Supporting Information

Inhibition of *Plasmodium falciparum* Hsp90 contributes to the antimalarial activities of aminoalcohol-carbazoles

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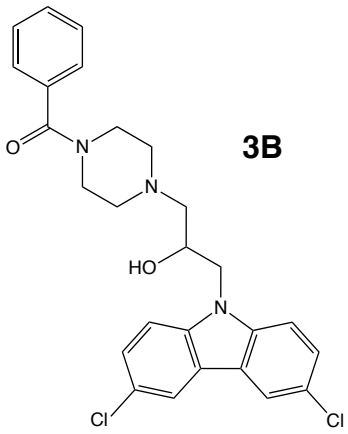
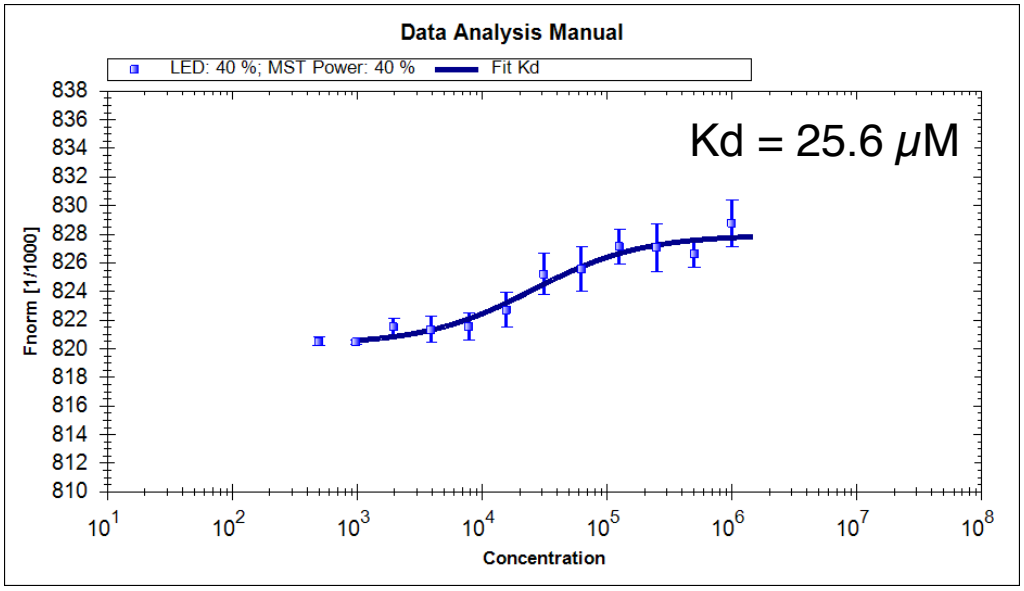




Supporting Information Figure S1. Binding of compound **3B** to PfHsp90

Supporting Information Tables S1-S4

Table S1. Top 10 compounds from docking

ZINC ID	Compound ID	Amber score
ZINC01118762	SJ000134266	-43.873257
ZINC19634654	SJ000147301	-46.434292 *
ZINC19634654	SJ000147301	-47.499771 *
ZINC19691242	SJ000112772	-46.258263
ZINC19691349	SJ000188011	-44.285931
ZINC19791426	SJ000291464	-54.179558
ZINC04187893	SJ000054598	-47.792870
ZINC53175258	SJ000147017	-51.419125
ZINC53201303	SJ000146788	-54.627930
ZINC00759143	SJ000111021	-38.935078

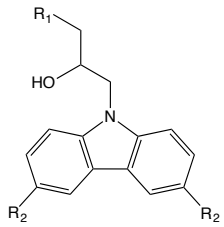
Footnotes:

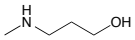
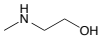
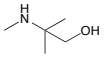
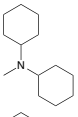
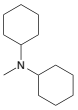
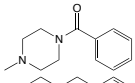
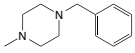
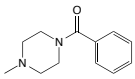
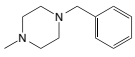
- Compound IDs are from ref. 21
- Compound 5E corresponds to SJ000111021
- Asterisks indicate one compound with two prominent binding poses
- The charges of the ligands were attributed by ZINC database
- The protein model (PfHsp90) was charged by AMBER99 forcefield

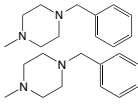
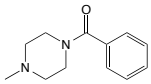
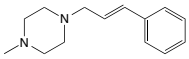
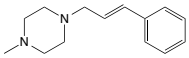
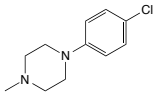
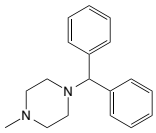
Table S2: Precision docking (Glide, XP mode) of 5E and 5B in PfHsp90

see separate Excel file

Supporting Information Table S3. Structures, biochemical and biological activities of all tested compounds (including all those of Table 1 and only partially tested ones)



Compound	R1	R2	Pf IC50 (nM)	L6 IC50 (nM)	Thermopho-resis shift (unit)	Kd (μM)
Group 2						
3D		H			0.245	
2G		H			3.625	
2E		H	162	3668	1.488	
4B		H			0.765	
4A		H			3.950	
3H		H	10149	6219	0.490	
2C		H	2082	7211	0.725	
2F		H	1436	26483	2.705	
1G		H	7786	6853	1.110	
5A		Cl	86	3339	5.875	
1D		H	12709	7375	0.240	
3F		H	4969	37666	0.600	
5G		Cl	1556	975	3.845	
5E		Cl	70	2613	8.385	
2A		H			0.540	
1H		Cl			1.370	
1F		Br	2084	11585	6.870	
1E		Cl	1231	9723	8.190	
1C		Br	1672	3657	0.41	
Group 1						
2H		Br	2342	10210	6.945	
2D*		Br	95	3673	6.640	
3B		Cl	1130	9723	6.710	25.6
5B		Cl	82	3599	6.405	28.1

2B		H	994	10786	6.685
3G		H			5.120
3A		H	14912	25155	3.335
1B		Br			4.795
1A		Cl			6.605
3E		Cl			4.970
3C		H			2.755

* This compound is identical to compound **14a** in ref. 28

Table S4. Microscale thermophoresis assays

	Absolute thermophoresis signal						Relative thermophoresis shift
Compound	Run1	Run2	Run3	Run4	Average	Standard deviation	
DMSO	817.92	820.58	819.08	819.24	819.21	1.089143394	0.000
IND31119	828.08	828.61	830.54	830.37	829.40	1.239220185	10.195
GMY	844.09	847.43	859.25	862.37	853.29	8.887209911	34.080
3A	822.49	822.59			822.54	0.070710678	3.335
3B	826.26	825.57			825.92	0.487903679	6.710
3C	821.41	822.51			821.96	0.777817459	2.755
3D	819.82	819.08			819.45	0.523259018	0.245
3E	824.82	823.53			824.18	0.912167748	4.970
3F	818.17	819.04			818.61	0.615182900	0.600
3G	824.69	823.96			824.33	0.516187950	5.120
3H	818.33	819.10			818.72	0.544472222	0.490
4A	815.14	815.37			815.26	0.162634560	3.950
4B	818.59	818.29			818.44	0.212132034	0.765
1A	826.01	825.61			825.81	0.282842712	6.605
1B	823.34	824.66			824.00	0.933380951	4.795
1C	819.65	819.59	818.47	817.47	818.80	1.036709538	0.410
1D	819.81	818.12			818.97	1.195010460	0.240
1E	828.67	826.12			827.40	1.803122292	8.190
1F	826.45	825.70			826.08	0.530330086	6.870
1G	819.57	821.06			820.32	1.053589104	1.110
1H	820.50	820.65			820.58	0.106066017	1.370
2A	820.02	819.47			819.75	0.388908730	0.540
2B	825.26	824.07	827.13	827.10	825.89	1.495660389	6.685
2C	819.33	820.53			819.93	0.848528137	0.725
2D	826.09	825.60			825.85	0.346482323	6.640
2E	821.69	822.88	819.43	818.77	820.69	1.920943778	1.488
2F	822.39	821.43			821.91	0.678822510	2.705
2G	823.25	822.41			822.83	0.593969696	3.625
2H	825.86	826.44			826.15	0.410121933	6.945
5A	825.75	824.41			825.08	0.947523087	5.875
5B	824.98	826.24			825.61	0.890954544	6.405
5E	810.99	810.65			810.82	0.240416306	8.385
5G	815.46	815.26			815.36	0.141421356	3.845