Supplementary Data

Structural and biological evaluation of halogen derivatives of 1,9-pyrazoloanthrones towards the design of specific potent inhibitor of c-Jun-N-terminal kinase (JNK)

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^{1}H and ^{13}C NMR Spectra of Anthrapyrazolone halogen derivatives

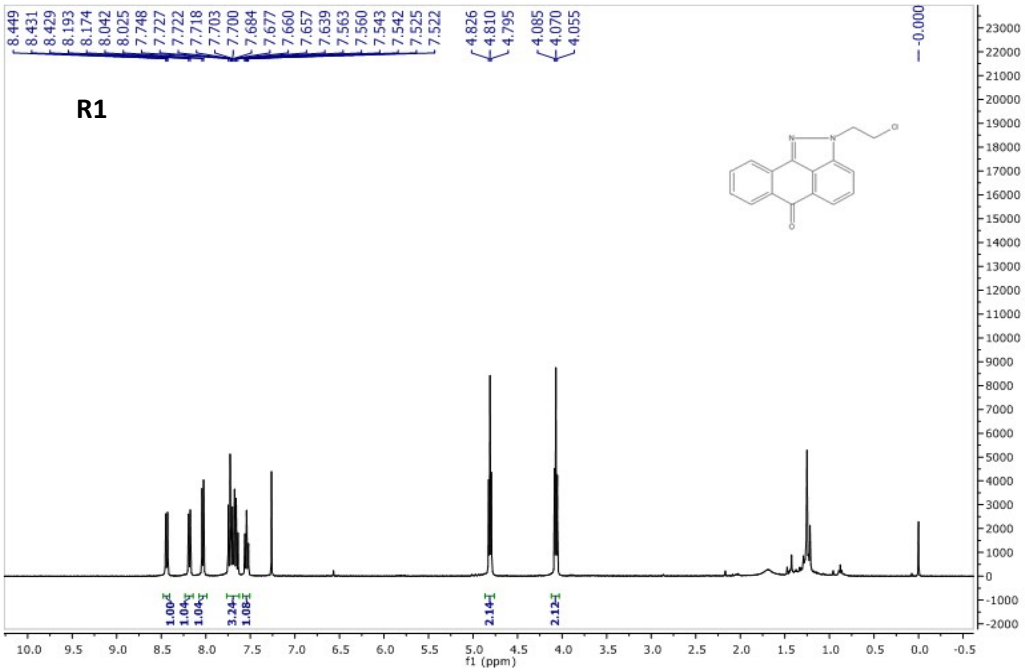


Fig. S1a ^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **R1**.

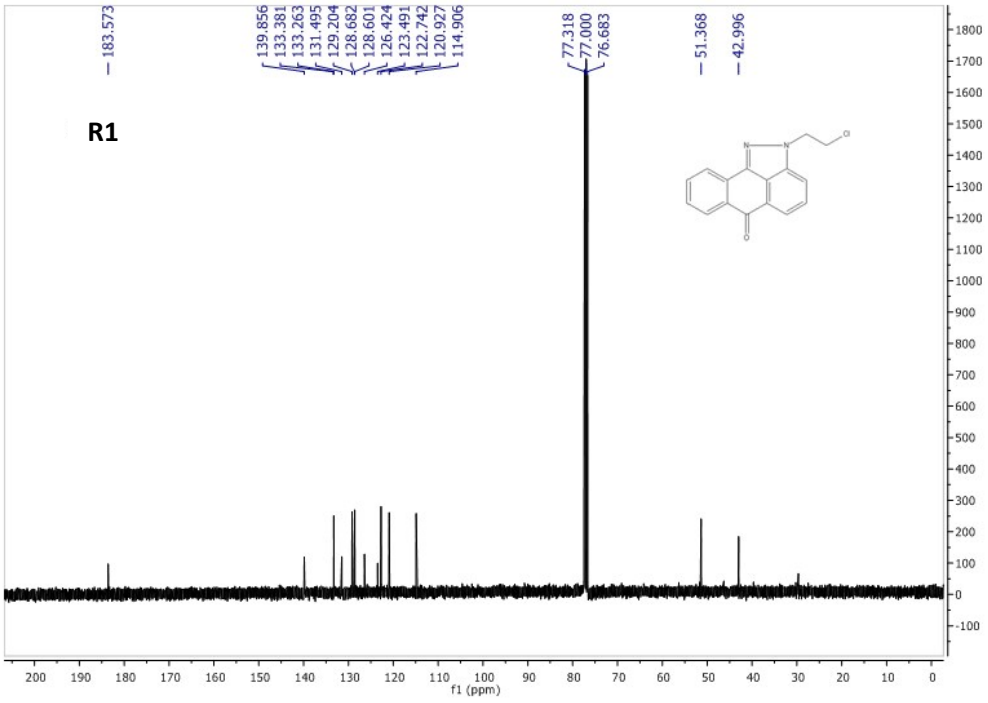


Fig. S1b ^{13}C NMR (100 MHz, $CDCl_3$) spectra of compound **R1**.

