Electronic Supplementary Information

Exploring synthetic avenues for the effective synthesis of selenium and tellurium containing multifunctional redox agents

Susanne Mecklenburg, Saad Shaaban, Lalla A. Ba, Torsten Burkholz, Thomas Schneider, Britta Diesel, Alexandra K. Kiemer, Anne Röseler, Katja Becker, Jörg Reichrath, Alexandra Stark, Wolfgang Tilgen, Muhammad Abbas, Ludger A. Wessjohann, Florenz Sasse and Claus Jacob*

S1. Synthesis of individual compounds

Compound 7, 4-(3-methyl-1,4-naphthoquinone-2-yl)butanoic acid 10, 6-(1,4-naphthoquinone-2-ylamino)hexanoic acid (16), 3-(3-methyl-1,4-naphthoquinone-2-ylthio)propanoic acid (19), 1,4,7,10-tetraazacyclododecane (18), 1-(4,7,10-tri-tert-butyloxy carbonyl-1,4,7,10-tetraazacyclododecane-1-yl)propane-1-one 20, 3-(3-methyl-1,4-naphthoquinone-2-ylthio)-1-(1,4,7,10-tetraazacyclododecane-1-yl)propane-1-one 21, 2-(3-methyl-1,4-dioxo-1,4-di hydronaphthalen-2-ylselanyl)acetaldehyde, 3-(3-methyl-1,4-dioxo-1,4-dihydronaphthalen-2-ylthio)propanoic acid, compound 26, compound 27, compound 28, compound 29 were synthesized according the literature.
2-(3-(phenylthio)propylamino)-1,4-naphthoquinone (4)

![Chemical Structure](image)

3-(phenylthio)propane-1-amine (167.3 mg, 1.00 mmol) was dissolved in 10 ml EtOH and added dropwise to a solution of 1,4-naphthoquinone (158.2 mg, 1.00 mmol) in 10 ml EtOH. The reaction was stirred for three days on air and in the dark. The precipitated solid was filtered off, washed thoroughly with EtOH and purified by silica gel column chromatography (CH$_2$Cl$_2$) to obtain a bright orange solid (88.4 mg, 0.27 mmol).

Yield: 27.3%.

C$_{19}$H$_{17}$NO$_2$S (MW = 323.41 g/mol).

TLC: $R_f$ = 0.25 (CH$_2$Cl$_2$).

Mp = 175-177°C.

$^1$H NMR (CDCl$_3$): $\delta$ = 2.00 (quint, 2 H, H$_{11}$, $^3$J$_{HH}$ = 6.9), 3.01 (t, 2 H, H$_{12}$, $^3$J$_{HH}$ = 6.9), 3.34 (q, 2 H, H$_{10}$, $^3$J$_{HH}$ = 6.6), 5.73 (s, 1 H, H$_3$), 5.93 (br s, 1 H, NH), 7.20 (m, 1 H, H$_{16}$), 7.30 (m, 2 H, H$_{15}$), 7.37 (m, 2 H, H$_{14}$), 7.61 (dt, 2 H, H$_6$ or H$_7$, not assigned (n.a.), $^3$J$_{HH}$ = 7.6, $^4$J$_{HH}$ = 1.3), 7.73 (dt, 2 H, H$_6$ or H$_7$, n.a., $^3$J$_{HH}$ = 7.6, $^4$J$_{HH}$ = 1.3), 8.04 (dd, 2 H, H$_5$ or H$_8$, n.a., $^3$J$_{HH}$ = 7.6, $^4$J$_{HH}$ = 1.0), 8.10 (dd, 2 H, H$_5$ or H$_8$, n.a., $^3$J$_{HH}$ = 7.6, $^4$J$_{HH}$ = 1.0).

$^{13}$C NMR (CDCl$_3$): $\delta$ = 27.4, 31.3, 41.1 (C$_{10,11,12}$, n.a.), 101.0 (C$_3$), 126.20, 126.26, 126.57, 131.98, 134.76 (C$_{5,6,7,8,16}$, n.a.), 129.10, 129.91 (C$_{14,15}$, n.a.), 130.49, 133.59, 135.35, (C$_{4a,8a,13}$, n.a.), 147.79 (C$_2$), 181.8, 182.9 (C$_{1,4}$, n.a.).
LC-MS: R_t, m/z (%) = not ionisable.


**2-(3-(phenylselenyl)propylamino)-1,4-naphthoquinone (5)**

The same procedure used for the preparation of 4 was applied in the reaction of 3-(phenylselenyl)propane-1-amine (428.3 mg, 2.00 mmol) with 1,4-naphthoquinone (316.3 mg, 2.00 mmol). After appropriate workup (silica gel column chromatography with CH_2Cl_2) a bright orange solid (150.3 mg, 0.41 mmol) was obtained.

Yield: 20.3%.

C_{19}H_{17}NO_2Se (MW = 370.30 g/mol).

TLC: R_f = 0.25 (CH_2Cl_2).

Mp = 161°C.

