Supporting information to the paper

Catalytic Chain-Breaking Pyridinol Antioxidants

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General Experimental Details

For ^1H NMR analysis (CDCl_3), 500, 400 and 300 MHz spectrometers were used. ^{13}C spectra were recorded at 125, 100 and 75 MHz. NMR chemical shifts are reported in ppm referenced to the solvent peak of CDCl_3 (7.26 ppm for ^1H and 77.16 ppm for ^{13}C , respectively). Mass spectra reported are for ions of ^{80}Se . ES-MS data were obtained using direct inlet of a dilute methanol solution of compound. Microwave reactions were carried out in a focused microwave reactor equipped with an IR sensor for continuous monitoring of the reaction temperature. Melting points, obtained using a Stuart Scientific melting point apparatus, are uncorrected. THF was dried by distillation over sodium/benzophenone. 3-Hydroxy-6-methyl-2-pyridyl phenyl telluride (**10a**), 3-hydroxy-6-methyl-2-pyridyl phenyl selenide (**10b**) and 3-hydroxy-6-methyl-2-pyridyl phenyl sulfide (**10c**) were prepared according to the literature.¹

Synthetic procedures

6-Bromo-3-pyridinol: 3-Amino-6-bromopyridine (1.73 g, 10 mmol) was dissolved in HBF_4 (5 mL, 50 % aq.) and water (5 mL) was added. To the resulting brownish solution, cooled to 0°C in an ice-bath, NaNO_2 (759 mg, 11 mmol) in water (5 mL) was added dropwise. The resulting yellowish heterogenous reaction mixture was stirred for 1 h at this temperature. After addition of water (5 mL), the mixture was stirred in an oil-bath for 5 h at 100°C (gas evolution). The cooled reaction mixture was then neutralized by addition of NaHCO_3 (5 % aq.) and the product extracted with ethyl acetate (5 x 35 mL). After drying (Na_2SO_4) and evaporation in *vacuo*, the resulting brownish solid was purified by column chromatography (SiO_2) using pentane/ethyl acetate (9:1) to give 1.04 g (60 %) of the title compound, mp $137\text{--}138^\circ\text{C}$ (lit. $135.5\text{--}136.5^\circ\text{C}$)²

5-Hydroxy-2-pyridyl *n*-Octyl Telluride (7a): To the solution of lithiated 6-bromo-3-pyridinol prepared as described below (compound **7c**), finely ground elemental tellurium (0.762 mg, 6 mmol) was added at -78°C . The cooling bath was then removed and stirring continued for an additional 4 h at room temperature. The reaction mixture was then poured onto crushed ice and kept in the open air overnight. After evaporation of the solvent in *vacuo*, the residue was washed with some pentane to remove any dialkyl ditelluride present and dissolved in EtOH (10 mL). To the remaining stirred dark red solution of crude bis-(5-hydroxy-2-pyridyl)ditelluride under N_2 , NaBH_4 (0.18 g, 5 mmol) was added in portions until the colour of the reaction mixture had permanently faded away. Octyl bromide (1.0 g, 5

mmol) was added and stirring continued for 1 h when the contents of the reaction flask was poured into brine and extracted with Et₂O (15 mL x 4). After drying over Na₂SO₄ and evaporation in *vacuo* the product was purified by column chromatography using pentane/ethyl acetate (86:14) as an eluent. The title compound was obtained as a colourless solid (0.442 g, 66 %), mp 56-57 °C. ¹H NMR δ 8.18 (d, *J* = 3.1, 1H), 7.52 (dm, *J* = 8.4, 1H), 7.04 (dd, *J* = 8.4, 3.0, 1H), 3.01 (t, *J* = 7.5, 2H), 1.81 (m, 2H), 1.35-1.19 (several peaks, 10H), 0.86 (t, *J* = 6.9, 3H). ¹³C NMR δ 153.2, 139.0, 134.6, 126.1, 124.9, 32.2, 32.0, 32.0, 29.3, 29.0, 22.8, 14.2, 10.0. Anal. calcd for C₁₃H₂₁NOTe: C 46.62; H 6.32. Found: C, 46.49; H, 6.25.

5-Hydroxy-2-pyridyl *n*-Octyl Selenide (7b) was prepared according to the procedure for sulphide **7c**, using di-*n*-octyl diselenide instead of di-*n*-octyl disulfide. Yield: 65 %, mp 44-45 °C ¹H NMR δ 8.13 (d, *J* = 3.0, 1H), 7.34 (dm, *J* = 8.6, 1H), 7.15 (dd, *J* = 3.0, 8.6, 1H), 3.02 (t, *J* = 7.6, 2H), 1.71 (m, 2H), 1.39-1.23 (several peaks, 10H), 0.86 (t, *J* = 7.1, 3H). ¹³C NMR δ 152.6, 143.5, 137.8, 128.5, 125.6, 31.9, 30.4, 30.0, 29.3, 29.2, 27.8, 22.8, 14.2. Anal. calcd for C₁₃H₂₁NOSe: C 54.56; H 7.39. Found: C, 54.87; H, 7.39.

5-Hydroxy-2-pyridyl *n*-Octyl Sulfide (7c): To 6-bromo-3-pyridinol (348 mg, 2 mmol) in THF (10 mL) under N₂ at -78°C was added dropwise *t*-BuLi (3.5 mL 1.7 M solution in pentane; 6 mmol). Then, di-*n*-octyl disulfide (872 mg, 3 mmol, 6 eq.) was added at -78°C and the reaction mixture stirred for 30 min at this temperature and an additional 3h at room temperature. After pouring the reaction mixture into NaHCO₃ (5 % aq.), extraction with Et₂O, drying over Na₂SO₄ and concentration in *vacuo*, the crude product was purified by column chromatography using pentane/ethyl acetate (88:12) as an eluent to yield the title compound as a colourless solid (403 mg, 84 %), mp 70-71 °C. ¹H NMR δ 8.12 (d, *J* = 2.7, 1H), 7.23 (dd, *J* = 8.6, 2.7, 1H), 7.17 (d, *J* = 8.6, 1H), 6.68 (bs, 1H), 3.02 (t, *J* = 7.3, 2H), 1.63 (m, 2H), 1.43-1.30 (several peaks, 10H), 0.86 (t, *J* = 7.1, 3H). ¹³C NMR δ 151.9, 148.8, 136.9, 125.9, 125.0, 32.7, 31.9, 29.4, 29.3, 29.3, 29.0, 22.8, 14.2.

