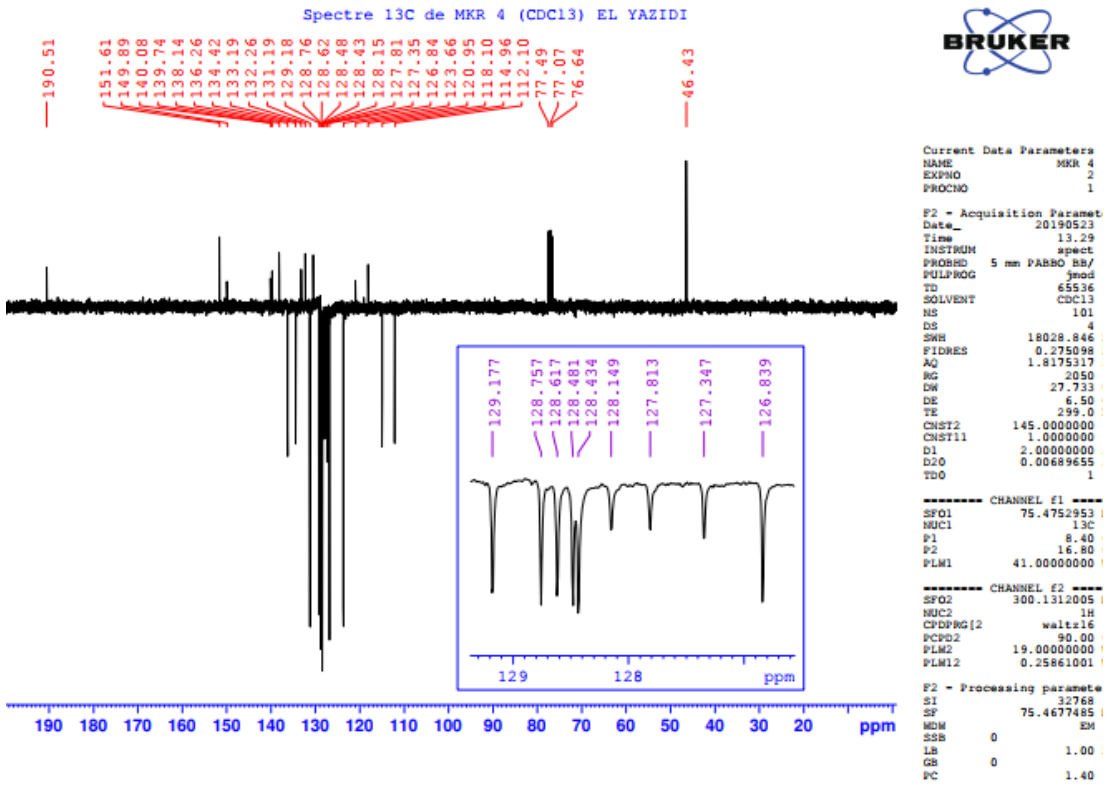


Figure S22. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound (**5c**)

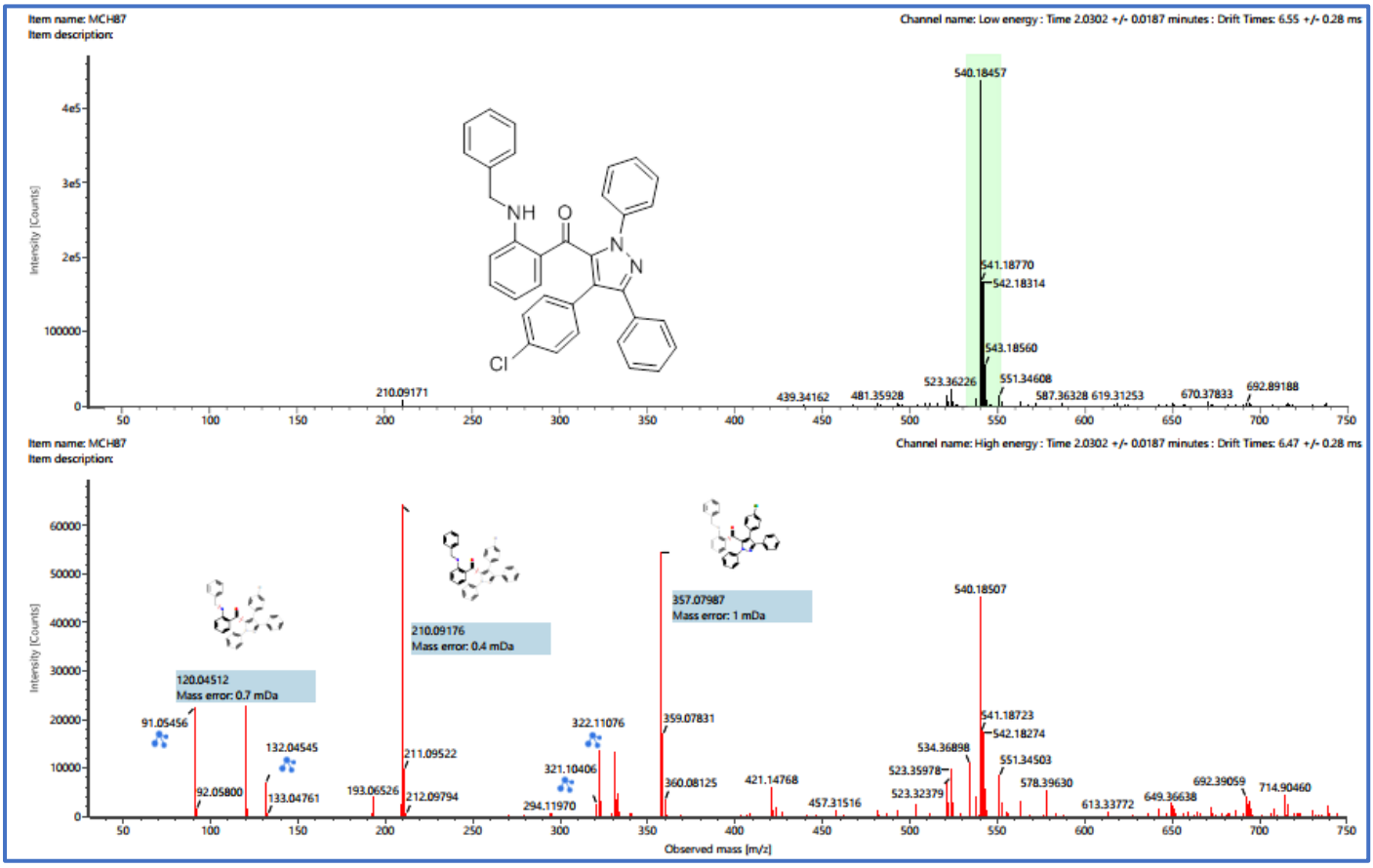


Figure S23. Mass spectrum of compound (**5c**)

f) 5-(2-benzylaminobenzoyl)-1,3-diphenyl-4-(p-tolyl)-1H-pyrazole (5d)

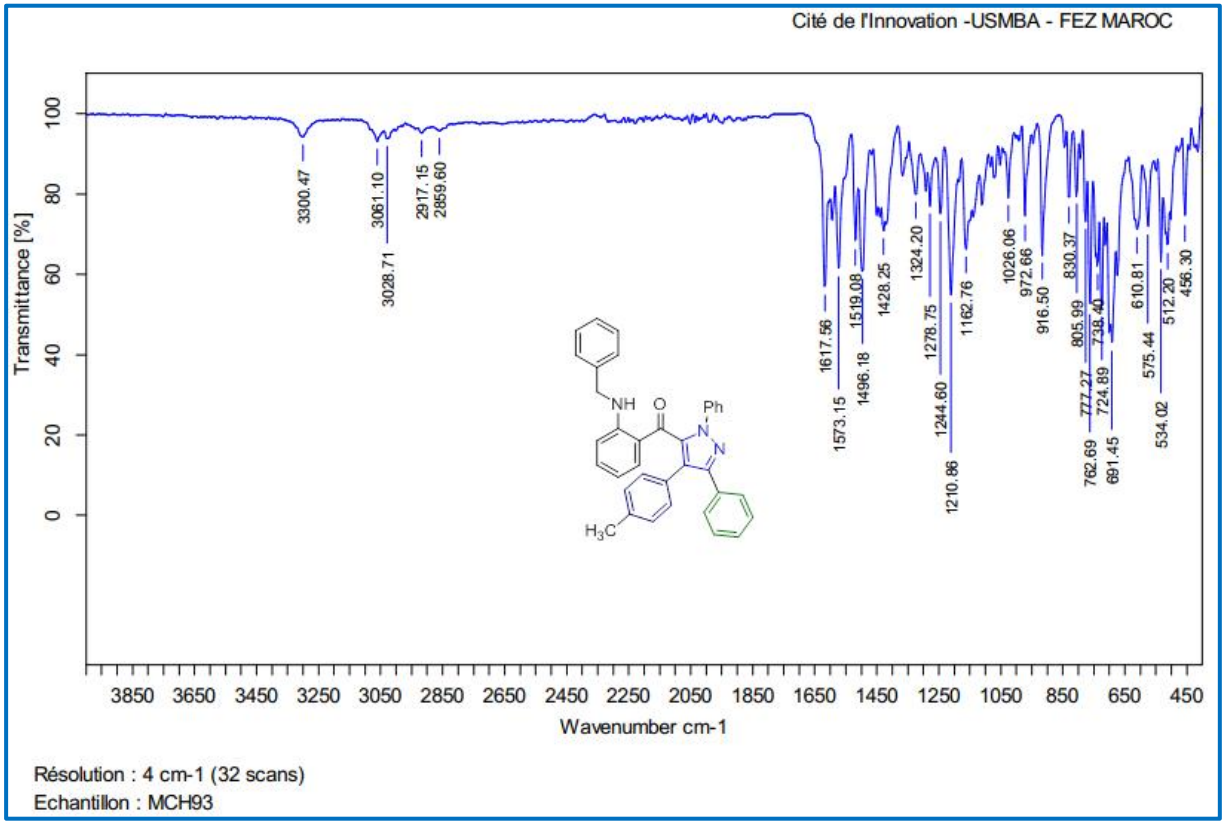


Figure S24. IR spectrum of compound (**5d**)

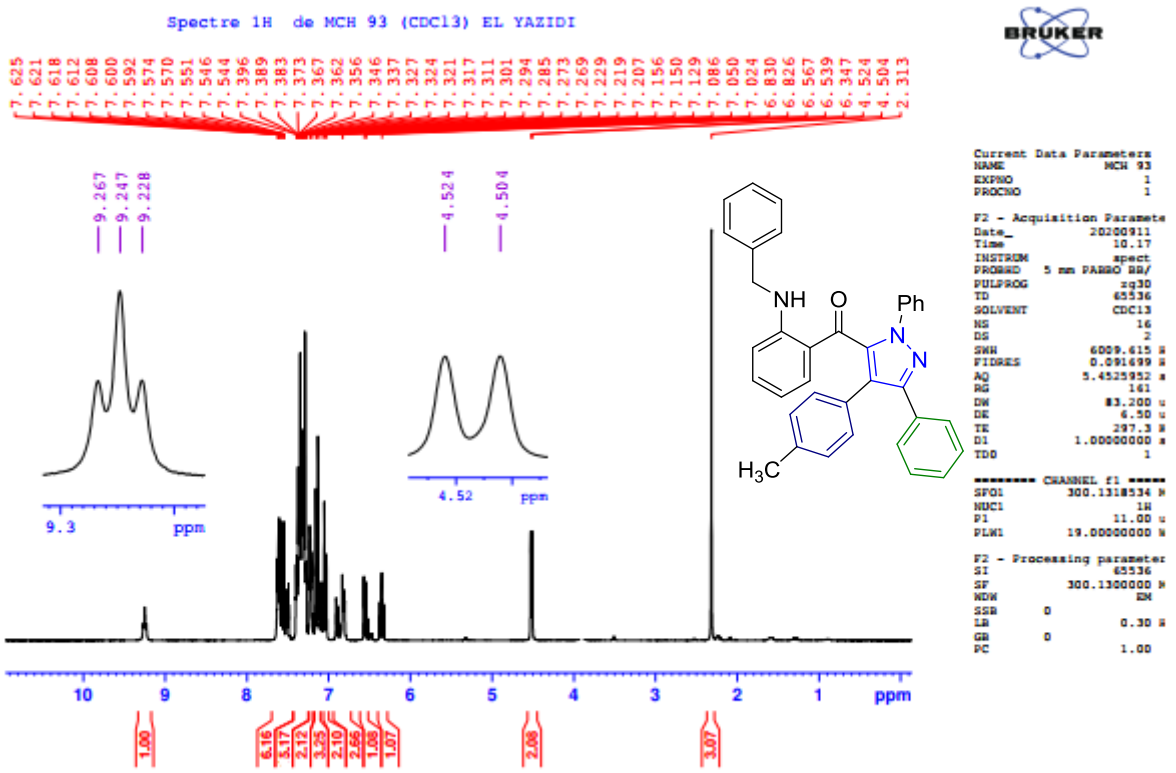


Figure S25. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound (**5d**)

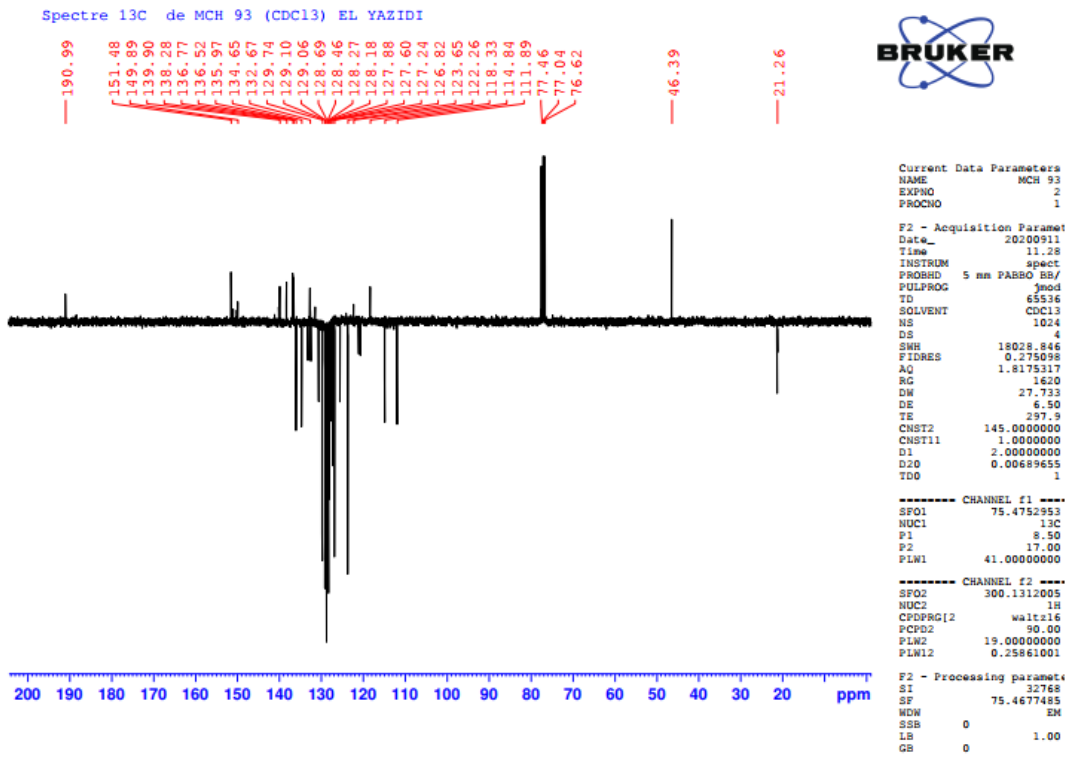


Figure S26. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound (**5d**)

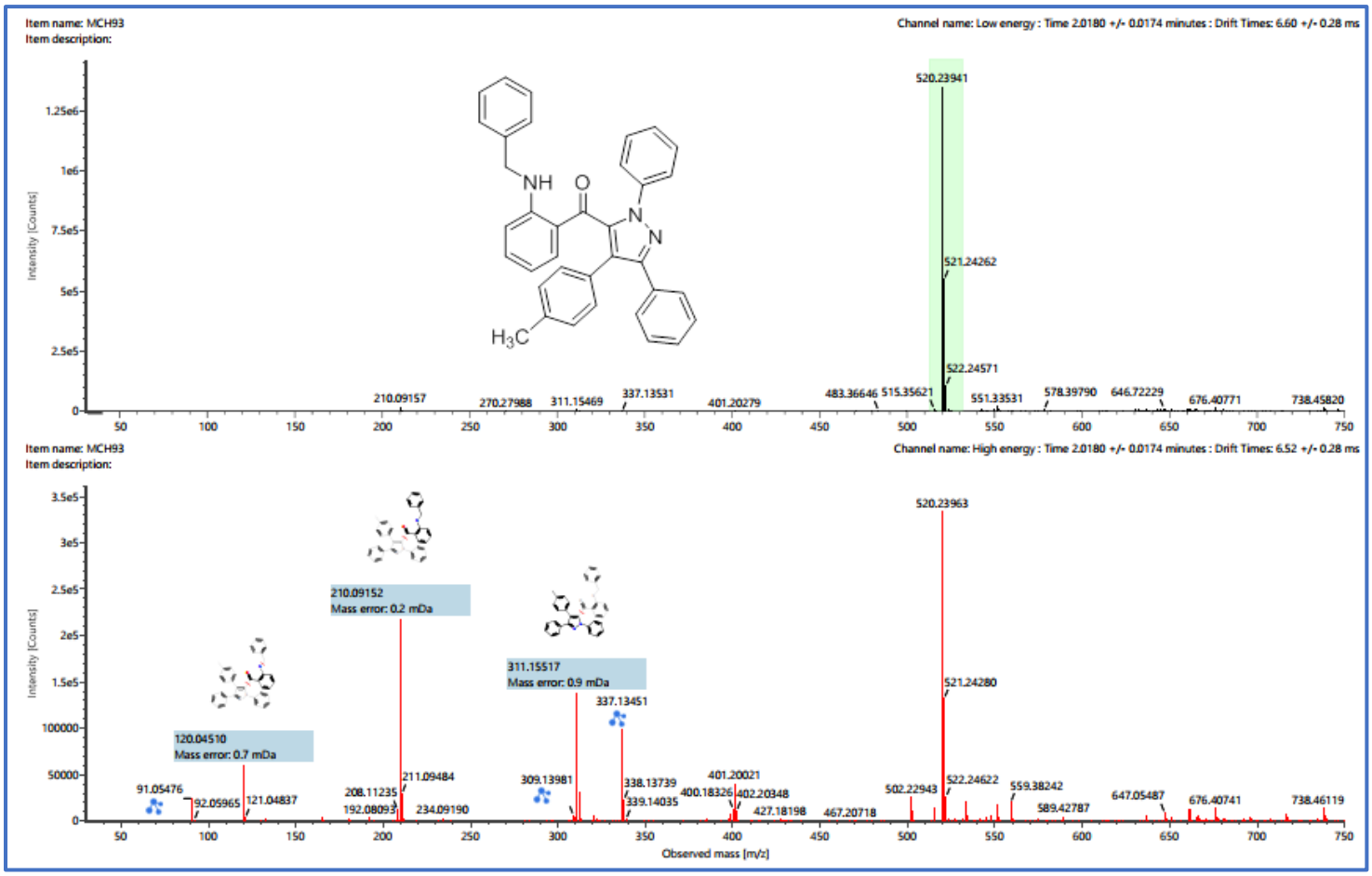


Figure S27. Mass spectrum of compound (**5d**)

g) 5-(2-allylaminobenzoyl)-1,3,4-triphenyl-1H-pyrazole 6a

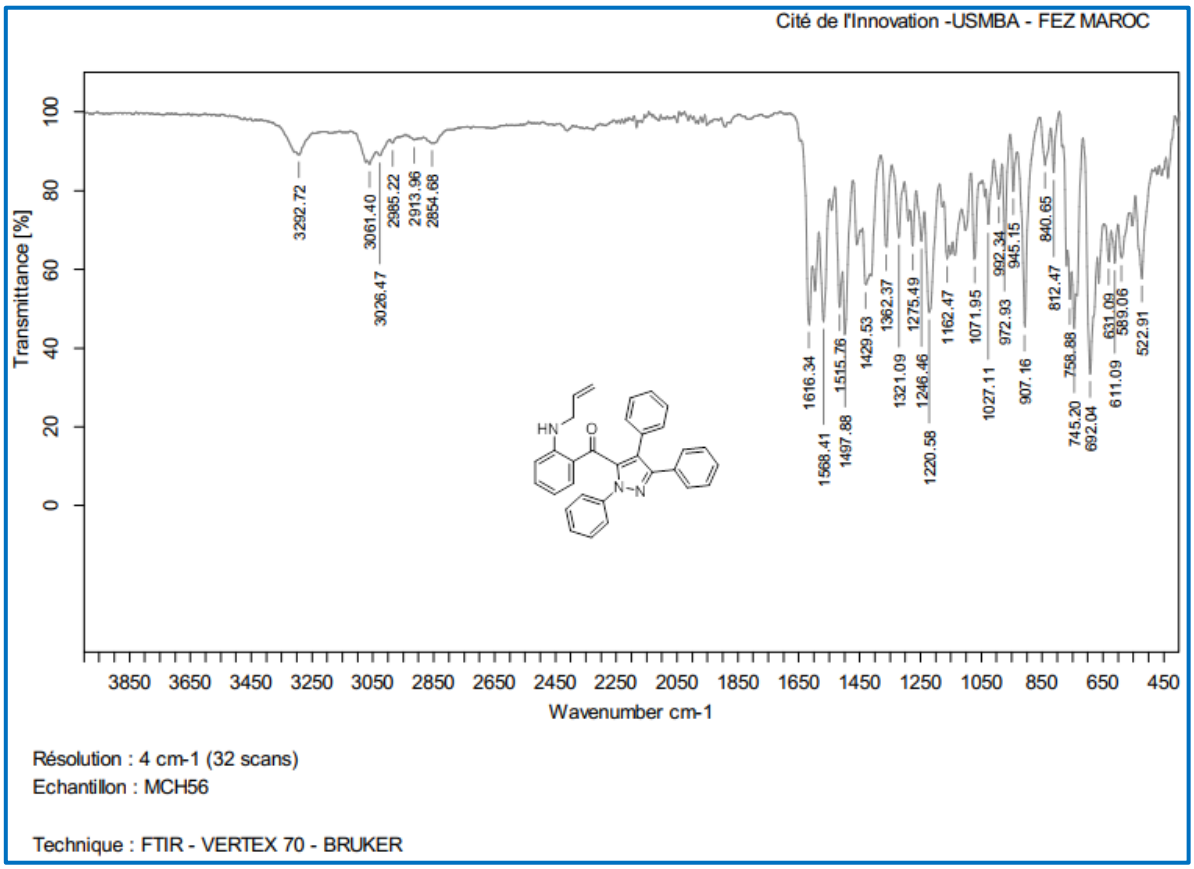


Figure S28. IR spectrum of compound (**6a**)

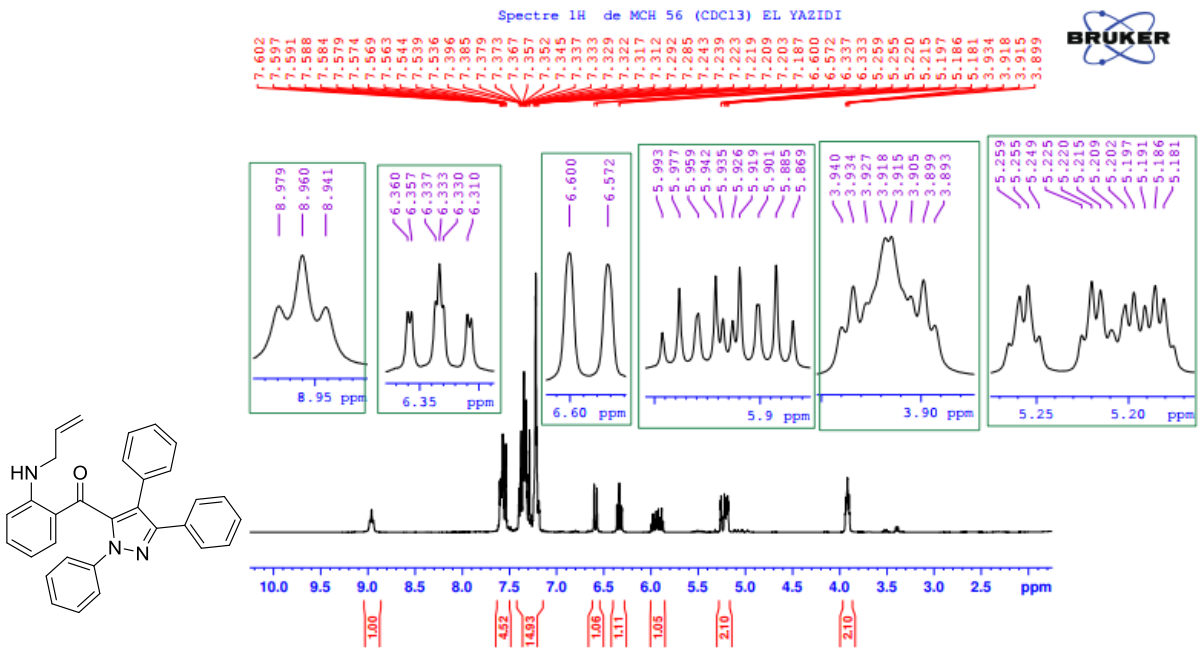


Figure S29. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound (**6a**)

