Electronic Supplementary Material

Exploring the Trifluoromenadione Core as a Template to design Antimalarial Redox-Active Agents Interacting with Glutathione Reductase

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Table S1. Redox potentials derived from cyclovoltammograms of menadione **2**, its analogues **3**, **6**, **7**, and **15**, and methylene blue (MB) as reference.

Figure S1. Cyclic Voltammetry of 1 mM t-Butylmenadione 15, and of fluoromenadione 6.

Figure S2. LC-MS traces showing the formation of lawsone 4 from trifluoromenadione 3 at pH 7.0.

 $_{15}$ Figure S3. $^1\mathrm{H}$ and $^{13}\mathrm{C}$ NMR spectra for 3, 5, 8 and 12.

	E _{pc1} (V)	E _{pa1} (V)	$\Delta E_{p}(V)$	E ⁰ ₁ (V)	$I_{\rm pc}/_{\rm Ipa}$	E _{pc2} (V)	E _{pa2} (V)	ΔEp (V)	$E_{2}^{0}(V)$	I_{pc}/I_{pa}
2	-0.703	-0.597	0.106	-0.65	0.93	-1.161	-0.982	0.179	-1.075	0.95
15	-0.754	-0.651	0.103	-0.702	0.94	-1.305	-1.05	0.255	-1.178	0.82
6	-0.540	-0.408	0.132	ND	0.42	-0.673	-0.569	0.104	ND	0.36
7	-0.425	-0.345	0.08	-0.385	0.58	-0.962	-0.760	0.202	ND	0.12
3	-0.352	-0.265	0.087	-0.308	0.96	-0.956	-0.797	0.159	-0.876	0.96
MB*	-0.272	-0.151	0.121	-0.151	0.99	nd	nd	nd	nd	nd

Table S1. Redox potentials derived from cyclovoltammograms of menadione 2 and its analogues.

nd: not determined (*MB = methylene blue)

5



Figure S1. Cyclic Voltammetry

Cyclic voltammograms of 1 mM *t*-Butylmenadione **15** (left), and fluoromenadione **6** (right) solutions were recorded at platine electrode in CH_2Cl_2 with 0.1 M Bu₄NBF₄ as supporting electrolyte at 0.2 V s⁻¹ scan rate.



Figure S2. LC-MS traces showing the formation of lawsone 4 from trifluoromenadione 3 at pH 7.0.

Trifluoromenadione 3

AUC	Area Peak at 0.4 min	С (µМ)		
exp 1	29691	11,19		
exp 2	21859	8,24		
AUC: Area under Curve				

Lawsone 4

AUC	Area Peak at 0.15 min	С (µМ)	
exp 1	2399	0,95	
exp 2	2080	0,82	

30 min



Trifluoromenadione 3

AUC	Area Peak at 0.4 min	C (µM)
exp 1	26149	9,86
exp 2	11803	4,45

Lawsone 4

AUC	Area Peak at 0.15 min	С (µМ)
exp 1	3936	1,55
exp 2	4398	1,74



Trifluoromenadione 3

AUC	Area peak at 0.4 min	С (µМ)
exp 1	14658	5,53
exp 2	11020	4,15

Lawsone 4

AUC	Area peak at 0.15 min	С (µМ)
exp 1	8606	3,40
exp 2	9406	3,72

3 h 30



Trifluoromenadione 3

AUC	Area peak at 0.4 min	C (µM)
exp 1	5285	1,9 9
exp 2	2387	0,90

Lawsone 4

AUC	Area peak at 0.15 min	С (µМ)
exp 1	17310	6,84
exp 2	14816	5,85



Trifluoromenadione 3

AUC	Area peak at 0.4 min	C (µM)
exp 1	731	0,28
exp 2	1590	0,60

Lawsone 4

5

10

15

AUC	Area peak at 0.15 min	С (µМ)
exp 1	23815	9,41
exp 2	21774	8,60

Figure S3. ¹H and ¹³C NMR spectra for 3, 5, 8 and 12.



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