3-Hydroxy-2-pyridyl *n*-Octyl Telluride (8a) was prepared from 2-bromo-3-pyridinol by using the procedure for telluride **7a**. Yield: 62 %, mp 83-84 °C. ¹H NMR δ 8.14 (dd, *J* = 4.6, 1.6, 1H), 7.15 (dd, *J* = 8.2, 1.6, 1H), 7.08 (dd, *J* = 8.2, 4.6, 1H), 3.02 (t, *J* = 7.5, 2H), 1.79 (m, 2H), 1.37-1.23 (several peaks, 10H), 0.86 (t, *J* = 6.9, 3H). ¹³C NMR δ 155.3, 142.8, 130.7, 123.3, 119.9, 32.2, 31.9, 31.9, 29.3, 29.0, 22.8, 14.2, 9.6. Anal. calcd for C₁₃H₂₁NOTe: C 46.62; H 6.32. Found: C, 46.66; H, 6.40.

3-Hydroxy-2-pyridyl *n*-Octyl Selenide (8b) was prepared from 2-bromo-3-pyridinol by using the procedure for selenide **7b**. Yield: 50 %, mp 88-89 °C. ¹H NMR δ 8.15 (dd, *J* = 4.7,

1.5, 1H), 7.29 (dm, $J = 8.1$, 1H), 7.13 (dd, $J = 8.1$, 4.8, 1H), 5.30 (s, 1H), 3.10 (t, $J = 7.5$, 2H), 1.70 (m, 2H), 1.43-1.24 (several peaks, 10H), 0.86 (t, $J = 7.1$, 3H). ^{13}C NMR δ 152.9, 142.2, 141.8, 123.0, 121.1, 31.9, 30.6, 30.0, 29.2, 29.1, 27.7, 22.7, 14.2. Anal. calcd for $\text{C}_{13}\text{H}_{21}\text{NOSe}$: C 54.54; H 7.39. Found: C, 54.39; H, 7.48.

3-Hydroxy-2-pyridyl *n*-Octyl Sulfide (8c) was prepared from 2-bromo-3-pyridinol according to the procedure for sulphide **7c**. Yield: 77 %, mp 101-103 °C. ^1H NMR δ 8.13 (dd, $J = 4.8$, 1.5, 1H), 7.22 (ddm, $J = 8.1$, 1.5, 1H), 7.06 (dd, $J = 8.1$, 4.8, 1H), 3.12 (t, $J = 7.3$, 2H), 1.63 (m, 2H), 1.41-1.24 (several peaks, 10H), 0.87 (t, $J = 7.1$, 3H). ^{13}C NMR δ 151.9, 144.4, 141.6, 122.6, 121.7, 33.2, 31.9, 29.9, 29.3, 29.2, 28.9, 22.8, 14.2. Anal. calcd for $\text{C}_{13}\text{H}_{21}\text{NOS}$: C 65.23; H 8.84. Found: C, 65.17; H, 9.09.

3-Hydroxy-6-methyl-2-pyridyl *n*-Octyl Telluride (9a) was prepared from 2-iodo-6-methyl-3-pyridinol according to the procedure for telluride **7a**. Yield: 54 %. ^1H NMR δ 7.03 (d, $J = 8.2$, 1H), 6.90 (dm, $J = 8.2$, 1H), 2.97 (t, $J = 7.4$, 2H), 2.47 (s, 3H), 1.80 (m, 2H), 1.23-1.34 (several peaks, 10H), 0.86 (t, $J = 7.1$, 3H). ^{13}C NMR δ 152.8, 151.9, 128.7, 123.3, 120.1, 32.1, 32.0, 31.9, 29.3, 29.0, 23.4, 22.8, 14.2, 10.2. Anal Calcd for $\text{C}_{14}\text{H}_{23}\text{NOTe}$: C, 48.19, H, 6.64. Found: C, 48.34; H, 6.73.

3-Hydroxy-6-methyl-2-pyridyl *n*-Octyl Selenide (9b) was prepared from 2-iodo-6-methyl-3-pyridinol according to the procedure for sulphide **9c**, using di-*n*-octyl diselenide instead of di-*n*-octyl disulfide. Yield: 60 %. ^1H NMR δ 7.09 (d, $J = 8.2$, 1H), 6.94 (dm, $J = 8.2$, 1H), 3.01 (t, $J = 7.3$, 2H), 2.47 (s, 3H), 1.68 (m, 2H), 1.38-1.24 (several peaks, 10 H), 0.87 (t, $J = 6.9$, 3H). ^{13}C NMR δ 151.2, 150.7, 139.6, 123.4, 121.6, 31.9, 30.8, 29.9, 29.2, 29.1, 28.9, 23.5, 22.8, 14.2. Anal Calcd for $\text{C}_{14}\text{H}_{23}\text{NOSe}$: C, 56.02; H, 7.72. Found: C, 56.25; H, 7.86.

