SUPPORTING INFORMATION FOR:

S-(2-Pyridinyl)-1,1,3,3-Tetramethylthiouronium Hexafluorophosphate. A New Reagent for the Synthesis of 2-Pyridinethiol Esters

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All moisture-sensitive reactions were performed in an inert, dry atmosphere of argon in oven-dried glassware. Reagent grade solvents were used for either chromatography or extraction. THF was distilled from Na/benzophenone under argon; methylene chloride, toluene, triethylamine and diisopropylethylamine were distilled from CaH₂ under argon. Analytical thin-layer chromatography (TLC) was performed using Merck silica gel 60 F-254 plates. The plates were visualized first with UV illumination followed by charring with 5% *p*-anisaldehyde in 95:5:1 EtOH:AcOH:H₂SO₄ or Verghn's reagent (12.5 g of ammonium molybdate and 0.5 g of ceric sulfate dissolved in 250 mL of 10% aq H₂SO₄). Flash chromatography was performed using silica gel (230-400 mesh). The solvent compositions reported for all chromatographic separations are on a volume/volume (v/v) basis. ¹H NMR spectra were recorded at either 200 or 300 MHz and are reported in parts per million (ppm) on the δ scale relative to residual CHCl₃ (δ 7.25), ¹³C NMR spectra were recorded at either 50 or 75 MHz and are reported in parts per million (ppm) on the δ scale relative to CDCl₃ (δ 77.00).

Tetramethylchloroformamidinium Hexafluorophosphate (5). Tetramethyl urea (3.00 mL, 25.0 mmol) was dissolved in 10 mL of dry toluene under argon with stirring. The solution was cooled to 0°C with an ice bath and a ~20% phosgene solution in toluene (26 mL, ~ 50 mmol) was added in 3 minutes. The mixture was kept 10 minutes at RT, then was heated at 60°C for 15 minutes. After cooling to RT, 85 mL of dry ether was added, the mixture was stirred for 5 minutes, and then the liquid was decanted. The remaining solid was washed with dry ether (3 $\times$ 10 mL), then dissolved in 125 mL of methylene chloride. A saturated aqueous solution of ammonium hexafluorophosphate (13 mL) was

added with stirring. After 5 minutes, the two layers were separated, the organic layer was washed with 15 mL of water and concentrated under reduced pressure. The resulting white solid was washed with ether (3 × 12 mL) and dried under reduced pressure over phosphorus pentoxide. Yield = quantitative; mp 100-101 °C; ¹H NMR (300 MHz, CDCl₃) δ 3.26 (*bs*, 12H; NCH₃); ¹³C NMR (75 MHz, CDCl₃) δ 43.84 (CH₃), 159.41 (C).

***S*-(2-Pyridinyl)-1,1,3,3-tetramethylthiuronium Hexafluorophosphate (6).**

Tetramethylchloroformamidinium hexafluorophosphate (4.49 g, 16.0 mmol) and 2-mercaptopyridine (1.78 g, 16.0 mmol) were dissolved in 10 mL of freshly distilled methylene chloride. Triethylamine (2.23 mL, 16.0 mmol) was added dropwise at RT (a white smoke evolved) and the reaction mixture was stirred for 10 minutes. It was then concentrated under reduced pressure and the resulting crude orange oil was crystallized from a mixture 3:1 methanol-isopropanol to obtain a white solid which was washed with isopropanol and dried under reduced pressure over phosphorus pentoxide (4.15 g, 73%). mp 109 °C; ¹H NMR (200 MHz, CDCl₃) δ 3.28 (*s*, 12H; NCH₃), 7.32 (*ddd*, 1H, *J* = 0.9, 4.8, 7.5 Hz; H-5'), 7.51 (*ddd*, 1H, *J* = 0.9, 0.9, 7.9 Hz; H-3'), 7.81 (*ddd*, 1H, *J* = 1.9, 7.5, 7.9 Hz; H-4'), 8.52 (*ddd*, 1H, *J* = 0.9, 1.9, 4.8 Hz; H-6'); ¹³C NMR (50 MHz, CDCl₃) δ 44.06 (CH₃), 123.70 (CH), 125.42 (CH), 138.82 (CH), 151.07 (C), 151.26 (CH), 172.07 (C); IR (KBr) 3060, 2940, 1610, 1569, 1402, 1259, 840 cm⁻¹; HRMS (FAB) *m/z*, calc. for C₁₀H₁₆N₃S (M⁺ - PF₆) 210.11, obsd. 210.105.

