Supporting Information

Sirtuin 1-activating derivatives belonging to the anilinopyridine class displaying *in vivo* cardioprotective activities

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Figure S1. HPLC chromatogram of compound 8.



PDA Ch2 254nm

Peak#	Ret. Time	Area	Area%	Height
1	9,728	26244	0,297	685
2	10,246	21512	0,243	1026
3	10,379	10220	0,115	982
4	11,006	8711411	98,438	1452342
5	11,722	1024	0,012	264
6	11,887	9975	0,113	1949
7	12,076	8881	0,100	1513
8	12,267	27860	0,315	5478
9	12,458	7702	0,087	1927
10	12,766	17963	0,203	4795
11	13,449	3698	0,042	519
12	13,660	1610	0,018	360
13	13,883	1585	0,018	306
Total		8849685	100,000	1472146

Figure S2. HPLC chromatogram of compound 9.





PDA	Ch2	254nm
PDA	Ch2	254nm

Peak#	Ret. Time	Area	Area%	Height
1	10,535	11022579	96,988	1046996
2	11,229	1415	0,012	345
3	11,337	8518	0,075	2046
4	11,477	2101	0,018	523
5	11,803	2882	0,025	574
6	12,185	78256	0,689	14641
7	12,368	64639	0,569	11867
8	12,579	161685	1,423	34154
9	13,430	12771	0,112	2557
10	13,621	1016	0,009	177
11	13,800	7874	0,069	1743
12	14,037	1112	0,010	100
Total		11364848	100,000	1115723

Figure S3. HPLC chromatogram of compound 10.



PDA Ch2 254nm

Peak#	Ret. Time	Area	Area%	Height
1	10,721	10952112	98,540	1358082
2	11,025	4146	0,037	1157
3	11,320	1102	0,010	320
4	11,476	1731	0,016	428
5	12,175	39528	0,356	7277
6	12,358	29496	0,265	5677
7	12,569	82134	0,739	16005
8	13,111	1107	0,010	275
9	13,533	1962	0,018	234
10	13,865	1065	0,010	164
Total	5 7	11114382	100,000	1389619

Figure S4. HPLC chromatogram of compound 11.



PDA Ch2 254nm

Peak#	Ret. Time	Area	Area%	Height
1	11,111	6659221	99,025	859526
2	11,950	1616	0,024	483
3	12,132	5577	0,083	1494
4	12,321	3389	0,050	656
5	12,429	7240	0,108	1536
6	12,591	3248	0,048	674
7	12,714	2597	0,039	576
8	12,789	2086	0,031	518
9	12,956	3464	0,052	648
10	13,169	1589	0,024	311
11	13,284	4621	0,069	1047
12	13,355	3560	0,053	928
13	13,473	1049	0,016	336
14	13,667	4952	0,074	852
15	14,197	2379	0,035	262
16	14,605	1820	0,027	354
17	14,882	2546	0,038	482
18	15,224	5857	0,087	490
19	16,691	2410	0,036	342
20	17,125	4460	0,066	369
21	18,368	1088	0,016	105

Peak#	Ret. Time	Area	Area%	Height
Total		6724770	100,000	871988

Figure S5. HPLC chromatogram of compound 12.



PDA Ch2 254nm

Peak#	Ret. Time	Area	Area%	Height
1	11,136	10739228	99,424	1380323
2	12,626	2110	0,020	545
3	12,714	6023	0,056	1019
4	13,164	9502	0,088	960
5	13,341	12407	0,115	1708
6	13,482	2018	0,019	610
7	13,652	9458	0,088	1609
8	14,604	1009	0,009	179
9	14,891	1642	0,015	324
10	15,204	9434	0,087	878
11	16,726	2105	0,019	248
12	17,155	2949	0,027	231
13	18,192	1768	0,016	177
14	18,428	1738	0,016	181
Total		10801391	100,000	1388992

Figure S6. HPLC chromatogram of compound 13.





PDA Ch2 254nm

Peak#	Ret. Time	Area	Area%	Height
1	10,811	8076023	98,610	885569
2	12,414	22530	0,275	1907
3	12,699	9478	0,116	1016
4	12,907	1269	0,015	159
5	13,067	4137	0,051	773
6	13,154	5117	0,062	985
7	13,377	39466	0,482	5608
8	13,659	8743	0,107	1201
9	14,611	1196	0,015	241
10	14,893	2274	0,028	415
11	15,237	8333	0,102	699
12	15,538	1882	0,023	259
13	16,724	1776	0,022	238
14	17,171	3356	0,041	260
15	17,719	1558	0,019	113
16	18,195	1198	0,015	128
17	18,442	1528	0,019	157
Total		8189866	100,000	899728

Figure S7. HPLC chromatogram of compound 14.



PDA Ch2 254nm

Peak#	Ret. Time	Area	Area%	Height
1	8,455	4167	0,044	242
2	10,800	9068261	96,524	961042
3	11,543	151190	1,609	10250
4	11,730	38814	0,413	6092
5	11,931	16244	0,173	1664
6	12,322	19953	0,212	2074
7	12,417	12736	0,136	2257
8	12,555	4323	0,046	875
9	12,696	14629	0,156	1273
10	12,981	6806	0,072	671
11	13,147	7800	0,083	858
12	13,337	10927	0,116	1163
13	13,459	3464	0,037	679
14	13,647	5683	0,060	805
15	13,952	2194	0,023	239
16	14,190	2412	0,026	293
17	14,590	2135	0,023	406
18	14,867	3084	0,033	586
19	15,209	7729	0,082	760
20	16,678	2762	0,029	394
21	17,109	5232	0,056	424

Peak#	Ret. Time	Area	Area%	Height
22	17,674	2093	0,022	160
23	18,123	1099	0,012	101
24	18,377	1100	0,012	130
Total		9394835	100,000	993439



10,0

12,5

15,0

17,5

min

7,5

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PDA C	h2 254nm			
Peak#	Ret. Time	Area	Area%	Height
1	11,413	128483	1,145	8654
2	11,607	110571	0,985	9843
3	11,966	14408	0,128	2411
4	12,169	4179	0,037	937
5	12,489	10714501	95,451	1858054
6	12,888	13488	0,120	3753
7	13,018	1191	0,011	408
8	13,185	1826	0,016	420
9	13,383	25436	0,227	4191
10	13,545	57768	0,515	13034
11	13,658	123069	1,096	27649
12	14,196	4447	0,040	275
13	14,660	2648	0,024	469
14	14,936	4056	0,036	644
15	15,323	6065	0,054	591
16	16,813	3353	0,030	415
17	17,161	2776	0,025	366
18	17,308	3084	0,027	408
19	17,825	2507	0,022	204
20	18 574	1262	0.011	114

5,0

2,5

0,0

Peak#	Ret. Time	Area	Area%	Height
Total		11225117	100,000	1932838

Figure S9. HPLC chromatogram of compound 16.



PDA C	h2	254nm

Peak#	Ret. Time	Area	Area%	Height
1	10,347	2796	0,024	210
2	11,351	61877	0,521	3035
3	11,565	54870	0,462	4694
4	11,770	12806	0,108	1924
5	11,920	19663	0,166	2410
6	12,077	20918	0,176	3021
7	12,669	11617332	97,794	1624225
8	13,155	4787	0,040	779
9	13,339	3759	0,032	868
10	13,458	10797	0,091	1955
11	13,690	36794	0,310	5434
12	14,135	1850	0,016	207
13	14,586	2851	0,024	387
14	15,013	4415	0,037	603
15	15,370	3407	0,029	520
16	15,499	1407	0,012	237
17	15,936	1304	0,011	162
18	16,172	8410	0,071	1055
19	16,793	3196	0,027	421
20	18,728	6209	0,052	592

Peak#	Ret. Time	Area	Area%	Height
Total	8	11879446	100,000	1652740

Figure S10. HPLC chromatogram of compound 17.





PDA Ch2 254nm

Peak#	Ret. Time	Area	Area%	Height
1	6,106	34198	0,354	1142
2	10,039	6626	0,069	413
3	10,521	1518	0,016	306
4	10,754	1995	0,021	318
5	11,084	7360	0,076	730
6	11,310	2261	0,023	393
7	11,455	6635	0,069	1234
8	11,592	5599	0,058	1088
9	11,711	5377	0,056	1025
10	12,022	9539610	98,739	1812064
11	12,427	31226	0,323	5398
12	12,725	1026	0,011	310
13	13,088	1241	0,013	290
14	13,220	1598	0,017	287
15	13,579	6279	0,065	1127
16	13,806	1051	0,011	204
17	14,176	2355	0,024	430
18	15,174	1376	0,014	173
19	16,195	2614	0,027	408
20	16,401	1449	0,015	237

Figure S11. HPLC chromatogram of compound 18.



Peak#	Ret. Time	Area	Area%	Height
1	9,128	16616	0,152	1148
2	11,016	113209	1,038	4397
3	11,357	53593	0,491	4388
4	11,570	56047	0,514	5040
5	11,784	14585	0,134	1887
6	11,928	12631	0,116	1990
7	12,378	10563886	96,880	1421615
8	12,679	1957	0,018	834
9	12,972	1967	0,018	290
10	13,141	5727	0,053	1126
11	13,248	2462	0,023	580
12	13,330	3085	0,028	627
13	13,536	16147	0,148	2165
14	13,696	9077	0,083	1813
15	13,806	7763	0,071	1447
16	14,212	2039	0,019	288
17	14,630	1739	0,016	158
18	15,403	9902	0,091	1337
19	15,942	1129	0,010	143
20	16,825	3363	0,031	435

Peak#	Ret. Time	Area	Area%	Height
21	18,780	7133	0,065	710
Total		10904054	100,000	1452418

Figure S12. HPLC chromatogram of compound 19.



PDA Ch2 254nm

Peak#	Ret. Time	Area	Area%	Height
1	12,503	29074	0,654	2850
2	12,767	4324537	97,303	832912
3	13,178	9815	0,221	2020
4	13,365	5359	0,121	787
5	13,547	15663	0,352	3669
6	13,654	17088	0,384	2691
7	13,771	16563	0,373	3147
8	14,173	3864	0,087	409
9	14,375	3011	0,068	423
10	15,092	2010	0,045	270
11	15,251	2307	0,052	361
12	15,450	8812	0,198	835
13	17,155	1176	0,026	146
14	17,693	2212	0,050	138
15	18,667	1510	0,034	161
16	18,997	1424	0,032	131
Total		444423	100,000	850951

Figure S13. HPLC chromatogram of compound 20.



PDA Ch2 254nm

Peak#	Ret. Time	Area	Area%	Height
1	11,401	100338	1,044	7465
2	11,594	111440	1,160	9703
3	11,951	2226	0,023	603
4	12,449	13031	0,136	1741
5	12,680	15191	0,158	2368
6	12,880	9286605	96,663	1789745
7	13,269	31291	0,326	6604
8	13,598	13936	0,145	2865
9	13,705	9464	0,099	2508
10	13,859	11646	0,121	2976
11	14,639	2616	0,027	369
12	14,925	1541	0,016	201
13	15,288	7846	0,082	605
Total		9607172	100,000	1827752

Figure S14. HPLC chromatogram of compound 21.



PDA Ch2 254nm	
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Peak#	Ret. Time	Area	Area%	Height
1	11,295	98595	0,623	4759
2	12,262	15320505	96,871	872130
3	12,639	3261	0,021	927
4	12,768	13225	0,084	2542
5	12,914	4183	0,026	1169
6	13,095	21362	0,135	4583
7	13,340	12864	0,081	1862
8	13,566	256487	1,622	48750
9	13,924	35425	0,224	4908
10	14,299	5286	0,033	655
11	14,508	4518	0,029	730
12	14,873	26836	0,170	4656
13	15,061	3318	0,021	574
14	15,455	3851	0,024	415
15	16,248	2756	0,017	253
16	16,739	2836	0,018	378
Total		15815308	100,000	949290

Figure S15. HPLC chromatogram of compound 22.



PDA	Ch2	254nm

Peak#	Ret. Time	Area	Area%	Height
1	10,300	32320	0,099	1391
2	11,373	93886	0,288	5099
3	11,624	149045	0,457	13896
4	11,792	84190	0,258	10353
5	12,607	32025622	98,299	2247278
6	12,824	20853	0,064	7899
7	13,028	28520	0,088	5972
8	13,181	14665	0,045	3036
9	13,339	10283	0,032	2759
10	13,524	15743	0,048	3026
11	13,625	15292	0,047	1968
12	13,836	2255	0,007	630
13	14,109	5490	0,017	969
14	14,260	4217	0,013	560
15	14,634	5095	0,016	746
16	14,748	5509	0,017	771
17	15,173	45976	0,141	6952
18	15,460	3525	0,011	544
19	15,924	2974	0,009	200
20	16,805	7548	0,023	778

Peak#	Ret. Time	Area	Area%	Height
21	18,019	1469	0,005	165
22	18,720	5347	0,016	567
Total		32579822	100,000	2315559

Figure 16. HPLC chromatogram of compound 23.



Figure S17. ¹H-NMR and ¹³C-NMR of compound **8**.





Figure S18. ¹H-NMR and ¹³C-NMR of compound 9.





Figure S19. ¹H-NMR and ¹³C-NMR of compound 10.





Figure S20. ¹H-NMR and ¹³C-NMR of compound 11.





Figure S21. ¹H-NMR and ¹³C-NMR of compound 12.





Figure S22. ¹H-NMR and ¹³C-NMR of compound 13.



Figure S23. ¹H-NMR and ¹³C-NMR of compound 14.





Figure S24. ¹H-NMR and ¹³C-NMR of compound 15.





Figure S25. ¹H-NMR and ¹³C-NMR of compound 16.





Figure S26. ¹H-NMR and ¹³C-NMR of compound 17.



Figure S27. ¹H-NMR and ¹³C-NMR of compound 18.



Figure S28. ¹H-NMR and ¹³C-NMR of compound 19.



Figure S29. ¹H-NMR and ¹³C-NMR of compound 20.





Figure S30. ¹H-NMR and ¹³C-NMR of compound 21.





Figure S31. ¹H-NMR and ¹³C-NMR of compound 22.





Figure S32. ¹H-NMR and ¹³C-NMR of compound 23.



Figure S33. ESI-HRMS spectrum of compound 8.



Figure S34. ESI-HRMS spectrum of compound 9.



Figure S35. ESI-HRMS spectrum of compound 10.



Figure S36. ESI-HRMS spectrum of compound 11.



Figure S37. ESI-HRMS spectrum of compound 12.



Figure S38. ESI-HRMS spectrum of compound 13.



Figure S39. ESI-HRMS spectrum of compound 14.



Figure S40. ESI-HRMS spectrum of compound 15.



Figure S41. ESI-HRMS spectrum of compound 16.



Figure S42. ESI-HRMS spectrum of compound 17.



Figure S43. ESI-HRMS spectrum of compound 18.



Figure S44. ESI-HRMS spectrum of compound 19.



Figure S45. ESI-HRMS spectrum of compound 20.



Figure S46. ESI-HRMS spectrum of compound 21.



Figure S47. ESI-HRMS spectrum of compound 22.



Figure S48. ESI-HRMS spectrum of compound 23.



Figure 49. Structure of SIRT1 in complex with p53-AMC peptide (green) used for docking studies. The main portions of the two different subpockets are highlighted in orange and blue. For clarity, the side chains of R1, H2, and K3 of p53-AMC are not shown.