3-Hydroxy-6-methyl-2-pyridyl *n*-Octyl Sulfide (9c): 2-Iodo-6-methyl-3-pyridinol (235 mg, 1.0 mmol) and di-*n*-octyl disulfide (290 mg, 1.0 mmol) were added to a stirred mixture of CuI (3 mg, 0.015 mmol), Mg turnings (48 mg, 2.0 mmol) and 2,2'-bipyridyl (2.3 mg, 0.015 mmol) in DMF (5 mL). This mixture was heated to 200 °C in a sealed tube in a microwave reactor (300 W) for 6 h and then poured into water (15 mL). After extraction with Et₂O (20 mL x 4), the organic phase was washed with brine (50 mL), dried (MgSO₄), filtered, and evaporated in *vacuo*. Purification by flash chromatography using pentane/ethyl acetate (85:15) as eluent yielded 165 mg (65 %) of the title compound as an oil. ^1H NMR δ 7.09 (d, $J = 8.2$, 1H), 6.93 (d, $J = 8.2$, 1H), 5.93 (bs, 1H), 3.08 (t, $J = 7.3$, 2H), 2.48 (s, 3H), 1.62 (m, 2H), 1.42-1.27 (several peaks, 10H), 0.88 (t, 3H). ^{13}C NMR δ 150.8, 150.0, 142.4, 122.5, 122.0, 33.5, 31.9,

30.0, 29.3, 29.2, 28.9, 23.5, 22.8, 14.2. Anal Calcd for C₁₄H₂₃NOS: C, 66.36; H, 9.15.

Found: C, 66.14; H, 9.01.

2-Bromo-3-cyano-4,6-dimethylpyridine (12) was prepared according to the procedure for 2-bromo-3-cyano-5-methoxy-4,6-dimethylpyridine below, using 3-cyano-4,6-dimethyl-2-pyridinol as a starting material. Yield: 96 %, mp 116-117 °C. ¹H NMR δ 7.09 (m, 1H), 2.56 (d, *J* = 0.58, 3H), 2.53 (d, *J* = 0.73, 3H). ¹³C NMR δ 163.0, 154.3, 143.6, 123.6, 115.5, 111.8, 24.6, 20.9.

2-Bromo-3-cyano-5-methoxy-4,6-dimethylpyridine: Into a round-bottomed flask (200 mL) equipped with a refluxing condenser, 3-cyano-5-methoxy-4,6-dimethyl-2-pyridinol (1.90 g, 10.9 mmol), Bu₄NBr (4.80 g, 14.9 mmol), P₂O₅ (4.09 g, 28.8 mmol), toluene (110 mL) and a stirring bar were placed. The mixture was heated for 14 h under reflux. The toluene layer was decanted and washed with a saturated solution of NaHCO₃ (30 mL) and then with water (50 mL). To the oily residue left in the flask was added water (50 mL) and then powdered NaHCO₃ portionwise until there were no further evolution of gas. The mixture was extracted with CH₂Cl₂ (ca. 250 mL), washed with brine (50 mL x 2) and then with water (30 mL). The toluene and CH₂Cl₂ solutions were combined and dried (MgSO₄). Removal of the solvent in *vacuo* and filtration of the product through a short pad of silica (Φ 4 cm x 7 cm) eluting with pentane/CH₂Cl₂ (to remove any remaining tetrabutylammonium salts) afforded 2.23 g (84%) of the title compound as a white powder, mp 99-100 °C. ¹H NMR δ 3.76 (s, 3H), 2.54 (s, 3H), 2.50 (s, 3H). ¹³C NMR δ 158.0, 152.7, 147.1, 137.0, 115.2, 113.2, 60.7, 19.8, 15.3.

2-Bromo-4,6-dimethylpyridine-3-carboxylic acid amide (13) was prepared according to the procedure for 2-bromo-5-methoxy-4,6-dimethylpyridine-3-carboxylic acid amide below, using 2-bromo-3-cyano-4,6-dimethylpyridine as a starting material. Yield: 68 %, mp 179-180 °C. ¹H NMR δ 6.99 (s, 1H), 6.12 (bs, 1H), 5.78 (bs, 1H), 2.51 (s, 3H), 2.38 (s, 3H). ¹³C NMR δ 168.6, 160.2, 147.8, 137.5, 132.4, 124.4, 24.2, 19.5.

2-Bromo-5-methoxy-4,6-dimethylpyridine-3-carboxylic acid amide: To concentrated H₂SO₄ (2.16 mL 96%, 18 M; 39.0 mmol) in an Erlenmeyer flask (50 mL) heated at 90 °C in an oil bath, 2-bromo-3-cyano-5-methoxy-4,6-dimethylpyridine (2.70 g, 11.2 mmol) was added. The dark brown mixture was stirred at 100 °C for 3 h and then cooled to ca 90 °C. Water (7.0 mL) was added dropwise (**CAUTION!** Quick addition of water causes bumping) and the mixture quickly cooled down to 20 °C, and poured slowly into water (30 mL) in a beaker (250 mL). To this mixture, powdered NaHCO₃ was added in small portions until the

evolution of CO₂ had ceased. After extraction with CH₂Cl₂ (120 mL x 3), washing with brine (40 mL x 2), and drying over MgSO₄ and evaporation of the solvent afforded 2.57 g (88%) of the title compound as colorless needles: ¹H NMR δ 6.07 (br s, 1 H), 5.82 (br s, 1 H), 3.73 (s, 3 H), 2.49 (s, 3 H), 2.34 (s, 3 H). ¹³C NMR δ 168.0, 154.4, 153.2, 140.6, 134.0, 130.7, 60.5, 19.3, 13.5.

3-Amino-2-bromo-4,6-dimethylpyridine (14) was prepared according to the procedure for 3-amino-2-bromo-5-methoxy-4,6-dimethylpyridine below, using 2-bromo-4,6-dimethylpyridine-3-carboxylic acid amide as a starting material. Yield: 84 %, mp 61-62 °C. ¹H NMR δ 6.82 (s, 1H), 4.01 (bs, 2H), 2.41 (s, 3H), 2.19 (s, 3H). ¹³C NMR δ 148.0, 137.5, 132.7, 128.6, 124.8, 22.9, 18.0.

