SUPPORTING INFORMATION

FOR

Phenyl-Guanidine Derivatives as Potential Therapeutic Agents for Glioblastoma Multiforme: Catalytic Syntheses, Cytotoxic Effects and DNA Affinity

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Table S1. Crystal data and structure refinement for complex **13**.

Empirical formula	$C_{15}H_{19}F_6N_3$.Toluene
Formula weight	447.46
Temperature, K	150(2)
Wavelength, Å	0.71073
Crystal system	Tetragonal
Space group	$I4_1/a$
a, Å	23.863(7)
b, Å	23.863(7)
c, Å	16.635(5)
α,°	90
β,°	90
γ,°	90
Volume, Å^3	9473(6)
Z	16
Density (calculated), g/cm^3	1.255
Absorption coefficient, mm^{-1}	0.108
F(000)	3744
Crystal size, mm^3	0.53 x 0.45 x 0.34
Index ranges	-28 ≤ h ≤ 28, -28 ≤ k ≤ 27, -19 ≤ l ≤ 19
Reflections collected	29923
Independent reflections	4177 [R(int) = 0.1009]
Data / restraints / parameters	4177 / 436 / 386
Goodness-of-fit on F^2	1.031
Final R indices [I>2σ(I)]	R_1 = 0.0743, wR_2 = 0.1653
R indices (all data)	R_1 = 0.1337, wR_2 = 0.1946

Largest diff. peak and hole, e.Å^{-3}	0.475 and -0.588

Table S2. Bond lengths [Å] and angles [deg] for **13**.

Bond distances [Å]

N1-C1	1.316(4)
N1-C11	1.398(4)
N2-C1	1.344(4)
N2-C2	1.465(4)
N3-C1	1.364(4)
N3-C5	1.453(4)
F4-C18	1.330(5)
F5-C18	1.307(4)
F6-C18	1.318(4)
C2-C4	1.511(5)
C2-C3	1.510(5)
C5-C7	1.507(5)
C5-C6	1.517(4)
C11-C16	1.385(4)
C11-C12	1.388(4)
C12-C13	1.379(4)
C13-C14	1.373(5)
C13-C18	1.495(5)
C14-C15	1.387(5)
C15-C16	1.381(5)
C15-C17A	1.436(11)
C15-C17	1.462(8)
C17-F2	1.315(9)
C17-F1	1.322(9)
C17-F3	1.325(10)
F1A-C17A	1.341(13)
F2A-C17A	1.354(12)
F3A-C17A	1.350(12)
C20_1-C21_1	1.463(13)
C21_1-C26_1	1.375(10)
C21_1-C22_1	1.388(10)
C22_1-C23_1	1.363(9)
C23_1-C24_1	1.339(9)
C24_1-C25_1	1.379(10)
C25_1-C26_1	1.366(10)
C20_2-C21_2	1.39(3)
C21_2-C26_2	1.375(14)
C21_2-C22_2	1.381(14)
C22_2-C23_2	1.369(14)
C23_2-C24_2	1.390(14)
C24_2-C25_2	1.364(14)
C25_2-C26_2	1.358(14)

Bond Angles (deg)

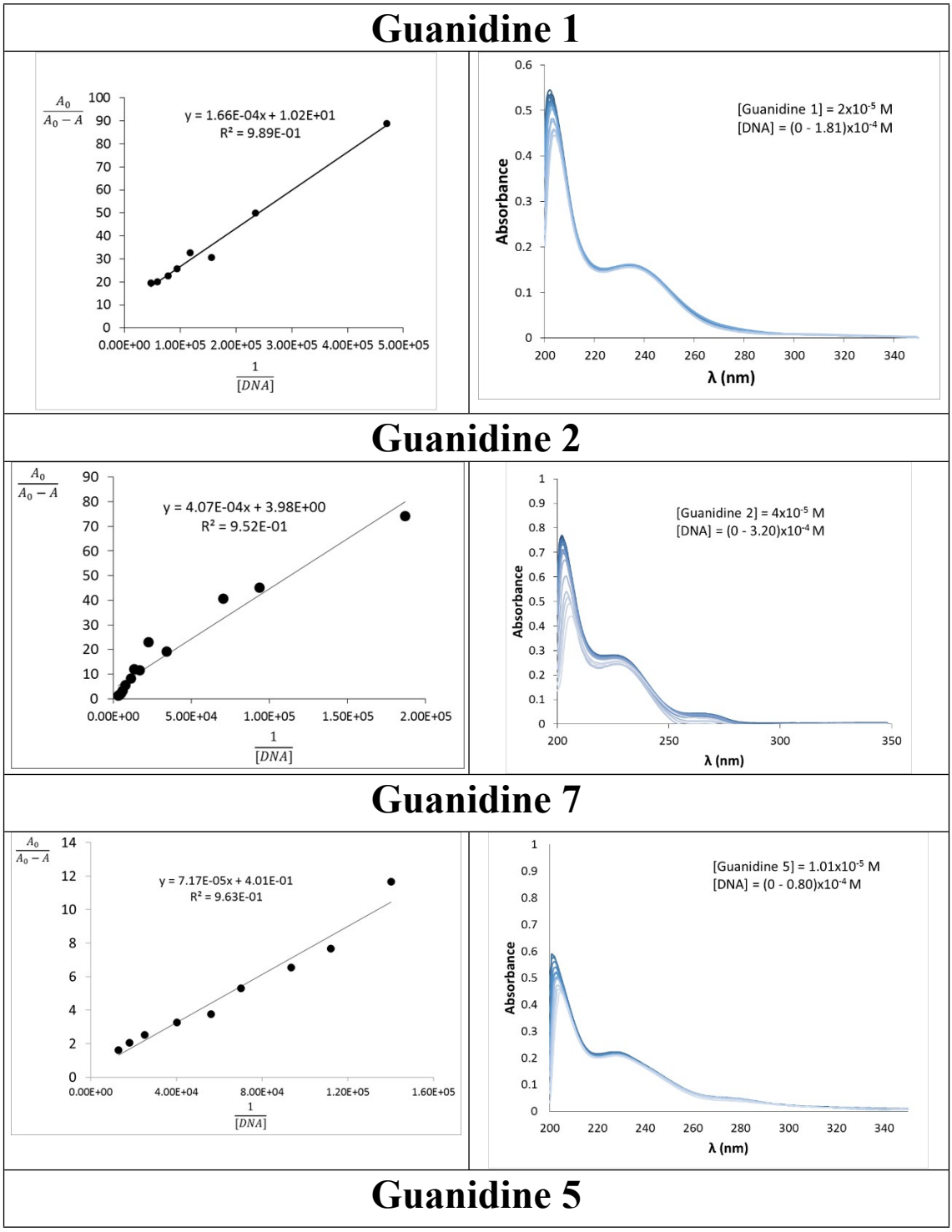
C1-N1-C11	121.9(3)
C1-N2-C2	124.0(3)
C1-N3-C5	125.6(3)
N1-C1-N2	119.2(3)
N1-C1-N3	125.8(3)
N2-C1-N3	114.9(3)
N2-C2-C4	107.9(3)
N2-C2-C3	110.9(3)
C4-C2-C3	112.4(3)
N3-C5-C7	112.1(3)
N3-C5-C6	107.1(3)
C7-C5-C6	111.6(3)
C16-C11-C12	117.7(3)
C16-C11-N1	122.8(3)
C12-C11-N1	119.2(3)
C13-C12-C11	121.3(3)
C14-C13-C12	120.7(3)
C14-C13-C18	119.4(3)
C12-C13-C18	119.8(3)
C13-C14-C15	118.7(3)
C16-C15-C14	120.5(3)
C16-C15-C17A	122.6(7)
C14-C15-C17A	116.2(6)
C16-C15-C17	117.5(5)
C14-C15-C17	121.7(5)
C15-C16-C11	121.2(3)
F5-C18-F6	107.2(4)
F5-C18-F4	105.2(3)
F6-C18-F4	105.6(4)
F5-C18-C13	113.3(3)
F6-C18-C13	113.0(3)
F4-C18-C13	111.9(3)
F2-C17-F1	106.8(9)
F2-C17-F3	107.0(8)
F1-C17-F3	106.9(8)
F2-C17-C15	110.4(7)
F1-C17-C15	112.0(8)
F3-C17-C15	113.4(7)
F1A-C17A-F3A	99.2(13)
F1A-C17A-F2A	99.8(13)
F3A-C17A-F2A	99.6(11)
F1A-C17A-C15	117.9(15)
F3A-C17A-C15	115.4(11)
F2A-C17A-C15	121.1(10)
C26_1-C21_1-C22_1	118.4(7)
C26_1-C21_1-C20_1	119.1(8)
C22_1-C21_1-C20_1	122.5(8)
C23_1-C22_1-C21_1	120.2(7)

