

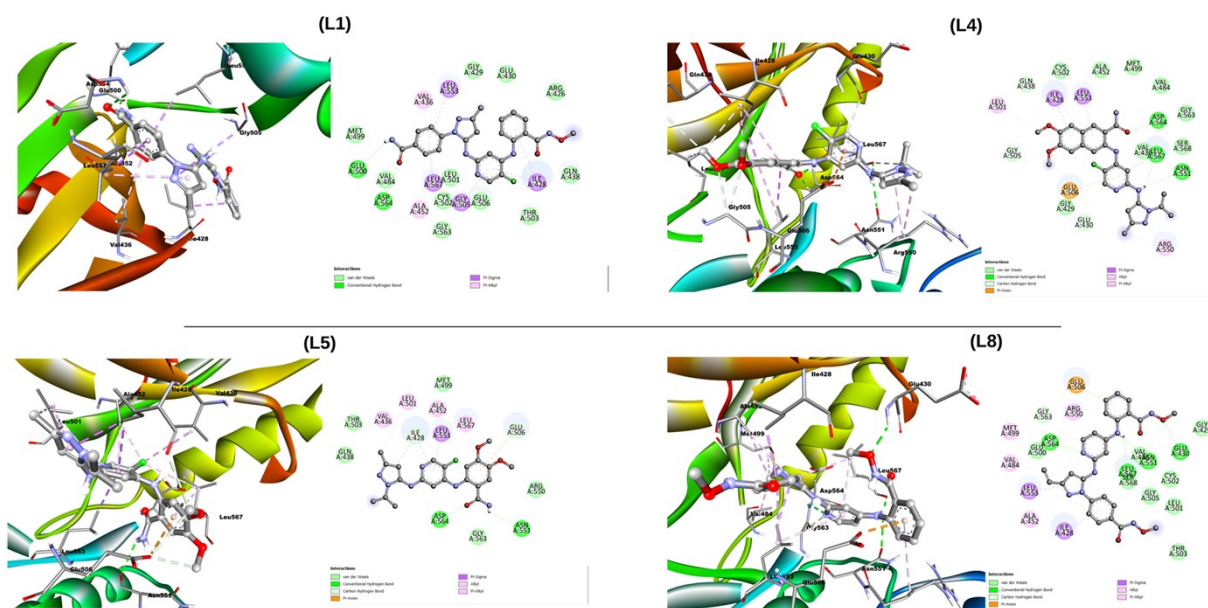


Figure S1: 2D and 3D visualization of the interactions of newly designed molecules and the FAK protein

Table S1: FAK protein interactions with the investigated ligands

compo und	name	parent	distan ce	category	types	from	from chemistry	to	to chemistr y	Affinity (kcal/mol)
L1	A:ASP564:HN - d:***1:O	Ligand Non-bond Monitor	2,989 91	Hydrogen Bond	Conventional Hydrogen Bond	A:ASP564: HN	H-Donor	d:***1:O	H- Acceptor	-9,1
	d:***1:H - A:GLU500:O	Ligand Non-bond Monitor	2,441 82	Hydrogen Bond	Conventional Hydrogen Bond	d:***1:H	H-Donor	A:GLU500: O	H- Acceptor	
	A:ILE428:CG2 - d:***1	Ligand Non-bond Monitor	3,871 94	Hydrophob ic	Pi-Sigma	A:ILE428: CG2	C-H	d:***1	Pi- Orbitals	
	A:ILE428:CD1 - d:***1	Ligand Non-bond Monitor	3,691 95	Hydrophob ic	Pi-Sigma	A:ILE428: CD1	C-H	d:***1	Pi- Orbitals	
	A:GLY505:CA - d:***1	Ligand Non-bond Monitor	3,917 48	Hydrophob ic	Pi-Sigma	A:GLY505: CA	C-H	d:***1	Pi- Orbitals	
	A:LEU553:CD1 - d:***1	Ligand Non-bond Monitor	3,854 75	Hydrophob ic	Pi-Sigma	A:LEU553: CD1	C-H	d:***1	Pi- Orbitals	
	A:LEU567:CD1 - d:***1	Ligand Non-bond Monitor	3,608 35	Hydrophob ic	Pi-Sigma	A:LEU567: CD1	C-H	d:***1	Pi- Orbitals	
	d:***1 - A:LEU567	Ligand Non-bond Monitor	5,432 9	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:LEU567	Alkyl	
	d:***1 - A:VAL436	Ligand Non-bond Monitor	5,368 64	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:VAL436	Alkyl	
	d:***1 - A:ALA452	Ligand Non-bond Monitor	4,945 86	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:ALA452	Alkyl	
L2	d:***1:N - A:GLU506:OE1	Ligand Non-bond Monitor	3,294 69	Electrostat ic	Attractive Charge	d:***1:N	Positive	A:GLU506: OE1	Negative	-9,3
	A:ASP564:HN - d:***1:O	Ligand Non-bond Monitor	2,275 62	Hydrogen Bond	Conventional Hydrogen Bond	A:ASP564: HN	H-Donor	d:***1:O	H- Acceptor	
	d:***1:H - A:ILE428:O	Ligand Non-bond Monitor	2,669 91	Hydrogen Bond	Conventional Hydrogen Bond	d:***1:H	H-Donor	A:ILE428: O	H- Acceptor	
	d:***1:C - A:ASN551:OD1	Ligand Non-bond Monitor	3,573 7	Hydrogen Bond	Carbon Hydrogen Bond	d:***1:C	H-Donor	A:ASN551: OD1	H- Acceptor	
	d:***1:C - A:ASP564:O	Ligand Non-bond Monitor	3,610 35	Hydrogen Bond	Carbon Hydrogen Bond	d:***1:C	H-Donor	A:ASP564: O	H- Acceptor	
	d:***1:C - A:SER568:OG	Ligand Non-bond Monitor	3,201 2	Hydrogen Bond	Carbon Hydrogen Bond	d:***1:C	H-Donor	A:SER568: OG	H- Acceptor	
	A:LEU553:CD1 -	Ligand Non-bond	3,645	Hydrophob	Pi-Sigma	A:LEU553:	C-H	d:***1	Pi-	

	d:***1	Monitor	24	ic		CD1			Orbitals	
	A:LEU567:CD1 - d:***1	Ligand Non-bond Monitor	3,618 23	Hydrophobic	Pi-Sigma	A:LEU567:CD1	C-H	d:***1	Pi-Orbitals	
	d:***1:C - A:LEU501	Ligand Non-bond Monitor	4,376 8	Hydrophobic	Alkyl	d:***1:C	Alkyl	A:LEU501	Alkyl	
	d:***1 - A:ILE428	Ligand Non-bond Monitor	5,488 13	Hydrophobic	Pi-Alkyl	d:***1	Pi-Orbitals	A:ILE428	Alkyl	
	d:***1 - A:ALA452	Ligand Non-bond Monitor	4,277 75	Hydrophobic	Pi-Alkyl	d:***1	Pi-Orbitals	A:ALA452	Alkyl	
	d:***1 - A:LEU501	Ligand Non-bond Monitor	5,304 4	Hydrophobic	Pi-Alkyl	d:***1	Pi-Orbitals	A:LEU501	Alkyl	
	d:***1 - A:CYS502	Ligand Non-bond Monitor	5,161 32	Hydrophobic	Pi-Alkyl	d:***1	Pi-Orbitals	A:CYS502	Alkyl	
	d:***1 - A:ILE428	Ligand Non-bond Monitor	4,455 46	Hydrophobic	Pi-Alkyl	d:***1	Pi-Orbitals	A:ILE428	Alkyl	
	d:***1 - A:LEU501	Ligand Non-bond Monitor	4,988 38	Hydrophobic	Pi-Alkyl	d:***1	Pi-Orbitals	A:LEU501	Alkyl	
	d:***1 - A:ILE428	Ligand Non-bond Monitor	4,634 26	Hydrophobic	Pi-Alkyl	d:***1	Pi-Orbitals	A:ILE428	Alkyl	
	d:***1 - A:VAL436	Ligand Non-bond Monitor	4,407 76	Hydrophobic	Pi-Alkyl	d:***1	Pi-Orbitals	A:VAL436	Alkyl	
L3	A:ASP564:HN - d:***1:O	Ligand Non-bond Monitor	2,236 18	Hydrogen Bond	Conventional Hydrogen Bond	A:ASP564:HN	H-Donor	d:***1:O	H-Acceptor	-8,6
	d:***1:H - A:ASN551:OD1	Ligand Non-bond Monitor	2,312 25	Hydrogen Bond	Conventional Hydrogen Bond	d:***1:H	H-Donor	A:ASN551:OD1	H-Acceptor	
	d:***1:C - A:GLU430:O	Ligand Non-bond Monitor	3,409 39	Hydrogen Bond	Carbon Hydrogen Bond	d:***1:C	H-Donor	A:GLU430:O	H-Acceptor	
	A:LEU553:CD1 - d:***1	Ligand Non-bond Monitor	3,503 28	Hydrophobic	Pi-Sigma	A:LEU553:CD1	C-H	d:***1	Pi-Orbitals	
	A:ALA452 - d:***1	Ligand Non-bond Monitor	3,917 12	Hydrophobic	Alkyl	A:ALA452	Alkyl	d:***1	Alkyl	
	A:VAL484 - d:***1	Ligand Non-bond Monitor	4,276 46	Hydrophobic	Alkyl	A:VAL484	Alkyl	d:***1	Alkyl	
	d:***1 - A:MET499	Ligand Non-bond Monitor	4,851 92	Hydrophobic	Alkyl	d:***1	Alkyl	A:MET499	Alkyl	
	d:***1 - A:LEU553	Ligand Non-bond Monitor	5,252 51	Hydrophobic	Alkyl	d:***1	Alkyl	A:LEU553	Alkyl	
	d:***1 - A:LEU567	Ligand Non-bond	4,394	Hydrophobic	Pi-Alkyl	d:***1	Pi-Orbitals	A:LEU567	Alkyl	

		Monitor	88	ic						
	d:***1 - A:ALA452	Ligand Non-bond Monitor	5,157 68	Hydrophobic	Pi-Alkyl	d:***1	Pi-Orbitals	A:ALA452	Alkyl	
L4	A:ASP564:HN - d:***1:O	Ligand Non-bond Monitor	2,057 64	Hydrogen Bond	Conventional Hydrogen Bond	A:ASP564: HN	H-Donor	d:***1:O	H-Acceptor	8,6
	d:***1:H - d:***1:O	Ligand Non-bond Monitor	2,036 5	Hydrogen Bond	Conventional Hydrogen Bond	d:***1:H	H-Donor	d:***1:O	H-Acceptor	
	d:***1:H - A:ASN551:OD1	Ligand Non-bond Monitor	2,427 51	Hydrogen Bond	Conventional Hydrogen Bond	d:***1:H	H-Donor	A:ASN551: OD1	H-Acceptor	
	d:***1:H - A:LEU567:O	Ligand Non-bond Monitor	2,710 08	Hydrogen Bond	Conventional Hydrogen Bond	d:***1:H	H-Donor	A:LEU567: O	H-Acceptor	
	A:GLY505:CA - d:***1:O	Ligand Non-bond Monitor	3,258 14	Hydrogen Bond	Carbon Hydrogen Bond	A:GLY505: CA	H-Donor	d:***1:O	H-Acceptor	
	A:GLY505:CA - d:***1:O	Ligand Non-bond Monitor	3,552 68	Hydrogen Bond	Carbon Hydrogen Bond	A:GLY505: CA	H-Donor	d:***1:O	H-Acceptor	
	d:***1:C - A:GLN438:OE1	Ligand Non-bond Monitor	3,743 63	Hydrogen Bond	Carbon Hydrogen Bond	d:***1:C	H-Donor	A:GLN438: OE1	H-Acceptor	
	d:***1:C - A:GLU430:O	Ligand Non-bond Monitor	3,275 43	Hydrogen Bond	Carbon Hydrogen Bond	d:***1:C	H-Donor	A:GLU430: O	H-Acceptor	
	d:***1:C - A:LEU567:O	Ligand Non-bond Monitor	3,411 95	Hydrogen Bond	Carbon Hydrogen Bond	d:***1:C	H-Donor	A:LEU567: O	H-Acceptor	
	A:GLU506:OE2 - d:***1	Ligand Non-bond Monitor	4,622 3	Electrostatic	Pi-Anion	A:GLU506: OE2	Negative	d:***1	Pi-Orbitals	
	A:ILE428:CD1 - d:***1	Ligand Non-bond Monitor	3,576 46	Hydrophobic	Pi-Sigma	A:ILE428: CD1	C-H	d:***1	Pi-Orbitals	
	A:LEU553:CD1 - d:***1	Ligand Non-bond Monitor	3,990 36	Hydrophobic	Pi-Sigma	A:LEU553: CD1	C-H	d:***1	Pi-Orbitals	
	A:LEU567:CB - d:***1	Ligand Non-bond Monitor	3,851 94	Hydrophobic	Pi-Sigma	A:LEU567: CB	C-H	d:***1	Pi-Orbitals	
	d:***1:C - A:ILE428	Ligand Non-bond Monitor	4,351 96	Hydrophobic	Alkyl	d:***1:C	Alkyl	A:ILE428	Alkyl	
	d:***1:C - A:ILE428	Ligand Non-bond Monitor	4,100 65	Hydrophobic	Alkyl	d:***1:C	Alkyl	A:ILE428	Alkyl	
	d:***1:C - A:LEU501	Ligand Non-bond Monitor	4,381 77	Hydrophobic	Alkyl	d:***1:C	Alkyl	A:LEU501	Alkyl	
	d:***1:C - A:ARG550	Ligand Non-bond Monitor	4,000 69	Hydrophobic	Alkyl	d:***1:C	Alkyl	A:ARG550	Alkyl	
	d:***1 - A:ILE428	Ligand Non-bond	5,312	Hydrophobic	Pi-Alkyl	d:***1	Pi-Orbitals	A:ILE428	Alkyl	

		Monitor	3	ic						
	d:***1 - A:LEU553	Ligand Non-bond Monitor	5,188 83	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:LEU553	Alkyl	
	d:***1 - A:ARG550	Ligand Non-bond Monitor	4,212 23	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:ARG550	Alkyl	
L5	A:ASP564:HN - d:***1:O	Ligand Non-bond Monitor	1,975 29	Hydrogen Bond	Conventional Hydrogen Bond	A:ASP564: HN	H-Donor	d:***1:O	H- Acceptor	-7,9
	d:***1:H - A:ASN551:O	Ligand Non-bond Monitor	2,971 83	Hydrogen Bond	Conventional Hydrogen Bond	d:***1:H	H-Donor	A:ASN551: O	H- Acceptor	
	d:***1:C - A:GLU506:OE2	Ligand Non-bond Monitor	3,648 52	Hydrogen Bond	Carbon Hydrogen Bond	d:***1:C	H-Donor	A:GLU506: OE2	H- Acceptor	
	d:***1:C - A:ILE428:O	Ligand Non-bond Monitor	3,577 59	Hydrogen Bond	Carbon Hydrogen Bond	d:***1:C	H-Donor	A:ILE428: O	H- Acceptor	
	d:***1:C - A:GLU506:OE2	Ligand Non-bond Monitor	3,456 78	Hydrogen Bond	Carbon Hydrogen Bond	d:***1:C	H-Donor	A:GLU506: OE2	H- Acceptor	
	A:GLU506:OE2 - d:***1	Ligand Non-bond Monitor	4,268 95	Electrostat ic	Pi-Anion	A:GLU506: OE2	Negative	d:***1	Pi- Orbitals	
	A:ILE428:CD1 - d:***1	Ligand Non-bond Monitor	3,913 43	Hydrophob ic	Pi-Sigma	A:ILE428: CD1	C-H	d:***1	Pi- Orbitals	
	A:ILE428:CD1 - d:***1	Ligand Non-bond Monitor	3,834 55	Hydrophob ic	Pi-Sigma	A:ILE428: CD1	C-H	d:***1	Pi- Orbitals	
	A:LEU553:CD1 - d:***1	Ligand Non-bond Monitor	3,783 63	Hydrophob ic	Pi-Sigma	A:LEU553: CD1	C-H	d:***1	Pi- Orbitals	
	A:ALA452 - d:***1:C17	Ligand Non-bond Monitor	3,624 01	Hydrophob ic	Alkyl	A:ALA452	Alkyl	d:***1:C17	Alkyl	
	d:***1:C17 - A:VAL436	Ligand Non-bond Monitor	4,821 41	Hydrophob ic	Alkyl	d:***1:C17	Alkyl	A:VAL436	Alkyl	
	d:***1:C17 - A:LEU567	Ligand Non-bond Monitor	4,876 79	Hydrophob ic	Alkyl	d:***1:C17	Alkyl	A:LEU567	Alkyl	
	d:***1:C - A:LEU501	Ligand Non-bond Monitor	4,284 98	Hydrophob ic	Alkyl	d:***1:C	Alkyl	A:LEU501	Alkyl	
	d:***1 - A:ALA452	Ligand Non-bond Monitor	4,412 3	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:ALA452	Alkyl	
	d:***1 - A:LEU567	Ligand Non-bond Monitor	4,372 11	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:LEU567	Alkyl	
	d:***1 - A:LEU501	Ligand Non-bond Monitor	5,322 76	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:LEU501	Alkyl	
L6	A:CYS502:HN -	Ligand Non-bond	1,993	Hydrogen	Conventional	A:CYS502:	H-Donor	d:***1:N	H-	-10

	d:***1:N	Monitor	04	Bond	Hydrogen Bond	HN			Acceptor	
	A:ASP564:HN - d:***1:O	Ligand Non-bond Monitor	2,140 71	Hydrogen Bond	Conventional Hydrogen Bond	A:ASP564: HN	H-Donor	d:***1:O	H- Acceptor	
	d:***1:H - A:CYS502:O	Ligand Non-bond Monitor	2,226 68	Hydrogen Bond	Conventional Hydrogen Bond	d:***1:H	H-Donor	A:CYS502: O	H- Acceptor	
	d:***1:H - d:***1:O	Ligand Non-bond Monitor	2,408 31	Hydrogen Bond	Conventional Hydrogen Bond	d:***1:H	H-Donor	d:***1:O	H- Acceptor	
