Simple Thiazocine-2-acetic Acid Derivatives via Ring Closing Metathesis

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Supplemental Information

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Experimental Section (Introduction and compounds 7-12 and 13-20)

All reagents were used without purification unless otherwise noted. Silica gel (70-230 mesh, 60 Å) was used for column chromatography. Melting points were taken on a Fisher-Johns melting point apparatus and are uncorrected. IR spectra were recorded in chloroform solution. NMR spectra were recorded in CDCl₃ solution unless otherwise noted (¹H NMR at 400 MHz and ¹³C NMR at 100 MHz). Mass spectra were obtained under electron impact at 70 eV. Gen2 refers to Grubbs' second Generation catalyst [CAS registry number 246047-72-3, 1,3-bis(2,4,6-trimethylphenyl)-2-imidazolidinylidene)dichloro(phenylmethylene)(tricyclohexylphosphine)ruthenium].

Methyl γ -bromocrotonate was prepared according to the literature:³⁵ ¹H NMR δ 6.95 (m, 1H), 5.99 (dt, 1H, J = 15.6, 1.2 Hz), 3.97 (dd, 2H, J = 7.6, 1.2 Hz), 3.71 (s, 3H); ¹³C NMR δ 165.9, 141.9, 124.1, 51.8, 29.0. *N*-Allyl-4-methylbenzensulfonamide was prepared according to the literature: mp 62-63 °C (lit.³⁶ 63-65 °C); ¹H NMR δ 7.73 (d, 2H, J = 8.0 Hz), 7.29 (d, 2H, J = 8.0 Hz), 5.70 (m, 1H), 5.14 (dd, 1H, J = 17.2, 1.2 Hz), 5.08 (dd, 1H, J = 9.2, 1.2 Hz), 4.50 (br s, 1H), 3.56 (t, 2H, J = 6.0 Hz), 2.41 (s, 3H); ¹³C NMR δ 143.5, 137.0, 133.0, 129.7, 127.1, 117.7, 45.8, 21.5.

(2*E*)-4-[allyl[(4-methylphenyl)sulfonyl]amino]but-2-enoic acid (7). To an ice-cooled solution of LiOH·H₂O (1.5 eq, 0.95 g, 22.5 mmol) in H₂O (40 mL) and THF (40 mL) was added at 0 °C a solution of **1** (4.64 g, 15 mmol) in THF (40 mL). This mixture was stirred at 0 °C for 3 h under a nitrogen atmosphere, then extracted with EtOAc. The aqueous layer was acidified with 5% HCl solution followed by extraction with EtOAc. The combined organic layers were dried over anhydrous Na₂SO₄ and concentrated *in vacuo* to

give 4.22 g (95%) of **7** as a white solid, which was used directly for preparation of **8** or **14**. ^1H NMR δ 7.68 (d, 2H, J = 8.0 Hz), 7.30 (d, 2H, J = 8.0 Hz), 6.81 (dt, 1H, J = 15.6, 5.6 Hz), 5.85 (dt, 1H, J = 15.6, 1.6 Hz), 5.59 (m, 1H), 5.17-5.10 (m, 2H), 3.93 (dd, 2H, J = 5.6, 1.6 Hz), 3.79 (d, 2H, J = 6.4 Hz), 2.42 (s, 3H); ^{13}C NMR δ 174.6, 145.3, 143.8, 136.7, 132.2, 129.8, 127.2, 119.9, 117.6, 50.6, 47.3, 21.6.

***N*-allyl-*N*-[(2*E*)-4-(1*H*-indol-1-yl)-4-oxobut-2-enyl]-4-methylbenzenesulfonamide (**8**).** Method 1: To an ice-cooled solution of **7** (0.71 g, 2.4 mmol) in THF (25 mL) was added dropwise oxalyl chloride (12.0 eq, 2.52 mL, 28.9 mmol) at 0 °C. The resulting mixture was stirred at room temperature for 24 h and concentrated *in vacuo*. The residue was used directly for the following reaction. To a well-stirred mixture of indole (1.1 eq, 0.31 g, 2.7 mmol), powdered NaOH (1.5 eq, 0.14 g, 3.6 mmol) and tetrabutylammonium hydrogen sulfate (0.01 eq, 0.01 g) in CH_2Cl_2 (15 mL) was added dropwise a solution of above residue in CH_2Cl_2 (10 mL) in an ice-water bath. The resulting mixture was stirred at 0 °C for 15 min and at room temperature for 3 h, poured into ice-water, and extracted with CH_2Cl_2 . The combined organic layers were washed with distilled water, dried over anhydrous Na_2SO_4 , and concentrated *in vacuo*. Column chromatography on silica gel (EtOAc/hexane, 1:9) gave 0.24 g (25%) of **8** as a sticky liquid.

