Supporting Information

Diastereoselective Diels–Alder Reactions of *N*-Sulfonyl-1-aza-1,3-butadienes With Optically Active Enol Ethers: An Asymmetric Variant of the 1-Azadiene Diels–Alder Reaction

Ryan C. Clark, Steven S. Pfeiffer, and Dale L. Boger*

Department of Chemistry and the Skaggs Institute for Chemical Biology
The Scripps Research Institute
10550 North Torrey Pines Road, La Jolla, California 92037

General Procedure for the Preparation of *N*-Sulfonyl-1-aza-1,3-butadienes 1, 20–25a.

Ethyl (*E*)-4-[(Phenylsulfonyl)imino]-2-butenoate (1). A solution of ethyl 4-oxo-2-butenoate (2.00 g, 15.6 mmol) and benzenesulfonamide (2.53 g, 16.1 mmol) in anhydrous CH_2Cl_2 (60 mL) was cooled to –10 °C under nitrogen, then treated dropwise sequentially with Et_3N (5.0 mL, 36 mmol) and $TiCl_4$ (1 M in CH_2Cl_2, 9.2 mL, 9.2 mmol). The resulting mixture was stirred at 0 °C for 4 h, at 25 °C for 30 min, before being filtered through a plug of Celite and concentrated to afford a brown solid. This solid was stirred in ether for 2 h, filtered, and the filtrate concentrated under reduced pressure to yield **1** (3.50 g, 84%) as a pale yellow solid of suitable purity for use in Diels–Alder reactions. Boger, D. L.; Corbett, W. L.; Curran, T. T.; Kasper, A. M. *J. Am. Chem. Soc.* **1991**, *113*, 1713.

Ethyl (*E*)-4-[(Methylsulfonyl)imino]-2-butenoate (20a): Boger, D. L.; Corbett, W. L.; Curran, T. T.; Kasper, A. M. *J. Am. Chem. Soc.* **1991**, *113*, 1713.

Ethyl (*E*)-4-[(*tert*-Butylsulfonyl)imino]-2-butenoate (21a): 885 mg, 85%; ^{1}H NMR (acetone-d_6, 400 MHz) δ 8.85 (d, 1H, J = 9.2 Hz), 7.28 (dd, 1H, J = 9.2, 15.7 Hz), 7.11 (d, 1H, J = 15.9 Hz), 4.28 (q, 2H, J = 7.1 Hz), 1.40 (s, 9H), 1.31 (t, 3H, J = 7.1 Hz); ^{13}C NMR (acetone-d_6, 125 MHz) δ 173.7, 166.2, 141.9, 139.9, 63.0, 25.5, 24.9, 15.3; IR (film) ν_{max} 2983, 1719, 1598, 1306, 1259, 1190, 1126, 809, 780, 677 cm^{-1}; HR ESI-TOF *m/z* 246.0804 ([M – H]$^-$, $C_{10}H_{17}NO_4S$ requires 246.0805).

Ethyl (*E*)-4-[(2-Nitrophenylsulfonyl)imino]-2-butenoate (22a): 586 mg, 48%; ^{1}H NMR (C_6D_6, 500 MHz) δ 8.48 (d, 1H, J = 9.4 Hz), 8.02 (dd, 1H, J = 1.4, 7.9 Hz), 7.06 (dd, 1H, J = 9.4, 15.7 Hz), 6.77 (dd, 1H, J = 1.2, 7.9 Hz), 6.55 (dt, 1H, J = 1.3, 7.8 Hz), 6.45 (dt, 1H, J = 1.4, 7.8 Hz), 5.83 (d, 1H, J = 15.7 Hz), 3.79 (q, 2H, J = 7.1 Hz), 0.82 (t, 3H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.7, 163.9, 141.2, 137.5, 135.1, 132.8, 132.2, 130.8, 130.6, 124.9, 61.7, 13.9; IR (film) ν_{max} 3097, 2985, 1719, 1594, 1543, 1364, 1304, 1262, 1168, 784, 740 cm^{-1}; HR ESI-TOF *m/z* 313.0488 (M + H$^+$, $C_{12}H_{12}N_2O_6S$ requires 313.0489).

Ethyl (*E*)-4-[(4-Nitrophenylsulfonyl)imino]-2-butenoate (23a): 1.28 g, 52%; ^{1}H NMR (C_6D_6, 500 MHz) δ 8.27 (d, 1H, J = 9.7 Hz), 7.58 (m, 2H), 7.49 (m, 2H), 6.95 (dd, 1H, J = 9.5, 15.8 Hz), 5.78 (d, 1H, J = 15.8 Hz), 3.82 (q, 2H, J = 7.1 Hz), 0.84 (t, 3H, J = 7.1 Hz); ^{13}C NMR (C_6D_6, 125 MHz) δ 170.0, 163.6, 150.6, 143.2, 140.4, 137.0, 129.2, 124.1, 61.4, 13.8; IR (film) ν_{max} 3107, 2983, 1721, 1596, 1532, 1351, 1306, 1260, 1192, 1166 cm^{-1}; HR ESI-TOF *m/z* 313.0491 (M + H$^+$, $C_{12}H_{12}N_2O_6S$ requires 313.0489).

Ethyl (*E*)-4-[(2-Trifluoromethylphenylsulfonyl)imino]-2-butenoate (24a): 103 mg, 79%; ^{1}H NMR (acetone-d_6, 400 MHz) δ 8.89 (qd, 1H, J = 1.0, 8.6 Hz), 8.40 (m, 1H), 8.05 (m, 3H), 7.23 (dd, 1H, J = 8.5, 15.7 Hz), 7.16 (d, 1H, J = 15.6 Hz), 4.27 (q, 2H, J = 7.1 Hz), 1.30 (t, 3H, *J* = 7.1 Hz); ^{13}C NMR (acetone-d_6, 100 MHz) δ 172.6, 165.8, 143.1, 139.4, 137.6, 136.5, 135.2, 134.5, 130.5 (q, *J* = 6.2 Hz), 130.1 (q, *J* = 33.4 Hz), 124.6 (q, *J* = 273.6 Hz), 63.0, 15.2; IR (film) ν_{max} 3084, 2986, 1722, 1594, 1441, 1338, 1310, 1270, 1167, 1119, 1096, 1036, 704, 775, 719 cm^{-1}; HR ESI-TOF *m/z* 336.0514 (M + H$^+$, $C_{13}H_{12}F_3NO_4S$ requires 336.0512).

Ethyl (*E*)-4-[(2,4-Difluorophenylsulfonyl)imino]-2-butenoate (25a): 84 mg, 71%; ^{1}H NMR (acetone-d_6, 400 M Hz) δ 8.98 (ddd, 1H, *J* = 0.3, 1.9, 8.3 Hz), 8.09 (dt, 1H, *J* = 6.3, 8.5 Hz), 7.36 (m, 2H), 7.26 (dd, 1H, *J* = 8.3, 15.7 Hz), 7.19 (d, 1H, *J* = 15.2 Hz), 4.27 (q, 2H, *J* = 7.1 Hz), 1.30 (t, 3H, *J* = 7.1 Hz); ^{13}C NMR (acetone-d_6, 100 MHz) δ 173.8, 168.7 (dd, *J* = 12.0Hz, *J* = 257.0Hz), 165.9, 162.2 (dd, *J* = 13.4Hz, *J* = 259.0Hz), 143.4, 139.4, 134.4 (d, *J* = 11.6Hz), 123.9 (dd, *J* = 3.8Hz, *J* = 14.4Hz), 114.5 (dd, *J* = 3.7Hz, *J* = 22.6Hz), 107.9 (dd, *J* = 25.0Hz, *J* = 26.8Hz), 63.1, 15.3; IR (film) ν_{max} 3105, 2986, 1722, 1602, 1481, 1433, 1338, 1306, 1277, 1170, 1074, 971, 791, 680 cm^{-1}; HR ESI-TOF *m/z* 304.0451 (M + H$^+$, $C_{12}H_{11}F_2NO_4$ requires 304.0450).

General Procedures for the Preparation of Enol Ethers 2–19a.

Method A: (*R*)-(1-(vinyloxy)ethyl)benzene (3a). A solution of mercury(II) acetate (130 mg, 0.409 mmol) in ethyl vinyl ether (4 mL) was treated with (*R*)-1-phenylethanol (500 mg, 4.09 mmol), and the resulting solution was stirred under nitrogen at 40 °C for 18 h. After cooling, flash chromatography (Al_2O_3, activated basic Brockmann (III), hexanes) yielded **3a** (263 mg, 43%) as a colorless oil. (a) Posner, G. H.; Wettlaufer, D. G. *Tetrahedron Lett.* **1986**, *27*, 667. (b) Chiellini, E. *Macromolecules* **1970**, *3*, 527.

Method B: (*S*)-3-(vinyloxy)-2-pyrrolidinone (19a). A solution of mercury(II) trifluoroacetate (211 mg, 0.495 mmol) in ethyl vinyl ether (95 mL) was treated with (*S*)-3-hydroxy-2-pyrrolidinone (1.00 g, 9.89 mmol) and Et_3N (70 µL, 0.495 mmol), and the resulting suspension was stirred under nitrogen at 25 °C for 60 h. After concentrating to 30 mL in vacuo, flash chromatography (SiO_2, EtOAc), followed by recrystallization afforded **19a** as a white solid (789 mg, 63%): mp 69 °C (white prisms, 4:1 hexanes–EtOAc); ^{1}H NMR (acetone-d_6, 400 MHz) δ 7.00 (br s, 1H), 6.53 (dd, 1H, *J* = 6.6, 14.1 Hz), 4.41 (dd, 1H, *J* = 7.2, 7.7 Hz), 4.32 (dd, 1H, *J* = 1.7, 14.1 Hz), 4.00 (dd, 1H, *J* = 1.7, 6.6 Hz), 3.35 (m, 2H), 2.54 (m, 1H), 2.01 (m, 1H); ^{13}C NMR (C_6D_6, 125 MHz) δ 175.5, 151.0, 89.4, 75.6, 38.9, 27.9; IR (film) ν_{max} 3229, 2914, 1704, 1626, 1296, 1192 cm^{-1}; HR ESI-TOF *m/z* 150.0525 (M + Na$^+$, $C_6H_9NO_2$ requires 150.0525); $[\alpha]^{23}_{D}$ –78 (*c* 0.77, $CHCl_3$).

Method C: (*S*)-(1-(vinyloxy)decyl)benzene (7a). A solution of (*S*)-1-phenyl-1-decanol (2.34 g, 10.0 mmol) in ethyl vinyl ether (5 mL) was treated with trifluoroacetic acid (7.4 µL, 0.1 mmol), and the solution was stirred for 3 d at 25 °C. Excess ethyl vinyl ether and trifluoroacetic acid were removed by a stream of nitrogen. The residue was dissolved in CH_2Cl_2 (12.6 mL), cooled to 0 °C, and treated dropwise sequentially with Et_3N (1.67 mL, 12.0 mmol) and TMSOTf (1.99 mL, 11.0 mmol). The solution was stirred at 0 to 25 °C for 5 h, then treated with aqueous 1 N NaOH (4 mL) and diluted with hexanes (150 mL). The organic layer was washed with water (2 × 50 mL) and dried ($MgSO_4$). The solvent was removed in vacuo and the residue was purified by flash chromatography (SiO_2, hexanes) to afford **7a** (1.65 g, 63%) as a colorless oil: ^{1}H NMR (acetone-d_6, 500 MHz) δ 7.30 (m, 5H), 6.36 (dd, 1H, *J* = 6.7, 14.1 Hz), 4.81 (dd, 1H, *J* = 5.7, 7.6 Hz), 4.17 (dd, 1H, *J* = 1.4, 14.2 Hz), 3.88 (dd, 1H, *J* = 1.4, 6.6 Hz), 1.85 (m, 1H), 1.71 (m, 1H), 1.41 (m, 1H), 1.28 (m, 13H), 0.87 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 150.8, 141.9, 128.3, 127.4, 126.2, 89.0, 81.6, 37.9, 31.8, 29.5, 29.4, 29.2, 29.5, 25.5, 22.6, 14.1; IR (film) ν_{max} 2925, 2854, 1634, 1615, 1190 cm^{-1}; GC/MS *m/z* 260 (M$^+$, $C_{18}H_{28}O$ requires 260); $[\alpha]^{23}_{D}$ –29 (*c* 0.50, THF).

(*R*)-benzyl 2-phenyl-2-(vinyloxy)acetate (14a): Method C, 608 mg, 55%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.49 (m, 2H), 7.38 (m, 3H), 7.32 (m, 3H), 7.24 (m, 2H), 6.51 (dd, 1H, *J* = 6.8 Hz, 14.3 Hz), 5.35 (s, 1H), (d, 1H, *J* = 12.3 Hz), 5.13 (d, 1H, *J* = 12.4 Hz), 4.30 (dd, 1H, *J* = 2.7, 14.3 Hz), 4.16 (dd, 1H, *J* = 2.7, 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.4, 149.7, 135.1, 134.9, 128.9, 128.6, 128.4, 128.3, 128.0, 127.0, 89.6, 78.5, 67.0; IR (film) ν_{max} 3033, 2955, 1755, 1640, 1621, 1163 cm^{-1}; HR ESI-TOF *m/z* 291.0983 (M$^+$ + Na, $C_{17}H_{16}O_3$ requires 291.0992); $[\alpha]^{23}_{D}$ –23 (*c* 0.50, THF).

(*R*)-methyl 2-(vinyloxy)propanoate (15a): Method C, 582 mg, 23%; ^{1}H NMR (C_6D_6, 400 MHz) δ 6.24 (dd, 1H, *J* = 6.8, 14.3 Hz), 4.25 (dd, 1H, *J* = 2.3, 14.3 Hz), 4.14 (q, 1H, *J* = 6.8 Hz), 3.96 (dd, 1H, *J* = 2.3, 6.8 Hz), 3.25 (s, 3H), 1.23 (d, 3H, *J* = 6.8 Hz); ^{13}C NMR (C_6D_6, 125 MHz) δ 171.7, 150.8, 88.3, 73.0, 51.4, 17.9; IR (film) ν_{max} 2990, 1760, 1639, 1621, 1448 cm^{-1}; GC/MS *m/z* 130 (M$^+$, $C_6H_{10}O_3$ requires 130); $[\alpha]^{23}_{D}$ +63 (*c* 0.50, THF).

(*S*)-benzyl 2-(vinyloxy)propanoate (16a): Method C, 236 mg, 42%; ^{1}H NMR (acetone-*d*$_6$, 500 MHz) δ 7.37 (m, 5H), 6.44 (dd, 1H, *J* = 6.8, 14.2 Hz), 5.19 (s, 2H), 4.53 (q, 1H, *J* = 6.8 Hz), 4.19 (dd, 1H, *J* = 2.1, 14.3 Hz), 4.01 (dd, 1H, *J* = 2.1, 6.7 Hz), 1.43 (d, 3H, *J* = 6.9 Hz); ^{13}C NMR (C_6D_6, 100 MHz) δ 171.2, 150.8, 136.1, 128.6, 128.5, 128.4, 88.4, 73.1, 66.5, 17.9; IR (film) ν_{max} 2989, 1757, 1639, 1621, 1456, 1190 cm^{-1}; HR ESI-TOF *m/z* 229.0839 (M + Na$^+$, $C_{12}H_{14}O_3$ requires 229.0835); $[\alpha]^{23}_{D}$ –53 (*c* 0.50, THF).

(*R*)-α-vinyloxy-γ-butyrolactone (18a): Method C, 300 mg, 20%; ^{1}H NMR (C_6D_6, 500 MHz) δ 6.27 (dd, 1H, *J* = 6.5, 14.1 Hz), 4.36 (dd, 1H, *J* = 2.1, 14.1 Hz), 4.03 (dd, 1H, *J* = 2.1, 6.5 Hz), 3.68 (dt, 1H, *J* = 3.2, 7.8 Hz), 3.43 (m, 1H), 3.17 (m, 1H), 1.42 (m, 1H), 1.34 (m, 1H); ^{13}C NMR (C_6D_6, 125 MHz) δ 172.9, 150.4, 90.2, 72.6, 64.6, 28.8; IR (film) ν_{max} 2994, 2921, 1781, 1624, 1173 cm^{-1}; GC/MS *m/z* 128 (M$^+$, $C_6H_8O_3$ requires 128.0473); $[\alpha]^{23}_{D}$ +66 (*c* 0.96, THF).

The remaining enol ethers were prepared as described in the references below (for compounds with two references the first (a) cites its main use in cycloaddition reactions and the second (b) cites its first report).

2a: Chiellini, E.; Marchetti, M.; Villiers, C.; Braud, C.; Vert, M. *Eur. Polymer J.* **1978**, *14*, 251.

***ent*-4a**: Boa, Andrew N.; Dawkins, David A.; Hergueta, Antonio R.; Jenkins, Paul R. *J. Chem. Soc., Perkin Trans. 1* **1994**, 953.

