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Supporting Information

***N*-Hydroxy-*N*-[1-(3-chlorobenzo[*b*]thien-2-yl)ethyl]urea (1b).** 2-Acetyl-3-chlorobenzo[*b*]thiophene was prepared from 3-chloro-2-chlorocarbonylbenzo[*b*]thiophene¹ by conversion to the *N*-methyl-*N*-methoxy amide and reaction with methylmagnesium bromide. This ketone was converted to **1b** using method 1a: mp 155-156 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.45 (d, *J*=7 Hz, 3H), 5.84 (q, *J*=7 Hz, 1H), 6.51 (bs, 2H), 7.47 (m, 2H), 7.75 (m, 1H), 7.99 (m, 1H), 9.60 (s, 1H), MS(DCI-NH₃) *m/z* 288 (M+NH₄)⁺, 271 (M+H)⁺. Anal. (C₁₁H₁₁ClN₂O₂S) C, H, N.

***N*-Hydroxy-*N*-[1-(4-chlorobenzo[*b*]thien-2-yl)ethyl]urea (1c).** Methyl 4-chlorobenzo[*b*]thiophene-2-carboxylate² was converted to 2-acetyl-7-chlorobenzo[*b*]thiophene by conversion to the *N,O*-dimethylhydroxamic acid and reaction with methyl magnesium bromide. The 2-acetyl-4-chlorobenzo[*b*]thiophene was converted to **1c** using method 1a: mp 157.5-158.5 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.54 (d, *J*=7 Hz, 3H), 5.61 (q, *J*=7 Hz, 1H), 6.51 (bs, 2H), 7.31 (m, 2H), 7.43 (m, 1H), 7.91 (d, *J*= 8 Hz, 1H), 9.34 (s, 1H), MS(DCI-NH₃) *m/z* 288 (M+NH₄)⁺, 271 (M+H)⁺. Anal. (C₁₁H₁₁ClN₂O₂S) C, H, N.

***N*-Hydroxy-*N*-[1-(5-fluorobenzo[*b*]thien-2-yl)ethyl]urea (1d).** 5-Fluorophenylbenzo[*b*]thiophene was prepared as described for **1g** using 4-fluorothiophenol instead of 4-*tert*-butyl thiophenol. 5-Fluorophenylbenzo[*b*]thiophene was converted to **1d** using method 3: mp 149-153 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.50 (d, *J*=7.5 Hz, 3H), 5.56 (m, 1H), 6.47 (bs, 2H), 7.13-7.29 (m, 2H), 7.57-7.77 (m, 1H), 7.81-7.95 (m, 1H), 9.26 (m, 1H). *M/z* (DCI-NH₃): 272 (M+NH₄)⁺, 255 (M+1)⁺. Anal. (C₁₁H₁₁FN₂O₂S): Calcd N: 11.01; Found N: 10.46.

***N*-Hydroxy-*N*-[1-(7-chlorobenzo[*b*]thien-2-yl)ethyl]urea (1e)** was prepared from ethyl 7-chlorobenzo[*b*]thiophene-2-carboxylate³ using the procedure described for **1c**: mp 157-159 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.53 (d, *J*=7 Hz, 3H), 5.49 (q, *J*=7 Hz,

1H), 6.51 (bs, 2H), 7.35-7.45 (m, 3H), 7.78 (m, 1H), 9.33 (s, 1H); MS (DCI-NH₃) m/z 288 (M+NH₄)⁺, 271 (M+H)⁺. Anal. : Calcd (C₁₁H₁₁ClN₂O₂S) C, H, N.

***N*-Hydroxy-*N*-[1-(3-methoxybenzo[*b*]thien-2-yl)ethyl]urea (1f).** To a stirred solution of thiosalicylic acid (10 g, 65 mmol) in 70% ethanol (250 mL) was added K₂CO₃ (8.97 g, 64.9 mmol). Chloroacetone (6.2 mL, 77.8 mmol) was added and the mixture was heated at reflux for 3 h and concentrated. The residue was dissolved in water and acidified to pH 1 with conc. HCl. The product precipitated and was collected and recrystallized from ethyl acetate / hexanes. Two crops were collected for a total of 10.2 g (81%) of 2-(2-oxothioproxy)benzoic acid. This acid (2.0 g, 10.3 mmol) was suspended in ether and excess diazomethane in ether was added. Excess diazomethane was destroyed by the addition of aqueous HCl. The ether layer was dried (MgSO₄) and concentrated to give methyl (2-oxothioproxy)benzoate (1.95 g, 85%).

To a stirred solution of the ester (1.9 g, 8.5 mmol) in methanol (40 mL) was added sodium methoxide (230 mg, 4.3 mmol). The reaction mixture was heated at reflux for 4 h and stirred for 15 h at room temperature. The reaction was concentrated and the residue diluted with 2N NaOH and ethyl acetate. The aqueous phase was acidified with concentrated HCl and the precipitated solid collected and dried to give 1.9 g (85%) of 3-hydroxy-2-acetylbenzo[*b*]thiophene. Treatment of this material with diazomethane as described above gave 2-acetyl-3-methoxybenzo[*b*]thiophene. 2-Acetyl-3-methoxybenzo[*b*]thiophene was converted to **1f** using method 1a: mp 158 °C (dec.); ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.42 (d, J=7.5 Hz, 3H), 3.91 (s, 3H), 5.81 (q, J=7.5 Hz, 1H), 6.42 (bs, 2H), 7.30-7.41 (m, 2H), 7.66-7.73 (m, 1H), 7.82-7.88 (m, 1H), 9.44 (s, 1H); MS (DCI-NH₃) m/z 284 (M+NH₄)⁺, 267 (M+H)⁺. Anal. (C₁₂H₁₄N₂O₃S) C, H, N.

***N*-[1-[5-(2,2-Dimethylethyl)benzo[*b*]thien-3-yl]ethyl]-*N*-hydroxyurea (1g).** A stirred suspension of 1-bromo-4-*tert*-butylbenzene (10 g, 47 mmol) in ether (100 mL) and magnesium metal (1.2 g, 49 mmol) was heated at reflux for 2 h. The mixture was cooled to 0 °C and sulfur (1.5 g) was added in portions over 10 min. The ice bath was removed

and the reaction mixture was stirred at room temperature for 1 hour. The mixture was poured into ice water, acidified with 10% HCl and extracted with ether. The organic extract was washed with sat'd NaCl and dried (MgSO₄). Concentration gave 4-*tert*-butylthiophenol as a cloudy yellow liquid (8.1 g) which was used without further purification.

To a stirred suspension of sodium hydride (2.0 g, 60%, 50 mmol) in THF (50 mL) was added a THF (25 mL) solution of the substituted thiophenol (prepared above) (8.1 g, 54 mmol) in THF (25 mL). The mixture was stirred for 0.5 h and bromoacetaldehyde diethyl acetal (9.3 g, 47 mmol) in ether (25 mL) was added. This mixture was stirred overnight at room temperature. Saturated NH₄Cl was added and the mixture concentrated. The residue was diluted with ether and washed with water. The organic extract was dried (MgSO₄) and concentrated. The residue was vacuum distilled to give 4-*tert*-butylphenyl-2-thiaproprionaldehyde diethyl acetal as a yellow oil 5.9 g (bp 142 °C / 1 mm Hg) (17%, 2 steps).

Phosphorous pentoxide and phosphoric acid were combined and heated at 130-135° for 0.75 h. The temperature was raised to 175 °C and the acetal prepared above (6.2 g, 2.2 mmol) was added dropwise. The hot solution was poured onto ice and extracted with ether. The combined organic extracts were dried (MgSO₄) and concentrated. The residue was filtered through a pad of silica gel, eluted with hexanes and concentrated to yield 2.26 g (54%) of 5-*tert*-butylbenzothiophene as a clear yellow liquid. 2-Acetyl-5-*tert*-butylbenzothiophene was prepared by metalation of the substituted benzo[b]thiophene with *n*-butyllithium and reaction with acetaldehyde followed by Jones oxidation in 43% yield (2 steps). 2-Acetyl-5-*tert*-butylbenzothiophene was converted to **1g** using method 1a: mp 151-153°C; ¹H NMR (300 MHz, DMSO-d₆) δ 134 (s, 9H), 1.50 (d, 3H), 5.55 (q, 1H), 6.44 (brs, 2H), 7.22 (s, 1H), 7.37 (dd, 1H), 7.74 (d, 1H), 7.77 (d, 1H), 9.21 (brs, 1H). MS(DCI-NH₃) m/z 310 (M+NH₄)⁺, 293 (M+H)⁺. Anal. (C₁₅H₂₀N₂O₂S) C, H, N.

***N*-Hydroxy-*N*-[1-(3-*tert*butylthiobenzo[*b*]thien-2-yl)methyl]urea (**1h**).** To a stirred solution of 3-bromo-benzo[*b*]thiophene-2-carboxaldehyde⁴ (0.2 g, 1.0 mmol) in ethanol (10 mL) was added K₂CO₃ (0.27 g, 2 mmol) and *tert*-butanethiol (0.23 mL, 2 mmol). The reaction was heated to 50 °C for 0.25 h and cooled. The mixture was diluted with water and extracted with ethyl acetate. The combined ethyl acetate layers were dried (MgSO₄) and concentrated to give 0.21 g (84 %) of 3-*tert*-butylthiobenzo[*b*]thiophene-2-carboxaldehyde which solidified on standing. This aldehyde was converted to **1h** using method 1a: mp 167 °C (dec.); ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.26 (s, 9H), 5.07 (s, 2H), 6.51 (bs, 2H), 7.33-7.48 (m, 2H), 7.95 (m, 2H), 9.55 (s, 1H), MS(DCI-NH₃) *m/z* 328 (M+NH₄)⁺, 311 (M+1)⁺. Anal. (C₁₄H₁₈N₂O₂S₂) C, H, N.

***N*-Hydroxy-*N*-[1-(3-phenylthiobenzo[*b*]thien-2-yl)methyl]urea (**1i**)** was prepared using thiophenol and 3-bromobenzo[*b*]thiophene-2-carboxaldehyde as described in **1h**: mp 165-167 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 5.03 (s, 2H), 6.51 (bs, 2H), 7.13 (m, 3H), 7.22 (m, 2H), 7.36 (m, 2H), 7.60 (d, *J*=4 Hz, 1H), 8.00 (d, *J*=4 Hz, 2H), 9.61 (s, 1H); MS (DCI-NH₃) *m/z* 348 (M+NH₄)⁺, 331 (M+H)⁺. Anal. (C₁₆H₁₄N₂O₂S₂) C, H, N.

***N*-Hydroxy-*N*-(1-benzo[*b*]thien-3-ylethyl)urea (**2**).** A solution of benzo[*b*]thiophene (20 g, 149 mmol) in nitroethane (100 mL) was added to a 0 °C stirred solution of AlCl₃ (59.7 g, 448 mmol) and acetyl chloride (10.6 mL, 149 mmol) in nitroethane (150 mL). The ice bath was removed and the mixture was allowed to stir for 15 h at room temperature. The mixture was poured onto ice (500 mL) and concentrated HCl (150 mL). The desired material was extracted with ethyl acetate. The organic extract was dried (MgSO₄) and concentrated. The residue was purified by flash column chromatography (SiO₂, eluting with 10% ethyl acetate / hexanes) to give the desired 3-acetylbenzo[*b*]thiophene as an oil 3.8 g (14%).

The 3-acetylbenzo[*b*]thiophene was converted to **2** by method 1a: mp 180 °C (dec.); ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.50 (d, *J*=7 Hz, 3H), 5.73 (q, 1H), 6.35 (br s, 2H), 7.30-

7.43 (m, 2H), 7.67 (s, 1H), 7.90-8.00 (m, 2H), 8.96 (s, 1H). M/z (EI): 236 (M)⁺. Anal. (C₁₁H₁₂N₂O₂S) C, H, N.

***N*-Hydroxy-*N*-(1-benzo[*b*]thien-2-ylethyl)urea 1,1-dioxide (3).** *N*-Acetoxy-1-*N*-[1-benzo[*b*]thien-2-yl]ethyl]urea was prepared from **1a**¹⁸ in THF in the presence of triethylamine and acetyl chloride. To a 0 °C stirred solution of *N*-acetoxy-1-*N*-[1-benzo[*b*]thien-2-yl]ethyl]urea (0.1 g, 0.36 mmol) in glacial acetic acid (2 mL) was added peracetic acid (0.2 g, 1.1 mmol) in acetic acid (1 mL). The mixture was stirred overnight and then poured into sat'd NaHCO₃. The mixture was extracted with ethyl acetate, dried (MgSO₄) and concentrated. The residue (0.126 g) was dissolved in 20% aqueous THF and lithium hydroxide hydrate (0.03 g, 0.72 mmol) was added. The mixture was stirred 0.5 h, neutralized with 2N HCl and the mixture was extracted with ethyl acetate. The combined organic extracts were washed with brine, dried (MgSO₄) and concentrated to give 0.69 g (71 %) of a clear foam: ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.42 (d, 3H), 5.29 (m, 2H), 6.57 (brs, 2H), 7.38 (s, 1H), 7.58 (m, 2H), 7.67 (m, 1H), 7.84 (d, 1H), 9.36 (s, 1H). Anal. (C₁₁H₁₂N₂O₄S) C, H, N.

***N*-Hydroxy-*N*-[1-(4-methylphenyl)ethyl]urea (4b)** was prepared using method 1a from 4-methoxyacetophenone: mp 134-135 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.38 (d, *J*=7 Hz, 3H), 2.26 (s, 3H), 5.25 (q, *J*=7 Hz, 1H), 6.27 (bs, 2H), 7.09 (d, *J*=8 Hz, 2H), 7.21 (d, *J*=8 Hz, 2H), 9.00 (s, 1H); MS (DCI-NH₃) *m/z* 212 (M+NH₄)⁺, 195 (M+H)⁺. Anal. (C₁₀H₁₄N₂O₂• 0.25 H₂O) C, H, N.

***N*-Hydroxy-*N*-[1-(4-phenylphenyl)ethyl]urea (4c)** was prepared using method 1b from 4-phenylacetophenone: mp 157-158 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.44 (d, 3H), 5.33 (q, 1H), 6.44 (brs, 2H), 7.32-7.50 (m, 5H), 7.56-7.67 (m, 4H), 9.12 (brs, 1H); MS (DCI-NH₃) *m/z* 274 (M+NH₄)⁺, 257 (M+H)⁺. Anal. (C₁₅H₁₆N₂O₂• 1.0 H₂O) : Calcd C: 65.67; Found C: 66.15.

***N*-Hydroxy-*N*-[1-(4-bromophenyl)ethyl]urea (4d)** was prepared using method 1a from 4-bromoacetophenone: mp 138-140 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.40 (d, *J*=7

Hz, 3H), 5.26 (q, J=7 Hz, 1H), 6.31 (bs, 2H), 7.29 (d, J=8 Hz, 2H), 7.49 (d, J=8 Hz, 2H), 9.10 (s, 1H); MS (DCI-NH₃) m/z 278, 276 (M+NH₄)⁺, 261, 259 (M+H)⁺. Anal. : Calcd (C₉H₁₁BrN₂O₂) C, H, N.

N-Hydroxy-N-[1-(4-phenylmethoxyphenyl)ethyl]urea (4e) was prepared using method 1a from 4-hydroxyacetophenone and benzylbromide: mp 140-141 °C; ¹H NMR (300 MHz, DMSO-d₆) δ 1.37 (d, 3H), 5.08 (s, 2H), 5.24 (q, 1H), 6.25 (s, 2H), 6.92 (d, 2H), 7.25 (d, 2H), 7.30-7.50 (m, 5H), 8.90 (s, 1H); MS (EI) m/z 286 (M)⁺. Anal. (C₁₆H₁₈N₂O₃• 1.0 H₂O) C, H, N.