Method 2: To a solution of **14** (1.10 g, 2.78 mmol) in dioxane (50 mL) was added a solution of DDQ (6.0 eq, 3.78 g, 16.68 mmol) in dioxane (30 mL) at 55 °C through a syringe. The resulting mixture was then heated to 70 °C and stirred for 3 days. The mixture was vacuum filtered and the filtrate was concentrated *in vacuo*. The residue was then stirred in MeOH (60 mL) at room temperature for 1 h. After the evaporation of

MeOH, the residue was diluted with CH₂Cl₂ (100 mL), washed with 5% NaHCO₃ solution followed by distilled water and concentrated *in vacuo*. Column chromatography on silica gel (EtOAc/hexane, 1:4) gave 0.98 g (89%) of **8** as a sticky liquid: IR 1690 cm⁻¹; ¹H NMR δ 8.45 (d, 1H, *J* = 7.6 Hz), 7.72 (d, 2H, *J* = 8.4 Hz), 7.55 (d, 1H, *J* = 7.6 Hz), 7.39 (d, 1H, *J* = 4.0 Hz), 7.36-7.25 (m, 4H), 6.98 (dt, 1H, *J* = 15.2, 5.2 Hz), 6.76 (dt, 1H, *J* = 15.2, 1.6 Hz), 6.64 (dd, 1H, *J* = 4.0, 0.8 Hz), 5.64 (m, 1H), 5.19-5.14 (m, 2H), 4.05 (dd, 2H, *J* = 5.2, 1.6 Hz), 3.85 (d, 2H, *J* = 6.4 Hz), 2.39 (s, 3H); ¹³C NMR δ 163.3, 144.1, 143.8, 136.7, 135.7, 132.3, 130.6, 130.0, 127.2, 125.1, 124.6, 123.9, 123.0, 120.9, 119.9, 116.7, 109.4, 50.9, 47.7, 21.5; MS [*m/z* (rel intensity)] 394 (M⁺, 27), 278 (8), 239 (13), 155 (69), 123 (6), 117 (60).

***N*-allyl-*N*-[2-(allylthio)-4-(1*H*-indol-1-yl)-4-oxobutyl]-4-methylbenzenesulfonamide (**9**).** To an ice-cooled solution of allyl mercaptan (1.2 eq, 0.07 mL, 0.9 mmol) and Et₃N (1.2 eq, 0.125 mL, 0.9 mmol) in CH₂Cl₂ (10 mL) was added a solution of **8** (0.30 g, 0.75 mmol) in CH₂Cl₂ (6 mL) at 0 °C. The resulting mixture was stirred at 0 °C for 15 min and at room temperature for 6 h, then diluted with CH₂Cl₂, washed with 5% HCl solution followed by distilled water. The organic layer was dried over anhydrous Na₂SO₄, and concentrated *in vacuo*. Column chromatography on silica gel (EtOAc/hexane, 1:4) gave 0.28 g (80%) of **9** as a sticky liquid: IR 1705 cm⁻¹; ¹H NMR δ 8.47 (d, 1H, *J* = 8.0 Hz), 7.67 (d, 2H, *J* = 8.0 Hz), 7.55 (d, 1H, *J* = 7.6 Hz), 7.47 (d, 1H, *J* = 4.0 Hz), 7.36-7.26 (m, 4H), 6.64 (d, 1H, *J* = 3.6 Hz), 5.76 (m, 1H), 5.56 (m, 1H), 5.23-5.02 (m, 4H), 3.89-3.78 (m, 2H), 3.57-3.46 (m, 3H), 3.29-3.06 (m, 4H), 2.40 (s, 3H); ¹³C NMR δ 169.3, 143.7, 136.3, 135.7, 134.5, 132.5, 130.4, 129.8, 127.3,

125.0, 124.7, 123.7, 120.8, 120.0, 117.6, 116.7, 109.3, 52.0, 51.8, 39.1, 38.6, 35.5, 21.5;
MS [m/z (rel intensity)] 313 (65), 224 (72), 155 (89), 117 (68).

