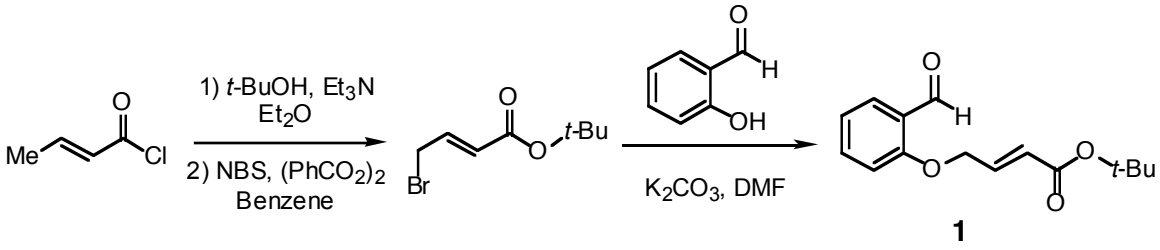
General Procedures. Proton NMR spectra were recorded on a Varian 400 spectrometer. Proton chemical shifts are reported in ppm (δ) relative to internal tetramethylsilane (TMS, δ 0.0 ppm), or with the solvent reference relative to TMS employed as an internal standard ($CDCl_3$, δ 7.26 ppm). Data are reported as follows: chemical shift (multiplicity [singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m)], coupling constants [Hz], integration). Carbon NMR spectra were recorded on a Varian 400 (100 MHz) or 500 (125 MHz) spectrometers with complete proton decoupling. Carbon chemical shifts are reported in ppm (δ) relative to TMS with the respective solvent resonance as the internal standard ($CDCl_3$, δ 77.0 ppm). All NMR spectra were acquired at ambient temperature. Analytical thin-layer chromatography (TLC) was performed using Silica Gel 60Å F254 precoated plates (0.25 mm thickness). TLC R_f values are reported. Visualization was accomplished by irradiation with a UV lamp and/or staining with $KMnO_4$, cerium ammonium molybdenate (CAM), or ninhydrin solutions. Flash column chromatography was performed using Silica Gel 60Å (32-63 micron). Optical rotations were recorded on a Rudolph Research Analytical Autopol IV Automatic polarimeter at the sodium D line (path length 50 mm). High resolution mass spectra were acquired in the Mass Spectrometry facility at Boston College (Chestnut Hill, MA). The method of ionization is indicated in parenthesis. Chiral Analytical normal phase HPLC was performed on a Hewlett-Packard 1100 Series chromatograph equipped with a diode array detector (214 nm and 254 nm).

All reactions were carried out in a nitrogen atmosphere employing oven-dried glassware. All solvents were distilled prior to use using the appropriate drying agents. Thiazolyl

alanine was either purchased from PepTech Corporation (Burlington, MA) or received as a donation from Synthetech Inc. (Albany, OR); all remaining amino acids and coupling reagents were purchased from Advanced ChemTech (Louisville, KY). All other chemicals were purchased form Aldrich Chemical Company (Milwaukee, WI); and solvents were purchased from Fisher Scientific.

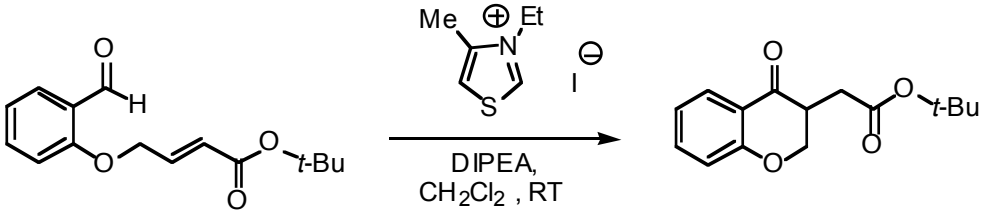
Preparation of *tert*-butyl substrate(s)



4-(2-Formyl-phenoxy)-but-2-enoic acid *tert*-butyl ester (1):[1] 4-Bromo-tert-butyl crontonate was synthesized by a known literature procedure.[2] **^{1}H NMR** ($CDCl_3$, 400 MHz) □ 10.56 (s, 1H), 7.86 (d, J=7.6 Hz, 1H), 7.55 (t, J=8.0 Hz, 1H), 7.07 (t, J=7.6 Hz, 1H), 7.00 (m, 1H), 6.95 (d, J=8.4, 1H), 6.13 (d, J=15.6 Hz, 1H), 4.81 (dd, J=2.4, 4.4 Hz, 2H), 1.50 (s, 9H); **^{13}C NMR** ($CDCl_3$, 100 MHz) □ 189.0, 164.8, 160.1, 139.7, 135.7, 128.5, 124.9, 124.1, 121.2, 112.4, 80.9, 66.9, 28.2; **TLC** R_f 0.17 (10% EtOAc/Hexanes); **IR** (neat, cm^{-1}) 2987, 2873, 1722, 1697, 1621; **Exact mass calcd for** $[C_{15}H_{18}O_4Na]+$ requires *m/z* = 285.1103, found *m/z* = 285.1108 (ESI).

[1] For the synthesis of **2** see: Ciganek, E. *Synthesis*, **1995**, 1311-1314.
[2] For the synthesis of **1** see: Orsini, F; Pelizzoni, F; Ricca, G. *Synthetic Communications*, **1982**, *12*, 1147-1154.

General Procedure for the Preparation of Racemic Product

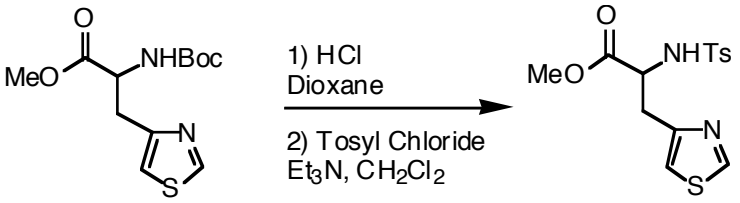


1 **2**

(4-Oxo-chroman-3-yl)-acetic acid *tert*-butyl ester (2): A flame dried 5 mL round bottom flask and stir bar, under an atmosphere of nitrogen, was charged with 4-(2-formyl-phenoxy)-but-2-enoic acid *tert*-butyl ester (0.15 mmol) followed by thiazolium salt (0.030 mmol). To the above reaction vessel was added methylene chloride (0.60 mL) via syringe, followed by diisopropyl ethylamine (DIPEA) (0.026 mL, 0.15 mmol). The reaction was stirred at ambient temperature under a positive pressure of nitrogen for 48 hours. The reaction was purified immediately by silica gel chromatography eluting with 5% EtOAc/hexanes to yield the desired product. **^{1}H NMR** ($CDCl_3$, 400 MHz) □ 7.90 (dd, J=1.6, 7.6 Hz, 1H), 7.48 (dt, J=7.2, 15.6 Hz, 1H), 7.02 (t, J=7.6 Hz, 1H), 6.97 (d, J=8.0 Hz, 1H), 4.58 (dd, J=5.2, 10.8 Hz, 1H), 4.29 (t, J=11.6 Hz, 1H), 3.28 (m, 1H), 2.85 (dd, J=4.8, 16.8 Hz, 1H), 2.33 (dd, J=8.0, 16.8 Hz, 1H), 1.47 (s, 9H); **^{13}C NMR** ($CDCl_3$, 100 MHz) □ 192.4, 170.3, 161.5, 135.7, 127.2, 121.3, 120.4, 117.7, 81.2, 70.3, 42.7, 31.7, 28.1; **TLC** R_f 0.57 (25% EtOAc/Hexanes); **IR** (neat, cm^{-1}) 2980, 2930, 1728, 1702, 1608, 1482; **HPLC** analysis – Chiracel AD column, 97:3 hexane:isopropanol, 1.0 mL/min. t_r=16.7 minutes, t_r=18.5 minutes. **Exact mass calcd for** $[C_{15}H_{18}O_4Na]+$ requires *m/z* = 285.1103. found *m/z* = 285.1103 (ESI).