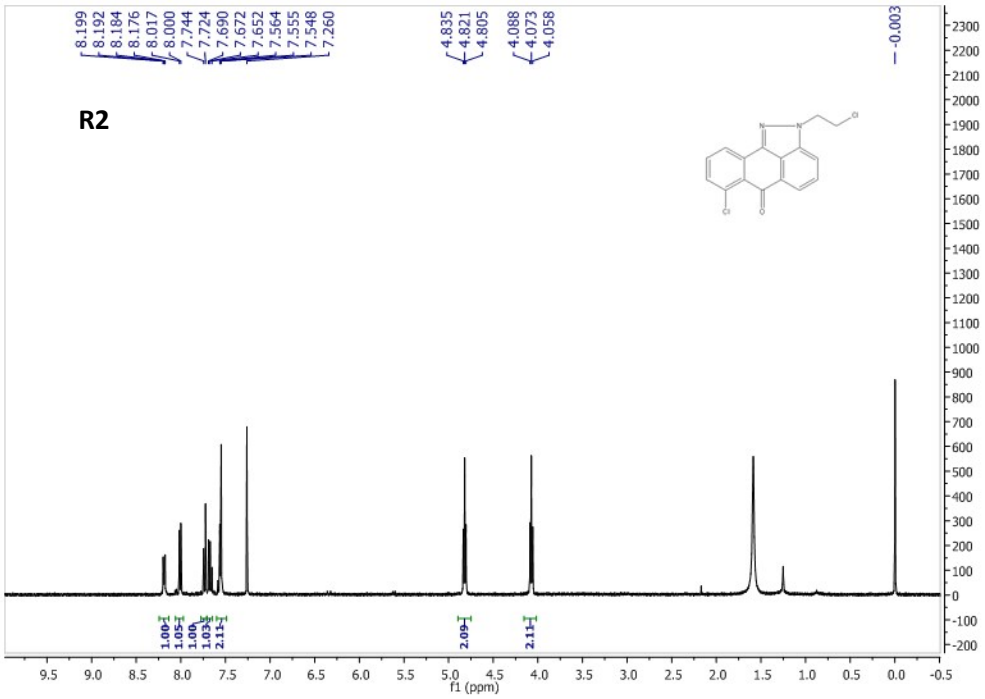


Fig. S1c ^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **R2**.

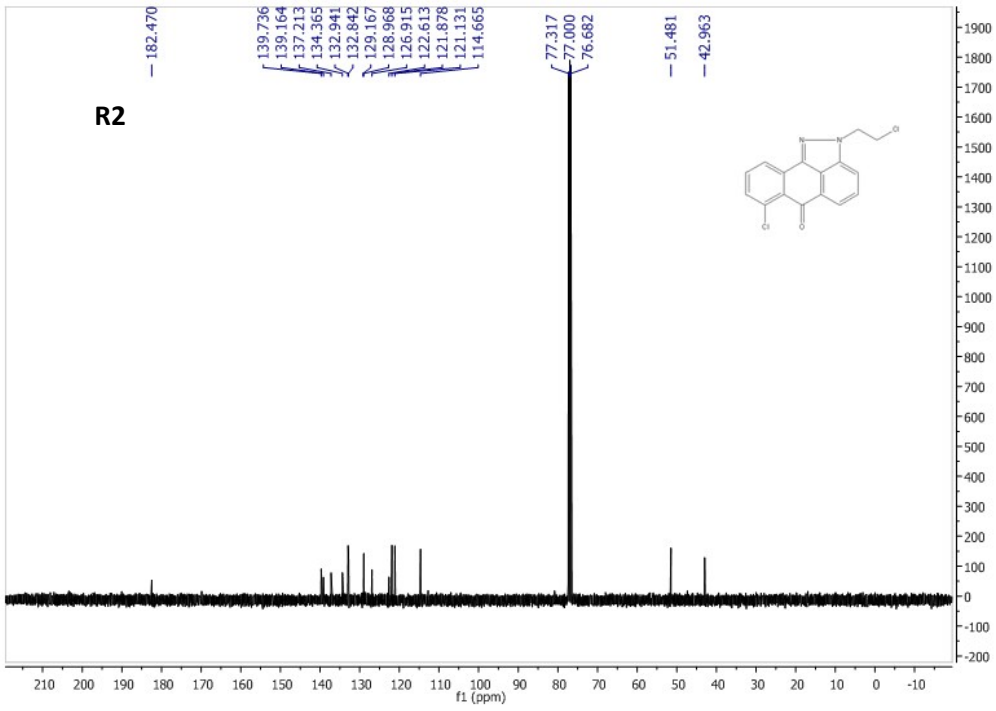


Fig. S1d ^{13}C NMR (100 MHz, $CDCl_3$) spectra of compound **R2**.