***N*-allyl-*N*-[2-(allylsulfinyl)-4-(1*H*-indol-1-yl)-4-oxobutyl]-4-methylbenzenesulfonamide (10).** To an ice-cooled solution of **9** (1.5 g, 3.21 mmol) in CH₂Cl₂ (25 mL) was added slowly a solution of *m*-CPBA (1.0 eq) in CH₂Cl₂ (20 mL). The resulting mixture was stirred at 0 °C for 15 min and put in a freezer (-20 °C) overnight. The reaction mixture was then poured into 5% NaHCO₃ solution. After separating and saving the organic layer, the aqueous layer was extracted with CH₂Cl₂. The combined organic layers were washed with distilled water, dried over anhydrous Na₂SO₄, and concentrated *in vacuo*. Column chromatography on silica gel (EtOAc/hexane, 3:2) gave 1.12 g (72%) of **10** as a sticky liquid (as a mixture of two diastereomers in a 2:3 ratio): IR 1698 cm⁻¹, ¹H NMR δ 8.38 (d, 1H, *J* = 7.6 Hz), 7.69 (d, 2H, *J* = 8.0 Hz), 7.55 (d, 1H, *J* = 7.6 Hz), 7.47 (d, 1H, *J* = 3.6 Hz), 7.36-7.25 (m, 4H), 6.67 (d, 1H, *J* = 4.0 Hz), 5.97 (m, 1H), 5.59 (m, 1H), 5.48-5.43 (m, 2H), 5.22 (dd, 1H, *J* = 17.2, 1.2 Hz), 5.16 (dd, 1H, *J* = 10.0, 1.2 Hz), 3.86 (d, 2H, *J* = 6.4 Hz), 3.79 (m, 1H), 3.69 (m, 1H), 3.64-3.59 (m, 2H), 3.57 (m, 1H), 3.48 (m, 1H), 3.43 (dd, 1H, *J* = 7.2, 2.0 Hz), 2.39 (s, 3H); ¹³C NMR δ 168.6, 144.0, 135.6, 132.4, 130.4, 130.0, 127.4, 127.2, 126.0, 125.3, 124.4, 124.0, 123.9, 121.1, 120.5, 116.5, 110.2, 54.2, 52.5, 51.0, 44.7, 34.1, 21.5.

***N*-allyl-*N*-[2-(allylsulfonyl)-4-(1*H*-indol-1-yl)-4-oxobutyl]-4-methylbenzenesulfonamide (11).** To an ice-cooled solution of **9** (0.28 g, 0.60 mmol) in CH₂Cl₂ (8 mL) was added a solution of *m*-CPBA (2.0 eq) in CH₂Cl₂ (6 mL). The

resulting mixture was stirred at room temperature for 12 h and poured into 5% NaHCO₃ solution. After separating and saving the organic layer, the aqueous layer was extracted with CH₂Cl₂. The combined organic layers were washed with distilled water, dried over anhydrous Na₂SO₄, and concentrated *in vacuo*. Column chromatography on silica gel (EtOAc/hexane, 3:7) gave 0.17 g (57%) of **11** as a sticky liquid: IR 1703 cm⁻¹; ¹H NMR δ 8.42 (d, 1H, *J* = 8.0 Hz), 7.68 (d, 2H, *J* = 8.0 Hz), 7.56 (d, 1H, *J* = 7.6 Hz), 7.48 (d, 1H, *J* = 4.0 Hz), 7.35-7.33 (m, 1H), 7.30-7.26 (m, 3H), 6.67 (dd, 1H, *J* = 4.0, 0.4 Hz), 5.93 (m, 1H), 5.59-5.48 (m, 3H), 5.23 (dd, 1H, *J* = 17.2, 1.2 Hz), 5.16 (dd, 1H, *J* = 10.0, 1.2 Hz), 4.37 (m, 1H), 3.99-3.78 (m, 4H), 3.70-3.59 (m, 2H), 3.53-3.46 (m, 2H), 2.39 (s, 3H); ¹³C NMR δ 168.0, 144.2, 135.6, 135.2, 131.8, 130.5, 130.0, 127.5, 125.7, 125.3, 124.4, 124.1, 124.0, 121.1, 121.0, 116.5, 110.2, 58.8, 54.9, 52.4, 46.2, 32.6, 21.5.