2-Methoxymethoxyacrylic Acid (7f). In a 50-mL 2-neck round-bottom flask, methoxymethyl vinyl ether (0.200 g, 2.27 mmol) was dissolved in 4 mL of dry THF under argon with stirring. The solution was cooled to -78 °C and a 1.1 M solution of *sec*-butyllithium in cyclohexane (2.10 mL, 2.27 mmol) was added dropwise. The reaction mixture was stirred 10 minutes at -78 °C and 1 h between -35 and -25 °C; it was then cooled to -78 °C and CO₂ was bubbled into the flask through a calcium sulfate tube for 10 minutes. Solid CO₂ was then added and the mixture was left warming to 0 °C. An aqueous 1 M solution of HCl was added until the pH reached 4 (pH paper) and the aqueous layer was extracted with ether. The pH was lowered to 2 with more HCl and the extraction was repeated. The combined organic layers were dried over magnesium sulfate, filtered and concentrated under reduced pressure to afford 0.208 g (69% yield) of product as a white solid. *R_f* 0.15 (1:1 hexanes/ethyl acetate); mp 45-47 °C; ¹H NMR (200 MHz, CDCl₃) δ 3.44 (*s*, 3H; OCH₃), 5.06 (*s*, 2H; OCH₂O), 5.13 (*d*, 1H, *J* = 2.5 Hz; H_A-3), 5.63 (*d*, 1H, *J* = 2.5 Hz; H_B-3), 8.20 (*bs*, 1H; OH); ¹³C NMR (50 MHz, CDCl₃) δ 56.39 (CH₃), 94.71 (CH₂), 101.02 (CH₂), 148.19 (C), 167.27 (C); IR (NaCl) 2981, 2938, 1725, 1633, 1205, 1156, 1102, 1010 cm⁻¹; HRMS (EI) *m/z*, calc. for C₅H₈O₄ (M⁺) 132.04 obsd. 132.043.

General Procedure for the Preparation of 2-Pyridinethiol Esters (8a-f). To an ice-cold solution of the acid (1.0 mmol) in 10 mL of freshly distilled methylene chloride, *S*-(2-pyridinyl)-1,1,3,3-tetramethylthiuronium hexafluorophosphate (1.2 mmol), diisopropylethylamine (1.2 mmol) and 4-(dimethylamino)-pyridine (0.12 mmol) were added in this order under argon with stirring. The reaction mixture was stirred overnight and the temperature was allowed to reach RT. The mixture was then concentrated under reduced pressure to obtain an oil which was partitioned between ether and 10 mL of a

10% aqueous solution of sodium carbonate. The aqueous layer was extracted three times with ether, the combined organic layer was dried over magnesium sulfate, filtered and concentrated under reduced pressure. The yellow oil obtained was filtered through a 4 cm plug of silica gel, using a mixture 4:1 ether-pentane as eluent. For the product **8e**, the plug of silica was first washed with 200 mL of a 1:1 ether-pentane mixture with 3% of triethylamine followed by 200 mL of a 1:1 ether-pentane mixture.

Thiobenzoic Acid, S-Pyridin-2-yl Ester (8a). Yield = 94%; white solid; R_f 0.26 (4:1 hexanes-ethyl acetate); mp 45-48 °C ^1H NMR (300 MHz, CDCl_3) δ 7.32 (*ddd*, 1H, J = 1.4, 4.9, 7.1 Hz; H-5'), 7.45-7.65 (*m*, 3H), 7.70-7.81 (*m*, 2H), 8.01 (*m*, 1H), 8.67 (*ddd*, 1H, J = 0.8, 1.9, 4.9 Hz; H-6'); ^{13}C NMR (50 MHz, CDCl_3) δ 123.52 (CH), 127.39 (CH), 128.68 (CH), 130.72 (CH), 133.77 (CH), 136.36 (CH), 137.05 (CH), 150.33 (CH), 151.11 (C), 189.13 (C); IR (NaCl) 3037, 2962, 1684, 1577, 1458, 1426, 1124, 908 cm^{-1} ; HRMS (EI) m/z , calc. for $\text{C}_{12}\text{H}_9\text{NOS}$ (M^+) 215.04 obsd. 215.039.

Thiobutyric Acid, S-Pyridin-2-yl Ester (8b). Yield = 83%; pale yellow oil; R_f 0.55 (1:1 hexanes-ethyl acetate); ^1H NMR (200 MHz, CDCl_3) δ 0.95 (*t*, 3H, J = 7.4 Hz; H-4), 1.71 (*sext*, 2H, J = 7.4 Hz; H-3), 2.64 (*t*, 2H, J = 7.4 Hz; H-2), 7.23 (*ddd*, 1H, J = 1.3, 4.9, 7.4 Hz; H-5'), 7.56 (*ddd*, 1H, J = 0.9, 1.3, 7.9 Hz; H-3'), 7.67 (*ddd*, 1H, J = 1.9, 7.4, 7.9 Hz; H-4'), 8.57 (*ddd*, 1H, J = 0.9, 1.9, 4.9 Hz; H-6'); ^{13}C NMR (50 MHz, CDCl_3) δ 13.37 (CH_3), 18.84 (CH_2), 45.91 (CH_2), 123.30 (CH), 129.98 (CH), 136.93 (CH), 150.23 (CH), 151.51 (C), 196.29 (C); IR (NaCl) 3065, 2967, 2930, 1716, 1579, 1459, 1427, 1118, 998 cm^{-1} ; HRMS (EI) m/z , calc. for $\text{C}_9\text{H}_{12}\text{NOS}$ (MH^+) 182.06 obsd. 182.063.

3-Phenyl-thioacrylic Acid, S-Pyridin-2-yl Ester (8c). Yield = 85%; white solid; R_f 0.47 (1:1 hexanes-ethyl acetate); mp 78 °C; ^1H NMR (200 MHz, CDCl_3) δ 6.77 (*d*, 1H, J = 15.1 Hz; H-2), 7.26 (*ddd*, 1H, J = 3.0, 4.9, 5.6 Hz; H-5'), 7.37 (*m*, 2H; arom.), 7.53 (*m*, 2H; arom.), 7.67 (*d*, 1H, J = 15.1 Hz; H-3), 7.72 (*m*, 2H; arom.), 8.61 (*ddd*, 1H, J = 1.1, 1.7, 4.9 Hz; H-6'); ^{13}C NMR (50 MHz, CDCl_3) δ 123.36 (CH), 124.06 (CH), 128.45 (CH), 128.87 (CH), 130.00 (CH), 130.80 (CH), 133.64 (C), 136.93 (CH), 142.05 (CH), 150.22 (CH), 151.46 (C), 186.70 (C); IR (KBr) 3049, 2918, 1676, 1610, 1569, 1449, 1418, 1021, 754 cm^{-1} ; HRMS (EI) m/z , calc. for $\text{C}_{14}\text{H}_{11}\text{NOS}$ (M^+) 241.06 obsd. 241.055

But-2-enethioic Acid, S-Pyridin-2-yl Ester (8d). Yield = 63%; pale yellow oil; R_f 0.43 (3:2 hexanes-ethyl acetate); ^1H NMR (200 MHz, CDCl_3) δ 1.87 (*dd*, 3H, J = 1.7, 6.0 Hz; H-4), 6.16 (*dq*, 1H, J = 1.7, 15.4 Hz; H-2), 6.98 (*dq*, 1H, J = 6.9, 15.4 Hz; H-3), 7.22 (*ddd*, 1H, J = 1.6, 4.9, 7.1 Hz; H-5'), 7.61 (*ddd*, 1H, J = 1.0, 1.6, 7.9 Hz; H-3'), 7.69 (*ddd*, 1H, J = 1.9, 7.1, 7.9 Hz; H-4'), 8.56 (*ddd*, 1H, J = 1.0, 1.9, 4.9 Hz; H-6'); ^{13}C NMR (50 MHz, CDCl_3) δ 18.00 (CH_3), 123.26 (CH), 129.33 (CH), 130.08 (CH), 136.86 (CH), 142.76 (CH), 150.16 (CH), 151.43 (C), 186.64 (C); IR (NaCl) 3045, 2980, 1689, 1639, 1589, 1452, 1427, 1049 cm^{-1} .