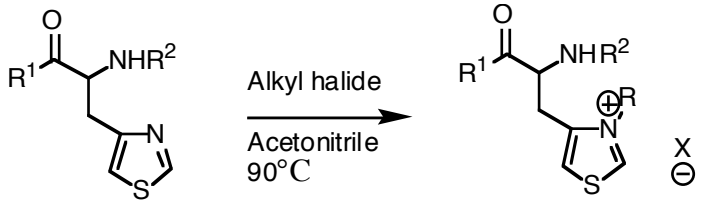
General Procedures for the preparation of Catalysts:

Representative Sulfonylation Procedure

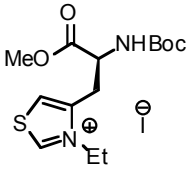


***N*$^{\alpha}$-(4-methylphenylsulfonyl)-l-thiazolyl alanine methyl ester:** A 25 mL round bottom flask with a stir bar was charged with Boc-thiazolyl alanine methyl ester (0.079 g, 0.27 mmol) and 5 mL of dioxane. HCl (g) was bubbled through the solution until a white solid began to precipitate. Once the bubbling ceased, the flask was capped with a septum vented with a small-gauged needle through the septum. After stirring vigorously for thirty minutes, the dioxane was removed to deliver thiazolyl alanine di-hydrochloride as a white solid. The solid was dried under vacuum for 4h. The salt was suspended in 5 mL of dry methylene chloride and treated with triethylamine (0.19 mL, 1.36 mmol) and *p*-toluenesulfonyl chloride. The reaction was stirred under nitrogen for 12h at ambient temperature. The reaction mixture was transferred to a separatory funnel and diluted with 20 mL of methylene chloride, washed with water (2 x 25 mL), sat. $NaHCO_3$ (2 x 25 mL), water (25 mL), brine (25 mL), dried over Na_2SO_4, and filtered. The solvent was removed under reduced pressure to afford a brown solid. Purification using silica gel chromatography eluting with 10%-40% ethyl acetate/hexanes delivered the desired product as a white solid (0.064 g, 70% yield).

General Method for Alkylation of Thiazolyl alanine Derivatives.

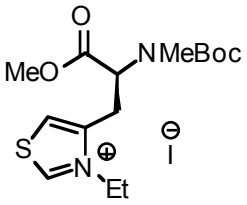


To a sealed tube was added thiazolyl alanine (peptide or modified amino acid) (100 mg), 1 mL of acetonitrile and 2 mL of alkyl halide. The tube was sealed tightly and heated to 90 °C for 48h or until complete by TLC. The reaction mixture was cooled to ambient temperature and then loaded directly onto a silica gel column and eluted with 250 mL of 50% ethyl acetate/hexanes to remove the alkyl halide. The catalyst was then eluted with 10% MeOH/CH_2Cl_2 and is UV-active and stains with iodine-silica gel. Isolated yield ranges from 35-50%.



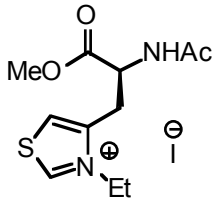
4a

N-Boc-3-ethylthiazolyl-3-ium alanine methyl ester; iodide (4a): ^{1}H NMR ($CDCl_3$, 400 MHz) 10.72 (s, 1H), 8.14 (s, 1H), 5.88 (bd, J=7.2 Hz, 1H), 4.71 (m, 2H), 3.82 (s, 3H), 3.55 (m, 2H), 1.74 (t, 14.4 Hz, 3H), 1.40 (s, 9H); **^{13}C NMR** ($CDCl_3$, 100 MHz) 170.5, 158.9, 155.5, 145.7, 124.0, 80.9, 53.3, 52.1, 49.3, 30.1, 28.2, 15.5; **TLC** R_f 0.32 (10% MeOH/CH_2Cl_2); **Exact Mass calcd for** $[C_{14}H_{23}N_2O_4S]+$ requires *m/z* = 315.1379, found *m/z* = 315.1372 (ESI).



4b

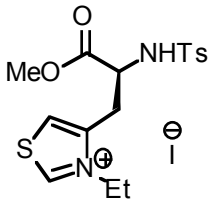
N-Boc-N-methyl-3-ethylthiazolyl-3-ium alanine methyl ester; iodide (4b): ^{1}H NMR ($CDCl_3$, 400 MHz) □ 10.83 (s, 1H), 8.20 (s, 1H), 4.92 (m, 1H), 4.75 (m, 2H), 3.77 (s, 3H), 3.62 (m, 1H), 3.48 (m, 1H), 2.92 (s, 3H), 1.73 (t, J=7.2 Hz, 3H), 1.44 (s, 9H); **^{13}C NMR** ($CDCl_3$, 100 MHz) □ 170.0, 159.0, 155.9, 146.0, 123.1, 81.4, 58.5, 52.9, 49.5, 34.1, 28.3, 27.4, 15.7; **TLC** R_f 0.57 (10% MeOH/CH_2Cl_2); **Exact Mass calcd for** $[C_{15}H_{25}N_2O_4S]$+ requires *m/z* = 329.1235, found *m/z* = 329.1529 (ESI).



4c

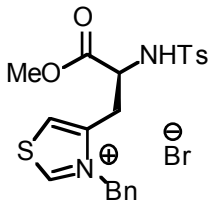
N-Acetyl-3-ethylthiazolyl-3-ium alanine methyl ester; iodide (4c): ^{1}H NMR ($CDCl_3$, 5% CD_3OD, 400 MHz) □ 10.18 (d, J=2.8 Hz, 1H), 8.19 (d, J=7.6 Hz, 1H), 8.12 (s, 1 H), 4.94 (m, 1H), 4.63 (q, J=7.2 Hz, 2H), 3.81 (s, 3H), 3.55 (m, 2H), 2.04 (s, 3H), 1.70 (t, J=7.6 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 5% CD_3OD, 100 MHz) □ 171.3, 169.9, 157.6, 145.1,

123.4, 53.0, 50.1, 49.0, 28.8, 22.6, 15.0; **TLC** R_f 0.25 (15% MeOH/CH_2Cl_2); **Exact Mass calcd for** $[C_{11}H_{17}N_2O_3SNa]+$ requires *m/z* = 257.0960. found *m/z* = 257.0962 (ESI).