1-[[4-[4-(methylphenyl)sulfonyl]-1-oxido-3,4,5,8-tetrahydro-2*H*-1,4-thiazocin-2-yl]acetyl]-1*H*-indole (12). To a solution of **10** (0.79 g, 1.63 mmol, 1:1 ratio) in CH₂Cl₂ (10 mL) was added a solution of Gen 2 catalyst (10% mol, 0.14 g) in CH₂Cl₂ (8 mL) under a nitrogen atmosphere. The resulting mixture was refluxed for 2.5 h, cooled to room temperature and concentrated *in vacuo*, Column chromatography of the residue on silica gel (EtOAc) gave 0.36 g (48%) of **12** as a white solid (a mixture of two diastereomers in a 2:3 ratio): mp 149-51 °C.

minor diastereomer: ¹H NMR δ 8.39 (d, 1H, *J* = 8.0 Hz), 7.66 (d, 2H, *J* = 8.4 Hz), 7.54 (d, 1H, *J* = 7.6 Hz), 7.41 (d, 1H, *J* = 4.0 Hz), 7.35-7.25 (m, 4H), 6.64 (d, 1H, *J* = 4.0 Hz), 5.90 (m, 1H), 5.64 (m, 1H), 4.42 (m, 1H), 4.17-3.79 (m, 5H), 3.47 (dd, 1H, *J* = 17.2, 6.0 Hz), 3.09-3.03 (m, 2H), 2.36 (s, 3H).

major diastereomer: IR 1702 cm^{-1} ; ^1H NMR δ 8.32 (d, 1H, $J = 8.4$ Hz), 7.59 (d, 2H, $J = 8.4$ Hz), 7.54 (d, 1H, $J = 7.2$ Hz), 7.47 (d, 1H, $J = 4.0$ Hz), 7.34-7.26 (m, 4H), 6.66 (d, 1H, $J = 4.0$ Hz), 5.95 (dt, 1H, $J = 11.6, 3.2$ Hz), 5.84 (m, 1H), 4.44 (m, 1H), 4.30 (d, 1H, $J = 18.4$ Hz), 3.99 (dd, 1H, $J = 14.0, 8.8$ Hz), 3.91 (m, 1H), 3.83 (dd, 1H, $J = 17.2, 2.4$ Hz), 3.74-3.64 (m, 2H), 3.26 (dd, 1H, $J = 14.0, 2.4$ Hz), 3.16 (dd, 1H, $J = 17.2, 10.0$ Hz), 2.39 (s, 3H); ^{13}C NMR δ 168.0, 167.5, 144.2, 144.1, 135.6, 135.5, 134.0, 133.7, 132.7, 130.4, 130.1, 130.0, 127.4, 127.1, 125.4, 125.3, 124.3, 124.1, 124.0, 121.1, 118.8, 116.4, 116.3, 110.3, 110.2, 55.4, 51.2, 49.9, 49.2, 48.8, 48.1, 46.2, 44.6, 34.7, 33.6, 21.46. Anal. Calcd for $\text{C}_{23}\text{H}_{24}\text{O}_5\text{N}_2\text{S}_2$: C, 60.51; H, 5.30; N, 6.14. Found: C, 60.18; H, 5.43; N, 6.00 (on diastereomer mixture).

***N*-Allyl-*N*-[(2*E*)-4-(2,3-dihydro-1*H*-indol-1-yl)-4-oxobut-2-enyl]-4-methylbenzenesulfonamide (**14**).** To an ice-cooled solution of **7** (0.68 g, 2.3 mmol) in THF (25 mL) was added dropwise oxalyl chloride (12.0 eq, 2.41 mL, 27.66 mmol) at 0 °C. The resulting mixture was stirred at room temperature for 24 h then concentrated *in vacuo* and the residue was used directly in the following reaction. To an ice-cooled solution of indoline (1.2 eq, 0.33 g, 2.8 mmol), pyridine (10.0 eq, 1.88 mL, 23.1 mmol) and DMAP (0.05 g) in CH_2Cl_2 (15 mL) was added slowly a solution of the above residue in CH_2Cl_2 (15 mL) at 0 °C. The resulting mixture was stirred at 0 °C for 15 min and at room temperature overnight. The solution was poured into 5% aqueous HCl and extracted with CH_2Cl_2 . The combined organic layers were washed with 5% HCl solution followed by distilled water, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Column chromatography on silica gel (EtOAc/hexane, 2:3) gave 0.59 g (64%) of **14** as a