N-Hydroxy-N-[1-[4-(1-phenyl)ethoxyphenyl]ethyl]urea (4g) was prepared using method 1a from 4-hydroxyacetophenone and 1-bromoethylbenzene: mp 125-130 °C; ¹H NMR (300 MHz, DMSO-d₆) δ 1.32 (d, J=7 Hz, 3H), 1.53 (d, J=6 Hz, 3H), 5.19 (q, J=7 Hz, 1H), 5.95 (q, J=6 Hz, 1H), 6.23 (bs, 2H), 6.81 (m, 2H), 7.15 (m, 2H), 7.22-7.43 (m, 4H), 8.95 (s, 1H), MS(DCI-NH₃) m/z 301(M+H)⁺. Anal. (C₁₇H₂₀N₂O₃) C, H, N.

N-Hydroxy-N-[1-(3-phenoxyphenyl)ethyl] urea (4h) was prepared using method 1a from 3-phenoxyacetophenone. 3-Phenoxyacetophenone was prepared by Ullman reaction of 3-bromoacetophenone and phenol: mp 96-98 °C; ¹H NMR (300 MHz, DMSO-d₆) δ 1.38 (d, J=7 Hz, 3H), 5.28 (q, J=7 Hz, 1H), 6.33 (bs, 2H), 6.84 (m, 1H), 6.96-7.05 (m, 3H), 7.13 (m, 2H), 7.25-7.45 (m, 3H), 9.09 (s, 1H), MS (DCI-NH₃) m/z 290 (M+NH₄)⁺. Anal. (C₁₅H₁₆N₂O₃) C, H, N.

N-Hydroxy-N-[1-(2-naphthyl)ethyl]urea (4i) was prepared using method 1a from 2-acetonaphthone: mp 140-142 °C; NMR (300 MHz, DMSO-d₆) δ 1.51 (d, 3H), 5.46 (q, 1H), 6.34 (bs, 2H), 7.45-7.54 (m, 3H), 7.81-7.90 (m, 4H), 9.11 (s, 1H); MS (EI) m/z 230 (M)⁺. Anal. (C₁₃H₁₄N₂O₂• 0.75 H₂O) C, H, N.

N-Hydroxy-N-(1-indol-2-ylethyl)urea (4l) To a stirred -70 °C solution of indole (11.7 g, 100 mmol) in dry THF (100 mL) was added n-butyllithium (40 mL, 2.5 M in hexanes, 100 mmol). After 0.5 h the mixture was added via cannula to an excess of carbon dioxide (dry ice, 18 g) in THF (100 mL). The solution was warmed to room temperature and

concentrated. Benzene (50 mL) was added and the mixture was distilled to remove water. The residue was dissolved in THF (100 mL) and cooled to -70 °C. To this stirred solution was added t-butyllithium (63 mL, 1.6 M in pentane, 100 mmol) and the mixture was stirred at -70 °C for 1 hour. A THF (100 mL) solution of *N,O*-dimethyl acetohydroxamic acid (10.3 g, 100 mmol) was added and the reaction stirred for 2 h at -70 °C and then at 0 °C for 1 h. Sat'd NH₄Cl (20 mL) was added and the mixture was extracted with ethyl acetate. The organic extract was dried (Na₂SO₄) and concentrated. The residue was purified by flash column chromatography (SiO₂, eluting with methylene chloride) to afford 2-acetylindole as a white solid (10.4 g, 66%).

This ketone was converted to **4l** using method 1a: mp 159-160 °C; ¹H NMR (300 MHz, DMSO-d₆) δ 1.48 (d, J=7 Hz, 3H), 5.46 (q, J=7 Hz, 1H), 6.28 (s, 1H), 6.45 (bs, 2H), 6.93 (m, 1H), 7.03 (m, 1H), 7.33 (m, 1H), 7.43 (m, 1H), 8.05 (s, 1H), 10.75 (bs, 1H) MS (DCI-NH₃) m/z 237 (M+NH₄)⁺, 220 (M+H)⁺. Anal. (C₁₁H₁₃N₃O₂) C, H, N.

***N*-Hydroxy-*N*-[1-(1-methylindol-2-yl)ethyl]urea (4m)** To a stirred solution of 2-acetyl indole (prepared in ex. **4l**) (15 g, 0.94 mmol) and sodium hydroxide (32 g) in water (300 mL) was added dimethyl sulfate (67.5 g) and the mixture was heated at 85 °C for 4 hours. The reaction mixture was then cooled and 1-methyl-2-acetyl indole collected and dried.

1-Methyl-2-acetyl indole was converted to **4m** using method 1a: mp 137-139 °C; ¹H NMR (300 MHz, DMSO-d₆) δ 1.48 (d, J=7 Hz, 3H), 3.75 (s, 3H), 5.70 (q, 1H), 6.15 (bs, 2H), 6.70 (s, 1H), 6.94 (m, 1H), 7.15 (m, 1H), 7.35 (m, 1H), 7.65 (m, 1H), 8.90 (s, 1H). IR: 3300, 1660, 1580. MS (DCI-NH₃) m/z 251 (M+NH₄)⁺, 234 (M+H)⁺. Anal. (C₁₂H₁₅N₃O₂) C, H, N.

***N*-Hydroxy-*N*-[1-(1-methylindol-3-yl)ethyl]urea (4n)** was prepared using method 1a and 1-methyl-3-acetyl indole: mp 149-150 °C; ¹H NMR (300 MHz, DMSO-d₆) δ 1.46 (d, J=7.5 Hz, 3H), 3.74 (s, 3H), 5.66 (q, 1H), 6.18 (bs, 2H), 6.94-7.15 (m, 2H), 7.24 (s, 1H), 7.36 (m, 1H), 7.64 (m, 1H), 8.88 (s, 1H); MS (DCI-NH₃) m/z 251 (M+NH₄)⁺, 234 (M+H)⁺. Anal. (C₁₂H₁₅N₃O₂) C, H, N.

***N*-Hydroxy-*N*-[(1-methyl-benzo[*b*]imidazol-2-yl)methyl]-*N'*-methylurea (4o)** was prepared from 2-chloromethyl-1-methylbenzimidazole using method 6 and substituting methyl isocyanate for trimethylsilyl isocyanate: mp 145-147 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 2.64 (d, *J*=4.5 Hz, 2H), 3.78 (s, 3H), 4.81 (s, 2H), 7.08 (m, 1H), 7.21 (m, 2H), 7.52 (m, 1H), 7.59 (m, 1H), 9.39 (s, 1H); MS (DCI-NH₃) *m/z* 235 (M+H)⁺. Anal. : Calcd (C₁₁H₁₄N₄O₂•1.0H₂O): C, H, N.

***N*-(1-Benzo[*b*]fur-2-ylethyl)-*N*-hydroxyurea (4p)** was prepared from 2-acetylbenzo[*b*]furan using method 1a: mp 147-150 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.46 (d, 3H), 5.47 (q, 1H), 6.48 (brs, 2H), 7.22 (m, 2H), 7.50 (d, 1H), 7.58 (m, 1H), 9.18 (s, 1H); MS (DCI-NH₃) *m/z* 238 (M+NH₄)⁺, 221 (M+H)⁺. Anal. (C₁₁H₁₂N₂O₃) C, H, N.

***N*-[1-(5-Chlorobenzo[*b*]fur-2-yl)ethyl]-*N*-hydroxyurea (4q).** To a stirred suspension of K₂CO₃ (17.3 g, 125 mmol) in acetone (100 mL) was added 5-chlorosalicylaldehyde (15.6 g, 100 mmol) and chloroacetone (90%, 12.0 g). The mixture was heated at reflux for 24 h, cooled and concentrated. The residue was poured into ice / 6N HCl and extracted with ethyl acetate. The organic extracts were dried (Na₂SO₄) and concentrated to give 2-acetyl-5-chlorobenzo[*b*]furan as a crystalline solid 8.24 g (42%). 2-Acetyl-5-chlorobenzo[*b*]furan was converted to **4q** using method 1a: mp 173.5-175 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.46 (d, *J*=7.0, 3H), 5.46 (q, *J*=7.0, 1H), 6.50 (bs, 2H), 6.73 (s, 1H), 7.27 (dd, *J*= 8.8 Hz, *J*=2.2 Hz, 1H), 7.55 (d, *J*=8.8 Hz, 1H), 7.66 (d, *J*=2.2 Hz, 1H), 9.21 (s, 1H); MS (DCI-NH₃) *m/z* 255 (M+H)⁺. Anal. (C₁₁H₁₁ClN₂O₃) C, H, N.

***N*-hydroxy-*N*-[1-(5-methoxybenzo[*b*]fur-2-yl)ethyl]urea (4r)** was prepared using 4-methoxysalicylaldehyde instead of 4-chlorosalicylaldehyde as described for **4q**: mp 149-151 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.44 (d, *J*=7 Hz, 3H), 3.76 (s, 3H), 5.43 (q, *J*=7 Hz, 1H), 6.47 (bs, 2H), 6.65 (m, 1H), 6.83 (dd, *J*=2.6 Hz, *J*=9.2 Hz, 1H), 7.08 (d, *J*=2.6 Hz, 1 H), 7.39 (d, *J*=9.2 Hz, 1H), 9.17 (s, 1H); MS (DCI-NH₃) *m/z* 251 (M+H)⁺. Anal. (C₁₂H₁₄N₂O₄) C, H, N.

***N*-[1-(Dibenzofuran-4-yl)ethyl]-*N*-hydroxyurea (4s)** was prepared from 4-acetyldibenzofuran using method 1a: mp 171-173 °C; ¹H NMR (DMSO-d₆) δ 1.52 (d, J = 7 Hz, 3H), 5.48 (q, J = 7 Hz, 1H), 6.34 (s, 2H), 7.39 (dt, J = 0.9 Hz, J = 7.5 Hz, 1H), 7.51 (m, 2H), 7.62 (d, J = 8.6 Hz, 1H), 7.69 (d, J = 8.2 Hz, 1H), 8.10 (d, J = 1.5 Hz, 1H), 8.14 (m, 1H), 9.11 (s, 1H); MS (DCI-NH₃) m/z 271 (M+H)⁺. Anal. (C₁₅H₁₄N₂O₃) C, H, N.

***N*-Hydroxy-*N*-[1-(thieno[2,3-*b*]thien-2-yl)methyl] urea (4t)**. 2-Acetyl-thieno[2,3-*b*]thiophene⁵ was converted to **4t** using method 1a: mp 167 °C (dec.); ¹H NMR (300 MHz, DMSO-d₆) δ 1.48 (d, J=7 Hz, 3H), 5.52 (q, J=7 Hz, 1H), 6.43 (bs, 2H), 7.16 (s, 1H), 7.24 (d, J=6 Hz, 1H), 7.55 (d, J=6 Hz, 2H), 9.23 (s, 1H), MS(DCI-NH₃) m/z 260 (M+NH₄)⁺, 243 (M+1)⁺. Anal. (C₉H₁₀N₂O₂S₂) C, H, N.

***N*-(1-Benzo[*b*]thien-2-ylethyl)-*N*-hydroxyacetamide (5a)**. *N*-Acetoxy-*N*-(1-benzo[*b*]thien-2-ylethyl)-*N*-hydroxyacetamide was prepared from *N*-(1-benzo[*b*]thien-2-ylethyl)hydroxylamine¹⁸ with excess acetyl chloride and triethylamine in THF: mp 138 °C (dec.); ¹H NMR (300 MHz, DMSO-d₆) δ 1.50 (d, J=7 Hz, 3H), 2.12 (bs, 3H), 5.69 (m, 1H), 6.86 (bs, 2H), 7.34 (m, 3H), 7.80 (m, 1H), 7.91 (m, 1H), MS(DCI-NH₃) m/z 296 (M+NH₄)⁺, 279 (M+1)⁺. Anal. (C₁₃H₁₄N₂O₃S) C, H, N.

Mono-deacylation of this material with lithium hydroxide / IPA / water provided **5a**: mp 108-110 °C (dec.); ¹H NMR (300 MHz, DMSO-d₆) δ 1.56 (d, J=7 Hz, 3H), 2.02 (s, 3H), 5.90 (m, 1H), 7.29-7.38 (m, 3H), 7.75-7.92 (m, 2H), 9.75 (bs, 1H), MS(DCI-NH₃) m/z 253 (M+NH₄)⁺, 236 (M+H)⁺. Anal. (C₁₂H₁₃NO₂S) C, H, N.

2-(Benzo[*b*]thien-2yl)propionic acid-*N*-hydroxy-*N*-methylamide (5b) 2-(Benzo[*b*]thien-2yl)propionic acid was prepared from metalation of benzo[*b*]thiophene, reaction with methyl pyruvate and reduction with tin(II)chloride. The acid was converted to **5b** by acid chloride formation and reaction with *N*-methylhydroxylamine: glass; ¹H NMR (300 MHz, DMSO-d₆) δ 1.43 (d, J=7 Hz, 3H), 3.13 (s, 3H), 4.69 (q, J=7 Hz, 1H),

7.22 (s, 1H), 7.24-7.37 (m, 2H), 7.75 (m, 1H), 7.87 (m, 1H), 10.10 (s, 1H), MS(DCI-NH₃) m/z 253 (M+NH₄)⁺. Anal. (C₁₂H₁₃NO₂S) C, H, N.

***N*-(1-Benzo[b]thien-2-ylethyl)urea (5c)** was prepared by reduction of *N*-(1-benzo[b]thien-2-ylethyl)-*N*-hydroxyurea¹⁸ with TiCl₃⁶: mp 205-206 °C; ¹H NMR (300 MHz, DMSO-d₆) δ 1.48 (d, J=7 Hz, 3H), 5.04 (m, 1H), 6.58 (d, J=8 Hz, 1H), 7.22 (s, 1H), 7.31 (m, 2H), 7.75 (m, 1H), 7.89 (m, 1H), MS(DCI-NH₃) m/z 238 (M+NH₄)⁺, 221 (M+H)⁺. Anal. (C₁₁H₁₂N₂OS) C, H, N.

***N*-(1-Benzo[b]thien-2-ylethyl)-*N*-methoxyurea (5d)** To a 0 °C stirred DMF (25 mL) solution of *N*-(1-benzo[b]thien-2-ylethyl)-*N*-hydroxyurea¹⁸ (2.0 g, 8.46 mmol) was added NaH (0.36 g, 8.88 mmol, 60%) and methyl iodide (1.26 g, 8.88 mmol). The mixture was stirred 0.5 h at room temperature and poured into sat'd NH₄Cl. The mixture was extracted with ethyl acetate, the combined extracts were dried (MgSO₄) and concentrated. The resulting solid was recrystallized from ethyl acetate / hexanes to give 0.76 g (36%) of **5d** as a white solid: mp 162 °C (dec.); ¹H NMR (300 MHz, DMSO-d₆) δ 1.52 (d, J=7 Hz, 3H), 3.66 (s, 3H), 5.29 (bs, 2H), 5.72 (q, J=7 Hz, 1H), 7.27 (m, 1H), 7.32 (m, 2H), 7.72 (m, 1H), 7.79 (m, 1H); MS (DCI-NH₃) m/z 268 (M+NH₄)⁺, 251 (M+H)⁺. Anal. (C₁₂H₁₄N₂O₂S) C, H, N.