^1H NMR (CDCl_3): δ = 2.01 (quint, 2 H, H^{11}, \textit{3}J_{\text{HH}} = 6.9), 2.97 (t, 2 H, H^{12}, \textit{3}J_{\text{HH}} = 6.9), 3.31 (q, 2 H, H^{10}, \textit{3}J_{\text{HH}} = 6.3), 5.72 (s, 1 H, H^{3}), 5.89 (br s, 1 H, NH), 7.26 (m, 3 H, H^{15,16}), 7.52 (m, 2 H, H^{14}), 7.61 (dt, 2 H, H^6 or H^7, n.a., \textit{3}J_{\text{HH}} = 7.6, \textit{4}J_{\text{HH}} = 1.3), 7.72 (dt, 2 H, H^6 or H^7, n.a., \textit{3}J_{\text{HH}} = 7.6, \textit{4}J_{\text{HH}} = 1.3), 8.03 (dd, 2 H, H^5 or H^8, n.a., \textit{3}J_{\text{HH}} = 7.6, \textit{4}J_{\text{HH}} = 1.0), 8.10 (dd, 2 H, H^5 or H^8, n.a., \textit{3}J_{\text{HH}} = 7.6, \textit{4}J_{\text{HH}} = 1.0).
$^{13}$C NMR (CDCl$_3$): $\delta = 24.8, 28.3, 42.0$ (C$^{10,11,12}$, n.a.), 101.0 (C$^3$), 126.1, 126.2, 127.3, 131.9, 134.7 (C$^{5,6,7,8,16}$, n.a.), 129.2, 133.0 (C$^{14,15}$, n.a.), 129.3, 130.4, 133.5 (C$^{4a,8a,13}$, n.a.), 147.7 (C$^2$, n.a.), 181.8, 182.8 (C$^{1,4}$, n.a.).

NMR data including COSY spectroscopy:

$^1$H NMR (CDCl$_3$): $\delta = 2.01$ (quint, 2 H, H$^{11}$, $3J_{HH} = 6.9$), 2.97 (t, 2 H, H$^{12}$, $3J_{HH} = 6.9$), 3.31 (q, 2 H, H$^{10}$, $3J_{HH} = 6.3$), 5.72 (s, 1 H, H$^3$), 5.89 (br s, 1 H, NH), 7.26 (m, 3 H, H$^{15,16}$), 7.52 (m, 2 H, H$^{14}$), 7.61 (dt, 2 H, H$^7$, $3J_{HH} = 7.6$, $4J_{HH} = 1.3$), 7.72 (dt, 2 H, H$^6$, $3J_{HH} = 7.6$, $4J_{HH} = 1.3$), 8.03 (dd, 2 H, H$^8$, $3J_{HH} = 7.6$, $4J_{HH} = 1.0$), 8.10 (dd, 2 H, H$^5$, $3J_{HH} = 7.6$, $4J_{HH} = 1.0$).

$^{13}$C NMR (CDCl$_3$): $\delta = 24.8$ (C$^{12}$), 28.3 (C$^{11}$), 42.0 (C$^{10}$), 101.0 (C$^3$), 126.1 (C$^5$), 126.2 (C$^8$), 127.3 (C$^{16}$), 129.2 (C$^{15}$), 129.3 (C$^{13}$), 130.4 (C$^{8a}$), 131.9 (C$^7$), 133.0 (C$^{14}$), 133.5 (C$^{4a}$), 134.7 (C$^6$), 147.7 (C$^2$), 181.8 (C$^1$), 182.8 (C$^4$).

LC-MS: $R_t = 11.7$ min, m/z (%) 372.1 (100) [M+H]$^+$. HRMS: [M+H]$^+$ calcd 372.0502, [M+H]$^+$ found 372.0402.

**2,5-bis(3-(phenylselenyl)propylamino)-1,4-benzoquinone (6)**

Following the procedure for the preparation of 4 and 5, 3-(phenylselenyl)propane-1-amine (1.67 g, 3.14 mmol) was reacted with 1,4-benzoquinone (108.1 mg, 1.00 mmol). A red solid (183.8 mg, 0.35 mmol) was obtained.
Yield: 34.5%.

C\textsubscript{24}H\textsubscript{26}N\textsubscript{2}O\textsubscript{2}Se\textsubscript{2} (MW = 532.40 g/mol).

TLC: \( R_f = 0.21 \) (CH\textsubscript{2}Cl\textsubscript{2}).

Mp = 164-166\degree C.

\(^1\)H NMR (CDCl\textsubscript{3}): \( \delta = 2.01 \) (quint, 4 H, H\textsubscript{11}, \( \tilde{J}_{HH} = 6.9 \)), 2.93 (t, 4 H, H\textsubscript{12}, \( \tilde{J}_{HH} = 6.9 \)), 3.28 (q, 4 H, H\textsubscript{10}, \( \tilde{J}_{HH} = 6.6 \)), 5.29 (s, 2 H, H\textsubscript{3}), 6.54 (br s, 2 H, NH), 7.27 (m, 6 H, H\textsubscript{15,16}), 7.51 (m, 4 H, H\textsubscript{14}).

\(^{13}\)C NMR (CDCl\textsubscript{3}): \( \delta = 24.9, 28.5, 42.0 \) (C\textsubscript{10,11,12}, n.a.), 93.2 (C\textsubscript{3}), 127.5 (C\textsubscript{16}), 129.1 (C\textsubscript{13}), 151.3 (C\textsubscript{2}), 129.2, 133.1 (C\textsubscript{14,15}, n.a.), 178.4 (C\textsubscript{1}).

LC-MS: \( R_t = 12.9 \) min, m/z (%) 535.0 (100) [M+H]\(^+\).

HRMS: [M+H]\(^+\) calcd 535.0402, [M+H]\(^+\) found 535.0285

\textbf{1,4-bis(3-(phenylselenyl)propyl)piperazine (8)}

Piperazine (2.7 mg, 0.73 mmol) was dissolved in 25 ml dry THF. A solution of 3-(phenylselenyl)propanal (310.3 mg, 1.46 mmol) in 18 ml THF was added dropwise at room temperature over a period of 10 min. After 15 min sodium triacetoxyborohydride (308.5 mg, 1.46 mmol) was added and the reaction was stirred at room temperature overnight. The solvent was evaporated under reduced pressure and the crude product was purified by silica
gel column chromatography (CH$_2$Cl$_2$/MeOH 95:5) to yield a beige solid (109.6 mg, 0.22 mmol).