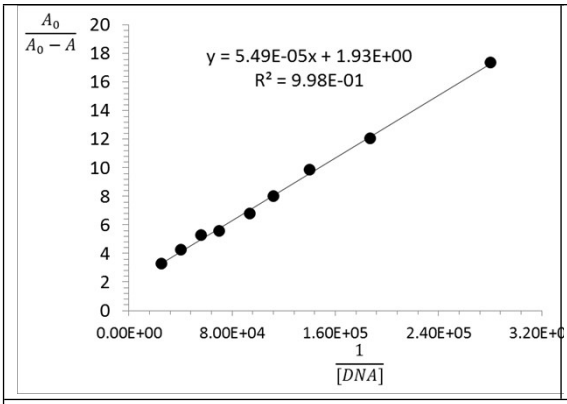
C24_1-C23_1-C22_1	122.4(8)
C23_1-C24_1-C25_1	117.1(8)
C26_1-C25_1-C24_1	122.8(9)
C21_1-C26_1-C25_1	119.0(8)
C20_2-C21_2-C26_2	118.5(19)
C20_2-C21_2-C22_2	121.2(19)
C26_2-C21_2-C22_2	120.3(17)
C23_2-C22_2-C21_2	122.4(18)
C22_2-C23_2-C24_2	117.0(17)
C25_2-C24_2-C23_2	119.2(17)
C26_2-C25_2-C24_2	124.1(18)
C25_2-C26_2-C21_2	116.5(17)

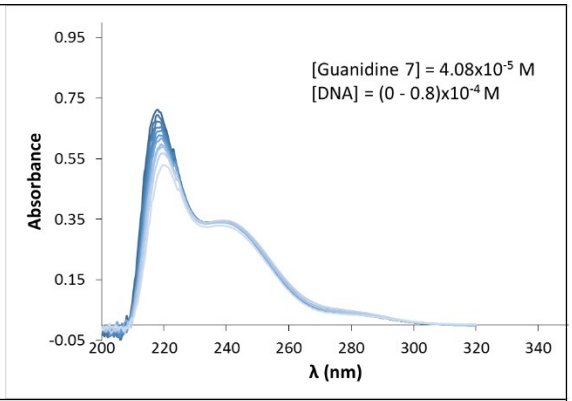
Table S3. Calculated octanol-water partition coefficients for guanidines **1-14.**

Compound	**clog *P***
1	2.837
2	2.953
3	3.684
4	2.977
5	3.622
6	3.515
7	3.646
8	4.543
9	3.732
10	2.592
11	2.894
12	4.819
13	4.532
14	3.662
TMZ	2.837

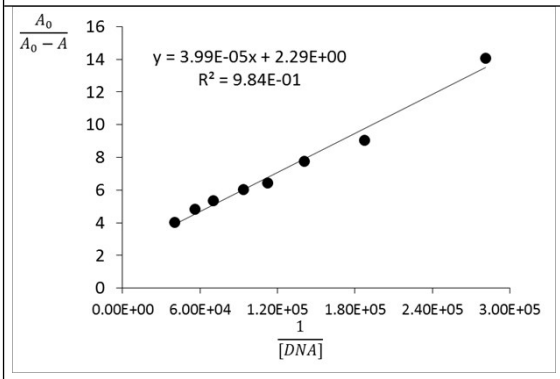
Figure S1. Changes in the UV spectrum of Guanidine 1, 2, 5, 7, 8, 12 and 14 through its titration with salmon sperm DNA at 300K (right). Plot of $A_0/(A_0 - A)$ *versus* 1/[DNA] for the titration of 1, 2, 5, 7, 8, 12 and 14 with sperm DNA (left).