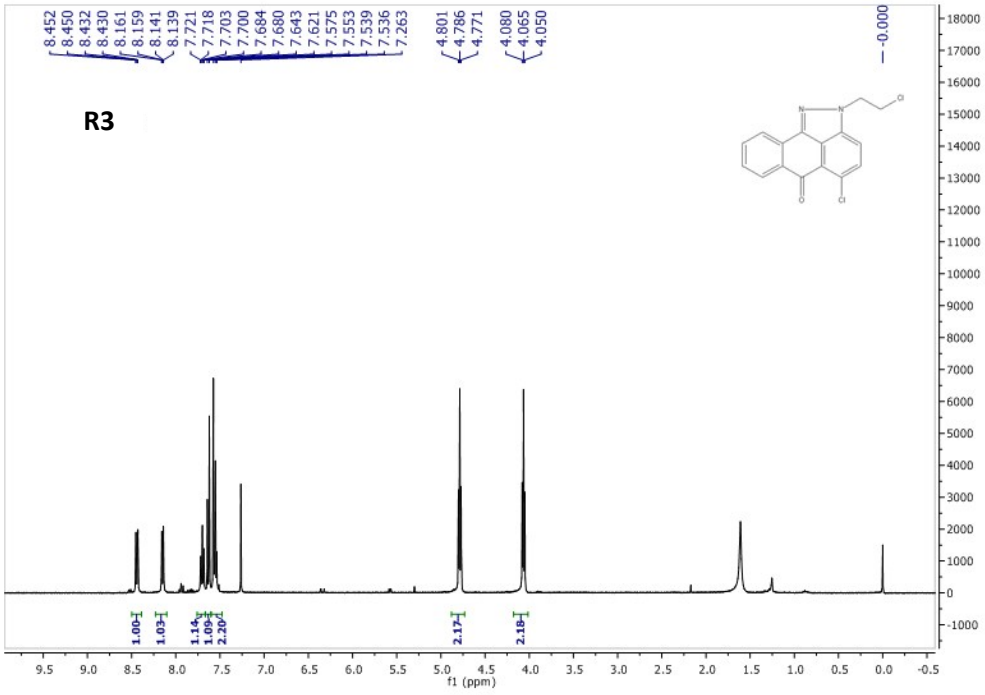


Fig. S1e ^{1}H NMR (400 MHz, $CDCl_3$) spectra of compound **R3**.

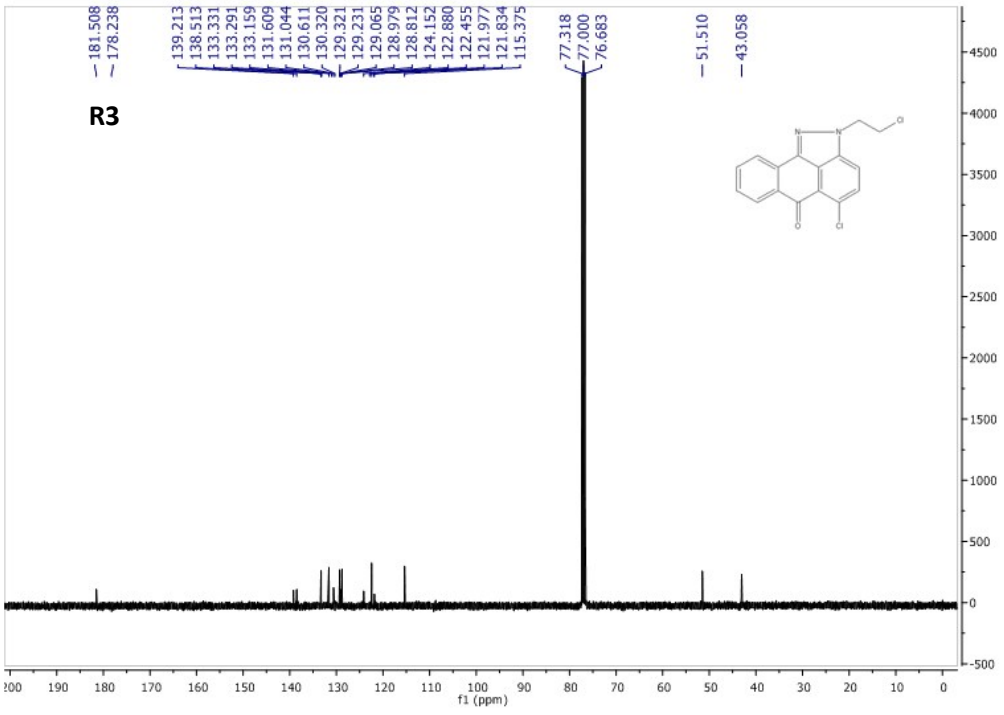


Fig. S1f ^{13}C NMR (100 MHz, $CDCl_3$) spectra of compound **R3**.