***N*-(1-Benzo[b]thien-2-ylethyl)-*N*-benzyloxyurea (5e)** was prepared from benzylbromide and *N*-(1-benzo[b]thien-2-ylethyl)-*N*-hydroxyurea¹⁸ using the procedure described for **5d**: mp 123-124 °C (dec.); ¹H NMR (300 MHz, DMSO-d₆) δ 1.61 (d, J=7 Hz, 3H), 4.75 (m, 2H), 5.56 (q, J=7 Hz, 1H), 6.68 (bs, 2H), 7.73 (m, 8H), 7.79 (m, 1H), 7.90 (m, 1H). MS(DCI-NH₃) m/z 344 (M+NH₄)⁺, 327 (M+H)⁺. Anal. (C₁₈H₁₈N₂O₂S) C, H, N.

***N*-(1-Benzo[b]thien-2-ylethyl)-*N*-ethoxyhydroxyurea (5f)** 2-Acetylbenzo[b]thiophene oxime was converted to *O*-hydroxyethyl-2-acetylbenzo[b]thiophene oxime using lithium metal and ethylene oxide⁷. This oxime was converted to **5f** using method 1a: mp 182-183 °C (dec.); ¹H NMR (300 MHz, DMSO-d₆) δ 1.61 (d, J=7 Hz, 3H), 3.52 (m, 2H),

3.73 (m, 1H), 3.86 (m, 1H), 5.19 (t, J=5 Hz, 1H), 5.54 (q, J=7 Hz, 1H), 6.88 (bs, 2H), 7.33 (m, 3H), 7.79 (m, 1H), 7.90 (m, 1H); MS (DCI-NH₃) m/z 298 (M+NH₄)⁺, 281 (M+H)⁺. Anal. (C₁₃H₁₆N₂O₃S) C, H, N.

***N*-(1-Benzo[b]thien-2-ylethyl)-*N*-hydroxytrifluoroacetamide (5g)** was prepared from *N*-(1-benzo[b]thien-2-ylethyl)hydroxylamine¹⁸ by diacylation with trifluoroacetic anhydride (5 eq) and pyridine (5 eq) in CH₂Cl₂ to give the ditrifluoroacetate in 76% yield. This diacylated material was treated in 20 % aqueous THF (50 mL) with lithium hydroxide monohydrate (2 eq) to give **5g** after chromatography (41%): mp 137-140 °C (dec.); ¹H NMR (300 MHz, DMSO-d₆) δ 1.67 (d, J=7 Hz, 3H), 5.85 (q, J=7 Hz, 1H), 7.36 (m, 2H), 7.43 (s, 1H), 7.84 (m, 1H), 7.94 (m, 1H) 10.79 (s, 1H), MS(DCI-NH₃) m/z 307 (M+NH₄)⁺. Anal. (C₁₂H₁₀F₃NO₂S) C, H, N.

***N*-(1-Benzo[b]thien-2-ylethyl)-*N'*-methyl-*N'*-hydroxyurea (5h)** *N*-(1-Benzo[b]thien-2-ylethyl)amine was prepared from *N*-(1-benzo[b]thien-2-ylethyl)hydroxylamine¹⁸ with Raney nickel in methanol at 4 atm H₂ (98%). This material was converted to **5h** with *N*-methylhydroxylamine using method 1b: mp 111-112 °C (dec.); ¹H NMR (300 MHz, DMSO-d₆) δ 1.56 (d, J=7 Hz, 3H), 2.89 (s, 3H), 5.12 (m, 1H), 7.23 (s, 1H), 7.25-7.37 (m, 3H), 7.76 (m, 1H), 7.88 (m, 1H), 9.45 (s, 1H); MS (DCI-NH₃) m/z 268 (M+NH₄)⁺, 251 (M+H)⁺. Anal. (C₁₂H₁₄N₂O₂S) C, H, N.

***N*-hydroxy-*N*-(1-Benzo[b]thien-2-ylethyl)formamide (5i)** was prepared using *N*-(1-benzo[b]thien-2-ylethyl)hydroxylamine¹⁸, acetyl formyl anhydride (prepared by reaction of sodium formate and acetyl chloride) and triethylamine in THF: mp 115-116.5°C; ¹H NMR (300 MHz, DMSO-d₆) δ 1.61 (s, 3H), 5.4-5.8 (br d, 1H), 7.3-7.4 (m, 3H), 7.77-7.95 (m, 2H), 8.23-8.36 (br d, 1H), 9.8 (br d, 1H). IR (CHCl₃): 160, 2890. MS (DCI-NH₃) m/z 239 (M+NH₄)⁺, 222 (M+H)⁺. Anal (C₁₁H₁₁NO₂S) C, H, N.

***N*-(1-Benzo[b]thien-2-ylethyl)ethyl-*N*-hydroxythiocarbamate (5j)** was prepared using *N*-(1-benzo[b]thien-2-ylethyl)hydroxylamine¹⁸, ethyl thiochloroformate and triethylamine in THF (34%): mp 117-119 °C (dec.); ¹H NMR (300 MHz, DMSO-d₆) δ

1.20 (t, $J=7.5$ Hz, 3H), 2.75 (q, $J=7.5$ Hz, 1H), 4.95 (s, 2H), 7.29-7.40 (m, 3H), 7.82 (m, 1H), 7.93 (m, 1H), 10.42 (s, 1H), MS(DCI-NH₃) m/z 299 (M+NH₄)⁺, 282 (M+H)⁺. Anal. (C₁₃H₁₅NO₂S₂) C, H, N.

***N*-(1-Benzo[b]thien-2-ylethyl)-*N*'-hydroxy-*N*'-carbamoylmethylurea (5k).** *N*-(1-Benzo[b]thien-2-ylethyl)-*N*-hydroxy-*N*'-carboethoxymethylurea was prepared by reaction of *N*-(1-benzo[b]thien-2-ylethyl)hydroxylamine¹⁸ and ethyl isocyanatoacetate. To a -78 °C stirred suspension of NH₄Cl in CH₂Cl₂ was added trimethylaluminum (3.2 mmol). The reaction was stirred at -78 °C for 0.25 h and at -20 °C for 0.5 h. The reaction was warmed to room temperature and benzo[b]thien-2-ylethyl)-*N*'-hydroxy-*N*'-carboethoxymethylurea (0.5 g, 1.6 mmol) in CH₂Cl₂ (5 mL) was added. The reaction was heated to reflux for 3 days. HCl (2 mL, 1.6 M solution) was added and the precipitated solid was collected and dried to give 0.2 g (43%) of **5k**: mp 165 °C (dec.); ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.53 (d, $J=7$ Hz, 3H), 3.64 (m, 2H), 5.56 (q, $J=7$ Hz, 1H), 7.10-7.20 (m, 3H), 7.82 (m, 1H), 7.93 (m, 1H), 10.42 (s, 1H), MS(DCI-NH₃) m/z 294 (M+H)⁺. Anal. (C₁₃H₁₅N₃O₃S•1.0 H₂O) C, H, N.

***N*-(1-Benzo[b]thien-2-ylethyl)-*N*-hydroxy-*N*'-carbamoylurea (5l).** Pyridine (30 mL) was added to a mixture of urea (7.27 g, 120 mmol) and phenyl chloroformate (8.94 g, 57.1 mmol). The mixture became exothermic then solidified. The solid was washed with pyridine and ethyl acetate to afford *N*-carbophenoxyurea as a white solid. A stirred solution of *N*-(1-benzo[b]thien-2-ylethyl)hydroxylamine¹⁸ (0.5g, 2.6 mmol) and *N*-carbophenoxyurea (0.47 g, 2.6 mmol) in dioxane (12 mL) was heated to 75 °C for 48 h. The reaction was concentrated and the residue was recrystallized from ethanol / hexanes to give 0.13 g (18%) of **5l**: mp 180 °C (dec.); ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.59 (d, $J=7$ Hz, 3H), 5.67 (q, $J=7$ Hz, 1H), 7.15 (bs, 1H), 7.33 (m, 3H), 7.65 (bs, 1H), 7.80 (m, 1H), 7.91 (m, 1H), 10.01 (s, 1H); MS (DCI-NH₃) m/z 280 (M+1)⁺. Anal. (C₁₂H₁₃N₃O₃S•0.25 H₂O) C, H, N.

***N*-(1-Benzo[b]thien-2-ylethyl)-*N*-hydroxysemicarbazide (5m).** To a stirred solution of **5j** (0.28 g, 1 mmol) in ethanol (10 mL) containing EtMgBr (0.1 mmol, 0.03 mL of 3M solution in ether) was added hydrazine (0.96 g, 3 mmol) and the mixture heated at 75 °C for 4 days. The solvent was removed and the residue chromatographed (SiO₂, eluting with 5% CHCl₃ / MeOH) to give **5m** (165 mg, 65%): mp 150-152 °C (dec.); ¹H NMR (300 MHz, DMSO-d₆) δ 1.58 (d, J=7 Hz, 3H), 4.51(bs, 2H), 5.60 (q, J=7 Hz, 1H), 7.20-8.00 (m, 5H), 9.28 (s, 1H), 9.35 (s, 1H); MS (DCI-NH₃) m/z 269(M+NH₄)⁺, 252 (M+H)⁺. Anal. (C₁₁H₁₃N₃O₂S): C, H, N.

***N*-(1-Benzo[b]thien-2-ylethyl)-*N*-hydroxy-*N'*-methylurea (5n)** was prepared using *N*-(1-benzo[b]thien-2-ylethyl)hydroxylamine¹⁸ and methyl isocyanate as described in method 1a: mp 149-150 °C; ¹H NMR (300 MHz, DMSO-d₆) δ 1.51 (d, 3H, J=7.5 Hz), 2.60 (d, 3H), 5.55 (q, 1H, J=7.5 Hz), 6.98 (m, 1H), 7.24-7.37 (m, 3H), 7.73-7.79 (m, 1H), 7.85-7.91 (m, 1H), 9.17 (s, 1H); MS (DCI-NH₃) m/z 268 (M+NH₄)⁺, 251 (M+H)⁺. Anal. (C₁₂H₁₄N₂O₂S) C, H, N.

***N*-(1-Benzo[b]thien-2-ylethyl)-*N*-hydroxy-*N'*-ethylurea (5o)** was prepared using *N*-(1-benzo[b]thien-2-ylethyl)hydroxylamine¹⁸ and ethyl isocyanate as described in method 1a: mp 138-139 °C; ¹H NMR (300 MHz, DMSO-d₆) δ 1.01 (t, 3H, J=7.5 Hz), 1.52 (d, 3H, J=7.5 Hz), 3.00-3.18 (m, 2H), 5.56 (q, 1H, J=7.5), 7.05 (m, 1H), 7.22-7.40 (m, 3H), 7.70-7.95 (m, 2H), 9.18 (g, 1H); MS (DCI-NH₃) m/z 282 (M+NH₄)⁺, 265 (M+H)⁺. Anal (C₁₃H₁₆N₂O₂S) C, H, N.

***N*-(1-Benzo[b]thien-2-ylethyl)-*N*-hydroxy-*N'*-allylurea (5p)** was prepared using *N*-(1-benzo[b]thien-2-ylethyl)hydroxylamine¹⁸ and allyl isocyanate as described in method 1a: mp 123-125°C; ¹H NMR (DMSO-d₆) δ 1.52 (d, J = 7 Hz, 3H), 3.68 (m, 2H), 4.98 (m, 1H), 5.05 (m, 1H), 5.56 (q, J = 7 Hz, 1H), 5.79 (m, 1H), 7.16 (t, J = 6.1 Hz, 1H), 7.30 (m, 3H), 7.77 (dd, J = 6.8 Hz, J = 2.4 Hz, 1H), 7.88 (m, J = 7.9 Hz, 1H), 9.26 (s, 1H); MS (DCI-NH₃) m/z 277 (M + H)⁺. Anal. (C₁₄H₁₆N₂O₂S) C, H, N.

***N*-(1-Benzo[b]thien-2-ylethyl)*N*-hydroxy-*N*',*N*'-dimethyl urea (5q)** was prepared using *N*-(1-benzo[b]thien-2-ylethyl)hydroxylamine¹⁸ and dimethylcarbonyl chloride with triethylamine in THF at 60 °C for 2 h: mp 139-141°C; ¹H NMR (300 MHz, DMSO-d₆) δ 1.54 (d, J = 7.5 Hz, 3H), 2.87 (s, 6H), 5.24 (q, 1H), 7.25-7.37 (m, 3H), 7.74-7.79 (m, 1H), 7.85-7.91 (m, 1H), 8.92 (s, 1H); MS (DCI-NH₃) m/z 282 (M+NH₄)⁺, 264 (M+H)⁺. Anal. (C₁₃H₁₆N₂O₂S): C, H, N.

***N*-(1-Benzo[b]thien-2-ylethyl)-*N*-hydroxy-*N*'-butylurea (5r)** was prepared using *N*-(1-benzo[b]thien-2-ylethyl)hydroxylamine¹⁸ and butyl isocyanate as described in method 1a: mp 108-110°C; ¹H NMR (DMSO-d₆) δ 0.83 (t, J = 7.0 Hz, 3H), 1.24 (m, 2H), 1.36 (m, 2H), 1.51 (d, J = 7 Hz, 3H), 5.54 (q, J = 7 Hz, 1H), 7.01 (t, J = 5.9 Hz, 1H), 7.25 (s, 1H), 7.31 (m, 2H), 7.76 (m, 1H), 7.87 (m, 1H), 9.18 (s, 1H); MS (DCI-NH₃) m/z 293 (M + H)⁺. Anal. (C₁₅H₂₀N₂O₂S) C, H, N.

***N*-(1-Benzo[b]thien-2-ylethyl)-*N*-hydroxy-*N*'-pentylurea (5s)** was prepared using *N*-(1-benzo[b]thien-2-ylethyl)hydroxylamine¹⁸ and *n*-pentyl isocyanate as described in method 1a. The isocyanate was prepared as follows: To a stirred solution of *n*-hexanoic acid (0.75 mL, 6.0 mmol) in benzene (30 mL) was added diphenylphosphoryl azide (1.30 mL, 6.10 mmol) and triethylamine (0.85 mL, 6.10 mmol). The solution was heated at reflux for 1h and allowed to cool. This solution of isocyanate was reacted with *N*-(1-benzo[b]thien-2-ylethyl)hydroxylamine to obtain **5s**: mp 98-100 °C ¹H NMR (DMSO-d₆) δ 0.83 (t, J = 7 Hz, 3H), 1.20 (m, 4H), 1.39 (m, 2H), 1.51 (d, J = 7 Hz, 3H), 3.03 (q, J = 6.7 Hz, 2H), 5.54 (q, J = 7 Hz, 1H), 6.99 (t, J = 5.9 Hz, 1H), 7.25 (s, 1H), 7.30 (m, 2H), 7.76 (m, 1H), 7.86 (m, 1H), 9.17 (s, 1H); MS (DCI-NH₃) m/z 307 (M + H)⁺. Anal. (C₁₆H₂₂N₂O₂S) C, H, N.

***N*-(1-Benzo[b]thien-2-ylethyl)-*N*-hydroxy-*N*'-phenylurea (5t)** was prepared using *N*-(1-benzo[b]thien-2-ylethyl)hydroxylamine¹⁸ and phenyl isocyanate as described in method 1a: mp 167-169 °C; ¹H NMR (DMSO-d₆) δ 1.60 (d, J = 7 Hz, 3H), 5.70 (q, J = 7 Hz, 1H), 6.89 (m, 1H), 7.21-7.37 (m, 5H), 7.64 (m, 2H), 7.79 (m, 1H), 7.89 (m, 1H),

9.06 (s, 1H), 9.69 (s, 1H); MS (DCI-NH₃) m/z 330 (M+NH₄)⁺, 313 (M + H)⁺. Anal. (C₁₇H₁₆N₂O₂S) C, H, N.