***ent*-5a**: Posner, G. H.; Wettlaufer, D. G. *Tetrahedron Lett.* **1986**, *27*, 667.

6a: Carruthers, W.; Coggins, P.; Weston, J. B. *J. Chem. Soc., Chem. Commun.* **1991**, 117.

8a: Prapansiri, V.; Thornton, E. R. *Tetrahedron Lett.* **1991**, *32*, 3147.

***ent*-9a**: Boa, A. N.; Booth, S. E.; Dawkins, D. A.; Jenkins, P. R.; Fawcett, J.; Russell, D. R. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1277.

10a: Denmark, S. E.; Schnute, M. E. *J Org. Chem.* **1991**, *56*, 6738.

11a: Denmark, S. E.; Thorarensen, A. *J. Org. Chem.* **1996**, *61*, 6727.

12a: Fringuelli, F.; Matteucci, M.; Piermatti, O.; Pizzo, F.; Burla, M. C. *J. Org. Chem.* **2001**, *66*, 4661.

13a: (a) Dujardin, G.; Molato, S.; Brown, E. *Tetrahedron: Asymmetry* **1993**, *4*, 193. (b) Basagni, D.; Liquori, A. M.; Pispisa, B. *Ric. Sci. Rend., Sez. A* **1964**, *7*, 155.

17a: Dujardin, G.; Rossignol, S.; Brown, E. *Synthesis* **1998**, *5*, 763.

General Procedure for the Preparation of Tetrahydropyridines 2–25b.

2b: A solution of **2a** (9.9 mg, 0.063 mmol) in anhydrous toluene (0.1 mL) was treated with **1** (11.2 mg, 0.042 mmol) and the solution was stirred under nitrogen for 60 h at 25 °C. The solvent was removed by a stream of nitrogen yielding a light orange oil: diagnostic ^{1}H NMR (C_6D_6, 500 MHz) δ 5.29 (td, 1H, *J* = 1.9, 8.6 Hz, int. 0.06), 5.27 (td, 1H, *J* = 1.9, 8.7 Hz, int. 0.06), 5.22 (ddd, 1H, *J* = 1.4, 5.0, 8.1 Hz, int. 0.74), 5.19 (ddd, 1H, *J* = 1.5, 5.2, 8.3 Hz, int. 1.00); HR ESI-TOF *m/z* 446.1978 (M + Na$^+$, $C_{22}H_{33}NO_5S$ requires 446.1972).

3b: diagnostic signals for the crude reaction product: ^{1}H NMR (acetone-*d$_6$*, 400 MHz) δ 5.59 (dt, 1H, *J* = 1.5, 2.7 Hz, int. 0.25), 5.17 (dt, 1H, *J* = 1.6, 2.5 Hz, int. 0.05), 5.13 (dt, 1H, *J* = 1.5, 2.7 Hz, int. 1.00); HR ESI-TOF *m/z* 438.1352 (M + Na$^+$, $C_{22}H_{25}NO_5S$ requires 438.1346).

3b-major endo: Purified by flash chromatography (SiO_2, 10–20% EtOAc–hexanes) followed by recrystallization from hexanes to afford **3b** as white needles (100 mg, 55%): mp 117 °C; ^{1}H NMR (acetone-*d$_6$*, 500 MHz) δ 7.74 (m, 2H), 7.68 (m, 1H), 7.59 (m, 2H), 7.36 (m, 4H), 7.29 (m, 1H), 6.64 (td, 1H, *J* = 1.6, 8.3 Hz), 5.37 (ddd, 1H, *J* = 1.6, 5.3, 8.3 Hz), 5.14 (dt, 1H, *J* = 1.6, 2.7 Hz), 4.92 (q, 1H, *J* = 6.5 Hz), 4.10 (qdd, 2H, *J* = 7.1, 10.8, 16.5), 2.89 (m, 1H), 2.48 (tdd, 1H, *J* = 1.4, 2.9, 13.7 Hz), 1.26 (t, 3H, *J* = 7.1 Hz), 1.24 (d, 3H, *J* = 6.5 Hz), 1.10 (ddd, 1H, *J* = 2.4, 7.6, 13.7 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 172.3, 143.3, 139.0, 132.8, 129.1, 128.3, 127.4, 126.6, 126.5, 122.8, 108.0, 78.8, 73.9, 60.8, 33.8, 28.7, 24.2, 14.2; IR (film) ν_{max} 2978, 1732, 1447, 1361, 1173, 1046, 927, 729, 689 cm^{-1}; HR ESI-TOF *m/z* 438.1352 (M + Na$^+$, $C_{22}H_{25}NO_5S$ requires 438.1346); $[\alpha]^{23}_D$ –235 (*c* 0.39, $CHCl_3$).

4b: diagnostic signals for the crude reaction product: ^{1}H NMR (acetone-*d$_6$*, 400 MHz) δ 5.55 (dt, 1H, *J* = 1.5, 2.6 Hz, int. 0.23), 5.13 (dt, 1H, *J* = 1.4, 2.7 Hz, int. 0.05), 5.08 (dt, 1H, *J* = 1.5, 2.5 Hz, int. 1.00); HR ESI-TOF *m/z* 466.1657 (M + Na$^+$, $C_{24}H_{29}NO_5S$ requires 466.1659).

5b: diagnostic signals for the crude reaction product: ^{1}H NMR (acetone-*d$_6$*, 400 MHz) δ 5.51 (dt, 1H, *J* = 1.5, 2.7 Hz, int. 0.18), 5.09 (dt, 1H, *J* = 1.2, 2.5 Hz, int. 0.09), 5.05 (dt, 1H, *J* = 1.5, 2.7 Hz, int. 1.00); HR ESI-TOF *m/z* 466.1665 (M + Na$^+$, $C_{24}H_{29}NO_5S$ requires 466.1659).

6b: diagnostic signals for the crude reaction product (72 h): ^{1}H NMR (acetone-*d$_6$*, 400 MHz) δ 5.49 (dt, 1H, *J* = 1.5, 2.6 Hz, int. 0.19), 5.03 (dt, 1H, *J* = 1.2, 2.6 Hz, int. 0.15), 4.98 (dt, 1H, *J* = 1.5, 2.7 Hz, int. 1.00); HR ESI-TOF *m/z* 480.1810 (M + Na$^+$, $C_{25}H_{31}NO_5S$ requires 480.1815).

6b-major endo: Purified by flash chromatography (SiO_2, 5–30% EtOAc–hexanes) followed by recrystallization from hexanes to afford **6b** as white prisms (35 mg, 19%): mp 128 °C; ^{1}H NMR (C_6D_6, 400 MHz) δ 7.58 (d, 2H, *J* = 7.2 Hz), 7.33 (m, 2H), 7.25 (t, 2H, *J* = 7.7 Hz), 7.13 (m, 1H), 6.81 (m, 1H), 6.72 (m, 3H), 5.26 (ddd, 1H, *J* = 1.5, 5.1, 8.3 Hz), 5.18 (dt, 1H, *J* = 1.5, 2.7 Hz), 4.85 (s, 1H), 4.08 (q, 2H, *J* = 7.1 Hz) 2.62 (tdd, 1H, *J* = 1.3, 2.7, 13.6 Hz), 2.29 (m, 1H), 1.04 (t, 3H, *J* = 7.1 Hz), 0.95 (s, 9H), 0.78 (ddd, 1H, *J* = 2.5, 7.9, 13.6 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) 171.9, 139.0, 139.0, 132.8, 129.1, 127.4, 127.2, 126.6, 122.8, 108.3, 85.7, 79.0, 60.8, 34.9, 33.9, 28.4, 25.9, 14.0; IR (film) ν_{max} 2954, 1732, 1447, 1363, 1209, 1172, 1042, 730, 690 cm^{-1}; HR ESI-TOF *m/z* 480.1810 (M + Na$^+$, $C_{25}H_{31}NO_5S$ requires 480.1815); $[\alpha]^{23}_D$ +270 (*c* 0.43, $CHCl_3$).

7b: diagnostic signals for the crude reaction product: ^{1}H NMR (acetone-*d$_6$*, 400 MHz) δ 5.54 (dt, 1H, *J* = 1.5, 2.6 Hz, int. 0.23), 5.13 (dt, 1H, *J* = 1.1, 2.6 Hz, int. 0.06), 5.09 (dt, 1H, *J* = 1.5, 2.7 Hz, int. 1.00); HR ESI-TOF *m/z* 550.2595 (M + Na$^+$, $C_{30}H_{41}NO_5S$ requires 550.2597).

8b: diagnostic signals for the crude reaction product: ^{1}H NMR (acetone-*d$_6$*, 400 MHz) δ 5.39 (ddd, 1H, *J* = 1.5, 5.2, 8.1 Hz, int. 1.00), 5.31 (td, 1H, *J* = 1.7, 8.4 Hz, int. 0.10), 5.24 (ddd, 1H, *J* = 1.5, 5.1, 8.1 Hz, int. 0.19); HR ESI-TOF *m/z* 506.1961 (M + Na$^+$, $C_{27}H_{35}NO_5S$ requires 506.1972).

9b: diagnostic signals for the crude reaction product: ^{1}H NMR (acetone-d_6, 400 MHz) δ 5.66 (dt, 1H, *J* = 1.5, 2.6 Hz, int. 0.24), 5.21 (dt, 1H, *J* = 1.5, 2.7 Hz, int. 1.00); HR ESI-TOF *m/z* 488.1497 (M + Na$^+$, $C_{26}H_{27}NO_5S$ requires 488.1502).

10b: diagnostic signals for the crude reaction product: ^{1}H NMR (C_6D_6, 400 MHz) δ 5.33 (dt, 1H, *J* = 1.5, 2.7, int. 0.13), 4.76 (dt, 1H, *J* = 1.0, 2.6 Hz, int. 0.05), 4.61 (dt, 1H, *J* = 1.6, 2.6 Hz, int. 1.00); HR ESI-TOF *m/z* 492.1809 (M + Na$^+$, $C_{26}H_{31}NO_5S$ requires 492.1815).

11b: diagnostic signals for the crude reaction product (48 h): ^{1}H NMR (acetone-d_6, 400 MHz) δ 5.39 (ddd, 1H, *J* = 1.6, 5.1, 8.4 Hz, int. 0.49), 5.29 (ddd, 1H, *J* = 1.6, 5.3, 8.3 Hz, int. 1.00), 5.25 (td, 1H, *J* = 1.9, 8.6 Hz, int. 0.44), 5.14 (td, 1H, *J* = 1.9, 8.6 Hz, int. 0.78); HR ESI-TOF *m/z* 534.2284 (M + Na$^+$, $C_{29}H_{37}NO_5S$ requires 534.2285).

12b: diagnostic signals for the crude reaction product: ^{1}H NMR (C_6D_6, 400 MHz) δ 5.48 (dt, 1H, *J* = 1.6, 2.6 Hz, int. 1.00), 5.41 (dt, 1H, *J* = 1.6, 2.6 Hz, int. 0.33); HR ESI-TOF *m/z* 470.1981 (M + Na$^+$, $C_{24}H_{33}NO_5S$ requires 470.1972).

12b-major endo: Purified by flash chromatography (SiO_2, 5–15% EtOAc–hexanes) followed by recrystallization from hexanes to afford **12b** as large white prisms (73 mg, 44%): mp 116 °C; ^{1}H NMR (C_6D_6, 400 MHz) δ 7.58 (m, 2H), 6.88 (m, 3H), 6.72 (td, 1H, *J* = 1.5, 8.3 Hz), 5.48 (dt, 1H, *J* = 1.5, 2.5 Hz), 5.21 (ddd, 1H, *J* = 1.4, 5.2, 8.2 Hz), 4.47 (td, 1H, *J* = 4.6, 9.4 Hz), 4.00 (m, 2H), 2.74 (m, 1H), 2.56 (tdd, 1H, *J* = 1.2, 2.7, 13.5 Hz), 2.30 (m, 2H), 2.12 (ddq, 1H, *J* = 2.0, 5.1, 7.2 Hz), 2.01 (ddd, 1H, *J* = 2.8, 4.1, 14.2 Hz), 1.83 (tt, 1H, *J* = 3.1, 5.9 Hz), 1.73 (dt, 1H, *J* = 2.0, 5.9 Hz), 1.30 (d, 3H, *J* = 7.4 Hz), 1.11 (m, 4H), 1.02 (t, 3H, *J* = 7.1 Hz), 0.94 (s, 3H), 0.84 (ddd, 1H, *J* = 2.3, 7.6, 13.5 Hz); ^{13}C NMR (C_6D_6, 100 MHz) δ 171.5, 140.2, 132.4, 129.1, 126.8, 122.8, 108.7, 82.2, 77.9, 60.5, 48.0, 45.7, 41.8, 38.5, 36.7, 34.2, 33.9, 29.1, 27.7, 23.8, 21.4, 14.2; IR (film) ν_{max} 2983, 2937, 2900, 1732, 1349, 1266, 1172, 1046, 920, 739 cm^{-1}; HR ESI-TOF *m/z* 470.1981 (M + Na$^+$, $C_{24}H_{33}NO_5S$ requires 470.1972); $[\alpha]^{23}_D$ –220 (*c* 0.14, $CHCl_3$).

13b: diagnostic signals for the crude reaction product: ^{1}H NMR (acetone-d_6, 400 MHz) δ 5.56 (dt, 1H, *J* = 1.3, 2.7 Hz, int. 0.08), 5.50 (dt, 1H, *J* = 1.5, 2.7 Hz, int. 0.29), 5.48 (dt, 1H, *J* = 1.4, 2.7 Hz, int. 0.19), 5.41 (dt, 1H, *J* = 1.6, 2.6 Hz, int. 1.00); HR ESI-TOF *m/z* 472.2126 (M + Na$^+$, $C_{24}H_{35}NO_5S$ requires 472.2128).

14b: diagnostic signals for the crude reaction product: ^{1}H NMR (C_6D_6, 400 MHz) δ 5.99 (dt, 1H, *J* = 1.5, 2.6 Hz, int. 1.00), 5.35 (dt, 1H, *J* = 1.4, 2.7 Hz, int. 0.47); HR ESI-TOF *m/z* 558.1553 (M + Na$^+$, $C_{29}H_{29}NO_7S$ requires 558.1557).

15b: diagnostic signals for the crude reaction product: ^{1}H NMR (C_6D_6, 400 MHz) δ 5.86 (dt, 1H, *J* = 1.6, 2.7, int. 1.00), 5.81 (dt, 1H, *J* = 1.5, 2.7 Hz, int. 0.09), 5.39 (dt, 1H, *J* = 1.4, 2.6 Hz, int. 0.11); HR ESI-TOF *m/z* 420.1084 (M + Na$^+$, $C_{18}H_{23}NO_7S$ requires 420.1087).

16b: diagnostic signals for the crude reaction product: ^{1}H NMR (C_6D_6, 400 MHz) δ 5.86 (dt, 1H, *J* = 1.6, 2.6, int. 1.00), 5.79 (dt, 1H, *J* = 1.5, 2.6 Hz, int. 0.09), 5.41 (dt, 1H, *J* = 1.4, 2.7 Hz, int. 0.11); HR ESI-TOF *m/z* 496.1398 (M + Na$^+$, $C_{24}H_{27}NO_7S$ requires 496.14).

17b: diagnostic signals for the crude reaction product (1 M, $CHCl_3$): ^{1}H NMR (acetone-d_6, 400 MHz) δ 5.79 (dt, 1H, *J* = 1.5, 2.7 Hz, int. 1.00), 5.75 (dt, 1H, *J* = 1.5, 2.8 Hz, int. 0.08), 5.63 (dt, 1H, *J* = 1.5, 2.7 Hz, int. 0.17); HR MALDI-FTMS *m/z* 446.1223 (M + Na$^+$, $C_{20}H_{25}NO_7S$ requires 446.1244).

17b-major endo: 72 mg, 46%; ^{1}H NMR (C_6D_6, 400 MHz) δ 7.50 (m, 2H), 6.83 (m, 3H), 6.70 (td, 1H, *J* = 1.7, 8.3 Hz), 6.07 (dt, 1H, *J* = 1.6, 2.7 Hz), 5.17 (ddd, 1H, *J* = 1.6, 5.1, 8.3 Hz), 4.60 (s, 1H), 3.90 (m, 2H), 3.25 (d, 1H, *J* = 8.8 Hz), 3.09 (d, 1H, *J* = 8.8 Hz), 2.74 (tdd, 1H, *J* = 1.2, 2.7, 14.1 Hz), 2.23 (m, 1H), 0.93 (t, 3H, *J* = 7.1 Hz), 0.84 (ddd, 1H, *J* = 2.6, 8.0, 14.1 Hz), 0.80 (s, 6H); ^{13}C NMR (C_6D_6, 100 MHz) δ 174.7, 170.9, 139.0, 132.7, 129.2, 126.8, 122.1, 108.9, 80.6, 77.8, 75.3, 60.3, 39.6, 33.5, 28.1, 21.9, 19.0, 13.9; IR (film) ν_{max} 2965, 1775, 1734, 1368, 1339, 1173, 1055 cm^{-1}; HR MALDI-FTMS *m/z* 446.1223 (M + Na$^+$, $C_{20}H_{25}NO_7S$ requires 446.1244); $[\alpha]^{23}_D$ –133 (*c* 0.61, THF).

17b-minor endo: 6.5 mg, 4%; ^{1}H NMR (C_6D_6, 400 MHz) δ 7.61 (m, 2H), 6.93 (m, 3H), 6.74 (td, 1H, *J* = 1.5, 8.3 Hz), 5.57 (dt, 1H, *J* = 1.5, 2.6 Hz), 5.27 (ddd, 1H, *J* = 1.5, 5.2, 8.3 Hz), 4.38 (s, 1H), 3.98 (m, 2H), 3.28 (d, 1H, *J* = 8.7 Hz), 3.11 (d, 1H, *J* = 8.7 Hz), 2.68 (tdd, 1H, *J* = 1.2, 2.7, 13.9 Hz), 2.32 (m, 1H), 1.06 (t, 3H, *J* = 7.1 Hz), 0.89 (ddd, 1H, *J* = 2.4, 7.9, 14.1 Hz), 0.81 (s, 3H), 0.76 (s, 3H); ^{13}C NMR (C_6D_6, 100 MHz) δ 172.7, 171.3, 139.8, 132.7, 129.2, 127.0, 122.4, 107.8, 81.3, 78.4, 75.0, 61.0, 40.0, 33.8, 27.4, 22.9, 19.3, 14.1; HR ESI-TOF *m/z* 446.1242 (M + Na$^+$, $C_{20}H_{25}NO_7S$ requires 446.1244).

17b-exo: 6.1 mg, 4%; ^{1}H NMR (C_6D_6, 400 MHz) δ 7.52 (m, 2H), 6.77 (m, 3H), 6.69 (ddd, 1H, *J* = 1.4, 2.6, 8.3 Hz), 6.00 (m, 1H), 5.26 (td, 1H, *J* = 1.8, 8.4 Hz), 4.73 (s, 1H), 3.72 (m, 2H), 3.38 (tdd, 1H, *J* = 2.3, 5.5, 12.6 Hz), 3.25 (d, 1H, *J* = 8.8 Hz), 3.10 (d, 1H, *J* = 8.8 Hz), 2.36 (dddd, 1H, *J* = 1.6, 3.0, 5.7, 13.4 Hz), 1.11 (dt, 1H, *J* = 2.6, 13.1 Hz), 0.77 (t, 3H, *J* = 7.0 Hz), 0.75 (s, 3H), 0.71 (s, 3H); ^{13}C NMR (C_6D_6, 100 MHz) δ 174.9, 169.8, 138.6, 132.9, 129.3, 126.8, 123.1, 108.7, 81.2, 77.6, 75.3, 60.7, 39.7, 34.4, 28.4, 22.2, 19.5, 13.9; HR ESI-TOF *m/z* 424.1426 (M + H$^+$, $C_{20}H_{25}NO_7S$ requires 424.1244).

18b: diagnostic signals for the crude reaction product (1 M, $CHCl_3$): ^{1}H NMR (acetone-*d*$_6$, 400 MHz) δ 6.05 (dt, 1H, *J* = 1.4, 2.8 Hz, int. 0.04), 5.97 (dt, 1H, *J* = 1.5, 2.7 Hz, int. 1.00), 5.39 (dt, 1H, *J* = 1.4, 2.6 Hz, int. 0.06); HR ESI-TOF *m/z* 418.0934 (M + Na$^+$, $C_{18}H_{21}NO_7S$ requires 418.0931).

18b-major endo: 80 mg, 56%; ^{1}H NMR (acetone-*d*$_6$, 500 MHz) δ 7.59 (m, 2H), 6.94 (m, 3H), 6.70 (td, 1H, *J* = 1.5, 8.4 Hz), 5.94 (dt, 1H, *J* = 1.5, 2.5 Hz), 5.15 (ddd, 1H, *J* = 1.4, 5.3, 8.1 Hz), 4.72 (t, 1H, *J* = 8.8 Hz), 3.94 (m, 2H), 3.51 (dt, 1H, *J* = 2.7, 8.7 Hz), 3.20 (dt, 1H, *J* = 6.5, 9.4 Hz), 2.63 (tdd, 1H, *J* = 1.3, 2.7, 13.9 Hz), 2.30 (m, 1H), 1.77 (m, 1H), 1.67 (m, 1H), 0.99 (t, 3H, *J* = 7.1 Hz), 0.82 (ddd, 1H, *J* = 2.5, 7.7, 13.9 Hz); ^{13}C NMR (acetone-*d*$_6$, 100 MHz) δ 176.5, 173.2, 140.7, 135.3, 131.4, 128.5, 123.7, 110.4, 82.6, 72.0, 66.7, 61.9, 35.0, 31.2, 29.9, 15.4; IR (film) ν_{max} 2985, 1783, 1732, 1447, 1337, 1171, 1048, 927, 733, 689; HR ESI-TOF *m/z* 418.0934 (M + Na$^+$, $C_{18}H_{21}NO_7S$ requires 418.0931); $[\alpha]^{23}_D$ –134 (*c* 0.75, $CHCl_3$).

19b: diagnostic signals for the crude reaction product (1 M, $CHCl_3$, 48 h): ^{1}H NMR (acetone-*d*$_6$, 500 MHz) δ 5.92 (dt, 1H, *J* = 1.5, 2.7 Hz, int. 1.02), 5.89 (dt, 1H, *J* = 1.4 Hz, 2.8 Hz, int. 0.02); diagnostic ^{1}H NMR (C_6D_6, 500 MHz) δ 5.29 (td, 1H, *J* = 1.7, 8.3 Hz, int. 0.02), 5.16 (ddd, 1H, *J* = 1.5, 5.3, 8.3 Hz, int. 1.02); HR ESI-TOF *m/z* 395.1275 (M + H$^+$, $C_{18}H_{22}N_2O_6S$ requires 395.1271).

19b-major endo: 117 mg, 80%; mp 134 °C (white prisms, 2:1 EtOAc–hexanes); Extraction of crude reaction mixture with 1 N HCl (aq) prior to column chromatography removes excess dieneophile; ^{1}H NMR (acetone-*d*$_6$, 500 MHz) δ 7.85 (m, 2H), 7.69 (m, 3H), 6.85 (bs, 1H), 6.62 (td, 1H, *J* = 1.6, 8.3 Hz), 5.93 (dt, 1H, *J* = 1.5, *J* = 2.7 Hz), 5.31 (ddd, 1H, *J* = 1.6, 5.3, 8.3 Hz), 4.37 (t, 1H, *J* = 8.1 Hz), 4.02 (m, 2H), 3.25 (m, 2H), 2.89 (m, 1H), 2.64 (tdd, 1H, *J* = 1.5, 2.9, 13.9 Hz), 2.29 (m, 1H), 1.74 (m, 1H), 1.18 (ddd, 1H, *J* = 2.5, 7.7, 13.8 Hz), 1.17 (t, 3H, *J* = 7.1 Hz); ^{13}C NMR (C_6D_6, 125 MHz) δ 176.4, 171.5, 139.7, 132.5, 129.2, 128.3, 127.0, 122.8, 81.0, 72.4, 60.4, 38.2, 33.9, 28.7, 28.5, 14.2; IR (film) ν_{max} 3250, 2984, 1713, 1447, 1337, 1171, 1046, 926, 732, 689 cm^{-1}; HR ESI-TOF *m/z* 395.1275 (M + H$^+$, $C_{18}H_{22}N_2O_6S$ requires 395.1271); [α]$^{23}_{D}$ +185 (*c* 0.53, $CHCl_3$).

20b: diagnostic signals for the crude reaction product (0.3 M, $CHCl_3$, 24 h): ^{1}H NMR (acetone-*d$_6$*, 400 MHz) δ 5.84 (dt, 1H, *J* = 1.5, 2.8 Hz), 5.28 (ddd, 1H, *J* = 1.6, 5.4, 8.4 Hz); HR ESI-TOF 355.0920 (M + Na$^+$, $C_{13}H_{20}N_2O_6S$ requires 355.0934).

21b-major endo: 0.3 M, $CHCl_3$, 24 h: 58 mg, 76%; mp 120 °C (white needles, EtOAc–hexanes); ^{1}H NMR (acetone-*d$_6$*, 400 MHz) δ 6.80 (s, 1H), 6.53 (td, 1H, *J* = 1.7, 8.4 Hz), 5.79 (m, 1H), 5.15 (ddd, 1H, *J* = 1.7, 5.1, 8.4 Hz), 4.48 (t, 1H, *J* = 8.0 Hz), 4.05 (qq, 2H, *J* = 7.1, 10.8 Hz), 3.24 (m, 2H), 3.09 (tdd, 1H, *J* = 1.4, 5.1, 8.0 Hz), 2.91 (m, 1H), 2.30 (dddd, 1H, *J* = 3.3, 6.8, 8.1, 12.9 Hz), 2.11 (ddd, 1H, *J* = 2.2, 7.9, 13.8 Hz), 1.77 (tdd, 1H, *J* = 7.9, 8.6, 12.9 Hz), 1.36 (s, 9H), 1.19 (t, 3H, *J* = 7.1 Hz); ^{13}C NMR (acetone-*d$_6$*, 125 MHz) δ 176.6, 173.7, 126.2, 105.7, 83.2, 74.3, 63.9, 61.8, 39.8, 35.3, 31.4, 30.2, 25.7, 15.4; IR (film) ν_{max} 3250, 2983, 1712, 1325, 1202, 1144, 1045, 931, 707 cm^{-1}; HR ESI-TOF *m/z* 397.1408 (M + Na$^+$, $C_{16}H_{26}N_2O_6S$ requires 397.1404); [α]$^{23}_{D}$ +47 (*c* 0.52, $CHCl_3$).

22b-major endo: 0.3 M, $CHCl_3$, 24 h: 168 mg, 60%; ^{1}H NMR (acetone-*d$_6$*, 400 M Hz) δ 8.15 (ddd, 1H, *J* = 0.7, 1.5, 7.4 Hz), 7.95 (m, 3H), 6.86 (s, 1H), 6.61 (td, 1H, *J* = 1.6, 8.4 Hz), 6.01 (m, 1H), 5.38 (ddd, 1H, *J* = 1.6, 5.3, 8.4 Hz), 4.29 (t, 1H, *J* = 8.0 Hz), 4.06 (qq, 2H, *J* = 7.1, 10.7 Hz), 3.25 (m, 2H), 3.05 (m, 1H), 2.85 (m, 1H), 2.29 (dddd, 1H, *J* = 3.6, 6.4, 8.2, 12.9 Hz), 1.77 (m, 2H), 1.20 (t, 3H, *J* = 7.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.5, 172.2, 147.8, 134.2, 132.1, 132.0, 130.8, 124.4, 122.0, 107.9, 81.5, 73.0, 60.8, 38.6, 33.7, 29.2, 28.3, 14.0; IR (film) ν_{max} 3249, 3098, 2985, 2902, 1712, 1546, 1371, 1176, 1045, 928, 908, 717, 732 cm^{-1}; HR ESI-TOF *m/z* 440.1121 (M + H$^+$, $C_{18}H_{21}N_3O_8S$ requires 440.1122); [α]$^{23}_{D}$ +96 (*c* 1.1, $CHCl_3$).

23b: diagnostic signals for the crude reaction product (0.3 M, $CHCl_3$, 24 h): ^{1}H NMR (acetone-*d*$_6$, 400 MHz) δ 5.99 (dt, 1H, *J* = 1.5, 2.7 Hz), 5.39 (ddd, 1H, *J* = 1.6, 5.3, 8.3 Hz); HR ESI-TOF *m/z* 462.0939 (M + Na$^+$, $C_{18}H_{21}N_3O_8S$ requires 462.0941).

24b: diagnostic signals for the crude reaction product (0.3 M, $CHCl_3$, 24 h): ^{1}H NMR (acetone-*d$_6$*, 400 MHz) δ 6.02 (m, 1H), 5.33 (ddd, 1H, *J* = 1.7, 5.3, 8.4 Hz); HR ESI-TOF *m/z* 485.0966 (M + Na$^+$, $C_{19}H_{21}F_3N_2O_6S$ requires 485.0965).

25b: diagnostic signals for the crude reaction product (0.3 M, $CHCl_3$, 24 h): ^{1}H NMR (acetone-*d$_6$*, 400 MHz) δ 5.99 (m, 1H), 5.32 (ddd, 1H, *J* = 1.6, 5.3, 8.4 Hz); HR ESI-TOF *m/z* 453.0902 (M + Na$^+$, $C_{18}H_{20}F_2N_2O_6S$ requires 453.0902).

Cycloadduct Transformations.

26: A suspension of $Pd(OH)_2/C$ (20%, 5 mg, 0.01 mmol) in ethanol (0.75 mL) was treated with a solution **17b** (213 mg, 0.503 mmol) in ethanol (0.75 mL), and the mixture was stirred under an atmosphere of hydrogen at 25 °C for 18 h. The reaction mixture was filtered through a plug of Celite (0.75 × 2 cm), which was then flushed with ethanol (10 mL). The solvent was removed in vacuo to yield **26** as a colorless oil (214 mg, 100%): ^{1}H NMR (C_6D_6, 500 MHz) δ 7.61 (m, 2H), 6.90 (m, 3H), 6.07 (t, 1H, *J* = 2.7 Hz), 4.26 (s, 1H), 4.03 (qd, 1H, *J* = 7.1, 10.8 Hz), 3.87 (qd, 1H, *J* = 7.2, 10.8 Hz), 3.73 (dt, 1H, *J* = 2.9, 13.4 Hz), 3.50 (ddd, 1H, *J* = 2.5, 4.7, 13.7 Hz), 3.24 (d, 1H, *J* = 8.8 Hz), 3.04 (d, 1H, *J* = 8.8 Hz), 2.58 (qd, 1H, *J* = 2.1, 14.2 Hz), 1.90 (m, 1H), 1.74 (m, 1H), 1.32 (ddd, 1H, *J* = 3.6, 6.7, 14.3 Hz), 0.95 (t, 3H, *J* = 7.1 Hz), 0.84 (m, 1H), 0.83 (s, 3H), 0.80 (s, 3H); ^{13}C NMR (C_6D_6, 125 MHz) δ 175.1, 173.6, 142.0, 132.4, 129.3, 127.2, 82.4, 78.4, 75.5, 60.4, 39.9, 37.8, 33.5, 32.0, 24.2, 22.7, 19.4, 14.3; IR (film) ν_{max} 2965, 1792, 1769, 1728, 1447, 1341, 1199, 1165, 1111, 1079 cm^{-1}; HR ESI-TOF *m/z* 448.1396 (M + Na$^+$, $C_{20}H_{27}NO_7S$ requires 448.14); [α]$^{23}_{D}$ +17 (*c* 0.51, THF).

27: A solution of **26** (26.8 mg, 0.0630 mmol) in THF–H_2O (1:3, 0.5 mL) was treated with TFA (1 μL, 0.013 mmol) and stirred at 75 °C for 22 h. The reaction mixture was diluted with CH_2Cl_2 (15 mL), and the organic layer was washed with water (2 × 5 mL), saturated aqueous NaCl (1 × 5 mL) and dried ($MgSO_4$). The solvent was removed in vacuo and the residue was purified by flash chromatography (SiO_2, 20% EtOAc–hexanes) to afford **27** as a colorless oil in a 14:1 (*trans*:*cis*) ratio of C2 epimers (13 mg, 66%): ^1H NMR (acetone-d_6, 500 MHz) δ 7.88 (m, 2H), 7.64 (m, 1H), 7.57 (m, 2H), 5.75 (td, 1H, *J* = 2.9, 4.8 Hz), 4.97 (d, 1H, *J* = 4.8 Hz), 4.07 (q, 2H, *J* = 7.1 Hz), 3.59 (ddd, 1H, *J* = 2.4, 4.6, 12.2 Hz), 3.06 (dt, 1H, *J* = 2.9, 12.7 Hz), 2.82 (tt, 1H, *J* = 3.7, 12.7 Hz), 2.07 (m, 1H), 1.96 (m, 1H), 1.68 (dt, 1H, *J* = 3.0, 13.1 Hz), 1.55 (dq, 1H, *J* = 4.7, 13.0 Hz), 1.19 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (acetone-d_6, 125 MHz) δ 175.8, 142.2, 134.2, 130.7, 129.4, 77.4, 61.8, 41.1, 37.1, 36.5, 29.2, 15.4; IR (film) ν_{max} 3500, 2964, 1732, 1447, 1331, 1260, 1153, 1094, 922 cm^{-1}; HR ESI-TOF *m/z* 336.0874 (M + Na^+, $C_{14}H_{19}NO_5S$ requires 336.0876).

28: A solution of **26** (34.0 mg, 0.0799 mmol) in EtOH (1.0 mL) was treated with TFA (1 μL, 0.013 mmol) and stirred at 75 °C for 22 h. The reaction mixture was diluted with CH_2Cl_2 (15 mL), and the organic layer was washed with water (2 × 5 mL), saturated aqueous NaCl (1 × 5 mL) and dried ($MgSO_4$). The solvent was removed in vacuo and the residue was purified by flash chromatography (SiO_2, 10–20% EtOAc–hexanes) to afford **28** as a colorless oil in a 7:1 (*trans*:*cis*) ratio of C2 epimers (20 mg, 80%): ^1H NMR (acetone-d_6, 600 MHz) δ 7.89 (m, 2H), 7.68 (m, 1H), 7.62 (m, 2H), 5.34 (t, 1H, *J* = 2.7 Hz), 4.04 (q, 2H, *J* = 7.1 Hz), 3.68 (ddd, 1H, *J* = 2.1, 4.3, 13.5 Hz), 3.52 (qd, 1H, *J* = 7.0, 9.6 Hz), 3.44 (qd, 1H, *J* = 7.0, 9.3 Hz), 3.11 (dt, 1H, *J* = 2.8, 13.3 Hz), 2.73 (tt, 1H, *J* = 3.6, 12.7 Hz), 2.10 (m, 1H), 1.82 (m, 1H), 1.47 (dt, 1H, *J* = 3.1, 13.2 Hz), 1.28 (dq, 1H, *J* = 4.7, 13.1 Hz), 1.17 (t, 3H, *J* = 7.2 Hz), 1.09 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (acetone-d_6, 600 MHz) δ 175.5, 142.9, 134.4, 131.0, 128.8, 83.6, 64.2, 61.8, 41.4, 37.0, 34.1, 28.5, 16.1, 15.4; IR (film) ν_{max} 2916, 1732, 1446, 1332, 1259, 1157, 1071, 924, 746, 689, 617 cm^{-1}; HR ESI-TOF *m/z* 364.1187 (M + Na^+, $C_{16}H_{23}NO_5S$ requires 364.1189).

29: A suspension of $Pd(OH)_2/C$ (20% Pd, 2 mg, 0.004 mmol) in ethanol (1.0 mL) was treated with **19b** (20 mg, 0.0507 mmol), and the mixture was stirred under an atmosphere of hydrogen at 25 °C for 14 h. The reaction mixture was filtered through a plug of Celite (0.75 × 2 cm), which was then flushed with ethanol (5 mL). The solvent was removed in vacuo to yield **29** as a colorless oil (20 mg, 100%): ^1H NMR (acetone-d_6, 300 MHz) δ 7.91 (m, 2H), 7.66 (m, 3H), 6.84 (s, 1H), 5.78 (t, 1H, *J* = 2.8 Hz), 4.04 (m, 3H), 3.52 (m, 2H), 3.23 (m, 2H), 2.54 (m, 2H), 2.17 (m, 1H), 1.98 (m, 1H), 1.73 (m, 2H), 1.41 (m, 1H), 1.18 (t, 3H, *J* = 7.1 Hz); ^{13}C NMR (acetone-d_6, 150 MHz) δ 176.5, 175.1, 143.1, 134.4, 131.1, 128.7, 84.1, 74.5, 61.6, 39.7, 39.4, 35.0, 33.6, 30.0, 26.0, 15.4; IR (film) ν_{max} 3249, 2983, 1713, 1342, 1199, 1163, 1076, 935 cm^{-1}; HR ESI-TOF *m/z* 419.1234 (M + Na^+, $C_{18}H_{24}N_2O_6S$ requires 419.1247); $[\alpha]^{23}_D$ –35 (*c* 1.0, $CHCl_3$).

30: A solution of **29** (30 mg, 0.076 mmol) in THF (0.75 mL) and water (0.75 mL) was treated with trifluoroacetic acid (1 μL, 0.013 mmol) and stirred at 25 °C for 18 h. The reaction mixture was diluted with CH_2Cl_2 (5 mL) and the organic layer was washed with water (2 × 2 mL) and saturated aqueous NaCl (1 × 2 mL), dried over $MgSO_4$ and the solvent was removed in vacuo. The residue was purified by flash chromatography (SiO_2, 20% EtOAc–hexanes) to afford **30** as a colorless oil as a 14:1 (*trans*:*cis*) ratio of C2 epimers (24 mg, 88%): ^1H NMR (acetone-d_6, 500 MHz) δ 7.89 (m, 2H), 7.60 (m, 3H), 5.76 (m, 1H), 4.88 (d, 1H, *J* = 5.2 Hz), 4.08 (q, 2H, *J* = 7.2 Hz), 3.60 (ddd, 1H, *J* = 2.2, 4.4, 12.2 Hz), 3.06 (dt, 1H, *J* = 2.8, 12.7 Hz), 2.83 (m, 1H), 2.08 (m, 1H), 1.96 (m, 1H), 1.68 (dt, 1H, *J* = 3.0, 13.1 Hz), 1.55 (dq, 1H, *J* = 4.7, 13.0 Hz), 1.19 (t, 3H, *J* = 7.1 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 175.7, 142.3, 134.2, 130.7, 129.4, 77.4, 61.8, 41.1, 37.1, 36.5, 29.2, 15.4; IR (film) ν_{max} 3500, 2978, 1732, 1447, 1331, 1260, 1163, 1094, 922 cm^{-1}; HR ESI-TOF *m/z* 336.0874 (M + Na$^+$, $C_{14}H_{19}NO_5S$ requires 336.0876).

31: A solution of **29** (23.9 mg, 0.0603 mmol) in EtOH (1.0 mL) was treated with TFA (1 μL, 0.013 mmol) and stirred at 75 °C for 3 h. The reaction mixture was diluted with CH_2Cl_2 (15 mL), and the organic layer was washed with water (2 × 5 mL), saturated aqueous NaCl (1 × 5 mL) and dried ($MgSO_4$). The solvent was removed in vacuo and the residue was purified by flash chromatography (SiO_2, 10–20% EtOAc–hexanes) to afford **31** as a colorless oil in a 7:1 (*trans*:*cis*) ratio of C2 epimers (19.4 mg, 94%): ^{1}H NMR (acetone-d_6, 600 MHz) δ 7.89 (m, 2H), 7.68 (m, 1H), 7.62 (m, 2H), 5.34 (t, 1H, *J* = 2.7 Hz), 4.04 (q, 2H, *J* = 7.1 Hz), 3.68 (ddd, 1H, *J* = 2.1, 4.5, 13.5 Hz), 3.52 (qd, 1H, *J* = 7.1, 9.5 Hz), 3.44 (qd, 1H, *J* = 7.0, 9.5 Hz), 3.11 (dt, 1H, *J* = 2.8, 13.3 Hz), 2.73 (tt, 1H, *J* = 3.6, 12.6 Hz), 2.10 (tdd, 1H, *J* = 2.1, 3.9, 13.5 Hz), 1.82 (m, 1H), 1.47 (dt, 1H, *J* = 3.1, 13.2 Hz), 1.28 (dq, 1H, *J* = 4.7, 13.1 Hz), 1.17 (t, 3H, *J* = 7.2 Hz), 1.09 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (acetone-d_6, 500 MHz) δ 175.5, 142.9, 134.4, 131.0, 128.8, 83.6, 64.2, 61.8, 41.4, 37.0, 34.1, 28.5, 16.1, 15.4; IR (film) ν_{max} 2916, 1732, 1446, 1332, 1259, 1157, 1071, 924, 746, 689, 617 cm^{-1}; HR ESI-TOF *m/z* 364.1189 (M + Na$^+$, $C_{16}H_{23}NO_5S$ requires 364.1189).

32: A suspension of $Pd(OH)_2/C$ (20% Pd, 2 mg, 0.004 mmol) in ethanol (1.0 mL) was treated with Et_3N (1.0 μL, 0.007 mmol), then **21b** (20 mg, 0.0534 mmol), and the mixture was stirred under an atmosphere of hydrogen at 25 °C for 40 h. The reaction mixture was filtered through a plug of Celite (0.75 × 1 cm), which was then flushed with ethanol (5 mL). The solvent was removed in vacuo to yield **32** as a colorless oil (17 mg, 85%): ^{1}H NMR (acetone-d_6, 600 MHz) δ 6.84 (s, 1H), 5.50 (t, 1H, *J* = 2.5 Hz), 4.42 (t, 1H, *J* = 8.1 Hz), 4.07 (q, 2H, *J* = 7.1 Hz), 3.58 (dt, 1H, *J* = 2.8, 13.2 Hz), 3.39 (m, 1H), 3.27 (m, 2H), 2.69 (m, 1H), 2.61 (qd, 1H, *J* = 2.3, 13.8 Hz), 2.36 (m, 1H), 2.13 (m, 1H), 2.08 (ddd, 1H, *J* = 3.1, 6.3, 13.8 Hz), 1.83 (m, 2H), 1.35 (s, 9H), 1.21 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR (acetone-d_6, 150 MHz) δ 176.7, 175.3, 85.3, 74.2, 62.1, 61.6, 41.0, 39.7, 35.1, 34.3, 30.3, 26.7, 25.5, 15.4; IR (film) ν_{max} 3351, 2980, 1713, 1314, 1199, 1135, 1075, 933 cm^{-1}; HR ESI-TOF *m/z* 399.1559 (M + Na$^+$, $C_{16}H_{28}N_2O_6S$ requires 399.156); $[\alpha]^{23}_{D}$ –30 (*c* 0.10, $CHCl_3$).