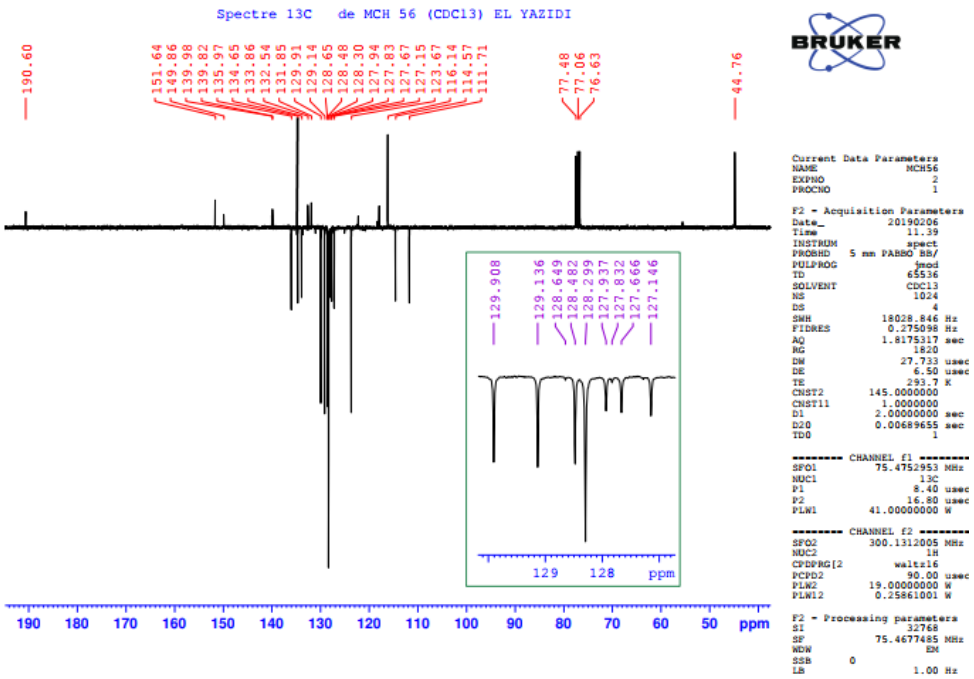


Figure S30. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound (**6a**)

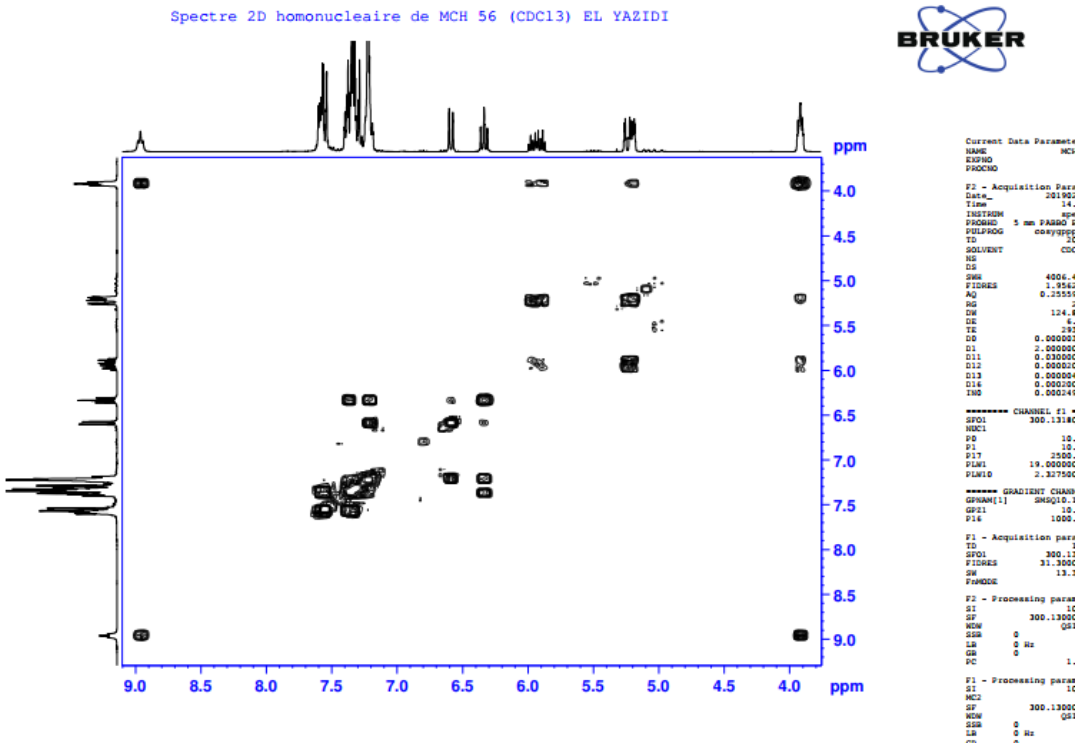


Figure S31. 2D-NMR spectrum of compound (**6a**)

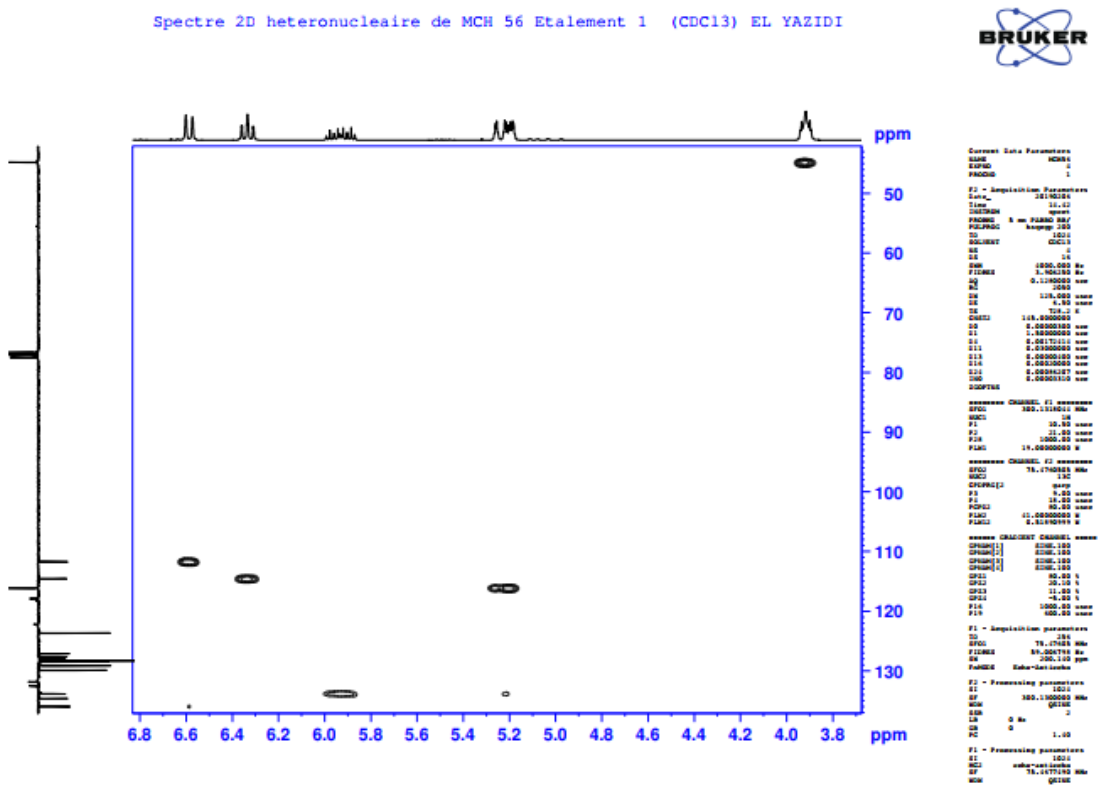


Figure S32. 2D-NMR spectrum of compound (**6a**)

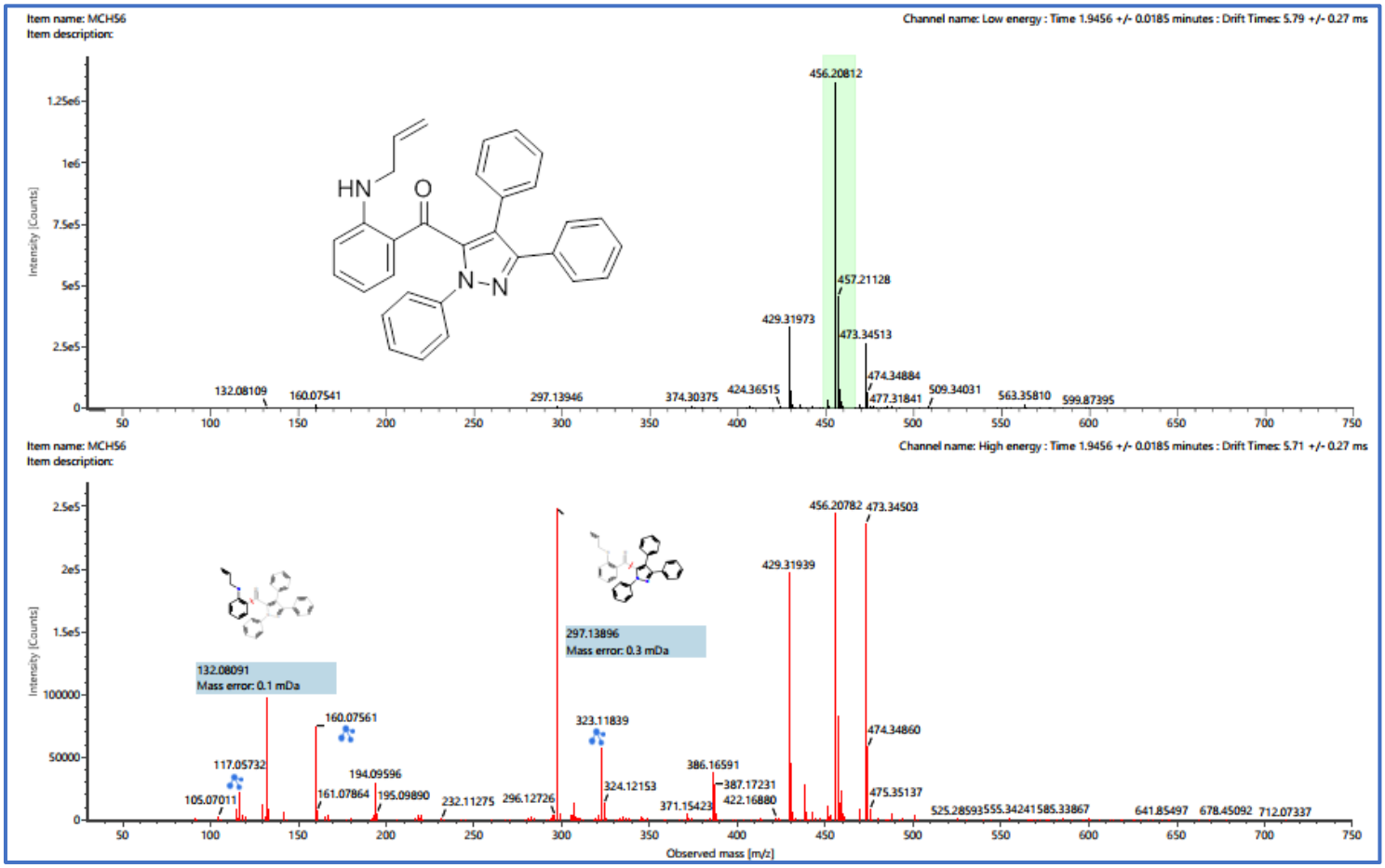


Figure S 33. Mass spectrum of compound (**6a**)

h) 5-(2-allylaminobenzoyl)-4-(4-methoxyphenyl)-1,3-diphenyl-1H-pyrazole (6b)

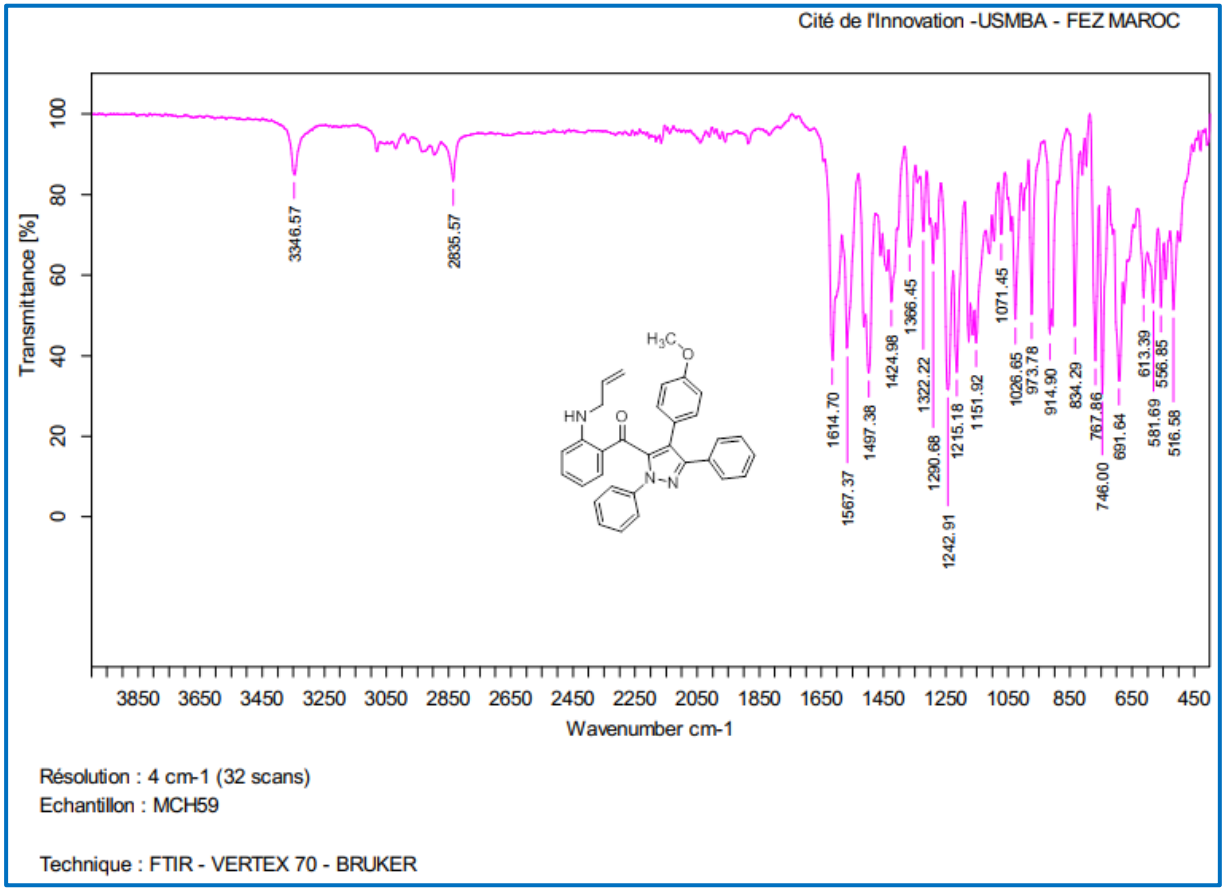


Figure S34. IR spectrum of compound (**6b**)

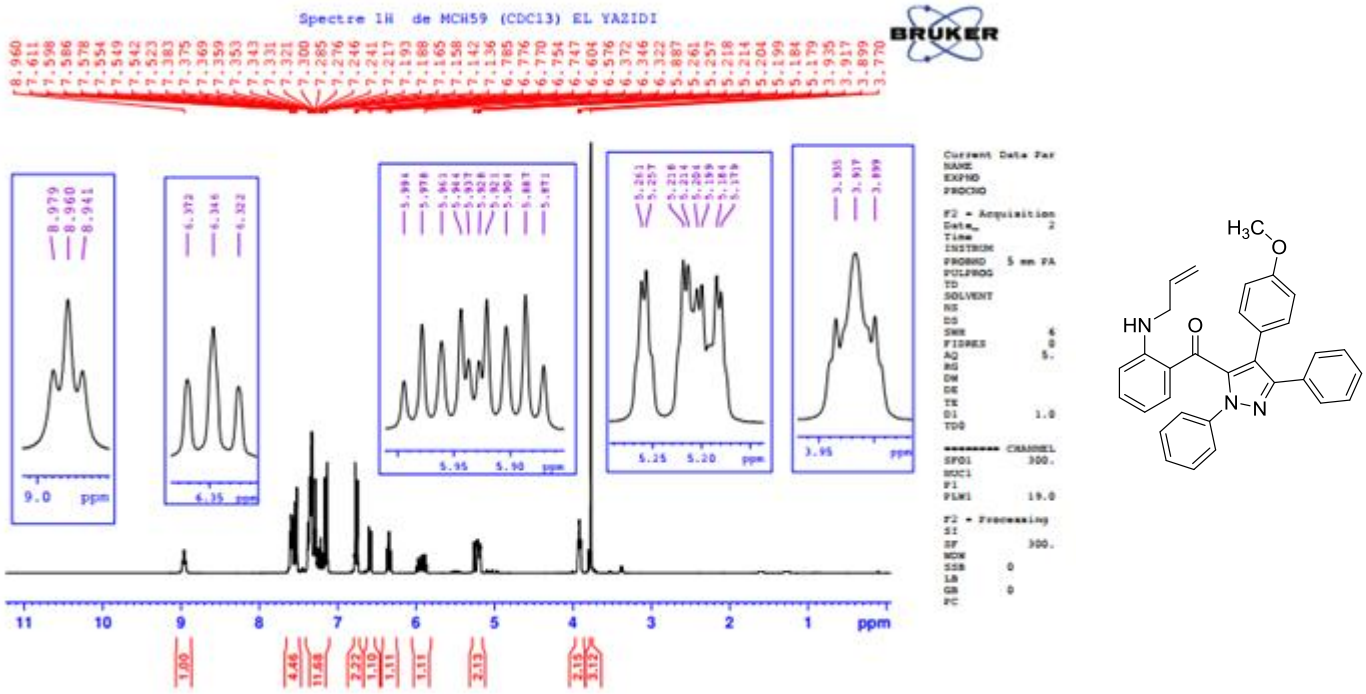


Figure S35. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound (**6b**)

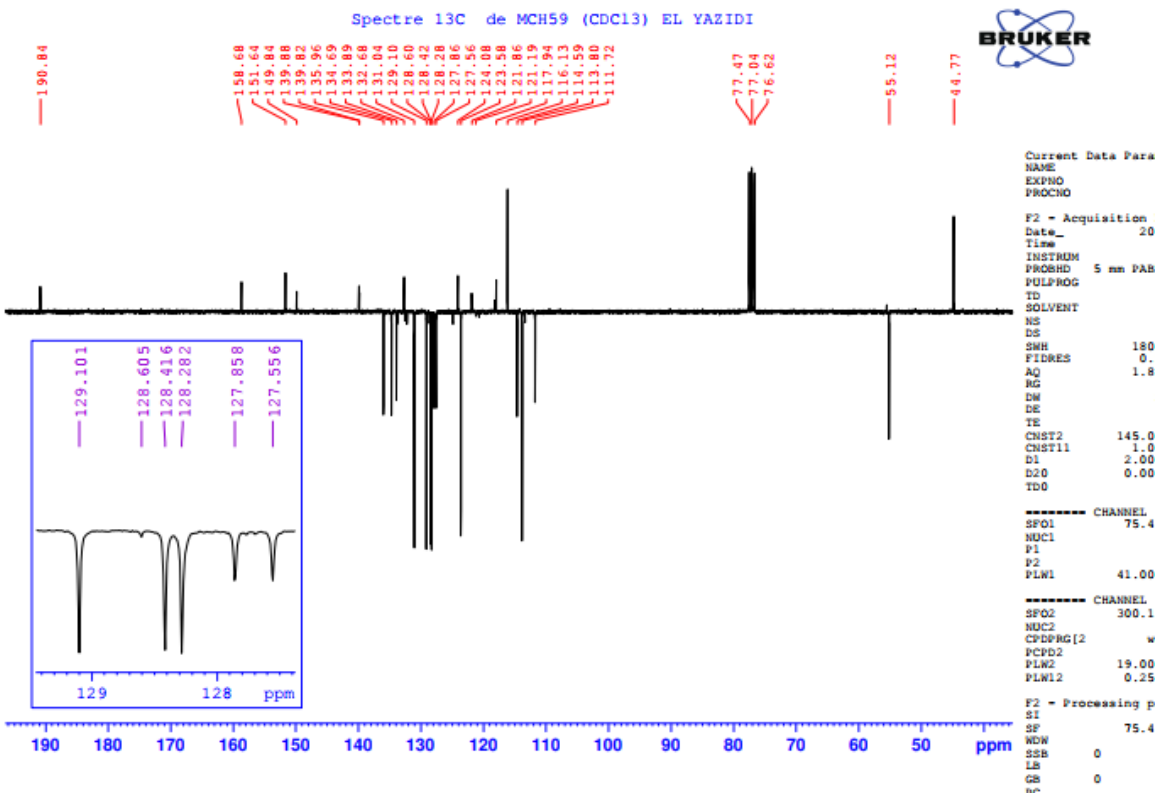


Figure S36. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound (**6b**)

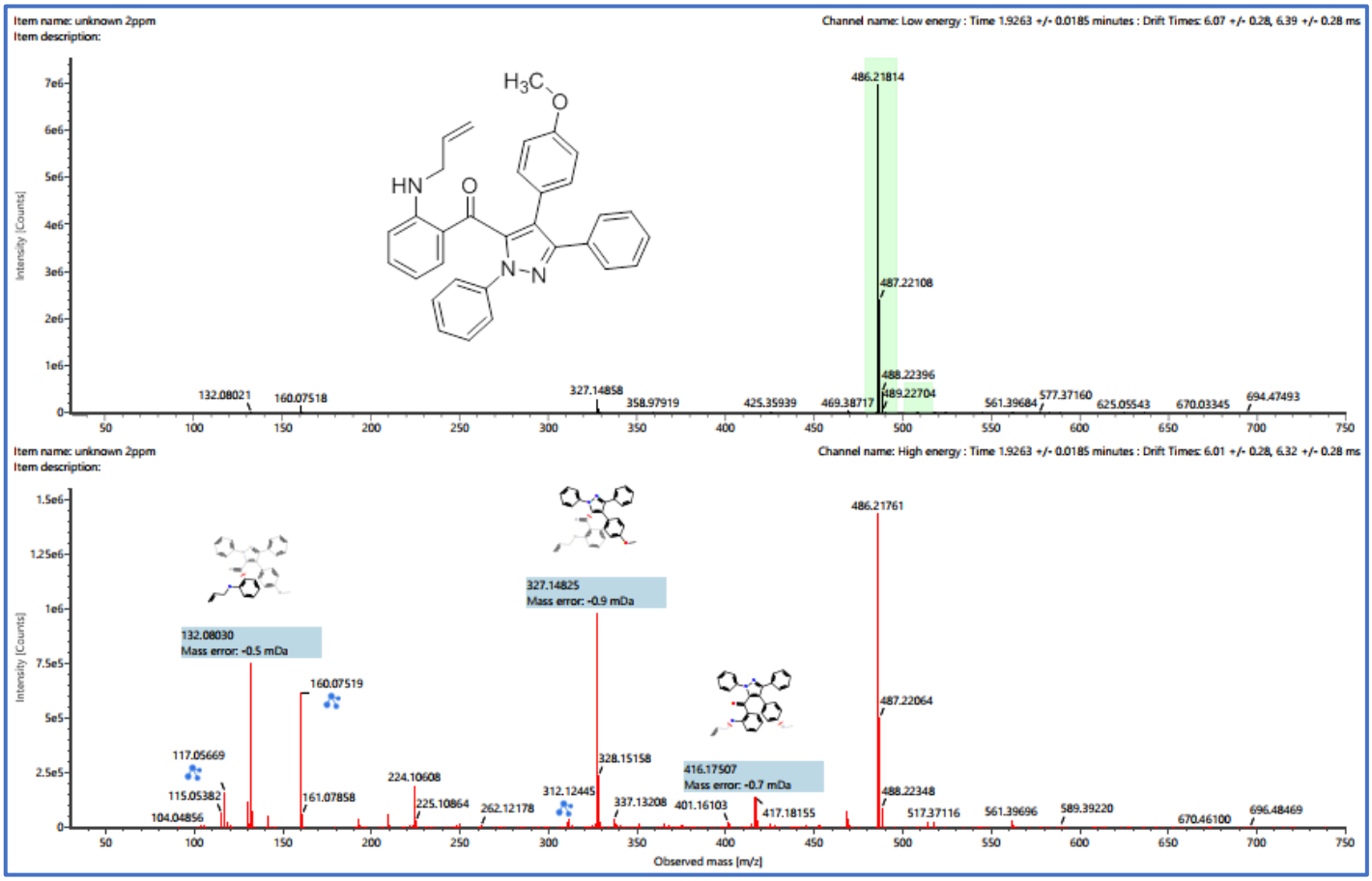


Figure S37. Mass spectrum of compound (**6b**)

i) 5-(2-allylaminobenzoyl)-4-(4-chlorophenyl)-1,3-diphenyl-1H-pyrazole (6c)