***N*-(1-Benzo[b]thien-2-ylethyl)-*N*-hydroxy-*N'*-benzylurea (5u)** was prepared using *N*-(1-benzo[b]thien-2-ylethyl)hydroxylamine¹⁸ and benzyl isocyanate as described in method 1a: mp 175-176 °C; ¹H NMR (DMSO-d₆) δ 1.54 (d, J = 6.9 Hz, 3H), 4.24 (d, J=6.5 Hz, 2H), 5.57 (q, J = 7 Hz, 1H), 7.27 (m, 1H), 7.32 (m, 5H), 7.61 (t, J=6.5 Hz, 2H), 7.76 (m, 1H), 7.88 (m, 1H), 9.31 (s, 1H); MS (DCI-NH₃) m/z 327 (M + H)⁺. Anal. (C₁₈H₁₈N₂O₂S) C, H, N.

***N*-(1-Benzo[b]thien-2-ylethyl)-*N*-hydroxy-*N'*-hydroxyethylurea (5v)**. To a stirred solution of the *N*-hydroxy-*N'*-carboethoxymethylurea (see **5k**) (5.2 g, 16.13 mmol) in THF (40 mL) was added lithium borohydride (18 mL, 36 mmol, 2 M in THF). The reaction was stirred at room temperature overnight and methanol was added (35 mL). The mixture was stirred for 4 h and concentrated. The mixture was diluted with 10% citric acid and ethyl acetate. The aqueous layer was washed with ethyl acetate and the organic layers combined, dried (MgSO₄) and concentrated. The solid residue was recrystallized (EtOAc / hexanes) to give 3.61 g (80%) of **5v**: mp 133-135 °C; ¹H NMR (DMSO-d₆) δ 1.51 (d, J=7 Hz, 3H), 3.13 (m, 2H), 3.39 (q, J=6.8 Hz), 4.65 (t, J=5.5 Hz, 1H), 5.56 (q, J=7 Hz, 1H), 6.90 (t, J=5.7 Hz, 1H), 7.26 (bs, 1H), 7.31 (m, 2H), 7.76 (m, 1H), 7.88 (m, 1H), 9.24 (s, 1H); MS (DCI-NH₃) m/z 281 (M + H)⁺. Anal. (C₁₃H₁₆N₂O₃S) C, H, N.

***N*-(1-Benzo[b]thien-2-ylethyl)-*N*-hydroxy-*N'*-hydroxypentylurea (5w)**. *N*-(1-Benzo[b]thien-2-ylethyl)-*N*-hydroxy-*N'*-(methyl 5-pentanoate)urea was prepared in (77%) from *N*-(1-benzo[b]thien-2-ylethyl)hydroxylamine¹⁸ and the isocyanate prepared from adipic acid mono methyl ester by the procedure described in the preparation of **5s**. This urea was converted to **5w** (56%) using the procedure described for **5v**: mp 130-131.5 °C; ¹H NMR (DMSO-d₆) δ 1.33 (d, J=7 Hz, 3H), 1.39 (t, J=7 Hz, 2H), 1.63 (m, 2H), 3.12 (m, 4H), 4.52 (m, 3H), 7.50 (t, J=5.5 Hz, 1H), 7.56 (m, 1H), 7.89 (m, 3H), 8.14

(t, J=5.5 Hz, 1H), 8.37 (dd, J=7.8 Hz, J= 1.3 Hz, 1H), 8.86 (s, 1H); MS (DCI-NH₃) m/z 323 (M + H)⁺. Anal. (C₁₆H₂₂N₂O₃S) C, H, N.

***N*-(1-Benzo[b]thien-2-ylethyl)-*N*-hydroxy-*N'*-acetylurea (5x)** was prepared using *N*-(1-benzo[b]thien-2-ylethyl)hydroxylamine¹⁸ and acyl isocyanate⁸ as described in method 1a: mp 134-136.5 °C; ¹H NMR (DMSO-d₆) δ 1.59 (d, J=7 Hz, 3H), 2.25 (2, 2H), 5.69 (q, J=7 Hz, 1H), 7.34 (m, 3H), 7.80 (m, 1H), 7.90 (m, 1H), 9.36 (bs, 1H), 9.98 (s, 1H); MS (DCI-NH₃) m/z 296 (M + NH₄)⁺; 279 (M + H)⁺. Anal. (C₁₃H₁₄N₂O₃S) C, H, N.

***N*-(1-Benzo[b]thien-2-ylethyl)-*N*-hydroxy-*N'*-carboxymethylurea (5y)** was prepared from *N'*-carboethoxymethyl-*N*-(1-benzo[b]thien-2-ylethyl)-*N*-hydroxyurea (see **5k**) by hydrolysis with lithium hydroxide in isopropanol / water as described in ex. **5g**: mp 138 °C (dec.); ¹H NMR (DMSO-d₆) δ 1.53 (d, J=7 Hz, 3H), 3.72 (m, 2H), 5.55 (q, J=7 Hz, 1H), 7.20-7.37 (m, 4H), 7.77 (m, 1H), 7.89 (m, 1H), 9.39 (s, 1H); MS (DCI-NH₃) m/z 312 (M + NH₄)⁺; 295 (M + H)⁺. Anal. (C₁₃H₁₄N₂O₄S) C, H, N.

***N*-(1-Benzo[b]thien-2-ylethyl)-*N,N'*-dihydroxyurea (5z)** was prepared using *N*-(1-benzo[b]thien-2-ylethyl)hydroxylamine¹⁸ and hydroxylamine instead of NH₄OH using procedure as described in method 1b: mp 132-134 °C (dec.); NMR (300 MHz, DMSO-d₆) δ 1.52 (d, J=7.5 Hz, 3H), 5.49 (q, J=7.5 Hz, 1H), 7.26-7.37 (m, 3H), 7.74-7.92 (m, 2H), 8.42 (bs, 1H), 9.15 (bs, 1H), 9.00 (s, 1H); MS (DCI-NH₃) m/z 270 (M+NH₄)⁺, 253 (M+H)⁺. Anal. (C₁₁H₁₂N₂O₃S) C, H, N.

***N*-(1-Benzo[b]thien-2-ylethyl)-*N*-hydroxythiourea (6)** was prepared using *N*-(1-benzo[b]thien-2-ylethyl)hydroxylamine¹⁸ and isothiocyanate as described by method 1a: mp 165°C (dec.); NMR (300 MHz, DMSO-d₆) δ 1.58 (d, J=7.5 Hz, 3H), 6.83 (m, 1H), 7.26-7.37 (m, 3H), 7.53-7.62 (s, 1H), 7.75-7.92 (m, 2H), 7.92-8.02 (bs, 1H), 9.28 (bs, 1H); MS (DCI-NH₃) m/z 270 (M+NH₄)⁺, 253 (M+H)⁺ Anal. (C₁₁H₁₂N₂OS₂) C, H, N.

***N*-(1-Fur-2-ylethyl)-*N*-hydroxyurea (7a)** was prepared using method 1a from 2-acetylfuran: mp 143-144 °C (dec.); ¹H NMR (DMSO-d₆) δ 1.36 (d, J=7 Hz, 3H), 5.31

(q, $J=7$ Hz, 1H), 6.23 (m, 1H), 6.38 (m, 3H), 7.53 (m, 1H), 9.04 (s, 1H); MS (DCI-NH₃) m/z 188 (M+H)⁺, 171 (M + H)⁺. Anal. (C₇H₁₀N₂O₃) C, H, N.

***N*-(1-Fur-3-ylethyl)-*N*-hydroxyurea (7b).** 3-Acetylfuran was prepared from 3-furaldehyde by addition of methyl magnesium bromide and Swern oxidation. This ketone was converted to **7b** using method 1a: mp 128-130 °C (dec.); ¹H NMR (DMSO-d₆) δ 1.31 (d, $J=7.5$ Hz, 3H), 5.17 (q, $J=7.5$ Hz, 1H), 6.35 (bs, 2H), 6.39 (m, 1H), 7.50 (m, 1H), 7.54 (m, 1H), 8.98 (s, 1H); MS (DCI-NH₃) m/z 171 (M + H)⁺. Anal. (C₇H₁₀N₂O₃) C, H, N.

***N*-Fur-2-ylmethyl-*N*-hydroxyurea (7c)** was prepared using method 1a from 2-furaldehyde: mp 128-131 °C (dec.); ¹H NMR (DMSO-d₆) δ 4.48 (s, 2H), 6.27 (m, 1H), 6.40 (m, 3H), 7.57 (m, 1H), 9.39 (s, 1H); MS (DCI-NH₃) m/z 157 (M + H)⁺. Anal. (C₆H₈N₂O₃) C, H, N.

***N*-Fur-3-ylmethyl-*N*-hydroxyurea (7d)** was prepared using method 1a from 3-furaldehyde: mp 125-128 °C (dec.); ¹H NMR (DMSO-d₆) δ 4.31 (s, 2H), 6.34 (bs, 2H), 6.40 (m, 1H), 7.56 (m, 2H), 9.30 (s, 1H); MS (DCI-NH₃) m/z 174 (M + NH₄)⁺; 157 (M + H)⁺. Anal. (C₆H₈N₂O₃) C, H, N.

***N*-[1-(2,5-Dimethylfur-3-yl)ethyl]-*N*-hydroxyurea (7e)** was prepared using method 1a from 2,5-dimethyl-3-acetylfuran: mp 145-146 °C; ¹H NMR (DMSO-d₆) δ 1.25 (d, $J=7.5$ Hz, 3H), 2.26 (s, 6H), 5.09 (q, $J=7.5$ Hz, 1H), 6.00 (s, 1H), 6.23 (bs, 2H), 8.95 (s, 1H); MS (DCI-NH₃) m/z 216 (M + NH₄)⁺; 199 (M + H)⁺. Anal. (C₉H₁₄N₂O₃) C, H, N.

***N*-[1-(2,5-Dimethylfur-3-yl)methyl]-*N*-hydroxyurea (7f)** was prepared using method 1a from 2,5-dimethylfuran-3-carboxaldehyde: mp 115-117 °C; ¹H NMR (DMSO-d₆) δ 2.16 (s, 6H), 4.17 (s, 2H), 5.90 (s, 1H), 6.23 (bs, 2H), 8.95 (s, 1H); MS (DCI-NH₃) m/z 207 (M + NH₄)⁺; 195 (M + H)⁺. Anal. (C₈H₁₂N₂O₃) C, H, N.

***N*-Hydroxy-*N*-[1-(2-methylfur-3-yl)methyl]urea (7g).** Methyl 2-methyl-3-furancarboxylate was reduced in ether with LAH to give 2-methyl-3-hydroxymethylfuran. This alcohol was converted to **7g** using method 7: mp 97-98 °C;

^1H NMR (CDCl_3) δ 1.65 (bs, 1H), 2.30 (s, 3H), 4.47 (s, 2H), 5.27 (bs, 2H), 6.36 (d, $J=2$ Hz, 1H), 7.25 (d, $J=2$ Hz, 1H); MS (DCI- NH_3) m/z 188 ($\text{M} + \text{NH}_4$) $^+$; 171 ($\text{M} + \text{H}$) $^+$. Anal. ($\text{C}_7\text{H}_{10}\text{N}_2\text{O}_3$) C, H, N.

***N*-Hydroxy-*N*-[1-(2,5-dimethylthien-3-yl)ethyl]urea (7h).** 3-Acetyl-5-methylfuran was prepared by methyl magnesium bromide addition to 5-methyl-3-furfural and subsequent Swern oxidation. This ketone was converted to **7h** using method 1a: mp 131-133 °C; ^1H NMR (DMSO-d_6) δ 1.28 (d, $J=7$ Hz, 3H), 2.20 (m, 3H), 5.10 (q, $J=7$ Hz, 1H), 6.00 (m, 1H), 6.31 (bs, 2H), 7.29 (s, 1H), 8.93 (s, 1H); MS (DCI- NH_3) m/z 202 ($\text{M} + \text{NH}_4$) $^+$; 185 ($\text{M} + \text{H}$) $^+$. Anal. ($\text{C}_8\text{H}_{12}\text{N}_2\text{O}_3$) C, H, N.

***N*-Hydroxy-*N*-[1-(5-methylfur-2-yl)methyl]urea (7i)** was prepared using method 1a from 5-methyl-2-furfural: mp 105 °C (dec.); ^1H NMR (DMSO-d_6) δ 2.21 (s, 3H), 4.39 (bs, 2H), 5.98 (m, 1H), 6.13 (d, $J=3$ Hz, 1H), 6.37 (bs, 2H), 9.33 (s, 1H); MS (DCI- NH_3) m/z 188 ($\text{M} + \text{NH}_4$) $^+$; 171 ($\text{M} + \text{H}$) $^+$. Anal. ($\text{C}_7\text{H}_{10}\text{N}_2\text{O}_3$) C, H, N.

***N*-Hydroxy-*N*-[1-(5-methylfur-2-yl)ethyl]urea (7j)** was prepared using method 1a from 2-acetyl-5-methylfuran: mp 116-118°C; ^1H NMR (300 MHz, DMSO-d_6) δ 1.32 (d, $J=7.5$ Hz, 3H), 2.21 (s, 3H), 5.25 (q, $J=7.5$, 1H), 5.95 (m, 1H), 6.08 (m, 1H), 6.36 (bs, 2H), 8.90 (s, 1H). IR (KBr): 3450, 3360, 3320, 2880, 1640, 1480. MS (DCI- NH_3) m/z 202 ($\text{M} + \text{NH}_4$) $^+$; 185 ($\text{M} + \text{H}$) $^+$ Anal. ($\text{C}_8\text{H}_{12}\text{N}_2\text{O}_3$) C, H, N.

***N*-Hydroxy-*N*-[1-(5-phenylfur-2-yl)ethyl]urea (7k).** To a 0 °C stirred solution of furan (10.2 g, 150 mmol) in THF (100 mL) was added *n*-butyllithium (60 mL, 150 mmol, 2.5 M in hexane). The mixture was stirred for 3 hours at 0 °C and transferred via cannula to a stirred suspension of zinc chloride (20.1 g, 150 mmol) in THF (100 mL). The mixture was stirred 1 h and a solution of tetrakis(triphenylphosphine) palladium (0.57g, 0.5 mmol) in tetrahydrofuran was added at room temperature. Bromobenzene (15.7g, 100 mmol) was added and the reaction was warmed to 50 °C and stirred for 24 h. The mixture was cooled and 0.1N HCl (100 mL) was added. The mixture was diluted with ether and the organic layer was washed with sat'd Na_2CO_3 , brine, dried with (MgSO_4)

and concentrated. The residue was distilled (50-55 °C/0.6-0.9 mm Hg) to give 12 g (84%) of 2-phenylfuran.

To a 0 °C stirred solution of 2-phenylfuran (12g, 83.2 mmol) in THF was added *n*-butyllithium (33.6 mL, 84 mmol, 2.5M in hexanes). The mixture was stirred 0.5 h and *N,O*-dimethylacetohydroxamic acid was added and the reaction was stirred at -20 °C for 1 h and at room temperature for 2 h. Sat'd NH₄Cl was added and the mixture was extracted with ether. The organic layer was washed with brine and dried (MgSO₄). Concentration gave 15.2 g (98%) of 2-acetyl-5-phenylfuran. The ketone was converted to **7k** using method 1a: mp 133-136 °C; ¹H NMR (300 MHz, DMSO-d₆) δ 1.41 (d, J=6.9 Hz, 3H), 5.38 (q, J=6.9 Hz, 1H), 6.35 (dd, J=1 Hz, J=3.3 Hz, 1H), 6.48 (s, 2H), 6.85 (d, 1H), 7.22-7.45 (m, 3H), 7.62-7.68 (m, 2H), 9.11 (s, 1H). IR (CDCl₃): 3450, 3440, 1570, 1425, 1650. MS (DCI-NH₃) m/z 264 (M + NH₄)⁺; 247 (M + H)⁺. Anal. (C₁₃H₁₄N₂O₃) C, H, N.