Yield: 30.2 %.

C$_{22}$H$_{30}$N$_2$Se$_2$ (MW = 480.41 g/mol).

TLC: $R_f$ = 0.25 (CH$_2$Cl$_2$/MeOH 95:5).

Mp = 61-63°C.

$^1$H NMR (CDCl$_3$): $\delta$ = 1.90 (quint, 4 H, H$^6$, $^3J_{HH}$ = 7.3), 2.45 (t, 12 H, H$^5$ or H$^7$, n.a., H$^8$, $^3J_{HH}$ = 7.3), 2.96 (t, 4 H, H$^5$ or H$^7$, n.a., $^3J_{HH}$ = 7.3), 7.27 (m, 6 H, H$^{1,2}$), 7.52 (m, 4 H, H$^3$).

$^{13}$C NMR (CDCl$_3$): $\delta$ = 25.6, 27.4 (C$^5,6$), 53.1 (C$^8$), 58.0 (C$^7$), 126.6 (C$^1$), 128.9, 132.4 (C$^{2,3}$, n.a.) 130.5 (C$^4$).

LC-MS: $R_t$ = 7.4 min, m/z (%) 482.9 (100) [M+H]$^+$.


4-(3-methyl-1,4-naphthoquinone-2-yl)-N-(3-(phenylselenyl)propyl)butanamide (11)

The method employed for the synthesis of 11 has been derived from the literature, where similar molecules have been recorded, yet without selenium.$^{10}$ Briefly, N-methylmorpholine (101.2 mg, 1.00 mmol) in 3 ml dry CHCl$_3$ was added to a solution of 4-(3-methyl-1,4-naphthoquinone-2-yl)butanoic acid$^2$ (10) (258.3 mg, 1.00 mmol) in 3 ml of dry CHCl$_3$ at 0
°C. After 15 min ethylchloroformate (108.5 mg, 1.00 mmol) in 3 ml dry CHCl₃ was added and after additional 30 min at 0 °C, 3-(phenylselenyl)propane-1-amine (214.2 mg, 1.00 mmol) in 3 ml dry CHCl₃ was added. The reaction mixture was stirred at 0 °C for 1 h and afterwards at room temperature overnight. The solvent was evaporated under reduced pressure and the crude product purified by silica gel column chromatography (CH₂Cl₂/MeOH 95:5). A yellowish brown solid (323.4 mg, 0.71 mmol) was obtained.

Yield: 71.2%.

C₂₄H₂₅NO₃Se (MW = 454.42 g/mol).

TLC: Rf = 0.65 (CH₂Cl₂/MeOH 95:5).

Mp = 79-80°C.

¹H NMR (CDCl₃): δ = 1.79 (quint, 2 H, H¹⁰ or H¹⁵, n.a., ³JHH = 7.9), 1.92 (quint, 2 H, H¹⁰ or H¹⁵, n.a., ³JHH = 7.3), 2.19 (s, 3 H, CH₃), 2.24 (t, 2 H, H⁹ or H¹¹ or H¹⁶, n.a., ³JHH = 7.3), 2.64 (t, 2 H, H⁹ or H¹¹ or H¹⁶, n.a., ³JHH = 7.9), 2.93 (t, 2 H, H⁹ or H¹¹ or H¹⁶, n.a., ³JHH = 7.3), 3.37 (q, 2 H, H¹⁴, ³JHH = 6.6), 5.93 (br s, 1 H, NH), 7.23 (m, 3 H, H¹⁹,²⁰), 7.48 (m, 2 H, H¹⁸), 7.68 (m, 2 H, H⁶,⁷), 8.05 (m, 2 H, H⁵,⁸).

¹³C NMR (CDCl₃): δ = 12.7 (CH₃), 24.2, 25.0, 26.3, 29.9, 36.0, 39.3 (C⁹,¹⁰,¹¹,¹⁴,¹⁵,¹⁶, n.a.), 126.2, 126.9, 129.1, 132.7, 133.3, 133.4 (C⁵,⁶,⁷,⁸,¹⁸,¹⁹,²⁰, n.a.), 129.9, 132.0, 132.1, 144.0, 146.2 (C²,³,⁴a,⁸a,¹⁷, n.a.), 172.1 (C¹²), 184.9, 185.1 (C¹⁴, n.a.).

LC-MS: Rᵣ = 9.9 min, m/z (%) 456.0 (100) [M+H]+.

4-(3-methyl-1,4-naphthoquinone-2-yl)-N-(3-(phenyltelluryl)propyl)butanamide (12)

Based on the preparation of 11, 4-(3-methyl-1,4-naphthoquinone-2-yl)butanoic acid\(^2\) (10) (258.3 mg, 1.00 mmol) was reacted with 3-(phenyltelluryl)propane-1-amine (262.8 mg, 1.00 mmol) using N-methylmorpholine (101.2 mg, 1 mmol) and ethylchloroformate (108.5 mg, 1.00 mmol) to result in a yellowish brown solid (201.8 mg, 0.40 mmol).

Yield: 40.1%.
C\(_{24}\)H\(_{25}\)NO\(_3\)Te (MW = 503.06 g/mol).
TLC: \(R_f = 0.51\) (CH\(_2\)Cl\(_2\)/MeOH 95:5).
Mp = 58°C.

\(^1\)H NMR (CDCl\(_3\)): \(\delta = 1.79\) (quint, 2 H, H\(^{10}\) or H\(^{15}\), n.a., \(3J_{HH} = 7.9\)), 2.01 (quint, 2 H, H\(^{10}\) or H\(^{15}\), n.a., \(3J_{HH} = 6.9\)), 2.20 (s, 3 H, CH\(_3\)), 2.22 (t, 2 H, H\(^9\) or H\(^{11}\) or H\(^{16}\), n.a., \(3J_{HH} = 6.9\)), 2.64 (t, 2 H, H\(^9\) or H\(^{11}\) or H\(^{16}\), n.a., \(3J_{HH} = 7.9\)), 2.89 (t, 2 H, H\(^9\) or H\(^{11}\) or H\(^{16}\), n.a., \(3J_{HH} = 7.6\)), 3.33 (q, 2 H, H\(^{14}\), \(3J_{HH} = 6.6\)), 5.79 (br s, 1 H, NH), 7.18 (m, 2 H, H\(^{19}\)), 7.26 (m, 1 H, H\(^{20}\)), 7.69 (m, 2 H, H\(^6,7\)), 7.72 (m, 2 H, H\(^{18}\)), 8.07 (m, 2 H, H\(^{5,8}\)).

\(^13\)C NMR (CDCl\(_3\)): \(\delta = 5.0\) (C\(^{16}\)), 24.2, 26.3, 31.6, 36.1, 41.1 (C\(^{9,10,11,14,15}\), n.a.), 12.7 (CH\(_3\)), 111.5 (C\(^{17}\)), 132.0, 132.1, 144.1, 146.2 (C\(^{2,3,4a,8a}\), n.a.), 126.3, 127.7, 129.2, 133.4, 133.5, 138.5 (C\(^{5,6,7,8,18,19,20}\), n.a.), 172.1 (C\(^{12}\)), 184.9, 185.1 (C\(^{14}\), n.a.).
NMR data including COSY spectroscopy:

\(^1\)H NMR (CDCl\(_3\)): \(\delta = 1.79\) (quint, 2 H, H\(_{10}\), \(\text{J}_{HH} = 7.9\)), 2.01 (quint, 2 H, H\(_{15}\), \(\text{J}_{HH} = 6.9\)), 2.20 (s, 3 H, CH\(_3\)), 2.22 (t, 2 H, H\(_{11}\), \(\text{J}_{HH} = 6.9\)), 2.64 (t, 2 H, H\(_9\), \(\text{J}_{HH} = 7.9\)), 2.89 (t, 2 H, H\(_{16}\), \(\text{J}_{HH} = 7.6\)), 3.33 (q, 2 H, H\(_{14}\), \(\text{J}_{HH} = 6.6\)), 5.79 (br s, 1 H, NH), 7.18 (m, 2 H, H\(_{19}\)), 7.26 (m, 1 H, H\(_{20}\)), 7.69 (m, 2 H, H\(_{6,7}\), thereof H\(_6\) in the low field and H\(_7\) in the high field of the signal), 7.72 (m, 2 H, H\(_{18}\)), 8.07 (m, 2 H, H\(_{5,8}\), thereof H\(_5\) in the low field and H\(_8\) in the high field of the signal).

\(^{13}\)C NMR (CDCl\(_3\)): \(\delta = 5.0\) (C\(_{16}\)), 12.7 (CH\(_3\)), 24.2 (C\(_{10}\)), 26.3 (C\(_9\)), 31.6 (C\(_{15}\)), 36.1 (C\(_{11}\)), 41.1 (C\(_{14}\)), 111.5 (C\(_{17}\)), 126.3 (C\(_{5,8}\)), 127.7 (C\(_{20}\)), 129.2 (C\(_{19}\)), 132.0 (C\(_{8a}\)), 132.1 (C\(_{4a}\)), 133.4, 133.5 (C\(_{6,7}\), n.a.), 138.5 (C\(_{18}\)), 144.1 (C\(_3\)), 146.2 (C\(_2\)), 172.1 (C\(_{12}\)), 184.9 (C\(_{1}\)), 185.1 (C\(_4\)).

LC-MS: \(R_t = 10.3\) min, m/z (%) 506.0 (100) [M+H]\(^+\).

HRMS: [M+H]\(^+\) calcd 506.0974, [M+H]\(^+\) found 506.0834.

**4,4’-(3,6-dimethyl-1,4-benzoquinone-2,5-diyl)dibutanoic acid (13)**

[Diagram of 4,4’-(3,6-dimethyl-1,4-benzoquinone-2,5-diyl)dibutanoic acid (13)]

2,5-dimethyl-1,4-benzoquinone (1.50 g, 10.02 mmol) and glutaric acid (14.53 g, 110.0 mmol) were mixed in 100 ml of 30 % aqueous CH\(_3\)CN and heated to 65°C. After all solids had dissolved, silver nitrate (1.25 g, 7.36 mmol) was added, followed by a solution of ammonium peroxodisulfate (6.53 g, 28.62 mmol) in 50 ml aqueous CH\(_3\)CN (dropwise over a period of 2 h). The reaction was heated for another 1 h at 65 °C before it was cooled and stirred overnight. 300 ml CH\(_2\)Cl\(_2\) and 200 ml H\(_2\)O were added and under addition of NaCl phases
were separated. The aqueous phase was extracted with CH₂Cl₂ (3 x 50 mL). The combined organic phases were washed with H₂O (5 x 100 mL) and dried over Na₂SO₄. After evaporation of the solvent under reduced pressure the crude yellowish brown oil was purified by using silica gel column chromatography (CH₂Cl₂/MeOH 95:5) to yield a orange solid (679 mg, 2.20 mmol).

Yield: 22%.