3-Amino-2-bromo-5-methoxy-4,6-dimethylpyridine (19): To a solution of KOH (1.15 g, 20.6 mmol) in water (3 mL) in an Erlenmeyer flask (50 mL) at 0 °C, Br₂ (0.623 g, 0.200 mL, 3.9 mmol) was added dropwise by syringe. The resulting lemon-yellow solution was stirred for 5 min at this temperature and 2-bromo-5-methoxy-4,6-dimethylpyridine-3-carboxylic acid amide (0.777 g, 3.0 mmol) was added. After stirring for another 5 min, a mixture of water and THF (1 mL of each) was added slowly to the resulting yellow suspension and stirring continued for 10 min at 0 °C. The flask was then placed in an oil bath preheated to 70 °C and stirred for 0.5 h (the color of the solution turned to reddish orange). The temperature of the oil-bath was raised to 90 °C and stirring continued for another 3 h. The cooled brown residue was subjected to aqueous work-up. After extraction with CH₂Cl₂ (150 mL x 2), washing with brine (50 mL x 2), and drying over MgSO₄, removal of the solvent afforded the title compound (0.693 g, ~100%) as pale yellow needles, mp 96-97 °C ¹H NMR δ 3.91 (br s, 2H), 3.64 (s, 1H), 2.33 (s, 3H), 2.09 (s, 3H). ¹³C NMR δ 153.0, 141.6, 138.6, 125.4, 122.7, 60.5, 18.4, 10.9.

2-Bromo-4,6-dimethyl-3-pyridinol (15) was prepared according to the procedure for 6-bromo-3-pyridinol, using 3-amino-2-bromo-4,6-dimethylpyridine as a starting material. Yield: 43 %, mp 106-107 °C. ¹H NMR δ 6.84 (s, 1H), 5.78 (br s, 1H), 2.39 (s, 3H), 2.24 (s, 3H). ¹³C NMR δ 150.6, 146.1, 135.4, 129.6, 125.8, 23.1, 16.5.

2-Bromo-5-methoxy-4,6-dimethyl-3-pyridinol was prepared according to the procedure for 6-bromo-3-pyridinol, using 3-amino-2-bromo-5-methoxy-4,6-dimethylpyridine as a starting material. Yield: 54 %, mp 103-104 °C. ¹H NMR δ 5.79 (s, 1H), 3.69 (s, 3H), 2.38 (s, 3H), 2.21 (s, 3H). ¹³C NMR δ 153.7, 146.7, 144.5, 128.6, 123.4, 60.4, 18.5, 10.2.

3-Hydroxy-4,6-dimethyl-2-pyridyl *n*-Octyl Telluride (16a) was prepared according to the procedure for pyridinol **7a**, using 2-bromo-4,6-dimethyl-3-pyridinol as a starting material. Yield: 44 %. ^1H NMR δ 6.80 (s, 1H), 6.15 (bs, 1H), 2.93 (t, $J = 7.7$, 2H), 2.43 (s, 3H), 2.22 (s, 3H), 1.76 (m, 2H), 1.35-1.23 (several peaks, 10H), 0.86 (t, $J = 7.2$, 3H). ^{13}C NMR δ 151.9, 151.6, 131.1, 127.8, 125.5, 32.0, 32.0, 31.9, 29.3, 29.0, 23.4, 22.8, 16.7, 14.2, 10.6. Anal. calcd for $\text{C}_{15}\text{H}_{25}\text{NOTe}$: C 49.64; H 7.02. Found: C, 49.46; H, 6.94.

3-Hydroxy-4,6-dimethyl-2-pyridyl *n*-Octyl Selenide (16b) was prepared according to the procedure for pyridinol **7b**, using 2-bromo-4,6-dimethyl-3-pyridinol as a starting material. Yield: 60 %. ^1H NMR δ 6.84 (s, 1H), 6.10 (bs, 1H), 3.08 (t, $J = 7.2$, 2H), 2.53 (s, 3H), 2.29 (s, 3H), 1.68 (m, 2H), 1.37-1.23 (several peaks, 10H), 0.86 (t, $J = 7.0$, 3H). ^{13}C NMR δ 150.6, 149.9, 138.1, 133.0, 125.6, 31.9, 30.8, 29.9, 29.5, 29.3, 29.1, 23.4, 22.8, 16.3, 14.2. Anal. calcd for $\text{C}_{15}\text{H}_{25}\text{NOSe}$: C 57.32; H 8.02. N 4.46 Found: C, 57.37; H, 8.03 N 4.48.

3-Hydroxy-4,6-dimethyl-2-pyridyl *n*-Octyl Sulfide (16c) was prepared according to the procedure for pyridinol **7c**, using 2-bromo-4,6-dimethyl-3-pyridinol as a starting material. Yield: 35 %, ^1H NMR δ 6.80 (s, 1H), 5.91 (s, 1H), 3.03 (t, $J = 7.4$, 2H), 2.42 (s, 3H), 2.23 (s, 3H), 1.61 (m, 2H), 1.41-1.20 (several peaks, 10 H), 0.87 (t, $J = 7.1$, 3H). ^{13}C NMR δ 150.3, 149.0, 140.7, 132.8, 124.8, 34.4, 31.9, 30.2, 29.3, 29.2, 28.9, 23.6, 22.8, 15.9, 14.22. EI-MS: 267.8 $[\text{M}+\text{H}]^+$, 290.0 $[\text{M}+\text{Na}]^+$, 266.0 $[\text{M}-\text{H}]^-$. Anal. calcd for $\text{C}_{15}\text{H}_{25}\text{NOS}$: C 67.37; H 9.42; N 5.24. Found: C, 66.99; H, 9.21 N 4.92.

3-Hydroxy-5-methoxy-4,6-dimethyl-2-pyridyl *n*-Octyl Telluride (18a) was prepared according to the procedure for pyridinol **7a**, using 2-bromo-5-methoxy-4,6-dimethyl-3-pyridinol as a starting material. Yield: 54 %. ^1H NMR δ 5.98 (s, 1H), 3.73 (s, 3H), 2.87 (t, $J = 7.6$, 2H), 2.44 (s, 3H), 2.23 (s, 3H), 1.77 (m, 2H), 1.32-1.22 (several peaks, 10H), 0.86 (t, $J = 7.2$, 3H). ^{13}C NMR δ 154.3, 152.7, 146.1, 124.2, 121.4, 60.5, 32.0, 31.9, 29.3, 29.0, 22.8, 22.5, 19.1, 14.2, 10.7, 10.2.