***N*-Hydroxy-*N*-[1-(5-phenylfuran-2-yl)methyl]urea (7l)**. 5-Phenylfuran-2-carboxaldehyde was prepared from 2-phenylfuran and *N,N*-dimethylformamide as described in **7k** and converted to **7l** using method 1a: mp 149 °C (dec.); ¹H NMR (DMSO-d₆) δ 4.53 (bs, 2H), 6.39 (d, J=3 Hz, 1H), 6.49 (bs, 2H), 6.87 (d, J=3 Hz, 1H), 7.26 (m, 1H), 7.41 (m, 2H), 7.66 (m, 2H), 9.48 (s, 1H); MS (DCI-NH₃) m/z 250 (M + NH₄)⁺; 233 (M + H)⁺. Anal. (C₁₂H₁₂N₂O₃) C, H, N.

***N*-Hydroxy-*N*-[5-(2,4,6-trimethylphenyl)-furan-2-ylethyl]urea (7m)**. 2-(2,4,6-Trimethylphenyl)furan was prepared from 2-bromomesitylene as described in **7k** and converted to **7m** using method 1a: mp 139-141 °C; ¹H NMR (300 MHz, DMSO-d₆) δ 1.40 (d, J=6.9 Hz, 3H), 2.13 (s, 6H), 2.25 (s, 3H), 5.35 (q, 6.9 Hz, 1H), 6.28-6.32 (m, 2H), 6.39 (s, 2H), 6.91 (s, 2H), 9.07 (s, 1H). IR (CDCl₃): 3530, 2360, 2340, 1670, 1560. MS (DCI-NH₃) m/z 306 (M + NH₄)⁺; 289 (M + H)⁺. Anal. (C₁₆H₂₀N₂O₃) C, H, N.

***N*-Hydroxy-*N*-[1-(5-pyrid-2-ylfuran-2-yl)ethyl]urea (7n)** was prepared from furan and 2-bromopyridine using the procedure described for **7k**: mp 185-187 °C (dec.); ¹H NMR

(DMSO- d_6) δ 1.43 (d, $J=7.5$ Hz, 3H), 5.39 (m, 1H), 6.41 (m, 1H), 6.48 (bs, 2H), 7.00 (d, $J=3$ Hz, 1H), 7.26 (m, 1H), 7.64 (m, 1H), 7.84 (m, 1H), 8.55 (m, 1H), 9.14 (s, 1H); MS (DCI-NH₃) m/z 248(M + H)⁺. Anal. (C₁₂H₁₃N₃O₃•0.5H₂O) Calcd C, 56.24 ; Found: C, 56.69.

***N*-Hydroxy-*N*-[1-[5-(2-phenylethenyl)fur-2-yl]ethyl]urea (7o)** . To a -78 °C stirred solution of diethyl benzylphosphonate (9.2g, 40.3 mmol) was added *n*-butyl lithium (16 mL, 2.5 M in hexanes). After 15 min furfural (3.4 mL, 40.3 mmol) was added. The reaction was stirred for 15 min at -78 °C and at room temperature for 5 h. Sat'd NH₄Cl was added and the mixture diluted with ether and water. The ether layer was dried (MgSO₄) and concentrated. The residue was purified by column chromatography (SiO₂, eluting with CH₂Cl₂ / pentane (1:10)) to give 2.8 g (38%) of 2-(2-phenylethenyl)furan.

The 2-(2-phenylethenyl)furan was converted to **7o** as described for 2-phenylfuran in the procedure given for **7k**: mp 140-143°C NMR (300 MHz, DMSO- d_6) δ 1.60 (d, $J = 7.2$ Hz, 3H), 5.35 (q, 1H, 7.2 Hz), 6.32 (dd, $J=1$ Hz, $J=3.3$ Hz, 1H), 6.46 (d, 3.3 Hz, 1H), 6.49 (s, 2H), 6.90 (d, $J=16.5$ Hz, 1H), 7.07 (d, $J=16.5$ Hz, 1H), 7.20-7.40 (m, 3H), 7.50-7.60 (m, 2H), 9.11 (s, 1H). IR (CDCl₃): 3470, 1655, 1575, 1445. MS (DCI-NH₃) m/z 290 (M + NH₄)⁺; 273 (M + H)⁺. Anal. (C₁₅H₁₆N₂O₃•0.5 H₂O) Calcd N: 9.95; Found N: 9.37.

***N*-1-(5-Butylfur-2-yl)ethyl-*N*-hydroxyurea (7p)**. 2-Acetyl-5-*n*-butylfuran was prepared by Friedel Crafts acylation of 2-*n*-butylfuran with acetyl-*p*-toluenesulfonate in benzene. This ketone was converted to **7p** using method 1a: mp 105-107.5°C; ¹H NMR (300 MHz, DMSO- d_6) δ 0.89 (t, 3H), 1.32 (m, 5H), 1.53 (m, 2H), 5.74 (m, 1H), 5.95 (m, 1H), 6.08 (m, 1H), 6.36 (br s, 2H), 8.97 (s, 1H); MS (DCI-NH₃) m/z 244 (M + NH₄)⁺, 227 (M+H)⁺. Anal. (C₁₁H₁₈N₂O₃): C, H, N.

***N*-hydroxy-*N*-[1-(5-hydroxymethylfur-2-yl)methyl]urea (7q)** was prepared using method 1a from 5-(hydroxymethyl)furfural: mp 122 °C (dec.); ¹H NMR (DMSO- d_6) δ 4.34 (d, $J=6$ Hz, 2H), 4.45 (s, 2H), 5.16 (t, $J=6$ Hz, 1H), 6.18 (m, 2H), 6.48 (bs, 2H), 9.48 (s, 1H); MS (DCI-NH₃) m/z 204 (M + NH₄)⁺. Anal. (C₇H₁₀N₂O₄•0.25H₂O) C, H, N.

***N*-1-(5-Ethoxymethylfur-2-yl)methyl-*N*-hydroxyurea (7r)**. 5-(Ethoxymethyl)furfuralhydroxylamine was obtained as a side product from the reduction of 5-(hydroxymethyl)furfural oxime from **7q** and converted separately to **7r** using method 1a: mp 81 °C (dec.); ¹H NMR (DMSO-d₆) δ 1.11 (d, J=7.5 Hz, 3H), 3.45 (d, J=7.5 Hz, 2H), 4.32 (s, 2H), 4.45 (s, 2H), 6.21 (d, J=3 Hz, 1H), 6.32 (d, J=3 Hz, 1H), 6.40 (bs, 2H), 9.40 (s, 1H); MS (DCI-NH₃) m/z 232 (M + NH₄)⁺. Anal. (C₉H₁₄N₂O₄) C, H, N.

***N*-1-(5-Benzyloxymethylfur-2-yl)ethyl-*N*-hydroxyurea (7s)**. 2-(Benzyloxymethyl)furan was obtained by reaction of 2-lithiofuran with benzyloxymethyl chloride in ether (61%). The substituted furan was converted to **7s** as described for **7k**: mp 121 °C (dec.); ¹H NMR (DMSO-d₆) δ 1.35 (d, J=7.5 Hz, 3H), 4.40 (s, 2H), 4.48 (s, 2H), 5.30 (q, J=7.5 Hz, 1H), 6.20 (d, J=3 Hz, 1H), 6.35 (d, J=3 Hz, 1H), 6.42 (bs, 2H), 7.27-7.38 (m, 5H), 9.06 (s, 1H); MS (DCI-NH₃) m/z 308 (M + NH₄)⁺. Anal. (C₁₅H₁₈N₂O₄•0.25H₂O) C, H, N.

***N*-1-(5-Carboxymethylfur-2-yl)ethyl-*N*-hydroxyurea (7t)**. 5-Acetyl-2-carbomethoxyfuran was prepared by the reaction of dilithio-2-carboxyfuran and *N,O*-dimethylacetohydroxamic acid followed by esterification in methanol / HCl (76% over 2 steps). This ketone was converted to **7t** using method 1a: mp 171-172 °C (dec.); ¹H NMR (DMSO-d₆) δ 1.38 (d, J=7 Hz, 3H), 5.34 (q, J=7.5 Hz, 1H), 6.41 (m, 1H), 6.46 (bs, 2H), 7.12 (d, J=4 Hz, 1H), 9.15 (s, 1H); MS (DCI-NH₃) m/z 232 (M + NH₄)⁺; 215 (M + H)⁺. Anal. (C₈H₁₀N₂O₅•0.5H₂O) C, H, N.

***N*-1-(5-*N*-Benzylcarboxamidofur-2-yl)ethyl-*N*-hydroxyurea (7u)**. 5-Acetyl-2-(*N*-benzylcarboxamido)furan was prepared by reaction of benzylamine and 5-acetyl-2-(chlorocarbonyl)furan, which was prepared from 5-acetyl-2-(carboxy)furan as described in the preparation of **7t**. This ketone was converted to **7u** using method 1a: mp 169 °C; ¹H NMR (DMSO-d₆) δ 1.38 (d, J=7 Hz, 3H), 4.41 (d, J=6 Hz, 2H), 5.34 (q, J=7 Hz, 1H), 6.39 (m, 1H), 6.49 (bs, 2H), 7.05 (d, J=3 Hz; 1H), 7.20-7.35 (m, 5H), 8.77 (t, J=5 Hz;

1H), 9.13 (s, 1H); MS (DCI-NH₃) m/z 321 (M + NH₄)⁺. Anal. (C₁₅H₁₇N₃O₄•0.25H₂O) C, H, N.

N-Hydroxy-N-(1-thien-2-yl)ethylurea (8a) was prepared using method 1a from 2-acetylthiophene: mp 129 °C (dec.); ¹H NMR (DMSO-d₆) δ 1.42 (d, J=7 Hz, 3H), 5.49 (q, J=7 Hz, 1H), 6.38 (bs, 2H), 6.94 (m, 2H), 7.36 (m, 1H), 9.13 (s, 1H); MS (DCI-NH₃) m/z 187 (M + H)⁺. Anal. (C₇H₁₀N₂O₂S) C, H, N.

N-Hydroxy-N-(1-thien-3-yl)ethylurea (8b) was prepared using method 1a from 3-acetylthiophene: mp 138.5-140 °C; ¹H NMR (DMSO-d₆) δ 1.39 (d, J=7 Hz, 3H), 5.32 (q, J=7 Hz, 1H), 6.33 (bs, 2H), 7.05 (m, 1H), 7.27 (m, 1H), 7.42 (m, 1H), 9.03 (s, 1H); MS (DCI-NH₃) m/z 204 (M + NH₄)⁺; 187 (M + H)⁺. Anal. (C₇H₁₀N₂O₂S) C, H, N.

N-[1-(2,5-Dimethylthien-3-yl)ethyl]-N-hydroxyurea (8c) was prepared using method 1a from 2,5-dimethyl-3-acetylthiophene: mp 146-147 °C; ¹H NMR (DMSO-d₆) δ 1.29 (d, J=7.5 Hz, 3H), 2.29 (s, 3H), 2.32 (s, 3H), 5.23 (q, J=7.5 Hz, 1H), 6.21 (bs, 2H), 6.74 (s, 1H), 9.02 (s, 1H); MS (DCI-NH₃) m/z 232 (M + NH₄)⁺; 215 (M + H)⁺. Anal. (C₉H₁₄N₂O₂S) C, H, N.

N-Hydroxy-N-[1-(3-methylthien-2-yl)ethyl]urea (8d) was prepared using method 1a from 2-acetyl-3-methylthiophene: mp 131 °C (dec.); ¹H NMR (DMSO-d₆) δ 1.35 (d, J=7 Hz, 3H), 2.16 (s, 3H), 5.09 (q, J=7 Hz, 1H), 6.30 (bs, 2H), 6.78 (d, J=6 Hz, 1H), 7.25 (d, J=6 Hz, 1H), 9.16 (s, 1H); MS (DCI-NH₃) m/z 218 (M + NH₄)⁺; 201 (M + H)⁺. Anal. (C₈H₁₂N₂O₂S) C, H, N.

N-Hydroxy-N-[1-(3-methylthien-2-yl)methyl]urea (8e) was prepared using method 1a from 3-methylthiophene-2-carboxaldehyde: mp 110 °C (dec.); ¹H NMR (DMSO-d₆) δ 2.17 (s, 3H), 4.56 (bs, 2H), 6.35 (m, 1H), 6.81 (d, J=6 Hz, 1H), 7.28 (d, J=6 Hz, 1H), 9.38 (s, 1H); MS (DCI-NH₃) m/z 204 (M + NH₄)⁺; 187 (M + H)⁺. Anal. (C₇H₁₀N₂O₂S) C, H, N.

N-Hydroxy-N-[1-(5-methylthien-2-yl)ethyl]urea (8f) was prepared using method 1a from 2-acetyl-5-methylthiophene: mp 130-131 °C; ¹H NMR (300 MHz, DMSO-d₆) δ

1.38 (d, 3H), 2.38 (s, 3H), 5.39 (q, 1H), 6.36 (brs, 2H), 6.59 (m, 1H), 6.70 (m, 1H), 9.08 (s, 1H). M/z (CI-NH₃): 218 (M+NH₄)⁺, 201 (M+1)⁺, 125. Anal. (C₈H₁₂N₂O₂S) C, H, N.

***N*-Hydroxy-*N*-[1-(5-phenylthien-2-yl)ethyl]urea (8g)** was prepared from 2-phenylthiophene as described for **7k**: mp 150-151.5 °C (dec.); ¹H NMR (DMSO-d₆) δ 1.46 (d, J=7 Hz, 3H), 5.49 (q, J=7 Hz, 1H), 6.45 (bs, 2H), 6.95 (d, J=3 Hz, 1H), 7.25-7.34 (m, 2H), 7.39 (m, 2H), 7.60 (m, 2H), 9.21 (s, 1H); MS (DCI-NH₃) m/z 280 (M + NH₄)⁺; 263 (M + H)⁺. Anal. (C₁₃H₁₄N₂O₂S•0.5H₂O) C, H, N.

***N*-Hydroxy-*N*-[1-[5-(pyrid-2-yl)thien-2-yl]ethyl]urea (8h)** was prepared from thiophene and 2-bromopyridine using the procedure described for **7k**: foam; ¹H NMR (DMSO-d₆) δ 1.46 (d, J=7.5 Hz, 3H), 5.94 (q, J=7 Hz, 1H), 6.43 (bs, 2H), 6.96 (d, J=4 Hz, 1H), 7.23 (m, 1H), 7.60 (d, J=4 Hz, 1H), 7.83 (m, 2H), 8.49 (m, 1H), 9.21 (s, 1H); MS (DCI-NH₃) m/z 264 (M + H)⁺. Anal. (C₁₂H₁₃N₃O₂S•0.5H₂O) Calcd N, 15.43; Found: N, 14.81.

***N*-Hydroxy-*N*-[1-(5-thien-2-ylthien-2-yl)ethyl]urea (8i)** was from 2,2'-dithienyl (Lancaster) using method 2: mp 154-155 °C; ¹H NMR (DMSO-d₆) δ 1.44 (d, J=7 Hz, 3H), 5.46 (q, J=7 Hz, 1H), 6.43 (bs, 2H), 6.89 (d, J=3 Hz, 1H), 7.08 (m, 2H), 7.22 (dd, J=4 Hz, J=1 Hz, 1H), 7.47 (dd, J=4 Hz, J=1 Hz, 1H), 9.23 (s, 1H); MS (DCI-NH₃) m/z 264 (M + NH₄)⁺. Anal. (C₁₁H₁₂N₂O₂S₂) C, H, N.

***N*-[1-(5-Benzylthien-2-yl)ethyl]*N*-hydroxyurea (8j)**. 2-Acetyl-5-benzylthiophene was prepared by Friedel Crafts acylation of 2-benzylthiophene⁹ with acetyl chloride and tin tetrachloride. This ketone was converted to **8j** using method 1a: mp 117-120 °C; ¹H NMR (DMSO-d₆) δ 1.37 (d, J=7.5 Hz, 3H), 4.06 (s, 2H), 5.39 (q, J=7.5 Hz, 1H), 6.43 (bs, 2H), 6.71 (m, 2H), 7.27 (m, 5H), 9.10 (s, 1H); MS (DCI-NH₃) m/z 294 (M + NH₄)⁺; 277 (M + H)⁺. Anal. (C₁₄H₁₆N₂O₂S) C, H, N.

***N*-Hydroxy-*N*-[1-[5-(2-phenylethenyl)thien-2-yl]ethyl]urea (8l)** was prepared from thiophene-2-carboxaldehyde using the procedure described for **7o**: mp 160.5-163 °C; ¹H

NMR (DMSO- d_6) δ 1.44 (d, $J=7.5$ Hz, 3H), 5.46 (q, $J=7.5$ Hz, 1H), 6.42 (bs, 2H), 6.84 (d, $J=12$ Hz, 1H), 6.87 (m, 1H), 7.01 (m, 1H), 7.24 (m, 1H), 7.36 (m, 3H), 7.55 (m, 2H), 9.20 (s, 1H); MS (DCI-NH₃) m/z 306 (M + NH₄)⁺; 289 (M + H)⁺. Anal. (C₁₅H₁₆N₂O₂S) C, H, N.

***N*-Hydroxy-*N*-[1-[5-(2-thien-2-ylethenyl)thien-2-yl]methyl]urea (8m).** 5-(2-Thien-2-ylethenyl)-2-thiophenecarboxaldehyde was prepared from diethyl thien-2-yl-phosphonate and thiophene-2-carboxaldehyde as described for **7o**, and after metalation substituting DMF for *N,O*-dimethylacetohydroxamic acid. This aldehyde was converted to **8m** using method 1a: mp 164-167 °C; ¹H NMR (DMSO- d_6) δ 4.60 (s, 2H), 6.42 (bs, 2H), 6.89 (d, $J=4$ Hz, 1H), 6.98-7.08 (m, 4H), 7.02 (m, 1H), 7.44 (d, $J=5$ Hz, 1H), 9.47 (s, 1H); MS (DCI-NH₃) m/z 298 (M + NH₄)⁺. Anal. (C₁₂H₁₂N₂O₂S₂) C, H, N.

***N*-1-(1-Cyclopropyl)methyl-*N*-hydroxyurea (9a)** was prepared by method 1a from 1-cyclopropanecarboxaldehyde: mp 108-109 °C; ¹H NMR (DMSO- d_6) δ 0.18 (m, 2H), 0.40 (m, 2H), 1.01 (m, 1H), 3.19 (d, $J=6.5$ Hz, 2H), 6.21 (bs, 2H), 9.24 (s, 1H); MS (DCI-NH₃) m/z 148 (M + H)⁺. Anal. (C₅H₁₀N₂O₂) C, H, N.

***N*-1-(1-Cyclopropyl)ethyl-*N*-hydroxyurea (9b)** was prepared using method 1a from 1-cyclopropyl methyl ketone: mp 94-97 °C; ¹H NMR (DMSO- d_6) δ 0.14 (m, 2H), 0.22-0.37 (m, 2H), 0.43 (m, 2H), 1.09 (d, $J=3$ Hz, 3H), 3.33 (m, 1H), 6.23 (bs, 2H), 8.94 (s, 1H); MS (DCI-NH₃) m/z 145 (M + NH₄)⁺. Anal. (C₆H₁₂N₂O₂) C, H, N.

***N*-Cyclobutylmethyl-*N*-hydroxyurea (9c).** Cyclobutanecarboxaldehyde was prepared by Swern oxidation of cyclobutanemethanol. This aldehyde was converted to **9c** using method 1a: mp 112-113 °C; ¹H NMR (DMSO- d_6) δ 1.68 (m, 2H), 1.80 (m, 4H), 1.97 (m, 2H), 2.55 (m, 1H), 3.34 (d, $J=7$ Hz, 2H), 6.20 (bs, 2H), 9.13 (s, 1H); MS (DCI-NH₃) m/z 145 (M + H)⁺. Anal. (C₆H₁₂N₂O₂) C, H, N.

***N*-Cyclopentylmethyl-*N*-hydroxyurea (9d)** was prepared from cyclopentylmethanol as described for **7c**: mp 115-116 °C; ¹H NMR (DMSO- d_6) δ 1.19 (m, 2H), 1.51 (m, 4H),

1.64 (m, 2H), 2.18 (m, 1H), 3.24 (d, J=7 Hz, 2H), 6.20 (bs, 2H), 9.17 (s, 1H); MS (DCI-NH₃) m/z 159 (M + H)⁺. Anal. (C₇H₁₄N₂O₂) C, H, N.

N-Cyclohexylmethyl-N-hydroxyurea (9e) was prepared from cyclohexane carboxaldehyde by the oxime reduction method using NaBH₃CN as described in ex. 12d. The hydroxylamine derivative was converted to 9e using method 1a: mp 143-144.5 °C; ¹H NMR (DMSO-d₆) δ 0.86 (m, 2H), 1.16 (m, 3H), 1.65 (m, 6H), 3.16 (d, J=7 Hz, 2H), 6.15 (bs, 2H), 9.16 (s, 1H); MS (DCI-NH₃) m/z 190 (M+NH₄)⁺. Anal. (C₈H₁₆N₂O₂) C, H, N.

N-Hydroxy-N-[[5-(phenylthio)fur-2-yl]methyl]urea (10a) was prepared from 5-thiophenoxyfuran-2-carboxaldehyde¹⁰ using method 1a: mp 118-120 °C; ¹H NMR (DMSO-d₆) δ 4.50 (s, 2H), 6.44 (d, J=4 Hz, 1H), 6.48 (bs, 2H), 6.91 (d, J=4 Hz, 1H), 7.21-7.26 (m, 3H), 7.28-7.37 (m, 2H), 9.47 (s, 1H); MS (DCI-NH₃) m/z 282 (M + NH₄)⁺. Anal. (C₁₂H₁₂N₂O₃S) C, H, N.

N-Hydroxy-N-[[5-(phenoxy)fur-2-yl]methyl]urea (10b) was prepared from phenol and 5-nitrofuran-2-carboxaldehyde using the procedure described for 11f: mp 118-120 °C; ¹H NMR (DMSO-d₆) δ 4.40 (s, 2H), 5.71 (d, J=4 Hz, 1H), 6.28 (d, J=4 Hz, 1H), 6.43 (bs, 2H), 7.05 (m, 2H), 7.16 (m, 1H), 7.40 (m, 2H), 9.40 (s, 1H); MS (DCI-NH₃) m/z 266 (M + NH₄)⁺; 249 (M + H)⁺. Anal. (C₁₂H₁₂N₂O₄) C, H, N.

N-[5-(4-Fluorophenoxy)fur-2-yl]methyl-N-hydroxyurea (10c) was prepared from 5-(4-fluorophenoxy)furan-2-carboxaldehyde¹⁸ using method 1a: mp 125-126 °C; ¹H NMR (DMSO-d₆) δ 4.39 (s, 2H), 5.68 (d, J=3 Hz, 1H), 6.28 (d, J=3 Hz, 1H), 6.43 (bs, 2H), 7.11 (m, 2H), 7.23 (m, 2H), 9.40 (s, 1H); MS (DCI-NH₃) m/z 284 (M + NH₄)⁺; 267 (M + H)⁺. Anal. (C₁₂H₁₁FN₂O₄) C, H, N.

N-Hydroxy-N-[[3-(phenylthio)thien-2-yl]methyl]urea (11a). To a stirred suspension of 3-bromothiophene-2-carboxaldehyde¹¹ (1.9 g, 10 mmol) and powdered potassium carbonate (3.04 g, 22 mmol) was added thiophenol (2.2 g, 20 mmol). The mixture was stirred overnight at room temperature and concentrated. The mixture was diluted with

water and ether and the aqueous layer was extracted with ether. The combined ether extracts were dried (MgSO_4) and concentrated. The residue was purified by flash column chromatography (SiO_2 , eluting with 3% ethyl acetate / hexanes) to give 3-(phenylthio)thiophene-2-carboxaldehyde as a yellow oil. This aldehyde was converted to **11a** using method 1a: mp 99-100.5 °C; ^1H NMR (DMSO-d_6) δ 4.77 (s, 2H), 6.47 (bs, 2H), 6.95 (d, $J=6$ Hz, 1H), 7.10-7.21 (m, 3H), 7.24-7.33 (m, 2H), 7.59 (d, $J=6$ Hz, 1H), 9.51 (s, 1H); MS (DCI- NH_3) m/z 298 ($\text{M} + \text{NH}_4$) $^+$; 281 ($\text{M} + \text{H}$) $^+$. Anal. ($\text{C}_{12}\text{H}_{12}\text{N}_2\text{O}_2\text{S}_2$) C, H, N.

***N*-Hydroxy-*N*-[[4-(phenylthio)thien-2-yl]methyl]urea (11b)**. To a -78 °C stirred solution of 2-(4-bromothiophen-2-yl)-1,3-dioxolane¹² (25 g, 131 mmol) in ether was added *n*-butyllithium (15 mL, 37.4 mmol, 2.5 M in hexanes). The reaction was stirred 10 min and diphenyldisulfide (8.2 g, 37.4 mmol) was added as a solid. The reaction was warmed to room temperature, diluted with water and the ether layer was separated. The ether solution was dried (MgSO_4) and concentrated. The residue was purified by flash column chromatography (SiO_2 , eluting with 10 % ethyl acetate / hexanes) to give 6.05 g (67%) of 2-((4-phenylthio)thien-2-yl)-1,3-dioxolane as an oil. The dioxolane (6.05g, 23 mmol) was dissolved in dioxane (45 mL) and 10 % HCl (45 mL). The mixture was stirred 0.5 h at room temperature and concentrated. The mixture was diluted with water and extracted with ethyl acetate. The ethyl acetate extracts were dried (MgSO_4) and concentrated to give 5.06 (100%) of 4-(phenylthio)thiophene-2-carboxaldehyde. This aldehyde was converted to **11b** using method 1a: mp 111-113 °C; ^1H NMR (DMSO-d_6) δ 4.62 (s, 2H), 6.46 (bs, 2H), 6.94 (d, $J=1$ Hz, 1H), 7.16-7.25 (m, 3H), 7.28-7.36 (m, 2H), 7.63 (d, $J=1$ Hz, 1H), 9.50 (s, 1H); MS (DCI- NH_3) m/z 298 ($\text{M} + \text{NH}_4$) $^+$; 281 ($\text{M} + \text{H}$) $^+$. Anal. ($\text{C}_{12}\text{H}_{12}\text{N}_2\text{O}_2\text{S}_2$) C, H, N.

***N*-Hydroxy-*N*-[[5-(phenylthio)thien-2-yl]methyl]urea (11c)** was prepared from 5-bromothiophene-2-carboxaldehyde and thiophenol as described for **11a**: mp 126-128 °C; ^1H NMR (DMSO-d_6) 4.63 (s, 2H), 6.47 (bs, 2H), 7.02 (d, $J=4$ Hz, 1H), 7.27-7.37 (m,

6H), 9.53 (s, 1H); MS (DCI-NH₃) m/z 298 (M + NH₄)⁺; 281 (M + H)⁺. Anal. (C₁₂H₁₂N₂O₂S₂) C, H, N.

N-Hydroxy-N-[[3-(phenoxy)thien-2-yl]methyl]urea (11d). A suspension of 3-bromothiophene (100g, 610 mmol), phenol (61.2 g, 650 mmol), copper bronze (5 g) and potassium carbonate (30 g, 220 mmol) was heated to 150 °C for 7 days. The mixture was cooled, diluted with chloroform (300 mL) and filtered. The solids were washed with chloroform and the chloroform extracts combined, washed with 10% NaOH, water, dried (MgSO₄) and concentrated. The residue was distilled to give 31 g (29%) of 3-phenoxythiophene (bp 80 °C, 3 mm Hg). This substituted thiophene was selectively metalated (with LDA in THF) in the 2 position and converted to **11d** by the procedure described for **7k**: mp 132-133.5 °C; ¹H NMR (DMSO-d₆) δ 4.55 (s, 2H), 6.43 (bs, 2H), 6.72 (d, J=6 Hz, 1H), 6.95 (m, 2H), 7.06 (m, 1H), 7.33 (m, 2H), 7.46 (d, J=6 Hz, 1H), 9.44 (s, 1H); MS (DCI-NH₃) m/z 282 (M + NH₄)⁺; 265 (M + H)⁺. Anal. (C₁₂H₁₂N₂O₃S•0.25H₂O) C, H, N.

N-Hydroxy-N-[[4-(phenoxy)thien-2-yl]methyl]urea (11e). 3-Phenoxythiophene was prepared from 3-bromothiophene as described for 3-phenoxyfuran in the procedure for **11d**.

To a 0 °C stirred solution of 3-phenoxythiophene (9.5 g, 53.9 mmol) in ether (200 mL) was added n-butyllithium (24 mL, 60 mmol). The reaction was stirred for 0.25 h and trimethylsilylchloride was added (6.45 g, 59.4 mmol). The reaction was stirred 0.25 h longer and n-butyllithium was added (24 mL, 60 mmol). The mixture was stirred an additional 0.25 h, DMF (14 mL) was added and the reaction was warmed to room temperature overnight. Water was added (5 mL) and the mixture was diluted with ether. The organic solution was washed with brine, dried (MgSO₄) and concentrated. The residue was purified by flash column chromatography (SiO₂, eluting with 5% ether / hexanes) to give 12.1 g (83%) of 4-phenoxy-5-trimethylsilylthiophene-2-carboxaldehyde as a yellow oil. This aldehyde was converted to **11e** using method 1a (TMS group

removed under conditions of reduction of oxime): mp 120-122 °C; ¹H NMR (DMSO-d₆) δ 4.57 (s, 2H), 6.46 (bs, 2H), 6.78 (bs, 2H), 7.03 (m, 2H), 7.12 (m, 1H), 7.38 (m, 2H), 9.49 (s, 1H); MS (DCI-NH₃) m/z 282 (M + NH₄)⁺; 265 (M + H)⁺. Anal. (C₁₂H₁₂N₂O₃S) C, H, N.

***N*-Hydroxy-*N*-[[5-(phenoxy)thien-2-yl]methyl]urea (11f).** To a stirred suspension of sodium hydride (1.05 g, 35 mmol, 80%) in DMSO (100 mL) was added phenol (3.3 g, 35 mmol) and the mixture stirred 0.5 h. To the reaction was added a DMSO (30 mL) solution of 5-nitrothiophene-2-carboxaldehyde (5 g, 32 mmol). The reaction was stirred 0.5 h and poured into water. The mixture was thoroughly extracted with ether and the combined extracts were washed with brine. The extracts were dried (MgSO₄) and concentrated to give crude 5-phenoxythiophene-2-carboxaldehyde. This aldehyde was converted to **11f** using method 1a: mp 114-116 °C; ¹H NMR (DMSO-d₆) δ 4.53 (s, 2H), 6.42 (bs, 2H), 6.49 (d, J=4 Hz, 1H), 6.73 (d, J=4 Hz, 1H), 7.13 (m, 3H), 7.40 (m, 2H), 9.45 (s, 1H); MS (DCI-NH₃) m/z 282 (M + NH₄)⁺; 265 (M + H)⁺. Anal. (C₁₂H₁₂N₂O₃S) C, H, N.