white solid: mp 123-5 °C; IR 1666 cm⁻¹; ¹H NMR δ 8.22 (d, 1H, *J* = 7.2 Hz), 7.69 (d, 2H, *J* = 8.4 Hz), 7.28 (d, 2H, *J* = 8.0 Hz), 7.17 (t, 2H, *J* = 7.6 Hz), 7.00 (t, 1H, *J* = 7.6 Hz), 6.77 (dt, 1H, *J* = 14.8, 5.2 Hz), 6.37 (d, 1H, *J* = 14.8 Hz), 5.61 (m, 1H), 5.15-5.11 (m, 2H), 4.10-4.05 (m, 2H), 3.98 (d, 2H, *J* = 4.8 Hz), 3.81 (d, 2H, *J* = 6.4 Hz), 3.16 (t, 2H, *J* = 7.6 Hz), 2.39 (s, 3H); ¹³C NMR δ 163.2, 143.6, 142.7, 140.2, 136.9, 132.3, 131.5, 129.8, 127.5, 127.1, 124.5, 123.9, 119.6, 117.4, 50.4, 48.0, 47.6, 27.9, 21.4; MS [*m/z* (rel intensity)] 396 (M⁺, 10), 241 (4), 155 (29), 119 (83). Anal. Calcd for C₂₂H₂₄O₃N₂S: C, 66.64; H, 6.10; N, 7.07. Found: C, 66.56; H, 6.16; N, 7.07.

***N*-allyl-*N*-[2-(allylthio)-4-(2,3-dihydro-1*H*-indol-1-yl)-4-oxobutyl]-4-methylbenzenesulfonamide (**15**).** To an ice-cooled solution of allyl mercaptan (3.0 eq, 0.36 mL, 4.5 mmol) and sodium methoxide (1.12 eq, 0.09 g, 1.7 mmol) in MeOH (15 mL) and THF (5 mL) was added a solution of **14** (0.59 g, 1.5 mmol) in THF (10 mL) at 0 °C. The resulting mixture was stirred at 0 °C for 15 min. The solution was then poured into ice water and extracted with CH₂Cl₂. The combined organic layers were washed with distilled water, dried over anhydrous Na₂SO₄, and concentrated *in vacuo*. Column chromatography on silica gel (EtOAc/hexane, 3:7) gave 0.67 g (95%) of **15** as a sticky liquid: IR 1659 cm⁻¹; ¹H NMR δ 8.22 (d, 1H, *J* = 8.8 Hz), 7.65 (d, 2H, *J* = 8.4 Hz), 7.27 (d, 2H, *J* = 8.4 Hz), 7.16 (t, 2H, *J* = 7.2 Hz), 6.98 (t, 1H, *J* = 7.2 Hz), 5.78 (m, 1H), 5.49 (m, 1H), 5.19-5.04 (m, 4H), 4.11-4.05 (m, 2H), 3.84 (d, 2H, *J* = 6.4 Hz), 3.55-3.42 (m, 2H), 3.28-3.13 (m, 5H), 3.00 (dd, 1H, *J* = 16.8, 4.4 Hz), 2.65 (dd, 1H, *J* = 16.8, 7.6 Hz), 2.39 (s, 3H); ¹³C NMR δ 168.7, 143.4, 143.0, 136.7, 134.6, 132.3, 131.3, 129.7, 127.4,

127.2, 124.5, 123.6, 119.8, 117.4, 117.0, 51.5, 51.4, 48.1, 39.0, 38.7, 35.4, 27.9, 21.5; MS [m/z (rel intensity)] 315 (25), 224 (21), 155 (52), 119 (65).

1-[[4-[4-(methylphenyl)sulfonyl]-1,1-dioxido-3,4,5,8-tetrahydro-2H-1,4-thiazocin-2-yl]acetyl]-1H-indole (16). To a solution of **11** (0.07 g, 0.14 mmol) in CH₂Cl₂ (4 mL) was added a solution of commercial Gen 2 catalyst (5% mol, 0.006 g) in CH₂Cl₂ (3 mL) under a nitrogen atmosphere. The mixture was refluxed until TLC showed the reaction to be complete, cooled to room temperature and concentrated *in vacuo*. Column chromatography of the residue on silica gel (EtOAc/hexane, 3:2) gave 0.06 g (91%) of **16** as a white solid: mp 237-9 °C; IR 1711 cm⁻¹; ¹H NMR δ 8.32 (d, 1H, *J* = 8.0 Hz), 7.65 (d, 2H, *J* = 8.4 Hz), 7.55 (d, 1H, *J* = 7.2 Hz), 7.45 (d, 1H, *J* = 4.0 Hz), 7.34-7.25 (m, 4H), 6.67 (d, 1H, *J* = 4.0 Hz), 5.88 (d, 1H, *J* = 12.4 Hz), 5.79 (m, 1H), 4.80 (m, 1H), 4.42-4.35 (m, 2H), 4.02-3.92 (m, 2H), 3.79-3.73 (m, 2H), 3.22 (dd, 1H, *J* = 13.2, 3.2 Hz), 3.03 (dd, 1H, *J* = 17.6, 10.8 Hz), 2.39 (s, 3H); ¹³C NMR δ 167.1, 144.4, 135.5, 133.8, 130.4, 130.2, 127.3, 125.4, 124.3, 124.1, 121.2, 117.7, 116.3, 110.6, 60.4, 53.1, 49.8, 49.1, 30.2, 21.5. Anal. Calcd for C₂₃H₂₄O₅N₂S₂: C, 58.46; H, 5.12; N, 5.93. Found: C, 58.18; H, 5.28; N, 5.76.