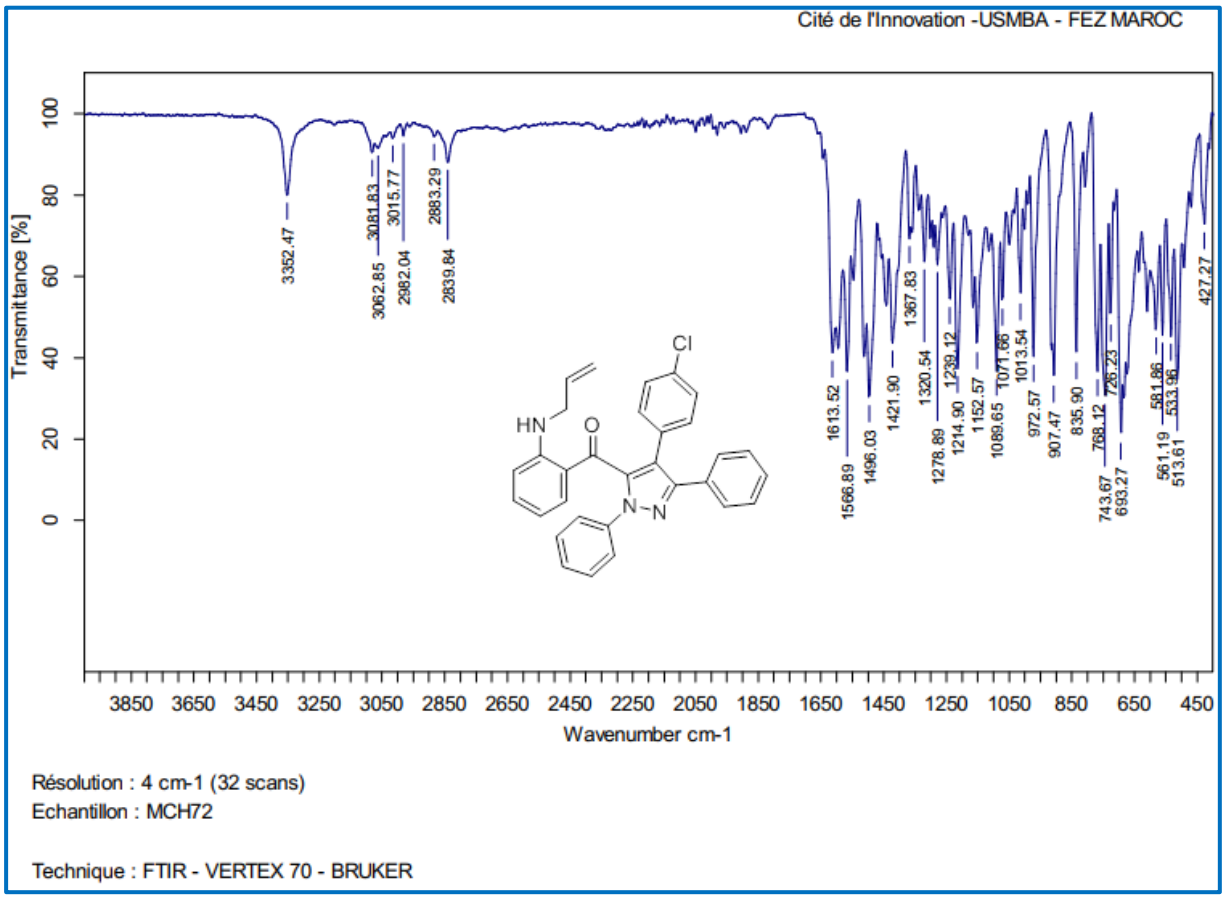


Figure S38. IR spectrum of compound (**6c**)

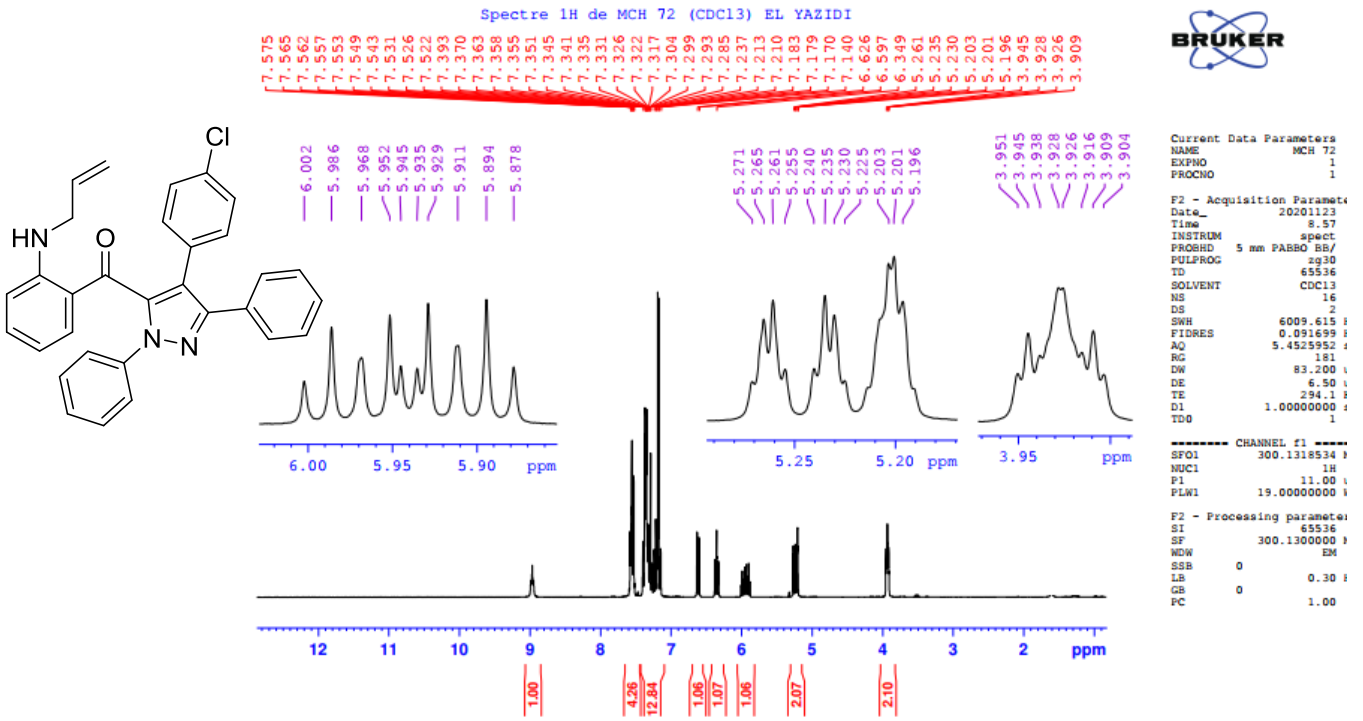


Figure S39. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound (**6c**)

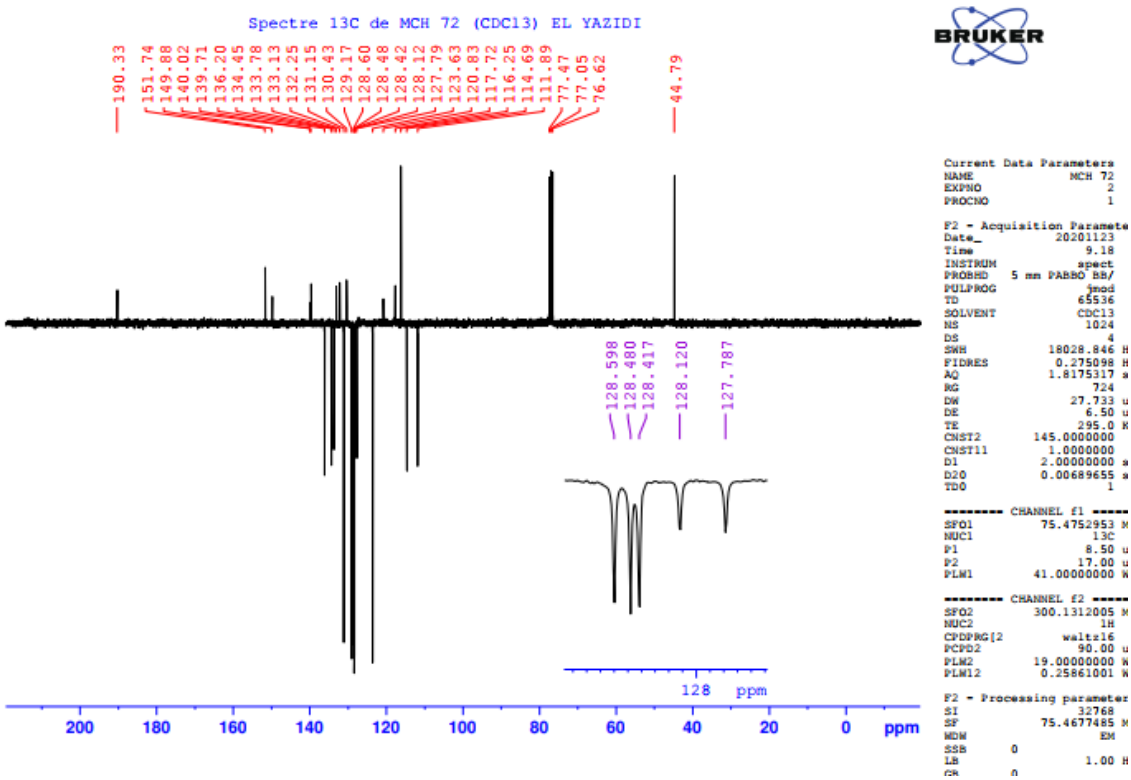


Figure S40. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound (**6c**)

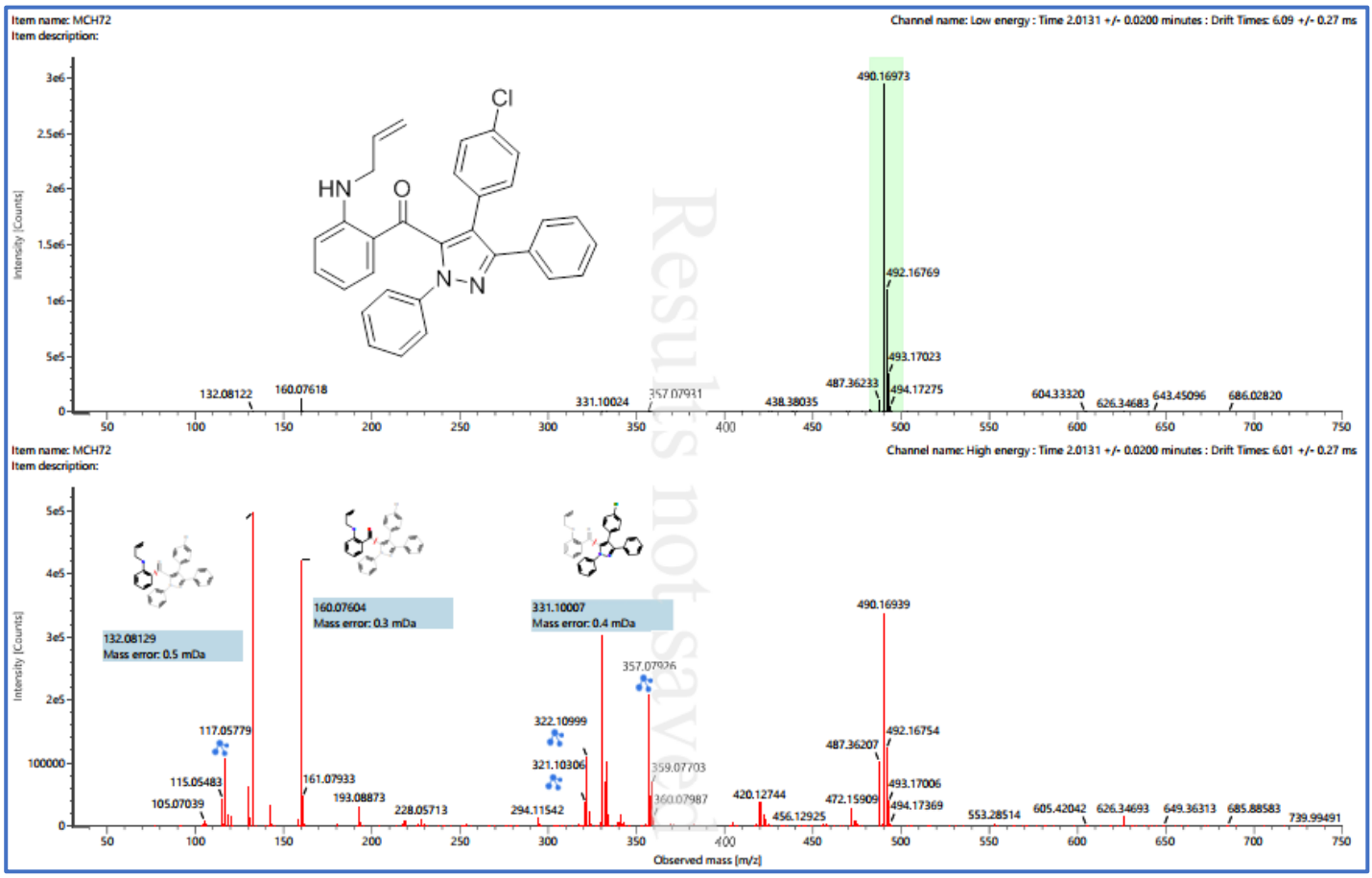


Figure S41. Mass spectrum of compound (**6c**)

j) 5-(2-propargylaminobenzoyl)-1,3,4-triphenyl-1H-pyrazole (7a)

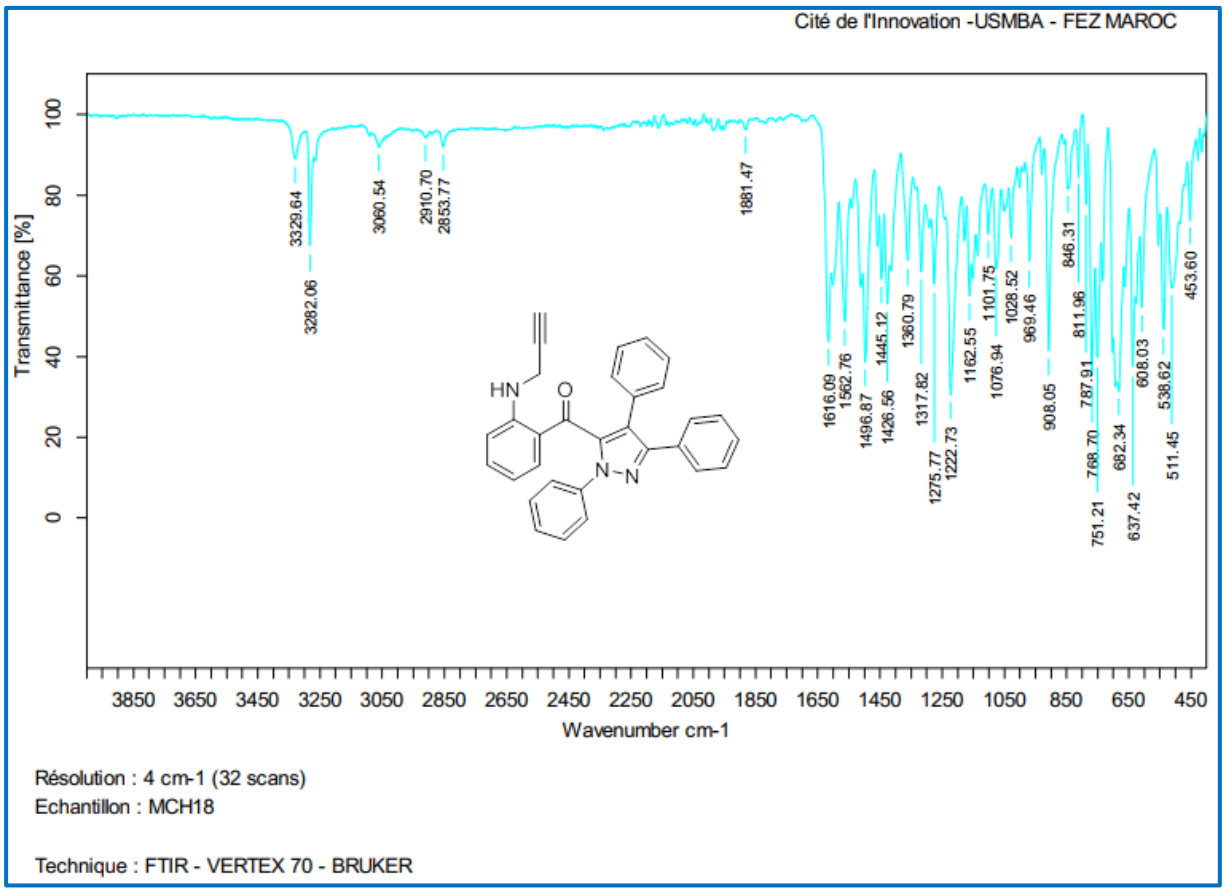


Figure S42. IR spectrum of compound (**7a**)

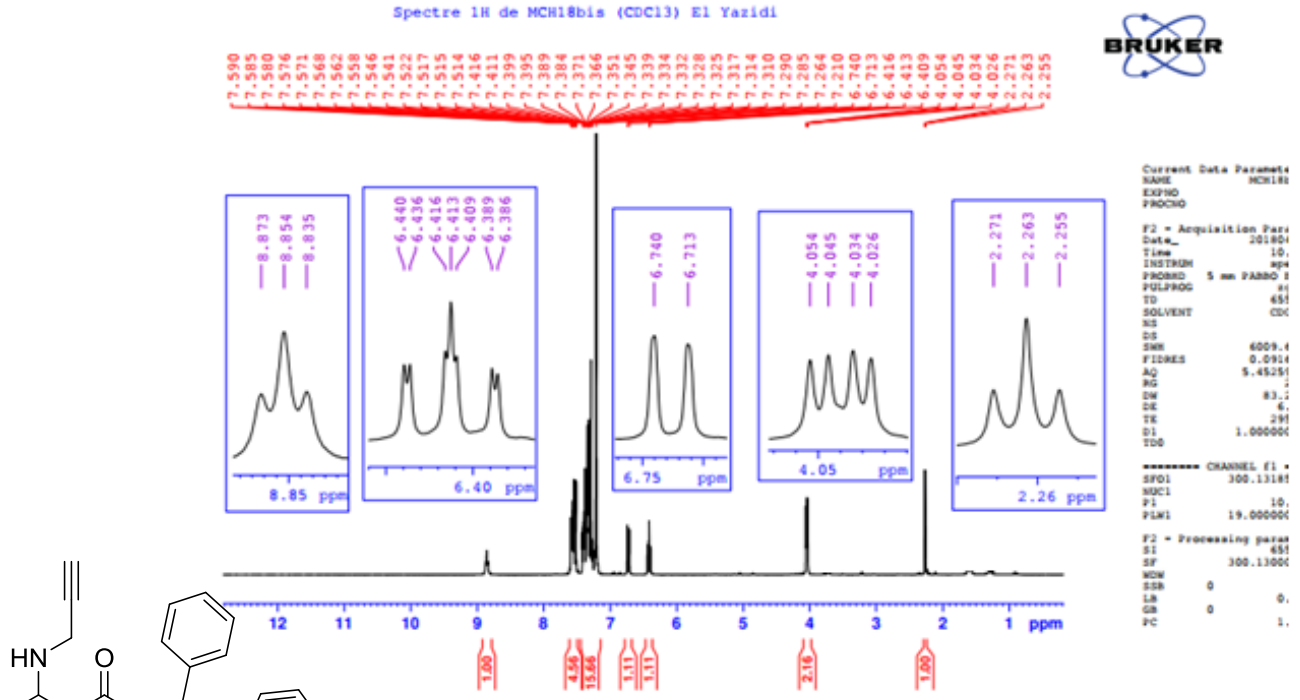


Figure S43. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound (**7a**)

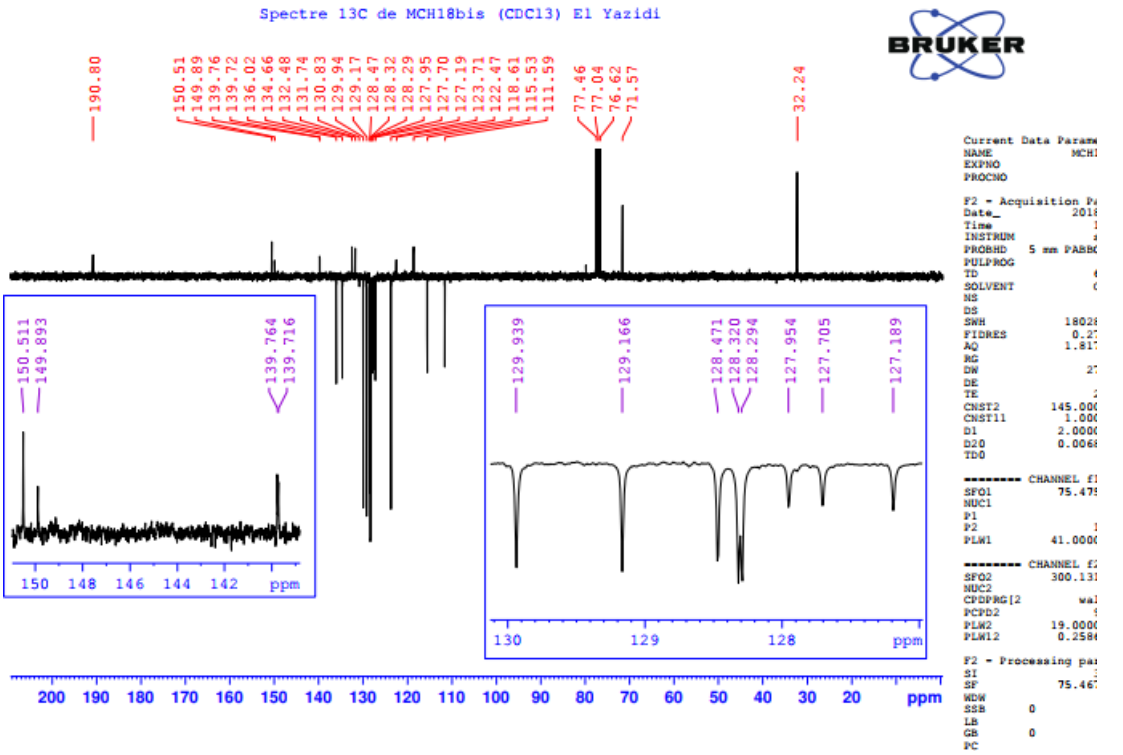


Figure S44. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound (**7a**)

