Supplementary Material

Synthesis and *In Vitro* Antimycobacterial Activity of Novel *N*-Arylpiperazines Containing an Ethane-1,2-diyl Connecting Chain

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Table S1. Observed R_f values and calculated R_M parameters (RP-TLC) of the evaluated compounds **8a–h** using stationary phases (silica gel plates) impregnated with a variously concentrated silicone oil in heptane.

Entry	1%		3%		5%	
	R_f	R_M	R_f	R_M	R_f	R_M
8a	0.78	-0.55	0.59	-0.16	0.53	-0.05
8b	0.69	-0.35	0.52	-0.03	0.44	0.11
8c	0.59	-0.16	0.42	0.42	0.27	0.44
8d	0.49	0.01	0.27	0.27	0.19	0.64
8e	0.51	-0.02	0.39	0.19	0.36	0.25
8f	0.39	0.19	0.33	0.31	0.28	0.41
8g	0.29	0.39	0.21	0.58	0.22	0.55
8h	0.19	0.63	0.13	0.83	0.13	0.83

Table S2. Observed values of capacity factors *k* (RP-HPLC) of the investigated compounds **8a–h**, which were determined in the methanol (MeOH)/water mobile phases containing a varying volume ratio (*v*/*v*) of the organic modifier.

Entry	*k*; MeOH/water (*v*/*v*)			
	k; 60:40	*k*; 70:30	*k*; 80:20	*k*; 85:15
8a	4.091	1.770	0.925	0.699
8b	4.951	2.778	1.245	0.879
8c	5.898	3.561	1.466	1.023
8d	6.738	5.039	1.769	1.185
8e	3.098	1.456	0.822	0.637
8f	4.524	2.053	1.023	0.757
8g	5.394	3.108	1.342	0.956
8h	7.598	4.627	1.736	1.173

Table S3. Relationships between the log k_w values and *in vitro* activity (in the log (1/*MIC* [M]) units) of the compounds under the study.

Equation No.	Strain (Days of Cultivation)/Series	Equation	Statistical Descriptors
Eq. (S1)	[1] ***MT* (14-d)/ 8a–d**	log (1/*MIC* [M]) = 2.4188 (±0.0431) × log k_w – 2.2686 (±0.1129)	[3] *RSS*=0.0003, [4] *R*=0.9997, [5] *Adj.* R^2=0.9991, [6] *RMSE*=0.0119, [7] *NoR*=0.0168, [8] *F*=3143.04, [9] *Prob>F*=0.0003 ***, [10] *n*=4
Eq. (S2)	***MT* (14-d)/ 8e–h**	log (1/*MIC* [M]) = 1.4933 (±0.1864) × log k_w + 0.7816 (±0.4762)	*RSS*=0.0235, *R*=0.9849, *Adj.* R^2=0.9547, *RMSE*=0.1085, *NoR*=0.1534, *F*=64.20, *Prob>F*=0.0152 **, *n*=4
Eq. (S3)	***MT* (21-d)/ 8a–d**	log (1/*MIC* [M]) = 2.4188 (±0.0431) × log k_w – 2.2686 (±0.1129)	*RSS*=0.0003, *R*=0.9997, *Adj.* R^2=0.9991, *RMSE*=0.0119, *NoR*=0.0168, *F*=3143.04, *Prob>F*=0.0003 ***, *n*=4
Eq. (S4)	***MT* (21-d)/ 8e–h**	log (1/*MIC* [M]) = 1.5162 (±0.4007) × log k_w + 0.6506 (±1.0239)	*RSS*=0.1088, *R*=0.9367, *Adj.* R^2=0.8162, *RMSE*=0.2332, *NoR*=0.3298, *F*=14.32, *Prob>F*=0.0633, *n*=4
Eq. (S5)	[2] ***MK* (7-d)/ 8a–d**	log (1/*MIC* [M]) = 1.4282 (±0.3673) × log k_w + 0.4700 (±0.9610)	*RSS*=0.0205, *R*=0.9398, *Adj.* R^2=0.8248, *RMSE*=0.1011, *NoR*=0.1430, *F*=15.12, *Prob>F*=0.0602, *n*=4

[1] *MT*, *Mycobacterium tuberculosis* My 331/88 (*M. tuberculosis* $H_{37}R_v$); [2] *MT*, *Mycobacterium kansasii* My 235/80; [3] *RSS*, residual sum of squares; [4] *R*, correlation coefficient; [5] *Adj.* R^2, adjusted coefficent of determination; [6] *RMSE*, root mean squared error (standard deviation); [7] *NoR*, norm of residuals; [8] *F*, Fisher´s significance ratio (Fisher´s *F*-test); [9] *Prob>F*, probability of obtaining the *F* Ratio (significance of a whole model); [10] *n*, number of cases (points). The indication of a significance level of the *F* Ratio: * (one star), statistically significant; ** (two stars), statistically very significant; *** (three stars), statistically extremely significant. The insignificant relationships were indicated by a red colour.

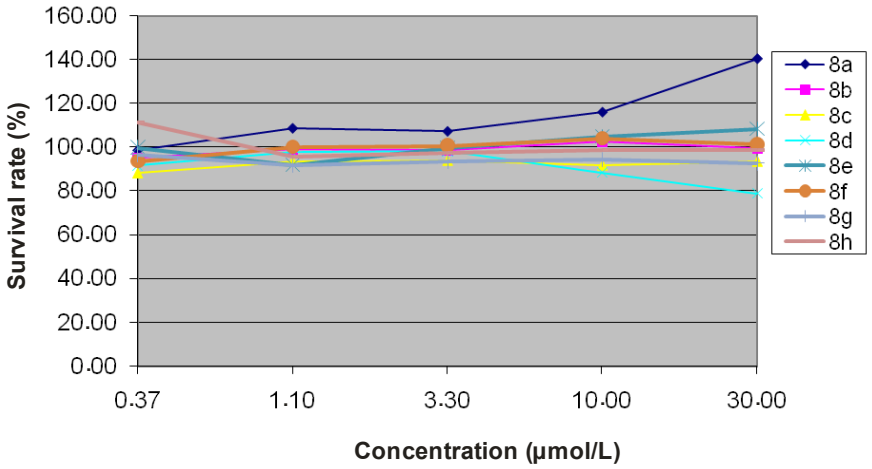

Figure S1. Survival rate curves of the compounds **8a–h** in a THP-1 cell line after the 24 h treatment.