N-allyl-N-[2-(allylsulfinyl)-4-(2,3-dihydro-1H-indol-1-yl)-4-oxobutyl]-4-methylbenzenesulfonamide (17). To an ice-cooled solution of **15** (0.85 g, 1.81 mmol) in CH₂Cl₂ (20 mL) was added slowly a solution of *m*-CPBA (1.0 eq) in CH₂Cl₂ (10 mL). The resulting mixture was stirred at 0 °C for 15 min and put in a freezer (-20 °C) overnight. The reaction mixture was then poured into 5% NaHCO₃ solution. After separating and saving the organic layer, the aqueous layer was extracted with CH₂Cl₂.

The combined organic layers were washed with distilled water, dried over anhydrous Na_2SO_4 , and concentrated *in vacuo*. Column chromatography on silica gel (EtOAc) gave 0.87 g (99%) of **17** as a sticky liquid (a mixture of two diastereomers present in a ratio of 2:3).

minor diastereomer: IR 1656 cm^{-1} ; ^1H NMR δ 8.14 (d, 1H, $J = 7.6\text{ Hz}$), 7.67 (d, 2H, $J = 8.0\text{ Hz}$), 7.28 (d, 2H, $J = 8.0\text{ Hz}$), 7.18-7.15 (m, 2H), 7.00 (m, 1H), 5.95 (m, 1H), 5.53 (m, 1H), 5.44-5.40 (m, 2H), 5.21 (dd, 1H, $J = 17.2, 1.6\text{ Hz}$), 5.14 (dd, 1H, $J = 10.0, 0.8\text{ Hz}$), 4.12-4.06 (m, 2H), 3.84 (d, 2H, $J = 6.8\text{ Hz}$), 3.70-3.54 (m, 4H), 3.38 (dd, 1H, $J = 13.2, 3.6\text{ Hz}$), 3.20 (t, 2H, $J = 8.4\text{ Hz}$), 3.12 (dd, 1H, $J = 17.6, 4.4\text{ Hz}$), 2.91 (dd, 1H, $J = 17.6, 8.0\text{ Hz}$), 2.39 (s, 3H); ^{13}C NMR δ 167.8, 143.8, 142.6, 135.9, 132.3, 131.2, 129.9, 127.4, 127.3, 126.3, 124.7, 124.0, 123.6, 120.3, 116.9, 54.3, 52.1, 51.3, 48.0, 44.7, 34.2, 27.9, 21.5.

major diastereomer: IR 1656 cm^{-1} ; ^1H NMR δ 8.17 (d, 1H, $J = 8.8\text{ Hz}$), 7.68 (d, 2H, $J = 8.0\text{ Hz}$), 7.28 (d, 2H, $J = 8.0\text{ Hz}$), 7.17 (m, 2H), 7.01 (td, 1H, $J = 7.2, 1.6\text{ Hz}$), 5.87 (m, 1H), 5.53-5.39 (m, 3H), 5.22-5.11 (m, 2H), 4.17-4.06 (m, 2H), 3.87-3.84 (m, 3H), 3.59 (dd, 1H, $J = 14.4, 9.2\text{ Hz}$), 3.54 (dd, 1H, $J = 13.6, 8.0\text{ Hz}$), 3.40 (dd, 1H, $J = 12.8, 7.2\text{ Hz}$), 3.30 (dd, 1H, $J = 14.4, 6.4\text{ Hz}$), 3.22-3.13 (m, 3H), 2.68 (dd, 1H, $J = 18.0, 4.8\text{ Hz}$), 2.39 (s, 3H); ^{13}C NMR δ 168.1, 143.8, 142.8, 135.9, 132.4, 132.0, 131.3, 129.9, 127.3, 127.2, 126.0, 124.7, 123.9, 120.4, 116.9, 54.9, 52.1, 51.7, 48.0, 29.0, 28.0, 21.5; MS [m/z (rel intensity)] 396 (9), 241 (9), 155 (35), 119 (100) for diastereomer mixture.