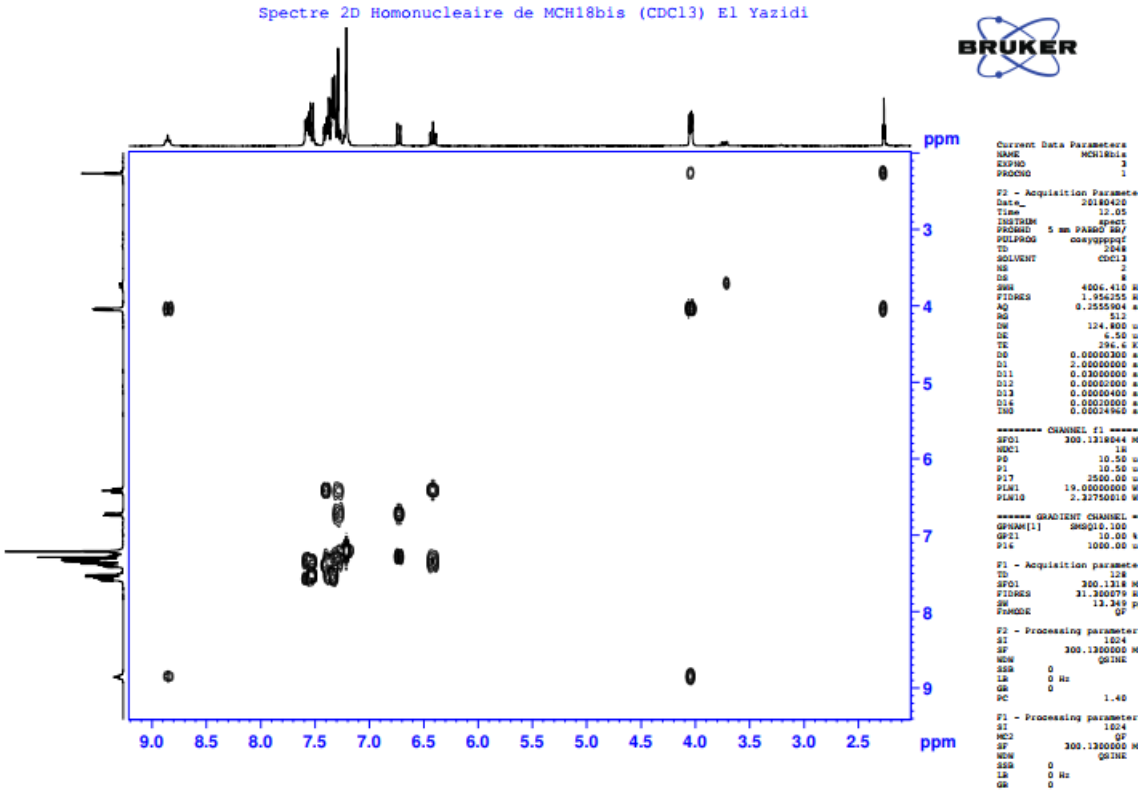


Figure S45. 2D-NMR spectrum of compound (**7a**)

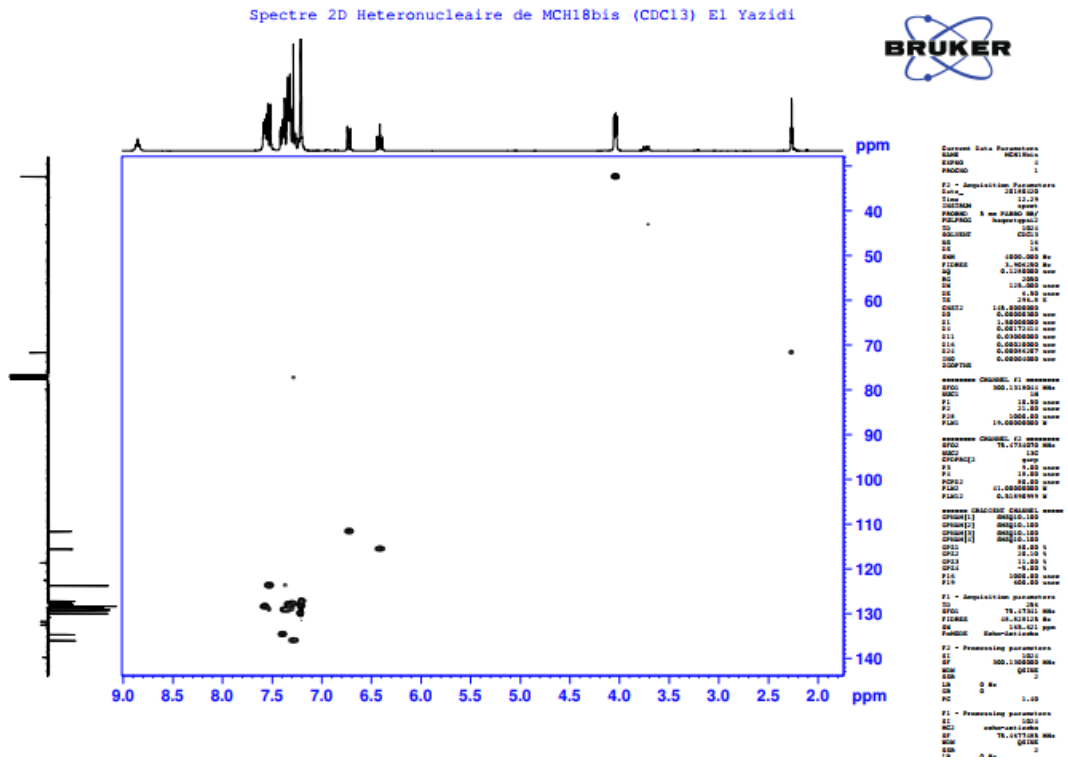


Figure S46. 2D-NMR spectrum of compound (**7a**)

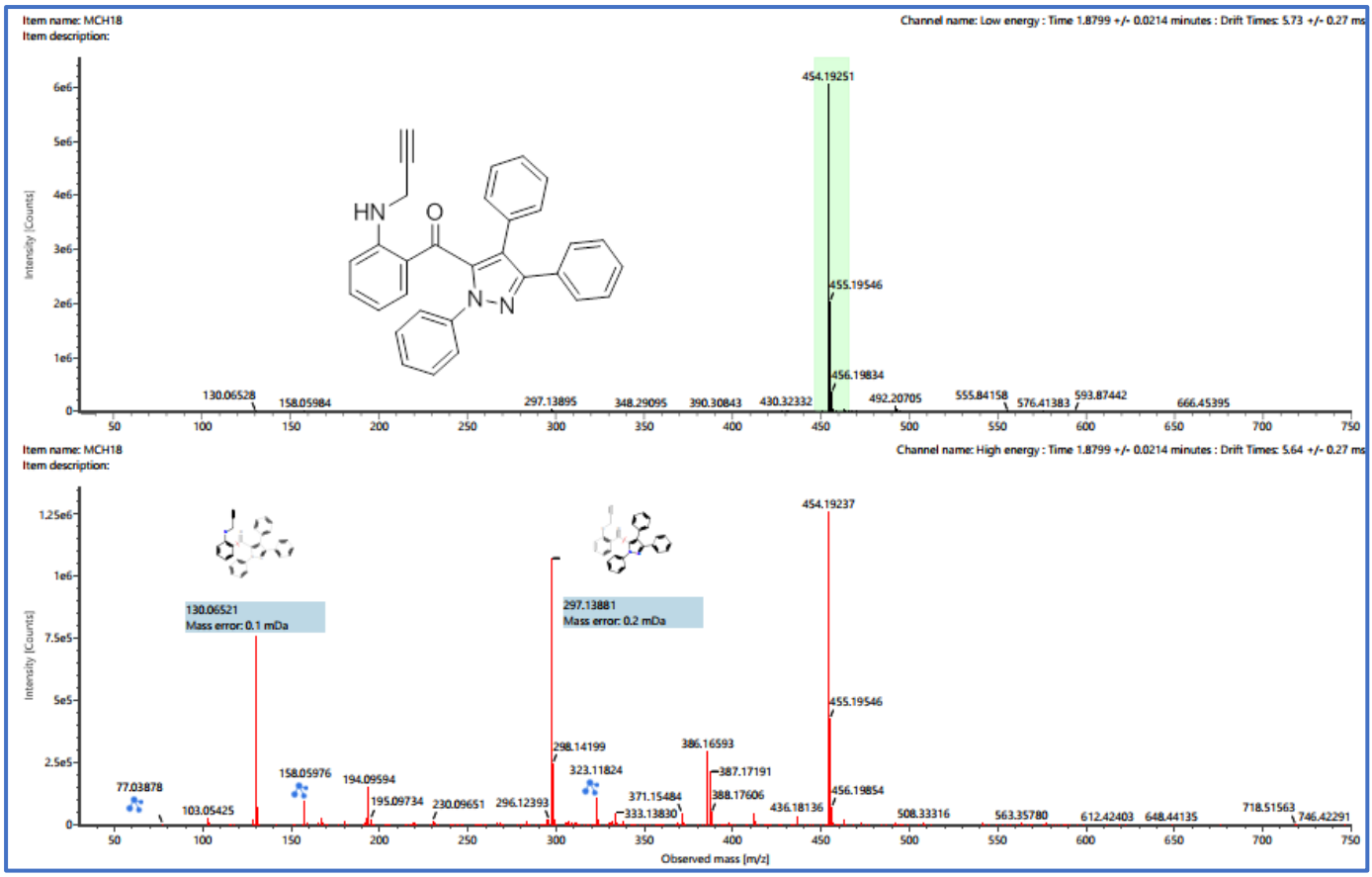


Figure S47. Mass spectrum of compound (**7a**)

k) 4-(4-methoxyphenyl)-5-(2-propargylaminobenzoyl)-1,3-diphenyl-1H-pyrazole (7b)

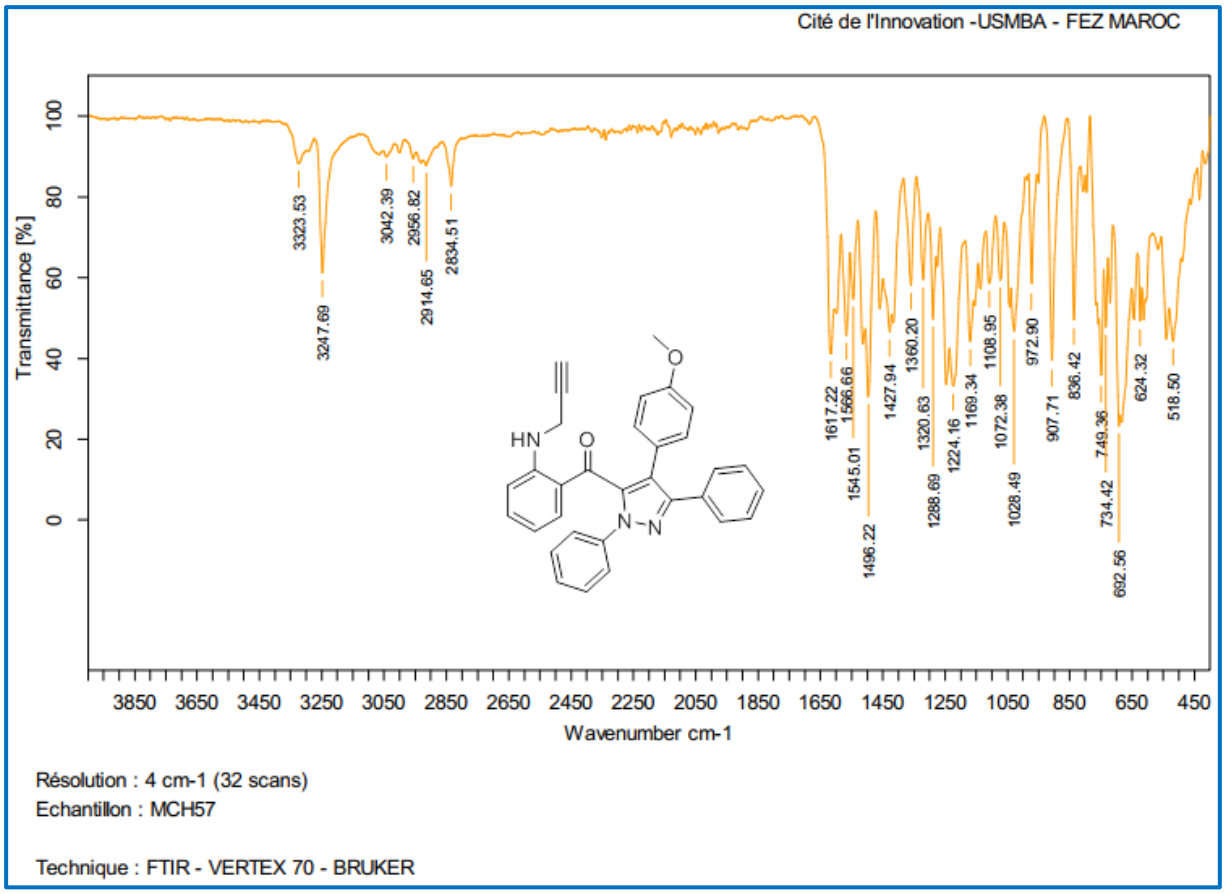


Figure S48. IR spectrum of compound (**7b**)

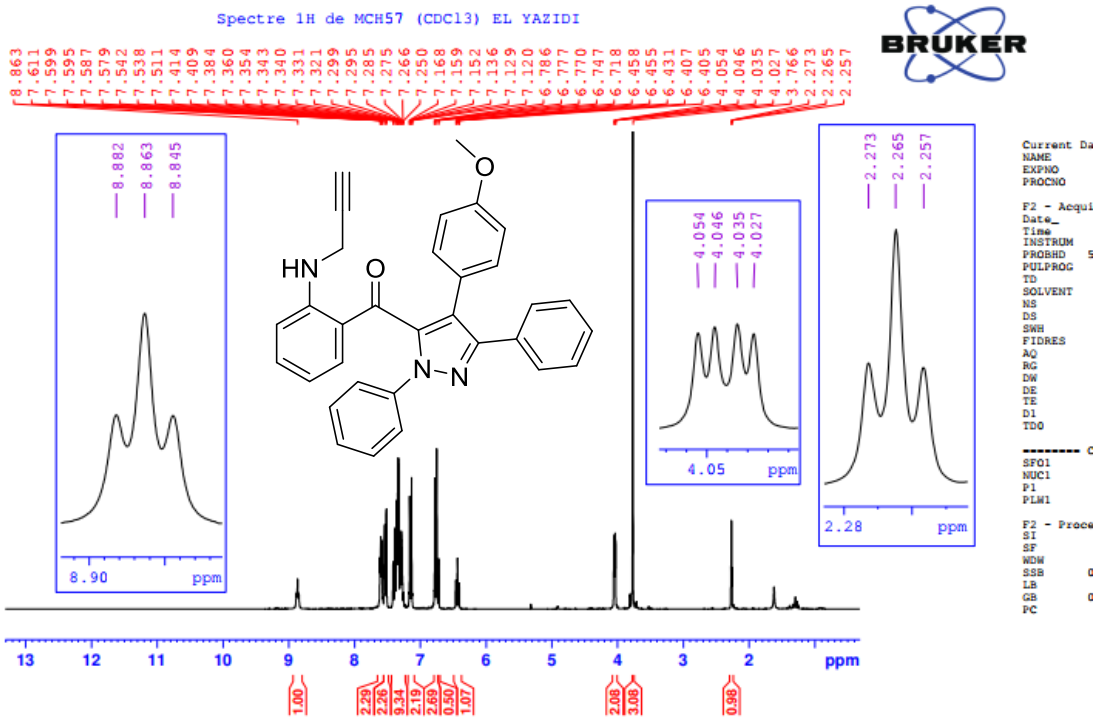


Figure S49. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound (**7b**)

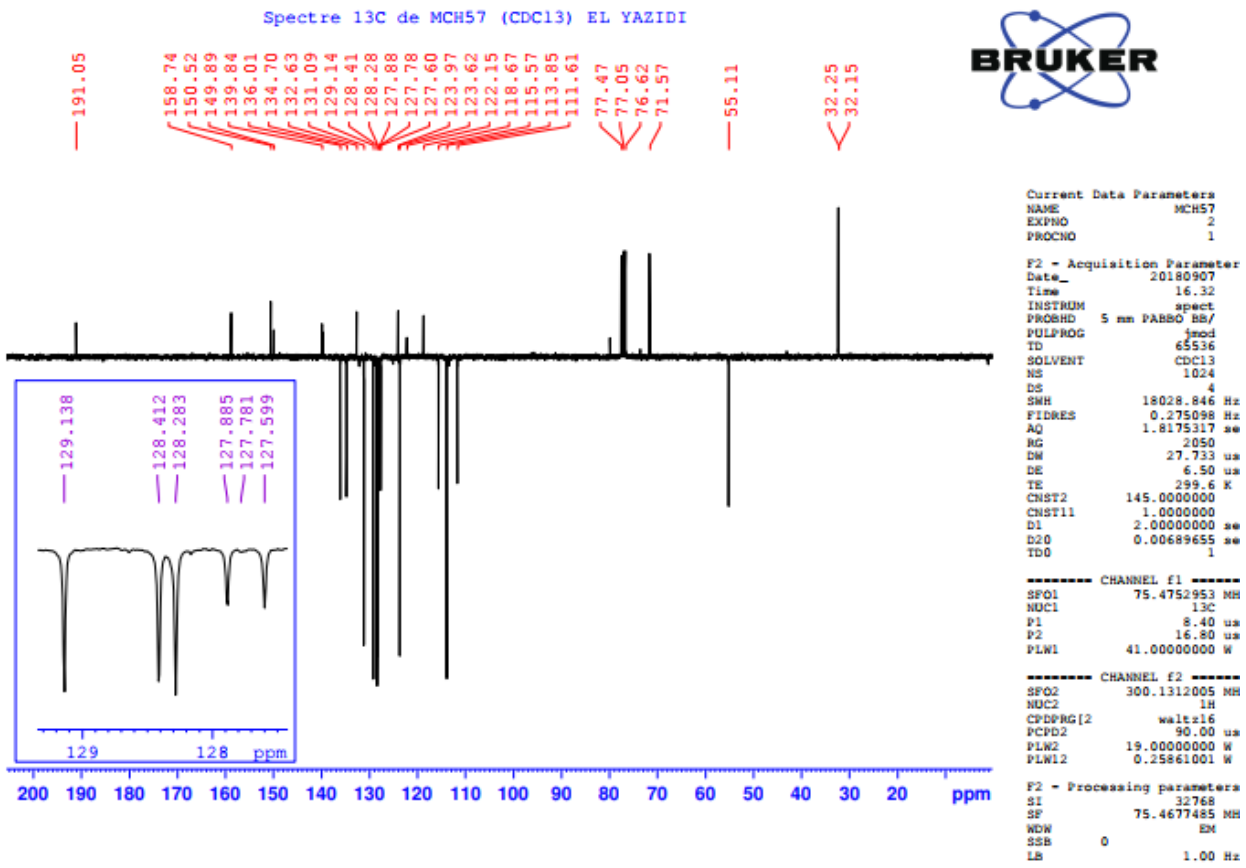


Figure S50. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound (**7b**)

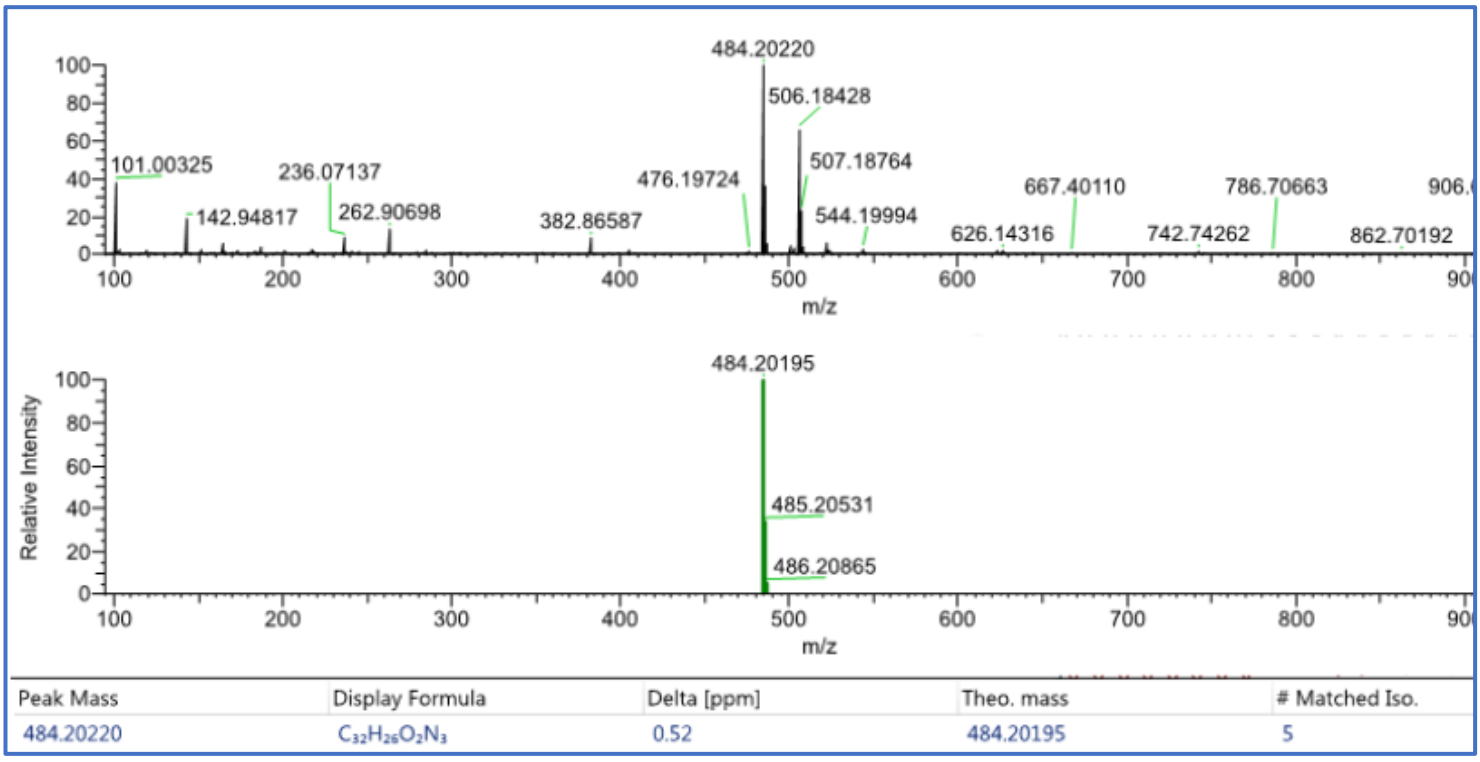


Figure S51. Mass spectrum of compound (**7b**)

l) 5-(2-methylaminobenzoyl)-1,3,4-triphenyl-1H-pyrazole (8a)

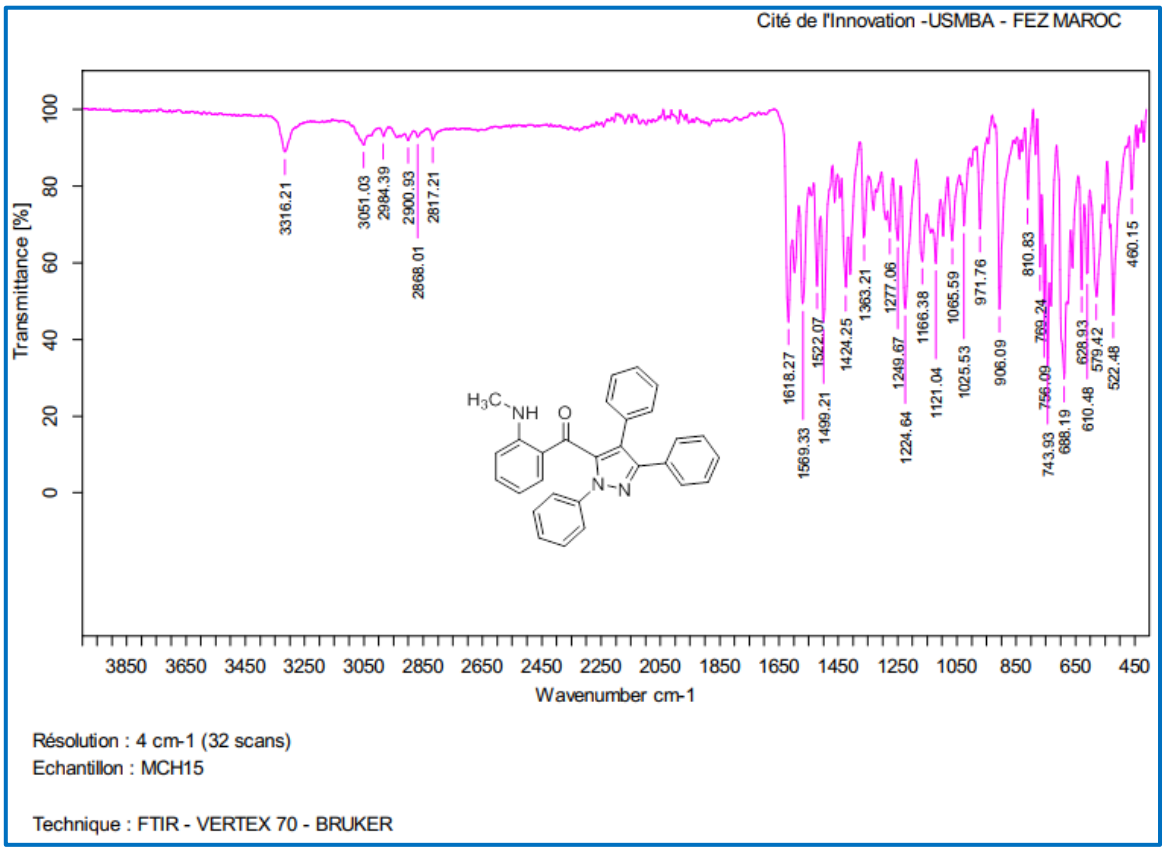


Figure S52. IR spectrum of compound (**8a**)