	A:GLY563:CA - d:***1:O	Ligand Non-bond Monitor	3,404 46	Hydrogen Bond	Carbon Hydrogen Bond	A:GLY563: CA	H-Donor	d:***1:O	H- Acceptor	
	d:***1:C - A:GLU500:O	Ligand Non-bond Monitor	3,660 65	Hydrogen Bond	Carbon Hydrogen Bond	d:***1:C	H-Donor	A:GLU500: O	H- Acceptor	
	d:***1:C - A:ASN551:OD1	Ligand Non-bond Monitor	3,485 98	Hydrogen Bond	Carbon Hydrogen Bond	d:***1:C	H-Donor	A:ASN551: OD1	H- Acceptor	
	d:***1:C - A:ASP564:O	Ligand Non-bond Monitor	3,637 94	Hydrogen Bond	Carbon Hydrogen Bond	d:***1:C	H-Donor	A:ASP564: O	H- Acceptor	
	d:***1:C - A:SER568:OG	Ligand Non-bond Monitor	3,236 32	Hydrogen Bond	Carbon Hydrogen Bond	d:***1:C	H-Donor	A:SER568: OG	H- Acceptor	
	A:LEU553:CD1 - d:***1	Ligand Non-bond Monitor	3,562 96	Hydrophob ic	Pi-Sigma	A:LEU553: CD1	C-H	d:***1	Pi- Orbitals	
	A:LEU567:CD1 - d:***1	Ligand Non-bond Monitor	3,571 31	Hydrophob ic	Pi-Sigma	A:LEU567: CD1	C-H	d:***1	Pi- Orbitals	
	d:***1:C - A:ILE428	Ligand Non-bond Monitor	4,776 88	Hydrophob ic	Alkyl	d:***1:C	Alkyl	A:ILE428	Alkyl	
	d:***1 - A:ALA452	Ligand Non-bond Monitor	4,051 02	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:ALA452	Alkyl	
	d:***1 - A:LEU501	Ligand Non-bond Monitor	5,269 53	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:LEU501	Alkyl	
	d:***1 - A:CYS502	Ligand Non-bond Monitor	5,068 31	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:CYS502	Alkyl	
	d:***1 - A:ILE428	Ligand Non-bond Monitor	4,129 26	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:ILE428	Alkyl	
	d:***1 - A:ILE428	Ligand Non-bond Monitor	5,332 34	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:ILE428	Alkyl	
	d:***1 - A:LEU501	Ligand Non-bond Monitor	5,172 43	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:LEU501	Alkyl	
	d:***1 - A:VAL436	Ligand Non-bond Monitor	4,561 38	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:VAL436	Alkyl	
L7	d:***1:H -	Ligand Non-bond	2,133	Hydrogen	Conventional	d:***1:H	H-Donor	A:CYS502:	H-	-9,2

	A:CYS502:O	Monitor	13	Bond	Hydrogen Bond			O	Acceptor	
	d:***1:H - A:THR503:O	Ligand Non-bond Monitor	2,425 24	Hydrogen Bond	Conventional Hydrogen Bond	d:***1:H	H-Donor	A:THR503: O	H- Acceptor	
	d:***1:C - A:LEU567:O	Ligand Non-bond Monitor	3,632 73	Hydrogen Bond	Carbon Hydrogen Bond	d:***1:C	H-Donor	A:LEU567: O	H- Acceptor	
	A:ILE428:CD1 - d:***1	Ligand Non-bond Monitor	3,856 31	Hydrophob ic	Pi-Sigma	A:ILE428: CD1	C-H	d:***1	Pi- Orbitals	