1-[[4-[4-(methylphenyl)sulfonyl]-1-oxido-3,4,5,8-tetrahydro-2H-1,4-thiazocin-2-yl]acetyl]indoline (18). To a solution of **17** (0.58 g, 1.193 mmol) in CH_2Cl_2 (12 mL) was

added a solution of commercial Gen 2 catalyst (10% mol, 0.10 g) in CH₂Cl₂ (10 mL) under a nitrogen atmosphere. The resulting mixture was refluxed for 21 h, cooled to room temperature and concentrated *in vacuo*. Column chromatography of the residue on silica gel (EtOAc) gave 0.22 g (40%) of **18** as a mixture of two diastereomers in a 3:4 ratio).

minor diastereomer: ¹H NMR δ 8.14 (d, 1H, *J* = 7.6 Hz), 7.67 (d, 2H, *J* = 8.0 Hz), 7.28 (d, 2H, *J* = 8.0 Hz), 7.19-7.15 (m, 2H), 7.02 (m, 1H), 5.89 (dt, 1H, *J* = 11.6, 3.2 Hz), 5.64 (m, 1H), 4.47 (m, 1H), 4.21-3.71 (m, 7H), 3.19 (t, 2H, *J* = 8.4 Hz), 3.04-2.95 (m, 2H), 2.57 (dd, 1H, *J* = 17.2, 4.0 Hz), 2.39 (s, 3H); ¹³C NMR δ 166.7, 144.0, 142.5, 134.2, 134.0, 131.2, 130.0, 127.5, 127.4, 124.7, 124.2, 118.9, 116.9, 49.1, 48.0, 46.6, 44.6, 37.5, 34.9, 28.0, 21.5.

major diastereomer: IR 1655 cm⁻¹; ¹H NMR δ 8.06 (d, 1H, *J* = 8.0 Hz), 7.59 (d, 2H, *J* = 8.8 Hz), 7.27 (d, 2H, *J* = 8.0 Hz), 7.17-7.11 (m, 2H), 7.00 (m, 1H), 5.88 (dt, 1H, *J* = 11.6, 4.0 Hz), 5.80 (m, 1H), 4.39 (m, 1H), 4.28-3.61 (m, 7H), 3.30 (td, 2H, *J* = 14.0, 2.8 Hz), 3.18 (t, 2H, *J* = 8.4 Hz), 2.66 (dd, 1H, *J* = 16.8, 10.0 Hz), 2.38 (s, 3H); ¹³C NMR δ 167.3, 144.1, 142.4, 134.2, 134.0, 132.7, 130.0, 127.4, 127.1, 124.7, 124.1, 118.5, 116.7, 55.6, 49.8, 48.6, 48.3, 48.0, 33.5, 28.0, 21.5; MS [*m/z* (rel intensity)] 155 (26), 119 (88) for diastereomer mixture.

***N*-allyl-*N*-[2-(allylsulfonyl)-4-(2,3-dihydro-1*H*-indol-1-yl)-4-oxobutyl]-4-methylbenzenesulfonamide (**19**).** To an ice-cooled solution of **15** (0.62 g, 1.32 mmol) in CH₂Cl₂ (20 mL) was added a solution of *m*-CPBA (2.0 eq) in CH₂Cl₂ (10 mL). The resulting mixture was stirred at room temperature for 16 h, poured into 5% NaHCO₃ solution. After separating and saving the organic layer, the aqueous layer was extracted

with CH₂Cl₂. The combined organic layers were washed with distilled water, dried over anhydrous Na₂SO₄, and concentrated *in vacuo*. Column chromatography on silica gel (EtOAc/hexane, 3:7) gave 0.62 g (94%) of **19** as a sticky liquid: IR 1658 cm⁻¹; ¹H NMR δ 8.17 (d, 1H, *J* = 8.0 Hz), 7.68 (d, 2H, *J* = 8.4 Hz), 7.28 (d, 2H, *J* = 8.4 Hz), 7.19-7.16 (m, 2H), 7.01 (td, 1H, *J* = 7.6, 0.8 Hz), 5.91 (m, 1H), 5.56-5.43 (m, 3H), 5.21 (dd, 1H, *J* = 17.2, 1.2 Hz), 5.14 (dd, 1H, *J* = 10.0, 1.2 Hz), 4.28 (m, 1H), 4.18-4.06 (m, 2H), 3.96-3.77 (m, 4H), 3.64 (dd, 1H, *J* = 14.4, 9.6 Hz), 3.45 (dd, 1H, *J* = 14.4, 5.2 Hz), 3.20 (t, 2H, *J* = 8.4 Hz), 3.13 (dd, 1H, *J* = 18.0, 6.4 Hz), 3.05 (dd, 1H, *J* = 18.0, 5.6 Hz), 2.40 (s, 3H); ¹³C NMR δ 167.1, 144.0, 142.6, 135.6, 131.7, 131.3, 129.9, 127.4, 125.4, 124.7, 124.1, 124.0, 120.6, 116.8, 58.5, 54.9, 51.8, 47.9, 45.7, 32.6, 27.9, 21.5; MS [*m/z* (rel intensity)] 347 (16), 155 (43), 119 (100).