4d

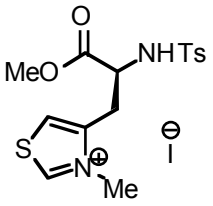
N-Tosyl-3-ethylthiazolyl-3-ium alanine methyl ester; iodide (4d): ^{1}H NMR (400 MHz, $CDCl_3$) 10.56 (d, J=2.8 Hz, 1H), 8.27 (d, J=2.4 Hz, 1H), 7.60 (d, J=8.4 Hz, 2H), 7.30 (d, J=8.0 Hz, 2H), 7.21 (s, 1H), 4.74 (m, 2H), 4.40 (br s, 1H), 3.59 (ABX, J_{ab1}=15.6, J_{ab2}=15.6, J_{ax}=9.23, J_{bx}=3.97 Hz, 2H), 3.50 (s, 3H), 2.42 (s, 3H), 1.65 (m, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) 169.5, 158.0, 144.8, 143.9, 136.6, 129.8, 127.2, 125.0, 54.5, 53.3, 49.4, 30.0, 21.6, 15.7; **TLC** R_f 0.20 (10% MeOH/CH_2Cl_2); **Exact Mass calcd for** $[C_{16}H_{21}N_2O_4S_2]+$ requires *m/z* = 369.0943. found *m/z* = 369.0946 (ESI).



4e

N-Tosyl-3-benzylthiazolyl-3-ium alanine methyl ester; bromide (4d): ^{1}H NMR (400 MHz, $CDCl_3$) 8.64 (d, J = 1.6 Hz, 1H), 8.40 (s, 1H), 7.96-7.88 (m, 3H), 7.77 (dd, J=8.9,

2.2 Hz, 1H), 7.68-7.58 (m, 2H), 7.03 (d, J=1.2 Hz, 1H), 6.00 (d, J=8.79 Hz, 1H), 4.4 (ddd, J=14.6, 8.8, 5.9 Hz, 1H), 3.42 (s, 3H), 3.25 (dq, J=14.7, 5.9 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) 170.8, 152.7, 151.8, 136.5, 134.4, 131.7, 129.7, 129.0, 128.6, 128.2, 127.6, 127.3, 122.2, 115.9, 55.4, 52.4, 34.1; **TLC** R_f 0.38 (15% MeOH/CH_2Cl_2); **Exact mass calcd for** $[C_{21}H_{23}N_2O_4S_2]$+ requires *m/z* = 431.1099, found *m/z* = 431.1097 (ESI).



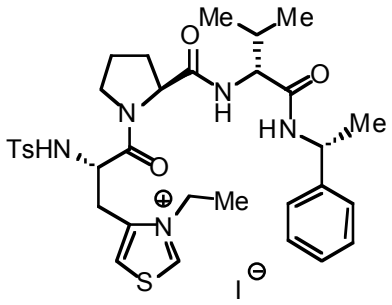
4f

N-Tosyl-3-methylthiazolyl-3-ium alanine methyl ester; iodide (4d): ^{1}H NMR (CD_3OD, 400 MHz) 8.12 (s, 1H), 7.72 (d, J=8.4 Hz, 2H), 7.40 (d, J=8.4 Hz, 2H), 4.46 (dd, J=9.2, 4.4 Hz, 1H), 4.28 (s, 3H), 3.54 (dd, J=14.0, 4.8 Hz, 1H), 3.53 (s, 3H), 3.31 (dd, J=15.2, 8.8 Hz, 1H), 2.47 (s, 3H); **^{13}C NMR** (CD_3OD, 100 MHz) 170.8, 147.2, 145.0, 144.5, 138.6, 130.6, 128.1, 124.9, 55.8, 53.3, 41.1, 31.4, 21.6; **TLC** R_f 0.33 (15% MeOH/CH_2Cl_2); **Exact Mass calcd for** $[C_{15}H_{19}N_2O_4S_2]$+ requires *m/z* = 355.0786, found *m/z* = 355.0772 (ESI); **X-ray crystal**: Obtained from MeOH/CH_2Cl_2. X-ray data available from Cambridge Crystallographic Data Centre (CCDC Number: 251033) as well as at the end of the supplementary information (p 19-27)

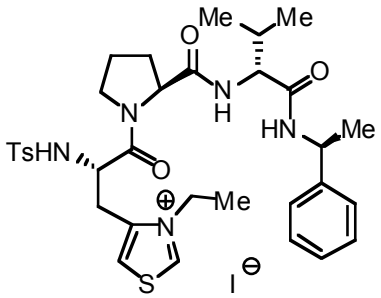
General Preparation of Peptides.

All peptides were prepared employing standard solution phase coupling techniques, utilizing commercially available Boc-protected amino acid derivatives with EDC (1-(3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride) as the coupling agent and HOBt (1-hydroxybenzotriazole) as a racemization suppressant.[3]

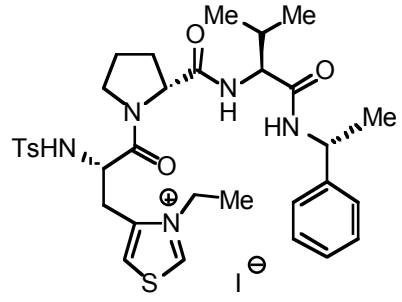
N-Terminal Peptides



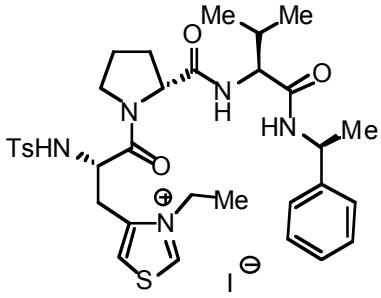
5a
$C_{33}H_{44}N_5O_5S_2^+$
Exact Mass: 654.2778
Mass Found (ESI): 654.2783



5b
$C_{33}H_{44}N_5O_5S_2^+$
Exact Mass: 654.2778
Mass Found (ESI): 654.2776



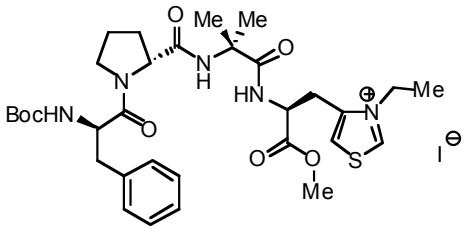
5c
$C_{33}H_{44}N_5O_5S_2^+$
Exact Mass: 654.2778
Mass Found (ESI): 654.2769



5d
$C_{33}H_{44}N_5O_5S_2^+$
Exact Mass: 654.2778
Mass Found (ESI): 654.2770

[3] Bodanszky, M.; Bodanszky, A. *The Practice of Peptide Synthesis*: Springer-Verlag: Berlin, 1993.