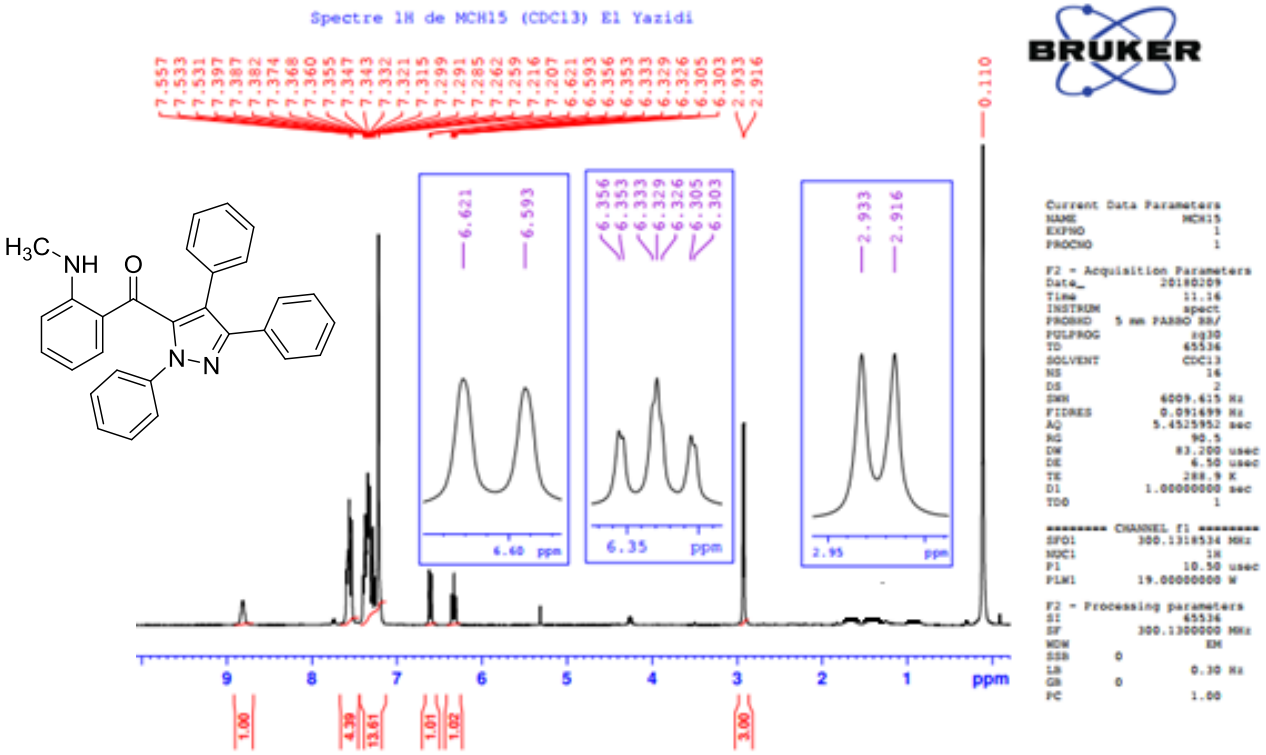


Figure S53. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound (**8a**)

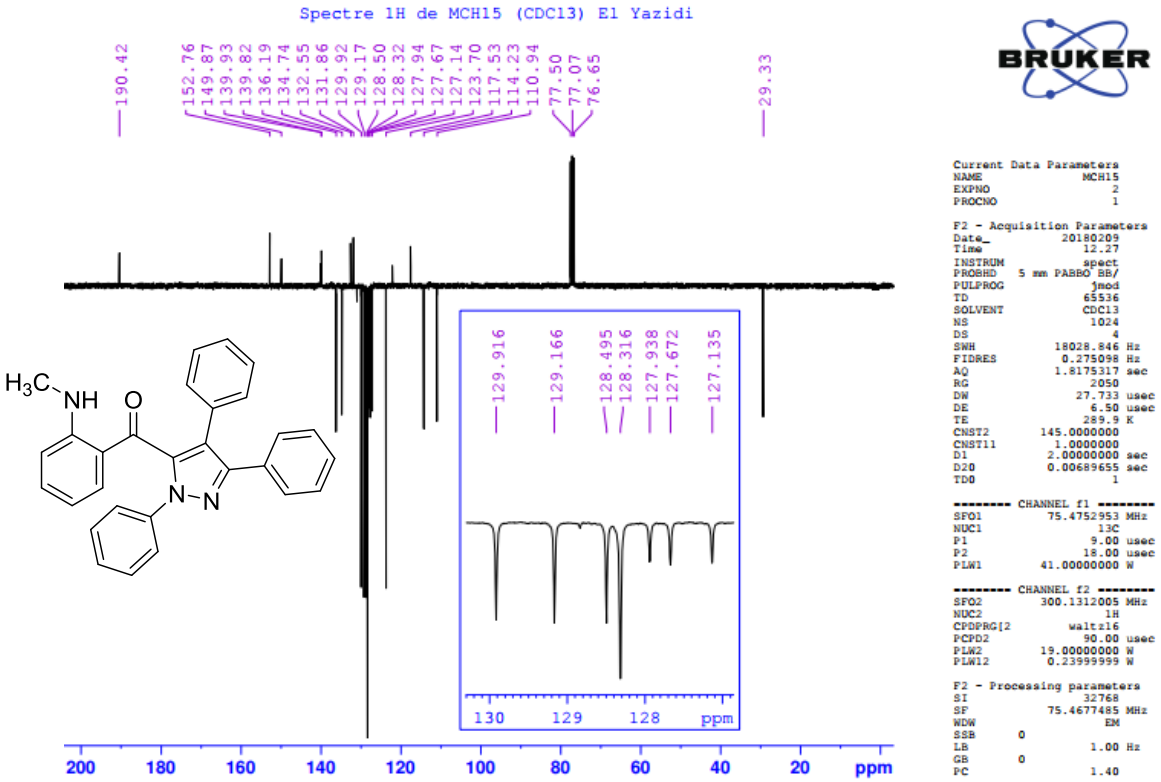


Figure S54. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound (**8a**)

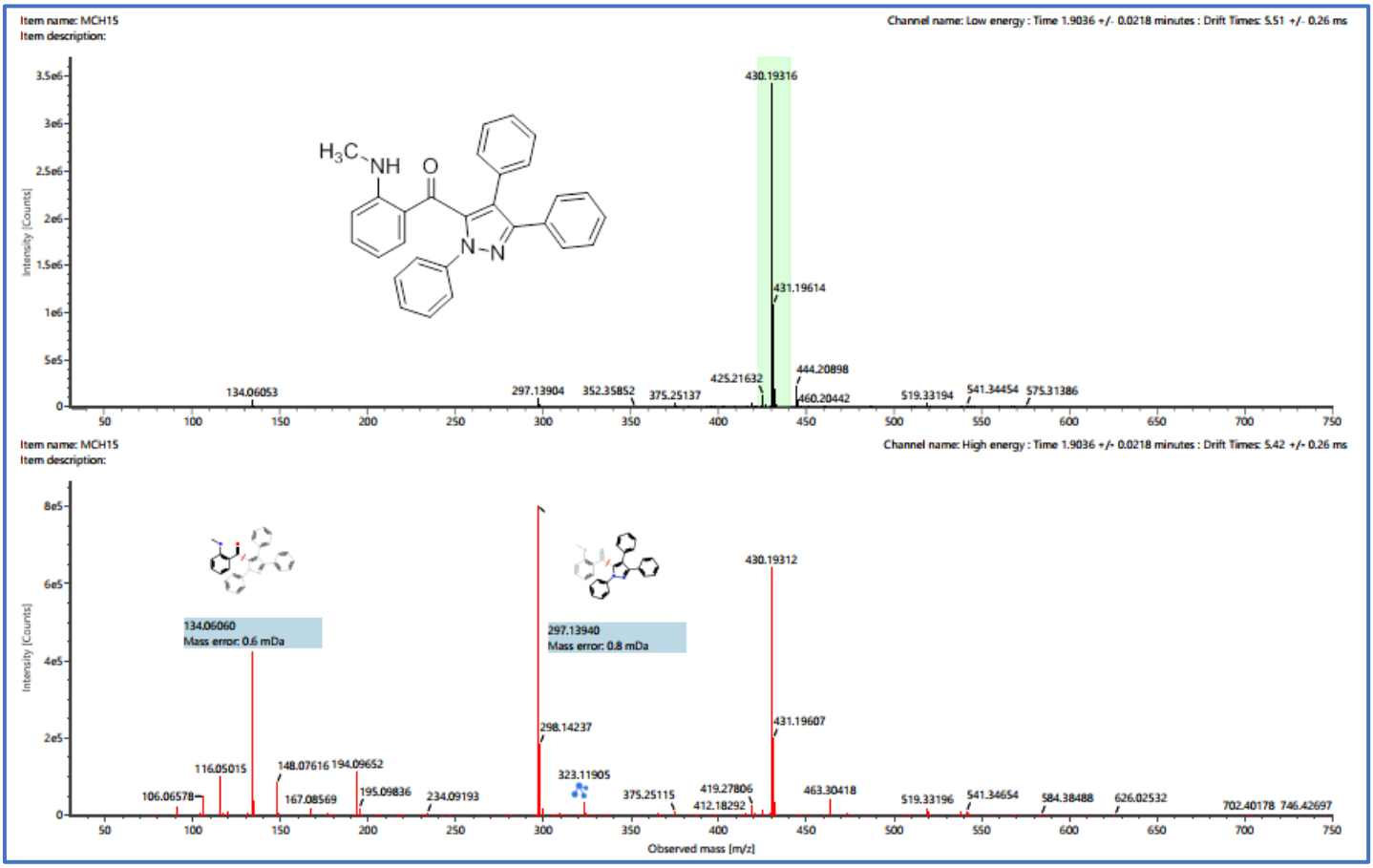


Figure S55. Mass spectrum of compound (**8a**)

m) 4-(4-methoxyphenyl)-5-(2-methylaminobenzoyl)-1,3-diphenyl-1H-pyrazole (8b)

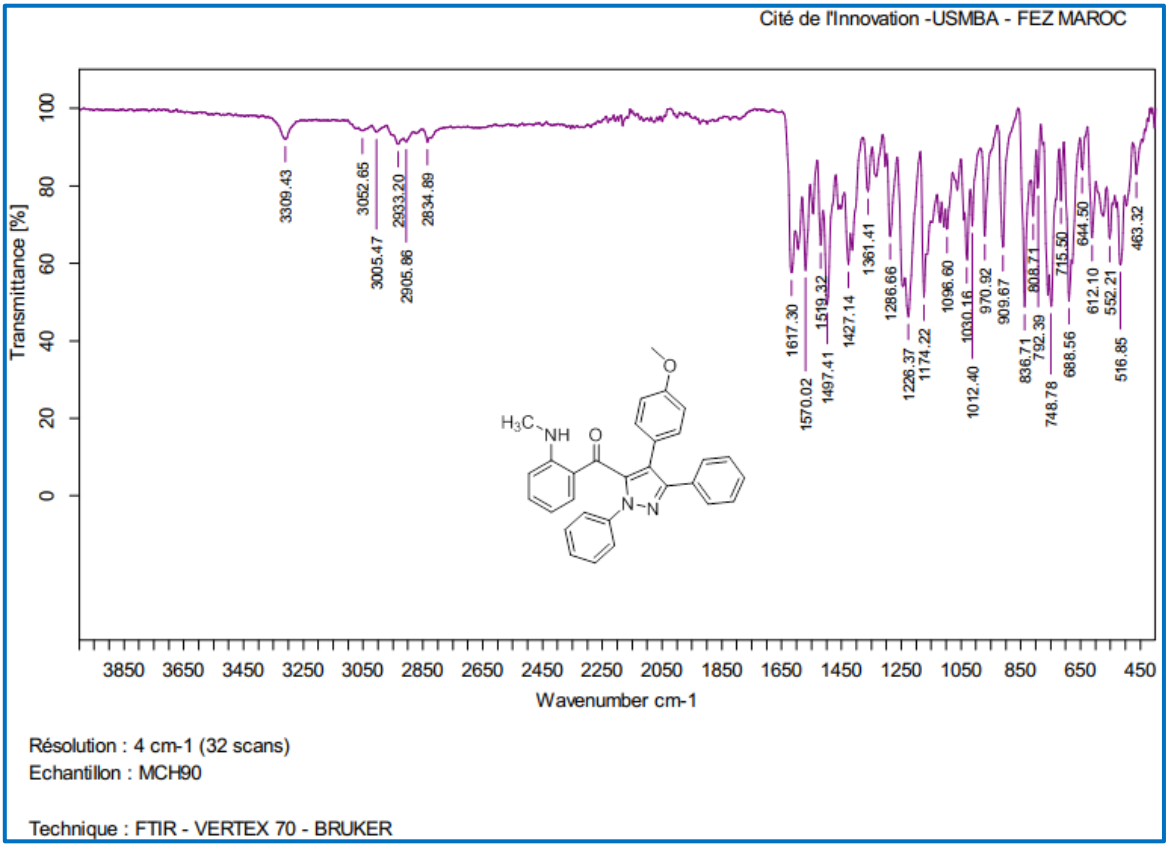


Figure S56. IR spectrum of compound (**8b**)

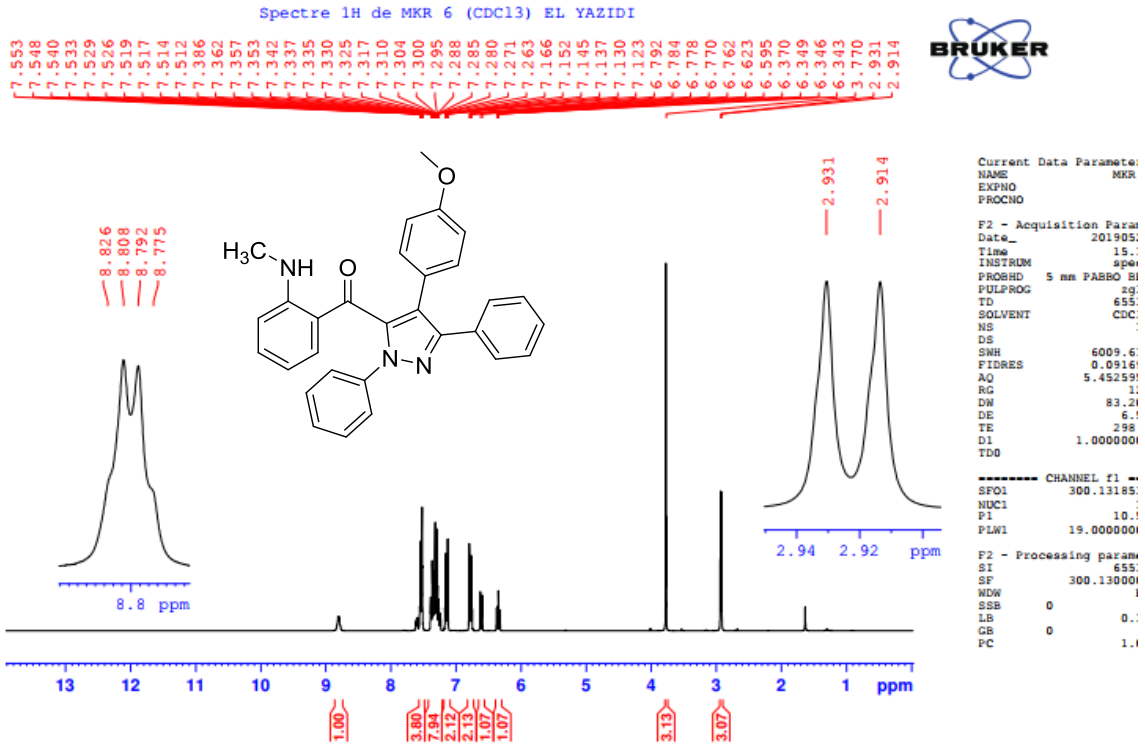


Figure S57. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound (**8b**)

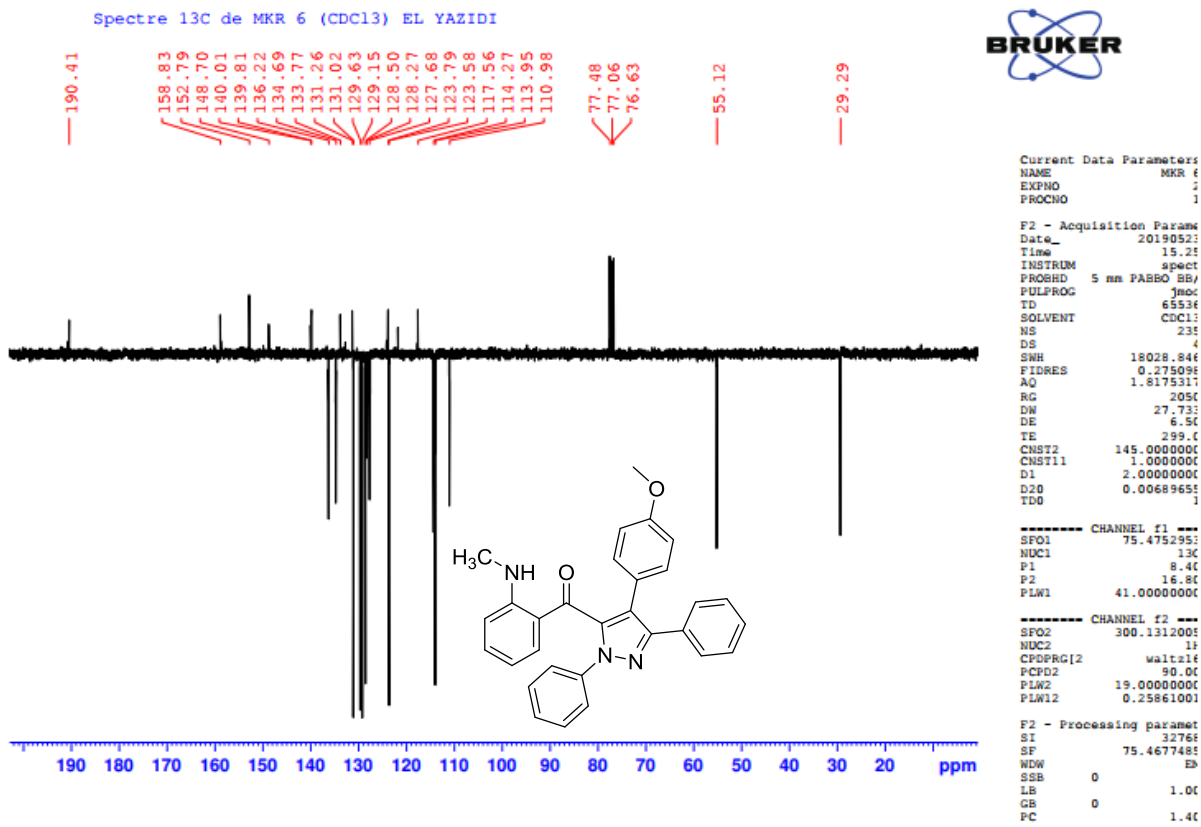


Figure S58. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound (**8b**)

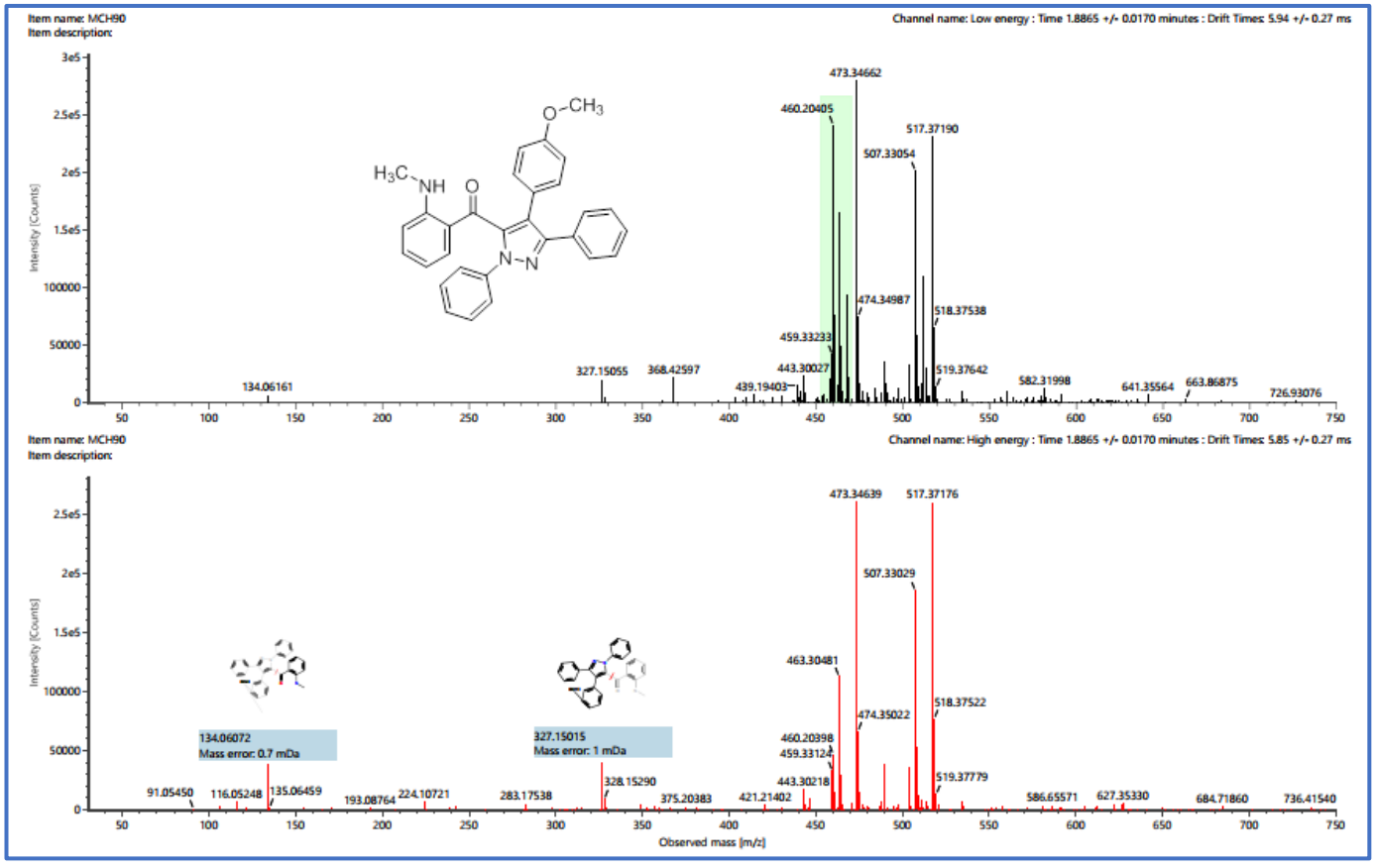


Figure S59. Mass spectrum of compound (**8b**)

n) 4-(4-chlorophenyl)-5-(2-methylaminobenzoyl)-1,3-diphenyl-1H-pyrazole (8c)

