

Supplementary Material

Dual action of dipyridthiazine and quinobenzothiazine derivatives – anticancer and cholinesterase- inhibiting activity

Jakub Jończyk¹, Justyna Godyń¹, Ewelina Stawarska¹, Beata Morak-Młodawska², Małgorzata Jeleń², Krystian Pluta², Barbara Malawska^{1*}

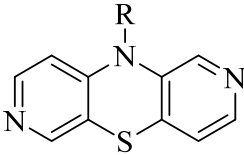
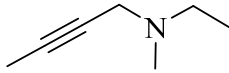
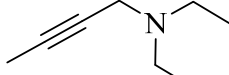
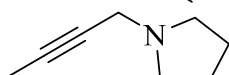
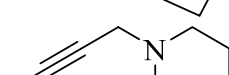
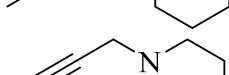
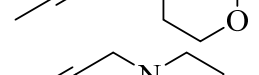
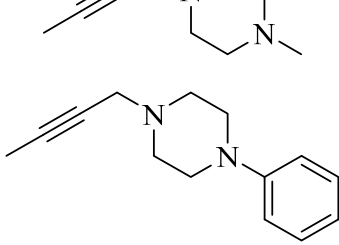
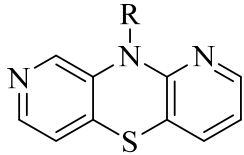
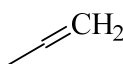
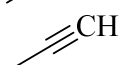
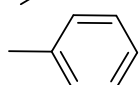
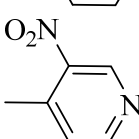
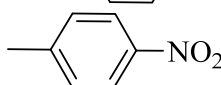
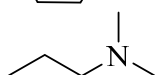
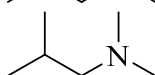
¹Department of Physicochemical Drug Analysis, Faculty of Pharmacy, Jagiellonian University Medical College, Kraków 30-688, Poland

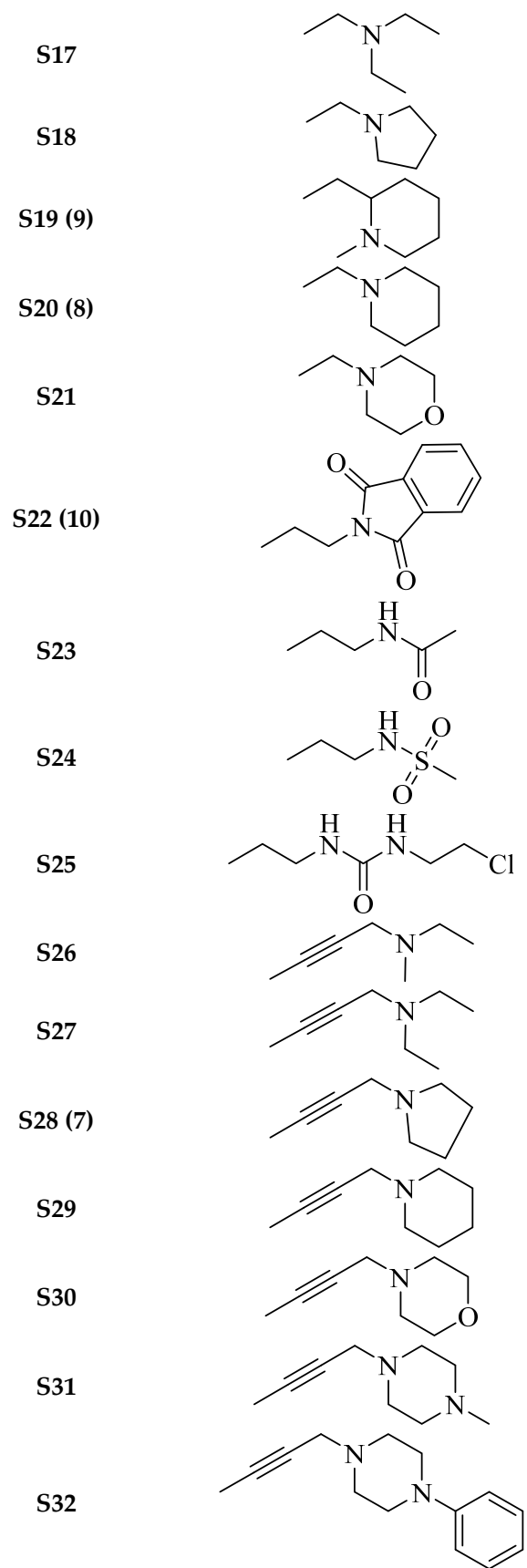
²The Medical University of Silesia in Katowice, Faculty of Pharmaceutical Sciences in Sosnowiec, Department of Organic Chemistry, Jagiellońska 4, 41-200 Sosnowiec, Poland,

Content

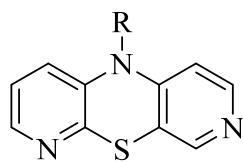
1. **Table S1.** Structures of tested compounds.
2. **Table S2.** Effects of azaphenothiazines **1-25** on the cancer cell lines and phytohemagglutinin-induced blood lymphocyte proliferation
3. ¹H NMR of compound **1**
4. ¹³C NMR of compound **1**
5. FAB MS of compound **1**
6. ¹H NMR of compound **2**
7. ¹³C NMR of compound **2**
8. FAB MS of compound **2**
9. ¹H NMR of compound **3**
10. ¹³C NMR of compound **3**
11. FAB MS of compound **3**

Table S1. Structures of tested compounds.

Dipyridothiazines	Compound	R
isomer 2,7-diaza 	S1	
	S2 (11)	
	S3 (12)	
	S4 (13)	
	S5	
	S6	
	S7	
isomer 1,8-diaza 	S8	H
	S9	CH ₃
	S10	
	S11	
	S12	
	S13	
	S14	
	S15 (6)	
	S16	

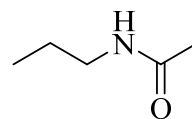


isomer 3,6-diaza

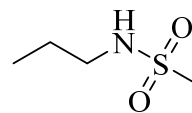


S33	H
S34	CH ₃
S35	
S36	
S37	
S38	
S39	
S40	
S41	
S42	
S43	
S44	
S45	
S46 (17)	
S47	
S48	
S49 (18)	

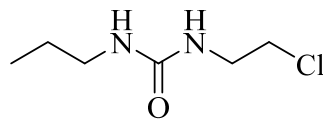
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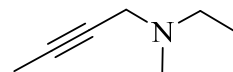
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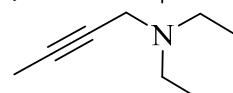
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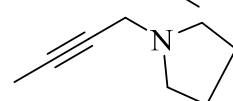
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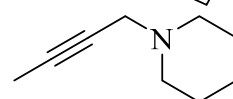
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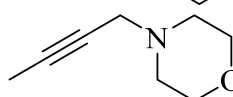
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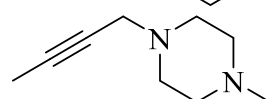
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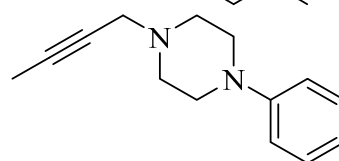
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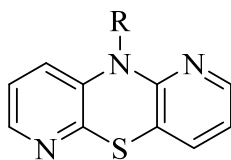
S58



S59



isomer 1,6-diaza



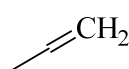
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H

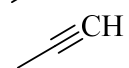
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CH₃

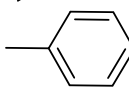
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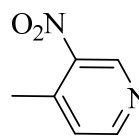
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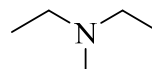
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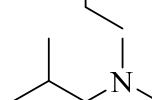
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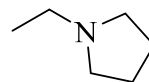
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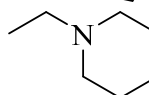
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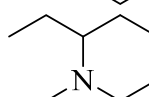
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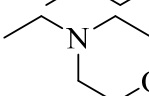
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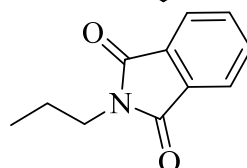
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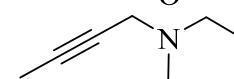
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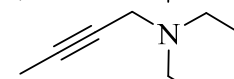
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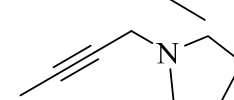
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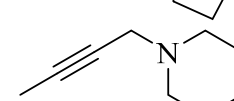
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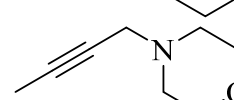
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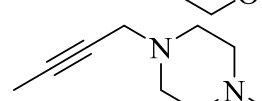
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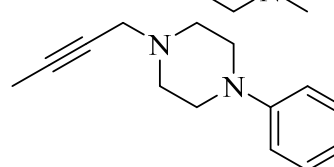
S77 (3)



S78



S79



N-substituted
quinobenzothiazines

Compound

Z

R

S80 (19)

9-F

H

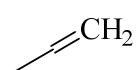
S81 (20)

9-F

CH₃

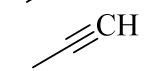
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9-F



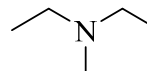
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9-F



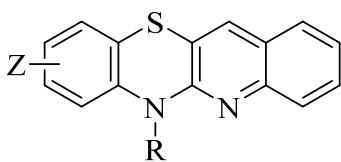
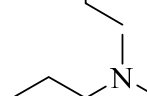
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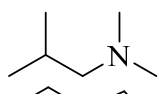
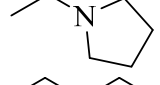
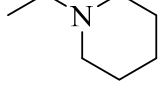
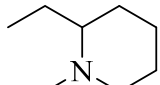
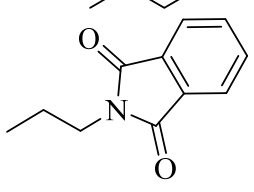
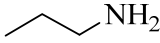
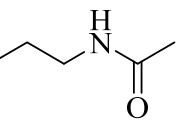
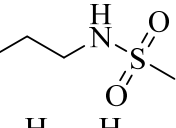
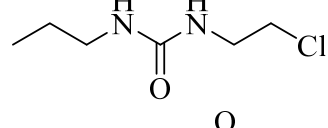
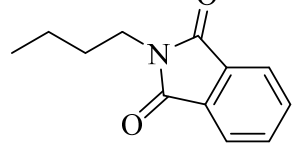
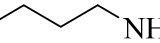
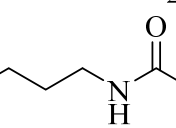
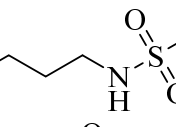
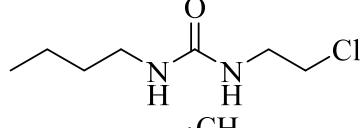
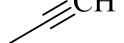
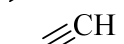
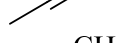
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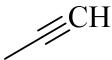
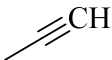
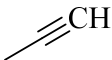
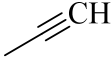
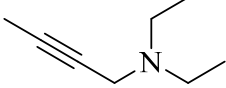
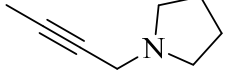
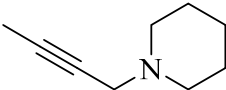


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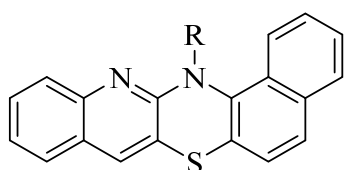
9-F



S86	9-F	
S87	9-F	
S88 (23)	9-F	
S89	9-F	
S90	9-F	
S91 (21)	9-F	
S92	9-F	
S93	9-F	
S94	9-F	
S95	9-F	
S96 (22)	9-F	
S97	9-F	
S98	9-F	
S99	9-F	
S100	8-Cl	
S101	9-Cl	
S102	9-Br	

S103	9-CF ₃	
S104	9-OCH ₃	
S105	9-SCH ₃	
S106	10-Cl	
S107 (24)	9-SCH ₃	
S108 (25)	9-SCH ₃	
S109	9-SCH ₃	

N-substituted
quinaphthaphthiazines



Compound

R

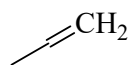
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H

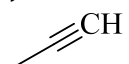
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CH₃

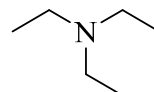
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S113



S114



Compound

R

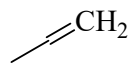
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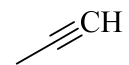
S116

CH₃

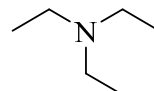
S117



S118



S119



N-substituted
diquinothiazine

Compound

R

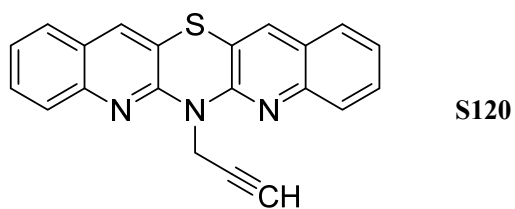
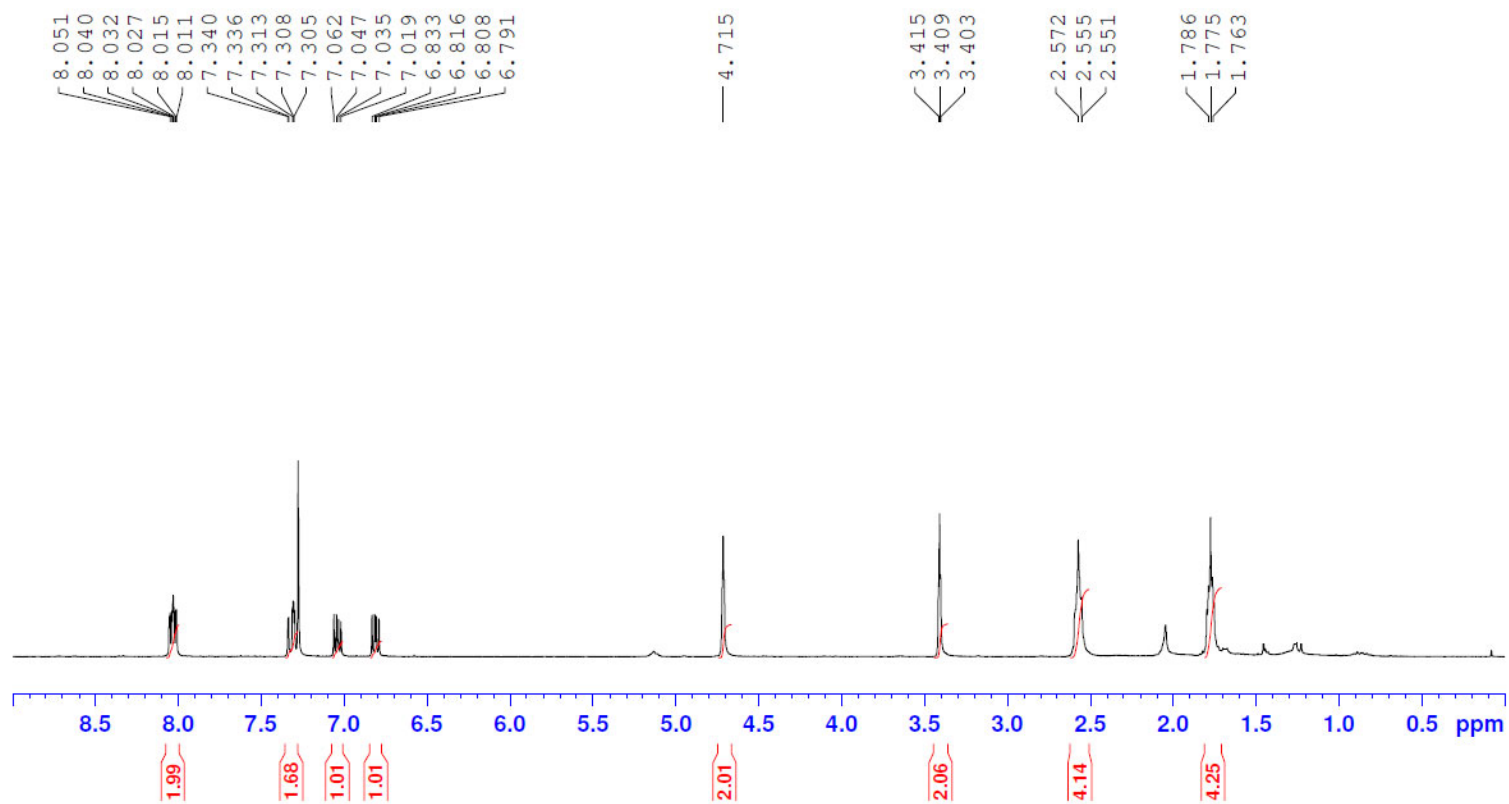


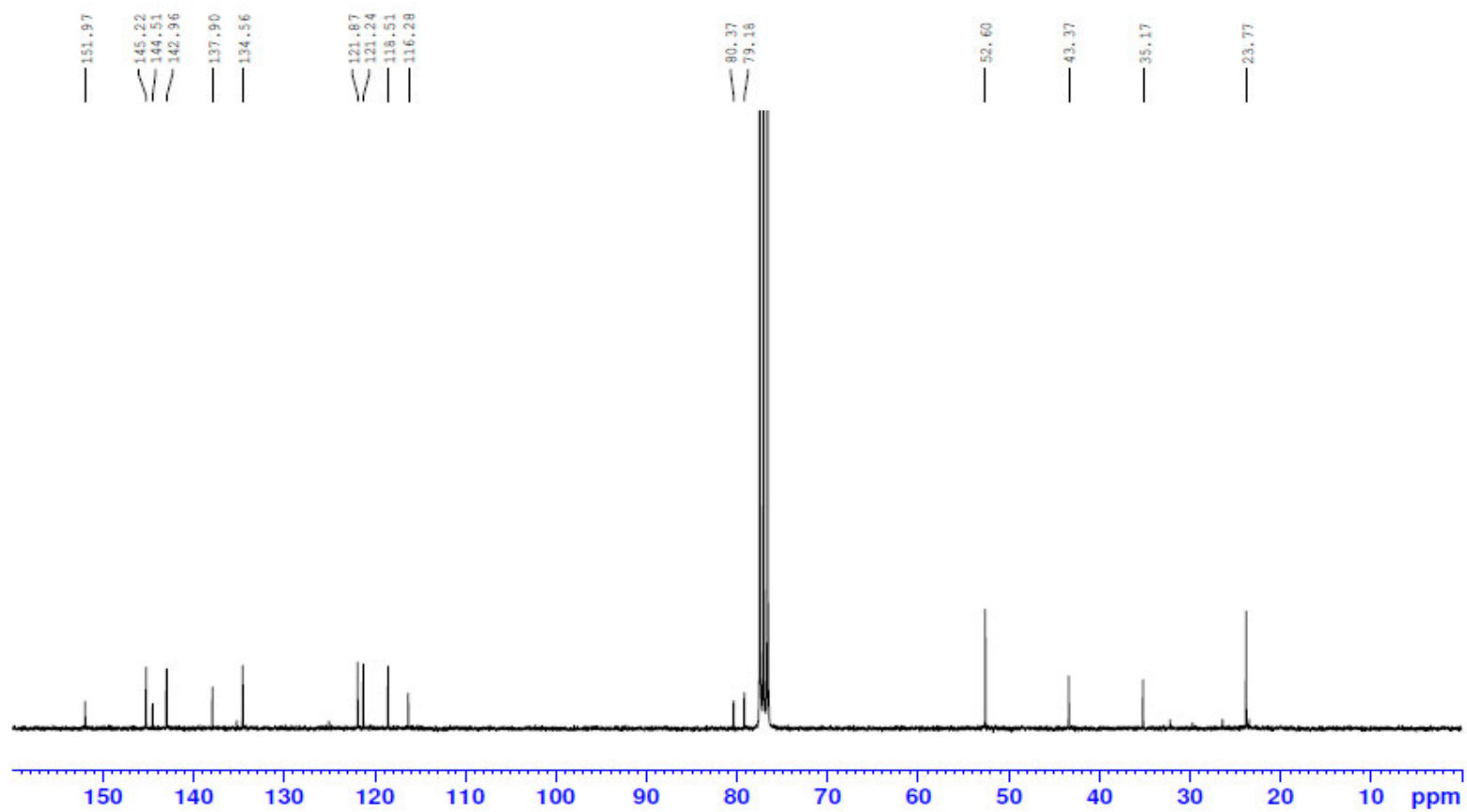
Table S2. Effects of azaphenothiazines **1-25** on the cancer cell lines and phytohemagglutinin-induced blood lymphocyte (PBMC) proliferation

No	Anticancer and antiproliferative activity [(IC ₅₀ in μ M and inhibition in % (μ M))]	Ref.
1	No tested	-
2	No tested	-
3	No tested	-
4	SNB-19 96.0; C-32 50.0; MCF-7 28.8	33
5	SNB-19 > 100; C-32 > 100; MCF-7 21.1	33
6	L-1210 19.2; SV948 47.6	34
7	SNB-19 > 100; C-32 > 100; T47D >100	35
8	PBMC 0.5% (32.0)	34
9	PBMC 7.0% (30.7)	34
10	PBMC 12.5% (25.8)	34
11	SNB-19 > 100; C-32 100; T47D > 100	35
12	SNB-19 > 100; C-32 > 100; T47D > 100	35
13	SNB-19 > 100; C-32 73.8; T47D > 100	35
14	SNB-19 0.35; C-32 4.9; MDA-MB231 9.1	32
15	SNB-19 0.34; C-32 1.7; MDA-MB231 19.5	32
16	SNB-19 > 100; C-32 > 100; MDA-MB231 > 100	32
17	SNB-19 > 100; C-32 > 100; MCF-7 87.1	36
18	SNB-19 > 100; C-32 > 100; MCF-7 > 100	36
19	PBMC 100% (37.3)	37
20	PBMC 27.8% (3.5)	31
21	No tested	-
22	No tested	-
23	PBMC 88.4% (2.6)	31
24	PBMC 94.2% (23.9)	30
25	PBMC 92.2% (24.0)	30

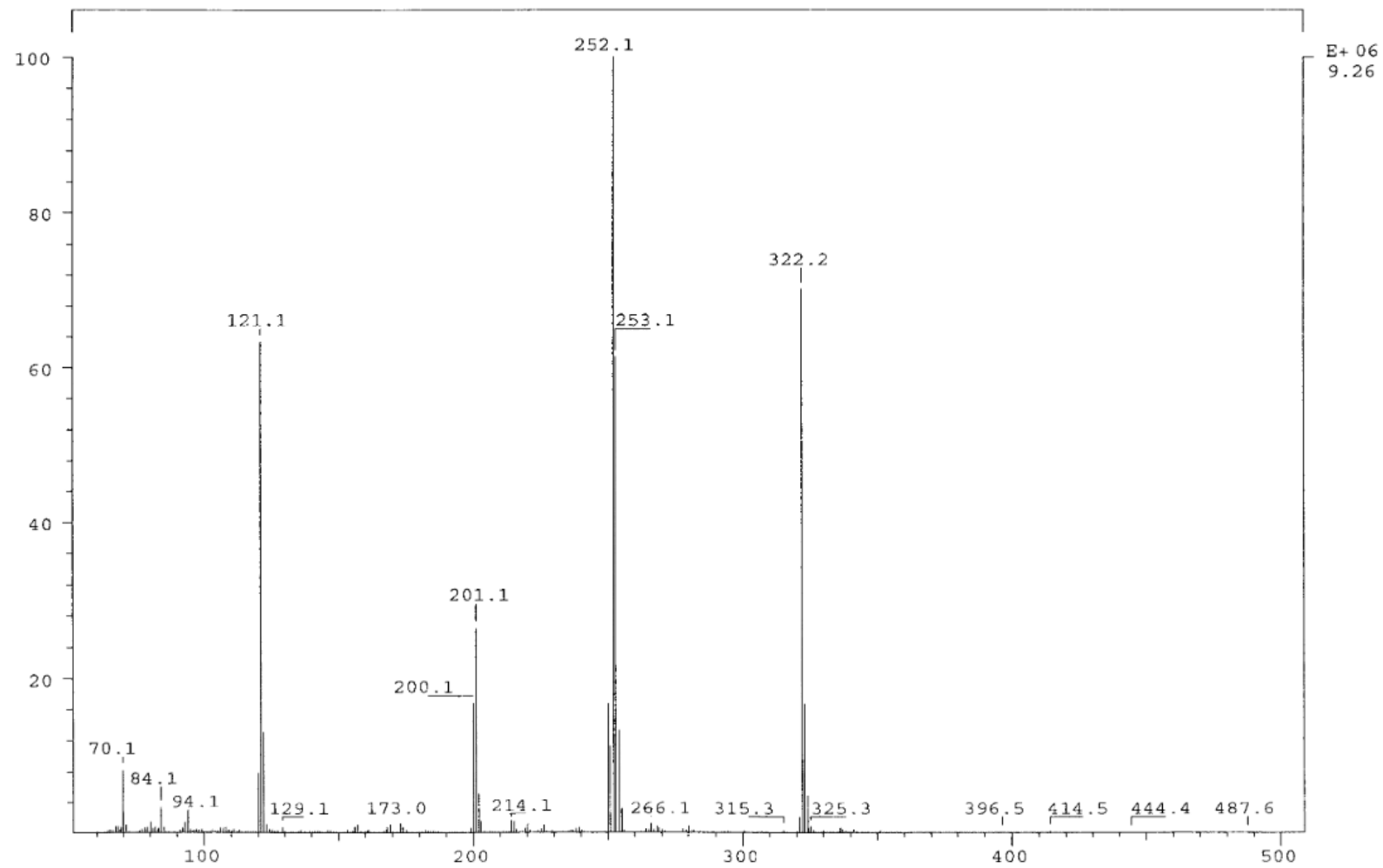
3. ^1H NMR of compound 1



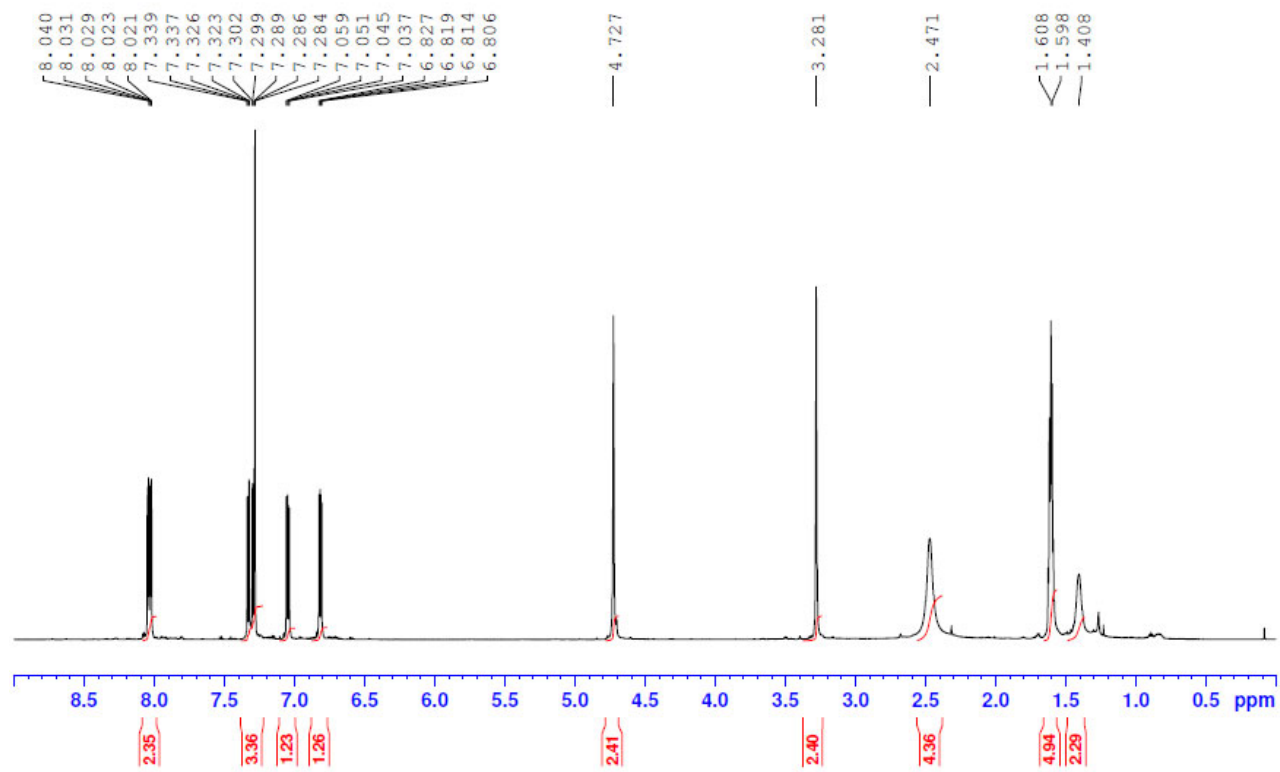
4. ^{13}C NMR of compound 1



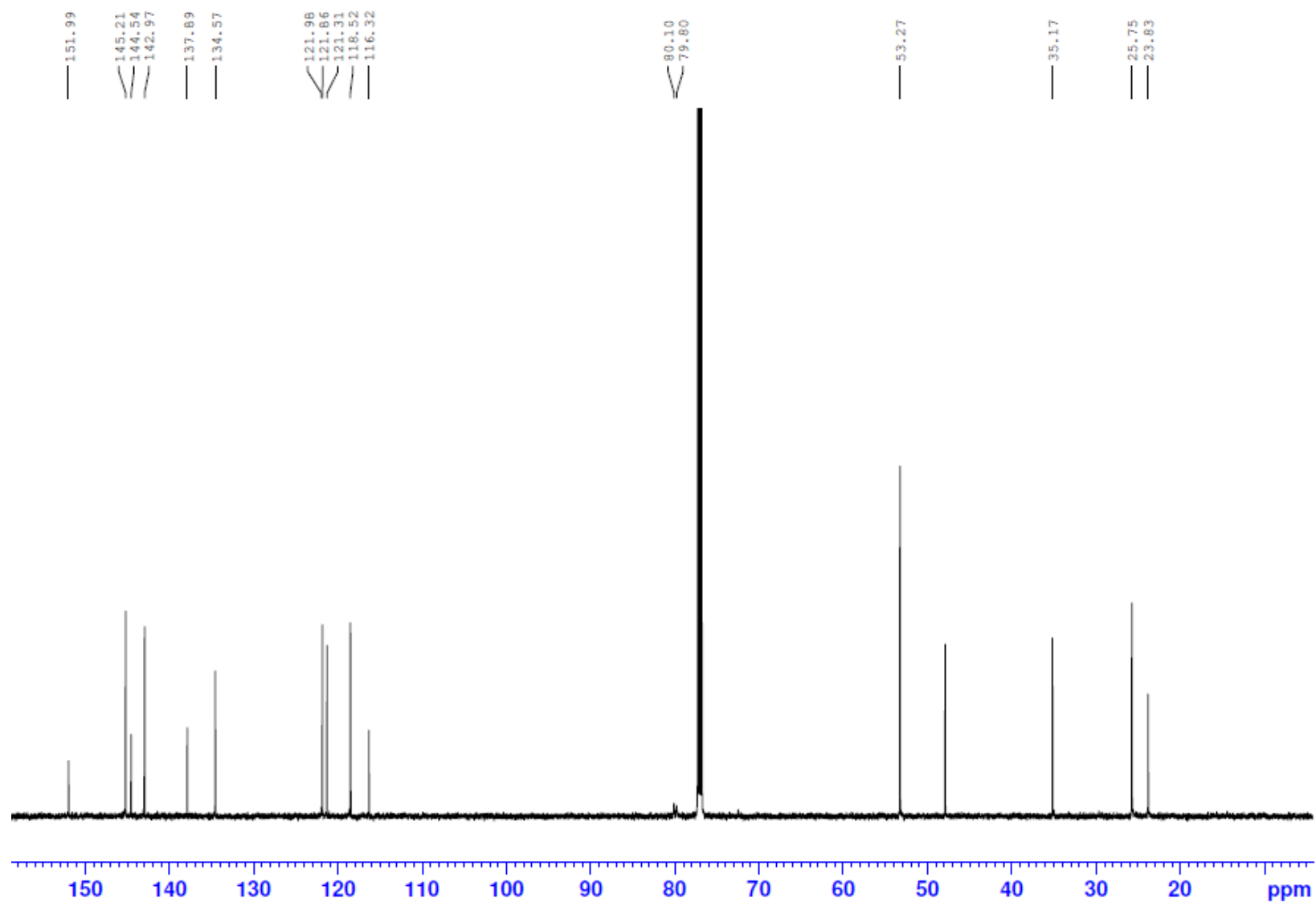
5. FAB MS of compound 1



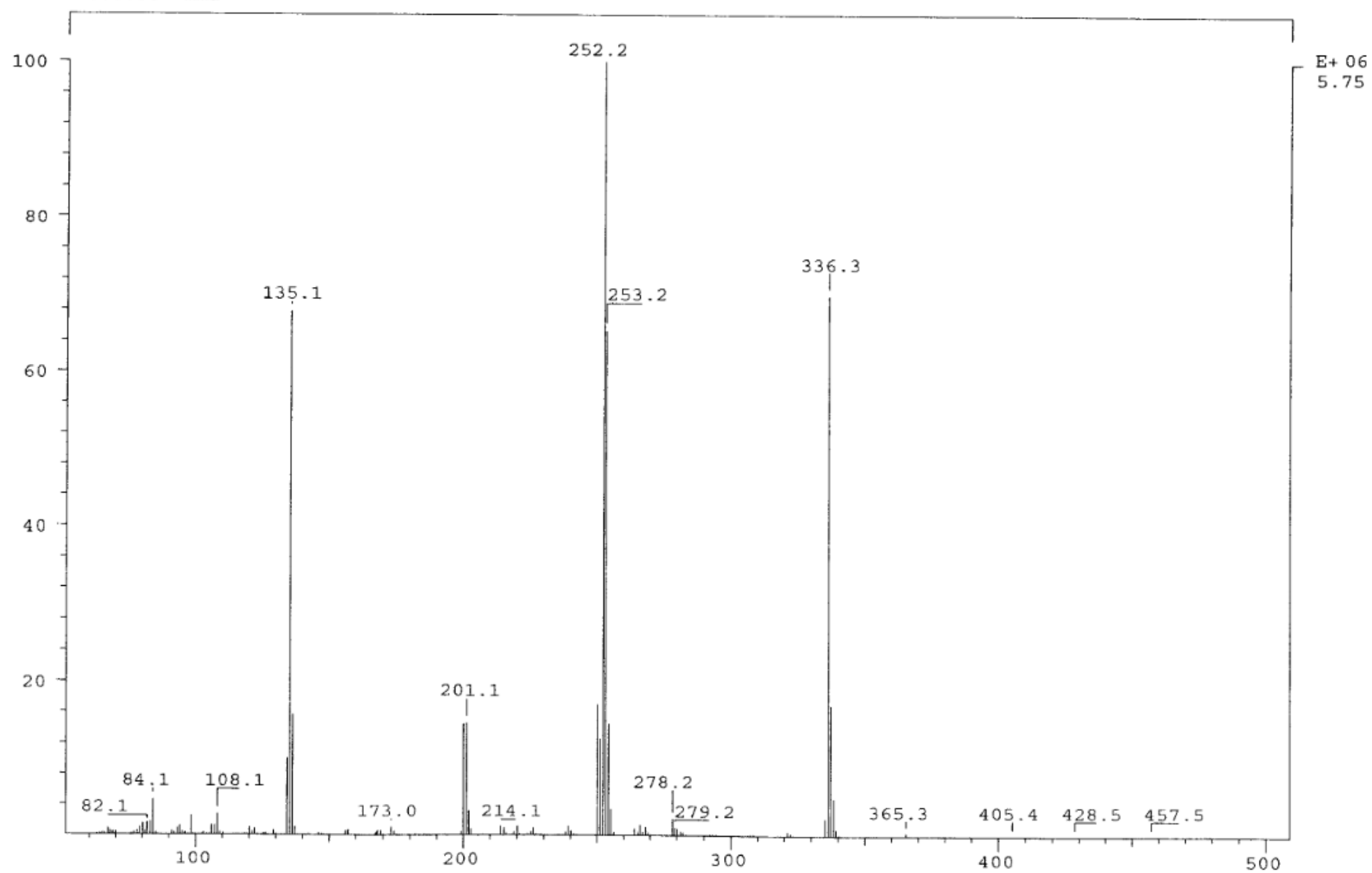
6. ^1H NMR of compound 2



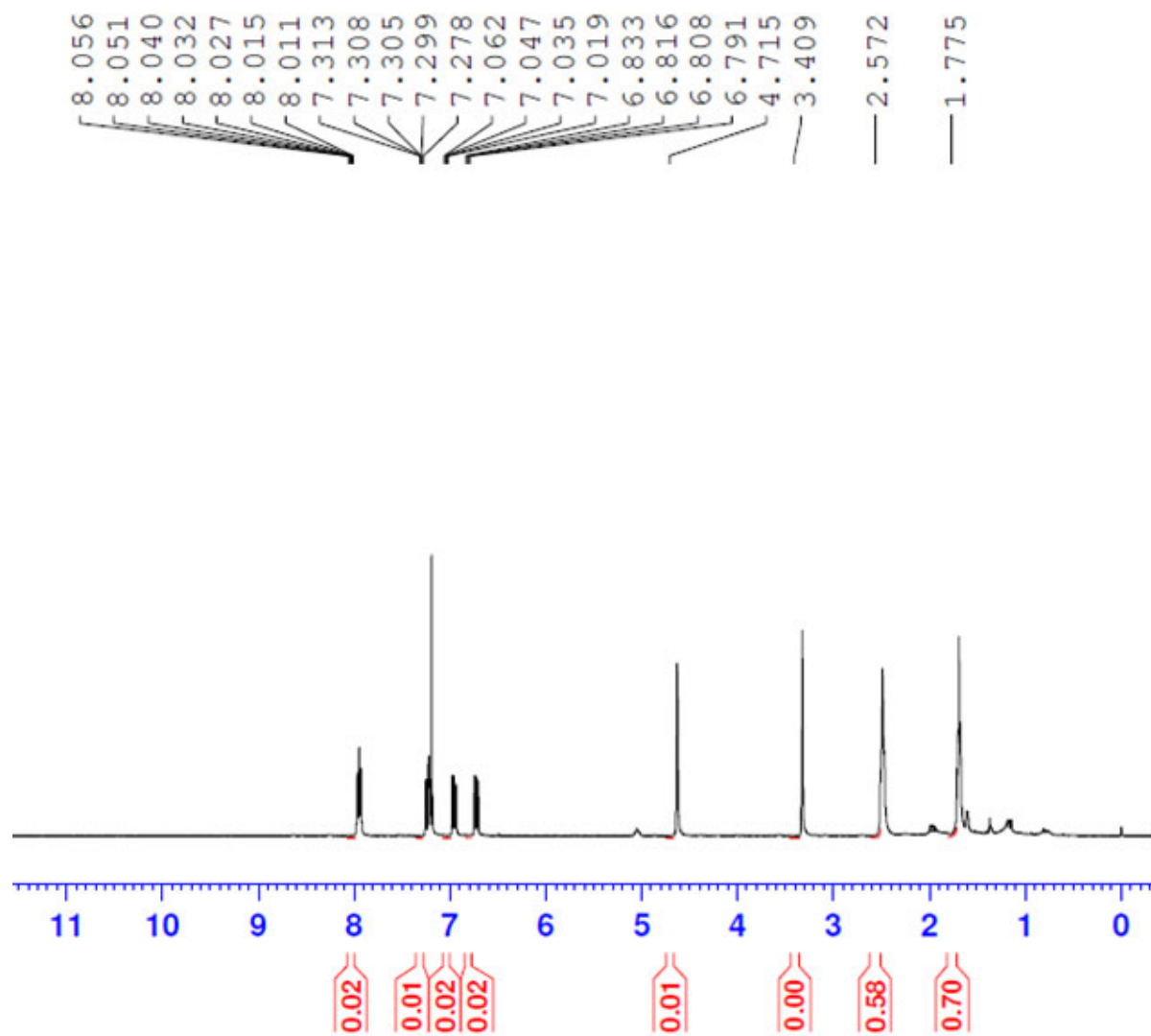
7. ^{13}C NMR of compound 2



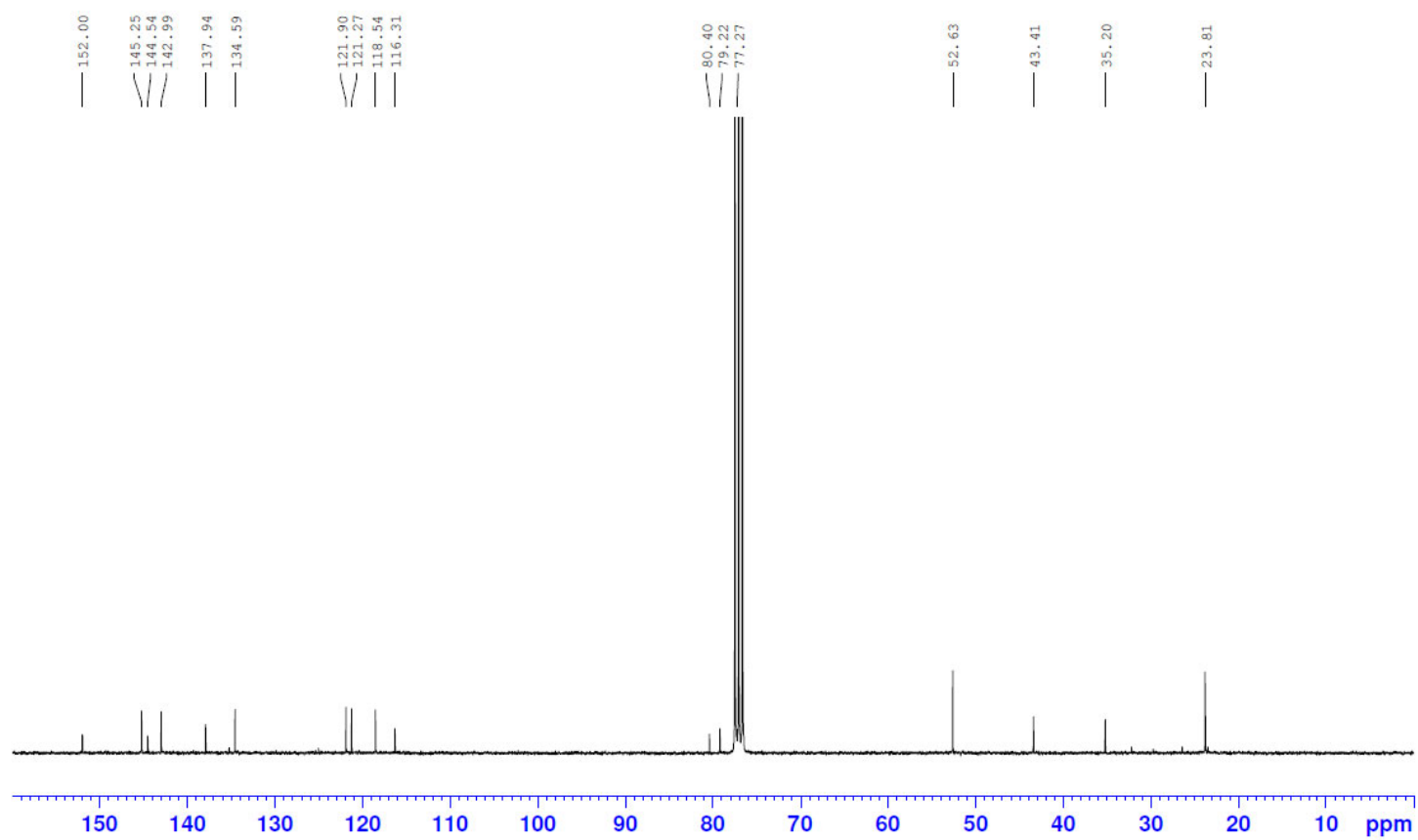
8. FAB MS of compound 2



9. ^1H NMR of compound 3



10. ^{13}C NMR of compound 3



11. FAB MS of compound 3