	d:***1:C - A:VAL484	Ligand Non-bond Monitor	3,966 48	Hydrophob ic	Alkyl	d:***1:C	Alkyl	A:VAL484	Alkyl	
	d:***1:C - A:MET499	Ligand Non-bond Monitor	3,711 43	Hydrophob ic	Alkyl	d:***1:C	Alkyl	A:MET499	Alkyl	
	d:***1 - A:ALA452	Ligand Non-bond Monitor	3,867 15	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:ALA452	Alkyl	
	d:***1 - A:LEU553	Ligand Non-bond Monitor	4,853 56	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:LEU553	Alkyl	
	d:***1 - A:VAL436	Ligand Non-bond Monitor	4,648 84	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:VAL436	Alkyl	
	d:***1 - A:LEU567	Ligand Non-bond Monitor	4,861 93	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:LEU567	Alkyl	
L8	A:GLU430:HN - d:***1:O	Ligand Non-bond Monitor	2,268 73	Hydrogen Bond	Conventional Hydrogen Bond	A:GLU430: HN	H-Donor	d:***1:O	H- Acceptor	-9,4
	A:ASP564:HN - d:***1:N	Ligand Non-bond Monitor	2,755 59	Hydrogen Bond	Conventional Hydrogen Bond	A:ASP564: HN	H-Donor	d:***1:N	H- Acceptor	
	d:***1:H - A:ASN551:OD1	Ligand Non-bond Monitor	2,895 32	Hydrogen Bond	Conventional Hydrogen Bond	d:***1:H	H-Donor	A:ASN551: OD1	H- Acceptor	
	d:***1:H - A:LEU567:O	Ligand Non-bond Monitor	2,122 97	Hydrogen Bond	Conventional Hydrogen Bond	d:***1:H	H-Donor	A:LEU567: O	H- Acceptor	
	A:GLY563:CA - d:***1:N	Ligand Non-bond Monitor	3,422 05	Hydrogen Bond	Carbon Hydrogen Bond	A:GLY563: CA	H-Donor	d:***1:N	H- Acceptor	
	d:***1:C - A:ASP564:O	Ligand Non-bond Monitor	3,711 03	Hydrogen Bond	Carbon Hydrogen Bond	d:***1:C	H-Donor	A:ASP564: O	H- Acceptor	
	A:GLU506:OE2 - d:***1	Ligand Non-bond Monitor	3,760 2	Electrostat ic	Pi-Anion	A:GLU506: OE2	Negative	d:***1	Pi- Orbitals	
	A:ILE428:CD1 - d:***1	Ligand Non-bond Monitor	3,438 14	Hydrophob ic	Pi-Sigma	A:ILE428: CD1	C-H	d:***1	Pi- Orbitals	
	A:LEU553:CD1 - d:***1	Ligand Non-bond Monitor	3,562 25	Hydrophob ic	Pi-Sigma	A:LEU553: CD1	C-H	d:***1	Pi- Orbitals	
	A:ALA452 -	Ligand Non-bond	4,322	Hydrophob	Alkyl	A:ALA452	Alkyl	d:***1:C	Alkyl	

	d:***1:C	Monitor	32	ic						
	d:***1:C - A:VAL484	Ligand Non-bond Monitor	3,665 31	Hydrophob ic	Alkyl	d:***1:C	Alkyl	A:VAL484	Alkyl	
	d:***1:C - A:MET499	Ligand Non-bond Monitor	3,962 29	Hydrophob ic	Alkyl	d:***1:C	Alkyl	A:MET499	Alkyl	
	d:***1 - A:LEU553	Ligand Non-bond Monitor	5,184 77	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:LEU553	Alkyl	
	d:***1 - A:LEU567	Ligand Non-bond Monitor	4,876 88	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:LEU567	Alkyl	