C₁₆H₂₀O₆ (MW = 308.33 g/mol).

R_f = 0.11 (CH₂Cl₂/MeOH 95:5).

¹H NMR (CDCl₃): δ = 2.05 (m, 4 H, H¹₀), 2.08 (s, 6 H, CH₃), 2.35 (m, 4 H, H⁹ or H¹¹, n.a.), 2.66 (m, 4 H, H⁹ or H¹¹, n.a.).

¹H NMR (CD₃OD): δ = 0.18 (m, 4 H, H¹₀), 0.49 (s, 6 H, CH₃), 0.79 (m, 4 H, (m, 4 H, H⁹ or H¹¹, n.a.), 1.00 (m, 4 H, H⁹ or H¹¹, n.a.).

¹³C NMR (CDCl₃): δ = 12.2 (CH₃), 24.9, 26.8, 34.6 (C⁹,¹⁰,¹¹, n.a.), 142.1, 142.7 (C²,³, n.a.), 177.0 (C¹₂), 188.5 (C¹).

LC-MS: R_t = 6.5 min, m/z (%) 308.94 (100) [M+H]⁺.

4,4'-(3,6-dimethyl-1,4-benzoquinone-2,5-diyl)bis(N-(3-(phenylselenyl)propyl)butanamide) (14):
Based on the preparation of 11, 4,4’-(3,6-dimethyl-1,4-benzoquinone-2,5-diyl)dibutanoic acid (13) (102.8 mg, 0.33 mmol) was reacted with 3-(phenylselenyl)propane-1-amine (142.7 mg, 0.66 mmol) using N-methylmorpholine (67.5 mg, 0.66 mmol) and ethylchloroformate (72.3 mg, 0.66 mmol). The crude product was purified by silica gel column chromatography (CH$_2$Cl$_2$/MeOH 98:2). A light yellow solid (109.2 mg, 0.16 mmol) was obtained.

Yield: 47.2%.

C$_{34}$H$_{42}$N$_2$O$_4$Se$_2$ (MW = 700.63 g/mol).

TLC: R$_f$ = 0.24 (CH$_2$Cl$_2$/MeOH 98:2).

Mp = 114-116°C.

$^1$H NMR (CDCl$_3$): δ = 1.71 (quint, 4 H, H$^{10}$ or H$^{15}$, n.a., $^3J_{HH}$ = 7.9), 1.91 (quint, 4 H, H$^{10}$ or H$^{15}$, n.a., $^3J_{HH}$ = 7.3), 2.02 (s, 6 H, CH$_3$), 2.18 (t, 4 H, H$^9$ or H$^{11}$ or H$^{16}$, n.a., $^3J_{HH}$ = 7.3), 2.48 (t, 4 H, H$^9$ or H$^{11}$ or H$^{16}$, n.a., $^3J_{HH}$ = 7.9), 2.92 (t, 4 H, H$^9$ or H$^{11}$ or H$^{16}$, n.a., $^3J_{HH}$ = 7.3), 3.36 (q, 4 H, H$^{14}$, $^3J_{HH}$ = 6.6), 5.84 (br s, 2 H, NH), 7.25 (m, 6 H, H$^{19,20}$), 7.48 (m, 4 H, H$^{18}$).

$^{13}$C NMR (CDCl$_3$): δ = 12.1 (CH$_3$), 24.3, 25.0, 25.9, 29.9, 36.1, 39.3 (C$^{9,10,11,14,15,16}$, n.a.), 127.0 (C$^{20}$), 129.1, 132.7 (C$^{18,19}$, n.a.), 129.9, 140.9, 143.5 (C$^{23,17}$, n.a.), 172.2 (C$^{12}$), 187.6 (C$^1$).

LC-MS: R$_t$ = 10.5 min, m/z (%) 703.1 (100) [M+H]$^+$.  
HRMS: [M+H]$^+$ calcd 703.1553, [M+H]$^+$ found 703.1356
Based on the preparation of 14, 4,4'-(3,6-dimethyl-1,4-benzoquinone-2,5-diyl) dibutanoic acid (13) (205.6 mg, 0.66 mmol) was reacted with 3-(phenyltelluryl)propane-1-amine (350.4 mg, 1.32 mmol) using N-methylmorpholine (134.9 mg, 1.32 mmol) and ethylchloroformate (144.7 mg, 1.32 mmol). After purification by silica gel column chromatography (CH$_2$Cl$_2$/MeOH 98:2) a yellowish brown solid (298.6 mg, 0.37 mmol) was obtained.

Yield: 56.1%.

C$_{34}$H$_{42}$N$_2$O$_4$Te$_2$ (MW = 797.91 g/mol).

TLC: $R_f$ = 0.40 (CH$_2$Cl$_2$/MeOH 98:2).

Mp = 99-103°C

$^1$H NMR (CDCl$_3$): $\delta$ = 1.69 (quint, 4 H, H$_{10}$ or H$_{15}$, n.a., $^3$$J_{HH}$ = 7.9), 1.99 (quint, 4 H, H$_{10}$ or H$_{15}$, n.a., $^3$$J_{HH}$ = 7.3), 2.00 (s, 6 H, CH$_3$), 2.15 (t, 4 H, H$_9$ or H$_{11}$ or H$_{16}$, n.a., $^3$$J_{HH}$ = 7.3), 2.46 (t, 4 H, H$_9$ or H$_{11}$ or H$_{16}$, n.a., $^3$$J_{HH}$ = 7.9), 2.86 (t, 4 H, H$_9$ or H$_{11}$ or H$_{16}$, n.a., $^3$$J_{HH}$ = 7.6), 3.31 (q, 4 H, H$_{14}$, $^3$$J_{HH}$ = 6.3), 5.71 (br s, 2 H, NH), 7.18 (m, 4 H, H$_{19}$), 7.26 (m, 2 H, H$_{20}$), 7.71 (m, 4 H, H$_{18}$).
$^{13}$C NMR (CDCl$_3$): $\delta$ = 4.9 (C$^{16}$), 24.3, 25.9, 31.6, 36.0, 41.0 (C$^{9,10,11,14,15}$, n.a.), 12.1 (CH$_3$), 111.4 (C$^{17}$), 140.9, 143.5 (C$^{2,3}$, n.a.), 127.7 (C$^{20}$), 129.2, 138.5 (C$^{18,19}$, n.a.), 172.2 (C$^{12}$), 187.5 (C$^1$).

LC-MS: $R_t = 11.0$ min, m/z (%) 801.7 (100) [M+H]$^+$.  

6-(1,4-naphthoquinone-2-ylamino)-N-(3-(phenylselenyl)propyl)hexanamide (17)

As described earlier, 6-(1,4-naphthoquinone-2-ylamino)hexanoic acid (16) (278.3 mg, 1.00 mmol) and 3-(phenylselenyl)propane-1-amine (214.2 mg, 1.00 mmol) were reacted in presence of $N$-methylmorpholine (101.2 mg, 1.00 mmol) and ethylchloroformate (108.5 mg, 1.00 mmol). After appropriate workup (silica gel column chromatography with CH$_2$Cl$_2$), an orange-red solid (124.9 mg, 0.26 mmol) was obtained.

Yield: 25.8%.

C$_{25}$H$_{28}$N$_2$O$_3$Se (MW = 483.46 g/mol).

TLC: $R_f = 0.50$ (CH$_2$Cl$_2$/MeOH 95:5).

Mp = 124-126°C.

$^1$H NMR (CDCl$_3$): $\delta$ = 1.41 (m, 2 H, H$^{12}$), 1.68 (m, 4 H, H$^{11,13}$), 1.90 (quint, 2 H, H$^{18}$, $^3$J$_{HH} = 6.9$), 2.15 (t, 2 H, H$^{14}$, $^3$J$_{HH} = 7.3$), 2.90 (t, 2 H, H$^{19}$, $^3$J$_{HH} = 7.3$), 3.17 (q, 2 H, H$^{10}$ or H$^{17}$, n.a., $^3$J$_{HH} = 6.3$), 3.35 (m, 2 H, H$^{10}$ or H$^{17}$, n.a.), 5.63 (br s, 1 H, NH), 5.70 (s, 1 H, H$^3$), 5.90 (br s,
1H, NH), 7.24 (m, 3 H, H^{22,23}), 7.47 (m, 2 H, H^{21}), 7.60 (dt, 1 H, H^{6} or H^{7}, n.a., \(^3\)J_{HH} = 7.6, \(^4\)J_{HH} = 1.3), 7.71 (dt, 1 H, H^{6} or H^{7}, n.a., \(^3\)J_{HH} = 7.6, \(^4\)J_{HH} = 1.3), 8.03 (dd, 1 H, H^{5} or H^{8}, n.a., \(^3\)J_{HH} = 7.9, \(^4\)J_{HH} = 1.0), 8.08 (dd, 1 H, H^{5} or H^{8}, n.a., \(^3\)J_{HH} = 7.9, \(^4\)J_{HH} = 1.0).

\(^{13}\)C NMR (CDCl\(_3\)): \(\delta = 25.08, 25.16, 26.6, 27.9, 29.9, 36.3, 39.2, 42.3\) (C^{10,11,12,13,14,17,18,19}, n.a.), 100.7 (C^{3}), 126.1, 126.2, 127.0, 131.9, 134.7 (C^{5,6,7,23}, n.a.), 129.1, 132.7 (C^{21,22}, n.a.), 129.9, 130.5, 133.6 (C^{8a}), n.a.), 147.9 (C^{2}), 172.5 (C^{15}), 181.9, 182.9 (C^{14}, n.a.).

NMR data including COSY spectroscopy:

\(^1\)H NMR (CDCl\(_3\)): \(\delta = 1.41\) (m, 2 H, H^{12}), 1.68 (m, 4 H, H^{11,13}), 1.90 (quint, 2 H, H^{18}, \(^3\)J_{HH} = 6.9), 2.15 (t, 2 H, H^{14}, \(^3\)J_{HH} = 7.3), 2.90 (t, 2 H, H^{19}, \(^3\)J_{HH} = 7.3), 3.17 (q, 2 H, H^{10}, \(^3\)J_{HH} = 6.3), 3.35 (m, 2 H, H^{17}), 5.63 (br s, 1 H, NH, H^{16}), 5.70 (s, 1 H, H^{3}), 5.90 (br s, 1 H, NH, H^{9}), 7.24 (m, 3 H, H^{22,23}), 7.47 (m, 2 H, H^{21}), 7.60 (dt, 1 H, H^{7}, \(^3\)J_{HH} = 7.6, \(^4\)J_{HH} = 1.3), 7.71 (dt, 1 H, H^{6}, \(^3\)J_{HH} = 7.6, \(^4\)J_{HH} = 1.3), 8.03 (dd, 1 H, H^{5}, \(^3\)J_{HH} = 7.9, \(^4\)J_{HH} = 1.0), 8.08 (dd, 1 H, H^{5}, \(^3\)J_{HH} = 7.9, \(^4\)J_{HH} = 1.0).

\(^{13}\)C NMR (CDCl\(_3\)): \(\delta = 25.08\) (C^{19}), 25.16 (C^{13}), 26.6 (C^{12}), 27.9 (C^{11}), 29.9 (C^{18}), 36.3 (C^{14}), 39.2 (C^{17}), 42.3 (C^{10}), 100.7 (C^{3}), 126.1 (C^{5}), 126.2 (C^{8}), 127.0 (C^{23}), 129.1 (C^{22}), 129.9 (C^{20}), 130.5 (C^{8a}), 131.9 (C^{7}), 132.7 (C^{21}), 133.6 (C^{4a}), 134.7 (C^{6}), 147.9 (C^{2}), 172.2 (C^{15}), 181.9 (C^{1}), 182.9 (C^{4}).

LC-MS: R\(_t = 8.8\) min, m/z (%) 484.9 (100) [M+H]\(^+\).

HRMS: [M+H]\(^+\) calcd 485.1343, [M+H]\(^+\) found 485.1320.
6-(1,4-naphthoquinone-2-ylamino)-N-(3-(phenyltelluryl)propyl)hexanamide (18)

Similar to the preparation of 17, 6-(1,4-naphthoquinone-2-ylamino)hexanoic acid (16) (191.5 mg, 0.67 mmol) and 3-(phenyltelluryl)propane-1-amine (175.0 mg, 0.67 mmol) were reacted in presence of N-methylmorpholine (67.4 mg, 0.67 mmol) and ethylchloroformate (72.3 mg, 0.67 mmol). After appropriate workup, an orange-red solid (250.3 mg, 0.47 mmol) was obtained.

Yield: 70.6%.

C$_{25}$H$_{28}$N$_2$O$_3$Te (MW = 532.10 g/mol).

TLC: R$_f$ = 0.36 (CH$_2$Cl$_2$/MeOH 95:5).

Mp = 105-107°C.

$^1$H NMR (CDCl$_3$): δ = 1.40 (m, 2 H, H$_{12}$), 1.67 (m, 4 H, H$_{11,13}$), 1.99 (m, 2 H, H$_{18}$), 2.13 (t, 2 H, H$_{14}$, $^3$J$_{HH}$ = 7.6), 2.86 (t, 2 H, H$_{19}$, $^3$J$_{HH}$ = 7.6), 3.17 (m, 2 H, H$_{10}$ or H$_{17}$, n.a.), 3.31 (m, 2 H, H$_{10}$ or H$_{17}$, n.a.), 5.55 (br s, 1 H, NH), 5.70 (s, 1 H, H$_3$), 5.90 (br s, 1 H, NH), 7.19 (m, 2 H, H$_{22}$), 7.27 (m, 1 H, H$_{23}$), 7.60 (dt, 1 H, H$_6$ or H$_7$, n.a., $^3$J$_{HH}$ = 7.6, $^4$J$_{HH}$ = 1.3), 7.71 (m, 3 H, H$_6$ or H$_7$, H$_{21}$), 8.03 (dd, 1 H, H$_5$ or H$_8$, n.a., $^3$J$_{HH}$ = 7.6, $^4$J$_{HH}$ = 1.3), 8.08 (dd, 1 H, H$_5$ or H$_8$, n.a., $^3$J$_{HH}$ = 7.6, $^4$J$_{HH}$ = 1.3).

$^{13}$C NMR (CDCl$_3$): δ = 5.0 (C$_{19}$), 25.1, 26.6, 27.9, 31.6, 36.3, 41.0, 42.3 (C$_{10,11,12,13,14,17,18}$, n.a.), 100.7 (C$_3$), 111.5 (C$_{20}$), 126.1, 126.2, 127.7, 131.9, 134.7 (C$_{5,8,6,7,23}$, n.a.) 129.2, 138.5 C$_{21,22}$, n.a.), 130.5, 133.6 (C$_{4a,8a}$, n.a.), 147.9 (C$_2$), 172.5 (C$_{15}$), 181.8, 182.9 (C$_{14}$, n.a.)
NMR data including COSY spectroscopy:

$^1$H NMR (CDCl$_3$): $\delta = 1.40$ (m, 2 H, H$_{12}$), 1.67 (m, 4 H, H$_{11,13}$), 1.99 (m, 2 H, H$_8$), 2.13 (t, 2 H, H$_{14}$, $^3J_{HH} = 7.6$), 2.86 (t, 2 H, H$_{19}$, $^3J_{HH} = 7.6$), 3.17 (m, 2 H, H$_{10}$), 3.31 (m, 2 H, H$_{17}$), 5.55 (br s, 1 H, NH, H$_{16}$), 5.70 (s, 1 H, H$_3$), 5.90 (br s, 1 H, NH, H$_9$), 7.19 (m, 2 H, H$_{22}$), 7.27 (m, 1 H, H$_{23}$), 7.60 (dt, 1 H, H$_7$, $^3J_{HH} = 7.6$, $^4J_{HH} = 1.3$), 7.71 (m, 3 H, H$_{6,21}$), 8.03 (dd, 1 H, H$_8$, $^3J_{HH} = 7.6$, $^4J_{HH} = 1.3$), 8.08 (dd, 1 H, H$_8$, $^3J_{HH} = 7.6$, $^4J_{HH} = 1.3$).

$^{13}$C NMR (CDCl$_3$): $\delta = 5.0$ (C$_{19}$), 25.1 (C$_{13}$), 26.6 (C$_{12}$), 27.9 (C$_{11}$), 31.6 (C$_{18}$), 36.3 (C$_{14}$), 41.0 (C$_{17}$), 42.3 (C$_{10}$), 100.7 (C$_3$), 111.5 (C$_{20}$), 126.1 (C$_5$), 126.2 (C$_8$), 127.7 (C$_{23}$), 129.2 (C$_{22}$), 130.5 (C$_{8a}$), 131.9 (C$_7$), 133.6 (C$_{4a}$), 134.7 (C$_6$), 138.5 (C$_{21}$), 147.9 (C$_2$), 172.5 (C$_{15}$), 181.8 (C$_1$), 182.9 (C$_4$).

LC-MS: $R_t = 12.4$ min, m/z (%) 535.2 (100) [M+H]$^+$.  

S2. SK-Mel-5 and HL-60 cell culture studies

SK-Mel-5 (human melanoma) and HL-60 (human leukemia) cell lines were cultured at 37°C in RPMI 1640 medium containing 10% FCS gold and 100U/mL penicillin and 100 µg/mL streptomycin. Cell viability was determined using a variation of the standard Methylthiazolyldiphenyltetrazolium bromide (MTT) assay.$^{11-13}$ To test the pro- or antioxidative properties of compounds, SK-Mel-5 cells were placed in wells of a 96-well plate (4 x 10$^4$ cells per well) and grown for 20 h to reach confluency. The medium was removed and cells were incubated with new medium containing the test compounds (5 to 200 µM). They were then incubated at 37°C for 24 h in the absence and presence of 1 mM H$_2$O$_2$. At
this point, the medium was removed and the MTT assay carried out. HL-60 cells were treated accordingly, yet an initial cell density of $9 \times 10^4$ cells per well was used.

S3. Activity assay against *Plasmodium falciparum*

**Cultivation of *Plasmodium falciparum* and drug sensitivity tests.** *P. falciparum* (3D7-Netherlands strain) was grown in continuous culture as described by Trager and Jensen\(^\text{14}\) with slight modifications. Unless otherwise stated, parasites were maintained at 1 to 10% parasitemia and 3.3% hematocrit in an RPMI 1640 culture medium supplemented with A+ erythrocytes, 0.5% lipid-rich bovine serum albumin (Albumax), 9 mM (0.16%) glucose, 0.2 mM hypoxanthine, 2.1 mM L-glutamine, and 22 µg/ml gentamicin. All incubations were carried out at 37°C in 3% $\text{O}_2$, 3% $\text{CO}_2$, and 94% $\text{N}_2$. Synchronization of parasites in culture to ring stages was carried out by treatment with 5% (w/v) sorbitol.\(^\text{15}\)

Isotopic drug sensitivity assays by means of the semi-automated microdilution technique\(^\text{16}\) were employed to investigate the susceptibility of the malaria parasites to the various compounds. The method depends on the incorporation of radioactive $^3\text{H}$-hypoxanthine which is taken up by the parasite as a precursor of purine deoxynucleotides for DNA synthesis and was performed according to the modifications of Fivelman and colleagues.\(^\text{17}\) In 96 well microtitre plates (Nunc\(^\text{®}\)), a two-fold serial dilution of the starting concentration of each drug to be tested was carried out. Parasites were incubated at a parasitemia of 0.25% (>70% ring forms) and 1.25% hematocrit in hypoxanthine free medium. After 48 hours, 0.5 µCi $^3\text{H}$-hypoxanthine was added into each well and the plates were incubated for another 24 h. The cells of each well were harvested on a glass fibre filter (Perkin-Elmer, Rodgau-Jügesheim,
Germany), washed and dried. Their radioactivity in counts per minute was considered to be proportional to the respective growth of *P. falciparum* in the well.

S4. Activity assay against *Trichophyton rubrum*

Activity against *Trichophyton rubrum* was measured in a plate assay. Briefly, agar plates containing streptomycin (40 ug/ml), penicillin (40 Units/ml) and cycloheximide (500 ug/ml) were prepared. The plates were placed on top of an ‘injection mask’, which formally divides the plate into eight equally-sized sectors and contains an inner and outer ring. Small amounts of *Trichophyton rubrum* samples obtained from patients were transferred onto the plate with a diluting loop, and positioned at the intersections of the sectors with the outer ring. The agar plate was stored in an incubator at 26°C for 6-10 days, during which time the dermatophytes grew to a size of around 1 cm in diameter. In order to test the ability of compounds to slow down or inhibit the further growth of the dermatophyte, cellulose plates soaked in compound (10 μl per plate) were added at the intersections of the sectors with the inner ring. The agar plates were returned to the incubator and the distance between the dermatophyte and the compound-containing plates was measured after 0, 2, 4, 6, 8 and 10 days. Incubations with DMSO as well as empty cellulose plates were used as negative controls, ketoconazol served as positive control and benchmark.

S5. 58-cell line screening at the National Cancer Institute (NCI)

The 58 cancer cell line screen for was performed at the National Cancer Institute (NCI) at the NIH (US). These single-dose tests (at 10 μM) were performed for cell lines clustered in cells
representing leukaemia, non-small cell lung cancer, colon cancer, cancer of the central nervous system, melanoma, ovarian cancer, renal cancer, prostate cancer and breast cancer.\textsuperscript{18,19} All tests follow a standard protocol for cytotoxicity screens, details of which can be obtained from the NCI website at http:\texttt{//dtp.nci.nih.gov}. Based on the results obtained as part of the single-dose testing, compounds with a particular activity were then selected for five-dose tests (10\textsuperscript{-8}, 10\textsuperscript{-7}, 10\textsuperscript{-6}, 10\textsuperscript{-5}, 10\textsuperscript{-4} M) and \textsc{LC}_{50} determination.
Summary of results obtained for 18 in the one-dose screen. Details are provided in the text.
S6. $^{13}$C NMR spectra of novel compounds
Literature:


