Experimental and analytical data

N-hydroxy-3-(4-methoxybenzenesulfonyl)-4-phenylbutyramide (compound **2**)

Step (a), scheme 1
To a solution of 12.1 mL (45.8 mmol) of t-butyl diethylphosphonoacetate in 100 mL of THF under argon at 25 °C was added 1.83 g (45.8 mmol) of 60% NaH in oil dispersion. The reaction mixture was stirred at 25 °C for 45 min and 5.4 mL (42 mmol) of phenylacetaldehyde was added. After 30 min at 25 °C the reaction was partitioned between 1N HCl and ethyl ether. The organic layer was dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. Purification by flash silica gel chromatography afforded 6.3 g (69%) of the α,β-unsaturated ester as a yellow oil.

Step (c), scheme 1
A solution of 6.3 g (29 mmol) of the t-butyl ester in 100 mL of CH_2Cl_2 and 30 mL of trifluoroacetic acid was stirred at 25 °C for 18 hours. The reaction was concentrated *in vacuo* to afford 4.67 g (100 %) of the α, β-unsaturated acid as a yellow crystalline solid.

Step (d), scheme 1
A mixture of 2.0 g (13 mmol) of the α, β-unsaturated acid, 1.8 mL (15 mmol) of 4-methoxybenzenethiol, and 0.4 mL (4 mmol) of piperidine was heated at 110 °C in a pressure vessel for 18 hours. The reaction was partitioned between ethyl ether and 1N HCl. The organic layer was dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. Purification by flash silica gel chromatography afforded 3.1 g (82%) of the thioether as a white crystalline solid.

Step (e), scheme 1
To a solution of 1.0 g (3.3 mmol) of the thioether in 30 mL of CH_2Cl_2 at 25 °C under argon was added 0.2 mL of DMF followed by 4.1 mL (8.3 mmol) of 2.0 M oxalyl chloride in CH_2Cl_2. After stirring at 25 °C for 1.5 hours, 2.1 mL (16 mmol) of O-trimethylsilylhydroxylamine was added and this was then stirred at 25 °C for 10 min. The reaction was partitioned between CH_2Cl_2 and 1N HCl. The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification by flash silica gel chromatography afforded 0.86 g (82%) of the hydroxamic acid as a yellow crystalline solid.

Step (f), scheme 1
To a solution of 0.86 g (2.7 mmol) of the hydroxamic acid in 50 mL of methanol at 0 °C was dropped in a solution of 2.5 g (4.1 mmol) of Oxone® dissolved in 15 mL of water. After stirring for 18 hours at 25 °C the reaction was concentrated *in vacuo*, then partitioned between ethyl acetate and water. The organic layer was dried over anhydrous Na_2SO_4 then concentrated *in vacuo*. Purification by flash silica gel chromatography and crystallization from CH_2Cl_2/hexanes afforded 0.38 g (40%) of N-hydroxy-3-(4-methoxybenzenesulfonyl)-4-phenylbutyramide as a white crystalline solid; mp 118-120 °C; ^1H NMR (DMSO-d_6) δ (TMS) 10.5 (s, 1H), 8.8 (s, 1H), 7.7-7.85 (d, 2H), 7.05-7.3

(m, 7H), 3.85 (s, 3H), 3.8-3.95 (m, 1H), 3.0-3.1 (m, 1H), 2.6-2.75 (m, 1H), 2.4-2.55 (m, 1H), 2.05-2.15 (m, 1H); MS (FAB) *m/e* 350 ($M+H^+$); Anal. ($C_{17}H_{19}NO_5S$) C, H, N.

N-hydroxy-3-(4-methoxybenzenesulfonyl)-5-phenylpentanamide (compound **3**)
Using the procedure for the preparation of compound **2** and substituting hydrocinnamaldehyde in the place of phenylacetaldehyde, produced N-hydroxy-3-(4-methoxybenzenesulfonyl)-5-phenylpentanamide as an off-white crystalline solid; mp 65-68 °C; ^1H NMR (DMSO-d_6) δ (TMS) 10.6 (s, 1H), 8.95 (s, 1H), 7.7-7.85 (d, 2H), 7.05-7.35(m, 7H), 3.45-3.6 (m, 1H), 3.85 (s, 3H), 2.45-2.8 (m, 3H), 2.2-2.35 (m, 1H), 1.85-2.1 (m, 1H), 1.6-1.8 (m, 1H); MS (FAB) *m/e* 364 ($M+H^+$); Anal. ($C_{18}H_{21}NO_5S$) C, H, N.

N-hydroxy-3-(4-methoxybenzenesulfonyl)-6-phenylhexanamide (compound **4**)
To a solution of 20 mL (40 mmol) of oxalyl chloride in 100 mL of CH_2Cl_2 at -78 °C under argon was added dropwise 5.7 mL (80 mmol) of DMSO. After stirring for 1 hour at -78 °C, 5.0 g (33 mmol) of 4-phenylbutanol dissolved in 20 mL of CH_2Cl_2 was added dropwise over 5 min. After stirring for 2 hours at -78 °C, 23 mL (166 mmol) of triethylamine was added dropwise over 5 min. The reaction was then stirred at -78 °C for 0.5 hours, 0 °C for 1 hour, and 25 °C for 1 hour. The reaction was partitioned between CH_2Cl_2 and 1N HCl. The organic layer was washed well with water, dried over anhydrous $MgSO_4$ and concentrated *in vacuo* to afford 5.0 g (100%) of 4-phenylbutrylaldehyde in the form of a yellow oil which was used without further purification.

Using the procedure for the preparation of compound **2** and using 4-phenylbutrylaldehyde (as prepared above) as the starting aldehyde, produced N-hydroxy-3-(4-methoxybenzenesulfonyl)-6-phenylhexanamide as a white foam; mp 43-46 °C; ^1H NMR (DMSO-d_6) δ (TMS) 10.55 (s, 1H), 8.85 (s, 1H), 7.65-7.8 (d, 2H), 7.05-7.35 (m, 7H), 3.9 (s, 3H), 3.45-3.6 (m, 1H), 2.4-2.65 (m, 3H), 2.05-2.2 (m, 1H), 1.3-1.85 (m, 4H); MS (FAB) *m/e* 378 ($M+H^+$); Anal. ($C_{19}H_{23}NO_5S$) C, H, N.

N-hydroxy-3-(4-methoxybenzenesulfonyl)-7-phenylheptanamide (compound **5**)
Oxidation of 5-phenylpentanol using the procedure used for the preparation of compound **4**, followed by step (a) scheme 1 described for the preparation of compound **2**, provided t-butyl 7-phenyl-hept-2-enoate.
Step (b), scheme 1
To a solution of 4-methoxybenzenethiol (1.5 g; 11 mmol) in THF (7 mL) was added n-BuLi (2.5 M in hexane; 0.3 mL; 0.7 mmol) at 0 °C under nitrogen. This mixture was added to a solution of t-butyl 7-phenyl-hept-2-enoate (2.0 g; 7.7 mmol) in THF (15 mL) at 0 °C and the reaction was allowed to warm and stir at 20 °C for 3 hours. The reaction was concentrated *in vacuo* and purified by column chromatography using 5% Et_2O/petroleum ether to obtain t-butyl 7-phenyl-3-phenylsulfanyl-heptanoate.
Continuing with steps (c, e-f) scheme 1 employed for the preparation of compound **2**, produced N-hydroxy-3-(4-methoxybenzenesulfonyl)-7-phenylheptanamide as a white foam; ^1H NMR (300 MHz, CD_3OD) δ 7.80 (d, J = 9.1 Hz, 2H), 7.25-7.20 (m, 2H),

7.15-7.08 (m, 5H), 3.89 (s, 3H), 3.61-3.53 (m, 1H), 2.64 (dd, J = 15.1, 5.0 Hz, 1H), 2.51 (t, J = 7.4 Hz, 2H), 2.24 (dd, J = 15.1, 8.2 Hz, 1H), 1.89-1.78 (m, 1H), 1.58-1.25 (m, 5H); MS (FAB) *m/e* 392 ($M+H^+$); Anal. ($C_{20}H_{25}NO_5S$) C, H, N.

N-hydroxy-3-(3,4-dimethoxybenzenesulfonyl)-7-phenylheptanamide (compound **6**)
Using the procedure for the preparation of compound **5** and substituting 3,4-dimethoxybenzenethiol for 4-methoxybenzenethiol, produced N-hydroxy-3-(3,4-dimethoxybenzenesulfonyl)-7-phenylheptanamide as a white solid; mp 157-159 °C; ^1H NMR (300 MHz, d_6-DMSO) δ 10.50 (s, 1H), 8.88 (s, 1H), 7.40 (d, J = 8.4 Hz, 1H), 7.06-7.30 (m, 7H), 3.82 (s, 3H), 3.80 (s, 3H), 3.50 (m, 1H), 2.40 (m, 2H), 2.11 (dd, J = 14.5, 8.9 Hz, 1H), 1.72 (m, 1H), 1.2-1.54 (m, 6H); MS (FAB) *m/e* 422 ($M+H^+$); Anal. ($C_{21}H_{27}NO_6S$) C, H, N.

N-hydroxy-3-(4-methoxybenzenesulfonyl)-3-methyl-7-phenylheptanamide (compound **7**)
Preparation of 6-phenyl-hexan-2-one:
To a solution of 2.0 g (11 mmol) of 5-phenylvaleric acid in 75 mL of CH_2Cl_2 at 0 °C under argon was added 2 drops of DMF followed by 7.0 mL (14 mmol) of oxalyl chloride. The reaction was stirred at 25 °C for 1 hour, then 1.4 g (14 mmol) of N,O-dimethylhydroxylamine hydrochloride and 2.7 mL (34 mmol) of pyridine were added sequentially and stirred for 72 hours at 25 °C. The reaction was partitioned between CH_2Cl_2 and 1N HCl. The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to give 2.5g (100%) of N-methoxy-N-methyl-6-phenylhexanamide as a yellow oil which was used without further purification.
To a solution of 2.5 g (11 mmol) of N-methoxy-N-methyl-6-phenylhexanamide in 50 mL of THF at -78 °C under argon was added 9.0 mL (12 mmol) of 1.4 M MeLi in diethyl ether. The reaction was stirred for 0.5 hours at -78 °C and was quenched by addition of 1N HCl. The reaction was partitioned between diethyl ether and water. The organic layer was dried over anhydrous $MgSO_4$ and concentrated *in vacuo* to give 2.0 g (100%) of 6-phenyl-hexan-2-one which was used without further purification.

Using the procedure for the preparation of compound **2** and substituting 6-phenyl-hexan-2-one (as prepared above) in the place of phenylacetaldehyde produced N-hydroxy-3-(4-methoxybenzenesulfonyl)-3-methyl-7-phenylheptanamide as a white solid; mp 52-55 °C; ^1H NMR ($CDCl_3$) δ (TMS) 9.35 (s, 1H), 7.6-8.1 (bs, 1H), 7.65-7.8 (d, 2H), 7.25-7.35 (m, 2H), 7.1-7.25 (m, 3H), 6.95-7.05 (d, 2H), 3.9 (s, 3H), 2.5-2.75 (m, 4H), 1.7-1.95 (m, 2H), 1.45-1.7 (m, 4H), 1.35 (s, 3H); MS (FAB) *m/e* 406 ($M+H^+$); Anal. ($C_{21}H_{27}NO_5S$) C,H,N.

(2R*, 3R*)-N-hydroxy-3-(4-methoxybenzenesulfonyl)-2-methyl-7-phenylheptanamide, (compound **8**)
t-Butyl phosphonoacetate (10.3 g, 40.7 mmol) was dissolved in THF (40 mL) and cooled to 0 °C. Sodium hexamethyldisilazane (43 mL, 1.0 M in THF) was added slowly and after 10 min methyl iodide (3.3 mL, 53 mmol) was added and the reaction was allowed to stir at 25 °C for 15 h. The reaction was diluted with ether and washed with 2N HCl, dried ($MgSO_4$) and concentrated *in vacuo* to provide t-butyl 2-diethylphosphonopropionate which was used without further purification.

Using the procedure for the preparation of compound **5** and substituting t-butyl 2-diethylphosphonopropionate (prepared above) in the place of t-butyl diethylphosphonoacetate, produced (2R*, 3R*)-N-hydroxy-3-(4-methoxybenzenesulfonyl)-2-methyl-7-phenylheptanamide, **8**, (contaminated with 10 % of the 2R*, 3S*-diastereomer); ^{1}H NMR (300 MHz, DMSO) δ 10.60 (s, 1H), 8.88 (bs, 1H), 7.76 (d, J = 8.7 Hz, 2H), 7.24 (t, J = 7.7 Hz, 2H), 7.16-7.12 (m, 3H), 7.06 (d, J = 7.0 Hz, 2H), 3.85 (s, 3H), 3.34-3.27 (m, 1H), 2.65-2.58 (m, 1H), 2.40-2.31 (m, 2H), 1.62-1.05 (m, 6H), 1.19 (d, J = 6.9 Hz, 3H); MS (FAB) *m/e* 406 ($M+H^+$); Anal. ($C_{21}H_{27}NO_5S$) C, H,N.

(2R*, 3S*)-N-hydroxy-3-(4-methoxybenzenesulfonyl)-2-methyl-7-phenylheptanamide, (compound **1**)

Diisopropylamine (58 mL, 410 mmol) was dissolved in THF (125 mL) and cooled to 0 °C. n-BuLi (160 mL, 400 mmol) was added over 15 min and after stirring 10 min at 0 °C, propionic acid (15.0 g, 200 mmol) was added over 20 min. The ice bath was then removed and the reaction was warmed to 50 °C. As the reaction thickened an additional 200 mL of THF was added to aid mixing. After a total of 45 min at the elevated temperature the reaction was again cooled to 0 °C and a solution of 5-phenylpentanal (26.0 g, 160 mmol) in THF (75 mL) was added dropwise over 2h. The reaction was stirred an additional 30 min and then the reaction was quenched by the addition of 2N HCl (400 mL). After shaking, the organic layer was separated, washed with brine and concentrated *in vacuo*. The crude reaction was purified by column chromatography using 1 to 3% MeOH/CH_2Cl_2 to obtain 13.5 g (36%) of the β-hydroxy acid, **9**, as a 1:1 mixture of diastereomers.

Step (a), scheme 2

3-Hydroxy-2-methyl-7-phenylheptanoic acid, **9**, (1.10 g, 4.7 mmol) was added to a solution of triphenylphosphine (1.94 g, 7.4 mmol) and Aldrithiol-2® (1.54 g, 7.0 mmol) in chloroform (45 mL). After stirring for 20 min the mixture was added slowly over 5 min to a heated suspension of $Hg(OSO_2CH_3)_2$ (3.6 g, 9.2 mmol) in CH_3CN (115 mL) using a 48 °C bath. After the completion of the addition, the reaction was heated for 1 min and then rapidly cooled to 25 °C. The reaction was filtered through celite, washed with CH_2Cl_2, concentrated *in vacuo* and purified by column chromatography using 20 % ether/pet ether to obtain 0.35 g (34%) of the faster eluting *anti*-isomer, **11**; ^{1}H NMR (300MHz, $CDCl_3$) δ 7.31–7.21 (m, 2H), 7.19–7.15 (m, 3H), 4.18–4.12 (m, 1H), 3.19 (dt, J = 7.6, 3.7 Hz, 1H), 2.63 (t, J = 7.6 Hz, 2H), 1.94–1.60 (m, 4H), 1.55–1.40 (m, 2H), 1.35 (d, J = 7.6 Hz, 3H) and 0.33 g (32%) of the slower eluting *syn*-isomer, **10**; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31-7.26 (m, 2H), 7.21-7.15 (m, 3H), 4.53-4.47 (m, 1H), 3.69 (dt, J = 7.8, 6.6 Hz, 1H), 2.62 (t, J = 7.6 Hz, 2H), 1.78-1.40 (m, 9H), 1.23 (d, J = 7.8 Hz, 3H).

Step (b), scheme 2

A solution of 1N NaOH (1.6 mL, 1.6 mmol) was added to a solution of 4-methoxybenzenethiol (0.32 g, 2.3 mmol) in iPrOH (2 mL) at 0 °C. This mixture was then added dropwise to a solution of β-lactone **10** (0.33 g, 1.5 mmol) in THF (3 mL) at °C and the reaction was stirred at room temperature for 1.5 h. The reaction was neutralized with

a solution of HCl(g) in ether, concentrated *in vacuo* and purified by flash column chromatography using 1-5 % MeOH/CH_2Cl_2 to provide 0.515 g (90%) of acid **12**.

Step (c), scheme 2

Oxalyl chloride (2M in CH_2Cl_2, 2.1 mL, 4.2 mmol) was added to a solution of carboxylic acid **12** (0.51 g, 1.4 mmol) in CH_2Cl_2 (8 mL) at 0 °C. The reaction was warmed to 25 °C, and after 25 min the reaction was concentrated *in vacuo* and azeotroped from chloroform. The residue was dissolved in CH_2Cl_2 (5 mL) and O-TMS hydroxylamine (0.42 g, 4 mmol) was added dropwise at 0 °C. After 10 min, 1N HCl (5 mL) and CH_2Cl_2 (5 mL) were added, and the reaction was vigorously stirred 2 min. The organic phase was separated and the aqueous phase was back-extracted twice. The combined organic phase was dried ($MgSO_4$) and concentrated *in vacuo* to yield 0.49 g (93%) of the hydroxamic acid as a white foam.

Step (d), scheme 2

The sulfide-hydroxamic acid from above (0.49 g, 1.3 mmol) was dissolved in MeOH (10 mL)/ THF (10 mL) and cooled to 0 °C. A solution of Oxone® (1.6 g, 2.6 mmol) in water (10 mL) was added dropwise over 2 min at 0 °C. After stirring 4h at 25 °C, the reaction was partitioned between CH_2Cl_2 and water. The aqueous layer was back-extracted, and the organic layers were combined, dried ($MgSO_4$) and concentrated *in vacuo* to yield 0.49 g (95%) of the sulfonyl hydroxamic acid, **1**, as a white foam; ^{1}H NMR (300 MHz, DMSO) δ 10.57 (s, 1H), 8.75 (bs, 1H), 7.76 (d, J = 8.6 Hz, 2H), 7.24 (t, J = 7.7 Hz, 2H), 7.16-7.13 (m, 3H), 7.06 (d, J = 7.0 Hz, 2H), 3.85 (s, 3H), 3.43-3.38 (m, 1H), 2.88-2.83 (m, 1H), 2.42-2.35 (m, 2H), 1.75-1.67 (m, 2H), 1.41-1.30 (m, 2H), 1.23-1.10 (m, 2H), 1.06 (d, J = 7.1 Hz, 3H); MS (FAB) *m/e* 406 ($M+H^+$); Anal. ($C_{21}H_{27}NO_5S$) C, H, N.