	d:***1 - A:ARG550	Ligand Non-bond Monitor	5,000 15	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:ARG550	Alkyl	
	d:***1 - A:ALA452	Ligand Non-bond Monitor	4,598 49	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:ALA452	Alkyl	
	d:***1 - A:LEU567	Ligand Non-bond Monitor	5,374 29	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:LEU567	Alkyl	
	d:***1 - A:LEU553	Ligand Non-bond Monitor	5,136 56	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:LEU553	Alkyl	
L9	A:GLU430:HN - d:***1:O	Ligand Non-bond Monitor	2,338 46	Hydrogen Bond	Conventional Hydrogen Bond	A:GLU430: HN	H-Donor	d:***1:O	H- Acceptor	-9,5
	A:ASP564:HN - d:***1:N	Ligand Non-bond Monitor	2,738 26	Hydrogen Bond	Conventional Hydrogen Bond	A:ASP564: HN	H-Donor	d:***1:N	H- Acceptor	
	d:***1:H - A:ASN551:OD1	Ligand Non-bond Monitor	2,617 25	Hydrogen Bond	Conventional Hydrogen Bond	d:***1:H	H-Donor	A:ASN551: OD1	H- Acceptor	
	d:***1:H - A:LEU567:O	Ligand Non-bond Monitor	2,430 93	Hydrogen Bond	Conventional Hydrogen Bond	d:***1:H	H-Donor	A:LEU567: O	H- Acceptor	
	d:***1:C - A:ASN551:O	Ligand Non-bond Monitor	3,707 02	Hydrogen Bond	Carbon Hydrogen Bond	d:***1:C	H-Donor	A:ASN551: O	H- Acceptor	
	A:GLU506:OE2 - d:***1	Ligand Non-bond Monitor	3,862 12	Electrostat ic	Pi-Anion	A:GLU506: OE2	Negative	d:***1	Pi- Orbitals	
	A:ILE428:CD1 - d:***1	Ligand Non-bond Monitor	3,597 96	Hydrophob ic	Pi-Sigma	A:ILE428: CD1	C-H	d:***1	Pi- Orbitals	
	A:LEU553:CD1 - d:***1	Ligand Non-bond Monitor	3,453 89	Hydrophob ic	Pi-Sigma	A:LEU553: CD1	C-H	d:***1	Pi- Orbitals	
	A:ALA452 - d:***1:C	Ligand Non-bond Monitor	3,716 31	Hydrophob ic	Alkyl	A:ALA452	Alkyl	d:***1:C	Alkyl	
	d:***1:C - A:VAL484	Ligand Non-bond Monitor	4,124 84	Hydrophob ic	Alkyl	d:***1:C	Alkyl	A:VAL484	Alkyl	
	d:***1:C -	Ligand Non-bond	4,192	Hydrophob	Alkyl	d:***1:C	Alkyl	A:MET499	Alkyl	

	A:MET499	Monitor	34	ic						
	d:***1 - A:LEU553	Ligand Non-bond Monitor	4,977 88	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:LEU553	Alkyl	
	d:***1 - A:LEU567	Ligand Non-bond Monitor	4,727 21	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:LEU567	Alkyl	
	d:***1 - A:ALA452	Ligand Non-bond Monitor	4,289 84	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:ALA452	Alkyl	
	d:***1 - A:LEU553	Ligand Non-bond Monitor	4,870 43	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:LEU553	Alkyl	
	d:***1 - A:ARG550	Ligand Non-bond Monitor	5,207 06	Hydrophob ic	Pi-Alkyl	d:***1	Pi-Orbitals	A:ARG550	Alkyl	