2-Methylthioacrylic Acid, S-Pyridin-2-yl Ester (8e). Yield = 50%; pale yellow oil; R_f 0.54 (1:1 hexanes-ethyl acetate); ^1H NMR (200 MHz, CDCl_3) δ 1.98 (*dd*, 1H, J = 0.9, 1.6 Hz; CH_3), 5.73 (*q*, 1H, J = 1.6 Hz; H_A -3), 6.20 (*q*, 1H, J = 0.9 Hz; H_B -3H), 7.27 (*ddd*, 1H, J = 1.3, 4.9, 7.4 Hz; H-5'), 7.60 (*ddd*, 1H, J = 0.9, 1.3, 7.9 Hz; H-3'), 7.72 (*ddd*, 1H, J =

1.9, 7.4, 7.9 Hz; H-4'), 8.61 (*ddd*, 1H, $J = 0.9, 1.9, 4.9$ Hz; H-6'); ^{13}C NMR (50 MHz, CDCl_3) δ 18.03 (CH_3), 123.42 (CH), 124.48 (CH_2), 130.63 (CH), 137.00 (CH), 143.37 (C), 150.36 (CH), 151.42 (C), 190.53 (C); IR (NaCl) 3038, 2972, 2912, 1683, 1578, 1457, 1427, 1031 cm^{-1} .

2-Methoxymethoxythioacrylic Acid, S-Pyridin-2-yl Ester (8f). Yield = 67%; pale yellow oil; R_f 0.39 (1:1 hexanes-ethyl acetate); ^1H NMR (200 MHz, CDCl_3) δ 3.49 (*s*, 3H; OCH_3), 4.79 (*d*, 1H, $J = 2.7$ Hz; $\text{H}_A\text{-3}$), 5.10 (*s*, 2H; OCH_2O), 5.39 (*d*, 1H, $J = 2.7$ Hz; $\text{H}_A\text{-3}$), 7.24 (*ddd*, 1H, $J = 1.3, 4.8, 7.4$ Hz; H-5'), 7.60 (*ddd*, 1H, $J = 0.9, 1.3, 7.9$ Hz; H-3'), 7.73 (*ddd*, 1H, $J = 1.9, 7.4, 7.9$ Hz; H-4'), 8.62 (*ddd*, 1H, $J = 0.9, 1.9, 4.8$ Hz; H-6'); ^{13}C NMR (50 MHz, CDCl_3) δ 56.56 (CH_3), 94.86 (CH_2), 94.97 (CH_2), 123.56 (CH), 130.62 (CH), 137.02 (CH), 150.46 (CH), 151.18 (C), 153.41 (C), 187.09 (C); IR (NaCl) 3055, 3006, 2973, 2940, 2235, 1699, 1627, 1578, 1458, 1283, 1162, 1009, 976 cm^{-1} .

¹H NMR
(300 MHz, CDCl₃)

**^{13}C NMR
(75 MHz, CDCl_3)**

6

7f

^1H NMR
(300 MHz, CDCl_3)

**^{13}C NMR
(75 MHz, CDCl_3)**

7f

**^{13}C NMR
(75 MHz, CDCl_3)**

¹H NMR
(300 MHz, CDCl₃)

^{13}C NMR
(75 MHz, CDCl_3)

¹H NMR
(300 MHz, CDCl₃)

8c

^{13}C NMR
(75 MHz, CDCl_3)

¹H NMR
(300 MHz, CDCl₃)

^{13}C NMR
(75 MHz, CDCl_3)

^1H NMR
(300 MHz, CDCl_3)

8

¹H NMR
(300 MHz, CDCl₃)

8f

**^{13}C NMR
(75 MHz, CDCl_3)**