C-Terminal Peptides

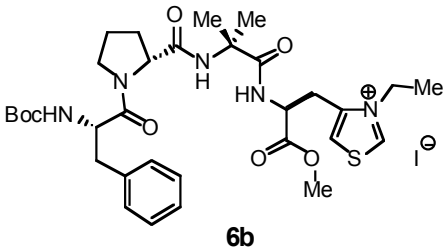


6a

$C_{32}H_{46}N_5O_7S^+$

Exact Mass: 644.3112

Mass Found (ESI): 644.3118

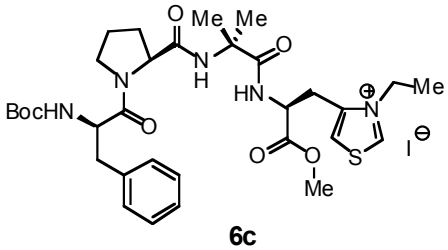


6b

$C_{32}H_{46}N_5O_7S^+$

Exact Mass: 644.3112

Mass Found (ESI): 644.3112

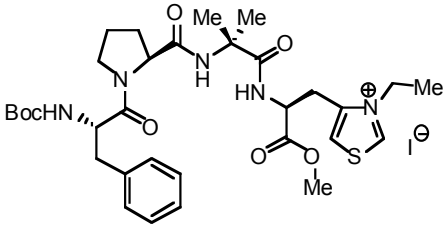


6c

$C_{32}H_{46}N_5O_7S^+$

Exact Mass: 644.3112

Mass Found (ESI): 644.3107



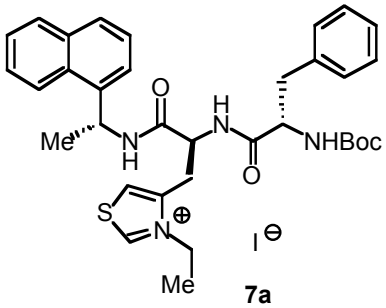
6d

$C_{32}H_{46}N_5O_7S^+$

Exact Mass: 644.3112

Mass Found (ESI): 644.3114

Dipeptides

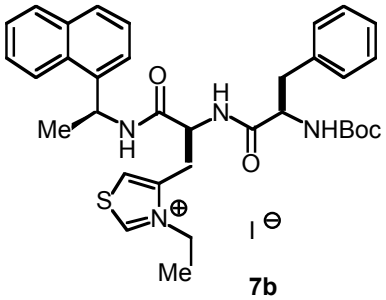


7a

$C_{34}H_{41}N_4O_4S^+$

Exact Mass: 601.2843

Mass Found (ESI): 601.2841

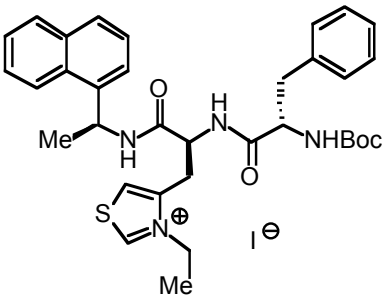


7b

$C_{34}H_{41}N_4O_4S^+$

Exact Mass: 601.2843

Mass Found (ESI): 601.2847

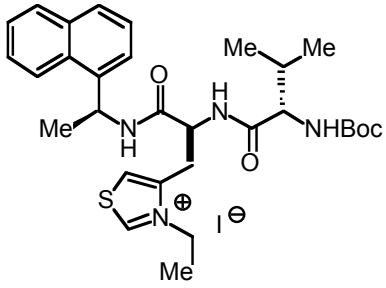


7c

$C_{34}H_{41}N_4O_4S^+$

Exact Mass: 601.2843

Mass Found (ESI): 601.2834

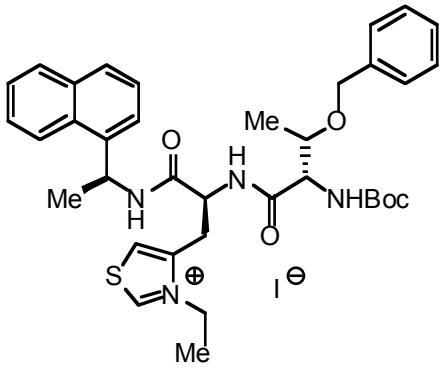


7d

$C_{30}H_{41}N_4O_4S^+$

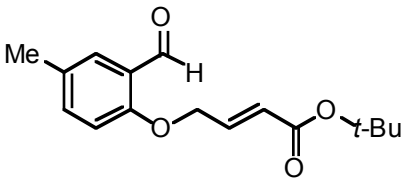
Exact Mass: 553.2843

Mass Found (ESI): 553.2847



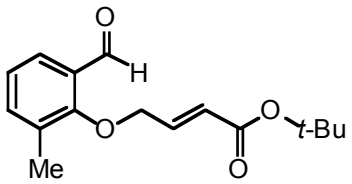
7e

4-[2-(3-Benzyloxy-2-tert-butoxycarbonylamino-butyrylamino)-2-(1-naphthalen-1-yl-ethylcarbamoyl)-ethyl]-3-ethyl-thiazol-3-ium; iodide (7e): ^{1}H NMR ($CDCl_3$, 400 MHz) □ 9.86 (s, 1H), 8.27 (d, J=8.3 Hz, 1H), 8.14 (bd, J=7.7 Hz, 1H), 7.88 (d, J=8.0 Hz, 1H), 7.79 (m, 1H), 7.66 (d, J=7.2 Hz, 1H), 7.59-7.46 (m, 4H), 7.36-7.27 (m, 3H), 6.75 (s, 1H), 6.00 (apparent pentet, 1H), 5.32 (bd, J=8.3 Hz, 1H), 4.92 (bd, J=5.6 Hz, 1H), 4.74-4.58 (m, 3H), 4.46 (m, 2H), 4.28 (dd, J=7.7, 2.8 Hz, 1H), 4.14 (s, 1H), 3.29 (ABX, J_{ax}=5.9, Hz, J_{bx}=7.3 Hz, J_{ab}=15.2 Hz, 2H), 1.67 (d, J=6.1 Hz, 3H), 1.52 (t, J=7.2 Hz, 3H), 1.47 (bs, 12H), 1.12 (d, J=5.9 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 100 MHz) □ 170.7, 167.1, 157.5, 145.3, 138.7, 137.7, 133.6, 130.7, 129.0, 128.8, 128.3, 127.8, 127.6, 127.5, 126.4, 125.7, 124.3, 123.3, 122.4, 74.5, 71.2, 58.7, 51.4, 50.0, 45.0, 30.2, 28.5, 21.0, 15.8, 15.3; **TLC** R_f 0.65 (15% MeOH/CH_2Cl_2); **Exact Mass Calcd for** $[C_{36}H_{45}NO_5S]$+ requires *m/z* = 645.111, found *m/z* = 645.3135 (ESI); **[□]$_D$**= 21.0 (*1.0*, CH_2Cl_2).



8a

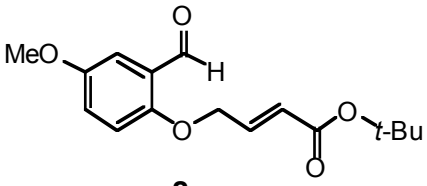
4-(2-Formyl-4-methyl-phenoxy)-but-2-enoic acid *tert*-butyl ester (8a): ^{1}H NMR ($CDCl_3$, 400 MHz) 10.53 (s, 1H), 7.65 (d, J=2.0 Hz, 1H), 7.34 (dd, J=8.4, 2.0 Hz, 1H), 7.00 (dt, J=15.7, 4.1 Hz, 1H), 6.84 (d, J=8.4 Hz, 1H), 6.12 (dt, J=15.8, 2.0 Hz, 1H), 4.77 (dd, J=4.1, 2.0 Hz, 2H), 2.32 (s, 3H), 1.50 (s, 9H); **^{13}C NMR** ($CDCl_3$, 100 MHz) 189.2, 164.9, 158.2, 146.9, 140.0, 136.3, 130.7, 128.5, 124.6, 124.0, 112.5, 80.7, 67.0, 28.2, 20.4; **IR** (film, cm^{-1}) 2760, 1715, 1690; **TLC** R_f 0.53 (25% EtoAc/Hexanes); **Exact Mass Calcd for** $[C_{16}H_{20}O_4Na]+$ requires *m/z* = 299.1259, found *m/z* = 299.1272 (ESI).