HR-MS

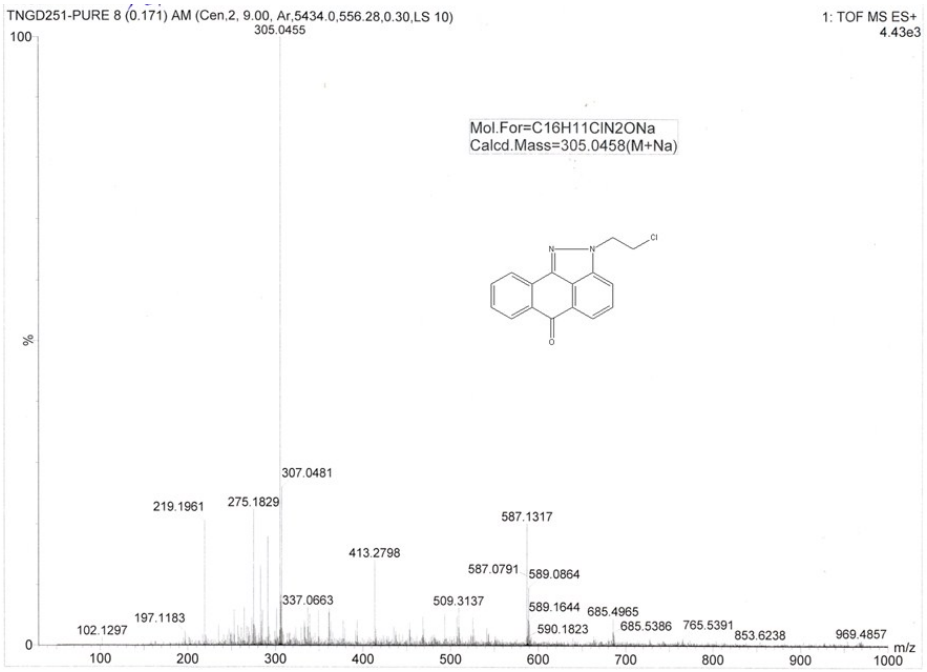


Fig. S1g HR-MS of **R1**

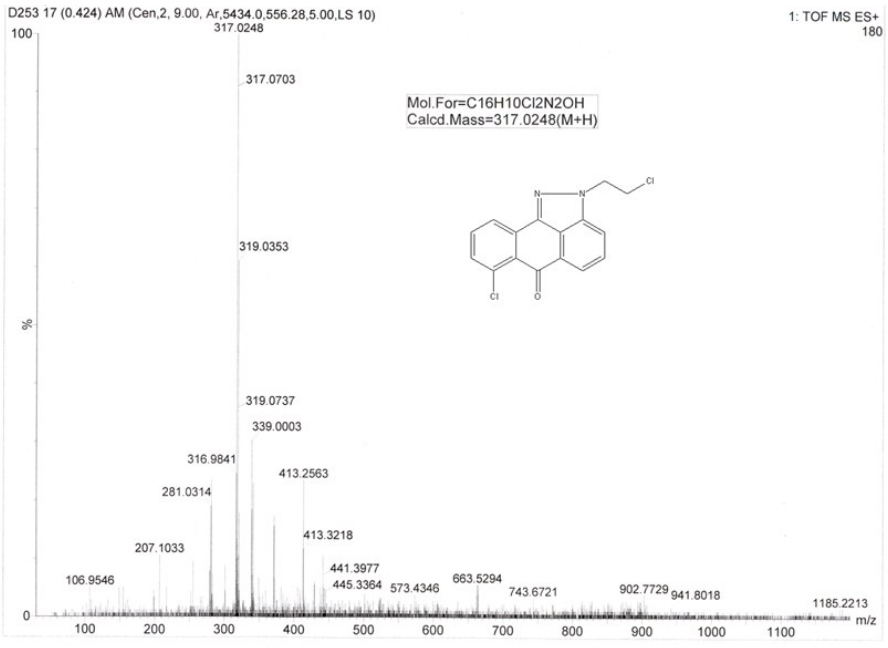


Fig. S1h HR-MS of **R2**