33: A solution of **32** (7.1 mg, 0.0189 mmol) in THF (375 μL) and water (125 μL) was treated with trifluoroacetic acid (0.5 μL, 0.0065 mmol) and stirred at 25 °C for 60 h. The reaction mixture was diluted with CH_2Cl_2 (3 mL) and the organic layer was washed with water (2 × 1 mL) and saturated aqueous NaCl (1 × 1 mL), dried over $MgSO_4$ and the solvent was removed in vacuo. The residue was purified by flash chromatography (SiO_2, 20% EtOAc–hexanes) to afford **33** as a colorless oil in a 20:1 (*trans*:*cis*) ratio of C2 epimers (4.7 mg, 85%): ^{1}H NMR (acetone-d_6, 500 MHz) δ 5.45 (m, 1H), 4.77 (s, 1H), 4.11 (q, 2H, *J* = 7.1 Hz), 3.54 (d, 1H, *J* = 11.1 Hz), 3.41 (dt, 1H, *J* = 2.6, 13.1 Hz), 2.90 (tt, 1H, *J* = 3.6, 12.6 Hz), 2.10 (m, 1H), 1.98 (m, 1H), 1.75 (dt, 1H, *J* = 2.2, 13.0 Hz), 1.64 (dq, 1H, *J* = 4.6, 12.9 Hz), 1.33 (s, 9H), 1.22 (t, 3H, *J* = 7.1 Hz); ^{13}C NMR (acetone-d_6, 150 MHz) δ 175.9, 78.5, 61.8, 42.6, 40.2, 36.8, 33.2, 25.3, 24.2, 15.4; IR (film) ν_{max} 3494, 2979, 1732, 1317, 1260, 1187, 1130, 1048, 922, 672 cm^{-1}; HR ESI-TOF *m/z* 316.1188 (M + Na$^+$, $C_{12}H_{23}NO_5S$ requires 316.1189).

34: A solution of **32** (7.1 mg, 0.0189 mmol) in EtOH (0.5 mL) was treated with TFA (0.5 μL, 0.0065 mmol) and stirred at 25 °C for 33 h. The reaction mixture was diluted with CH_2Cl_2 (3 mL), and the organic layer was washed with water (2 × 1 mL), saturated aqueous NaCl (1 × 1 mL) and dried ($MgSO_4$). The solvent was removed in vacuo and the residue was purified by flash chromatography (SiO_2, 10–20% EtOAc–hexanes) to afford **34** as a colorless oil in a 4:1

(*trans*:*cis*) ratio of C2 epimers (5.8 mg, 95%): ^{1}H NMR (acetone-d_6, 500 MHz) δ 5.09 (t, 1H, *J* = 2.4 Hz), 4.11 (q, 2H, *J* = 7.1 Hz), 3.55 (m, 3H), 3.23 (dt, 1H, *J* = 2.7, 13.3 Hz), 2.88 (tt, 1H, *J* = 3.8, 12.6 Hz), 2.15 (m, 1H), 1.96 (m, 1H), 1.73 (m, 2H), 1.35 (s, 9H), 1.22 (t, 3H, *J* = 7.1 Hz), 1.17 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (acetone-d_6, 500 MHz) δ 175.9, 84.2, 64.1, 62.3, 61.8, 42.9, 37.1, 35.0, 29.4, 25.5, 16.3, 15.4; IR (film) ν_{max} 2976, 1732, 1320, 1187, 1134, 927, 668 cm^{-1}; HR ESI-TOF *m/z* 344.1502 (M + Na$^+$, $C_{14}H_{27}NO_5S$ requires 344.1502).

35: A suspension of $Pd(OH)_2/C$ (20% Pd, 2.5 mg, 0.0046 mmol) in ethanol (1.0 mL) was treated with **22b** (20 mg, 0.0455 mmol), and the mixture was stirred under an atmosphere of hydrogen at 25 °C for 72 h. The reaction mixture was filtered through a plug of Celite (0.75 × 1 cm), which was then flushed with ethanol (5 mL). The solvent was removed in vacuo to yield **35** as a colorless oil (13.1 mg, 73%): ^{1}H NMR (acetone-d_6, 600 MHz) δ 7.64 (dd, 1H, *J* = 1.6, 8.1 Hz), 7.32 (ddd, 1H, *J* = 1.6, 7.3, 8.5 Hz), 6.92 (d, 1H, *J* = 7.8 Hz), 6.79 (s, 1H), 6.72 (ddd, 1H, *J* = 1.0, 7.1, 8.0 Hz), 5.80 (t, 1H, *J* = 2.9 Hz), 5.72 (d, 2H, *J* = 8.5 Hz), 4.19 (t, 1H, *J* = 8.1 Hz), 4.06 (m, 2H), 3.46 (m, 2H), 3.25 (m, 2H), 2.55 (tt, 1H, *J* = 2.6, 5.4 Hz), 2.44 (ddd, 1H, *J* = 2.4, 4.4, 13.9 Hz), 2.31 (m, 1H), 1.87 (m, 3H), 1.43 (tdd, 1H, *J* = 5.3, 12.6, 13.4 Hz), 1.20 (t, 3H, *J* = 7.1 Hz); ^{13}C NMR (acetone-d_6, 150 MHz) δ 176.7, 175.2, 148.2, 135.8, 131.4, 122.8, 119.3, 118.0, 83.8, 73.7, 61.6, 39.7, 39.1, 35.2, 33.4, 30.2, 26.0, 15.4; IR (film) ν_{max} 3464, 3371, 2919, 1722, 1621, 1485, 1455, 1321, 1202, 1147, 1076, 934, 753 cm^{-1}; HR ESI-TOF *m/z* 434.1353 (M + Na$^+$, $C_{18}H_{25}N_3O_6S$ requires 434.1356); $[\alpha]^{23}_D$ –65 (*c* 0.17, $CHCl_3$).

36: A solution of **35** (5.8 mg, 0.0141 mmol) in EtOH (0.5 mL) was treated with TFA (0.5 μL, 0.0065 mmol) and stirred at 25 °C for 33 h. The reaction mixture was diluted with CH_2Cl_2 (3 mL), and the organic layer was washed with water (2 × 1 mL), saturated aqueous NaCl (1 × 1 mL) and dried ($MgSO_4$). The solvent was removed in vacuo and the residue was purified by flash chromatography (SiO_2, 20% EtOAc–hexanes) to afford **36** as a colorless oil in a 2.5:1 ratio (*trans*:*cis*) of C2 epimers (4.2 mg, 96%). Spectroscopic data for the major diastereoisomer: ^{1}H NMR (acetone-d_6, 600 M Hz) δ 7.54 (m, 1H), 7.34 (m, 1H), 6.89 (m, 1H), 6.81 (m, 1H), 6.44 (s, 1H), 5.48 (t, 1H, *J* = 2.9 Hz), 4.14 (q, 2H, *J* = 7.2 Hz), 3.40 (ddd, 1H, *J* = 2.7, 4.3, 11.6 Hz), 2.85 (m, 1H), 2.64 (ddd, 1H, *J* = 2.9, 11.9, 13.1 Hz), 2.32 (m, 1H), 2.09 (m, 1H), 1.98 (ddd, 1H, *J* = 3.7, 12.9, 14.2 Hz), 1.74 (ddd, 1H, *J* = 4.4, 13.0, 26.0 Hz), 1.23 (t, 3H, *J* = 7.4 Hz); ^{13}C NMR (acetone-d_6, 150 M Hz) δ 175.4, 144.7, 135.0, 126.9, 119.1, 118.0, 117.6, 66.2, 62.0, 42.5, 36.8, 33.0, 28.5, 15.4; IR (film) ν_{max} 3369, 2936, 1732, 1606, 1505, 1485, 1327, 1172, 900, 751 cm^{-1}; HR ESI-TOF *m/z* 311.1053 (M + H$^+$, $C_{14}H_{18}N_2O_4S$ requires 311.106).