1-[[4-[4-(methylphenyl)sulfonyl]-1,1-dioxido-3,4,5,8-tetrahydro-2*H*-1,4-thiazocin-2-yl]acetyl]indoline (20). To a solution of **19** (0.31 g, 0.62 mmol) in CH₂Cl₂ (10 mL) was added a solution of commercial Gen 2 catalyst (5% mol, 0.026 g) in CH₂Cl₂ (5 mL) under a nitrogen atmosphere. The mixture was refluxed until TLC showed the reaction to be complete, then cooled to room temperature and concentrated *in vacuo*. Column chromatography of the residue on silica gel (EtOAc) gave 0.26 g (89%) of **20** as a white solid: mp 267-9 °C; IR 1651 cm⁻¹; ¹H NMR δ 8.05 (d, 1H, *J* = 8.0 Hz), 7.65 (d, 2H, *J* = 8.4 Hz), 7.29 (d, 2H, *J* = 8.0 Hz), 7.15 (dd, 2H, *J* = 15.6, 7.6 Hz), 7.01 (td, 1H, *J* = 7.6, 1.2 Hz), 5.86 (d, 1H, *J* = 11.6 Hz), 5.75 (m, 1H), 4.85 (dd, 1H, *J* = 13.6, 7.2 Hz), 4.41 (d, 1H, *J* = 19.6 Hz), 4.06-4.02 (m, 2H), 3.97-3.85 (m, 2H), 3.69 (d, 2H, *J* = 19.2 Hz), 3.26-3.17 (m, 4H), 2.51 (dd, 1H, *J* = 17.2, 10.4 Hz), 2.39 (s, 3H); ¹³C NMR δ 166.2, 144.3,

142.4, 134.0, 131.3, 130.1, 127.4, 127.2, 124.8, 124.3, 117.4, 116.7, 53.1, 52.9, 49.7, 49.2, 47.9, 29.9, 27.9, 21.5; MS [m/z (rel intensity)] 474 (M^+ , 1), 155 (26), 119 (100).
Anal. Calcd for $C_{23}H_{26}O_5N_2S_2$: C, 58.21; H, 5.52; N, 5.90. Found: C, 57.98; H, 5.69; N, 5.85.

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¹H NMR Spectrum of 1

¹³C NMR Spectrum of 1

^1H NMR Spectrum of 2

¹³C NMR Spectrum of 2

¹H NMR Spectrum of 3

¹³C NMR Spectrum of 3

¹H NMR Spectrum of 4

^{13}C NMR Spectrum of 4

^1H NMR Spectrum of 5 (High R_f diastereomer)

^{13}C NMR Spectrum of 5 (High R_f diastereomer)

^1H NMR Spectrum of 5 (Low R_f diastereomer)

^{13}C NMR Spectrum of 5 (Low R_f diastereomer)

^1H NMR Spectrum of 6

¹³C NMR Spectrum of 6

^1H NMR Spectrum of 7

^{13}C NMR Spectrum of 7

^1H NMR Spectrum of 8

¹³C NMR Spectrum of 8

^1H NMR Spectrum of 9

¹³C NMR Spectrum of 9

¹H NMR Spectrum of 10

^{13}C NMR Spectrum of 10

¹H NMR Spectrum of 11

^{13}C NMR Spectrum of 11

¹H NMR Spectrum of 12

^{13}C NMR Spectrum of 12

¹H NMR Spectrum of 14

¹³C NMR Spectrum of 14

^1H NMR Spectrum of 15

^{13}C NMR Spectrum of 15

¹H NMR Spectrum of 16

^{13}C NMR Spectrum of 16

¹H NMR Spectrum of 17

^{13}C NMR Spectrum of 17

¹H NMR Spectrum of 18

^{13}C NMR Spectrum of 18

¹H NMR Spectrum of 19

^{13}C NMR Spectrum of 19

^1H NMR Spectrum of 20

¹³C NMR Spectrum of 20

¹H NMR Spectrum of 21

¹³C NMR Spectrum of 21