8b

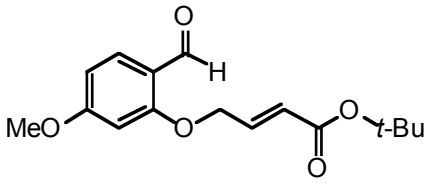
4-(2-Formyl-6-methyl-phenoxy)-but-2-enoic acid *tert*-butyl ester (8b): ^{1}H NMR ($CDCl_3$, 400 MHz) 10.30 (s, 1H), 7.67 (d, J=8.1 Hz, 1H), 7.45 (d, J=7.6 Hz, 1H), 7.16 (t, J=7.6 Hz, 1H), 6.98 (dt, J=15.7, 1.9 Hz, 1H), 4.58 (dd, J=4.3, 2.0 Hz, 2H), 2.32 (s, 3H), 1.51 (s, 9H); **^{13}C NMR** ($CDCl_3$, 100 MHz) 189.3, 164.8, 159.4, 140.0, 137.3,

132.0, 129.0, 126.5, 124.5, 123.7, 80.5, 73.5, 28.0, 15.6; **IR** (film, cm^{-1}) 2741, 1715, 1669; **TLC** R_f 0.60 (25% EtoAc/Hexanes); **Exact Mass Calcd for** $[C_{16}H_{20}O_4Na]+$ requires *m/z* = 299.1259, found *m/z* = 299.1254 (ESI).



8c

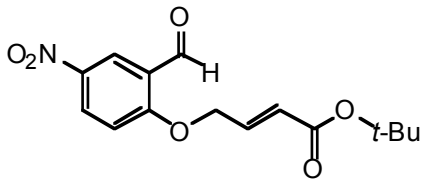
4-(2-Formyl-4-methoxy-phenoxy)-but-2-enoic acid *tert*-butyl ester (8c): ^{1}H NMR ($CDCl_3$, 400 MHz) 10.51 (s, 1H), 7.33 (d, J=3.3 Hz, 1H), 7.12 (dd, J=9.1, 3.3 Hz, 1H), 6.99 (dt, J=15.7, 4.2 Hz, 1H), 6.90 (d, J=9.0 Hz, 1H), 6.12 (dt, J=15.8, 1.8 Hz, 1H), 4.76 (dd, J=4.1, 2.0 Hz, 2H), 3.80 (s, 3H), 1.50 (s, 9H); **^{13}C NMR** ($CDCl_3$; 100 MHz) 188.7, 164.8, 158.8, 153.8, 140.0, 125.2, 123.9, 123.1, 114.3, 110.4, 80.7, 67.6, 55.7, 28.1; **IR** (film, cm^{-1}) 2753, 1715, 1690; **TLC** R_f 0.40 (25% EtoAc/Hexanes); **Exact Mass Calcd for** $[C_{16}H_{20}O_5Na]+$ requires *m/z* = 315.1208, found *m/z* = 315.1209 (ESI).



8d

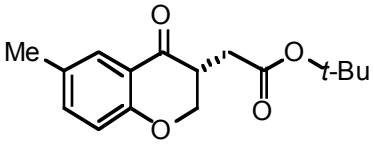
4-(2-Formyl-5-methoxy-phenoxy)-but-2-enoic acid *tert*-butyl ester (8d): ^{1}H NMR ($CDCl_3$, 400 MHz) 10.38 (s, 1H), 7.83 (d, J=11.7 Hz, 1H), 6.98 (dt, J=15.5, 3.9 Hz, 1H), 6.57 (dd, J=8.73, 2.2 Hz, 1H), 6.39 (d, J=2.2 Hz, 1H), 6.12 (dt, J=15.72, 2.0 Hz, 1H), 4.76 (dd, J=4.1, 2.0 Hz, 2H), 3.86 (s, 3H), 1.50 (s, 9H); **^{13}C NMR** ($CDCl_3$, 100

MHz) δ 187.5, 165.8, 164.8, 161.7, 139.5, 130.5, 124.1, 119.0, 106.1, 98.8, 80.8, 66.8, 55.6, 28.2; **IR** (film, cm^{-1}) 2766, 1715, 1686; **TLC** R_f 0.33 (25% EtoAc/Hexanes); **Exact Mass Calcd for** $[C_{16}H_{20}O_5Na]+$ requires *m/z* = 315.1208, found *m/z* = 315.1202 (ESI).



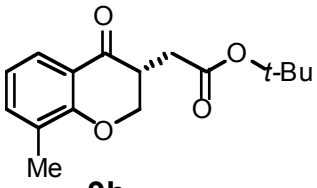
8e

4-(2-Formyl-4-nitro-phenoxy)-but-2-enoic acid *tert*-butyl ester (8e): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.53 (s, 1H), 8.66 (d, J=2.9 Hz, 1H), 8.43 (dd, J=9.17, 2.9 Hz, 1H), 7.16 (dt, J=15.8, 4.4 Hz, 1H), 6.14 (dt, J=15.8, 2.0 Hz, 1H), 5.03 (dd, J=4.3, 1.9 Hz, 2H), 1.51 (s, 9H); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ 186.7, 164.3, 163.6, 141.7, 138.0, 130.4, 125.1, 124.7, 124.6, 113.0, 81.2, 67.9, 28.1; **IR** (film, cm^{-1}) 2766, 1709, 1665; **TLC** R_f 0.23 (25% EtoAc/Hexanes); **Exact Mass Calcd for** $[C_{15}H_{17}NO_6Na]+$ requires *m/z* = 330.0954, found *m/z* = 330.0960 (ESI).



9a

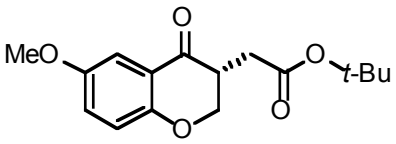
(6-Methyl-4-oxo-chroman-3-yl)-acetic acid *tert*-butyl ester (9a): **^{1}H NMR** ($CDCl_3$, 400 MHz) 7.68 (s, 1H), 7.28 (d, J=6.3 Hz, 1H), 6.87 (d, J=8.4 Hz, 1H), 4.55 (dt, J=5.9, 5.17 Hz, 1H), 4.26 (t, J=11.3 Hz, 1H), 3.26 (m, 1H), 2.84 (dd, J=16.7, 4.7 Hz, 1H), 2.34 (q, J=8.4 Hz, 1H), 2.31 (s, 3H), 1.48 (s, 9H); **^{13}C NMR** ($CDCl_3$, 100 MHz) 192.7, 170.3, 159.6, 136.8, 130.8, 126.8, 120.0, 117.5, 81.2, 70.3, 42.8, 31.8, 28.1, 20.5; **IR** (film, cm^{-1}) 1740, 1702; **TLC** R_f 0.66 (25% EtoAc/Hexanes); **Exact Mass Calcd for** $[C_{16}H_{20}O_4Na]+$ requires *m/z* = 299.1259, found *m/z* = 299.1251 (ESI); **HPLC** Chiralcel AD, 2% 2-propanol/hexane, 1.0 mL/min, 20 °C, t_r = 9.3 min (major), t_r = 13.3 min (minor).