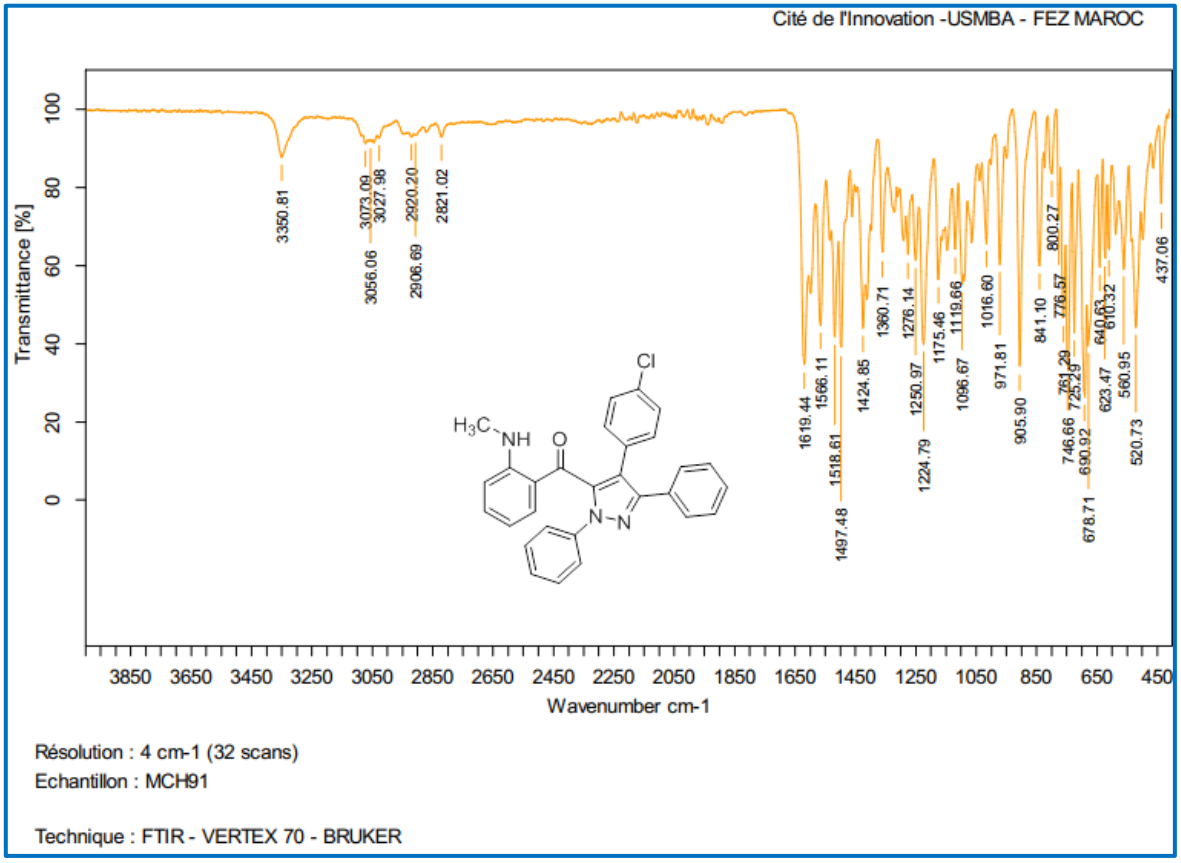


Figure S60. IR spectrum of compound (**8c**)

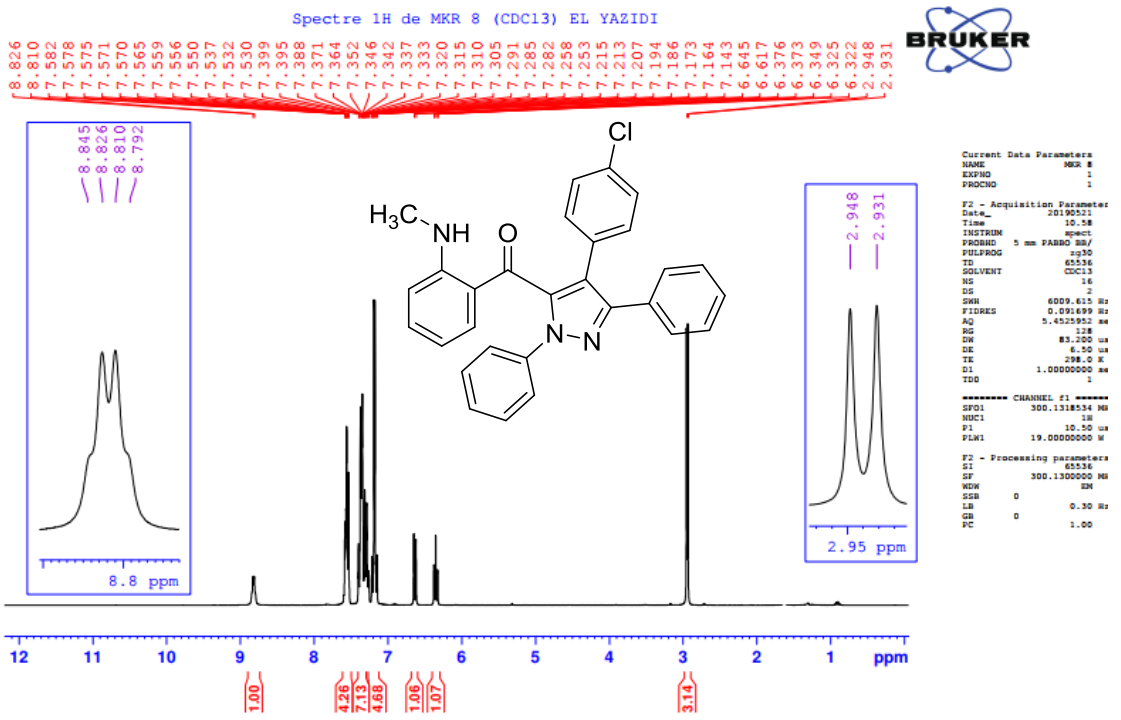


Figure S61. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound (**8c**)

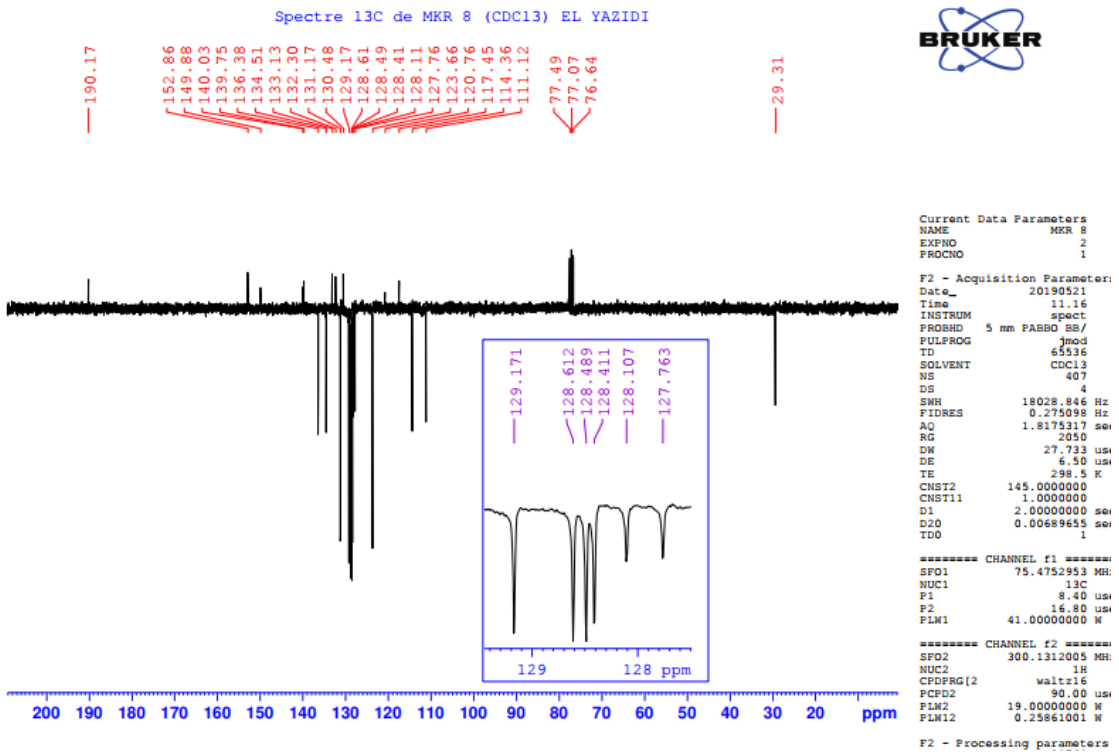


Figure S62. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound (**8c**)

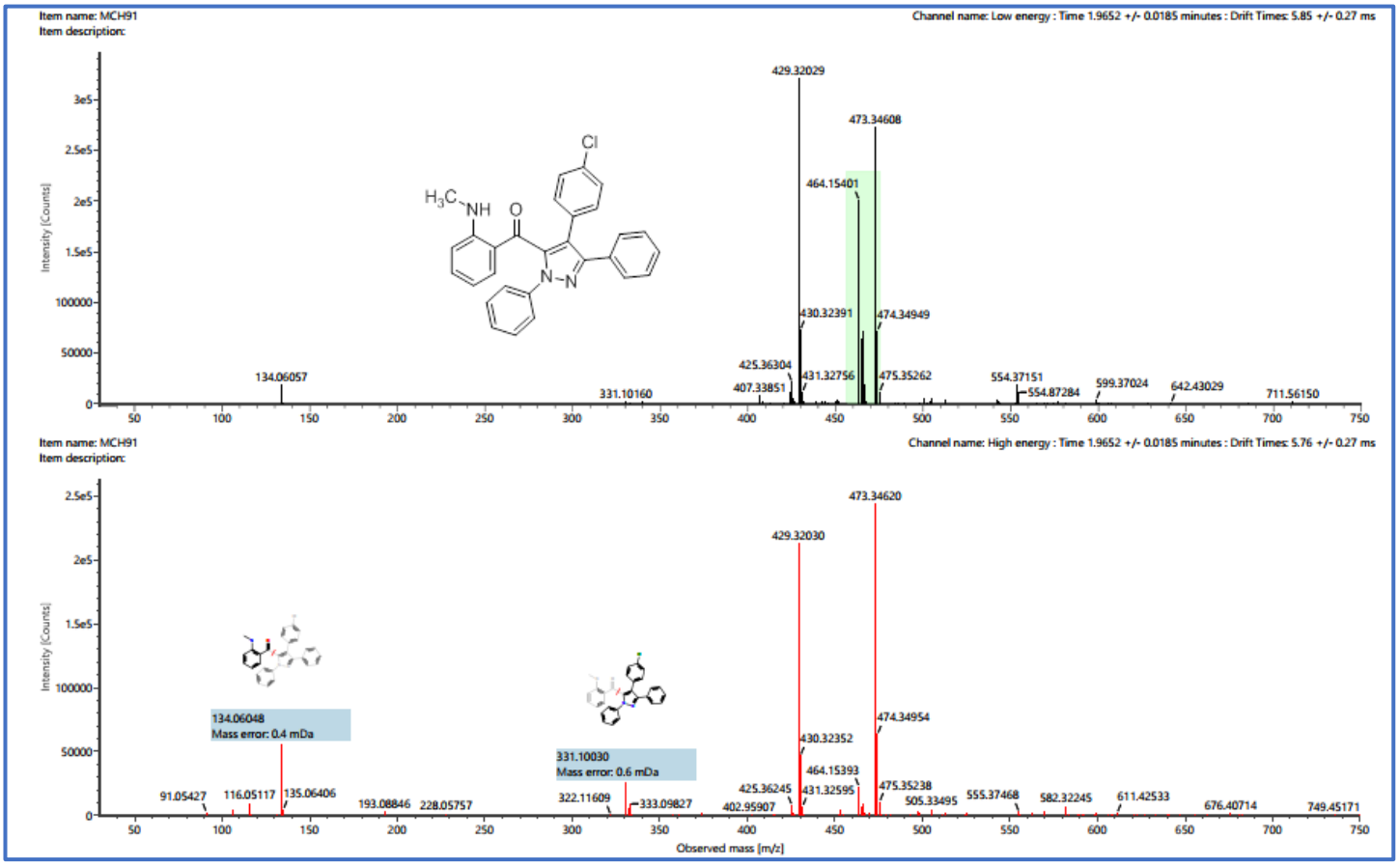


Figure S63. Mass spectrum of compound (**8c**)

o) 5-(2-methylaminobenzoyl)-1,3-diphenyl-4-(p-tolyl)-1H-pyrazole (8d)

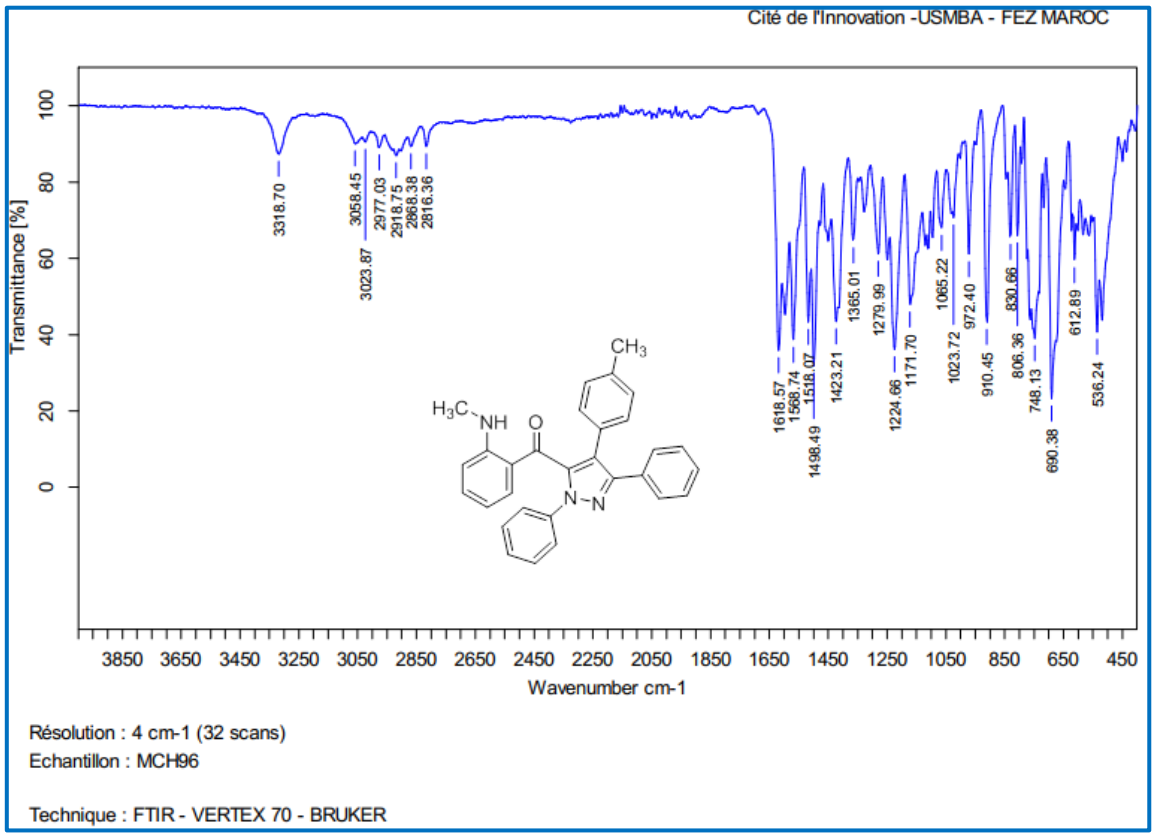


Figure S64. IR spectrum of compound (**8d**)

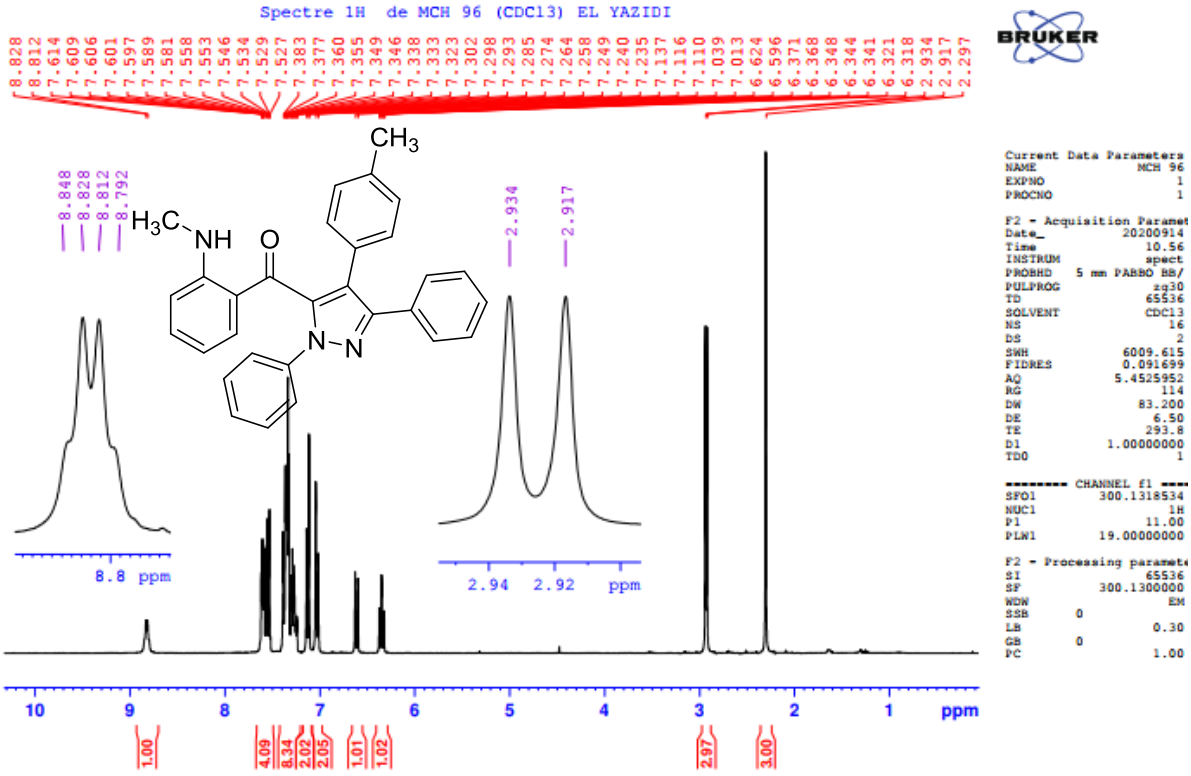


Figure S65. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound (**8d**)

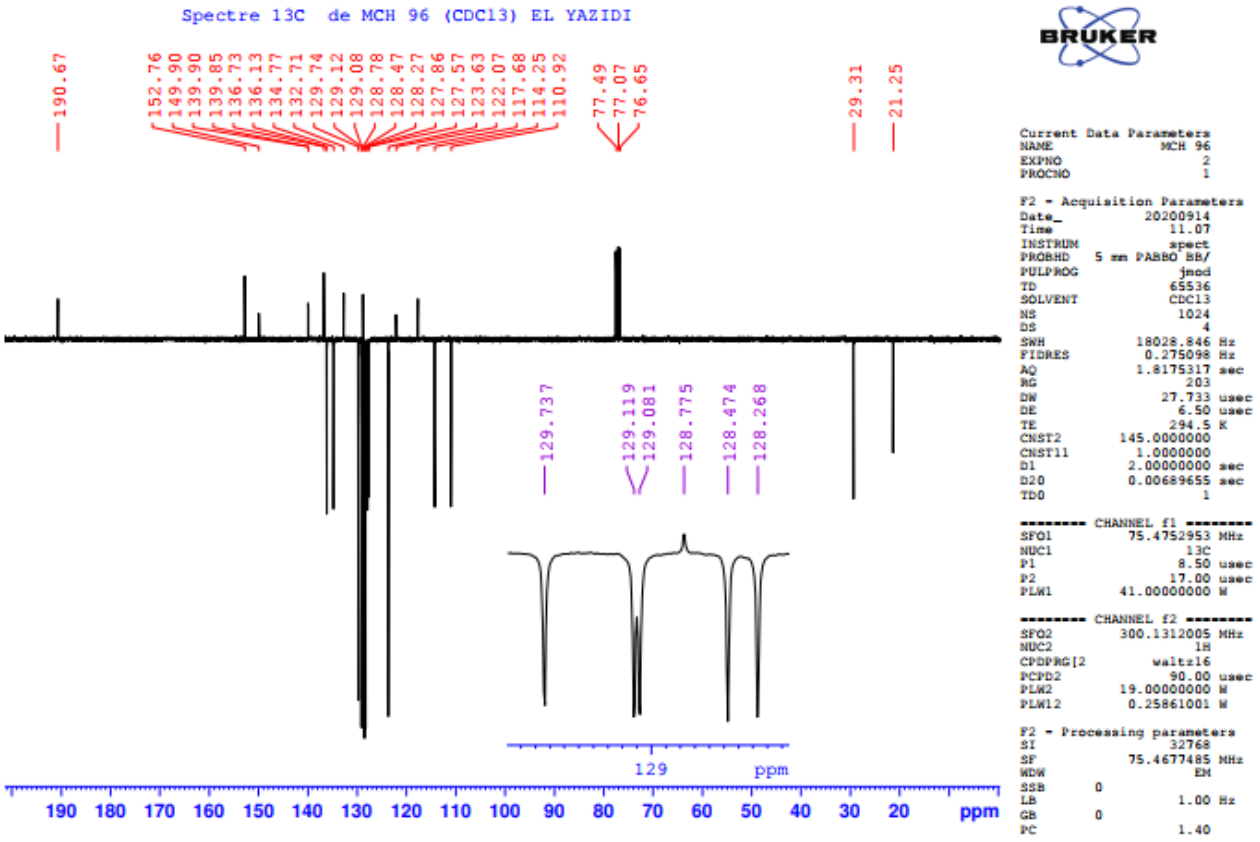


Figure S66. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound (**8d**)

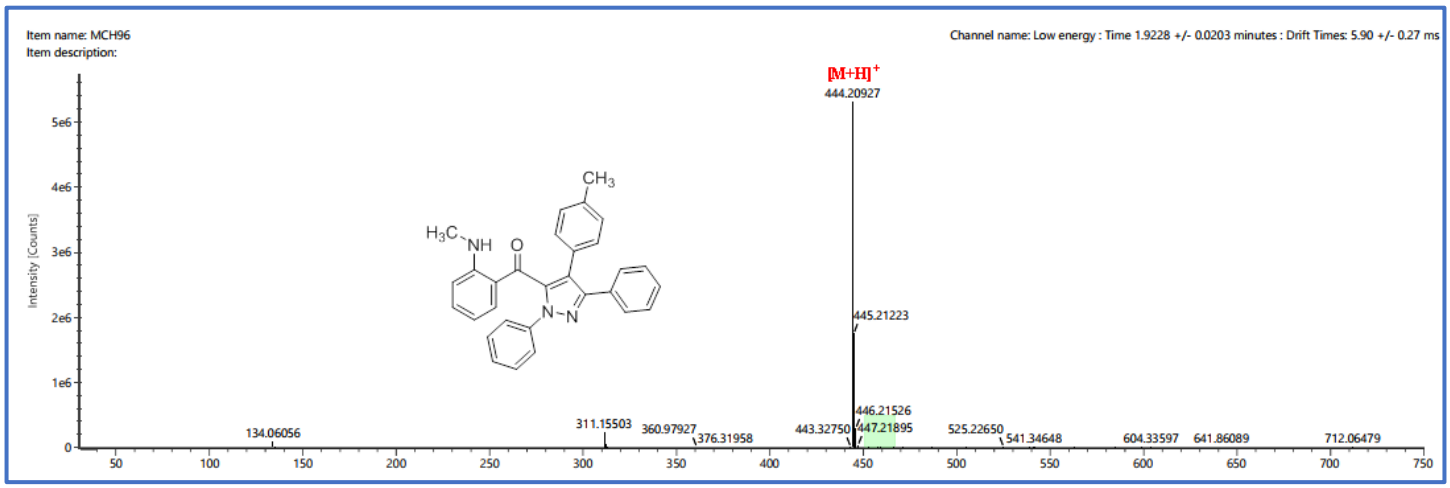


Figure S67. Mass spectrum of compound (**8d**)

p) 5-(2-dimethylaminobenzoyl)-1,3,4-triphenyl-1H-pyrazole (9a)