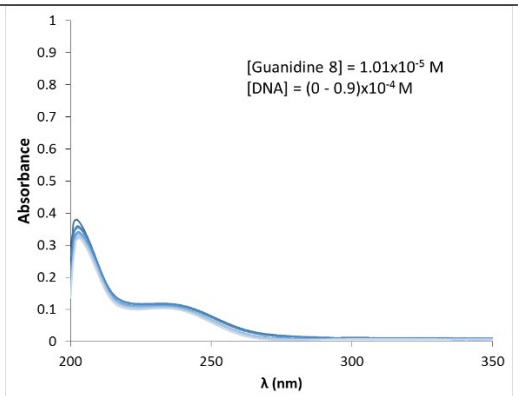




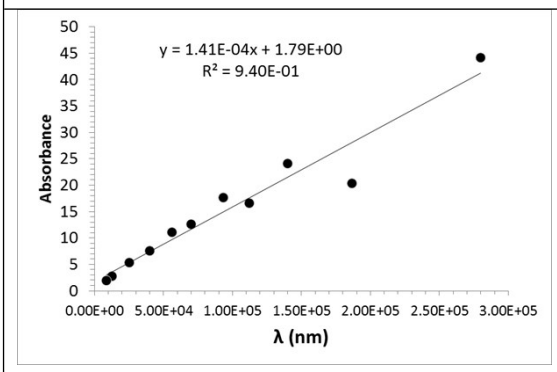


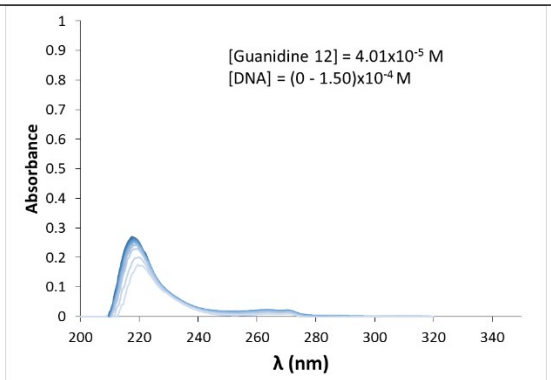
Guanidine 8



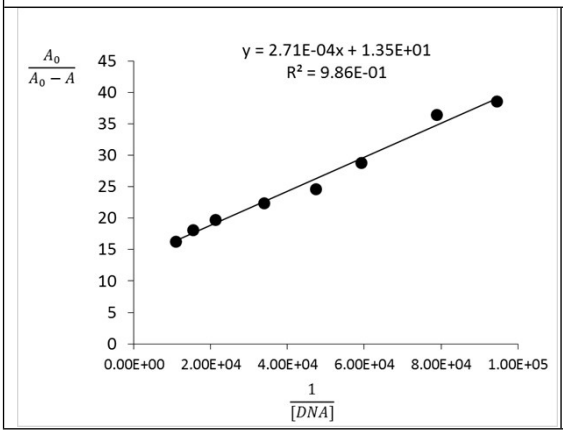


Guanidine 12





Guanidine 14



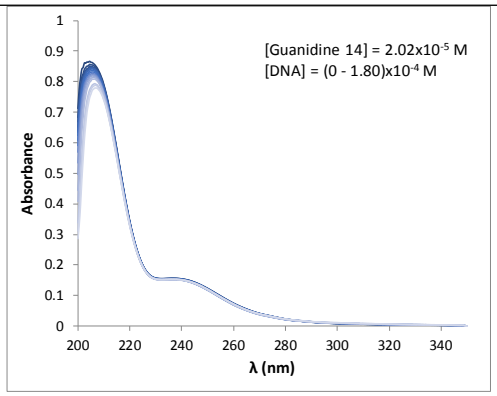


Figure S2. (right) Changes in the fluorescence spectrum of EB-DNA complex in the presence of different amounts of Guanidine **1** and **8** at 300K. (left) Stern-Volmer plot of quenching of EB-DNA with Guanidine **1** and **8**; [EB] and [DNA] were fixed at 29 and 32.0 μM, respectively. Fluorescence intensity was measured at 622 nm

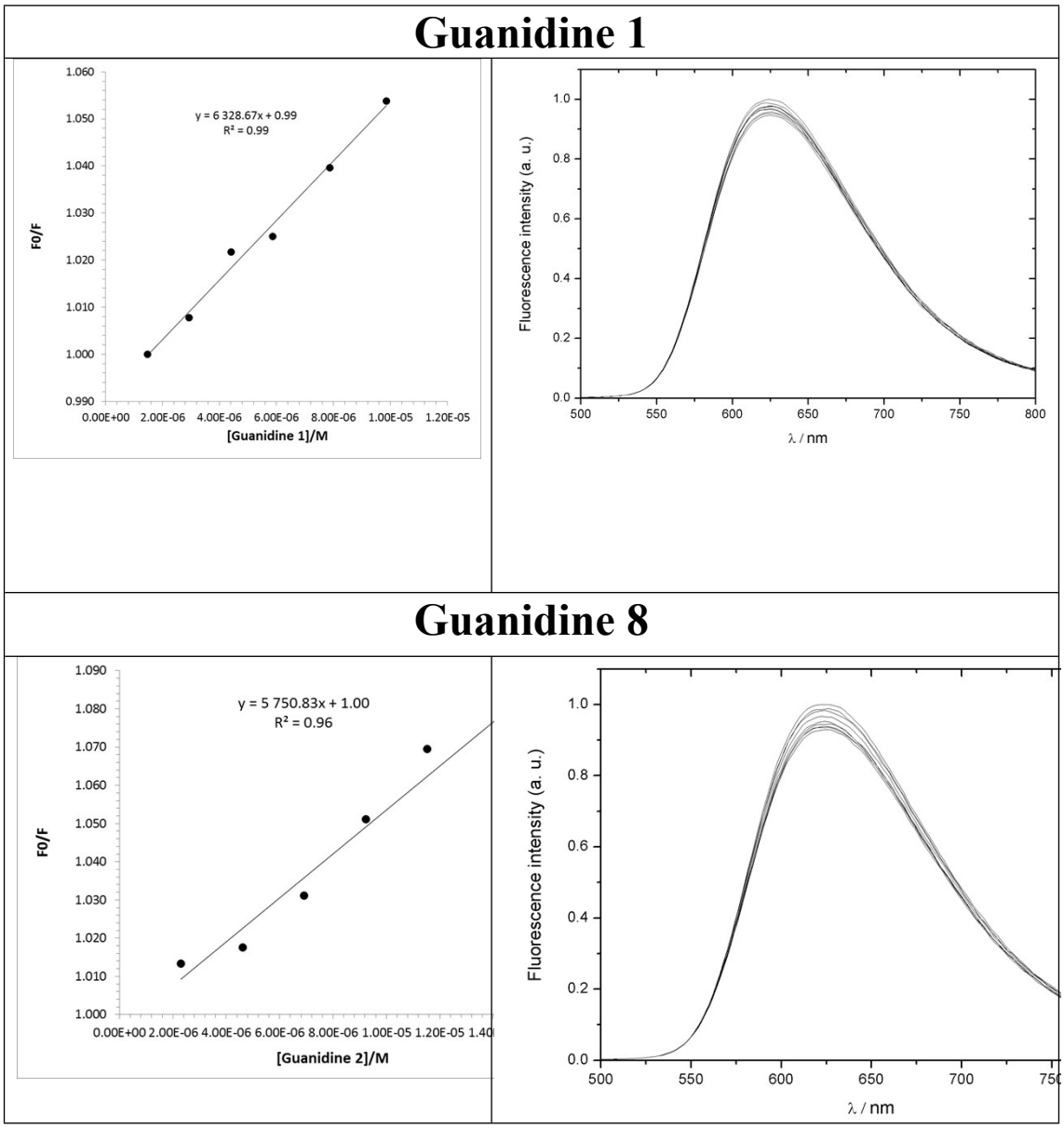
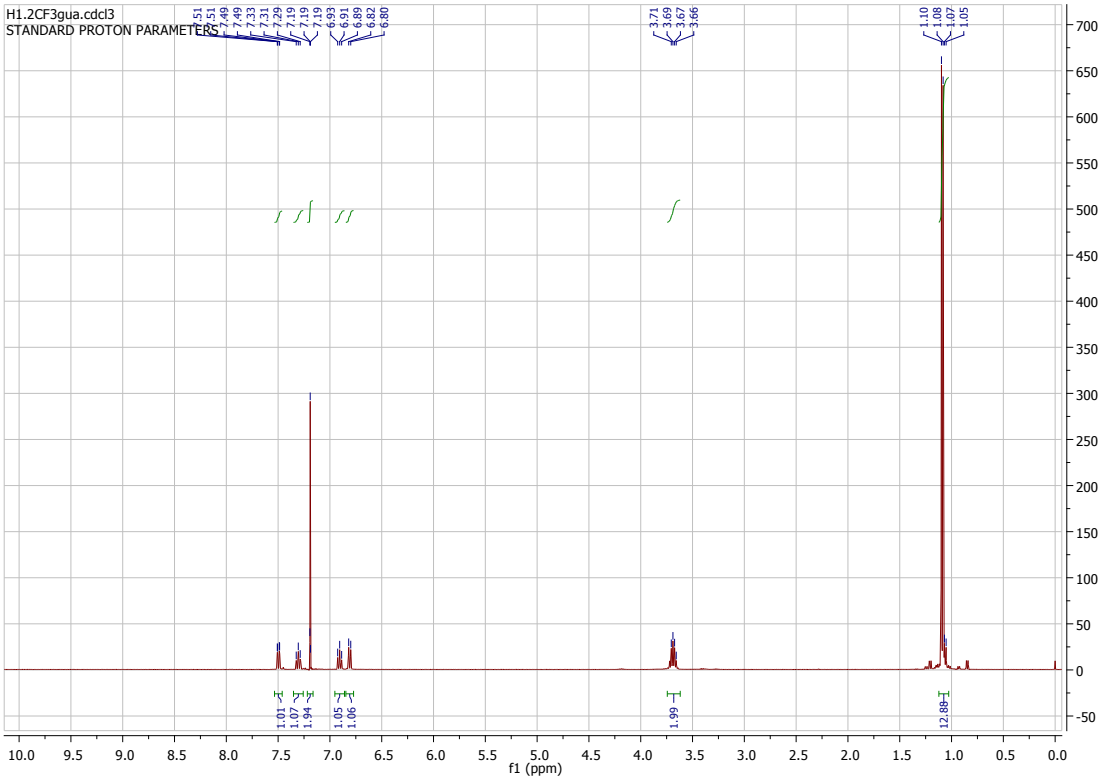
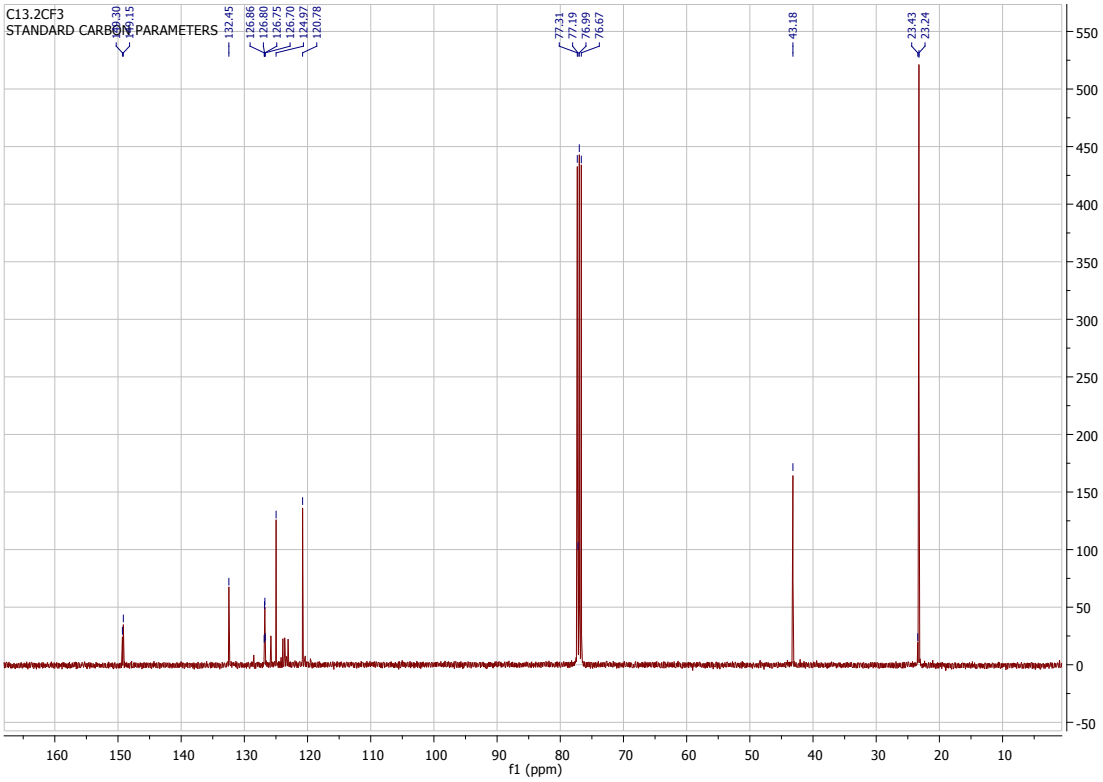