9b

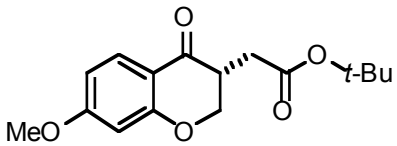
(8-Methyl-4-oxo-chroman-3-yl)-acetic acid *tert*-butyl ester (9b): ^{1}H NMR ($CDCl_3$, 400 MHz) 7.44 (d, J=8.0 Hz, 1H), 7.33 (d, J=6.5 Hz, 1H), 6.92 (t, J=7.5 Hz, 1H), 4.62 (dd, J=11.2, 5.3 Hz, 1H), 4.27 (t, J=11.5 Hz, 1H), 3.26 (m, 1H), 2.85 (dd, J=16.7, 4.8 Hz, 1H), 2.32 (dd, J=16.6, 8.35 Hz, 1H), 2.24 (s, 3H), 1.48 (s, 9H); **^{13}C NMR** ($CDCl_3$, 100 MHz) 192.8, 170.4, 159.8, 136.6, 126.9, 124.8, 120.7, 120.1, 81.1, 70.2, 42.7, 42.7, 31.8, 28.2, 15.7; **IR** (film, cm^{-1}) 1728, 1702; **TLC** R_f 0.81 (25% EtoAc/Hexanes); **Exact**

Mass Calcd for $[C_{16}H_{20}O_4Na]+$ requires *m/z* = 299.1259, found *m/z* = 299.1259 (ESI); **HPLC** Chiralcel AD, 2% ethanol/hexane, 1.0 mL/min, 20 °C, t_r = 14.4 min (major), t_r = 16.7 min (minor).



9c

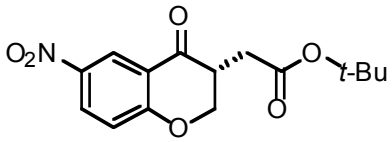
(6-Methoxy-4-oxo-chroman-3-yl)-acetic acid *tert*-butyl ester (9c): ^{1}H NMR ($CDCl_3$, 400 MHz) 7.32 (d, J=3.2 Hz, 1H), 7.09 (dd, J=9.0 Hz, J=3.1 Hz, 1H), 6.89 (d, J=9.0 Hz, 1H), 4.53 (dd, J=11.0, 5.2 Hz, 1H), 4.25 (t, J=11.0 Hz, 1H), 3.79 (s, 3H), 3.24 (m, 1H), 2.83 (dd, J=16.7, 4.8 Hz, 1H), 2.35 (dd, J=16.8, 8.3 Hz, 1H), 1.47 (s, 9H); **^{13}C NMR** ($CDCl_3$, 100 MHz) 192.6, 170.3, 156.3, 154.0, 125.0, 120.3, 119.0, 107.6, 81.2, 70.4, 42.8, 31.9, 28.2; **IR** (film, cm^{-1}) 1734, 1690; **TLC** R_f 0.48 (25% EtoAc/Hexanes); **Exact Mass Calcd for** $[C_{16}H_{20}O_5Na]+$ requires *m/z* = 315.1208, found *m/z* = 315.1207 (ESI); **HPLC** Chiralcel AD, 2% 2-propanol/hexane, 1.0 mL/min, 20 °C, t_r = 14.7 min (major), t_r = 17.2 min (minor).



9d

(7-Methoxy-4-oxo-chroman-3-yl)-acetic acid *tert*-butyl ester (9d): ^{1}H NMR ($CDCl_3$, 400 MHz) 7.83 (d, J=8.8 Hz, 1H), 6.58 (dd, J=8.9, 2.4 Hz, 1H), 6.40 (d, J=2.4 Hz, 1H),

4.56 (dd, J=11.0, 5.2 Hz, 1H), 4.27 (t, J=11.3 Hz, 1H), 3.84 (s, 3H), 3.21 (m, 1H), 2.85 (dd, J=16.7, 4.6 Hz, 1H), 2.30 (dd, J=16.7, 8.6 Hz, 1H), 1.54 (s, 9H); **^{13}C NMR** ($CDCl_3$, 100 MHz) 191.1, 165.7, 163.5, 129.0, 114.4, 110.0, 100.6, 81.1, 70.6, 55.7, 42.4, 31.8, 28.2; **IR** (film, cm^{-1}) 1740, 1683; **TLC** R_f 0.51 (25% EtoAc/Hexanes); **Exact Mass Calcd for** $[C_{16}H_{20}O_5Na]+$ requires *m/z* = 315.1208, found *m/z* = 315.1208 (ESI); **HPLC** Chiralcel AD, 2% 2-propanol/hexane, 1.0 mL/min, 20 °C, t_r = 20.6 min (major), t_r = 23.9 min (minor)



9e

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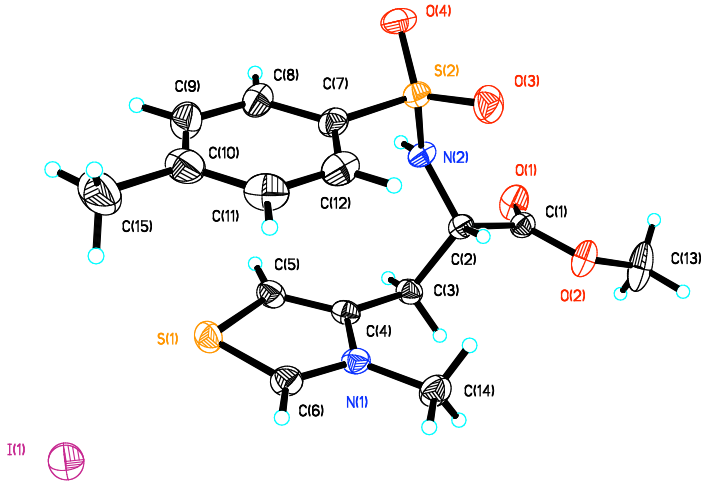
(6-Nitro-4-oxo-chroman-3-yl)-acetic acid *tert*-butyl ester (9e): ^{1}H NMR ($CDCl_3$, 400 MHz) 8.80 (d, J=2.8 Hz, 1H), 8.33 (dd, J=9.1, 2.7 Hz, 1H), 7.11 (d, J=9.2 Hz, 1H), 4.73 (dd, 11.4, 5.6 Hz, 1H), 4.43 (t, J=11.9 Hz, 1H), 3.33 (m, 1H), 2.86 (dd, J=17.1, 4.5 Hz, 1H), 2.43 (dd, J=17.0, 7.9 Hz, 1H), 1.48 (s, 9H); **^{13}C NMR** ($CDCl_3$, 100 MHz) 190.4, 169.7, 165.4, 142.0, 130.1, 123.8, 120.0, 119.0, 81.6, 70.8, 53.5, 42.4, 31.2, 28.2; **IR** (film, cm^{-1}) 1734, 1709; **TLC** R_f 0.45 (25% EtOAc/Hexanes); **Exact Mass Calcd for** $[C_{15}H_{17}NO_6Na]+$ requires *m/z* = 330.0954, found *m/z* = 330.0954 (ESI); **HPLC** Chiralcel AD, 1% 2-propanol/hexane, 1.0 mL/min, 20 °C, t_r = 62.3 min, t_r = 75.6 min.

