**SUPPORTING INFORMATION**

*Title:* Synthesis of 7- and 8-Functionalized 2-Aminophenoxazinones via Cyclocondensation of 2-Aminophenols

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**General methods**

All solvents for chromatographic separation were distilled before use. Commercially available reagents, diphenyl diselenide (6e), and bis(2-nitrophenyl) diselenide (6f) were used without further purification. MeOH was distilled prior to hydrogenation of nitrophenol compounds. Et₂O was distilled slowly over a mixture of LAH and CaH₂ powders using a water bath. Freshly distilled MeCN was redistilled twice over P₂O₅ to obtain the anhydrous solvent for preparation of ebselen. 2-Phenyl-1,2-benzisoselenazol-3(2H)-one (ebselen) (6a) was prepared from anthranilic acid and elemental selenium via the formation of 2,2’-dicarboxydiphenyl diselenide, followed by 2-(chloroseleno)benzoyl chloride...
tandem selenenylation-acylation of aniline (Liebig's Ann. Chem. 1993, 1239–1244). Bis[2-(N-phenylcarbamoyl)phenyl]diselenide (6b) was prepared by hydrogenation of ebselen (6a) with H₂NHN₂·H₂O using the literature procedure (Liebig's Ann. Chem. 1993, 1239–1244). The catalysts 6c and 6d were synthesized from the corresponding arylmagnesium bromides and elemental selenium (J. Am. Chem. Soc. 1975, 97, 5434–5447). Bis(2-nitro-4-trifluoromethylphenyl)diselenide (6g) was obtained by LiSeSeLi-mediated selenenylation of the corresponding 2-nitro-4-trifluoromethyl-1-chlorobenzene as reported in our previous work (Synth. Commun. 2009, 39, 251–266). Questiomyacin A was obtained by 2-aminophenol cyclocondensation with literature procedure (Synth. Commun. 2007, 37, 1779–1789). 2-Aminophenols 1b,c and 1f were prepared from the corresponding 2-nitrophenols by hydrogenation by alkaline KBF₄ in the presence of Pd on activated charcoal, via a modified literature procedure (Synth. Commun. 2007, 37, 1779–1789). 4-Bromo-2-nitrophenol was prepared by the nitration of 4-bromophenol with Bi(NO₃)₃·5H₂O using a scaled up (multigram scale) version of the grinding procedure described by Sun et al. (J. Org. Chem. 2005, 70, 9071–9073). Preparative column chromatography was performed on Merck Si60 silica gel (63–200 μm) as the stationary phase. Analytical TLC was performed on PET foils precoated with silica gel (Merck silica gel, 60 F254), and were made visual under UV light (λmax = 254 nm), or by staining with iodine steam. Melting points were determined on an Electrothermal IA 91100 digital melting-point apparatus using the standard open capillary method. IR spectra were recorded as KBr plates on a Perkin–Elmer 2000 FT-IR spectrometer. Absorption maxima are reported in wavenumbers (cm⁻¹). ¹H and ¹³C NMR spectra were recorded in CDCl₃ or DMSO-d₆ on a Bruker DRX 300 Spectrometer (300.1 for ¹H and 75.4 for ¹³C) or on a Bruker Avance 600 Spectrometer (600.6 for ¹H and 151.0 for ¹³C) at 295 K. Chemical shifts (δ) are given in parts per million (ppm) downfield relative to TMS, and coupling constants (J) are in Hz. Residual solvent central signals were recorded as follows: CDCl₃, δH = 7.263, δC = 77.00; DMSO-d₆, δH = 2.50, δC = 39.43. When measured, DEPT signals are referred to as (+) or (−). High-resolution mass spectra (HRMS) of new compounds (2b, 2c, 3d, 3f and 4e) were recorded on a Waters LCD Premier XE instrument, and only the [M + H]⁺ molecular species are reported. UV/VIS spectra were recorded on Hewlett-Packard HP 8752 spectrophotometer. All known products were characterized by ¹H NMR, ¹³C NMR and IR spectroscopy, and were identified by comparison of their spectral data and melting points with those reported in the literature. The NMR parameters for compound 2a were calculated with GIAO/DFT/B3LYP/6-31G(d,p) level. See also Chemical Abstract on SciFinder for ¹H NMR and ¹³C NMR spectra calculated using Advanced Chemistry Development, Inc. (ACD/Labs) Software V11.01 (© 1994–2014 ACD.Labs).

4-Bromo-2-nitrophenol

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\begin{array}{c}
\text{NO}_2 \\
\text{O} \\
\text{H}
\end{array}
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Yield: 5.64 g (62%); yellow plates; mp 88–89 °C (Synth. Commun. 2015, 45, 143–150, mp 89.0–90.5 °C). The analytical sample was obtained by recrystallization from light petroleum ether (20 mL/g). Yellow prisms; 5.56 g (61%): mp 114–116 °C (light petroleum ether)
(J. Org. Chem. 1958, 23, 1800–1802, mp 116 °C); IR (KBr): 3437, 3273, 3100, 1615, 1533, 1473, 1316, 1237, 1141, 836, 662, 629, 529 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ = 10.49 (s, 1 H, OH), 8.24 (d, J = 2.4 Hz, 1 H), 7.66 (dd, J = 8.9, 2.4 Hz, 1 H), 7.08 (d, J = 8.9 Hz, 1 H); ¹³C NMR (75 MHz, CDCl₃): δ = 154.1 (C), 140.3 (CH), 134.0 (C), 127.3 (CH), 121.7 (CH), 111.7 (C). IR, ¹H NMR, and ¹³C NMR data are in consistent with literature values (Synth. Commun. 2015, 45, 143–150: see the Supporting Information).

2-Amino-4-fluorophenol (1b)

Yield: 1.14 g (90%); pale brown crystals; mp 133–135 °C (CHCl₃) (Zh. Obsch. Khim. 1975, 45, 2414–2422, mp 135–136 °C); ¹H NMR (300 MHz, DMSO-d₆): δ = 8.92 (s, 1 H, OH), 6.55 (dd, J = 8.6 Hz, ¹J_{HF} = 5.6 Hz, 1 H, ArH), 6.36 (dd, ¹J_{HF} = 10.8 Hz, J = 3.1 Hz, 1 H, ArH), 6.12 (ddd, J = 8.6, 3.1 Hz, ²J_{HF} = 8.7 Hz, 1 H, ArH), 4.85 (br s, 2 H, NH₂); ¹³C NMR (75 MHz, DMSO-d₆): δ = 156.3 (d, ¹J_{CF} = 231.0 Hz, CF), 140.1 (d, ²J_{CF} = 1.7 Hz, C), 138.0 (d, ³J_{CF} = 11.4 Hz, C), 114.0 (d, ³J_{CF} = 10.0 Hz, CH), 100.9 (d, ²J_{CF} = 22.6 Hz, CH), 100.6 (d, ²J_{CF} = 26.3 Hz, CH). ¹H NMR data is consistent with literature values (Inorg. Chem. 2009, 48, 2908–2918).

2-Amino-5-fluorophenol (1c)

Yield: 0.77 g (61%); pale brown crystals; mp 142.0–142.5 °C (CHCl₃) (Chem. Eur. J. 2011, 17, 9076–9082, mp 140–143 °C); IR (KBr): 3380, 3315, 3400–2200 (br), 1623, 1525, 1459, 1291, 1257, 1208, 1156, 1130, 971, 894, 843, 775, 729, 609, 464 cm⁻¹; ¹H NMR (300 MHz, DMSO-d₆): δ = 6.56 (dd, J = 8.1 Hz, ¹J_{HF} = 6.4 Hz, 1 H, ArH), 6.55 (br s, 1 H, OH), 6.48 (dd, ²J_{HF} = 10.3 Hz, J = 2.7 Hz, 1 H, ArH), 6.37 (ddd, ³J_{HF} = 9.2 Hz, J = 8.1, 2.7 Hz, 1 H, ArH), 4.77 (br s, 2 H, NH₂); ¹³C NMR (151 MHz, DMSO-d₆): δ = 154.8 (d, ¹J_{CF} = 232.1 Hz, CF), 145.2 (d, ³J_{CF} = 10.7 Hz, C), 131.8 (C), 114.7 (d, ³J_{CF} = 8.9 Hz, CH), 104.8 (d, ²J_{CF} = 21.4 Hz, CH), 102.0 (d, ²J_{CF} = 24.9 Hz, CH). ¹H NMR data is consistent with literature values (Inorg. Chem. 2009, 48, 7937–7946).

2-Amino-4-bromophenol (1f)

Yield: 1.63 g (87%); grey plates; mp 127–128 °C (CHCl₃) (J. Org. Chem. 1990, 55, 2736–2742, mp 130–133 °C); IR (KBr): 3375, 3308, 3069, 3019, 1602, 1498, 1445, 1279, 1206, 873, 846, 804, 772, 630, 453 cm⁻¹; ¹H NMR (300 MHz, DMSO-d₆): δ = 9.27 (s, 1 H, OH), 6.71 (d, J = 2.4 Hz, 1 H, ArH), 6.55 (d, J = 8.3 Hz, 1 H, ArH), 6.48 (dd, J = 8.3, 2.4 Hz, 1 H, ArH), 4.81 (br s, 2 H, NH₂); ¹H NMR (600 MHz, DMSO-d₆): δ = 9.29 (s, 1 H, OH), 6.71 (d, J = 2.4 Hz, 1 H, ArH), 6.55 (d, J = 8.3 Hz, 1 H, ArH), 6.49 (dd, J = 8.3, 2.4 Hz, 1 H, ArH), 4.78 (br s, 2 H, NH₂); ¹³C NMR (75 MHz, DMSO-d₆): δ = 143.2 (C), 138.7 (C), 118.1 (CH), 116.0 (CH), 115.6 (CH), 110.6 (C). ¹H NMR data is consistent with literature values (Inorg. Chem. 2009, 48, 2908–2918).
Aminophenoxazinone 2–5: General Procedure

To a mixture of 2-aminophenol (1a–i) (1 equiv) and ebselen (6a) (0.08–5 mol%) in t-BuOH (5 mL/mmol), was added 30% aq H$_2$O$_2$ (1.2–5.0 equiv), and the reaction mixture was stirred at mild temperature (0–20 °C) or at solvent reflux temperature (+82 °C) for 20 h (Table 1). Next, a catalytic amount of Pt/C and the sat. solution of NaHCO$_3$ in brine (7.5%, 25 mL/mmol) were added and the mixture stirred vigorously until evolution of CO$_2$ and O$_2$ had ceased. The mixture was extracted with CHCl$_3$ (×5) until red or orange color of the phenoxazinone chromophore had disappeared. The combined organic layers were dried over anhydrous Na$_2$SO$_4$ and filtered. Silica gel (70–230 mesh, 10 g/mmol) was added, the solvent was removed in vacuum, and the residue was poured on a silica gel column (70–230 mesh) and subjected to purification. Products 2a–f, 3d, 3f and 4e were isolated by elution with CHCl$_3$–EtOAc (5:1 to 3:1, v/v), and product 5i was isolated by elution with EtOAc. In the cases of products 2g–h, the precipitate formed during the reaction was collected by filtration, washed several times with t-BuOH–H$_2$O (4:1, v/v) and H$_2$O, and then dried in air. The results are given in Table 1. The 2-amino-8-methyl-3H-phenoxazin-3-one (2a) and new compounds 2b, 2c, 3d, 3f and 4e were fully characterized.

**CAUTION:** Reactions containing fluorinated aminophenols 1b and 1c should be handled with extreme care due to the possible evolution of extremely toxic HF. Moreover, waste brine containing fluoroorganic residues and NaF can be harmful to the environment, human health and animals, so all manipulations of the waste require special attention. Safety precautions including nitrile, or natural rubber gloves are recommended.

2-Amino-8-methyl-3H-phenoxazin-3-one (2a)

The general procedure starting from 2-amino-4-methylphenol (1a) (0.62 g, 5.0 mmol), ebselen (6a) (69 mg, 0.25 mmol, 5 mol%) and H$_2$O$_2$ (2.0 mL, 20 mmol, 4.0 equiv) at r.t. was employed, with separation by column chromatography (CHCl$_3$–EtOAc, 5:1, v/v) to afford 2e (145 mg, 26%) as a red powder: mp 240–243 °C (CHCl$_3$); $R_f$ = 0.38 (CHCl$_3$–EtOAc, 5:1, v/v); IR (KBr): 3404, 3307, 3244, 2918, 1587 (br), 1569, 1477, 1431, 1206, 1180, 843, 799, 583, 562 cm$^{-1}$; $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ = 7.51 (s, 1 H, H-9), 7.39 (d, $J$ = 8.4 Hz, 1 H, H-6), 7.28 (dd, $J$ = 8.4, 1.6 Hz, 1 H, H-7), 6.78 (br s, 2 H, NH$_2$), 6.35 (s, 1 H, H-1), 6.33 (s, 1 H, H-4), 2.39 (s, 3H, CH$_3$); $^1$H NMR (600 MHz, DMSO-$d_6$): $\delta$ = 7.51 (s, 1 H, H-9), 7.39 (d, $J$ = 8.3 Hz, 1 H, H-6), 7.28 (d, $J$ = 8.3 Hz, 1 H, H-7), 6.77 (br s, 2 H, NH$_2$), 6.35 (s, 1 H, H-1 or H-4), 6.33 (s, 1 H, H-1 or H-4), 2.39 (s, 3 H, CH$_3$); $^1$H NMR (600 MHz, DMSO-$d_6$ + 1 equiv of TFA): $\delta$ = 7.49 (s, 1 H, H-9), 7.40 (d, $J$ = 8.3 Hz, 1 H, H-6), 7.28 (d, $J$ = 8.3 Hz, 1 H, H-7), 6.36 (s, 2 H, H-1 and H-4), 2.39 (s, 3 H, CH$_3$); $^1$H NMR (600 MHz, DMSO-$d_6$ + 5 equiv of TFA): $\delta$ = 7.46 (s, 1 H, H-9), 7.42 (d, $J$ = 8.3 Hz, 1 H, H-6), 7.27 (d, $J$ = 8.3 Hz, 1 H, H-7), 6.41 (s, 1 H, H-1 or H-4), 6.38 (s, 1 H, H-1 or H-4), 2.39 (s, 3 H, CH$_3$); $^{13}$C NMR (75 MHz, DMSO-$d_6$): $\delta$ = 180.1 (C), 148.9 (C), 148.1 (C), 147.3 (C), 140.0 (C), 134.7 (C), 133.5 (C), 129.8 (CH), 127.6 (CH), 115.5 (CH),
103.2 (CH), 98.4 (CH), 20.4 (CH₃); UV/VIS (MeOH): λ<sub>max</sub> = 239 nm (log ε = 4.465), 440 nm (log ε = 4.392); HRMS (EI): m/z [M + H]<sup>+</sup> calcd for C<sub>13</sub>H<sub>11</sub>N₂O₂: 227.0815; found: 227.0812; Anal. Calcd for C<sub>13</sub>H<sub>10</sub>N₂O₂: C, 69.02; H, 4.46; N, 12.38. Found: C, 68.96; H, 4.64; N, 12.35. Spectroscopic data discrepancies were found for integrations (J. Med. Chem. 2013, 56, 3310–3317, reported in the Supporting Information) of the benzene ring region and for the proton and carbon chemical shifts.

In particular, signal of the methyl group reported at 2.09 ppm and 31.1 ppm did not occur at all in our <sup>1</sup>H NMR and <sup>13</sup>C NMR spectrum, whereas instead a resonance at 2.39 ppm and 20.4 ppm, respectively, was measured in DMSO-d₆.

2-Amino-8-fluoro-3H-phenoxazin-3-one (2b)

The general procedure starting from 2-amino-4-fluorophenol (1b) (0.254 g, 2.0 mmol), ebselen (6a) (5.5 mg, 20 μmol, 1 mol%) and H<sub>2</sub>O<sub>2</sub> (0.60 mL, 6.0 mmol, 3.0 equiv) at 0–5 °C (ice–water bath) was employed, with purification of the crude product by column chromatography (CHCl₃–EtOAc, 5:1, v/v) to afford 2b (57.5 mg, 25%) as a red powder; mp 301–303 °C (CHCl₃) (with decomposition); R<sub>f</sub> = 0.42 (CHCl₃–EtOAc, 5:1, v/v); IR (KBr): 3476, 3394, 3367, 3335, 3265, 3204, 3045, 1613 (br), 1581, 1476, 1253, 1203, 1146, 869, 850, 804, 520, 471 cm<sup>–1</sup>; <sup>1</sup>H NMR (300 MHz, DMSO-<em>d</em><sub>6</sub>): δ = 7.56 (dd, <sup>3</sup>J = 9.0, <sup>4</sup>J<sub>HF</sub> = 5.1 Hz, 1 H, H-6), 7.53 (dd, <sup>3</sup>J<sub>HF</sub> = 9.3 Hz, <sup>4</sup>J = 3.0 Hz, 1 H, H-9), 7.32 (ddd, <sup>3</sup>J = 9.0 Hz, <sup>4</sup>J<sub>HF</sub> = 8.4 Hz, <sup>5</sup>J = 3.0 Hz, 1 H, H-7), 7.00 (br s, 2 H, NH₂), 6.36 (s, 1 H, H-1 or H-4), 6.34 (s, 1 H, H-1 or H-4); <sup>13</sup>C NMR (75 MHz, DMSO-<em>d</em><sub>6</sub>): δ = 180.1 (C), 158.6 (d, <sup>3</sup>J<sub>CF</sub> = 23.7 Hz, CH), 129.1 (d, <sup>3</sup>J<sub>CF</sub> = 12.6 Hz, C), 115.6 (d, <sup>2</sup>J<sub>CF</sub> = 25.0 Hz, CH), 112.9 (d, <sup>2</sup>J<sub>CF</sub> = 23.7 Hz, CH), 103.4 (C), 103.3 (CH), 97.8 (CH); UV/VIS (MeOH): λ<sub>max</sub> = 230 nm (log ε = 4.482), 438 nm (log ε = 4.487), 425 nm (log ε = 4.463), 437 nm (log ε = 4.472); HRMS (EI): m/z [M + H]<sup>+</sup> calcd for C<sub>12</sub>H<sub>10</sub>FNO<sub>2</sub>: 231.0564; found: 231.0578; Anal. Calcd for C<sub>12</sub>H<sub>11</sub>FNO<sub>2</sub>: C, 62.61; H, 3.07; N, 12.17. Found: C, 62.30; H, 3.10; N, 12.25. Caution: it is advisable to use a falcon round-bottom polypropylene tube (which has no detrimental effect on the reaction yield) because formation of HF causes tarnishing a glass flasks.

2-Amino-7-fluoro-3H-phenoxazin-3-one (2c)

The general procedure starting from 2-amino-5-fluorophenol (1c) (0.636 g, 5.0 mmol), ebselen (6a) (6.9 mg, 25 μmol, 0.5 mol%) and H<sub>2</sub>O<sub>2</sub> (1.5 mL, 15 mmol, 3 equiv) at r.t. was employed, with purification of the crude product by column chromatography (CHCl₃–EtOAc, 5:1, v/v) to afford 2c (351 mg, 61%) as a red powder; mp 255–256 °C (CHCl₃); R<sub>f</sub> = 0.37 (CHCl₃–EtOAc, 5:1, v/v); IR (KBr): 3494, 3398, 3265 (br), 3200, 3046, 1694 (br), 1580 (br), 1471, 1287, 1267, 1244, 1191, 1102, 969, 851, 512, 481 cm<sup>–1</sup>; <sup>1</sup>H NMR (300 MHz, DMSO-<em>d</em><sub>6</sub>): δ = 7.75 (dd, <sup>3</sup>J = 8.7 Hz, <sup>4</sup>J<sub>HF</sub> = 6.0 Hz, 1 H, H-9), 7.48 (dd, <sup>3</sup>J<sub>HF</sub> = 9.3 Hz, <sup>4</sup>J = 2.4 Hz, 1 H, H-6), 7.27 (ddd, <sup>3</sup>J = 8.7 Hz, <sup>3</sup>J<sub>HF</sub> = 8.7 Hz, <sup>4</sup>J = 2.4 Hz, 1 H, H-8), 6.79 (br s, 2 H,
NH₂), 6.37 (s, 1 H, H-1 or H-4), 6.34 (s, 1 H, H-1 or H-4); 13C NMR (151 MHz, DMSO-d6): δ = 180.0 (C), 160.9 (d, 1JCF = 248.1 Hz, CF), 148.3 (C), 147.5 (d, 2JCF = 2.9 Hz, C), 147.1 (C), 142.4 (d, 3JCF = 13.4 Hz, C), 130.7 (d, 4JCF = 2.6 Hz, C), 129.3 (d, 5JCF = 10.0 Hz, CH), 112.9 (d, 6JCF = 23.3 Hz, CH), 103.7 (CH), 103.3 (d, 7JCF = 27.5 Hz, CH), 98.3 (CH); UV/VIS (MeOH): λmax = 236 nm (log ε = 4.445), 414 nm (log ε = 4.357), 426 nm (log ε = 4.369); HRMS (EI): m/z [M + H]⁺ calcd for C₁₀H₁₂F₃N₂O₂: 231.0564; found: 231.0563; Anal. Caled for C₁₀H₁₂F₃N₂O₂: C, 62.61; H, 3.07; N, 12.17. Found: C, 62.30; H, 3.10; N, 12.25. Caution: it is advisable to use a falcon round-bottom polypropylene tube (which has no detrimental effect on the reaction yield) because formation of HF causes tarnishing a glass flasks.

2-Amino-8-chloro-3H-phenoxazin-3-one (2d) The general procedure starting from 2-amino-4-chlorophenol (1d) (287 mg, 2.0 mmol), ebselen (6a) (2.7 mg, 10 μmol, 0.5 mol%) and H₂O₂ (0.60 mL, 6.0 mmol, 3 equiv) at r.t. was employed, with purification of the crude product by column chromatography (CHCl₃–EtOAc, 2:1, v/v), to afford 2d (163 mg, 66%) as a red powder: mp 270–271 °C (CHCl₃) (Chin. Chem. Lett. 2006, 17, 1141–1144, mp 268–270 °C); Rf = 0.38 (CHCl₃–EtOAc, 5:1, v/v); IR (KBr): 3455, 3367, 3045, 1607 (br), 1572, 1493, 1207, 1188, 1072, 870, 811, 581, 487 cm⁻¹; ¹H NMR (300 MHz, DMSO-d₆): δ = 7.73 (d, J = 2.4 Hz, 1 H, H-9), 7.52 (d, J = 8.7 Hz, 1 H, H-6), 7.46 (dd, J = 8.7, 2.4 Hz, 1 H, H-7), 6.99 (br s, 2 H, NH₂), 6.36 (s, 1 H, H-1 or H-4), 6.33 (s, 1 H, H-1 or H-4); ¹³C NMR (151 MHz, DMSO-d₆): δ = 180.1 (C), 149.0 (C), 148.7 (C), 147.7 (C), 140.6 (C), 134.5 (C), 128.6 (C), 127.9 (CH), 126.5 (CH), 117.4 (CH), 103.6 (CH), 98.0 (CH). IR and ¹H NMR data are consistent with literature values (Chin. Chem. Lett. 2006, 17, 1141–1144).

2-Amino-7-chloro-3H-phenoxazin-3-one (2e) The general procedure starting from 2-amino-5-chlorophenol (1e) (287 mg, 2.0 mmol), ebselen (6a) (5.4 mg, 20 μmol, 1 mol%) and H₂O₂ (0.40 mL, 4.0 mmol, 2 equiv) at 0–5 °C (ice–water bath) was employed, with purification of the crude product by column chromatography (CHCl₃–EtOAc, 5:1, v/v) to afford 2e (1.9 g, 72%) as a red powder: mp 297–298 °C (CHCl₃) (Synth. Commun. 2007, 37, 1779–1789, mp 296–297 °C); Rf = 0.38 (CHCl₃–EtOAc, 5:1, v/v); IR (KBr): 3402, 3305, 3247, 1574 (br), 1463, 1440, 1289, 1173, 1071, 924, 824, 541 (br) cm⁻¹; ¹H NMR (300 MHz, DMSO-d₆): δ = 7.67 (d, J = 8.6 Hz, 1 H, H-9), 7.62 (d, J = 2.0 Hz, 1 H, H-6), 7.40 (dd, J = 8.6, 2.0 Hz, 1 H, H-8), 6.87 (br s, 2 H, NH₂), 6.34 (s, 2 H, H-1, H-4); ¹³C NMR (75 MHz, DMSO-d₆): δ = 180.2 (C), 148.33 (C), 148.27 (C), 147.4 (C), 142.2 (C), 132.7 (C), 131.9 (C), 129.0 (CH), 125.4 (CH), 115.9 (CH), 103.7 (CH), 98.2 (CH). IR data are consistent with literature values (Synth. Commun. 2007, 37, 1779–1789).
2-Amino-8-bromo-3H-phenoxazin-3-one (2f)

The general procedure starting from 2-amino-4-bromophenol (1f) (376 mg, 2.0 mmol), ebselen (6a) (5.5 mg, 20 μmol, 1.0 mol%) and H₂O₂ (0.60 mL, 6.0 mmol, 3 equiv) at 0–5 °C (ice–water bath) was employed, with purification of the crude product by column chromatography (CHCl₃–EtOAc, 3:1; v/v), to afford 2f (151 mg, 52%) as a red powder: mp 235–246 °C (EtOAc) (with decomposition) (Bull. Soc. Chim. Fr. 1923, 33, 1823–1832); R$_f$ = 0.65 (CHCl₃–EtOAc, 3:1; v/v); IR (KBr): 3456, 3368, 3046, 1606 (br); 1H NMR (300 MHz, DMSO-d$_6$): $\delta$ = 7.86 (d, J = 2.0 Hz, 1 H, H-9), 7.58 (dd, J = 8.8, 2.0 Hz, 1 H, H-7), 7.46 (d, J = 8.8 Hz, 1 H, H-6), 7.00 (br s, 2 H, NH$_2$), 6.37 (s, 1 H, H-1 or H-4), 6.33 (s, 1 H, H-1 or H-4); $^{13}$C NMR (75 MHz, DMSO-d$_6$): $\delta$ = 180.2 (C), 149.0 (C), 148.7 (C), 147.8 (C), 141.2 (C), 135.0 (C), 130.7 (C), 129.6 (CH), 117.9 (CH), 116.5 (C), 103.7 (CH), 98.0 (CH); UV/VIS (MeOH): $\lambda_{max}$ = 248 nm (log $\varepsilon$ = 4.239), 420 nm (log $\varepsilon$ = 4.227), 434 nm (log $\varepsilon$ = 4.167); HRMS: m/z [M + H]$^+$ calcld for C$_{12}$H$_8$BrN$_2$O$_2$: 290.9764; found 290.9756; Anal. Calcd for C$_{12}$H$_8$BrN$_2$O$_2$: C, 49.51; H, 2.27; Br, 27.32; N, 9.40.

2-Amino-8-carboxy-3H-phenoxazin-3-one (2g)

The general procedure starting from 2-amino-4-carboxyphenol (1g) (1.53 g, 10 mmol), ebselen (6a) (137 mg, 0.50 mmol, 5 mol%) and H₂O₂ (4.0 mL, 40 mmol, 4 equiv) at r.t. was employed, and the precipitate formed during the reaction was collected by filtration, washed with t-BuOH–H₂O (4:1; v/v) and H₂O, and dried in air to afford 2g (1.11 g, 87%) as a red brown powder: mp > 300 °C (Chem. Ber. 1896, 29, 1756–1760, mp > 300 °C); IR (KBr): 3466, 3351, 3300–2200 (COOH), 1701, 1578 (br), 1264, 1203, 1188, 764, 539 cm$^{-1}$; 1H NMR (300 MHz, DMSO-d$_6$): $\delta$ = 13.00 (br s, 1 H, COOH), 8.16 (d, J = 1.4 Hz, 1 H, H-9); 7.96 (dd, J = 8.5, 1.4 Hz, 1 H, H-7), 7.56 (d, J = 8.5 Hz, 1 H, H-6), 6.92 (br s, 2 H, NH$_2$), 6.40 (s, 1 H, H-1 or H-4), 6.37 (s, 1 H, H-1 or H-4); $^{13}$C NMR (75 MHz, DMSO-d$_6$): $\delta$ = 180.3 (C), 166.3 (C), 148.9 (C), 148.6 (C), 147.5 (C), 144.8 (C), 133.3 (C), 129.0 (CH), 128.9 (CH), 127.6 (C), 116.2 (CH), 104.0 (CH), 98.2 (CH). 1H NMR and $^{13}$C NMR data are consistent with literature values. (J. Biol. Chem. 2006, 281, 36944–36951).

2-Amino-7-carboxy-3H-phenoxazin-3-one (2h)

The general procedure starting from 2-amino-5-carboxyphenol (1h) (1.53 g, 10 mmol), ebselen (6a) (137 mg, 0.50 mmol, 5 mol%) and H₂O₂ (5.0 mL, 50 mmol, 5 equiv) at r.t. was employed, and the precipitate formed during the reaction was collected by filtration, washed with t-BuOH–H₂O (4:1; v/v) and H₂O, and dried in air to afford 2h (0.97 g, 76%) as a dark red powder; mp > 300 °C; IR (KBr): 3451, 3400–2200 (COOH), 3340, 3043, 1705, 1606 (br), 1443, 1284, 1184, 875, 775, 765, 697, 537 cm$^{-1}$; 1H NMR
(300 MHz, DMSO-\textit{d}_6): \delta = 12.80 (br s, 1 H, COOH), 7.91 (d, \textit{J} = 1.6 Hz, 1 H, H-6), 7.89 (dd, \textit{J} = 8.9, 1.6 Hz, 1 H, H-8), 7.75 (d, \textit{J} = 8.9 Hz, 1 H, H-9), 7.09 (br, 2 H, NH_2), 6.40 (s, 1 H, H-1 or H-4), 6.37 (s, 1 H, H-1 or H-4); \textsuperscript{13}C NMR (75 MHz, DMSO-\textit{d}_6): \delta = 180.2 (C), 166.1 (C), 149.6 (C), 149.0 (C), 148.1 (C), 141.4 (C), 136.8 (C), 129.7 (C), 127.7 (CH), 125.6 (CH), 116.6 (CH), 103.7 (CH), 98.1 (CH). \textsuperscript{1}H NMR and \textsuperscript{13}C NMR data are consistent with literature values. (Appl. Environ. Microbiol. 2002, 68, 4965–4970).

2-Amino-4,8-dichloro-1H-phenoxazin-1-one (3d)

The general procedure starting from 2-amino-4-chlorophenol (1d) (287 mg, 2.0 mmol), ebselen (6a) (27 mg, 0.10 mmol, 5 mol%) and H_2O_2 (1.0 mL, 10 mmol, 5 equiv) at gentle reflux temperature (+82 °C) was employed, with purification of the crude product by column chromatography (CHCl_3–EtOAc, 5:1, v/v), to afford 3d (146 mg, 52%) as a red powder: mp 228–230 °C (CHCl_3); \textit{R}_f = 0.86 (CHCl_3–EtOAc, 5:1, v/v); IR (KBr): 3460, 3344, 3332 (br), 3071, 1599 (br), 1572, 1489, 1455, 1421, 1395, 1280, 1212, 1188, 1074, 944, 868, 843, 804, 585, 498 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (300 MHz, DMSO-\textit{d}_6): \delta = 7.83 (d, \textit{J} = 1.5 Hz, 1 H, H-9), 7.60–7.50 (m, 2 H, H-6, H-7), 7.21 (br s, 2 H, NH_2), 6.39 (s, 1 H, H-3); \textsuperscript{13}C NMR (75 MHz, DMSO-\textit{d}_6): \delta = 177.5 (C), 148.9 (C), 144.1 (2-C), 140.7 (C), 133.7 (C), 128.92 (CH), 128.85 (C), 127.0 (CH), 117.4 (CH), 102.8 (C), 102.6 (CH); HRMS (EI): m/z [M + H]\textsuperscript{+} calcd for C_{12}H_{7}Cl_{2}N_{2}O_{2}: 280.9879; found: 280.9880. Anal. Calcd for C_{12}H_{7}Br_{2}N_{2}O_{2}Cl_{2}: C, 51.27; H, 2.15; N, 9.97; Cl, 25.22. Found; C, 51.42; H, 2.02; N, 10.02; Cl, 25.00.

2-Amino-4,8-dibromo-1H-phenoxazin-1-one (3f)

The general procedure starting from 2-amino-4-bromophenol (1f) (376 mg, 2.0 mmol), ebselen (6a) (27 mg, 0.10 mmol, 5 mol%) and H_2O_2 (1.0 mL, 10 mmol, 5 equiv) at gentle reflux temperature (+82 °C) was employed, with purification of the crude product by column chromatography (CHCl_3–EtOAc, 5:1, v/v), to afford 3f (236 mg, 64%) as a red powder: mp > 300 °C (EtOAc); \textit{R}_f = 0.80 (CHCl_3–EtOAc, 5:1, v/v); IR (KBr): 3464, 3323 (br), 3081, 1654, 1599 (br), 1543, 1490, 1451, 1368, 1274, 1211, 1184, 841, 816, 431 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (300 MHz, DMSO-\textit{d}_6): \delta = 7.92 (d, \textit{J} = 2.3 Hz, 1 H, H-9), 7.63 (dd, \textit{J} = 8.8, 2.3 Hz, 1 H, H-7), 7.49 (d, \textit{J} = 8.8 Hz, 1 H, H-6), 7.17 (br s, 2 H, NH_2), 6.39 (s, 1 H, H-3); \textsuperscript{13}C NMR (75 MHz, DMSO-\textit{d}_6): \delta = 177.4 (C), 149.3 (C), 146.0 (C), 144.7 (C), 141.3 (C), 134.3 (C), 131.8 (CH), 130.0 (CH), 117.7 (CH), 116.6 (C), 102.7 (CH), 94.3 (C); UV/VIS (MeOH): \lambda_{\text{max}} = 254 nm (log \varepsilon = 4.406), 419 nm (log \varepsilon = 4.341), 435 nm (log \varepsilon = 4.365); HRMS (EI): m/z [M + H]\textsuperscript{+} central signal calcd for C_{12}H_{7}Br_{2}N_{2}O_{2}: 370.8848; found: 370.8867. Anal. Calcd for C_{12}H_{6}Br_{2}N_{2}O_{2}C: 38.95; H, 1.63; Br, 43.19; N, 7.57. Found; C, 39.22; H, 1.57; Br, 43.48; N, 7.39.
4-Amino-1,7-dichloro-3H-phenoxazin-3-one (4e)

The general procedure starting from 2-amino-5-chlorophenol (1e) (287 mg, 2.0 mmol), ebselen (6a) (27 mg, 0.10 mmol, 5 mol%) and H$_2$O$_2$ (1.0 mL, 10 mmol, 5 equiv) at gentle reflux temperature (+82 °C) was employed, with purification of the crude product by column chromatography (CHCl$_3$–EtOAc, 5:1, v/v), to afford 4e (171 mg, 61%) as a red powder: mp 284 °C (CHCl$_3$); $R_f$ = 0.86 (CHCl$_3$–EtOAc, 5:1, v/v); $R_f$ = 0.47 (CHCl$_3$); IR (KBr): 3480, 3375 (br), 3048, 1659, 1599 (br), 1457, 1429, 1308, 1186, 1077, 942, 923, 844, 821, 589 cm$^{-1}$; $^1$H NMR (300 MHz, DMSO-d$_6$): $\delta$ = 7.80 (d, $J$ = 8.6 Hz, 1 H, H-9), 7.70 (d, $J$ = 2.2 Hz, 1 H, H-6), 7.46 (dd, $J$ = 8.6, 2.2 Hz, 1 H, H-8), 7.11 (br s, 2 H, NH$_2$), 6.38 (s, 1 H, H-2); $^{13}$C NMR (75 MHz, DMSO-d$_6$): $\delta$ = 177.7 (C), 148.7 (C), 143.9 (C), 143.6 (C), 142.4 (C), 133.1 (C), 132.0 (C), 129.5 (CH), 125.6 (CH), 115.9 (CH), 103.0 (C), 102.7 (CH); HRMS (EI): m/z [M + H]$^+$ calcd for C$_{12}$H$_7$Cl$_2$N$_2$O$_2$: 280.9879; found: 280.9880; Anal. Calcd for C$_{12}$H$_6$N$_2$O$_2$Cl$_2$: C, 51.27; H, 2.15; N, 9.97; Cl, 25.22. Found: C, 51.18; H, 2.25; N, 10.08; Cl, 25.40.

2-Amino-4,4a-dihydro-4a,7-dimethyl-3H-phenoxazin-3-one (5i)

The general procedure starting from 2-amino-5-methylphenol (1i) (3.08 g, 25 mmol), ebselen (6a) (5.5 mg, 0.08 mol%) and H$_2$O$_2$ (3.0 mL, 30 mmol, 1.2 equiv) at 0–5 °C (ice–water bath) was employed, with purification of the crude product by filtration other Si60 silica gel (0.063–0.2 mm) eluted with EtOAc, to afford 5i (2.75 g, 91%) as a orange powder; mp 230–231 °C (EtOAc) (Synth. Commun. 2007, 37, 1779–1789, mp 231 °C); $R_f$ = 0.62 (EtOAc); IR (KBr): 3401, 3288, 3165 (br), 3033, 2969, 2951, 1695, 1623 (br), 1534, 1491, 1394, 1288, 1108, 1064, 813, 571 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 7.21 (d, $J$ = 8.1 Hz, 1 H, H-9), 6.84 (dd, $J$ = 8.1, 1.2 Hz, 1 H, H-8), 6.72 (d, $J$ = 1.2 Hz, 1 H, H-6), 6.22 (s, 1 H, H-1), 4.63 (br s, 2 H, NH$_2$), 3.10 (s, 2 H, CH$_2$), 2.33 (s, 3 H, CH$_3$-7), 1.24 (s, 3 H, CH$_3$-4); $^{13}$C NMR (151 MHz, CDCl$_3$): $\delta$ = 191.2 (C), 160.2 (C), 144.3 (C), 144.2 (C), 138.6 (C), 132.2 (C), 126.3 (CH), 123.4 (CH), 117.0 (CH), 109.4 (CH), 71.4 (C), 49.5 (CH$_2$), 22.4 (CH$_3$), 21.5 (CH$_3$); $^{13}$C NMR (151 MHz, DMSO-d$_6$): $\delta$ = 191.5 (C), 160.8 (C), 146.4 (C), 143.8 (C), 136.5 (C), 132.6 (C), 125.4 (CH), 116.5 (CH), 105.9 (CH), 70.9 (C), 49.1 (CH$_2$), 22.0 (CH$_3$), 20.9 (CH$_3$). $^1$H NMR data is consistent with literature values (Tetrahedron Lett. 2015, 56, 1060–1062. $^{13}$C NMR data appeared in DMSO-d$_6$ generally is consistent with literature values (Chem. Lett. 1996, 819–820) but signal reported as 77.1 ppm did not occur in our spectrum, whereas instead a resonance at 70.9 ppm and fourteen new signals we were observed due to equilibrium with 2-amino-4a,7-dimethyl-4aH-phenoxazin-3-ol; $^{13}$C NMR (151 MHz, DMSO-d$_6$): $\delta$ = 183.4 (C), 152.9 (C), 151.2 (C), 147.2 (C), 144.1 (C), 136.1 (C), 134.4 (C), 127.6 (CH), 120.4 (CH), 119.6 (CH), 116.4 (CH), 94.6 (CH), 20.6 (CH$_3$), 17.7 (CH$_3$). The equilibrium with CDCl$_3$ we do not observed (Fig. S73–S80).
2-Phenyl-1,2-benzisoselenazol-3(2H)-one – ebselen (6a)

![Chemical Structure](image)

The solution of 2-(chloroseleno)benzoyl chloride (1.27 g, 5.0 mmol) in anhydrous MeCN (20 mL) was added dropwise at r.t. to a stirred solution of aniline (1.53 mL, 16.5 mmol) in anhydrous MeCN (25 mL) over 1.5 h. The reaction was continued for additional 2 h (with TLC control), before H₂O (75 mL) was added dropwise and the mixture was allowed to stand for 30 min. The formed precipitate was collected by filtration, washed with H₂O (2·3 mL), dried in air and recrystallized from EtOAc to afford pale orange prisms of 2-phenyl-1,2-benzisoselenazol-3(2H)-one (ebselen) (6a) (1.1 g, 80%): mp 181.0–181.5 °C (EtOAc) (Liebigs Ann. Chem. 1993, 1239–1244, mp 181–182 °C); ¹H NMR (600 MHz, CDCl₃): δ = 8.13 (d, J = 7.9 Hz, 1 H, ArH), 7.68–7.65 (m, 2 H, ArH), 7.64 (d, J = 8.0 Hz, 2 H, ArH), 7.48 (dd, J = 7.9, 6.2, 1.8 Hz, 1 H, ArH), 7.44 (dd, J = 8.0, 7.4 Hz, 2 H, ArH), 7.29 (t, J = 7.4 Hz, 1 H, ArH). ¹H NMR data is consistent with literature values (Org. Lett. 2010, 12, 5394–5397, see the Supporting Information).

Bis[2-(N-phenylcarbamoyl)phenyl]diselenide (6b)

![Chemical Structure](image)

Compound 6b was prepared by the hydrogenation of ebselen (6a) with H₂NNH₂·H₂O with literature procedure (Liebigs Ann. Chem. 1993, 1239–1244) to afford colorless powder; mp 262.5–264.0 °C (EtOH) (Liebigs Ann. Chem. 1993, 1239–1244, mp 262–264 °C); ¹H NMR (600 MHz, DMSO-d₆): δ = 10.56 (s, 2 H, NH), 7.96 (d, J = 7.5 Hz, 2 H, ArH), 7.80 (d, J = 8.0 Hz, 2 H, ArH), 7.77 (d, J = 7.9 Hz, 4 H, ArH), 7.46 (dd, J = 8.0 Hz, J = 6.9 Hz, 2 H, ArH), 7.42 (dd, J = 7.5 Hz, J = 6.9 Hz, 2 H, ArH), 7.40 (dd, J = 7.9 Hz, J = 7.3 Hz, 4 H, ArH), 7.16 (t, J = 7.3 Hz, 2 H, ArH). ¹H NMR data is consistent with literature values (Bioorg. Med. Chem. Lett. 2006, 16, 5334–5338).

Bis[3,5-bis(trifluoromethyl)phenyl]diselenide (6c)

The literature procedure of diphenyl diselenides preparation (J. Am. Chem. Soc. 1975, 97, 5434–5447) starting from 3,5-bis(trifluoromethyl)phenyl-magnesium bromide (60 mmol) and elemental selenium 4.75 g (60 mmol) followed aerobic oxidation of the corresponding benzeneselenol was employed, with separation by column chromatography (silica gel, 70–230 mesh, 130 g) by slow elution with degassed hexane, to afford 6c (11.4 g, 19.5 mmol, 65%) as pale yellow crystals: mp 70.5–
71.5 °C (pentane) (J. Chem. Soc., Perkin Trans. 1 2001, 224–228, mp 65 °C); \(^1\)H NMR (600 MHz, CDCl\(_3\)): \(\delta = 8.03\) (s, 4 H, ArH), 7.79 (s, 2 H, ArH). \(^1\)H NMR data is consistent with literature values (J. Chem. Soc., Perkin Trans. 1 2001, 224–228).

**Bis(3-trifluoromethylphenyl)diselenide (6d)**

The literature procedure of diphenyl diselenides preparation (J. Am. Chem. Soc. 1975, 97, 5434–5447) starting from 3-trifluoromethylphenylmagnesium bromide (60 mmol) and elemental selenium 4.75 g (60 mmol) followed aerobic oxidation of the corresponding benzeneselenol was employed, with separation by column chromatography (silica gel, 70–230 mesh, 130 g) by slow elution with degassed hexane, to afford 6d (11.4 g, 25.4 mmol, 85 %) as orange oil: (Org. Lett. 2012, 14, 1074–1077, oil); \(^1\)H NMR (600 MHz, CDCl\(_3\)): \(\delta = 7.85\) (s, 2 H, ArH), 7.77 (d, \(J = 7.8\) Hz, 2 H, ArH), 7.53 (d, \(J = 7.7\) Hz, 2 H, ArH), 7.41 (dd, \(J = 7.8\) Hz, \(J = 7.7\) Hz, 2 H, ArH). \(^1\)H NMR data is consistent with literature values (Org. Lett. 2012, 14, 1074–1077, see the Supporting Information).

**Bis(2-nitro-4-trifluoromethylphenyl)diselenide (6g)**

The literature procedure (Synth. Commun. 2009, 39, 251–266) starting from 2-nitro-4-trifluoromethylchlorobenzene and LiSeSeLi prepared from elementary selenium and lithium (Phosphorus, Sulfur, Silicon Relat. Elem. 2008, 183, 970–985) was employed, with purification of the crude product by recrystallization from MeCN, to afford 6g as a yellow needles; mp 180–182 °C (MeCN) (Ann. Polish Chem. Soc. 2004, 1282–1285, mp 180–182 °C), (Synth. Commun. 2009, 39, 251–266, mp 180–182); IR (KBr): 3103, 1618, 1566, 1535, 1521, 1331, 1300, 1158, 1141, 1032, 1084, 844, 708 cm\(^{-1}\). \(^1\)H NMR and \(^13\)C NMR data are consistent with literature values (Synth. Commun. 2009, 39, 251–266).
Fig. S1 $^1$H NMR (300.132 MHz, CDCl$_3$) spectrum of 4-bromo-2-nitrophenol

Fig. S2 $^1$H NMR (300.132 MHz, CDCl$_3$) expansion spectrum of 4-bromo-2-nitrophenol
Fig. S3 $^{13}$C NMR (75.475 MHz, CDCl$_3$) spectrum of 4-bromo-2-nitrophenol

Fig. S4 $^{13}$C NMR (75.475 MHz, CDCl$_3$) expansion spectrum of 4-bromo-2-nitrophenol
Fig. S5 $^1$H NMR (300.132 MHz, DMSO-$d_6$) spectrum of 2-amino-4-fluorophenol (1b)

Fig. S6 $^1$H NMR (300.132 MHz, DMSO-$d_6$) expansion spectrum of 2-amino-4-fluorophenol (1b)
Fig S7 $^{13}$C NMR (75.475 MHz, DMSO-$d_6$) spectrum of 2-amino-4-fluorophenol (1b)

Fig S8 $^{13}$C NMR (75.475 MHz, DMSO-$d_6$) expansion spectrum of 2-amino-4-fluorophenol (1b)
Fig S9 $^{13}$C NMR (75.475 MHz, DMSO-d$_6$) dept-135 spectrum of 2-amino-4-fluorophenol (1b)

Fig S10 $^{13}$C NMR (75.475 MHz, DMSO-d$_6$) dept-135 expansion spectrum of compound 1b
Fig. S11 $^1$H NMR (300.132 MHz, DMSO-$d_6$) spectrum of 2-amino-5-fluorophenol (1c)

Fig. S12 $^1$H NMR (300.132 MHz, DMSO-$d_6$) expansion spectrum of 2-amino-5-fluorophenol (1c)
Fig S13 $^{13}$C NMR (151.031 MHz, DMSO-$d_6$) spectrum of 2-amino-5-fluorophenol (1c)

Fig S14 $^{13}$C NMR (151.031 MHz, DMSO-$d_6$) expansion spectrum of compound 1c
Fig. S15 \( ^1\text{H NMR} \) (300.132 MHz, DMSO-\( d_6 \)) spectrum of 2-amino-4-bromophenol (1f)

Fig. S16 \( ^1\text{H NMR} \) (300.132 MHz, DMSO-\( d_6 \)) expansion spectrum of 2-amino-4-bromophenol (1f)
**Fig. S17** $^1$H NMR (600.584 MHz, DMSO-d$_6$) expansion spectrum of 2-amino-4-bromophenol (1f)

**Fig. S18** $^{13}$C NMR (75.475 MHz, DMSO-d$_6$) spectrum of 2-amino-4-bromophenol (1f)
Fig. S19 $^1$H NMR (300.132 MHz, DMSO-d$_6$) spectrum of 2-amino-8-methylphenoxazin-3-one 2a

Fig. S20 $^1$H NMR (300.132 MHz, DMSO-d$_6$) expansion spectrum of compound 2a
Fig. S21 $^{13}$C NMR (75.475 MHz, DMSO-$d_6$) spectrum of 2-amino-8-methylphenoxazin-3-one 2a

Fig. S22 $^{13}$C NMR (75.475 MHz, DMSO-$d_6$) expansion spectrum of compound 2a
Fig. S23 $^1$H NMR (300.132 MHz, DMSO-$d_6$) spectrum of 2-amino-8-fluorophenoxazin-3-one 2b

Fig. S24 $^1$H NMR (300.132 MHz, DMSO-$d_6$) expansion spectrum of compound 2b
Fig. S25 $^{13}$C NMR (75.475 MHz, DMSO-$d_6$) spectrum of 2-amino-8-fluorophenoxazin-3-one 2b

Fig. S26 $^{13}$C NMR (75.475 MHz, DMSO-$d_6$) expansion spectrum of compound 2b
Fig. S27 $^1$H NMR (300.132 MHz, DMSO-$d_6$) spectrum of 2-amino-7-fluorophenoxazin-3-one 2c

Fig. S28 $^1$H NMR (300.132 MHz, DMSO-$d_6$) expansion spectrum of compound 2c
Fig. S29 $^{13}$C NMR (151.03 MHz, DMSO-$d_6$) spectrum of 2-amino-7-fluoro-$3H$-phenoxazin-3-one ($2c$)

Fig. S30 $^{13}$C NMR (151.03 MHz, DMSO-$d_6$) expansion spectrum of compound $2c$
Fig. S3 $^{13}$C NMR (75.475 MHz, DMSO-$d_6$) dept-135 spectrum of compound 2c

Fig. S2 $^{13}$C NMR (75.475 MHz, DMSO-$d_6$) dept-135 expansion spectrum of compound 2c
Fig. S33 $^1$H NMR (300.132 MHz, DMSO-$d_6$) spectrum of 2-amino-8-chlorophenoxazin-3-one 2d

Fig. S34 $^1$H NMR (300.132 MHz, DMSO-$d_6$) expansion spectrum of compound 2d
**Fig. S35** $^{13}$C NMR (151.031 MHz, DMSO-$d_6$) spectrum of 2-amino-8-chlorophenoxazin-3-one **2d**

![13C NMR spectrum of 2-amino-8-chlorophenoxazin-3-one 2d](image)

**Fig. S36** $^{13}$C NMR (151.031 MHz, DMSO-$d_6$) expansion spectrum of compound **2d**

![13C NMR expansion spectrum of compound 2d](image)
Fig. S37 $^1$H NMR (300.132 MHz, DMSO-$d_6$) spectrum of 2-amino-7-chlorophenoxazin-3-one 2e

Fig. S38 $^1$H NMR (300.132 MHz, DMSO-$d_6$) expansion spectrum of compound 2e
Fig. S39 $^{13}$C NMR (75.475 MHz, DMSO-d$_6$) spectrum of 2-amino-7-chlorophenoxazin-3-one 2e

Fig. S40 $^{13}$C NMR (75.475 MHz, DMSO-d$_6$) expansion spectrum of compound 2e
Fig. S41 $^1$H NMR (300.132 MHz, DMSO-$d_6$) spectrum of 2-amino-8-bromophenoxazin-3-one $2f$

Fig. S42 $^1$H NMR (300.132 MHz, DMSO-$d_6$) expansion spectrum of compound $2f$
Fig. S43 $^{13}$C NMR (75.475 MHz, DMSO-d$_6$) spectrum of 2-amino-8-bromophenoxazin-3-one 2f

Fig. S44 $^{13}$C NMR (75.475 MHz, DMSO-d$_6$) expansion spectrum of compound 2f
Fig. S45 $^{13}$C NMR (75.475 MHz, DMSO-$d_6$) dept-135 spectrum of compound 2f

Fig. S46 $^{13}$C NMR (75.475 MHz, DMSO-$d_6$) dept-135 expansion spectrum of compound 2f
Fig. S47 $^1$H NMR (300.132 MHz, DMSO-d$_6$) spectrum of 2-amino-8-carboxyphenoxazin-3-one 2g

Fig. S48 $^1$H NMR (300.132 MHz, DMSO-d$_6$) expansion spectrum of compound 2g
Fig. S49 $^{13}$C NMR (75.475 MHz, DMSO-$d_6$) spectrum of 2-amino-8-carboxyphenoxazin-3-one $2g$

Fig. S50 $^{13}$C NMR (75.475 MHz, DMSO-$d_6$) expansion spectrum of compound $2g$
Fig. S51 $^1$H NMR (300.132 MHz, DMSO-$d_6$) spectrum of 2-amino-7-carboxyphenoxazin-3-one 2h

Fig. S52 $^1$H NMR (300.132 MHz, DMSO-$d_6$) expansion spectrum of compound 2h
Fig. S53 $^{13}$C NMR (75.475 MHz, DMSO-$d_6$) spectrum of 2-amino-7-carboxyphenoxazin-3-one 2h

Fig. S54 $^{13}$C NMR (75.475 MHz, DMSO-$d_6$) expansion spectrum of compound 2h
Fig. S55 $^1$H NMR (300.132 MHz, DMSO-$d_6$) spectrum of 2-amino-4,8-dichlorophenoxazin-1-one 3d

Fig. S56 $^1$H NMR (300.132 MHz, DMSO-$d_6$) expansion spectrum of compound 3d
Fig. S57 $^{13}$C NMR (75.475 MHz, DMSO-d$_6$) spectrum of 2-amino-4,8-dichlorophenoxazin-1-one 3d

Fig. S58 $^{13}$C NMR (75.475 MHz, DMSO-d$_6$) expansion spectrum of compound 3d
Fig. S59 $^{13}$C NMR (75.475 MHz, DMSO-$d_6$) dept-135 spectrum of compound 3d

Fig. S60 $^{13}$C NMR (75.475 MHz, DMSO-$d_6$) dept-135 expansion spectrum of compound 3d
Fig. S61 $^1$H NMR (300.132 MHz, DMSO-$d_6$) spectrum of 4-amino-4,8-dibromophenoxazin-1-one 3f

Fig. S62 $^1$H NMR (300.132 MHz, DMSO-$d_6$) expansion spectrum of compound 3f
Fig. S63 $^{13}$C NMR (75.475 MHz, DMSO-d$_6$) spectrum of 2-amino-4,8-dibromophenoxazin-1-one 3f

Fig. S64 $^{13}$C NMR (75.475 MHz, DMSO-d$_6$) expansion spectrum of compound 3f
Fig. S6 $^{13}$C NMR (75.475 MHz, DMSO-$d_6$) dept-135 spectrum of compound 3f

Fig. S6 $^{13}$C NMR (75.475 MHz, DMSO-$d_6$) dept-135 expansion spectrum of compound 3f
Fig. S67 $^1$H NMR (300.132 MHz, DMSO-$d_6$) spectrum of 4-amino-1,7-dichlorophenoxazin-3-one 4e

Fig. S68 $^1$H NMR (300.132 MHz, DMSO-$d_6$) expansion spectrum of compound 4e
Fig. S60 $^{13}$C NMR (75.475 MHz, DMSO-d$_6$) spectrum of 4-amino-1,7-dichlorophenoxazin-3-one 4e

Fig. S70 $^{13}$C NMR (75.475 MHz, DMSO-d$_6$) expansion spectrum of compound 4e
Fig. S71 $^{13}$C NMR (75.475 MHz, DMSO-$d_6$) dept-135 spectrum of compound 4e

Fig. S72 $^{13}$C NMR (75.475 MHz, DMSO-$d_6$) dept-135 expansion spectrum of compound 4e
Fig. S73 $^1$H NMR (300.132 MHz, CDCl$_3$) spectrum of 2-amino-4a,7-dimethylphenoxazin-3-one 5i

Fig. S74 $^1$H NMR (300.132 MHz, CDCl$_3$) expansion spectrum of compound 5i
Fig. S75 $^{13}$C NMR (151.031 MHz, CDCl$_3$) spectrum of compounds 5i

Fig. S76 $^{13}$C NMR (151.031 MHz, CDCl$_3$) dept-135 spectrum of compound 5i
**Fig. S7** $^{13}$C NMR (151.031 MHz, DMSO-$d_6$) spectrum of compound 5i

**Fig. S8** $^{13}$C NMR (151.031 MHz, DMSO-$d_6$) expansion spectrum of compound 5i
Fig. S79 $^{13}$C NMR (151.031 MHz, DMSO-$d_6$) dept-135 spectrum of compound 5i

Fig. S80 $^{13}$C NMR (151.031 MHz, DMSO-$d_6$) expansion spectrum of 2-amino-4α,7-dimethyl-4αH-phenoxazin-3-ol (5i-B) with 5i-A core signals extraction
Fig. S81 $^1$H NMR (600.584 MHz, CDCl$_3$) spectrum of 2-phenyl-1,2-benziselenazol-3(2$H$)-one (6)

Fig. S82 $^1$H NMR (600.584 MHz, CDCl$_3$) expansion spectrum of ebselen (6)
Fig. S83 $^1$H NMR (600.584 MHz, DMSO-$d_6$) spectrum of 2-cabramoylphenyl diselenide 6b

Fig. S84 $^1$H NMR (600.584 MHz, DMSO-$d_6$) expansion spectrum of 2-cabramoylphenyl diselenide 6b
Fig. S85 $^1$H NMR (600.584 MHz, CDCl$_3$) spectrum of 3,5-bis(trifluoromethyl)diphenyl diselenide 6c

Fig. S86 $^1$H NMR (600.584 MHz, CDCl$_3$) expansion spectrum of diphenyl diselenide 6c
Fig. S8 ¹H NMR (600.584 MHz, CDCl₃) spectrum of 3-(trifluoromethyl)diphenyl diselenide (6d)

Fig. S88 ¹H NMR (300.13 MHz, CDCl₃) spectrum of 3-(trifluoromethyl)diphenyl diselenide (6d)
Fig. S89 $^1$H NMR (600.584 MHz, DMSO-$d_6$) spectrum of 2-aminophenol and 2-amino-4-methylphenol cross-coupling by NaIO$_3$ to mixture of questiomyacin A and compound 2a
Fig. S90 $^1$H NMR (300.13 MHz, DMSO-d$_6$) spectrum of questiomycin A

Fig. S91 $^1$H NMR (300.13 MHz, DMSO-d$_6$) expansion spectrum of questiomycin A
Fig. S92 $^1$H NMR (600.584 MHz, DMSO-$_d_6$) spectrum of compound 2a with CF$_3$COOH (1 eq)

Fig. S93 $^1$H NMR (600.584 MHz, DMSO-$_d_6$) expansion spectrum of 2a with CF$_3$COOH (1 eq)
Fid. S94 $^1$H NMR (600.584 MHz, DMSO-$d_6$) spectrum of compound 2a with CF$_3$COOH (5 eq)

Fid. S95 $^1$H NMR (600.584 MHz, DMSO-$d_6$) expansion spectrum of 2a with CF$_3$COOH (5 eq)
Fig. S96 UV/VIS (MeOH) spectrum of compound 2a

Fig. S97 UV/VIS (MeOH) spectrum of compound 2b
Fig. S98 UV/VIS (MeOH) spectrum of compound 2c

Fig. S99 UV/VIS (MeOH) spectrum of compound 2f
Fig. S100 UV/VIS (MeOH) spectrum of compound 3f
During the cyclocondensation of 2-amino-4-methylphenol to compound 2a, the methyl group present in substrate molecule 1a is lost in oxidative reaction conditions. The UV-visible spectrum of compound 2a (Fig. S96) showed striking similarities to the UV spectra of various known compounds, such as questiomycin A (Synth. Commun. 2007, 37, 1779–1789), actinocene (Synth. Commun. 2007, 37, 1779–1789), cinnabarinic acid (J. Med. Chem. 2013, 56, 3310–3317), elloxazinones A and B (J. Antibiot. 2007, 60, 277–284), bezzeramycin A (Eur. J. Org. Chem. 2010, 231–235, see the Supporting Information), pitucamycin (J. Nat. Prod. 2010, 73, 1461–1464), and venezueline E (Bioorg. Med. Chem. Lett. 2013, 23, 301–304, see the Supporting Information), with comparison to chandrananimycin E (J. Antibiot. 2015; doi:10.1038/ja.2015.10), suggesting that 2a belongs to the group of 2-amino phenoxazinone. Its empirical formula was assigned to be C_{13}H_{11}N_{2}O_{2} by HRMS (EI) (m/z = 227.0812 for [M + H]^{+}; calcd. 227.0815 for (C_{13}H_{11}N_{2}O_{2}). The measured accurate mass of the protonated 2a was m/z = 227.0812, which corresponded to an empirical formula of C_{13}H_{11}N_{2}O_{2} [M + H]^{+}, which an error of 1.30 ppm between the measured accurate mass and calculated exact mass, which indicated nine degrees of unsaturation. The $^{13}$C NMR spectrum (Fig. S21-S22) showed 13 carbon signals: one methyl ($\delta_{C}$ 20.4), five methines, and seven quaternary carbon atoms including one carbonyl group ($\delta_{C}$ 180.1). In addition to broad signal at 6.78 ppm the $^1$H NMR spectrum in DMSO-d$_6$ of 2a exhibits seven resonances corresponding to one aliphatic methyl group and five methine protons. The proton and carbon signals were correlated by $^1$H-$^1$H and $^1$H-$^{13}$C 2D spectroscopy (Fig. S102-S104). The remaining signal did not give any correlation in the HSQC experiment and must thus be attached to heteroatom. This is very close to the spectrum of questiomycin A – 2-amino-3H-phenoxazin-3-one, apart for the additional carbon at a $\delta_C$ of 20.4 and the replacement of a C8 tertiary carbon by a quaternary carbon at a $\delta_C$ of 134.7 ppm.
Fig. S102 $^1$H COSY (600.584 MHz, DMSO-d$_6$) experiment for 2-amino-8-methyl-3$H$-phenoxazin-3-one (2a) at 298 K
Fig. S103 $^1$H-$^{13}$C HSQC (600.584 MHz for $^1$H, and 151.031 MHz for $^{13}$C, DMSO-$d_6$) experiment for 2-amino-8-methyl-$3H$-phenoxazin-3-one (2a) at 298 K
Fig. S104 $^1$H, $^{13}$C HMBC (600.584 MHz for $^1$H, and 151.031 MHz for $^{13}$C, DMSO-d$_6$) experiment for 2-amino-8-methyl-3H-phenoxazin-3-one (2a) at 298 K
Fig. S105 $^1$H NMR (600.584 MHz, DMSO-$d_6$) spectrum of compound 2a at 298K

Fig. S106 $^1$H NMR (600.584 MHz, DMSO-$d_6$) expansion spectrum of compound 2a at 298K
Fig. S107 $^{13}$C NMR (151.031 MHz, DMSO-d$_6$) spectrum of compound 2a at 298K

Fig. S108 $^{13}$C NMR (151.031 MHz, DMSO-d$_6$) expansion spectrum of compound 2a at 298K
Fig. S109 Correlation of experimental $^{13}$C NMR chemical shifts with calculated for compound 2a