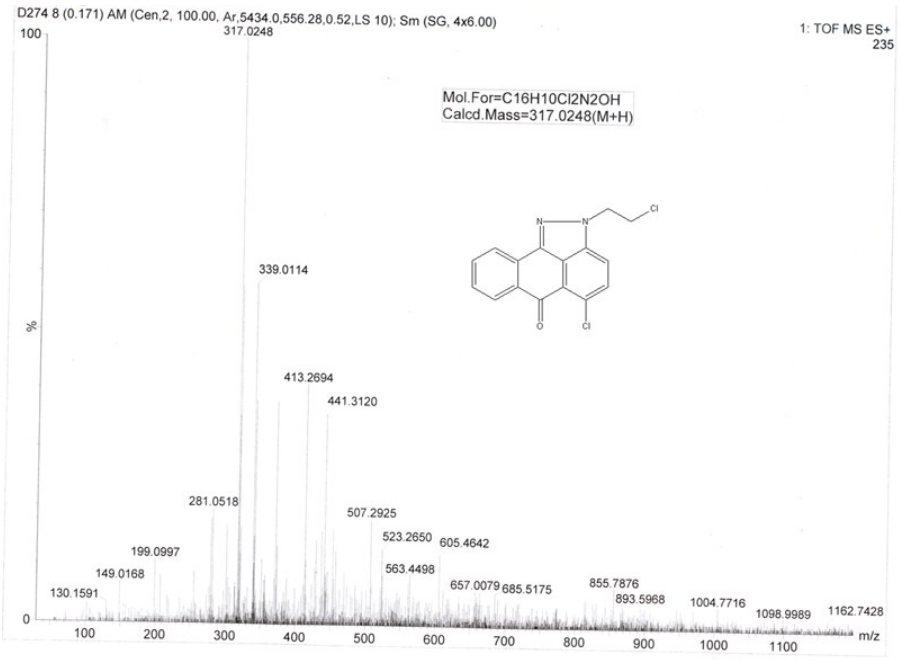


Fig. S1i HR-MS of **R3**

Computational alanine scanning

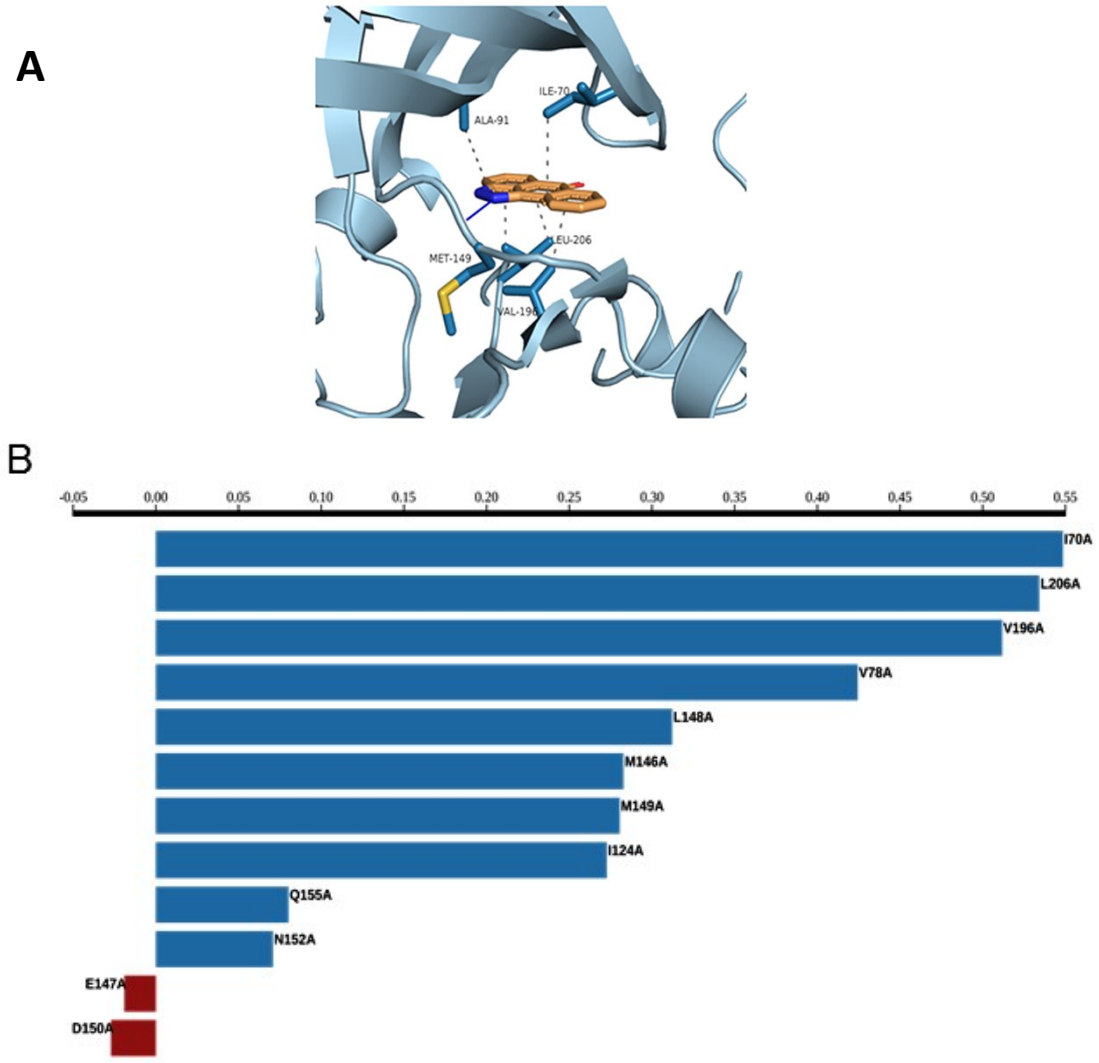
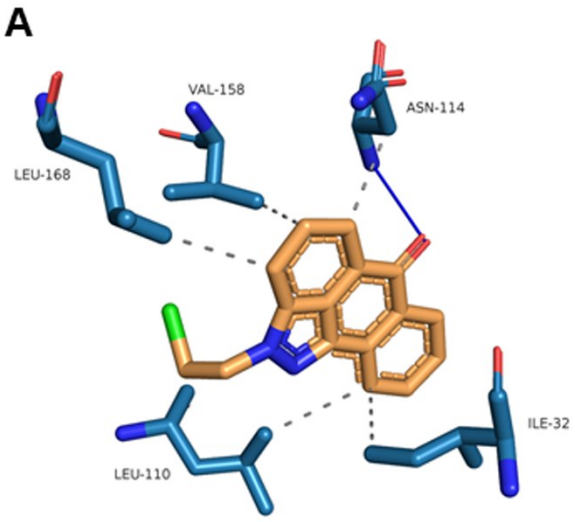