3-Hydroxy-5-methoxy-4,6-dimethyl-2-pyridyl *n*-Octyl Selenide (18b) was prepared according to the procedure for pyridinol **7b**, using 2-bromo-5-methoxy-4,6-dimethyl-3-pyridinol as a starting material. Yield: 64 %. ^1H NMR δ 3.72 (s, 3H), 3.19 (t, $J = 7.6$, 2H), 2.44 (s, 3H), 2.20 (s, 3H), 1.72 (m, 2H), 1.44-1.26 (several peaks, 10H), 0.88 (t, 3H). ^{13}C NMR δ 154.1, 151.0, 144.9, 132.4, 126.1, 60.4, 31.9, 30.8, 29.9, 29.6, 29.2, 29.1, 22.7, 18.7, 14.1, 9.9. EI-MS; 346.4 $[\text{M}+\text{H}]^+$ (most abundant). Anal. calcd for $\text{C}_{16}\text{H}_{27}\text{NO}_2\text{Se}$: C 55.8; H 7.9; N 4.1. Found: C, 55.4; H, 7.7, N, 3.9

2-Bromo-5-methoxy-4,6-dimethylpyridine: 3-Amino-2-bromo-5-methoxy-4,6-dimethylpyridine (231 mg, 1.00 mmol) was dissolved in HBF₄ (0.5 mL, 50 % aq. solution), water (0.5 mL) was added and the resulting brownish solution cooled to 0°C. NaNO₂ (83 mg, 1.2 mmol) in water (0.5 mL) was added dropwise at 0°C. The resulting solution was stirred for 1 h at this temperature when hypophosphorous acid (0.491 mL 50% in H₂O, 4.74 mmol) was quickly added. The mixture was then heated under reflux for 15 min, cooled to ambient temperature and neutralized with NaHCO₃ (5 % aq.). After extraction with CH₂Cl₂ (3 x 25 mL), drying (Na₂SO₄) and concentration *in vacuo*, the brown residue was purified by column chromatography (SiO₂) eluting with CH₂Cl₂ to give the title compound (80 mg, 37 % yield) in the first fraction, ¹H NMR δ 7.12 (s, 1H), 3.71 (s, 3 H), 2.46 (s, 3 H), 2.43 (s, 3 H). ¹³C NMR δ 153.5, 153.2, 143.2, 134.8, 127.7, 60.2, 19.1, 15.7. and 2-bromo-5-methoxy-4,6-dimethyl-3-pyridinol (87 mg, 38 % yield) in the second fraction.

6-Bromo-2,4-dimethyl-3-pyridinol (20): To a solution of 2-bromo-5-methoxy-4,6-dimethylpyridine (216 mg, 1 mmol) in CH₂Cl₂ (10 mL), was added BBr₃ (2 mL 1.0 M solution in CH₂Cl₂; 2 mmol) at -78°C under N₂. After stirring for 30 min at this temperature and then 16 h at ambient temperature, the reaction mixture was poured into cold water (10 mL) and NaHCO₃ (5 % aq.) was added. After extraction with CH₂Cl₂ (3 x 20 mL), drying over Na₂SO₄ and evaporation *in vacuo*, the resulting brownish solid was purified by column chromatography eluting with ethyl acetate/pentane (16:84), the title compound was obtained as a colourless solid (150 mg, 78 %), mp 105-106 °C. ¹H NMR δ 7.1 (s, 1 H), 6.42 (br s, 1H), 2.43 (s, 3 H), 2.23 (s, 3 H). ¹³C NMR δ 149.4, 146.4, 137.0, 130.3, 127.6, 18.7, 15.9.

5-Hydroxy-4,6-dimethyl-2-pyridyl *n*-Octyl Telluride (21a) was prepared according to the procedure for pyridinol **7a**, using 6-bromo-2,4-dimethyl-3-pyridinol as a starting material. Yield: 47 %. ¹H NMR δ 7.21(s, 1H), 3.04 (t, *J* = 7.7, 2H), 2.48 (s, 3H), 2.21 (s, 3H), 1.86 (m, 2H), 1.38-1.26 (several peaks, 10H), 0.87 (t, *J* = 7.0, 3H). ¹³C NMR δ 148.2, 146.1, 132.9, 132.3, 127.4, 32.3, 32.2, 32.0, 29.3, 29.1, 22.8, 19.0, 15.2, 14.2, 9.7.

5-Hydroxy-4,6-dimethyl-3-pyridyl *n*-Octyl Selenide (21b): To the solution of dilithiated 6-bromo-2,4-dimethyl-3-pyridinol prepared as described below (compound **19c**), finely ground elemental selenium (0.32 g, 4.0 mmol) was added and stirring continued for 2h. The reaction mixture was then poured onto crushed ice and kept in the open air for 2h when a solution of saturated aqueous NH₄Cl was added. Extraction with Et₂O (3 x 50 mL), drying and evaporation afforded crude bis-(5-hydroxy-4,6-dimethyl-3-pyridyl) diselenide which was dissolved in EtOH and cooled to 0°C under N₂. NaBH₄ (0.34 g, 10 mmol) was added in one

portion and the reaction mixture was stirred for 30 min at room temperature, resulting in a faint yellowish solution. *n*-Octyl bromide (2.0 g, 10 mmol) was added by syringe and stirring continued for an additional 1 h when the reaction mixture was poured into water. Extraction with Et₂O (3 x 20 mL), drying over Na₂SO₄, evaporation and purification by column chromatography eluting with pentane/ethyl acetate (90:10) afforded 0.185 g (54 %) of the title compound as a light yellow oil. ¹H NMR δ 7.00 (s, 1H), 4.78 (br s, 1H), 3.06 (t, *J* = 7.6, 2H), 2.45 (s, 3H), 2.20 (s, 3H), 1.74 (m, 2H), 1.42-1.23 (several peaks, 10 H), 0.87 (t, *J* = 7.0, 3H). ¹³C NMR δ 147.4, 145.2, 143.7, 133.1, 126.4, 32.0, 30.7, 30.2, 29.3, 29.3, 27.0, 22.8, 18.9, 15.4, 14.

5-Hydroxy-4,6-dimethyl-2-pyridyl *n*-Octyl Sulfide (21c): To a solution of 6-bromo-2,4-dimethyl-3-pyridinol (0.202 g, 1.0 mmol) in THF (15 mL) was added dropwise *t*-BuLi (1.8 mL 1.7 M in pentane; 3 mmol) at -78 °C. The solution was stirred for 20 min at this temperature and 15 min at room temperature. The reaction mixture was again cooled to -78 °C and di-*n*-octyl disulfide (0.58 g, 2 mmol) was added dropwise and stirring was continued for 1 h at room temperature. A saturated solution of NH₄Cl was added and the mixture was extracted with ether (3 x 25 mL). Drying over Na₂SO₄, removal of the solvent *in vacuo* and purification of the crude product by column chromatography using ethylacetate/ pentane (13:87) as eluent afforded the title compound (0.17 g, 64 %). ¹H NMR δ 6.86 (s, 1H), 4.82 (bs, 1H), 3.04 (t, *J* = 7.6, 2H), 2.44 (s, 3H), 2.20 (s, 3H), 1.64 (m, 2 H), 1.41-1.26 (several peaks, 10H), 0.87 (t, *J* = 7.0, 3H). ¹³C NMR δ 148.4, 146.8, 144.8, 133.3, 123.0, 32.0, 31.8, 29.7, 29.3, 29.3, 29.0, 22.8, 19.0, 15.7, 14.3.

2-Bromo-3-methoxy-4,6-dimethyl-pyridine (22): 2-Bromo-4,6-dimethyl-3-pyridinol (300 mg, 1.5 mmol) was dissolved in dry DMF (2.5 mL) and K₂CO₃ (225 mg, 1.6 mmol) was added. After stirring for 30 min at room temperature, methyl iodide (0.1 mL, 1.6 mmol) was added dropwise and stirring was continued for 4 h. The reaction mixture was poured into water (5 ml) and extracted with CH₂Cl₂ (5 mL x 3). Drying of the organic phase over Na₂SO₄, filtration and evaporation *in vacuo* gave 320 mg (100%) of the title compound as a yellow oil. ¹H NMR (500 MHz) δ 6.91 (s, 1H), 3.81 (s, 3H), 2.45 (s, 3H), 2.30 (s, 3H), ¹³C NMR (75 MHz) δ 154.3, 150.6, 142.6, 136.4, 125.4, 60.6, 23.4, 16.3.

Di-*n*-octyl ditelluride was prepared in 19 % yield by alkylation of disodium ditelluride prepared by phenylhydrazine reduction of elemental tellurium in analogy with a literature procedure.³ Spectroscopic data were in good agreement with literature.⁴

3-Methoxy-4,6-dimethyl-2-pyridyl *n*-Octyl Telluride (23): To 2-bromo-3-methoxy-4,6-dimethyl-pyridine (180 mg, 0.83 mmol) in THF (6 mL) under N₂ at -78 °C was added dropwise *t*-BuLi (1 ml, 1.7 M solution in pentane; 1.7 mmol) and the reaction was stirred at this temperature for 30 minutes. Then, di-*n*-octyl ditelluride (450 mg, 0.93 mmol) was added and the reaction mixture was stirred for 15 min at -78 °C and an additional 2 h at room temperature. After pouring the reaction mixture into NaHCO₃ (5 % aq.), extraction with Et₂O, drying over Na₂SO₄ and concentration in *vacuo*, the crude product was purified by column chromatography using pentane/ethyl acetate (9:1) as an eluent to yield the title compound as a yellow oil (180 mg, 57 %). ¹H NMR (500 MHz) δ 6.68 (s, 1H), 3.78 (s, 3H), 3.12 (t, *J* = 7.7 Hz, 2H), 2.43 (s, 3H), 2.21 (s, 3H), 1.88 (m, 2H), 1.45-1.20 (overlapping multiplets, 10H), 0.88 (t, *J* = 7.3, 3H). ¹³C NMR (100 MHz) δ 155.5, 154.3, 137.0, 136.0, 122.9, 60.4, 32.5, 32.1, 32.0, 29.4, 29.2, 23.7, 22.8, 15.9, 14.3, 8.2. Anal. calcd for C₁₆H₂₇NOTe: C, 50.98; H, 7.22; N, 3.72. Found: C, 51.12; H, 7.24; N, 3.76.

3-Hydroxy-2-pyridyl *n*-Octyl Telluroxide (24): To a solution of 3-hydroxy-2-pyridyl *n*-octyl telluride (150 mg, 0.45 mmol) in CH₂Cl₂ (6 ml), *tert*-butyl hydroperoxide (70 % aq soln, 52 μ L; 0.54 mmol) was slowly added at ambient temperature. After stirring for 1 h the solvent was evaporated in *vacuo* to give the title compound as a white solid in quantitative yield. Reduction with NaHSO₃ (aq, sat)/diethyl ether cleanly and quantitatively returned the telluride starting material in the organic phase.

3-Hydroxy-4,6-dimethyl-2-pyridyl *n*-Octyl Telluroxide (25) was prepared from 3-hydroxy-4,6-dimethyl-2-pyridyl *n*-octyl telluride using the procedure for telluroxide **24**.

HPLC Peroxidation Assay.

In the experimental setup (schematically shown in Figure S1), linoleic acid and the antioxidant to be evaluated were vigorously stirred in chlorobenzene at 42°C with an aqueous solution of *N*-acetylcysteine (NAC). 2,2'-Azobis(2,4-dimethylvaleronitrile) (AMVN) was added as an initiator in the organic phase and the progress of peroxidation monitored by HPLC (conjugated diene hydroperoxide formation). For comparison of catalyst efficiency, inhibition times (*T*_{inh}) and inhibited rates of peroxidation, *R*_{inh}, were determined by least-squares methods from absorbance/time plots as previously described.^{5,6}

Figure S1. Two-phase model used for studying regeneration of chain-breaking antioxidants.

Figure S2. Inhibition time recorded with compound **16a** in the presence of various amounts of N-acetylcysteine (1, 0.5, 0.25, 0.125 0.0625 and 0 mM) in the aqueous phase.

Homogenous Phase Autoxidations. Kinetic measurements with peroxy radicals were performed by studying the inhibited autoxidation of styrene or cumene in chlorobenzene at 303 K, initiated by AIBN (0.05 M), in the presence of variable amounts ($1\text{--}20 \times 10^{-6}\text{M}$) of pyridinols, or α -tocopherol (α -TOH) or its synthetic analogue 2,2,5,7,8-pentamethyl-6-chromanol as reference antioxidants. The autoxidation was followed by monitoring the oxygen consumption in an oxygen uptake apparatus built in our laboratory and based on a Validyne DP15 differential pressure transducer, which have been previously described. The rate of initiation R_i was measured in a preliminary set of experiments from the length of the inhibition period T_{inh} , using α -TOH as a reference antioxidant: $R_i = 2 [\alpha\text{-TOH}] / T_{inh}$. Integration of the oxygen consumption trace afforded the rate of reaction with peroxy

radicals k_{inh} , according to the equation $\Delta[O_2]_t = -k_p/k_{inh} [RH] \ln(1-t/T_{inh})$. The k_p values of styrene and cumene at 303° are 41 and 0.32 M⁻¹s⁻¹ respectively.⁷

In order to evaluate the co-antioxidant behaviour of thiols towards pyridinols autoxidation studies were performed by adding 1-10 equivalents of *N*-(*t*-butoxycarbonyl)-cysteine methyl ester (LipCys), a lipid soluble analogue of NAC, to the autoxidating mixture. Each measurement was averaged over 3-5 independent determinations.

Figure S3. Length of the induction period observed during the autoxidation of styrene in chlorobenzene initiated by AIBN at 30 °C in the presence of ($\circ$) **8a** and ($\bullet$) **24** and LipCys 9.5×10^{-5} M.

Figure S4. Oxygen consumption observed during the autoxidation of styrene in chlorobenzene initiated by AIBN at 30 °C in the presence of **16a** (1.3×10^{-5} M). The arrows indicate the injection of LipCys (9.5×10^{-5} M). After around 13000 sec oxygen contained in the system is completely consumed.

p*K_a* Values. The p*K_a*'s of the pyridinols were determined by recording the UV-vis spectra at a number of different pH values. The spectral differences between the pyridinols and the deprotonated counterpart were used to generate p*K_a* plots from which the p*K_a* could be determined.

Estimated error: < 0.5 p*K_a* -units.

Pulse Radiolysis. Radiolysis of water results in the formation of OH[•], e_{aq}⁻, H[•], H₂O₂, H₂ and H₃O⁺, with OH[•] and e_{aq}⁻ being the major radical species with primary radiation chemical yields of 0.28 μmol J⁻¹ each above pH 3. N₂O-saturated solutions were used throughout in order to convert the reducing solvated electron into the oxidizing hydroxyl radical ($G_{\text{OH}} = 5.6 \times 10^{-7}$ mol J⁻¹).⁸ Millipore Milli-Q filtered water was used throughout. The pulse radiolysis equipment consists of a linear accelerator delivering 3 MeV electrons and a computerized optical detection system.⁹ The pulses were of 5-10 ns duration, giving doses of 3-6 Gy. For dosimetry a N₂O-saturated 10⁻² KSCN solution was used.¹⁰ The Gε value of (SCN)₂^{•-} was taken to be 4.78 x 10⁻⁴ m² J⁻¹ at 500 nm.

The procedures were previously described.¹¹ Estimated uncertainty in potentials ± 20 mV.

Cyclic Voltammetry. Cyclic voltammetry was performed with a Potentiostat/Galvanostat interfaced to a base PC. The cell was a standard three-electrode setup using a 3 mm diameter glassy carbon working electrode, a platinum coil counter electrode, and a calomel reference electrode. Acetonitrile was of the purest grade available, and the supporting electrolyte, 0.1 M tetrabutylammonium perchlorate (TBAP), was recrystallized from 10 % hexane in ethyl acetate. The scan rate was 500 mV s⁻¹, and full IR compensation was employed in all measurements. Each measurement was averaged over 3-5 independent determinations. None of the oxidation processes studied were reversible. Therefore, peak potentials, E_p , were reported.

Assay for Thiol Peroxidase Activity. Initial rates recorded for the reduction of hydrogen peroxide (3.75 mM) in methanol by thiophenol (1 mM) at 25 °C in the presence of catalyst (0.01 mM) were recorded by monitoring the UV absorption of diphenyl disulfide at 305 nm. Initial rates were measured at least six times and calculated for the first 60 s of reaction. The rate of disulfide formation was corrected for the slow spontaneous thiol oxidation by subtracting the rate of disulfide formation in a control experiment run without added catalyst.¹²

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^1H NMR spectrum of **7a**.

^{13}C NMR spectrum of **7a**.

^1H NMR spectrum of **7b**.

^{13}C NMR spectrum of **7b**.

¹H NMR spectrum of **7c**.

^{13}C NMR spectrum of **7c**.

¹H NMR spectrum of **8a**.

STANDARD 1H OBSERVE

Pulse Sequence: s2pul

Solvent: cdcl3

Temp. 25.0 C / 298.1 K

File: OrthoOHPyTeOctyl_1H

PULSE SEQUENCE: s2pul

Pulse 37.1 degrees

Acq. time 3.744 sec

Width 6000.6 Hz

8 repetitions

OBSERVE H1, 399.98 MHz

DATA PROCESSING

Line broadening 0.2 Hz

Ft size 65536

Total time 1 minute

^{13}C NMR spectrum of **8a**.

¹H NMR spectrum of **8b**.

Pulse Sequence: s2pul
 Solvent: cdcl3
 Temp: 25.0 C / 298.1 K
 File: h11-thomas-rewriting_ortho_se_pyridinol_lh_4_sep_cdcl3_500
 INOVA-500 Unit500
 User: henrik
 Date: 2007
 PULSE SEQUENCE: s2pul
 Pulse: 73.5 degrees
 Acq. time: 3.000 sec
 Width: 8000.0 Hz
 F2: 500.136131 MHz
 OBSERVATION: 499.94 MHz
 DATA PROCESSING
 Line broadening: 0.2 Hz
 FT size: 65536
 Total time: 1 minutes

¹³C NMR spectrum of **8b**.

¹H NMR spectrum of **8c**.

¹³C NMR spectrum of **8c**.

¹H NMR spectrum of **9a**.

^{13}C NMR spectrum of **9a**.

¹H NMR spectrum of **9b**.

^{13}C NMR spectrum of **9b**.

¹H NMR spectrum of **9c**.

¹H Observe

Archive directory: /home/vnmr1/vnmrSYS/data
Sample directory:

Pulse Sequence: s2pul

Solvent: CDCl₃
Temp. 25.0 C / 298.1 K
File: PyOHSeOctyl_1H

PULSE SEQUENCE: s2pul
Pulse 43.2 degrees
Acq. time 3.700 sec
Width 4800.8 Hz
8 repetitions
OBSERVE H1, 300.03 MHz
DATA PROCESSING
Line broadening 0.2 Hz
Ft size 65536
Total time 1 minute

^{13}C NMR spectrum of **9c**.

^1H NMR spectrum of **12**.

^{13}C NMR spectrum of **12**.

User: henrikj
 Date: Mar 9 2007
 PULSE SEQUENCE: zgpg30
 Relax. delay 1.500 sec
 Pulse 64.5 degrees
 Acq. time 1.199 sec
 Width 25000.0 Hz
 18000 repetitions
 OBSERVE C13, 100.58 MHz
 DECOUPLE H1, 399.98 MHz
 Power 48 dB
 Continuously on
 200000 scans
 Multiscan gated
 Single precision data
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 65536
 Total time 13.5 hours

¹H NMR spectrum of **2-Bromo-3-cyano-5-methoxy-4,6-dimethylpyridine**.

¹³C NMR spectrum of **2-Bromo-3-cyano-5-methoxy-4,6-dimethylpyridine**.

^1H NMR spectrum of **13**.

Width 25000.0 Hz
6672 repetitions
OBSERVE C13, 100.58 MHz
DECOUPLE H1, 399.98 MHz
Power 48 dB
continuously on
WALTZ-16 modulated
Single precision data
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 5.0 hours

¹H NMR spectrum of **2-Bromo-5-methoxy-4,6-dimethyl-3-carboxylic acid amide**.

¹³C NMR spectrum of **2-Bromo-5-methoxy-4,6-dimethyl-3-carboxylic acid amide**.

^1H NMR spectrum of **14**.

^{13}C NMR spectrum of **14**.

¹H NMR spectrum of **19**.

^{13}C NMR spectrum of **19**.

Temp. 25.0 C / 298.1 K
File: OMe2MeNH2PyBr_13C

PULSE SEQUENCE: s2pul
Relax. delay 3.000 sec
Pulse 64.5 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
32 repetitions
OBSERVE C13, 100.58 MHz
DECOUPLE H1, 399.98 MHz
Power 48 dB
continuously on
WALTZ-16 modulated
Single precision data
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 2 minutes

¹H NMR spectrum of **15**.

^{13}C NMR spectrum of **15**.

¹³H NMR spectrum of **2-Bromo-5-methoxy-4,6-dimethyl-3-pyridinol**.

¹³C NMR spectrum of **2-Bromo-5-methoxy-4,6-dimethyl-pyridinol**.

¹H NMR spectrum of **16a**.

¹³C NMR spectrum of **16a**.

¹H NMR spectrum of **16b**.

^{13}C NMR spectrum of **16b**.

¹H NMR spectrum of **16c**.

STANDARD PROTON PARAMETERS

Pulse Sequence: #2pul
 Solvent: cdcl3
 Temp: 25.0 C / 298.1 K
 File: b1-75_andra_kolonnuppreingen_1H_CDCL3
 INOVA-500 "unity500"
 User: henrikj
 Date: Oct 16 2007
 PULSE SEQUENCE: #2pul
 Pulse 73.5 degrees
 Acq. time 3.000 sec
 Width 8000.0 Hz
 16 repetitions
 OBSERVED F1: 499.94 MHz
 PROCESSED F1: 499.94 MHz
 Line broadening 0.2 Hz
 FT size 65536
 Total time 1 minute

¹H NMR spectrum of **16c**.

¹H NMR spectrum of **18a**.

^{13}C NMR spectrum of **18a**.

¹H NMR spectrum of **18b**.

¹³C NMR spectrum of **18b**.

¹H NMR spectrum of **2-Bromo-5-methoxy-4,6-dimethylpyridine**.

¹³C NMR spectrum of **2-Bromo-5-methoxy-4,6-dimethylpyridine**.

¹H NMR spectrum of **20**.

^{13}C NMR spectrum of **20**.

^1H NMR spectrum of **21a**.

^1H NMR spectrum of **21a**.

¹H NMR spectrum of **21b**.

¹³C NMR spectrum of **21b**.

¹³H NMR spectrum of **21c**.

¹³C NMR spectrum of **21c**.

¹H NMR spectrum of **22**.

¹³C NMR spectrum of **22**.

¹H NMR spectrum of **23**.

experiment 145
Pulse Sequence: s2pul
Solvent: cdcl3
Temp: 25.0 C / 298.1 K
File: h1_exp145_nycdcl3_1h_cdcl3_500
INOVA-500 "unity500"
User: henrikj
Date: May 20 2009
Pulse Sequence: s2pul
Pulse 73.5 degrees
Pulse 15.0 degrees
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.93 MHz
DATA PROCESSING
FID Processing 0.2 Hz
FT 65353
Total time 1 minute

¹³C NMR spectrum of **23**.