***N*-Hydroxy-*N*-[[5-(4-chlorophenylthio)thien-2-yl]methyl]urea (11g)** was prepared from 4-chlorothiophenol and 5-bromothiophene-2-carboxaldehyde using the procedure described for **11a**: mp 155-160 °C; ¹H NMR (DMSO-d₆) δ 4.64 (s, 2H), 6.47 (bs, 2H), 7.04 (d, J=4 Hz, 1H), 7.20 (m, 2H), 7.28 (d, J=4 Hz, 1H), 7.40 (m, 2H), 9.54 (s, 1H); MS (DCI-NH₃) m/z 332 (M + NH₄)⁺; 315 (M + H)⁺. Anal. (C₁₂H₁₁ClN₂O₂S₂•0.5H₂O) C, H, N.

***N*-3-(Fur-2-yl)prop-2-enyl-*N*-hydroxyurea (12a)** was prepared using method 1a from 3-(2-furyl)acrolein: mp. 118-121 °C; ¹H-NMR (300 MHz, DMSO-d₆) δ 4.06 (d, J=7 Hz, 2H), 6.06 (dt, J= 15 Hz, J=7 Hz, 1H), 6.34 (bs, 2H), 6.37-6.50 (m, 3H), 7.59 (d, J=2 Hz, 1H), 9.31 (s, 1H), MS (DCI-NH₃) m/z 200 (M + NH₄)⁺, 183 (M + H)⁺. Anal. (C₈H₁₀N₂O₃) C, H, N.

***N*-4-(Fur-2-yl)-3-buten-2-yl-*N*-hydroxyurea (12b)** was prepared from 2-furaldehyde as described for **12d**: mp. 123-124 °C; ¹H-NMR (300 MHz, DMSO-d₆) δ: 1.20 (d, 3H), 4.78 (quintet, 1H), 6.12 (d-d, 1H), 6.35 (m+s, 4H), 6.47 (d-d, 1H), 7.6 (d, 1H), 9.05 (s, 1H), IR (KBr): 3480, 3320, 3240, 3180, 1640 cm⁻¹; MS (DCI-NH₃) m/z 214 (M + NH₄)⁺, 197 (M+H)⁺. Anal. (C₉H₁₂N₂O₃) C, H, N.

***N*-3-(Fur-3-yl)-prop-2-enyl-*N*-hydroxyurea (12c)** was prepared from 3-furaldehyde and acetaldehyde as described for **12d**: mp 136-137 °C; ¹H NMR (DMSO-d₆) δ 4.03 (m, 2H), 5.96 (m, 1H), 6.32-6.42 (m, 3H), 6.70 (d, J=3.3 Hz, 1H), 7.61 (m, 1H), 7.70 (bs, 1H), 9.30 (s, 1H); MS (DCI-NH₃) m/z 200 (M + NH₄)⁺; 183 (M + H)⁺. Anal. (C₈H₁₀N₂O₃) Calcd C, 52.73 H, 5.54; N, 15.38; Found: C, 52.39; H, 5.55; N, 15.05.

***N*-4-(Fur-3-yl)-3-buten-2-yl-*N*-hydroxyurea (12d)**. To a room temperature stirred solution of 3-furaldehyde (8.65 mL, 0.1 mole) and acetone (22 mL) in methanol (20 mL) was added 15% potassium hydroxide (1.7 mL) dropwise. The reaction was stirred for 3h at room temperature and acidified with acetic acid to pH 5. The solution was concentrated and extracted with ethyl acetate (150 mL). The organic extract was washed with water and brine, dried (MgSO₄) and concentrated. The residue was purified by flash column chromatography (SiO₂, eluting with hexanes / ethyl acetate 10:1) to afford 13.2 g (97%) of 2-(fur-3-yl)ethenyl methyl ketone: mp 33-36 °C. The ketone was converted to the oxime using hydroxylamine hydrochloride and NaOAc in methanol / water (2:1) (83%). The oxime was reduced to the hydroxylamine derivative by an alternative procedure with NaCNBH₃ as follows: To a solution of the oxime of 2-(fur-3-yl)-ethenyl methyl ketone (6.62 g, 40 mmol) in acetic acid (100 mL) was added NaBH₃CN (5.03 g, 80 mmol) in small portions (every 0.5 h) over a period of 5 h. The mixture was concentrated and the residue neutralized with sat'd NaHCO₃ and solid NaHCO₃. The mixture was extracted with ethyl acetate and the combined organic extracts were dried (MgSO₄) and concentrated. The residue was purified by flash column chromatography (SiO₂, eluting with CH₂Cl₂ / ethyl acetate 3:1) to afford 6 g of hydroxylamine derivative

that was used for urea formation without further characterization. The hydroxylamine derivative was converted to **12d** in 54% using method 1a: mp 122-123 °C; ¹H-NMR (300 MHz, DMSO d₆) δ 1.20 (d, 3H), 4.75 (quintet, 1H), 6.0 (d-d, 1H), 6.32 (m, 3H), 6.7 (d, 1H), 7.62 (d, 1H), 7.7 (s, 1H), 9.0 (s, 1H), IR (KBr): 3440, 3340, 3260, 3200, 1660 cm⁻¹. MS (DCI-NH₃) m/z 214 (M+NH₄)⁺; 197 (M+H)⁺. Anal. (C₉H₁₂N₂O₃) C, H, N.

N-Hydroxy-N-[3-(5-methylfur-2-yl)-prop-2-enyl]urea (12e) was prepared from 5-methylfuran-2-carboxaldehyde and acetaldehyde as described for **12d**, with the reduction of the oxime as originally described in method 1a: mp 131-133 °C; ¹H NMR (DMSO-d₆) δ 2.28 (s, 3H), 4.03 (d, J=7.5 Hz, 2H), 5.95 (m, 1H), 6.07 (m, 1H), 6.24 (m, 1H), 6.33 (d, J=16 Hz, 1H), 6.37 (bs, 2H), 9.30 (s, 1H); MS (DCI-NH₃) m/z 197 (M + H)⁺. Anal. (C₉H₁₂N₂O₃) C, H, N.

N-Hydroxy-N-[4-(1-methylfur-3-yl)-3-buten-2-yl]urea (12f). To a stirred solution of 5-methyl-2-furfural (2.0 g, 18 mmol) in toluene (50 mL) was added 1-triphenylphosphoranylidene-2-propanone (6.1 g, 19 mmol, Aldrich) and the mixture heated to reflux overnight. The mixture was cooled, filtered through a pad of silica gel and concentrated. The residue was purified by flash column chromatography (SiO₂, eluting with 40% ether / hexanes) to give 2.6 g (96%) of 2-(1-methylfur-3-yl)ethenyl methyl ketone. The ketone was converted to **12f** using method 1a: mp 122-124.5 °C; ¹H NMR (DMSO-d₆) δ 1.19 (d, J=7.5 Hz, 3H), 2.26 (s, 3H), 4.74 (m, 1H), 6.01 (m, 1H), 6.06 (m, 1H), 6.25 (m, 2H), 6.25 (m, 2H), 6.36 (bs, 2H), 9.00 (s, 1H); MS (DCI-NH₃) m/z 211 (M + H)⁺. Anal. (C₁₀H₁₄N₂O₃•0.25 H₂O) Calcd C, 55.93 ; Found: C, 56.49.

N-Hydroxy-N-[3-(5-phenylfur-2-yl)-prop-2-enyl]urea (12g) was prepared from 5-phenyl-2-furaldehyde (see **7k**) as described for **12e**: mp 158-159 °C; ¹H NMR (DMSO-d₆) δ 4.10 (d, J=7 Hz, 2H), 6.15-6.28 (m, 1H), 6.35-6.50 (m, 3H), 6.52 (d, J=4 Hz, 1H), 6.97 (d, J=4 Hz, 1H), 7.29 (m, 1H), 7.43 (m, 2H), 7.73 (m, 2H), 9.36 (s, 1H); MS (DCI-NH₃) m/z 276 (M+NH₄)⁺, 259 (M + H)⁺. Anal. (C₁₄H₁₄N₂O₃•0.25 H₂O) C, H, N.

***N*-Hydroxy-*N*-[4-(thien-3-yl)-3-buten-2-yl]urea (13b)** was prepared from thiophene-3-carboxaldehyde as described for **12d**: mp 133-134 °C; ¹H-NMR (300 MHz, DMSO-d₆) δ 1.2 (d, 3H), 4.8 (m, 1H), 6.15 (d-d, 1H), 6.35 (s, 2H), 6.5 (d, 1H), 7.28 (d-d, 1H), 7.4 (d-d, 1H), 7.5 (d-d, 1H), 9.03 (s, 1H), IR (KBr): 3400, 3360, 1625 cm⁻¹. MS (DCI-NH₃) m/z 230 (M+NH₄)⁺. Anal. (C₉H₁₂N₂O₂S) C, H, N.

***N*-[1-*trans*-[2-(2-Furyl)cyclopropyl]methyl]-*N*-hydroxyurea (14a)** was prepared using method 1a from *trans*-2-(2-furyl)-1-cyclopropyl carboxaldehyde¹³: mp 108-110 °C; ¹H NMR (300 MHz, DMSO-d₆) δ 0.86 (m, 2H), 1.40 (m, 1H), 1.87 (m, 1H), 3.35 (m, 2H), 6.03 (d, 1H, J = 3.5 Hz), 6.30 (m, 3H), 7.42 (m, 1H), 9.33 (s, 1H); MS (DCI-NH₃) m/z 197(M+H)⁺. Anal. (C₉H₁₂N₂O₃) C, H, N.

***N*-[1-*trans*-[2-(2-Furfuryl)cyclopropyl]ethyl]-*N*-hydroxyurea (14b)** was prepared using method 1a from *trans*-2-(2-furyl)-1-cyclopropyl methyl ketone¹³: oil; ¹H NMR (300 MHz, DMSO-d₆) (mixture of 4 diastereomers) δ 0.83 (m, 2H), 1.12 (m, 3H), 1.21-1.47 (m, 1H), 1.83-1.96 (m, 1H), 3.61 (m, 1H), 5.94-6.07 (m, 1H), 6.23-6.36 (m, 3H), 7.37-7.49 (m, 1H), 9.01 and 9.03 and 9.04 and 9.06 (s, 1H); MS (DCI-NH₃) m/z 211 (M+H)⁺. Anal. (C₁₀H₁₄N₂O₃•0.5H₂O) Calcd N, 12.77 ; Found: N, 12.13.

***N*-[1-*trans*-[2-(3-Furyl)cyclopropyl]methyl]-*N*-hydroxyurea (14c)** was prepared using method 1a from *trans*-2-(3-furyl)-1-cyclopropyl carboxaldehyde¹³: mp 108.5-110.5 °C; ¹H NMR (300 MHz, DMSO-d₆) δ 0.69 (m, 1H), 0.77 (m, 1H), 1.19 (m, 1H), 1.63 (m, 1H), 3.31 (d, 2H, J = 7 Hz), 6.25 (m, 1H), 6.28 (bs, 2H), 7.44 (bs, 1H), 7.51 (t, 1H, J = 2 Hz), 9.28 (s, 1H); MS (DCI-NH₃) m/z 197 (M+H)⁺. Anal. (C₉H₁₂N₂O₃) C, H, N.

***N*-[1-*trans*-[2-(3-Furyl)cyclopropyl]ethyl]-*N*-hydroxyurea (14d)** was prepared using method 1a from *trans*-2-(3-furyl)-1-cyclopropyl methyl ketone¹³: mp 128-130 °C; ¹H NMR (300 MHz, DMSO-d₆) (90:10 ratio of diastereomers) δ 0.70 (m, 2H), 1.11 (d, 3H, J = 7 Hz), 1.18 (m, 1H), 1.70 (m, 1H), 3.56 (m, 1H), 6.24 (m, 1H), 6.30 (bs, 2H), 7.39 (m, 1H), 7.49 (t, 1H, J = 2 Hz), 8.96 and 8.97 (s, 1H); MS (DCI-NH₃) m/z 211 (M+H)⁺. Anal. (C₁₀H₁₄N₂O₃) C, H, N.

***N*-[1-*trans*-[2-(3-Phenoxyphenyl)cyclopropyl]methyl]-*N*-hydroxyurea (14e)** was prepared using method 1a from *trans*-2-(3-phenoxyphenyl)-1-cyclopropyl carboxaldehyde¹³: mp 81.5-83.0 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 0.82-0.95 (m, 2H), 1.32 (m, 1H), 1.85 (m, 1H), under DMSO (2H), 6.27 (bs, 2H), 6.73 (m, 2H), 6.83 (d, 1H, *J* = 8 Hz), 6.99 (m, 2H), 7.13 (t, 1H, *J* = 7.5 Hz), 7.24 (t, 1H, *J* = 7.5 Hz), 7.48 (m, 2H), 9.30 (s, 1H); MS (DCI-NH₃) *m/z* 299 (M+H)⁺. Anal. (C₁₇H₁₈N₂O₃) C, H, N.

***N*-[1-*trans*-[2-(3-Phenoxyphenyl)cyclopropyl]ethyl]-*N*-hydroxyurea (14f)** was prepared using method 1a from *trans*-2-(3-phenoxyphenyl)-1-cyclopropyl methyl ketone¹³: mp 132-134 °C; ¹H NMR (300 MHz, DMSO-*d*₆) (85:15 mixture of diastereomers) δ 0.86 (t, 2H, *J* = 7 Hz), 1.13 (d, 3H, *J* = 7 Hz), 1.33 (m, 1H), 1.92 (m, 1H), 3.62 (m, 1H), 6.27 (bs, 2H), 6.71 (m, 2H), 6.82 (d, 1H, *J* = 8 Hz), 6.99 (m, 2H), 7.09-7.25 (m, 2H), 7.39 (m, 2H), 8.98 & 9.00 (s, 1H); MS (M+H)⁺=313; Anal. (C₁₈H₂₀N₂O₃) C, H, N.

***N*-Hydroxy-*N*-[3-(3-phenoxyphenyl)-2-propynyl]urea (15a)**. 3-Phenoxyphenylacetylene was prepared from 3-phenoxybenzaldehyde by the Corey-Fuchs procedure.¹⁴ The acetylene was treated with *n*-butyllithium in THF and reacted with acetaldehyde to give 3-(3-phenoxyphenyl)-2-propynol. This alcohol was converted to **15a** using method 6: mp 139-141 °C; ¹H NMR (DMSO-*d*₆) δ 4.30 (s, 2H), 6.57 (s, 2H), 6.93 (m, 1H), 7.05 (m, 3H), 7.19 (m, 2H), 7.41 (m, 3H), 9.59 (s, 1H); MS (DCI-NH₃) *m/z* 300 (M+NH₄)⁺, 283 (M+H)⁺. Anal. (C₁₆H₁₄N₂O₃) C, H, N.

***N*-Hydroxy-*N*-[4-(3-phenoxyphenyl)-3-butyn-2-yl]urea (15b)** was prepared from 3-phenoxyphenylacetylene and acetaldehyde as described for **15a**: mp 110-115 °C; ¹H NMR (DMSO-*d*₆) δ 1.33 (d, 3H, *J* = 7 Hz), 5.10 (q, 1H, *J* = 7 Hz), 6.52 (br s, 2H), 6.91 (m, 1H), 7.05 (m, 3H), 7.18 (m, 2H), 7.41 (m, 3H), 9.32 (s, 1H), IR (KBr) 3300, 3200, 1665, 1590, 1580, 1485, 1220 cm⁻¹; MS (DCI-NH₃) *m/z* 314 (M+NH₄)⁺, 297 (M+H)⁺. Anal (C₁₇H₁₆N₂O₃•0.25H₂O) C, H, N.