Figure S3. NMR spectra of **3**, **4**, **5**, **9**, **13** and **14**.

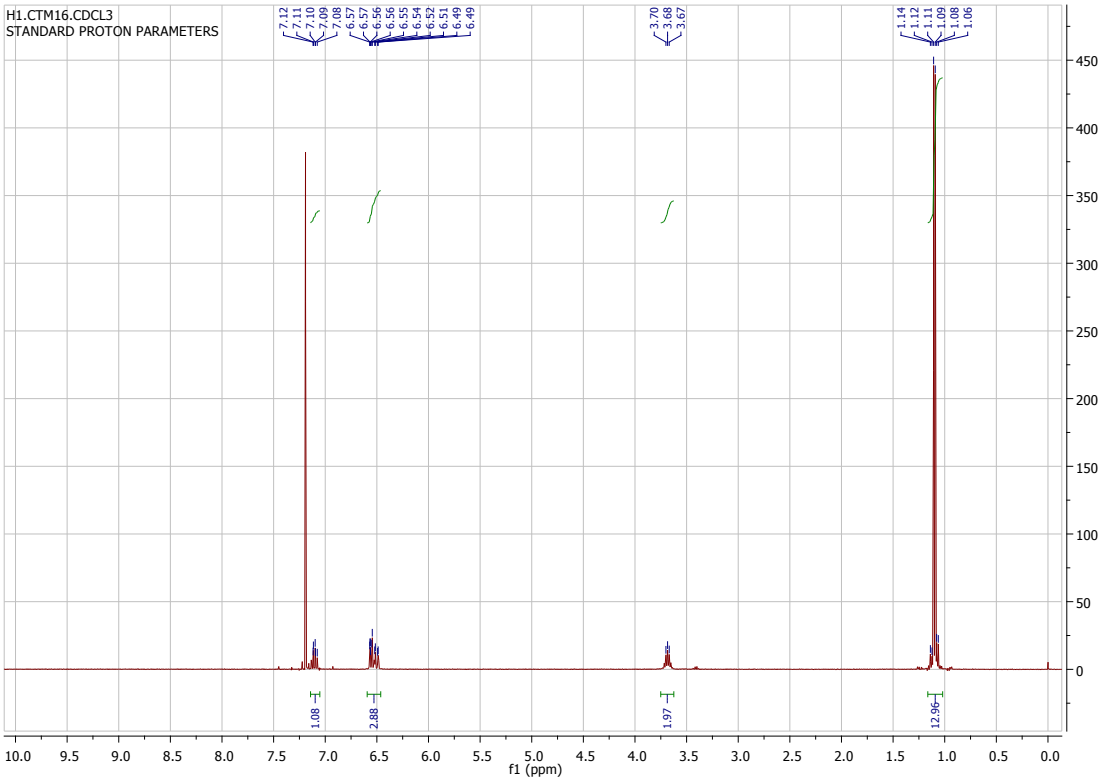
^{1}H-NMR of **3** in $CDCl_3$, 298K.



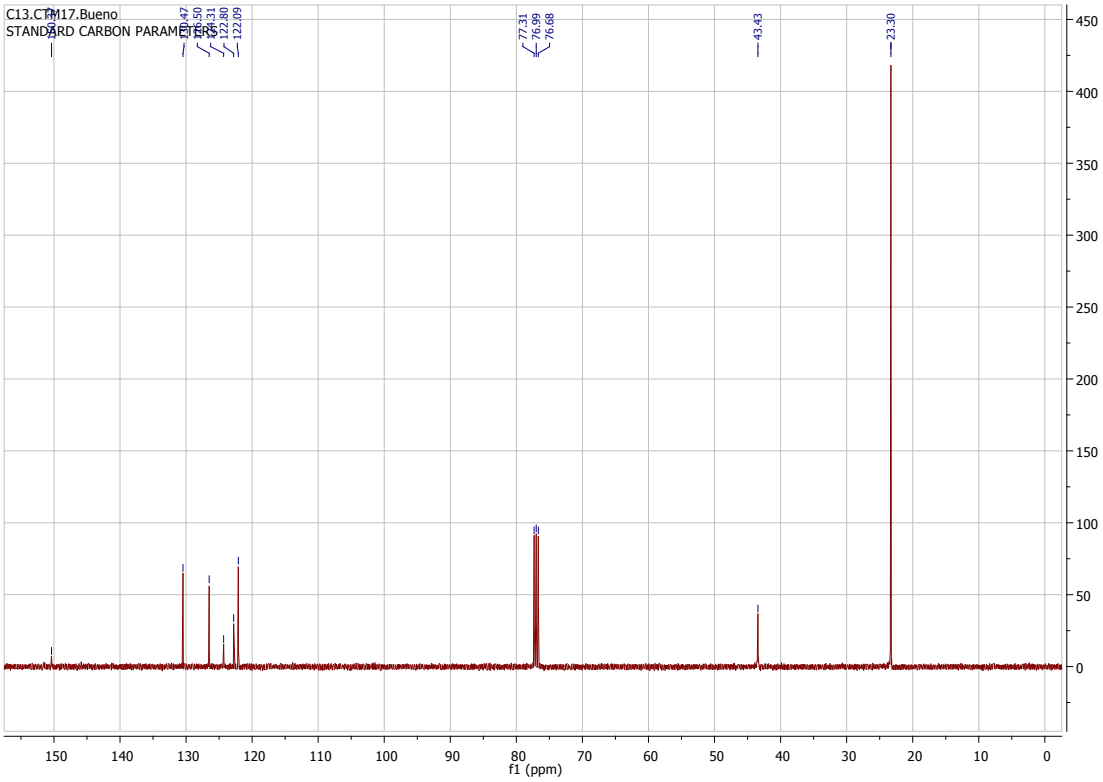
^{13}C-NMR of **3** in $CDCl_3$, 298K.



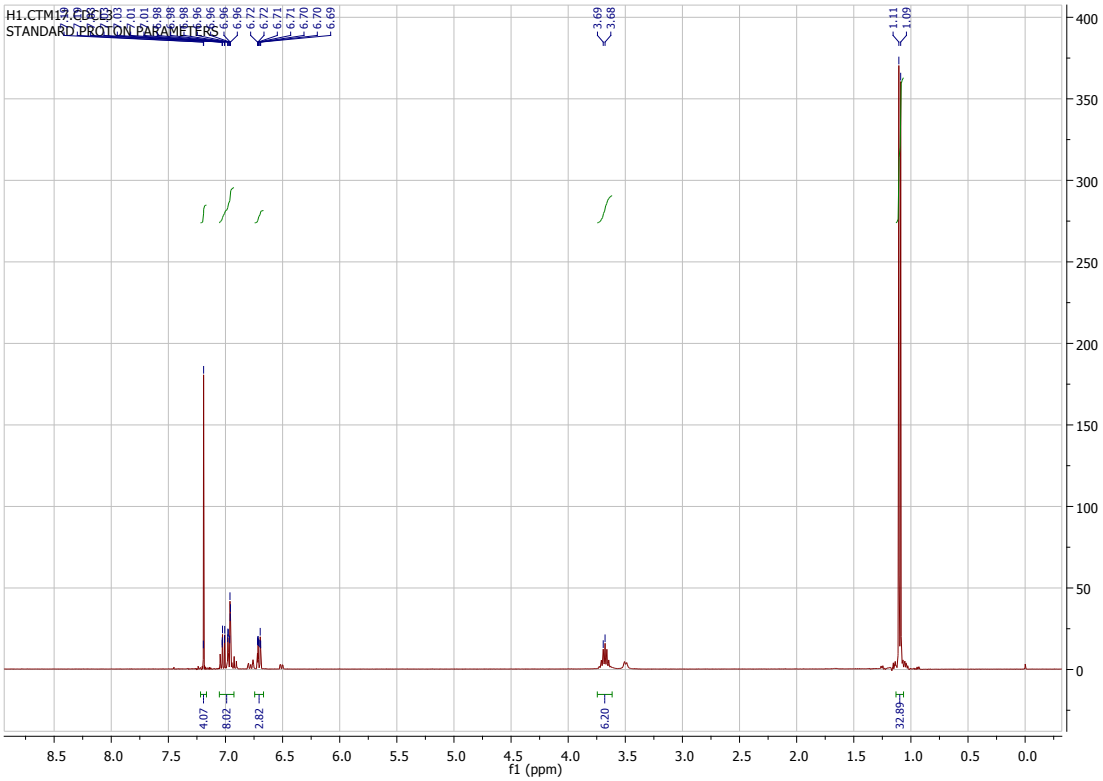
^{1}H-NMR of **4** in $CDCl_3$, 298K.



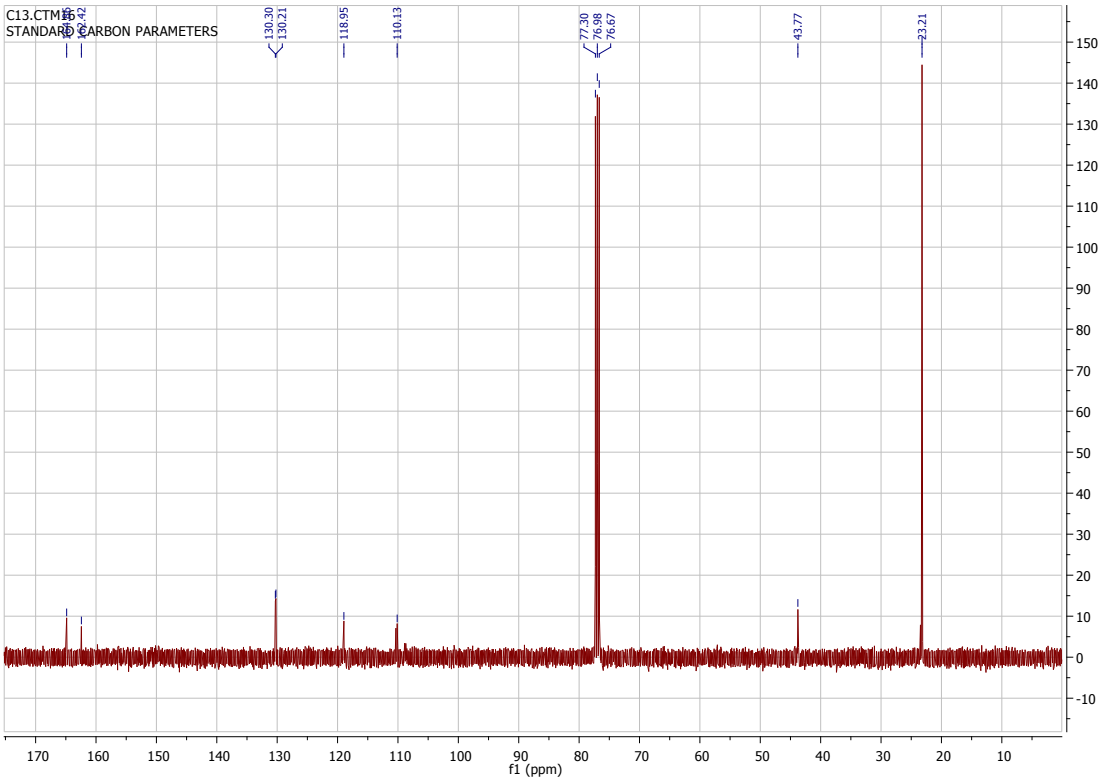
^{13}C-NMR of **4** in $CDCl_3$, 298K.



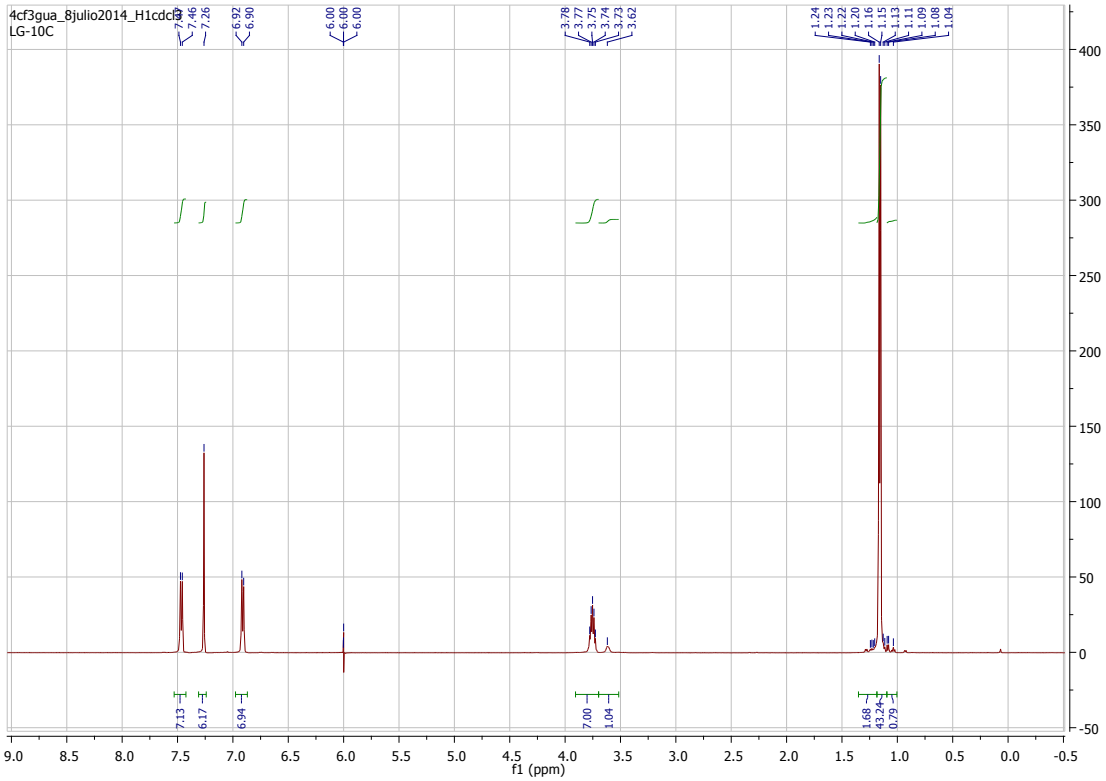
^{1}H-NMR of **5** in $CDCl_3$, 298K.



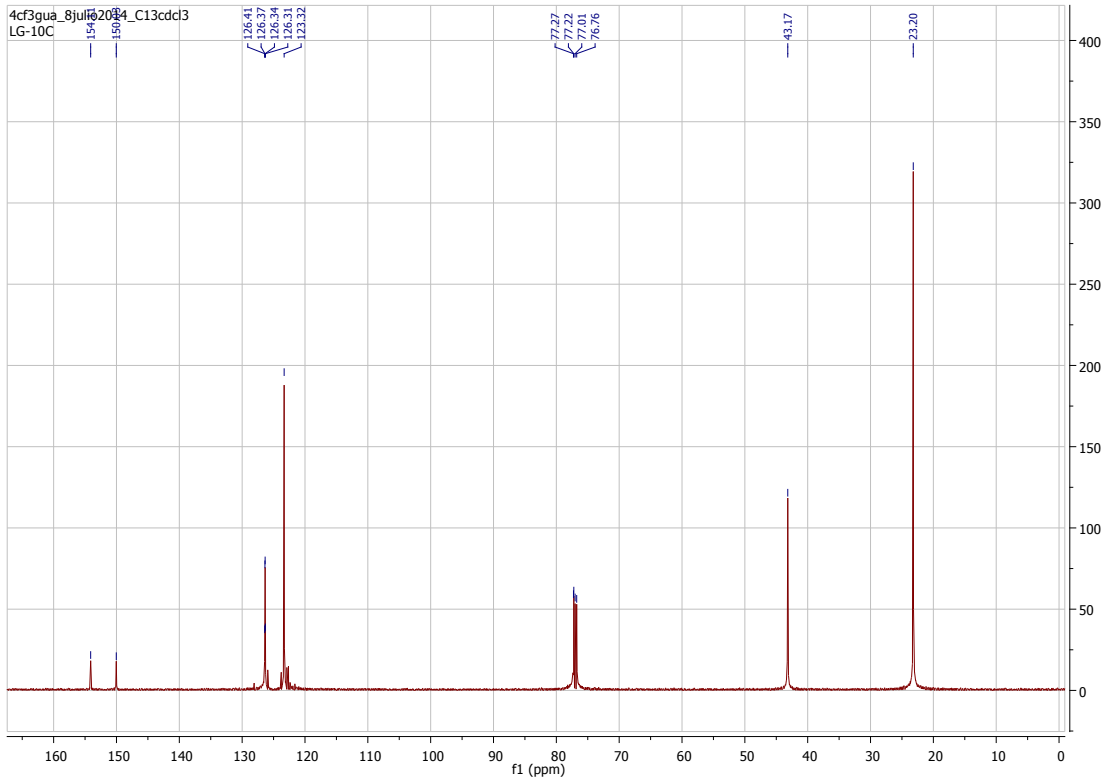
^{13}C-NMR of **5** in $CDCl_3$, 298K.



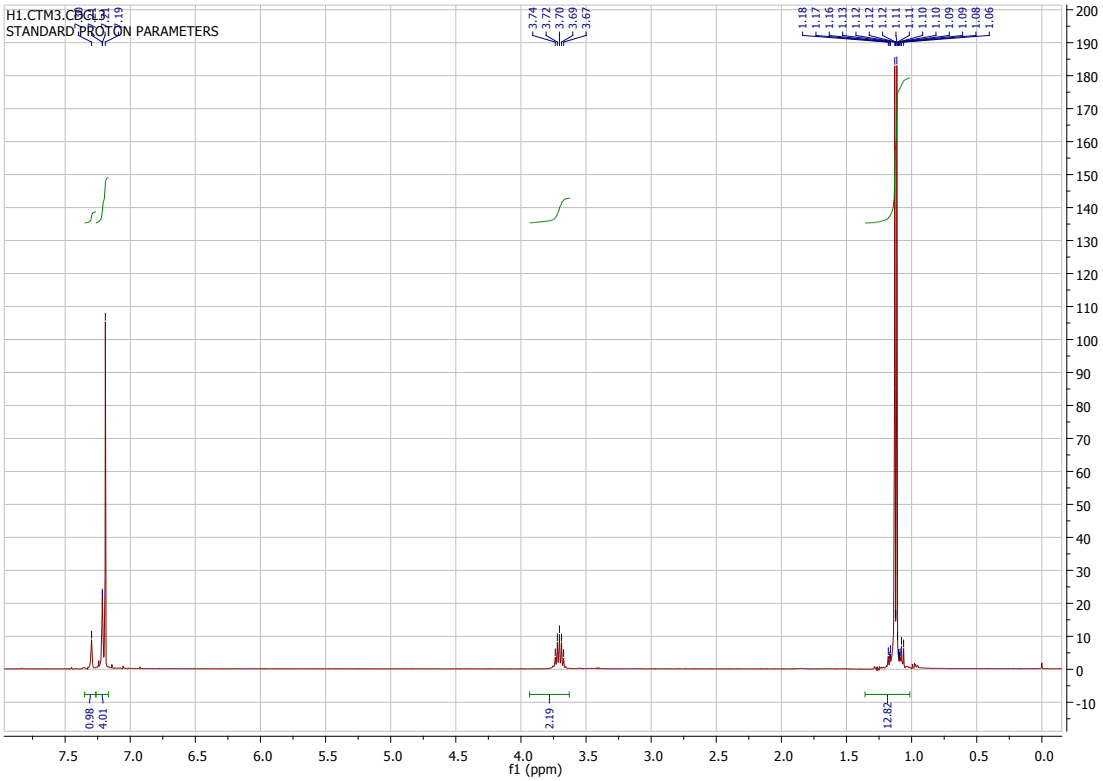
^{1}H-NMR of **9** in $CDCl_3$, 298K.



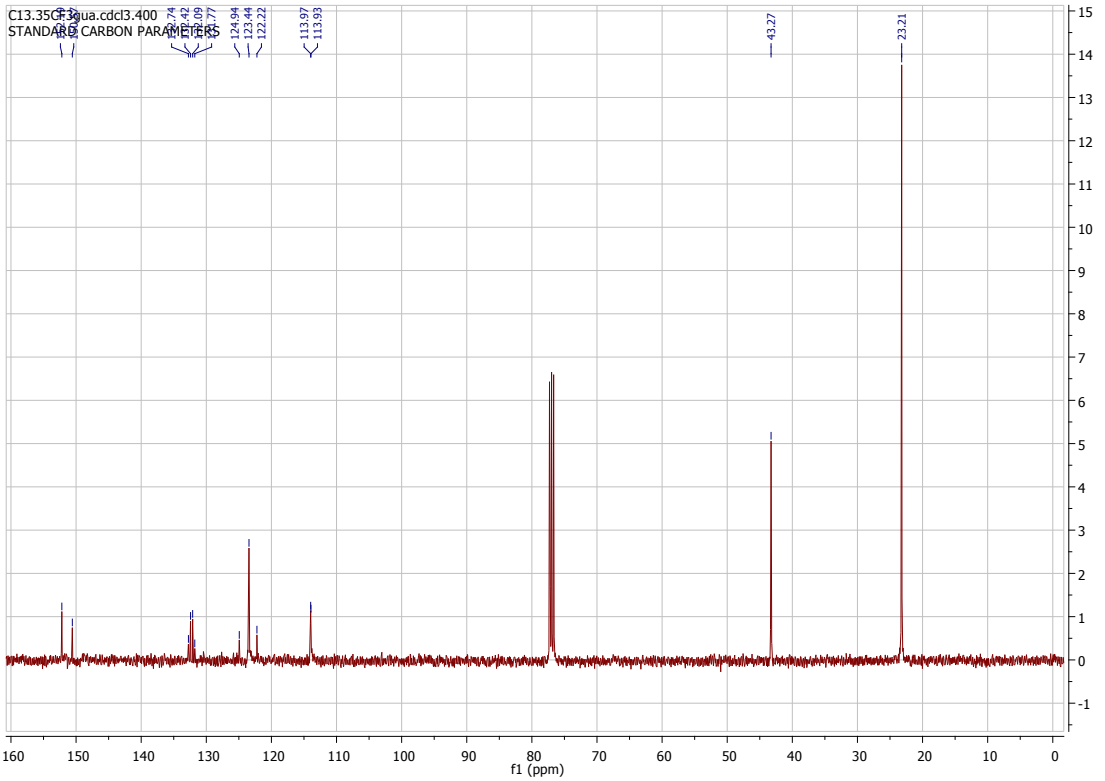
^{13}C-NMR of **9** in $CDCl_3$, 298K.



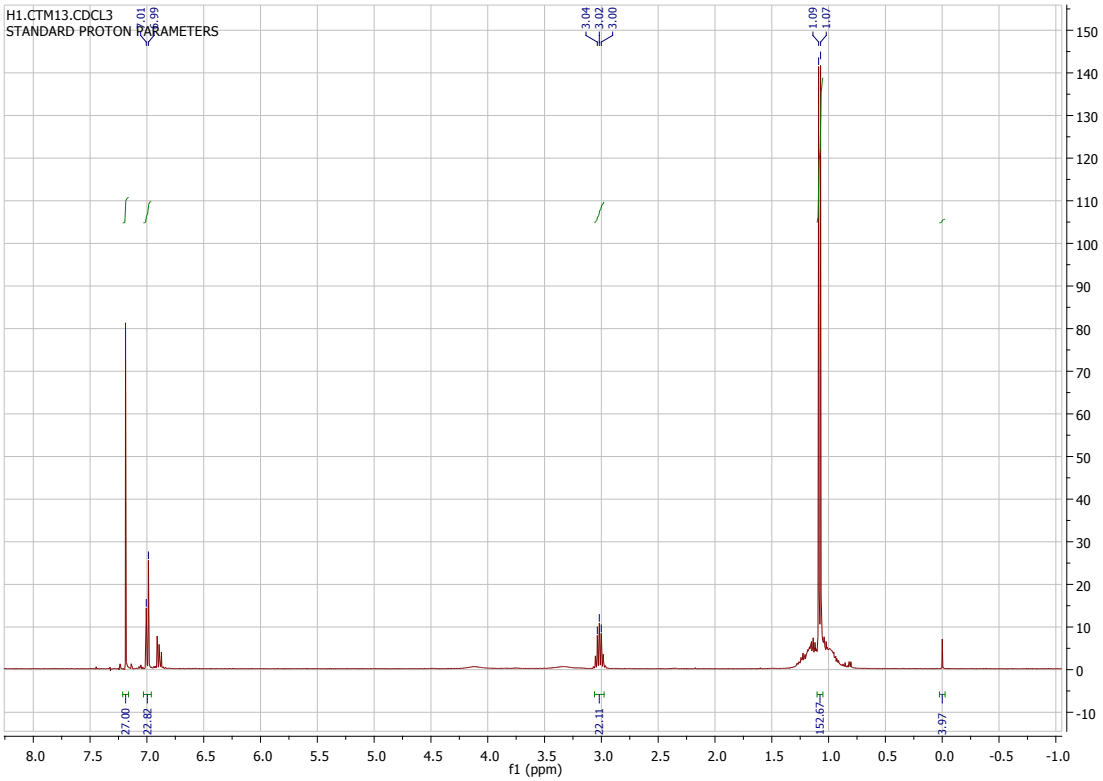
^{1}H-NMR of **13** in $CDCl_3$, 298K.



^{13}C-NMR of **13** in $CDCl_3$, 298K.



^{1}H-NMR of **14** in $CDCl_3$, 298K.



^{13}C-NMR of **14** in $CDCl_3$, 298K.

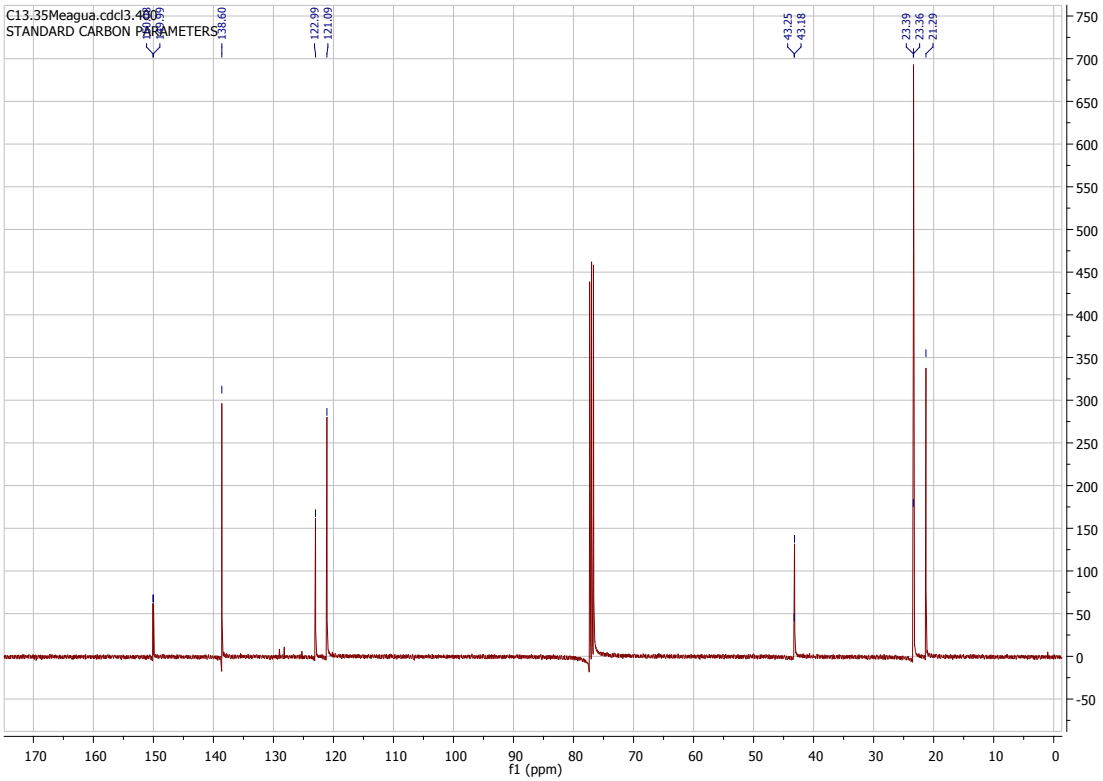
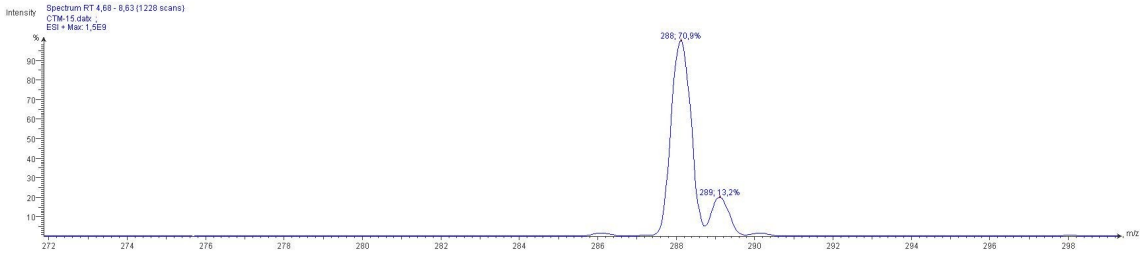
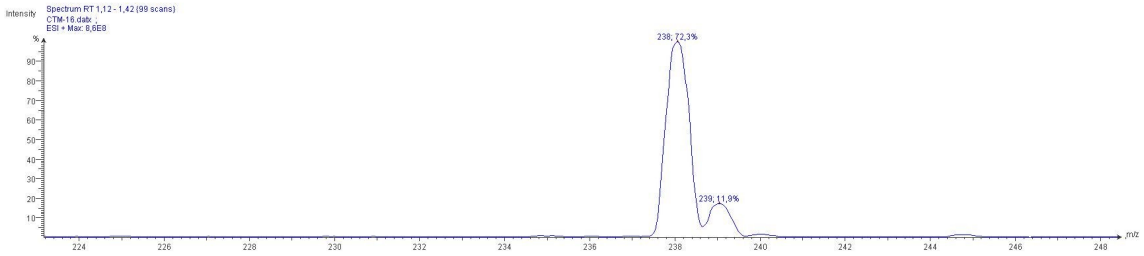


Figure S4. Mass spectra of **3**, **4**, **5**, **9**, **13** and **14**.

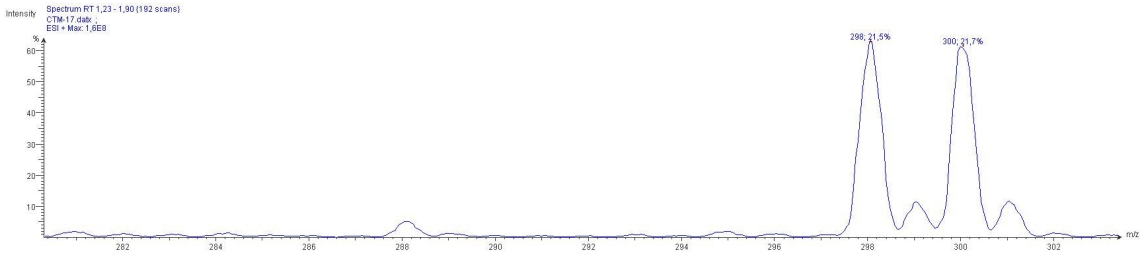
Compound **3**



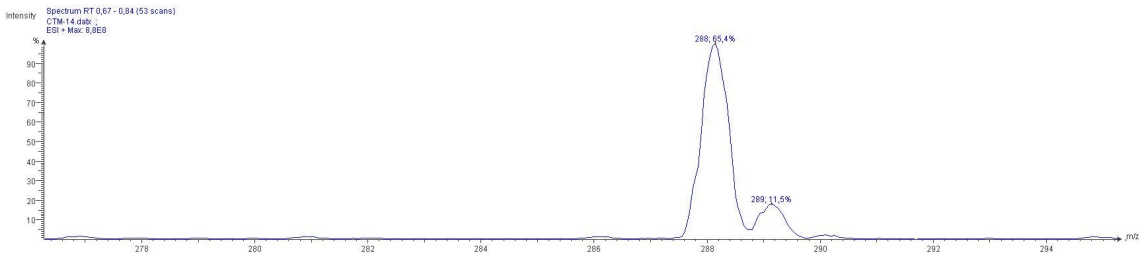
Compound **4**



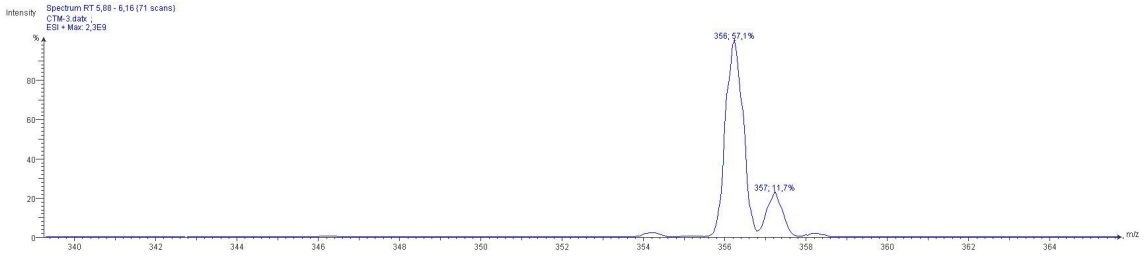
Compound **5**



Compound **9**



Compound **13**



Compound **14**