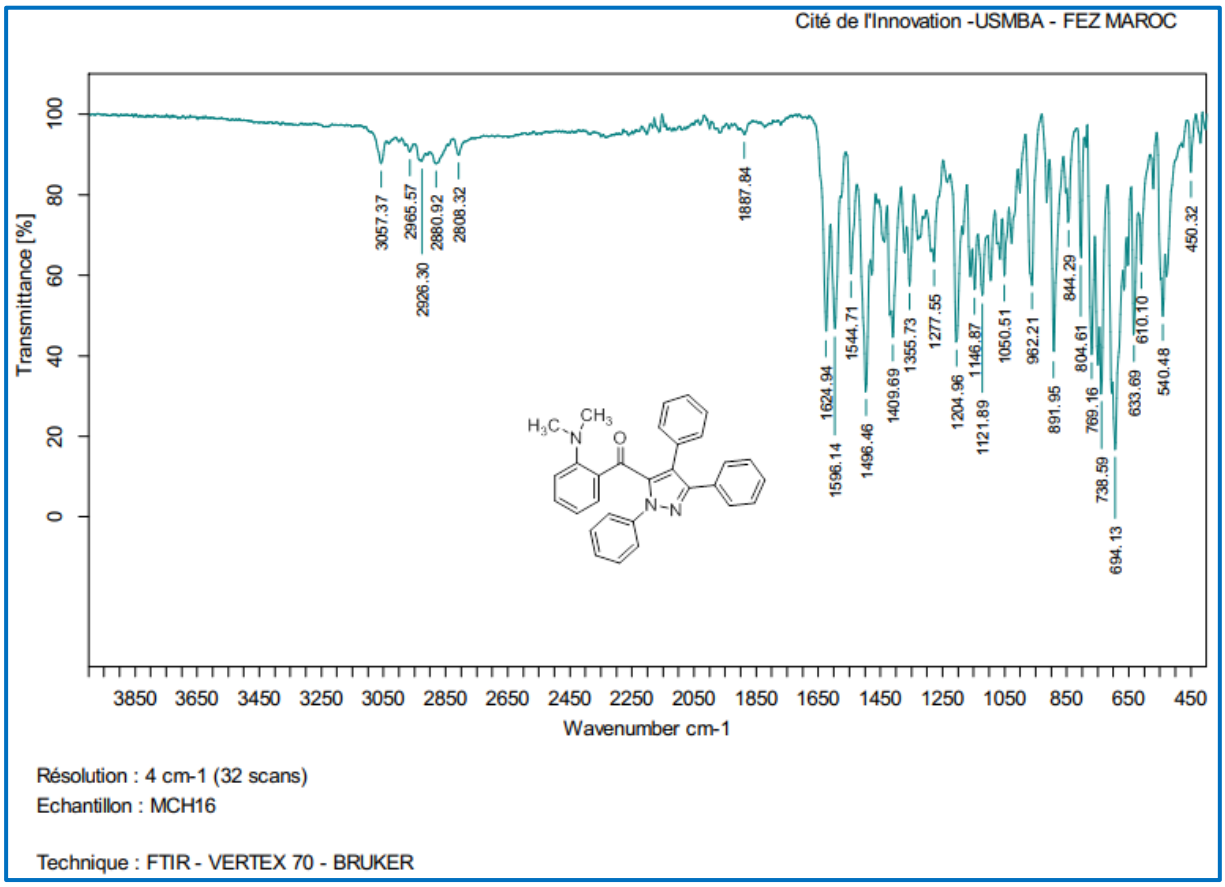


Figure S68. IR spectrum of compound (**9a**)

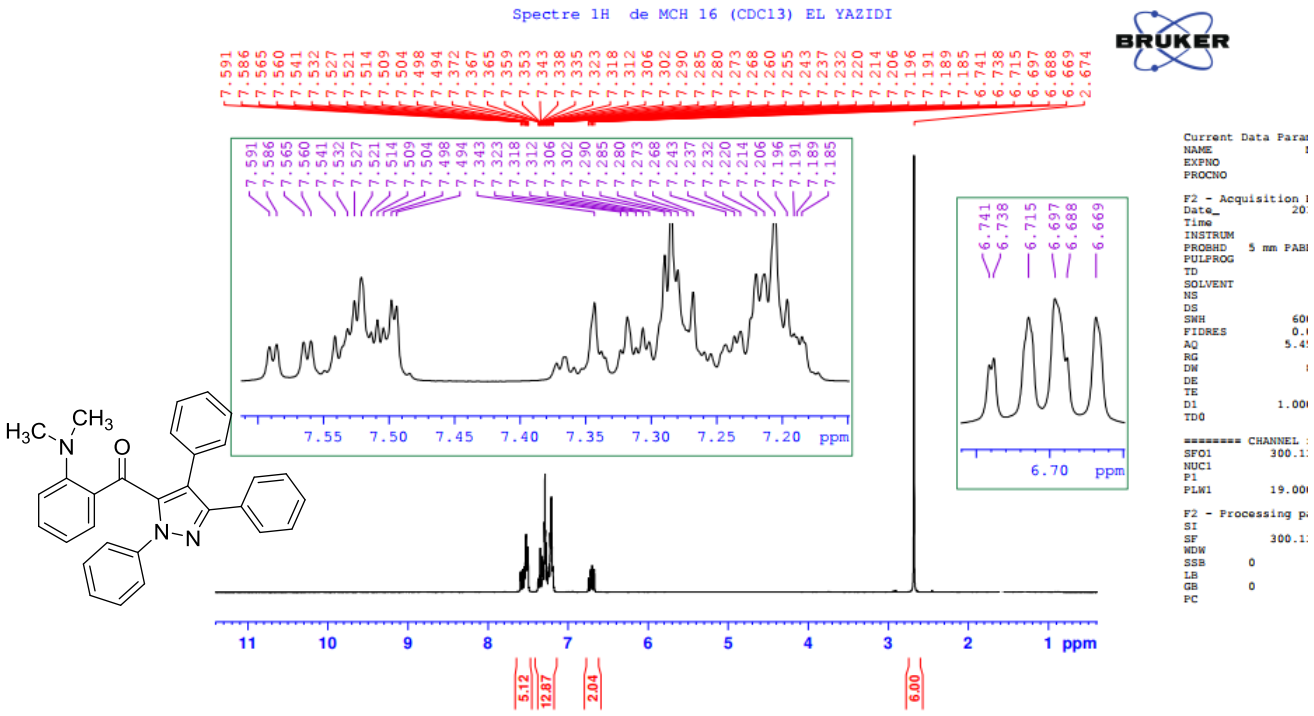


Figure S69. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound (**9a**)

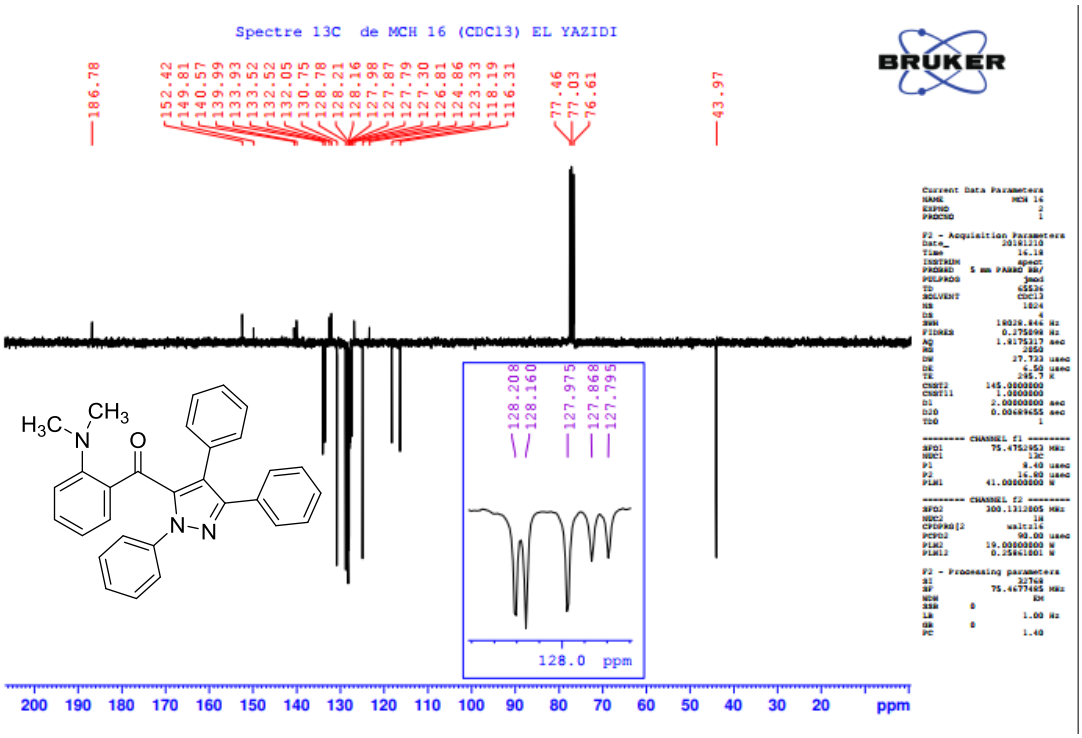


Figure S70. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound (**9a**)

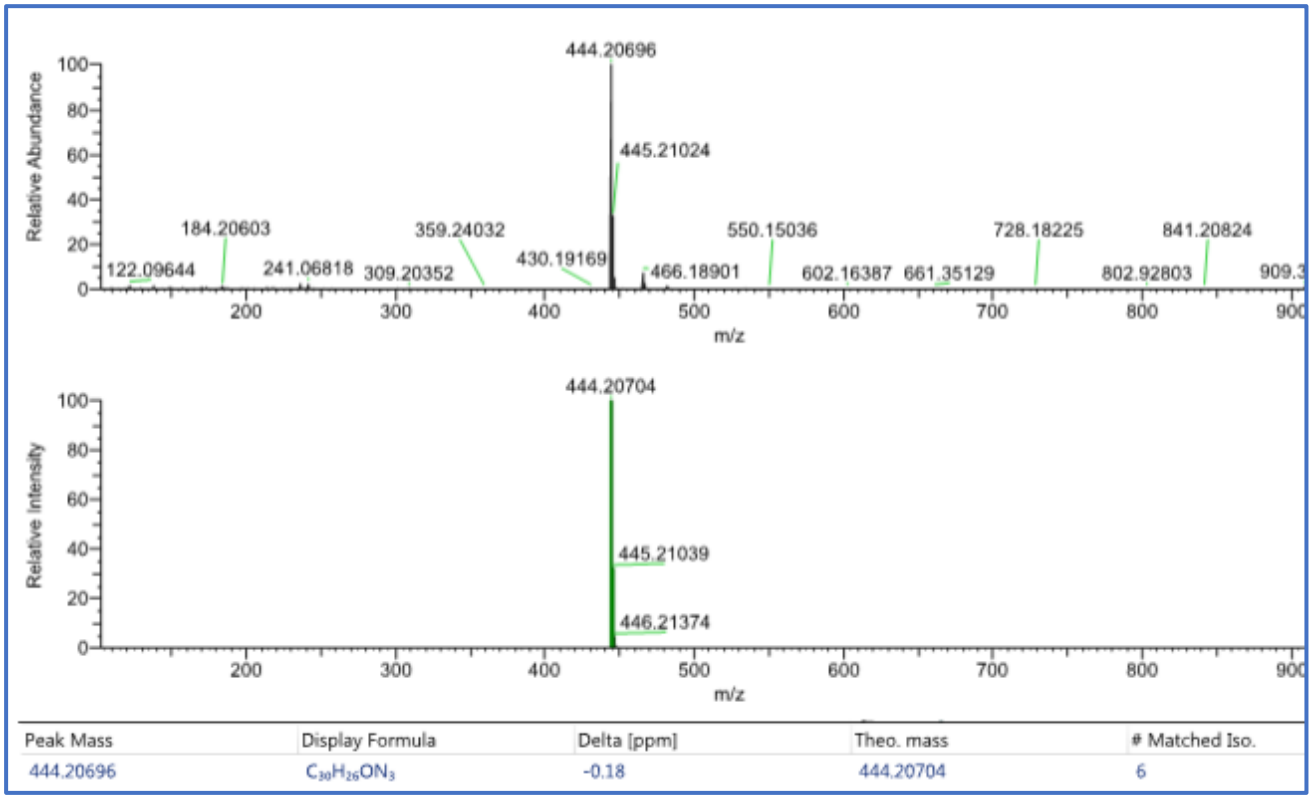


Figure S71. Mass spectrum of compound (**9a**)

q) 4-(4-methoxyphenyl)-5-(2-dimethylaminobenzoyl)-1,3-diphenyl-1H-pyrazole (9b)

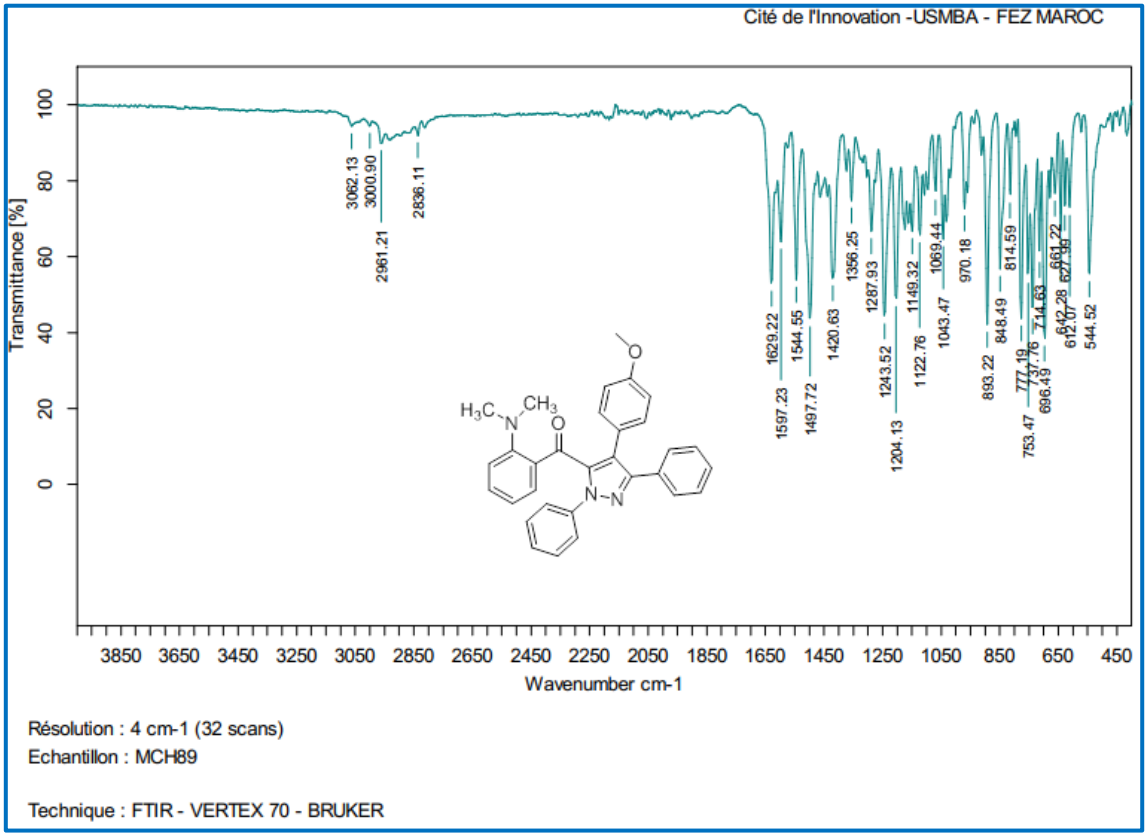


Figure S72. IR spectrum of compound (**9b**)

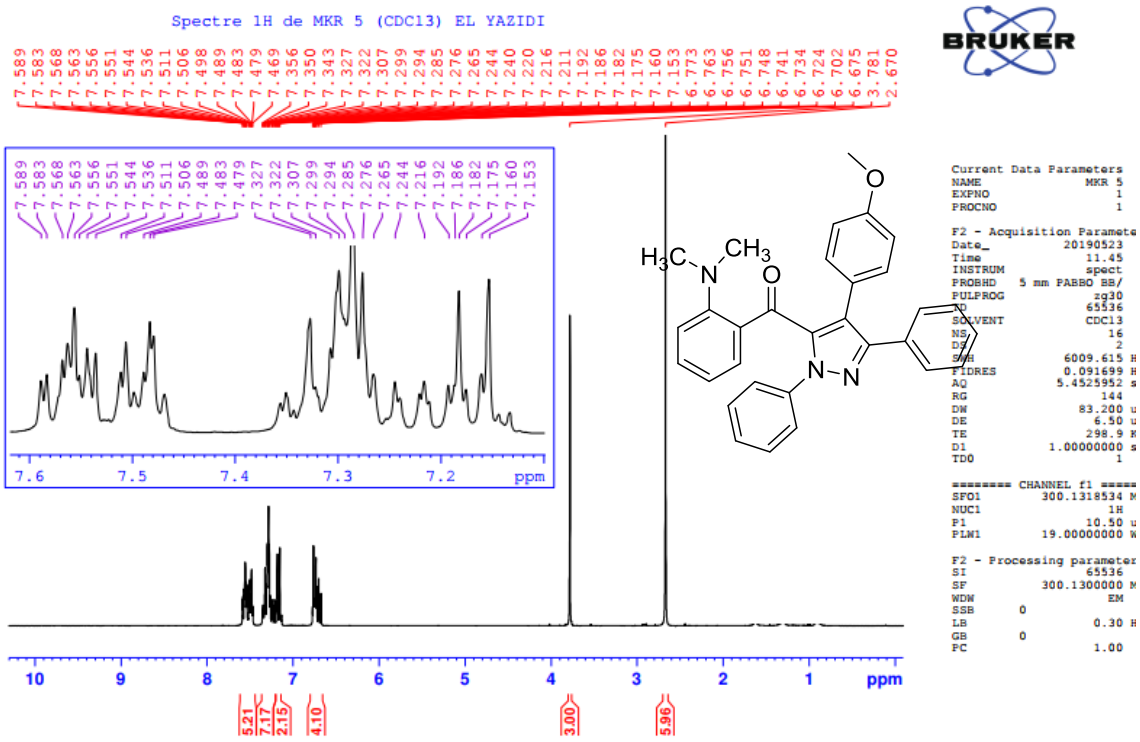


Figure S73. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound (**9b**)

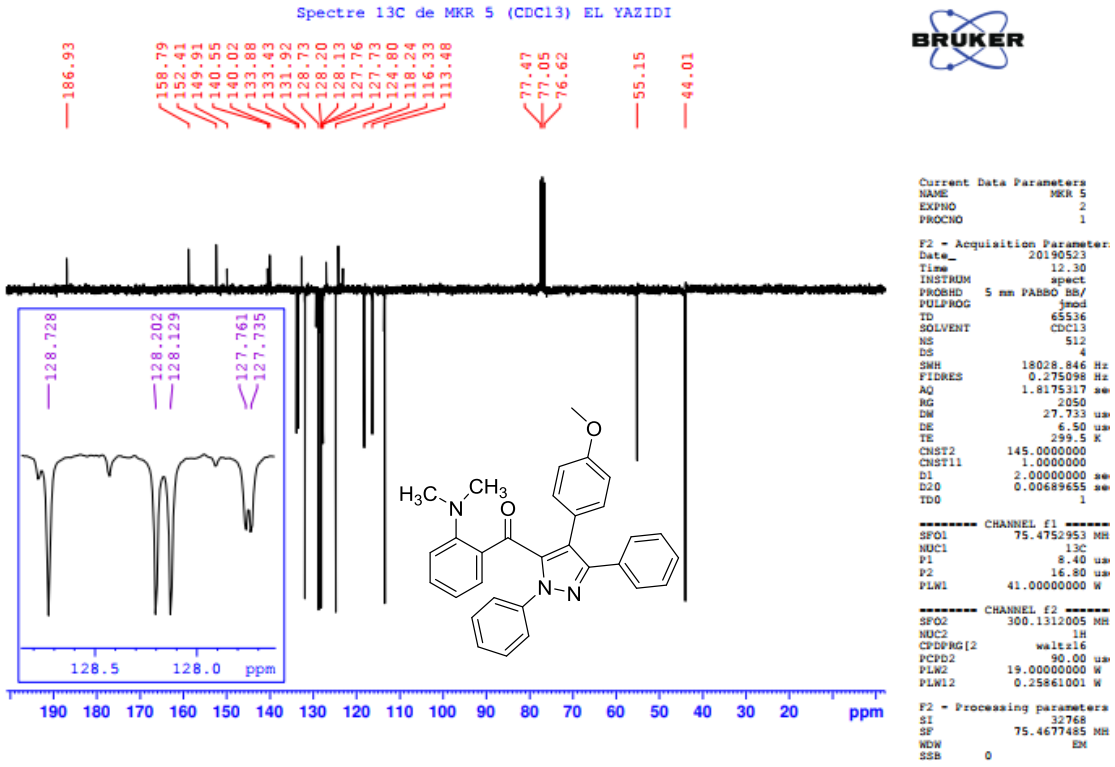


Figure S74. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound (**9b**)

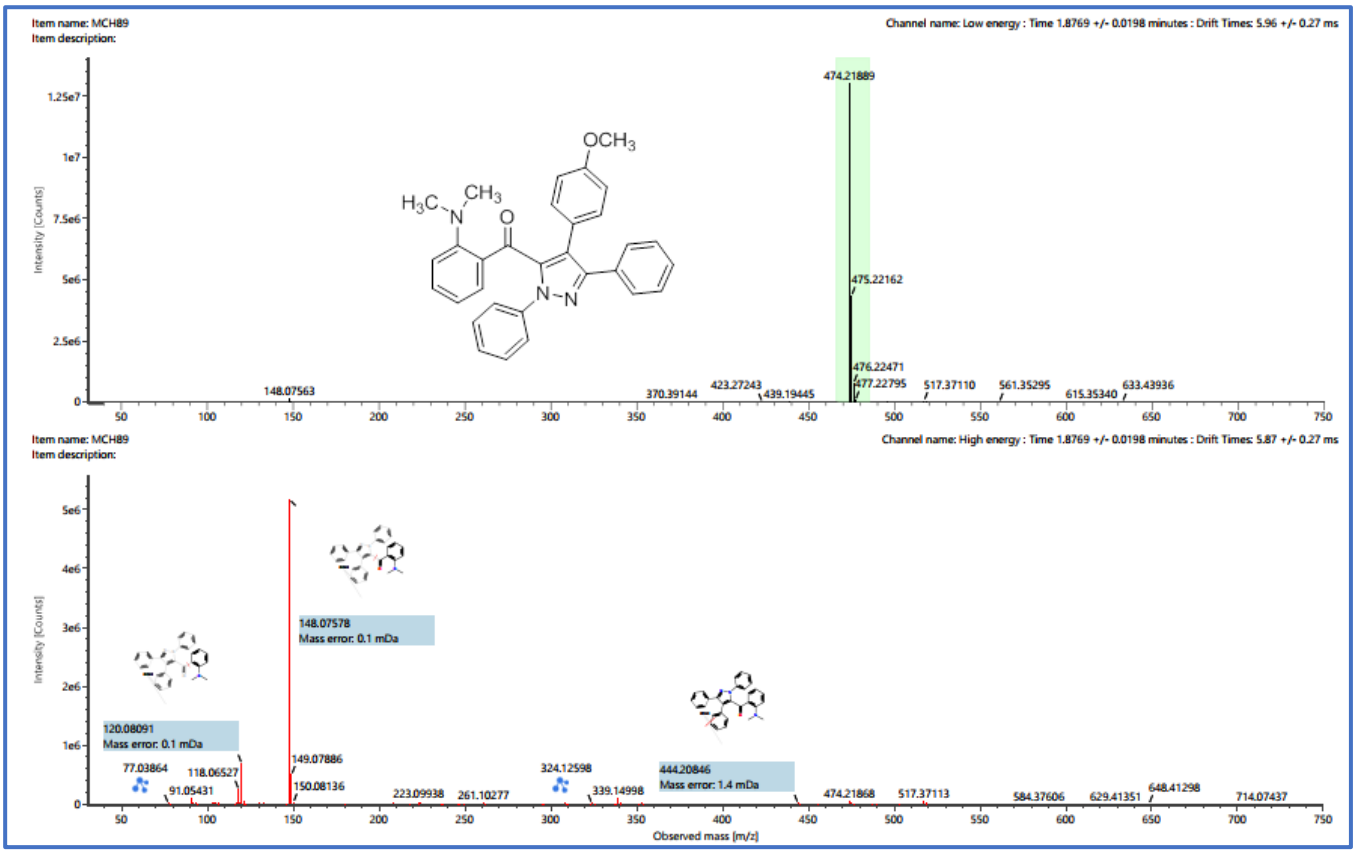


Figure S75. Mass spectrum of compound (**9b**)

r) 4-(4-chlorophenyl)-5-(2-dimethylaminobenzoyl)-1,3-diphenyl-1H-pyrazole (9c)

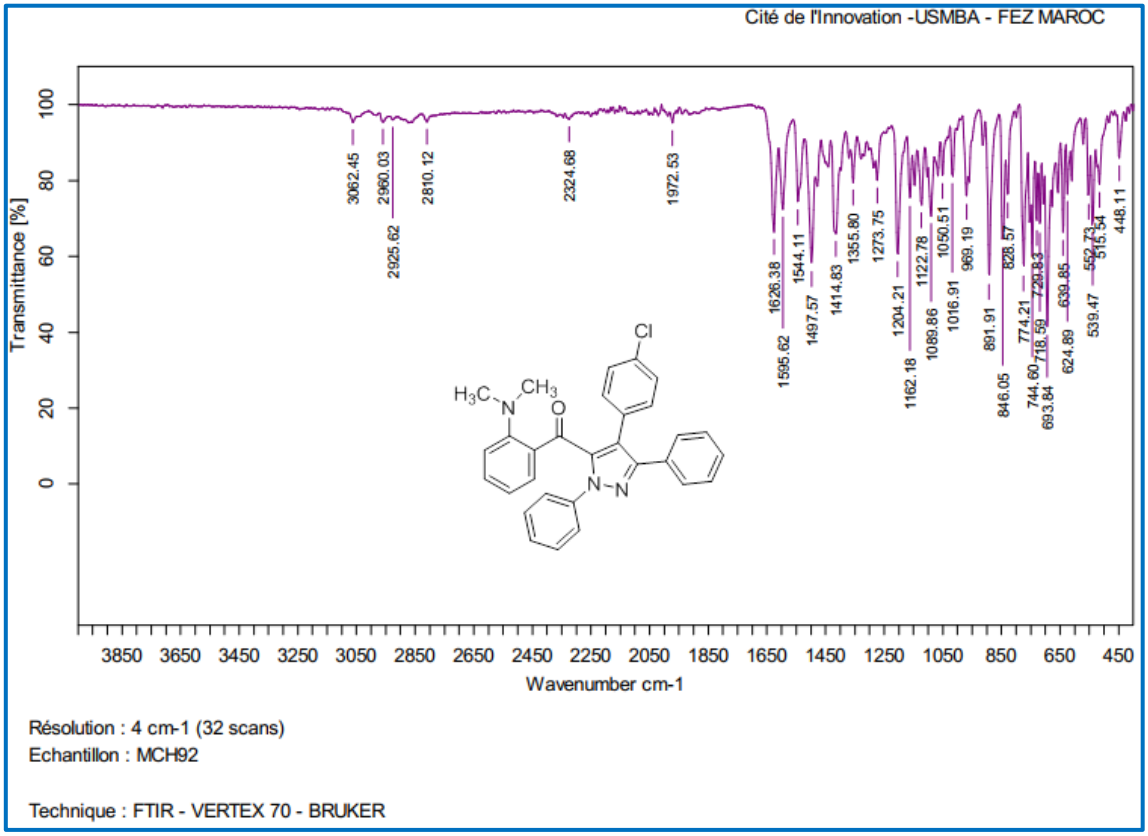


Figure S76. IR spectrum of compound (**9c**)

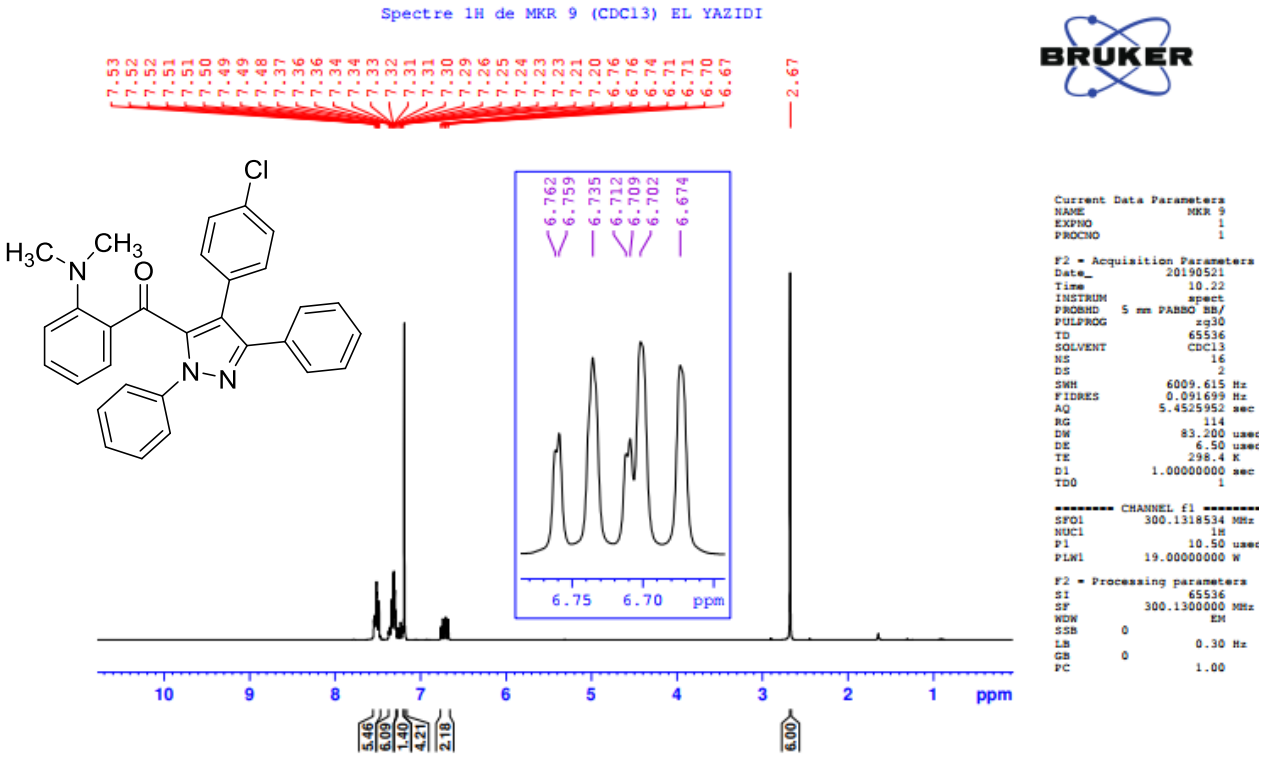


Figure S77. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound (**9c**)

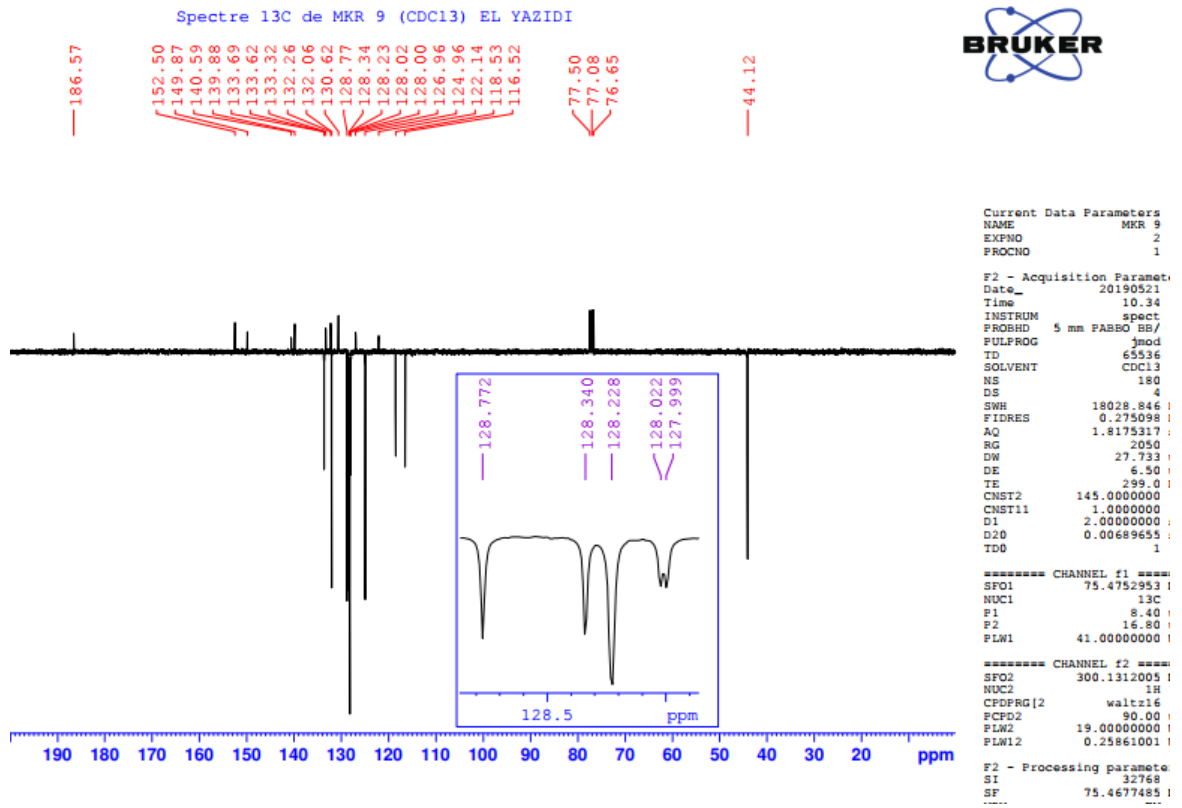


Figure S78. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound (**9c**)

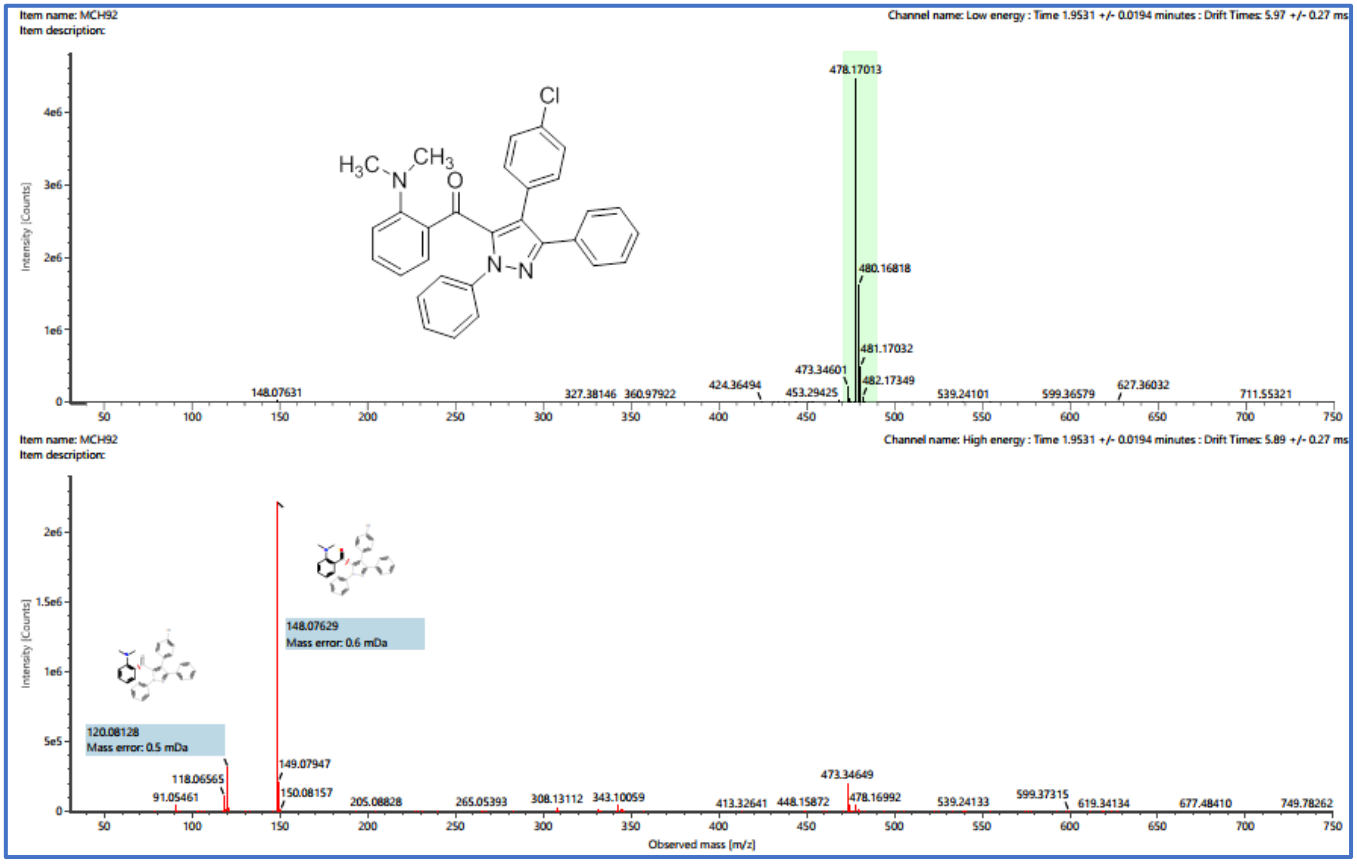


Figure S79. Mass spectrum of compound (**9c**)

s) 5-(2-dimethylaminobenzoyl)-1,3-diphenyl-4-(p-tolyl)-1H-pyrazole (9d)

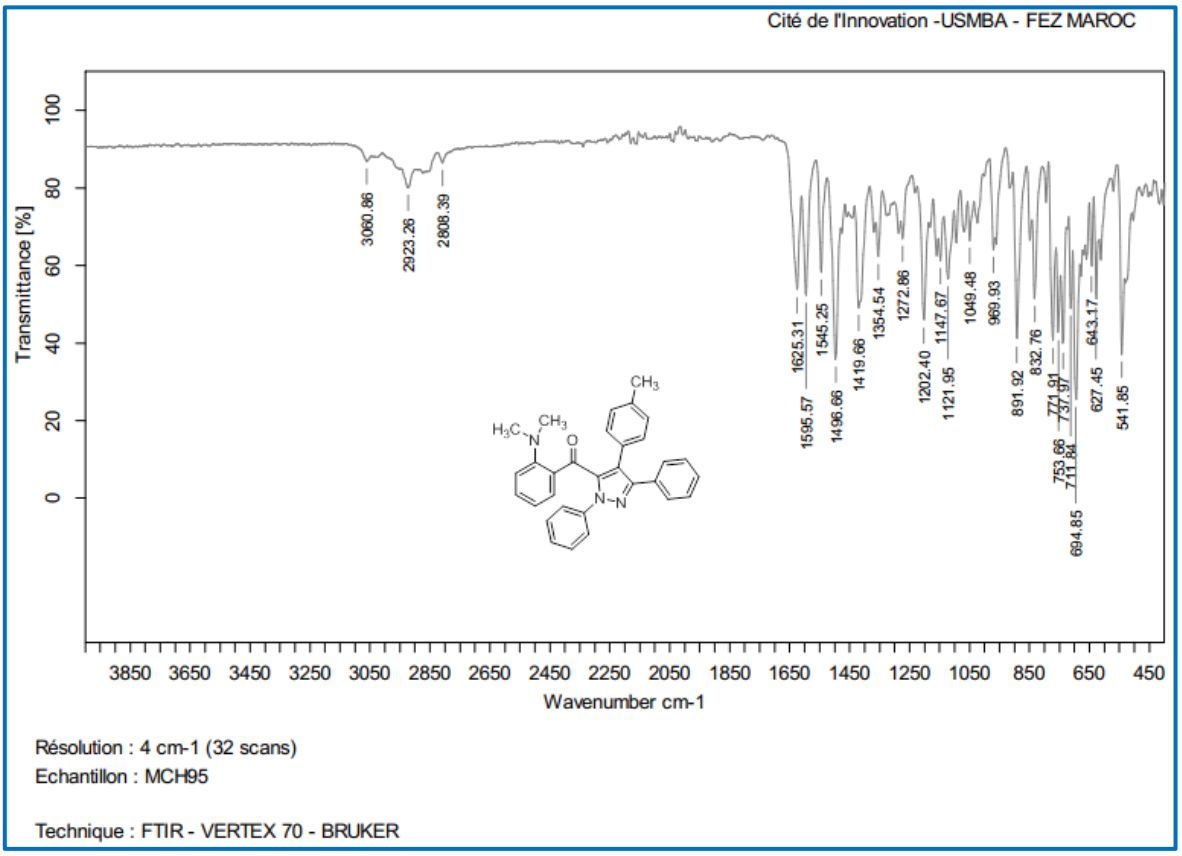


Figure S80. IR spectrum of compound (**9d**)

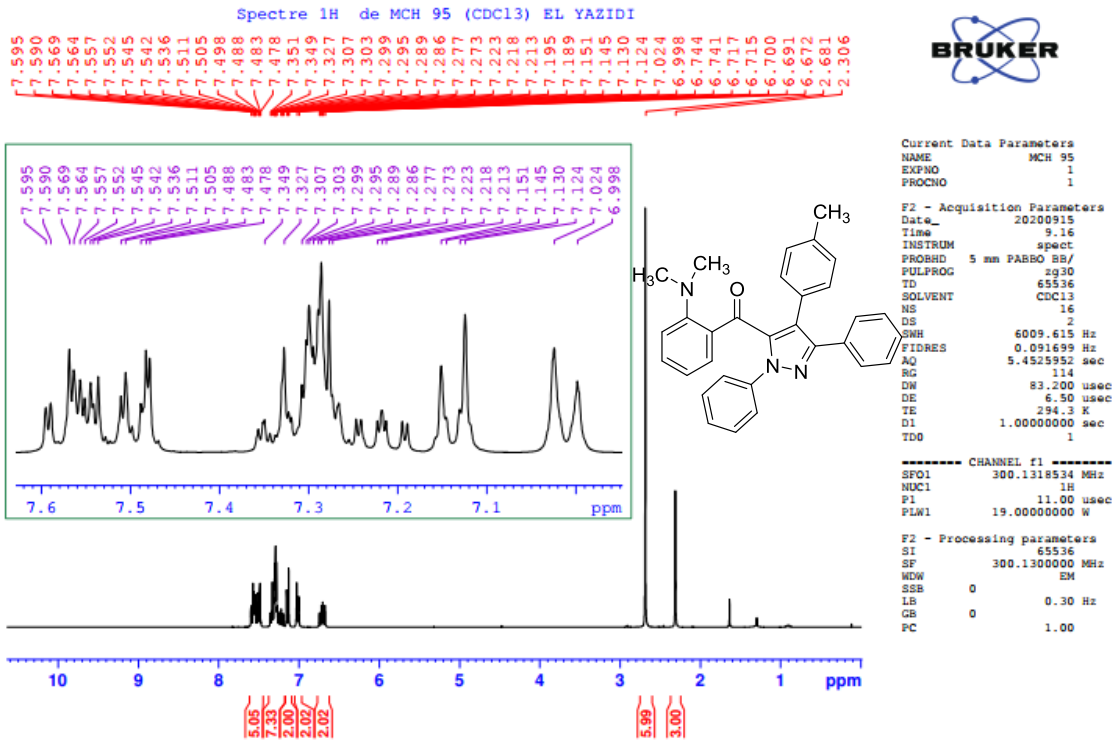


Figure S81. ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of compound (**9d**)

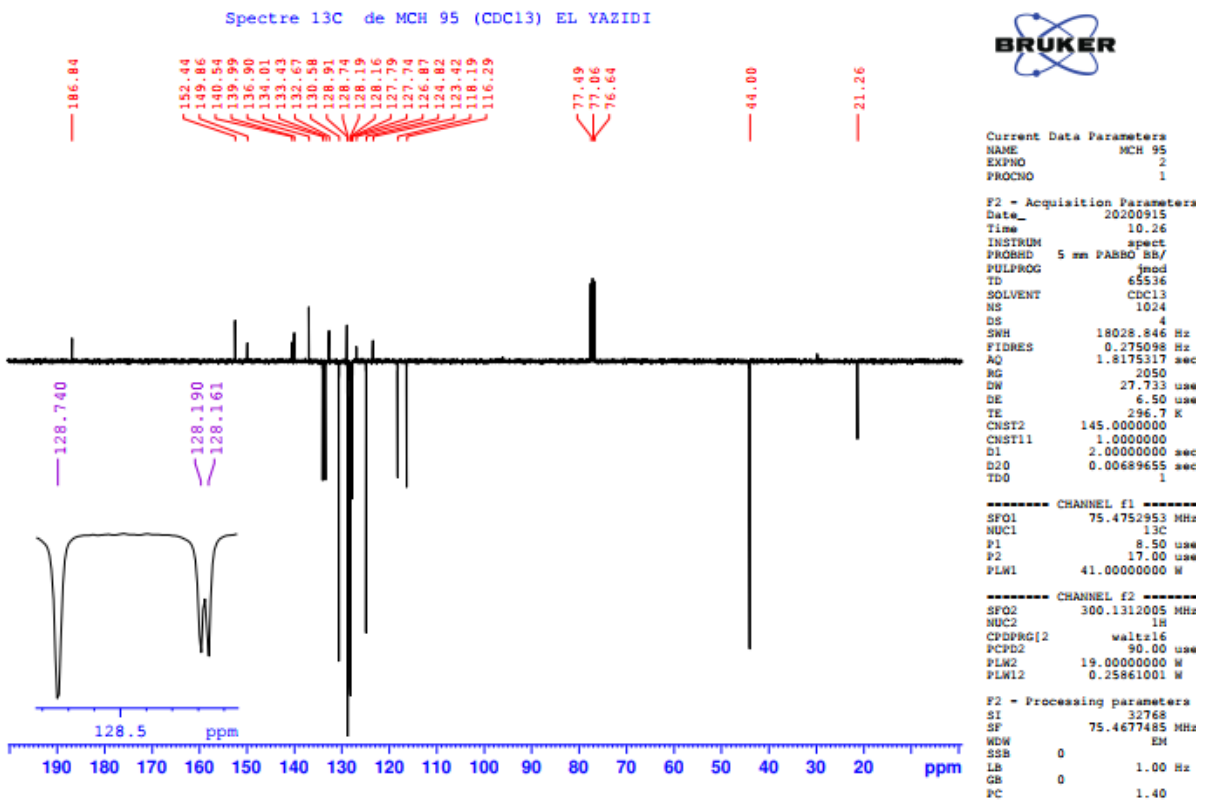


Figure S82. ^{13}C NMR spectrum (75 MHz, $CDCl_3$) of compound (**9d**)

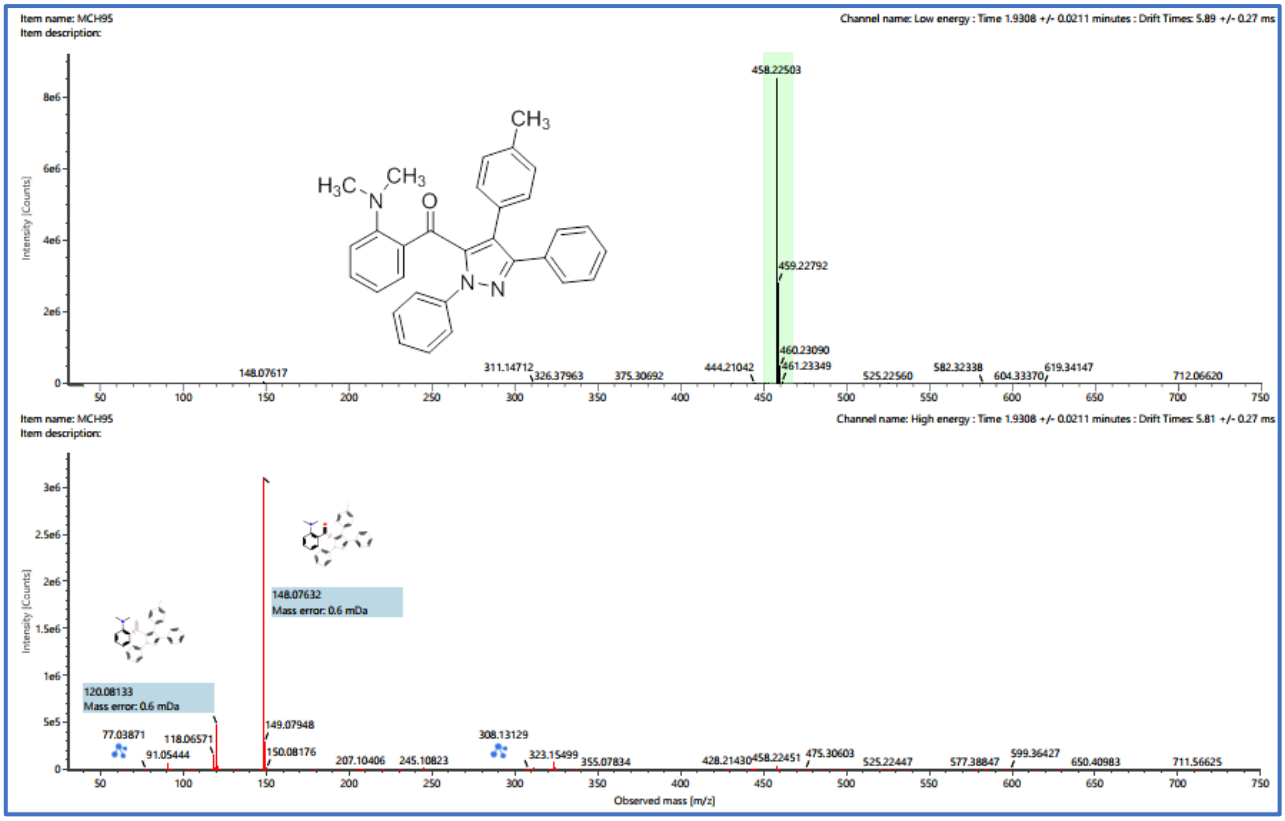


Figure S83. Mass spectrum of compound (**9d**)

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