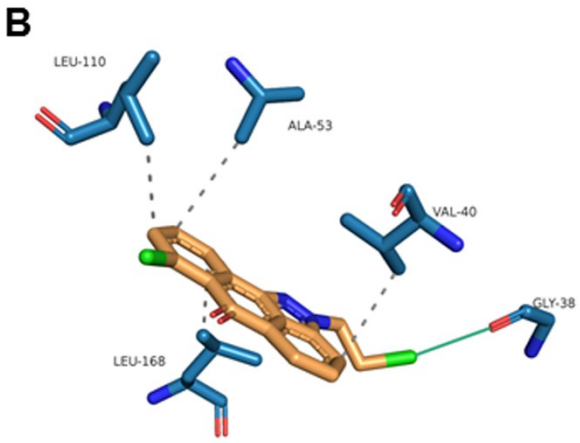
Figure S2 Analysis of the protein (JNK3) and ligand (SP600125) interaction depicts the interacting residues at the active site. **(A)** Dotted lines are hydrophobic interactions and hydrogen bond is represented by blue line. The ligand interacts with the protein predominantly by hydrophobic interactions. (**B**) The ΔΔG values, depicting the loss in the binding energy between JNK3 and SP600125 because of alanine mutations are shown in Fig 2B. This plot ranks the important residues for protein ligand interaction.

Protein (JNK1/2/3), and Ligand (R1/R2/R3) interactions obtained from PLIP server

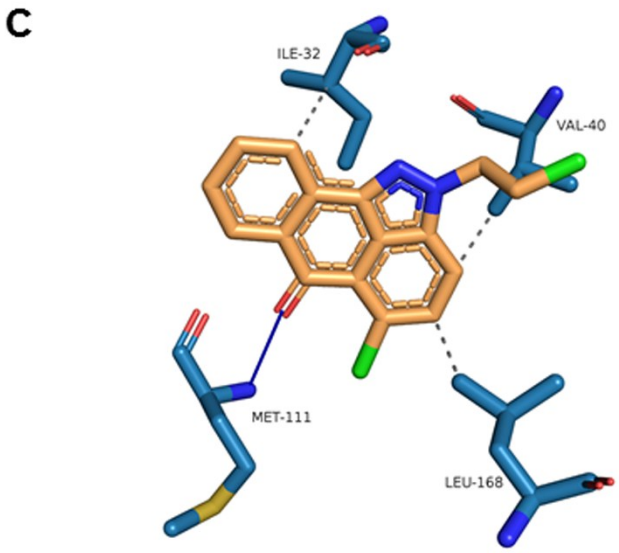
a.)