TAE- 226	A:CYS502:HN - d:***1:N	Ligand Non-bond Monitor	1,937 18	Hydrogen Bond	Conventional Hydrogen Bond	A:CYS502: HN	H-Donor	d:***1:N	H- Acceptor	-9,3
	d:***1:H - A:CYS502:O	Ligand Non-bond Monitor	1,856 65	Hydrogen Bond	Conventional Hydrogen Bond	d:***1:H	H-Donor	A:CYS502: O	H- Acceptor	
	d:***1:O - A:GLU506:OE2	Ligand Non-bond Monitor	3,264 12	Hydrogen Bond	Conventional Hydrogen Bond	d:***1:O	H-Donor	A:GLU506: OE2	H- Acceptor	
	d:***1:H - A:ILE428:O	Ligand Non-bond Monitor	2,204 07	Hydrogen Bond	Conventional Hydrogen Bond	d:***1:H	H-Donor	A:ILE428: O	H- Acceptor	
	d:***1:C - A:GLU500:O	Ligand Non-bond Monitor	3,606 22	Hydrogen Bond	Carbon Hydrogen Bond	d:***1:C	H-Donor	A:GLU500: O	H- Acceptor	
	d:***1:C - A:GLN438:OE1	Ligand Non-bond Monitor	3,322 78	Hydrogen Bond	Carbon Hydrogen Bond	d:***1:C	H-Donor	A:GLN438: OE1	H- Acceptor	
	d:***1:C - A:THR503:O	Ligand Non-bond Monitor	3,333 85	Hydrogen Bond	Carbon Hydrogen Bond	d:***1:C	H-Donor	A:THR503: O	H- Acceptor	
	d:***1:C - A:ILE428:O	Ligand Non-bond Monitor	3,496 86	Hydrogen Bond	Carbon Hydrogen Bond	d:***1:C	H-Donor	A:ILE428: O	H- Acceptor	
	A:ILE428:CD1 - d:***1	Ligand Non-bond Monitor	3,887 74	Hydrophob ic	Pi-Sigma	A:ILE428: CD1	C-H	d:***1	Pi- Orbitals	
	A:LEU553:CD1 - d:***1	Ligand Non-bond Monitor	3,492 12	Hydrophob ic	Pi-Sigma	A:LEU553: CD1	C-H	d:***1	Pi- Orbitals	
	A:ILE428 - d:***1	Ligand Non-bond Monitor	4,693 7	Hydrophob ic	Alkyl	A:ILE428	Alkyl	d:***1	Alkyl	
	A:ALA452 - d:***1:Cl6	Ligand Non-bond Monitor	3,770 93	Hydrophob ic	Alkyl	A:ALA452	Alkyl	d:***1:Cl6	Alkyl	
	d:***1:Cl6 - A:MET499	Ligand Non-bond Monitor	4,839 8	Hydrophob ic	Alkyl	d:***1:Cl6	Alkyl	A:MET499	Alkyl	
	d:***1:C -	Ligand Non-bond	4,246	Hydrophob	Alkyl	d:***1:C	Alkyl	A:LEU501	Alkyl	

	A:LEU501	Monitor	67	ic						
	d:***1 - A:ALA452	Ligand Non-bond Monitor	4,074 28	Hydrophobic	Pi-Alkyl	d:***1	Pi-Orbitals	A:ALA452	Alkyl	
	d:***1 - A:LEU501	Ligand Non-bond Monitor	5,268 23	Hydrophobic	Pi-Alkyl	d:***1	Pi-Orbitals	A:LEU501	Alkyl	
	d:***1 - A:CYS502	Ligand Non-bond Monitor	4,974 32	Hydrophobic	Pi-Alkyl	d:***1	Pi-Orbitals	A:CYS502	Alkyl	
	d:***1 - A:LEU553	Ligand Non-bond Monitor	4,786 08	Hydrophobic	Pi-Alkyl	d:***1	Pi-Orbitals	A:LEU553	Alkyl	
	d:***1 - A:LEU567	Ligand Non-bond Monitor	4,674 69	Hydrophobic	Pi-Alkyl	d:***1	Pi-Orbitals	A:LEU567	Alkyl	

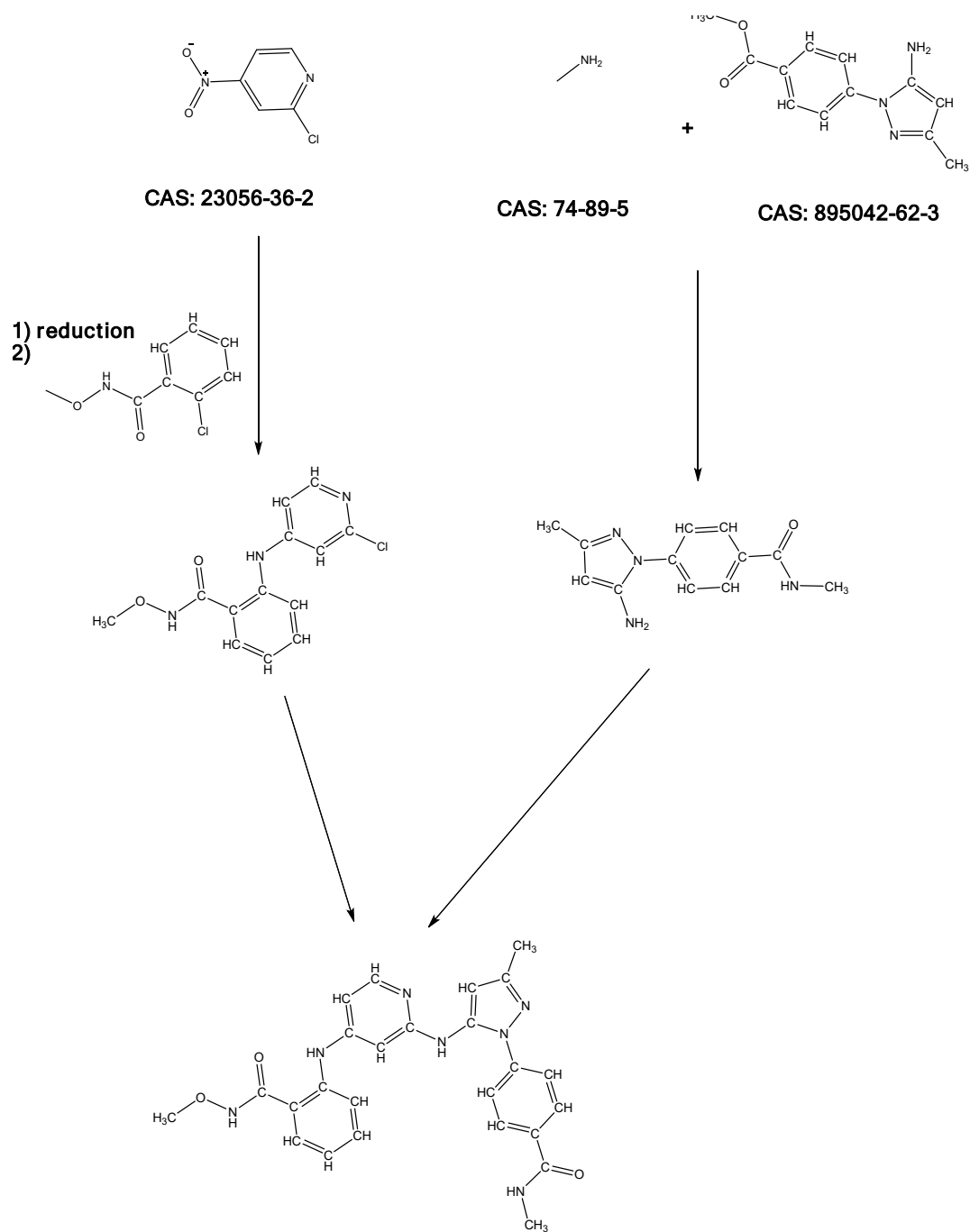


Figure S2: Proposed synthesis pathway for L9