***N*-Hydroxy-*N*-[4-[3-(4-fluorophenoxy)phenyl]-3-butyn-2-yl]urea (15c).** 3 - (4-fluorophenoxy)benzaldehyde was prepared as described for 3-phenoxybenzaldehyde in ex. 4 h. 3-(4-Fluorophenoxy)phenylacetylene was prepared from 3-(4-fluorophenoxy)benzaldehyde as described for **15a** and converted to **15c** as described for **15b**: mp 139-140 °C; ¹H NMR (DMSO-d₆) δ 1.33 (d, J = 7 Hz, 3H), 5.10 (q, J = 7 Hz, 1H), 6.55 (s, 2H), 6.87 (m, 1H), 7.03 (m, 1H), 7.13 (m, 3H), 7.25 (t, J = 8 Hz, 1H), 7.37 (t, J = 8 Hz, 1H), 9.33 (s, 1H); MS (DCI-NH₃) m/z 332 (M+NH₄)⁺, 315 (M+H)⁺. Anal. (C₁₇H₁₅FN₂O₃) C, H, N.

***N*-[4-(3-Furyl)-3-butyn-2-yl]-*N*-hydroxyurea (15d)** was prepared from 3-ethynylfuran as described for **15b**: mp 152-154 °C; ¹H NMR (DMSO-d₆) δ 1.33 (d, J = 7 Hz, 3H), 5.09 (q, J = 7 Hz, 1H), 6.51 (s, 2H), 6.55 (m, 1H), 7.7 (m, 1H), 7.95 (m, 1H), 9.31 (s, 1H); MS (DCI-NH₃) m/z 212 (M+NH₄)⁺, 195 (M+H)⁺. Anal (C₉H₁₀N₂O₃• 0.25H₂O) Calcd H, 5.32 ; Found: H, 5.86.

***N*-[4-(2-Furyl)-3-butyn-2-yl]-*N*-hydroxyurea (15e)** was prepared from 2-ethynylfuran as described for **15b**: mp 141-142 °C; ¹H NMR (DMSO-d₆) δ 1.35 (d, J = 7 Hz, 3H), 5.15 (q, J = 7 Hz, 1H), 6.52 (dd, J = 1.5, J=3 Hz, 1H), 6.58 (s, 2H), 6.72 (d, J = 4.5 Hz, 1H), 7.68 (m, 1H), 9.38 (s, 1H); MS (DCI-NH₃) m/z 195 (M+H)⁺. Anal (C₉H₁₀N₂O₃• 0.25H₂O) C, H, N.

***N*-[4-(2-Benzo[*b*]thienyl)-3-butyn-2-yl]-*N*-hydroxyurea(15f).** 2 - Ethynylbenzo[*b*]thiophene, prepared from benzo[*b*]thiophene-2-carboxaldehyde¹⁵ and converted to **15f** as described for **15b**: mp 168-169 °C; ¹H NMR (300 MHz, DMSO-d₆) δ 1.40 (d, J = 7 Hz, 3H), 5.20 (q, J = 7 Hz, 1H), 6.61 (s, 2H), 7.42 (m, 2H), 7.61 (s, 1H), 7.85 (m, 1H), 7.95 (m, 1H), 9.42 (s, 1H); MS (DCI-NH₃) m/z 261 (M + H)⁺. Anal (C₁₃H₁₂N₂O₂S) Calcd C, 59.98. Found: C, 59.49.

***N*-Benzo[*b*]thien-2-ylmethyl-*N*-hydroxyurea (16a)** was prepared using method 1a from benzo[*b*]thiophene-2-carboxaldehyde¹⁵: mp 170.5-172 °C; ¹H NMR (300 MHz, DMSO-d₆) δ 4.74 (s, 2H), 6.47 (brs, 2H), 7.23 (m, 2H), 7.78 (m, 1H), 7.90 (m, 1H), 9.53

(s, 1H); MS m/z (DCI-NH₃): 240 (M+NH₄)⁺, 223 (M+H)⁺. Anal. (C₁₀H₁₀N₂O₂S) C, H, N.

(R) and (S) -N-(1-Benzo[b]thien-2-ylethyl)-N-hydroxyurea (16b) (16c). A diastereomeric mixture of *O*-(*R*)-*O*-methylmandelate derivatives were prepared from **1a** (0.68 g, 4.1 mmol) by the method of Trost¹⁶ and after HPLC separation (eluting with 1:1 ether, CH₂Cl₂) provided 0.597 g (37%) of the faster moving diastereomer, 0.712 g (46%) of the slower moving diastereomer and 0.243 g (15%) of a mixture of diastereomers. X-ray analysis showed the faster moving diastereomer to have the (R,R) configuration. The diastereomers were treated separately with K₂CO₃ in methanol to give: R isomer (**16b**) of **1a**: mp 150-151 °C; [α]_D²³ = +44.5 °(C = 1.00 MeOH)

Anal. (C₁₁H₁₂N₂O₂S): C, H, N.

S isomer (**16c**) of **1a**: mp 150-151 °C; [α]_D²³ = -46.8 °(C = 1.02 MeOH)

Anal. (C₁₁H₁₂N₂O₂S): C, H, N.

N-[3-[5-(4-Fluorophenoxy)-2-furyl]-1,1-dimethyl-2-propynyl]-N-hydroxyurea (17e).

To a stirred solution of 4-[5-(4-fluorophenoxy)-2-furyl]-3-butyn-2-ol¹⁸ (8 g, 32.5 mmol) in CH₂Cl₂ (200 mL) was added MnO₂ (22.62 g, 260 mmol) in portions over 2 h. The mixture was heated to 40 °C for 0.5 h and cooled. The mixture was filtered and concentrated. The residue was purified by flash column chromatography (eluted with 10 % ethyl acetate / hexanes) to give 5.6 g (70%) of the desired ketone. Treatment of this ketone in THF with methyl magnesium bromide provided 3-[5-(4-fluorophenoxy)-2-furyl]-1,1-dimethyl-2-propynol in 79 %. This alcohol was converted to **17e** using method 7: mp 105-106 °C; ¹H NMR (300 MHz, DMSO-d₆) δ 1.58 (s, 6H), 5.77 (d, J=4 Hz, 1H), 6.45 (brs, 2H), 6.68 (d, J=4 Hz, 1H), 7.15-7.30 (m, 4H), 9.44 (s, 1H); MS m/z (DCI-NH₃): 319 (M+H)⁺. Anal. (C₁₆H₁₅FN₂O₄) C, H, N.

N-[3-[5-(4-Fluorophenoxy)-2-furyl]-1-spirocyclobutyl-2-propynyl]-N-hydroxyurea (17f). 5-(4-Fluorophenoxy)-2-furylethyne¹⁸ was metalated with LDA and reacted with cyclobutanone to give 3-[5-(4-fluorophenoxy)-2-furyl]-1-spirocyclobutyl-2-propynol.

This alcohol was converted to **17f** using method 7: mp 160-161 °C; ¹H NMR (300 MHz, DMSO-d₆) δ 1.79-1.99 (m, 2H), 2.66 (m, 2H), 2.57 (m, 2H), 5.78 (d, J=4 Hz, 1H), 6.49 (bs, 2H), 6.73 (d, J=4 Hz, 1H), 7.16-7.30 (m, 4H), 9.46 (s, 1H); MS m/z (DCI-NH₃): 331 (M+H)⁺. Anal. (C₁₇H₁₅FN₂O₄•0.25 H₂O) C, H, N.

***N*-[1-*trans*-[2-[5-(4-Fluorophenoxy)-2-furyl]cyclopropyl]methyl]-*N*-hydroxyurea**

(17h). *Trans*-2-(5-(4-fluorophenoxy)-2-furyl)-1-cyclopropyl carboxaldehyde was prepared from 5-(4-fluorophenoxy)-furan-2-carboxaldehyde¹⁸ by the method¹³ reported for *trans*-2-(2-furyl)-1-cyclopropyl carboxaldehyde (see **14a**). This aldehyde was converted to **17h** using method 1: oil; ¹H NMR (300 MHz, DMSO-d₆) δ 0.83 (m, 2H), 1.36 (m, 1H), 1.79 (m, 1H), 3.33 (m, 2H, obscured by H₂O), 6.03 (d, 1H, J = 4 Hz), 6.28 (bs, 2H), 7.07 (m, 2H), 7.23 (m, 2H), 9.31 (s, 1H); MS (DCI-NH₃) m/z 324 (M+NH₄)⁺, 307 (M+H)⁺. Anal. (C₁₅H₁₅FN₂O₄) Calcd C, 58.82, H, 4.49, N, 9.15; Found: C, 58.48, H, 5.36, N, 8.51.

5-(4-Fluorophenoxy)fur-2-ylmethyloximyl-*O*-2-ethyl-*N*-hydroxyurea (17i). Under a nitrogen atmosphere was dissolved lithium metal (0.07 g, 10 mmol) in MeOH (15 mL) and EtOH (15 mL).⁷ To this stirred solution was added acetone oxime (2.0 g, 27 mmol) and the mixture heated to 60 °C; Ethylene oxide (2.2 mL, 46 mmol) was added and the mixture was stirred 1 h. Additional ethylene oxide (1.0 mL) was added and the reaction was heated 1 h. The mixture was cooled, excess acetic acid was added and concentrated. The residue was purified by column chromatography (SiO₂, eluting with 20% ethyl acetate / hexanes and 50% ethyl acetate / hexanes) to give 2.08 g of 2-propyloximyl-2-*O*-ethanol as a clear oil. This material was heated to reflux in 6 N HCl for 3 h. The mixture was cooled and concentrated to give 0.48 g (15%) of *O*-(ethan-1-ol)hydroxylamine hydrochloride. 5-(4-Fluorophenoxy)fur-2-ylmethyloximyl-*O*-2-ethan-1-ol was prepared from 5-(4-fluorophenoxy)furan-2-carboxaldehyde¹⁸ and *O*-(ethan-1-ol)hydroxylamine hydrochloride as described in method 1a. This hydroxyethyl derivative was converted using method 9 to give **17i** as a 2/1 mixture of *Z/E* isomers: oil; ¹H NMR (300 MHz,

DMSO- d_6) δ 3.58 (t, J=6 Hz, 0.66H), 3.67 (t, J=6 Hz; 1.34 H), 4.15 (t, J=6 Hz, 0.66H), 4.26 (t, J=6 Hz, 1.34H), 5.82 (d, J= 4 Hz, 1H), 6.30 (bs, 2H), 6.79 (d, J=4 Hz, 0.33H), 7.20-7.33 (m, 4.67H), 7.46 (s, 0.67H), 8.00 (s, 0.33H), 9.38 (s, 0.33H), 9.42 (s, 0.67H); MS m/z (DCI-NH₃): 341 (M+NH₄)⁺, 324 (M+H)⁺. Anal. (C₁₄H₁₄FN₃O₅) C, H, N.

5-(4-Fluorophenoxy)fur-2-ylmethyl-E-oximyl-O-2-(1-methyl)ethyl-N-hydroxyurea

(17j). *O*-(1-Methylethan-1-ol)hydroxylamine hydrochloride was prepared as described in example **17i** using propylene oxide instead of ethylene oxide. This material was converted to **17j** using the procedure described in example **17i**. A single isomer was purified by chromatography and shown by X-ray analysis to have the E oxime geometry: mp 124-124.5 °C; ¹H NMR (300 MHz, DMSO- d_6) δ 0.99 (d J=6 Hz, 3H), 3.87 (dd, J=6 Hz, J=11 Hz, 1H), 4.10 (dd, J=7.5 Hz, J=11 Hz, 1H), 4.40 (m, 1H), 5.79 (d, J=4 Hz, 1 H), 6.27 (bs, 2H), 6.78 (d, J=4 Hz, 2H), 7.20-7.33 (m, 4H), 7.97 (s, 1H), 9.01 (s, 1H). M/z (CI-NH₃): 338 (M+H)⁺. Anal. (C₁₅H₁₆FN₃O₅) C, H, N.

(Z)-N-[2-Fluoro-3-[5-(4-fluorophenoxy)-2-furyl]-1-methyl-2-propenyl]-N-

hydroxyurea (17k). To a 0 °C stirred suspension of 0.7g NaH (0.7 g, 23.3 mmol, 80%) was added ethyl (diethoxyphosphoryl)fluoroacetate¹⁷ (5.64 g, 23.3 mmol). The reaction was stirred 15 min and 5-(4-fluorophenoxy)-2-furfural (4.0 g, 19.4 mmol) in 3 mL THF was added. The reaction was stirred for 1 h at room temperature and concentrated. The residue was purified by flash column chromatography (SiO₂, eluting with 20 % ethyl acetate / hexanes) to give 1.09 g (19%) of the E [cis (H-F)] and 2.45 g (45%) of the Z [trans (H-F)] isomers. Z isomer: ¹H NMR (300 MHz) (CDCl₃) δ 1.35 (t, J =6.8 Hz, 3H), 4.31 (q, J = 6.8, 7.7 Hz, 2H), 5.56 (d, J= 3.4 Hz, 1H), 6.81 (d, J =33.5 Hz, 1H), 6.81 (d, J= 3.4 Hz, 1H), 7.03-7.26 (m, 4H); MS (DCI/NH₃) m/z 312 (M+NH₄)⁺, 295 (M+H)⁺.

To a stirred isopropyl alcohol (10 mL) solution of (Z) ethyl 2-fluoro-3-[5-(4-fluorophenoxy)-2-furyl] acrylate (2.59 g, 8.81 mmol) was added 15.4 mL of 1M LiOH (15.4 mmol, 1 M aqueous). The reaction was stirred 1 h and poured into cold 1N H₃PO₄ and extracted with ethyl acetate. The combined organic extracts were washed with brine,

dried (MgSO_4) and evaporated to yield 2.20 g (94 %) of the desired acid: ^1H NMR (300 MHz) (CDCl_3) δ 5.58 (d, $J=3.75$ Hz, 1H), 6.94 (d, $J= 32.25$ Hz, 1H), 6.90 (d, $J=3.75$ Hz, 1H), 7.05-7.13 (m, 4H); MS (DCI/ NH_3) m/z 284 ($\text{M}+\text{NH}_4$) $^+$, 267 ($\text{M}+\text{H}$) $^+$.

This acid was converted to (Z) 2-fluoro-1-[5-(4-fluorophenoxy)-2-furyl]buten-3-one by conversion to the acid chloride followed by *N,O*-dimethylhydroxylamine (76%) and methyl magnesium bromide (32%). This methyl ketone was converted to **17k** using method 1a: mp 160-162 °C; ^1H NMR (300 MHz) (DMSO- d_6) δ 1.24 (d, $J=7.5$ Hz, 3H), 4.97 (m, 1H), 5.78 (d, $J= 39.0$ Hz, 1H), 5.81 (d, $J= 3$ Hz, 1H), 6.48 (m, 3H), 7.14 (m, 2H), 7.25 (m, 2H), 9.24 (s, 1H); MS (DCI- NH_3) m/z 284 ($\text{M}+\text{NH}_4$) $^+$, 267 ($\text{M}+\text{H}$) $^+$.

Anal. ($\text{C}_{15}\text{H}_{14}\text{F}_2\text{N}_2\text{O}_4$): C, H, N.

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