General experimental for X-Ray crystallographic anaylsis:

Data was collected using a Bruker APEX CCD (charged coupled deviced) based diffractometer equipped with an LT-2 low temperature apparatus operating at 193 K. A suitable crystal was chosen and mounted on a glass fiber using grease. Data was measured using omega scans of 0.3° per frame for 30 seconds, such that a hemisphere was collected. A total of 1305 frames were collected with a maximum resolution of 0.90 Å. Cell parameters were retrieved using SMART[i] software and refined using SAINT on all observed reflections. Data reduction was performed using the SAINT software[ii], which corrects for Lp and decay. Absorption corrections were applied using SADABS supplied by George Sheldrick. The structures ware solved by the direct method using the SHELXS-97[iii] program and refined by least squares method on F^2, SHELXL-97[iv], incorporated in SHELXTL-PC V 6.10[v].

All non-hydrogen atoms are refined anisotropically. Hydrogens were calculated by geometrical methods and refined as a riding model. The crystal used for the diffraction study showed no decomposition during data collection. All drawings are done at 30% ellipsoids.



[i] SMART V5.626 (NT) Software for the CCD Detector Systems; Bruker Analytical X-ray Systems, Madison, WI (2001)
[ii] SAINT V 5.01 (NT) Software for the CCD Detector Systems; Bruker Analytical X-ray Systems, Madison, WI (2001)
[iii] Sheldrick, G. M. SHELXS-90, *Program for the Solution of Crystal Structure*, University of Göttingen, Germany, 1990
[iv] Sheldrick, G. M. SHELXL-97, *Program for the Refinement of Crystal Structure*, University of Göttingen, Germany, 1997.
[v] SHELXTL 6.0 (PC-Version), Program Library for Structure Solution and Molecular Graphics; Bruker Analytical X-ray Systems, Madison, WI (1998)

Table 1. Crystal data and structure refinement for jtb43t.

Identification code	jtb43t	
Empirical formula	C15 H19 I N2 O4 S2	
Formula weight	482.34	
Temperature	193(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P1	
Unit cell dimensions	a = 7.2693(6) Å	a= 80.624(2)°.
	b = 7.7618(7) Å	b= 72.296(2)°.
	c = 8.7263(7) Å	g = 85.313(2)°.
Volume	462.51(7) $Å^3$	
Z	1	
Density (calculated)	1.732 Mg/m^3	
Absorption coefficient	1.978 mm^{-1}	
F(000)	240	
Crystal size	0.20 x 0.20 x 0.20 mm^3	
Theta range for data collection	2.48 to 28.34°.	
Index ranges	-9<=h<=9, -10<=k<=9, -10<=l<=11	
Reflections collected	3450	
Independent reflections	2761 [R(int) = 0.0300]	
Completeness to theta = 28.34°	98.4 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2761 / 3 / 217	
Goodness-of-fit on F^2	1.080	
Final R indices [I>2sigma(I)]	R1 = 0.0190, wR2 = 0.0477	
R indices (all data)	R1 = 0.0190, wR2 = 0.0477	
Absolute structure parameter	-0.043(11)	
Largest diff. peak and hole	0.738 and -0.356 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3)
for jtb43t. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
I(1)	7017	9773	6922	32(1)
S(2)	1136(1)	7907(1)	399(1)	25(1)
S(1)	5953(1)	10259(1)	3161(1)	28(1)
N(1)	2867(6)	11897(4)	3052(5)	22(1)
O(2)	-991(4)	13401(3)	-688(3)	31(1)
C(3)	3005(5)	12411(4)	94(5)	23(1)
C(1)	605(4)	12514(4)	-1369(4)	22(1)
N(2)	2056(3)	9714(3)	-610(3)	23(1)
C(12)	1447(6)	7475(5)	3511(6)	32(1)
C(7)	2299(4)	7212(4)	1895(4)	25(1)
O(1)	1417(4)	12664(3)	-2800(3)	34(1)
C(2)	1368(4)	11392(4)	-87(4)	21(1)
C(5)	5493(4)	10752(4)	1333(4)	26(1)
C(4)	3800(4)	11655(4)	1450(3)	22(1)
C(8)	4122(5)	6391(4)	1439(5)	31(1)
C(6)	3860(5)	11247(4)	4074(4)	27(1)
O(3)	-848(3)	8270(3)	1210(4)	37(1)
O(4)	1660(4)	6653(3)	-712(3)	37(1)
C(14)	953(5)	12765(5)	3609(4)	30(1)
C(9)	5059(6)	5814(5)	2594(5)	37(1)
C(11)	2408(6)	6906(5)	4644(5)	38(1)
C(13)	-1751(6)	14660(7)	-1777(6)	50(1)
C(10)	4241(7)	6037(5)	4206(6)	39(1)
C(15)	5282(9)	5434(7)	5449(8)	56(1)

Table 3. Bond lengths [Å] and angles [°] for jtb43t.

S(2)-O(3)	1.428(3)
S(2)-O(4)	1.433(3)
S(2)-N(2)	1.607(3)
S(2)-C(7)	1.754(4)
S(1)-C(6)	1.676(3)
S(1)-C(5)	1.705(3)
N(1)-C(6)	1.326(5)
N(1)-C(4)	1.393(5)
N(1)-C(14)	1.472(5)
O(2)-C(1)	1.325(4)
O(2)-C(13)	1.446(5)
C(3)-C(4)	1.487(5)
C(3)-C(2)	1.541(4)
C(1)-O(1)	1.199(4)
C(1)-C(2)	1.516(4)
N(2)-C(2)	1.450(3)
C(12)-C(11)	1.374(7)
C(12)-C(7)	1.398(6)
C(7)-C(8)	1.394(4)
C(5)-C(4)	1.350(4)
C(8)-C(9)	1.378(6)
C(9)-C(10)	1.384(6)
C(11)-C(10)	1.416(7)
C(10)-C(15)	1.498(7)
O(3)-S(2)-O(4)	120.43(17)
O(3)-S(2)-N(2)	107.54(14)
O(4)-S(2)-N(2)	106.32(16)
O(3)-S(2)-C(7)	107.59(17)
O(4)-S(2)-C(7)	106.69(16)
N(2)-S(2)-C(7)	107.72(15)
C(6)-S(1)-C(5)	90.61(16)
C(6)-N(1)-C(4)	113.5(3)

