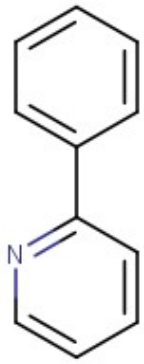
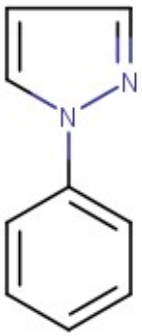
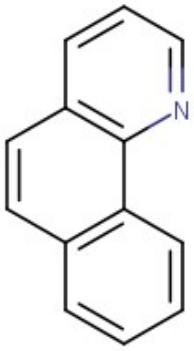
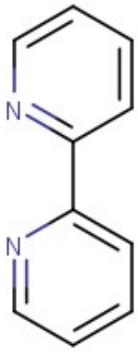
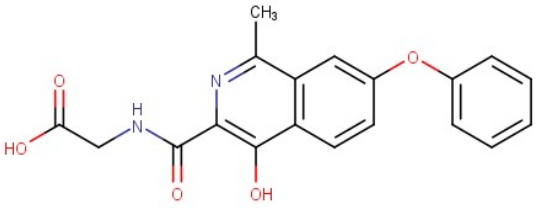
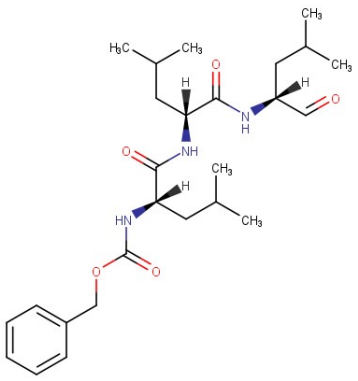
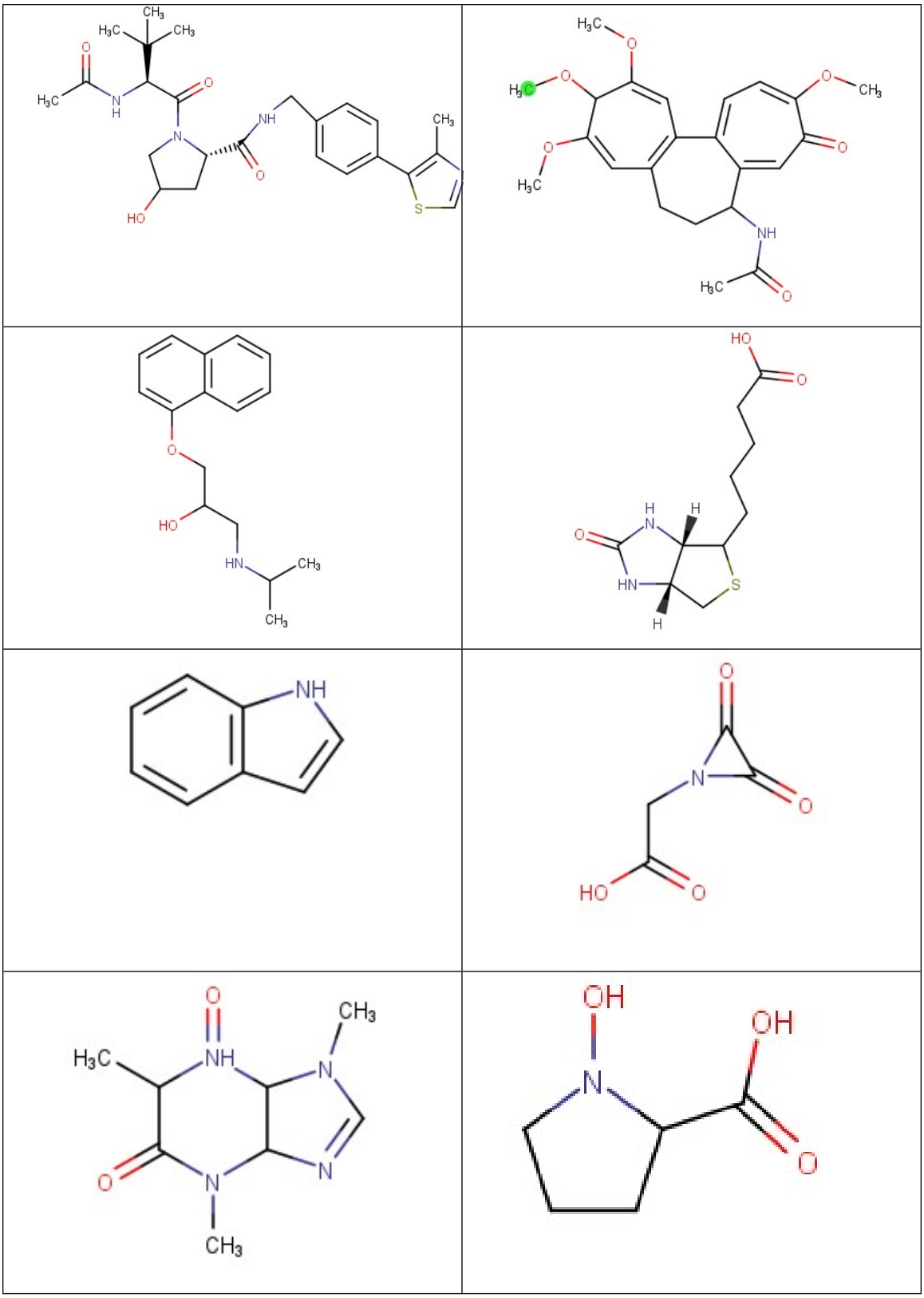
Electronic Supplementary Material (ESI) for RSC Advances.

TABLES

Table 1. Selected molecules form literature survey:



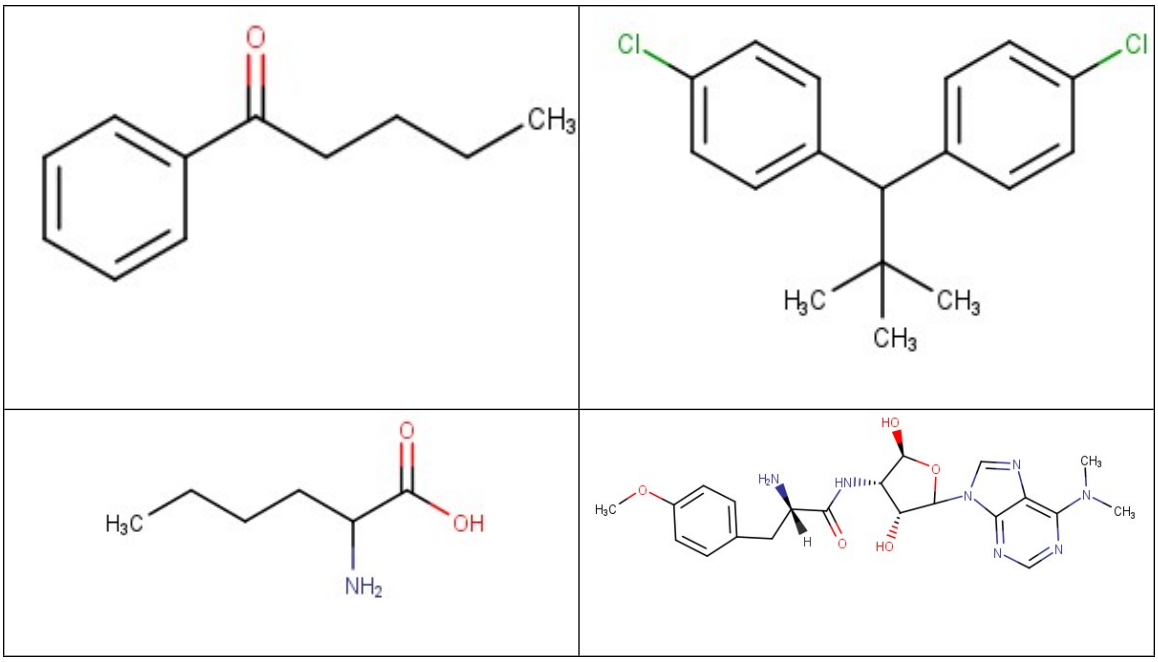
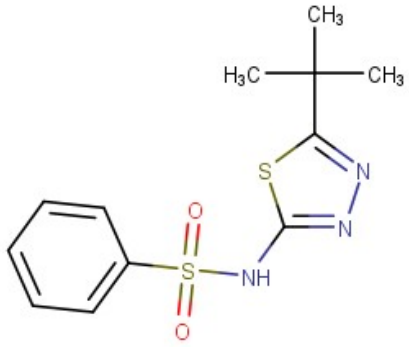
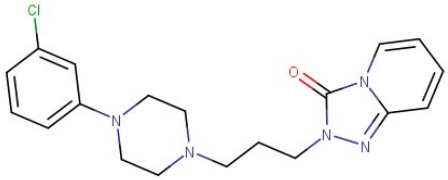
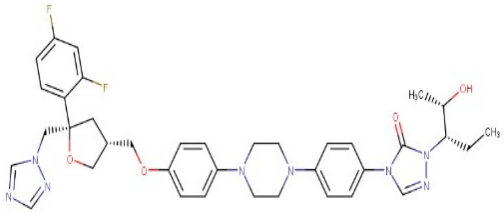
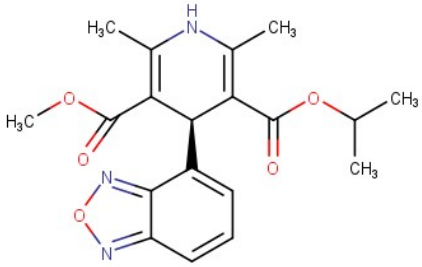
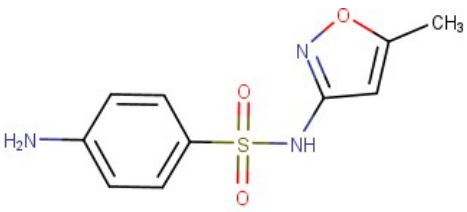
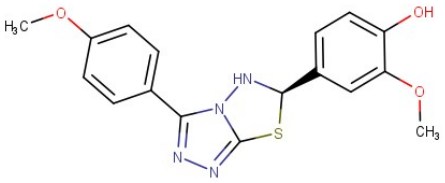
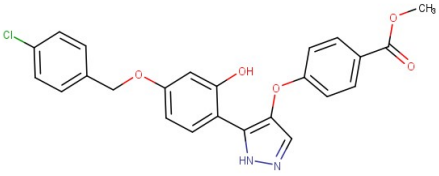
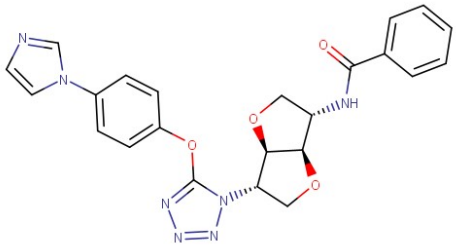
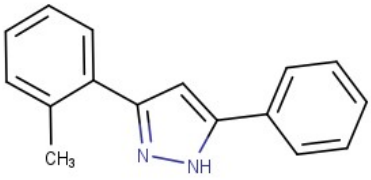


Table 2. List of scaffolds generated from pharmacophore modelling by Zinc pharmar:

1	**2**
3	**4**

5	 6 
7 	 8
9 	 10
11 	 12
13 	 14

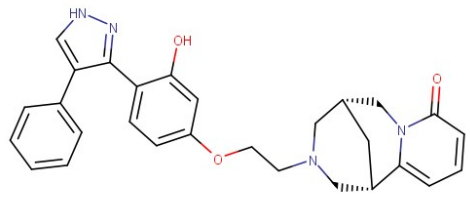
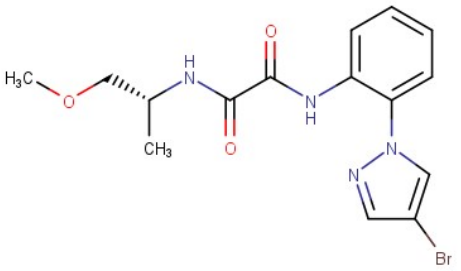
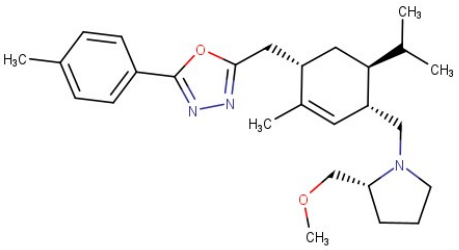
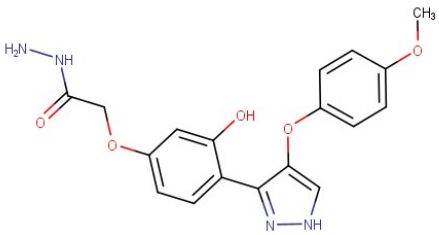
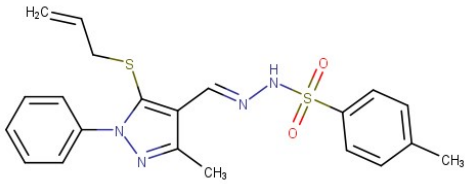
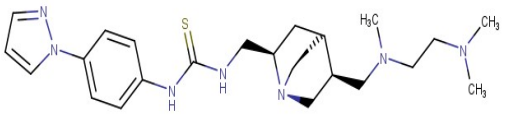
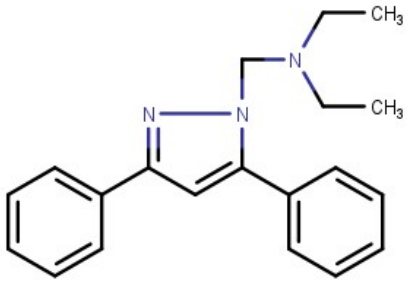
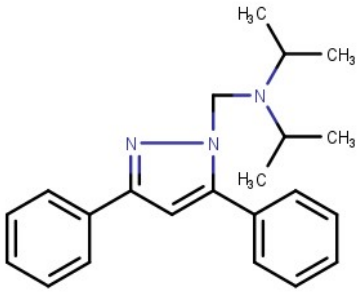
 **15**	 **16**
 **17**	 **18**
 **19**	 **20**

Table 3. List of designed novel molecules:

Compound code	2D Images
CDEA	
CDIPA	

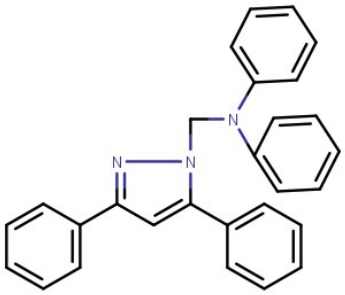
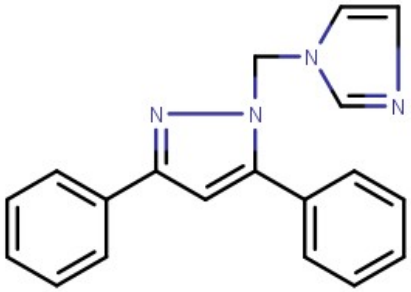
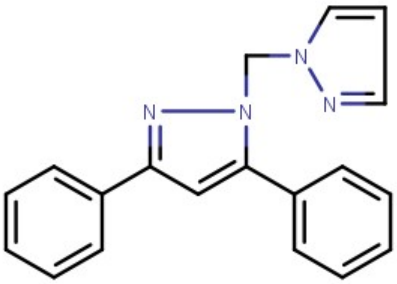
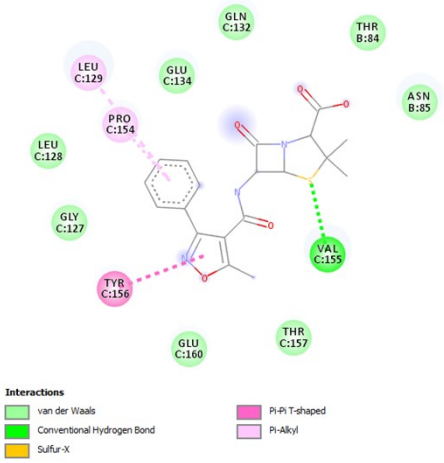
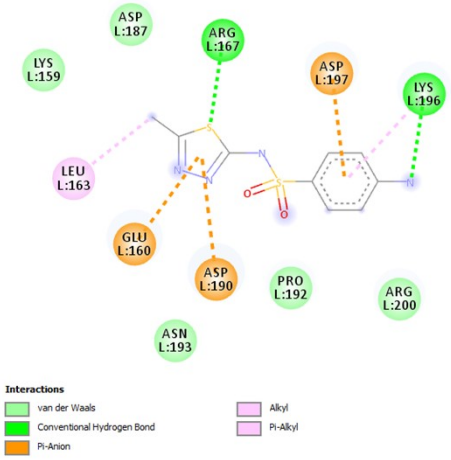
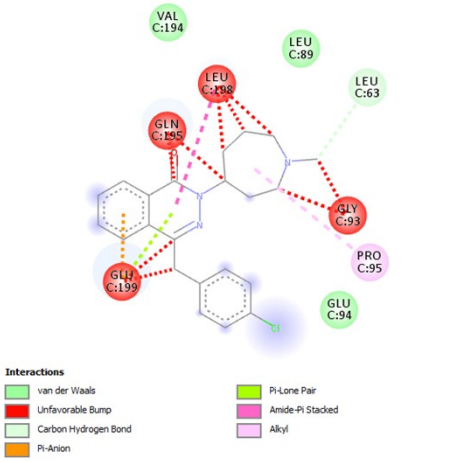
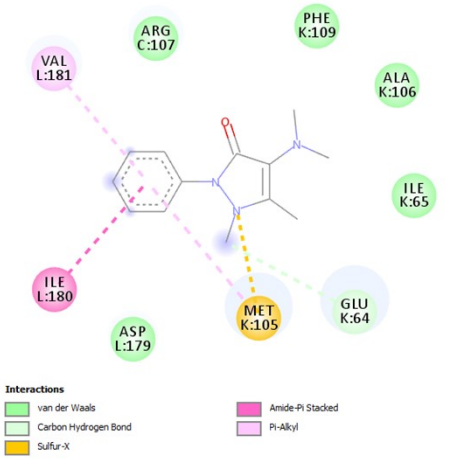
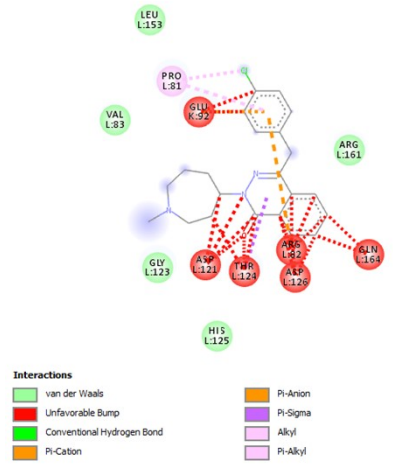
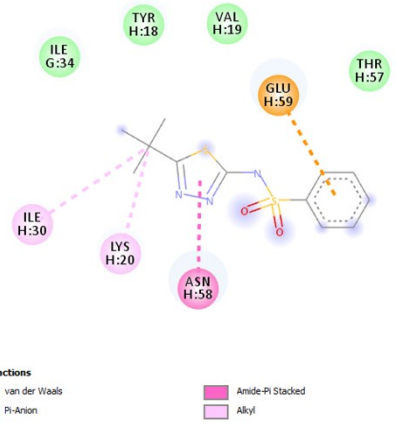
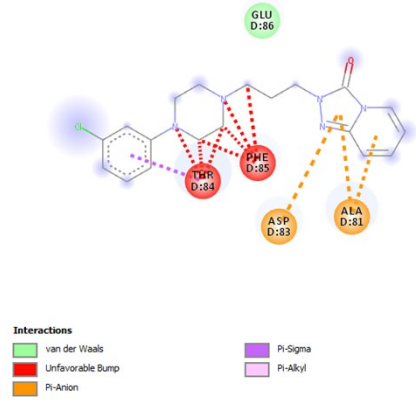
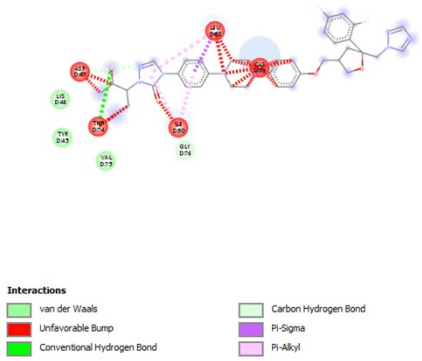
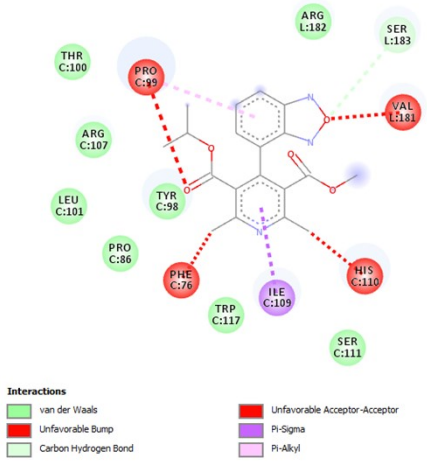
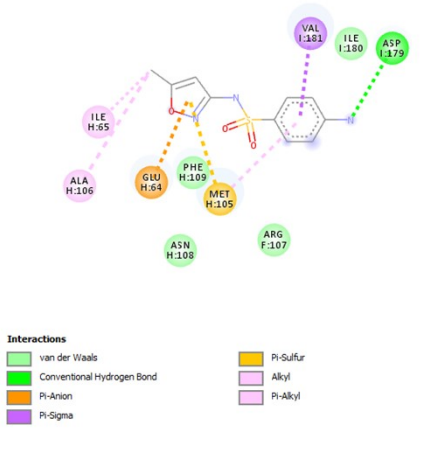
CDPA	
CI	
CP	

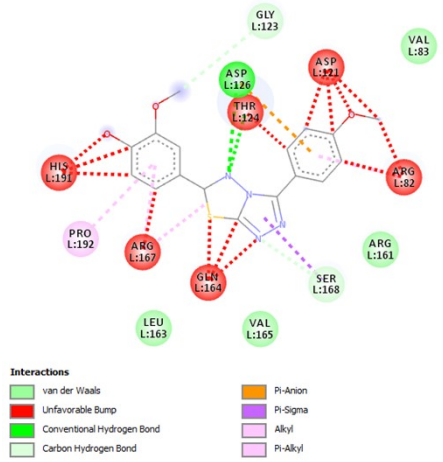
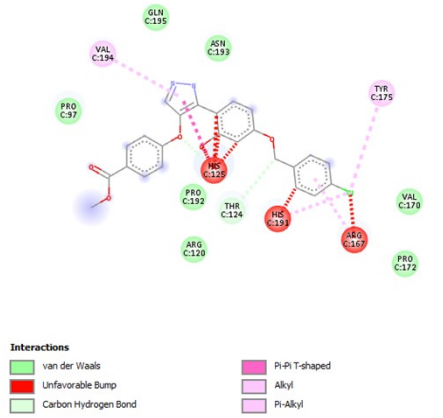
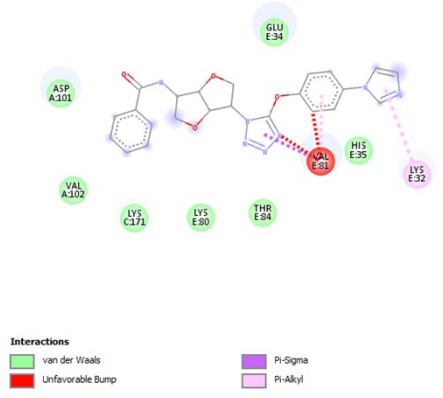
Table 4. Binding affinity and 2D interactions of top HITS:

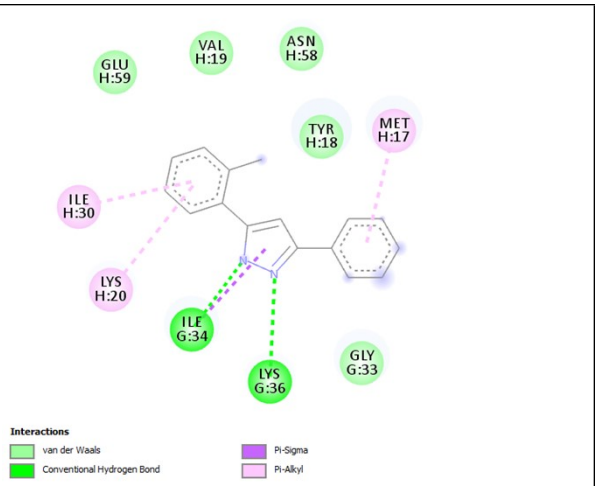
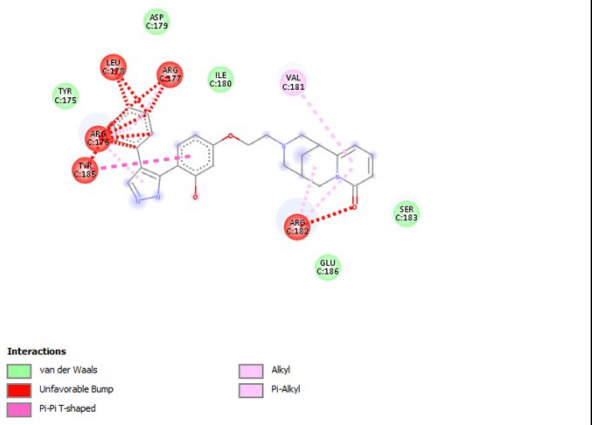
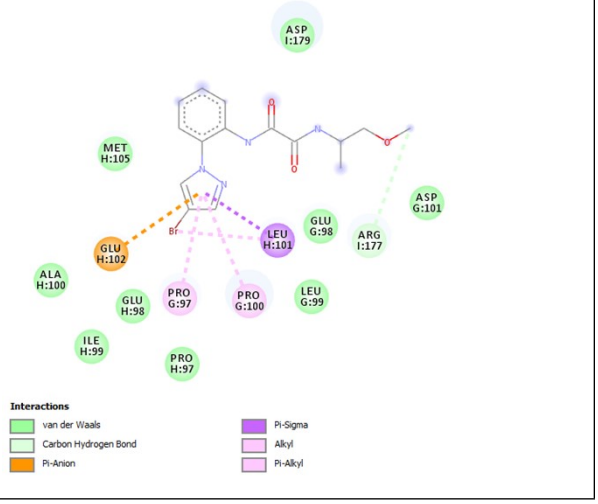
S NO	Binding affinity	2D interaction image
1	**-5.6**	

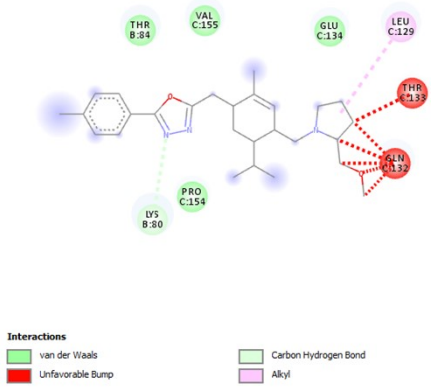
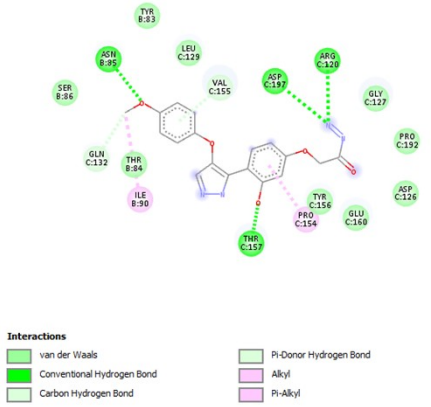
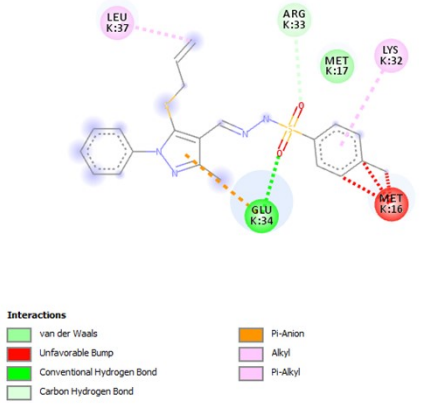
2	**-4.7**	 ASP L:187 ARG L:167 LYS L:159 ASP L:197 LYS L:196 LEU L:163 GLU L:160 ASP L:190 PRO L:192 ARG L:200 ASN L:193 Interactions van der Waals Conventional Hydrogen Bond Pi-Anion Alkyl Pi-Alkyl
3	**12.6**	 VAL C:194 LEU C:89 LEU C:63 GLN C:195 GLY C:93 PRO C:95 GLU C:199 GLU C:94 Interactions van der Waals Unfavorable Bump Carbon Hydrogen Bond Pi-Anion Pi-Lone Pair Amide-Pi Stacked Alkyl
4	**-6.6**	 ARG C:107 PHE K:109 VAL L:181 ALA K:106 ILE K:65 ILE L:180 MET K:105 GLU K:64 ASP L:179 Interactions van der Waals Carbon Hydrogen Bond Sulfur-X Amide-Pi Stacked Pi-Alkyl

5	**7.5**	 LEU L:153 PRO L:81 GLU K:92 VAL L:83 ARG L:161 ARG L:82 GLN L:164 GLY L:123 ASP L:121 THR L:124 ASP L:126 HIS L:125 Interactions van der Waals Unfavorable Bump Conventional Hydrogen Bond Pi-Cation Pi-Anion Pi-Sigma Alkyl Pi-Alkyl
6	**-3.7**	 TYR H:18 VAL H:19 ILE G:34 THR H:57 GLU H:59 ILE H:30 LYS H:20 ASN H:58 Interactions van der Waals Pi-Anion Amide-Pi Stacked Alkyl
7	**4.6**	 GLU D:86 PHE D:85 THR D:84 ASP D:83 ALA D:81 Interactions van der Waals Unfavorable Bump Pi-Anion Pi-Sigma Pi-Alkyl

8	**3.3**	 Interactions van der Waals Unfavorable Bump Conventional Hydrogen Bond Carbon Hydrogen Bond Pi-Sigma Pi-Alkyl
9	**-7.2**	 ARG L:182 SER L:183 THR C:100 PRO C:99 VAL L:181 ARG C:107 TYR C:98 LEU C:101 PRO C:86 PHE C:76 ILE C:109 HIS C:110 TRP C:117 SER C:111 Interactions van der Waals Unfavorable Bump Carbon Hydrogen Bond Unfavorable Acceptor-Acceptor Pi-Sigma Pi-Alkyl
10	**-5.0**	 VAL I:181 ILE I:180 ASP I:179 ILE H:65 ALA H:106 GLU H:64 PHE H:109 MET H:105 ASN H:108 ARG F:107 Interactions van der Waals Conventional Hydrogen Bond Pi-Anion Pi-Sigma Pi-Sulfur Alkyl Pi-Alkyl

11	**12.8**	
12	**6.5**	
13	**-0.8**	

14	**-7.5**	
15	**9.2**	
16	**-6.5**	

17	**5.5**	
18	**-7.8**	
19	**3.6**	

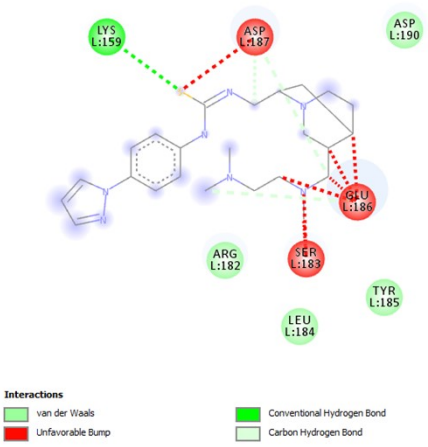
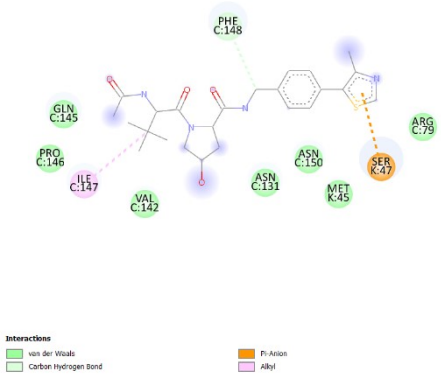
20	**1.2**	
CO-CRYSTAL	**-6.2**	

Table 5. Physical characterization data of synthesized compounds:

S.NO.	Sample code	Mol. formula	Mol. Weight	Melting point(°C)	Rf value	Yield (%)	Color (Powder)
1	CP	$C_{19}H_{16}N_4$	300.365	135-140	0.52	85	White
2	CI	$C_{19}H_{16}N_4$	300.365	140-145	0.36	79	White
3	CDPA	$C_{28}H_{23}N_3$	401.513	135-145	0.21	86	White
4	CDEA	$C_{20}H_{23}N_3$	305.425	155-160	0.42	86	White
5	CDIPA	$C_{22}H_{27}N_3$	333.479	175-180	0.64	86	White

Table 6. Wound size of the rat with days

Groups	Wound size (mm)			
	Day 3	Day 7	Day 11	Day 15
Control	18.7	18.4	17.6	15.5
Low dose 75mg/Kg	18.1	17.4	15.3	13.3
High dose 150mg/Kg	17.4	16.6	12.0	8.1

FIGURE

Figure 1. Primary output page

Input Molecules view details: visualization of the detected features

#	Molecule	Atoms	Features	Spatial Features	Aromatic	Hydrophobic	Donors	Acceptors	Negatives	Positives
1	1.mol2	19	4	4	2	0	0	1	0	1
2	4.mol2	20	4	4	2	0	0	2	0	0
3	2.mol2	19	4	4	2	0	0	1	0	1
4	17.mol2	21	9	8	0	4	1	3	1	0
5	3.mol2	23	4	4	3	0	0	1	0	0
6	7.mol2	65	19	18	2	8	3	6	0	0
7	15.mol2	26	5	5	1	3	0	1	0	0
8	14.mol2	16	6	6	0	1	0	4	1	0
9	9.mol2	40	9	7	2	2	2	3	0	0
10	16.mol2	37	11	11	2	9	0	0	0	0
11	13.mol2	28	7	7	0	3	1	3	0	0
12	10.mol2	16	4	3	2	0	1	0	0	1
13	8.mol2	57	21	21	0	14	1	6	0	0
14	12.mol2	15	8	6	0	0	2	5	1	0
15	18.mol2	62	20	17	3	4	5	8	0	0
16	11.mol2	16	4	3	2	0	1	0	0	1
17	6.mol2	75	24	24	1	15	3	5	0	0
18	5.mol2	41	13	12	3	1	2	6	1	0

Figure 2. The figure displays parts of the main output page obtained for input with eighteen HIF-mimetics.

Sort by score

Number of Aligned Molecules: 10

Score	Jmol	Features	Spatial Features	Aromatic	Hydrophobic	Donors	Acceptors	Negatives	Positives	Molecules
14.230	Jmol	3	3	0	0	0	3	0	0	12.mol2 17.mol2 14.mol2 9.mol2 8.mol2 18.mol2 6.mol2 5.mol2 13.mol2 7.mol2

Number of Aligned Molecules: 9

Score	Jmol	Features	Spatial Features	Aromatic	Hydrophobic	Donors	Acceptors	Negatives	Positives	Molecules
13.500	Jmol	3	3	0	0	1	2	0	0	6.mol2 7.mol2 8.mol2 12.mol2 18.mol2 5.mol2 9.mol2 13.mol2 17.mol2
10.945	Jmol	3	3	0	1	0	2	0	0	14.mol2 17.mol2 7.mol2 9.mol2 8.mol2 18.mol2 6.mol2 5.mol2 13.mol2

Number of Aligned Molecules: 8

Score	Jmol	Features	Spatial Features	Aromatic	Hydrophobic	Donors	Acceptors	Negatives	Positives	Molecules
24.875	Jmol	3	3	2	0	0	1	0	0	2.mol2 1.mol2 4.mol2 3.mol2 7.mol2 9.mol2 18.mol2 5.mol2
13.500	Jmol	3	3	0	0	1	2	0	0	12.mol2 17.mol2 7.mol2 8.mol2 18.mol2 6.mol2 5.mol2 13.mol2
10.436	Jmol	3	3	0	1	0	2	0	0	14.mol2 17.mol2 7.mol2 8.mol2 18.mol2 6.mol2 5.mol2 13.mol2
9.900	Jmol	3	3	0	1	1	1	0	0	17.mol2 7.mol2 13.mol2 8.mol2 18.mol2 6.mol2 9.mol2 5.mol2
9.334	Jmol	3	3	0	1	0	2	0	0	7.mol2 8.mol2 18.mol2 6.mol2 5.mol2 17.mol2 9.mol2 13.mol2

Number of Aligned Molecules: 7

Score	Jmol	Features	Spatial Features	Aromatic	Hydrophobic	Donors	Acceptors	Negatives	Positives	Molecules
13.576	Jmol	4	4	0	1	0	3	0	0	14.mol2 17.mol2 8.mol2 18.mol2 6.mol2 9.mol2 5.mol2
9.334	Jmol	3	3	0	1	1	1	0	0	17.mol2 9.mol2 18.mol2 6.mol2 5.mol2 7.mol2 8.mol2
8.731	Jmol	3	3	0	1	1	1	0	0	5.mol2 17.mol2 13.mol2 8.mol2 9.mol2 6.mol2 18.mol2
8.731	Jmol	3	3	0	1	0	2	0	0	5.mol2 17.mol2 8.mol2 6.mol2 7.mol2 9.mol2 13.mol2
5.940	Jmol	3	3	0	2	0	1	0	0	6.mol2 17.mol2 7.mol2 15.mol2 8.mol2 18.mol2 9.mol2
5.940	Jmol	3	3	0	2	0	1	0	0	8.mol2 17.mol2 7.mol2 15.mol2 6.mol2 9.mol2 18.mol2

Figure 3. Pharmacophore output page describes the top-scoring candidate pharmacophore model.

Pharmacophore features:

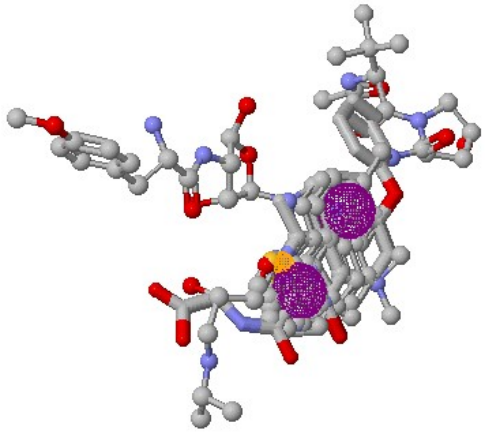
Score	Features	Spatial Features	Aromatic	Hydrophobic	Donors	Acceptors	Negatives	Positives
24.875	3	3	2	0	0	1	0	0

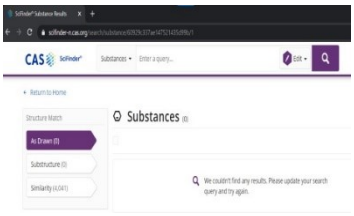
Molecule Name	Show Molecule:	Show Features:
2*		
1		
4		
3		
7		
9		
18		
5		

* pivot molecule

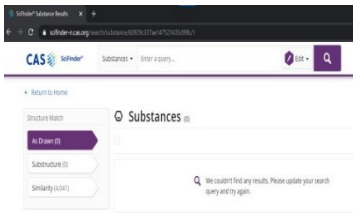
Download Pharmacophore and Alignment File

Figure 4. Generated pharmacophore in ZINCPharmer.

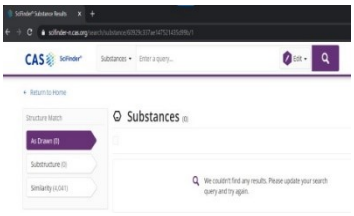




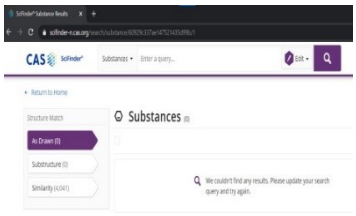
Pyrazole derivative



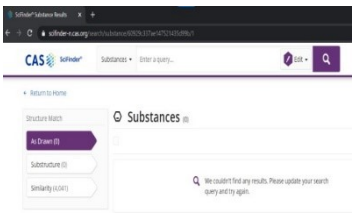
Imidazole derivative



Diphenylamine derivative



Diethylamine derivative



Diisopropylamine derivative

Figure 5. Sci-finder results of the compounds

Figure 6. Structure of 4W9H protein

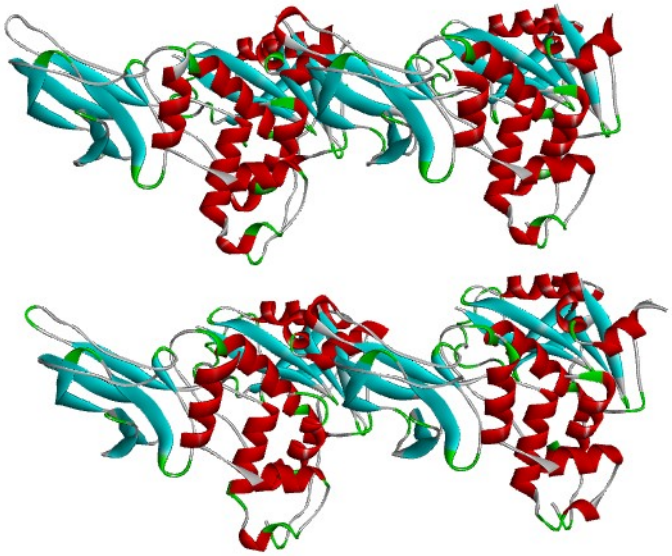


Figure 7. Ramachandran plot

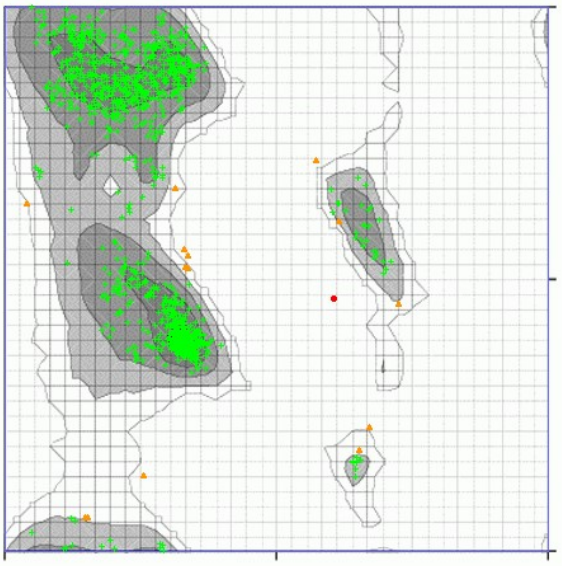


Figure 8. Egg model

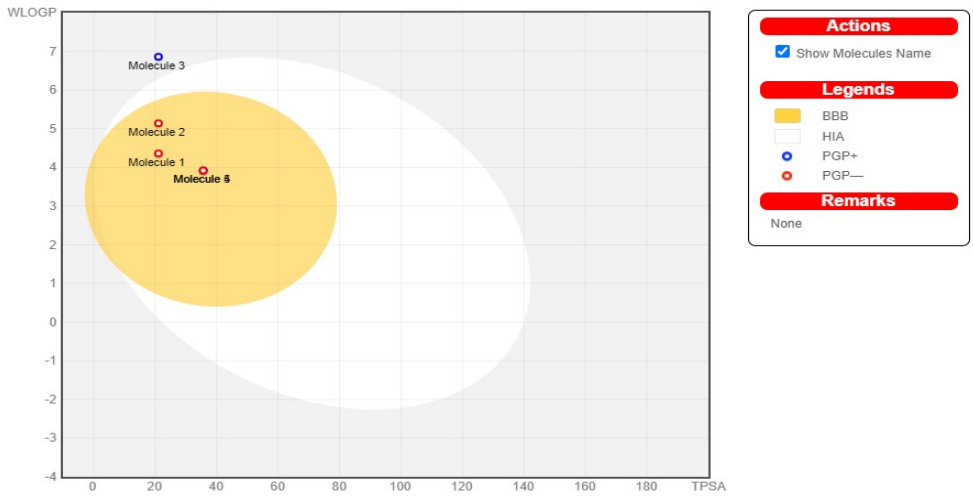
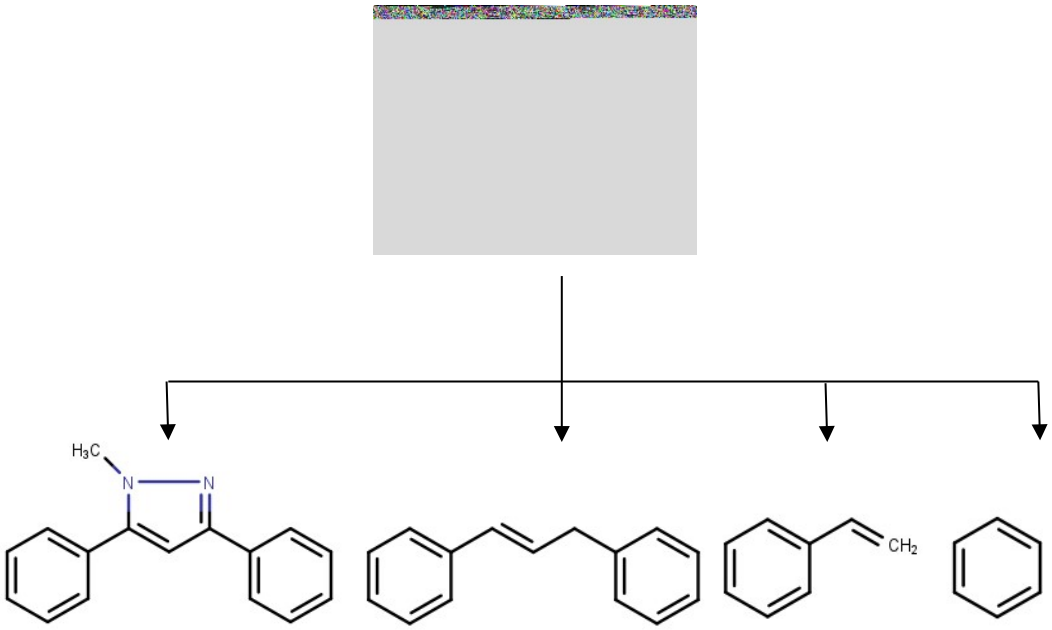


Figure 9. Synthesized pyrazole analogues

Figure 10. Mass fragmentation of compound CI



(m/z+5)-228 **(m/z+4)-187** **(m/z+4)-104** **(m/z+1)-76**

Figure 11. IR spectra of compound CI

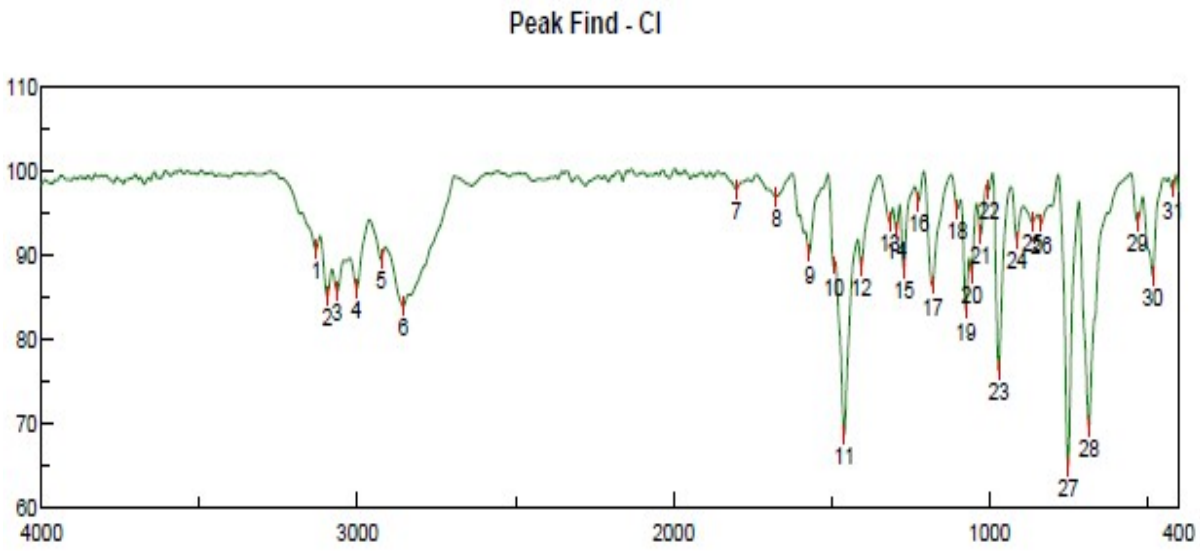


Figure 12. ^{1}H spectra of compound CI

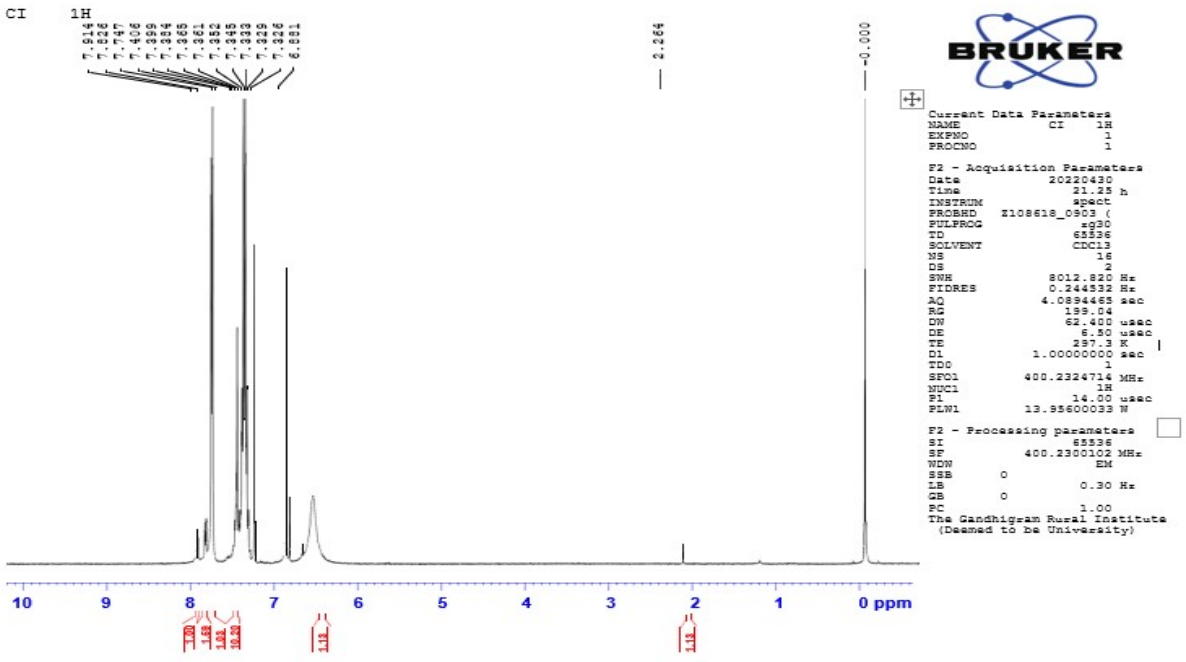


Figure 13. ^{13} C spectra of compound CI

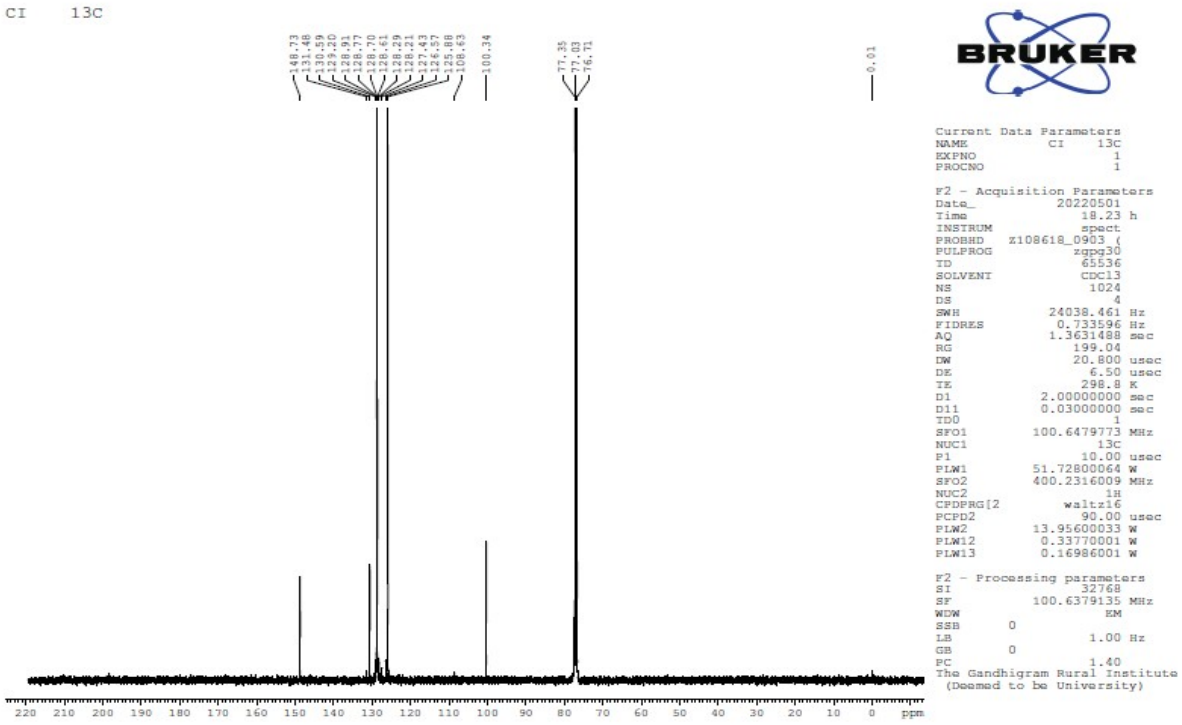


Figure 14. Mass spectra of compound CI

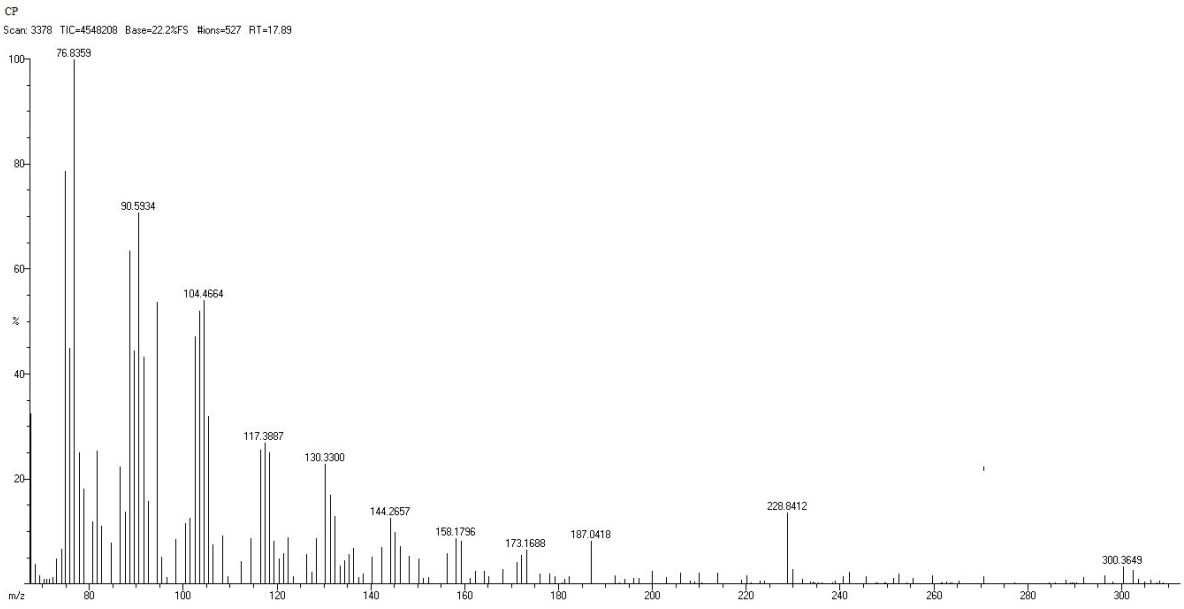
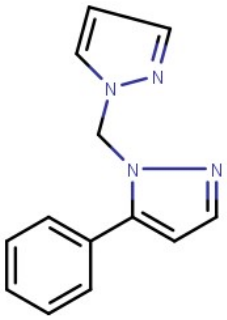
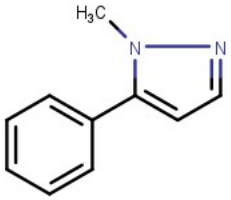
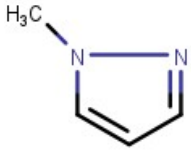


Figure 15. Mass fragmentation of compound CP







(m/z-1)-224 **(m/z+2)- 154** **(m/z+2)-77**

Figure 16. IR spectra of compound CP

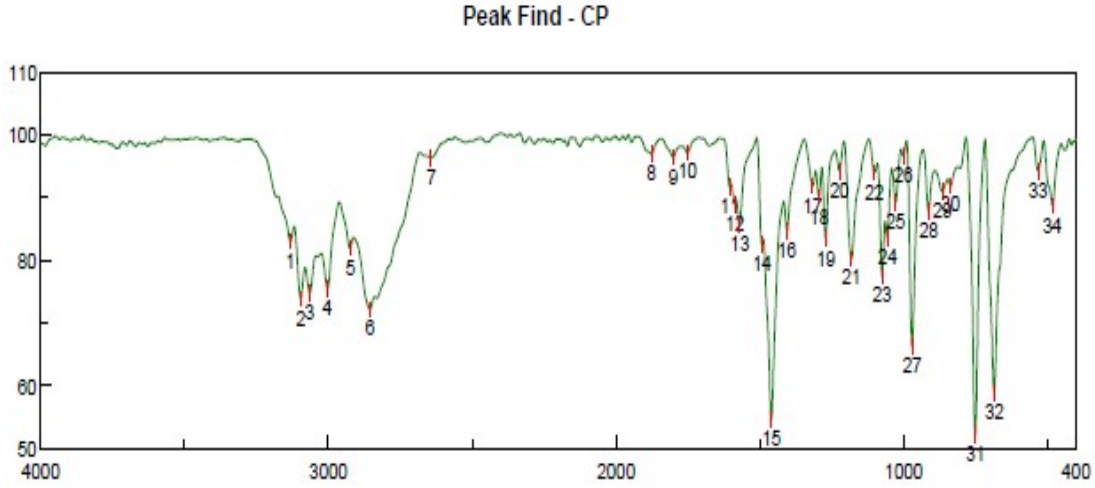


Figure 17. H1 spectra of compound CP

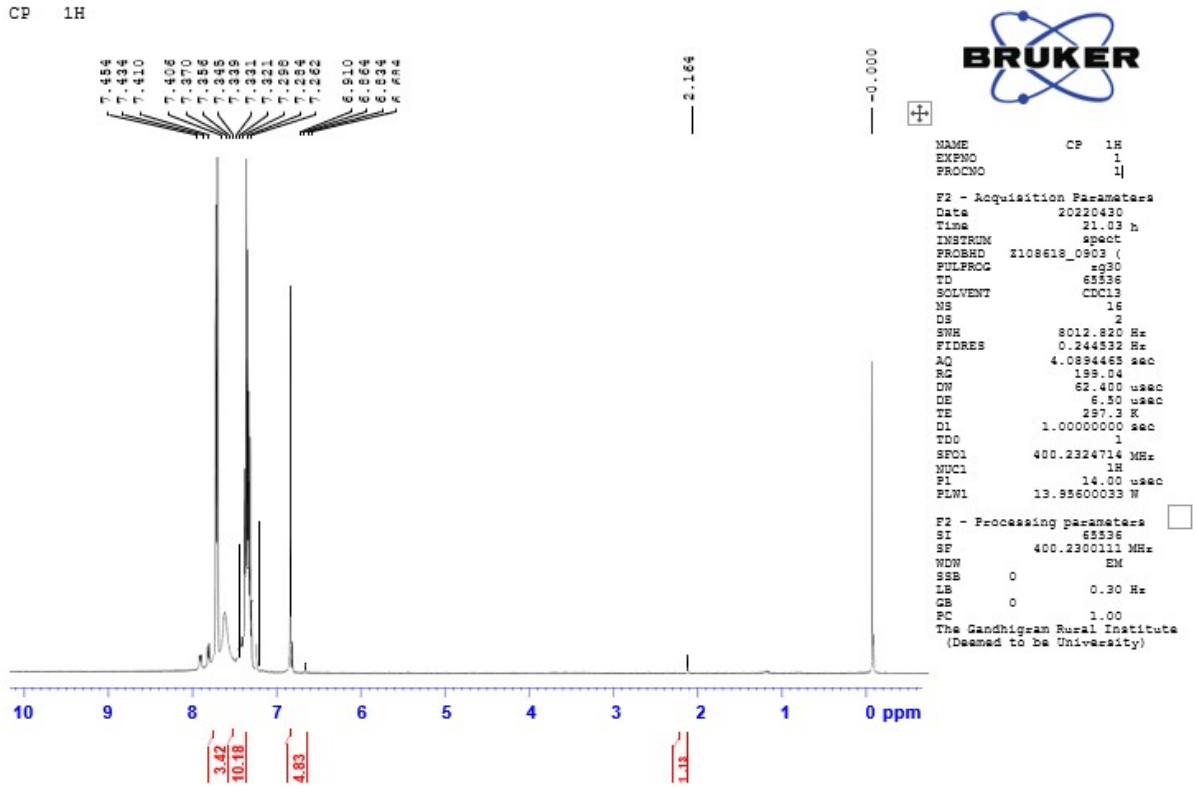


Figure 18. C13 spectra of compound CP

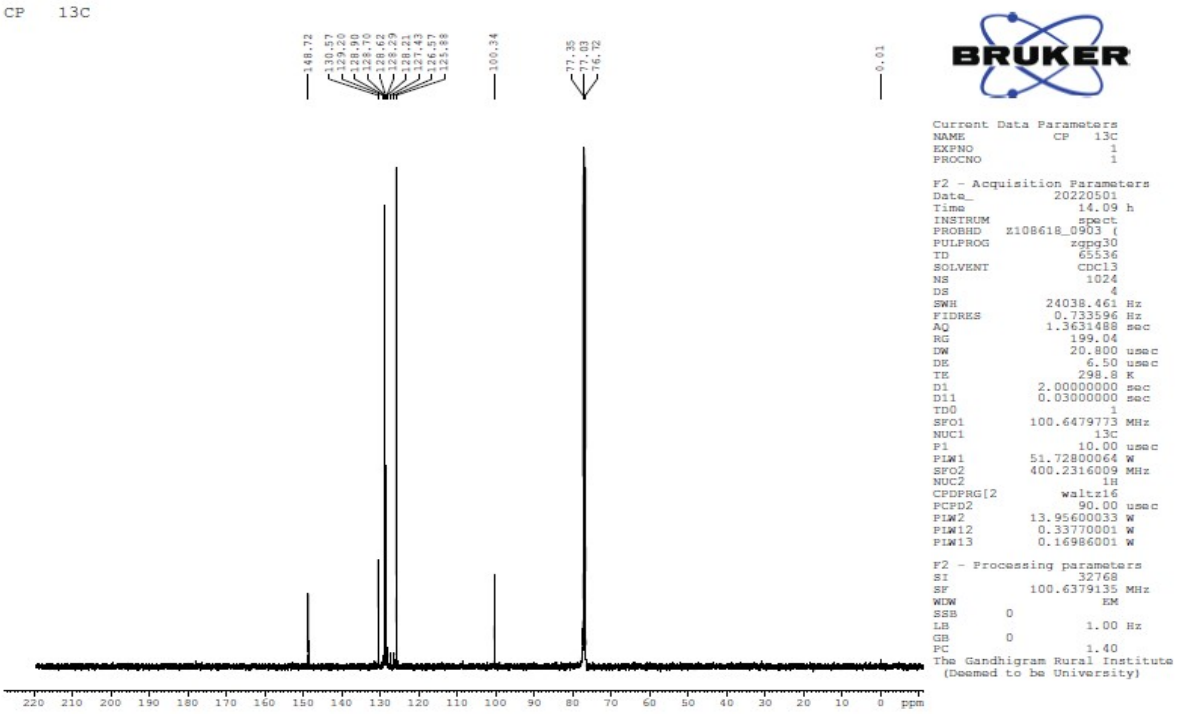


Figure 19. Mass spectra of compound CP

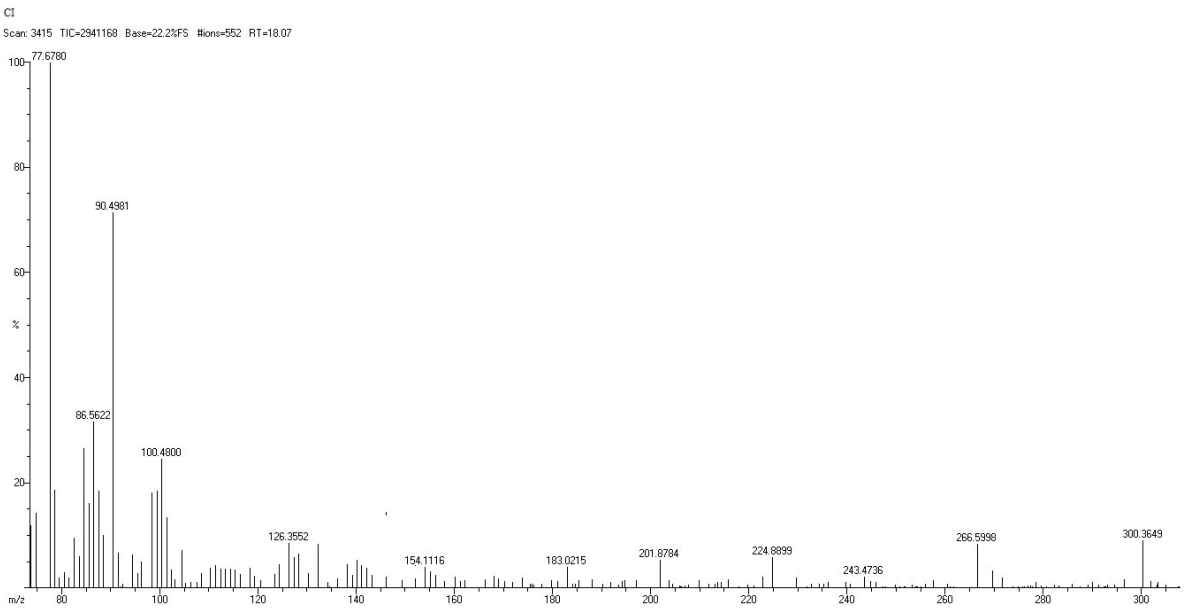
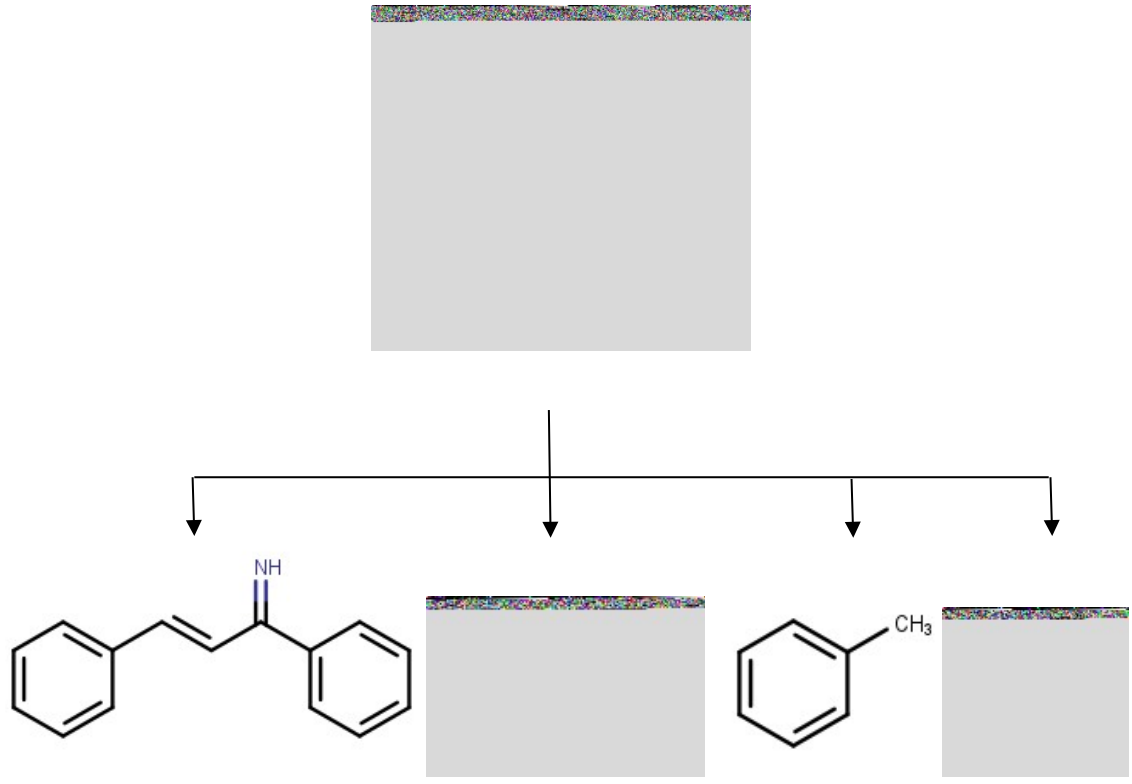


Figure 20. Mass fragmentation of compound CDPA



(m/z-3)-208 **(m/z+3)-99** **(m/z+4)-93** **(m/z+2)-75**

Figure 21. IR spectra of compound CDPA

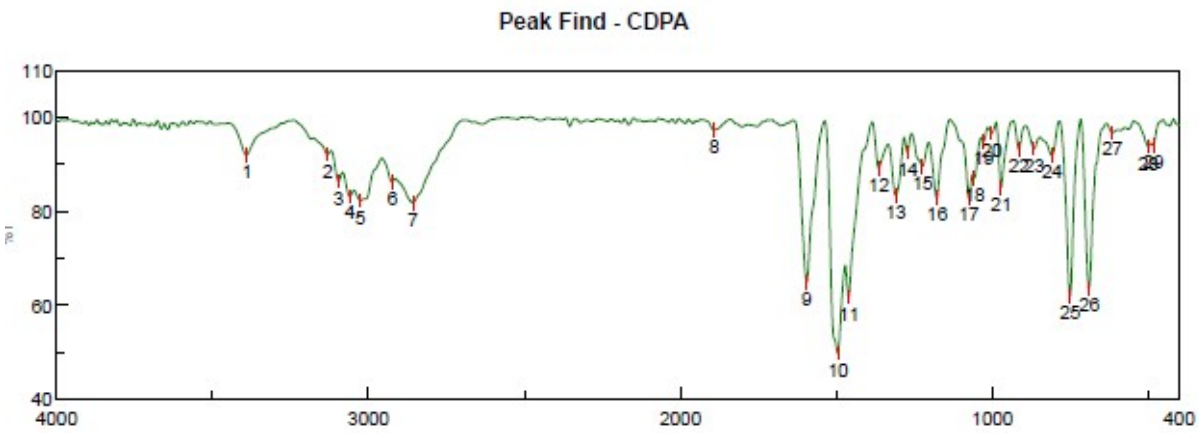


Figure 22. H1 spectra of compound CDPA

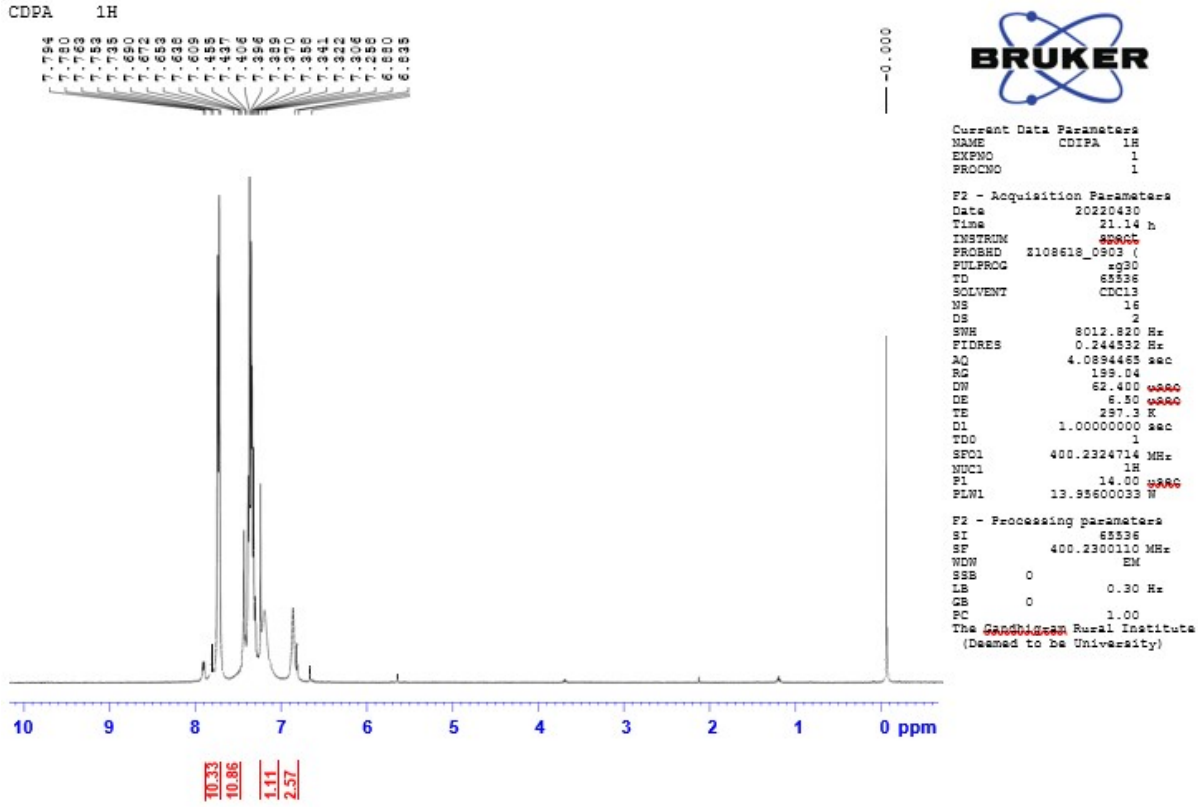


Figure 23. C13 spectra of compound CDPA

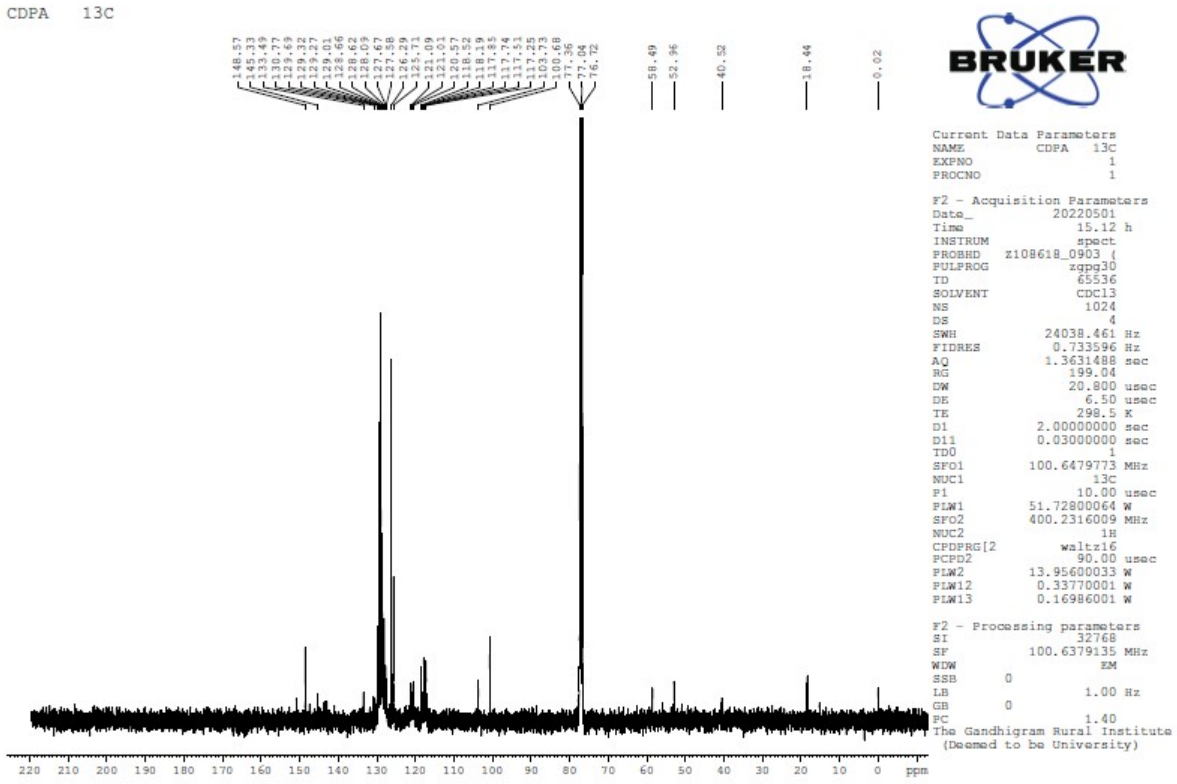


Figure 24. Mass spectra of compound CDPA

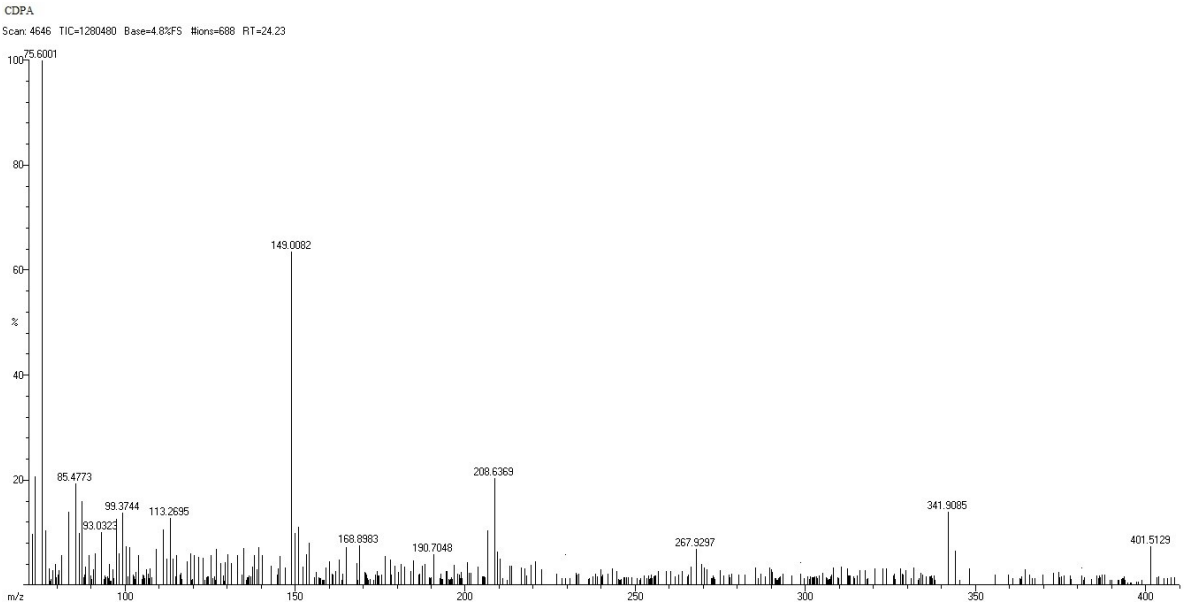
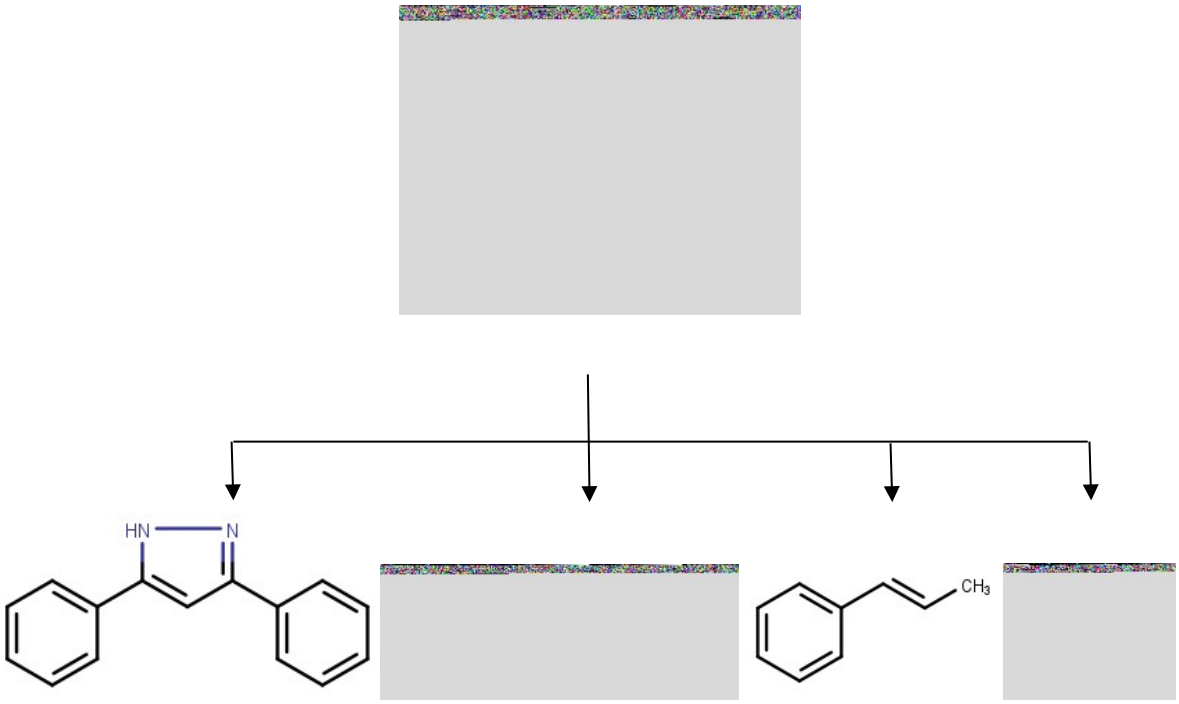


Figure 25. Mass fragmentation of compound CDEA



(m/z+1)-218 **(m/z+5)-196** **(m/z+2)-122** **(m/z-3)-89**

Figure 26. IR spectra of compound CDEA

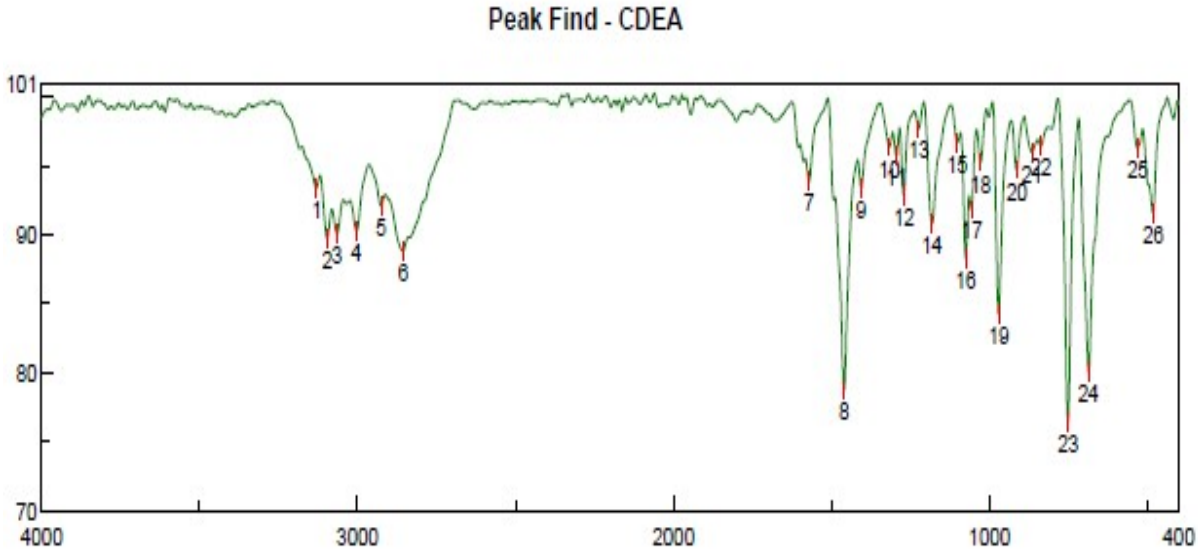


Figure 27. H1 spectra of compound CDEA

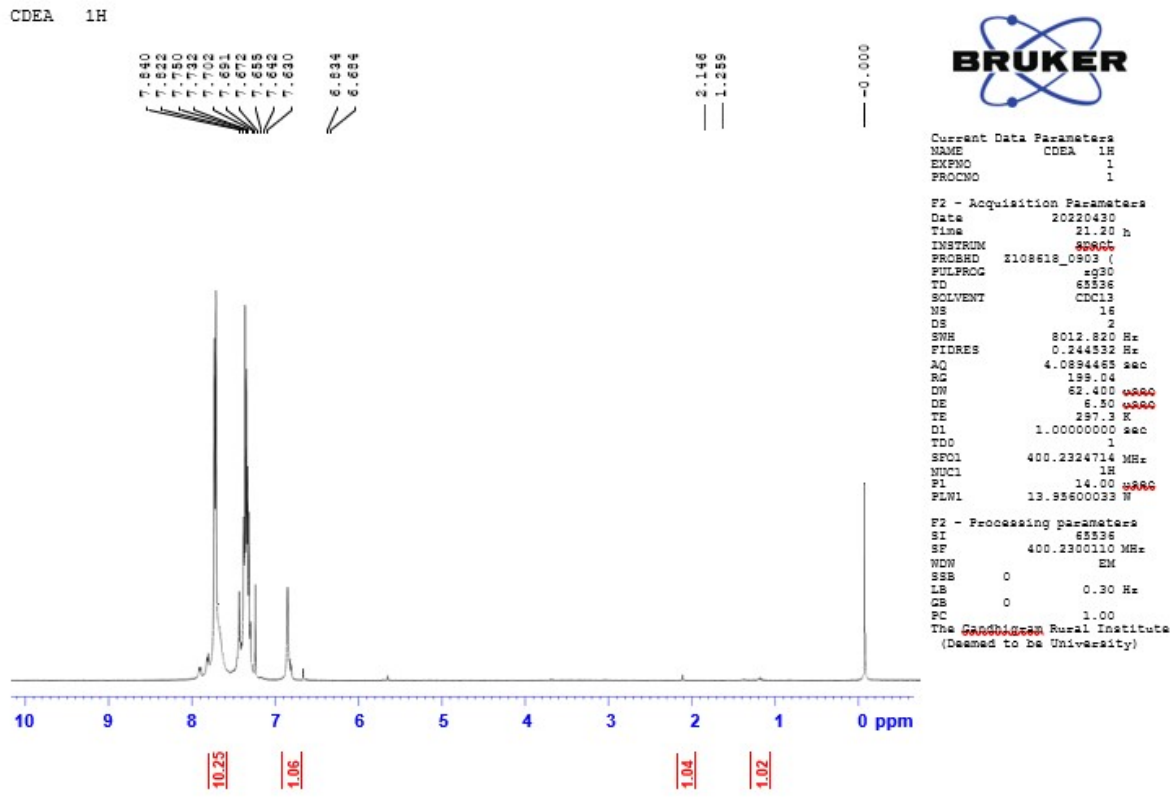


Figure 28. C13 spectra of compound CDEA

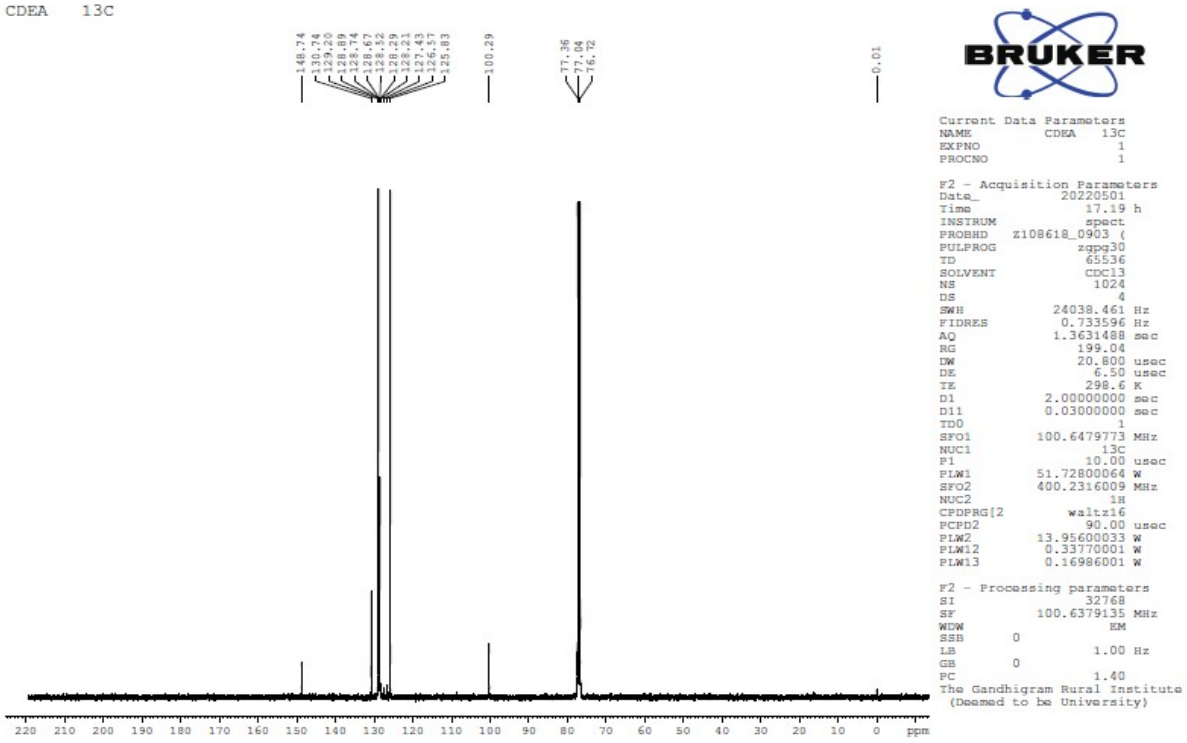


Figure 29. Mass spectra of compound CDEA

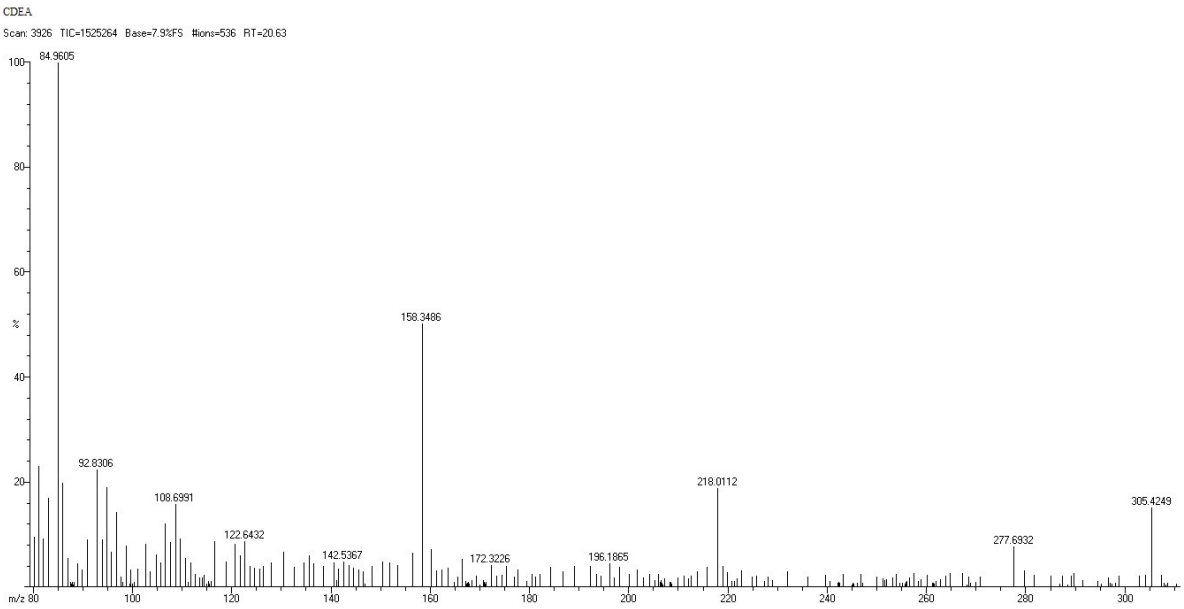
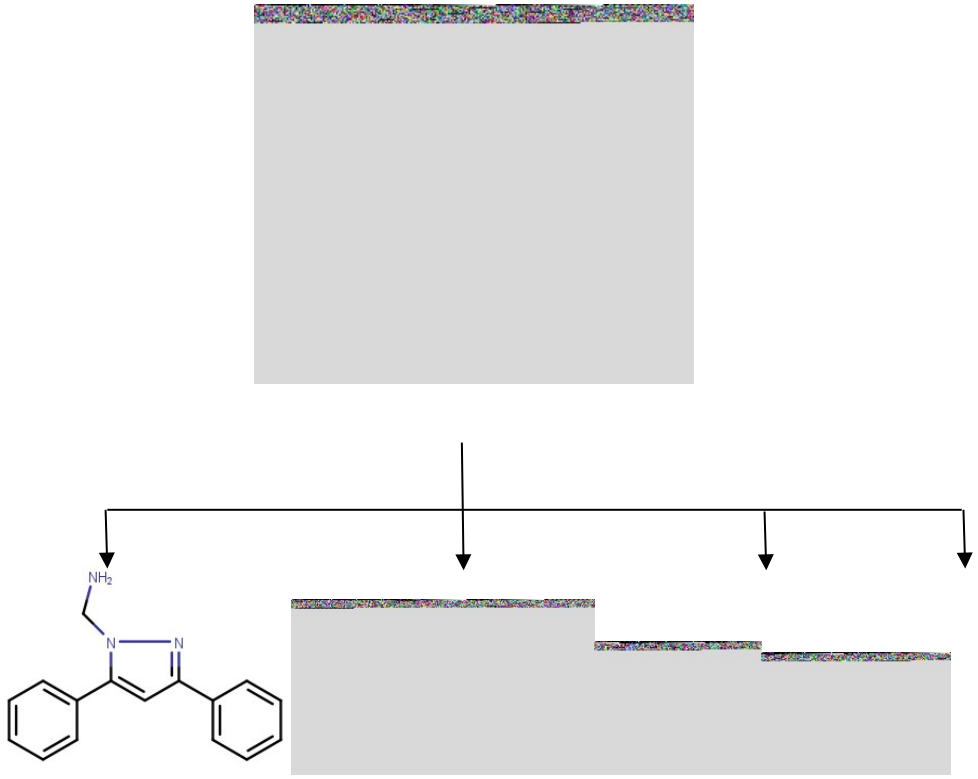


Figure 30. Mass fragmentation of compound CDPA



(m/z+)-247 **(m/z+5)-200** **(m/z-5)-107** **(m/z-4)-93**

Figure 31. IR spectra of compound CDIPA

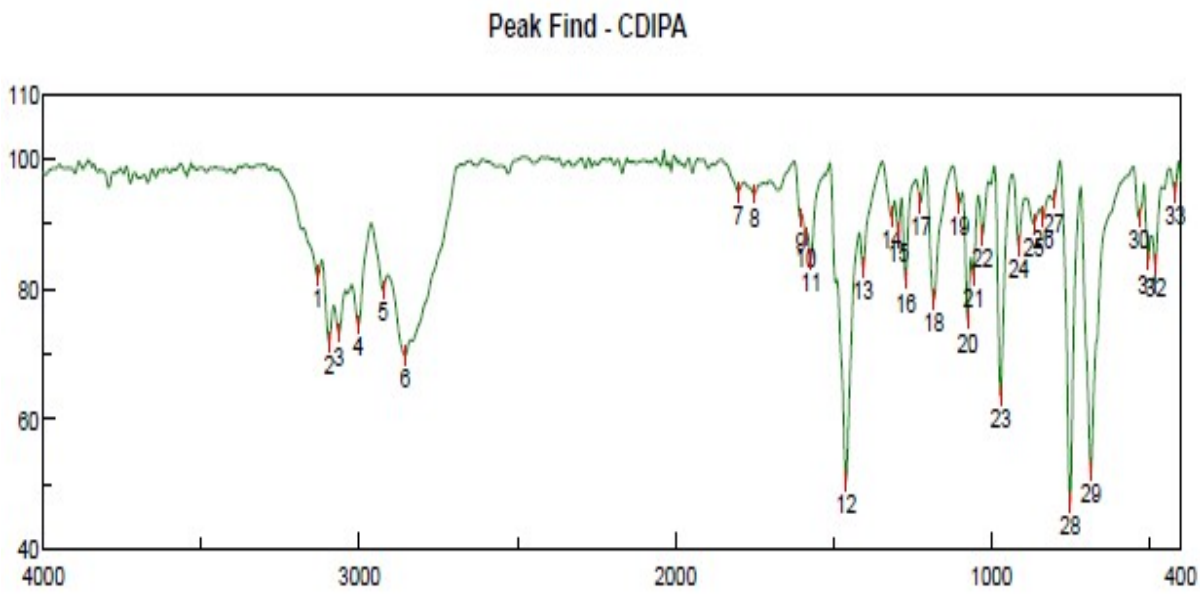


Figure 32. H1 spectra of compound CDIPA

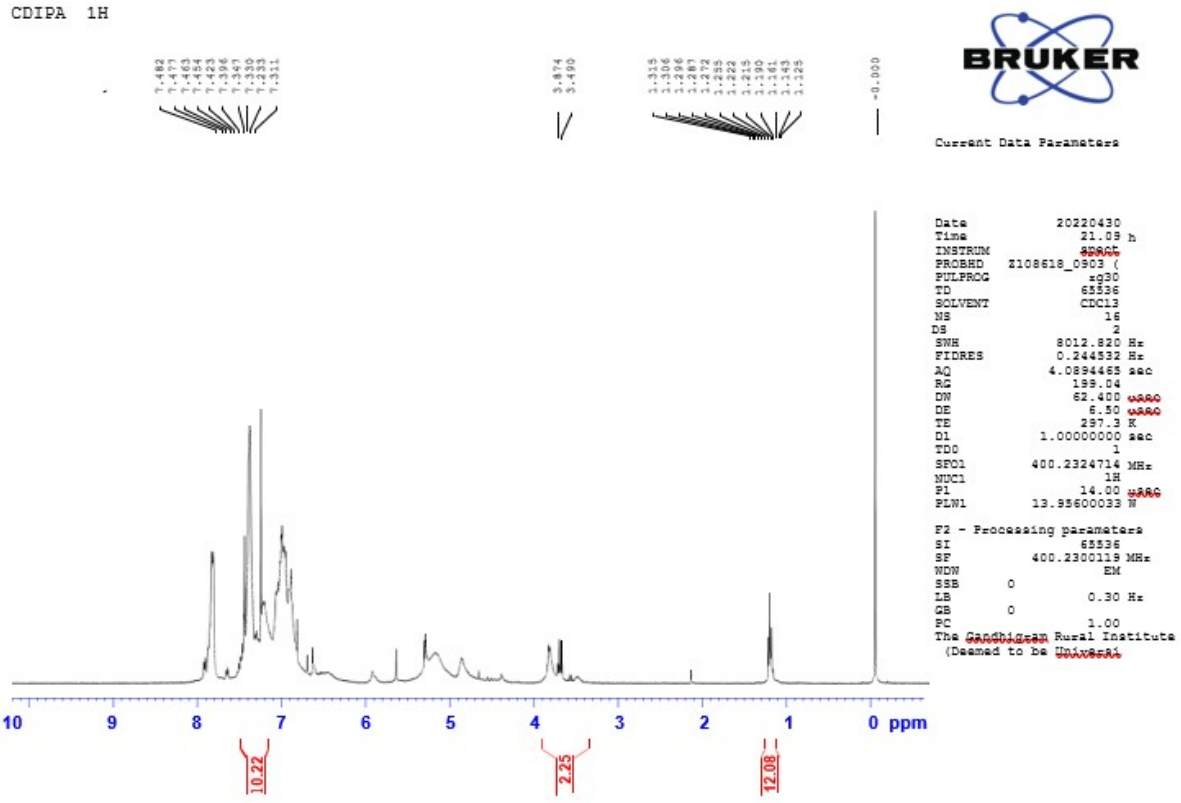


Figure 33. C13 spectra of compound CDIPA

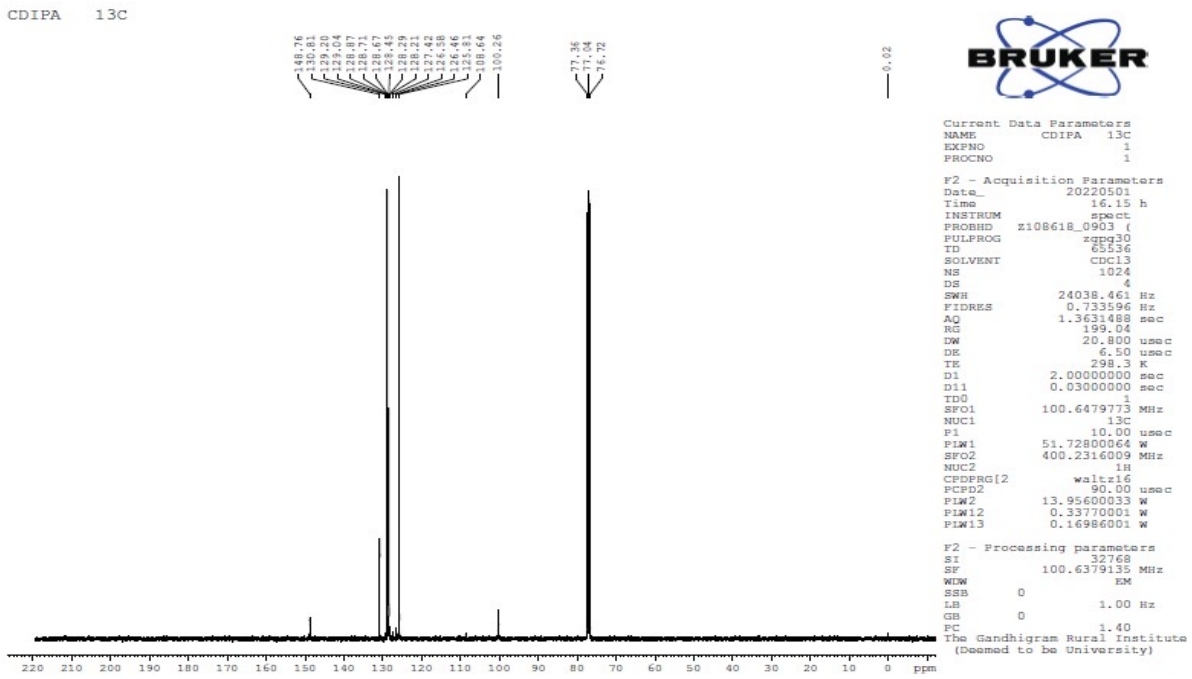


Figure 34. Mass spectra of compound CDIPA

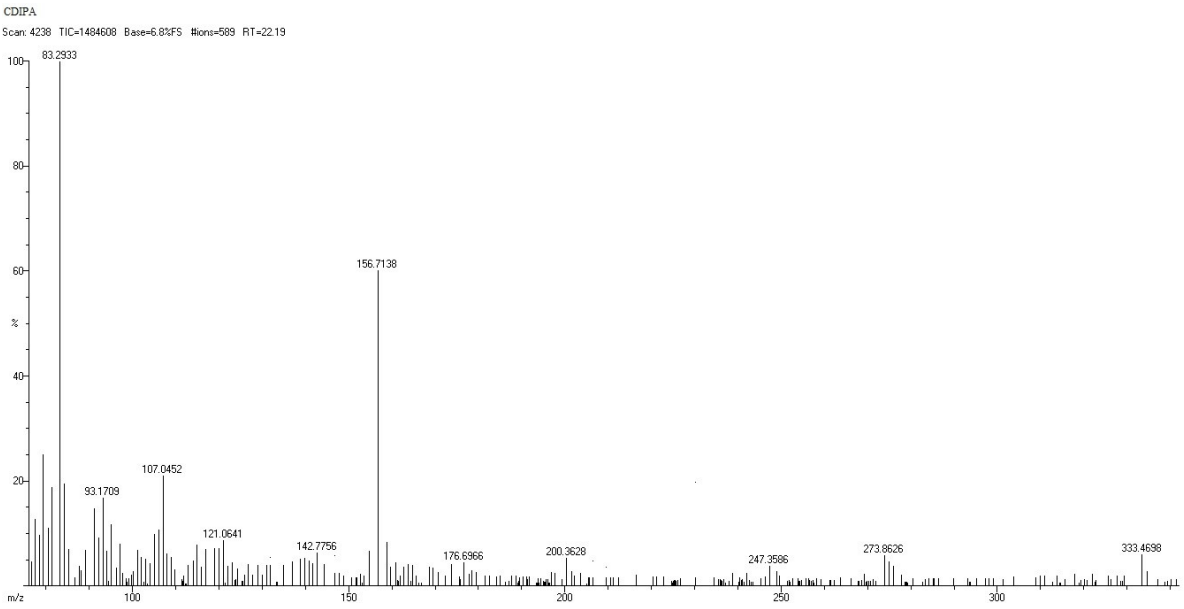


Figure 34. Graphical correlation of % viability with concentration µg/ml of the synthesized compounds. (X-concentration in µg/ml and Y-% viability)

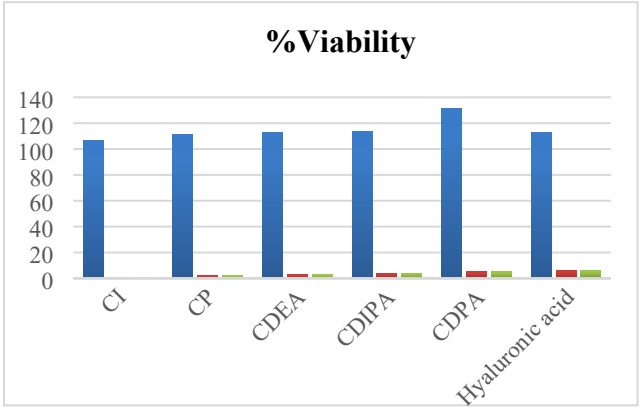


Figure 35. Effect of test drug (CI) on wound contraction