R1

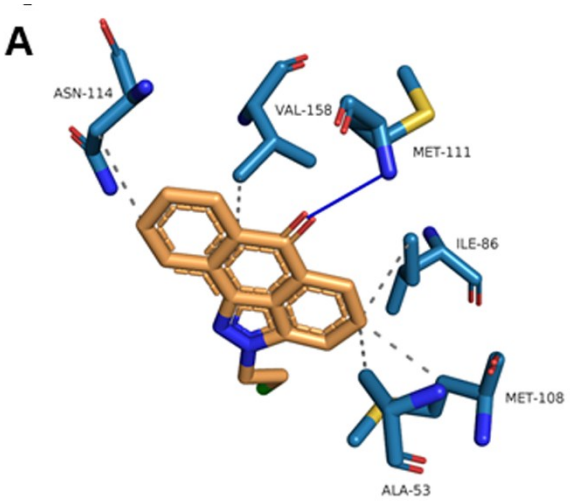


R2

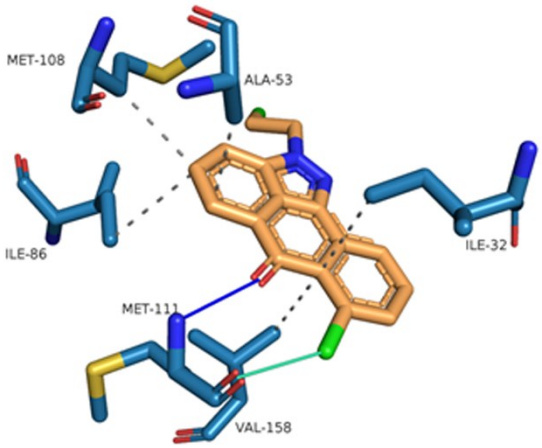


R3

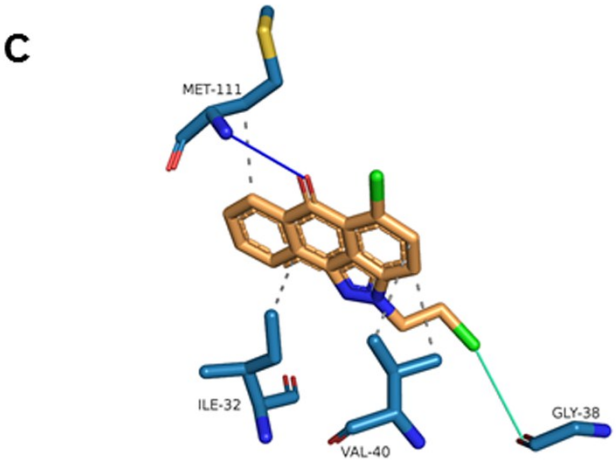
b.)


A
ASN-114
VAL-158
MET-111
ILE-86
MET-108
ALA-53

R1


B
MET-108
ALA-53
ILE-86
ILE-32
MET-111
VAL-158

R2


C
MET-111
ILE-32
VAL-40
GLY-38

R3

c.)

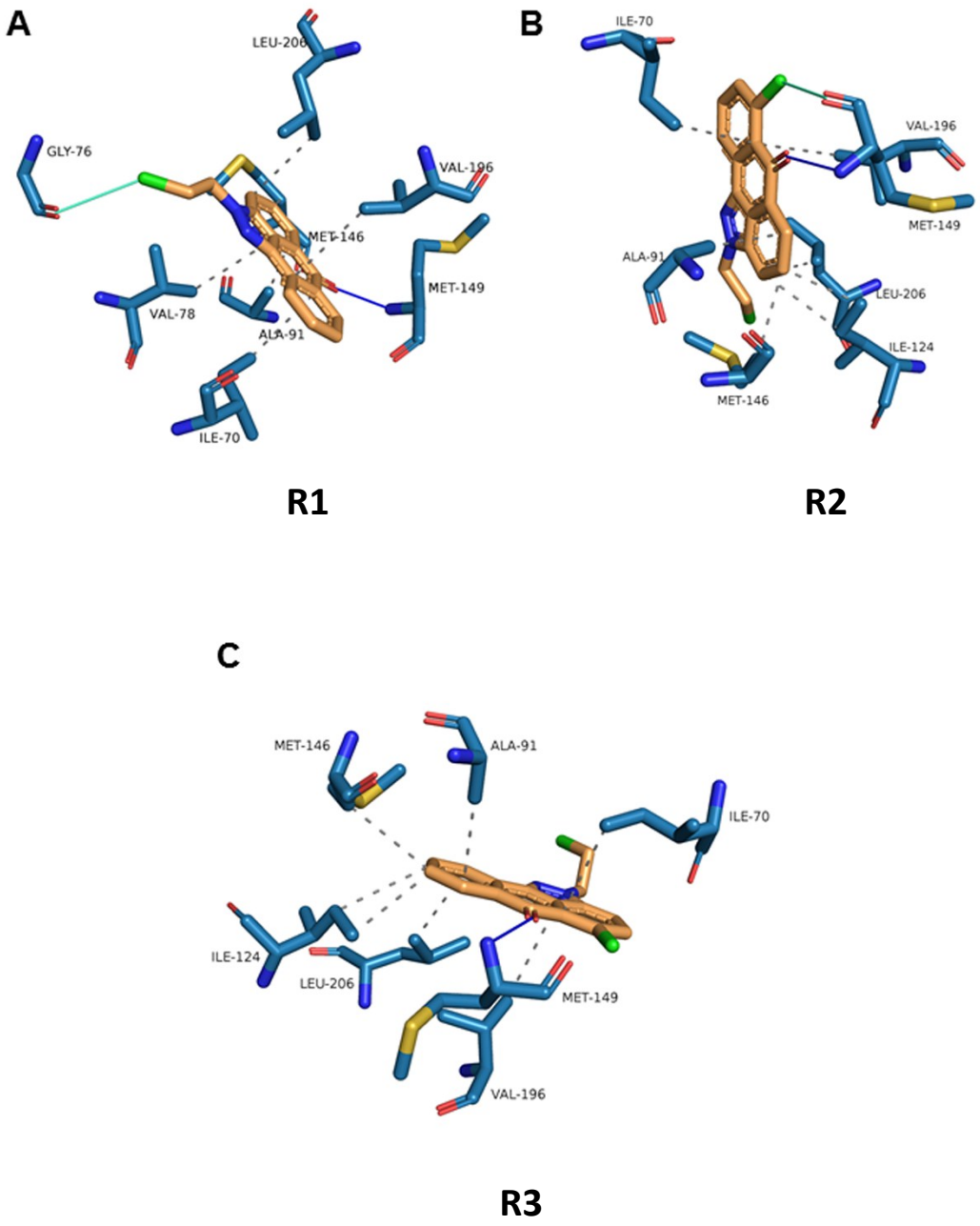


Fig. S3a–S3c shows the interactions between JNK1:R1/R2/R3, JNK2:R1/R2/R3 and JNK3:R1/R2/R3 respectively. The structures are generated by docking. The structure corresponding to the lowest binding energy from the ensemble is taken in each case. The dotted lines are hydrophobic interactions, the green lines depict hydrogen bonds and halogen bonds are represented by blue lines.

Table S1

Gene Primers

S. No.	Gene (mouse)	Primer sequence
1	*Ccl2* forward	5’-taaaaacctggatcggaaccaaa-3’
	Ccl2 reverse	5’-gcattagcttcagatttacgggt-3’
2	*Ccl4* forward	5’-ttcctgctgtttctcttacacct-3’
	Ccl4 reverse	5’-ctgtctgcctcttttggtcag-3’
3	*Ccl5* forward	5’-ttccctgtcatcgcttgctct-3’
	Ccl5 reverse	5’-cggatggagatgccgatttt-3’
4	*Ccl11* forward	5’-gaatcaccaacaacagatgcac-3’
	Ccl11 reverse	5’-atcctggacccacttcttctt-3’
5	*Ccl12* forward	5’-atttccacacttctatgcctcct-3’
	Ccl12 reverse	5’-atccagtatggtcctgaagatca-3’
6	*Cxcl5* forward	5’-gttccatctcgccattcatgc-3’
	Cxcl5 reverse	5’-gcggctatgactgaggaagg-3’
7	*Cxcl9* forward	5’-tcttttcctcttgggcatcatctt-3’
	Cxcl9 reverse	5’-tttccccctcttttgctttttctt-3’
8	*Cxcl10* forward	5’-ccaagtgctgccgtcattttc-3’
	Cxcl10 reverse	5’-tccctatggccctcattctca-3’

9	*Cxcl11* forward	5’-ggcttccttatgttcaaacaggg-3’
	Cxcl11 reverse	5’-gccgttactcgggtaaattaca-3’
10	*Gapdh* forward	5’-gagccaaacgggtcatcatct-3’
	Gapdh reverse	5’-gaggggccatccacagtctt-3’