C(6)-N(1)-C(14)	121.7(3)
C(4)-N(1)-C(14)	124.7(3)
C(1)-O(2)-C(13)	116.3(3)
C(4)-C(3)-C(2)	115.4(3)
O(1)-C(1)-O(2)	124.8(3)
O(1)-C(1)-C(2)	124.1(3)
O(2)-C(1)-C(2)	110.9(3)
C(2)-N(2)-S(2)	122.4(2)
C(11)-C(12)-C(7)	119.7(4)
C(8)-C(7)-C(12)	119.9(4)
C(8)-C(7)-S(2)	118.5(3)
C(12)-C(7)-S(2)	121.6(3)
N(2)-C(2)-C(1)	109.3(2)
N(2)-C(2)-C(3)	111.9(2)
C(1)-C(2)-C(3)	106.2(2)
C(4)-C(5)-S(1)	112.2(2)
C(5)-C(4)-N(1)	110.9(3)
C(5)-C(4)-C(3)	127.1(3)
N(1)-C(4)-C(3)	122.0(3)
C(9)-C(8)-C(7)	119.7(3)
N(1)-C(6)-S(1)	112.7(3)
C(8)-C(9)-C(10)	121.6(4)
C(12)-C(11)-C(10)	121.0(4)
C(9)-C(10)-C(11)	118.0(4)
C(9)-C(10)-C(15)	121.4(5)
C(11)-C(10)-C(15)	120.5(4)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for jtb43t. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
I(1)	30(1)	40(1)	23(1)	-6(1)	-5(1)	2(1)
S(2)	24(1)	18(1)	33(1)	-4(1)	-10(1)	0(1)
S(1)	29(1)	34(1)	24(1)	-6(1)	-12(1)	4(1)
N(1)	28(2)	19(1)	21(2)	-3(1)	-9(1)	0(1)
O(2)	26(1)	32(1)	29(1)	1(1)	-5(1)	9(1)
C(3)	26(2)	21(2)	22(2)	-2(1)	-10(1)	-2(1)
C(1)	22(1)	22(1)	23(1)	-5(1)	-6(1)	1(1)
N(2)	25(1)	19(1)	25(1)	-6(1)	-4(1)	2(1)
C(12)	32(2)	27(2)	33(2)	-4(2)	-2(2)	-2(1)
C(7)	26(1)	18(1)	29(2)	0(1)	-7(1)	-1(1)
O(1)	37(1)	42(1)	21(1)	-4(1)	-9(1)	11(1)
C(2)	23(1)	19(1)	20(1)	-4(1)	-6(1)	1(1)
C(5)	27(1)	30(1)	23(1)	-6(1)	-9(1)	-2(1)
C(4)	26(1)	20(1)	20(1)	-2(1)	-8(1)	-5(1)
C(8)	29(2)	28(2)	35(2)	-5(1)	-8(1)	4(1)
C(6)	33(2)	28(2)	21(1)	-5(1)	-9(1)	1(1)
O(3)	22(1)	32(1)	54(2)	0(1)	-9(1)	-4(1)
O(4)	50(1)	23(1)	47(2)	-13(1)	-23(1)	3(1)
C(14)	30(2)	32(2)	26(2)	-9(1)	-6(1)	5(1)
C(9)	36(2)	32(2)	47(2)	-2(1)	-19(2)	3(1)
C(11)	50(2)	36(2)	29(2)	-3(1)	-10(2)	-8(2)
C(13)	34(2)	61(3)	43(2)	7(2)	-9(2)	22(2)
C(10)	55(3)	26(2)	41(2)	5(1)	-26(2)	-9(2)
C(15)	73(3)	46(3)	62(3)	3(2)	-46(3)	-9(2)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3)for jtb43t.

	x	y	z	U(eq)
H(3A)	4051	12486	-915	27
H(3B)	2525	13592	251	27
H(2A)	2991	9684	-1492	28
H(12A)	236	8031	3817	39
H(2B)	337	11222	948	25
H(5A)	6313	10435	367	31
H(8A)	4703	6234	362	37
H(6A)	3441	11330	5179	32
H(14A)	615	12777	4760	44
H(14B)	8	12142	3373	44
H(14C)	989	13944	3057	44
H(9A)	6271	5261	2281	45
H(11A)	1845	7095	5715	46
H(13A)	-2900	15225	-1162	74
H(13B)	-2056	14073	-2551	74
H(13C)	-803	15517	-2339	74
H(15A)	6496	4879	4945	83
H(15B)	4510	4617	6302	83
H(15C)	5507	6421	5896	83

Table 6. Torsion angles [°] for jtb43t.

C(13)-O(2)-C(1)-O(1)	-1.4(5)
C(13)-O(2)-C(1)-C(2)	173.8(4)
O(3)-S(2)-N(2)-C(2)	30.0(3)
O(4)-S(2)-N(2)-C(2)	160.2(2)
C(7)-S(2)-N(2)-C(2)	-85.7(3)
C(11)-C(12)-C(7)-C(8)	-0.6(5)
C(11)-C(12)-C(7)-S(2)	179.9(3)
O(3)-S(2)-C(7)-C(8)	165.1(3)
O(4)-S(2)-C(7)-C(8)	34.6(3)
N(2)-S(2)-C(7)-C(8)	-79.2(3)
O(3)-S(2)-C(7)-C(12)	-15.4(3)
O(4)-S(2)-C(7)-C(12)	-145.9(3)
N(2)-S(2)-C(7)-C(12)	100.3(3)
S(2)-N(2)-C(2)-C(1)	-118.5(3)
S(2)-N(2)-C(2)-C(3)	124.0(3)
O(1)-C(1)-C(2)-N(2)	-44.9(4)
O(2)-C(1)-C(2)-N(2)	139.9(3)
O(1)-C(1)-C(2)-C(3)	76.0(4)
O(2)-C(1)-C(2)-C(3)	-99.2(3)
C(4)-C(3)-C(2)-N(2)	-68.3(4)
C(4)-C(3)-C(2)-C(1)	172.4(3)
C(6)-S(1)-C(5)-C(4)	0.6(3)
S(1)-C(5)-C(4)-N(1)	-1.6(3)
S(1)-C(5)-C(4)-C(3)	175.2(3)
C(6)-N(1)-C(4)-C(5)	2.0(4)
C(14)-N(1)-C(4)-C(5)	-177.4(3)
C(6)-N(1)-C(4)-C(3)	-175.0(3)
C(14)-N(1)-C(4)-C(3)	5.6(5)
C(2)-C(3)-C(4)-C(5)	103.8(4)
C(2)-C(3)-C(4)-N(1)	-79.7(4)
C(12)-C(7)-C(8)-C(9)	1.2(5)
S(2)-C(7)-C(8)-C(9)	-179.3(3)
C(4)-N(1)-C(6)-S(1)	-1.6(4)

C(14)-N(1)-C(6)-S(1)	177.8(3)
C(5)-S(1)-C(6)-N(1)	0.5(3)
C(7)-C(8)-C(9)-C(10)	-0.4(6)
C(7)-C(12)-C(11)-C(10)	-0.8(6)
C(8)-C(9)-C(10)-C(11)	-0.9(6)
C(8)-C(9)-C(10)-C(15)	-178.9(4)
C(12)-C(11)-C(10)-C(9)	1.6(6)
C(12)-C(11)-C(10)-C(15)	179.6(4)

Symmetry transformations used to generate equivalent atoms: